pyPESTO Documentation

Release 0.2.10

The pyPESTO developers

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USER'S GUIDE

Version: 0.2.10
Source code: https://github.com/icb-dcm/pypesto

CHAPTER

ONE

INSTALL AND UPGRADE

1.1 Requirements

This package requires Python 3.7 or later. It is tested on Linux using Travis continuous integration.

1.1.1 I cannot use my system's Python distribution, what now?

Several Python distributions can co-exist on a single system. If you don't have access to a recent Python version via your system's package manager (this might be the case for old operating systems), it is recommended to install the latest version of the Anaconda Python 3 distribution.

Also, there is the possibility to use multiple virtual environments via:

```
python3 -m virtualenv ENV_NAME
source ENV_NAME/bin/activate
```

where ENV_NAME denotes an individual environment name, if you do not want to mess up the system environment.

1.2 Install from PIP

The package can be installed from the Python Package Index PyPI via pip:

```
pip3 install pypesto
```

1.3 Install from GIT

If you want the bleeding edge version, install directly from github:

```
pip3 install git+https://github.com/icb-dcm/pypesto.git
```

If you need to have access to the source code, you can download it via:

```
git clone https://github.com/icb-dcm/pypesto.git
```

and then install from the local repository via:

```
cd pypesto
pip3 install .
```

1.4 Upgrade

If you want to upgrade from an existing previous version, replace `install` by `install --upgrade` in the above commands.

1.5 Install optional packages and external dependencies

- pyPESTO includes multiple convenience methods to simplify parameter estimation for models generated using the toolbox AMICI. To use AMICI, install it via pip:

  ```
  pip3 install amici
  ```

  or, in case of problems, follow the full instructions from the AMICI documentation.

- This package inherently supports optimization using the dlib toolbox. To use it, install dlib via:

  ```
  pip3 install dlib
  ```

- All external dependencies can be installed through this shell script.

CHAPTER

TWO

EXAMPLES

We provide a collection of example notebooks to get a better idea of how to use pyPESTO, and illustrate core features.

The notebooks can be run locally with an installation of jupyter (`pip install jupyter`), or online on Google Colab or nbviewer, following the links at the top of each notebook. At least an installation of pyPESTO is required, which can be performed by

```
# install if not done yet
!pip install pypesto --quiet
```

Potentially, further dependencies may be required.

2.1 Getting started

2.1.1 Rosenbrock banana

Here, we perform optimization for the Rosenbrock banana function, which does not require an AMICI model. In particular, we try several ways of specifying derivative information.

[1]:
```
# install if not done yet
# %pip install pypesto --quiet
```

[2]:
```
import pypesto
import pypesto.visualize as visualize
import numpy as np
import scipy as sp
import matplotlib.pyplot as plt
from mpl_toolkits.mplot3d import Axes3D

%matplotlib inline
```

Define the objective and problem

[3]:
```
# first type of objective
objective1 = pypesto.Objective(fun=sp.optimize.rosen,
                               grad=sp.optimize.rosen_der,
                               hess=sp.optimize.rosen_hess)

# second type of objective
def rosen2(x):
    return (sp.optimize.rosen(x),
            sp.optimize.rosen_der(x),
            sp.optimize.rosen_hess(x))
objective2 = pypesto.Objective(fun=rosen2, grad=True, hess=True)

dim_full = 10
lb = -5 * np.ones((dim_full, 1))
ub = 5 * np.ones((dim_full, 1))

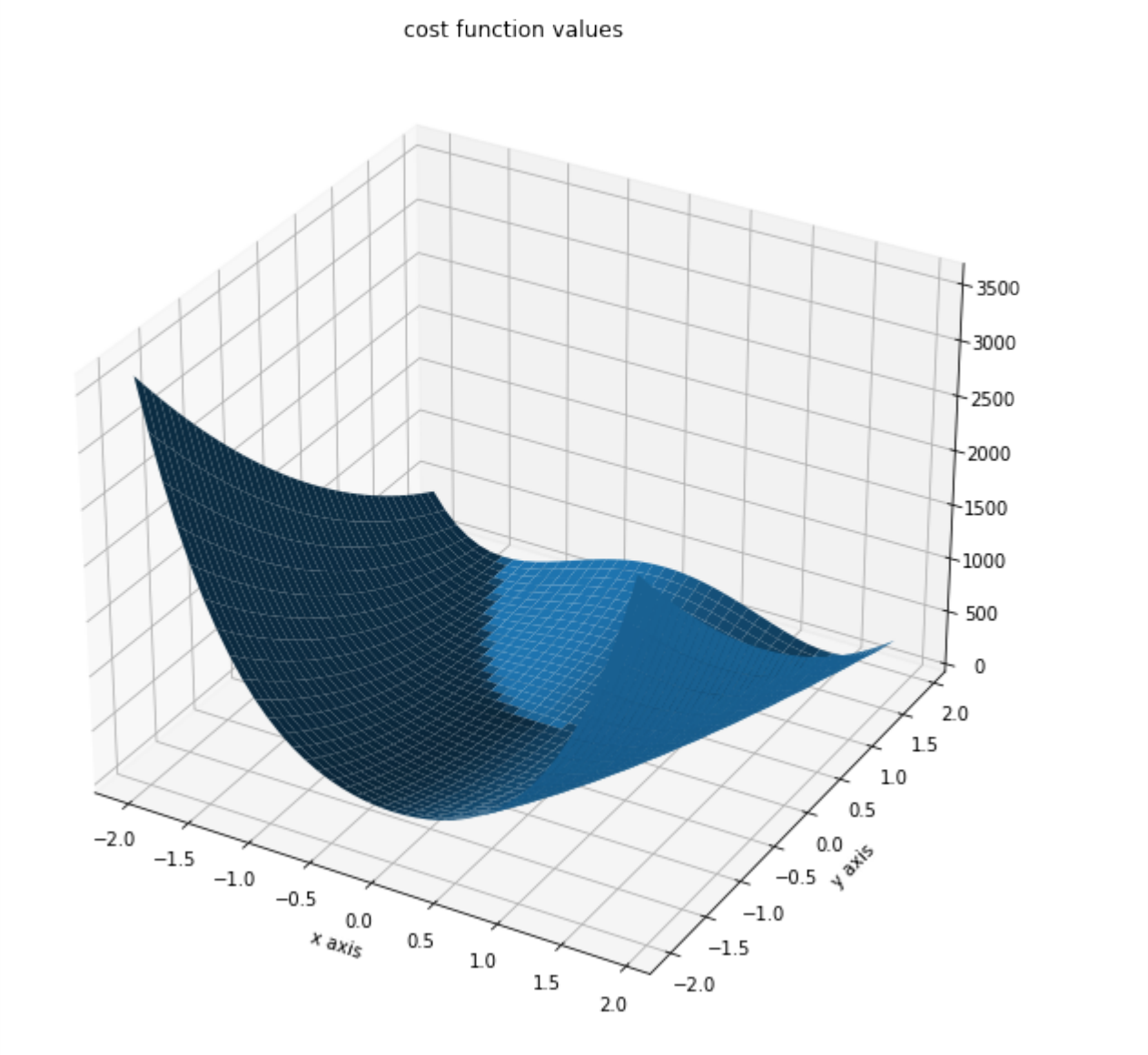
problem1 = pypesto.Problem(objective=objective1, lb=lb, ub=ub)
problem2 = pypesto.Problem(objective=objective2, lb=lb, ub=ub)
```

Illustration

[4]:
```
x = np.arange(-2, 2, 0.1)
y = np.arange(-2, 2, 0.1)
x, y = np.meshgrid(x, y)
z = np.zeros_like(x)
for j in range(0, x.shape[0]):
    for k in range(0, x.shape[1]):
        z[j,k] = objective1([x[j,k], y[j,k]], (0,))
```

[5]:
```
fig = plt.figure()
fig.set_size_inches(*(14,10))
ax = plt.axes(projection='3d')
ax.plot_surface(X=x, Y=y, Z=z)
plt.xlabel('x axis')
plt.ylabel('y axis')
ax.set_title('cost function values')
```

[5]:
```
Text(0.5, 0.92, 'cost function values')
```



Run optimization

[6]:
```
import pypesto.optimize as optimize
```

[7]:
```
# create different optimizers
optimizer_bfgs = optimize.ScipyOptimizer(method='l-bfgs-b')
optimizer_tnc = optimize.ScipyOptimizer(method='TNC')
optimizer_dogleg = optimize.ScipyOptimizer(method='dogleg')

# set number of starts
n_starts = 20

# save optimizer trace
history_options = pypesto.HistoryOptions(trace_record=True)
```

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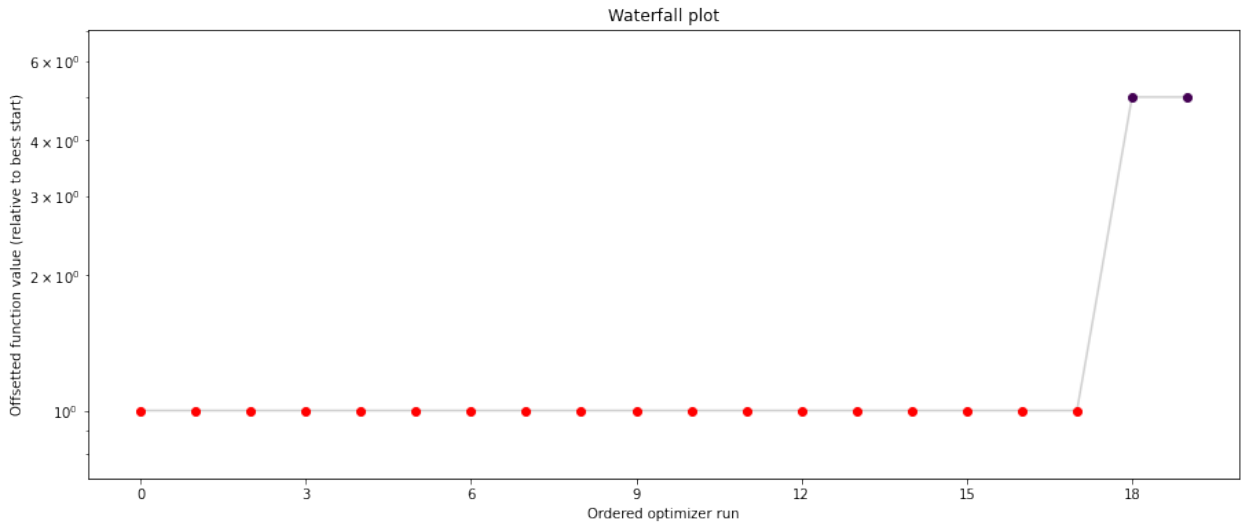
```
# Run optimizaitons for different optimzers
result1_bfgs = optimize.minimize(
    problem=problem1, optimizer=optimizer_bfgs,
    n_starts=n_starts, history_options=history_options,
    filename=None)
result1_tnc = optimize.minimize(
    problem=problem1, optimizer=optimizer_tnc,
    n_starts=n_starts, history_options=history_options,
    filename=None)
result1_dogleg = optimize.minimize(
    problem=problem1, optimizer=optimizer_dogleg,
    n_starts=n_starts, history_options=history_options,
    filename=None)

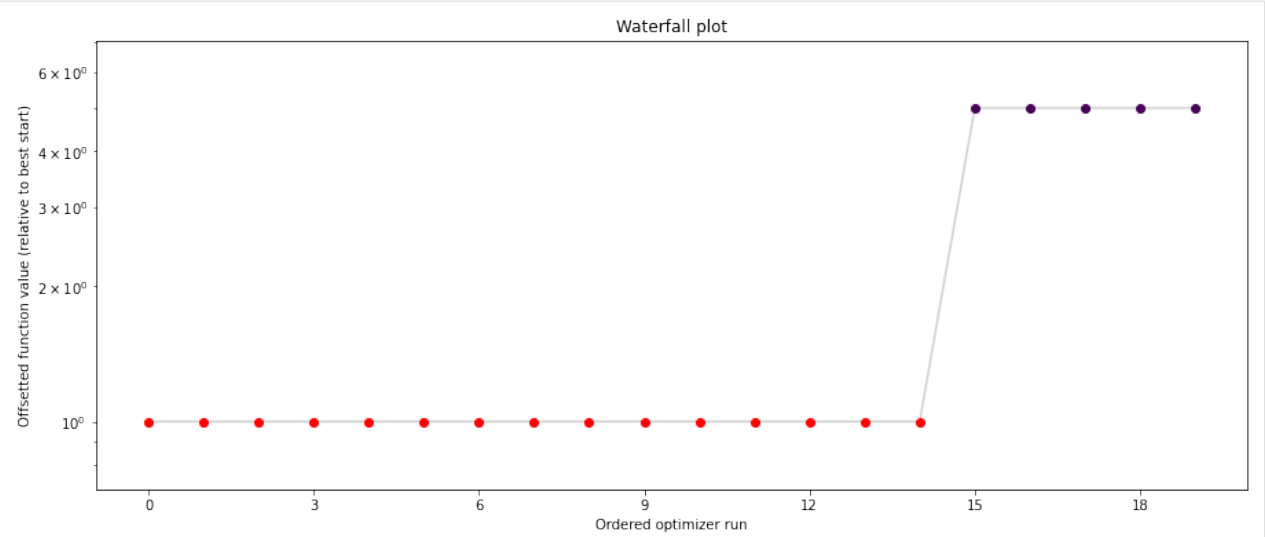
# Optimize second type of objective
result2 = optimize.minimize(
    problem=problem2, optimizer=optimizer_tnc,
    n_starts=n_starts, filename=None)
```

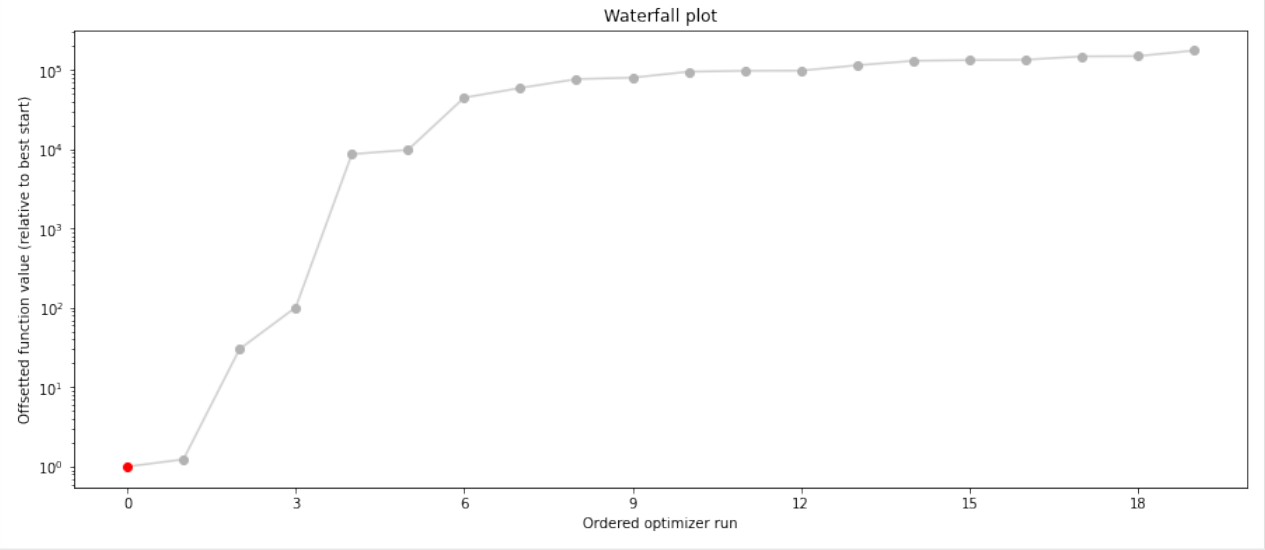
```
100%|| 20/20 [00:00<00:00, 23.57it/s]
100%|| 20/20 [00:01<00:00, 13.47it/s]
100%|| 20/20 [00:00<00:00, 259.22it/s]
100%|| 20/20 [00:01<00:00, 10.49it/s]
```

Visualize and compare optimization results

[8]:
```
# plot separated waterfalls
visualize.waterfall(result1_bfgs, size=(15,6))
visualize.waterfall(result1_tnc, size=(15,6))
visualize.waterfall(result1_dogleg, size=(15,6));
```

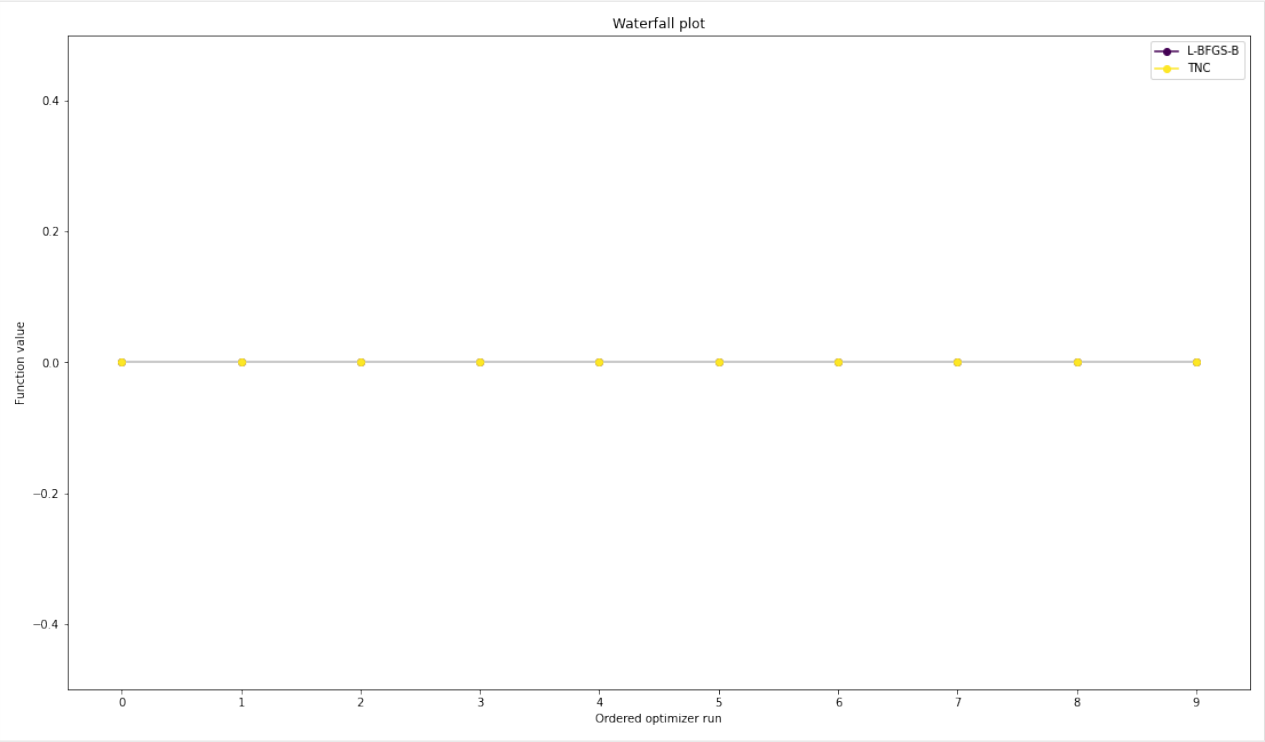






We can now have a closer look, which method perfomred better: Let's first compare bfgs and TNC, since both methods gave good results. How does the fine convergence look like?

[9]:
```
# plot one list of waterfalls
visualize.waterfall(
    [result1_bfgs, result1_tnc],
    legends=['L-BFGS-B', 'TNC'],
    start_indices=10,
    scale_y='lin',
);
```

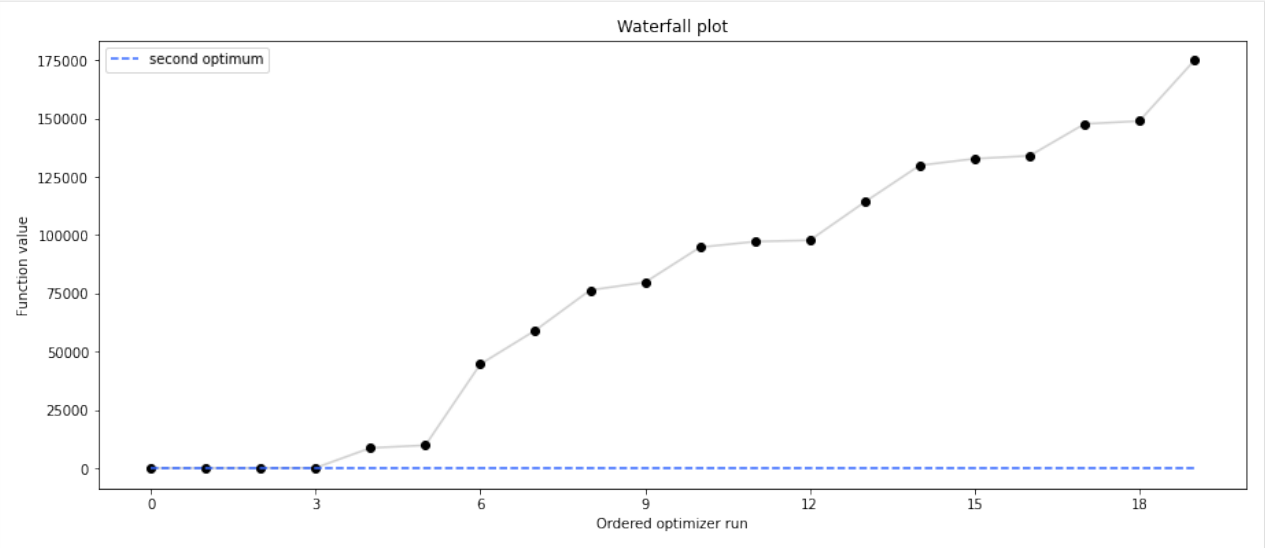


[10]:
```
# retrieve second optimum
all_x = result1_bfgs.optimize_result.get_for_key('x')
all_fval = result1_bfgs.optimize_result.get_for_key('fval')
x = all_x[19]
fval = all_fval[19]
print('Second optimum at: ' + str(fval))

# create a reference point from it
ref = {'x': x, 'fval': fval, 'color': [
    0.2, 0.4, 1., 1.], 'legend': 'second optimum'}
ref = visualize.create_references(ref)

# new waterfall plot with reference point for second optimum
visualize.waterfall(
    result1_dogleg,
    size=(15,6),
    scale_y='lin',
    y_limits=[-1, 101],
    reference=ref,
    colors=[0., 0., 0., 1.],
);
```

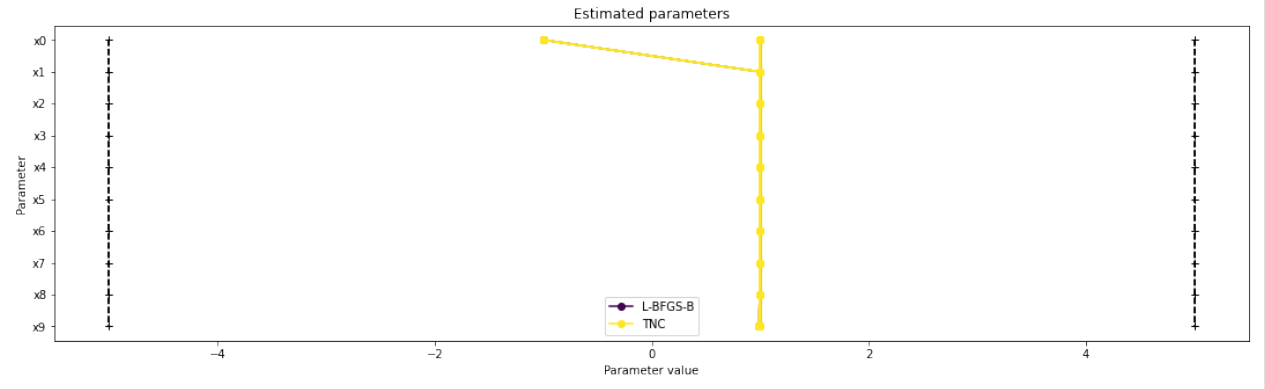
```
Second optimum at: 3.986579112988829
```

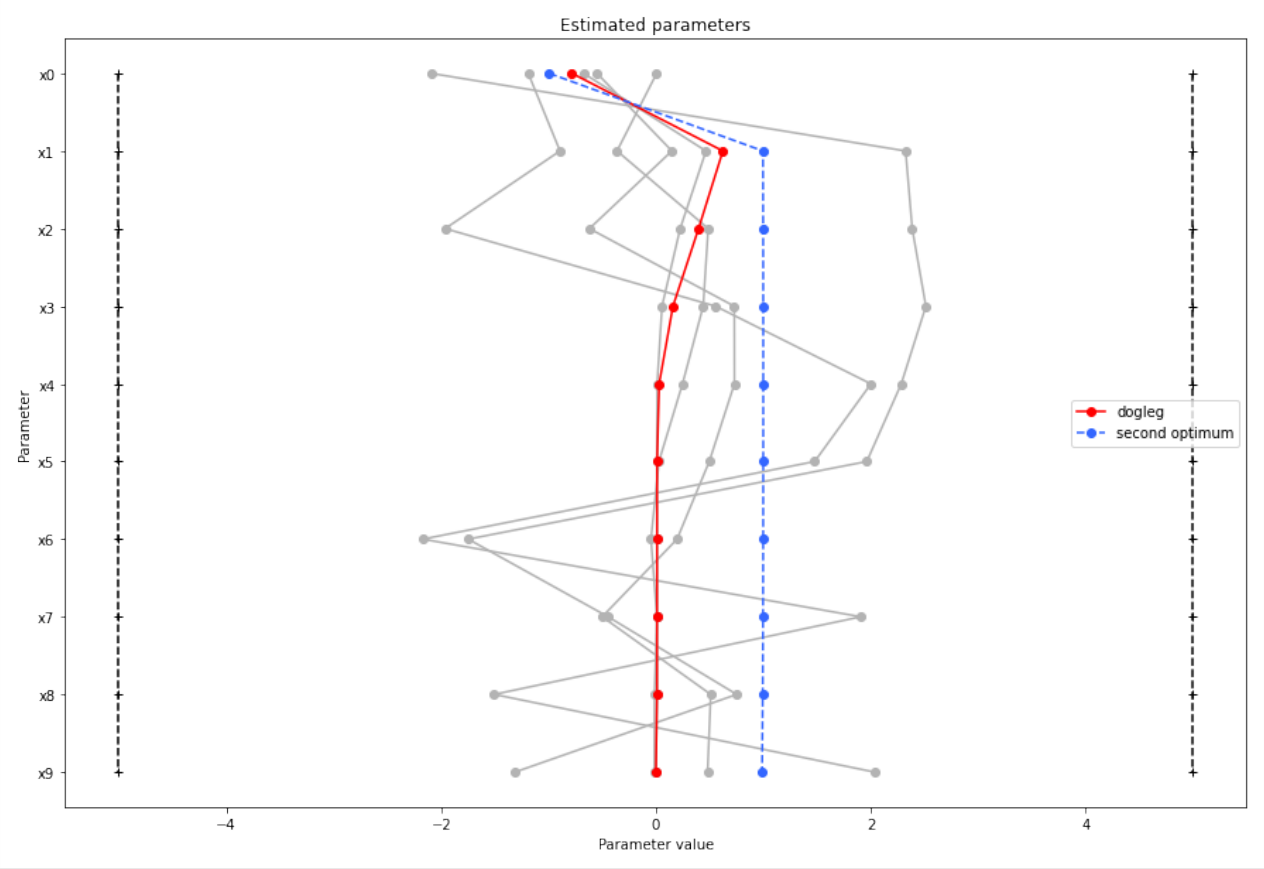


Visualize parameters

There seems to be a second local optimum. We want to see whether it was also found by the dogleg method

[11]:
```
visualize.parameters(
    [result1_bfgs, result1_tnc],
    legends=['L-BFGS-B', 'TNC'],
    balance_alpha=False,
)
visualize.parameters(
    result1_dogleg,
    legends='dogleg',
    reference=ref,
    size=(15,10),
    start_indices=[0, 1, 2, 3, 4, 5],
    balance_alpha=False,
);
```





If the result needs to be examined in more detail, it can easily be exported as a pandas.DataFrame:

[12]:
```
df = result1_tnc.optimize_result.as_dataframe(
    ['fval', 'n_fval', 'n_grad', 'n_hess', 'n_res',
     'n_sres', 'time'],
)
df.head()
```

[12]:

	fval	n_fval	n_grad	n_hess	n_res	n_sres	time
0	1.700177e-12	234	234	0	0	0	0.095119
1	5.863075e-12	254	254	0	0	0	0.102610
2	6.024982e-12	201	201	0	0	0	0.074668
3	1.022637e-11	231	231	0	0	0	0.086636
4	1.491191e-11	170	170	0	0	0	0.072328

Optimizer history

Let's compare optimzer progress over time.

[13]:
```
# plot one list of waterfalls
visualize.optimizer_history(
    [result1_bfgs, result1_tnc],
    legends=['L-BFGS-B', 'TNC'],
    reference=ref,
)
# plot one list of waterfalls
```

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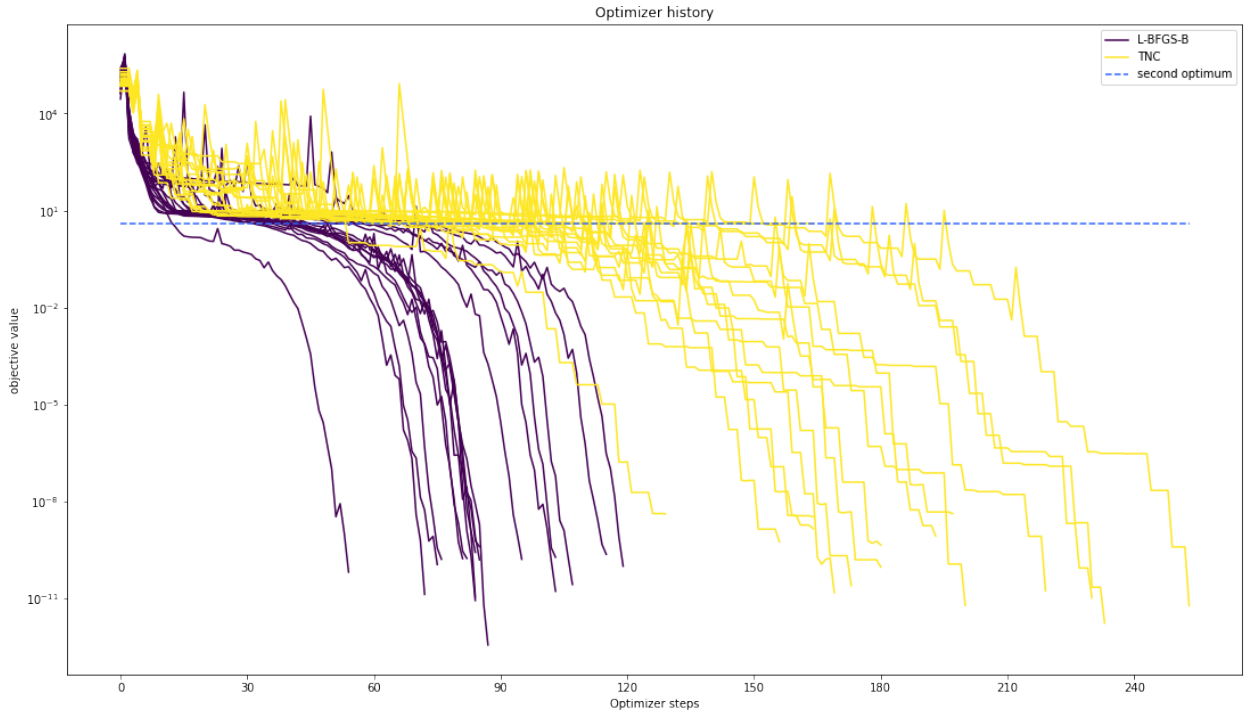
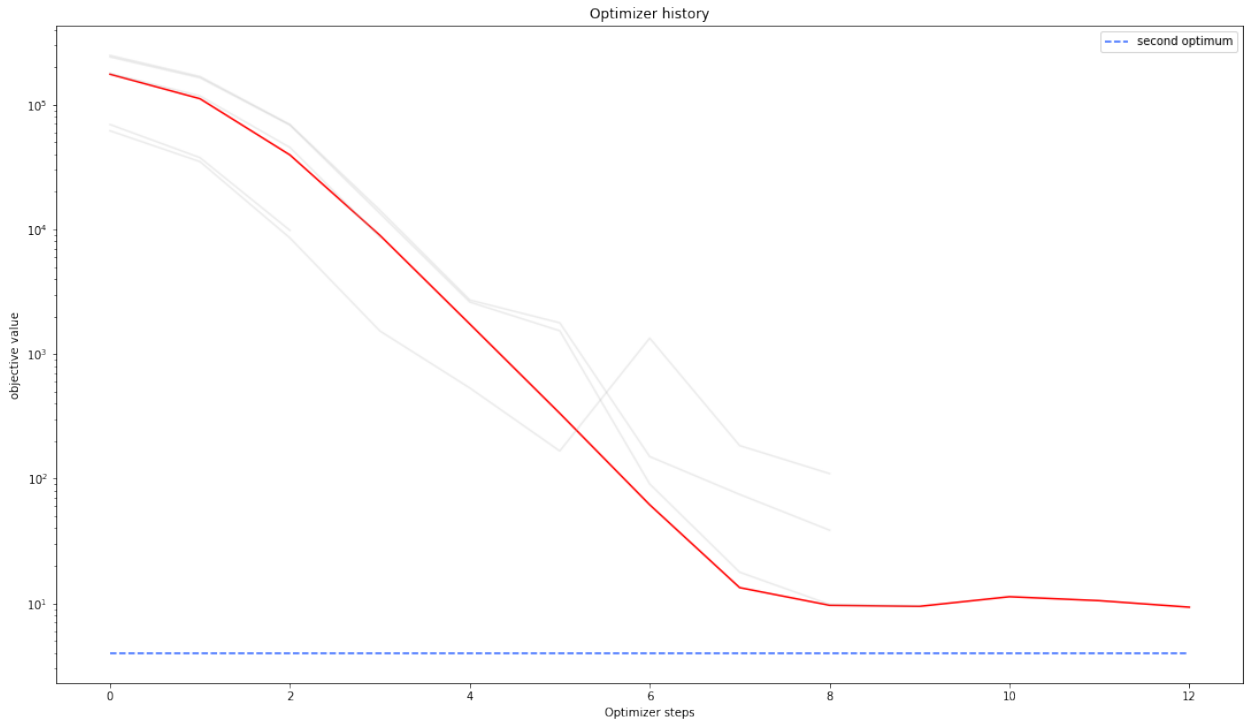
```
visualize.optimizer_history(
    result1_dogleg,
    reference=ref,
);
```

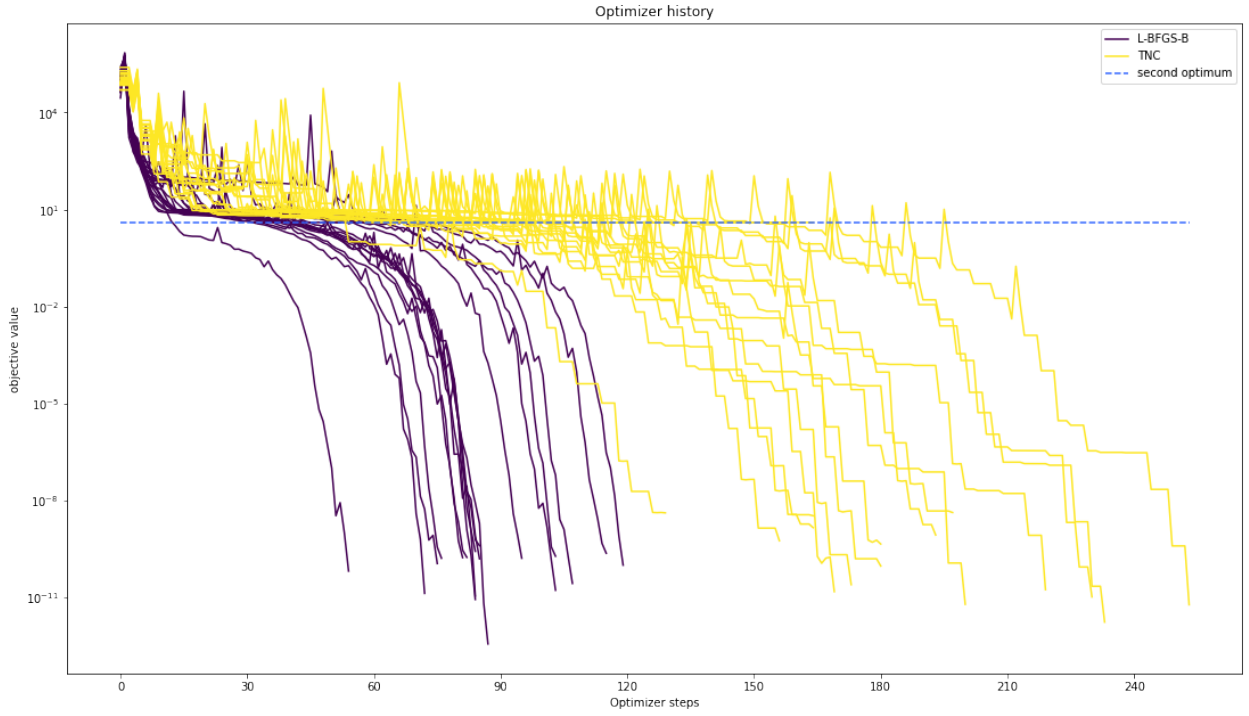


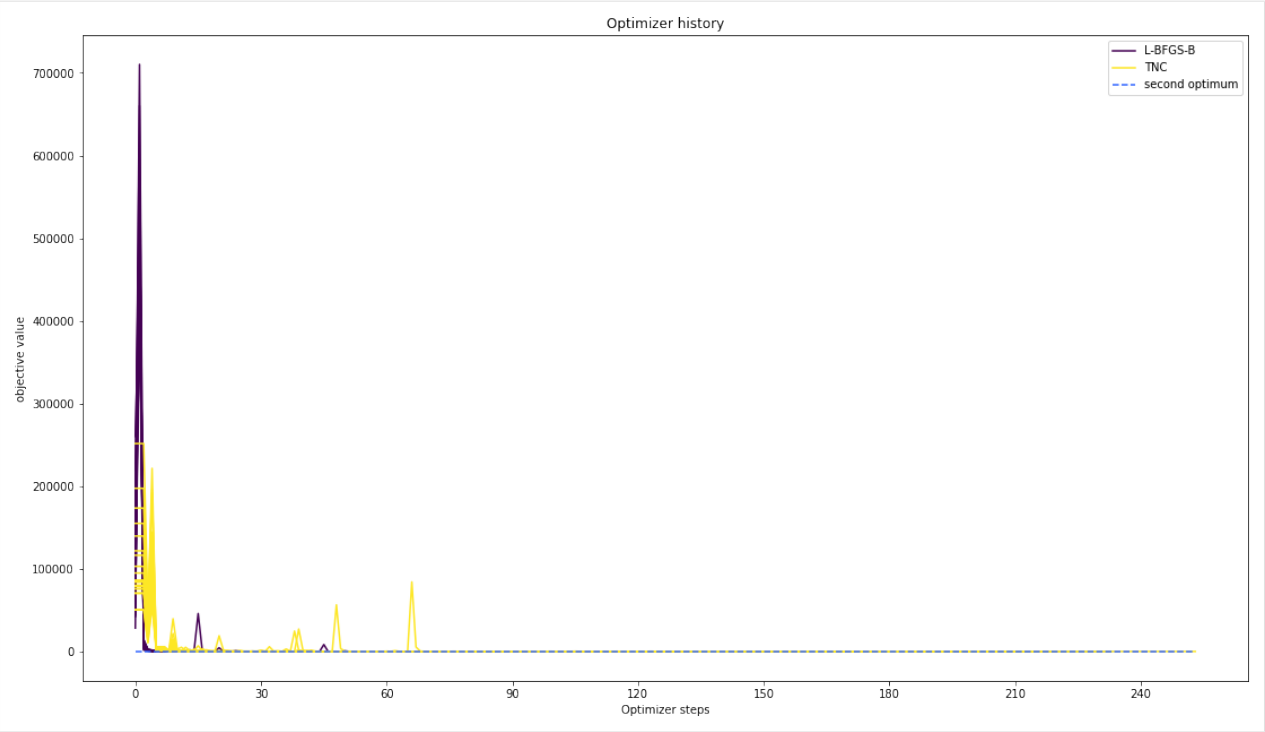


We can also visualize this usign other scalings or offsets. . .

[14]:
```
# plot one list of waterfalls
visualize.optimizer_history(
    [result1_bfgs, result1_tnc],
    legends=['L-BFGS-B', 'TNC'],
    reference=ref,
    offset_y=0.,
)

# plot one list of waterfalls
visualize.optimizer_history(
    [result1_bfgs, result1_tnc],
    legends=['L-BFGS-B', 'TNC'],
    reference=ref,
    scale_y='lin',
    y_limits=[-1., 11.],
);
```





Compute profiles

The profiling routine needs a problem, a results object and an optimizer.

Moreover it accepts an index of integer (profile_index), whether or not a profile should be computed.

Finally, an integer (result_index) can be passed, in order to specify the local optimum, from which profiling should be started.

[15]:
```
import pypesto.profile as profile
```

[16]:
```
# compute profiles
profile_options = profile.ProfileOptions(min_step_size=0.0005,
    delta_ratio_max=0.05,
    default_step_size=0.005,
    ratio_min=0.01,
)

result1_bfgs = profile.parameter_profile(
    problem=problem1,
    result=result1_bfgs,
    optimizer=optimizer_bfgs,
    profile_index=np.array([1, 1, 1, 0, 0, 1, 0, 1, 0, 0, 0]),
    result_index=0,
    profile_options=profile_options,
    filename=None,
)

# compute profiles from second optimum
result1_bfgs = profile.parameter_profile(
    problem=problem1,
```

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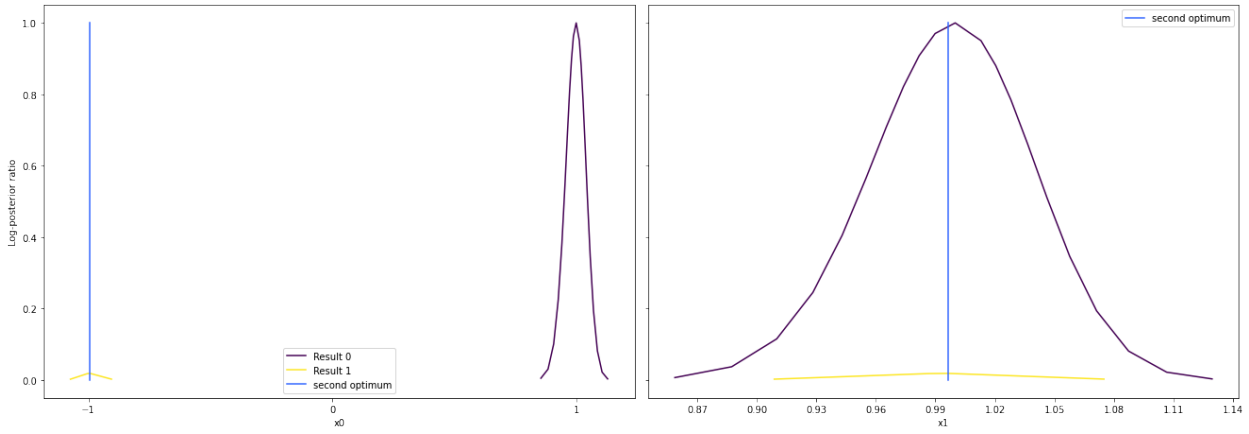
```
    result=result1_bfgs,
    optimizer=optimizer_bfgs,
    profile_index=np.array([1, 1, 1, 0, 0, 1, 0, 1, 0, 0, 0]),
    result_index=19,
    profile_options=profile_options,
    filename=None,
)
```

```
100%|| 11/11 [00:00<00:00, 27.63it/s]
100%|| 11/11 [00:00<00:00, 86.06it/s]
```

Visualize and analyze results

pypesto offers easy-to-use visualization routines:

[17]:
```
# specify the parameters, for which profiles should be computed
ax = visualize.profiles(
    result1_bfgs,
    profile_indices = [0,1,2,5,7],
    reference=ref,
    profile_list_ids=[0, 1],
);
```



Approximate profiles

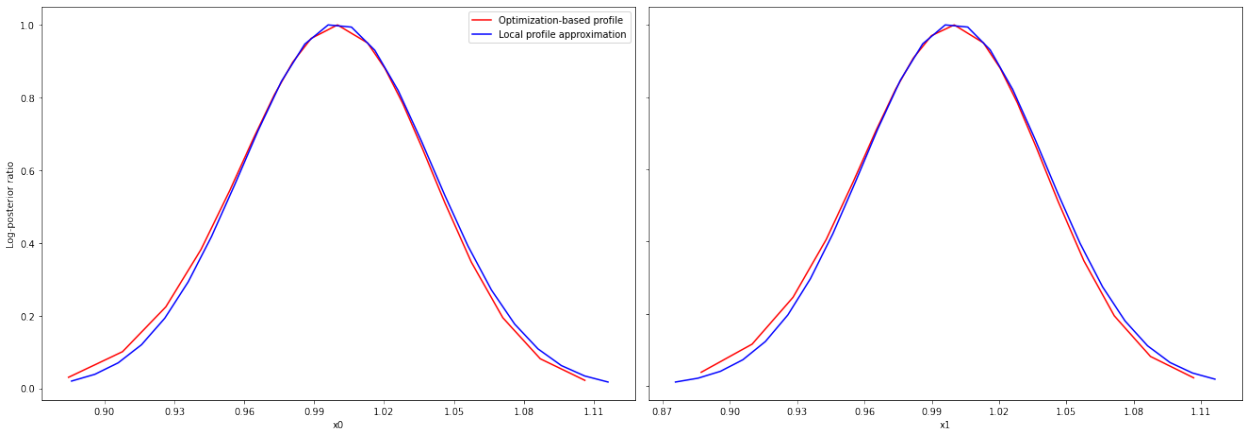
When computing the profiles is computationally too demanding, it is possible to employ to at least consider a normal approximation with covariance matrix given by the Hessian or FIM at the optimal parameters.

[18]:
```
result1_tnc = profile.approximate_parameter_profile(
    problem=problem1,
    result=result1_bfgs,
    profile_index=np.array([1, 1, 1, 0, 0, 1, 0, 1, 0, 0, 0]),
    result_index=0,
    n_steps=1000,
)
```

```
Computing Hessian/FIM as not available in result.
```

These approximate profiles require at most one additional function evaluation, can however yield substantial approximation errors:

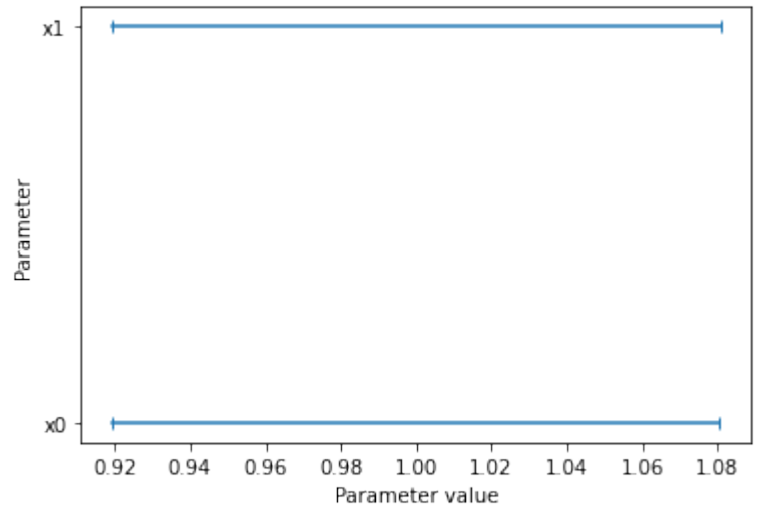
[19]:
```
axes = visualize.profiles(
    result1_bfgs,
    profile_indices = [0,1,2,5,7],
    profile_list_ids=[0, 2],
    ratio_min=0.01,
    colors=[(1,0,0,1), (0,0,1,1)],
    legends=[
        "Optimization-based profile",
        "Local profile approximation",
    ],
);
```



We can also plot approximate confidence intervals based on profiles:

[20]:
```
visualize.profile_cis(
    result1_bfgs,
    confidence_level=0.95,
    profile_list=2,
)
```

[20]:
```
<AxesSubplot:xlabel='Parameter value', ylabel='Parameter'>
```



2.2 PEtab and AMICI

2.2.1 AMICI Python example "Boehm"

This is an example using the "boehm_ProteomeRes2014.xml" model to demonstrate and test SBML import and AMICI Python interface.

[ ]:
```
# install if not done yet
# !apt install libatlas-base-dev swig
# %pip install pypesto[amici] --quiet
```

[1]:
```
import libsbml
import importlib
import amici
import pypesto
import os
import sys
import numpy as np
import matplotlib.pyplot as plt

# temporarily add the simulate file
sys.path.insert(0, 'boehm_JProteomeRes2014')

from benchmark_import import DataProvider

# sbml file
sbml_file = 'boehm_JProteomeRes2014/boehm_JProteomeRes2014.xml'

# name of the model that will also be the name of the python module
model_name = 'boehm_JProteomeRes2014'

# output directory
model_output_dir = 'tmp/' + model_name
```

The example model

Here we use `libsbml` to show the reactions and species described by the model (this is independent of AMICI).

[2]:
```
sbml_reader = libsbml.SBMLReader()
sbml_doc = sbml_reader.readSBML(os.path.abspath(sbml_file))
sbml_model = sbml_doc.getModel()
dir(sbml_doc)
print(os.path.abspath(sbml_file))
print('Species: ', [s.getId() for s in sbml_model.getListOfSpecies()])


print('\nReactions:')
for reaction in sbml_model.getListOfReactions():
    reactants = ' + '.join(
        ['%s %s'%(int(r.getStoichiometry())
                  if r.getStoichiometry() > 1 else '', r.getSpecies())
         for r in reaction.getListOfReactants()])
    products  = ' + '.join(
        ['%s %s'%(int(r.getStoichiometry())
                  if r.getStoichiometry() > 1 else '', r.getSpecies())
```

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```
        for r in reaction.getListOfProducts()])
    reversible = '<' if reaction.getReversible() else ''
    print('%3s: %10s %1s->%10s\t\t[%s]' % (
        reaction.getId(),
        reactants,
        reversible,
        products,
        libsbml.formulaToL3String(reaction.getKineticLaw().getMath())))
```

```
/home/yannik/pypesto/doc/example/boehm_JProteomeRes2014/boehm_JProteomeRes2014.xml
Species:  ['STAT5A', 'STAT5B', 'pApB', 'pApA', 'pBpB', 'nucpApA', 'nucpApB', 'nucpBpB
↪']

Reactions:
v1_v_0:   2 STAT5A  ->      pApA              [cyt * BaF3_Epo * STAT5A^2 * k_phos]
v2_v_1:  STAT5A +  STAT5B  ->      pApB               [cyt * BaF3_Epo * STAT5A *␣
↪STAT5B * k_phos]
v3_v_2:   2 STAT5B  ->      pBpB              [cyt * BaF3_Epo * STAT5B^2 * k_phos]
v4_v_3:       pApA  ->   nucpApA              [cyt * k_imp_homo * pApA]
v5_v_4:       pApB  ->   nucpApB              [cyt * k_imp_hetero * pApB]
v6_v_5:       pBpB  ->   nucpBpB              [cyt * k_imp_homo * pBpB]
v7_v_6:    nucpApA  ->  2 STAT5A              [nuc * k_exp_homo * nucpApA]
v8_v_7:    nucpApB  -> STAT5A +  STAT5B               [nuc * k_exp_hetero * nucpApB]
v9_v_8:    nucpBpB  ->  2 STAT5B              [nuc * k_exp_homo * nucpBpB]
```

Importing an SBML model, compiling and generating an AMICI module

Before we can use AMICI to simulate our model, the SBML model needs to be translated to C++ code. This is done by `amici.SbmlImporter`.

[3]:
```
# Create an SbmlImporter instance for our SBML model
sbml_importer = amici.SbmlImporter(sbml_file)
```

In this example, we want to specify fixed parameters, observables and a σ parameter. Unfortunately, the latter two are not part of the SBML standard. However, they can be provided to `amici.SbmlImporter.sbml2amici` as demonstrated in the following.

Constant parameters

Constant parameters, i.e. parameters with respect to which no sensitivities are to be computed (these are often parameters specifying a certain experimental condition) are provided as a list of parameter names.

[4]:
```
constantParameters = ['ratio', 'specC17']
```

Observables

We used SBML's `AssignmentRule <http://sbml.org/Software/libSBML/5.13.0/docs//python-api/classlibsbml_1_1_rule.html>`__ as a non-standard way to specify *Model outputs* within the SBML file. These rules need to be removed prior to the model import (AMICI does at this time not support these Rules). This can be easily done using `amici.assignmentRules2observables()`.

In this example, we introduced parameters named `observable_*` as targets of the observable AssignmentRules. Where applicable we have `observable_*_sigma` parameters for σ parameters (see below).

[5]:
```
# Retrieve model output names and formulae from AssignmentRules and remove the␣
↪respective rules
observables = amici.assignmentRules2observables(
        sbml_importer.sbml, # the libsbml model object
        filter_function=lambda variable: variable.getId().startswith('observable_')␣
↪and not variable.getId().endswith('_sigma')
    )
print('Observables:', observables)
```

```
Observables: {'observable_pSTAT5A_rel': {'name': 'observable_pSTAT5A_rel', 'formula':
↪'(100 * pApB + 200 * pApA * specC17) / (pApB + STAT5A * specC17 + 2 * pApA *␣
↪specC17)'}, 'observable_pSTAT5B_rel': {'name': 'observable_pSTAT5B_rel', 'formula':
↪'-(100 * pApB - 200 * pBpB * (specC17 - 1)) / (STAT5B * (specC17 - 1) - pApB + 2 *␣
↪pBpB * (specC17 - 1))'}, 'observable_rSTAT5A_rel': {'name': 'observable_rSTAT5A_rel
↪', 'formula': '(100 * pApB + 100 * STAT5A * specC17 + 200 * pApA * specC17) / (2 *␣
↪pApB + STAT5A * specC17 + 2 * pApA * specC17 - STAT5B * (specC17 - 1) - 2 * pBpB *␣
↪(specC17 - 1))'}}
```

σ parameters

To specify measurement noise as a parameter, we simply provide a dictionary with (preexisting) parameter names as keys and a list of observable names as values to indicate which sigma parameter is to be used for which observable.

[6]:
```
sigma_vals = ['sd_pSTAT5A_rel', 'sd_pSTAT5B_rel', 'sd_rSTAT5A_rel']
observable_names = observables.keys()
sigmas = dict(zip(list(observable_names), sigma_vals))
print(sigmas)
```

```
{'observable_pSTAT5A_rel': 'sd_pSTAT5A_rel', 'observable_pSTAT5B_rel': 'sd_pSTAT5B_rel
↪', 'observable_rSTAT5A_rel': 'sd_rSTAT5A_rel'}
```

Generating the module

Now we can generate the python module for our model. `amici.SbmlImporter.sbml2amici` will symbolically derive the sensitivity equations, generate C++ code for model simulation, and assemble the python module.

[7]:
```
sbml_importer.sbml2amici(model_name,
                         model_output_dir,
                         verbose=False,
                         observables=observables,
                         constantParameters=constantParameters,
                         sigmas=sigmas,
  )
```

Importing the module and loading the model

If everything went well, we need to add the previously selected model output directory to our PYTHON_PATH and are then ready to load newly generated model:

[8]:
```
sys.path.insert(0, os.path.abspath(model_output_dir))
model_module = importlib.import_module(model_name)
```

And get an instance of our model from which we can retrieve information such as parameter names:

[9]:
```
model = model_module.getModel()

print("Model parameters:", list(model.getParameterIds()))
print("Model outputs:   ", list(model.getObservableIds()))
print("Model states:    ", list(model.getStateIds()))
```

```
Model parameters: ['Epo_degradation_BaF3', 'k_exp_hetero', 'k_exp_homo', 'k_imp_hetero
↪', 'k_imp_homo', 'k_phos', 'sd_pSTAT5A_rel', 'sd_pSTAT5B_rel', 'sd_rSTAT5A_rel']
Model outputs:    ['observable_pSTAT5A_rel', 'observable_pSTAT5B_rel', 'observable_
↪rSTAT5A_rel']
Model states:     ['STAT5A', 'STAT5B', 'pApB', 'pApA', 'pBpB', 'nucpApA', 'nucpApB',
↪'nucpBpB']
```

Running simulations and analyzing results

After importing the model, we can run simulations using `amici.runAmiciSimulation`. This requires a `Model` instance and a `Solver` instance. Optionally you can provide measurements inside an `ExpData` instance, as shown later in this notebook.

[10]:
```
h5_file = 'boehm_JProteomeRes2014/data_boehm_JProteomeRes2014.h5'
dp = DataProvider(h5_file)
```

[11]:
```
# set timepoints for which we want to simulate the model
timepoints = amici.DoubleVector(dp.get_timepoints())
model.setTimepoints(timepoints)

# set fixed parameters for which we want to simulate the model
model.setFixedParameters(amici.DoubleVector(np.array([0.693, 0.107])))

# set parameters to optimal values found in the benchmark collection
model.setParameterScale(2)
model.setParameters(amici.DoubleVector(np.array(
    [-1.568917588,
     -4.999704894,
     -2.209698782,
     -1.786006548,
     4.990114009,
     4.197735488,
     0.585755271,
     0.818982819,
     0.498684404,
    ]
)))

# Create solver instance
solver = model.getSolver()
```

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```
# Run simulation using model parameters from the benchmark collection and default␣
↪solver options
rdata = amici.runAmiciSimulation(model, solver)
```

[12]:
```
# Create edata
edata = amici.ExpData(rdata, 1.0, 0)

# set observed data
edata.setObservedData(amici.DoubleVector(dp.get_measurements()[0][:, 0]), 0)
edata.setObservedData(amici.DoubleVector(dp.get_measurements()[0][:, 1]), 1)
edata.setObservedData(amici.DoubleVector(dp.get_measurements()[0][:, 2]), 2)

# set standard deviations to optimal values found in the benchmark collection
edata.setObservedDataStdDev(amici.DoubleVector(np.array(16*[10**0.585755271])), 0)
edata.setObservedDataStdDev(amici.DoubleVector(np.array(16*[10**0.818982819])), 1)
edata.setObservedDataStdDev(amici.DoubleVector(np.array(16*[10**0.498684404])), 2)
```

[13]:
```
rdata = amici.runAmiciSimulation(model, solver, edata)

print('Chi2 value reported in benchmark collection: 47.9765479')
print('chi2 value using AMICI:')
print(rdata['chi2'])
```

```
Chi2 value reported in benchmark collection: 47.9765479
chi2 value using AMICI:
47.97654321200259
```

Run optimization using pyPESTO

[14]:
```
# create objective function from amici model
# pesto.AmiciObjective is derived from pesto.Objective,
# the general pesto objective function class

model.requireSensitivitiesForAllParameters()


solver.setSensitivityMethod(amici.SensitivityMethod_forward)
solver.setSensitivityOrder(amici.SensitivityOrder_first)


objective = pypesto.AmiciObjective(model, solver, [edata], 1)
```

[15]:
```
import pypesto.optimize as optimize

# create optimizer object which contains all information for doing the optimization
optimizer = optimize.ScipyOptimizer()

optimizer.solver = 'bfgs'
```

[16]:
```
# create problem object containing all information on the problem to be solved
x_names = ['x' + str(j) for j in range(0, 9)]
problem = pypesto.Problem(objective=objective,
```

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```
                        lb=-5*np.ones((9)), ub=5*np.ones((9)),
                        x_names=x_names)
```

[17]:
```
# do the optimization
result = optimize.minimize(problem=problem,
                           optimizer=optimizer,
                           n_starts=10) # 200
```

```
  0%|          | 0/10 [00:00<?, ?it/s][Warning] AMICI:CVODES:CVode:ERR_FAILURE: AMICI␣
↪ERROR: in module CVODES in function CVode : At t = 27.1575 and h = 3.02895e-06, the␣
↪error test failed repeatedly or with |h| = hmin.
[Warning] AMICI:simulation: AMICI forward simulation failed at t = 27.157468:
AMICI failed to integrate the forward problem

[Warning] AMICI:CVODES:CVode:ERR_FAILURE: AMICI ERROR: in module CVODES in function␣
↪CVode : At t = 27.1575 and h = 3.02895e-06, the error test failed repeatedly or␣
↪with |h| = hmin.
[Warning] AMICI:simulation: AMICI forward simulation failed at t = 27.157468:
AMICI failed to integrate the forward problem

[Warning] AMICI:CVODES:CVode:ERR_FAILURE: AMICI ERROR: in module CVODES in function␣
↪CVode : At t = 27.1575 and h = 3.02895e-06, the error test failed repeatedly or␣
↪with |h| = hmin.
[Warning] AMICI:simulation: AMICI forward simulation failed at t = 27.157468:
AMICI failed to integrate the forward problem

 20%|        | 2/10 [00:04<00:16,  2.01s/it][Warning] AMICI:CVODES:CVode:ERR_FAILURE:␣
↪AMICI ERROR: in module CVODES in function CVode : At t = 198.1 and h = 2.52411e-05,␣
↪the error test failed repeatedly or with |h| = hmin.
[Warning] AMICI:simulation: AMICI forward simulation failed at t = 198.099706:
AMICI failed to integrate the forward problem

[Warning] AMICI:CVODES:CVode:ERR_FAILURE: AMICI ERROR: in module CVODES in function␣
↪CVode : At t = 197.924 and h = 2.91098e-05, the error test failed repeatedly or␣
↪with |h| = hmin.
[Warning] AMICI:simulation: AMICI forward simulation failed at t = 197.924166:
AMICI failed to integrate the forward problem

[Warning] AMICI:CVODES:CVode:ERR_FAILURE: AMICI ERROR: in module CVODES in function␣
↪CVode : At t = 197.924 and h = 2.91098e-05, the error test failed repeatedly or␣
↪with |h| = hmin.
[Warning] AMICI:simulation: AMICI forward simulation failed at t = 197.924166:
AMICI failed to integrate the forward problem

[Warning] AMICI:CVODES:CVode:ERR_FAILURE: AMICI ERROR: in module CVODES in function␣
↪CVode : At t = 197.924 and h = 2.91098e-05, the error test failed repeatedly or␣
↪with |h| = hmin.
[Warning] AMICI:simulation: AMICI forward simulation failed at t = 197.924166:
AMICI failed to integrate the forward problem

 30%|       | 3/10 [00:05<00:13,  1.92s/it][Warning] AMICI:CVODES:CVode:ERR_FAILURE:␣
↪AMICI ERROR: in module CVODES in function CVode : At t = 125.014 and h = 1.7682e-05,
↪ the error test failed repeatedly or with |h| = hmin.
[Warning] AMICI:simulation: AMICI forward simulation failed at t = 125.014377:
AMICI failed to integrate the forward problem

[Warning] AMICI:CVODES:CVode:ERR_FAILURE: AMICI ERROR: in module CVODES in function␣
↪CVode : At t = 125.014 and h = 1.7682e-05, the error test failed repeatedly or␣
↪|h| = hmin.
```

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```
[Warning] AMICI:simulation: AMICI forward simulation failed at t = 125.014377:
AMICI failed to integrate the forward problem

[Warning] AMICI:CVODES:CVode:ERR_FAILURE: AMICI ERROR: in module CVODES in function␣
↪CVode : At t = 125.014 and h = 1.7682e-05, the error test failed repeatedly or with␣
↪|h| = hmin.
[Warning] AMICI:simulation: AMICI forward simulation failed at t = 125.014377:
AMICI failed to integrate the forward problem

 50%|     | 5/10 [00:08<00:08,  1.74s/it][Warning] AMICI:CVODES:CVode:ERR_FAILURE:␣
↪AMICI ERROR: in module CVODES in function CVode : At t = 162.24 and h = 3.05789e-06,
↪ the error test failed repeatedly or with |h| = hmin.
[Warning] AMICI:simulation: AMICI forward simulation failed at t = 162.239689:
AMICI failed to integrate the forward problem

[Warning] AMICI:CVODES:CVode:ERR_FAILURE: AMICI ERROR: in module CVODES in function␣
↪CVode : At t = 162.24 and h = 3.05789e-06, the error test failed repeatedly or with␣
↪|h| = hmin.
[Warning] AMICI:simulation: AMICI forward simulation failed at t = 162.239689:
AMICI failed to integrate the forward problem

 70%|   | 7/10 [00:18<00:08,  2.96s/it][Warning] AMICI:CVODES:CVode:ERR_FAILURE:␣
↪AMICI ERROR: in module CVODES in function CVode : At t = 25.5245 and h = 5.70238e-
↪06, the error test failed repeatedly or with |h| = hmin.
[Warning] AMICI:simulation: AMICI forward simulation failed at t = 25.524541:
AMICI failed to integrate the forward problem

[Warning] AMICI:CVODES:CVode:ERR_FAILURE: AMICI ERROR: in module CVODES in function␣
↪CVode : At t = 25.5245 and h = 5.70238e-06, the error test failed repeatedly or␣
↪with |h| = hmin.
[Warning] AMICI:simulation: AMICI forward simulation failed at t = 25.524541:
AMICI failed to integrate the forward problem

100%|| 10/10 [00:23<00:00,  2.37s/it]
```

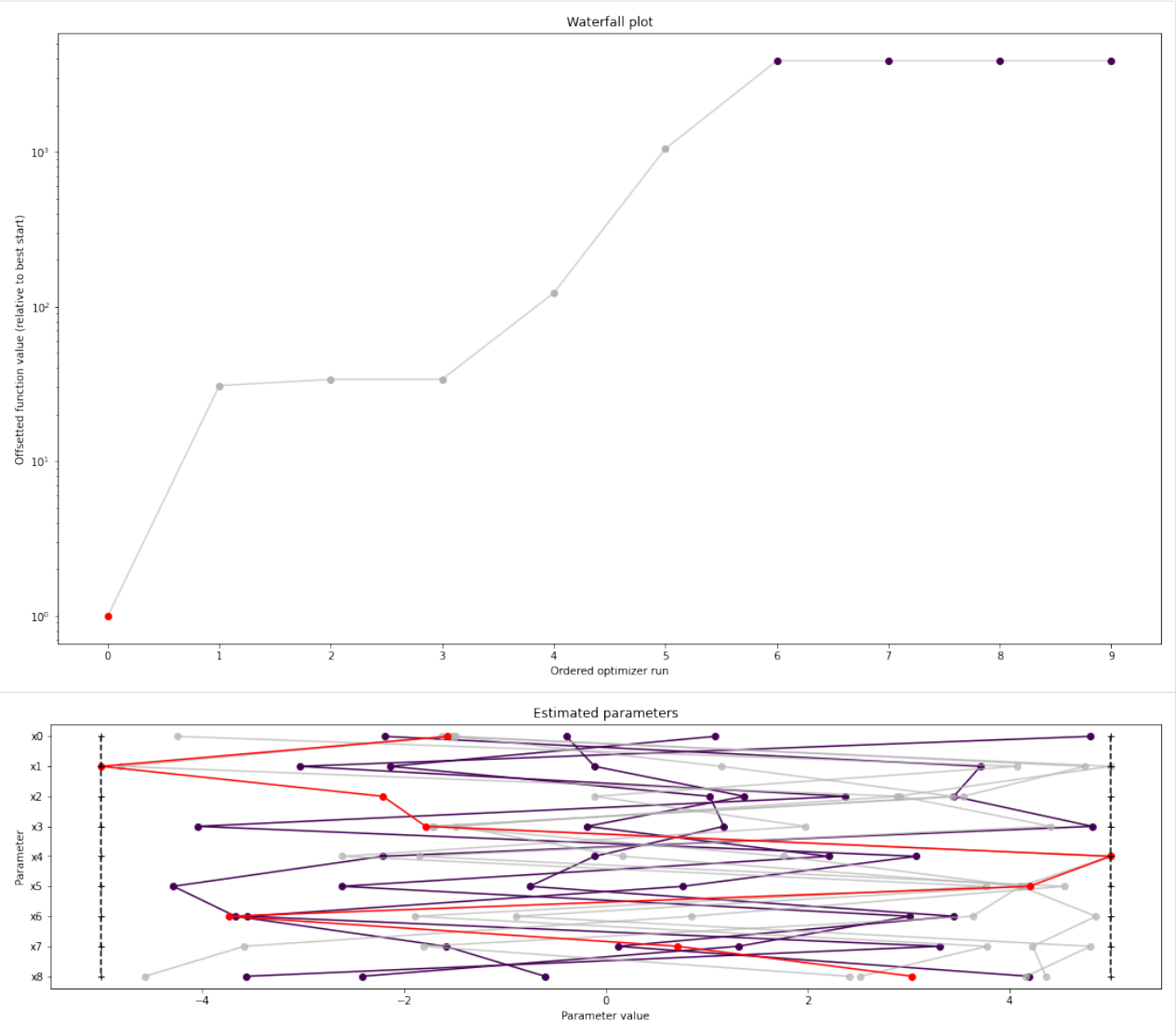
Visualization

Create waterfall and parameter plot

[18]:
```
# waterfall, parameter space,
import pypesto.visualize as visualize

visualize.waterfall(result)
visualize.parameters(result)
```

[18]:
```
<AxesSubplot:title={'center':'Estimated parameters'}, xlabel='Parameter value',␣
↪ylabel='Parameter'>
```



2.2.2 Model import using the Petab format

In this notebook, we illustrate how to use pyPESTO together with PEtab and AMICI. We employ models from the benchmark collection, which we first download:

[ ]:
```
# install if not done yet
# !apt install libatlas-base-dev swig
# %pip install pypesto[amici,petab] --quiet
```

[1]:
```
import pypesto
import pypesto.petab
import pypesto.optimize as optimize
import pypesto.visualize as visualize
import amici
import petab

import os
```

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```
import numpy as np
import matplotlib.pyplot as plt

%matplotlib inline

!git clone --depth 1 https://github.com/Benchmarking-Initiative/Benchmark-Models-
↪PEtab.git tmp/benchmark-models || (cd tmp/benchmark-models && git pull)

folder_base = "tmp/benchmark-models/Benchmark-Models/"
```

```
fatal: destination path 'tmp/benchmark-models' already exists and is not an empty␣
↪directory.
Already up to date.
```

Import

Manage PEtab model

A PEtab problem comprises all the information on the model, the data and the parameters to perform parameter estimation. We import a model as a `petab.Problem`.

[2]:
```
# a collection of models that can be simulated

#model_name = "Zheng_PNAS2012"
model_name = "Boehm_JProteomeRes2014"
#model_name = "Fujita_SciSignal2010"
#model_name = "Sneyd_PNAS2002"
#model_name = "Borghans_BiophysChem1997"
#model_name = "Elowitz_Nature2000"
#model_name = "Crauste_CellSystems2017"
#model_name = "Lucarelli_CellSystems2018"
#model_name = "Schwen_PONE2014"
#model_name = "Blasi_CellSystems2016"

# the yaml configuration file links to all needed files
yaml_config = os.path.join(folder_base, model_name, model_name + '.yaml')

# create a petab problem
petab_problem = petab.Problem.from_yaml(yaml_config)
```

Import model to AMICI

The model must be imported to pyPESTO and AMICI. Therefore, we create a `pypesto.PetabImporter` from the problem, and create an AMICI model.

[3]:
```
importer = pypesto.petab.PetabImporter(petab_problem)

model = importer.create_model()

# some model properties
print("Model parameters:", list(model.getParameterIds()), '\n')
print("Model const parameters:", list(model.getFixedParameterIds()), '\n')
```

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```
print("Model outputs:   ", list(model.getObservableIds()), '\n')
print("Model states:    ", list(model.getStateIds()), '\n')
```

```
Using existing amici model in folder /Users/pauljonasjost/Documents/GitHub_Folders/
↪pyPESTO/doc/example/amici_models/Boehm_JProteomeRes2014.
```

```
Model parameters: ['Epo_degradation_BaF3', 'k_exp_hetero', 'k_exp_homo', 'k_imp_hetero
↪', 'k_imp_homo', 'k_phos', 'ratio', 'specC17', 'noiseParameter1_pSTAT5A_rel',
↪'noiseParameter1_pSTAT5B_rel', 'noiseParameter1_rSTAT5A_rel']

Model const parameters: []

Model outputs:    ['pSTAT5A_rel', 'pSTAT5B_rel', 'rSTAT5A_rel']

Model states:     ['STAT5A', 'STAT5B', 'pApB', 'pApA', 'pBpB', 'nucpApA', 'nucpApB',
↪'nucpBpB']
```

Create objective function

To perform parameter estimation, we need to define an objective function, which integrates the model, data, and noise model defined in the PEtab problem.

