"Heta compiler" is a framework for the development and management of Quantitative Systems Pharmacology modeling platforms

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MOTIVATION & OBJECTIVES

Today the pharmacology modeling is evolving towards complex mechanism-based dynamical modeling and involves a large amount of biological and clinical data.

There are some specific properties of a typical QSP project:

- include hundreds components, processes, cell types, and several drugs;
- team involves people with different expertise and background;
- simulation and data processing may require of different tools and formats;

The objective of the study is the development of the infrastructure and the workflow:

1. storing the QSP models and data in integrated infrastructure,
2. support incremental platform's updates,
3. support of models written in human-readable text and table-like formats,
4. export models and data to different popular formats on the fly.

HETA LANGUAGE

Heta is a human-readable modeling language for Quantitative Systems Pharmacology (QSP) and Systems Biology (SB).

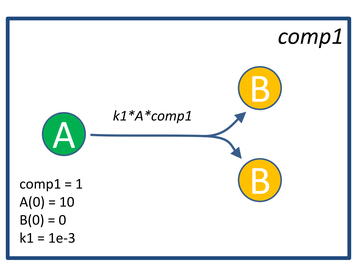
Heta language represents the dynamic model in a process-description format i.e. as interacting components that describe volumes, concentrations, amounts, rates, and others. The Heta code can be represented as ordinary differential equations (ODEs) which are generated "on the fly".

Features:

- Human-readable/writable code can be used for model creation, modification, or integration.
- Easy code parsing and transformation for potential implementation into different tools and frameworks.
- Modularity: QSP platform can be subdivided into several files and spaces for better project management.
- Reusability: modeling platforms should be easily extended for other projects.
- Reach annotation capabilities for better code revision and reporting.
- Simple transformation to popular modeling formats: Matlab, R, Simbiology, DBSolve, SBML, etc.

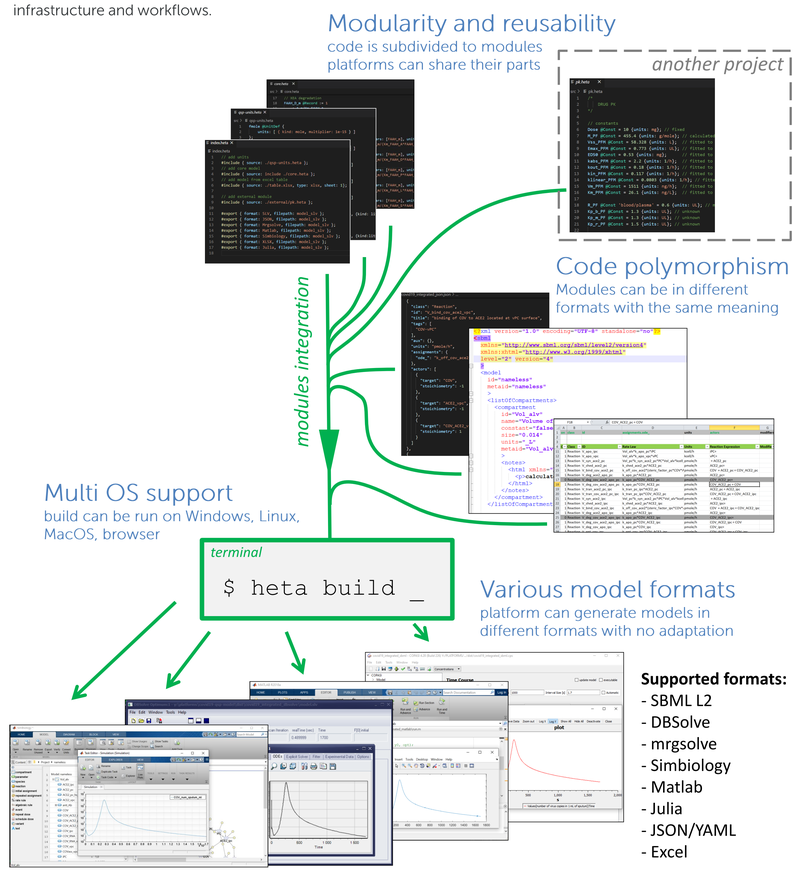
HETA CODE EXAMPLE

```
/*
  Hello World!
*/
comp1 @Compartment .= 1;
A @Species { compartment: comp1 };
B @Species { compartment: comp1 };
r1 @Reaction { actors: A => 2B };

// math
A .= 10;
B .= 0;
r1 := k1*A*comp1;

k1 @Const = 1e-3;

#export { format: SBML, filepath: sbml };
#export { format: Mrgsolve, filepath: mrgsolve };
```



HETA COMPILER & BENEFITS

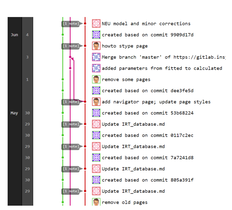
Heta compiler is a supporting tool for the development of QSP modeling platforms. It integrates different code formats into modeling platform and produces runnable simulation code. It can be used as a framework for modeling projects of any size and complexity. It is flexible and can be easily integrated the existing infrastructure and workflows.



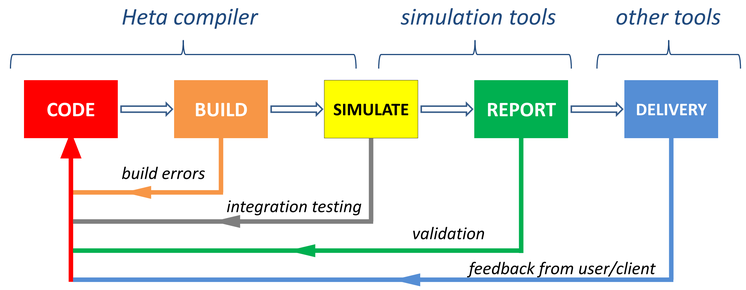
INTEGRATION WITH VERSION CONTROL

The Heta-based infrastructure is friendly for version control systems like Git and SVN. Usage of version control system add benefits to the Heta workflow:

- Storing of a platform history and results with important steps.
- Controllable and manageable code sharing with the remote synchronization.
- Working tasks distribution and delegation.
- Usage of automatization facilities (CI/CD) like GitHub actions, GitLab runner, etc.
- Delivery of results to users/clients.



WORKFLOW FOR QSP PLATFORMS



Continuous development

IMPLEMENTATION

Open source QSP platforms (shared on GitHub)

- heta-case-mini: A demo example of QSP platform developed with Heta and qs3p-js.
- FAAH inhibitor model: A platform describing Fatty Acid Amide Hydrolase inhibition in human.
- COVID-19 QSP model: A model describing SARS-CoV-2 virus and host cell life cycles

QSP projects for the development of middle-scale and large-scale models:

- Alzheimer-consortium QSP platform
- A set of InSysBio projects with more than 1000 components each.

Web applications

- Immune Response Template A Quantitative Systems Pharmacology (QSP) platform of immune system and tool for development of QSP and mechanistic models related to immune response.
- mAb-app PK/RO simulator for anti-PD-1 monoclonal Antibodies (Shiny app)

REFERENCES & CONTACTS

Heta project homepage:
https://hetalang.github.io

Video tutorial
https://rb.gy/xgpkft

GitHub repository
hetalang/heta-compiler

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http://insysbio.com

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