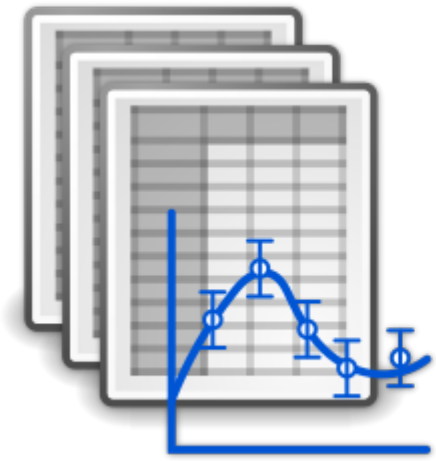
PEtab

Release latest

Mar 18, 2021

Data format



PEtab

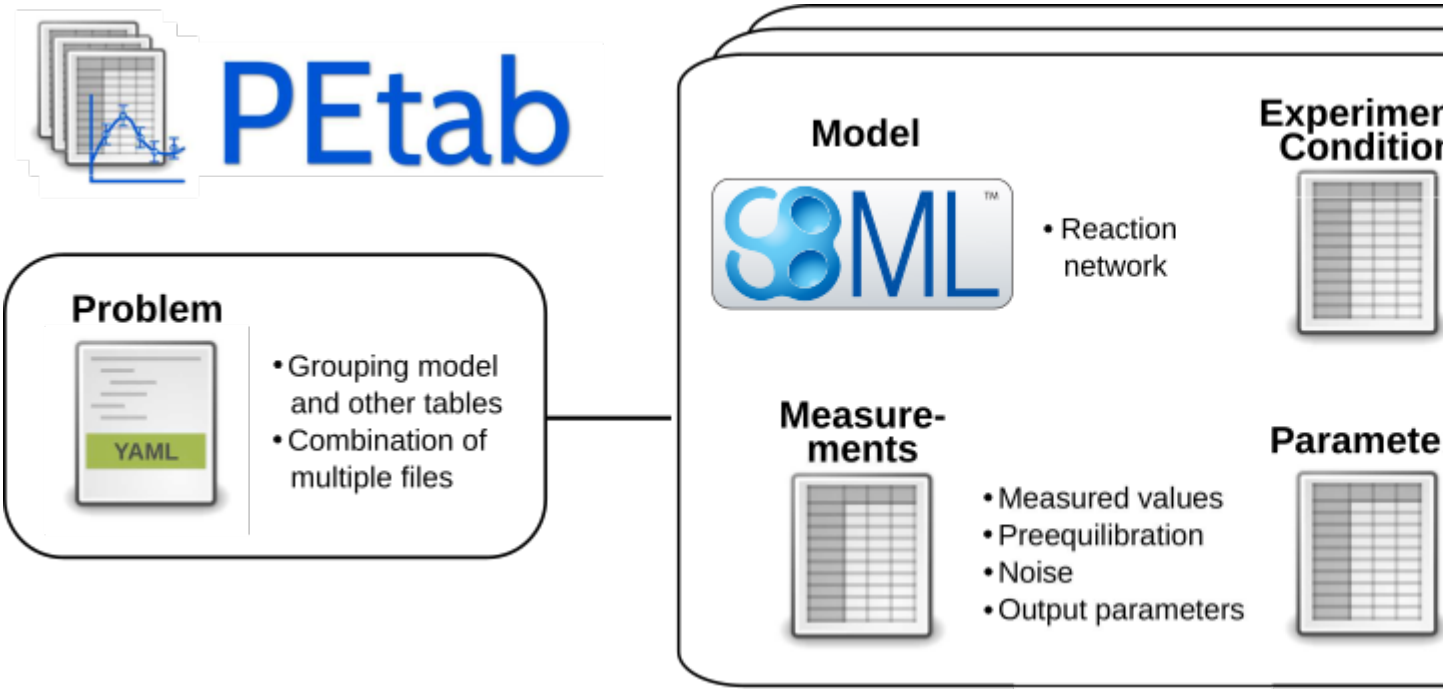
PEtab is a data format for specifying parameter estimation problems in systems biology. This repository provides extensive documentation and a Python library for easy access and validation of *PEtab* files.

CHAPTER 1

About PEtab

PEtab is built around SBML and based on tab-separated values (TSV) files. It is meant as a standardized way to provide information for parameter estimation, which is out of the current scope of SBML. This includes for example:

- Specifying and linking measurements to models
  - Defining model outputs
  - Specifying noise models
- Specifying parameter bounds for optimization
- Specifying multiple simulation condition with potentially shared parameters



CHAPTER 2

Documentation

Documentation of the PEtab data format and Python library is available at https://petab.readthedocs.io/en/latest/.

CHAPTER 3

Examples

A wide range of PEtab examples can be found in the systems biology parameter estimation benchmark problem collection.

CHAPTER 4

PEtab support in systems biology tools

Where PEtab is supported (in alphabetical order):

- AMICI (Example)
- A PEtab -> COPASI converter
- d2d (HOWTO)
- dMod (HOWTO)
- MEIGO (HOWTO)
- parPE
- pyABC (Example)
- pyPESTO (Example)
- SBML2Julia (Tutorial)

If your project or tool is using PEtab, and you would like to have it listed here, please let us know.

4.1 PEtab features supported in different tools

The following list provides an overview of supported PEtab features in different tools, based on passed test cases of the PEtab test suite:

ID	Test	AMICI>=0.10.20	Copasi	D2D	dMod	MEIGO	ParPE	pyABC>=0.10.1	pyPESTO>=0.0.11	SBML2Julia
1	Basic simulation	+++	+–	+++	+++	+++	–+	+++	+++	+++
2	Multiple simulation conditions	+++	+–	+++	+++	+++	–+	+++	+++	+++
3	Numeric observable parameter overrides in measurement table	+++	+–	+++	+++	+++	–+	+++	+++	+++
4	Parametric observable parameter overrides in measurement table	+++	+–	+++	+++	+++	–+	+++	+++	+++
5	Parametric overrides in condition table	+++	+–	+++	+++	+++	–+	+++	+++	+++
6	Time-point specific overrides in the measurement table	—	—	+++	+++	+++	—	—	—	+++
7	Observable transformations to log10 scale	+-+	+–	+++	++-	+++	–+	+-+	+-+	+++
8	Replicate measurements	+++	+–	+++	+++	+++	–+	+++	+++	+++
9	Pre-equilibration	+++	+–	+++	+++	+++	–+	+++	+++	+++
10	Partial pre-equilibration	+++	—	+++	+++	+++	–+	+++	+++	+++
11	Numeric initial concentration in condition table	+++	+–	+++	+++	+++	–+	+++	+++	+++
12	Numeric initial compartment sizes in condition table	—	+–	+++	+++	+++	—	—	—	+++
13	Parametric initial concentrations in condition table	+++	+–	+++	+++	+++	–+	+++	+++	+++
14	Numeric noise parameter overrides in measurement table	+++	+–	+++	+++	+++	–+	+++	+++	+++
15	Parametric noise parameter overrides in measurement table	+++	+–	+++	+++	+++	–+	+++	+++	+++
16	Observable transformations to log scale	+-+	+–	+++	++-	+++	–+	+-+	+-+	+++

Legend:

- First character indicates whether computing simulated data is supported and simulations are correct (+) or not (-).
- Second character indicates whether computing chi2 values of residuals are supported and correct (+) or not (-).
- Third character indicates whether computing likelihoods is supported and correct (+) or not (-).

CHAPTER 5

Using PEtab

If you would like to use PEtab yourself, please have a look at:

- a PEtab tutorial going through the individual steps of setting up a parameter estimation problem in PEtab, independently of any specific software
- the PEtab format reference
- the example models provided in the benchmark collection.
- the tutorials provided with each of the softwares supporting PEtab

To convert your existing parameter estimation problem to the PEtab format, you will have to:

1. Specify your model in SBML.
2. Create a condition table.
3. Create a table of observables.
4. Create a table of measurements.
5. Create a parameter table.

If you are using Python, some handy functions of the PEtab library can help you with that. This include also a PEtab validator called `petablint` which you can use to check if your files adhere to the PEtab standard. If you have further questions regarding PEtab, feel free to post an issue at our github repository.

CHAPTER 6

PEtab Python library

PEtab comes with a Python package for creating, checking, visualizing and working with PEtab files. This library is available on pypi and the easiest way to install it is running

It will require Python>=3.6 to run.

Development versions of the PEtab library can be installed using

(replace `develop` by the branch or commit you would like to install).

When setting up a new parameter estimation problem, the most useful tools will be:

- The **PEtab validator**, which is now automatically installed using Python entrypoints to be available as a shell command from anywhere called `petablint`
- `petab.create_parameter_df` to create the parameter table, once you have set up the model, condition table, observable table and measurement table
- `petab.create_combine_archive` to create a COMBINE Archive from PEtab files

6.1 Library examples

Examples for PEtab Python library usage:

- Validation
- Visualization

CHAPTER 7

Getting help

If you have any question or problems with PEtab, feel free to post them at our GitHub issue tracker.

CHAPTER 8

Contributing to PEtab

Contributions and feedback to PEtab are very welcome, see our contribution guide.

8.1 PEtab data format specification

Format version: 1

This document explains the PEtab data format.

8.1.1 Purpose

Providing a standardized way for specifying parameter estimation problems in systems biology, especially for the case of Ordinary Differential Equation (ODE) models.

8.1.2 Scope

The scope of PEtab is the full specification of parameter estimation problems in typical systems biology applications. In our experience, a typical setup of data-based modeling starts either with (i) the model of a biological system that is to be calibrated, or with (ii) experimental data that are to be integrated and analyzed using a computational model. Measurements are linked to the biological model by an observation and noise model. Often, measurements are taken after some perturbations have been applied, which are modeled as derivations from a generic model (Figure 1A). Therefore, one goal was to specify such a setup in the least redundant way. Furthermore, we wanted to establish an intuitive, modular, machine- and human-readable and -writable format that makes use of existing standards.

8.1.3 Overview

The PEtab data format specifies a parameter estimation problem using a number of text-based files (Systems Biology Markup Language (SBML) and Tab-Separated Values (TSV)) (Figure 2), i.e.

- An SBML model [SBML]