[4]:
```
import libsbml
converter_config = libsbml.SBMLLocalParameterConverter()\
    .getDefaultProperties()
petab_problem.sbml_document.convert(converter_config)

obj = importer.create_objective()

# for some models, hyperparamters need to be adjusted
#obj.amici_solver.setMaxSteps(10000)
#obj.amici_solver.setRelativeTolerance(1e-7)
#obj.amici_solver.setAbsoluteTolerance(1e-7)
```

```
Using existing amici model in folder /Users/pauljonasjost/Documents/GitHub_Folders/
↪pyPESTO/doc/example/amici_models/Boehm_JProteomeRes2014.
```

We can request variable derivatives via `sensi_orders`, or function values or residuals as specified via `mode`. Passing `return_dict`, we obtain the direct result of the AMICI simulation.

[5]:
```
ret = obj(petab_problem.x_nominal_scaled, mode='mode_fun', sensi_orders=(0,1), return_
↪dict=True)
print(ret)
```

```
{'fval': 138.22199566457704, 'grad': array([ 2.20546436e-02,  5.53227499e-02,  5.
↪78876640e-03,  5.42272184e-03,
       -4.51595808e-05,  7.91009669e-03,  0.00000000e+00,  1.07876837e-02,
        2.40388572e-02,  1.91925085e-02,  0.00000000e+00]), 'rdatas': [<amici.numpy.
↪ReturnDataView object at 0x7fdb9a293c40>]}
```

The problem defined in PEtab also defines the fixing of parameters, and parameter bounds. This information is contained in a `pypesto.Problem`.

[6]:
```
problem = importer.create_problem(obj)
```

In particular, the problem accounts for the fixing of parametes.

[7]:
```
print(problem.x_fixed_indices, problem.x_free_indices)
```

```
[6, 10] [0, 1, 2, 3, 4, 5, 7, 8, 9]
```

The problem creates a copy of he objective function that takes into account the fixed parameters. The objective function is able to calculate function values and derivatives. A finite difference check whether the computed gradient is accurate:

[8]:
```
objective = problem.objective
ret = objective(petab_problem.x_nominal_free_scaled, sensi_orders=(0,1))
print(ret)
```

```
(138.22199566457704, array([ 2.20546436e-02,  5.53227499e-02,  5.78876640e-03,  5.
↪42272184e-03,
       -4.51595808e-05,  7.91009669e-03,  1.07876837e-02,  2.40388572e-02,
        1.91925085e-02]))
```

[9]:
```
eps = 1e-4

def fd(x):
    grad = np.zeros_like(x)
    j = 0
    for i, xi in enumerate(x):
        mask = np.zeros_like(x)
        mask[i] += eps
        valinc, _ = objective(x+mask, sensi_orders=(0,1))
        valdec, _ = objective(x-mask, sensi_orders=(0,1))
        grad[j] = (valinc - valdec) / (2*eps)
        j += 1
    return grad

fdval = fd(petab_problem.x_nominal_free_scaled)
print("fd: ", fdval)
print("l2 difference: ", np.linalg.norm(ret[1] - fdval))
```

```
fd:  [ 0.02993985  0.05897443 -0.00149735 -0.00281785 -0.00925273  0.01197046
  0.01078638  0.02403756  0.01919121]
l2 difference:  0.017256061672716528
```

In short

All of the previous steps can be shortened by directly creating an importer object and then a problem:

[10]:
```
importer = pypesto.petab.PetabImporter.from_yaml(yaml_config)
problem = importer.create_problem()
```

```
Using existing amici model in folder /Users/pauljonasjost/Documents/GitHub_Folders/
↪pyPESTO/doc/example/amici_models/Boehm_JProteomeRes2014.
```

Run optimization

Given the problem, we can perform optimization. We can specify an optimizer to use, and a parallelization engine to speed things up.

[11]:
```
optimizer = optimize.ScipyOptimizer()

# engine = pypesto.engine.SingleCoreEngine()
engine = pypesto.engine.MultiProcessEngine()

# do the optimization
result = optimize.minimize(problem=problem, optimizer=optimizer,
                           n_starts=10, engine=engine)
```

```
Engine set up to use up to 8 processes in total. The number was automatically␣
↪determined and might not be appropriate on some systems.
Performing parallel task execution on 8 processes.
100%|| 10/10 [00:00<00:00, 131.88it/s]
Using existing amici model in folder /Users/pauljonasjost/Documents/GitHub_Folders/
↪pyPESTO/doc/example/amici_models/Boehm_JProteomeRes2014.
Using existing amici model in folder /Users/pauljonasjost/Documents/GitHub_Folders/
↪pyPESTO/doc/example/amici_models/Boehm_JProteomeRes2014.
Using existing amici model in folder /Users/pauljonasjost/Documents/GitHub_Folders/
↪pyPESTO/doc/example/amici_models/Boehm_JProteomeRes2014.
Using existing amici model in folder /Users/pauljonasjost/Documents/GitHub_Folders/
↪pyPESTO/doc/example/amici_models/Boehm_JProteomeRes2014.
Using existing amici model in folder /Users/pauljonasjost/Documents/GitHub_Folders/
↪pyPESTO/doc/example/amici_models/Boehm_JProteomeRes2014.
Executing task 2.
Using existing amici model in folder /Users/pauljonasjost/Documents/GitHub_Folders/
↪pyPESTO/doc/example/amici_models/Boehm_JProteomeRes2014.
Using existing amici model in folder /Users/pauljonasjost/Documents/GitHub_Folders/
↪pyPESTO/doc/example/amici_models/Boehm_JProteomeRes2014.
Using existing amici model in folder /Users/pauljonasjost/Documents/GitHub_Folders/
↪pyPESTO/doc/example/amici_models/Boehm_JProteomeRes2014.
Executing task 1.
Executing task 0.
Executing task 3.
Executing task 4.
Executing task 6.
Executing task 5.
Executing task 7.
Final fval=249.7460, time=0.3161s, n_fval=20.
Using existing amici model in folder /Users/pauljonasjost/Documents/GitHub_Folders/
↪pyPESTO/doc/example/amici_models/Boehm_JProteomeRes2014.
Final fval=249.7460, time=0.3418s, n_fval=17.
Using existing amici model in folder /Users/pauljonasjost/Documents/GitHub_Folders/
↪pyPESTO/doc/example/amici_models/Boehm_JProteomeRes2014.
Executing task 8.
Executing task 9.
Final fval=249.7460, time=0.6842s, n_fval=39.
[Warning] AMICI:CVODES:CVode:ERR_FAILURE: AMICI ERROR: in module CVODES in function␣
↪CVode : At t = 116.84 and h = 1.9371e-05, the error test failed repeatedly or with␣
↪|h| = hmin.
[Warning] AMICI:simulation: AMICI forward simulation failed at t = 116.839896:
AMICI failed to integrate the forward problem

[Warning] AMICI:CVODES:CVode:ERR_FAILURE: AMICI ERROR: in module CVODES in function␣
↪CVode : At t = 116.84 and h = 1.9371e-05, the error test failed repeatedly or with␣
↪|h| = hmin.
```

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```
[Warning] AMICI:simulation: AMICI forward simulation failed at t = 116.839896:
AMICI failed to integrate the forward problem

[Warning] AMICI:CVODES:CVode:ERR_FAILURE: AMICI ERROR: in module CVODES in function␣
↪CVode : At t = 116.84 and h = 1.9371e-05, the error test failed repeatedly or with␣
↪|h| = hmin.
[Warning] AMICI:simulation: AMICI forward simulation failed at t = 116.839896:
AMICI failed to integrate the forward problem

Final fval=159.0527, time=1.7929s, n_fval=102.
[Warning] AMICI:CVODES:CVode:ERR_FAILURE: AMICI ERROR: in module CVODES in function␣
↪CVode : At t = 89.1085 and h = 1.38467e-05, the error test failed repeatedly or␣
↪with |h| = hmin.
[Warning] AMICI:simulation: AMICI forward simulation failed at t = 89.108509:
AMICI failed to integrate the forward problem

Final fval=147.5440, time=2.7005s, n_fval=167.
Final fval=156.3410, time=2.5897s, n_fval=136.
Final fval=154.7306, time=2.6399s, n_fval=104.
[Warning] AMICI:CVODES:CVode:ERR_FAILURE: AMICI ERROR: in module CVODES in function␣
↪CVode : At t = 168.714 and h = 4.02611e-05, the error test failed repeatedly or␣
↪with |h| = hmin.
[Warning] AMICI:simulation: AMICI forward simulation failed at t = 168.714402:
AMICI failed to integrate the forward problem

[Warning] AMICI:CVODES:CVode:ERR_FAILURE: AMICI ERROR: in module CVODES in function␣
↪CVode : At t = 168.714 and h = 4.02611e-05, the error test failed repeatedly or␣
↪with |h| = hmin.
[Warning] AMICI:simulation: AMICI forward simulation failed at t = 168.714402:
AMICI failed to integrate the forward problem

[Warning] AMICI:CVODES:CVode:ERR_FAILURE: AMICI ERROR: in module CVODES in function␣
↪CVode : At t = 168.714 and h = 4.02611e-05, the error test failed repeatedly or␣
↪with |h| = hmin.
[Warning] AMICI:simulation: AMICI forward simulation failed at t = 168.714402:
AMICI failed to integrate the forward problem

Final fval=149.5878, time=3.3350s, n_fval=171.
Final fval=149.5882, time=3.8314s, n_fval=172.
Parameters obtained from history and optimizer do not match: [-1.56379081 -3.2217545 ␣
↪ 5.          5.          -1.89883736  4.35504207
  0.9094744   0.80931241  1.07766644], [-1.56378624 -3.22180774  5.          5.      ␣
↪  -1.89885149  4.355015
  0.9094958   0.80930196  1.07768133]
Final fval=171.1341, time=4.0903s, n_fval=187.
```

Visualize

The results are contained in a `pypesto.Result` object. It contains e.g. the optimal function values.

[12]:
```
result.optimize_result.get_for_key('fval')
```

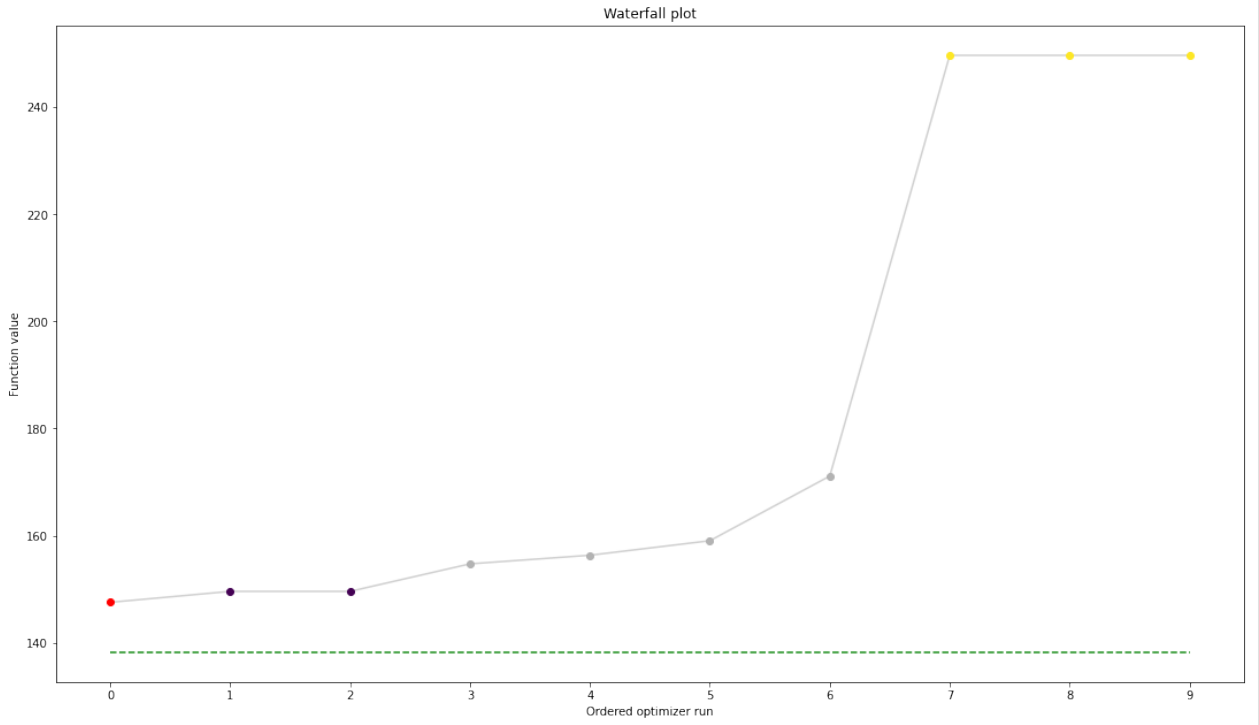
[12]:
```
[147.5440308019394,
 149.5878368928219,
 149.58822002126522,
 154.7306294235784,
 156.3410332994205,
 159.05273185070513,
 171.1340766484108,
 249.74597383547857,
 249.7459974423845,
 249.74599767995497]
```

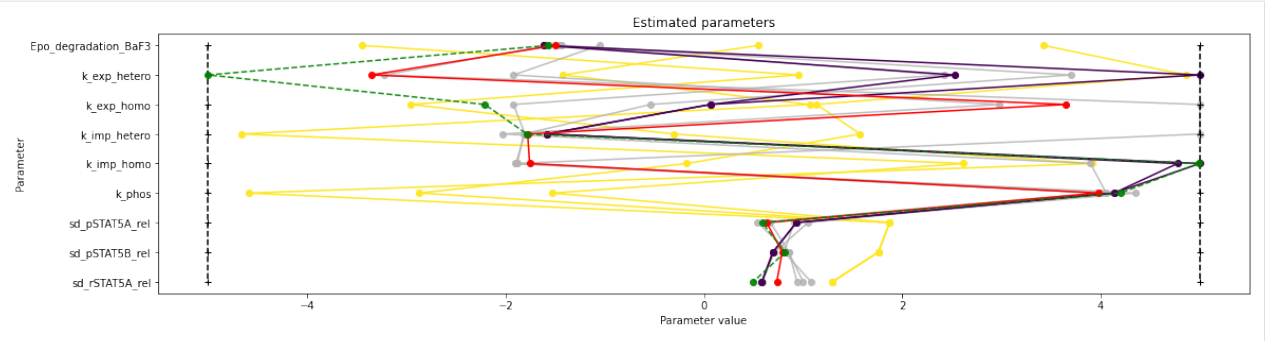
We can use the standard pyPESTO plotting routines to visualize and analyze the results.

[13]:
```
ref = visualize.create_references(
    x=petab_problem.x_nominal_scaled, fval=obj(petab_problem.x_nominal_scaled))

visualize.waterfall(result, reference=ref, scale_y='lin')
visualize.parameters(result, reference=ref)
```

[13]:
```
<AxesSubplot:title={'center':'Estimated parameters'}, xlabel='Parameter value',␣
↪ylabel='Parameter'>
```

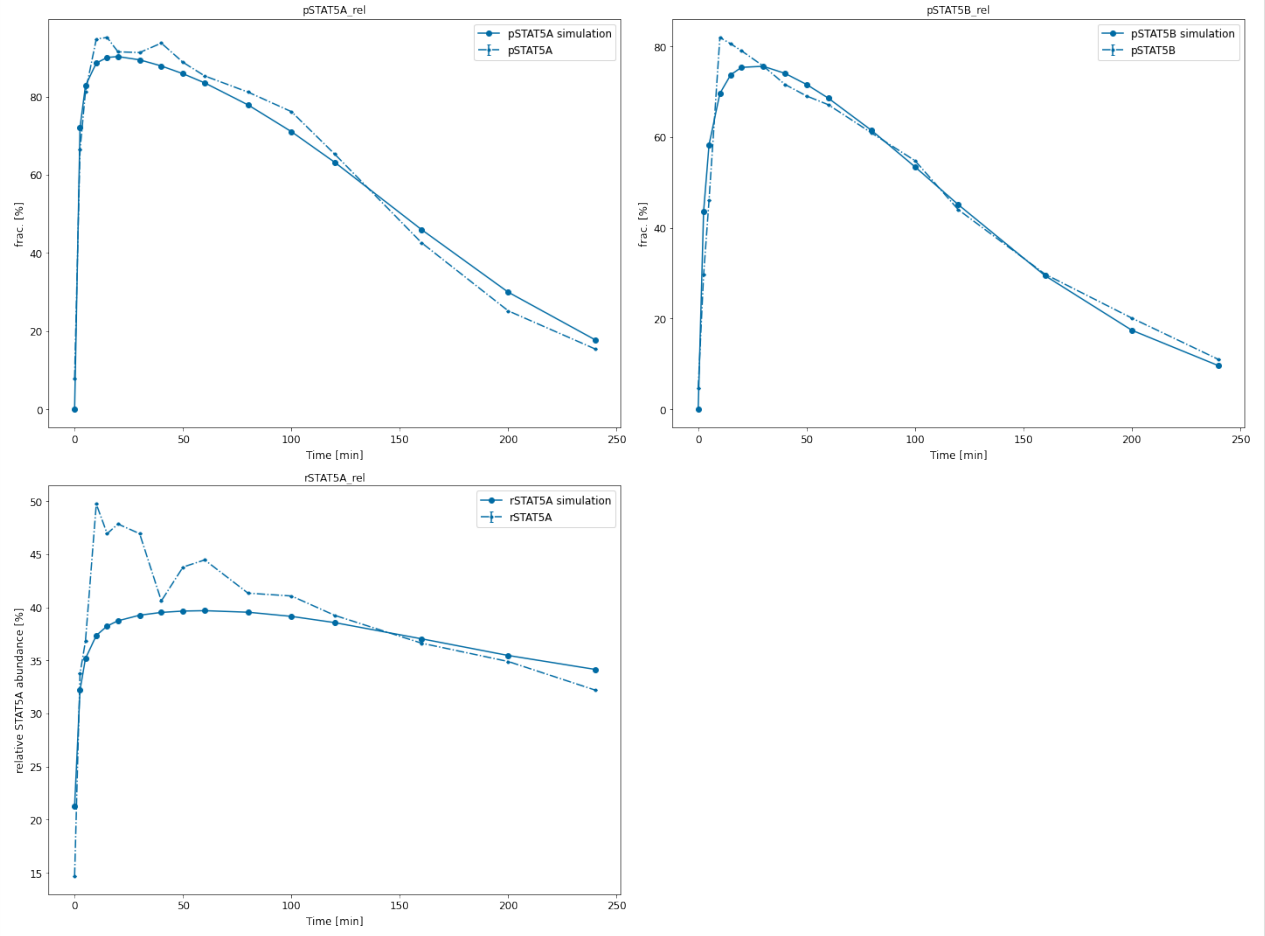




We can also conveniently visualize the model fit. This plots the petab visualization using optimized parameters.

[14]:
```
# we need to explicitely import the method
from pypesto.visualize.model_fit import visualize_optimized_model_fit
visualize_optimized_model_fit(petab_problem=petab_problem,
                              result=result)
```

[14]:
```
{'plot1': <AxesSubplot:title={'center':'pSTAT5A_rel'}, xlabel='Time [min]', ylabel=
↪'frac. [%]'>,
 'plot2': <AxesSubplot:title={'center':'pSTAT5B_rel'}, xlabel='Time [min]', ylabel=
↪'frac. [%]'>,
 'plot3': <AxesSubplot:title={'center':'rSTAT5A_rel'}, xlabel='Time [min]', ylabel=
↪'relative STAT5A abundance [%]'>}
```



2.3 Algorithms and features

2.3.1 Fixed parameters

In this notebook we will show how to use fixed parameters. Therefore, we employ our Rosenbrock example. We define two problems, where for the first problem all parameters are optimized, and for the second we fix some of them to specified values.

[ ]:
```
# install if not done yet
# %pip install pypesto --quiet
```

Define problem

[1]:
```
import pypesto
import pypesto.optimize as optimize
import pypesto.visualize as visualize
import numpy as np
import scipy as sp
import matplotlib.pyplot as plt

%matplotlib inline
```

[2]:
```
objective = pypesto.Objective(fun=sp.optimize.rosen,
                              grad=sp.optimize.rosen_der,
                              hess=sp.optimize.rosen_hess)

dim_full = 5
lb = -2 * np.ones((dim_full,1))
ub = 2 * np.ones((dim_full,1))

problem1 = pypesto.Problem(objective=objective, lb=lb, ub=ub)

x_fixed_indices = [1, 3]
x_fixed_vals = [1, 1]
problem2 = pypesto.Problem(objective=objective, lb=lb, ub=ub,
                           x_fixed_indices=x_fixed_indices,
                           x_fixed_vals=x_fixed_vals)
```

Optimize

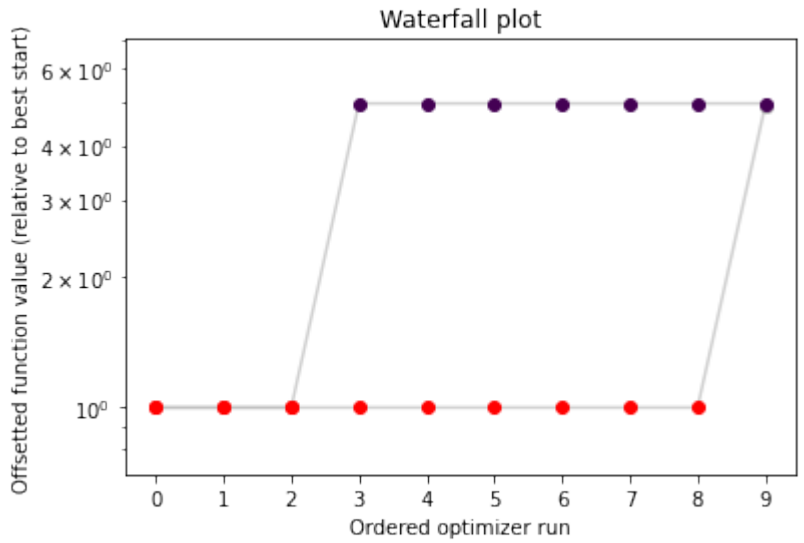
[3]:
```
optimizer = optimize.ScipyOptimizer()
n_starts = 10

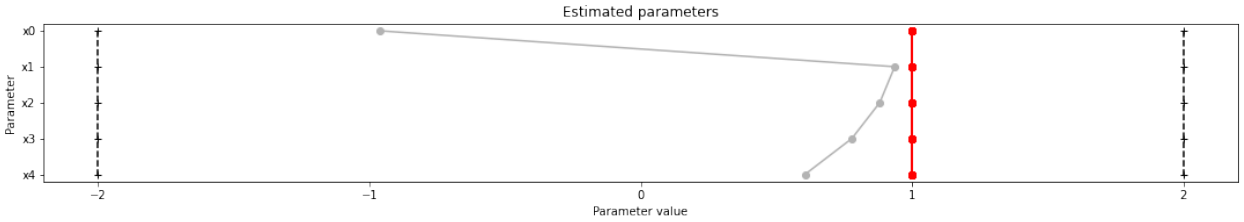
result1 = optimize.minimize(problem=problem1, optimizer=optimizer,
                            n_starts=n_starts, filename=None)
result2 = optimize.minimize(problem=problem2, optimizer=optimizer,
                            n_starts=n_starts, filename=None)
```

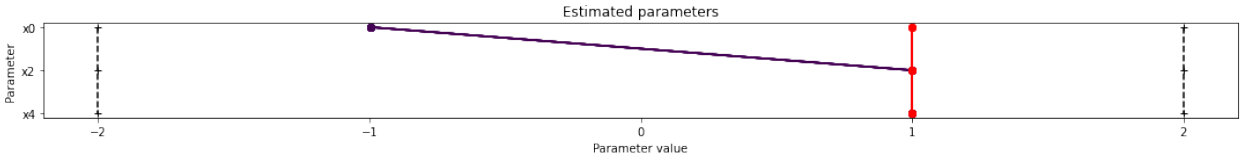
Visualize

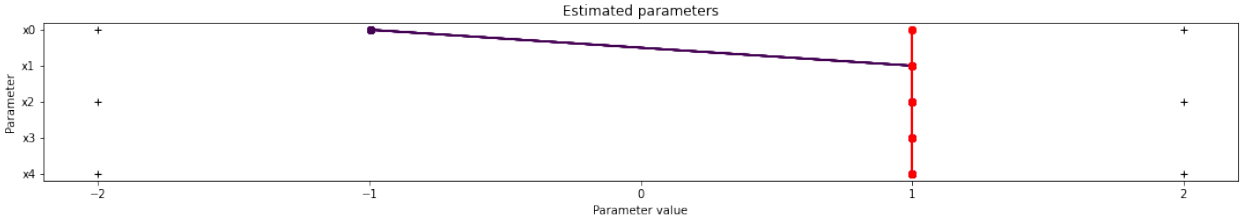
[4]:
```
fig, ax = plt.subplots()
visualize.waterfall(result1, ax)
visualize.waterfall(result2, ax)
visualize.parameters(result1)
visualize.parameters(result2)
visualize.parameters(result2, parameter_indices='all')
```

[4]:
```
<matplotlib.axes._subplots.AxesSubplot at 0x7ff3da236a20>
```









[5]:
```
result1.optimize_result.as_dataframe(['fval', 'x', 'grad'])
```

[5]:
```
           fval                                                  x  \
0  2.563931e-14  [0.9999999859217336, 0.9999999812160436, 0.999...
```

(continues on next page)

(continued from previous page)

```
1  4.103854e-14  [1.0000000033181213, 1.00000001070042, 1.00000...
2  2.430040e-13  [0.9999999979980921, 0.9999999872750013, 0.999...
3  2.993261e-12  [1.0000000655628785, 1.0000002137366326, 1.000...
4  3.028019e-11  [1.0000002263273202, 0.9999999457510741, 1.000...
5  1.504857e-10  [1.0000008747306284, 1.000001813929941, 1.0000...
6  3.713657e-10  [1.0000011952242212, 1.000001771893066, 1.0000...
7  4.012393e-10  [0.9999986079063197, 0.9999988670990364, 0.999...
8  5.247717e-10  [1.000000368254703, 1.0000009022274876, 0.9999...
9  3.930839e+00  [-0.9620510415103535, 0.9357394330313418, 0.88...

                                                  grad
0  [-3.7771869883630873e-06, 3.2004378806360524e-...
1  [-1.6190347383411735e-06, 5.768553691118231e-0...
2  [3.4844693764909735e-06, 4.6873211372756083e-0...
3  [-3.291322500031286e-05, 6.600823794056182e-07...
4  [0.00020321414758544783, -0.000184783444508992...
5  [-2.4037728901340504e-05, -1.168240814877157e-...
6  [0.00024981346612303615, 0.0001962351003382311...
7  [-0.000663297051531534, 0.000537723456872972, ...
8  [-6.555069341760695e-05, 0.0009407121705420637...
9  [-1.109923131625834e-06, 5.109232684041842e-06...
```

[6]:
```
result2.optimize_result.as_dataframe(['fval', 'x', 'grad'])
```

[6]:
```
           fval                                                  x  \
0  4.679771e-17  [0.9999999998641961, 1.0, 1.0000000002266116, ...
1  4.825331e-16  [0.9999999995848748, 1.0, 0.9999999991941183, ...
2  1.394704e-14  [1.0000000026325193, 1.0, 0.9999999987812758, ...
3  3.989975e+00  [-0.9949747468838975, 1.0, 0.9999999999585671,...
4  3.989975e+00  [-0.9949747461383964, 1.0, 0.9999999963588824,...
5  3.989975e+00  [-0.9949747436177196, 1.0, 0.9999999894437084,...
6  3.989975e+00  [-0.9949747458936441, 1.0, 0.99999997533737, 1...
7  3.989975e+00  [-0.9949747793023977, 1.0, 1.000000023888003, ...
8  3.989975e+00  [-0.9949748033666262, 1.0, 1.0000000080319777,...
9  3.989975e+00  [-0.994974648260114, 1.0, 0.9999999725753793, ...

                                                  grad
0  [-1.0891474676223493e-07, nan, 2.2706484163692...
1  [-3.329303753527845e-07, nan, -8.0749345757971...
2  [2.1112804950914665e-06, nan, -1.2211616799204...
3  [-4.2116658605095836e-08, nan, -4.151572285811...
4  [5.468066182068299e-07, nan, -3.64839985427999...
5  [2.5380648831507813e-06, nan, -1.0577404068293...
6  [7.40153570877311e-07, nan, -2.471195460075688...
7  [-2.5651750697797127e-05, nan, 2.3935779637870...
8  [-4.466176453288284e-05, nan, 8.0480417566767e...
9  [7.78676721049365e-05, nan, -2.747946901432181...
```

2.3.2 Definition of Priors:

In this notebook we demonstrate how to include prior knowledge into a parameter inference problem, in particular how to define (log-)priors for parameters. If you want to maximize your posterior distribution, you need to define

- A (negative log-)likelihood
- A (log-)prior

The posterior is then built as an `AggregatedObjective`. If you import a problem via `PEtab` and the priors are contained in the parameter table, the definition of priors is done automatically.

CAUTION: The user needs to specify the **negative** *log-likelihood*, while the *log-prior* is internally mulitplied by -1.

[ ]:
```
# install if not done yet
# %pip install pypesto --quiet
```

[1]:
```
import numpy as np
import scipy as sp

import pypesto
```

Example: Rosenbrock Banana

We will use the Rosenbrock Banana

$$f(x,\theta) = \sum_{i=1}^{N} \underbrace{100 \cdot (x_i - x_{i-1}^2)^2}_{\text{"negative log-likelihood"}} + \underbrace{(x_{i-1} - 1)^2}_{\text{"Gaussian log-prior"}} \tag{2.1}$$

as an example. Here we interpret the first term as the *negative log-likelihood* and the second term as Gaussian *log-prior* with mean 1 and standard deviation $1/\sqrt{2}$.

Note that the second term is only equivalent to the negative log-distribution of a Gaussian up to a constant.

Define the negative log-likelihood

[2]:
```
n_x = 5


def rosenbrock_part_1(x):
    """
    Calculate obj. fct + gradient of the "likelihood" part.
    """
    obj = sum(100.0*(x[1:] - x[:-1]**2.0)**2.0)

    grad = np.zeros_like(x)
    grad[:-1] += -400 * (x[1:] - x[:-1]**2.0) * x[:-1]
    grad[1:] += 200 * (x[1:] - x[:-1]**2.0)

    return (obj, grad)

neg_log_likelihood = pypesto.Objective(fun=rosenbrock_part_1, grad=True)
```

Define the log-prior

A prior on an individual paramater is defined in a `prior_dict`, which contains the following key-value pairs:

- `index`: Index of the parameter
- `density_fun`: (Log-)posterior. (Scalar function!)
- `density_dx`: d/dx (Log-)posterior (optional)
- `density_ddx`: $d^{2/dx}2$ (Log-)posterior (optional)

A `prior_dict` can be either obtained by `get_parameter_prior_dict` for several common priors, or defined by the user.

[3]:
```
from pypesto.objective.priors import get_parameter_prior_dict

# create a list of prior dicts...
prior_list = []
mean = 1
std_dev = 1 / np.sqrt(2)

for i in range(n_x-1):
    prior_list.append(get_parameter_prior_dict(i, 'normal', [mean, std_dev]))

# create the prior
neg_log_prior = pypesto.objective.NegLogParameterPriors(prior_list)
```

Define the negative log-posterior and the problem

The negative log-posterior is defined as an `AggregatedObjective`. Since optimization/visualization is not the main focus of this notebook, the reader is referred to other examples for a more in-depth presentation of these.

[4]:
```
neg_log_posterior = pypesto.objective.AggregatedObjective([neg_log_likelihood, neg_
↪log_prior])

lb = -5 * np.ones((n_x, 1))
ub = 5 * np.ones((n_x, 1))

problem = pypesto.Problem(objective=neg_log_posterior,
                          lb=lb,
                          ub=ub)
```

Optimize

[5]:
```
import pypesto.optimize as optimize

result = optimize.minimize(problem=problem, n_starts=10, filename=None)
```

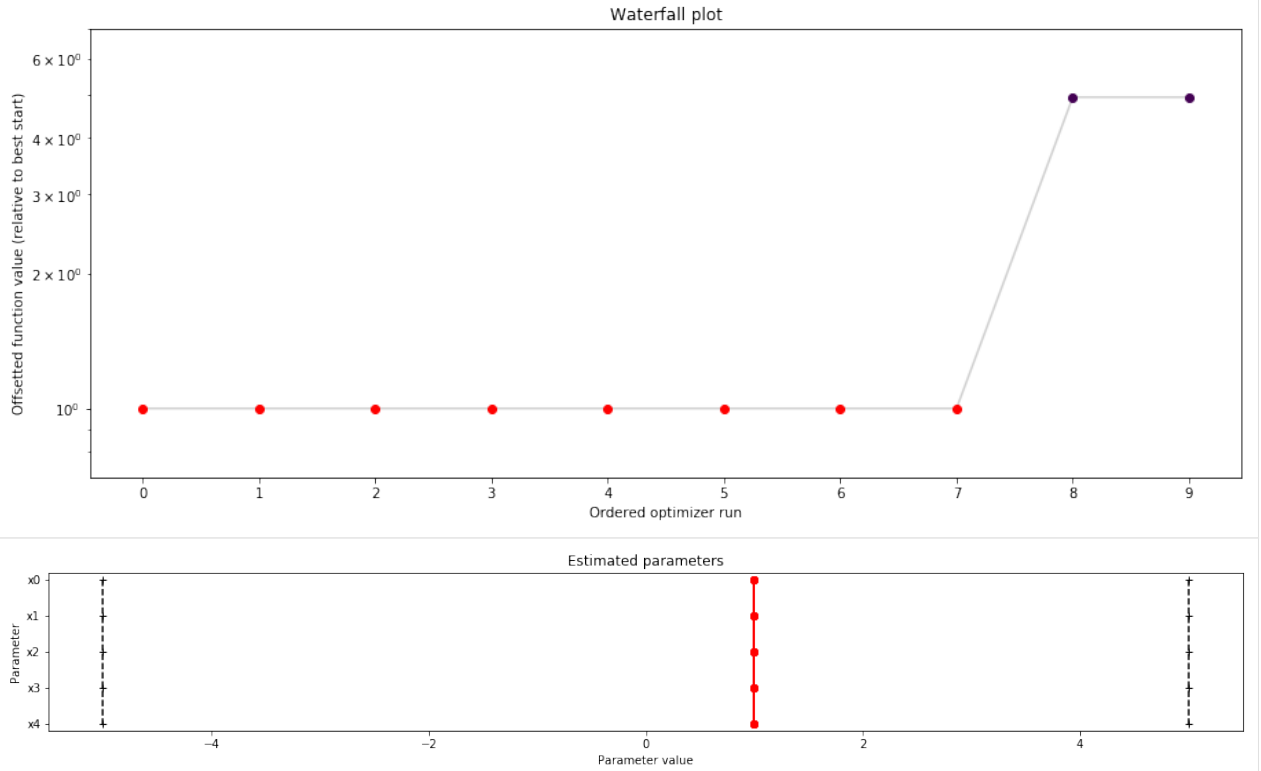
Some basic visualizations

[6]:
```
import pypesto.visualize as visualize

visualize.waterfall(result, size=(15,6))

# parallel coordinates plot for best 5 fits
visualize.parameters(result, start_indices=5)
```

[6]:
```
<matplotlib.axes._subplots.AxesSubplot at 0x12faa1908>
```



[ ]:
```
```

2.3.3 A sampler study

In this notebook, we perform a short study of how various samplers implemented in pyPESTO perform.

[1]:
```
# install if not done yet
# !apt install libatlas-base-dev swig
# %pip install pypesto[amici,petab,pymc3,emcee] --quiet
```

The pipeline

First, we show a typical workflow, fully integrating the samplers with a PEtab problem, using a toy example of a conversion reaction.

[2]:
```
import pypesto
import pypesto.petab
import pypesto.optimize as optimize
import pypesto.sample as sample
import pypesto.visualize as visualize
import petab

# import to petab
petab_problem = petab.Problem.from_yaml(
    "conversion_reaction/conversion_reaction.yaml")
# import to pypesto
importer = pypesto.petab.PetabImporter(petab_problem)
# create problem
problem = importer.create_problem()
```

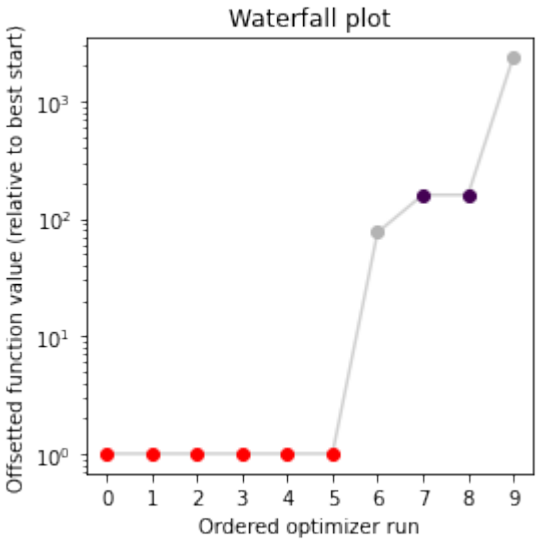
```
Using existing amici model in folder /home/yannik/pypesto/doc/example/amici_models/
↪conversion_reaction_0.
```

Commonly, as a first step, optimization is performed, in order to find good parameter point estimates.

[3]:
```
result = optimize.minimize(problem, n_starts=10, filename=None)
```

```
100%|| 10/10 [00:02<00:00,  3.59it/s]
```

[4]:
```
ax = visualize.waterfall(result, size=(4,4))
```



Next, we perform sampling. Here, we employ a `pypesto.sample.AdaptiveParallelTemperingSampler` sampler, which runs Markov Chain Monte Carlo (MCMC) chains on different temperatures. For each chain, we employ a `pypesto.sample.AdaptiveMetropolisSampler`. For more on the samplers see below or the API documentation.

[5]:
```
sampler = sample.AdaptiveParallelTemperingSampler(
    internal_sampler=sample.AdaptiveMetropolisSampler(),
    n_chains=3)
```

For the actual sampling, we call the `pypesto.sample.sample` function. By passing the result object to the function, the previously found global optimum is used as starting point for the MCMC sampling.

[6]:
```
%%time
result = sample.sample(problem, n_samples=10000, sampler=sampler,
                       result=result, filename=None)
```

```
100%|| 10000/10000 [01:27<00:00, 114.52it/s]
Elapsed time: 88.83624044499999
```

```
CPU times: user 1min 16s, sys: 12.8 s, total: 1min 28s
Wall time: 1min 27s
```

When the sampling is finished, we can analyse our results. A first thing to do is to analyze the sampling burn-in:

[7]:
```
sample.geweke_test(result)
```

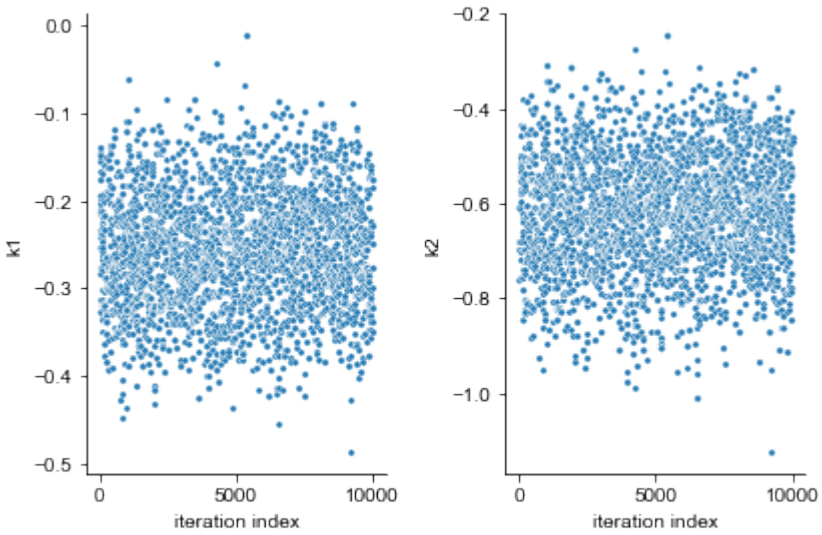
```
Geweke burn-in index: 0
```

[7]:
```
0
```

pyPESTO provides functions to analyse both the sampling process as well as the obtained sampling result. Visualizing the traces e.g. allows to detect burn-in phases, or fine-tune hyperparameters. First, the parameter trajectories can be visualized:

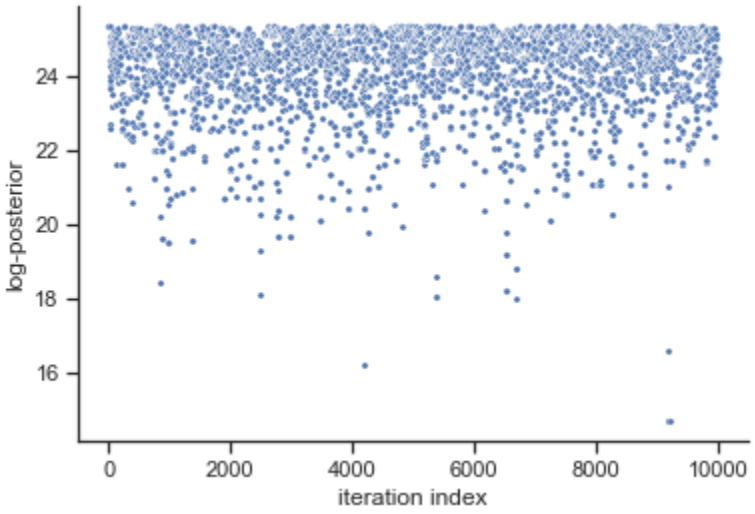
[8]:
```
sample.geweke_test(result)
ax = visualize.sampling_parameter_traces(result, use_problem_bounds=False)
```

```
Geweke burn-in index: 0
```



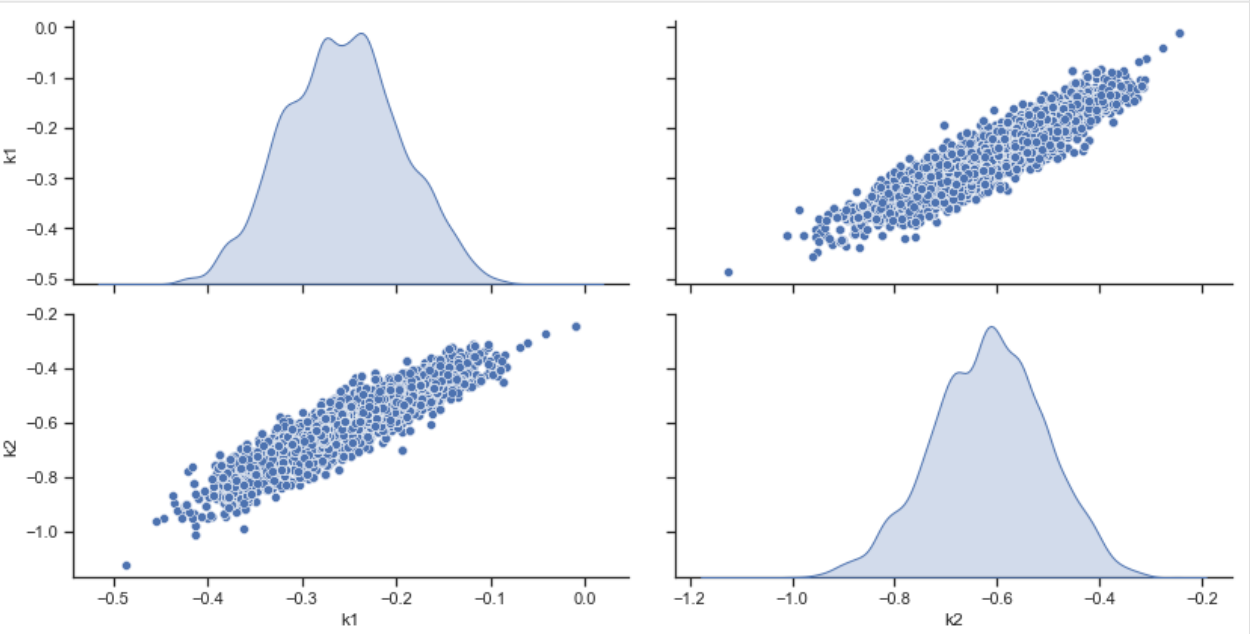
Next, also the log posterior trace can be visualized:

[9]:
```
ax = visualize.sampling_fval_traces(result)
```



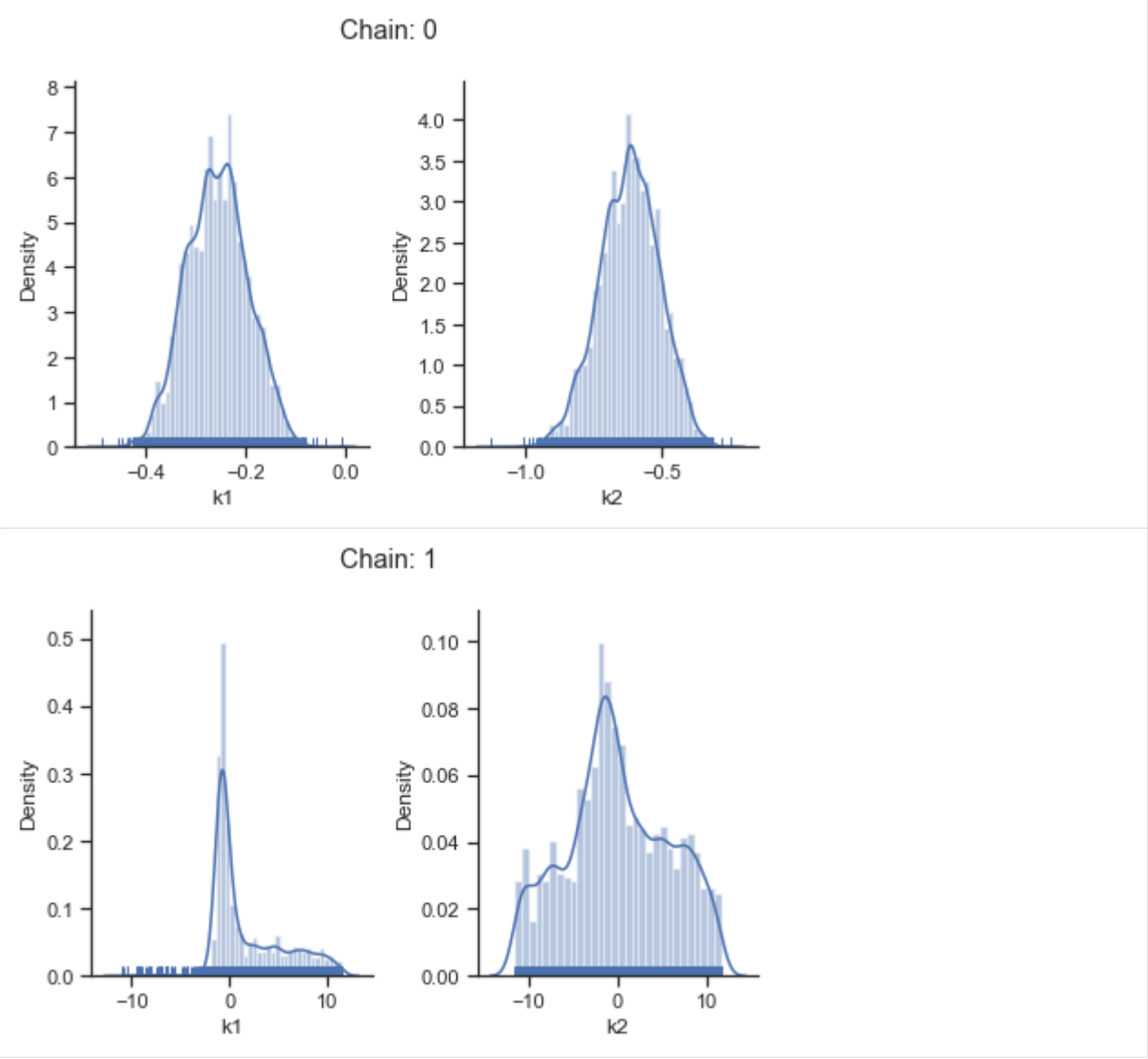
To visualize the result, there are various options. The scatter plot shows histograms of 1-dim parameter marginals and scatter plots of 2-dimensional parameter combinations:

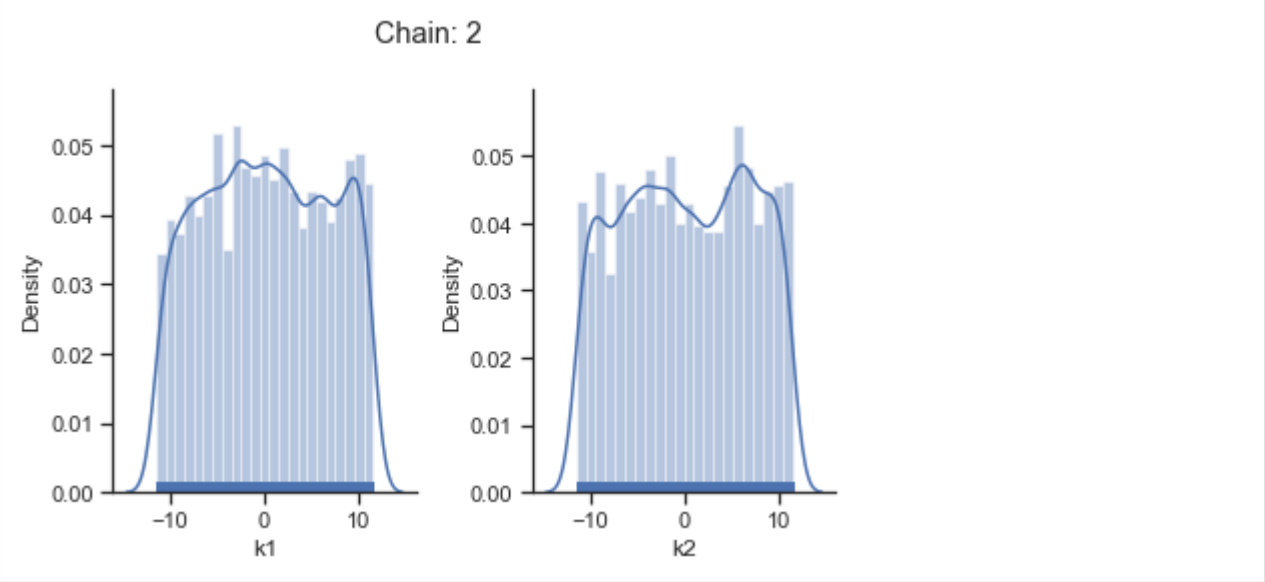
[10]:
```
ax = visualize.sampling_scatter(result, size=[13,6])
```



`sampling_1d_marginals` allows to plot e.g. kernel density estimates or histograms (internally using seaborn):

[11]:
```
for i_chain in range(len(result.sample_result.betas)):
    visualize.sampling_1d_marginals(
        result, i_chain=i_chain, suptitle=f"Chain: {i_chain}")
```


Chain: 0
Density
k1
k2
Chain: 1
Density
k1
k2



That's it for the moment on using the sampling pipeline.

1-dim test problem

To compare and test the various implemented samplers, we first study a 1-dimensional test problem of a gaussian mixture density, together with a flat prior.

[12]:
```
import numpy as np
from scipy.stats import multivariate_normal
import seaborn as sns
import pypesto
import pypesto.sample as sample
import pypesto.visualize as visualize

def density(x):
    return 0.3*multivariate_normal.pdf(x, mean=-1.5, cov=0.1) + \
        0.7*multivariate_normal.pdf(x, mean=2.5, cov=0.2)

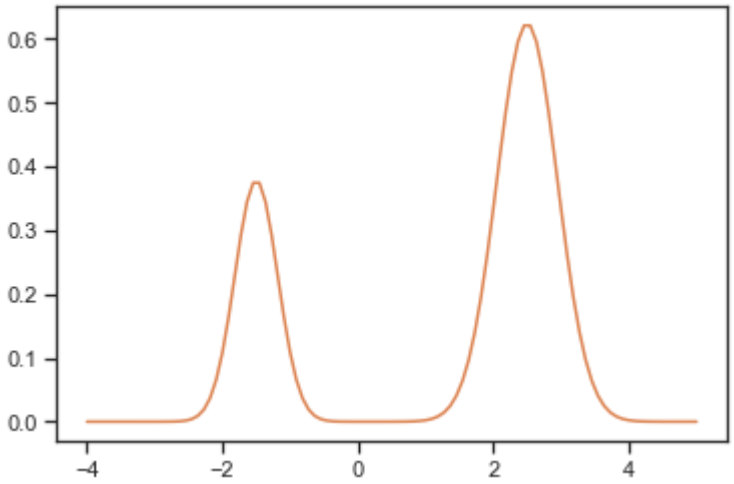
def nllh(x):
    return - np.log(density(x))

objective = pypesto.Objective(fun=nllh)
problem = pypesto.Problem(
    objective=objective, lb=-4, ub=5, x_names=['x'])
```

The likelihood has two separate modes:

[13]:
```
xs = np.linspace(-4, 5, 100)
ys = [density(x) for x in xs]

ax = sns.lineplot(xs, ys, color='C1')
```



Metropolis sampler

For this problem, let us try out the simplest sampler, the `pypesto.sample.MetropolisSampler`.

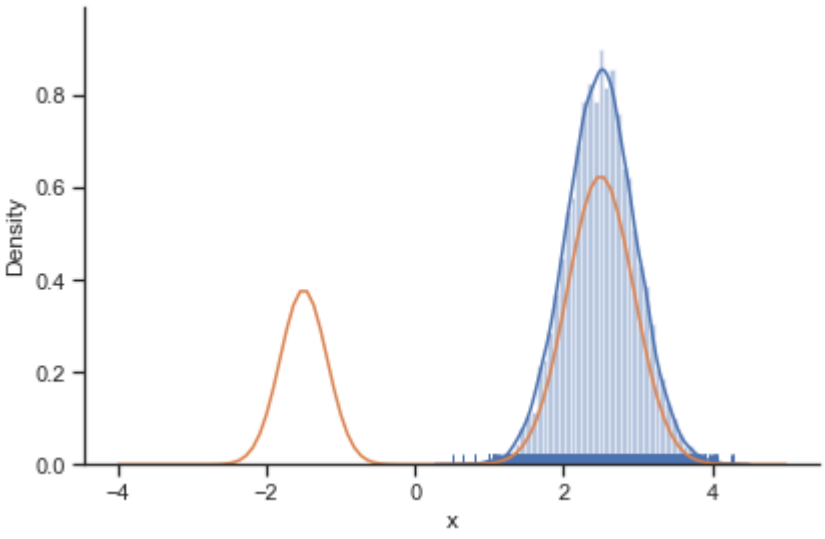
[14]:
```
sampler = sample.MetropolisSampler({'std': 0.5})
result = sample.sample(problem, 1e4, sampler,
                       x0=np.array([0.5]), filename=None)
```

```
100%|| 10000/10000 [00:04<00:00, 2133.34it/s]
Elapsed time: 4.838635854999993
```

[15]:
```
sample.geweke_test(result)
ax = visualize.sampling_1d_marginals(result)
ax[0][0].plot(xs, ys)
```

```
Geweke burn-in index: 0
```

[15]:
```
[<matplotlib.lines.Line2D at 0x7f3c41012490>]
```



The obtained posterior does not accurately represent the distribution, often only capturing one mode. This is because it is hard for the Markov chain to jump between the distribution's two modes. This can be fixed by choosing a higher proposal variation `std`:

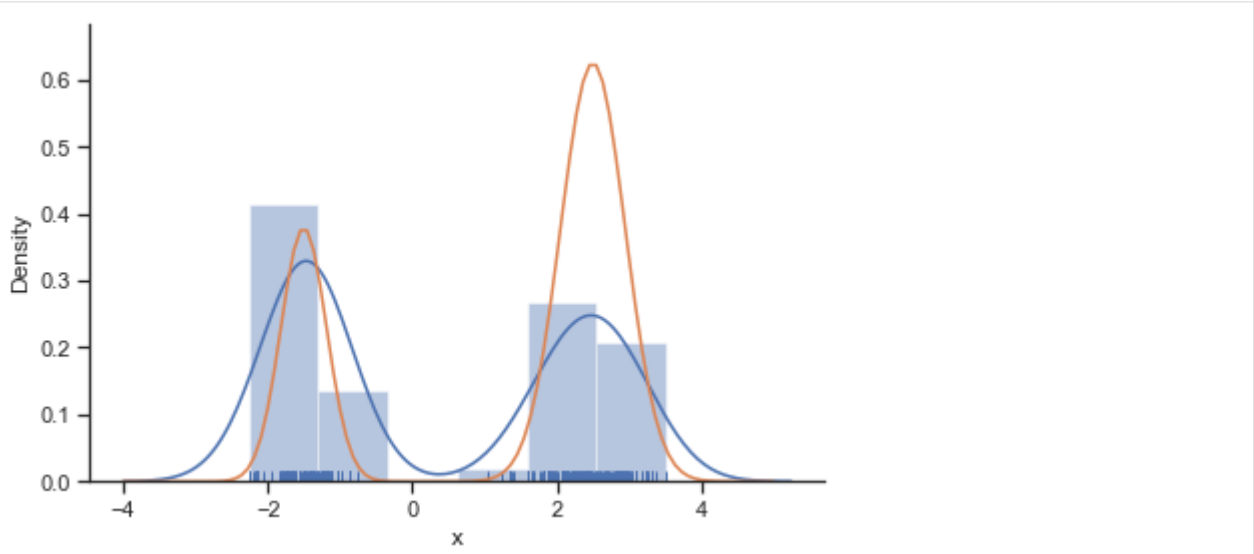
[16]:
```
sampler = sample.MetropolisSampler({'std': 1})
result = sample.sample(problem, 1e4, sampler,
                       x0=np.array([0.5]), filename=None)
```

```
100%|| 10000/10000 [00:04<00:00, 2179.96it/s]
Elapsed time: 4.922243723000008
```

[17]:
```
sample.geweke_test(result)
ax = visualize.sampling_1d_marginals(result)
ax[0][0].plot(xs, ys)
```

```
Geweke burn-in index: 9500
```

[17]:
```
[<matplotlib.lines.Line2D at 0x7f3c2acc22e0>]
```



In general, MCMC have difficulties exploring multimodel landscapes. One way to overcome this is to used parallel tempering. There, various chains are run, lifting the densities to different temperatures. At high temperatures, proposed steps are more likely to get accepted and thus jumps between modes more likely.

Parallel tempering sampler

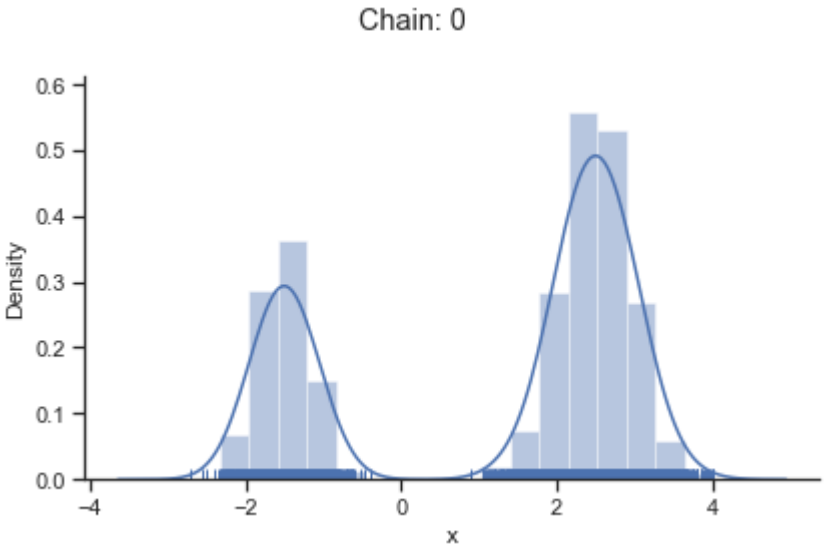
In pyPESTO, the most basic parallel tempering algorithm is the `pypesto.sample.ParallelTemperingSampler`. It takes an `internal_sampler` parameter, to specify what sampler to use for performing sampling the different chains. Further, we can directly specify what inverse temperatures `betas` to use. When not specifying the `betas` explicitly but just the number of chains `n_chains`, an established near-exponential decay scheme is used.

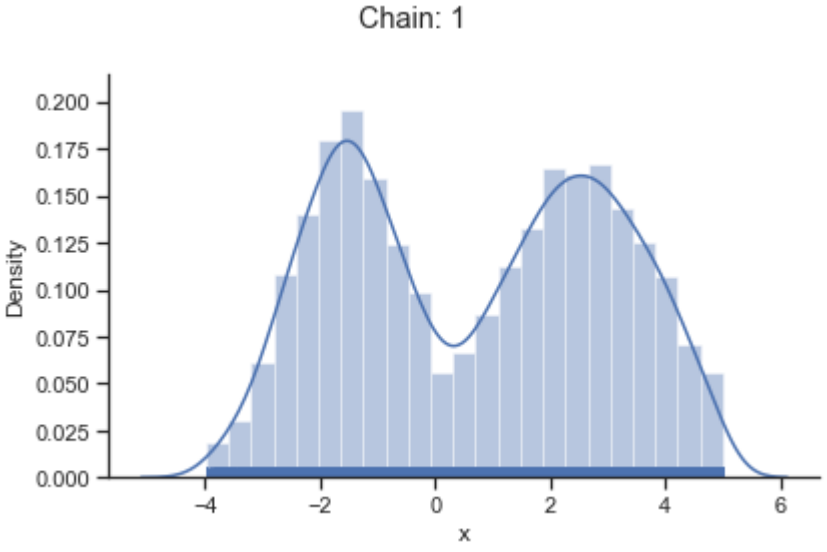
[18]:
```
sampler = sample.ParallelTemperingSampler(
    internal_sampler=sample.MetropolisSampler(),
    betas=[1, 1e-1, 1e-2])
result = sample.sample(problem, 1e4, sampler,
                       x0=np.array([0.5]), filename=None)
```

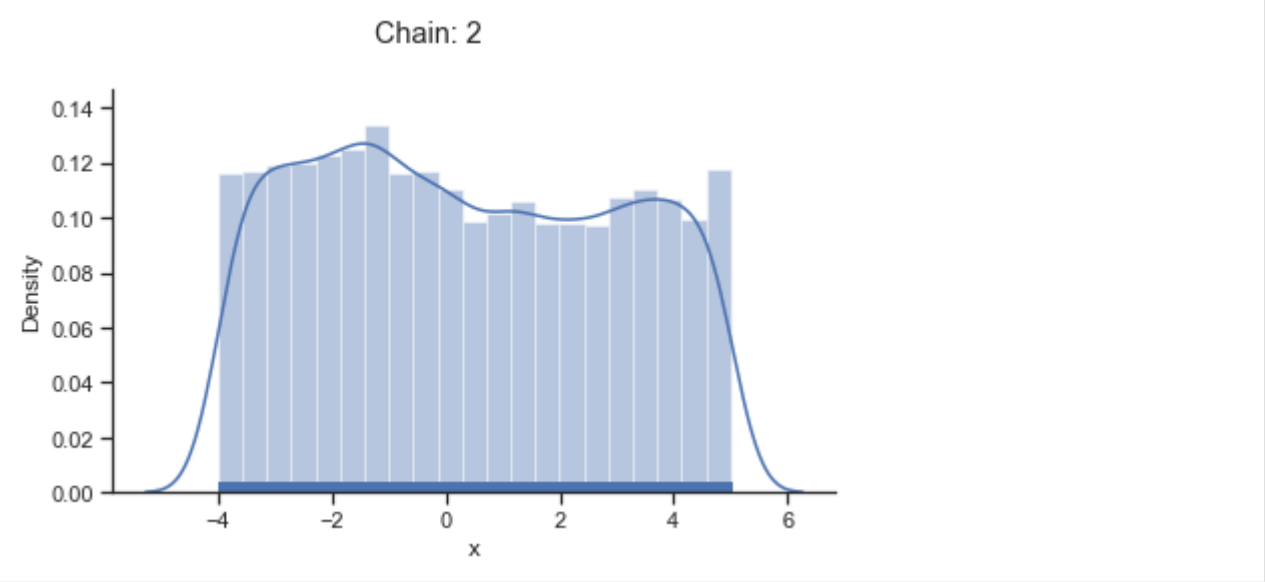
```
100%|| 10000/10000 [00:19<00:00, 524.68it/s]
Elapsed time: 19.971183034000006
```

[19]:
```
sample.geweke_test(result)
for i_chain in range(len(result.sample_result.betas)):
    visualize.sampling_1d_marginals(
        result, i_chain=i_chain, suptitle=f"Chain: {i_chain}")
```

```
Geweke burn-in index: 1000
```







Of interest is here finally the first chain at index `i_chain=0`, which approximates the posterior well.

Adaptive Metropolis sampler

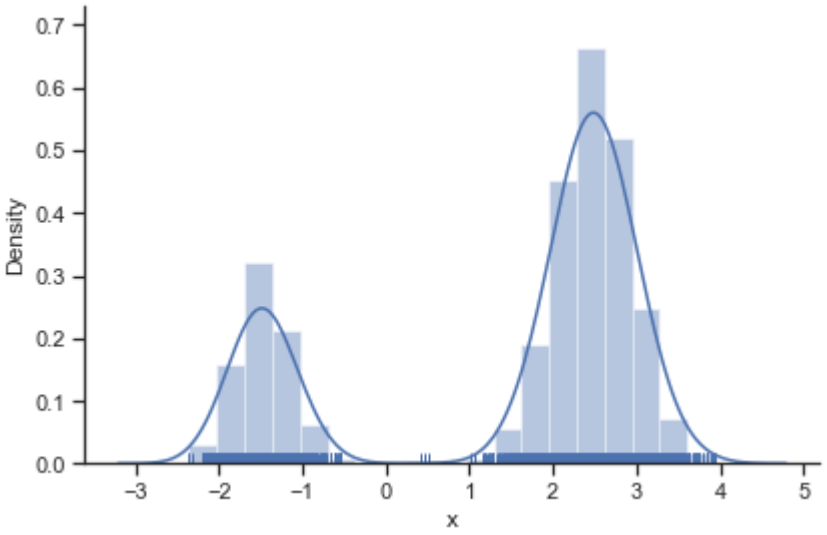
The problem of having to specify the proposal step variation manually can be overcome by using the `pypesto.sample.AdaptiveMetropolisSampler`, which iteratively adjusts the proposal steps to the function landscape.

[20]:
```
sampler = sample.AdaptiveMetropolisSampler()
result = sample.sample(problem, 1e4, sampler,
                       x0=np.array([0.5]), filename=None)
```

```
100%|| 10000/10000 [00:05<00:00, 1692.54it/s]
Elapsed time: 5.962580276000011
```

[21]:
```
sample.geweke_test(result)
ax = visualize.sampling_1d_marginals(result)
```

