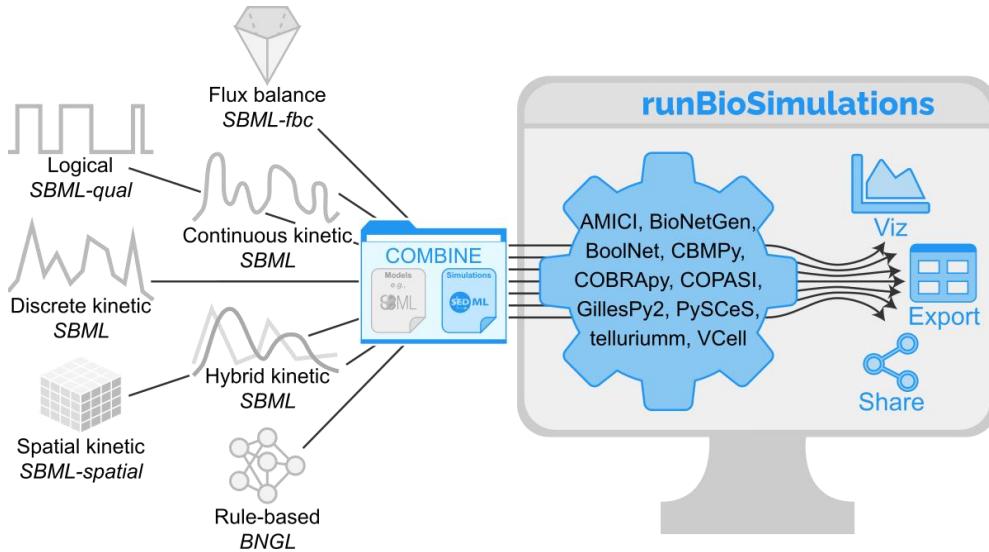


BioSimulations: HDF5/HSDS-powered platform for biosimulation



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Conflicts of interest

Formic Labs

“OS” for life science R&D

Actively recruiting

formiclabs.io

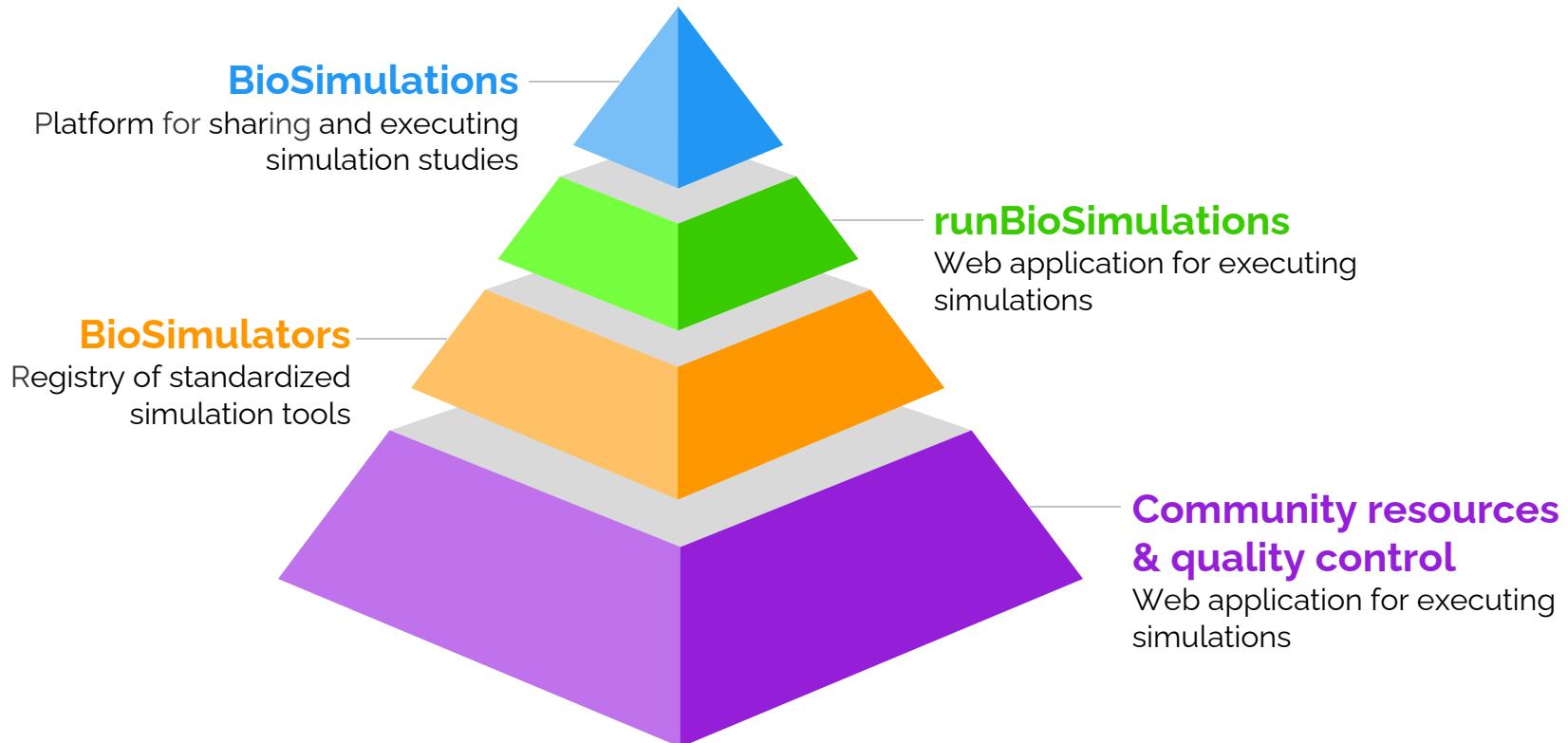
Motivation

- Precision medicine and bioengineering need **more comprehensive and more predictive models**
- Such models need to **integrate multiple modeling methodologies** across scales