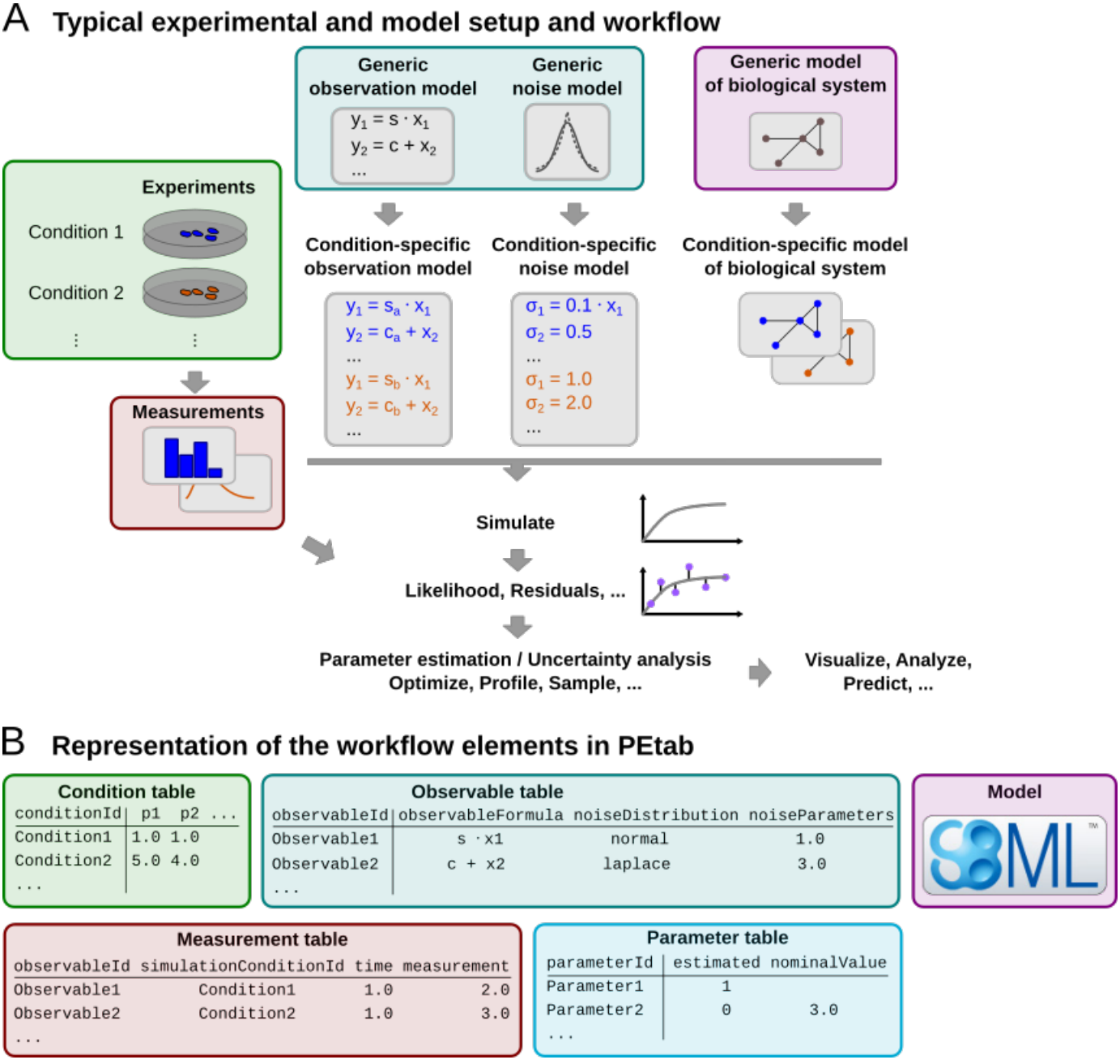


Fig. 1: **Figure 1: A common setup for data-based modeling studies and its representation in PEtab.**

- A measurement file to fit the model to [TSV]
- A condition file specifying model inputs and condition-specific parameters [TSV]
- An observable file specifying the observation model [TSV]
- A parameter file specifying optimization parameters and related information [TSV]
- (optional) A simulation file, which has the same format as the measurement file, but contains model simulations [TSV]
- (optional) A visualization file, which contains specifications how the data and/or simulations should be plotted by the visualization routines [TSV]

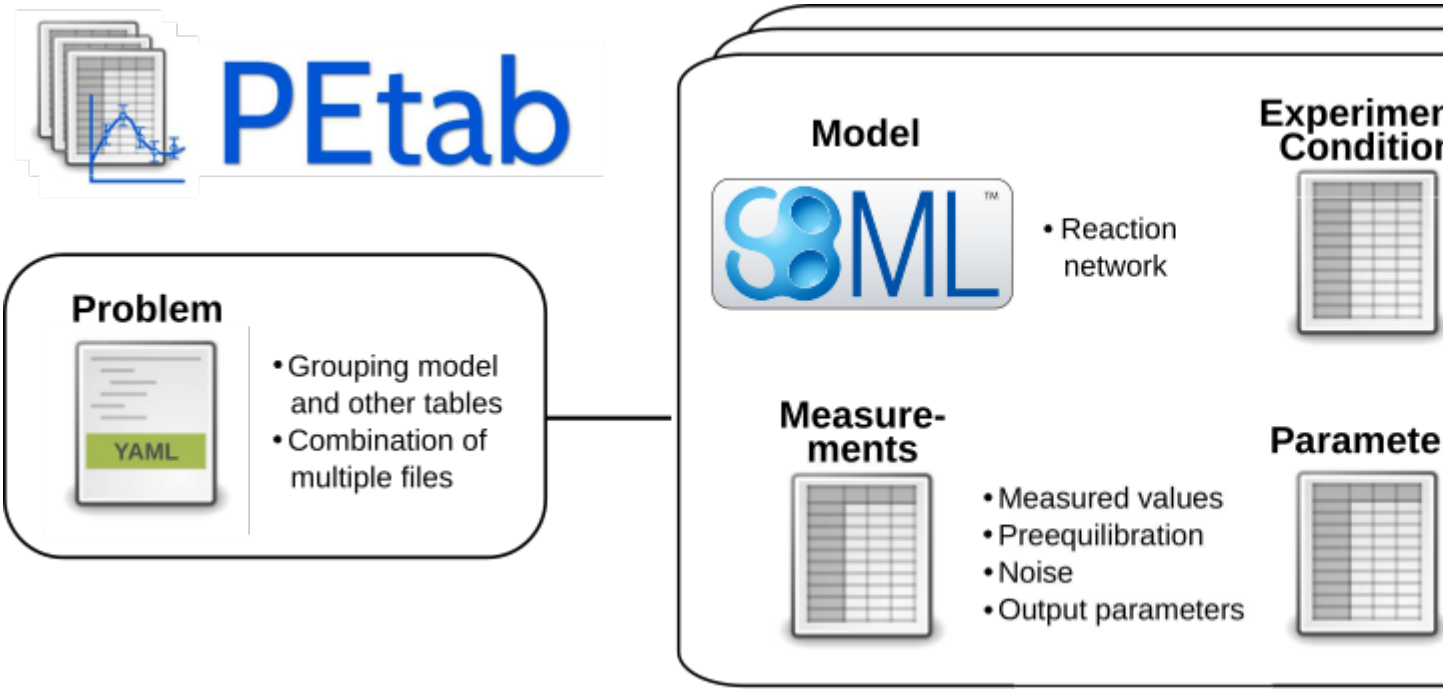


Fig. 2: **Figure 2: Files constituting a PEtab problem.**

Figure 1B shows how those files relate to a common setup for data-based modeling studies.

The following sections will describe the minimum requirements of those components in the core standard, which should provide all information for defining the parameter estimation problem.

Extensions of this format (e.g. additional columns in the measurement table) are possible and intended. However, while those columns may provide extra information for example for plotting, downstream analysis, or for more efficient parameter estimation, they should not affect the optimization problem as such.

General remarks

- All model entities, column names and row names are case-sensitive
- Fields in "[]" are optional and may be left empty.

8.1.4 SBML model definition

The model must be specified as valid SBML. There are no further restrictions.

8.1.5 Condition table

The condition table specifies parameters, or initial values of species and compartments for specific simulation conditions (generally corresponding to different experimental conditions).

This is specified as a tab-separated value file in the following way:

conditionId	[conditionName]	parameterOrSpeciesOrCompartmentId1	...	parameterOrSpeciesOrCompartmentId${n}
STRING	[STRING]	NUMERIC|STRING	...	NUMERIC|STRING
e.g.				
conditionId1	[conditionName1]	0.42	...	parameterId
conditionId2	...	...	...	...
...	...	...	...	

Row- and column-ordering are arbitrary, although specifying `conditionId` first may improve human readability.

Additional columns are *not* allowed.

Detailed field description

- `conditionId` [STRING, NOT NULL]

  Unique identifier for the simulation/experimental condition, to be referenced by the measurement table described below. Must consist only of upper and lower case letters, digits and underscores, and must not start with a digit.

- `conditionName` [STRING, OPTIONAL]

  Condition names are arbitrary strings to describe the given condition. They may be used for reporting or visualization.

- `${parameterOrSpeciesOrCompartmentId1}`

  Further columns may be global parameter IDs, IDs of species or compartments as defined in the SBML model. Only one column is allowed per ID. Values for these condition parameters may be provided either as numeric values, or as IDs defined in the SBML model, the parameter table or both.

  - `${parameterId}`

    The values will override any parameter values specified in the model.

  - `${speciesId}`

    If a species ID is provided, it is interpreted as the initial concentration/amount of that species and will override the initial concentration/amount given in the SBML model or given by a preequilibration condition. If `NaN` is provided for a condition, the result of the preequilibration (or initial concentration/amount from the SBML model, if no preequilibration is defined) is used.

  - `${compartmentId}`

    If a compartment ID is provided, it is interpreted as the initial compartment size.

8.1.6 Measurement table

A tab-separated values files containing all measurements to be used for model training or validation.

Expected to have the following named columns in any (but preferably this) order:

observableId	[preequilibrationConditionId]	simulationConditionId	measurement	time
observableId	[conditionId]	conditionId	NUMERIC	NUMERIC|inf
...	...	...	...	...

(wrapped for readability)

...	[observableParameters]	[noiseParameters]
...	[parameterId|NUMERIC[;parameterId|NUMERIC][...]]	[parameterId|NUMERIC[;parameterId|NUMERIC][...]]
...	...	...

Additional (non-standard) columns may be added. If the additional plotting functionality of PEtab should be used, such columns could be

...	[datasetId]	[replicateId]
...	[datasetId]	[replicateId]
...	...	...

where `datasetId` is a necessary column to use particular plotting functionality, and `replicateId` is optional, which can be used to group replicates and plot error bars.

Detailed field description

- `observableId` [STRING, NOT NULL, REFERENCES(observables.observableID)]

  Observable ID as defined in the observables table described below.

- `preequilibrationConditionId` [STRING OR NULL, REFERENCES(conditionsTable.conditionID), OPTIONAL]

  The `conditionId` to be used for preequilibration. E.g. for drug treatments, the model would be preequilibrated with the no-drug condition. Empty for no preequilibration.

- `simulationConditionId` [STRING, NOT NULL, REFERENCES(conditionsTable.conditionID)]

  `conditionId` as provided in the condition table, specifying the condition-specific parameters used for simulation.

- `measurement` [NUMERIC, NOT NULL]

  The measured value in the same units/scale as the model output.

- `time` [NUMERIC OR STRING, NOT NULL]

  Time point of the measurement in the time unit specified in the SBML model, numeric value or `inf` (lower-case) for steady-state measurements.

- `observableParameters` [NUMERIC, STRING OR NULL, OPTIONAL]

  This field allows overriding or introducing condition-specific versions of output parameters defined in the observation model. The model can define observables (see below) containing place-holder parameters which can be replaced by condition-specific dynamic or constant parameters. Placeholder parameters must be named `observableParameter${n}_${observableId}` with `n` ranging from 1 (not 0) to the number of placeholders for the given observable, without gaps. If the observable specified under `observableId` contains no placeholders, this field must be empty. If it contains `n > 0` placeholders, this field must hold `n` semicolon-separated numeric values or parameter names. No trailing semicolon must be added.

Different lines for the same `observableId` may specify different parameters. This may be used to account for condition-specific or batch-specific parameters. This will translate into an extended optimization parameter vector.

All placeholders defined in the observation model must be overwritten here. If there are no placeholders used, this column may be omitted.

- `noiseParameters` [NUMERIC, STRING OR NULL, OPTIONAL]

  The measurement standard deviation or `NaN` if the corresponding sigma is a model parameter.

  Numeric values or parameter names are allowed. Same rules apply as for `observableParameters` in the previous point.

- `datasetId` [STRING, OPTIONAL]

  The datasetId is used to group certain measurements to datasets. This is typically the case for data points which belong to the same observable, the same simulation and preequilibration condition, the same noise model, the same observable transformation and the same observable parameters. This grouping makes it possible to use the plotting routines which are provided in the PEtab repository.

- `replicateId` [STRING, OPTIONAL]

  The replicateId can be used to discern replicates with the same `datasetId`, which is helpful for plotting e.g. error bars.

8.1.7 Observables table

Parameter estimation requires linking experimental observations to the model of interest. Therefore, one needs to define observables (model outputs) and respective noise models, which represent the measurement process. Since parameter estimation is beyond the scope of SBML, there exists no standard way to specify observables (model outputs) and respective noise models. Therefore, in PEtab observables are specified in a separate table as described in the following. This allows for a clear separation of the observation model and the underlying dynamic model, which allows, in most cases, to reuse any existing SBML model without modifications.

The observable table has the following columns:

observableId	[observableName]	observableFormula
STRING	[STRING]	STRING
e.g.		
relativeTotalProtein1	Relative abundance of Protein1	observableParameter1_relativeTotalProtein1 * (protein1 + phospho_protein1)
...	...	...