```
Geweke burn-in index: 0
```



Adaptive parallel tempering sampler

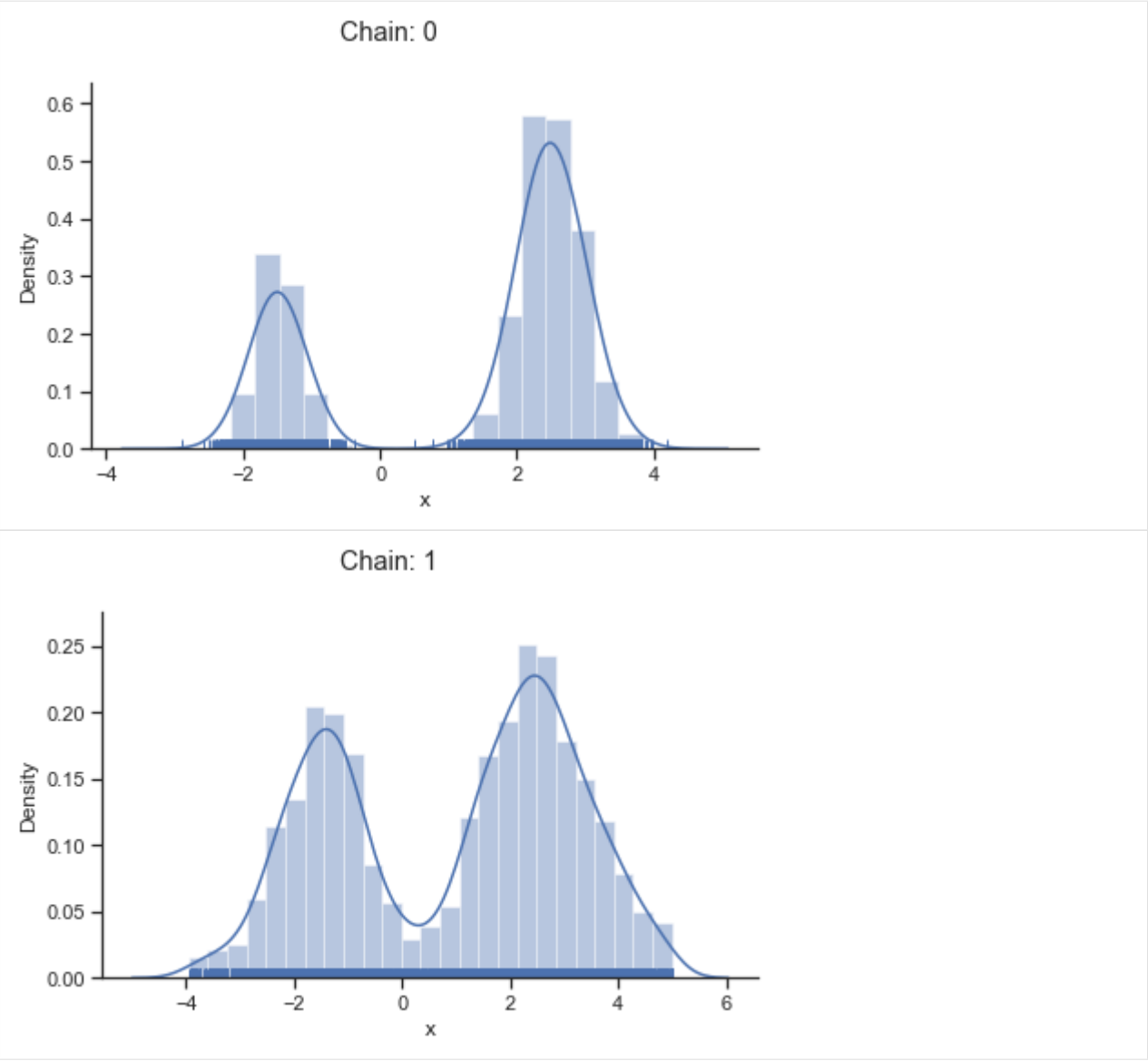
The `pypesto.sample.AdaptiveParallelTemperingSampler` iteratively adjusts the temperatures to obtain good swapping rates between chains.

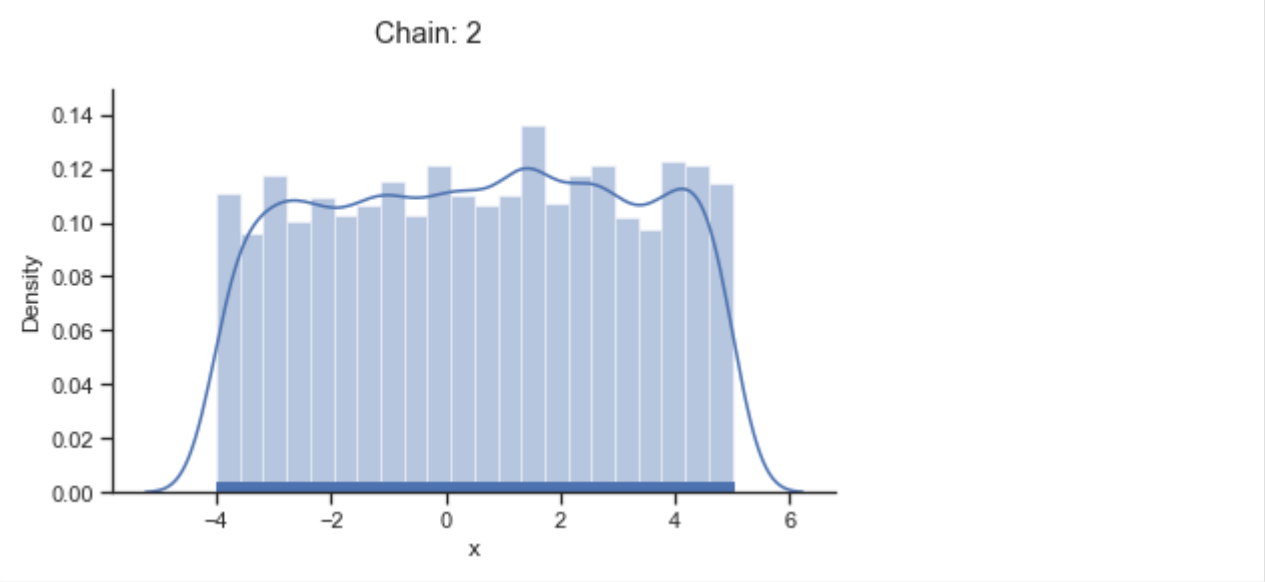
[22]:
```
sampler = sample.AdaptiveParallelTemperingSampler(
    internal_sampler=sample.AdaptiveMetropolisSampler(), n_chains=3)
result = sample.sample(problem, 1e4, sampler,
                       x0=np.array([0.5]), filename=None)
```

```
100%|| 10000/10000 [00:20<00:00, 481.04it/s]
Elapsed time: 20.773585252000004
```

[23]:
```
sample.geweke_test(result)
for i_chain in range(len(result.sample_result.betas)):
    visualize.sampling_1d_marginals(
        result, i_chain=i_chain, suptitle=f"Chain: {i_chain}")
```

```
Geweke burn-in index: 0
```


Chain: 0
Density
x
Chain: 1
Density
x



[24]:
```
result.sample_result.betas
```

[24]:
```
array([1.00000000e+00, 2.25534913e-01, 2.00000000e-05])
```

Pymc3 sampler

[25]:
```
sampler = sample.Pymc3Sampler()
result = sample.sample(problem, 1e4, sampler,
                       x0=np.array([0.5]), filename=None)
```

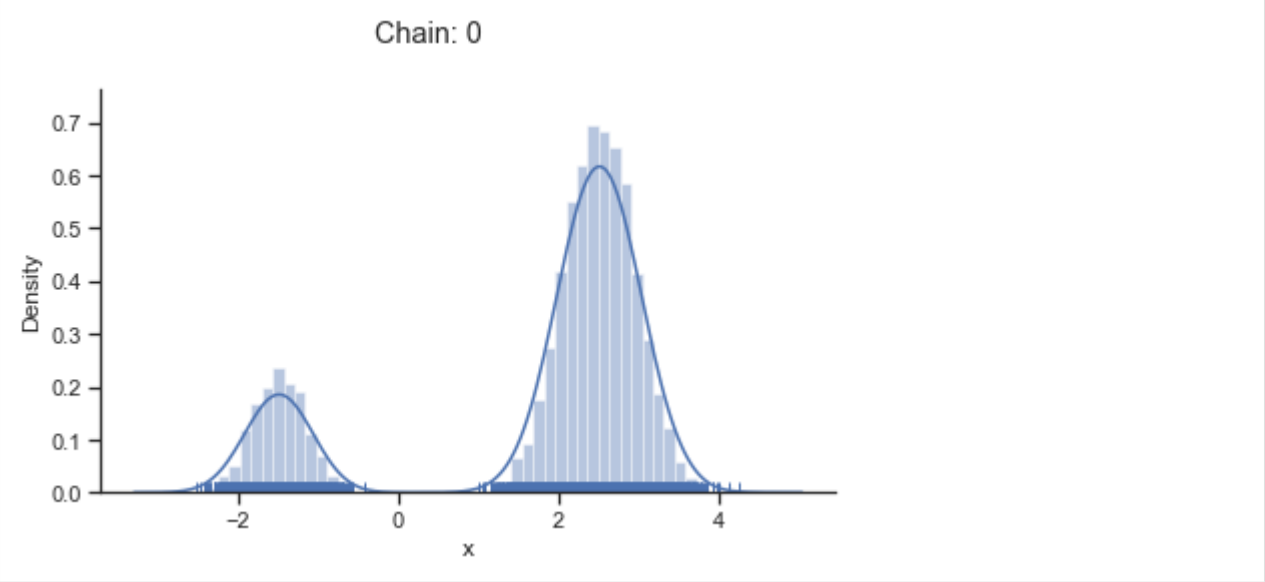
```
Auto-assigning NUTS sampler...
Initializing NUTS using jitter+adapt_diag...
Initializing NUTS failed. Falling back to elementwise auto-assignment.
Sequential sampling (1 chains in 1 job)
Slice: [x]
```

```
<IPython.core.display.HTML object>
```

```
Sampling 1 chain for 1_000 tune and 10_000 draw iterations (1_000 + 10_000 draws␣
↪total) took 42 seconds.
Only one chain was sampled, this makes it impossible to run some convergence checks
Elapsed time: 51.85952766199998
```

[26]:
```
sample.geweke_test(result)
for i_chain in range(len(result.sample_result.betas)):
    visualize.sampling_1d_marginals(
        result, i_chain=i_chain, suptitle=f"Chain: {i_chain}")
```

```
Geweke burn-in index: 0
```



If not specified, pymc3 chooses an adequate sampler automatically.

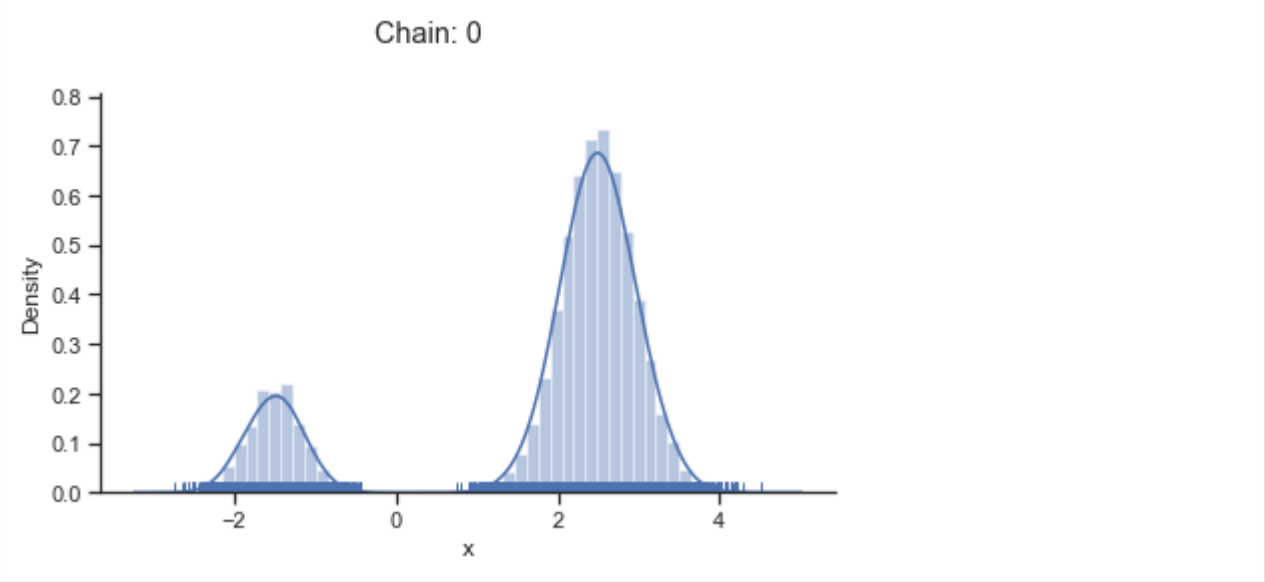
Emcee sampler

[27]:
```
sampler = sample.EmceeSampler(nwalkers=10, run_args={'progress': True})
result = sample.sample(problem, int(1e4), sampler,
                       x0=np.array([0.5]), filename=None)
```

```
100%|| 10000/10000 [00:48<00:00, 206.19it/s]
Elapsed time: 48.12011979000002
```

[28]:
```
sample.geweke_test(result)
for i_chain in range(len(result.sample_result.betas)):
    visualize.sampling_1d_marginals(
        result, i_chain=i_chain, suptitle=f"Chain: {i_chain}")
```

```
Geweke burn-in index: 25000
```



2-dim test problem: Rosenbrock banana

The adaptive parallel tempering sampler with chains running adaptive Metropolis samplers is also able to sample from more challenging posterior distributions. To illustrates this shortly, we use the Rosenbrock function.

[29]:
```
import scipy.optimize as so
import pypesto

# first type of objective
objective = pypesto.Objective(fun=so.rosen)

dim_full = 4
lb = -5 * np.ones((dim_full, 1))
ub = 5 * np.ones((dim_full, 1))

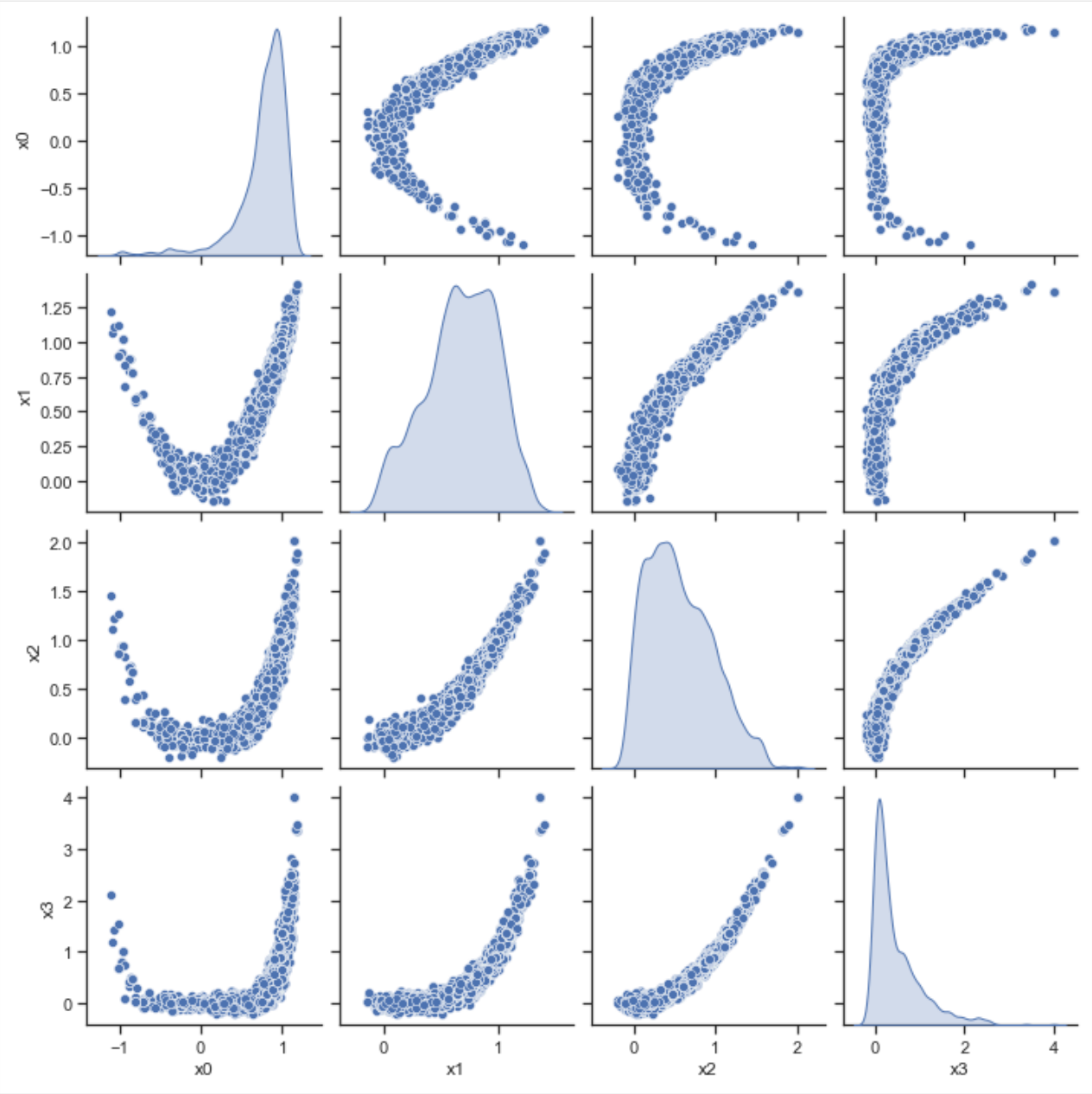
problem = pypesto.Problem(objective=objective, lb=lb, ub=ub)
```

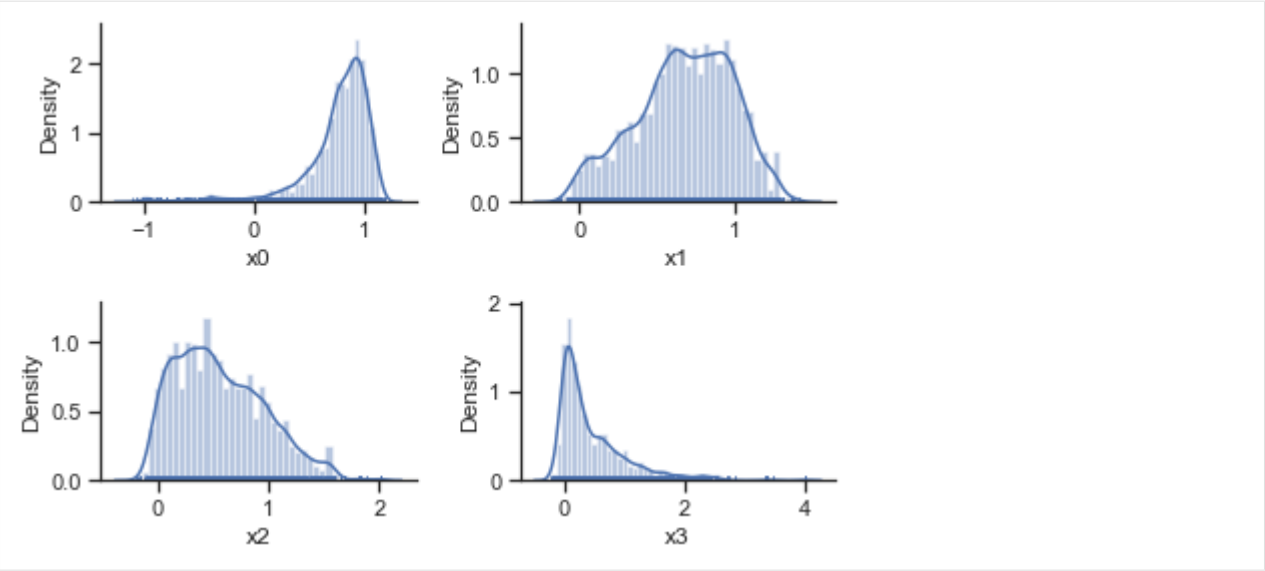
[30]:
```
sampler = sample.AdaptiveParallelTemperingSampler(
    internal_sampler=sample.AdaptiveMetropolisSampler(), n_chains=10)
result =sample.sample(problem, 1e4, sampler,
                      x0=np.zeros(dim_full), filename=None)
```

```
100%|| 10000/10000 [00:51<00:00, 194.85it/s]
Elapsed time: 51.031069281999976
```

[31]:
```
sample.geweke_test(result)
ax = visualize.sampling_scatter(result)
ax = visualize.sampling_1d_marginals(result)
```

```
Geweke burn-in index: 500
```


x0
x1
x2
x3



2.3.4 MCMC sampling diagnostics

In this notebook, we illustrate how to assess the quality of your MCMC samples, e.g. convergence and auto-correlation, in pyPESTO.

[ ]:
```
# install if not done yet
# !apt install libatlas-base-dev swig
# %pip install pypesto[amici,petab] --quiet
```

The pipeline

First, we load the model and data to generate the MCMC samples from. In this example we show a toy example of a conversion reaction, loaded as a PEtab problem.

[1]:
```
import pypesto
import pypesto.petab
import pypesto.optimize as optimize
import pypesto.sample as sample
import pypesto.visualize as visualize

import petab
import numpy as np
import logging
import matplotlib.pyplot as plt

# log diagnostics
logger = logging.getLogger("pypesto.sample.diagnostics")
logger.setLevel(logging.INFO)
logger.addHandler(logging.StreamHandler())

# import to petab
petab_problem = petab.Problem.from_yaml(
    "conversion_reaction/multiple_conditions/conversion_reaction.yaml")
# import to pypesto
```

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```
importer = pypesto.petab.PetabImporter(petab_problem)
# create problem
problem = importer.create_problem()
```

Create the sampler object, in this case we will use adaptive parallel tempering with 3 temperatures.

[2]:
```
sampler = sample.AdaptiveParallelTemperingSampler(
    internal_sampler=sample.AdaptiveMetropolisSampler(),
    n_chains=3)
```

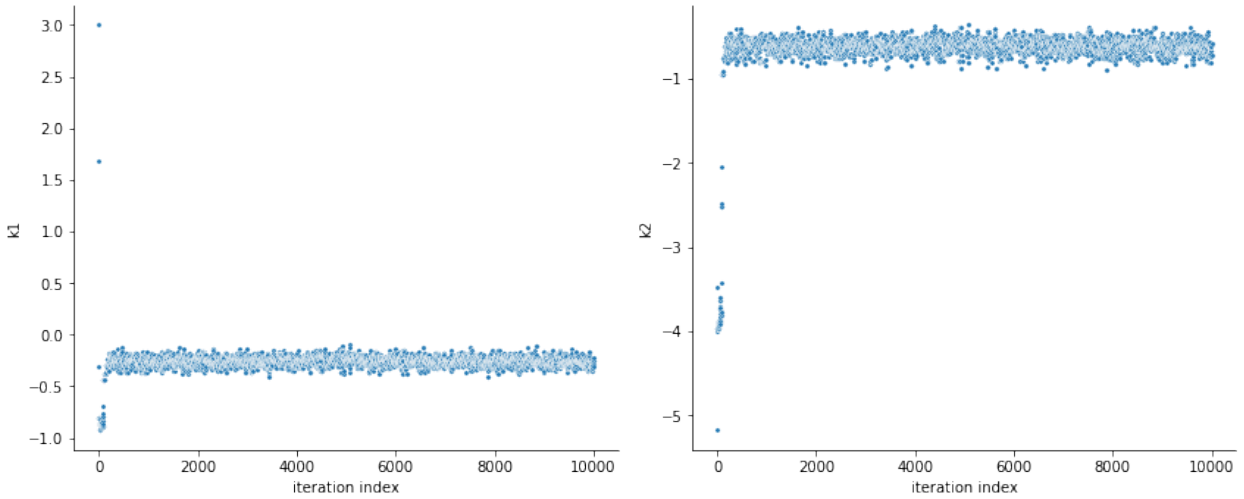
First, we will initiate the MCMC chain at a "random" point in parameter space, e.g. $\theta_{start} = [3, -4]$

[3]:
```
result = sample.sample(problem, n_samples=10000, sampler=sampler,
                       x0=np.array([3,-4]), filename=None)
elapsed_time = result.sample_result.time
print(f'Elapsed time: {round(elapsed_time,2)}')
```

```
100%|| 10000/10000 [00:44<00:00, 225.23it/s]
```

```
Elapsed time: 54.85
```

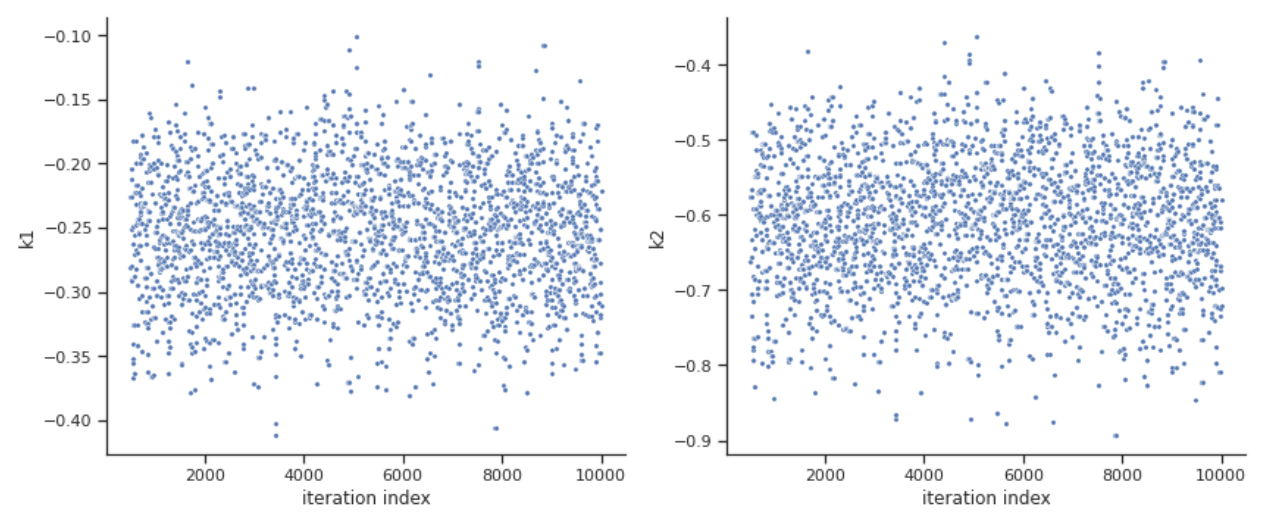
[4]:
```
ax = visualize.sampling_parameter_traces(result, use_problem_bounds=False, size=(12,
↪5))
```



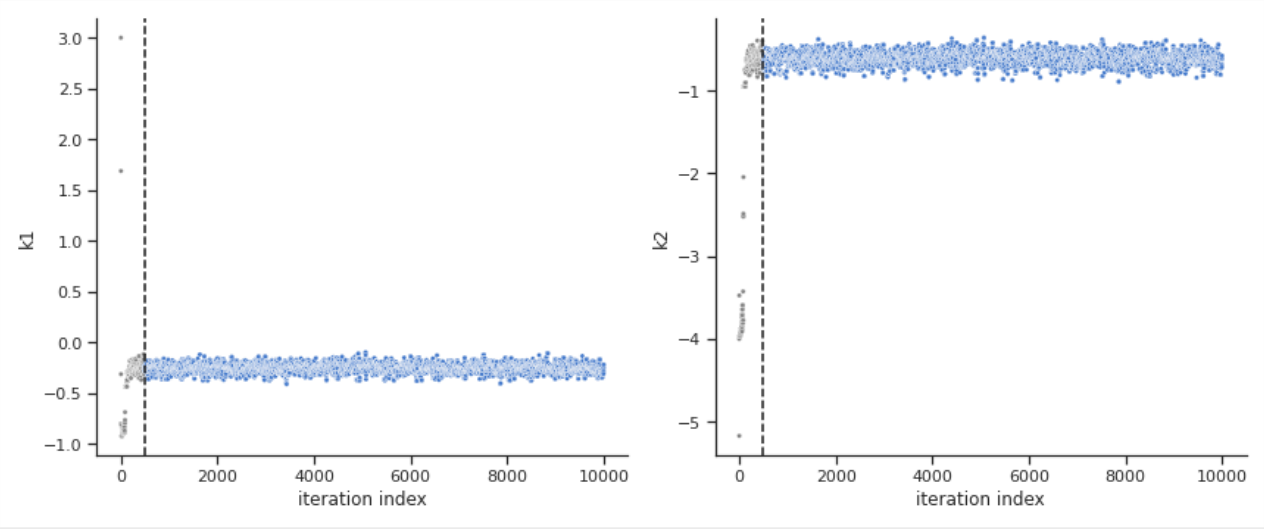
By visualizing the chains, we can see a warm up phase occurring until convergence of the chain is reached. This is commonly known as "burn in" phase and should be discarded. An automatic way to evaluate and find the index of the chain in which the warm up is finished can be done by using the Geweke test.

[5]:
```
sample.geweke_test(result=result)
ax = visualize.sampling_parameter_traces(result, use_problem_bounds=False, size=(12,
↪5))
```

```
Geweke burn-in index: 500
```



[6]:
```
ax = visualize.sampling_parameter_traces(result, use_problem_bounds=False, full_
↪trace=True, size=(12,5))
```



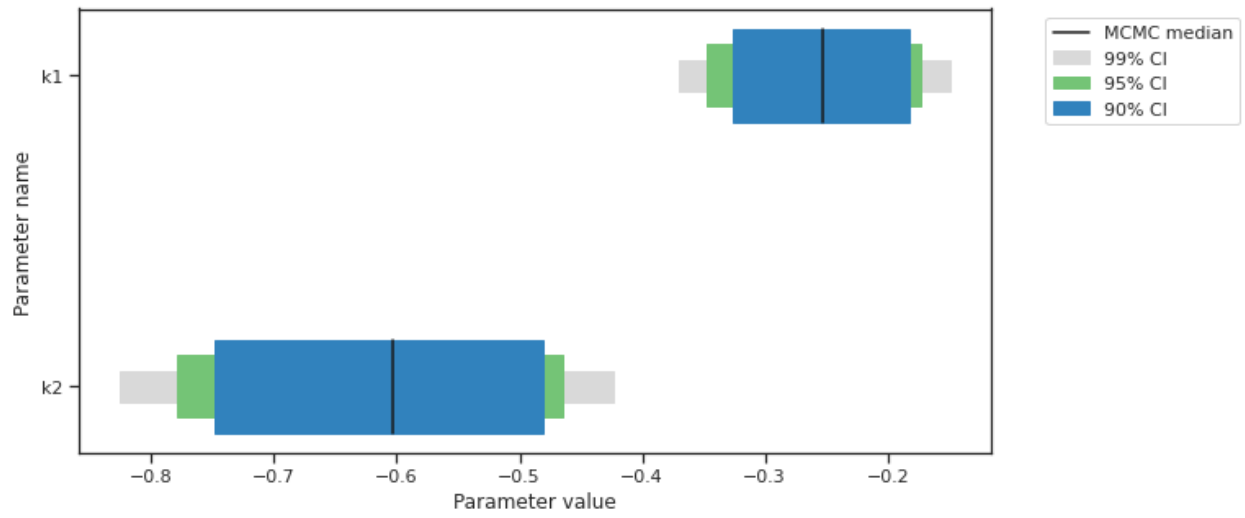
Calculate the effective sample size per computation time. We save the results in a variable as we will compare them later.

[7]:
```
sample.effective_sample_size(result=result)
ess = result.sample_result.effective_sample_size
print(f'Effective sample size per computation time: {round(ess/elapsed_time,2)}')
```

```
Estimated chain autocorrelation: 8.482536903793251
Estimated effective sample size: 1001.947062942551
```

```
Effective sample size per computation time: 18.27
```

[8]:
```
alpha = [99, 95, 90]
ax = visualize.sampling_parameter_cis(result, alpha=alpha, size=(10,5))
```



Predictions can be performed by creating a parameter ensemble from the sample, then applying a predictor to the ensemble. The predictor requires a simulation tool. Here, AMICI is used. First, the predictor is setup.

[9]:
```
from pypesto.C import AMICI_STATUS, AMICI_T, AMICI_X, AMICI_Y
from pypesto.predict import AmiciPredictor


# This post_processor will transform the output of the simulation tool
# such that the output is compatible with the next steps.
def post_processor(amici_outputs, output_type, output_ids):
    outputs = [
        amici_output[output_type] if amici_output[AMICI_STATUS] == 0
        else np.full((len(amici_output[AMICI_T]), len(output_ids)), np.nan)
        for amici_output in amici_outputs
    ]
    return outputs


# Setup post-processors for both states and observables.
from functools import partial
amici_objective = result.problem.objective
state_ids = amici_objective.amici_model.getStateIds()
observable_ids = amici_objective.amici_model.getObservableIds()
post_processor_x = partial(
    post_processor,
    output_type=AMICI_X,
    output_ids=state_ids,
)
post_processor_y = partial(
    post_processor,
    output_type=AMICI_Y,
    output_ids=observable_ids,
)

# Create pyPESTO predictors for states and observables
predictor_x = AmiciPredictor(
    amici_objective,
    post_processor=post_processor_x,
```

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```
    output_ids=state_ids,
)
predictor_y = AmiciPredictor(
    amici_objective,
    post_processor=post_processor_y,
    output_ids=observable_ids,
)
```

Next, the ensemble is created.

[10]:
```
from pypesto.ensemble import Ensemble
from pypesto.C import EnsembleType

# corresponds to only the estimated parameters
x_names = result.problem.get_reduced_vector(result.problem.x_names)

# Create the ensemble with the MCMC chain from parallel tempering with the real␣
↪temperature.
ensemble = Ensemble.from_sample(
    result,
    chain_slice=slice(None, None, 2),  # Optional argument: only use every second␣
↪vector in the chain.
    x_names=x_names,
    ensemble_type=EnsembleType.sample,
    lower_bound=result.problem.lb,
    upper_bound=result.problem.ub
)
```

The predictor is then applied to the ensemble to generate predictions.

[11]:
```
from pypesto.engine import MultiProcessEngine

# Currently, parallelization of predictions is supported with the
# `pypesto.engine.MultiProcessEngine` and `pypesto.engine.MultiThreadEngine`
# engines. If no engine is specified, the `pypesto.engine.SingleCoreEngine`
# engine is used.
engine = MultiProcessEngine()

ensemble_prediction = ensemble.predict(predictor_x, prediction_id=AMICI_X,␣
↪engine=engine)
```

```
Engine set up to use up to 8 processes in total. The number was automatically␣
↪determined and might not be appropriate on some systems.
100%|| 8/8 [00:00<00:00, 641.55it/s]
```

[12]:
```
from pypesto.C import CONDITION, OUTPUT

credibility_interval_levels = [90, 95, 99]

ax = visualize.sampling_prediction_trajectories(
    ensemble_prediction,
    levels=credibility_interval_levels,
    size=(10,5),
    labels={'A': 'state_A', 'condition_0': 'cond_0'},
    axis_label_padding=60,
    groupby=CONDITION,
    condition_ids=['condition_0', 'condition_1'],  # `None` for all conditions
```

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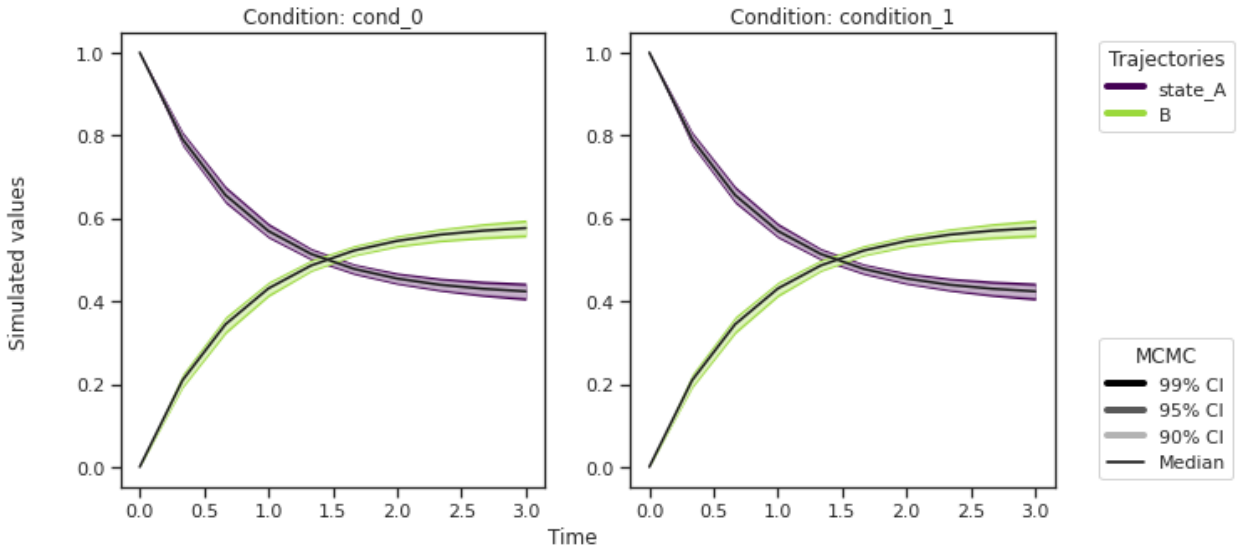
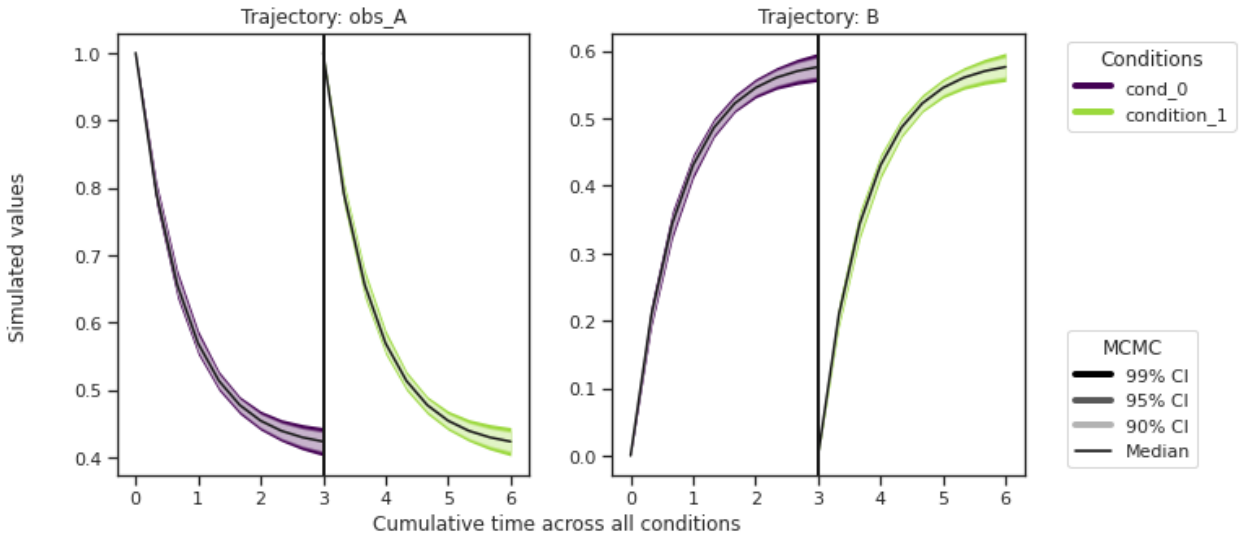
```
    output_ids=['A', 'B'],  # `None` for all outputs
)
```



[13]:
```
ax = visualize.sampling_prediction_trajectories(
    ensemble_prediction,
    levels=credibility_interval_levels,
    size=(10,5),
    labels={'A': 'obs_A', 'condition_0': 'cond_0'},
    axis_label_padding=60,
    groupby=OUTPUT,
)
```



Predictions are stored in `ensemble_prediction.prediction_summary`.

Commonly, as a first step, optimization is performed, in order to find good parameter point estimates.

[14]:
```
res = optimize.minimize(problem, n_starts=10, filename=None)
```

```
100%|| 10/10 [00:02<00:00,  4.72it/s]
```

By passing the result object to the function, the previously found global optimum is used as starting point for the MCMC sampling.

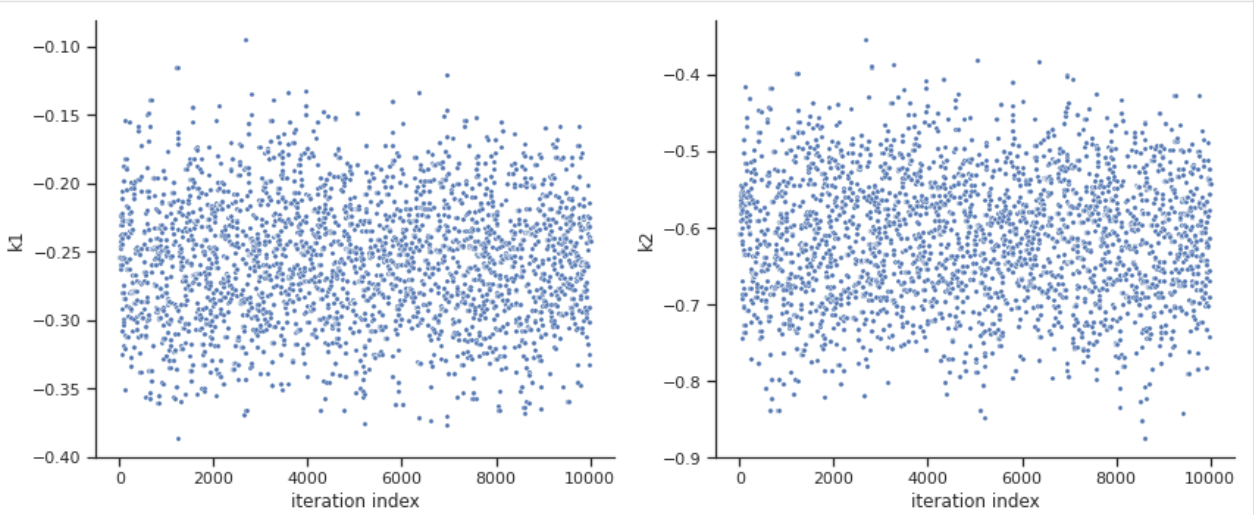
[15]:
```
res = sample.sample(problem, n_samples=10000, sampler=sampler,
                    result=res, filename=None)
elapsed_time = res.sample_result.time
print('Elapsed time: '+str(round(elapsed_time,2)))
```

```
100%|| 10000/10000 [00:42<00:00, 237.21it/s]
```

```
Elapsed time: 52.21
```

When the sampling is finished, we can analyse our results. pyPESTO provides functions to analyse both the sampling process as well as the obtained sampling result. Visualizing the traces e.g. allows to detect burn-in phases, or fine-tune hyperparameters. First, the parameter trajectories can be visualized:

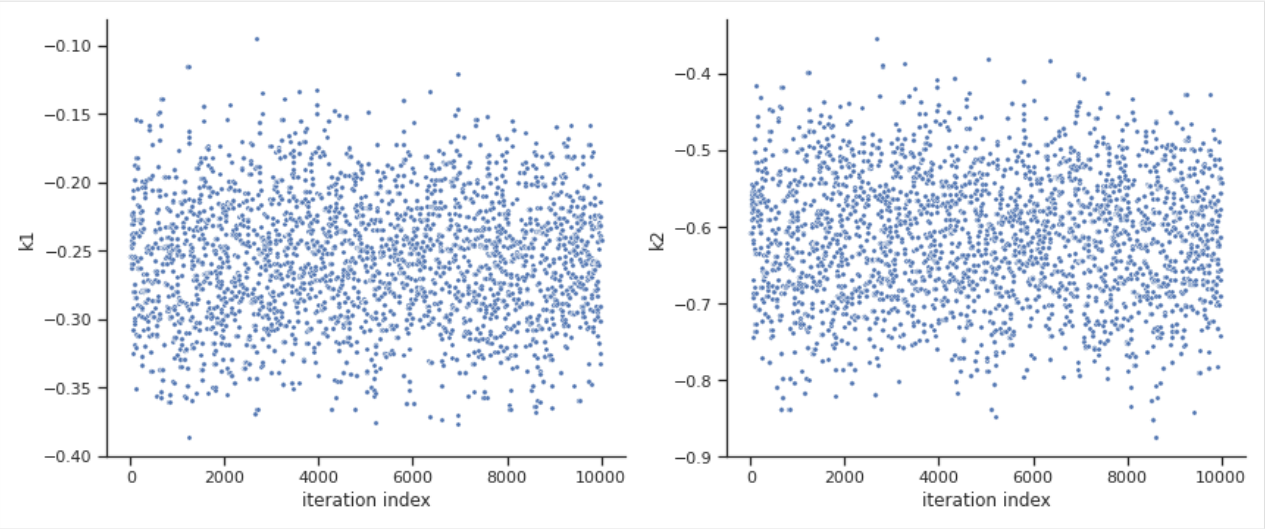
[16]:
```
ax = visualize.sampling_parameter_traces(res, use_problem_bounds=False, size=(12,5))
```



By visual inspection one can see that the chain is already converged from the start. This is already showing the benefit of initiating the chain at the optimal parameter vector. However, this may not be always the case.

[17]:
```
sample.geweke_test(result=res)
ax = visualize.sampling_parameter_traces(res, use_problem_bounds=False, size=(12,5))
```

```
Geweke burn-in index: 0
```

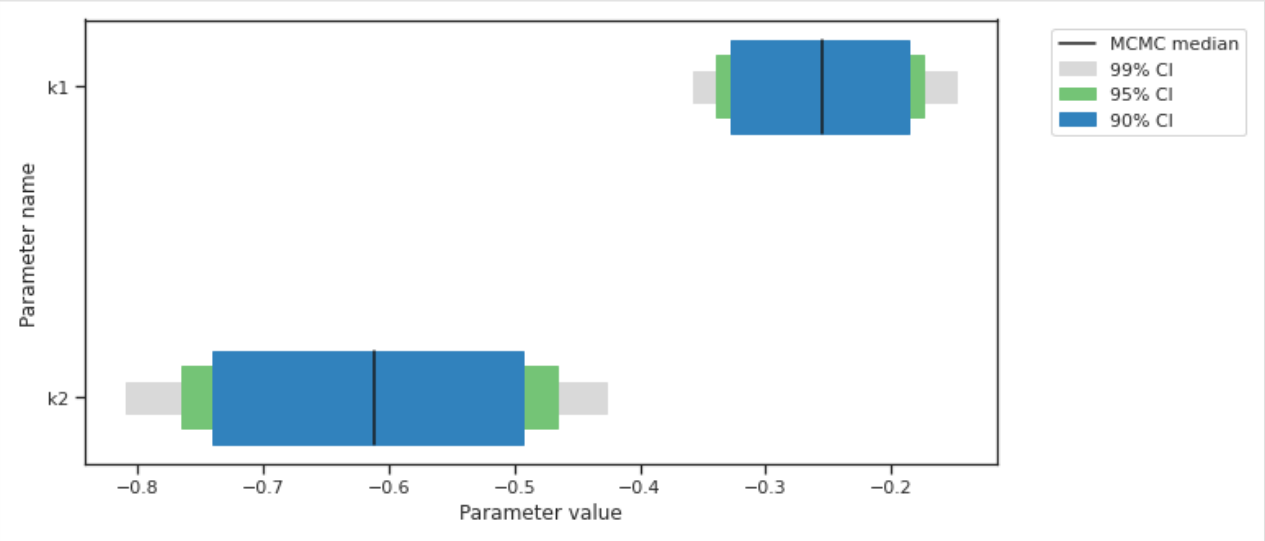


[18]:
```
sample.effective_sample_size(result=res)
ess = res.sample_result.effective_sample_size
print(f'Effective sample size per computation time: {round(ess/elapsed_time,2)}')
```

```
Estimated chain autocorrelation: 7.213987603646274
Estimated effective sample size: 1217.5572307365612
```

```
Effective sample size per computation time: 23.32
```

[19]:
```
percentiles = [99, 95, 90]
ax = visualize.sampling_parameter_cis(res, alpha=percentiles, size=(10,5))
```



[20]:
```
# Create the ensemble with the MCMC chain from parallel tempering with the real␣
↪temperature.
ensemble = Ensemble.from_sample(
    res,
    x_names=x_names,
    ensemble_type=EnsembleType.sample,
    lower_bound=res.problem.lb,
    upper_bound=res.problem.ub
```

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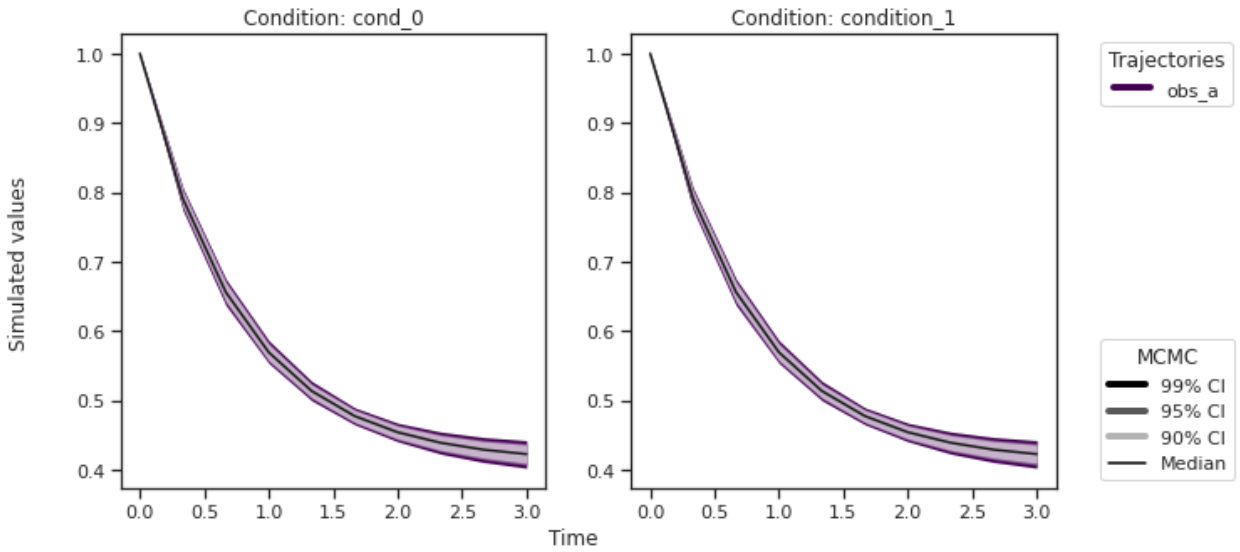
```
)

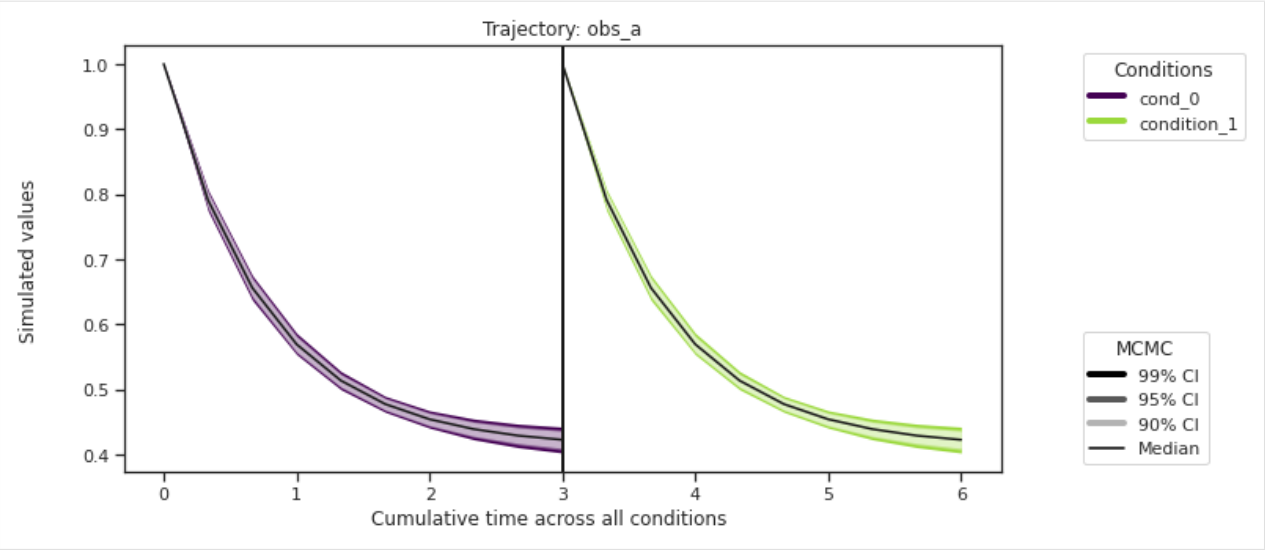
ensemble_prediction = ensemble.predict(predictor_y, prediction_id=AMICI_Y,␣
↪engine=engine)
```

```
100%|| 8/8 [00:00<00:00, 2219.21it/s]
```

[21]:
```
ax = visualize.sampling_prediction_trajectories(
    ensemble_prediction,
    levels=credibility_interval_levels,
    size=(10,5),
    labels={'A': 'obs_A', 'condition_0': 'cond_0'},
    axis_label_padding=60,
    groupby=CONDITION,
)
```



[22]:
```
ax = visualize.sampling_prediction_trajectories(
    ensemble_prediction,
    levels=credibility_interval_levels,
    size=(10,5),
    labels={'A': 'obs_A', 'condition_0': 'cond_0'},
    axis_label_padding=60,
    groupby=OUTPUT,
)
```



Custom timepoints can also be specified, either for each condition - `amici_objective.set_custom_timepoints(..., timepoints=...)`

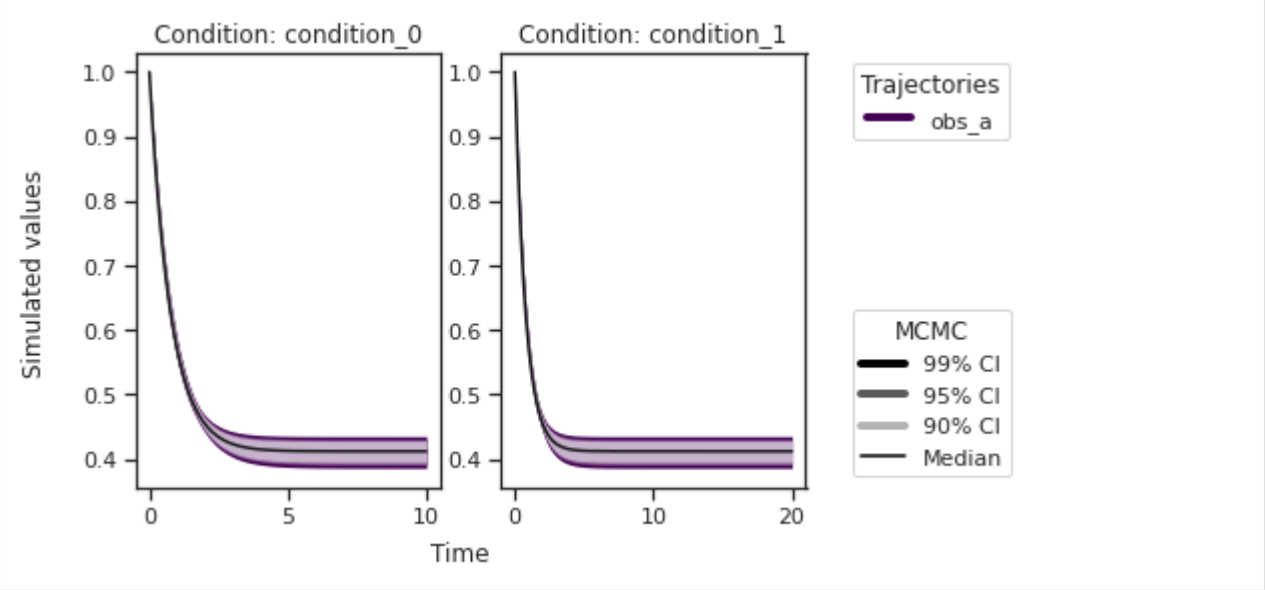
or for all conditions - `amici_objective.set_custom_timepoints(..., timepoints_global=...)`.

[23]:
```
# Create a custom objective with new output timepoints.
timepoints = [np.linspace(0, 10, 100), np.linspace(0, 20, 200)]
amici_objective_custom = amici_objective.set_custom_timepoints(timepoints=timepoints)

# Create an observable predictor with the custom objective.
predictor_y_custom = AmiciPredictor(
    amici_objective_custom,
    post_processor=post_processor_y,
    output_ids=observable_ids,
)

# Predict then plot.
ensemble_prediction = ensemble.predict(predictor_y_custom, prediction_id=AMICI_Y,␣
↪engine=engine)
ax = visualize.sampling_prediction_trajectories(
    ensemble_prediction,
    levels=credibility_interval_levels,
    groupby=CONDITION,
)
```

```
100%|| 8/8 [00:00<00:00, 1193.09it/s]
```



2.3.5 Storage

This notebook illustrates how simulations and results can be saved to file.

[ ]:
```
# install if not done yet
# %pip install pypesto --quiet
```

[1]:
```
import pypesto
import pypesto.optimize as optimize
import pypesto.visualize as visualize
from pypesto.store import (save_to_hdf5, read_from_hdf5)

import numpy as np
import scipy as sp
import matplotlib.pyplot as plt
import tempfile

%matplotlib inline
```

Define the objective and problem

[2]:
```
objective = pypesto.Objective(fun=sp.optimize.rosen,
                              grad=sp.optimize.rosen_der,
                              hess=sp.optimize.rosen_hess)

dim_full = 10
lb = -3 * np.ones((dim_full, 1))
ub = 3 * np.ones((dim_full, 1))

problem = pypesto.Problem(objective=objective, lb=lb, ub=ub)

# create optimizers
optimizer = optimize.ScipyOptimizer(method='l-bfgs-b')
```

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```
# set number of starts
n_starts = 20
```

Objective function traces

During optimization, it is possible to regularly write the objective function trace to file. This is useful e.g. when runs fail, or for various diagnostics. Currently, pyPESTO can save histories to 3 backends: in-memory, as CSV files, or to HDF5 files.

Memory History

To record the history in-memory, just set `trace_record=True` in the `pypesto.HistoryOptions`. Then, the optimization result contains those histories:

[3]:
```
# record the history
history_options = pypesto.HistoryOptions(trace_record=True)

# Run optimizaitons
result = optimize.minimize(
    problem=problem, optimizer=optimizer,
    n_starts=n_starts, history_options=history_options,
    filename=None)
```

```
  0%|          | 0/20 [00:00<?, ?it/s]Executing task 0.
Final fval=0.0000, time=0.0218s, n_fval=94.
Executing task 1.
Final fval=0.0000, time=0.0142s, n_fval=61.
Executing task 2.
Final fval=0.0000, time=0.0191s, n_fval=72.
Executing task 3.
Final fval=0.0000, time=0.0185s, n_fval=76.
Executing task 4.
Final fval=0.0000, time=0.0227s, n_fval=81.
 25%|       | 5/20 [00:00<00:00, 48.89it/s]Executing task 5.
Final fval=0.0000, time=0.0258s, n_fval=83.
Executing task 6.
Final fval=0.0000, time=0.0270s, n_fval=90.
Executing task 7.
Final fval=3.9866, time=0.0278s, n_fval=77.
Executing task 8.
Final fval=0.0000, time=0.0308s, n_fval=98.
Executing task 9.
Final fval=0.0000, time=0.0256s, n_fval=96.
 50%|     | 10/20 [00:00<00:00, 39.43it/s]Executing task 10.
Final fval=0.0000, time=0.0224s, n_fval=68.
Executing task 11.
Final fval=0.0000, time=0.0172s, n_fval=64.
Executing task 12.
Final fval=0.0000, time=0.0220s, n_fval=79.
Executing task 13.
Final fval=0.0000, time=0.0277s, n_fval=92.
Executing task 14.
Final fval=0.0000, time=0.0198s, n_fval=70.
```

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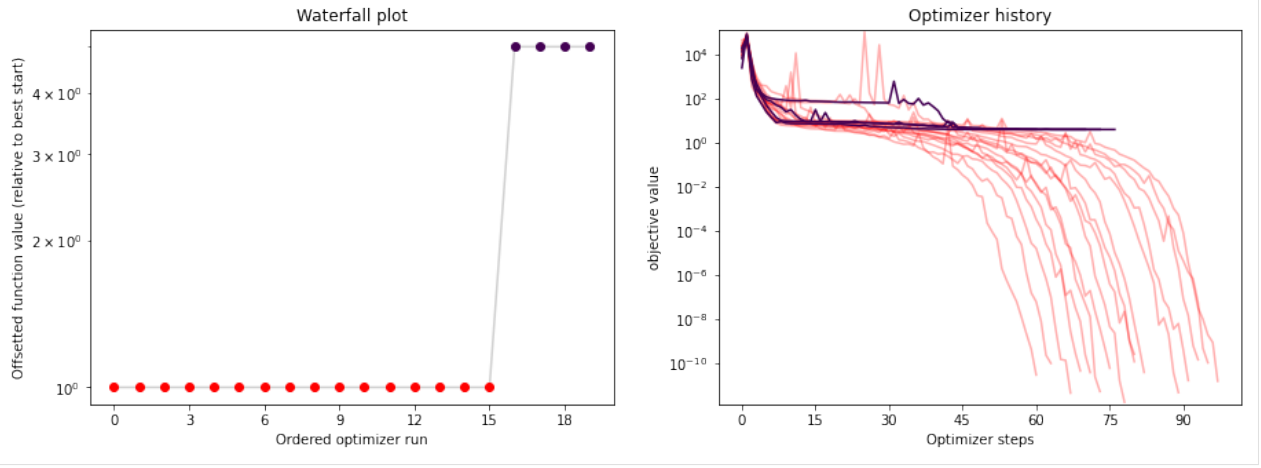
```
 75%|  | 15/20 [00:00<00:00, 41.09it/s]Executing task 15.
Final fval=0.0000, time=0.0253s, n_fval=81.
Executing task 16.
Final fval=3.9866, time=0.0226s, n_fval=61.
Executing task 17.
Final fval=3.9866, time=0.0307s, n_fval=74.
Executing task 18.
Final fval=3.9866, time=0.0236s, n_fval=71.
Executing task 19.
Final fval=0.0000, time=0.0175s, n_fval=74.
100%|| 20/20 [00:00<00:00, 40.68it/s]
```

Now, in addition to queries on the result, we can also access the

[4]:
```
print("History type: ", type(result.optimize_result.list[0].history))
# print("Function value trace of best run: ", result.optimize_result.list[0].history.
↪get_fval_trace())

fig, ax = plt.subplots(1, 2)
visualize.waterfall(result, ax=ax[0])
visualize.optimizer_history(result, ax=ax[1])
fig.set_size_inches((15, 5))
```

```
History type:  <class 'pypesto.objective.history.MemoryHistory'>
```



CSV History

The in-memory storage is however not stored anywhere. To do that, it is possible to store either to CSV or HDF5. This is specified via the `storage_file` option. If it ends in `.csv`, a `pypesto.objective.history.CsvHistory` will be employed; if it ends in `.hdf5` a `pypesto.objective.history.Hdf5History`. Occurrences of the substring `{id}` in the filename are replaced by the multistart id, allowing to maintain a separate file per run (this is necessary for CSV as otherwise runs are overwritten).

