



HetaProject – a Single Open Source Platform for Modeling, Simulation and Parameters Estimation in QSP

InSysBio

QSP Company

Ivan Borisov¹, Evgeny Metelkin¹

¹ InSysBio, Moscow, Russia

QSP CHALLENGES

A typical QSP project requires

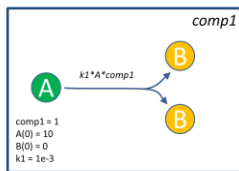
- model's development in a human-readable and tabular formats;
- integration between modeling and simulation environments;
- solving large-scale ODE models;
- running parallel Monte Carlo and Virtual Patients simulations;
- solving multi-conditional parameter estimation problems;

Software, which could establish the linkage between emerging QSP frameworks and fast computational methods, is of utmost importance for the field.

HETA LANGUAGE

Heta is a modeling language for Quantitative Systems Pharmacology (QSP) and Systems Biology (SB) [1]. It represents the dynamic models as interacting components that describe volumes, concentrations, amounts, rates.

```
// hello world!
//
comp1 @compartment {
  A @species { compartment: comp1 };
  B @species { compartment: comp1 };
  r1 @reaction { actors: A => B };
}
// math
A := 10;
B := 0;
r1 := k1*A*comp1;
k1 @const := 1e-3;
#export { format: SBML, filepath: sbml };
#export { format: Hrgsolve, filepath: hrgsolve };
```



HETACOMPILER

HetaCompiler converts Heta-based models into a number of formats to perform simulations. Currently it supports export to Matlab, R, Simbiology, DBSolve, SBML and Julia HetaSimulator.



HETASIMULATOR

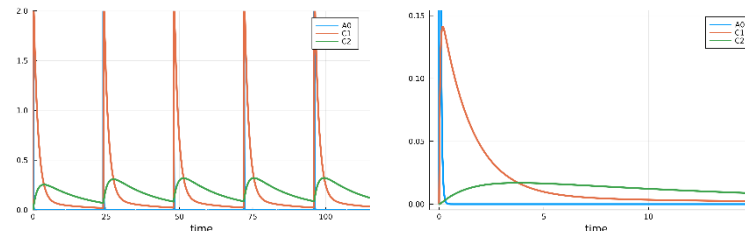
HetaSimulator is a Julia-based simulation and parameters estimation platform. **HetaSimulator** allows the user to run single, Monte-Carlo and Virtual Patients simulations. It supports single and multi-conditional fitting and provides tabular data input for both simulation conditions and experimental measurements.

HetaSimulator exports three main functions: **sim**, **mc** and **fit**.

The usage of the functions is illustrated by a small pharmacokinetic model with 3 state variables A0, C1, C2 and events describing drug dosage regime.

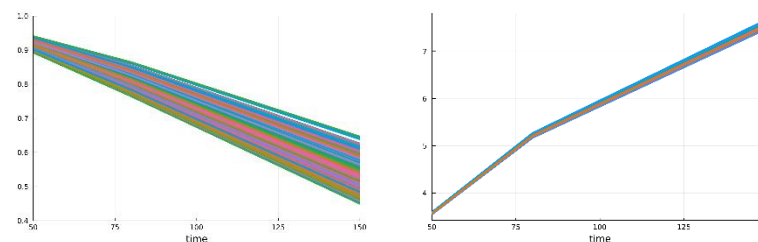
HetaSimulator.sim supports :

- single and multi-conditional simulations;
- configurable solver options with access to 300+ ODE solvers from DifferentialEquations.jl package [2];
- simulation arguments, including parameters' values, events setup, output variables, saving options, etc;



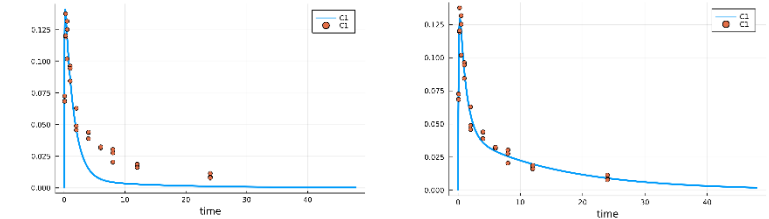
HetaSimulator.mc supports :

- parallel Monte-Carlo and Virtual Patients simulations;
- timeseries statistics generation;



HetaSimulator.fit supports :

- single and multi-conditional fitting;
- tabular input data format for experimental measurements;
- various measurement error distributions;



CONCLUSIONS

HetaProject is a single platform for models development and validation in the QSP field. It was released as an ecosystem of open-source software packages. It can be used as the modeling and simulation environment in QSP project of any size and complexity.

REFERENCES

- [1] E. Metelkin. "Heta compiler" is a framework for the development and management of Quantitative Systems Pharmacology modeling platforms. American Conference on Pharmacometrics 11, 2020
- [2] Rackauckas, C., Nie, Q. DifferentialEquations.jl – A Performant and Feature-Rich Ecosystem for Solving Differential Equations in Julia. Journal of open research software, 5, 2017

CONTACTS



HetaSimulator:

<https://github.com/hetalan/g/HetaSimulator.jl>



Video tutorial

<https://rb.gy/xgpkft>

dev@insysbio.com
<http://insysbio.com>

3 September 2021, PAGE, Virtual