(wrapped for readability)

...	[observableTransformation]	noiseFormula	[noiseDistribution]
...	[lin(default)|log|log10]	STRING|NUMBER	[laplace|normal]
...	e.g.		
...	lin	noiseParameter1_relativeTotalProtein1	normal
...	...	...	...

Detailed field description

- `observableId` [STRING]

Unique identifier for the given observable. Must consist only of upper and lower case letters, digits and underscores, and must not start with a digit. This is referenced by the `observableId` column in the measurement table.

- [`observableName`] [STRING, OPTIONAL]

  Name of the observable. Only used for output, not for identification.

- `observableFormula` [STRING]

  Observation function as plain text formula expression. May contain any symbol defined in the SBML model (including model time `time`) or parameter table. In the simplest case just an SBML species ID or an `AssignmentRule` target.

  May introduce new parameters of the form `observableParameter${n}_${observableId}`, which are overridden by `observableParameters` in the measurement table (see description there).

- `observableTransformation` [STRING, OPTIONAL]

  Transformation of the observable and measurement for computing the objective function. Must be one of `lin`, `log` or `log10`. Defaults to `lin`. The measurements and model outputs are both assumed to be provided in linear space.

- `noiseFormula` [NUMERIC|STRING]

  Measurement noise can be specified as a numerical value which will default to a Gaussian noise model if not specified differently in `noiseDistribution` with standard deviation as provided here. In this case, the same standard deviation is assumed for all measurements for the given observable.

  Alternatively, some formula expression can be provided to specify more complex noise models. A noise model which accounts for relative and absolute contributions could, e.g., be defined as:

```
noiseParameter1_observable_pErk + noiseParameter2_observable_pErk*pErk
```

  with `noiseParameter1_observable_pErk` denoting the absolute and `noiseParameter2_observable_pErk` the relative contribution for the observable `observable_pErk` corresponding to species `pErk`. IDs of noise parameters that need to have different values for different measurements have the structure: `noiseParameter${indexOfNoiseParameter}_${observableId}` to facilitate automatic recognition. The specific values or parameters are assigned in the `noiseParameters` field of the *measurement table* (see above). Any parameters named `noiseParameter${1..n}_${observableId}` *must* be overwritten in the measurement table.

- `noiseDistribution` [STRING: 'normal' or 'laplace', OPTIONAL]

  Assumed noise distribution for the given measurement. Only normally or Laplace distributed noise is currently allowed (log-normal and log-Laplace are obtained by setting `observableTransformation` to `log`, similarly for `log10`). Defaults to `normal`. If `normal`, the specified `noiseParameters` will be interpreted as standard deviation (*not* variance). If `Laplace` ist specified, the specified `noiseParameter` will be interpreted as the scale, or diversity, parameter.

Noise distributions

For `noiseDistribution`, `normal` and `laplace` are supported. For `observableTransformation`, `lin`, `log` and `log10` are supported. Denote by y the simulation, m the measurement, and σ the standard deviation of a normal, or the scale parameter of a laplace model, as given via the `noiseFormula` field. Then we have the following effective noise distributions.

- Normal distribution:

$$\pi(m|y,\sigma) = \frac{1}{\sqrt{2\pi}\sigma} \exp\left(-\frac{(m-y)^2}{2\sigma^2}\right)$$

- Log-normal distribution (i.e. log(m) is normally distributed):

$$\pi(m|y,\sigma) = \frac{1}{\sqrt{2\pi}\sigma m} \exp\left(-\frac{(\log m - \log y)^2}{2\sigma^2}\right)$$

- Log10-normal distribution (i.e. log10(m) is normally distributed):

$$\pi(m|y,\sigma) = \frac{1}{\sqrt{2\pi}\sigma m \log(10)} \exp\left(-\frac{(\log_{10} m - \log_{10} y)^2}{2\sigma^2}\right)$$

- Laplace distribution:

$$\pi(m|y,\sigma) = \frac{1}{2\sigma} \exp\left(-\frac{|m-y|}{\sigma}\right)$$

- Log-Laplace distribution (i.e. log(m) is Laplace distributed):

$$\pi(m|y,\sigma) = \frac{1}{2\sigma m} \exp\left(-\frac{|\log m - \log y|}{\sigma}\right)$$

- Log10-Laplace distribution (i.e. log10(m) is Laplace distributed):

$$\pi(m|y,\sigma) = \frac{1}{2\sigma m \log(10)} \exp\left(-\frac{|\log_{10} m - \log_{10} y|}{\sigma}\right)$$

The distributions above are for a single data point. For a collection $D = \{m_i\}_i$ of data points and corresponding simulations $Y = \{y_i\}_i$ and noise parameters $\Sigma = \{\sigma_i\}_i$, the current specification assumes independence, i.e. the full distributions is

$$\pi(D|Y,\Sigma) = \prod_i \pi(m_i|y_i,\sigma_i)$$

8.1.8 Parameter table

A tab-separated value text file containing information on model parameters.

This table *must* include the following parameters:

- Named parameter overrides introduced in the *conditions table*, unless defined in the SBML model
- Named parameter overrides introduced in the *measurement table*

and *must not* include:

- Placeholder parameters (see `observableParameters` and `noiseParameters` above)
- Parameters included as column names in the *condition table*
- Parameters that are AssignmentRule targets in the SBML model

it *may* include:

- Any SBML model parameter that was not excluded above

- Named parameter overrides introduced in the *conditions table*

One row per parameter with arbitrary order of rows and columns:

parameterId	[parameterName]	parameterScale	lowerBound	upperBound	nominalValue	estimate	...
STRING	[STRING]	log10|lin|log	NUMERIC	NUMERIC	NUMERIC	0|1	...
...	...	...	...	...	...	...	...

(wrapped for readability)

...	[initializationPriorType]	[initializationPriorParameters]	[objectivePriorType]	[objectivePriorParameters]
...	*see below*	*see below*	*see below*	*see below*
...	...	...	...	...

Additional columns may be added.

Detailed field description

- `parameterId` [STRING, NOT NULL]

  The `parameterId` of the parameter described in this row. This has to match the ID of a parameter specified in the SBML model, a parameter introduced as override in the condition table, or a parameter occurring in the `observableParameters` or `noiseParameters` column of the measurement table (see above).

- `parameterName` [STRING, OPTIONAL]

  Parameter name to be used e.g. for plotting etc. Can be chosen freely. May or may not coincide with the SBML parameter name.

- `parameterScale` [lin|log|log10]

  Scale of the parameter to be used during parameter estimation.

- `lowerBound` [NUMERIC]

  Lower bound of the parameter used for optimization. Optional, if `estimate==0`. Must be provided in linear space, independent of `parameterScale`.

- `upperBound` [NUMERIC]

  Upper bound of the parameter used for optimization. Optional, if `estimate==0`. Must be provided in linear space, independent of `parameterScale`.

- `nominalValue` [NUMERIC]

  Some parameter value to be used if the parameter is not subject to estimation (see `estimate` below). Must be provided in linear space, independent of `parameterScale`. Optional, unless `estimate==0`.

- `estimate` [BOOL 0|1]

  1 or 0, depending on, if the parameter is estimated (1) or set to a fixed value(0) (see `nominalValue`).

- `initializationPriorType` [STRING, OPTIONAL]

  Prior types used for sampling of initial points for optimization. Sampled points are clipped to lie inside the parameter boundaries specified by `lowerBound` and `upperBound`. Defaults to `parameterScaleUniform`.

Possible prior types are:

- *uniform*: flat prior on linear parameters
- *normal*: Gaussian prior on linear parameters
- *laplace*: Laplace prior on linear parameters
- *logNormal*: exponentiated Gaussian prior on linear parameters
- *logLaplace*: exponentiated Laplace prior on linear parameters
- *parameterScaleUniform* (default): Flat prior on original parameter scale (equivalent to "no prior")
- *parameterScaleNormal*: Gaussian prior on original parameter scale
- *parameterScaleLaplace*: Laplace prior on original parameter scale

- `initializationPriorParameters` [STRING, OPTIONAL]

  Prior parameters used for sampling of initial points for optimization, separated by a semicolon. Defaults to `lowerBound;upperBound`. The parameters are expected to be in linear scale except for the `parameterScale` priors, where the prior parameters are expected to be in parameter scale.

  So far, only numeric values will be supported, no parameter names. Parameters for the different prior types are:

  - uniform: lower bound; upper bound
  - normal: mean; standard deviation (**not** variance)
  - laplace: location; scale
  - logNormal: parameters of corresp. normal distribution (see: normal)
  - logLaplace: parameters of corresp. Laplace distribution (see: laplace)
  - parameterScaleUniform: lower bound; upper bound
  - parameterScaleNormal: mean; standard deviation (**not** variance)
  - parameterScaleLaplace: location; scale

- `objectivePriorType` [STRING, OPTIONAL]

  Prior types used for the objective function during optimization or sampling. For possible values, see `initializationPriorType`.

- `objectivePriorParameters` [STRING, OPTIONAL]

  Prior parameters used for the objective function during optimization. For more detailed documentation, see `initializationPriorParameters`.

8.1.9 Visualization table

A tab-separated value file containing the specification of the visualization routines which come with the PEtab repository. Plots are in general collections of different datasets as specified using their `datasetId` (if provided) inside the measurement table.

Expected to have the following columns in any (but preferably this) order:

plotId	[plotName]	[plotTypeSimulation]	[plotTypeData]
STRING	[STRING]	[LinePlot(default)|BarPlot|ScatterPlot]	[MeanAndSD(default)|MeanAndSEM|replicate;provided]
...	...	...	...

(wrapped for readability)

...	[datasetId]	[xValues]	[xOffset]	[xLabel]	[xScale]
...	[datasetId]	[time(default)|parameterOrStateId]	[NUMERIC]	[STRING]	[lin|log|log10|order]
...	...	...	...	...	...

(wrapped for readability)

...	[yValues]	[yOffset]	[yLabel]	[yScale]	[legendEntry]
...	[observableId]	[NUMERIC]	[STRING]	[lin|log|log10]	[STRING]
...	...	...	...	...	...

Detailed field description

- `plotId` [STRING, NOT NULL]

  An ID which corresponds to a specific plot. All datasets with the same plotId will be plotted into the same axes object.

- `plotName` [STRING, OPTIONAL]

  A name for the specific plot.

- `plotTypeSimulation` [STRING, OPTIONAL]

  The type of the corresponding plot, can be `LinePlot`, `BarPlot` and `ScatterPlot`. Default is `LinePlot`.

- `plotTypeData` [STRING, OPTIONAL]

  The type how replicates should be handled, can be `MeanAndSD`, `MeanAndSEM`, `replicate` (for plotting all replicates separately), or `provided` (if numeric values for the noise level are provided in the measurement table). Default is `MeanAndSD`.

- `datasetId` [STRING, NOT NULL, REFERENCES(measurementTable.datasetId), OPTIONAL]

  The datasets which should be grouped into one plot.

- `xValues` [STRING, OPTIONAL]

  The independent variable, which will be plotted on the x-axis. Can be `time` (default, for time resolved data), or it can be `parameterOrStateId` for dose-response plots. The corresponding numeric values will be shown on the x-axis.

- `xOffset` [NUMERIC, OPTIONAL]

  Possible data-offsets for the independent variable (default is `0`).

- `xLabel` [STRING, OPTIONAL]

  Label for the x-axis. Defaults to the entry in `xValues`.

- `xScale` [STRING, OPTIONAL]

  Scale of the independent variable, can be `lin`, `log`, `log10` or `order`. The `order` value should be used if values of the independent variable are ordinal. This value can only be used in combination with `LinePlot` value for the `plotTypeSimulation` column. In this case, points on x axis will be placed equidistantly from each other. Default is `lin`.

- `yValues` [observableId, REFERENCES(measurementTable.observableId), OPTIONAL]

  The observable which should be plotted on the y-axis.

- `yOffset` [NUMERIC, OPTIONAL]

  Possible data-offsets for the observable (default is `0`).

- `yLabel` [STRING, OPTIONAL]

  Label for the y-axis. Defaults to the entry in `yValues`.