[5]:
```
# record the history and store to CSV
history_options = pypesto.HistoryOptions(trace_record=True, storage_file='history_{id}
↪.csv')

# Run optimizaitons
result = optimize.minimize(
```

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```
    problem=problem, optimizer=optimizer,
    n_starts=n_starts, history_options=history_options,
    filename=None)
```

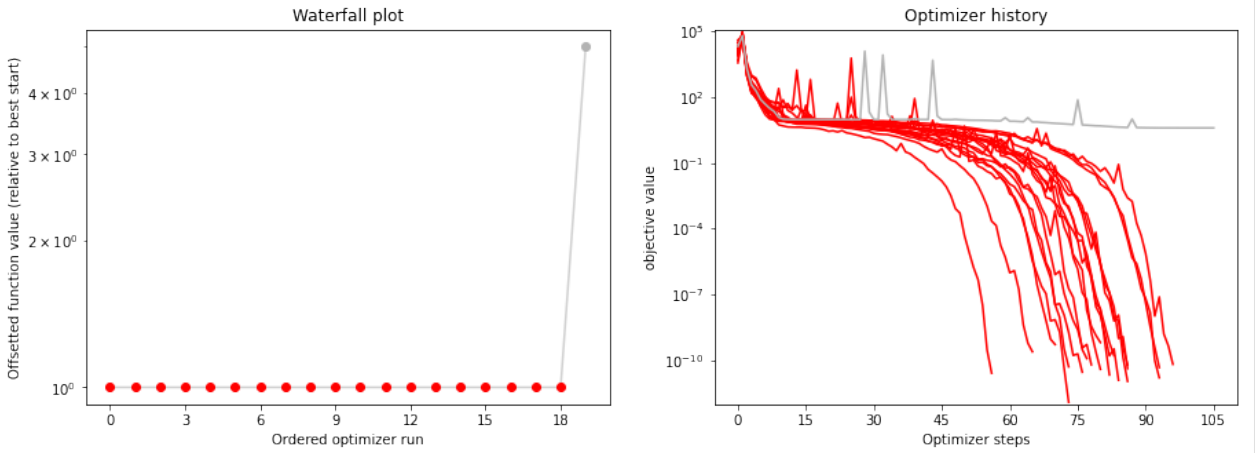
```
  0%|          | 0/20 [00:00<?, ?it/s]Executing task 0.
Final fval=0.0000, time=1.3848s, n_fval=87.
  5%|         | 1/20 [00:01<00:26,  1.39s/it]Executing task 1.
Final fval=0.0000, time=1.0376s, n_fval=66.
 10%|         | 2/20 [00:02<00:21,  1.18s/it]Executing task 2.
Final fval=0.0000, time=1.3995s, n_fval=87.
 15%|        | 3/20 [00:03<00:21,  1.28s/it]Executing task 3.
Final fval=0.0000, time=1.3883s, n_fval=87.
 20%|        | 4/20 [00:05<00:21,  1.33s/it]Executing task 4.
Final fval=0.0000, time=1.1283s, n_fval=74.
 25%|       | 5/20 [00:06<00:18,  1.25s/it]Executing task 5.
Final fval=0.0000, time=1.2335s, n_fval=81.
 30%|       | 6/20 [00:07<00:17,  1.25s/it]Executing task 6.
Final fval=3.9866, time=1.6121s, n_fval=106.
 35%|      | 7/20 [00:09<00:17,  1.37s/it]Executing task 7.
Final fval=0.0000, time=1.2220s, n_fval=77.
 40%|      | 8/20 [00:10<00:15,  1.32s/it]Executing task 8.
Final fval=0.0000, time=1.0812s, n_fval=71.
 45%|     | 9/20 [00:11<00:13,  1.25s/it]Executing task 9.
Final fval=0.0000, time=1.5227s, n_fval=78.
 50%|     | 10/20 [00:13<00:13,  1.33s/it]Executing task 10.
Final fval=0.0000, time=1.9653s, n_fval=97.
 55%|    | 11/20 [00:14<00:13,  1.53s/it]Executing task 11.
Final fval=0.0000, time=1.9667s, n_fval=94.
 60%|    | 12/20 [00:16<00:13,  1.66s/it]Executing task 12.
Final fval=0.0000, time=1.0537s, n_fval=57.
 65%|   | 13/20 [00:18<00:10,  1.48s/it]Executing task 13.
Final fval=0.0000, time=1.5494s, n_fval=81.
 70%|   | 14/20 [00:19<00:09,  1.50s/it]Executing task 14.
Final fval=0.0000, time=1.8838s, n_fval=94.
 75%|  | 15/20 [00:21<00:08,  1.62s/it]Executing task 15.
Final fval=0.0000, time=1.8472s, n_fval=84.
 80%|  | 16/20 [00:23<00:06,  1.69s/it]Executing task 16.
Final fval=0.0000, time=1.6928s, n_fval=85.
 85%| | 17/20 [00:25<00:05,  1.69s/it]Executing task 17.
Final fval=0.0000, time=1.4911s, n_fval=83.
 90%| | 18/20 [00:26<00:03,  1.63s/it]Executing task 18.
Final fval=0.0000, time=1.3229s, n_fval=74.
 95%|| 19/20 [00:27<00:01,  1.54s/it]Executing task 19.
Final fval=0.0000, time=1.5840s, n_fval=79.
100%|| 20/20 [00:29<00:00,  1.47s/it]
```

Note that for this simple cost function, saving to CSV takes a considerable amount of time. This overhead decreases for more costly simulators, e.g. using ODE simulations via AMICI.

[6]:
```
print("History type: ", type(result.optimize_result.list[0].history))
# print("Function value trace of best run: ", result.optimize_result.list[0].history.
↪get_fval_trace())

fig, ax = plt.subplots(1, 2)
visualize.waterfall(result, ax=ax[0])
visualize.optimizer_history(result, ax=ax[1])
fig.set_size_inches((15, 5))
```

```
History type:  <class 'pypesto.objective.history.CsvHistory'>
```



HDF5 History

Just as in CSV, writing the history to HDF5 takes a considerable amount of time. If a user specifies a HDF5 output file named `my_results.hdf5` and uses a parallelization engine, then: * a folder is created to contain partial results, named `my_results/` (the stem of the output filename) * files are created to store the results of each start, named `my_results/my_results_{START_INDEX}.hdf5` * a file is created to store the combined result from all starts, named `my_results.hdf5`. Note that this file depends on the files in the `my_results/` directory, so **cease to function** if `my_results/` is deleted.

[7]:
```
# record the history and store to CSV
history_options = pypesto.HistoryOptions(trace_record=True, storage_file='history.hdf5
↪')

# Run optimizaitons
result = optimize.minimize(
    problem=problem, optimizer=optimizer,
    n_starts=n_starts, history_options=history_options,
    filename=None)
```

```
  0%|          | 0/20 [00:00<?, ?it/s]Executing task 0.
Final fval=0.0000, time=0.5606s, n_fval=322.
  5%|         | 1/20 [00:00<00:10,  1.78it/s]Executing task 1.
Final fval=3.9866, time=0.3860s, n_fval=280.
 10%|         | 2/20 [00:00<00:08,  2.18it/s]Executing task 2.
Final fval=0.0000, time=0.5257s, n_fval=342.
 15%|        | 3/20 [00:01<00:08,  2.04it/s]Executing task 3.
Final fval=0.0000, time=0.4912s, n_fval=333.
 20%|        | 4/20 [00:01<00:07,  2.04it/s]Executing task 4.
Final fval=3.9866, time=0.3889s, n_fval=324.
 25%|       | 5/20 [00:02<00:06,  2.20it/s]Executing task 5.
Final fval=0.0000, time=0.4808s, n_fval=345.
 30%|       | 6/20 [00:02<00:06,  2.15it/s]Executing task 6.
Final fval=0.0000, time=0.4517s, n_fval=322.
 35%|      | 7/20 [00:03<00:05,  2.17it/s]Executing task 7.
Final fval=0.0000, time=0.5006s, n_fval=347.
 40%|      | 8/20 [00:03<00:05,  2.11it/s]Executing task 8.
Final fval=0.0000, time=0.4723s, n_fval=311.
```

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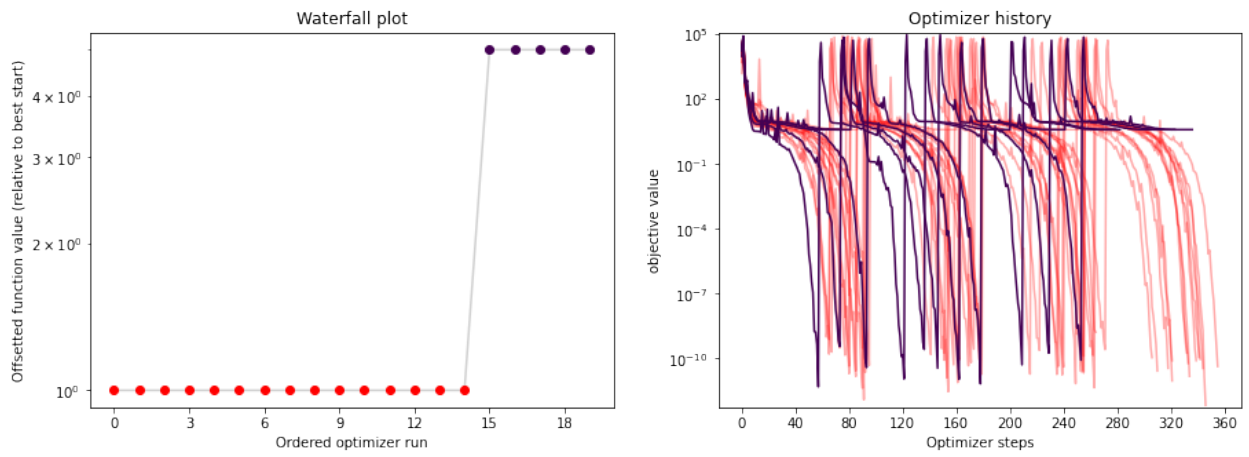
```
 45%|     | 9/20 [00:04<00:05,  2.11it/s]Executing task 9.
Final fval=0.0000, time=0.3521s, n_fval=307.
 50%|     | 10/20 [00:04<00:04,  2.29it/s]Executing task 10.
Final fval=3.9866, time=0.4401s, n_fval=283.
 55%|    | 11/20 [00:05<00:03,  2.28it/s]Executing task 11.
Final fval=0.0000, time=0.4453s, n_fval=356.
 60%|    | 12/20 [00:05<00:03,  2.27it/s]Executing task 12.
Final fval=0.0000, time=0.3788s, n_fval=335.
 65%|   | 13/20 [00:05<00:02,  2.37it/s]Executing task 13.
Final fval=0.0000, time=0.4477s, n_fval=334.
 70%|   | 14/20 [00:06<00:02,  2.32it/s]Executing task 14.
Final fval=0.0000, time=0.4339s, n_fval=319.
 75%|  | 15/20 [00:06<00:02,  2.31it/s]Executing task 15.
Final fval=0.0000, time=0.4260s, n_fval=343.
 80%|  | 16/20 [00:07<00:01,  2.32it/s]Executing task 16.
Final fval=3.9866, time=0.4394s, n_fval=313.
 85%| | 17/20 [00:07<00:01,  2.31it/s]Executing task 17.
Final fval=0.0000, time=0.2605s, n_fval=265.
 90%| | 18/20 [00:07<00:00,  2.62it/s]Executing task 18.
Final fval=0.0000, time=0.4477s, n_fval=340.
 95%|| 19/20 [00:08<00:00,  2.49it/s]Executing task 19.
Final fval=3.9866, time=0.5053s, n_fval=337.
100%|| 20/20 [00:08<00:00,  2.26it/s]
```

[8]:
```
print("History type: ", type(result.optimize_result.list[0].history))
# print("Function value trace of best run: ", result.optimize_result.list[0].history.
↪get_fval_trace())

fig, ax = plt.subplots(1, 2)
visualize.waterfall(result, ax=ax[0])
visualize.optimizer_history(result, ax=ax[1])
fig.set_size_inches((15, 5))
```

```
History type:  <class 'pypesto.objective.history.Hdf5History'>
```



Result storage

Result objects can be stored as HDF5 files. When applicable, this is preferable to just pickling results, which is not guaranteed to be reproducible in the future.

[9]:
```
# Run optimizaitons
result = optimize.minimize(
    problem=problem, optimizer=optimizer,
    n_starts=n_starts, filename=None)
```

```
  0%|          | 0/20 [00:00<?, ?it/s]Executing task 0.
Final fval=3.9866, time=0.0118s, n_fval=48.
Executing task 1.
Final fval=3.9866, time=0.0201s, n_fval=90.
Executing task 2.
Final fval=0.0000, time=0.0210s, n_fval=100.
Executing task 3.
Final fval=0.0000, time=0.0164s, n_fval=73.
Executing task 4.
Final fval=0.0000, time=0.0174s, n_fval=76.
Executing task 5.
Final fval=0.0000, time=0.0155s, n_fval=71.
 30%|       | 6/20 [00:00<00:00, 55.46it/s]Executing task 6.
Final fval=0.0000, time=0.0190s, n_fval=87.
Executing task 7.
Final fval=0.0000, time=0.0195s, n_fval=88.
Executing task 8.
Final fval=0.0000, time=0.0177s, n_fval=79.
Executing task 9.
Final fval=3.9866, time=0.0179s, n_fval=83.
Executing task 10.
Final fval=0.0000, time=0.0188s, n_fval=86.
Executing task 11.
Final fval=3.9866, time=0.0202s, n_fval=84.
 60%|    | 12/20 [00:00<00:00, 52.23it/s]Executing task 12.
Final fval=3.9866, time=0.0188s, n_fval=82.
Executing task 13.
Final fval=0.0000, time=0.0211s, n_fval=91.
Executing task 14.
Final fval=3.9866, time=0.0170s, n_fval=75.
Executing task 15.
Final fval=0.0000, time=0.0124s, n_fval=54.
Executing task 16.
Final fval=0.0000, time=0.0161s, n_fval=70.
Executing task 17.
Final fval=0.0000, time=0.0177s, n_fval=81.
 90%| | 18/20 [00:00<00:00, 53.48it/s]Executing task 18.
Final fval=0.0000, time=0.0187s, n_fval=82.
Executing task 19.
Final fval=3.9866, time=0.0163s, n_fval=75.
100%|| 20/20 [00:00<00:00, 53.45it/s]
```

[10]:
```
result.optimize_result.list[0:2]
```

[10]:
```
[{'id': '4',
  'x': array([1.00000001, 1.        , 1.        , 0.99999999, 0.99999999,
         1.00000001, 1.00000001, 1.00000004, 1.00000008, 1.00000014]),
  'fval': 2.6045655152986313e-13,
```

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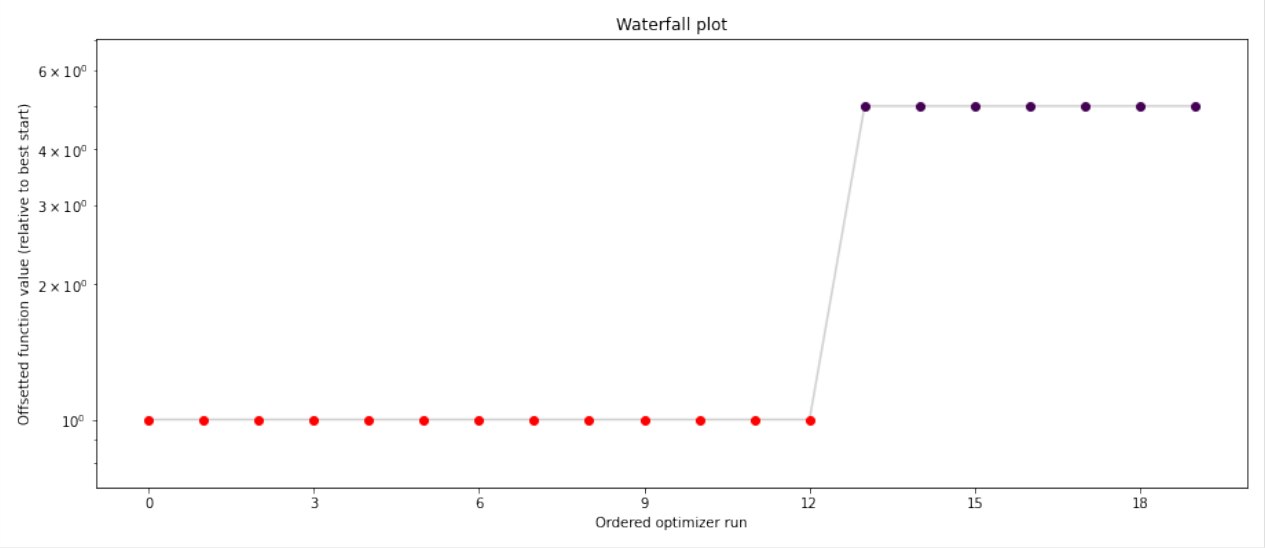
```
  'grad': array([ 7.38459033e-06, -4.78320167e-07, -6.50914679e-07, -1.47726642e-06,
         -1.39575141e-05,  9.14793168e-06, -7.58437136e-06,  4.50055738e-07,
          1.01219510e-05, -4.24214104e-06]),
  'hess': None,
  'res': None,
  'sres': None,
  'n_fval': 76,
  'n_grad': 76,
  'n_hess': 0,
  'n_res': 0,
  'n_sres': 0,
  'x0': array([ 0.33383114,  2.09297901, -1.77381628, -1.60663808, -2.85350433,
          0.71050093, -1.190691  ,  0.91974885, -2.34344618,  1.21791823]),
  'fval0': 18119.670540771178,
  'history': <pypesto.objective.history.History at 0x7ffd399536a0>,
  'exitflag': 0,
  'time': 0.017375946044921875,
  'message': 'CONVERGENCE: REL_REDUCTION_OF_F_<=_FACTR*EPSMCH'},
 {'id': '16',
  'x': array([1.        , 1.        , 1.00000001, 1.        , 1.00000001,
         1.00000003, 1.00000007, 1.00000009, 1.00000017, 1.00000039]),
  'fval': 7.312572536347769e-13,
  'grad': array([ 3.34432881e-06, -6.16413761e-06,  1.25983886e-05, -5.34613024e-06,
         -7.50765648e-06,  1.11777438e-06,  1.94167105e-05, -5.91496342e-06,
         -2.50337361e-05,  1.19659990e-05]),
  'hess': None,
  'res': None,
  'sres': None,
  'n_fval': 70,
  'n_grad': 70,
  'n_hess': 0,
  'n_res': 0,
  'n_sres': 0,
  'x0': array([ 2.58291438,  2.48719491,  2.93132676, -0.75290073,  0.34568409,
          0.60255167, -0.68200823, -1.01952663, -2.47953741,  2.14959561]),
  'fval0': 14770.270006296314,
  'history': <pypesto.objective.history.History at 0x7ffd496cea90>,
  'exitflag': 0,
  'time': 0.016092777252197266,
  'message': 'CONVERGENCE: REL_REDUCTION_OF_F_<=_FACTR*EPSMCH'}]
```

As usual, having obtained our result, we can directly perform some plots:

[11]:
```
# plot waterfalls
visualize.waterfall(result, size=(15,6))
```

[11]:
```
<AxesSubplot:title={'center':'Waterfall plot'}, xlabel='Ordered optimizer run',␣
↪ylabel='Offsetted function value (relative to best start)'>
```



Save optimization result as HDF5 file

The optimization result can be saved with `pypesto.store.write_result()`. This will write the problem and the optimization result, and the profiling and sampling results if available, to HDF5. All of them can be disabled with boolean flags (see the documentation)

[12]:
```
fn = tempfile.mktemp(".hdf5")

# Write result
save_to_hdf5.write_result(result, fn)
```

```
Warning: There is no sampling_result, which you tried to save to hdf5.
```

Read optimization result from HDF5 file

When reading in the stored result again, we recover the original optimization result:

[13]:
```
# Read result and problem
result = read_from_hdf5.read_result(fn)
```

```
WARNING: You are loading a problem.
This problem is not to be used without a separately created objective.
WARNING: You are loading a problem.
This problem is not to be used without a separately created objective.
WARNING: You are loading a problem.
This problem is not to be used without a separately created objective.
WARNING: You are loading a problem.
This problem is not to be used without a separately created objective.
Loading the sampling result failed. It is highly likely that no sampling result␣
↪exists within /var/folders/2f/bnywv1ns2_9g8wtzlf_74yzh0000gn/T/tmpewjf65r6.hdf5.
```

[14]:
```
result.optimize_result.list[0:2]
```

[14]:
```
[{'id': '4',
  'x': array([1.00000001, 1.        , 1.        , 0.99999999, 0.99999999,
```

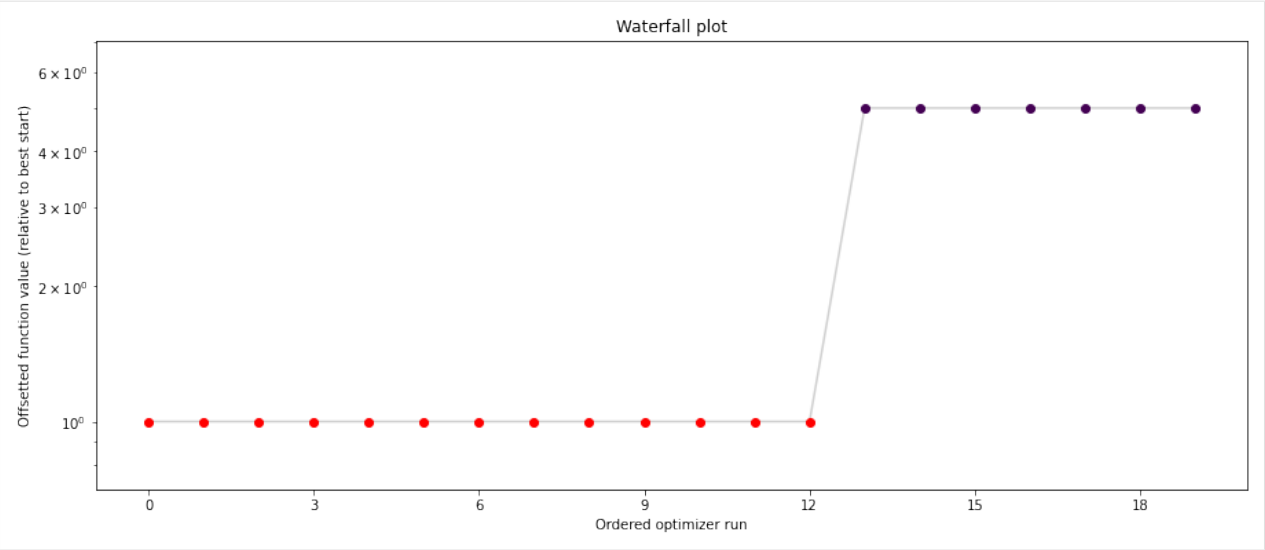
(continues on next page)

(continued from previous page)

```
        1.00000001, 1.00000001, 1.00000004, 1.00000008, 1.00000014]),
 'fval': 2.6045655152986313e-13,
 'grad': array([ 7.38459033e-06, -4.78320167e-07, -6.50914679e-07, -1.47726642e-06,
        -1.39575141e-05,  9.14793168e-06, -7.58437136e-06,  4.50055738e-07,
         1.01219510e-05, -4.24214104e-06]),
 'hess': None,
 'res': None,
 'sres': None,
 'n_fval': 76,
 'n_grad': 76,
 'n_hess': 0,
 'n_res': 0,
 'n_sres': 0,
 'x0': array([ 0.33383114,  2.09297901, -1.77381628, -1.60663808, -2.85350433,
         0.71050093, -1.190691  ,  0.91974885, -2.34344618,  1.21791823]),
 'fval0': 18119.670540771178,
 'history': None,
 'exitflag': 0,
 'time': 0.017375946044921875,
 'message': 'CONVERGENCE: REL_REDUCTION_OF_F_<=_FACTR*EPSMCH'},
{'id': '16',
 'x': array([1.        , 1.        , 1.00000001, 1.        , 1.00000001,
        1.00000003, 1.00000007, 1.00000009, 1.00000017, 1.00000039]),
 'fval': 7.312572536347769e-13,
 'grad': array([ 3.34432881e-06, -6.16413761e-06,  1.25983886e-05, -5.34613024e-06,
        -7.50765648e-06,  1.11777438e-06,  1.94167105e-05, -5.91496342e-06,
        -2.50337361e-05,  1.19659990e-05]),
 'hess': None,
 'res': None,
 'sres': None,
 'n_fval': 70,
 'n_grad': 70,
 'n_hess': 0,
 'n_res': 0,
 'n_sres': 0,
 'x0': array([ 2.58291438,  2.48719491,  2.93132676, -0.75290073,  0.34568409,
         0.60255167, -0.68200823, -1.01952663, -2.47953741,  2.14959561]),
 'fval0': 14770.270006296314,
 'history': None,
 'exitflag': 0,
 'time': 0.016092777252197266,
 'message': 'CONVERGENCE: REL_REDUCTION_OF_F_<=_FACTR*EPSMCH'}]
```

[15]:
```
# plot waterfalls
pypesto.visualize.waterfall(result, size=(15,6))
```

[15]:
```
<AxesSubplot:title={'center':'Waterfall plot'}, xlabel='Ordered optimizer run',␣
↪ylabel='Offsetted function value (relative to best start)'>
```



2.3.6 Save and load results as HDF5 files

[ ]:
```
# install if not done yet
# %pip install pypesto --quiet
```

[24]:
```
import pypesto
import numpy as np
import scipy as sp
import pypesto.optimize as optimize
import matplotlib.pyplot as plt
import pypesto.store as store
import pypesto.profile as profile
import pypesto.sample as sample
import tempfile

%matplotlib inline
```

In this notebook, we will demonstrate how to save and (re-)load optimization results, profile results and sampling results to an `.hdf5` file. The use case of this notebook is to generate visualizations from reloaded result objects.

Define the objective and problem

[25]:
```
objective = pypesto.Objective(fun=sp.optimize.rosen,
                              grad=sp.optimize.rosen_der,
                              hess=sp.optimize.rosen_hess)

dim_full = 20
lb = -5 * np.ones((dim_full, 1))
ub = 5 * np.ones((dim_full, 1))

problem = pypesto.Problem(objective=objective, lb=lb, ub=ub)
```

Fill result object with profile, sample, optimization

[26]:
```
# create optimizers
optimizer = optimize.ScipyOptimizer()

# set number of starts
n_starts = 10

# Optimization
result = pypesto.optimize.minimize(
    problem=problem, optimizer=optimizer,
    n_starts=n_starts, filename=None)
# Profiling
result = profile.parameter_profile(
    problem=problem, result=result,
    optimizer=optimizer, filename=None)
# Sampling
sampler = sample.AdaptiveMetropolisSampler()
result = sample.sample(problem=problem,
                       sampler=sampler,
                       n_samples=100000,
                       result=result,
                       filename=None)
```

```
100%|| 100000/100000 [00:29<00:00, 3431.32it/s]
```

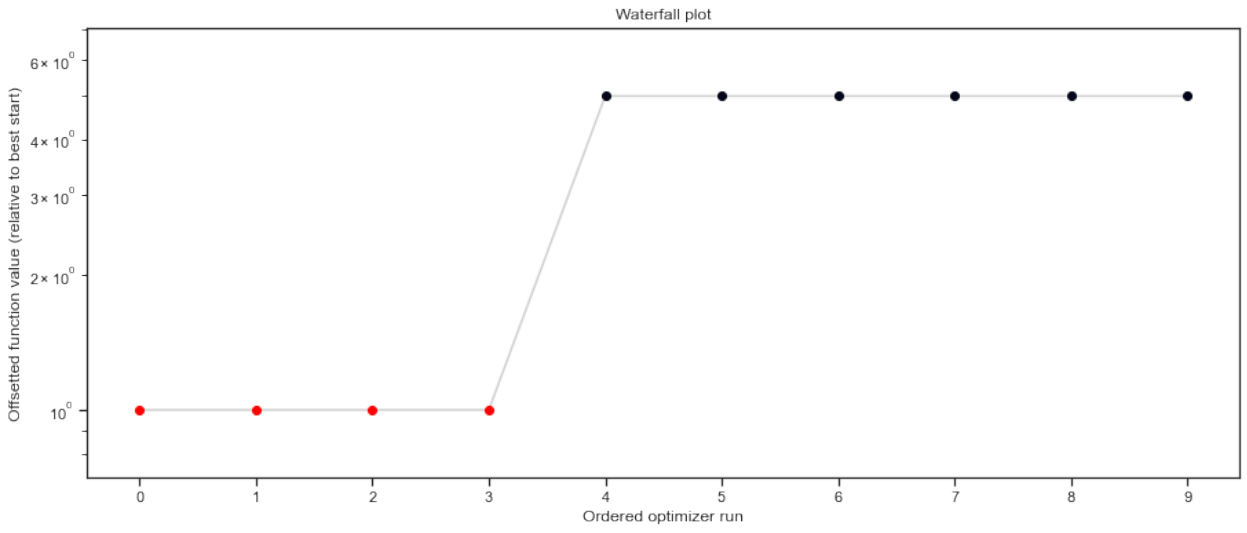
Plot results

We now want to plot the results (before saving).

[27]:
```
import pypesto.visualize

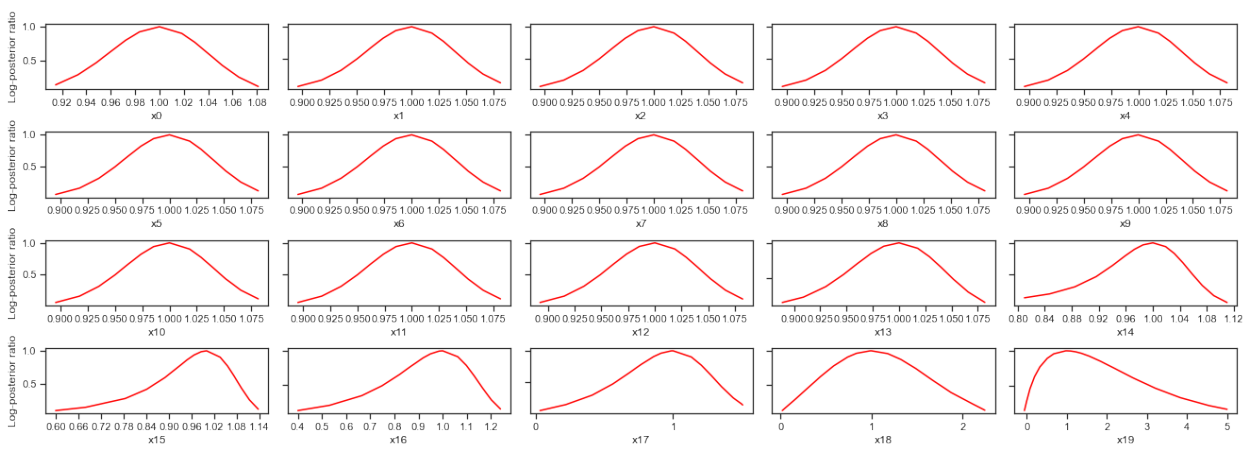
# plot waterfalls
pypesto.visualize.waterfall(result, size=(15,6))
```

[27]:
```
<AxesSubplot:title={'center':'Waterfall plot'}, xlabel='Ordered optimizer run',␣
↪ylabel='Offsetted function value (relative to best start)'>
```



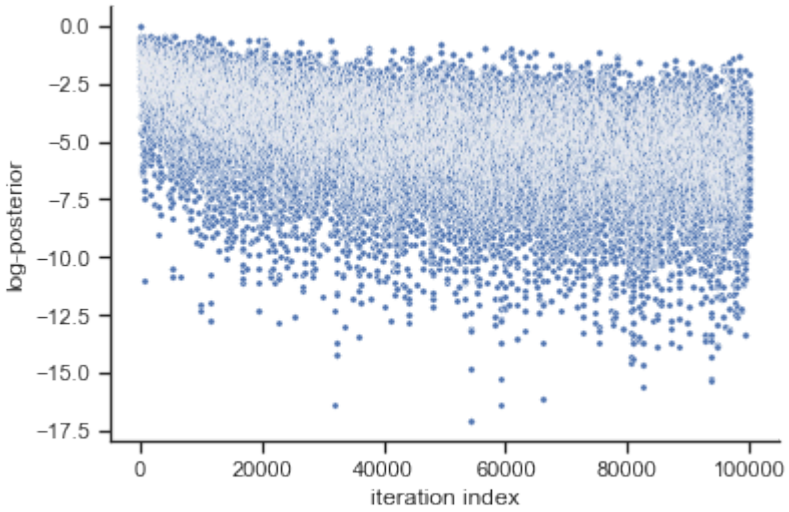
[28]:
```
# plot profiles
pypesto.visualize.profiles(result)
```

[28]:
```
[<AxesSubplot:xlabel='x0', ylabel='Log-posterior ratio'>,
 <AxesSubplot:xlabel='x1'>,
 <AxesSubplot:xlabel='x2'>,
 <AxesSubplot:xlabel='x3'>,
 <AxesSubplot:xlabel='x4'>,
 <AxesSubplot:xlabel='x5', ylabel='Log-posterior ratio'>,
 <AxesSubplot:xlabel='x6'>,
 <AxesSubplot:xlabel='x7'>,
 <AxesSubplot:xlabel='x8'>,
 <AxesSubplot:xlabel='x9'>,
 <AxesSubplot:xlabel='x10', ylabel='Log-posterior ratio'>,
 <AxesSubplot:xlabel='x11'>,
 <AxesSubplot:xlabel='x12'>,
 <AxesSubplot:xlabel='x13'>,
 <AxesSubplot:xlabel='x14'>,
 <AxesSubplot:xlabel='x15', ylabel='Log-posterior ratio'>,
 <AxesSubplot:xlabel='x16'>,
 <AxesSubplot:xlabel='x17'>,
 <AxesSubplot:xlabel='x18'>,
 <AxesSubplot:xlabel='x19'>]
```



[29]:
```
# plot samples
pypesto.visualize.sampling_fval_traces(result)
```

[29]:
```
<AxesSubplot:xlabel='iteration index', ylabel='log-posterior'>
```



Save result object in HDF5 File

[30]:
```
# create temporary file
fn = tempfile.mktemp(".hdf5")

# write result with write_result function.
# Choose which parts of the result object to save with
# corresponding booleans.
store.write_result(result=result,
                   filename=fn,
                   problem=True,
                   optimize=True,
                   profile=True,
                   sample=True)
```

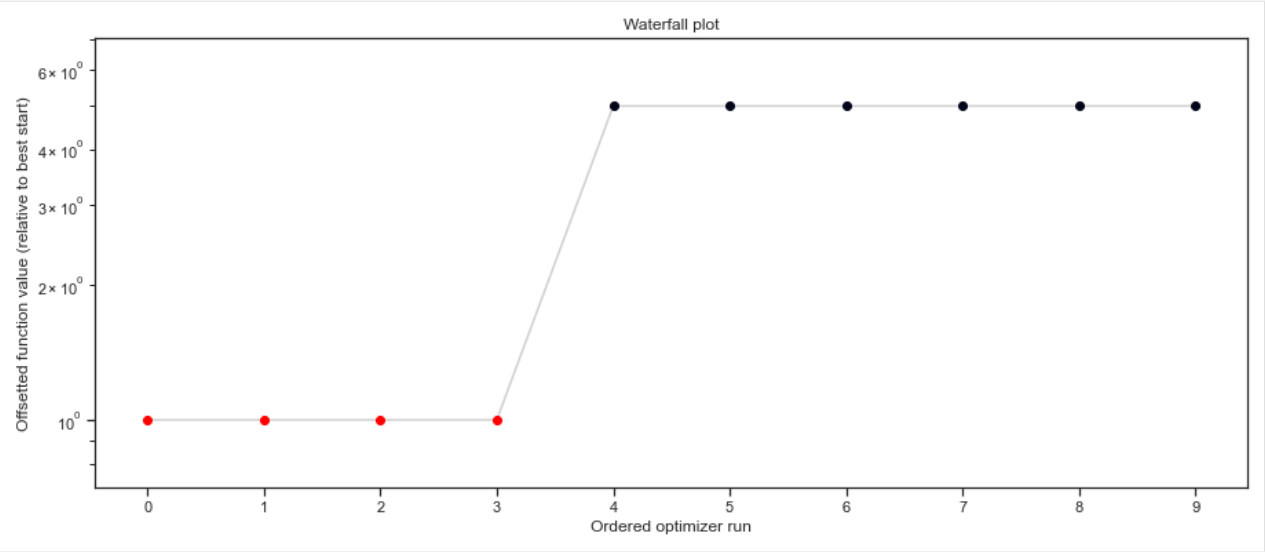
Reload results

[31]:
```
# Read result
result2 = store.read_result(fn)
```

Plot (reloaded) results

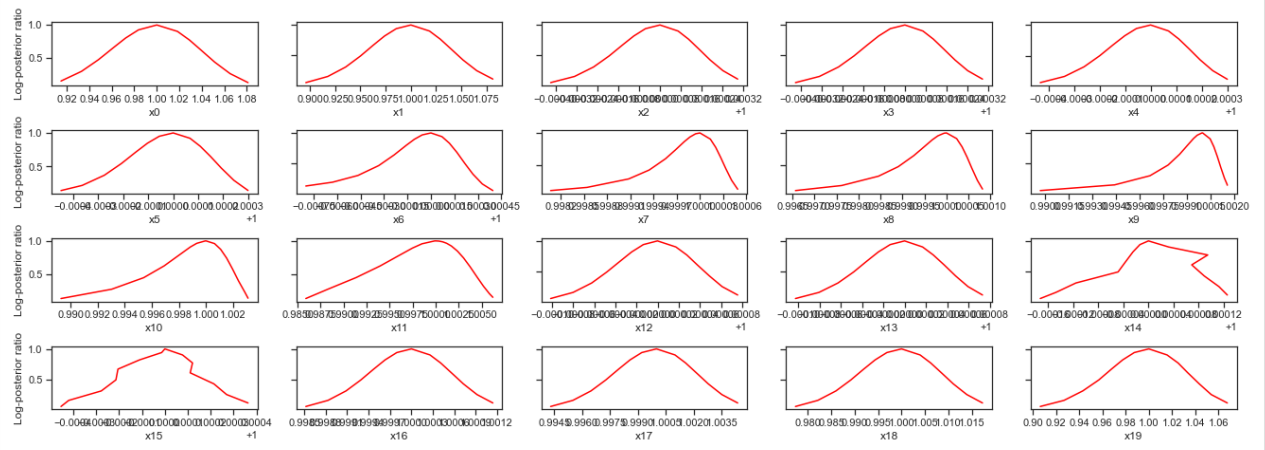
[32]:
```
# plot waterfalls
pypesto.visualize.waterfall(result2, size=(15,6))
```

[32]:
```
<AxesSubplot:title={'center':'Waterfall plot'}, xlabel='Ordered optimizer run',␣
↪ylabel='Offsetted function value (relative to best start)'>
```



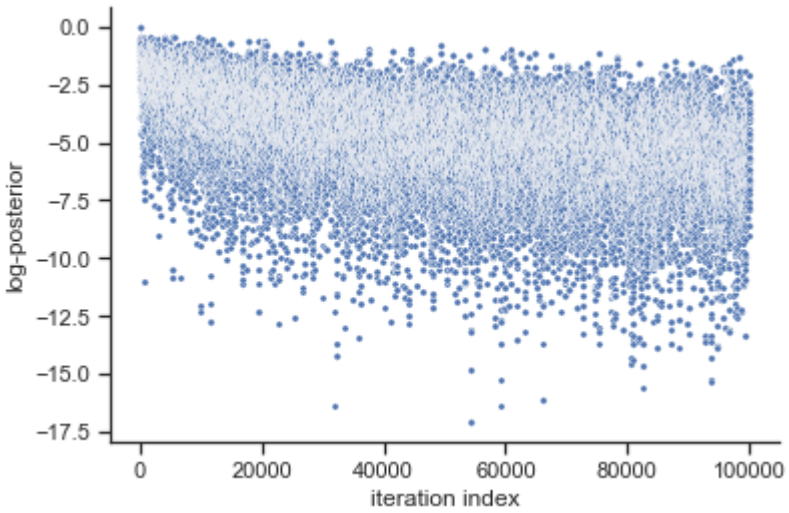
[33]:
```
# plot profiles
pypesto.visualize.profiles(result2)
```

[33]:
```
[<AxesSubplot:xlabel='x0', ylabel='Log-posterior ratio'>,
 <AxesSubplot:xlabel='x1'>,
 <AxesSubplot:xlabel='x2'>,
 <AxesSubplot:xlabel='x3'>,
 <AxesSubplot:xlabel='x4'>,
 <AxesSubplot:xlabel='x5', ylabel='Log-posterior ratio'>,
 <AxesSubplot:xlabel='x6'>,
 <AxesSubplot:xlabel='x7'>,
 <AxesSubplot:xlabel='x8'>,
 <AxesSubplot:xlabel='x9'>,
 <AxesSubplot:xlabel='x10', ylabel='Log-posterior ratio'>,
 <AxesSubplot:xlabel='x11'>,
 <AxesSubplot:xlabel='x12'>,
 <AxesSubplot:xlabel='x13'>,
 <AxesSubplot:xlabel='x14'>,
 <AxesSubplot:xlabel='x15', ylabel='Log-posterior ratio'>,
 <AxesSubplot:xlabel='x16'>,
 <AxesSubplot:xlabel='x17'>,
 <AxesSubplot:xlabel='x18'>,
 <AxesSubplot:xlabel='x19'>]
```



[34]:
```
# plot samples
pypesto.visualize.sampling_fval_traces(result2)
```

[34]:
```
<AxesSubplot:xlabel='iteration index', ylabel='log-posterior'>
```



For the saving of optimization history, we refer to *store.ipynb*.

2.4 Application examples

2.4.1 Conversion reaction

[ ]:
```
# install if not done yet
# !apt install libatlas-base-dev swig
# %pip install pypesto[amici] --quiet
```

[1]:
```
import importlib
import os
import sys
import numpy as np
import amici
import amici.plotting
import pypesto
import pypesto.optimize as optimize
import pypesto.visualize as visualize

# sbml file we want to import
sbml_file = 'conversion_reaction/model_conversion_reaction.xml'
# name of the model that will also be the name of the python module
model_name = 'model_conversion_reaction'
# directory to which the generated model code is written
model_output_dir = 'tmp/' + model_name
```

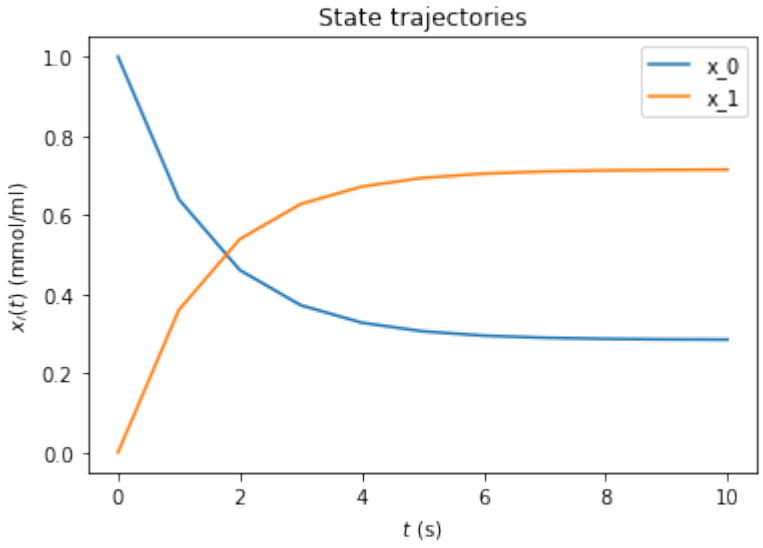
Compile AMICI model

[2]:
```
# import sbml model, compile and generate amici module
sbml_importer = amici.SbmlImporter(sbml_file)
sbml_importer.sbml2amici(model_name,
                         model_output_dir,
                         verbose=False)
```

Load AMICI model

[3]:
```
# load amici module (the usual starting point later for the analysis)
sys.path.insert(0, os.path.abspath(model_output_dir))
model_module = importlib.import_module(model_name)
model = model_module.getModel()
model.requireSensitivitiesForAllParameters()
model.setTimepoints(np.linspace(0, 10, 11))
model.setParameterScale(amici.ParameterScaling.log10)
model.setParameters([-0.3,-0.7])
solver = model.getSolver()
solver.setSensitivityMethod(amici.SensitivityMethod.forward)
solver.setSensitivityOrder(amici.SensitivityOrder.first)

# how to run amici now:
rdata = amici.runAmiciSimulation(model, solver, None)
amici.plotting.plotStateTrajectories(rdata)
edata = amici.ExpData(rdata, 0.2, 0.0)
```



Optimize

[4]:
```
# create objective function from amici model
# pesto.AmiciObjective is derived from pesto.Objective,
# the general pesto objective function class
objective = pypesto.AmiciObjective(model, solver, [edata], 1)

# create optimizer object which contains all information for doing the optimization
optimizer = optimize.ScipyOptimizer(method='ls_trf')

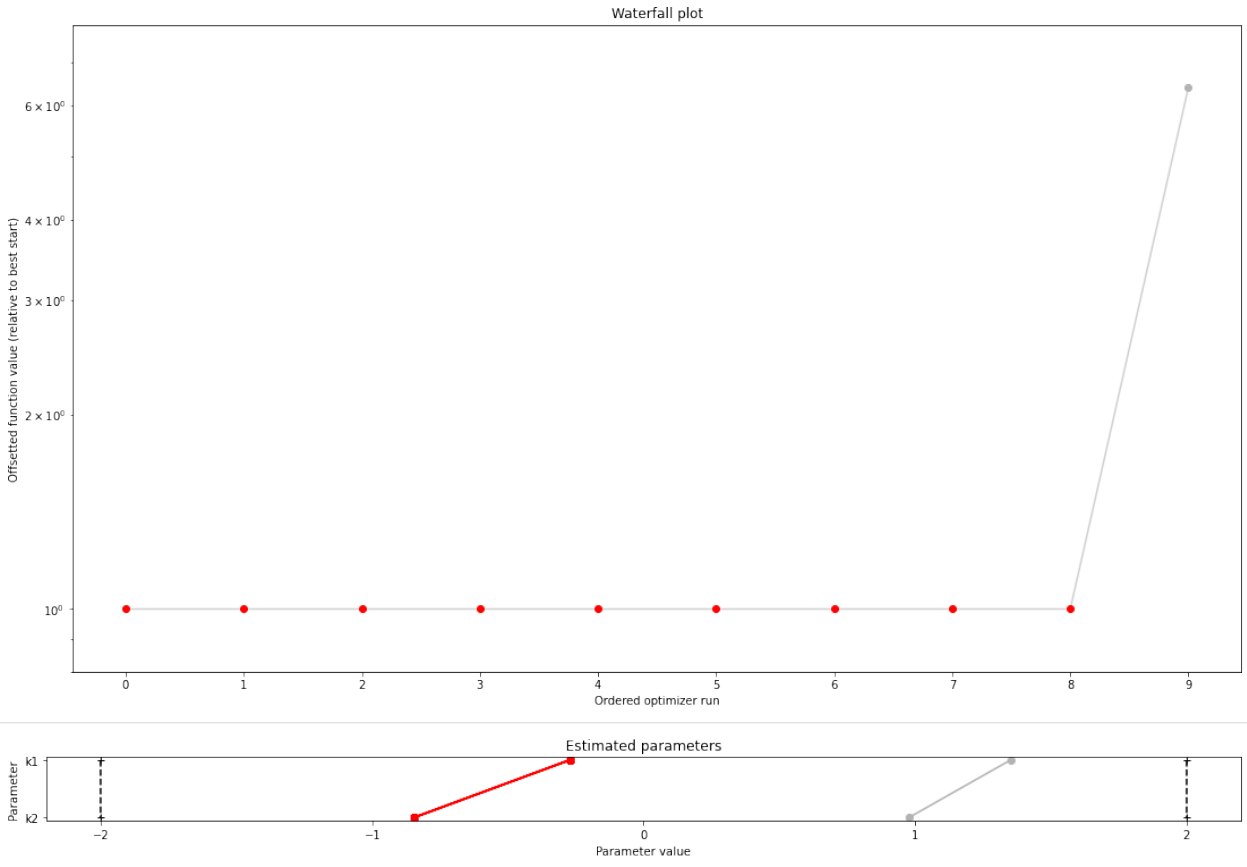
# create problem object containing all information on the problem to be solved
problem = pypesto.Problem(objective=objective,
                          lb=[-2,-2], ub=[2,2])

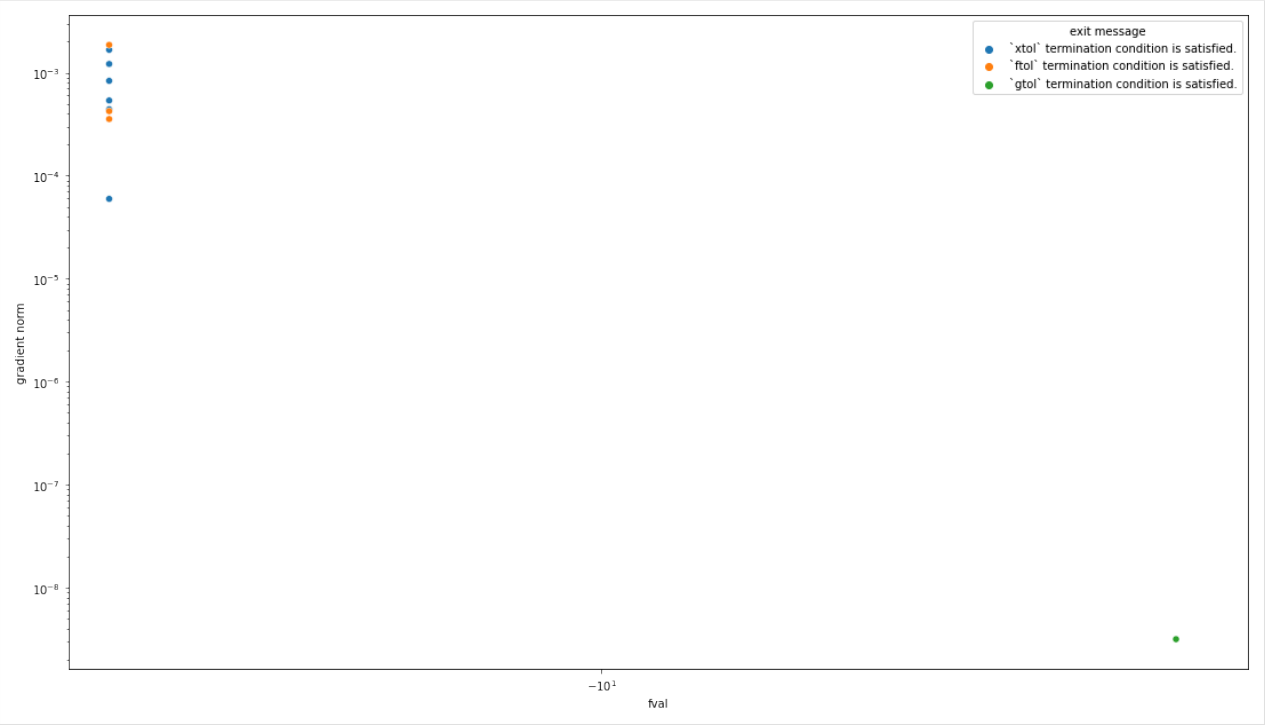
# do the optimization
result = optimize.minimize(problem=problem,
                           optimizer=optimizer,
                           n_starts=10, filename=None)
```

Visualize

[5]:
```
visualize.waterfall(result)
visualize.parameters(result)
visualize.optimizer_convergence(result)
```

[5]:
```
<AxesSubplot:xlabel='fval', ylabel='gradient norm'>
```





Profiles

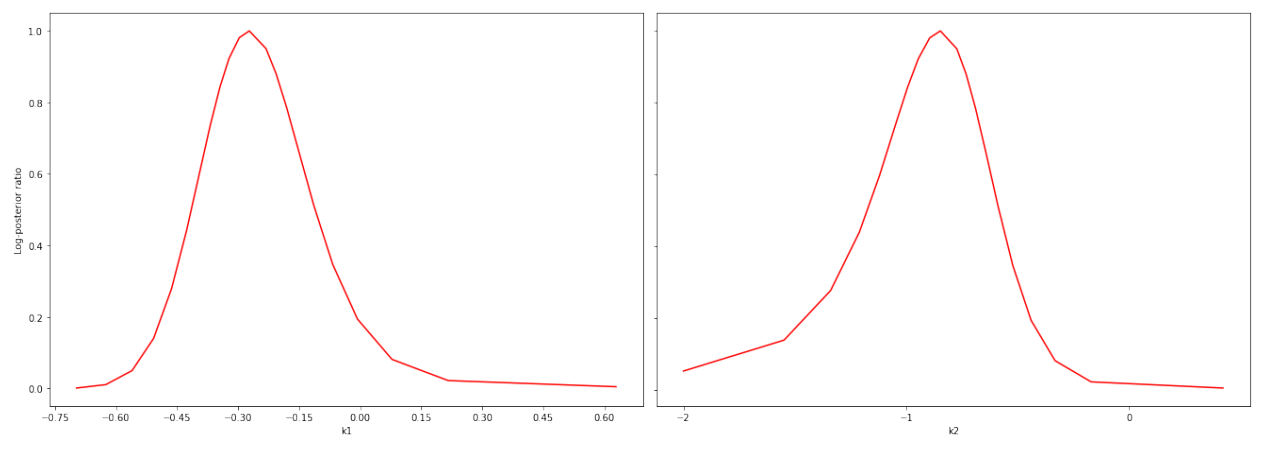
[6]:
```
import pypesto.profile as profile

profile_options = profile.ProfileOptions(min_step_size=0.0005,
    delta_ratio_max=0.05,
    default_step_size=0.005,
    ratio_min=0.01)

result = profile.parameter_profile(
    problem=problem,
    result=result,
    optimizer=optimizer,
    profile_index=np.array([1, 1, 1, 0, 0, 1, 0, 1, 0, 0, 0]),
    result_index=0,
    profile_options=profile_options,
    filename=None)
```

```
Parameters obtained from history and optimizer do not match: [-0.17103023], [-0.
↪17102486]
Parameters obtained from history and optimizer do not match: [-0.92272262], [-0.
↪92270649]
```

[7]:
```
# specify the parameters, for which profiles should be computed
ax = visualize.profiles(result)
```



Sampling

[8]:
```
import pypesto.sample as sample

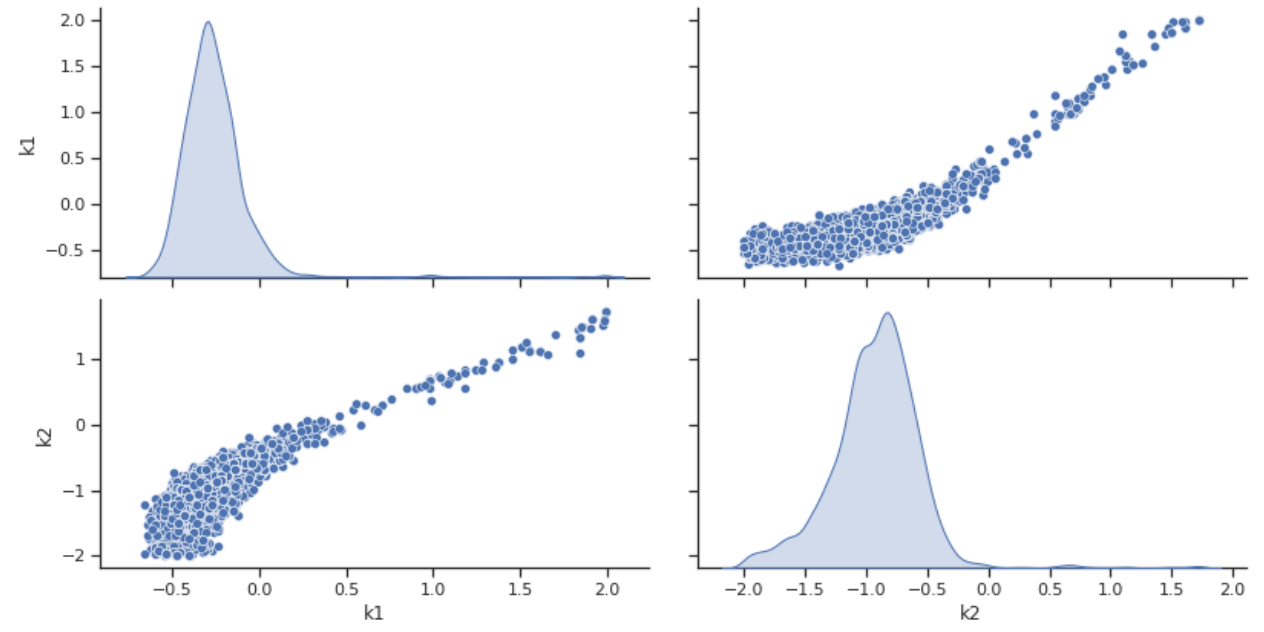
sampler = sample.AdaptiveParallelTemperingSampler(
    internal_sampler=sample.AdaptiveMetropolisSampler(),
    n_chains=3)

result = sample.sample(problem, n_samples=10000,
                       sampler=sampler, result=result,
                       filename=None)
```

```
100%|| 10000/10000 [00:33<00:00, 295.74it/s]
```

[9]:
```
ax = visualize.sampling_scatter(result, size=[13,6])
```

```
Burn in index not found in the results, the full chain will be shown.
You may want to use, e.g., 'pypesto.sample.geweke_test'.
```



Predict

[10]:
```
# Let's create a function, which predicts the ratio of x_1 and x_0
import pypesto.predict as predict

def ratio_function(amici_output_list):
    # This (optional) function post-processes the results from AMICI and must accept␣
↪one input:
    # a list of dicts, with the fields t, x, y[, sx, sy - if sensi_orders includes 1]
    # We need to specify the simulation condition: here, we only have one, i.e., it's␣
↪[0]
    x = amici_output_list[0]['x']
    ratio = x[:,1] / x[:,0]
    # we need to output also at least one simulation condition
    return [ratio]

# create pypesto prediction function
predictor = predict.AmiciPredictor(objective, post_processor=ratio_function, output_
↪ids=['ratio'])

# run prediction
prediction = predictor(x=model.getUnscaledParameters())
```

[11]:
```
dict(prediction)
```

[11]:
```
{'conditions': [{'timepoints': array([ 0.,  1.,  2.,  3.,  4.,  5.,  6.,  7.,  8.,  9.
↪, 10.]),
   'output_ids': ['ratio'],
   'x_names': ['k1', 'k2'],
   'output': array([0.        , 1.95196396, 2.00246152, 2.00290412, 2.00290796,
          2.00290801, 2.00290801, 2.00290799, 2.002908  , 2.00290801,
          2.002908  ]),
   'output_sensi': None}],
 'condition_ids': ['condition_0'],
 'comment': None,
 'parameter_ids': ['k1', 'k2']}
```

Analyze parameter ensembles

[12]:
```
# We want to use the sample result to create a prediction
from pypesto.ensemble import ensemble

# first collect some vectors from the sampling result
vectors = result.sample_result.trace_x[0, ::20, :]

# create the collection
my_ensemble = ensemble.Ensemble(vectors,
                                x_names=problem.x_names,
                                ensemble_type=ensemble.EnsembleType.sample,
                                lower_bound=problem.lb,
                                upper_bound=problem.ub)

# we can also perform an approximative identifiability analysis
summary = my_ensemble.compute_summary()
identifiability = my_ensemble.check_identifiability()
print(identifiability.transpose())
```

```
parameterId                k1        k2
parameterId                k1        k2
lowerBound                 -2        -2
upperBound                  2         2
ensemble_mean       -0.559689 -0.810604
ensemble_std         0.287255  0.364753
ensemble_median     -0.559689 -0.810604
within lb: 1 std         True      True
within ub: 1 std         True      True
within lb: 2 std         True      True
within ub: 2 std         True      True
within lb: 3 std         True      True
within ub: 3 std         True      True
within lb: perc 5        True      True
within lb: perc 20       True      True
within ub: perc 80       True      True
within ub: perc 95       True      True
```

[13]:
```
# run a prediction
ensemble_prediction = my_ensemble.predict(predictor, prediction_id='ratio_over_time')

# go for some analysis
prediction_summary = ensemble_prediction.compute_summary(percentiles_list=(1, 5, 10,␣
↪25, 75, 90, 95, 99))
dict(prediction_summary)
```

[13]:
```
{'mean': <pypesto.predict.result.PredictionResult at 0x7fe734b68760>,
 'std': <pypesto.predict.result.PredictionResult at 0x7fe734b698b0>,
 'median': <pypesto.predict.result.PredictionResult at 0x7fe734b69d60>,
 'percentile 1': <pypesto.predict.result.PredictionResult at 0x7fe734b69a30>,
 'percentile 5': <pypesto.predict.result.PredictionResult at 0x7fe734b69a60>,
 'percentile 10': <pypesto.predict.result.PredictionResult at 0x7fe734b69640>,
 'percentile 25': <pypesto.predict.result.PredictionResult at 0x7fe734b69610>,
 'percentile 75': <pypesto.predict.result.PredictionResult at 0x7fe734b693d0>,
 'percentile 90': <pypesto.predict.result.PredictionResult at 0x7fe734b69e20>,
 'percentile 95': <pypesto.predict.result.PredictionResult at 0x7fe734b692e0>,
 'percentile 99': <pypesto.predict.result.PredictionResult at 0x7fe734b69730>}
```

2.4.2 Optimization with Synthetic Data

In this notebook, optimization is performed with an SBML model and PEtab parameter estimation problem, which includes some measurements.

Next, optimization is performed with synthetic data as measurements, which is generated using PEtab and AMICI. The ability to recover the parameter vector that was used to generate the synthetic data is demonstrated.

Requirements

Additional requirements for this notebook can be installed with `pip install amici petab`.

[ ]:
```
# install if not done yet
# !apt install libatlas-base-dev swig
# %pip install pypesto[amici,petab] --quiet
```

1. Load required packages. PEtab provides a base class that is designed to be easily extended to support simulation with different tools. Here, the AMICI implementation of this base class is used.

[1]:
```
import amici.petab_simulate
import matplotlib.pyplot as plt
import petab
import pypesto.optimize
import pypesto.petab
import pypesto.visualize

# Helper function to get the maximum likelihood estimate as a dictionary from a␣
↪pyPESTO optimization result.
def get_x_mle(optimize_result, pypesto_problem, petab_problem, scaled=True):
    if not scaled:
        scaling = petab.parameters.get_optimization_parameter_scaling(petab_problem.
↪parameter_df)
    return {
        x_id: (petab.parameters.unscale(x_value, scaling[x_id]) if not scaled else x_
↪value)
        for x_id, x_value in zip(pypesto_problem.x_names, optimize_result.list[0]['x
↪'])
        #if x_id in scaling
    }
```

2.4.3 Standard Optimization

The PEtab problem is used to generate a pyPESTO problem, which is used to estimate model parameters.

2. Load a PEtab problem. The synthetic data returned by the PEtab-derived synthetic data generator (later, an instance of `amici.petab_simulate.PetabSimulator`) will be equivalent to switching the measurements in the PEtab problem's measurements table with simulated values.

[2]:
```
petab_yaml_filename = 'conversion_reaction/conversion_reaction.yaml'
petab_problem_original = petab.Problem.from_yaml(petab_yaml_filename)
```

3. Create a pyPESTO problem from the PEtab problem. Here, the original PEtab problem is used for parameter estimation (no synthetic data is generated).

[3]:
```
pypesto_importer_original = pypesto.petab.PetabImporter(petab_problem_original)
pypesto_problem_original = pypesto_importer_original.create_problem()
```

4. Estimate parameters. Multi-start local optimization with 100 starts is used, with the default pyPESTO optimizer.

[4]:
```
pypesto_result_original = pypesto.optimize.minimize(pypesto_problem_original, n_
↪starts=100)
```

```
Parameters obtained from history and optimizer do not match: [-0.25418068 -0.
↪60837086], [-0.25416788 -0.60834112]
```

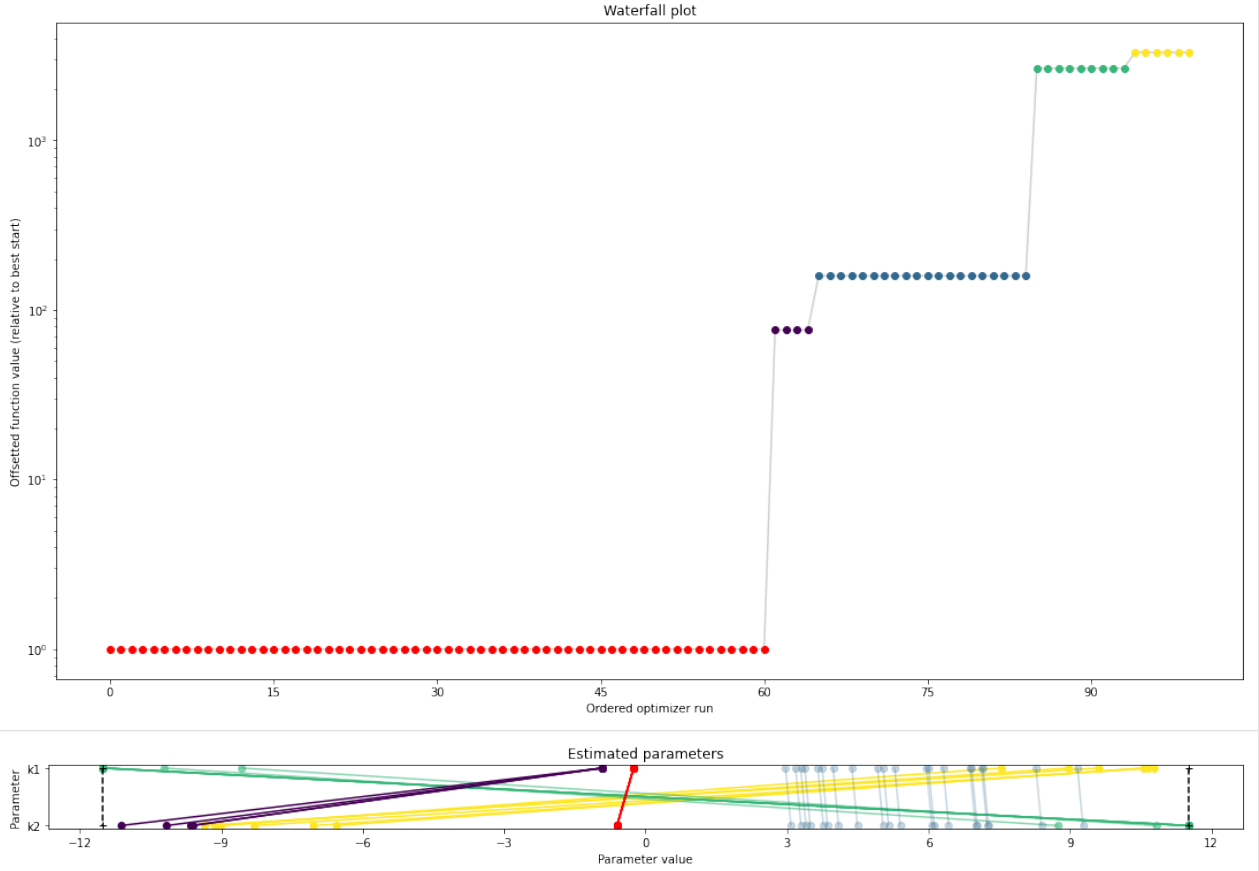
5. Visualize parameter estimation. Here, estimated values for `k1` and `k2` are shown, then a waterfall plot to indicate optimization quality, then a plot of the estimated parameters from the different starts to indicate identifiability.

Here, parameter estimation appears to have been successful. In the case of problematic parameter estimation, synthetic data can be used to determine whether parameter estimation can be used to identify known parameter values.

[5]:
```
x_mle_unscaled_original = get_x_mle(pypesto_result_original.optimize_result,
                                    pypesto_problem_original,
                                    petab_problem_original,
                                    scaled=False)
print('Parameters are estimated to be (linear scale):')
print('\n'.join([f'{x_id}: {x_value}' for x_id, x_value in x_mle_unscaled_original.
↪items()]))

pypesto.visualize.waterfall(pypesto_result_original);
pypesto.visualize.parameters(pypesto_result_original);
```

```
Parameters are estimated to be (linear scale):
k1: 0.7755615818811391
k2: 0.5442529577589637
```



2.4.4 Synthetic Optimization

Similar to the standard optimization, except the PEtab measurements table is replaced with synthetic data that is generated from specified parameters, with noise, and then used for optimization.

Here, parameters are specified with a dictionary that is used to update the original PEtab parameters table. An alternative is use a second PEtab YAML file that is identical to the original, except for the parameters table, which would now contain the parameter values to be used for synthetic data generation.

Noise

Noise is added to the simulated data according to the: - noise distribution in the PEtab observables table; - noise formula in the PEtab observables table, which is used to calculate the scale of the noise distribution; and - noise parameters in the PEtab measurements table, which are substituted into the noise formula for measurement-specific noise distribution scales.

6. As before, load a PEtab problem. This time, the parameters table is edited to contain parameters values that will be used for synthetic data generation (`synthetic_parameters`). Then, the simulator is used to generate synthetic data, which replaces the measurements table of the PEtab problem for parameter estimation in the next step.

Here, synthetic data also has noise added (`noise=True`), which is defined by the PEtab problem as described above. A noise scaling factor can also be specified (here, a small value - `noise_scaling_factor=0.01` - is used, to reduce noise such that the synthetic parameters are more likely to be recovered with parameter estimation).

The simulator working directory is then deleted along with its contents.

[6]:
```
petab_problem_synthetic = petab.Problem.from_yaml(petab_yaml_filename)

synthetic_parameters = {'k1': 1.5, 'k2': 2.5}
petab_problem_synthetic.parameter_df[petab.C.NOMINAL_VALUE].update(synthetic_
↪parameters)

simulator = amici.petab_simulate.PetabSimulator(petab_problem_synthetic)
# Optional: the AMICI simulator is provided a model, to avoid recompilation
petab_problem_synthetic.measurement_df = simulator.simulate(
    noise=True,
    noise_scaling_factor=0.01,
    amici_model=pypesto_problem_original.objective.amici_model,
)
simulator.remove_working_dir()
```

7. Create a pyPESTO problem from the edited PEtab problem, and estimate parameters.

[7]:
```
pypesto_importer_synthetic = pypesto.petab.PetabImporter(petab_problem_synthetic)
pypesto_problem_synthetic = pypesto_importer_synthetic.create_problem()
pypesto_result_synthetic = pypesto.optimize.minimize(pypesto_problem_synthetic, n_
↪starts=100)
```

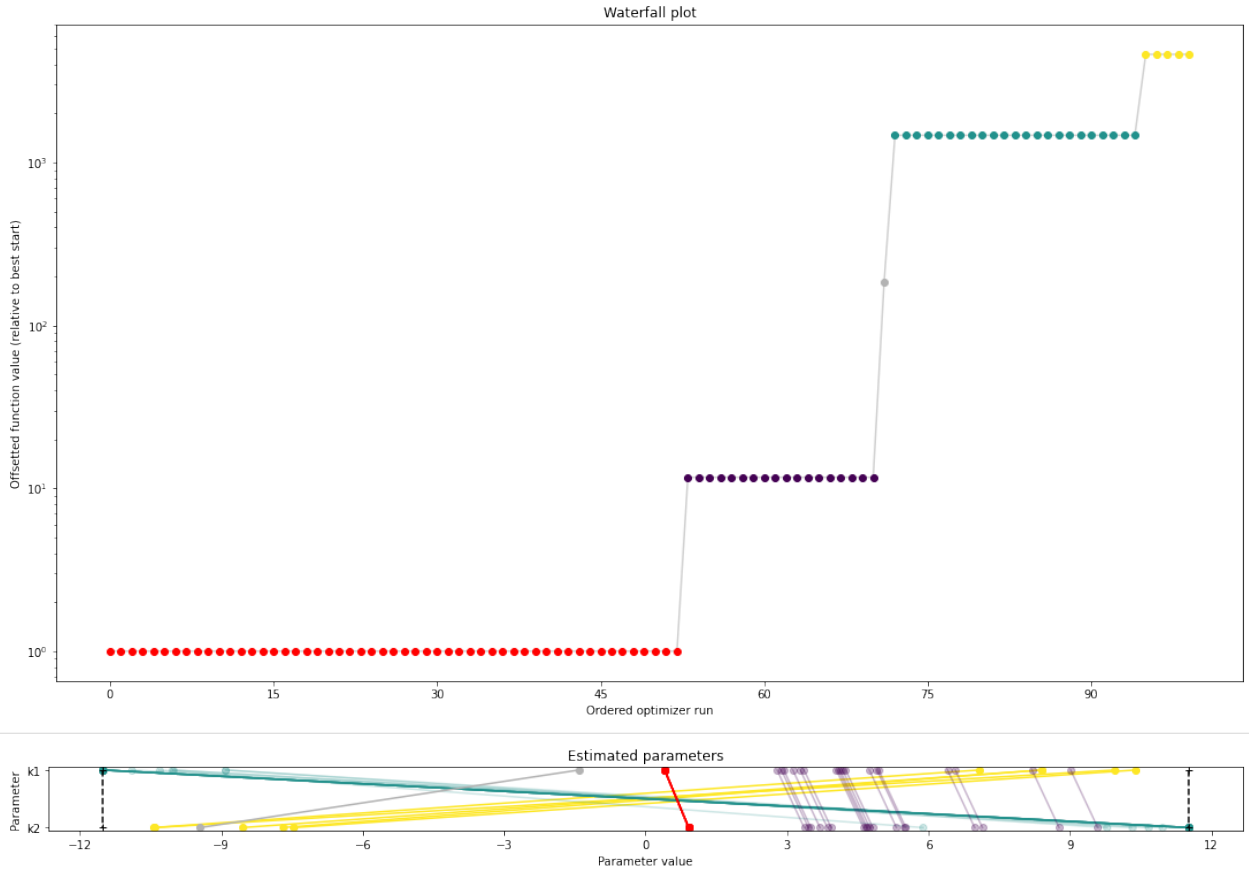
```
Function values from history and optimizer do not match: -24.31965832797165, 1439.
↪3853896684805
Parameters obtained from history and optimizer do not match: [0.10235171 0.50828654],␣
↪[-10.9022877   11.51292546]
```

8. Visualize parameter estimation. Here, the estimates for `k1` and `k2` are similar to the synthetic parameters, suggesting that parameter estimation works well with this PEtab problem and can be used to identify parameter values successfully (**caveat**: noise is reduced here; parameter estimation can be expected to perform worse with more realistically noisy data).

[8]:
```
x_mle_unscaled_synthetic = get_x_mle(pypesto_result_synthetic.optimize_result,
                                     pypesto_problem_synthetic,
                                     petab_problem_synthetic,
                                     scaled=False)
print('Parameters are estimated to be (linear scale):')
print('\n'.join([f'{x_id}: {x_value}' for x_id, x_value in x_mle_unscaled_synthetic.
↪items()]))

pypesto.visualize.waterfall(pypesto_result_synthetic);
pypesto.visualize.parameters(pypesto_result_synthetic);
```

```
Parameters are estimated to be (linear scale):
k1: 1.4969201262521281
k2: 2.494299196042553
```



CHAPTER

THREE

STORAGE

It is important to be able to store analysis results efficiently, easily accessible, and portable across systems. For this aim, pyPESTO allows to store results in efficient, portable HDF5 files. Further, optimization trajectories can be stored using various backends, including HDF5 and CSV.

In the following, describe the file formats. For detailed information on usage, consult the `doc/example/hdf5_storage.ipynb` and `doc/example/store.ipynb` notebook, and the API documentation for the `pypesto.objective.history` and `pypesto.storage` modules.

3.1 pyPESTO Problem

```
+ /problem/
  - Attributes:
    - filled by objective.get_config()
    - ...

  - lb [float n_par]
  - ub [float n_par]
  - lb_full [float n_par_full]
  - ub_full [float n_par_full]
  - dim [int]
  - dim_full [int]
  - x_fixed_values [float (n_par_full-n_par)]
  - x_fixed_indices [int (n_par_full-n_par)]
  - x_free_indices [int n_par]
  - x_names [str n_par_full]
```

3.2 Parameter estimation

3.2.1 Parameter estimation settings

Parameter estimation settings are saved in `/optimization/settings`.

3.2.2 Parameter estimation results

Parameter estimation results are saved in `/optimization/results/`.

Results per local optimization

Results of the `$n`'th multistart a saved in the format

```
+ /optimization/results/$n/
  - fval: [float]
      Objective function value of best iteration
  - x: [float n_par_full]
      Parameter set of best iteration
  - grad: [float n_par_full]
      Gradient of objective function at point x
  - hess: [float n_par_full x n_par_full]
      Hessian matrix of objective function at point x
  - n_fval: [int]
      Total number of objective function evaluations
  - n_grad: [int]
      Number of gradient evaluations
  - n_hess: [int]
      Number of Hessian evaluations
  - x0: [float n_par_full]
      Initial parameter set
  - fval0: [float]
      Objective function value at starting parameters
  - exitflag: [str] Some exit flag
  - time: [float] Execution time
  - message: [str] Some exit message
```

Trace per local optimization

When objective function call histories are saved to HDF5, they are under `/optimization/results/$n/trace/`.

```
+ /optimization/results/$n/trace/
  - fval: [float n_iter]
      Objective function value of best iteration
  - x: [float n_iter x n_par_full]
      Parameter set of best iteration
  - grad: [float n_iter x n_par_full]
      Gradient of objective function at point x
  - hess: [float n_iter x n_par_full x n_par_full]
      Hessian matrix of objective function at point x
  - time: [float n_iter] Executition time
  - chi2: [float n_iter x ...]
  - schi2: [float n_iter x ...]
```

3.3 Sampling

3.3.1 Sampling results

Sampling results are saved in `/sampling/results/`.