- `yScale` [STRING, OPTIONAL]

  Scale of the observable, can be `lin`, `log`, or `log10`. Default is `lin`.

- `legendEntry` [STRING, OPTIONAL]

  The name that should be displayed for the corresponding dataset in the legend and which defaults to the value in `datasetId`.

Extensions

Additional columns, such as `Color`, etc. may be specified.

Examples

Examples of the visualization table can be found in the Benchmark model collection, for example in the Chen_MSB2009 model.

8.1.10 YAML file for grouping files

To link the SBML model, measurement table, condition table, etc. in an unambiguous way, we use a YAML file.

This file also allows specifying a PEtab version (as the format is not unlikely to change in the future).

Furthermore, this can be used to describe parameter estimation problems comprising multiple models (more details below).

The format is described in the schema ../petab/petab_schema.yaml, which allows for easy validation.

Parameter estimation problems combining multiple models

Parameter estimation problems can comprise multiple models. For now, PEtab allows to specify multiple SBML models with corresponding condition and measurement tables, and one joint parameter table. This means that the parameter namespace is global. Therefore, parameters with the same ID in different models will be considered identical.

8.2 PEtab Tutorial

8.2.1 Overview

In the following, we demonstrate how to set up a parameter estimation problem in PEtab based on a realistic application example. To this end, we consider the model and experimental data by Boehm et al. (2014). The model describes the dynamics of phosphorylation and dimerization of the transcription factors STAT5A and STAT5B. A visualization and the corresponding reactions of the model are provided below, although the details of the model are not relevant for the purpose of this tutorial. For more details, we refer to the original publication (Boehm et al., 2014).

A PEtab problem consists of 1) an SBML model of a biological system, 2) condition, observable and measurement definitions, and 3) the specification of the parameters. We will show how to generate the respective files in the following.

8.2.2 1. The model

PEtab assumes that an SBML file of the model exists. Here, we use the SBML model provided in the original publication, which is also available on Biomodels (https://www.ebi.ac.uk/biomodels/BIOMD0000000591). For illustration purposes we slightly modified the SBML model and shortened some parts of the PEtab files. The full PEtab problem introduced in this tutorial is available online.

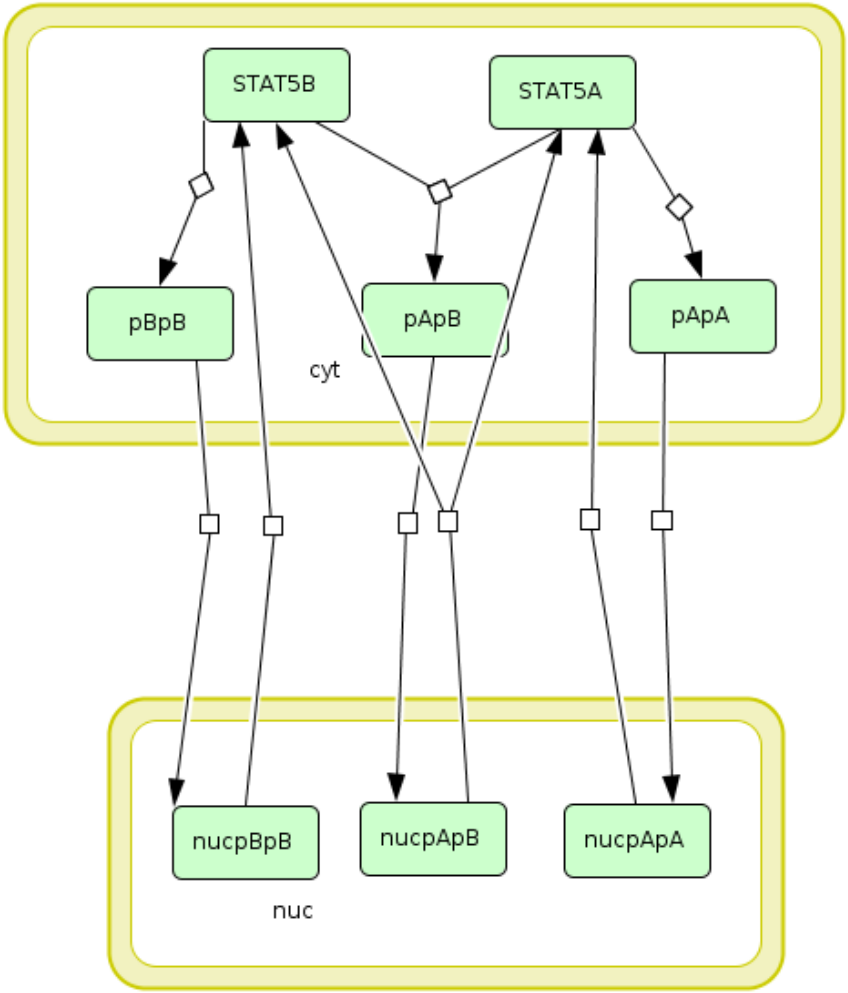


Fig. 3: Visualization of the model used as example in this tutorial. The model describes the dynamics of phosphorylation and dimerization of the transcription factors STAT5A and STAT5B.

Table 1: Reactions included in the example model.

ID	Reaction	Rate law
R1	2 STAT5A → pApA	cyt * BaF3_Epo * STAT5A^2 * k_phos
R2	STAT5A + STAT5B → pApB	cyt * BaF3_Epo * STAT5A * STAT5B * k_phos
R3	2 STAT5B → pBpB	cyt * BaF3_Epo * STAT5B^2 * k_phos
R4	pApA → nucpApA	cyt * k_imp_homo * pApA
R5	pApB → nucpApB	cyt * k_imp_hetero * pApB
R6	pBpB → nucpBpB	cyt * k_imp_homo * pBpB
R7	nucpApA → 2 STAT5A	nuc * k_exp_homo * nucpApA
R8	nucpApB → STAT5A + STAT5B	nuc * k_exp_hetero * nucpApB
R9	nucpBpB → 2 STAT5B	nuc * k_exp_homo * nucpBpB

8.2.3 2. Linking model and measurements

The model by Boehm et al. (2014) was calibrated on measurements on phosphorylation levels of STAT5A and STAT5B as well as relative STAT5A abundance for different timepoints between 0 - 240 minutes after stimulation with erythropoietin (Epo):

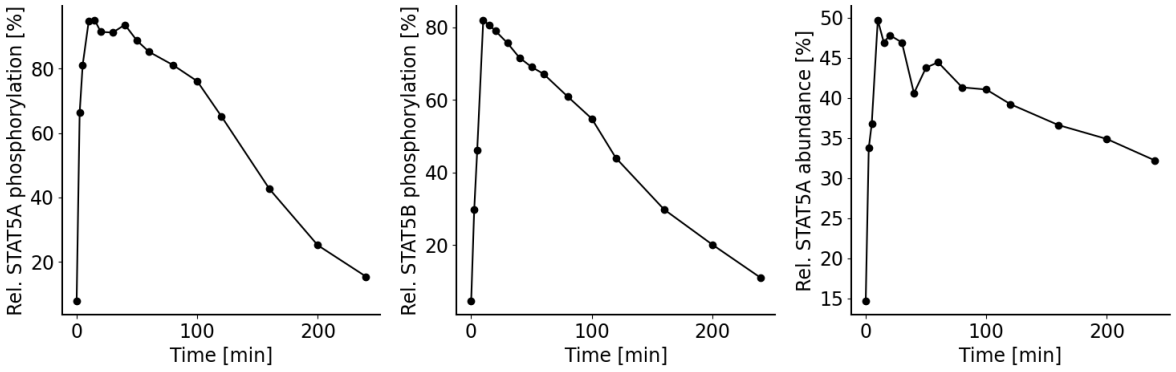


Fig. 4: Measurements considered for model calibration in our example.

To define a parameter estimation problem in PEtab, we need to map measurements to the model states. To this end, we need to 1) specify the experimental conditions the measurements were generated from, 2) specify observation functions and error models, and 3) specify the measurements themselves. For this, we need to define observation functions as well as experimental conditions under which a measurement was performed.

2.1 Specifying experimental conditions

All measurements were collected under the same experimental condition, which is a stimulation with Epo. This is specified in the experimental condition PEtab file, a tab-separated values (TSV) file[1], by providing a condition identifier and listing all condition-specific parameters and their respective values.

In the problem considered here, the relevant parameter is `Epo_concentration` which we want to set to a value of 1.25E-7, as the only condition-specific parameter. Since in this example we include data from only one single experiment, it would not be necessary to specify the condition parameter here, but instead the value could have been also set in the model or in the parameter table. However, the benefit of specifying it in the condition table is, that it allows us to easily add measurements from other experiments performed with different Epo concentrations later on.

[1] TSV files can be created using any standard spreadsheet application, or for small files, text editor.

The condition table looks as follows:

Table 2: Conditions table `experimental_conditions.tsv`.

conditionId	conditionName	Epo_concentration
epo_stimulation	Stimulation with 1.25E-7 Epo	1.25E-7

- *conditionId* is a unique identifier to define the different conditions and link them to the measurements (see measurement file below). Additional measurements e.g. for different Epo concentrations can be defined by adding new rows.
- *conditionName* can be used as a human readable description of the condition e.g. for plotting.

The following column headers (here *Epo_concentration*) refer to different parameters or species in the model, the values of which are overridden by these condition-specific values. Here, we define the Epo concentration, but additional columns could be used to e.g. set different initial concentrations of STAT5A/B. In addition to numeric values, also parameter identifiers can be used here to introduce condition specific optimization parameters.

2.2 Specifying the observation model

To link the model states to the measured values, we specify observation functions. Additionally, a noise model can be introduced to account for the measurement errors. In PEtab, this can be encoded in the observable file:

Table 3: Observables table `observables.tsv`.

observableId	observableName	...
pSTAT5A_rel	Rel. STAT5A phosphorylation [%]	...
pSTAT5B_rel	Rel. STAT5B phosphorylation [%]	...
rSTAT5A_rel	Rel. STAT5A abundance [%]	...

Table 4: Observables table `observables.tsv` (continued).

...	observableFormula	...
...	100*(2*pApA + pApB) / (2*pApA + pApB + STAT5A)	...
...	100*(2*pBpB + pApB) / (2*pBpB + pApB + STAT5B)	...
...	100*(STAT5A + pApB + 2*pApA) / (2 * pApB + 2* pApA + STAT5A + STAT5B + 2*pBpB)	...

Table 5: Observables table `observables.tsv` (continued).

...	noiseFormula	noiseDistribution
...	noiseParameter1_pSTAT5A_rel	normal
...	noiseParameter1_pSTAT5B_rel	normal
...	noiseParameter1_rSTAT5A_rel	normal

- *observableId* specifies a unique identifier to the observables that can be used to link them to the measurements (see below).
- *observableName* can be used as a human readable description of the observable. Here, this corresponds to the y-label in the figure above.
- *observableFormula* is a mathematical expression defining how the model output is calculated. The formula can consist of species and parameters defined in the SBML file. In our example, we measure e.g. the relative phosphorylation level of STAT5A (*pSTAT5A_rel*), which is the sum of all species containing phosphorylated STAT5A over the sum of all species containing any form of STAT5A.
- *noiseFormula* is used to describe the formula for the measurement noise. Together with *noiseDistribution*, it defines the noise model. In this example, we assume additive, normally distributed measurement noise. In

this scenario, `noiseParameter1_{observableId}` is the standard deviation of the measurement noise. Parameters following this naming scheme are expected to be overridden in a measurement-specific manner in the *noiseParameters* column of the measurement table (see below).