```
+ /sampling/results/
  - betas [float n_chains]
  - trace_neglogpost [float n_chains x (n_samples+1)]
  - trace_neglogprior [float n_chains x (n_samples+1)]
  - trace_x [float n_chains x (n_samples+1) x n_par]
  - Attributes:
    - time
```

3.4 Profiling

3.4.1 Profiling results

Profiling results are saved in `/profiling/$profiling_id/`, where `profiling_id` indicates the number of profilings done.

```
+/profiling/profiling_id/
  - $parameter_index/
    - exitflag_path [float n_iter]
    - fval_path [float n_iter]
    - gradnorm_path [float n_iter]
    - ratio_path [float n_iter]
    - time_path [float n_iter]
    - x_path [float n_par x n_iter]
    - Attributes:
      - time_total
      - IsNone
      - n_fval
      - n_grad
      - n_hess
```

CHAPTER

FOUR

API REFERENCE

4.1 pyPESTO

Parameter Estimation TOolbox for python.

class pypesto.**AmiciObjective**(*amici_model: Union[amici.Model, amici.ModelPtr], amici_solver: Union[amici.Solver, amici.SolverPtr], edatas: Union[Sequence[amici.ExpData], amici.ExpData], max_sensi_order: Optional[int] = None, x_ids: Optional[Sequence[str]] = None, x_names: Optional[Sequence[str]] = None, parameter_mapping: Optional[ParameterMapping] = None, guess_steadystate: Optional[bool] = None, n_threads: Optional[int] = 1, fim_for_hess: Optional[bool] = True, amici_object_builder: Optional[pypesto.objective.amici.AmiciObjectBuilder] = None, calculator: Optional[pypesto.objective.amici_calculator.AmiciCalculator] = None*)

Bases: pypesto.objective.base.ObjectiveBase

Allows to create an objective directly from an amici model.

__init__(*amici_model: Union[amici.Model, amici.ModelPtr], amici_solver: Union[amici.Solver, amici.SolverPtr], edatas: Union[Sequence[amici.ExpData], amici.ExpData], max_sensi_order: Optional[int] = None, x_ids: Optional[Sequence[str]] = None, x_names: Optional[Sequence[str]] = None, parameter_mapping: Optional[ParameterMapping] = None, guess_steadystate: Optional[bool] = None, n_threads: Optional[int] = 1, fim_for_hess: Optional[bool] = True, amici_object_builder: Optional[pypesto.objective.amici.AmiciObjectBuilder] = None, calculator: Optional[pypesto.objective.amici_calculator.AmiciCalculator] = None*)

Initialize objective.

Parameters

- **amici_model** – The amici model.
- **amici_solver** – The solver to use for the numeric integration of the model.
- **edatas** – The experimental data. If a list is passed, its entries correspond to multiple experimental conditions.
- **max_sensi_order** – Maximum sensitivity order supported by the model. Defaults to 2 if the model was compiled with o2mode, otherwise 1.
- **x_ids** – Ids of optimization parameters. In the simplest case, this will be the AMICI model parameters (default).

- **x_names** – Names of optimization parameters.
- **parameter_mapping** – Mapping of optimization parameters to model parameters. Format as created by *amici.petab_objective.create_parameter_mapping*. The default is just to assume that optimization and simulation parameters coincide.
- **guess_steadystate** – Whether to guess steadystates based on previous steadystates and respective derivatives. This option may lead to unexpected results for models with conservation laws and should accordingly be deactivated for those models.
- **n_threads** – Number of threads that are used for parallelization over experimental conditions. If amici was not installed with openMP support this option will have no effect.
- **fim_for_hess** – Whether to use the FIM whenever the Hessian is requested. This only applies with forward sensitivities. With adjoint sensitivities, the true Hessian will be used, if available. FIM or Hessian will only be exposed if *max_sensi_order>1*.
- **amici_object_builder** – AMICI object builder. Allows recreating the objective for pickling, required in some parallelization schemes.
- **calculator** – Performs the actual calculation of the function values and derivatives.

apply_custom_timepoints() → None
Apply custom timepoints, if applicable.

See the *set_custom_timepoints* method for more information.

apply_steadystate_guess(*condition_ix: int*, *x_dct: Dict*) → None
Apply steady state guess to *edatas[condition_ix].x0*.

Use the stored steadystate as well as the respective sensitivity (if available) and parameter value to approximate the steadystate at the current parameters using a zeroth or first order taylor approximation: x_ss(x') = x_ss(x) [+ dx_ss/dx(x)*(x'-x)]

call_unprocessed(*x: numpy.ndarray*, *sensi_orders: Tuple[int, ...]*, *mode: str*, *edatas: Sequence[amici.ExpData] = None*, *parameter_mapping: ParameterMapping = None*)
Call objective function without pre- or post-processing and formatting.

Returns A dict containing the results.

Return type result

check_gradients_match_finite_differences(*x: Optional[numpy.ndarray] = None*, **args*, ***kwargs*) → bool
Check if gradients match finite differences (FDs).

Parameters **x** (*The parameters for which to evaluate the gradient.*) –

Returns Indicates whether gradients match (True) FDs or not (False)

Return type bool

check_mode(*mode: str*) → bool
See *ObjectiveBase* documentation.

check_sensi_orders(*sensi_orders: Tuple[int, ...]*, *mode: str*) → bool
See *ObjectiveBase* documentation.

get_config() → dict
Return basic information of the objective configuration.

initialize()
See *ObjectiveBase* documentation.

par_arr_to_dct(*x: Sequence[float]*) → Dict[str, float]
Create dict from parameter vector.

reset_steadystate_guesses() → None
Reset all steadystate guess data.

set_custom_timepoints(*timepoints: Optional[Sequence[Sequence[Union[float, int]]]] = None*, *timepoints_global: Optional[Sequence[Union[float, int]]] = None*) → pypesto.objective.amici.AmiciObjective
Create a copy of this objective that is evaluated at custom timepoints.

The intended use is to aid in predictions at unmeasured timepoints.

Parameters

- **timepoints** – The outer sequence should contain a sequence of timepoints for each experimental condition.
- **timepoints_global** – A sequence of timepoints that will be used for all experimental conditions.

Returns

Return type The customized copy of this objective.

store_steadystate_guess(*condition_ix: int*, *x_dct: Dict*, *rdata: amici.ReturnData*) → None
Store condition parameter, steadystate and steadystate sensitivity.

Stored in steadystate_guesses if steadystate guesses are enabled for this condition.

class pypesto.**CsvHistory**(*file: str*, *x_names: Optional[Sequence[str]] = None*, *options: Optional[Union[pypesto.objective.history.HistoryOptions, Dict]] = None*, *load_from_file: bool = False*)
Bases: pypesto.objective.history.History

Stores a representation of the history in a CSV file.

Parameters

- **file** – CSV file name.
- **x_names** – Parameter names.
- **options** – History options.
- **load_from_file** – If True, history will be initialized from data in the specified file

__init__(*file: str*, *x_names: Optional[Sequence[str]] = None*, *options: Optional[Union[pypesto.objective.history.HistoryOptions, Dict]] = None*, *load_from_file: bool = False*)
Initialize self. See help(type(self)) for accurate signature.

finalize()
Finalize history. Called after a run.

get_chi2_trace(*ix: Optional[Union[Sequence[int], int]] = None*, *trim: bool = False*) → Union[Sequence[Union[float, numpy.ndarray, np.nan]], float, numpy.ndarray, np.nan]
Chi2 values.

Takes as parameter an index or indices and returns corresponding trace values. If only a single value is requested, the list is flattened.

get_fval_trace(*ix: Optional[Union[Sequence[int], int]] = None*, *trim: bool = False*) → Union[Sequence[Union[float, numpy.ndarray, np.nan]], float, numpy.ndarray, np.nan]

Return function values.

Takes as parameter an index or indices and returns corresponding trace values. If only a single value is requested, the list is flattened.

get_grad_trace(*ix: Optional[Union[Sequence[int], int]] = None*, *trim: bool = False*) → Union[Sequence[Union[float, numpy.ndarray, np.nan]], float, numpy.ndarray, np.nan]

Return gradients.

Takes as parameter an index or indices and returns corresponding trace values. If only a single value is requested, the list is flattened.

get_hess_trace(*ix: Optional[Union[Sequence[int], int]] = None*, *trim: bool = False*) → Union[Sequence[Union[float, numpy.ndarray, np.nan]], float, numpy.ndarray, np.nan]

Return hessians.

Takes as parameter an index or indices and returns corresponding trace values. If only a single value is requested, the list is flattened.

get_res_trace(*ix: Optional[Union[Sequence[int], int]] = None*, *trim: bool = False*) → Union[Sequence[Union[float, numpy.ndarray, np.nan]], float, numpy.ndarray, np.nan]

Residuals.

Takes as parameter an index or indices and returns corresponding trace values. If only a single value is requested, the list is flattened.

get_schi2_trace(*ix: Optional[Union[Sequence[int], int]] = None*, *trim: bool = False*) → Union[Sequence[Union[float, numpy.ndarray, np.nan]], float, numpy.ndarray, np.nan]

Chi2 sensitivities.

Takes as parameter an index or indices and returns corresponding trace values. If only a single value is requested, the list is flattened.

get_sres_trace(*ix: Optional[Union[Sequence[int], int]] = None*, *trim: bool = False*) → Union[Sequence[Union[float, numpy.ndarray, np.nan]], float, numpy.ndarray, np.nan]

Residual sensitivities.

Takes as parameter an index or indices and returns corresponding trace values. If only a single value is requested, the list is flattened.

get_time_trace(*ix: Optional[Union[Sequence[int], int]] = None*, *trim: bool = False*) → Union[Sequence[Union[float, numpy.ndarray, np.nan]], float, numpy.ndarray, np.nan]

Cumulative execution times.

Takes as parameter an index or indices and returns corresponding trace values. If only a single value is requested, the list is flattened.

get_x_trace(*ix: Optional[Union[Sequence[int], int]] = None*, *trim: bool = False*) → Union[Sequence[Union[float, numpy.ndarray, np.nan]], float, numpy.ndarray, np.nan]

Return parameters.

Takes as parameter an index or indices and returns corresponding trace values. If only a single value is requested, the list is flattened.

update(*x: numpy.ndarray, sensi_orders: Tuple[int, ...], mode: str, result: Dict[str, Union[float, numpy.ndarray]]*) → None
See *History* docstring.

class pypesto.**FD**(*obj: pypesto.objective.base.ObjectiveBase, grad: Optional[bool] = None, hess: Optional[bool] = None, sres: Optional[bool] = None, hess_via_fval: bool = True, delta_fun: Union[pypesto.objective.finite_difference.FDDelta, numpy.ndarray, float, str] = 1e-06, delta_grad: Union[pypesto.objective.finite_difference.FDDelta, numpy.ndarray, float, str] = 1e-06, delta_res: Union[pypesto.objective.finite_difference.FDDelta, float, numpy.ndarray, str] = 1e-06, method: str = 'central', x_names: Optional[List[str]] = None*)
Bases: pypesto.objective.base.ObjectiveBase

Finite differences (FDs) for derivatives.

Given an objective that gives function values and/or residuals, this class allows to flexibly obtain all derivatives calculated via FDs.

For the parameters *grad*, *hess*, *sres*, a value of None means that the objective derivative is used if available, otherwise resorting to FDs. True means that FDs are used in any case, False means that the derivative is not exported.

Note that the step sizes should be carefully chosen. They should be small enough to provide an accurate linear approximation, but large enough to be robust against numerical inaccuracies, in particular if the objective relies on numerical approximations, such as an ODE.

Parameters

- **grad** – Derivative method for the gradient (see above).
- **hess** – Derivative method for the Hessian (see above).
- **sres** – Derivative method for the residual sensitivities (see above).
- **hess_via_fval** – If the Hessian is to be calculated via finite differences: whether to employ 2nd order FDs via fval even if the objective can provide a gradient.
- **delta_fun** – FD step sizes for function values. Can be either a float, or a np.ndarray of shape (n_par,) for different step sizes for different coordinates.
- **delta_grad** – FD step sizes for gradients, if the Hessian is calculated via 1st order sensitivities from the gradients. Similar to *delta_fun*.
- **delta_res** – FD step sizes for residuals. Similar to *delta_fun*.
- **method** – Method to calculate FDs. Can be any of *FD.METHODS*: central, forward or backward differences. The latter two require only roughly half as many function evaluations, are however less accurate than central (O(x) vs O(x**2)).
- **x_names** – Parameter names that can be optionally used in, e.g., history or gradient checks.

Examples

Define residuals and objective function, and obtain all derivatives via FDs:

```
>>> from pypesto import Objective, FD
>>> import numpy as np
>>> x_obs = np.array([11, 12, 13])
>>> res = lambda x: x - x_obs
>>> fun = lambda x: 0.5 * sum(res(x)**2)
>>> obj = FD(Objective(fun=fun, res=res))
```

BACKWARD = 'backward'

CENTRAL = 'central'

FORWARD = 'forward'

METHODS = ['central', 'forward', 'backward']

__init__(*obj: pypesto.objective.base.ObjectiveBase, grad: Optional[bool] = None, hess: Optional[bool] = None, sres: Optional[bool] = None, hess_via_fval: bool = True, delta_fun: Union[pypesto.objective.finite_difference.FDDelta, numpy.ndarray, float, str] = 1e-06, delta_grad: Union[pypesto.objective.finite_difference.FDDelta, numpy.ndarray, float, str] = 1e-06, delta_res: Union[pypesto.objective.finite_difference.FDDelta, float, numpy.ndarray, str] = 1e-06, method: str = 'central', x_names: Optional[List[str]] = None*)

Initialize self. See help(type(self)) for accurate signature.

call_unprocessed(*x: numpy.ndarray, sensi_orders: Tuple[int, ...], mode: str, **kwargs*) → Dict[str, Union[float, numpy.ndarray, Dict]]

See *ObjectiveBase* for more documentation.

Main method to overwrite from the base class. It handles and delegates the actual objective evaluation.

property has_fun

Check whether function is defined.

property has_grad

Check whether gradient is defined.

property has_hess

Check whether Hessian is defined.

property has_res

Check whether residuals are defined.

property has_sres

Check whether residual sensitivities are defined.

class pypesto.**FDDelta**(*delta: Optional[Union[numpy.ndarray, float]] = None, test_deltas: Optional[numpy.ndarray] = None, update_condition: str = 'constant', max_distance: float = 0.5, max_steps: int = 30*)

Bases: object

Finite difference step size with automatic updating.

Reference implementation: https://github.com/ICB-DCM/PESTO/blob/master/private/getStepSizeFD.m

Parameters

- **delta** – (Initial) step size, either a float, or a vector of size (n_par,). If not None, this is used as initial step size.
- **test_deltas** – Step sizes to try out in step size selection. If None, a range [1e-1, 1e-2, ..., 1e-8] is considered.

- **update_condition** – A "good" step size may be a local property. Thus, this class allows updating the step size if certain criteria are met, in the `pypesto.objective.finite_difference.FDDelta.update()` function. FDDelta.CONSTANT means that the step size is only initially selected. FDDelta.DISTANCE means that the step size is updated if the current evaluation point is sufficiently far away from the last training point. FDDelta.STEPS means that the step size is updated *max_steps* evaluations after the last update. FDDelta.ALWAYS mean that the step size is selected in every call.
- **max_distance** – Coefficient on the distance between current and reference point beyond which to update, in the *FDDelta.DISTANCE* update condition.
- **max_steps** – Number of steps after which to update in the *FDDelta.STEPS* update condition.

ALWAYS = 'always'

CONSTANT = 'constant'

DISTANCE = 'distance'

STEPS = 'steps'

UPDATE_CONDITIONS = ['constant', 'distance', 'steps', 'always']

__init__(*delta: Optional[Union[numpy.ndarray, float]] = None*, *test_deltas: Optional[numpy.ndarray] = None*, *update_condition: str = 'constant'*, *max_distance: float = 0.5*, *max_steps: int = 30*)
Initialize self. See help(type(self)) for accurate signature.

get() → numpy.ndarray
Get delta vector.

update(*x: numpy.ndarray*, *fval: Optional[Union[float, numpy.ndarray]]*, *fun: Callable*, *fd_method: str*) → None
Update delta if update conditions are met.

Parameters

- **x** – Current parameter vector, shape (n_par,).
- **fval** – fun(x), to avoid re-evaluation. Scalar- or vector-valued.
- **fun** – Function whose 1st-order derivative to approximate. Scalar- or vector-valued.
- **fd_method** – FD method employed by `pypesto.objective.finite_difference.FD`, see there.

class pypesto.**Hdf5History**(*id: str*, *file: str*, *options: Optional[Union[pypesto.objective.history.HistoryOptions, Dict]] = None*)
Bases: `pypesto.objective.history.History`

Stores a representation of the history in an HDF5 file.

Parameters

- **id** – Id of the history
- **file** – HDF5 file name.
- **options** – History options.

__init__(*id: str*, *file: str*, *options: Optional[Union[pypesto.objective.history.HistoryOptions, Dict]] = None*)
Initialize self. See help(type(self)) for accurate signature.

finalize()
See *History* docstring.

get_chi2_trace(*ix: Optional[Union[Sequence[int], int]] = None*, *trim: bool = False*) → Union[Sequence[Union[float, numpy.ndarray, np.nan]], float, numpy.ndarray, np.nan]
Chi2 values.

Takes as parameter an index or indices and returns corresponding trace values. If only a single value is requested, the list is flattened.

get_fval_trace(*ix: Optional[Union[Sequence[int], int]] = None*, *trim: bool = False*) → Union[Sequence[Union[float, numpy.ndarray, np.nan]], float, numpy.ndarray, np.nan]
Return function values.

Takes as parameter an index or indices and returns corresponding trace values. If only a single value is requested, the list is flattened.

get_grad_trace(*ix: Optional[Union[Sequence[int], int]] = None*, *trim: bool = False*) → Union[Sequence[Union[float, numpy.ndarray, np.nan]], float, numpy.ndarray, np.nan]
Return gradients.

Takes as parameter an index or indices and returns corresponding trace values. If only a single value is requested, the list is flattened.

get_hess_trace(*ix: Optional[Union[Sequence[int], int]] = None*, *trim: bool = False*) → Union[Sequence[Union[float, numpy.ndarray, np.nan]], float, numpy.ndarray, np.nan]
Return hessians.

Takes as parameter an index or indices and returns corresponding trace values. If only a single value is requested, the list is flattened.

get_history_directory()
Return filepath.

get_res_trace(*ix: Optional[Union[Sequence[int], int]] = None*, *trim: bool = False*) → Union[Sequence[Union[float, numpy.ndarray, np.nan]], float, numpy.ndarray, np.nan]
Residuals.

Takes as parameter an index or indices and returns corresponding trace values. If only a single value is requested, the list is flattened.

get_schi2_trace(*ix: Optional[Union[Sequence[int], int]] = None*, *trim: bool = False*) → Union[Sequence[Union[float, numpy.ndarray, np.nan]], float, numpy.ndarray, np.nan]
Chi2 sensitivities.

Takes as parameter an index or indices and returns corresponding trace values. If only a single value is requested, the list is flattened.

get_sres_trace(*ix: Optional[Union[Sequence[int], int]] = None*, *trim: bool = False*) → Union[Sequence[Union[float, numpy.ndarray, np.nan]], float, numpy.ndarray, np.nan]
Residual sensitivities.

Takes as parameter an index or indices and returns corresponding trace values. If only a single value is requested, the list is flattened.

get_time_trace(*ix: Optional[Union[Sequence[int], int]] = None*, *trim: bool = False*) → Union[Sequence[Union[float, numpy.ndarray, np.nan]], float, numpy.ndarray, np.nan]
Cumulative execution times.

Takes as parameter an index or indices and returns corresponding trace values. If only a single value is requested, the list is flattened.

get_x_trace(*ix: Optional[Union[Sequence[int], int]] = None*, *trim: bool = False*) → Union[Sequence[Union[float, numpy.ndarray, np.nan]], float, numpy.ndarray, np.nan]
Return parameters.

Takes as parameter an index or indices and returns corresponding trace values. If only a single value is requested, the list is flattened.

static load(*id: str*, *file: str*)
Load the History object from memory.

property n_fval
See *HistoryBase* docstring.

property n_grad
See *HistoryBase* docstring.

property n_hess
See *HistoryBase* docstring.

property n_res
See *HistoryBase* docstring.

property n_sres
See *HistoryBase* docstring.

recover_options(*file: str*)
Recover options when loading the hdf5 history from memory.

Done by testing which entries were recorded.

property trace_save_iter
After how many iterations to store the trace.

update(*x: numpy.ndarray*, *sensi_orders: Tuple[int, ...]*, *mode: str*, *result: Dict[str, Union[float, numpy.ndarray]]*) → None
See *History* docstring.

class pypesto.**History**(*options: Optional[Union[pypesto.objective.history.HistoryOptions, Dict]] = None*)
Bases: pypesto.objective.history.HistoryBase

Track number of function evaluations only, no trace.

Parameters **options** – History options.

__init__(*options: Optional[Union[pypesto.objective.history.HistoryOptions, Dict]] = None*)
Initialize self. See help(type(self)) for accurate signature.

finalize()
See *HistoryBase* docstring.

property n_fval
See *HistoryBase* docstring.

property n_grad
See *HistoryBase* docstring.

property n_hess
See *HistoryBase* docstring.

property n_res
See *HistoryBase* docstring.

property n_sres
See *HistoryBase* docstring.

property start_time
See *HistoryBase* docstring.

update(*x: numpy.ndarray*, *sensi_orders: Tuple[int, ...]*, *mode: str*, *result: Dict[str, Union[float, numpy.ndarray]]*) → None
Update history after a function evaluation.

Parameters

- **x** – The parameter vector.
- **sensi_orders** – The sensitivity orders computed.
- **mode** – The objective function mode computed (function value or residuals).
- **result** – The objective function values for parameters *x*, sensitivities *sensi_orders* and mode *mode*.

class pypesto.**HistoryBase**
Bases: abc.ABC

Abstract base class for history objects.

Can be used as a dummy history, but does not implement any history functionality.

finalize()
Finalize history. Called after a run.

get_chi2_trace(*ix: Optional[Union[Sequence[int], int]] = None*, *trim: bool = False*) → Union[Sequence[float], float]
Chi2 values.

Takes as parameter an index or indices and returns corresponding trace values. If only a single value is requested, the list is flattened.

get_fval_trace(*ix: Optional[Union[Sequence[int], int]] = None*, *trim: bool = False*) → Union[Sequence[float], float]
Return function values.

Takes as parameter an index or indices and returns corresponding trace values. If only a single value is requested, the list is flattened.

get_grad_trace(*ix: Optional[Union[int, Sequence[int]]] = None*, *trim: bool = False*) → Union[Sequence[Union[numpy.ndarray, np.nan]], numpy.ndarray, np.nan]
Return gradients.

Takes as parameter an index or indices and returns corresponding trace values. If only a single value is requested, the list is flattened.

get_hess_trace(*ix: Optional[Union[int, Sequence[int]]] = None*, *trim: bool = False*) → Union[Sequence[Union[numpy.ndarray, np.nan]], numpy.ndarray, np.nan]
Return hessians.

Takes as parameter an index or indices and returns corresponding trace values. If only a single value is requested, the list is flattened.

get_res_trace(*ix: Optional[Union[int, Sequence[int]]] = None*, *trim: bool = False*) → Union[Sequence[Union[numpy.ndarray, np.nan]], numpy.ndarray, np.nan]
Residuals.

Takes as parameter an index or indices and returns corresponding trace values. If only a single value is requested, the list is flattened.

get_schi2_trace(*ix: Optional[Union[int, Sequence[int]]] = None*, *trim: bool = False*) → Union[Sequence[Union[numpy.ndarray, np.nan]], numpy.ndarray, np.nan]
Chi2 sensitivities.

Takes as parameter an index or indices and returns corresponding trace values. If only a single value is requested, the list is flattened.

get_sres_trace(*ix: Optional[Union[int, Sequence[int]]] = None*, *trim: bool = False*) → Union[Sequence[Union[numpy.ndarray, np.nan]], numpy.ndarray, np.nan]
Residual sensitivities.

Takes as parameter an index or indices and returns corresponding trace values. If only a single value is requested, the list is flattened.

get_time_trace(*ix: Optional[Union[Sequence[int], int]] = None*, *trim: bool = False*) → Union[Sequence[float], float]
Cumulative execution times.

Takes as parameter an index or indices and returns corresponding trace values. If only a single value is requested, the list is flattened.

get_trimmed_indices()
Get indices for a monotonically decreasing history.

get_x_trace(*ix: Optional[Union[Sequence[int], int]] = None*, *trim: bool = False*) → Union[Sequence[numpy.ndarray], numpy.ndarray]
Return parameters.

Takes as parameter an index or indices and returns corresponding trace values. If only a single value is requested, the list is flattened.

property n_fval
Return number of function evaluations.

property n_grad
Return number of gradient evaluations.

property n_hess
Return number of Hessian evaluations.

property n_res
Return number of residual evaluations.

property n_sres
Return number or residual sensitivity evaluations.

property start_time
Return start time.

update(*x: numpy.ndarray*, *sensi_orders: Tuple[int, ...]*, *mode: str*, *result: Dict[str, Union[float, numpy.ndarray]]*) → None
Update history after a function evaluation.

Parameters

- **x** – The parameter vector.
- **sensi_orders** – The sensitivity orders computed.

- **mode** – The objective function mode computed (function value or residuals).
- **result** – The objective function values for parameters *x*, sensitivities *sensi_orders* and mode *mode*.

class pypesto.**HistoryOptions**(*trace_record: bool = False*, *trace_record_grad: bool = True*, *trace_record_hess: bool = True*, *trace_record_res: bool = True*, *trace_record_sres: bool = True*, *trace_record_chi2: bool = True*, *trace_record_schi2: bool = True*, *trace_save_iter: int = 10*, *storage_file: Optional[str] = None*)

Bases: dict

Options for the objective that are used in optimization.

In addition implements a factory pattern to generate history objects.

Parameters

- **trace_record** – Flag indicating whether to record the trace of function calls. The trace_record_* flags only become effective if trace_record is True.
- **trace_record_grad** – Flag indicating whether to record the gradient in the trace.
- **trace_record_hess** – Flag indicating whether to record the Hessian in the trace.
- **trace_record_res** – Flag indicating whether to record the residual in the trace.
- **trace_record_sres** – Flag indicating whether to record the residual sensitivities in the trace.
- **trace_record_chi2** – Flag indicating whether to record the chi2 in the trace.
- **trace_record_schi2** – Flag indicating whether to record the chi2 sensitivities in the trace.
- **trace_save_iter** – After how many iterations to store the trace.
- **storage_file** – File to save the history to. Can be any of None, a "{filename}.csv", or a "{filename}.hdf5" file. Depending on the values, the *create_history* method creates the appropriate object. Occurrences of "{id}" in the file name are replaced by the *id* upon creation of a history, if applicable.

__init__(*trace_record: bool = False*, *trace_record_grad: bool = True*, *trace_record_hess: bool = True*, *trace_record_res: bool = True*, *trace_record_sres: bool = True*, *trace_record_chi2: bool = True*, *trace_record_schi2: bool = True*, *trace_save_iter: int = 10*, *storage_file: Optional[str] = None*)

Initialize self. See help(type(self)) for accurate signature.

static assert_instance(*maybe_options: Union[pypesto.objective.history.HistoryOptions, Dict]*) → pypesto.objective.history.HistoryOptions

Return a valid options object.

Parameters **maybe_options** (*HistoryOptions or dict*) –

create_history(*id: str*, *x_names: Sequence[str]*) → pypesto.objective.history.History

Create a *History* object; Factory method.

Parameters

- **id** – Identifier for the history.
- **x_names** – Parameter names.

class pypesto.**McmcPtResult**(*trace_x: numpy.ndarray*, *trace_neglogpost: numpy.ndarray*, *trace_neglogprior: numpy.ndarray*, *betas: Iterable[float]*, *burn_in: Optional[int] = None*, *time: float = 0.0*, *auto_correlation: Optional[float] = None*, *effective_sample_size: Optional[float] = None*, *message: Optional[str] = None*)

Bases: dict

The result of a sampler run using Markov-chain Monte Carlo.

Currently result object of all supported samplers. Can be used like a dict.

Parameters

- **trace_x** (*[n_chain, n_iter, n_par]*) – Parameters.
- **trace_neglogpost** (*[n_chain, n_iter]*) – Negative log posterior values.
- **trace_neglogprior** (*[n_chain, n_iter]*) – Negative log prior values.
- **betas** (*[n_chain]*) – The associated inverse temperatures.
- **burn_in** (*[n_chain]*) – The burn in index.
- **time** (*[n_chain]*) – The computation time.
- **auto_correlation** (*[n_chain]*) – The estimated chain autcorrelation.
- **effective_sample_size** (*[n_chain]*) – The estimated effective sample size.
- **message** (*str*) – Textual comment on the profile result.
- **Here** –
- **denotes the number of chains** (*n_chain*) –
- **the number of** (*n_iter*) –
- **(i.e.** (*iterations*) –
- **chain length)** (*the*) –
- **n_par the number of parameters.** (*and*) –

__init__(*trace_x: numpy.ndarray*, *trace_neglogpost: numpy.ndarray*, *trace_neglogprior: numpy.ndarray*, *betas: Iterable[float]*, *burn_in: Optional[int] = None*, *time: float = 0.0*, *auto_correlation: Optional[float] = None*, *effective_sample_size: Optional[float] = None*, *message: Optional[str] = None*)

Initialize self. See help(type(self)) for accurate signature.

class pypesto.**MemoryHistory**(*options: Optional[Union[pypesto.objective.history.HistoryOptions, Dict]] = None*)

Bases: pypesto.objective.history.History

Class for optimization history stored in memory.

Track number of function evaluations and keeps an in-memory trace of function evaluations.

Parameters **options** – History options.

__init__(*options: Optional[Union[pypesto.objective.history.HistoryOptions, Dict]] = None*)

Initialize self. See help(type(self)) for accurate signature.

get_chi2_trace(*ix: Optional[Union[Sequence[int], int]] = None*, *trim: bool = False*) → Union[Sequence[Union[float, numpy.ndarray, np.nan]], float, numpy.ndarray, np.nan]

Chi2 values.

Takes as parameter an index or indices and returns corresponding trace values. If only a single value is requested, the list is flattened.

get_fval_trace(*ix: Optional[Union[Sequence[int], int]] = None*, *trim: bool = False*) → Union[Sequence[Union[float, numpy.ndarray, np.nan]], float, numpy.ndarray, np.nan]

Return function values.

Takes as parameter an index or indices and returns corresponding trace values. If only a single value is requested, the list is flattened.

get_grad_trace(*ix: Optional[Union[Sequence[int], int]] = None*, *trim: bool = False*) → Union[Sequence[Union[float, numpy.ndarray, np.nan]], float, numpy.ndarray, np.nan]

Return gradients.

Takes as parameter an index or indices and returns corresponding trace values. If only a single value is requested, the list is flattened.

get_hess_trace(*ix: Optional[Union[Sequence[int], int]] = None*, *trim: bool = False*) → Union[Sequence[Union[float, numpy.ndarray, np.nan]], float, numpy.ndarray, np.nan]

Return hessians.

Takes as parameter an index or indices and returns corresponding trace values. If only a single value is requested, the list is flattened.

get_res_trace(*ix: Optional[Union[Sequence[int], int]] = None*, *trim: bool = False*) → Union[Sequence[Union[float, numpy.ndarray, np.nan]], float, numpy.ndarray, np.nan]

Residuals.

Takes as parameter an index or indices and returns corresponding trace values. If only a single value is requested, the list is flattened.

get_schi2_trace(*ix: Optional[Union[Sequence[int], int]] = None*, *trim: bool = False*) → Union[Sequence[Union[float, numpy.ndarray, np.nan]], float, numpy.ndarray, np.nan]

Chi2 sensitivities.

Takes as parameter an index or indices and returns corresponding trace values. If only a single value is requested, the list is flattened.

get_sres_trace(*ix: Optional[Union[Sequence[int], int]] = None*, *trim: bool = False*) → Union[Sequence[Union[float, numpy.ndarray, np.nan]], float, numpy.ndarray, np.nan]

Residual sensitivities.

Takes as parameter an index or indices and returns corresponding trace values. If only a single value is requested, the list is flattened.

get_time_trace(*ix: Optional[Union[Sequence[int], int]] = None*, *trim: bool = False*) → Union[Sequence[Union[float, numpy.ndarray, np.nan]], float, numpy.ndarray, np.nan]

Cumulative execution times.

Takes as parameter an index or indices and returns corresponding trace values. If only a single value is requested, the list is flattened.

get_x_trace(*ix: Optional[Union[Sequence[int], int]] = None*, *trim: bool = False*) → Union[Sequence[Union[float, numpy.ndarray, np.nan]], float, numpy.ndarray, np.nan]

Return parameters.

Takes as parameter an index or indices and returns corresponding trace values. If only a single value is requested, the list is flattened.

update(*x: numpy.ndarray, sensi_orders: Tuple[int, ...], mode: str, result: Dict[str, Union[float, numpy.ndarray]]*) → None
See *History* docstring.

class pypesto.**NegLogPriors**(*objectives: Sequence[pypesto.objective.base.ObjectiveBase], x_names: Optional[Sequence[str]] = None*)
Bases: pypesto.objective.aggregated.AggregatedObjective

Aggregates different forms of negative log-prior distributions.

Allows to distinguish priors from the likelihood by testing the type of an objective.

Consists basically of a list of individual negative log-priors, given in self.objectives.

class pypesto.**Objective**(*fun: Optional[Callable] = None, grad: Optional[Union[Callable, bool]] = None, hess: Optional[Callable] = None, hessp: Optional[Callable] = None, res: Optional[Callable] = None, sres: Optional[Union[Callable, bool]] = None, x_names: Optional[Sequence[str]] = None*)
Bases: pypesto.objective.base.ObjectiveBase

Objective class.

The objective class allows the user explicitly specify functions that compute the function value and/or residuals as well as respective derivatives.

Denote dimensions *n* = parameters, *m* = residuals.

Parameters

- **fun** – The objective function to be minimized. If it only computes the objective function value, it should be of the form

  ```
  fun(x) -> float
  ```

  where x is an 1-D array with shape (n,), and n is the parameter space dimension.

- **grad** – Method for computing the gradient vector. If it is a callable, it should be of the form

  ```
  grad(x) -> array_like, shape (n,).
  ```

  If its value is True, then fun should return the gradient as a second output.

- **hess** – Method for computing the Hessian matrix. If it is a callable, it should be of the form

  ```
  hess(x) -> array, shape (n, n).
  ```

  If its value is True, then fun should return the gradient as a second, and the Hessian as a third output, and grad should be True as well.

- **hessp** – Method for computing the Hessian vector product, i.e.

  ```
  hessp(x, v) -> array_like, shape (n,)
  ```

  computes the product H*v of the Hessian of fun at x with v.

- **res** – Method for computing residuals, i.e.

  ```
  res(x) -> array_like, shape(m,).
  ```

- **sres** – Method for computing residual sensitivities. If it is a callable, it should be of the form

  ```
  sres(x) -> array, shape (m, n).
  ```

If its value is True, then res should return the residual sensitivities as a second output.

- **x_names** – Parameter names. None if no names provided, otherwise a list of str, length dim_full (as in the Problem class). Can be read by the problem.

__init__(*fun: Optional[Callable] = None*, *grad: Optional[Union[Callable, bool]] = None*, *hess: Optional[Callable] = None*, *hessp: Optional[Callable] = None*, *res: Optional[Callable] = None*, *sres: Optional[Union[Callable, bool]] = None*, *x_names: Optional[Sequence[str]] = None*)

Initialize self. See help(type(self)) for accurate signature.

call_unprocessed(*x: numpy.ndarray*, *sensi_orders: Tuple[int, ...]*, *mode: str*, ***kwargs*) → Dict[str, Union[float, numpy.ndarray, Dict]]

Call objective function without pre- or post-processing and formatting.

Returns A dict containing the results.

Return type result

get_config() → dict

Return basic information of the objective configuration.

property has_fun

Check whether function is defined.

property has_grad

Check whether gradient is defined.

property has_hess

Check whether Hessian is defined.

property has_hessp

property has_res

Check whether residuals are defined.

property has_sres

Check whether residual sensitivities are defined.

class pypesto.**ObjectiveBase**(*x_names: Optional[Sequence[str]] = None*)

Bases: abc.ABC

Abstract objective class.

The objective class is a simple wrapper around the objective function, giving a standardized way of calling. Apart from that, it manages several things including fixing of parameters and history.

The objective function is assumed to be in the format of a cost function, log-likelihood function, or log-posterior function. These functions are subject to minimization. For profiling and sampling, the sign is internally flipped, all returned and stored values are however given as returned by this objective function. If maximization is to be performed, the sign should be flipped before creating the objective function.

Parameters **x_names** – Parameter names that can be optionally used in, e.g., history or gradient checks.

history

For storing the call history. Initialized by the methods, e.g. the optimizer, in *initialize_history()*.

pre_post_processor

Preprocess input values to and postprocess output values from __call__. Configured in *update_from_problem()*.

__call__(*x: numpy.ndarray*, *sensi_orders: Tuple[int, ...] = (0)*, *mode: str = 'mode_fun'*, *return_dict: bool = False*, ***kwargs*) → Union[float, numpy.ndarray, Tuple, Dict[str, Union[float, numpy.ndarray, Dict]]]

Obtain arbitrary sensitivities.

This is the central method which is always called, also by the get_* methods.

There are different ways in which an optimizer calls the objective function, and in how the objective function provides information (e.g. derivatives via separate functions or along with the function values). The different calling modes increase efficiency in space and time and make the objective flexible.

Parameters

- **x** – The parameters for which to evaluate the objective function.
- **sensi_orders** – Specifies which sensitivities to compute, e.g. (0,1) -> fval, grad.
- **mode** – Whether to compute function values or residuals.
- **return_dict** – If False (default), the result is a Tuple of the requested values in the requested order. Tuples of length one are flattened. If True, instead a dict is returned which can carry further information.

Returns By default, this is a tuple of the requested function values and derivatives in the requested order (if only 1 value, the tuple is flattened). If *return_dict*, then instead a dict is returned with function values and derivatives indicated by ids.

Return type result

__init__(*x_names: Optional[Sequence[str]] = None*)

Initialize self. See help(type(self)) for accurate signature.

abstract call_unprocessed(*x: numpy.ndarray*, *sensi_orders: Tuple[int, ...]*, *mode: str*, ***kwargs*) → Dict[str, Union[float, numpy.ndarray, Dict]]

Call objective function without pre- or post-processing and formatting.

Parameters

- **x** – The parameters for which to evaluate the objective function.
- **sensi_orders** – Specifies which sensitivities to compute, e.g. (0,1) -> fval, grad.
- **mode** – Whether to compute function values or residuals.

Returns A dict containing the results.

Return type result

check_grad(*x: numpy.ndarray*, *x_indices: Optional[Sequence[int]] = None*, *eps: float = 1e-05*, *verbosity: int = 1*, *mode: str = 'mode_fun'*, *order: int = 0*, *detailed: bool = False*) → pandas.core.frame.DataFrame

Compare gradient evaluation.

Firstly approximate via finite differences, and secondly use the objective gradient.

Parameters

- **x** – The parameters for which to evaluate the gradient.
- **x_indices** – Indices for which to compute gradients. Default: all.
- **eps** – Finite differences step size.
- **verbosity** – Level of verbosity for function output. 0: no output, 1: summary for all parameters, 2: summary for individual parameters.

- **mode** – Residual (MODE_RES) or objective function value (MODE_FUN) computation mode.
- **order** – Derivative order, either gradient (0) or Hessian (1).
- **detailed** – Toggle whether additional values are returned. Additional values are function values, and the central difference weighted by the difference in output from all methods (standard deviation and mean).

Returns gradient, finite difference approximations and error estimates.

Return type result

check_grad_multi_eps(**args*, *multi_eps: Optional[Iterable] = None*, *label: str = 'rel_err'*, ***kwargs*)

Compare gradient evaluation.

Equivalent to the *ObjectiveBase.check_grad* method, except multiple finite difference step sizes are tested. The result contains the lowest finite difference for each parameter, and the corresponding finite difference step size.

Parameters

- **ObjectiveBase.check_grad method parameters.** (*All*) –
- **multi_eps** – The finite difference step sizes to be tested.
- **label** – The label of the column that will be minimized for each parameter. Valid options are the column labels of the dataframe returned by the *ObjectiveBase.check_grad* method.

check_gradients_match_finite_differences(**args*, *x: Optional[numpy.ndarray] = None*, *x_free: Optional[Sequence[int]] = None*, *rtol: float = 0.01*, *atol: float = 0.001*, *mode: Optional[str] = None*, *order: int = 0*, *multi_eps=None*, ***kwargs*) → bool

Check if gradients match finite differences (FDs).

Parameters

- **rtol** (*relative error tolerance*) –
- **x** (*The parameters for which to evaluate the gradient*) –
- **x_free** (*Indices for which to compute gradients*) –
- **rtol** –
- **atol** (*absolute error tolerance*) –
- **mode** (*function values or residuals*) –
- **order** (*gradient order, 0 for gradient, 1 for hessian*) –
- **multi_eps** (*multiple test step width for FDs*) –

Returns Indicates whether gradients match (True) FDs or not (False)

Return type bool

check_mode(*mode: str*) → bool

Check if the objective is able to compute in the requested mode.

Either *check_mode* or the *fun_...* functions must be overwritten in derived classes.

Parameters **mode** – Whether to compute function values or residuals.

Returns Boolean indicating whether mode is supported

Return type flag

check_sensi_orders(*sensi_orders: Tuple[int, ...]*, *mode: str*) → bool
Check if the objective is able to compute the requested sensitivities.

Either *check_sensi_orders* or the *fun_...* functions must be overwritten in derived classes.

Parameters

- **sensi_orders** – Specifies which sensitivities to compute, e.g. (0,1) -> fval, grad.
- **mode** – Whether to compute function values or residuals.

Returns Boolean indicating whether combination of sensi_orders and mode is supported

Return type flag

get_config() → dict
Get the configuration information of the objective function.

Return it as a dictonary.

get_fval(*x: numpy.ndarray*) → float
Get the function value at x.

get_grad(*x: numpy.ndarray*) → numpy.ndarray
Get the gradient at x.

get_hess(*x: numpy.ndarray*) → numpy.ndarray
Get the Hessian at x.

get_res(*x: numpy.ndarray*) → numpy.ndarray
Get the residuals at x.

get_sres(*x: numpy.ndarray*) → numpy.ndarray
Get the residual sensitivities at x.

property has_fun
Check whether function is defined.

property has_grad
Check whether gradient is defined.

property has_hess
Check whether Hessian is defined.

property has_hessp

property has_res
Check whether residuals are defined.

property has_sres
Check whether residual sensitivities are defined.

initialize()
Initialize the objective function.

This function is used at the beginning of an analysis, e.g. optimization, and can e.g. reset the objective memory. By default does nothing.

static output_to_tuple(*sensi_orders: Tuple[int, ...]*, *mode: str*, ***kwargs: Union[float, numpy.ndarray]*) → Tuple
Return values as requested by the caller.

Usually only a subset of outputs is demanded. One output is returned as-is, more than one output are returned as a tuple in order (fval, grad, hess).

update_from_problem(*dim_full: int, x_free_indices: Sequence[int], x_fixed_indices: Sequence[int], x_fixed_vals: Sequence[float]*)

Handle fixed parameters.

Later, the objective will be given parameter vectors x of dimension dim, which have to be filled up with fixed parameter values to form a vector of dimension dim_full >= dim. This vector is then used to compute function value and derivatives. The derivatives must later be reduced again to dimension dim.

This is so as to make the fixing of parameters transparent to the caller.

The methods preprocess, postprocess are overwritten for the above functionality, respectively.

Parameters

- **dim_full** – Dimension of the full vector including fixed parameters.
- **x_free_indices** – Vector containing the indices (zero-based) of free parameters (complimentary to x_fixed_indices).
- **x_fixed_indices** – Vector containing the indices (zero-based) of parameter components that are not to be optimized.
- **x_fixed_vals** – Vector of the same length as x_fixed_indices, containing the values of the fixed parameters.

property x_names

Parameter names.

class pypesto.**OptimizeResult**

Bases: object

Result of the *pypesto.optimize.minimize()* function.

__init__()

Initialize self. See help(type(self)) for accurate signature.

append(*optimizer_result: pypesto.result.optimize.OptimizerResult*)

Append an optimizer result to the result object.

Parameters **optimizer_result** – The result of one (local) optimizer run.

as_dataframe(*keys=None*) → pandas.core.frame.DataFrame

Get as pandas DataFrame.

If keys is a list, return only the specified values, otherwise all.

as_list(*keys=None*) → Sequence

Get as list.

If keys is a list, return only the specified values.

Parameters **keys** (*list(str), optional*) – Labels of the field to extract.

get_for_key(*key*) → list

Extract the list of values for the specified key as a list.

sort()

Sort the optimizer results by function value fval (ascending).

class pypesto.**OptimizerHistory**(*history: pypesto.objective.history.History, x0: numpy.ndarray, lb: numpy.ndarray, ub: numpy.ndarray, generate_from_history: bool = False*)

Bases: object

Objective call history.

Container around a History object, which keeps track of optimal values.

fval0, fval_min
Initial and best function value found.

chi20, chi2_min
Initial and best chi2 value found.

x0, x_min
Initial and best parameters found.

grad_min
gradient for best parameters

hess_min
hessian (approximation) for best parameters

res_min
residuals for best parameters

sres_min
residual sensitivities for best parameters

Parameters

- **history** – History object to attach to this container. This history object implements the storage of the actual history.
- **x0** – Initial values for optimization.
- **lb** – Lower and upper bound. Used for checking validity of optimal points.
- **ub** – Lower and upper bound. Used for checking validity of optimal points.
- **generate_from_history** – If set to true, this function will try to fill attributes of this function based on the provided history.

__init__(*history: pypesto.objective.history.History*, *x0: numpy.ndarray*, *lb: numpy.ndarray*, *ub: numpy.ndarray*, *generate_from_history: bool = False*) → None
Initialize self. See help(type(self)) for accurate signature.

extract_from_history(*var: str*, *ix: int*) → bool
Get value of *var* at iteration *ix* and assign to *{var}_min*.

Parameters

- **var** (*Variable to extract, e.g. 'grad', 'x'.*) –
- **ix** (*Trace index.*) –

Returns Whether extraction and assignment worked. False in particular if the history value is nan.

Return type successful

finalize()
Finalize history.

update(*x: numpy.ndarray*, *sensi_orders: Tuple[int]*, *mode: str*, *result: Dict[str, Union[float, numpy.ndarray]]*) → None
Update history and best found value.

class pypesto.**OptimizerResult**(*id: Optional[str] = None*, *x: Optional[numpy.ndarray] = None*, *fval: Optional[float] = None*, *grad: Optional[numpy.ndarray] = None*, *hess: Optional[numpy.ndarray] = None*, *res: Optional[numpy.ndarray] = None*, *sres: Optional[numpy.ndarray] = None*, *n_fval: Optional[int] = None*, *n_grad: Optional[int] = None*, *n_hess: Optional[int] = None*, *n_res: Optional[int] = None*, *n_sres: Optional[int] = None*, *x0: Optional[numpy.ndarray] = None*, *fval0: Optional[float] = None*, *history: Optional[pypesto.objective.history.History] = None*, *exitflag: Optional[int] = None*, *time: Optional[float] = None*, *message: Optional[str] = None*)

Bases: dict

The result of an optimizer run.

Used as a standardized return value to map from the individual result objects returned by the employed optimizers to the format understood by pypesto.

Can be used like a dict.

id
Id of the optimizer run. Usually the start index.

x
The best found parameters.

fval
The best found function value, *fun(x)*.

grad
The gradient at *x*.

hess
The Hessian at *x*.

res
The residuals at *x*.

sres
The residual sensitivities at *x*.

n_fval
Number of function evaluations.

n_grad
Number of gradient evaluations.

n_hess
Number of Hessian evaluations.

n_res
Number of residuals evaluations.

n_sres
Number of residual sensitivity evaluations.

x0
The starting parameters.

fval0
The starting function value, *fun(x0)*.

history
Objective history.

exitflag
The exitflag of the optimizer.

time
Execution time.

message
Textual comment on the optimization result.

Type str

Notes

Any field not supported by the optimizer is filled with None.

__init__(*id: Optional[str] = None*, *x: Optional[numpy.ndarray] = None*, *fval: Optional[float] = None*, *grad: Optional[numpy.ndarray] = None*, *hess: Optional[numpy.ndarray] = None*, *res: Optional[numpy.ndarray] = None*, *sres: Optional[numpy.ndarray] = None*, *n_fval: Optional[int] = None*, *n_grad: Optional[int] = None*, *n_hess: Optional[int] = None*, *n_res: Optional[int] = None*, *n_sres: Optional[int] = None*, *x0: Optional[numpy.ndarray] = None*, *fval0: Optional[float] = None*, *history: Optional[pypesto.objective.history.History] = None*, *exitflag: Optional[int] = None*, *time: Optional[float] = None*, *message: Optional[str] = None*)
Initialize self. See help(type(self)) for accurate signature.

update_to_full(*problem:* pypesto.problem.Problem) → None
Update values to full vectors/matrices.

Parameters **problem** – problem which contains info about how to convert to full vectors or matrices

class pypesto.**PredictionConditionResult**(*timepoints: numpy.ndarray*, *output_ids: Sequence[str]*, *output: Optional[numpy.ndarray] = None*, *output_sensi: Optional[numpy.ndarray] = None*, *output_weight: Optional[float] = None*, *output_sigmay: Optional[numpy.ndarray] = None*, *x_names: Optional[Sequence[str]] = None*)
Bases: object

Light-weight wrapper for the prediction of one simulation condition.

It should provide a common api how amici predictions should look like in pyPESTO.

__init__(*timepoints: numpy.ndarray*, *output_ids: Sequence[str]*, *output: Optional[numpy.ndarray] = None*, *output_sensi: Optional[numpy.ndarray] = None*, *output_weight: Optional[float] = None*, *output_sigmay: Optional[numpy.ndarray] = None*, *x_names: Optional[Sequence[str]] = None*)
Initialize PredictionConditionResult.

Parameters

- **timepoints** – Output timepoints for this simulation condition
- **output_ids** – IDs of outputs for this simulation condition
- **output** – Postprocessed outputs (ndarray)
- **output_sensi** – Sensitivities of postprocessed outputs (ndarray)

- **output_weight** – LLH of the simulation
- **output_sigmay** – Standard deviations of postprocessed observables
- **x_names** – IDs of model parameter w.r.t to which sensitivities were computed

class pypesto.**PredictionResult**(*conditions: Sequence[Union[pypesto.result.predict.PredictionConditionResult, Dict]]*, *condition_ids: Optional[Sequence[str]] = None*, *comment: Optional[str] = None*)

Bases: object

Light-weight wrapper around prediction from pyPESTO made by an AMICI model.

Its only purpose is to have fixed format/api, how prediction results should be stored, read, and handled: as predictions are a very flexible format anyway, they should at least have a common definition, which allows to work with them in a reasonable way.

__init__(*conditions: Sequence[Union[pypesto.result.predict.PredictionConditionResult, Dict]]*, *condition_ids: Optional[Sequence[str]] = None*, *comment: Optional[str] = None*)

Initialize PredictionResult.

Parameters

- **conditions** – A list of PredictionConditionResult objects or dicts
- **condition_ids** – IDs or names of the simulation conditions, which belong to this prediction (e.g., PEtab uses tuples of preequilibration condition and simulation conditions)
- **comment** – An additional note, which can be attached to this prediction

write_to_csv(*output_file: str*)

Save predictions to a csv file.

Parameters **output_file** – path to file/folder to which results will be written

write_to_h5(*output_file: str*, *base_path: Optional[str] = None*)

Save predictions to an h5 file.

It appends to the file if the file already exists.

Parameters

- **output_file** – path to file/folder to which results will be written
- **base_path** – base path in the h5 file

class pypesto.**Problem**(*objective: pypesto.objective.base.ObjectiveBase*, *lb: Union[numpy.ndarray, List[float]]*, *ub: Union[numpy.ndarray, List[float]]*, *dim_full: Optional[int] = None*, *x_fixed_indices: Optional[Union[Iterable[SupportsInt], SupportsInt]] = None*, *x_fixed_vals: Optional[Union[Iterable[SupportsFloat], SupportsFloat]] = None*, *x_guesses: Optional[Iterable[float]] = None*, *x_names: Optional[Iterable[str]] = None*, *x_scales: Optional[Iterable[str]] = None*, *x_priors_defs: Optional[pypesto.objective.priors.NegLogPriors] = None*, *lb_init: Optional[Union[numpy.ndarray, List[float]]] = None*, *ub_init: Optional[Union[numpy.ndarray, List[float]]] = None*, *copy_objective: bool = True*)

Bases: object

The problem formulation.

A problem specifies the objective function, boundaries and constraints, parameter guesses as well as the parameters which are to be optimized.

Parameters

- **objective** – The objective function for minimization. Note that a shallow copy is created.

- **lb** – The lower and upper bounds for optimization. For unbounded directions set to +-inf.
- **ub** – The lower and upper bounds for optimization. For unbounded directions set to +-inf.
- **lb_init** – The lower and upper bounds for initialization, typically for defining search start points. If not set, set to lb, ub.
- **ub_init** – The lower and upper bounds for initialization, typically for defining search start points. If not set, set to lb, ub.
- **dim_full** – The full dimension of the problem, including fixed parameters.
- **x_fixed_indices** – Vector containing the indices (zero-based) of parameter components that are not to be optimized.
- **x_fixed_vals** – Vector of the same length as x_fixed_indices, containing the values of the fixed parameters.
- **x_guesses** – Guesses for the parameter values, shape (g, dim), where g denotes the number of guesses. These are used as start points in the optimization.
- **x_names** – Parameter names that can be optionally used e.g. in visualizations. If objective.get_x_names() is not None, those values are used, else the values specified here are used if not None, otherwise the variable names are set to ['x0', ... 'x{dim_full}']. The list must always be of length dim_full.
- **x_scales** – Parameter scales can be optionally given and are used e.g. in visualisation and prior generation. Currently the scales 'lin', 'log`and 'log10' are supported.
- **x_priors_defs** – Definitions of priors for parameters. Types of priors, and their required and optional parameters, are described in the *Prior* class.
- **copy_objective** – Whethter to generate a deep copy of the objective function before potential modification the problem class performs on it.

Notes

On the fixing of parameter values:

The number of parameters dim_full the objective takes as input must be known, so it must be either lb a vector of that size, or dim_full specified as a parameter.

All vectors are mapped to the reduced space of dimension dim in __init__, regardless of whether they were in dimension dim or dim_full before. If the full representation is needed, the methods get_full_vector() and get_full_matrix() can be used.

__init__(*objective: pypesto.objective.base.ObjectiveBase*, *lb: Union[numpy.ndarray, List[float]]*, *ub: Union[numpy.ndarray, List[float]]*, *dim_full: Optional[int] = None*, *x_fixed_indices: Optional[Union[Iterable[SupportsInt], SupportsInt]] = None*, *x_fixed_vals: Optional[Union[Iterable[SupportsFloat], SupportsFloat]] = None*, *x_guesses: Optional[Iterable[float]] = None*, *x_names: Optional[Iterable[str]] = None*, *x_scales: Optional[Iterable[str]] = None*, *x_priors_defs: Optional[pypesto.objective.priors.NegLogPriors] = None*, *lb_init: Optional[Union[numpy.ndarray, List[float]]] = None*, *ub_init: Optional[Union[numpy.ndarray, List[float]]] = None*, *copy_objective: bool = True*)

Initialize self. See help(type(self)) for accurate signature.

property dim

Return dimension only considering non fixed parameters.

fix_parameters(*parameter_indices: Union[Iterable[SupportsInt], SupportsInt]*, *parameter_vals: Union[Iterable[SupportsFloat], SupportsFloat]*) → None
Fix specified parameters to specified values.

full_index_to_free_index(*full_index: int*)
Calculate index in reduced vector from index in full vector.

Parameters **full_index** (*The index in the full vector.*) –

Returns free_index

Return type The index in the free vector.

get_full_matrix(*x: Optional[numpy.ndarray]*) → Optional[numpy.ndarray]
Map matrix from dim to dim_full. Usually used for hessian.

Parameters **x** (*array_like, shape=(dim, dim)*) – The matrix in dimension dim.

get_full_vector(*x: Optional[numpy.ndarray]*, *x_fixed_vals: Optional[Iterable[float]] = None*) → Optional[numpy.ndarray]
Map vector from dim to dim_full. Usually used for x, grad.

Parameters

- **x** (*array_like, shape=(dim,)*) – The vector in dimension dim.
- **x_fixed_vals** (*array_like, ndim=1, optional*) – The values to be used for the fixed indices. If None, then nans are inserted. Usually, None will be used for grad and problem.x_fixed_vals for x.

get_reduced_matrix(*x_full: Optional[numpy.ndarray]*) → Optional[numpy.ndarray]
Map matrix from dim_full to dim, i.e. delete fixed indices.

Parameters **x_full** (*array_like, ndim=2*) – The matrix in dimension dim_full.

get_reduced_vector(*x_full: Optional[numpy.ndarray]*, *x_indices: Optional[List[int]] = None*) → Optional[numpy.ndarray]
Keep only those elements, which indices are specified in x_indices.

If x_indices is not provided, delete fixed indices.

Parameters

- **x_full** (*array_like, ndim=1*) – The vector in dimension dim_full.
- **x_indices** – indices of x_full that should remain

property lb
Return lower bounds of free parameters.

property lb_init
Return initial lower bounds of free parameters.

normalize() → None
Process vectors.

Reduce all vectors to dimension dim and have the objective accept vectors of dimension dim.

print_parameter_summary() → None
Print a summary of parameters.

Include what parameters are being optimized and parameter boundaries.

set_x_guesses(*x_guesses: Iterable[float]*)
Set the x_guesses of a problem.

Parameters **x_guesses** –

property ub
Return upper bounds of free parameters.

property ub_init
Return initial upper bounds of free parameters.

unfix_parameters(*parameter_indices: Union[Iterable[SupportsInt], SupportsInt]*) → None
Free specified parameters.

property x_free_indices
Return non fixed parameters.

property x_guesses
Return guesses of the free parameter values.

class pypesto.**ProfileResult**
Bases: object

Result of the profile() function.

It holds a list of profile lists. Each profile list consists of a list of *ProfilerResult* objects, one for each parameter.

__init__()
Initialize self. See help(type(self)) for accurate signature.

append_empty_profile_list() → int
Append an empty profile list to the list of profile lists.

Returns The index of the created profile list.

Return type index

append_profiler_result(*profiler_result: Optional[pypesto.result.profile.ProfilerResult] = None*, *profile_list: Optional[int] = None*) → None
Append the profiler result to the profile list.

Parameters

- **profiler_result** – The result of one profiler run for a parameter, or None if to be left empty.
- **profile_list** – Index specifying the profile list to which we want to append. Defaults to the last list.

get_profiler_result(*i_par: int*, *profile_list: Optional[int] = None*)
Get the profiler result at parameter index *i_par* of *profile_list*.

Parameters

- **i_par** – Integer specifying the profile index.
- **profile_list** – Index specifying the profile list. Defaults to the last list.

set_profiler_result(*profiler_result: pypesto.result.profile.ProfilerResult*, *i_par: int*, *profile_list: Optional[int] = None*) → None
Write a profiler result to the result object.

Parameters

- **profiler_result** – The result of one (local) profiler run.
- **i_par** – Integer specifying the parameter index where to put profiler_result.
- **profile_list** – Index specifying the profile list. Defaults to the last list.

class pypesto.**ProfilerResult**(*x_path: numpy.ndarray*, *fval_path: numpy.ndarray*, *ratio_path: numpy.ndarray*, *gradnorm_path: numpy.ndarray = nan*, *exitflag_path: numpy.ndarray = nan*, *time_path: numpy.ndarray = nan*, *time_total: float = 0.0*, *n_fval: int = 0*, *n_grad: int = 0*, *n_hess: int = 0*, *message: Optional[str] = None*)

Bases: dict

The result of a profiler run.

The standardized return value from pypesto.profile, which can either be initialized from an OptimizerResult or from an existing ProfilerResult (in order to extend the computation).

Can be used like a dict.

x_path
The path of the best found parameters along the profile (Dimension: n_par x n_profile_points)

fval_path
The function values, fun(x), along the profile.

ratio_path
The ratio of the posterior function along the profile.

gradnorm_path
The gradient norm along the profile.

exitflag_path
The exitflags of the optimizer along the profile.

time_path
The computation time of the optimizer runs along the profile.

time_total
The total computation time for the profile.

n_fval
Number of function evaluations.

n_grad
Number of gradient evaluations.

n_hess
Number of Hessian evaluations.

message
Textual comment on the profile result.

Notes

Any field not supported by the profiler or the profiling optimizer is filled with None. Some fields are filled by pypesto itself.

__init__(*x_path: numpy.ndarray*, *fval_path: numpy.ndarray*, *ratio_path: numpy.ndarray*, *gradnorm_path: numpy.ndarray = nan*, *exitflag_path: numpy.ndarray = nan*, *time_path: numpy.ndarray = nan*, *time_total: float = 0.0*, *n_fval: int = 0*, *n_grad: int = 0*, *n_hess: int = 0*, *message: Optional[str] = None*)
Initialize self. See help(type(self)) for accurate signature.

append_profile_point(*x: numpy.ndarray*, *fval: float*, *ratio: float*, *gradnorm: float = nan*, *time: float = nan*, *exitflag: float = nan*, *n_fval: int = 0*, *n_grad: int = 0*, *n_hess: int = 0*) → None
Append a new point to the profile path.

Parameters

- **x** – The parameter values.
- **fval** – The function value at *x*.
- **ratio** – The ratio of the function value at *x* by the optimal function value.
- **gradnorm** – The gradient norm at *x*.
- **time** – The computation time to find *x*.
- **exitflag** – The exitflag of the optimizer (useful if an optimization was performed to find *x*).
- **n_fval** – Number of function evaluations performed to find *x*.
- **n_grad** – Number of gradient evaluations performed to find *x*.
- **n_hess** – Number of Hessian evaluations performed to find *x*.

flip_profile() → None
Flip the profiling direction (left-right).

Profiling direction needs to be changed once (if the profile is new), or twice if we append to an existing profile. All profiling paths are flipped in-place.

class pypesto.**Result**(*problem=None*)
Bases: object

Universal result object for pypesto.

The algorithms like optimize, profile, sample fill different parts of it.

problem
The problem underlying the results.

Type *pypesto.Problem*

optimize_result
The results of the optimizer runs.

profile_result
The results of the profiler run.

sample_result
The results of the sampler run.

__init__(*problem=None*)
Initialize self. See help(type(self)) for accurate signature.

class pypesto.**SampleResult**
Bases: object

Result of the sample() function.

__init__()
Initialize self. See help(type(self)) for accurate signature.

4.2 Objective

class pypesto.objective.**AggregatedObjective**(*objectives: Sequence[pypesto.objective.base.ObjectiveBase]*, *x_names: Optional[Sequence[str]] = None*)

Bases: pypesto.objective.base.ObjectiveBase

Aggregates multiple objectives into one objective.

__init__(*objectives: Sequence[pypesto.objective.base.ObjectiveBase]*, *x_names: Optional[Sequence[str]] = None*)

Initialize objective.

Parameters

- **objectives** – Sequence of pypesto.ObjectiveBase instances
- **x_names** – Sequence of names of the (optimized) parameters. (Details see documentation of x_names in *pypesto.ObjectiveBase*)

call_unprocessed(*x: numpy.ndarray*, *sensi_orders: Tuple[int, ...]*, *mode: str*, ***kwargs*) → Dict[str, Union[float, numpy.ndarray, Dict]]

See *ObjectiveBase* for more documentation.

Main method to overwrite from the base class. It handles and delegates the actual objective evaluation.

check_mode(*mode: str*) → bool

See *ObjectiveBase* documentation.

check_sensi_orders(*sensi_orders: Tuple[int, ...]*, *mode: str*) → bool

See *ObjectiveBase* documentation.

get_config() → dict

Return basic information of the objective configuration.

initialize()

See *ObjectiveBase* documentation.

class pypesto.objective.**AmiciCalculator**

Bases: object

Class to perform the AMICI call and obtain objective function values.

__call__(*x_dct: Dict*, *sensi_orders: Tuple[int]*, *mode: str*, *amici_model: Union[amici.Model, amici.ModelPtr]*, *amici_solver: Union[amici.Solver, amici.SolverPtr]*, *edatas: List[amici.ExpData]*, *n_threads: int*, *x_ids: Sequence[str]*, *parameter_mapping: ParameterMapping*, *fim_for_hess: bool*)

Perform the actual AMICI call.

Called within the AmiciObjective.__call__() method.

Parameters

- **x_dct** – Parameters for which to compute function value and derivatives.
- **sensi_orders** – Tuple of requested sensitivity orders.
- **mode** – Call mode (function value or residual based).
- **amici_model** – The AMICI model.
- **amici_solver** – The AMICI solver.
- **edatas** – The experimental data.

- **n_threads** – Number of threads for AMICI call.
- **x_ids** – Ids of optimization parameters.
- **parameter_mapping** – Mapping of optimization to simulation parameters.
- **fim_for_hess** – Whether to use the FIM (if available) instead of the Hessian (if requested).

__init__()
Initialize self. See help(type(self)) for accurate signature.

initialize()
Initialize the calculator. Default: Do nothing.

class pypesto.objective.**AmiciObjectBuilder**
Bases: abc.ABC

Allows to build AMICI model, solver, and edatas.

This class is useful for pickling an *pypesto.AmiciObjective*, which is required in some parallelization schemes. Therefore, this class itself must be picklable.

abstract create_edatas(*model: Union[amici.Model, amici.ModelPtr]*) → Sequence[amici.ExpData]
Create AMICI experimental data.

abstract create_model() → Union[amici.Model, amici.ModelPtr]
Create an AMICI model.

abstract create_solver(*model: Union[amici.Model, amici.ModelPtr]*) → Union[amici.Solver, amici.SolverPtr]
Create an AMICI solver.

class pypesto.objective.**AmiciObjective**(*amici_model: Union[amici.Model, amici.ModelPtr]*, *amici_solver: Union[amici.Solver, amici.SolverPtr]*, *edatas: Union[Sequence[amici.ExpData], amici.ExpData]*, *max_sensi_order: Optional[int] = None*, *x_ids: Optional[Sequence[str]] = None*, *x_names: Optional[Sequence[str]] = None*, *parameter_mapping: Optional[ParameterMapping] = None*, *guess_steadystate: Optional[bool] = None*, *n_threads: Optional[int] = 1*, *fim_for_hess: Optional[bool] = True*, *amici_object_builder: Optional[pypesto.objective.amici.AmiciObjectBuilder] = None*, *calculator: Optional[pypesto.objective.amici_calculator.AmiciCalculator] = None*)
Bases: pypesto.objective.base.ObjectiveBase

Allows to create an objective directly from an amici model.

__init__(*amici_model: Union[amici.Model, amici.ModelPtr]*, *amici_solver: Union[amici.Solver, amici.SolverPtr]*, *edatas: Union[Sequence[amici.ExpData], amici.ExpData]*, *max_sensi_order: Optional[int] = None*, *x_ids: Optional[Sequence[str]] = None*, *x_names: Optional[Sequence[str]] = None*, *parameter_mapping: Optional[ParameterMapping] = None*, *guess_steadystate: Optional[bool] = None*, *n_threads: Optional[int] = 1*, *fim_for_hess: Optional[bool] = True*, *amici_object_builder: Optional[pypesto.objective.amici.AmiciObjectBuilder] = None*, *calculator: Optional[pypesto.objective.amici_calculator.AmiciCalculator] = None*)
Initialize objective.

Parameters

- **amici_model** – The amici model.
- **amici_solver** – The solver to use for the numeric integration of the model.
- **edatas** – The experimental data. If a list is passed, its entries correspond to multiple experimental conditions.
- **max_sensi_order** – Maximum sensitivity order supported by the model. Defaults to 2 if the model was compiled with o2mode, otherwise 1.
- **x_ids** – Ids of optimization parameters. In the simplest case, this will be the AMICI model parameters (default).
- **x_names** – Names of optimization parameters.
- **parameter_mapping** – Mapping of optimization parameters to model parameters. Format as created by *amici.petab_objective.create_parameter_mapping*. The default is just to assume that optimization and simulation parameters coincide.
- **guess_steadystate** – Whether to guess steadystates based on previous steadystates and respective derivatives. This option may lead to unexpected results for models with conservation laws and should accordingly be deactivated for those models.
- **n_threads** – Number of threads that are used for parallelization over experimental conditions. If amici was not installed with openMP support this option will have no effect.
- **fim_for_hess** – Whether to use the FIM whenever the Hessian is requested. This only applies with forward sensitivities. With adjoint sensitivities, the true Hessian will be used, if available. FIM or Hessian will only be exposed if *max_sensi_order>1*.
- **amici_object_builder** – AMICI object builder. Allows recreating the objective for pickling, required in some parallelization schemes.
- **calculator** – Performs the actual calculation of the function values and derivatives.

apply_custom_timepoints() → None
Apply custom timepoints, if applicable.

See the *set_custom_timepoints* method for more information.

apply_steadystate_guess(*condition_ix: int*, *x_dct: Dict*) → None
Apply steady state guess to *edatas[condition_ix].x0*.

Use the stored steadystate as well as the respective sensitivity (if available) and parameter value to approximate the steadystate at the current parameters using a zeroth or first order taylor approximation: x_ss(x') = x_ss(x) [+ dx_ss/dx(x)*(x'-x)]

call_unprocessed(*x: numpy.ndarray*, *sensi_orders: Tuple[int, ...]*, *mode: str*, *edatas: Sequence[amici.ExpData] = None*, *parameter_mapping: ParameterMapping = None*)
Call objective function without pre- or post-processing and formatting.

Returns A dict containing the results.

Return type result

check_gradients_match_finite_differences(*x: Optional[numpy.ndarray] = None*, **args*, ***kwargs*) → bool
Check if gradients match finite differences (FDs).

Parameters **x** (*The parameters for which to evaluate the gradient.*) –

Returns Indicates whether gradients match (True) FDs or not (False)

Return type bool

check_mode(*mode: str*) → bool
See *ObjectiveBase* documentation.

check_sensi_orders(*sensi_orders: Tuple[int, ...]*, *mode: str*) → bool
See *ObjectiveBase* documentation.

get_config() → dict
Return basic information of the objective configuration.

initialize()
See *ObjectiveBase* documentation.

par_arr_to_dct(*x: Sequence[float]*) → Dict[str, float]
Create dict from parameter vector.

reset_steadystate_guesses() → None
Reset all steadystate guess data.

set_custom_timepoints(*timepoints: Optional[Sequence[Sequence[Union[float, int]]]] = None*, *timepoints_global: Optional[Sequence[Union[float, int]]] = None*) → pypesto.objective.amici.AmiciObjective
Create a copy of this objective that is evaluated at custom timepoints.

The intended use is to aid in predictions at unmeasured timepoints.

Parameters

- **timepoints** – The outer sequence should contain a sequence of timepoints for each experimental condition.
- **timepoints_global** – A sequence of timepoints that will be used for all experimental conditions.

Returns

Return type The customized copy of this objective.

store_steadystate_guess(*condition_ix: int*, *x_dct: Dict*, *rdata: amici.ReturnData*) → None
Store condition parameter, steadystate and steadystate sensitivity.

Stored in steadystate_guesses if steadystate guesses are enabled for this condition.

class pypesto.objective.**CsvHistory**(*file: str*, *x_names: Optional[Sequence[str]] = None*, *options: Optional[Union[pypesto.objective.history.HistoryOptions, Dict]] = None*, *load_from_file: bool = False*)
Bases: pypesto.objective.history.History

Stores a representation of the history in a CSV file.

Parameters

- **file** – CSV file name.
- **x_names** – Parameter names.
- **options** – History options.
- **load_from_file** – If True, history will be initialized from data in the specified file

__init__(*file: str*, *x_names: Optional[Sequence[str]] = None*, *options: Optional[Union[pypesto.objective.history.HistoryOptions, Dict]] = None*, *load_from_file: bool = False*)
Initialize self. See help(type(self)) for accurate signature.

finalize()
Finalize history. Called after a run.

get_chi2_trace(*ix: Optional[Union[Sequence[int], int]] = None*, *trim: bool = False*) → Union[Sequence[Union[float, numpy.ndarray, np.nan]], float, numpy.ndarray, np.nan]
Chi2 values.

Takes as parameter an index or indices and returns corresponding trace values. If only a single value is requested, the list is flattened.

get_fval_trace(*ix: Optional[Union[Sequence[int], int]] = None*, *trim: bool = False*) → Union[Sequence[Union[float, numpy.ndarray, np.nan]], float, numpy.ndarray, np.nan]
Return function values.

Takes as parameter an index or indices and returns corresponding trace values. If only a single value is requested, the list is flattened.

get_grad_trace(*ix: Optional[Union[Sequence[int], int]] = None*, *trim: bool = False*) → Union[Sequence[Union[float, numpy.ndarray, np.nan]], float, numpy.ndarray, np.nan]
Return gradients.

Takes as parameter an index or indices and returns corresponding trace values. If only a single value is requested, the list is flattened.

get_hess_trace(*ix: Optional[Union[Sequence[int], int]] = None*, *trim: bool = False*) → Union[Sequence[Union[float, numpy.ndarray, np.nan]], float, numpy.ndarray, np.nan]
Return hessians.

Takes as parameter an index or indices and returns corresponding trace values. If only a single value is requested, the list is flattened.

get_res_trace(*ix: Optional[Union[Sequence[int], int]] = None*, *trim: bool = False*) → Union[Sequence[Union[float, numpy.ndarray, np.nan]], float, numpy.ndarray, np.nan]
Residuals.

Takes as parameter an index or indices and returns corresponding trace values. If only a single value is requested, the list is flattened.

get_schi2_trace(*ix: Optional[Union[Sequence[int], int]] = None*, *trim: bool = False*) → Union[Sequence[Union[float, numpy.ndarray, np.nan]], float, numpy.ndarray, np.nan]
Chi2 sensitivities.

Takes as parameter an index or indices and returns corresponding trace values. If only a single value is requested, the list is flattened.

get_sres_trace(*ix: Optional[Union[Sequence[int], int]] = None*, *trim: bool = False*) → Union[Sequence[Union[float, numpy.ndarray, np.nan]], float, numpy.ndarray, np.nan]
Residual sensitivities.

Takes as parameter an index or indices and returns corresponding trace values. If only a single value is requested, the list is flattened.

get_time_trace(*ix: Optional[Union[Sequence[int], int]] = None*, *trim: bool = False*) → Union[Sequence[Union[float, numpy.ndarray, np.nan]], float, numpy.ndarray, np.nan]
Cumulative execution times.

Takes as parameter an index or indices and returns corresponding trace values. If only a single value is requested, the list is flattened.

get_x_trace(*ix: Optional[Union[Sequence[int], int]] = None*, *trim: bool = False*) → Union[Sequence[Union[float, numpy.ndarray, np.nan]], float, numpy.ndarray, np.nan]
Return parameters.

Takes as parameter an index or indices and returns corresponding trace values. If only a single value is requested, the list is flattened.

update(*x: numpy.ndarray*, *sensi_orders: Tuple[int, ...]*, *mode: str*, *result: Dict[str, Union[float, numpy.ndarray]]*) → None
See *History* docstring.

class pypesto.objective.**FD**(*obj: pypesto.objective.base.ObjectiveBase*, *grad: Optional[bool] = None*, *hess: Optional[bool] = None*, *sres: Optional[bool] = None*, *hess_via_fval: bool = True*, *delta_fun: Union[pypesto.objective.finite_difference.FDDelta, numpy.ndarray, float, str] = 1e-06*, *delta_grad: Union[pypesto.objective.finite_difference.FDDelta, numpy.ndarray, float, str] = 1e-06*, *delta_res: Union[pypesto.objective.finite_difference.FDDelta, float, numpy.ndarray, str] = 1e-06*, *method: str = 'central'*, *x_names: Optional[List[str]] = None*)
Bases: pypesto.objective.base.ObjectiveBase

Finite differences (FDs) for derivatives.

Given an objective that gives function values and/or residuals, this class allows to flexibly obtain all derivatives calculated via FDs.

For the parameters *grad*, *hess*, *sres*, a value of None means that the objective derivative is used if available, otherwise resorting to FDs. True means that FDs are used in any case, False means that the derivative is not exported.

Note that the step sizes should be carefully chosen. They should be small enough to provide an accurate linear approximation, but large enough to be robust against numerical inaccuracies, in particular if the objective relies on numerical approximations, such as an ODE.

Parameters

- **grad** (*Optional[bool]*) – Derivative method for the gradient (see above).
- **hess** (*Optional[bool]*) – Derivative method for the Hessian (see above).
- **sres** (*Optional[bool]*) – Derivative method for the residual sensitivities (see above).
- **hess_via_fval** (*bool*) – If the Hessian is to be calculated via finite differences: whether to employ 2nd order FDs via fval even if the objective can provide a gradient.
- **delta_fun** (*pypesto.objective.finite_difference.FDDelta*) – FD step sizes for function values. Can be either a float, or a `np.ndarray` of shape (n_par,) for different step sizes for different coordinates.
- **delta_grad** (*pypesto.objective.finite_difference.FDDelta*) – FD step sizes for gradients, if the Hessian is calculated via 1st order sensitivities from the gradients. Similar to *delta_fun*.
- **delta_res** (*pypesto.objective.finite_difference.FDDelta*) – FD step sizes for residuals. Similar to *delta_fun*.

- **method** (*str*) – Method to calculate FDs. Can be any of *FD.METHODS*: central, forward or backward differences. The latter two require only roughly half as many function evaluations, are however less accurate than central (O(x) vs O(x**2)).
- **x_names** – Parameter names that can be optionally used in, e.g., history or gradient checks.

Examples

Define residuals and objective function, and obtain all derivatives via FDs:

```
>>> from pypesto import Objective, FD
>>> import numpy as np
>>> x_obs = np.array([11, 12, 13])
>>> res = lambda x: x - x_obs
>>> fun = lambda x: 0.5 * sum(res(x)**2)
>>> obj = FD(Objective(fun=fun, res=res))
```

BACKWARD = 'backward'

CENTRAL = 'central'

FORWARD = 'forward'

METHODS = ['central', 'forward', 'backward']

__init__(*obj: pypesto.objective.base.ObjectiveBase*, *grad: Optional[bool] = None*, *hess: Optional[bool] = None*, *sres: Optional[bool] = None*, *hess_via_fval: bool = True*, *delta_fun: Union[pypesto.objective.finite_difference.FDDelta, numpy.ndarray, float, str] = 1e-06*, *delta_grad: Union[pypesto.objective.finite_difference.FDDelta, numpy.ndarray, float, str] = 1e-06*, *delta_res: Union[pypesto.objective.finite_difference.FDDelta, float, numpy.ndarray, str] = 1e-06*, *method: str = 'central'*, *x_names: Optional[List[str]] = None*)

Initialize self. See help(type(self)) for accurate signature.

call_unprocessed(*x: numpy.ndarray*, *sensi_orders: Tuple[int, ...]*, *mode: str*, ***kwargs*) → Dict[str, Union[float, numpy.ndarray, Dict]]

See *ObjectiveBase* for more documentation.

Main method to overwrite from the base class. It handles and delegates the actual objective evaluation.

delta_fun: pypesto.objective.finite_difference.FDDelta

delta_grad: pypesto.objective.finite_difference.FDDelta

delta_res: pypesto.objective.finite_difference.FDDelta

grad: Optional[bool]

property has_fun

Check whether function is defined.

property has_grad

Check whether gradient is defined.

property has_hess

Check whether Hessian is defined.

property has_res

Check whether residuals are defined.

property has_sres

Check whether residual sensitivities are defined.

hess: Optional[bool]

hess_via_fval: bool

method: str

obj: pypesto.objective.base.ObjectiveBase

sres: Optional[bool]

class pypesto.objective.**FDDelta**(*delta: Optional[Union[numpy.ndarray, float]] = None, test_deltas: Optional[numpy.ndarray] = None, update_condition: str = 'constant', max_distance: float = 0.5, max_steps: int = 30*)

Bases: object

Finite difference step size with automatic updating.

Reference implementation: https://github.com/ICB-DCM/PESTO/blob/master/private/getStepSizeFD.m

Parameters

- **delta** (*Optional[Union[numpy.ndarray, float]]*) – (Initial) step size, either a float, or a vector of size (n_par,). If not None, this is used as initial step size.
- **test_deltas** (*numpy.ndarray*) – Step sizes to try out in step size selection. If None, a range [1e-1, 1e-2, . . . , 1e-8] is considered.
- **update_condition** (*str*) – A "good" step size may be a local property. Thus, this class allows updating the step size if certain criteria are met, in the pypesto.objective.finite_difference.FDDelta.update() function. FDDelta.CONSTANT means that the step size is only initially selected. FDDelta.DISTANCE means that the step size is updated if the current evaluation point is sufficiently far away from the last training point. FDDelta.STEPS means that the step size is updated *max_steps* evaluations after the last update. FDDelta.ALWAYS mean that the step size is selected in every call.
- **max_distance** (*float*) – Coefficient on the distance between current and reference point beyond which to update, in the *FDDelta.DISTANCE* update condition.
- **max_steps** (*int*) – Number of steps after which to update in the *FDDelta.STEPS* update condition.

ALWAYS = 'always'

CONSTANT = 'constant'

DISTANCE = 'distance'

STEPS = 'steps'

UPDATE_CONDITIONS = ['constant', 'distance', 'steps', 'always']

__init__(*delta: Optional[Union[numpy.ndarray, float]] = None, test_deltas: Optional[numpy.ndarray] = None, update_condition: str = 'constant', max_distance: float = 0.5, max_steps: int = 30*)

Initialize self. See help(type(self)) for accurate signature.

delta: Optional[Union[numpy.ndarray, float]]

get() → numpy.ndarray

Get delta vector.

max_distance: float

max_steps: int

steps: int

test_deltas: numpy.ndarray

update(*x: numpy.ndarray*, *fval: Optional[Union[float, numpy.ndarray]]*, *fun: Callable*, *fd_method: str*) → None
Update delta if update conditions are met.

Parameters

- **x** – Current parameter vector, shape (n_par,).
- **fval** – fun(x), to avoid re-evaluation. Scalar- or vector-valued.
- **fun** – Function whose 1st-order derivative to approximate. Scalar- or vector-valued.
- **fd_method** – FD method employed by `pypesto.objective.finite_difference.FD`, see there.

update_condition: str

updates: int

x0: Optional[numpy.ndarray]

class pypesto.objective.**Hdf5History**(*id: str*, *file: str*, *options: Optional[Union[pypesto.objective.history.HistoryOptions, Dict]] = None*)
Bases: pypesto.objective.history.History

Stores a representation of the history in an HDF5 file.

Parameters

- **id** – Id of the history
- **file** – HDF5 file name.
- **options** – History options.

__init__(*id: str*, *file: str*, *options: Optional[Union[pypesto.objective.history.HistoryOptions, Dict]] = None*)
Initialize self. See help(type(self)) for accurate signature.

finalize()
See *History* docstring.

get_chi2_trace(*ix: Optional[Union[Sequence[int], int]] = None*, *trim: bool = False*) → Union[Sequence[Union[float, numpy.ndarray, np.nan]], float, numpy.ndarray, np.nan]
Chi2 values.

Takes as parameter an index or indices and returns corresponding trace values. If only a single value is requested, the list is flattened.

get_fval_trace(*ix: Optional[Union[Sequence[int], int]] = None*, *trim: bool = False*) → Union[Sequence[Union[float, numpy.ndarray, np.nan]], float, numpy.ndarray, np.nan]
Return function values.

Takes as parameter an index or indices and returns corresponding trace values. If only a single value is requested, the list is flattened.

get_grad_trace(*ix: Optional[Union[Sequence[int], int]] = None*, *trim: bool = False*) → Union[Sequence[Union[float, numpy.ndarray, np.nan]], float, numpy.ndarray, np.nan]
Return gradients.

Takes as parameter an index or indices and returns corresponding trace values. If only a single value is requested, the list is flattened.

get_hess_trace(*ix: Optional[Union[Sequence[int], int]] = None*, *trim: bool = False*) → Union[Sequence[Union[float, numpy.ndarray, np.nan]], float, numpy.ndarray, np.nan]

Return hessians.

Takes as parameter an index or indices and returns corresponding trace values. If only a single value is requested, the list is flattened.

get_history_directory()

Return filepath.

get_res_trace(*ix: Optional[Union[Sequence[int], int]] = None*, *trim: bool = False*) → Union[Sequence[Union[float, numpy.ndarray, np.nan]], float, numpy.ndarray, np.nan]

Residuals.

Takes as parameter an index or indices and returns corresponding trace values. If only a single value is requested, the list is flattened.

get_schi2_trace(*ix: Optional[Union[Sequence[int], int]] = None*, *trim: bool = False*) → Union[Sequence[Union[float, numpy.ndarray, np.nan]], float, numpy.ndarray, np.nan]

Chi2 sensitivities.

Takes as parameter an index or indices and returns corresponding trace values. If only a single value is requested, the list is flattened.

get_sres_trace(*ix: Optional[Union[Sequence[int], int]] = None*, *trim: bool = False*) → Union[Sequence[Union[float, numpy.ndarray, np.nan]], float, numpy.ndarray, np.nan]

Residual sensitivities.

Takes as parameter an index or indices and returns corresponding trace values. If only a single value is requested, the list is flattened.

get_time_trace(*ix: Optional[Union[Sequence[int], int]] = None*, *trim: bool = False*) → Union[Sequence[Union[float, numpy.ndarray, np.nan]], float, numpy.ndarray, np.nan]

Cumulative execution times.

Takes as parameter an index or indices and returns corresponding trace values. If only a single value is requested, the list is flattened.

get_x_trace(*ix: Optional[Union[Sequence[int], int]] = None*, *trim: bool = False*) → Union[Sequence[Union[float, numpy.ndarray, np.nan]], float, numpy.ndarray, np.nan]

Return parameters.

Takes as parameter an index or indices and returns corresponding trace values. If only a single value is requested, the list is flattened.

static load(*id: str*, *file: str*)

Load the History object from memory.

property n_fval

See *HistoryBase* docstring.

property n_grad

See *HistoryBase* docstring.

property n_hess
See *HistoryBase* docstring.

property n_res
See *HistoryBase* docstring.

property n_sres
See *HistoryBase* docstring.

recover_options(*file: str*)
Recover options when loading the hdf5 history from memory.

Done by testing which entries were recorded.

property trace_save_iter
After how many iterations to store the trace.

update(*x: numpy.ndarray*, *sensi_orders: Tuple[int, ...]*, *mode: str*, *result: Dict[str, Union[float, numpy.ndarray]]*) → None
See *History* docstring.

class pypesto.objective.**History**(*options: Optional[Union[pypesto.objective.history.HistoryOptions, Dict]] = None*)
Bases: pypesto.objective.history.HistoryBase

Track number of function evaluations only, no trace.

Parameters **options** – History options.

__init__(*options: Optional[Union[pypesto.objective.history.HistoryOptions, Dict]] = None*)
Initialize self. See help(type(self)) for accurate signature.

finalize()
See *HistoryBase* docstring.

property n_fval
See *HistoryBase* docstring.

property n_grad
See *HistoryBase* docstring.

property n_hess
See *HistoryBase* docstring.

property n_res
See *HistoryBase* docstring.

property n_sres
See *HistoryBase* docstring.

property start_time
See *HistoryBase* docstring.

update(*x: numpy.ndarray*, *sensi_orders: Tuple[int, ...]*, *mode: str*, *result: Dict[str, Union[float, numpy.ndarray]]*) → None
Update history after a function evaluation.

Parameters

- **x** – The parameter vector.
- **sensi_orders** – The sensitivity orders computed.
- **mode** – The objective function mode computed (function value or residuals).

- **result** – The objective function values for parameters *x*, sensitivities *sensi_orders* and mode *mode*.

class pypesto.objective.**HistoryBase**

Bases: abc.ABC

Abstract base class for history objects.

Can be used as a dummy history, but does not implement any history functionality.

finalize()

Finalize history. Called after a run.

get_chi2_trace(*ix: Optional[Union[Sequence[int], int]] = None*, *trim: bool = False*) → Union[Sequence[float], float]

Chi2 values.

Takes as parameter an index or indices and returns corresponding trace values. If only a single value is requested, the list is flattened.

get_fval_trace(*ix: Optional[Union[Sequence[int], int]] = None*, *trim: bool = False*) → Union[Sequence[float], float]

Return function values.

Takes as parameter an index or indices and returns corresponding trace values. If only a single value is requested, the list is flattened.

get_grad_trace(*ix: Optional[Union[int, Sequence[int]]] = None*, *trim: bool = False*) → Union[Sequence[Union[numpy.ndarray, np.nan]], numpy.ndarray, np.nan]

Return gradients.

Takes as parameter an index or indices and returns corresponding trace values. If only a single value is requested, the list is flattened.

get_hess_trace(*ix: Optional[Union[int, Sequence[int]]] = None*, *trim: bool = False*) → Union[Sequence[Union[numpy.ndarray, np.nan]], numpy.ndarray, np.nan]

Return hessians.

Takes as parameter an index or indices and returns corresponding trace values. If only a single value is requested, the list is flattened.

get_res_trace(*ix: Optional[Union[int, Sequence[int]]] = None*, *trim: bool = False*) → Union[Sequence[Union[numpy.ndarray, np.nan]], numpy.ndarray, np.nan]

Residuals.

Takes as parameter an index or indices and returns corresponding trace values. If only a single value is requested, the list is flattened.

get_schi2_trace(*ix: Optional[Union[int, Sequence[int]]] = None*, *trim: bool = False*) → Union[Sequence[Union[numpy.ndarray, np.nan]], numpy.ndarray, np.nan]

Chi2 sensitivities.

Takes as parameter an index or indices and returns corresponding trace values. If only a single value is requested, the list is flattened.

get_sres_trace(*ix: Optional[Union[int, Sequence[int]]] = None*, *trim: bool = False*) → Union[Sequence[Union[numpy.ndarray, np.nan]], numpy.ndarray, np.nan]

Residual sensitivities.

Takes as parameter an index or indices and returns corresponding trace values. If only a single value is requested, the list is flattened.

get_time_trace(*ix: Optional[Union[Sequence[int], int]] = None*, *trim: bool = False*) → Union[Sequence[float], float]

Cumulative execution times.

Takes as parameter an index or indices and returns corresponding trace values. If only a single value is requested, the list is flattened.

get_trimmed_indices()
Get indices for a monotonically decreasing history.

get_x_trace(*ix: Optional[Union[Sequence[int], int]] = None*, *trim: bool = False*) → Union[Sequence[numpy.ndarray], numpy.ndarray]
Return parameters.

Takes as parameter an index or indices and returns corresponding trace values. If only a single value is requested, the list is flattened.

property n_fval
Return number of function evaluations.

property n_grad
Return number of gradient evaluations.

property n_hess
Return number of Hessian evaluations.

property n_res
Return number of residual evaluations.

property n_sres
Return number or residual sensitivity evaluations.

property start_time
Return start time.

update(*x: numpy.ndarray*, *sensi_orders: Tuple[int, ...]*, *mode: str*, *result: Dict[str, Union[float, numpy.ndarray]]*) → None
Update history after a function evaluation.

Parameters

- **x** – The parameter vector.
- **sensi_orders** – The sensitivity orders computed.
- **mode** – The objective function mode computed (function value or residuals).
- **result** – The objective function values for parameters *x*, sensitivities *sensi_orders* and mode *mode*.

class pypesto.objective.**HistoryOptions**(*trace_record: bool = False*, *trace_record_grad: bool = True*, *trace_record_hess: bool = True*, *trace_record_res: bool = True*, *trace_record_sres: bool = True*, *trace_record_chi2: bool = True*, *trace_record_schi2: bool = True*, *trace_save_iter: int = 10*, *storage_file: Optional[str] = None*)
Bases: dict

Options for the objective that are used in optimization.

In addition implements a factory pattern to generate history objects.

Parameters

- **trace_record** – Flag indicating whether to record the trace of function calls. The trace_record_* flags only become effective if trace_record is True.
- **trace_record_grad** – Flag indicating whether to record the gradient in the trace.

- **trace_record_hess** – Flag indicating whether to record the Hessian in the trace.
- **trace_record_res** – Flag indicating whether to record the residual in the trace.
- **trace_record_sres** – Flag indicating whether to record the residual sensitivities in the trace.
- **trace_record_chi2** – Flag indicating whether to record the chi2 in the trace.
- **trace_record_schi2** – Flag indicating whether to record the chi2 sensitivities in the trace.
- **trace_save_iter** – After how many iterations to store the trace.
- **storage_file** – File to save the history to. Can be any of None, a "{filename}.csv", or a "{filename}.hdf5" file. Depending on the values, the *create_history* method creates the appropriate object. Occurrences of "{id}" in the file name are replaced by the *id* upon creation of a history, if applicable.

__init__(*trace_record: bool = False*, *trace_record_grad: bool = True*, *trace_record_hess: bool = True*, *trace_record_res: bool = True*, *trace_record_sres: bool = True*, *trace_record_chi2: bool = True*, *trace_record_schi2: bool = True*, *trace_save_iter: int = 10*, *storage_file: Optional[str] = None*)
Initialize self. See help(type(self)) for accurate signature.

static assert_instance(*maybe_options: Union[pypesto.objective.history.HistoryOptions, Dict]*) → pypesto.objective.history.HistoryOptions
Return a valid options object.

Parameters **maybe_options** (*HistoryOptions or dict*) –

create_history(*id: str*, *x_names: Sequence[str]*) → pypesto.objective.history.History
Create a *History* object; Factory method.

Parameters

- **id** – Identifier for the history.
- **x_names** – Parameter names.

class pypesto.objective.**MemoryHistory**(*options: Optional[Union[pypesto.objective.history.HistoryOptions, Dict]] = None*)
Bases: pypesto.objective.history.History

Class for optimization history stored in memory.

Track number of function evaluations and keeps an in-memory trace of function evaluations.

Parameters **options** – History options.

__init__(*options: Optional[Union[pypesto.objective.history.HistoryOptions, Dict]] = None*)
Initialize self. See help(type(self)) for accurate signature.

get_chi2_trace(*ix: Optional[Union[Sequence[int], int]] = None*, *trim: bool = False*) → Union[Sequence[Union[float, numpy.ndarray, np.nan]], float, numpy.ndarray, np.nan]
Chi2 values.

Takes as parameter an index or indices and returns corresponding trace values. If only a single value is requested, the list is flattened.

get_fval_trace(*ix: Optional[Union[Sequence[int], int]] = None*, *trim: bool = False*) → Union[Sequence[Union[float, numpy.ndarray, np.nan]], float, numpy.ndarray, np.nan]
Return function values.

Takes as parameter an index or indices and returns corresponding trace values. If only a single value is requested, the list is flattened.

get_grad_trace(*ix: Optional[Union[Sequence[int], int]] = None*, *trim: bool = False*) → Union[Sequence[Union[float, numpy.ndarray, np.nan]], float, numpy.ndarray, np.nan]

Return gradients.

Takes as parameter an index or indices and returns corresponding trace values. If only a single value is requested, the list is flattened.

get_hess_trace(*ix: Optional[Union[Sequence[int], int]] = None*, *trim: bool = False*) → Union[Sequence[Union[float, numpy.ndarray, np.nan]], float, numpy.ndarray, np.nan]

Return hessians.

Takes as parameter an index or indices and returns corresponding trace values. If only a single value is requested, the list is flattened.

get_res_trace(*ix: Optional[Union[Sequence[int], int]] = None*, *trim: bool = False*) → Union[Sequence[Union[float, numpy.ndarray, np.nan]], float, numpy.ndarray, np.nan]

Residuals.

Takes as parameter an index or indices and returns corresponding trace values. If only a single value is requested, the list is flattened.

get_schi2_trace(*ix: Optional[Union[Sequence[int], int]] = None*, *trim: bool = False*) → Union[Sequence[Union[float, numpy.ndarray, np.nan]], float, numpy.ndarray, np.nan]

Chi2 sensitivities.

Takes as parameter an index or indices and returns corresponding trace values. If only a single value is requested, the list is flattened.

get_sres_trace(*ix: Optional[Union[Sequence[int], int]] = None*, *trim: bool = False*) → Union[Sequence[Union[float, numpy.ndarray, np.nan]], float, numpy.ndarray, np.nan]

Residual sensitivities.

Takes as parameter an index or indices and returns corresponding trace values. If only a single value is requested, the list is flattened.

get_time_trace(*ix: Optional[Union[Sequence[int], int]] = None*, *trim: bool = False*) → Union[Sequence[Union[float, numpy.ndarray, np.nan]], float, numpy.ndarray, np.nan]

Cumulative execution times.

Takes as parameter an index or indices and returns corresponding trace values. If only a single value is requested, the list is flattened.

get_x_trace(*ix: Optional[Union[Sequence[int], int]] = None*, *trim: bool = False*) → Union[Sequence[Union[float, numpy.ndarray, np.nan]], float, numpy.ndarray, np.nan]

Return parameters.

Takes as parameter an index or indices and returns corresponding trace values. If only a single value is requested, the list is flattened.

update(*x: numpy.ndarray*, *sensi_orders: Tuple[int, ...]*, *mode: str*, *result: Dict[str, Union[float, numpy.ndarray]]*) → None

See *History* docstring.

class pypesto.objective.**NegLogParameterPriors**(*prior_list: List[Dict], x_names: Optional[Sequence[str]] = None*)

Bases: pypesto.objective.base.ObjectiveBase

Implements Negative Log Priors on Parameters.

Contains a list of prior dictionaries for the individual parameters of the format

{'index': [int], 'density_fun': [Callable], 'density_dx': [Callable], 'density_ddx': [Callable]}

A prior instance can be added to e.g. an objective, that gives the likelihood, by an AggregatedObjective.

Notes

All callables should correspond to log-densities. That is, they return log-densities and their corresponding derivatives. Internally, values are multiplied by -1, since pyPESTO expects the Objective function to be of a negative log-density type.

__init__(*prior_list: List[Dict], x_names: Optional[Sequence[str]] = None*)
Initialize.

Parameters

- **prior_list** – List of dicts containing the individual parameter priors. Format see above.
- **x_names** – Sequence of parameter names (optional).

call_unprocessed(*x: numpy.ndarray, sensi_orders: Tuple[int, ...], mode: str*) → Dict[str, Union[float, numpy.ndarray, Dict]]
Call objective function without pre- or post-processing and formatting.

Returns A dict containing the results.

Return type result

check_mode(*mode*) → bool
See *ObjectiveBase* documentation.

check_sensi_orders(*sensi_orders: Tuple[int, ...], mode: str*) → bool
See *ObjectiveBase* documentation.

gradient_neg_log_density(*x*)
Evaluate the gradient of the negative log-density at x.

hessian_neg_log_density(*x*)
Evaluate the hessian of the negative log-density at x.

hessian_vp_neg_log_density(*x, p*)
Compute vector product of the hessian at x with a vector p.

neg_log_density(*x*)
Evaluate the negative log-density at x.

residual(*x*)
Evaluate the residual representation of the prior at x.

residual_jacobian(*x*)
Evaluate residual Jacobian.

Evaluate the Jacobian of the residual representation of the prior for a parameter vector x w.r.t. x, if available.

class pypesto.objective.**NegLogPriors**(*objectives: Sequence[pypesto.objective.base.ObjectiveBase]*, *x_names: Optional[Sequence[str]] = None*)

Bases: pypesto.objective.aggregated.AggregatedObjective

Aggregates different forms of negative log-prior distributions.

Allows to distinguish priors from the likelihood by testing the type of an objective.

Consists basically of a list of individual negative log-priors, given in self.objectives.

class pypesto.objective.**Objective**(*fun: Optional[Callable] = None*, *grad: Optional[Union[Callable, bool]] = None*, *hess: Optional[Callable] = None*, *hessp: Optional[Callable] = None*, *res: Optional[Callable] = None*, *sres: Optional[Union[Callable, bool]] = None*, *x_names: Optional[Sequence[str]] = None*)

Bases: pypesto.objective.base.ObjectiveBase

Objective class.

The objective class allows the user explicitly specify functions that compute the function value and/or residuals as well as respective derivatives.

Denote dimensions n = parameters, m = residuals.

Parameters

- **fun** – The objective function to be minimized. If it only computes the objective function value, it should be of the form

  ```
  fun(x) -> float
  ```

  where x is an 1-D array with shape (n,), and n is the parameter space dimension.

- **grad** – Method for computing the gradient vector. If it is a callable, it should be of the form

  ```
  grad(x) -> array_like, shape (n,).
  ```

  If its value is True, then fun should return the gradient as a second output.

- **hess** – Method for computing the Hessian matrix. If it is a callable, it should be of the form

  ```
  hess(x) -> array, shape (n, n).
  ```

  If its value is True, then fun should return the gradient as a second, and the Hessian as a third output, and grad should be True as well.

- **hessp** – Method for computing the Hessian vector product, i.e.

  ```
  hessp(x, v) -> array_like, shape (n,)
  ```

  computes the product H*v of the Hessian of fun at x with v.

- **res** – Method for computing residuals, i.e.

  ```
  res(x) -> array_like, shape(m,).
  ```

- **sres** – Method for computing residual sensitivities. If it is a callable, it should be of the form