2.3 Specifying measurements

The experimental data is linked to the conditions via the *conditionId* and to the observables via the *observableId*. This is defined in the PEtab measurement file:

Table 6: Measurement table `measurement_data.tsv`.

observableId	simulationConditionId	measurement	time	noiseParameters
pSTAT5A_rel	epo_stimulation	7.9	0	sd_pSTAT5A_rel
...	...	...	...	...
pSTAT5A_rel	epo_stimulation	15.4	240	sd_pSTAT5A_rel
pSTAT5B_rel	epo_stimulation	4.6	0	sd_pSTAT5B_rel
...	...	...	...	...
pSTAT5B_rel	epo_stimulation	10.96	240	sd_pSTAT5B_rel
rSTAT5A_rel	epo_stimulation	14.7	0	sd_rSTAT5A_rel
...	...	...	...	...
rSTAT5A_rel	epo_stimulation	32.2	240	sd_rSTAT5A_rel

- *observableId* references the *observableId* from the observable file.
- *simulationConditionId* references the *conditionId* from the experimental condition file.
- *measurement* defines the values that are measured for the respective observable and experimental condition.
- *time* is the time point at which the measurement was performed. For brevity, only the first and last time point of the example are shown here (the omitted measurements are indicated by "..." in the example).
- *noiseParameters* relates to the *noiseParameters* in the observables file. In our example, the measurement noise is unknown. Therefore we define parameters here which have to be estimated (see parameters sheet below). If the noise is known, e.g. from multiple replicates, numeric values can be used in this column.

8.2.4 3. Defining parameters

The model by Boehm et al. (2014) contains nine unknown parameters that need to be estimated from the experimental data. Additionally, it has two known parameters that are fixed to literature values.

The parameters file for this is given by:

Table 7: Parameter table `parameters.tsv`.

parameterId	parameterScale	lowerBound	upperBound	nominalValue	estimate
Epo_degradation_BaF3	log10	1E-5	1E+5		1
k_exp_hetero	log10	1E-5	1E+5		1
k_exp_homo	log10	1E-5	1E+5		1
k_imp_hetero	log10	1E-5	1E+5		1
k_imp_homo	log10	1E-5	1E+5		1
k_phos	log10	1E-5	1E+5		1
ratio	lin			0.693	0
sd_pSTAT5A_rel	log10	1E-5	1E+5		1
sd_pSTAT5B_rel	log10	1E-5	1E+5		1
sd_rSTAT5A_rel	log10	1E-5	1E+5		1

- *parameterId* references parameters defined in the SBML file. Additionally, parameters defined in the measurement table can be used here. In this example, the standard deviations for the different observables (*sd_{observableId}*) are estimated.
- *parameterScale* is the scale on which parameters are estimated. Often, a logarithmic scale improves optimization. Alternatively, a linear scale can be used, e.g. when parameters can be negative.
- *lowerBound* and *upperBound* define the bounds for the parameters used during optimization. These are usually biologically plausible ranges.
- *nominalValue* are known values used for simulation. The entry can be left empty, if a value is unknown and subject to optimization.
- *estimate* defines whether the parameter is subject to optimization (1) or if it is fixed (0) to the value in the nominalValue column.

8.2.5 4. Visualization file

Optionally, a visualization file can be specified in PEtab which defines how the measurement data and potentially model simulations are plotted. So far, the visualization files are only supported by the PEtab Python library. Here, we describe a file that specifies the visualization of the measurement data similar to the figure above.

Table 8: Visualization specification table `visualization_specification.tsv`.

plotId	plotTypeData	xLabel	yValues	yLabel
plot1	MeanAndSD	Time [min]	pSTAT5A_rel	Rel. STAT5A phosphorylation [%]
plot2	MeanAndSD	Time [min]	pSTAT5B_rel	Rel. STAT5B phosphorylation [%]
plot3	MeanAndSD	Time [min]	rSTAT5A_rel	Rel. STAT5A abundance [%]

- *plotId* corresponds to a specific plot. All lines which share the same *plotId* are combined into one plot.
- *plotTypeData* defines the plotting style of the measurement data. Here, we use mean and (if available) standard deviations.
- *xLabel* and *yLabel* are the labels of the x- and y-axes for the corresponding plot.
- *yValues* defines what is plotted. In this example the different observables are plotted individually.

There are various ways of further individualizing the plots, e.g. by defining legend entries or data plotted on log-scale (see the documentation for further information https://petab.readthedocs.io/en/latest/documentation_data_format.html#visualization-table).

8.2.6 5. YAML file

To group the previously mentioned PEtab files, a YAML file can be used, defining which files constitute a PEtab problem. While being optional, this makes it easier to import a PEtab problem into tools, and allows reusing files for different PEtab problems. This file has the following format (`Boehm_JProteomeRes2014.yaml`):

```
format_version: 1
parameter_file: parameters.tsv
problems:
  - condition_files:
    - experimental_conditions.tsv
    measurement_files:
    - measurement_data.tsv
    observable_files:
```

(continues on next page)

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```
  - observables.tsv
  sbml_files:
  - model_Boehm_JProteomeRes2014.xml
  visualization_files:
  - visualization_specification.tsv
```

The first line specifies the version this file and the files referenced adhere to. The current version number is 1. The second line references the parameter file. This is followed by a list of (sub-)problems, in this case only one, referencing the respective condition, measurement observable, model, and visualization files. There can be multiple of those files, e.g. for large numbers of measurements, one could split those up into separate files, e.g. by experimental condition or observable.

8.2.7 6. Model simulation

To simulate the model and compare it to the experimental data, the nominal parameters in the parameters file need to be set. As some parameters are a priori unknown, we here consider randomly sampled parameters to get a glance of model behaviour and fit to the data.

Table 9: Parameter table `parameters.tsv` with *nominalValue* set to random values.

parameterId	parameterScale	lowerBound	upperBound	nominalValue	estimate
Epo_degradation_BaF3	log10	1E-5	1E+5	0.105	1
k_exp_hetero	log10	1E-5	1E+5	1.85	1
k_exp_homo	log10	1E-5	1E+5	9.83	1
k_imp_hetero	log10	1E-5	1E+5	1048.96	1
k_imp_homo	log10	1E-5	1E+5	10.136	1
k_phos	log10	1E-5	1E+5	10.136	1
ratio	lin			0.693	0
sd_pSTAT5A_rel	log10	1E-5	1E+5	51.7	1
sd_pSTAT5B_rel	log10	1E-5	1E+5	0.257	1
sd_rSTAT5A_rel	log10	1E-5	1E+5	0.017	1

With this, the model can be simulated using the different tools that support PEtab. The easiest tool to get started with is probably COPASI which comes with a graphical user interface (see https://github.com/copasi/python-petab-importer for further instructions).

It is apparent from the figure, that the random parameters yield a poor fit of the model with the data. Therefore, it is important to optimize the parameters to improve the model fit. This can be done using various parameter estimation tools. Links to detailed descriptions how to use the individual toolboxes are provided at the PEtab Github page.

8.2.8 7. Further information

This tutorial only demonstrates a subset of PEtab functionality. For full reference, consult the PEtab reference. After finishing the implementation of the PEtab problem, its correctness can be verified using the PEtab library (see https://github.com/PEtab-dev/PEtab/blob/master/doc/example/example_petablint.ipynb for instructions). The PEtab problem can then be used as input to the supporting toolboxes to estimate the unknown parameters or calculate parameter uncertainties. Links to tutorials for the different tools can be found at the PEtab Github page (https://github.com/PEtab-dev/PEtab#petab-support-in-systems-biology-tools).

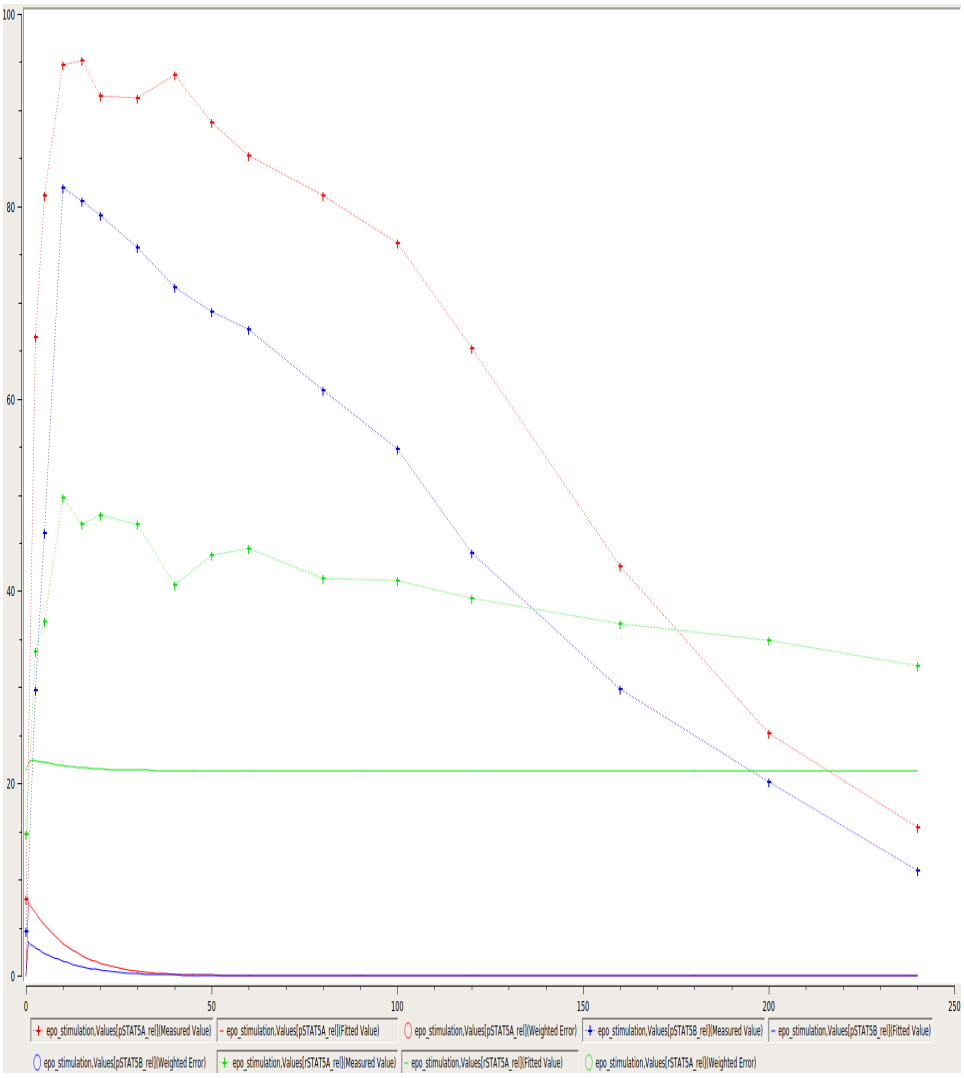

Fig. 5: Visualization of model outputs after simulation with random parameters and measurements in COPASI.

8.3 API Reference

petab
petab.composite_problem
petab.core
petab.conditions
petab.C
petab.lint
petab.measurements
petab.parameter_mapping
petab.parameters
petab.problem
petab.sampling
petab.sbml
petab.yaml
petab.visualize.data_overview
petab.visualize.helper_functions
petab.visualize. plot_data_and_simulation
petab.visualize.plotting_config

8.4 PEtab changelog

8.4.1 0.1 series

0.1.14

- Fix sampling of priors in `parameterScale` (#492)
- Clarify documentation of `parameterScale` priors
- Improvements in `petab.simulate` (#479):
  - Fix default noise distributions
  - Add option for non-negative synthetic data

0.1.13

- Fix for pandas 1.2.0 – use `get_handle` instead of `get_filepath_or_buffer`
- Fix erroneous `petab_test_suite` symlink (all #493)

0.1.12

- Documentation update:
  - Added SBML2Julia to list of tools supporting PEtab
  - Extended PEtab introduction
  - Tutorial for creating PEtab files
- Minor fix: Default argument for optional 'model' parameter in 'petab.lint.check_condition_df'' (#477)

0.1.11

- Function for generating synthetic data (#472)
- Minor documentation updates (#470)

0.1.10

- Fixed deployment setup, no further changes.*

0.1.9

Library:

- Allow URL as filenames for YAML files and SBML models (Closes #187) (#459)
- Allow model time in observable formulas (#445)
- Make float parsing from CSV round-trip (#444)
- Validator: Error message for missing IDs, with line numbers. (#467)
- Validator: Detect duplicated observable IDs (#446)
- Some documentation and CI fixes / updates
- Visualization: Add option to save visualization specification (#457)
- Visualization: Column XValue not mandatory anymore (#429)
- Visualization: Add sorting of indices of dataframes for the correct sorting of x-values (#430)
- Visualization: Default value for the column x_label in vis_spec (#431)

0.1.8

Library:

- Use `core.is_empty` to check for empty values (#434)
- Move tests to python 3.8 (#435)
- Update to libcombine 0.2.6 (#437)
- Make float parsing from CSV round-trip (#444)
- Lint: Allow model time in observable formulas (#445)
- Lint: Detect duplicated observable ids (#446)
- Fix likelihood calculation with missing values (#451)

Documentation:

- Move format documentation to restructuredtext format (#452)
- Document all noise distributions and observable scales (#452)
- Fix documentation for prior distribution (#449)

Visualization:

- Make XValue column non-mandatory (#429)

- Apply correct condition sorting (#430)
- Apply correct default x label (#431)

0.1.7

Documentation:

- Update coverage and links of supporting tools
- Update explanatory figure

0.1.6

Library:

- Fix handling of empty columns for residual calculation (#392)
- Allow optional fixing of fixed parameters in parameter mapping (#399)
- Fix function to flatten out time-point specific overrides (#404)
- Add function to create a problem yaml file (#398)
- Allow merging of multiple parameter files (#407)

Documentation:

- In README, add to the overview table the coverage for the supporting tools, and links and usage examples (various commits)
- Show REAMDE on readthedocs documentation front page (#400)
- Correct description of observable and noise formulas (#401)
- Update documentation on optional visualization values (#405, #419)

Visualization:

- Fix sorting problem (#396)
- More generously handle optional values (#405, #419)
- Create dataset id also for simulation dataframe (#408)
- Extend test suite for visualization (#418)

0.1.5

Library:

- New create empty observable function (issue 386) (#387)
- Deprecate petab.sbml.globalize_parameters (#381)
- Fix computing log10 likelihood (#380)
- Documentation update and typehints for visualization (#372)
- Ordered result of `petab.get_output_parameters`
- Fix missing argument to parameters.create_parameter_df

Documentation:

- Add overview of supported PEtab feature in toolboxes
- Add contribution guide
- Fix optional values in documentation (#378)

0.1.4

Library:

- Fixes / updates in functions for computing llh and chi2
- Allow and require output parameters defined in observable table to be defined in parameter table
- Fix merge_preeq_and_sim_pars_condition which incorrectly assumed lists instead of dicts
- Update parameter mapping to deal with species and compartments in condition table
- Removed `petab.migrations.sbml_observables_to_table`

  For converting older PEtab files to observable table format, use one of the previous releases
- Visualization:
  - Fix various issues with get_data_to_plot
  - Fixed various issues with expected presence of optional columns

0.1.3

File format:

- Updated documentation
- Observables table in YAML file now mandatory in schema (was implicitly mandatory before, as observable table was required already)

Library:

- petablint:
  - Fix: allow specifying observables file via CLI (Closes #302)
  - Fix: nominalValue is optional unless estimated!=1 anywhere (Fixes #303)
  - Fix: handle undefined observables more gracefully (Closes #300) (#351)
- Parameter mapping:
  - Fix / refactor parameter mapping (breaking change) (#344) (now performing parameter value and scale mapping together)
  - check optional measurement cols in mapping (#350)
- allow calculating llhs (#349), chi2 values (#348) and residuals (#345)
- Visualization
  - Basic Scatterplots & lot of bar plot fixes (#270)
  - Fix incorrect length of bool `bool_preequ` when subsetting with ind_meas (Closes #322)
- make libcombine optional (#338)

0.1.2

Library:

- Extensions and fixes for the visualization functions (#255, #262)
- Allow to extract fixed|free and scaled|non-scaled parameters (#256, #268, #273)
- Various fixes (esp. #264)
- Add function to get observable ids (#269)
- Improve documentation (esp. #289)
- Set default column for simulation results to 'simulation'
- Add support for COMBINE archives (#271)
- Fix sbml observables to table
- Improve prior and dataframe tests (#285, #286, #297)
- Add function to get parameter table with all default values (#288)
- Move tests to github actions (#281)
- Check for valid identifiers
- Fix handling of empty values in dataframes
- Allow to get numeric values in parameter mappings in scaled form (#308)

0.1.1

Library:

- Fix parameter mapping: include output parameters not present in SBML model
- Fix missing `petab/petab_schema.yaml` in source distribution
- Let get_placeholders return an (ordered) list of placeholders
- Deprecate `petab.problem.from_folder` and related functions (obsolete after introducing more flexible YAML files for grouping tables and models)

0.1.0

Data format:

- Introduce observables table instead of SBML assignment rules for defining observation model (#244) (moves observableTransformation and noiseModel from the measurement table to the observables table)
- Allow initial concentrations / sizes in condition table (#238)
- Fixes and clarifications in the format documentation
- Changes in prior columns of the parameter table (#222)
- Introduced separate version number of file format, this release being version 1

Library:

- Adaptations to new file formats
- Various bugfixes and clean-up, especially in visualization and validator

- Parameter mapping changed to include all model parameters and not only those differing from the ones defined inside the SBML model
- Introduced constants for all field names and string options, replacing most string literals in the code (#228)
- Added unit tests and additional format validation steps
- Optional parallelization of parameter mapping (#205)
- Extended documentation (in-source and example Jupyter notebooks)

0.0.2

Bugfix release

- Fix `petablint` error
- Fix minor issues in `petab.visualize`

0.0.1

Data format:

- Update format and documentation with respect to data and parameter scales (#169)
- Define YAML schema for grouping PEtab files, also allowing for more complex combinations of files (#183)

Library:

- Refactor library. Reorganize `petab.core` functions.
- Fix visualization w/o condition names #142
- Extend validator
- Removed deprecated functions petab.Problem.get_constant_parameters and petab.sbml.constant_species_to_parameters
- Minor fixes and extensions

8.4.2 0.0 series

0.0.0a17

Data format: *No changes*

Library:

- Extended visualization support
- Add helper function and test case to deal with timepoint-specific parameters flatten_timepoint_specific_output_overrides (#128) (Closes #125)
- Fix get_noise_distributions: so far we got 'normal' everywhere due to wrong grouping (#147)
- Fix create_parameter_df: Exclude rule targets (#149)
- Verify condition table column names occur as model parameters (Closes #150) (#151)
- More informative error messages in case of wrongly set observable and noise parameters (Closes #118) (#155)
- Update doc for copasi import and github installation (#158)

- Extend validator to check if all required parameters are present in parameter table (Closes #43) (#159)
- Setup documentation for RTD (#161)
- Handle None in petab.core.split_parameter_replacement_list (Closes #121)
- Fix(lint) correct handling of optional columns. Check before access.
- Remove obsolete generate_experiment_id.py (Closes #111) #166

0.0.0a16 and earlier

See git history

8.5 How to cite

Help us to promote PEtab: When using PEtab, please cite our preprint:

```
@misc{schmiester2020petab,
      title={PEtab -- interoperable specification of parameter estimation problems in␣
↪systems biology},
      author={Leonard Schmiester and Yannik Schälte and Frank T. Bergmann and Tacio␣
↪Camba and Erika Dudkin and Janine Egert and Fabian Fröhlich and Lara Fuhrmann and␣
↪Adrian L. Hauber and Svenja Kemmer and Polina Lakrisenko and Carolin Loos and Simon␣
↪Merkt and Wolfgang Müller and Dilan Pathirana and Elba Raimúndez and Lukas Refisch␣
↪and Marcus Rosenblatt and Paul L. Stapor and Philipp Städter and Dantong Wang and␣
↪Franz-Georg Wieland and Julio R. Banga and Jens Timmer and Alejandro F. Villaverde␣
↪and Sven Sahle and Clemens Kreutz and Jan Hasenauer and Daniel Weindl},
      year={2020},
      eprint={2004.01154},
      archivePrefix={arXiv},
      primaryClass={q-bio.QM}
}
```

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```
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8.8 Examples

The following examples should help to get a better idea of how to use the PEtab library.

8.8.1 Using petablint

`petablint` is a tool to validate a model against the PEtab standard. When you have installed PEtab, you can simply call it from the command line. It takes the following arguments:

[1]:
```
!petablint -h
```

```
usage: petablint [-h] [-v] [-s SBML_FILE_NAME] [-m MEASUREMENT_FILE_NAME]
                 [-c CONDITION_FILE_NAME] [-p PARAMETER_FILE_NAME]
                 [-y YAML_FILE_NAME | -n MODEL_NAME] [-d DIRECTORY]

Check if a set of files adheres to the PEtab format.

optional arguments:
  -h, --help            show this help message and exit
  -v, --verbose         More verbose output
  -s SBML_FILE_NAME, --sbml SBML_FILE_NAME
                        SBML model filename
  -m MEASUREMENT_FILE_NAME, --measurements MEASUREMENT_FILE_NAME
                        Measurement table
```

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```
  -c CONDITION_FILE_NAME, --conditions CONDITION_FILE_NAME
                        Conditions table
  -p PARAMETER_FILE_NAME, --parameters PARAMETER_FILE_NAME
                        Parameter table
  -y YAML_FILE_NAME, --yaml YAML_FILE_NAME
                        PEtab YAML problem filename
  -n MODEL_NAME, --model-name MODEL_NAME
                        Model name where all files are in the working
                        directory and follow PEtab naming convention.
                        Specifying -[smcp] will override defaults
  -d DIRECTORY, --directory DIRECTORY
```

Let's look at an example: In the example_Fujita folder, we have a PEtab configuration file `Fujita.yaml` telling which files belong to the Fujita model:

[2]:
```
!cat example_Fujita/Fujita.yaml
```

```
parameter_file: Fujita_parameters.tsv
petab_version: 0.0.0a17
problems:
- condition_files:
  - Fujita_experimentalCondition.tsv
  measurement_files:
  - Fujita_measurementData.tsv
  sbml_files:
  - Fujita_model.xml
```

To verify everything is ok, we can just call:

[3]:
```
!petablint -y example_Fujita/Fujita.yaml
```

If there were some inconsistency or error, we would see that here. `petablint` can be called in different ways. You can e.g. also pass SBML, measurement, condition, and parameter file directly, or, if the files follow PEtab naming conventions, you can just pass the model name.

8.8.2 Visualization of data and simulations

In this notebook, we illustrate the visualization functions of petab.

[1]:
```
from petab.visualize import plot_data_and_simulation
import matplotlib.pyplot as plt
```

[2]:
```
folder = "example_Isensee/"

data_file_path = folder + "Isensee_measurementData.tsv"
condition_file_path = folder + "Isensee_experimentalCondition.tsv"
visualization_file_path = folder + "Isensee_visualizationSpecification.tsv"
simulation_file_path = folder + "Isensee_simulationData.tsv"

# function to call, to plot data and simulations
ax = plot_data_and_simulation(data_file_path,
                              condition_file_path,
                              visualization_file_path,
```

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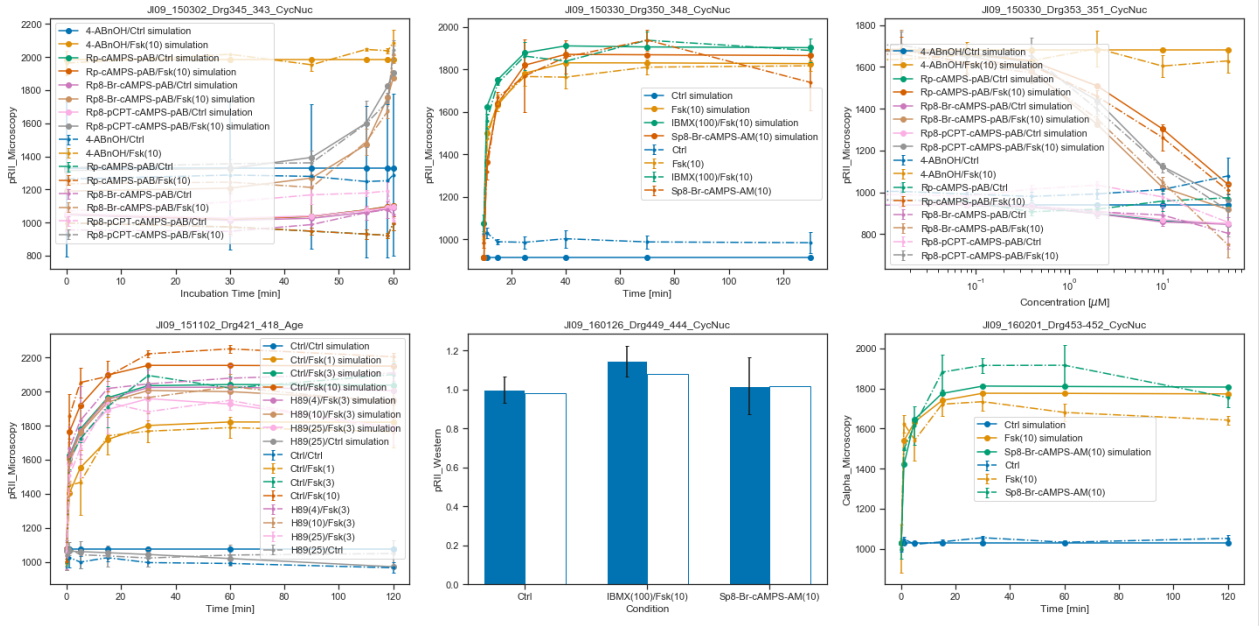
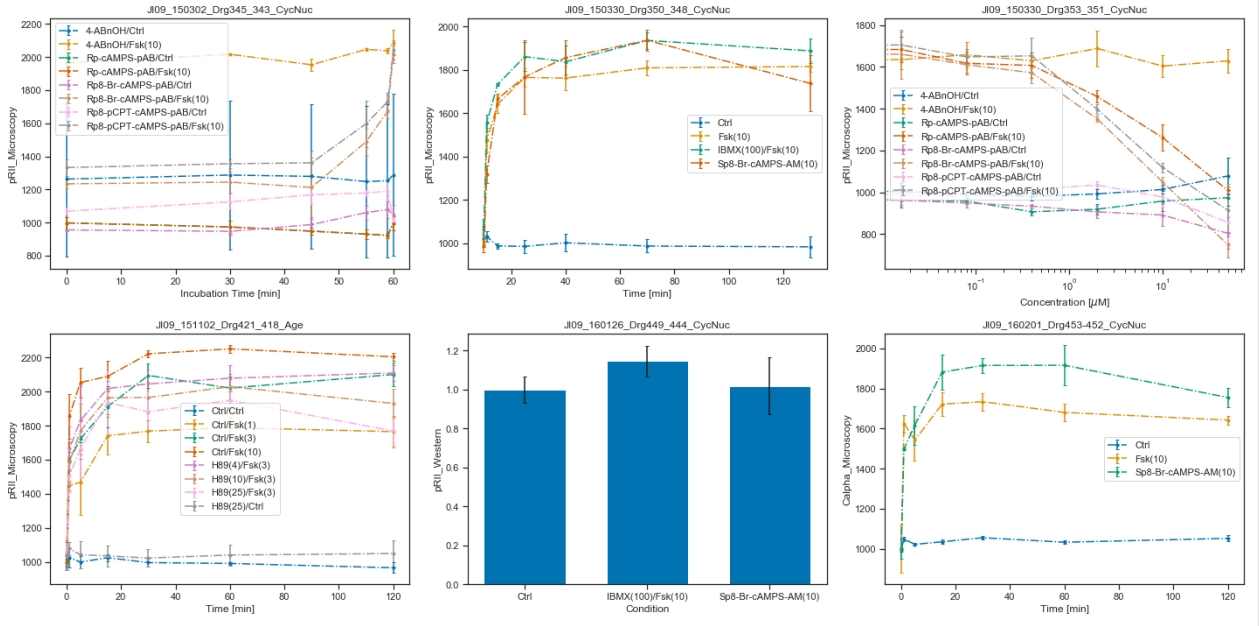
```
                                    simulation_file_path)
plt.show()
```



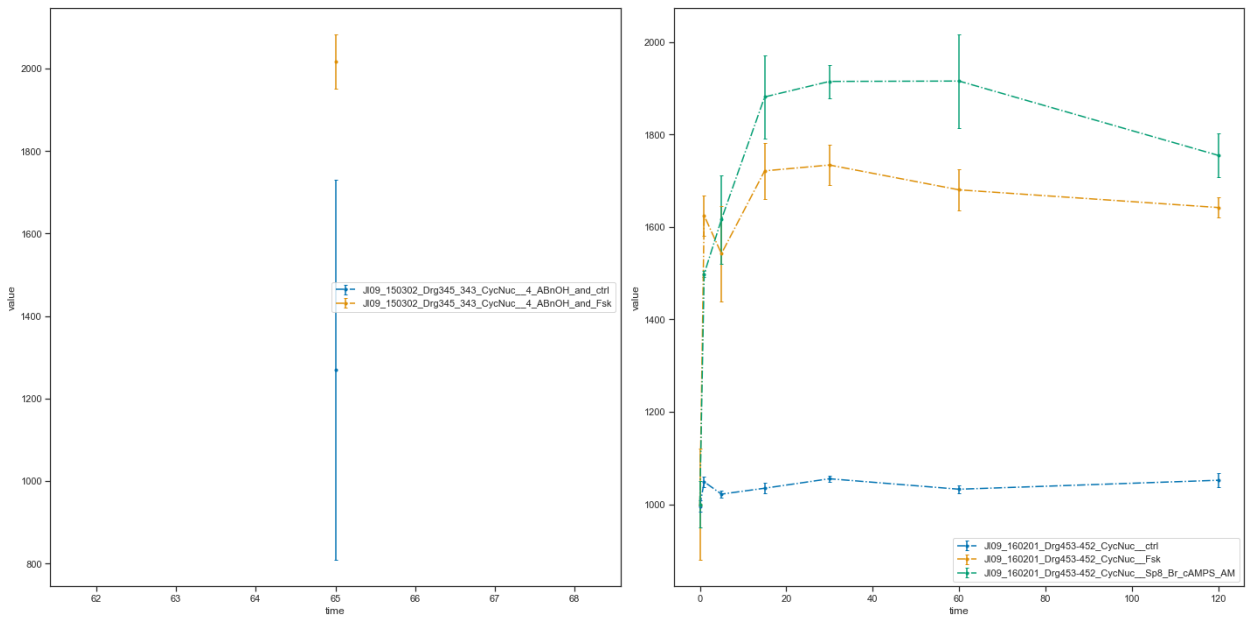
Now, we want to call the plotting routines without using the simulated data, only the visualization specification file.

[3]:
```
ax_without_sim = plot_data_and_simulation(
    data_file_path,
    condition_file_path,
    visualization_file_path)
plt.show()
```



We can also call the plotting routine without the visualization specification file, but by passing a list of lists as `dataset_id_list`. Each sublist corresponds to a plot, and contains the datasetIds which should be plotted. In this simply structured plotting routine, the independent variable will always be time.

[4]:
```
ax_without_sim = plot_data_and_simulation(
    data_file_path,
    condition_file_path,
    dataset_id_list = [['JI09_150302_Drg345_343_CycNuc__4_ABnOH_and_ctrl',
                        'JI09_150302_Drg345_343_CycNuc__4_ABnOH_and_Fsk'],
                       ['JI09_160201_Drg453-452_CycNuc__ctrl',
                        'JI09_160201_Drg453-452_CycNuc__Fsk',
                        'JI09_160201_Drg453-452_CycNuc__Sp8_Br_cAMPS_AM']])
plt.show()
```



Let's look more closely at the plotting routines, if no visualization specification file is provided. If such a file is missing, PEtab needs to know how to group the data points. For this, five options can be used: * dataset_id_list * sim_cond_id_lis * sim_cond_num_list * observable_id_list * observable_num_list

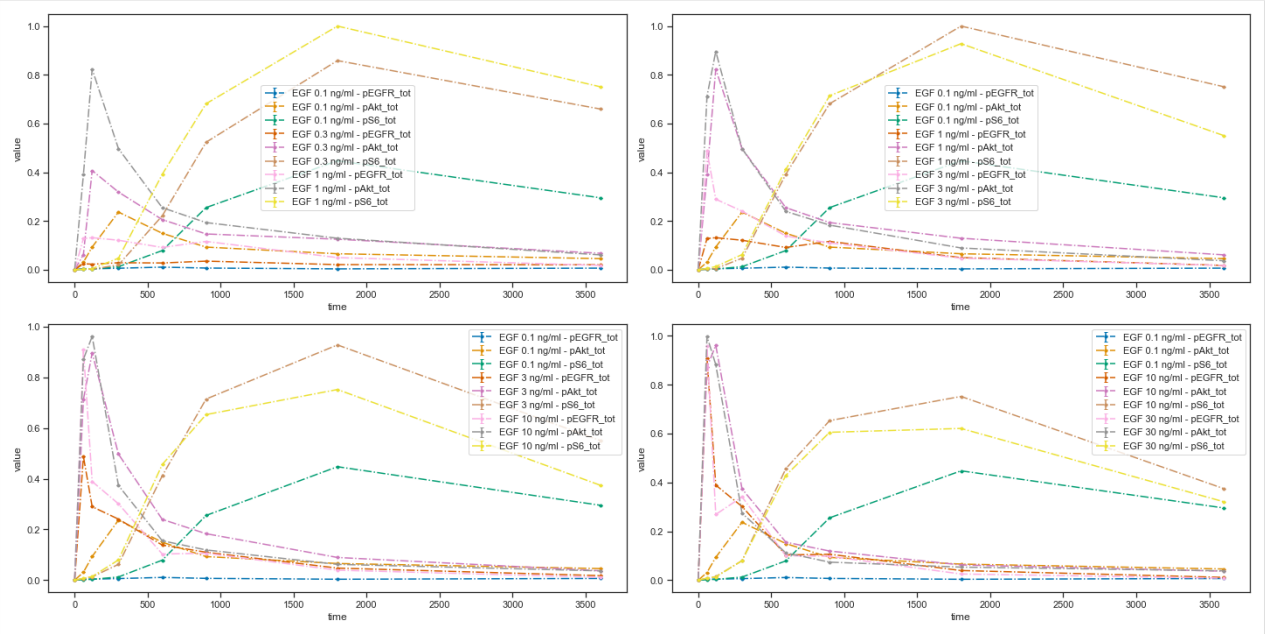
Each of them is a list of lists. Again, each sublist is a plot and its content are either simulation condition IDs or observable IDs (or their corresponding number when being enumerated) or the dataset IDs.

We want to illustrate this functionality by using a simpler example, a model published in 2010 by Fujita et al.