  ```
  sres(x) -> array, shape (m, n).
  ```

  If its value is True, then res should return the residual sensitivities as a second output.

- **x_names** – Parameter names. None if no names provided, otherwise a list of str, length dim_full (as in the Problem class). Can be read by the problem.

__init__(*fun: Optional[Callable] = None*, *grad: Optional[Union[Callable, bool]] = None*, *hess: Optional[Callable] = None*, *hessp: Optional[Callable] = None*, *res: Optional[Callable] = None*, *sres: Optional[Union[Callable, bool]] = None*, *x_names: Optional[Sequence[str]] = None*)
Initialize self. See help(type(self)) for accurate signature.

call_unprocessed(*x: numpy.ndarray*, *sensi_orders: Tuple[int, ...]*, *mode: str*, ***kwargs*) → Dict[str, Union[float, numpy.ndarray, Dict]]
Call objective function without pre- or post-processing and formatting.

Returns A dict containing the results.

Return type result

get_config() → dict
Return basic information of the objective configuration.

property has_fun
Check whether function is defined.

property has_grad
Check whether gradient is defined.

property has_hess
Check whether Hessian is defined.

property has_hessp

property has_res
Check whether residuals are defined.

property has_sres
Check whether residual sensitivities are defined.

class pypesto.objective.**ObjectiveBase**(*x_names: Optional[Sequence[str]] = None*)
Bases: abc.ABC

Abstract objective class.

The objective class is a simple wrapper around the objective function, giving a standardized way of calling. Apart from that, it manages several things including fixing of parameters and history.

The objective function is assumed to be in the format of a cost function, log-likelihood function, or log-posterior function. These functions are subject to minimization. For profiling and sampling, the sign is internally flipped, all returned and stored values are however given as returned by this objective function. If maximization is to be performed, the sign should be flipped before creating the objective function.

Parameters **x_names** – Parameter names that can be optionally used in, e.g., history or gradient checks.

history
For storing the call history. Initialized by the methods, e.g. the optimizer, in *initialize_history()*.

pre_post_processor
Preprocess input values to and postprocess output values from __call__. Configured in *update_from_problem()*.

__call__(*x: numpy.ndarray*, *sensi_orders: Tuple[int, ...] = (0)*, *mode: str = 'mode_fun'*, *return_dict: bool = False*, ***kwargs*) → Union[float, numpy.ndarray, Tuple, Dict[str, Union[float, numpy.ndarray, Dict]]]
Obtain arbitrary sensitivities.

This is the central method which is always called, also by the get_* methods.

There are different ways in which an optimizer calls the objective function, and in how the objective function provides information (e.g. derivatives via separate functions or along with the function values). The different calling modes increase efficiency in space and time and make the objective flexible.

Parameters

- **x** – The parameters for which to evaluate the objective function.
- **sensi_orders** – Specifies which sensitivities to compute, e.g. (0,1) -> fval, grad.
- **mode** – Whether to compute function values or residuals.
- **return_dict** – If False (default), the result is a Tuple of the requested values in the requested order. Tuples of length one are flattened. If True, instead a dict is returned which can carry further information.

Returns By default, this is a tuple of the requested function values and derivatives in the requested order (if only 1 value, the tuple is flattened). If *return_dict*, then instead a dict is returned with function values and derivatives indicated by ids.

Return type result

__init__(*x_names: Optional[Sequence[str]] = None*)
Initialize self. See help(type(self)) for accurate signature.

abstract call_unprocessed(*x: numpy.ndarray*, *sensi_orders: Tuple[int, ...]*, *mode: str*, ***kwargs*) → Dict[str, Union[float, numpy.ndarray, Dict]]
Call objective function without pre- or post-processing and formatting.

Parameters

- **x** – The parameters for which to evaluate the objective function.
- **sensi_orders** – Specifies which sensitivities to compute, e.g. (0,1) -> fval, grad.
- **mode** – Whether to compute function values or residuals.

Returns A dict containing the results.

Return type result

check_grad(*x: numpy.ndarray*, *x_indices: Optional[Sequence[int]] = None*, *eps: float = 1e-05*, *verbosity: int = 1*, *mode: str = 'mode_fun'*, *order: int = 0*, *detailed: bool = False*) → pandas.core.frame.DataFrame
Compare gradient evaluation.

Firstly approximate via finite differences, and secondly use the objective gradient.

Parameters

- **x** – The parameters for which to evaluate the gradient.
- **x_indices** – Indices for which to compute gradients. Default: all.
- **eps** – Finite differences step size.
- **verbosity** – Level of verbosity for function output. 0: no output, 1: summary for all parameters, 2: summary for individual parameters.
- **mode** – Residual (MODE_RES) or objective function value (MODE_FUN) computation mode.
- **order** – Derivative order, either gradient (0) or Hessian (1).
- **detailed** – Toggle whether additional values are returned. Additional values are function values, and the central difference weighted by the difference in output from all methods (standard deviation and mean).

Returns gradient, finite difference approximations and error estimates.

Return type result

check_grad_multi_eps(**args*, *multi_eps: Optional[Iterable] = None*, *label: str = 'rel_err'*, ***kwargs*)

Compare gradient evaluation.

Equivalent to the *ObjectiveBase.check_grad* method, except multiple finite difference step sizes are tested. The result contains the lowest finite difference for each parameter, and the corresponding finite difference step size.

Parameters

- **ObjectiveBase.check_grad method parameters.** (*All*) –
- **multi_eps** – The finite difference step sizes to be tested.
- **label** – The label of the column that will be minimized for each parameter. Valid options are the column labels of the dataframe returned by the *ObjectiveBase.check_grad* method.

check_gradients_match_finite_differences(**args*, *x: Optional[numpy.ndarray] = None*, *x_free: Optional[Sequence[int]] = None*, *rtol: float = 0.01*, *atol: float = 0.001*, *mode: Optional[str] = None*, *order: int = 0*, *multi_eps=None*, ***kwargs*) → bool

Check if gradients match finite differences (FDs).

Parameters

- **rtol** (*relative error tolerance*) –
- **x** (*The parameters for which to evaluate the gradient*) –
- **x_free** (*Indices for which to compute gradients*) –
- **rtol** –
- **atol** (*absolute error tolerance*) –
- **mode** (*function values or residuals*) –
- **order** (*gradient order, 0 for gradient, 1 for hessian*) –
- **multi_eps** (*multiple test step width for FDs*) –

Returns Indicates whether gradients match (True) FDs or not (False)

Return type bool

check_mode(*mode: str*) → bool

Check if the objective is able to compute in the requested mode.

Either *check_mode* or the *fun_...* functions must be overwritten in derived classes.

Parameters **mode** – Whether to compute function values or residuals.

Returns Boolean indicating whether mode is supported

Return type flag

check_sensi_orders(*sensi_orders: Tuple[int, ...]*, *mode: str*) → bool

Check if the objective is able to compute the requested sensitivities.

Either *check_sensi_orders* or the *fun_...* functions must be overwritten in derived classes.

Parameters

- **sensi_orders** – Specifies which sensitivities to compute, e.g. (0,1) -> fval, grad.
- **mode** – Whether to compute function values or residuals.

Returns Boolean indicating whether combination of sensi_orders and mode is supported

Return type flag

get_config() → dict
Get the configuration information of the objective function.

Return it as a dictonary.

get_fval(*x: numpy.ndarray*) → float
Get the function value at x.

get_grad(*x: numpy.ndarray*) → numpy.ndarray
Get the gradient at x.

get_hess(*x: numpy.ndarray*) → numpy.ndarray
Get the Hessian at x.

get_res(*x: numpy.ndarray*) → numpy.ndarray
Get the residuals at x.

get_sres(*x: numpy.ndarray*) → numpy.ndarray
Get the residual sensitivities at x.

property has_fun
Check whether function is defined.

property has_grad
Check whether gradient is defined.

property has_hess
Check whether Hessian is defined.

property has_hessp

property has_res
Check whether residuals are defined.

property has_sres
Check whether residual sensitivities are defined.

initialize()
Initialize the objective function.

This function is used at the beginning of an analysis, e.g. optimization, and can e.g. reset the objective memory. By default does nothing.

static output_to_tuple(*sensi_orders: Tuple[int, ...], mode: str, **kwargs: Union[float, numpy.ndarray]*) → Tuple
Return values as requested by the caller.

Usually only a subset of outputs is demanded. One output is returned as-is, more than one output are returned as a tuple in order (fval, grad, hess).

update_from_problem(*dim_full: int, x_free_indices: Sequence[int], x_fixed_indices: Sequence[int], x_fixed_vals: Sequence[float]*)
Handle fixed parameters.

Later, the objective will be given parameter vectors x of dimension dim, which have to be filled up with fixed parameter values to form a vector of dimension dim_full >= dim. This vector is then used to compute function value and derivatives. The derivatives must later be reduced again to dimension dim.

This is so as to make the fixing of parameters transparent to the caller.

The methods preprocess, postprocess are overwritten for the above functionality, respectively.

Parameters

- **dim_full** – Dimension of the full vector including fixed parameters.
- **x_free_indices** – Vector containing the indices (zero-based) of free parameters (complimentary to x_fixed_indices).
- **x_fixed_indices** – Vector containing the indices (zero-based) of parameter components that are not to be optimized.
- **x_fixed_vals** – Vector of the same length as x_fixed_indices, containing the values of the fixed parameters.

property x_names
Parameter names.

class pypesto.objective.**OptimizerHistory**(*history: pypesto.objective.history.History*, *x0: numpy.ndarray*, *lb: numpy.ndarray*, *ub: numpy.ndarray*, *generate_from_history: bool = False*)

Bases: object

Objective call history.

Container around a History object, which keeps track of optimal values.

fval0, fval_min
Initial and best function value found.

chi20, chi2_min
Initial and best chi2 value found.

x0, x_min
Initial and best parameters found.

grad_min
gradient for best parameters

hess_min
hessian (approximation) for best parameters

res_min
residuals for best parameters

sres_min
residual sensitivities for best parameters

Parameters

- **history** – History object to attach to this container. This history object implements the storage of the actual history.
- **x0** – Initial values for optimization.
- **lb** – Lower and upper bound. Used for checking validity of optimal points.
- **ub** – Lower and upper bound. Used for checking validity of optimal points.
- **generate_from_history** – If set to true, this function will try to fill attributes of this function based on the provided history.

__init__(*history: pypesto.objective.history.History*, *x0: numpy.ndarray*, *lb: numpy.ndarray*, *ub: numpy.ndarray*, *generate_from_history: bool = False*) → None
Initialize self. See help(type(self)) for accurate signature.

extract_from_history(*var: str*, *ix: int*) → bool
Get value of *var* at iteration *ix* and assign to *{var}_min*.

Parameters

- **var** (*Variable to extract, e.g. 'grad', 'x'.*) –
- **ix** (*Trace index.*) –

Returns Whether extraction and assignment worked. False in particular if the history value is nan.

Return type successful

finalize()
Finalize history.

update(*x: numpy.ndarray*, *sensi_orders: Tuple[int]*, *mode: str*, *result: Dict[str, Union[float, numpy.ndarray]]*) → None
Update history and best found value.

pypesto.objective.**res_to_chi2**(**args*, ***kwargs*)

pypesto.objective.**sres_to_schi2**(**args*, ***kwargs*)

4.3 Problem

A problem contains the objective as well as all information like prior describing the problem to be solved.

class pypesto.problem.**NegLogPriors**(*objectives: Sequence[pypesto.objective.base.ObjectiveBase]*, *x_names: Optional[Sequence[str]] = None*)
Bases: pypesto.objective.aggregated.AggregatedObjective

Aggregates different forms of negative log-prior distributions.

Allows to distinguish priors from the likelihood by testing the type of an objective.

Consists basically of a list of individual negative log-priors, given in self.objectives.

class pypesto.problem.**ObjectiveBase**(*x_names: Optional[Sequence[str]] = None*)
Bases: abc.ABC

Abstract objective class.

The objective class is a simple wrapper around the objective function, giving a standardized way of calling. Apart from that, it manages several things including fixing of parameters and history.

The objective function is assumed to be in the format of a cost function, log-likelihood function, or log-posterior function. These functions are subject to minimization. For profiling and sampling, the sign is internally flipped, all returned and stored values are however given as returned by this objective function. If maximization is to be performed, the sign should be flipped before creating the objective function.

Parameters **x_names** – Parameter names that can be optionally used in, e.g., history or gradient checks.

history
For storing the call history. Initialized by the methods, e.g. the optimizer, in *initialize_history()*.

pre_post_processor
Preprocess input values to and postprocess output values from __call__. Configured in *update_from_problem()*.

__call__(*x: numpy.ndarray*, *sensi_orders: Tuple[int, ...] = (0)*, *mode: str = 'mode_fun'*, *return_dict: bool = False*, ***kwargs*) → Union[float, numpy.ndarray, Tuple, Dict[str, Union[float, numpy.ndarray, Dict]]]
Obtain arbitrary sensitivities.

This is the central method which is always called, also by the get_* methods.

There are different ways in which an optimizer calls the objective function, and in how the objective function provides information (e.g. derivatives via separate functions or along with the function values). The different calling modes increase efficiency in space and time and make the objective flexible.

Parameters

- **x** – The parameters for which to evaluate the objective function.
- **sensi_orders** – Specifies which sensitivities to compute, e.g. (0,1) -> fval, grad.
- **mode** – Whether to compute function values or residuals.
- **return_dict** – If False (default), the result is a Tuple of the requested values in the requested order. Tuples of length one are flattened. If True, instead a dict is returned which can carry further information.

Returns By default, this is a tuple of the requested function values and derivatives in the requested order (if only 1 value, the tuple is flattened). If *return_dict*, then instead a dict is returned with function values and derivatives indicated by ids.

Return type result

__init__(*x_names: Optional[Sequence[str]] = None*)
Initialize self. See help(type(self)) for accurate signature.

abstract call_unprocessed(*x: numpy.ndarray*, *sensi_orders: Tuple[int, ...]*, *mode: str*, ***kwargs*) → Dict[str, Union[float, numpy.ndarray, Dict]]
Call objective function without pre- or post-processing and formatting.

Parameters

- **x** – The parameters for which to evaluate the objective function.
- **sensi_orders** – Specifies which sensitivities to compute, e.g. (0,1) -> fval, grad.
- **mode** – Whether to compute function values or residuals.

Returns A dict containing the results.

Return type result

check_grad(*x: numpy.ndarray*, *x_indices: Optional[Sequence[int]] = None*, *eps: float = 1e-05*, *verbosity: int = 1*, *mode: str = 'mode_fun'*, *order: int = 0*, *detailed: bool = False*) → pandas.core.frame.DataFrame
Compare gradient evaluation.

Firstly approximate via finite differences, and secondly use the objective gradient.

Parameters

- **x** – The parameters for which to evaluate the gradient.
- **x_indices** – Indices for which to compute gradients. Default: all.
- **eps** – Finite differences step size.

- **verbosity** – Level of verbosity for function output. 0: no output, 1: summary for all parameters, 2: summary for individual parameters.
- **mode** – Residual (MODE_RES) or objective function value (MODE_FUN) computation mode.
- **order** – Derivative order, either gradient (0) or Hessian (1).
- **detailed** – Toggle whether additional values are returned. Additional values are function values, and the central difference weighted by the difference in output from all methods (standard deviation and mean).

Returns gradient, finite difference approximations and error estimates.

Return type result

check_grad_multi_eps(**args*, *multi_eps: Optional[Iterable] = None*, *label: str = 'rel_err'*, ***kwargs*)

Compare gradient evaluation.

Equivalent to the *ObjectiveBase.check_grad* method, except multiple finite difference step sizes are tested. The result contains the lowest finite difference for each parameter, and the corresponding finite difference step size.

Parameters

- **ObjectiveBase.check_grad method parameters.** (*All*) –
- **multi_eps** – The finite difference step sizes to be tested.
- **label** – The label of the column that will be minimized for each parameter. Valid options are the column labels of the dataframe returned by the *ObjectiveBase.check_grad* method.

check_gradients_match_finite_differences(**args*, *x: Optional[numpy.ndarray] = None*, *x_free: Optional[Sequence[int]] = None*, *rtol: float = 0.01*, *atol: float = 0.001*, *mode: Optional[str] = None*, *order: int = 0*, *multi_eps=None*, ***kwargs*) → bool

Check if gradients match finite differences (FDs).

Parameters

- **rtol** (*relative error tolerance*) –
- **x** (*The parameters for which to evaluate the gradient*) –
- **x_free** (*Indices for which to compute gradients*) –
- **rtol** –
- **atol** (*absolute error tolerance*) –
- **mode** (*function values or residuals*) –
- **order** (*gradient order, 0 for gradient, 1 for hessian*) –
- **multi_eps** (*multiple test step width for FDs*) –

Returns Indicates whether gradients match (True) FDs or not (False)

Return type bool

check_mode(*mode: str*) → bool

Check if the objective is able to compute in the requested mode.

Either *check_mode* or the *fun_...* functions must be overwritten in derived classes.

Parameters **mode** – Whether to compute function values or residuals.

Returns Boolean indicating whether mode is supported

Return type flag

check_sensi_orders(*sensi_orders: Tuple[int, ...]*, *mode: str*) → bool
Check if the objective is able to compute the requested sensitivities.

Either *check_sensi_orders* or the *fun_...* functions must be overwritten in derived classes.

Parameters

- **sensi_orders** – Specifies which sensitivities to compute, e.g. (0,1) -> fval, grad.
- **mode** – Whether to compute function values or residuals.

Returns Boolean indicating whether combination of sensi_orders and mode is supported

Return type flag

get_config() → dict
Get the configuration information of the objective function.

Return it as a dictonary.

get_fval(*x: numpy.ndarray*) → float
Get the function value at x.

get_grad(*x: numpy.ndarray*) → numpy.ndarray
Get the gradient at x.

get_hess(*x: numpy.ndarray*) → numpy.ndarray
Get the Hessian at x.

get_res(*x: numpy.ndarray*) → numpy.ndarray
Get the residuals at x.

get_sres(*x: numpy.ndarray*) → numpy.ndarray
Get the residual sensitivities at x.

property has_fun
Check whether function is defined.

property has_grad
Check whether gradient is defined.

property has_hess
Check whether Hessian is defined.

property has_hessp

property has_res
Check whether residuals are defined.

property has_sres
Check whether residual sensitivities are defined.

initialize()
Initialize the objective function.

This function is used at the beginning of an analysis, e.g. optimization, and can e.g. reset the objective memory. By default does nothing.

static output_to_tuple(*sensi_orders: Tuple[int, ...], mode: str, **kwargs: Union[float, numpy.ndarray]*) → Tuple

Return values as requested by the caller.

Usually only a subset of outputs is demanded. One output is returned as-is, more than one output are returned as a tuple in order (fval, grad, hess).

update_from_problem(*dim_full: int, x_free_indices: Sequence[int], x_fixed_indices: Sequence[int], x_fixed_vals: Sequence[float]*)

Handle fixed parameters.

Later, the objective will be given parameter vectors x of dimension dim, which have to be filled up with fixed parameter values to form a vector of dimension dim_full >= dim. This vector is then used to compute function value and derivatives. The derivatives must later be reduced again to dimension dim.

This is so as to make the fixing of parameters transparent to the caller.

The methods preprocess, postprocess are overwritten for the above functionality, respectively.

Parameters

- **dim_full** – Dimension of the full vector including fixed parameters.
- **x_free_indices** – Vector containing the indices (zero-based) of free parameters (complimentary to x_fixed_indices).
- **x_fixed_indices** – Vector containing the indices (zero-based) of parameter components that are not to be optimized.
- **x_fixed_vals** – Vector of the same length as x_fixed_indices, containing the values of the fixed parameters.

property x_names

Parameter names.

class pypesto.problem.**Problem**(*objective: pypesto.objective.base.ObjectiveBase, lb: Union[numpy.ndarray, List[float]], ub: Union[numpy.ndarray, List[float]], dim_full: Optional[int] = None, x_fixed_indices: Optional[Union[Iterable[SupportsInt], SupportsInt]] = None, x_fixed_vals: Optional[Union[Iterable[SupportsFloat], SupportsFloat]] = None, x_guesses: Optional[Iterable[float]] = None, x_names: Optional[Iterable[str]] = None, x_scales: Optional[Iterable[str]] = None, x_priors_defs: Optional[pypesto.objective.priors.NegLogPriors] = None, lb_init: Optional[Union[numpy.ndarray, List[float]]] = None, ub_init: Optional[Union[numpy.ndarray, List[float]]] = None, copy_objective: bool = True*)

Bases: object

The problem formulation.

A problem specifies the objective function, boundaries and constraints, parameter guesses as well as the parameters which are to be optimized.

Parameters

- **objective** – The objective function for minimization. Note that a shallow copy is created.
- **lb** – The lower and upper bounds for optimization. For unbounded directions set to +-inf.
- **ub** – The lower and upper bounds for optimization. For unbounded directions set to +-inf.
- **lb_init** – The lower and upper bounds for initialization, typically for defining search start points. If not set, set to lb, ub.

- **ub_init** – The lower and upper bounds for initialization, typically for defining search start points. If not set, set to lb, ub.
- **dim_full** – The full dimension of the problem, including fixed parameters.
- **x_fixed_indices** – Vector containing the indices (zero-based) of parameter components that are not to be optimized.
- **x_fixed_vals** – Vector of the same length as x_fixed_indices, containing the values of the fixed parameters.
- **x_guesses** – Guesses for the parameter values, shape (g, dim), where g denotes the number of guesses. These are used as start points in the optimization.
- **x_names** – Parameter names that can be optionally used e.g. in visualizations. If objective.get_x_names() is not None, those values are used, else the values specified here are used if not None, otherwise the variable names are set to ['x0', ... 'x{dim_full}']. The list must always be of length dim_full.
- **x_scales** – Parameter scales can be optionally given and are used e.g. in visualisation and prior generation. Currently the scales 'lin', 'log`and 'log10' are supported.
- **x_priors_defs** – Definitions of priors for parameters. Types of priors, and their required and optional parameters, are described in the *Prior* class.
- **copy_objective** – Whethter to generate a deep copy of the objective function before potential modification the problem class performs on it.

Notes

On the fixing of parameter values:

The number of parameters dim_full the objective takes as input must be known, so it must be either lb a vector of that size, or dim_full specified as a parameter.

All vectors are mapped to the reduced space of dimension dim in __init__, regardless of whether they were in dimension dim or dim_full before. If the full representation is needed, the methods get_full_vector() and get_full_matrix() can be used.

__init__(*objective: pypesto.objective.base.ObjectiveBase*, *lb: Union[numpy.ndarray, List[float]]*, *ub: Union[numpy.ndarray, List[float]]*, *dim_full: Optional[int] = None*, *x_fixed_indices: Optional[Union[Iterable[SupportsInt], SupportsInt]] = None*, *x_fixed_vals: Optional[Union[Iterable[SupportsFloat], SupportsFloat]] = None*, *x_guesses: Optional[Iterable[float]] = None*, *x_names: Optional[Iterable[str]] = None*, *x_scales: Optional[Iterable[str]] = None*, *x_priors_defs: Optional[pypesto.objective.priors.NegLogPriors] = None*, *lb_init: Optional[Union[numpy.ndarray, List[float]]] = None*, *ub_init: Optional[Union[numpy.ndarray, List[float]]] = None*, *copy_objective: bool = True*)

Initialize self. See help(type(self)) for accurate signature.

property dim

Return dimension only considering non fixed parameters.

fix_parameters(*parameter_indices: Union[Iterable[SupportsInt], SupportsInt]*, *parameter_vals: Union[Iterable[SupportsFloat], SupportsFloat]*) → None

Fix specified parameters to specified values.

full_index_to_free_index(*full_index: int*)

Calculate index in reduced vector from index in full vector.

Parameters **full_index** (*The index in the full vector.*) –

Returns free_index

Return type The index in the free vector.

get_full_matrix(*x: Optional[numpy.ndarray]*) → Optional[numpy.ndarray]
Map matrix from dim to dim_full. Usually used for hessian.

Parameters **x** (*array_like, shape=(dim, dim)*) – The matrix in dimension dim.

get_full_vector(*x: Optional[numpy.ndarray]*, *x_fixed_vals: Optional[Iterable[float]] = None*) → Optional[numpy.ndarray]
Map vector from dim to dim_full. Usually used for x, grad.

Parameters

- **x** (*array_like, shape=(dim,)*) – The vector in dimension dim.
- **x_fixed_vals** (*array_like, ndim=1, optional*) – The values to be used for the fixed indices. If None, then nans are inserted. Usually, None will be used for grad and problem.x_fixed_vals for x.

get_reduced_matrix(*x_full: Optional[numpy.ndarray]*) → Optional[numpy.ndarray]
Map matrix from dim_full to dim, i.e. delete fixed indices.

Parameters **x_full** (*array_like, ndim=2*) – The matrix in dimension dim_full.

get_reduced_vector(*x_full: Optional[numpy.ndarray]*, *x_indices: Optional[List[int]] = None*) → Optional[numpy.ndarray]
Keep only those elements, which indices are specified in x_indices.

If x_indices is not provided, delete fixed indices.

Parameters

- **x_full** (*array_like, ndim=1*) – The vector in dimension dim_full.
- **x_indices** – indices of x_full that should remain

property lb
Return lower bounds of free parameters.

property lb_init
Return initial lower bounds of free parameters.

normalize() → None
Process vectors.

Reduce all vectors to dimension dim and have the objective accept vectors of dimension dim.

print_parameter_summary() → None
Print a summary of parameters.

Include what parameters are being optimized and parameter boundaries.

set_x_guesses(*x_guesses: Iterable[float]*)
Set the x_guesses of a problem.

Parameters **x_guesses** –

property ub
Return upper bounds of free parameters.

property ub_init
Return initial upper bounds of free parameters.

unfix_parameters(*parameter_indices: Union[Iterable[*SupportsInt*],* SupportsInt*]*) → None
Free specified parameters.

property x_free_indices
Return non fixed parameters.

property x_guesses
Return guesses of the free parameter values.

class pypesto.problem.**SupportsFloat**(**args*, ***kwargs*)
Bases: Protocol

An ABC with one abstract method __float__.

__init__(**args*, ***kwargs*)
Initialize self. See help(type(self)) for accurate signature.

class pypesto.problem.**SupportsInt**(**args*, ***kwargs*)
Bases: Protocol

An ABC with one abstract method __int__.

__init__(**args*, ***kwargs*)
Initialize self. See help(type(self)) for accurate signature.

4.4 Prediction

Generate predictions from simulations with specified parameter vectors, with optional post-processing.

class pypesto.predict.**AmiciPredictor**(*amici_objective: pypesto.objective.amici.AmiciObjective*, *amici_output_fields: Optional[Sequence[str]] = None*, *post_processor: Optional[Callable] = None*, *post_processor_sensi: Optional[Callable] = None*, *post_processor_time: Optional[Callable] = None*, *max_chunk_size: Optional[int] = None*, *output_ids: Optional[Sequence[str]] = None*, *condition_ids: Optional[Sequence[str]] = None*)
Bases: object

Do forward simulations/predictions for an AMICI model.

The user may supply post-processing methods. If post-processing methods are supplied, and a gradient of the prediction is requested, then the sensitivities of the AMICI model must also be post-processed. There are no checks here to ensure that the sensitivities are correctly post-processed, this is explicitly left to the user. There are also no safeguards if the postprocessor routines fail. This may happen if, e.g., a call to Amici fails, and no timepoints, states or observables are returned. As the AmiciPredictor is agnostic about the dimension of the postprocessor and also the dimension of the postprocessed output, these checks are also left to the user. An example for such a check is provided in the default output (see _default_output()).

__call__(*x: numpy.ndarray*, *sensi_orders: Tuple[int, ...] = (0)*, *mode: str = 'mode_fun'*, *output_file: str = ''*, *output_format: str = 'csv'*, *include_llh_weights: bool = False*, *include_sigmay: bool = False*) → pypesto.result.predict.PredictionResult
Call the predictor.

Simulate a model for a certain prediction function. This method relies on the AmiciObjective, which is underlying, but allows the user to apply any post-processing of the results, the sensitivities, and the timepoints.

Parameters

- **x** – The parameters for which to evaluate the prediction function.
- **sensi_orders** – Specifies which sensitivities to compute, e.g. (0,1) -> fval, grad.

- **mode** – Whether to compute function values or residuals.
- **output_file** – Path to an output file.
- **output_format** – Either 'csv', 'h5'. If an output file is specified, this routine will return a csv file, created from a DataFrame, or an h5 file, created from a dict.
- **include_llh_weights** – Boolean whether weights should be included in the prediction. Necessary for weighted means of Ensembles.
- **include_sigmay** – Boolean whether standard deviations should be included in the prediction output. Necessary for evaluation of weighted means of Ensembles.

Returns PredictionResult object containing timepoints, outputs, and output_sensitivities if requested

Return type results

__init__(*amici_objective: pypesto.objective.amici.AmiciObjective*, *amici_output_fields: Optional[Sequence[str]] = None*, *post_processor: Optional[Callable] = None*, *post_processor_sensi: Optional[Callable] = None*, *post_processor_time: Optional[Callable] = None*, *max_chunk_size: Optional[int] = None*, *output_ids: Optional[Sequence[str]] = None*, *condition_ids: Optional[Sequence[str]] = None*)

Initialize predictor.

Parameters

- **amici_objective** – An objective object, which will be used to get model simulations
- **amici_output_fields** – keys that exist in the return data object from AMICI, which should be available for the post-processors
- **post_processor** – A callable function which applies postprocessing to the simulation results and possibly defines different outputs than those of the amici model. Default are the observables (*pypesto.C.AMICI_Y*) of the AMICI model. This method takes a list of dicts (with the returned fields *pypesto.C.AMICI_T*, *pypesto.C.AMICI_X*, and *pypesto.C.AMICI_Y* of the AMICI ReturnData objects) as input. Safeguards for, e.g., failure of AMICI are left to the user.
- **post_processor_sensi** – A callable function which applies postprocessing to the sensitivities of the simulation results. Defaults to the observable sensitivities of the AMICI model. This method takes a list of dicts (with the returned fields *pypesto.C.AMICI_T*, *pypesto.C.AMICI_X*, *pypesto.C.AMICI_Y*, *pypesto.C.AMICI_SX*, and *pypesto.C.AMICI_SY* of the AMICI ReturnData objects) as input. Safeguards for, e.g., failure of AMICI are left to the user.
- **post_processor_time** – A callable function which applies postprocessing to the timepoints of the simulations. Defaults to the timepoints of the amici model. This method takes a list of dicts (with the returned field *pypesto.C.AMICI_T* of the amici ReturnData objects) as input. Safeguards for, e.g., failure of AMICI are left to the user.
- **max_chunk_size** – In some cases, we don't want to compute all predictions at once when calling the prediction function, as this might not fit into the memory for large datasets and models. Here, the user can specify a maximum chunk size of conditions, which should be simulated at a time. Defaults to None, meaning that all conditions will be simulated.
- **output_ids** – IDs of outputs, as post-processing allows the creation of customizable outputs, which may not coincide with those from the AMICI model (defaults to AMICI observables).
- **condition_ids** – List of identifiers for the conditions of the edata objects of the amici objective, will be passed to the PredictionResult at call.

class pypesto.predict.**PredictorTask**(*predictor: pypesto.predict.Predictor*, *x: Sequence[float]*, *sensi_orders: Tuple[int, ...]*, *mode: str*, *id: str*)

Bases: pypesto.engine.task.Task

Perform a single prediction with *pypesto.engine.Task*.

Designed for use with *pypesto.ensemble.Ensemble*.

predictor
The predictor to use.

x
The parameter vector to compute predictions with.

sensi_orders
Specifies which sensitivities to compute, e.g. (0,1) -> fval, grad.

mode
Whether to compute function values or residuals.

id
The input ID.

__init__(*predictor: pypesto.predict.Predictor*, *x: Sequence[float]*, *sensi_orders: Tuple[int, ...]*, *mode: str*, *id: str*)
Initialize self. See help(type(self)) for accurate signature.

execute() → pypesto.predict.PredictionResult
Execute and return the prediction.

4.5 PEtab

pyPESTO support for the PEtab data format.

class pypesto.petab.**PetabImporter**(*petab_problem: petab.Problem*, *output_folder: str = None*, *model_name: str = None*, *validate_petab: bool = True*)

Bases: pypesto.objective.amici.AmiciObjectBuilder

Importer for Petab files.

Create an *amici.Model*, an *objective.AmiciObjective* or a *pypesto.Problem* from Petab files.

MODEL_BASE_DIR = 'amici_models'

__init__(*petab_problem: petab.Problem*, *output_folder: str = None*, *model_name: str = None*, *validate_petab: bool = True*)
Initialize importer.

Parameters

- **petab_problem** – Managing access to the model and data.
- **output_folder** – Folder to contain the amici model. Defaults to './amici_models/{model_name}'.
- **model_name** – Name of the model, which will in particular be the name of the compiled model python module.
- **validate_petab** – Flag indicating if the PEtab problem shall be validated.

check_gradients(**args*, *rtol: float = 0.01*, *atol: float = 0.001*, *mode: Optional[Union[str, List[str]]] = None*, *multi_eps=None*, ***kwargs*) → bool
Check if gradients match finite differences (FDs).

Parameters

- **rtol** (*relative error tolerance*) –
- **atol** (*absolute error tolerance*) –
- **mode** (*function values or residuals*) –
- **objAbsoluteTolerance** (*absolute tolerance in sensitivity calculation*) –
- **objRelativeTolerance** (*relative tolerance in sensitivity calculation*) –
- **multi_eps** (*multiple test step width for FDs*) –

Returns **match**

Return type Whether gradients match FDs (True) or not (False)

compile_model (***kwargs*)
Compile the model.

If the output folder exists already, it is first deleted.

Parameters **kwargs** (Extra arguments passed to *amici.SbmlImporter.sbml2amici*.) –

create_edatas (*model: amici.Model = None*, *simulation_conditions=None*) → List[amici.ExpData]
Create list of amici.ExpData objects.

create_model (*force_compile: bool = False*, ***kwargs*) → amici.Model
Import amici model.

Parameters

- **force_compile** – If False, the model is compiled only if the output folder does not exist yet. If True, the output folder is deleted and the model (re-)compiled in either case.

  Warning: If *force_compile*, then an existing folder of that name will be deleted.

- **kwargs** (*Extra arguments passed to amici.SbmlImporter.sbml2amici*) –

create_objective (*model: amici.Model = None*, *solver: amici.Solver = None*, *edatas: Sequence[amici.ExpData] = None*, *force_compile: bool = False*, ***kwargs*) → pypesto.objective.amici.AmiciObjective
Create a *pypesto.AmiciObjective*.

Parameters

- **model** – The AMICI model.
- **solver** – The AMICI solver.
- **edatas** – The experimental data in AMICI format.
- **force_compile** – Whether to force-compile the model if not passed.
- ****kwargs** – Additional arguments passed on to the objective.

Returns A *pypesto.AmiciObjective* for the model and the data.

Return type objective

create_predictor(*objective: Optional[pypesto.objective.amici.AmiciObjective] = None*, *amici_output_fields: Optional[Sequence[str]] = None*, *post_processor: Optional[Callable] = None*, *post_processor_sensi: Optional[Callable] = None*, *post_processor_time: Optional[Callable] = None*, *max_chunk_size: Optional[int] = None*, *output_ids: Optional[Sequence[str]] = None*, *condition_ids: Optional[Sequence[str]] = None*) → pypesto.predict.amici_predictor.AmiciPredictor

Create a *pypesto.predict.AmiciPredictor*.

The *AmiciPredictor* facilitates generation of predictions from parameter vectors.

Parameters

- **objective** – An objective object, which will be used to get model simulations
- **amici_output_fields** – keys that exist in the return data object from AMICI, which should be available for the post-processors
- **post_processor** – A callable function which applies postprocessing to the simulation results. Default are the observables of the AMICI model. This method takes a list of ndarrays (as returned in the field ['y'] of amici ReturnData objects) as input.
- **post_processor_sensi** – A callable function which applies postprocessing to the sensitivities of the simulation results. Default are the observable sensitivities of the AMICI model. This method takes two lists of ndarrays (as returned in the fields ['y'] and ['sy'] of amici ReturnData objects) as input.
- **post_processor_time** – A callable function which applies postprocessing to the timepoints of the simulations. Default are the timepoints of the amici model. This method takes a list of ndarrays (as returned in the field ['t'] of amici ReturnData objects) as input.
- **max_chunk_size** – In some cases, we don't want to compute all predictions at once when calling the prediction function, as this might not fit into the memory for large datasets and models. Here, the user can specify a maximum number of conditions, which should be simulated at a time. Default is 0 meaning that all conditions will be simulated. Other values are only applicable, if an output file is specified.
- **output_ids** – IDs of outputs, if post-processing is used
- **condition_ids** – IDs of conditions, if post-processing is used

Returns A *pypesto.predict.AmiciPredictor* for the model, using the outputs of the AMICI model and the timepoints from the PEtab data

Return type predictor

create_prior() → Optional[pypesto.objective.priors.NegLogParameterPriors]

Create a prior from the parameter table.

Returns None, if no priors are defined.

create_problem(*objective: Optional[pypesto.objective.amici.AmiciObjective] = None*, *x_guesses: Optional[Iterable[float]] = None*, ***kwargs*) → *pypesto.problem.Problem*

Create a *pypesto.Problem*.

Parameters

- **objective** – Objective as created by *create_objective*.
- **x_guesses** – Guesses for the parameter values, shape (g, dim), where g denotes the number of guesses. These are used as start points in the optimization.
- ****kwargs** – Additional key word arguments passed on to the objective, if not provided.

Returns A *pypesto.Problem* for the objective.

Return type problem

create_solver(*model: amici.Model = None*) → amici.Solver
Return model solver.

create_startpoint_method() → Optional[pypesto.startpoint.base.StartpointMethod]
Create a startpoint method.

If the PEtab problem specifies an initializationPrior. Returns None, if no initializationPrior is specified.

static from_yaml(*yaml_config: Union[dict, str]*, *output_folder: Optional[str] = None*, *model_name: Optional[str] = None*) → pypesto.petab.importer.PetabImporter
Simplified constructor using a petab yaml file.

prediction_to_petab_measurement_df(*prediction: pypesto.result.predict.PredictionResult*, *predictor: Optional[pypesto.predict.amici_predictor.AmiciPredictor] = None*) → pandas.core.frame.DataFrame
Cast prediction into a dataframe.

If a PEtab problem is simulated without post-processing, then the result can be cast into a PEtab measurement or simulation dataframe

Parameters

- **prediction** – A prediction result as produced by an AmiciPredictor
- **predictor** – The AmiciPredictor function

Returns A dataframe built from the rdatas in the format as in self.petab_problem.measurement_df.

Return type measurement_df

prediction_to_petab_simulation_df(*prediction: pypesto.result.predict.PredictionResult*, *predictor: Optional[pypesto.predict.amici_predictor.AmiciPredictor] = None*) → pandas.core.frame.DataFrame
See *prediction_to_petab_measurement_df*.

Except a PEtab simulation dataframe is created, i.e. the measurement column label is adjusted.

rdatas_to_measurement_df(*rdatas: Sequence[amici.ReturnData]*, *model: amici.Model = None*) → pandas.core.frame.DataFrame
Create a measurement dataframe in the petab format.

Parameters

- **rdatas** – A list of rdatas as produced by pypesto.AmiciObjective.__call__(x, return_dict=True)['rdatas'].
- **model** – The amici model.

Returns A dataframe built from the rdatas in the format as in self.petab_problem.measurement_df.

Return type measurement_df

rdatas_to_simulation_df(*rdatas: Sequence[amici.ReturnData]*, *model: amici.Model = None*) → pandas.core.frame.DataFrame
See *rdatas_to_measurement_df*.

Execpt a petab simulation dataframe is created, i.e. the measurement column label is adjusted.

class pypesto.petab.**PetabImporterPysb**(*petab_problem: amici.petab_import_pysb.PysbPetabProblem*, *output_folder: str = None*)

Bases: pypesto.petab.importer.PetabImporter

Import for experimental PySB-based PEtab problems.

__init__(*petab_problem: amici.petab_import_pysb.PysbPetabProblem*, *output_folder: str = None*)

Initialize importer.

Parameters

- **petab_problem** – Managing access to the model and data.
- **output_folder** – Folder to contain the amici model.

compile_model(***kwargs*)

Compile the model.

If the output folder exists already, it is first deleted.

Parameters **kwargs** (Extra arguments passed to *amici.SbmlImporter.sbml2amici*.) –

4.6 Optimize

Multistart optimization with support for various optimizers.

class pypesto.optimize.**CmaesOptimizer**(*par_sigma0: float = 0.25*, *options: Optional[Dict] = None*)

Bases: pypesto.optimize.optimizer.Optimizer

Global optimization using cma-es.

Package homepage: https://pypi.org/project/cma-es/

__init__(*par_sigma0: float = 0.25*, *options: Optional[Dict] = None*)

Initialize.

Parameters

- **par_sigma0** – scalar, initial standard deviation in each coordinate. par_sigma0 should be about 1/4th of the search domain width (where the optimum is to be expected)
- **options** – Optimizer options that are directly passed on to cma.

is_least_squares()

Check whether optimizer is a least squares optimizer.

minimize(*problem: pypesto.problem.Problem*, *x0: numpy.ndarray*, *id: str*, *history_options: Optional[pypesto.objective.history.HistoryOptions] = None*, *optimize_options: Optional[pypesto.optimize.options.OptimizeOptions] = None*)

class pypesto.optimize.**DlibOptimizer**(*options: Optional[Dict] = None*)

Bases: pypesto.optimize.optimizer.Optimizer

Use the Dlib toolbox for optimization.

__init__(*options: Optional[Dict] = None*)

Initialize base class.

get_default_options()

Create default options specific for the optimizer.

is_least_squares()
Check whether optimizer is a least squares optimizer.

minimize(*problem: pypesto.problem.Problem*, *x0: numpy.ndarray*, *id: str*, *history_options: Optional[pypesto.objective.history.HistoryOptions] = None*, *optimize_options: Optional[pypesto.optimize.options.OptimizeOptions] = None*)

class pypesto.optimize.**FidesOptimizer**(*hessian_update: Optional[None] = 'Hybrid'*, *options: Optional[Dict] = None*, *verbose: Optional[int] = 20*)
Bases: pypesto.optimize.optimizer.Optimizer

Global/Local optimization using the trust region optimizer fides.

Package Homepage: https://fides-optimizer.readthedocs.io/en/latest

__init__(*hessian_update: Optional[None] = 'Hybrid'*, *options: Optional[Dict] = None*, *verbose: Optional[int] = 20*)
Initialize.

Parameters

- **options** – Optimizer options.
- **hessian_update** – Hessian update strategy. If this is None, a hybrid approximation that switches from the problem.objective provided Hessian (approximation) to a BFGS approximation will be used.

is_least_squares()
Check whether optimizer is a least squares optimizer.

minimize(*problem: pypesto.problem.Problem*, *x0: numpy.ndarray*, *id: str*, *history_options: Optional[pypesto.objective.history.HistoryOptions] = None*, *optimize_options: Optional[pypesto.optimize.options.OptimizeOptions] = None*)

class pypesto.optimize.**IpoptOptimizer**(*options: Optional[Dict] = None*)
Bases: pypesto.optimize.optimizer.Optimizer

Use IpOpt (https://pypi.org/project/ipopt/) for optimization.

__init__(*options: Optional[Dict] = None*)
Initialize.

Parameters **options** – Options are directly passed on to *cyipopt.minimize_ipopt*.

is_least_squares()
Check whether optimizer is a least squares optimizer.

minimize(*problem: pypesto.problem.Problem*, *x0: numpy.ndarray*, *id: str*, *history_options: Optional[pypesto.objective.history.HistoryOptions] = None*, *optimize_options: Optional[pypesto.optimize.options.OptimizeOptions] = None*)

class pypesto.optimize.**NLoptOptimizer**(*method=None*, *local_method=None*, *options: Optional[Dict] = None*, *local_options: Optional[Dict] = None*)
Bases: pypesto.optimize.optimizer.Optimizer

Global/Local optimization using NLopt.

Package homepage: https://nlopt.readthedocs.io/en/latest/

__init__(*method=None*, *local_method=None*, *options: Optional[Dict] = None*, *local_options: Optional[Dict] = None*)
Initialize.

Parameters

- **method** – Local or global Optimizer to use for minimization.
- **local_method** – Local method to use in combination with the global optimizer (for the MLSL family of solvers) or to solve a subproblem (for the AUGLAG family of solvers)
- **options** – Optimizer options. scipy option *maxiter* is automatically transformed into *maxeval* and takes precedence.
- **local_options** – Optimizer options for the local method

is_least_squares()
Check whether optimizer is a least squares optimizer.

minimize(*problem:* pypesto.problem.Problem, *x0:* *numpy.ndarray*, *id:* *str*, *history_options:* *Optional[pypesto.objective.history.HistoryOptions] = None*, *optimize_options:* *Optional[pypesto.optimize.options.OptimizeOptions] = None*)

class pypesto.optimize.**OptimizeOptions**(*allow_failed_starts:* *bool = True*, *report_sres:* *bool = True*, *report_hess:* *bool = True*, *history_beats_optimizer:* *bool = True*)

Bases: dict

Options for the multistart optimization.

Parameters

- **allow_failed_starts** – Flag indicating whether we tolerate that exceptions are thrown during the minimization process.
- **report_sres** – Flag indicating whether sres will be stored in the results object. Deactivating this option will improve memory consumption for large scale problems.
- **report_hess** – Flag indicating whether hess will be stored in the results object. Deactivating this option will improve memory consumption for large scale problems.
- **history_beats_optimizer** – Whether the optimal value recorded by pyPESTO in the history has priority over the optimal value reported by the optimizer (True) or not (False).

__init__(*allow_failed_starts:* *bool = True*, *report_sres:* *bool = True*, *report_hess:* *bool = True*, *history_beats_optimizer:* *bool = True*)
Initialize self. See help(type(self)) for accurate signature.

static assert_instance(*maybe_options:* *Union[pypesto.optimize.options.OptimizeOptions, Dict]*) → pypesto.optimize.options.OptimizeOptions
Return a valid options object.

Parameters **maybe_options** (OptimizeOptions *or* *dict*) –

class pypesto.optimize.**Optimizer**
Bases: abc.ABC

Optimizer base class, not functional on its own.

An optimizer takes a problem, and possibly a start point, and then performs an optimization. It returns an OptimizerResult.

__init__()
Initialize base class.

get_default_options()
Create default options specific for the optimizer.

abstract is_least_squares()
Check whether optimizer is a least squares optimizer.

abstract minimize(*problem: pypesto.problem.Problem, x0: numpy.ndarray, id: str, history_options: Optional[pypesto.objective.history.HistoryOptions] = None, optimize_options: Optional[pypesto.optimize.options.OptimizeOptions] = None*)

class pypesto.optimize.**PyswarmOptimizer**(*options: Optional[Dict] = None*)

Bases: pypesto.optimize.optimizer.Optimizer

Global optimization using pyswarm.

__init__(*options: Optional[Dict] = None*)
Initialize base class.

is_least_squares()
Check whether optimizer is a least squares optimizer.

minimize(*problem: pypesto.problem.Problem, x0: numpy.ndarray, id: str, history_options: Optional[pypesto.objective.history.HistoryOptions] = None, optimize_options: Optional[pypesto.optimize.options.OptimizeOptions] = None*)

class pypesto.optimize.**PyswarmsOptimizer**(*par_popsize: float = 10, options: Optional[Dict] = None*)

Bases: pypesto.optimize.optimizer.Optimizer

Global optimization using pyswarms.

Package homepage: https://pyswarms.readthedocs.io/en/latest/index.html

Parameters

- **par_popsize** – number of particles in the swarm, default value 10
- **options** – Optimizer options that are directly passed on to pyswarms. c1: cognitive parameter c2: social parameter w: inertia parameter Default values are (c1,c2,w) = (0.5, 0.3, 0.9)

Examples

Arguments that can be passed to options:

maxiter: used to calculate the maximal number of funcion evaluations. Default: 1000

__init__(*par_popsize: float = 10, options: Optional[Dict] = None*)
Initialize base class.

is_least_squares()
Check whether optimizer is a least squares optimizer.

minimize(*problem: pypesto.problem.Problem, x0: numpy.ndarray, id: str, history_options: Optional[pypesto.objective.history.HistoryOptions] = None, optimize_options: Optional[pypesto.optimize.options.OptimizeOptions] = None*)

class pypesto.optimize.**ScipyDifferentialEvolutionOptimizer**(*options: Optional[Dict] = None*)

Bases: pypesto.optimize.optimizer.Optimizer

Global optimization using scipy's differential evolution optimizer.

Package homepage: https://docs.scipy.org/doc/scipy/reference/generated /scipy.optimize.differential_evolution.html

Parameters **options** – Optimizer options that are directly passed on to scipy's optimizer.

Examples

Arguments that can be passed to options:

maxiter: used to calculate the maximal number of funcion evaluations by maxfevals = (maxiter + 1) * popsize * len(x) Default: 100

popsize: population size, default value 15

__init__(*options: Optional[Dict] = None*)
Initialize base class.

is_least_squares()
Check whether optimizer is a least squares optimizer.

minimize(*problem:* pypesto.problem.Problem, *x0:* *numpy.ndarray*, *id:* *str*, *history_options: Optional[pypesto.objective.history.HistoryOptions] = None*, *optimize_options: Optional[pypesto.optimize.options.OptimizeOptions] = None*)

class pypesto.optimize.**ScipyOptimizer**(*method: str = 'L-BFGS-B'*, *tol: float = 1e-09*, *options: Optional[Dict] = None*)
Bases: pypesto.optimize.optimizer.Optimizer

Use the SciPy optimizers.

Find details on the optimizer and configuration options at: https://docs.scipy.org/doc/scipy/reference/generated/scipy. optimize.minimize.html#scipy.optimize.minimize

__init__(*method: str = 'L-BFGS-B'*, *tol: float = 1e-09*, *options: Optional[Dict] = None*)
Initialize base class.

get_default_options()
Create default options specific for the optimizer.

is_least_squares()
Check whether optimizer is a least squares optimizer.

minimize(*problem:* pypesto.problem.Problem, *x0:* *numpy.ndarray*, *id:* *str*, *history_options: Optional[pypesto.objective.history.HistoryOptions] = None*, *optimize_options: Optional[pypesto.optimize.options.OptimizeOptions] = None*)

pypesto.optimize.**fill_result_from_history**(*result: pypesto.result.optimize.OptimizerResult*, *optimizer_history: pypesto.objective.history.OptimizerHistory*, *optimize_options: Optional[pypesto.optimize.options.OptimizeOptions] = None*) → pypesto.result.optimize.OptimizerResult
Overwrite some values in the result object with values in the history.

Parameters

- **result** (*Result as reported from the used optimizer.*) –
- **optimizer_history** (*History of function values recorded by the objective.*) –
- **optimize_options** (*Options on e.g. how to override.*) –

Returns **result**

Return type The in-place modified result.

pypesto.optimize.**minimize**(*problem:* pypesto.problem.Problem, *optimizer: Optional[pypesto.optimize.optimizer.Optimizer] = None*, *n_starts: int = 100*, *ids: Optional[Iterable[str]] = None*, *startpoint_method: Optional[Union[pypesto.startpoint.base.StartpointMethod, Callable, bool]] = None*, *result: Optional[pypesto.result.result.Result] = None*, *engine: Optional[pypesto.engine.base.Engine] = None*, *progress_bar: bool = True*, *options: Optional[pypesto.optimize.options.OptimizeOptions] = None*, *history_options: Optional[pypesto.objective.history.HistoryOptions] = None*, *filename: Optional[str] = 'Auto'*) → pypesto.result.result.Result

Do multistart optimization.

Parameters

- **problem** – The problem to be solved.
- **optimizer** – The optimizer to be used n_starts times.
- **n_starts** – Number of starts of the optimizer.
- **ids** – Ids assigned to the startpoints.
- **startpoint_method** – Method for how to choose start points. False means the optimizer does not require start points, e.g. for the 'PyswarmOptimizer'.
- **result** – A result object to append the optimization results to. For example, one might append more runs to a previous optimization. If None, a new object is created.
- **engine** – Parallelization engine. Defaults to sequential execution on a SingleCoreEngine.
- **progress_bar** – Whether to display a progress bar.
- **options** – Various options applied to the multistart optimization.
- **history_options** – Optimizer history options.
- **filename** – Name of the hdf5 file, where the result will be saved. Default is "Auto", in which case it will automatically generate a file named *year_month_day_optimization_result.hdf5*. Deactivate saving by setting filename to *None*.

Returns Result object containing the results of all multistarts in *result.optimize_result*.

Return type result

pypesto.optimize.**optimization_result_from_history**(*filename: str*, *problem:* pypesto.problem.Problem) → pypesto.result.result.Result

Convert a saved hdf5 History to an optimization result.

Used for interrupted optimization runs.

Parameters

- **filename** – The name of the file in which the information are stored.
- **problem** – Problem, needed to identify what parameters to accept.

Returns

- *A result object in which the optimization result is constructed from*
- *history. But missing "Time, Message and Exitflag" keys.*

pypesto.optimize.**read_result_from_file**(*problem: pypesto.problem.Problem, history_options: pypesto.objective.history.HistoryOptions, identifier: str*) → pypesto.result.optimize.OptimizerResult

Fill an OptimizerResult from history.

Parameters

- **problem** – The problem to find optimal parameters for.
- **identifier** – Multistart id.
- **history_options** – Optimizer history options.

pypesto.optimize.**read_results_from_file**(*problem: pypesto.problem.Problem, history_options: pypesto.objective.history.HistoryOptions, n_starts: int*) → pypesto.result.result.Result

Fill a Result from a set of histories.

Parameters

- **problem** – The problem to find optimal parameters for.
- **n_starts** – Number of performed multistarts.
- **history_options** – Optimizer history options.

4.7 Profile

class pypesto.profile.**ProfileOptions**(*default_step_size: float = 0.01, min_step_size: float = 0.001, max_step_size: float = 1.0, step_size_factor: float = 1.25, delta_ratio_max: float = 0.1, ratio_min: float = 0.145, reg_points: int = 10, reg_order: int = 4, magic_factor_obj_value: float = 0.5*)

Bases: dict

Options for optimization based profiling.

Parameters

- **default_step_size** – Default step size of the profiling routine along the profile path (adaptive step lengths algorithms will only use this as a first guess and then refine the update).
- **min_step_size** – Lower bound for the step size in adaptive methods.
- **max_step_size** – Upper bound for the step size in adaptive methods.
- **step_size_factor** – Adaptive methods recompute the likelihood at the predicted point and try to find a good step length by a sort of line search algorithm. This factor controls step handling in this line search.
- **delta_ratio_max** – Maximum allowed drop of the posterior ratio between two profile steps.
- **ratio_min** – Lower bound for likelihood ratio of the profile, based on inverse chi2-distribution. The default 0.145 is slightly lower than the 95% quantile 0.1465 of a chi2 distribution with one degree of freedom.
- **reg_points** – Number of profile points used for regression in regression based adaptive profile points proposal.

- **reg_order** – Maximum degree of regression polynomial used in regression based adaptive profile points proposal.
- **magic_factor_obj_value** – There is this magic factor in the old profiling code which slows down profiling at small ratios (must be >= 0 and < 1).

__init__(*default_step_size: float = 0.01*, *min_step_size: float = 0.001*, *max_step_size: float = 1.0*, *step_size_factor: float = 1.25*, *delta_ratio_max: float = 0.1*, *ratio_min: float = 0.145*, *reg_points: int = 10*, *reg_order: int = 4*, *magic_factor_obj_value: float = 0.5*)

Initialize self. See help(type(self)) for accurate signature.

static create_instance(*maybe_options: Union[pypesto.profile.options.ProfileOptions, Dict]*) → pypesto.profile.options.ProfileOptions

Return a valid options object.

Parameters **maybe_options** (*ProfileOptions or dict*) –

pypesto.profile.**approximate_parameter_profile**(*problem:* pypesto.problem.Problem, *result: pypesto.result.result.Result*, *profile_index: Optional[Iterable[int]] = None*, *profile_list: Optional[int] = None*, *result_index: int = 0*, *n_steps: int = 100*) → pypesto.result.result.Result

Calculate profile approximation.

Based on an approximation via a normal likelihood centered at the chosen optimal parameter value, with the covariance matrix being the Hessian or FIM.

Parameters

- **problem** – The problem to be solved.
- **result** – A result object to initialize profiling and to append the profiling results to. For example, one might append more profiling runs to a previous profile, in order to merge these. The existence of an optimization result is obligatory.
- **profile_index** – List with the profile indices to be computed (by default all of the free parameters).
- **profile_list** – Integer which specifies whether a call to the profiler should create a new list of profiles (default) or should be added to a specific profile list.
- **result_index** – Index from which optimization result profiling should be started (default: global optimum, i.e., index = 0).
- **n_steps** – Number of profile steps in each dimension.

Returns The profile results are filled into *result.profile_result*.

Return type result

pypesto.profile.**calculate_approximate_ci**(*xs: numpy.ndarray*, *ratios: numpy.ndarray*, *confidence_ratio: float*) → Tuple[float, float]

Calculate approximate confidence interval based on profile.

Interval bounds are linerly interpolated.

Parameters

- **xs** – The ordered parameter values along the profile for the coordinate of interest.
- **ratios** – The likelihood ratios corresponding to the parameter values.
- **confidence_ratio** – Minimum confidence ratio to base the confidence interval upon, as obtained via *pypesto.profile.chi2_quantile_to_ratio*.

Returns Bounds of the approximate confidence interval.

Return type lb, ub

pypesto.profile.**chi2_quantile_to_ratio**(*alpha: float = 0.95*, *df: int = 1*)

Compute profile likelihood threshold.

Transform lower tail probability *alpha* for a chi2 distribution with *df* degrees of freedom to a profile likelihood ratio threshold.

Parameters

- **alpha** – Lower tail probability, defaults to 95% interval.
- **df** – Degrees of freedom.

Returns Corresponds to a likelihood ratio.

Return type ratio

pypesto.profile.**parameter_profile**(*problem: pypesto.problem.Problem*, *result: pypesto.result.result.Result*, *optimizer: pypesto.optimize.optimizer.Optimizer*, *engine: Optional[pypesto.engine.base.Engine] = None*, *profile_index: Optional[Iterable[int]] = None*, *profile_list: Optional[int] = None*, *result_index: int = 0*, *next_guess_method: Union[Callable, str] = 'adaptive_step_regression'*, *profile_options: Optional[pypesto.profile.options.ProfileOptions] = None*, *progress_bar: bool = True*, *filename: Optional[str] = 'Auto'*) → pypesto.result.result.Result

Call to do parameter profiling.

Parameters

- **problem** – The problem to be solved.
- **result** – A result object to initialize profiling and to append the profiling results to. For example, one might append more profiling runs to a previous profile, in order to merge these. The existence of an optimization result is obligatory.
- **optimizer** – The optimizer to be used along each profile.
- **engine** – The engine to be used.
- **profile_index** – List with the parameter indices to be profiled (by default all free indices).
- **profile_list** – Integer which specifies whether a call to the profiler should create a new list of profiles (default) or should be added to a specific profile list.
- **result_index** – Index from which optimization result profiling should be started (default: global optimum, i.e., index = 0).
- **next_guess_method** – Function handle to a method that creates the next starting point for optimization in profiling.
- **profile_options** – Various options applied to the profile optimization.
- **progress_bar** – Whether to display a progress bar.
- **filename** – Name of the hdf5 file, where the result will be saved. Default is "Auto", in which case it will automatically generate a file named *year_month_day_profiling_result.hdf5*. Deactivate saving by setting filename to *None*.

Returns The profile results are filled into *result.profile_result*.

Return type result

pypesto.profile.**validation_profile_significance**(*problem_full_data: pypesto.problem.Problem*, *result_training_data: pypesto.result.result.Result*, *result_full_data: Optional[pypesto.result.result.Result] = None*, *n_starts: Optional[int] = 1*, *optimizer: Optional[pypesto.optimize.optimizer.Optimizer] = None*, *engine: Optional[pypesto.engine.base.Engine] = None*, *lsq_objective: bool = False*, *return_significance: bool = True*) → float

Compute significance of Validation Interval.

It is a confidence region/interval for a new validation experiment.[1] et al. (This method per default returns the significance = 1-alpha!)

The reasoning behind their approach is, that a validation data set is outside the validation interval, if fitting the full data set would lead to a fit $theta_{new}$, that does not contain the old fit $theta_{train}$ in their (Profile-Likelihood) based parameter-confidence intervals. (I.e. the old fit would be rejected by the fit of the full data.)

This method returns the significance of the validation data set (where *result_full_data* is the objective function for fitting both data sets). I.e. the largest alpha, such that there is a validation region/interval such that the validation data set lies outside this Validation Interval with probability alpha. (If one is interested in the opposite, set *return_significance=False*.)

Parameters

- **problem_full_data** – pypesto.problem, such that the objective is the negative-log-likelihood of the training and validation data set.
- **result_training_data** – result object from the fitting of the training data set only.
- **result_full_data** – pypesto.result object that contains the result of fitting training and validation data combined.
- **n_starts** – number of starts for fitting the full data set (if result_full_data is not provided).
- **optimizer** – optimizer used for refitting the data (if result_full_data is not provided).
- **engine** – engine for refitting (if result_full_data is not provided).
- **lsq_objective** – indicates if the objective of problem_full_data corresponds to a nllh (False), or a chi^2 value (True).
- **return_significance** – indicates, if the function should return the significance (True) (i.e. the probability, that the new data set lies outside the Confidence Interval for the validation experiment, as given by the method), or the largest alpha, such that the validation experiment still lies within the Confidence Interval (False). I.e. alpha = 1-significance.

[1] Kreutz, Clemens, Raue, Andreas and Timmer, Jens. "Likelihood based observability analysis and confidence intervals for predictions of dynamic models". BMC Systems Biology 2012/12. doi:10.1186/1752-0509-6-120

4.8 Sample

Draw samples from the distribution, with support for various samplers.

class pypesto.sample.**AdaptiveMetropolisSampler**(*options: Optional[Dict] = None*)
Bases: pypesto.sample.metropolis.MetropolisSampler

Metropolis-Hastings sampler with adaptive proposal covariance.

__init__(*options: Optional[Dict] = None*)
Initialize self. See help(type(self)) for accurate signature.

classmethod default_options()
Return the default options for the sampler.

initialize(*problem:* pypesto.problem.Problem, *x0: numpy.ndarray*)
Initialize the sampler.

class pypesto.sample.**AdaptiveParallelTemperingSampler**(*internal_sampler: pypesto.sample.sampler.InternalSampler, betas: Optional[Sequence[float]] = None, n_chains: Optional[int] = None, options: Optional[Dict] = None*)
Bases: pypesto.sample.parallel_tempering.ParallelTemperingSampler

Parallel tempering sampler with adaptive temperature adaptation.

adjust_betas(*i_sample: int, swapped: Sequence[bool]*)
Update temperatures as in Vousden2016.

classmethod default_options() → Dict
Get default options for sampler.

class pypesto.sample.**EmceeSampler**(*nwalkers: int = 1, sampler_args: Optional[dict] = None, run_args: Optional[dict] = None*)
Bases: pypesto.sample.sampler.Sampler

Use emcee for sampling.

Wrapper around https://emcee.readthedocs.io/en/stable/, see there for details.

__init__(*nwalkers: int = 1, sampler_args: Optional[dict] = None, run_args: Optional[dict] = None*)
Initialize sampler.

Parameters

- **nwalkers**(*The number of walkers in the ensemble.*)–
- **sampler_args** – Further keyword arguments that are passed on to emcee.EnsembleSampler.__init__.
- **run_args** – Further keyword arguments that are passed on to emcee.EnsembleSampler.run_mcmc.

get_samples() → pypesto.result.sample.McmcPtResult
Get the samples into the fitting pypesto format.

initialize(*problem:* pypesto.problem.Problem, *x0: Union[numpy.ndarray, List[numpy.ndarray]]*) → None
Initialize the sampler.

sample(*n_samples: int*, *beta: float = 1.0*) → None
Return the most recent sample state.

class pypesto.sample.**InternalSampler**(*options: Optional[Dict] = None*)
Bases: pypesto.sample.sampler.Sampler

Sampler to be used inside a parallel tempering sampler.

The last sample can be obtained via *get_last_sample* and set via *set_last_sample*.

abstract get_last_sample() → pypesto.sample.sampler.InternalSample
Get the last sample in the chain.

Returns The last sample in the chain in the exchange format.

Return type internal_sample

make_internal(*temper_lpost: bool*)
Allow the inner samplers to be used as inner samplers.

Can be called by parallel tempering samplers during initialization. Default: Do nothing.

Parameters **temper_lpost** – Whether to temperate the posterior or only the likelihood.

abstract set_last_sample(*sample: pypesto.sample.sampler.InternalSample*)
Set the last sample in the chain to the passed value.

Parameters **sample** – The sample that will replace the last sample in the chain.

class pypesto.sample.**MetropolisSampler**(*options: Optional[Dict] = None*)
Bases: pypesto.sample.sampler.InternalSampler

Simple Metropolis-Hastings sampler with fixed proposal variance.

__init__(*options: Optional[Dict] = None*)
Initialize self. See help(type(self)) for accurate signature.

classmethod default_options()
Return the default options for the sampler.

get_last_sample() → pypesto.sample.sampler.InternalSample
Get the last sample in the chain.

Returns The last sample in the chain in the exchange format.

Return type internal_sample

get_samples() → pypesto.result.sample.McmcPtResult
Get the samples into the fitting pypesto format.

initialize(*problem:* pypesto.problem.Problem, *x0: numpy.ndarray*)
Initialize the sampler.

make_internal(*temper_lpost: bool*)
Allow the inner samplers to be used as inner samplers.

Can be called by parallel tempering samplers during initialization. Default: Do nothing.

Parameters **temper_lpost** – Whether to temperate the posterior or only the likelihood.

sample(*n_samples: int*, *beta: float = 1.0*)
Load last recorded particle.

set_last_sample(*sample: pypesto.sample.sampler.InternalSample*)
Set the last sample in the chain to the passed value.

Parameters **sample** – The sample that will replace the last sample in the chain.

class pypesto.sample.**ParallelTemperingSampler**(*internal_sampler: pypesto.sample.sampler.InternalSampler*, *betas: Optional[Sequence[float]] = None*, *n_chains: Optional[int] = None*, *options: Optional[Dict] = None*)

Bases: pypesto.sample.sampler.Sampler

Simple parallel tempering sampler.

__init__(*internal_sampler: pypesto.sample.sampler.InternalSampler*, *betas: Optional[Sequence[float]] = None*, *n_chains: Optional[int] = None*, *options: Optional[Dict] = None*)
Initialize self. See help(type(self)) for accurate signature.

adjust_betas(*i_sample: int*, *swapped: Sequence[bool]*)
Adjust temperature values. Default: Do nothing.

classmethod default_options() → Dict
Return the default options for the sampler.

get_samples() → pypesto.result.sample.McmcPtResult
Concatenate all chains.

initialize(*problem:* pypesto.problem.Problem, *x0: Union[numpy.ndarray, List[numpy.ndarray]]*)
Initialize all samplers.

sample(*n_samples: int*, *beta: float = 1.0*)
Sample and swap in between samplers.

swap_samples() → Sequence[bool]
Swap samples as in Vousden2016.

class pypesto.sample.**Pymc3Sampler**(*step_function=None*, ***kwargs*)

Bases: pypesto.sample.sampler.Sampler

Wrapper around Pymc3 samplers.

Parameters

- **step_function** – A pymc3 step function, e.g. NUTS, Slice. If not specified, pymc3 determines one automatically (preferable).
- ****kwargs** – Options are directly passed on to *pymc3.sample*.

__init__(*step_function=None*, ***kwargs*)
Initialize self. See help(type(self)) for accurate signature.

get_samples() → pypesto.result.sample.McmcPtResult
Convert result from Pymc3 to McmcPtResult.

initialize(*problem:* pypesto.problem.Problem, *x0: numpy.ndarray*)
Initialize the sampler.

Parameters

- **problem** – The problem for which to sample.
- **x0** – Should, but is not required to, be used as initial parameter.

sample(*n_samples: int*, *beta: float = 1.0*)
Sample the problem.

Parameters

- **n_samples** – Number of samples to be computed.

- **beta** – Inverse temperature for the log probability function.

classmethod translate_options(*options*)
Translate options and fill in defaults.

Parameters **options** – Options configuring the sampler.

class pypesto.sample.**Sampler**(*options: Optional[Dict] = None*)
Bases: abc.ABC

Sampler base class, not functional on its own.

The sampler maintains an internal chain, which is initialized in *initialize*, and updated in *sample*.

__init__(*options: Optional[Dict] = None*)
Initialize self. See help(type(self)) for accurate signature.

classmethod default_options() → Dict
Set/Get default options.

Returns Default sampler options.

Return type default_options

abstract get_samples() → pypesto.result.sample.McmcPtResult
Get the generated samples.

abstract initialize(*problem: pypesto.problem.Problem, x0: Union[numpy.ndarray, List[numpy.ndarray]]*)
Initialize the sampler.

Parameters

- **problem** – The problem for which to sample.
- **x0** – Should, but is not required to, be used as initial parameter.

abstract sample(*n_samples: int, beta: float = 1.0*)
Perform sampling.

Parameters

- **n_samples** – Number of samples to generate.
- **beta** – Inverse of the temperature to which the system is elevated.

classmethod translate_options(*options*)
Translate options and fill in defaults.

Parameters **options** – Options configuring the sampler.

pypesto.sample.**auto_correlation**(*result: pypesto.result.result.Result*) → float
Calculate the autocorrelation of the MCMC chains.

Parameters **result** – The pyPESTO result object with filled sample result.

Returns Estimate of the integrated autocorrelation time of the MCMC chains.

Return type auto_correlation

pypesto.sample.**calculate_ci_mcmc_sample**(*result: pypesto.result.result.Result, ci_level: float = 0.95, exclude_burn_in: bool = True*) → Tuple[numpy.ndarray, numpy.ndarray]
Calculate parameter credibility intervals based on MCMC samples.

Parameters

- **result** – The pyPESTO result object with filled sample result.

- **ci_level** – Lower tail probability, defaults to 95% interval.

Returns Bounds of the MCMC percentile-based confidence interval.

Return type lb, ub

pypesto.sample.**calculate_ci_mcmc_sample_prediction**(*simulated_values: numpy.ndarray*, *ci_level: float = 0.95*) → Tuple[numpy.ndarray, numpy.ndarray]

Calculate prediction credibility intervals based on MCMC samples.

Parameters

- **simulated_values** – Simulated model states or model observables.
- **ci_level** – Lower tail probability, defaults to 95% interval.

Returns Bounds of the MCMC-based prediction confidence interval.

Return type lb, ub

pypesto.sample.**effective_sample_size**(*result: pypesto.result.result.Result*) → float

Calculate the effective sample size of the MCMC chains.

Parameters **result** – The pyPESTO result object with filled sample result.

Returns Estimate of the effective sample size of the MCMC chains.

Return type ess

pypesto.sample.**geweke_test**(*result: pypesto.result.result.Result*, *zscore: float = 2.0*) → int

Calculate the burn-in of MCMC chains.

Parameters

- **result** – The pyPESTO result object with filled sample result.
- **zscore** – The Geweke test threshold.

Returns Iteration where the first and the last fraction of the chain do not differ significantly regarding Geweke test -> Burn-In

Return type burn_in

pypesto.sample.**sample**(*problem: pypesto.problem.Problem*, *n_samples: int*, *sampler: Optional[pypesto.sample.sampler.Sampler] = None*, *x0: Optional[Union[numpy.ndarray, List[numpy.ndarray]]] = None*, *result: Optional[pypesto.result.result.Result] = None*, *filename: Optional[str] = 'Auto'*) → pypesto.result.result.Result

Call to do parameter sampling.

Parameters

- **problem** – The problem to be solved. If None is provided, a `pypesto.AdaptiveMetropolisSampler` is used.
- **n_samples** – Number of samples to generate.
- **sampler** – The sampler to perform the actual sampling.
- **x0** – Initial parameter for the Markov chain. If None, the best parameter found in optimization is used. Note that some samplers require an initial parameter, some may ignore it. x0 can also be a list, to have separate starting points for parallel tempering chains.
- **result** – A result to write to. If None provided, one is created from the problem.

- **filename** – Name of the hdf5 file, where the result will be saved. Default is "Auto", in which case it will automatically generate a file named *year_month_day_sampling_result.hdf5*. Deactivate saving by setting filename to *None*.

Returns A result with filled in sample_options part.

Return type result

4.9 Result

The pypesto.Result object contains all results generated by the pypesto components. It contains sub-results for optimization, profiling, sampling.

class pypesto.result.**McmcPtResult**(*trace_x: numpy.ndarray*, *trace_neglogpost: numpy.ndarray*, *trace_neglogprior: numpy.ndarray*, *betas: Iterable[float]*, *burn_in: Optional[int] = None*, *time: float = 0.0*, *auto_correlation: Optional[float] = None*, *effective_sample_size: Optional[float] = None*, *message: Optional[str] = None*)

Bases: dict

The result of a sampler run using Markov-chain Monte Carlo.

Currently result object of all supported samplers. Can be used like a dict.

Parameters

- **trace_x** (*[n_chain, n_iter, n_par]*) – Parameters.
- **trace_neglogpost** (*[n_chain, n_iter]*) – Negative log posterior values.
- **trace_neglogprior** (*[n_chain, n_iter]*) – Negative log prior values.
- **betas** (*[n_chain]*) – The associated inverse temperatures.
- **burn_in** (*[n_chain]*) – The burn in index.
- **time** (*[n_chain]*) – The computation time.
- **auto_correlation** (*[n_chain]*) – The estimated chain autcorrelation.
- **effective_sample_size** (*[n_chain]*) – The estimated effective sample size.
- **message** (*str*) – Textual comment on the profile result.
- **Here** –
- **denotes the number of chains** (*n_chain*) –
- **the number of** (*n_iter*) –
- **(i.e.** (*iterations*) –
- **chain length)** (*the*) –
- **n_par the number of parameters.** (*and*) –

__init__(*trace_x: numpy.ndarray*, *trace_neglogpost: numpy.ndarray*, *trace_neglogprior: numpy.ndarray*, *betas: Iterable[float]*, *burn_in: Optional[int] = None*, *time: float = 0.0*, *auto_correlation: Optional[float] = None*, *effective_sample_size: Optional[float] = None*, *message: Optional[str] = None*)

Initialize self. See help(type(self)) for accurate signature.

class pypesto.result.**OptimizeResult**

Bases: object

Result of the *pypesto.optimize.minimize()* function.

__init__()
Initialize self. See help(type(self)) for accurate signature.

append(*optimizer_result: pypesto.result.optimize.OptimizerResult*)
Append an optimizer result to the result object.

Parameters **optimizer_result** – The result of one (local) optimizer run.

as_dataframe(*keys=None*) → pandas.core.frame.DataFrame
Get as pandas DataFrame.

If keys is a list, return only the specified values, otherwise all.

as_list(*keys=None*) → Sequence
Get as list.

If keys is a list, return only the specified values.

Parameters **keys** (*list(str), optional*) – Labels of the field to extract.

get_for_key(*key*) → list
Extract the list of values for the specified key as a list.

sort()
Sort the optimizer results by function value fval (ascending).

class pypesto.result.**OptimizerResult**(*id: Optional[str] = None, x: Optional[numpy.ndarray] = None, fval: Optional[float] = None, grad: Optional[numpy.ndarray] = None, hess: Optional[numpy.ndarray] = None, res: Optional[numpy.ndarray] = None, sres: Optional[numpy.ndarray] = None, n_fval: Optional[int] = None, n_grad: Optional[int] = None, n_hess: Optional[int] = None, n_res: Optional[int] = None, n_sres: Optional[int] = None, x0: Optional[numpy.ndarray] = None, fval0: Optional[float] = None, history: Optional[pypesto.objective.history.History] = None, exitflag: Optional[int] = None, time: Optional[float] = None, message: Optional[str] = None*)

Bases: dict

The result of an optimizer run.

Used as a standardized return value to map from the individual result objects returned by the employed optimizers to the format understood by pypesto.

Can be used like a dict.

id
Id of the optimizer run. Usually the start index.

x
The best found parameters.

fval
The best found function value, *fun(x)*.

grad
The gradient at *x*.

hess
The Hessian at *x*.

res
The residuals at *x*.

sres
The residual sensitivities at *x*.

n_fval
Number of function evaluations.

n_grad
Number of gradient evaluations.

n_hess
Number of Hessian evaluations.

n_res
Number of residuals evaluations.

n_sres
Number of residual sensitivity evaluations.

x0
The starting parameters.

fval0
The starting function value, *fun(x0)*.

history
Objective history.

exitflag
The exitflag of the optimizer.

time
Execution time.

message
Textual comment on the optimization result.

Type str

Notes

Any field not supported by the optimizer is filled with None.

__init__(*id: Optional[str] = None*, *x: Optional[numpy.ndarray] = None*, *fval: Optional[float] = None*, *grad: Optional[numpy.ndarray] = None*, *hess: Optional[numpy.ndarray] = None*, *res: Optional[numpy.ndarray] = None*, *sres: Optional[numpy.ndarray] = None*, *n_fval: Optional[int] = None*, *n_grad: Optional[int] = None*, *n_hess: Optional[int] = None*, *n_res: Optional[int] = None*, *n_sres: Optional[int] = None*, *x0: Optional[numpy.ndarray] = None*, *fval0: Optional[float] = None*, *history: Optional[pypesto.objective.history.History] = None*, *exitflag: Optional[int] = None*, *time: Optional[float] = None*, *message: Optional[str] = None*)
Initialize self. See help(type(self)) for accurate signature.

update_to_full(*problem:* pypesto.problem.Problem) → None
Update values to full vectors/matrices.

Parameters **problem** – problem which contains info about how to convert to full vectors or matrices

class pypesto.result.**PredictionConditionResult**(*timepoints: numpy.ndarray, output_ids: Sequence[str], output: Optional[numpy.ndarray] = None, output_sensi: Optional[numpy.ndarray] = None, output_weight: Optional[float] = None, output_sigmay: Optional[numpy.ndarray] = None, x_names: Optional[Sequence[str]] = None*)

Bases: object

Light-weight wrapper for the prediction of one simulation condition.

It should provide a common api how amici predictions should look like in pyPESTO.

__init__(*timepoints: numpy.ndarray, output_ids: Sequence[str], output: Optional[numpy.ndarray] = None, output_sensi: Optional[numpy.ndarray] = None, output_weight: Optional[float] = None, output_sigmay: Optional[numpy.ndarray] = None, x_names: Optional[Sequence[str]] = None*)
Initialize PredictionConditionResult.

Parameters

- **timepoints** – Output timepoints for this simulation condition
- **output_ids** – IDs of outputs for this simulation condition
- **output** – Postprocessed outputs (ndarray)
- **output_sensi** – Sensitivities of postprocessed outputs (ndarray)
- **output_weight** – LLH of the simulation
- **output_sigmay** – Standard deviations of postprocessed observables
- **x_names** – IDs of model parameter w.r.t to which sensitivities were computed

class pypesto.result.**PredictionResult**(*conditions: Sequence[Union[pypesto.result.predict.PredictionConditionResult, Dict]], condition_ids: Optional[Sequence[str]] = None, comment: Optional[str] = None*)

Bases: object

Light-weight wrapper around prediction from pyPESTO made by an AMICI model.

Its only purpose is to have fixed format/api, how prediction results should be stored, read, and handled: as predictions are a very flexible format anyway, they should at least have a common definition, which allows to work with them in a reasonable way.

__init__(*conditions: Sequence[Union[pypesto.result.predict.PredictionConditionResult, Dict]], condition_ids: Optional[Sequence[str]] = None, comment: Optional[str] = None*)
Initialize PredictionResult.

Parameters

- **conditions** – A list of PredictionConditionResult objects or dicts
- **condition_ids** – IDs or names of the simulation conditions, which belong to this prediction (e.g., PEtab uses tuples of preequilibration condition and simulation conditions)

- **comment** – An additional note, which can be attached to this prediction

write_to_csv(*output_file: str*)
Save predictions to a csv file.

Parameters **output_file** – path to file/folder to which results will be written

write_to_h5(*output_file: str*, *base_path: Optional[str] = None*)
Save predictions to an h5 file.

It appends to the file if the file already exists.

Parameters

- **output_file** – path to file/folder to which results will be written
- **base_path** – base path in the h5 file

class pypesto.result.**ProfileResult**
Bases: object

Result of the profile() function.

It holds a list of profile lists. Each profile list consists of a list of *ProfilerResult* objects, one for each parameter.

__init__()
Initialize self. See help(type(self)) for accurate signature.

append_empty_profile_list() → int
Append an empty profile list to the list of profile lists.

Returns The index of the created profile list.

Return type index

append_profiler_result(*profiler_result: Optional[pypesto.result.profile.ProfilerResult] = None*, *profile_list: Optional[int] = None*) → None
Append the profiler result to the profile list.

Parameters

- **profiler_result** – The result of one profiler run for a parameter, or None if to be left empty.
- **profile_list** – Index specifying the profile list to which we want to append. Defaults to the last list.

get_profiler_result(*i_par: int*, *profile_list: Optional[int] = None*)
Get the profiler result at parameter index *i_par* of *profile_list*.

Parameters

- **i_par** – Integer specifying the profile index.
- **profile_list** – Index specifying the profile list. Defaults to the last list.

set_profiler_result(*profiler_result: pypesto.result.profile.ProfilerResult*, *i_par: int*, *profile_list: Optional[int] = None*) → None
Write a profiler result to the result object.

Parameters

- **profiler_result** – The result of one (local) profiler run.
- **i_par** – Integer specifying the parameter index where to put profiler_result.
- **profile_list** – Index specifying the profile list. Defaults to the last list.

class pypesto.result.**ProfilerResult**(*x_path: numpy.ndarray*, *fval_path: numpy.ndarray*, *ratio_path: numpy.ndarray*, *gradnorm_path: numpy.ndarray = nan*, *exitflag_path: numpy.ndarray = nan*, *time_path: numpy.ndarray = nan*, *time_total: float = 0.0*, *n_fval: int = 0*, *n_grad: int = 0*, *n_hess: int = 0*, *message: Optional[str] = None*)

Bases: dict

The result of a profiler run.

The standardized return value from pypesto.profile, which can either be initialized from an OptimizerResult or from an existing ProfilerResult (in order to extend the computation).

Can be used like a dict.

x_path
The path of the best found parameters along the profile (Dimension: n_par x n_profile_points)

fval_path
The function values, fun(x), along the profile.

ratio_path
The ratio of the posterior function along the profile.

gradnorm_path
The gradient norm along the profile.

exitflag_path
The exitflags of the optimizer along the profile.

time_path
The computation time of the optimizer runs along the profile.

time_total
The total computation time for the profile.

n_fval
Number of function evaluations.

n_grad
Number of gradient evaluations.

n_hess
Number of Hessian evaluations.

message
Textual comment on the profile result.

Notes

Any field not supported by the profiler or the profiling optimizer is filled with None. Some fields are filled by pypesto itself.

__init__(*x_path: numpy.ndarray*, *fval_path: numpy.ndarray*, *ratio_path: numpy.ndarray*, *gradnorm_path: numpy.ndarray = nan*, *exitflag_path: numpy.ndarray = nan*, *time_path: numpy.ndarray = nan*, *time_total: float = 0.0*, *n_fval: int = 0*, *n_grad: int = 0*, *n_hess: int = 0*, *message: Optional[str] = None*)
Initialize self. See help(type(self)) for accurate signature.

append_profile_point(*x: numpy.ndarray*, *fval: float*, *ratio: float*, *gradnorm: float = nan*, *time: float = nan*, *exitflag: float = nan*, *n_fval: int = 0*, *n_grad: int = 0*, *n_hess: int = 0*) → None

Append a new point to the profile path.

Parameters

- **x** – The parameter values.
- **fval** – The function value at x.
- **ratio** – The ratio of the function value at x by the optimal function value.
- **gradnorm** – The gradient norm at x.
- **time** – The computation time to find x.
- **exitflag** – The exitflag of the optimizer (useful if an optimization was performed to find x).
- **n_fval** – Number of function evaluations performed to find x.
- **n_grad** – Number of gradient evaluations performed to find x.
- **n_hess** – Number of Hessian evaluations performed to find x.

flip_profile() → None

Flip the profiling direction (left-right).

Profiling direction needs to be changed once (if the profile is new), or twice if we append to an existing profile. All profiling paths are flipped in-place.

class pypesto.result.**Result**(*problem=None*)

Bases: object

Universal result object for pypesto.

The algorithms like optimize, profile, sample fill different parts of it.

problem

The problem underlying the results.

Type *pypesto.Problem*

optimize_result

The results of the optimizer runs.

profile_result

The results of the profiler run.

sample_result

The results of the sampler run.

__init__(*problem=None*)

Initialize self. See help(type(self)) for accurate signature.

class pypesto.result.**SampleResult**

Bases: object

Result of the sample() function.

__init__()

Initialize self. See help(type(self)) for accurate signature.

4.10 Visualize

pypesto comes with various visualization routines. To use these, import pypesto.visualize.

class pypesto.visualize.**ReferencePoint**(*reference=None*, *x=None*, *fval=None*, *color=None*, *legend=None*)

Bases: dict

Reference point for plotting.

Should contain a parameter value and an objective function value, may also contain a color and a legend.

Can be used like a dict.

x
Reference parameters.

Type ndarray

fval
Function value, fun(x), for reference parameters.

Type float

color
Color which should be used for reference point.

Type RGBA, optional

auto_color
flag indicating whether color for this reference point should be assigned automatically or whether it was assigned by user

Type boolean

legend
legend text for reference point

Type str

__init__(*reference=None*, *x=None*, *fval=None*, *color=None*, *legend=None*)
Initialize self. See help(type(self)) for accurate signature.

pypesto.visualize.**assign_clustered_colors**(*vals*, *balance_alpha=True*, *highlight_global=True*)

Cluster and assign colors.

Parameters

- **vals** (*numeric list or array*) – List to be clustered and assigned colors.
- **balance_alpha** (*bool (optional)*) – Flag indicating whether alpha for large clusters should be reduced to avoid overplotting (default: True)
- **highlight_global** (*bool (optional)*) – flag indicating whether global optimum should be highlighted

Returns **colors** – One for each element in 'vals'.

Return type list of RGBA

pypesto.visualize.**assign_clusters**(*vals*)
Find clustering.

Parameters **vals** (*numeric list or array*) – List to be clustered.

Returns

- **clust** (*numeric list*) – Indicating the corresponding cluster of each element from 'vals'.
- **clustsize** (*numeric list*) – Size of clusters, length equals number of clusters.

pypesto.visualize.**assign_colors**(*vals*, *colors=None*, *balance_alpha=True*, *highlight_global=True*)

Assign colors or format user specified colors.

Parameters

- **vals** (*numeric list or array*) – List to be clustered and assigned colors.
- **colors** (*list, or RGBA, optional*) – list of colors, or single color
- **balance_alpha** (*bool (optional)*) – Flag indicating whether alpha for large clusters should be reduced to avoid overplotting (default: True)
- **highlight_global** (*bool (optional)*) – flag indicating whether global optimum should be highlighted

Returns **colors** – One for each element in 'vals'.

Return type list of RGBA

pypesto.visualize.**create_references**(*references=None*, *x=None*, *fval=None*, *color=None*, *legend=None*) → List[pypesto.visualize.reference_points.ReferencePoint]

Create a list of reference point objects from user inputs.

Parameters

- **references** (*ReferencePoint or dict or list, optional*) – Will be converted into a list of RefPoints
- **x** (*ndarray, optional*) – Parameter vector which should be used for reference point
- **fval** (*float, optional*) – Objective function value which should be used for reference point
- **color** (*RGBA, optional*) – Color which should be used for reference point.
- **legend** (*str*) – legend text for reference point

Returns **colors** – One for each element in 'vals'.

Return type list of RGBA

pypesto.visualize.**delete_nan_inf**(*fvals: numpy.ndarray*, *x: Optional[numpy.ndarray] = None*, *xdim: Optional[int] = 1*) → Tuple[numpy.ndarray, numpy.ndarray]

Delete nan and inf values in fvals.

If parameters 'x' are passed, also the corresponding entries are deleted.

Parameters

- **x** – array of parameters
- **fvals** – array of fval
- **xdim** – dimension of x, in case x dimension cannot be inferred

Returns

- *x* – array of parameters without nan or inf

- *fvals* – array of fval without nan or inf

pypesto.visualize.**ensemble_crosstab_scatter_lowlevel**(*dataset: numpy.ndarray*, *component_labels: Optional[Sequence[str]] = None*, ***kwargs*)

Plot cross-classification table of scatter plots for different coordinates.

Lowlevel routine for multiple UMAP and PCA plots, but can also be used to visualize, e.g., parameter traces across optimizer runs.

Parameters

- **dataset** – array of data points to be shown as scatter plot
- **component_labels** – labels for the x-axes and the y-axes

Returns A dictionary of plot axes.

Return type axs

pypesto.visualize.**ensemble_identifiability**(*ensemble: pypesto.ensemble.ensemble.Ensemble*, *ax: Optional[matplotlib.axes._axes.Axes] = None*, *size: Optional[Tuple[float]] = (12, 6)*)

Visualize identifiablity of parameter ensemble.

Plot an overview about how many parameters hit the parameter bounds based on a ensemble of parameters. confidence intervals/credible ranges are computed via the ensemble mean plus/minus 1 standard deviation. This highlevel routine expects a ensemble object as input.

Parameters

- **ensemble** – ensemble of parameter vectors (from pypesto.ensemble)
- **ax** – Axes object to use.
- **size** – Figure size (width, height) in inches. Is only applied when no ax object is specified

Returns **ax** – The plot axes.

Return type matplotlib.Axes

pypesto.visualize.**ensemble_scatter_lowlevel**(*dataset*, *ax: Optional[matplotlib.axes._axes.Axes] = None*, *size: Optional[Tuple[float]] = (12, 6)*, *x_label: str = 'component 1'*, *y_label: str = 'component 2'*, *color_by: Optional[Sequence[float]] = None*, *color_map: str = 'viridis'*, *background_color: Tuple[float, float, float, float] = (0.0, 0.0, 0.0, 1.0)*, *marker_type: str = '.'*, *scatter_size: float = 0.5*, *invert_scatter_order: bool = False*)

Create a scatter plot.

Parameters

- **dataset** – array of data points in reduced dimension
- **ax** – Axes object to use.
- **size** – Figure size (width, height) in inches. Is only applied when no ax object is specified
- **x_label** – The x-axis label

- **y_label** – The y-axis label
- **color_by** – A sequence/list of floats, which specify the color in the colormap
- **color_map** – A colormap name known to pyplot
- **background_color** – Background color of the axes object (defaults to black)
- **marker_type** – Type of plotted markers
- **scatter_size** – Size of plotted markers
- **invert_scatter_order** – Specifies the order of plotting the scatter points, can be important in case of overplotting

Returns **ax** – The plot axes.

Return type matplotlib.Axes

pypesto.visualize.**optimization_run_properties_one_plot**(*results: pypesto.result.result.Result*, *properties_to_plot: Optional[List[str]] = None*, *size: Tuple[float, float] = (18.5, 10.5)*, *start_indices: Optional[Union[int, Iterable[int]]] = None*, *colors: Optional[Union[List[float], List[List[float]]]] = None*, *legends: Optional[Union[str, List[str]]] = None*, *plot_type: str = 'line'*) → matplotlib.axes._axes.Axes

Plot stats for allproperties specified in properties_to_plot on one plot.

Parameters

- **results** – Optimization result obtained by 'optimize.py' or list of those
- **properties_to_plot** – Optimization run properties that should be plotted
- **size** – Figure size (width, height) in inches. Is only applied when no ax object is specified
- **start_indices** – List of integers specifying the multistarts to be plotted or int specifying up to which start index should be plotted
- **colors** – List of RGBA colors (one color per property in properties_to_plot), or single RGBA color. If not set and one result, clustering is done and colors are assigned automatically
- **legends** – Labels, one label per optimization property
- **plot_type** – Specifies plot type. Possible values: 'line' and 'hist'

Returns The plot axes.

Return type ax

Examples

optimization_properties_per_multistart(result1, properties_to_plot=['time'], colors=[.5, .9, .9, .3])

optimization_properties_per_multistart(result1, properties_to_plot=['time', 'n_grad'], colors=[[.5, .9, .9, .3], [.2, .1, .9, .5]])

pypesto.visualize.**optimization_run_properties_per_multistart**(*results: Union[pypesto.result.result.Result, Sequence[pypesto.result.result.Result]], properties_to_plot: Optional[List[str]] = None, size: Tuple[float, float] = (18.5, 10.5), start_indices: Optional[Union[int, Iterable[int]]] = None, colors: Optional[Union[List[float], List[List[float]]]] = None, legends: Optional[Union[str, List[str]]] = None, plot_type: str = 'line'*) → Dict[str, matplotlib.axes._subplots.AxesSubplot]

One plot per optimization property in properties_to_plot.

Parameters

- **results** – Optimization result obtained by 'optimize.py' or list of those
- **properties_to_plot** – Optimization run properties that should be plotted
- **size** – Figure size (width, height) in inches. Is only applied when no ax object is specified
- **start_indices** – List of integers specifying the multistarts to be plotted or int specifying up to which start index should be plotted
- **colors** – List of RGBA colors (one color per result in results), or single RGBA color. If not set and one result, clustering is done and colors are assigned automatically
- **legends** – Labels for line plots, one label per result object
- **plot_type** – Specifies plot type. Possible values: 'line' and 'hist'

Returns

- *ax*
- *The plot axes.*

Examples

optimization_properties_per_multistart(result1, properties_to_plot=['time'], colors=[.5, .9, .9, .3])

optimization_properties_per_multistart([result1, result2], properties_to_plot=['time'], colors=[[.5, .9, .9, .3], [.2, .1, .9, .5]])

optimization_properties_per_multistart(result1, properties_to_plot=['time', 'n_grad'], colors=[.5, .9, .9, .3])

optimization_properties_per_multistart([result1, result2], properties_to_plot=['time', 'n_fval'], colors=[[.5, .9, .9, .3], [.2, .1, .9, .5]])

pypesto.visualize.**optimization_run_property_per_multistart**(*results: Union[pypesto.result.result.Result, Sequence[pypesto.result.result.Result]], opt_run_property: str, axes: Optional[matplotlib.axes._axes.Axes] = None, size: Tuple[float, float] = (18.5, 10.5), start_indices: Optional[Union[int, Iterable[int]]] = None, colors: Optional[Union[List[float], List[List[float]]]] = None, legends: Optional[Union[str, List[str]]] = None, plot_type: str = 'line'*) → matplotlib.axes._axes.Axes

Plot stats for an optimization run property specified by opt_run_property.

It is possible to plot a histogram or a line plot. In a line plot, on the x axis are the numbers of the multistarts, where the multistarts are ordered with respect to a function value. On the y axis of the line plot the value of the corresponding parameter for each multistart is displayed.

Parameters

- **opt_run_property** – optimization run property to plot. One of the 'time', 'n_fval', 'n_grad', 'n_hess', 'n_res', 'n_sres'
- **results** – Optimization result obtained by 'optimize.py' or list of those
- **axes** – Axes object to use
- **size** – Figure size (width, height) in inches. Is only applied when no ax object is specified
- **start_indices** – List of integers specifying the multistarts to be plotted or int specifying up to which start index should be plotted
- **colors** – List of RGBA colors (one color per result in results), or single RGBA color. If not set and one result, clustering is done and colors are assigned automatically
- **legends** – Labels for line plots, one label per result object
- **plot_type** – Specifies plot type. Possible values: 'line', 'hist', 'both'

Returns The plot axes.

Return type ax

pypesto.visualize.**optimizer_convergence**(*result: pypesto.result.result.Result*, *ax: Optional[matplotlib.axes._axes.Axes] = None*, *xscale: str = 'symlog'*, *yscale: str = 'log'*, *size: Tuple[float] = (18.5, 10.5)*) → matplotlib.axes._axes.Axes

Visualize to help spotting convergence issues.

Scatter plot of function values and gradient values at the end of optimization. Optimizer exit-message is encoded by color. Can help identifying convergence issues in optimization and guide tolerance refinement etc.

Parameters

- **result** – Optimization result obtained by 'optimize.py'
- **ax** – Axes object to use.
- **size** – Figure size (width, height) in inches. Is only applied when no ax object is specified
- **xscale** – Scale for x-axis
- **yscale** – Scale for y-axis

Returns **ax** – The plot axes.

Return type matplotlib.Axes

pypesto.visualize.**optimizer_history**(*results*, *ax=None*, *size=(18.5, 10.5)*, *trace_x='steps'*, *trace_y='fval'*, *scale_y='log10'*, *offset_y=None*, *colors=None*, *y_limits=None*, *start_indices=None*, *reference=None*, *legends=None*)

Plot history of optimizer.

Can plot either the history of the cost function or of the gradient norm, over either the optimizer steps or the computation time.

Parameters

- **results** (*pypesto.Result or list*) – Optimization result obtained by 'optimize.py' or list of those
- **ax** (*matplotlib.Axes, optional*) – Axes object to use.
- **size** (*tuple, optional*) – Figure size (width, height) in inches. Is only applied when no ax object is specified
- **trace_x** (*str, optional*) – What should be plotted on the x-axis? Possibilities: 'time', 'steps' Default: 'steps'
- **trace_y** (*str, optional*) – What should be plotted on the y-axis? Possibilities: 'fval', 'gradnorm', 'stepsize' Default: 'fval'
- **scale_y** (*str, optional*) – May be logarithmic or linear ('log10' or 'lin')
- **offset_y** (*float, optional*) – Offset for the y-axis-values, as these are plotted on a log10-scale Will be computed automatically if necessary
- **colors** (*list, or RGBA, optional*) – list of colors, or single color color or list of colors for plotting. If not set, clustering is done and colors are assigned automatically
- **y_limits** (*float or ndarray, optional*) – maximum value to be plotted on the y-axis, or y-limits

- **start_indices** (*list or int*) – list of integers specifying the multistart to be plotted or int specifying up to which start index should be plotted
- **reference** (*list, optional*) – List of reference points for optimization results, containing et least a function value fval
- **legends** (*list or str*) – Labels for line plots, one label per result object

Returns **ax** – The plot axes.

Return type matplotlib.Axes

pypesto.visualize.**optimizer_history_lowlevel**(*vals*, *scale_y='log10'*, *colors=None*, *ax=None*, *size=(18.5, 10.5)*, *x_label='Optimizer steps'*, *y_label='Objective value'*, *legend_text=None*)

Plot optimizer history using list of numpy arrays.

Parameters

- **vals** (*list of numpy arrays*) – list of 2xn-arrays (x_values and y_values of the trace)
- **scale_y** (*str, optional*) – May be logarithmic or linear ('log10' or 'lin')
- **colors** (*list, or RGBA, optional*) – list of colors, or single color color or list of colors for plotting. If not set, clustering is done and colors are assigned automatically
- **ax** (*matplotlib.Axes, optional*) – Axes object to use.
- **size** (*tuple, optional*) – see waterfall
- **x_label** (*str*) – label for x-axis
- **y_label** (*str*) – label for y-axis
- **legend_text** (*str*) – Label for line plots

Returns **ax** – The plot axes.

Return type matplotlib.Axes

pypesto.visualize.**parameter_hist**(*result: pypesto.result.result.Result*, *parameter_name: str*, *bins: Union[int, str] = 'auto'*, *ax: Optional[matplotlib.Axes] = None*, *size: Optional[Tuple[float]] = (18.5, 10.5)*, *color: Optional[List[float]] = None*, *start_indices: Optional[Union[int, List[int]]] = None*)

Plot parameter values as a histogram.

Parameters

- **result** – Optimization result obtained by 'optimize.py'
- **parameter_name** – The name of the parameter that should be plotted
- **bins** – Specifies bins of the histogram
- **ax** – Axes object to use
- **size** – Figure size (width, height) in inches. Is only applied when no ax object is specified
- **color** – RGBA color.
- **start_indices** – List of integers specifying the multistarts to be plotted or int specifying up to which start index should be plotted

Returns The plot axes.

Return type ax

pypesto.visualize.**parameters**(*results: Union[pypesto.result.result.Result, Sequence[pypesto.result.result.Result]], ax: Optional[matplotlib.axes._axes.Axes] = None, parameter_indices: Union[str, Sequence[int]] = 'free_only', lb: Optional[Union[numpy.ndarray, List[float]]] = None, ub: Optional[Union[numpy.ndarray, List[float]]] = None, size: Optional[Tuple[float, float]] = None, reference: Optional[List[pypesto.visualize.reference_points.ReferencePoint]] = None, colors: Optional[Union[List[float], List[List[float]]]] = None, legends: Optional[Union[str, List[str]]] = None, balance_alpha: bool = True, start_indices: Optional[Union[int, Iterable[int]]] = None, scale_to_interval: Optional[Tuple[float, float]] = None*) → matplotlib.axes._axes.Axes

Plot parameter values.

Parameters

- **results** – Optimization result obtained by 'optimize.py' or list of those
- **ax** – Axes object to use.
- **parameter_indices** – Specifies which parameters should be plotted. Allowed string values are 'all' (both fixed and free parameters will be plotted) and 'free_only' (only free parameters will be plotted)
- **lb** – If not None, override result.problem.lb, problem.problem.ub. Dimension either result.problem.dim or result.problem.dim_full.
- **ub** – If not None, override result.problem.lb, problem.problem.ub. Dimension either result.problem.dim or result.problem.dim_full.
- **size** – Figure size (width, height) in inches. Is only applied when no ax object is specified
- **reference** – List of reference points for optimization results, containing at least a function value fval
- **colors** – list of RGBA colors, or single RGBA color If not set, clustering is done and colors are assigned automatically
- **legends** – Labels for line plots, one label per result object
- **balance_alpha** – Flag indicating whether alpha for large clusters should be reduced to avoid overplotting (default: True)
- **start_indices** – list of integers specifying the multistarts to be plotted or int specifying up to which start index should be plotted
- **scale_to_interval** – Tuple of bounds to which to scale all parameter values and bounds, or `None` to use bounds as determined by `lb, ub`.

Returns The plot axes.

Return type ax

pypesto.visualize.**parameters_lowlevel**(*xs: Sequence[Union[numpy.ndarray, List[float]]], fvals: Union[numpy.ndarray, List[float]], lb: Optional[Union[numpy.ndarray, List[float]]] = None, ub: Optional[Union[numpy.ndarray, List[float]]] = None, x_labels: Optional[Iterable[str]] = None, ax: Optional[matplotlib.axes._axes.Axes] = None, size: Optional[Tuple[float, float]] = None, colors: Optional[Sequence[Union[numpy.ndarray, List[float]]]] = None, linestyle: str = '-', legend_text: Optional[str] = None, balance_alpha: bool = True*) → matplotlib.axes._axes.Axes

Plot parameters plot using list of parameters.

Parameters

- **xs** – Including optimized parameters for each startpoint. Shape: (n_starts, dim).
- **fvals** – Function values. Needed to assign cluster colors.
- **lb** – The lower and upper bounds.
- **ub** – The lower and upper bounds.
- **x_labels** – Labels to be used for the parameters.
- **ax** – Axes object to use.
- **size** – see parameters
- **colors** – One for each element in 'fvals'.
- **linestyle** – linestyle argument for parameter plot
- **legend_text** – Label for line plots
- **balance_alpha** – Flag indicating whether alpha for large clusters should be reduced to avoid overplotting (default: True)

Returns The plot axes.

Return type ax

pypesto.visualize.**process_offset_y**(*offset_y: Optional[float], scale_y: str, min_val: float*) → float

Compute offset for y-axis, depend on user settings.

Parameters

- **offset_y** – value for offsetting the later plotted values, in order to ensure positivity if a semilog-plot is used
- **scale_y** – Can be 'lin' or 'log10', specifying whether values should be plotted on linear or on log10-scale
- **min_val** – Smallest value to be plotted

Returns offset_y – value for offsetting the later plotted values, in order to ensure positivity if a semilog-plot is used

Return type float

pypesto.visualize.**process_result_list**(*results*, *colors=None*, *legends=None*)

Assign colors and legends to a list of results, check user provided lists.

Parameters

- **results** (*list or pypesto.Result*) – list of pypesto.Result objects or a single pypesto.Result
- **colors** (*list, optional*) – list of RGBA colors
- **legends** (*str or list*) – labels for line plots

Returns

- **results** (*list of pypesto.Result*) – list of pypesto.Result objects
- **colors** (*list of RGBA*) – One for each element in 'results'.
- **legends** (*list of str*) – labels for line plots

pypesto.visualize.**process_y_limits**(*ax*, *y_limits*)

Apply user specified limits of y-axis.

Parameters

- **ax** (*matplotlib.Axes, optional*) – Axes object to use.
- **y_limits** (*ndarray*) – y_limits, minimum and maximum, for current axes object

Returns **ax** – Axes object to use.

Return type matplotlib.Axes, optional

pypesto.visualize.**profile_cis**(*result: pypesto.result.result.Result*, *confidence_level: float = 0.95*, *profile_indices: Optional[Sequence[int]] = None*, *profile_list: int = 0*, *color: Union[str, tuple] = 'C0'*, *show_bounds: bool = False*, *ax: Optional[matplotlib.axes._axes.Axes] = None*) → matplotlib.axes._axes.Axes

Plot approximate confidence intervals based on profiles.

Parameters

- **result** – The result object after profiling.
- **confidence_level** – The confidence level in (0,1), which is translated to an approximate threshold assuming a chi2 distribution, using *pypesto.profile.chi2_quantile_to_ratio*.
- **profile_indices** – List of integer values specifying which profiles should be plotted. Defaults to the indices for which profiles were generated in profile list *profile_list*.
- **profile_list** – Index of the profile list to be used.
- **color** – Main plot color.
- **show_bounds** – Whether to show, and extend the plot to, the lower and upper bounds.
- **ax** – Axes object to use. Default: Create a new one.

pypesto.visualize.**profile_lowlevel**(*fvals*, *ax=None*, *size: Tuple[float, float] = (18.5, 6.5)*, *color=None*, *legend_text: Optional[str] = None*, *show_bounds: bool = False*, *lb: Optional[float] = None*, *ub: Optional[float] = None*)

Lowlevel routine for plotting one profile, working with a numpy array only.

Parameters

- **fvals** (*numeric list or array*) – Values to plot.
- **ax** (*matplotlib.Axes, optional*) – Axes object to use.
- **size** (*tuple, optional*) – Figure size (width, height) in inches. Is only applied when no ax object is specified.

- **color** (*RGBA, optional*) – Color for profiles in plot.
- **legend_text** (*str*) – Label for line plots.
- **show_bounds** – Whether to show, and extend the plot to, the lower and upper bounds.
- **lb** – Lower bound.
- **ub** – Upper bound.

Returns **ax** – The plot axes.

Return type matplotlib.Axes

pypesto.visualize.**profiles**(*results: Union[pypesto.result.result.Result, Sequence[pypesto.result.result.Result]], ax=None, profile_indices: Optional[Sequence[int]] = None, size: Sequence[float] = (18.5, 6.5), reference: Optional[Union[pypesto.visualize.reference_points.ReferencePoint, Sequence[pypesto.visualize.reference_points.ReferencePoint]]] = None, colors=None, legends: Optional[Sequence[str]] = None, x_labels: Optional[Sequence[str]] = None, profile_list_ids: Union[int, Sequence[int]] = 0, ratio_min: float = 0.0, show_bounds: bool = False*)

Plot classical 1D profile plot.

Using the posterior, e.g. Gaussian like profile.

Parameters

- **results** (*list or pypesto.Result*) – List of or single *pypesto.Result* after profiling.
- **ax** (*list of matplotlib.Axes, optional*) – List of axes objects to use.
- **profile_indices** (*list of integer values*) – List of integer values specifying which profiles should be plotted.
- **size** (*tuple, optional*) – Figure size (width, height) in inches. Is only applied when no ax object is specified.
- **reference** (*list, optional*) – List of reference points for optimization results, containing at least a function value fval.
- **colors** (*list, or RGBA, optional*) – List of colors, or single color.
- **legends** (*list or str, optional*) – Labels for line plots, one label per result object.
- **x_labels** (*list of str*) – Labels for parameter value axes (e.g. parameter names).
- **profile_list_ids** (*int or list of ints, optional*) – Index or list of indices of the profile lists to be used for profiling.
- **ratio_min** – Minimum ratio below which to cut off.
- **show_bounds** – Whether to show, and extend the plot to, the lower and upper bounds.

Returns **ax** – The plot axes.

Return type matplotlib.Axes

pypesto.visualize.**profiles_lowlevel**(*fvals*, *ax=None*, *size: Tuple[float, float] = (18.5, 6.5)*, *color=None*, *legend_text: Optional[str] = None*, *x_labels=None*, *show_bounds: bool = False*, *lb_full=None*, *ub_full=None*)

Lowlevel routine for profile plotting.

Working with a list of arrays only, opening different axes objects in case.

Parameters

- **fvals** (*numeric list or array*) – Values to plot.
- **ax** (*list of matplotlib.Axes, optional*) – List of axes object to use.
- **size** (*tuple, optional*) – Figure size (width, height) in inches. Is only applied when no ax object is specified.
- **size** – Figure size (width, height) in inches. Is only applied when no ax object is specified.
- **color** (*RGBA, optional*) – Color for profiles in plot.
- **legend_text** (*List[str]*) – Label for line plots.
- **legend_text** – Label for line plots.
- **show_bounds** – Whether to show, and extend the plot to, the lower and upper bounds.
- **lb_full** – Lower bound.
- **ub_full** – Upper bound.

Returns **ax** – The plot axes.

Return type matplotlib.Axes

pypesto.visualize.**projection_scatter_pca**(*pca_coordinates: numpy.ndarray*, *components: Sequence[int] = (0, 1)*, ***kwargs*)

Plot a scatter plot for PCA coordinates.

Creates either one or multiple scatter plots, depending on the number of coordinates passed to it.

Parameters

- **pca_coordinates** – array of pca coordinates (returned as first output by the routine get_pca_representation) to be shown as scatter plot
- **components** – Components to be plotted (corresponds to columns of pca_coordinates)

Returns Either one axes object, or a dictionary of plot axes (depending on the number of coordinates passed)

Return type axs

pypesto.visualize.**projection_scatter_umap**(*umap_coordinates: numpy.ndarray*, *components: Sequence[int] = (0, 1)*, ***kwargs*)

Plot a scatter plots for UMAP coordinates.

Creates either one or multiple scatter plots, depending on the number of coordinates passed to it.

Parameters

- **umap_coordinates** – array of umap coordinates (returned as first output by the routine get_umap_representation) to be shown as scatter plot
- **components** – Components to be plotted (corresponds to columns of umap_coordinates)

Returns Either one axes object, or a dictionary of plot axes (depending on the number of coordinates passed)

Return type axs

pypesto.visualize.**projection_scatter_umap_original**(*umap_object: None*, *color_by: Optional[Sequence[float]] = None*, *components: Sequence[int] = (0, 1)*, ***kwargs*)

See *projection_scatter_umap* for more documentation.

Wrapper around umap.plot.points. Similar to *projection_scatter_umap*, but uses the original plotting routine from umap.plot.

Parameters

- **umap_object** – umap object (returned as second output by get_umap_representation) to be shown as scatter plot
- **color_by** – A sequence/list of floats, which specify the color in the colormap
- **components** – Components to be plotted (corresponds to columns of umap_coordinates)

Returns **ax** – The plot axes.

Return type matplotlib.Axes

pypesto.visualize.**sampling_1d_marginals**(*result: pypesto.result.result.Result*, *i_chain: int = 0*, *par_indices: Optional[Sequence[int]] = None*, *stepsize: int = 1*, *plot_type: str = 'both'*, *bw: str = 'scott'*, *suptitle: Optional[str] = None*, *size: Optional[Tuple[float, float]] = None*)

Plot marginals.

Parameters

- **result** – The pyPESTO result object with filled sample result.
- **i_chain** – Which chain to plot. Default: First chain.
- **par_indices** (*list of integer values*) – List of integer values specifying which parameters to plot. Default: All parameters are shown.
- **stepsize** – Only one in *stepsize* values is plotted.
- **plot_type** (*{'hist'|'kde'|'both'}*) – Specify whether to plot a histogram ('hist'), a kernel density estimate ('kde'), or both ('both').
- **bw** (*{'scott', 'silverman' | scalar | pair of scalars}*) – Kernel bandwidth method.
- **suptitle** – Figure super title.
- **size** – Figure size in inches.

Returns matplotlib-axes

Return type ax

pypesto.visualize.**sampling_fval_traces**(*result: pypesto.result.result.Result*, *i_chain: int = 0*, *full_trace: bool = False*, *stepsize: int = 1*, *title: Optional[str] = None*, *size: Optional[Tuple[float, float]] = None*, *ax: Optional[matplotlib.axes._axes.Axes] = None*)

Plot log-posterior (=function value) over iterations.

Parameters

- **result** – The pyPESTO result object with filled sample result.

- **i_chain** – Which chain to plot. Default: First chain.
- **full_trace** – Plot the full trace including warm up. Default: False.
- **stepsize** – Only one in *stepsize* values is plotted.
- **title** – Axes title.
- **size** (*ndarray*) – Figure size in inches.
- **ax** – Axes object to use.

Returns The plot axes.

Return type ax

pypesto.visualize.**sampling_parameter_cis**(*result: pypesto.result.result.Result*, *alpha: Optional[Sequence[int]] = None*, *step: float = 0.05*, *show_median: bool = True*, *title: Optional[str] = None*, *size: Optional[Tuple[float, float]] = None*, *ax: Optional[matplotlib.axes._axes.Axes] = None*) → matplotlib.axes._axes.Axes

Plot MCMC-based parameter credibility intervals.

Parameters

- **result** – The pyPESTO result object with filled sample result.
- **alpha** – List of lower tail probabilities, defaults to 95% interval.
- **step** – Height of boxes for projectile plot, defaults to 0.05.
- **show_median** – Plot the median of the MCMC chain. Default: True.
- **title** – Axes title.
- **size** (*ndarray*) – Figure size in inches.
- **ax** – Axes object to use.

Returns The plot axes.

Return type ax

pypesto.visualize.**sampling_parameter_traces**(*result: pypesto.result.result.Result*, *i_chain: int = 0*, *par_indices: Optional[Sequence[int]] = None*, *full_trace: bool = False*, *stepsize: int = 1*, *use_problem_bounds: bool = True*, *suptitle: Optional[str] = None*, *size: Optional[Tuple[float, float]] = None*, *ax: Optional[matplotlib.axes._axes.Axes] = None*)

Plot parameter values over iterations.

Parameters

- **result** – The pyPESTO result object with filled sample result.
- **i_chain** – Which chain to plot. Default: First chain.
- **par_indices** (*list of integer values*) – List of integer values specifying which parameters to plot. Default: All parameters are shown.
- **full_trace** – Plot the full trace including warm up. Default: False.
- **stepsize** – Only one in *stepsize* values is plotted.

- **use_problem_bounds** – Defines if the y-limits shall be the lower and upper bounds of parameter estimation problem.
- **suptitle** – Figure suptitle.
- **size** – Figure size in inches.
- **ax** – Axes object to use.

Returns The plot axes.

Return type ax

pypesto.visualize.**sampling_prediction_trajectories**(*ensemble_prediction: pypesto.ensemble.ensemble.EnsemblePrediction*, *levels: Union[float, Sequence[float]]*, *title: Optional[str] = None*, *size: Optional[Tuple[float, float]] = None*, *axes: Optional[matplotlib.axes._axes.Axes] = None*, *labels: Optional[Dict[str, str]] = None*, *axis_label_padding: int = 50*, *groupby: str = 'condition'*, *condition_gap: float = 0.01*, *condition_ids: Optional[Sequence[str]] = None*, *output_ids: Optional[Sequence[str]] = None*, *weighting: bool = False*) → matplotlib.axes._axes.Axes

Visualize prediction trajectory of an EnsemblePrediction.

Plot MCMC-based prediction credibility intervals for the model states or outputs. One or various credibility levels can be depicted. Plots are grouped by condition.

Parameters

- **result** – The pyPESTO result object with filled sample result.
- **levels** – Credibility levels, e.g. [95] for a 95% credibility interval. See the `_get_level_percentiles()` method for a description of how these levels are handled, and current limitations.
- **title** – Axes title.
- **size** (*ndarray*) – Figure size in inches.
- **axes** – Axes object to use.
- **labels** – Keys should be ensemble output IDs, values should be the desired label for that output. Defaults to output IDs.
- **axis_label_padding** – Pixels between axis labels and plots.
- **groupby** – Group plots by *pypesto.C.OUTPUT* or *pypesto.C.CONDITION*.
- **condition_gap** – Gap between conditions when *groupby == pypesto.C.CONDITION*.
- **condition_ids** – If provided, only data for the provided condition IDs will be plotted.
- **output_ids** – If provided, only data for the provided output IDs will be plotted.
- **weighting** – Whether weights should be used for trajectory.

Returns The plot axes.

Return type axes

pypesto.visualize.**sampling_scatter**(*result: pypesto.result.result.Result, i_chain: int = 0, stepsize: int = 1, suptitle: Optional[str] = None, diag_kind: str = 'kde', size: Optional[Tuple[float, float]] = None*)

Parameter scatter plot.

Parameters

- **result** – The pyPESTO result object with filled sample result.
- **i_chain** – Which chain to plot. Default: First chain.
- **stepsize** – Only one in *stepsize* values is plotted.
- **suptitle** – Figure super title.
- **diag_kind** – Visualization mode for marginal densities {'auto', 'hist', 'kde', None}
- **size** – Figure size in inches.

Returns The plot axes.

Return type ax

pypesto.visualize.**waterfall**(*results: Union[pypesto.result.result.Result, Sequence[pypesto.result.result.Result]], ax: Optional[matplotlib.axes._axes.Axes] = None, size: Optional[Tuple[float]] = (18.5, 10.5), y_limits: Optional[Tuple[float]] = None, scale_y: Optional[str] = 'log10', offset_y: Optional[float] = None, start_indices: Optional[Union[Sequence[int], int]] = None, reference: Optional[Sequence[pypesto.visualize.reference_points.ReferencePoint]] = None, colors: Optional[Union[Tuple[float, float, float, float], Sequence[Tuple[float, float, float, float]]]] = None, legends: Optional[Union[Sequence[str], str]] = None*)

Plot waterfall plot.

Parameters

- **results** – Optimization result obtained by 'optimize.py' or list of those
- **ax** (*matplotlib.Axes, optional*) – Axes object to use.
- **size** – Figure size (width, height) in inches. Is only applied when no ax object is specified
- **y_limits** (*float or ndarray, optional*) – maximum value to be plotted on the y-axis, or y-limits
- **scale_y** – May be logarithmic or linear ('log10' or 'lin')
- **offset_y** – offset for the y-axis, if it is supposed to be in log10-scale
- **start_indices** – Integers specifying the multistart to be plotted or int specifying up to which start index should be plotted
- **reference** – Reference points for optimization results, containing at least a function value fval
- **colors** – Colors or single color for plotting. If not set, clustering is done and colors are assigned automatically
- **legends** – Labels for line plots, one label per result object

Returns **ax** – The plot axes.

Return type matplotlib.Axes

pypesto.visualize.**waterfall_lowlevel**(*fvals*, *scale_y='log10'*, *offset_y=0.0*, *ax=None*, *size=(18.5, 10.5)*, *colors=None*, *legend_text=None*)

Plot waterfall plot using list of function values.

Parameters

- **fvals** (*numeric list or array*) – Including values need to be plotted.
- **scale_y** (*str, optional*) – May be logarithmic or linear ('log10' or 'lin')
- **offset_y** – offset for the y-axis, if it is supposed to be in log10-scale
- **ax** (*matplotlib.Axes, optional*) – Axes object to use.
- **size** (*tuple, optional*) – see waterfall
- **colors** (*list, or RGBA, optional*) – list of colors, or single color color or list of colors for plotting. If not set, clustering is done and colors are assigned automatically
- **legend_text** (*str*) – Label for line plots

Returns **ax** – The plot axes.

Return type matplotlib.Axes

4.11 Engines

The execution of the multistarts can be parallelized in different ways, e.g. multi-threaded or cluster-based. Note that it is not checked whether a single task itself is internally parallelized.

class pypesto.engine.**Engine**

Bases: abc.ABC

Abstract engine base class.

__init__()

Initialize self. See help(type(self)) for accurate signature.

abstract execute(*tasks: List[pypesto.engine.task.Task]*, *progress_bar: bool = True*)

Execute tasks.

Parameters

- **tasks** – List of tasks to execute.
- **progress_bar** – Whether to display a progress bar.

class pypesto.engine.**MultiProcessEngine**(*n_procs: Optional[int] = None*)

Bases: pypesto.engine.base.Engine

Parallelize the task execution using multiprocessing.

Parameters **n_procs** – The maximum number of processes to use in parallel. Defaults to the number of CPUs available on the system according to *os.cpu_count()*. The effectively used number of processes will be the minimum of *n_procs* and the number of tasks submitted.

__init__(*n_procs: Optional[int] = None*)

Initialize self. See help(type(self)) for accurate signature.

execute(*tasks: List[pypesto.engine.task.Task]*, *progress_bar: bool = True*)
Pickle tasks and distribute work over parallel processes.

Parameters

- **tasks** – List of tasks to execute.
- **progress_bar** – Whether to display a progress bar.

class pypesto.engine.**MultiThreadEngine**(*n_threads: Optional[int] = None*)
Bases: pypesto.engine.base.Engine

Parallelize the task execution using multithreading.

Parameters **n_threads** – The maximum number of threads to use in parallel. Defaults to the number of CPUs available on the system according to *os.cpu_count()*. The effectively used number of threads will be the minimum of *n_threads* and the number of tasks submitted.

__init__(*n_threads: Optional[int] = None*)
Initialize self. See help(type(self)) for accurate signature.

execute(*tasks: List[pypesto.engine.task.Task]*, *progress_bar: bool = True*)
Deepcopy tasks and distribute work over parallel threads.

Parameters

- **tasks** – List of tasks to execute.
- **progress_bar** – Whether to display a progress bar.

class pypesto.engine.**SingleCoreEngine**
Bases: pypesto.engine.base.Engine

Dummy engine for sequential execution on one core.

Note that the objective itself may be multithreaded.

__init__()
Initialize self. See help(type(self)) for accurate signature.

execute(*tasks: List[pypesto.engine.task.Task]*, *progress_bar: bool = True*)
Execute all tasks in a simple for loop sequentially.

Parameters

- **tasks** – List of tasks to execute.
- **progress_bar** – Whether to display a progress bar.

class pypesto.engine.**Task**
Bases: abc.ABC

Abstract Task class.

A task is one of a list of independent execution tasks that are submitted to the execution engine to be executed using the execute() method, commonly in parallel.

__init__()
Initialize self. See help(type(self)) for accurate signature.

abstract execute()
Execute the task and return its results.

4.12 Startpoint

Methods for selecting points that can be used as startpoints for multi-start optimization. Startpoint methods can be implemented by deriving from *pypesto.startpoint.StartpointMethod*.

class pypesto.startpoint.**CheckedStartpoints**(*use_guesses: bool = True*, *check_fval: bool = False*, *check_grad: bool = False*)

Bases: pypesto.startpoint.base.StartpointMethod, abc.ABC

Startpoints checked for function value and/or gradient finiteness.

__call__(*n_starts: int*, *problem:* pypesto.problem.Problem) → numpy.ndarray
Generate checked startpoints.

__init__(*use_guesses: bool = True*, *check_fval: bool = False*, *check_grad: bool = False*)
Initialize.

Parameters

- **use_guesses** – Whether to use guesses provided in the problem.
- **check_fval** – Whether to check function values at the startpoint, and resample if not finite.
- **check_grad** – Whether to check gradients at the startpoint, and resample if not finite.

check_and_resample(*xs: numpy.ndarray*, *lb: numpy.ndarray*, *ub: numpy.ndarray*, *objective: pypesto.objective.base.ObjectiveBase*) → numpy.ndarray
Check sampled points for fval, grad, and potentially resample ones.

Parameters

- **xs** (*Startpoints candidates, shape (n_starts, n_par)*) –
- **lb** (*Lower parameter bound.*) –
- **ub** (*Upper parameter bound.*) –
- **objective** (*Objective function, for evaluation.*) –

Returns Checked and potentially partially resampled startpoints, shape (n_starts, n_par).

Return type xs

abstract sample(*n_starts: int*, *lb: numpy.ndarray*, *ub: numpy.ndarray*) → numpy.ndarray
Actually sample startpoints.

While in this implementation, *__call__* handles the checking of guesses and resampling, this method defines the actual sampling.

Parameters

- **n_starts** (*Number of startpoints to generate.*) –
- **lb** (*Lower parameter bound.*) –
- **ub** (*Upper parameter bound.*) –

Returns xs

Return type Startpoints, shape (n_starts, n_par)

class pypesto.startpoint.**FunctionStartpoints**(*function: Callable*, *use_guesses: bool = True*, *check_fval: bool = False*, *check_grad: bool = False*)

Bases: pypesto.startpoint.base.CheckedStartpoints

Define startpoints via callable.

The callable should take the same arguments as the *__call__* method.

__init__(*function: Callable*, *use_guesses: bool = True*, *check_fval: bool = False*, *check_grad: bool = False*)
Initialize.

Parameters

- **function** (*The callable sampling startpoints.*) –
- **use_guesses** (*As in CheckedStartpoints.*) –
- **check_fval** (*As in CheckedStartpoints.*) –
- **check_grad** (*As in CheckedStartpoints.*) –

sample(*n_starts: int*, *lb: numpy.ndarray*, *ub: numpy.ndarray*) → numpy.ndarray
Call function.

class pypesto.startpoint.**LatinHypercubeStartpoints**(*use_guesses: bool = True*, *check_fval: bool = False*, *check_grad: bool = False*, *smooth: bool = True*)
Bases: pypesto.startpoint.base.CheckedStartpoints

Generate latin hypercube-sampled startpoints.

See e.g. https://en.wikipedia.org/wiki/Latin_hypercube_sampling.

__init__(*use_guesses: bool = True*, *check_fval: bool = False*, *check_grad: bool = False*, *smooth: bool = True*)
Initialize.

Parameters

- **use_guesses** – As in CheckedStartpoints.
- **check_fval** – As in CheckedStartpoints.
- **check_grad** – As in CheckedStartpoints.
- **smooth** – Whether a (uniformly chosen) random starting point within the hypercube [i/n_starts, (i+1)/n_starts] should be chosen (True) or the midpoint of the interval (False).

sample(*n_starts: int*, *lb: numpy.ndarray*, *ub: numpy.ndarray*) → numpy.ndarray
Call function.

class pypesto.startpoint.**NoStartpoints**
Bases: pypesto.startpoint.base.StartpointMethod

Dummy class generating nan points. Useful if no startpoints needed.

__call__(*n_starts: int*, *problem:* pypesto.problem.Problem) → numpy.ndarray
Generate a (n_starts, dim) nan matrix.

class pypesto.startpoint.**StartpointMethod**
Bases: abc.ABC

Startpoint generation, in particular for multi-start optimization.

Abstract base class, specific sampling method needs to be defined in sub-classes.

abstract __call__(*n_starts: int*, *problem:* pypesto.problem.Problem) → numpy.ndarray
Generate startpoints.

Parameters

- **n_starts** (*Number of starts.*) –
- **problem** (*Problem specifying e.g. dimensions, bounds, and guesses.*) –

Returns xs

Return type Startpoints, shape (n_starts, n_par)

class pypesto.startpoint.**UniformStartpoints**(*use_guesses: bool = True*, *check_fval: bool = False*, *check_grad: bool = False*)

Bases: pypesto.startpoint.base.FunctionStartpoints

Generate uniformly sampled startpoints.

__init__(*use_guesses: bool = True*, *check_fval: bool = False*, *check_grad: bool = False*)

Initialize.

Parameters

- **function** (*The callable sampling startpoints.*) –
- **use_guesses** (*As in CheckedStartpoints.*) –
- **check_fval** (*As in CheckedStartpoints.*) –
- **check_grad** (*As in CheckedStartpoints.*) –

pypesto.startpoint.**latin_hypercube**(*n_starts: int*, *lb: numpy.ndarray*, *ub: numpy.ndarray*, *smooth: bool = True*) → numpy.ndarray

Generate latin hypercube points.

Parameters

- **n_starts** – Number of points.
- **lb** – Lower bound.
- **ub** – Upper bound.
- **smooth** – Whether a (uniformly chosen) random starting point within the hypercube [i/n_starts, (i+1)/n_starts] should be chosen (True) or the midpoint of the interval (False).

Returns Latin hypercube points, shape (n_starts, n_x).

Return type xs

pypesto.startpoint.**to_startpoint_method**(*maybe_startpoint_method: Union[pypesto.startpoint.base.StartpointMethod, Callable, bool]*) → pypesto.startpoint.base.StartpointMethod

Create StartpointMethod instance if possible, otherwise raise.

Parameters **maybe_startpoint_method** – A StartpointMethod instance, or a Callable as expected by FunctionStartpoints.

Returns A StartpointMethod instance.

Return type startpoint_method

Raises **TypeError if arguments cannot be converted to a StartpointMethod.** –

pypesto.startpoint.**uniform**(*n_starts: int*, *lb: numpy.ndarray*, *ub: numpy.ndarray*) → numpy.ndarray

Generate uniform points.

Parameters

- **n_starts** (*Number of starts.*) –
- **lb** (*Lower bound.*) –
- **ub** (*Upper bound.*) –

Returns xs

Return type Uniformly sampled points in [lb, ub], shape (n_starts, n_x)

4.13 Storage

Saving and loading traces and results objects.

class pypesto.store.**OptimizationResultHDF5Reader**(*storage_filename: str*)
Bases: object

Reader of the HDF5 result files written by OptimizationResultHDF5Writer.

storage_filename
HDF5 result file name

__init__(*storage_filename: str*)
Initialize reader.

Parameters **storage_filename** (*str*) – HDF5 result file name

read() → pypesto.result.result.Result
Read HDF5 result file and return pyPESTO result object.

class pypesto.store.**OptimizationResultHDF5Writer**(*storage_filename: str*)
Bases: object

Writer of the HDF5 result files.

storage_filename
HDF5 result file name

__init__(*storage_filename: str*)
Initialize Writer.

Parameters **storage_filename** (*str*) – HDF5 result file name

write(*result: pypesto.result.result.Result*, *overwrite=False*)
Write HDF5 result file from pyPESTO result object.

class pypesto.store.**ProblemHDF5Reader**(*storage_filename: str*)
Bases: object

Reader of the HDF5 problem files written by ProblemHDF5Writer.

storage_filename
HDF5 problem file name

__init__(*storage_filename: str*)
Initialize reader.

Parameters **storage_filename** (*str*) – HDF5 problem file name

read(*objective: Optional[pypesto.objective.base.ObjectiveBase] = None*) → *pypesto.problem.Problem*
Read HDF5 problem file and return pyPESTO problem object.

Parameters **objective** – Objective function which is currently not saved to storage.

Returns A problem instance with all attributes read in.

Return type problem

class pypesto.store.**ProblemHDF5Writer**(*storage_filename: str*)
Bases: object

Writer of the HDF5 problem files.

storage_filename
HDF5 result file name

__init__(*storage_filename: str*)
Initialize writer.

Parameters **storage_filename** (*str*) – HDF5 problem file name

write(*problem*, *overwrite: bool = False*)
Write HDF5 problem file from pyPESTO problem object.

class pypesto.store.**ProfileResultHDF5Reader**(*storage_filename: str*)
Bases: object

Reader of the HDF5 result files written by OptimizationResultHDF5Writer.

storage_filename
HDF5 result file name

__init__(*storage_filename: str*)
Initialize reader.

Parameters **storage_filename** – HDF5 result file name

read() → pypesto.result.result.Result
Read HDF5 result file and return pyPESTO result object.

class pypesto.store.**ProfileResultHDF5Writer**(*storage_filename: str*)
Bases: object

Writer of the HDF5 result files.

storage_filename
HDF5 result file name

__init__(*storage_filename: str*)
Initialize Writer.

Parameters **storage_filename** (*str*) – HDF5 result file name

write(*result: pypesto.result.result.Result*, *overwrite: bool = False*)
Write HDF5 result file from pyPESTO result object.

class pypesto.store.**SamplingResultHDF5Reader**(*storage_filename: str*)
Bases: object

Reader of the HDF5 result files written by SamplingResultHDF5Writer.

storage_filename
HDF5 result file name

__init__(*storage_filename: str*)
Initialize reader.

Parameters **storage_filename** (*str*) – HDF5 result file name

read() → pypesto.result.result.Result
Read HDF5 result file and return pyPESTO result object.

class pypesto.store.**SamplingResultHDF5Writer**(*storage_filename: str*)
Bases: object

Writer of the HDF5 sampling files.

storage_filename
HDF5 result file name

__init__(*storage_filename: str*)
Initialize Writer.

Parameters **storage_filename** (*str*) – HDF5 result file name

write(*result: pypesto.result.result.Result*, *overwrite: bool = False*)
Write HDF5 sampling file from pyPESTO result object.

pypesto.store.**autosave**(*filename: str*, *result: pypesto.result.result.Result*, *store_type: str*, *overwrite: bool = False*)
Save the result of optimization, profiling or sampling automatically.

Parameters

- **filename** – Either the filename to save to or "Auto", in which case it will automatically generate a file named *year_month_day_{type}_result.hdf5*.
- **result** – The result to be saved.
- **store_type** – Either *optimize*, *sample* or *profile*. Depending on the method the function is called in.
- **overwrite** – Whether to overwrite the currently existing results.

pypesto.store.**get_or_create_group**(*f: Union[h5py._hl.files.File, h5py._hl.group.Group]*, *group_path: str*) → h5py._hl.group.Group
Return/create a group object for the group with group_path relative to f.

pypesto.store.**f**
should be checked

Type file or group where existence of a group with the path group_path

pypesto.store.**group_path**

Type the path or simply the name of the group that should exist in f

Returns hdf5 group object with specified path relative to f.

Return type grp

pypesto.store.**load_objective_config**(*filename: str*)
Load the objective information stored in f.

Parameters **filename** – The name of the file in which the information are stored.

Returns

- *A dictionary of the information, stored instead of the*
- *actual objective in problem.objective.*

pypesto.store.**read_result**(*filename: str*, *problem: bool = True*, *optimize: bool = False*, *profile: bool = False*, *sample: bool = False*) → pypesto.result.result.Result
Save the whole pypesto.Result object in an HDF5 file.

Parameters

- **filename** – The HDF5 filename.
- **problem** – Read the problem.
- **optimize** – Read the optimize result.
- **profile** – Read the profile result.
- **sample** – Read the sample result.

Returns Result object containing the results stored in HDF5 file.

Return type result

pypesto.store.**write_array**(*f: h5py._hl.group.Group*, *path: str*, *values: Collection*) → None
Write array to hdf5.

Parameters

- **f** – h5py.Group where dataset should be created
- **path** – path of the dataset to create
- **values** – array to write

pypesto.store.**write_result**(*result: pypesto.result.result.Result*, *filename: str*, *overwrite: bool = False*, *problem: bool = True*, *optimize: bool = False*, *profile: bool = False*, *sample: bool = False*)
Save whole pypesto.Result to hdf5 file.

Boolean indicators allow specifying what to save.

Parameters

- **result** – The *pypesto.Result* object to be saved.
- **filename** – The HDF5 filename.
- **overwrite** – Boolean, whether already existing results should be overwritten.
- **problem** – Read the problem.
- **optimize** – Read the optimize result.
- **profile** – Read the profile result.
- **sample** – Read the sample result.

4.14 Logging

Logging convenience functions.

pypesto.logging.**log**(*name: str = 'pypesto'*, *level: int = 20*, *console: bool = True*, *filename: str = ''*)
Log messages from *name* with *level* to any combination of console/file.

Parameters

- **name** – The name of the logger.
- **level** – The output level to use.
- **console** – If True, messages are logged to console.
- **filename** – If specified, messages are logged to a file with this name.

pypesto.logging.**log_level_active**(*logger: logging.Logger*, *level: int*) → bool
Check whether the requested log level is active in any handler.

This is useful in case log expressions are costly.

Parameters

- **logger** – The logger.
- **level** – The requested log level.

Returns Whether there is a handler registered that handles events of importance at least *level* and higher.

Return type active

pypesto.logging.**log_to_console**(*level: int = 20*)
Log to console.

Parameters the log method. (*See*) –

pypesto.logging.**log_to_file**(*level: int = 20*, *filename: str = '.pypesto_logging.log'*)
Log to file.

Parameters the log method. (*See*) –

4.15 Ensemble

class pypesto.ensemble.**Ensemble**(*x_vectors: numpy.ndarray*, *x_names: Optional[Sequence[str]] = None*, *vector_tags: Optional[Sequence[Tuple[int, int]]] = None*, *ensemble_type: Optional[pypesto.C.EnsembleType] = None*, *predictions: Optional[Sequence[pypesto.ensemble.ensemble.EnsemblePrediction]] = None*, *lower_bound: Optional[numpy.ndarray] = None*, *upper_bound: Optional[numpy.ndarray] = None*)
Bases: object

An ensemble is a wrapper around a numpy array.

It comes with some convenience functionality: It allows to map parameter values via identifiers to the correct parameters, it allows to compute summaries of the parameter vectors (mean, standard deviation, median, percentiles) more easily, and it can store predictions made by pyPESTO, such that the parameter ensemble and the predictions are linked to each other.

__init__(*x_vectors: numpy.ndarray*, *x_names: Optional[Sequence[str]] = None*, *vector_tags: Optional[Sequence[Tuple[int, int]]] = None*, *ensemble_type: Optional[pypesto.C.EnsembleType] = None*, *predictions: Optional[Sequence[pypesto.ensemble.ensemble.EnsemblePrediction]] = None*, *lower_bound: Optional[numpy.ndarray] = None*, *upper_bound: Optional[numpy.ndarray] = None*)
Initialize.

Parameters

- **x_vectors** – parameter vectors of the ensemble, in the format n_parameter x n_vectors
- **x_names** – Names or identifiers of the parameters
- **vector_tags** – Additional tag, which adds information about the the parameter vectors of the form (optimization_run, optimization_step) if the ensemble is created from an optimization result or (sampling_chain, sampling_step) if the ensemble is created from a sampling result.

- **ensemble_type** – Type of ensemble: Ensemble (default), sample, or unprocessed_chain Samples are meant to be representative, ensembles can be any ensemble of parameters, and unprocessed chains still have burn-ins
- **predictions** – List of EnsemblePrediction objects
- **lower_bound** – array of potential lower bounds for the parameters
- **upper_bound** – array of potential upper bounds for the parameters

check_identifiability() → pandas.core.frame.DataFrame
Check identifiability of ensemble.

Use ensemble mean and standard deviation to assess (in a rudimentary way) whether or not parameters are identifiable. Returns a dataframe with tuples, which specify whether or not the lower and the upper bounds are violated.

Returns DataFrame indicating parameter identifiability based on mean plus/minus standard deviations and parameter bounds

Return type parameter_identifiability

compute_summary(*percentiles_list: Sequence[int] = (5, 20, 80, 95)*)
Compute summary for the parameters of the ensemble.

Summary includes the mean, the median, the standard deviation and possibly percentiles. Those summary results are added as a data member to the EnsemblePrediction object.

Parameters **percentiles_list** – List or tuple of percent numbers for the percentiles

Returns Dict with mean, std, median, and percentiles of parameter vectors

Return type summary

static from_optimization_endpoints(*result: pypesto.result.result.Result*, *cutoff: float = inf*, *max_size: int = inf*, ***kwargs*)
Construct an ensemble from an optimization result.

Parameters

- **result** – A pyPESTO result that contains an optimization result.
- **cutoff** – Exclude parameters from the optimization if the nllh is higher than the *cutoff*.
- **max_size** – The maximum size the ensemble should be.

Returns

Return type The ensemble.

static from_optimization_history(*result: pypesto.result.result.Result*, *cutoff: float = inf*, *max_size: int = inf*, *max_per_start: int = inf*, *distribute: bool = True*, ***kwargs*)
Construct an ensemble from the history of an optimization.

Parameters

- **result** – A pyPESTO result that contains an optimization result with history recorded.
- **cutoff** – Exclude parameters from the optimization if the nllh is higher than the *cutoff*.
- **max_size** – The maximum size the ensemble should be.
- **max_per_start** – The maximum number of vectors to be included from a single optimization start.

- **distribute** – Boolean flag, whether the best (False) values from the start should be taken or whether the indices should be more evenly distributed.

Returns

Return type The ensemble.

static from_sample(*result: pypesto.result.result.Result*, *remove_burn_in: bool = True*, *chain_slice: Optional[slice] = None*, *x_names: Optional[Sequence[str]] = None*, *lower_bound: Optional[numpy.ndarray] = None*, *upper_bound: Optional[numpy.ndarray] = None*, ***kwargs*)

Construct an ensemble from a sample.

Parameters

- **result** – A pyPESTO result that contains a sample result.
- **remove_burn_in** – Exclude parameter vectors from the ensemble if they are in the "burn-in".
- **chain_slice** – Subset the chain with a slice. Any "burn-in" removal occurs first.
- **x_names** – Names or identifiers of the parameters
- **lower_bound** – array of potential lower bounds for the parameters
- **upper_bound** – array of potential upper bounds for the parameters

Returns

Return type The ensemble.

predict(*predictor: Callable*, *prediction_id: Optional[str] = None*, *sensi_orders: Tuple = (0)*, *default_value: Optional[float] = None*, *mode: str = 'mode_fun'*, *include_llh_weights: bool = False*, *include_sigmay: bool = False*, *engine: Optional[pypesto.engine.base.Engine] = None*, *progress_bar: bool = True*) → pypesto.ensemble.ensemble.EnsemblePrediction

Run predictions for a full ensemble.

User needs to hand over a predictor function and settings, then all results are grouped as EnsemblePrediction for the whole ensemble

Parameters

- **predictor** – Prediction function, e.g., an AmiciPredictor
- **prediction_id** – Identifier for the predictions
- **sensi_orders** – Specifies which sensitivities to compute, e.g. (0,1) -> fval, grad
- **default_value** – If parameters are needed in the mapping, which are not found in the parameter source, it can make sense to fill them up with this default value (e.g. *np.nan*) in some cases (to be used with caution though).
- **mode** – Whether to compute function values or residuals.
- **include_llh_weights** – Whether to include weights in the output of the predictor.
- **include_sigmay** – Whether to include standard deviations in the output of the predictor.
- **engine** – Parallelization engine. Defaults to sequential execution on a *SingleCoreEngine*.
- **progress_bar** – Whether to display a progress bar.

Returns

Return type The prediction of the ensemble.

class pypesto.ensemble.**EnsemblePrediction**(*predictor: Optional[Callable[[Sequence], pypesto.result.predict.PredictionResult]] = None*, *prediction_id: Optional[str] = None*, *prediction_results: Optional[Sequence[pypesto.result.predict.PredictionResult]] = None*, *lower_bound: Optional[Sequence[numpy.ndarray]] = None*, *upper_bound: Optional[Sequence[numpy.ndarray]] = None*)

Bases: object

Class of ensemble prediction.

An ensemble prediction consists of an ensemble, i.e., a set of parameter vectors and their identifiers such as a sample, and a prediction function. It can be attached to a ensemble-type object

__init__(*predictor: Optional[Callable[[Sequence], pypesto.result.predict.PredictionResult]] = None*, *prediction_id: Optional[str] = None*, *prediction_results: Optional[Sequence[pypesto.result.predict.PredictionResult]] = None*, *lower_bound: Optional[Sequence[numpy.ndarray]] = None*, *upper_bound: Optional[Sequence[numpy.ndarray]] = None*)

Initialize.

Parameters

- **predictor** – Prediction function, e.g., an AmiciPredictor, which takes a parameter vector as input and outputs a PredictionResult object
- **prediction_id** – Identifier for the predictions
- **prediction_results** – List of Prediction results
- **lower_bound** – Array of potential lower bounds for the predictions, should have the same shape as the output of the predictions, i.e., a list of numpy array (one list entry per condition), with the arrays having the shape of n_timepoints x n_outputs for each condition.
- **upper_bound** – array of potential upper bounds for the parameters

compute_chi2(*amici_objective: pypesto.objective.amici.AmiciObjective*)

Compute the chi^2 error of the weighted mean trajectory.

Parameters **amici_objective** – The objective function of the model, the parameter ensemble was created from.

Returns

Return type The chi^2 error.

compute_summary(*percentiles_list: Sequence[int] = (5, 20, 80, 95)*, *weighting: bool = False*, *compute_weighted_sigma: bool = False*) → Dict

Compute summary from the ensemble prediction results.

Summary includes the mean, the median, the standard deviation and possibly percentiles. Those summary results are added as a data member to the EnsemblePrediction object.

Parameters

- **percentiles_list** – List or tuple of percent numbers for the percentiles
- **weighting** – Whether weights should be used for trajectory.

- **compute_weighted_sigma** – Whether weighted standard deviation of the ensemble mean trajectory should be computed. Defaults to False.

Returns dictionary of predictions results with the keys mean, std, median, percentiles, ...

Return type summary

condense_to_arrays()

Add prediction result to EnsemblePrediction object.

Reshape the prediction results to an array and add them as a member to the EnsemblePrediction objects. It's meant to be used only if all conditions of a prediction have the same observables, as this is often the case for large-scale data sets taken from online databases or similar.

pypesto.ensemble.**get_covariance_matrix_parameters**(*ens: pypesto.ensemble.ensemble.Ensemble*) → numpy.ndarray

Compute the covariance of ensemble parameters.

Parameters **ens** – Ensemble object containing a set of parameter vectors

Returns covariance matrix of ensemble parameters

Return type covariance_matrix

pypesto.ensemble.**get_covariance_matrix_predictions**(*ens: Union[pypesto.ensemble.ensemble.Ensemble, pypesto.ensemble.ensemble.EnsemblePrediction], prediction_index: int = 0*) → numpy.ndarray

Compute the covariance of ensemble predictions.

Parameters

- **ens** – Ensemble object containing a set of parameter vectors and a set of predictions or EnsemblePrediction object containing only predictions
- **prediction_index** – index telling which prediction from the list should be analyzed

Returns covariance matrix of ensemble predictions

Return type covariance_matrix

pypesto.ensemble.**get_pca_representation_parameters**(*ens: pypesto.ensemble.ensemble.Ensemble, n_components: int = 2, rescale_data: bool = True, rescaler: Optional[Callable] = None*) → Tuple

PCA of parameter ensemble.

Compute the representation with reduced dimensionality via principal component analysis (with a given number of principal components) of the parameter ensemble.

Parameters

- **ens** – Ensemble objects containing a set of parameter vectors
- **n_components** – number of components for the dimension reduction
- **rescale_data** – flag indicating whether the principal components should be rescaled using a rescaler function (e.g., an arcsinh function)
- **rescaler** – callable function to rescale the output of the PCA (defaults to numpy.arcsinh)

Returns

- *principal_components* – principal components of the parameter vector ensemble
- *pca_object* – returned fitted pca object from sklearn.decomposition.PCA()

pypesto.ensemble.**get_pca_representation_predictions**(*ens: Union[pypesto.ensemble.ensemble.Ensemble, pypesto.ensemble.ensemble.EnsemblePrediction]*, *prediction_index: int = 0*, *n_components: int = 2*, *rescale_data: bool = True*, *rescaler: Optional[Callable] = None*) → Tuple

PCA of ensemble prediction.

Compute the representation with reduced dimensionality via principal component analysis (with a given number of principal components) of the ensemble prediction.

Parameters

- **ens** – Ensemble objects containing a set of parameter vectors and a set of predictions or EnsemblePrediction object containing only predictions
- **prediction_index** – index telling which prediction from the list should be analyzed
- **n_components** – number of components for the dimension reduction
- **rescale_data** – flag indicating whether the principal components should be rescaled using a rescaler function (e.g., an arcsinh function)
- **rescaler** – callable function to rescale the output of the PCA (defaults to numpy.arcsinh)

Returns

- *principal_components* – principal components of the parameter vector ensemble
- *pca_object* – returned fitted pca object from sklearn.decomposition.PCA()

pypesto.ensemble.**get_percentile_label**(*percentile: Union[float, int, str]*) → str

Convert a percentile to a label.

Labels for percentiles are used at different locations (e.g. ensemble prediction code, and visualization code). This method ensures that the same percentile is labeled identically everywhere.

The percentile is rounded to two decimal places in the label representation if it is specified to more decimal places. This is for readability in plotting routines, and to avoid float to string conversion issues related to float precision.

Parameters **percentile** – The percentile value that will be used to generate a label.

Returns

Return type The label of the (possibly rounded) percentile.

pypesto.ensemble.**get_spectral_decomposition_lowlevel**(*matrix: numpy.ndarray*, *normalize: bool = False*, *only_separable_directions: bool = False*, *cutoff_absolute_separable: float = 1e-16*, *cutoff_relative_separable: float = 1e-16*, *only_identifiable_directions: bool = False*, *cutoff_absolute_identifiable: float = 1e-16*, *cutoff_relative_identifiable: float = 1e-16*) → Tuple[numpy.ndarray, numpy.ndarray]

Compute the spectral decomposition of ensemble parameters or predictions.

Parameters

- **matrix** – symmetric matrix (typically a covariance matrix) of parameters or predictions
- **normalize** – flag indicating whether the returned Eigenvalues should be normalized with respect to the largest Eigenvalue
- **only_separable_directions** – return only separable directions according to cutoff_[absolute/relative]_separable
- **cutoff_absolute_separable** – Consider only eigenvalues of the covariance matrix above this cutoff (only applied when only_separable_directions is True)
- **cutoff_relative_separable** – Consider only eigenvalues of the covariance matrix above this cutoff, when rescaled with the largest eigenvalue (only applied when only_separable_directions is True)
- **only_identifiable_directions** – return only identifiable directions according to cutoff_[absolute/relative]_identifiable
- **cutoff_absolute_identifiable** – Consider only low eigenvalues of the covariance matrix with inverses above of this cutoff (only applied when only_identifiable_directions is True)
- **cutoff_relative_identifiable** – Consider only low eigenvalues of the covariance matrix when rescaled with the largest eigenvalue with inverses above of this cutoff (only applied when only_identifiable_directions is True)

Returns

- *eigenvalues* – Eigenvalues of the covariance matrix
- *eigenvectors* – Eigenvectors of the covariance matrix

pypesto.ensemble.**get_spectral_decomposition_parameters**(*ens: pypesto.ensemble.ensemble.Ensemble*, *normalize: bool = False*, *only_separable_directions: bool = False*, *cutoff_absolute_separable: float = 1e-16*, *cutoff_relative_separable: float = 1e-16*, *only_identifiable_directions: bool = False*, *cutoff_absolute_identifiable: float = 1e-16*, *cutoff_relative_identifiable: float = 1e-16*) → Tuple[numpy.ndarray, numpy.ndarray]

Compute the spectral decomposition of ensemble parameters.

Parameters

- **ens** – Ensemble object containing a set of parameter vectors
- **normalize** – flag indicating whether the returned Eigenvalues should be normalized with respect to the largest Eigenvalue
- **only_separable_directions** – return only separable directions according to cutoff_[absolute/relative]_separable
- **cutoff_absolute_separable** – Consider only eigenvalues of the covariance matrix above this cutoff (only applied when only_separable_directions is True)
- **cutoff_relative_separable** – Consider only eigenvalues of the covariance matrix above this cutoff, when rescaled with the largest eigenvalue (only applied when only_separable_directions is True)
- **only_identifiable_directions** – return only identifiable directions according to cutoff_[absolute/relative]_identifiable
- **cutoff_absolute_identifiable** – Consider only low eigenvalues of the covariance matrix with inverses above of this cutoff (only applied when only_identifiable_directions is True)
- **cutoff_relative_identifiable** – Consider only low eigenvalues of the covariance matrix when rescaled with the largest eigenvalue with inverses above of this cutoff (only applied when only_identifiable_directions is True)

Returns

- *eigenvalues* – Eigenvalues of the covariance matrix
- *eigenvectors* – Eigenvectors of the covariance matrix

pypesto.ensemble.**get_spectral_decomposition_predictions**(*ens: pypesto.ensemble.ensemble.Ensemble*, *normalize: bool = False*, *only_separable_directions: bool = False*, *cutoff_absolute_separable: float = 1e-16*, *cutoff_relative_separable: float = 1e-16*, *only_identifiable_directions: bool = False*, *cutoff_absolute_identifiable: float = 1e-16*, *cutoff_relative_identifiable: float = 1e-16*) → Tuple[numpy.ndarray, numpy.ndarray]

Compute the spectral decomposition of ensemble predictions.

Parameters

- **ens** – Ensemble object containing a set of parameter vectors and a set of predictions or EnsemblePrediction object containing only predictions
- **normalize** – flag indicating whether the returned Eigenvalues should be normalized with respect to the largest Eigenvalue
- **only_separable_directions** – return only separable directions according to cutoff_[absolute/relative]_separable
- **cutoff_absolute_separable** – Consider only eigenvalues of the covariance matrix above this cutoff (only applied when only_separable_directions is True)
- **cutoff_relative_separable** – Consider only eigenvalues of the covariance matrix above this cutoff, when rescaled with the largest eigenvalue (only applied when only_separable_directions is True)
- **only_identifiable_directions** – return only identifiable directions according to cutoff_[absolute/relative]_identifiable
- **cutoff_absolute_identifiable** – Consider only low eigenvalues of the covariance matrix with inverses above of this cutoff (only applied when only_identifiable_directions is True)
- **cutoff_relative_identifiable** – Consider only low eigenvalues of the covariance matrix when rescaled with the largest eigenvalue with inverses above of this cutoff (only applied when only_identifiable_directions is True)

Returns

- *eigenvalues* – Eigenvalues of the covariance matrix
- *eigenvectors* – Eigenvectors of the covariance matrix

pypesto.ensemble.**get_umap_representation_parameters**(*ens: pypesto.ensemble.ensemble.Ensemble*, *n_components: int = 2*, *normalize_data: bool = False*, ***kwargs*) → Tuple

UMAP of parameter ensemble.

Compute the representation with reduced dimensionality via umap (with a given number of umap components) of the parameter ensemble. Allows to pass on additional keyword arguments to the umap routine.

Parameters

- **ens** – Ensemble objects containing a set of parameter vectors
- **n_components** – number of components for the dimension reduction
- **normalize_data** – flag indicating whether the parameter ensemble should be rescaled with mean and standard deviation

Returns

- *umap_components* – first components of the umap embedding
- *umap_object* – returned fitted umap object from umap.UMAP()

pypesto.ensemble.**get_umap_representation_predictions**(*ens: Union[pypesto.ensemble.ensemble.Ensemble, pypesto.ensemble.ensemble.EnsemblePrediction]*, *prediction_index: int = 0*, *n_components: int = 2*, *normalize_data: bool = False*, ***kwargs*) → Tuple

UMAP of ensemble prediction.

Compute the representation with reduced dimensionality via umap (with a given number of umap components) of the ensemble predictions. Allows to pass on additional keyword arguments to the umap routine.

Parameters

- **ens** – Ensemble objects containing a set of parameter vectors and a set of predictions or EnsemblePrediction object containing only predictions
- **prediction_index** – index telling which prediction from the list should be analyzed
- **n_components** – number of components for the dimension reduction
- **normalize_data** – flag indicating whether the parameter ensemble should be rescaled with mean and standard deviation

Returns

- *umap_components* – first components of the umap embedding
- *umap_object* – returned fitted umap object from umap.UMAP()

pypesto.ensemble.**read_ensemble_prediction_from_h5**(*predictor: Optional[Callable[[Sequence], pypesto.result.predict.PredictionResult]]*, *input_file: str*)

Read an ensemble prediction from an HDF5 File.

pypesto.ensemble.**read_from_csv**(*path: str*, *sep: str = '\t'*, *index_col: int = 0*, *headline_parser: Optional[Callable] = None*, *ensemble_type: Optional[pypesto.C.EnsembleType] = None*, *lower_bound: Optional[numpy.ndarray] = None*, *upper_bound: Optional[numpy.ndarray] = None*)

Create an ensemble from a csv file.

Parameters

- **path** – path to csv file to read in parameter ensemble

- **sep** – separator in csv file
- **index_col** – index column in csv file
- **headline_parser** – A function which reads in the headline of the csv file and converts it into vector_tags (see constructor of Ensemble for more details)
- **ensemble_type** – Ensemble type: representative sample or random ensemble
- **lower_bound** – array of potential lower bounds for the parameters
- **upper_bound** – array of potential upper bounds for the parameters

Returns Ensemble object of parameter vectors

Return type result

pypesto.ensemble.**read_from_df**(*dataframe: pandas.core.frame.DataFrame*, *headline_parser: Optional[Callable] = None*, *ensemble_type: Optional[pypesto.C.EnsembleType] = None*, *lower_bound: Optional[numpy.ndarray] = None*, *upper_bound: Optional[numpy.ndarray] = None*)

Create an ensemble from a csv file.

Parameters

- **dataframe** – pandas.DataFrame to read in parameter ensemble
- **headline_parser** – A function which reads in the headline of the csv file and converts it into vector_tags (see constructor of Ensemble for more details)
- **ensemble_type** – Ensemble type: representative sample or random ensemble
- **lower_bound** – array of potential lower bounds for the parameters
- **upper_bound** – array of potential upper bounds for the parameters

Returns Ensemble object of parameter vectors

Return type result

pypesto.ensemble.**write_ensemble_prediction_to_h5**(*ensemble_prediction: pypesto.ensemble.ensemble.EnsemblePrediction*, *output_file: str*, *base_path: Optional[str] = None*)

Write an *EnsemblePrediction* to hdf5.

Parameters

- **ensemble_prediction** – The prediciton to be saved.
- **output_file** – The filename of the hdf5 file.
- **base_path** – An optional filepath where the file should be saved to.

CHAPTER

FIVE

CONTRIBUTE

5.1 Workflow

If you start working on a new feature or a fix, please create an issue on GitHub shortly describing the issue and assign yourself. Your startpoint should always be the `develop` branch, which contains the lastest updates.

Create an own branch or fork, on which you can implement your changes. To get your work merged, please:

1. create a pull request to the `develop` branch with a meaningful summary,
2. check that code changes are covered by tests, and all tests pass,
3. check that the documentation is up-to-date,
4. request a code review from the main developers.

5.2 Environment

If you contribute to the development of pyPESTO, install developer requirements via:

```
pip install -r requirements-dev.txt
```

This installs the tools described below.

5.2.1 Pre-commit hooks

Firstly, this installs a pre-commit tool. To add those hooks to the *.git* folder of your local clone such that they are run on every commit, run:

```
pre-commit install
```

When adding new hooks, consider manually running `pre-commit run --all-files` once as usually only the diff is checked. The configuration is specified in `.pre-commit-config.yaml`.

Should it be necessary to perform commits without pre-commit verification, use `git commit --no-verify` or the shortform `-n`.

5.2.2 Tox

Secondly, this installs the virtual testing tool tox, which we use for all tests, format and quality checks. Its configuration is specified in `tox.ini`. To run it locally, simply execute:

```
tox [-e flake8,doc]
```

with optional `-e` options specifying the environments to run, see `tox.ini` for details.

5.3 GitHub Actions

For automatic continuous integration testing, we use GitHub Actions. All tests are run there on pull requests and required to pass. The configuration is specified in `.github/workflows/ci.yml`.

5.4 Documentation

To make pyPESTO easily usable, we try to provide good documentation, including code annotation and usage examples. The documentation is hosted at pypesto.readthedocs.io and updated automatically on merges to the main branches. To create the documentation locally, first install the requirements via:

```
pip install .[doc]
```

and then compile the documentation via:

```
cd doc
make html
```

The documentation is then under `doc/_build`.

Alternatively, the documentation can be compiled and tested via a single line:

```
tox -e doc
```

When adding code, all modules, classes, functions, parameters, code blocks should be properly documented.

For docstrings, we follow the numpy docstring standard. Check here for a detailed explanation.

5.5 Unit tests

Unit tests are located in the `test` folder. All files starting with `test_` contain tests and are automatically run on GitHub Actions. Run them locally via e.g.:

```
tox -e base
```

with `base` covering basic tests, but some parts (`optimize`, `petab`, `...`) being in separate subfolders. This boils mostly down to e.g.:

```
pytest test/base
```

You can also run only specific tests.

Unit tests can be written with pytest or unittest.

Code changes should always be covered by unit tests. It might not always be easy to test code which is based on random sampling, but we still encourage general sanity and integration tests. We highly encourage a test-driven development style.

5.6 PEP8

We try to respect the PEP8 coding standards. We run flake8 as part of the tests. The flake8 plugins used are specified in `tox.ini` and the flake8 configuration is given in `.flake8`. You can run the checks locally via:

```
tox -e flake8
```

CHAPTER

SIX

DEPLOY

New production releases should be created every time the `main` branch is updated.

6.1 Versions

For version numbers, we use `A.B.C`, where

- `C` is increased for bug fixes,
- `B` is increased for new features and minor API breaking changes,
- `A` is increased for major API breaking changes,

as suggested by the Python packaging guide.

6.2 Create a new release

After new commits have been added via pull requests to the `develop` branch, changes can be merged to `main` and a new version of pyPESTO can be released.

6.2.1 Merge into main

1. create a pull request from `develop` to `main`,
2. check that all code changes are covered by tests and all tests pass,
3. check that the documentation is up-to-date,
4. adapt the version number in `pypesto/version.py` (see above),
5. update the release notes in `CHANGELOG.rst`,
6. request a code review,
7. merge into the origin `main` branch.

To be able to actually perform the merge, sufficient rights may be required. Also, at least one review is required.

6.2.2 Create a release on GitHub

After merging into `main`, create a new release on GitHub. This can be done either directly on the project GitHub website, or via the CLI as described in Git Basics - Tagging. In the release form,

- specify a tag with the new version as specified in `pypesto/version.py`,
- include the latest additions to `CHANGELOG.rst` in the release description.

6.3 Upload to PyPI

The upload to the python package index PyPI has been automatized via GitHub Actions and is triggered whenever a new release tag is published.

Should it be necessary to manually upload a new version to PyPI, proceed as follows: First, a so called "wheel" is created via:

```
python setup.py bdist_wheel
```

A wheel is essentially a zip archive which contains the source code and the binaries (if any).

This archive is uploaded using twine:

```
twine upload dist/pypesto-x.y.z-py3-non-any.wheel
```

replacing x.y.z by the respective version number.

For a more in-depth discussion see also the section on distributing packages of the Python packaging guide.

CHAPTER

SEVEN

RELEASE NOTES

7.1 0.2 series

7.1.1 0.2.10 (2022-01-06)

- **AMICI:**
  - Make AMICI objective report only what is being asked for (#777)
- **Optimization:**
  - (Breaking) Refactor startpoint generation with clear assignments; allow checking gradients (#769)
  - (Breaking) Prioritize history vs optimize result (#775)
- **Storage:**
  - Fix loading empty history and result generation from multiple histories (#764)
  - Fix autosave function for single-core (#770)
  - Fix potential autosave overwriting and typehints (#772)
  - Allow loading of partial results from history file (#783)
- **CI:**
  - Compile AMICI models without gradients in test suite (#774)
- **General:**
  - (Breaking) Create result sub-module; shift storage+result related functionality (#784)
  - Fix finite difference constant mode (#786)
  - Refactor ensemble module (#788)
  - Introduce general C constants file (#788)
  - Apply isort for automatic imports formatting (#785)
  - Reduce run log output (#789)
  - Various minor fixes (#765, #766, #768, #771)

7.1.2 0.2.9 (2021-11-03)

- **General:**
  - Automatically save results (#749)
  - Update all docstrings to numpy standard (#750)
  - Add Google Colab and nbviewer links to all notebooks for online execution (#758)
  - Option to not save hess and sres in result (#760)
  - Set minimum supported python version to 3.7 (#755)
- **Visualization:**
  - Parameterize start index in optimized model fit (#744)

7.1.3 0.2.8 (2021-10-28)

- **PEtab:**
  - Use correct measurement column name in *rdatas_to_simulation_df* (#721)
  - Visualize optimized model fit via PEtab problem (#725)
  - Un-ignore observable scaling tests (#742)
  - New function to plot model trajectory with custom time points (#739)
- **Optimization:**
  - OOD Refactor startpoint generation (#732)
  - Update to fides 0.6.0 (#733)
  - Correctly report FVAL vs CHI2 values in fides (#741)
- **Ensemble:**
  - Option for using weighted ensemble means (#702)
  - Default names and bounds for *Ensemble.from_sample* (#730)
- **Storage:**
  - Load optimization result from HDF5 history (#726)
- **General:**
  - Enable use of priors with least squares optimizers (#745)
  - Add temporary CITATION.cff file (#734)
  - Regular scheduled CI runs (#754)
  - Allow to not copy objective in problem (#756)
- **Fixes:**
  - Fix non-exported visualization in notebook (#729)
  - Mark some more tests as flaky (#704)
  - Fix minor data type and OOD issues in parameter and waterfall plots (#731)

7.1.4 0.2.7 (2021-07-30)

- **Finite Differences:**
  - Adaptive finite differences (#671)
  - Add helper function for checking gradients of objectives (#690)
  - Small bug fixes (#711, #714)
- **Storage:**
  - Store representation of the objective (#669)
  - Minor fixes in HDF5 history (#679)
  - HDF5 reader for ensemble predictions (#681)
  - Update storage demo jupyter notebook (#699)
  - Option to trim trace to be monotonically decreasing (#705)
- **General:**
  - Improved tests and bug fixes of validation intervals (#676, #685)
  - Add input file validation via PEtab linter for PEtab import (#678)
  - Remove default values from docstring (#680)
  - Minor fixes/improvements of ensembles (#687, #688)
  - Fix sorting of optimization values including *NaN* values (#691)
  - Specify axis limits for plotting (#693)
  - Minor fixes in visualization (#696)
  - Add installation option *all_optimizers* (#695)
  - Improve installation documentation (#689)
  - Update *pysb* and *BNG* version on GitHub Actions (#697)
  - Bug fix in steady state guesses (#715)

7.1.5 0.2.6 (2021-05-17)

- **Objective:**
  - Basic finite differences (#666)
  - Fix factor 2 in res/fval values (#619)
- **Optimization:**
  - Sort optimization results when appending (#668)
  - Read optimizer result from HDF5 (previously only CSV) (#663)
- **Storage:**
  - Load ensemble from HDF5 (#640)
- **CI:**
  - Add flake8 checks as pre-commit hook (#662)

  - Add efficient biological conversion reaction test model (#619)

- **General:**
  - No automatic import of the predict module (#657)
  - Assert unique problem parameter names (#665)
  - Load ensemble from optimization result with and without history usage (#640)
  - Calculate validation profile significance (#658)
  - Set pypesto screen logger to "INFO" by default (#667)
- **Minor fixes:**
  - Fix axis variable overwriting in *visualize.sampling_parameter_traces* (#665)

7.1.6 0.2.5 (2021-05-04)

- **Objectives:**
  - New Aesara objectve (#623, #629, #635)
- **Sampling:**
  - New Emcee sampler (#606)
  - Fix compatibility to new Theano version (#650)
- **Storage:**
  - Improve hdf5 storage documentation (#612)
  - Hdf5 history for MultiProcessEngine (#650)
  - Minor fixes (#637, #638, #645, #649)
- **Visualization:**
  - Fix bounds of parameter plots (#601)
  - Fix waterfall plots with multiple results (#611)
- **CI:**
  - Move CI tests on GitHub Actions to python 3.9 (#598)
  - Add issue template (#604)
  - Update BionetGen Link (#630)
  - Introduce project.toml (#634)
- **General:**
  - Introduce progress bar for optimization, profiles and ensembles (#641)
  - Extend gradient checking functionality (#644)
- **Minor fixes:**
  - Fix installation of ipopt (#599)
  - Fix Zenodo link (#601)
  - Fix duplicates in documentation (#603)
  - Fix least squares optimizers (#617 #631 #632)

  - Fix trust region options (#616)
  - Fix slicing for new AMICI release (#621)
  - Refactor and document latin hypercube sampling (#647)
  - Fix missing SBML name in PEtab import (#648)

7.1.7 0.2.4 (2021-03-12)

- **Ensembles/Sampling:**
  - General ensemble analysis, visualization, storage (#557, #565, #568)
  - Calculate and plot MCMC parameter and prediction CIs via ensemble definition, parallelize ensemble predictions (#490)
- **Optimization:**
  - New optimizer: SciPy Differential Evolution (#543)
  - Set fides default to hybrid (#578)
- **AMICI:**
  - Make *guess_steadystate* less restrictive (#561) and have a more intuitive default behavior (#562, #582)
  - Customize time points (#490)
- **Storage:**
  - Save HDF5 history with SingleCoreEngine (#564)
  - Add read/write function for whole results (#589)
- **Engines:**
  - MPI based distributed parallelization (#542)
- **Visualization:**
  - Speed up waterfall plots by resizing scales only once (#577)
  - Change waterfall default offset to 1 - minimum (#593)
- **CI:**
  - Move GHA CI tests to pull request level for better cooperability (#574)
  - Streamline test environments using tox and pre-commit hooks (#579)
  - Test profile and sampling storage (#585)
  - Update for Ubuntu 20.04, add rerun on failure (#587)
- Minor fixes (release notes #558, nlop tests #559, close files #495, visualization #554, deployment #560, flakiness #570, aggregated deepcopy #572, respect user-provided offsets #576, update to SWIG 4 #591, check overwrite in profile writing #566)

7.1.8 0.2.3 (2021-01-18)

- **New optimizers:**
  - FIDES (#506, #503 # 500)
  - NLopt (#493)
- **Extended PEtab support:**
  - PySB import (#437)
  - Support of PEtab's initializationPriors (#535)
  - Support of prior parameterScale{Normal,Laplace} (#520)
  - Example notebook for synthetic data generation (#482)
- **General new and improved functionality:**
  - Predictions (#544)
  - Move tests to GitHub Actions (#524)
  - Parallelize profile calculation (#532)
  - Save *x_guesses* in *pypesto.problem* (#494)
  - Improved finite difference gradients (#464)
  - Support of unconstrained optimization (#519)
  - Additional NaN check for fval, grad and hessian (#521)
  - Add sanity checks for optimizer bounds (#516)
- **Improvements in storage:**
  - Fix hdf5 export of optimizer history (#536)
  - Fix reading *x_names* from hdf5 history (#528)
  - Storage does not save empty arrays (#489)
  - hdf5 storage sampling (#546)
  - hdf5 storage parameter profiles (#546)
- **Improvements in the visualization routines:**
  - Plot parameter values as histogram (#485)
  - Fix y axis limits in waterfall plots (#503)
  - Fix color scheme in visualization (#498)
  - Improved visualization of optimization results (#486)
- Several small bug fixes (#547, #541, #538, #533, #512, #508)

7.1.9 0.2.2 (2020-10-05)

- New optimizer: CMA-ES (#457)
- New plot: Optimizer convergence summary (#446)
- **Fixes in visualization:**
  - Type checks for reference points (#460)
  - y_limits in waterfall plots with multiple results (#475)
- Support of new amici release (#469)
- **Multiple fixes in optimization code:**
  - Remove unused argument for dlib optimizer (#466)
  - Add check for installation of ipopt (#470)
  - Add maxiter as default option of dlib (#474)
- Numpy based subindexing in amici_util (#462)
- Check amici/PEtab installation (#477)

7.1.10 0.2.1 (2020-09-07)

- Example Notebook for prior functionality (#438)
- Changed parameter indexing in profiling routines (#419)
- Basic sanity checking for parameter fixing (#420)
- **Bug fixes in:**
  - Displaying of multi start optimization (#430)
  - AMICI error output (#428)
  - Axes scaling/limits in waterfall plots (#441)
  - Priors (PEtab import, error handling) (#448, #452, #454)
- Improved sampling diagnostics (e.g. effective samples size) (#426)
- Improvements and bug fixes in parameter plots (#425)

7.1.11 0.2.0 (2020-06-17)

Major:

- Modularize import, to import optimization, sampling and profiling separately (#413)

Minor:

- **Bug fixes in**
  - sampling (#412)
  - visualization (#405)
  - PEtab import (#403)
  - Hessian computation (#390)

- Improve hdf5 error output (#409)
- Outlaw large new files in GitHub commits (#388)

7.2 0.1 series

7.2.1 0.1.0 (2020-06-17)

Objective

- Write solver settings to stream to enable serialization for distributed systems (#308)
- **Refactor objective function (#347)**
  - Removes necessity for all of the nasty binding/undbinding in AmiciObjective
  - Substantially reduces the complexity of the AggregatedObjective class
  - Aggregation of functions with inconsistent sensi_order/mode support
  - Introduce ObjectiveBase as an abstract Objective class
  - Introduce FunctionObjective for objectives from functions
- Implement priors with gradients, integrate with PEtab (#357)
- Fix minus sign in AmiciObjective.get_error_output (#361)
- Implement a prior class, derivatives for standard models, interface with PEtab (#357)
- Use *amici.import_model_module* to resolve module loading failure (#384)

Problem

- Tidy up problem vectors using properties (#393)

Optimization

- Interface IpOpt optimizer (#373)

Profiles

- Tidy up profiles (#356)
- Refactor profiles; add locally approximated profiles (#369)
- Fix profiling and visualization with fixed parameters (#393)

Sampling

- Geweke test for sampling convergence (#339)
- Implement basic Pymc3 sampler (#351)
- Make theano for pymc3 an optional dependency (allows using pypesto without pymc3) (#356)
- Progress bar for MCMC sampling (#366)
- Fix Geweke test crash for small sample sizes (#376)
- In parallel tempering, allow to only temperate the likelihood, not the prior (#396)

History and storage

- Allow storing results in a pre-filled hdf5 file (#290)
- Various fixes of the history (reduced vs. full parameters, read-in from file, chi2 values) (#315)

- Fix proper dimensions in result for failed start (#317)
- Create required directories before creating hdf5 file (#326)
- Improve storage and docs documentation (#328)
- Fix storing x_free_indices in hdf5 result (#334)
- Fix problem hdf5 return format (#336)
- Implement partial trace extraction, simplify History API (#337)
- Save really all attributes of a Problem to hdf5 (#342)

Visualization

- Customizable xLabels and tight layout for profile plots (#331)
- Fix non-positive bottom ylim on a log-scale axis in waterfall plots (#348)
- Fix "palette list has the wrong number of colors" in sampling plots (#372)
- Allow to plot multiple profiles from one result (#399)

Logging

- Allow easier specification of only logging for submodules (#398)

Tests

- Speed up travis build (#329)
- Update travis test system to latest ubuntu and python 3.8 (#330)
- Additional code quality checks, minor simplifications (#395)

7.3 0.0 series

7.3.1 0.0.13 (2020-05-03)

- Tidy up and speed up tests (#265 and others).
- Basic self-implemented Adaptive Metropolis and Adaptive Parallel Tempering sampling routines (#268).
- Fix namespace sample -> sampling (#275).
- Fix covariance matrix regularization (#275).
- Fix circular dependency *PetabImporter* - *PetabAmiciObjective* via *AmiciObjectBuilder*, *PetabAmiciObjective* becomes obsolete (#274).
- Define *AmiciCalculator* to separate the AMICI call logic (required for hierarchical optimization) (#277).
- Define initialize function for resetting steady states in *AmiciObjective* (#281).
- Fix scipy least squares options (#283).
- Allow failed starts by default (#280).
- Always copy parameter vector in objective to avoid side effects (#291).
- Add Dockerfile (#288).
- Fix header names in CSV history (#299).

Documentation:

- Use imported members in autodoc (#270).
- Enable python syntax highlighting in notebooks (#271).

7.3.2 0.0.12 (2020-04-06)

- Add typehints to global functions and classes.
- Add *PetabImporter.rdatas_to_simulation_df* function (all #235).
- Adapt y scale in waterfall plot if convergence was too good (#236).
- Clarify that *Objective* is of type negative log-posterior, for minimization (#243).
- Tidy up *AmiciObjective.parameter_mapping* as implemented in AMICI now (#247).
- Add *MultiThreadEngine* implementing multi-threading aside the *MultiProcessEngine* implementing multi-processing (#254).
- Fix copying and pickling of *AmiciObjective* (#252, #257).
- Remove circular dependence history-objective (#254).
- Fix problem of visualizing results with failed starts (#249).
- Rework history: make thread-safe, use factory methods, make context-specific (#256).
- Improve PEtab usage example (#258).
- Define history base contract, enabling different backends (#260).
- Store optimization results to HDF5 (#261).
- Simplify tests (#263).

Breaking changes:

- *HistoryOptions* passed to *pypesto.minimize* instead of *Objective* (#256).
- *GlobalOptimizer* renamed to *PyswarmOptimizer* (#235).

7.3.3 0.0.11 (2020-03-17)

- Rewrite AmiciObjective and PetabAmiciObjective simulation routine to directly use amici.petab_objective routines (#209, #219, #225).
- Implement petab test suite checks (#228).
- Various error fixes, in particular regarding PEtab and visualization.
- Improve trace structure.
- Fix conversion between fval and chi2, fix FIM (all #223).

7.3.4 0.0.10 (2019-12-04)

- Only compute FIM when sensitivities are available (#194).
- Fix documentation build (#197).
- Add support for pyswarm optimizer (#198).
- Run travis tests for documentation and notebooks only on pull requests (#199).

7.3.5 0.0.9 (2019-10-11)

- Update to AMICI 0.10.13, fix API changes (#185).
- Start using PEtab import from AMICI to be able to import constant species (#184, #185)
- Require PEtab>=0.0.0a16 (#183)

7.3.6 0.0.8 (2019-09-01)

- Add logo (#178).
- Fix petab API changes (#179).
- Some minor bugfixes (#168).

7.3.7 0.0.7 (2019-03-21)

- Support noise models in Petab and Amici.
- Minor Petab update bug fixes.

7.3.8 0.0.6 (2019-03-13)

- Several minor error fixes, in particular on tests and steady state.

7.3.9 0.0.5 (2019-03-11)

- Introduce AggregatedObjective to use multiple objectives at once.
- Estimate steady state in AmiciObjective.
- Check amici model build version in PetabImporter.
- Use Amici multithreading in AmiciObjective.
- Allow to sort multistarts by initial value.
- Show usage of visualization routines in notebooks.
- Various fixes, in particular to visualization.

7.3.10 0.0.4 (2019-02-25)

- Implement multi process parallelization engine for optimization.
- Introduce PrePostProcessor to more reliably handle pre- and post-processing.
- Fix problems with simulating for multiple conditions.
- Add more visualization routines and options for those (colors, reference points, plotting of lists of result obejcts)

7.3.11 0.0.3 (2019-01-30)

- Import amici models and the petab data format automatically using pypesto.PetabImporter.
- Basic profiling routines.

7.3.12 0.0.2 (2018-10-18)

- Fix parameter values
- Record trace of function values
- Amici objective to directly handle amici models

7.3.13 0.0.1 (2018-07-25)

- Basic framework and implementation of the optimization

CHAPTER

EIGHT

AUTHORS

This package is mainly developed by:

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CHAPTER

NINE

CONTACT

Discovered an error? Need help? Not sure if something works as intended? Please contact us!

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CHAPTER

TEN

LICENSE

```
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CHAPTER

ELEVEN

LOGO

pyPESTO's logo can be found in multiple variants in the doc/logo directory on github, in svg and png format. It is made available under a creative commons CC0 license. You are encouraged to use it e.g. in presentations and posters.

We thank Patrick Beart for his contribution to the logo.

CHAPTER

TWELVE

INDICES AND TABLES

- genindex
- modindex
- search

PYTHON MODULE INDEX

p

INDEX

Symbols

A

B

C

D

E

F

G

H

I

L

M

N

O

P

R

S

X