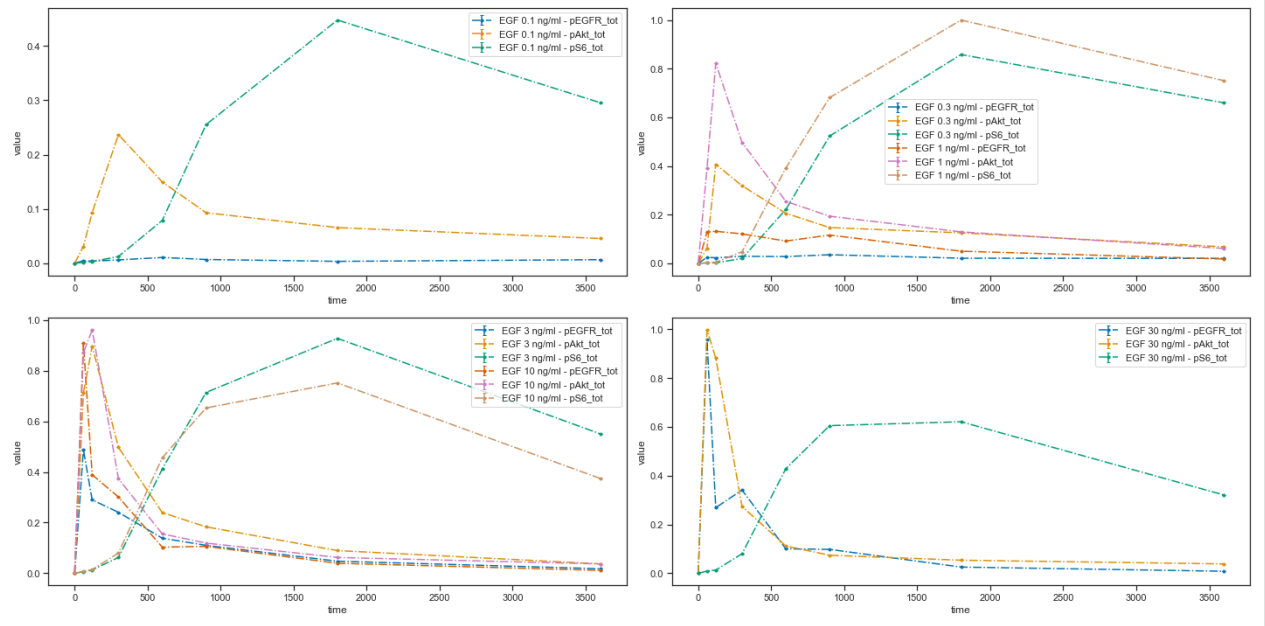
[5]:
```
data_file_path = "example_Fujita/Fujita_measurementData.tsv"
condition_file_path = "example_Fujita/Fujita_experimentalCondition.tsv"

# Plot 4 axes objects, plotting
# - in the first window all observables of the  1st, 2nd, and 3rd simulation condition
# - in the second window all observables of the 1st, 3rd, and 4th simulation condition
# - in the third window all observables of the  1st, 4th, and 5th simulation condition
# - in the fourth window all observables of the 1st, 5th, and 6th simulation condition
plot_data_and_simulation(data_file_path, condition_file_path,
                         sim_cond_num_list = [[0, 1, 2], [0, 2, 3], [0, 3, 4], [0, 4,␣
↪5]])
plt.show()
```

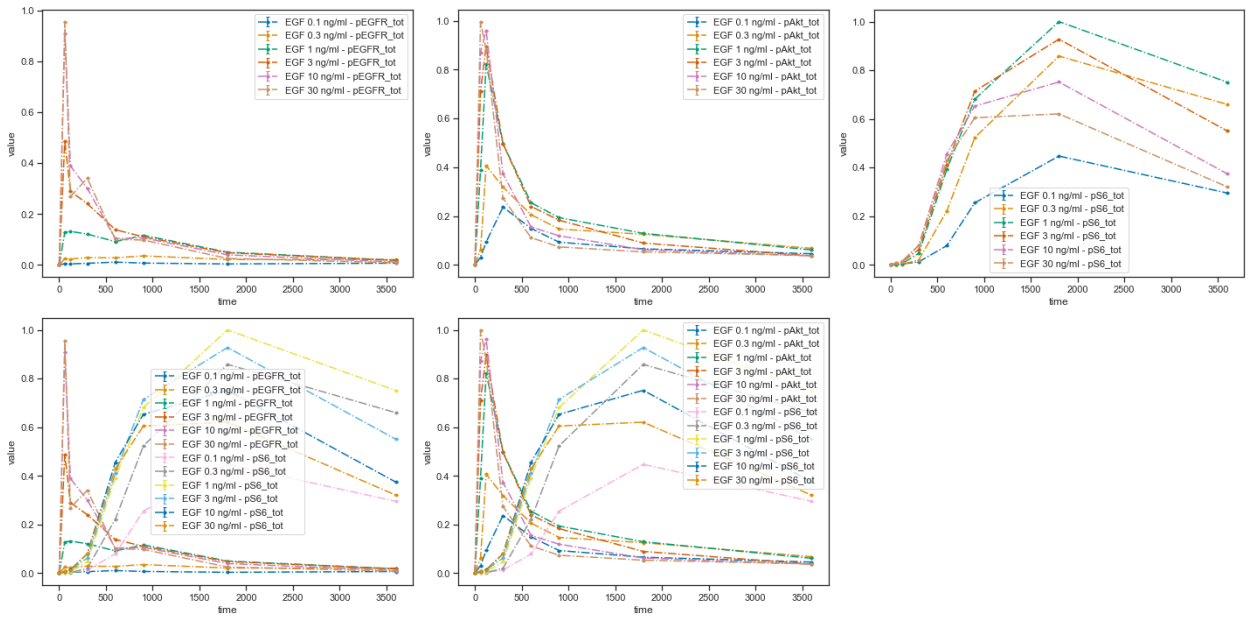
```
/home/polina/Documents/Development/PEtab/petab/visualize/helper_functions.py:157:␣
↪UserWarning: DatasetIds would have been available, but other grouping was requested.
↪ Consider using datasetId.
  warnings.warn("DatasetIds would have been available, but other "
```



[6]:
```
# Plot 4 axes objects, plotting
# - in the first window  all observables of the simulation condition 'model1_data1'
# - in the second window all observables of the simulation conditions 'model1_data2',
↪'model1_data3'
# - in the third window  all observables of the simulation conditions 'model1_data4',
↪'model1_data5'
# - in the fourth window all observables of the simulation condition 'model1_data6'
plot_data_and_simulation(
    data_file_path, condition_file_path,
    sim_cond_id_list = [['model1_data1'], ['model1_data2', 'model1_data3'],
                        ['model1_data4', 'model1_data5'], ['model1_data6']])
plt.show()
```

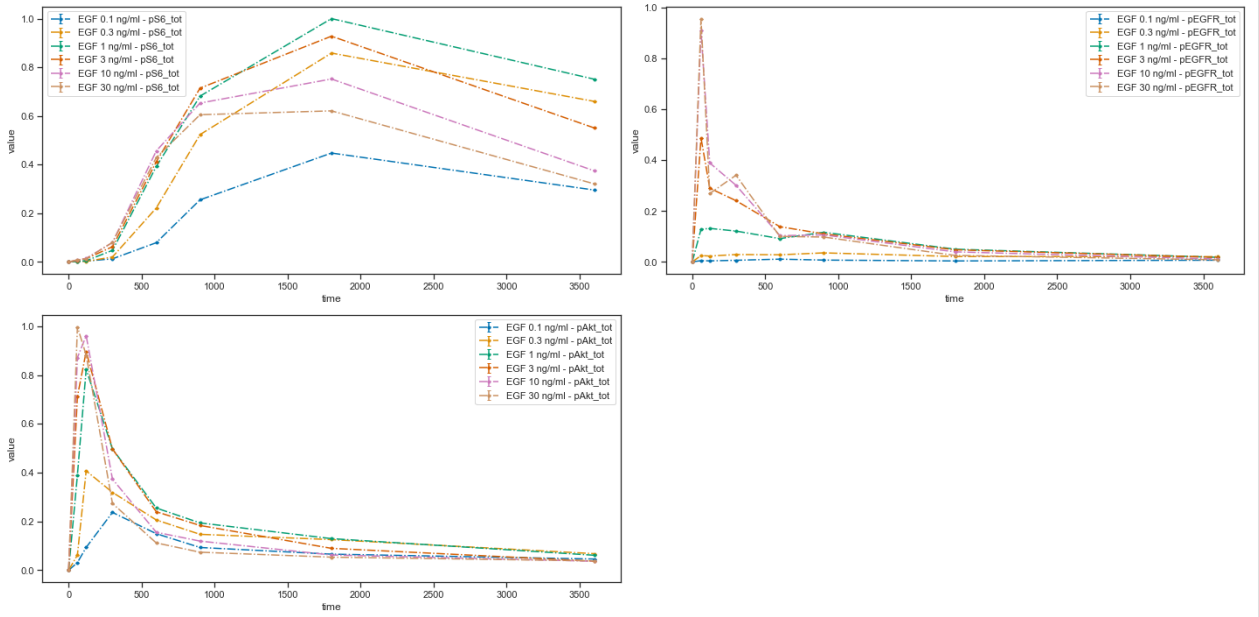


[7]:
```
# Plot 5 axes objects, plotting
# - in the first window  the 1st observable for all simulation conditions
# - in the second window the 2nd observable for all simulation conditions
# - in the third window  the 3rd observable for all simulation conditions
# - in the fourth window the 1st and 3rd observable for all simulation conditions
# - in the fifth window  the 2nd and 3rd observable for all simulation conditions
plot_data_and_simulation(
    data_file_path, condition_file_path,
    observable_num_list = [[0], [1], [2], [0, 2], [1, 2]])
plt.show()
```



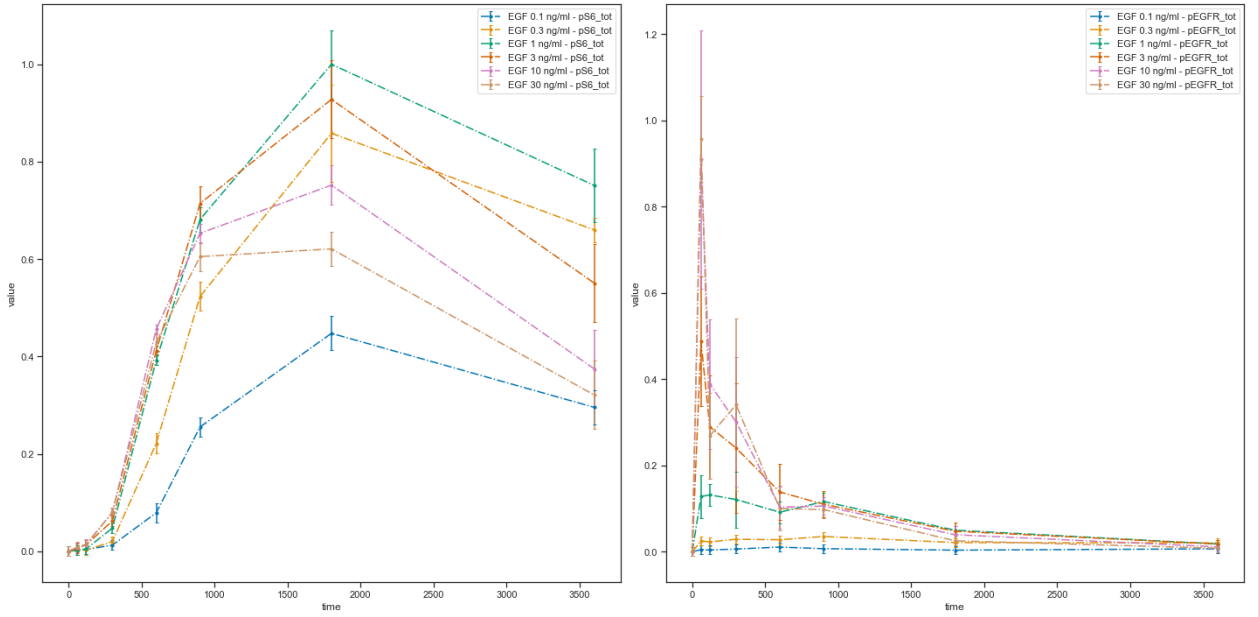
[8]:
```
# Plot 3 axes objects, plotting
# - in the first window  the observable 'pS6_tot' for all simulation conditions
# - in the second window the observable 'pEGFR_tot' for all simulation conditions
# - in the third window  the observable 'pAkt_tot' for all simulation conditions

plot_data_and_simulation(
    data_file_path, condition_file_path,
    observable_id_list = [['pS6_tot'], ['pEGFR_tot'], ['pAkt_tot']])
plt.show()
```



[9]:
```
# Plot 2 axes objects, plotting
# - in the first window  the observable 'pS6_tot' for all simulation conditions
# - in the second window the observable 'pEGFR_tot' for all simulation conditions
# - in the third window  the observable 'pAkt_tot' for all simulation conditions
# while using the noise values which are saved in the PEtab files

plot_data_and_simulation(
    data_file_path, condition_file_path,
    observable_id_list = [['pS6_tot'], ['pEGFR_tot']],
    plotted_noise='provided')
plt.show()
```



Examples of systems biology parameter estimation problems specified in PEtab can be found in the systems biology benchmark model collection.

CHAPTER 9

Indices and tables

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