- **Collaboration** is needed to achieve better models

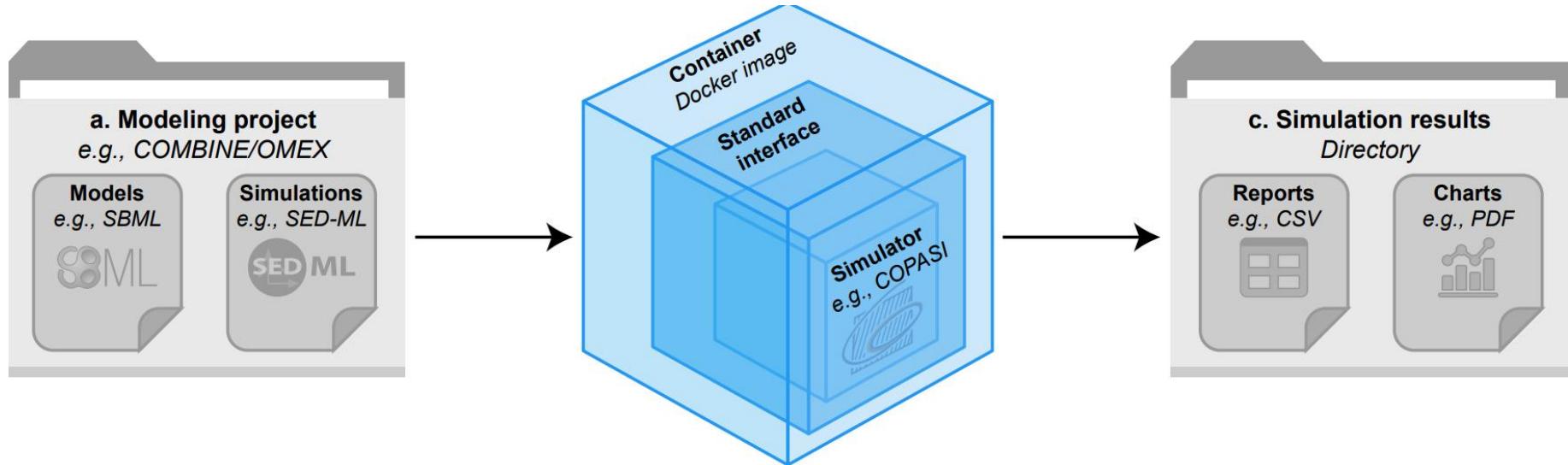
Goals

- Make it easier to **share, discover, and understand** modeling studies
 - Models
 - Simulation experiments and results
 - Data visualizations of results
- Make it easier to **reproduce and reuse** simulations
 - Find capable simulation tools
 - Edit model and simulation parameters
 - Re-paint figures with alternative simulation results
- Support a **broad range of modeling** across methods, biology, and scales

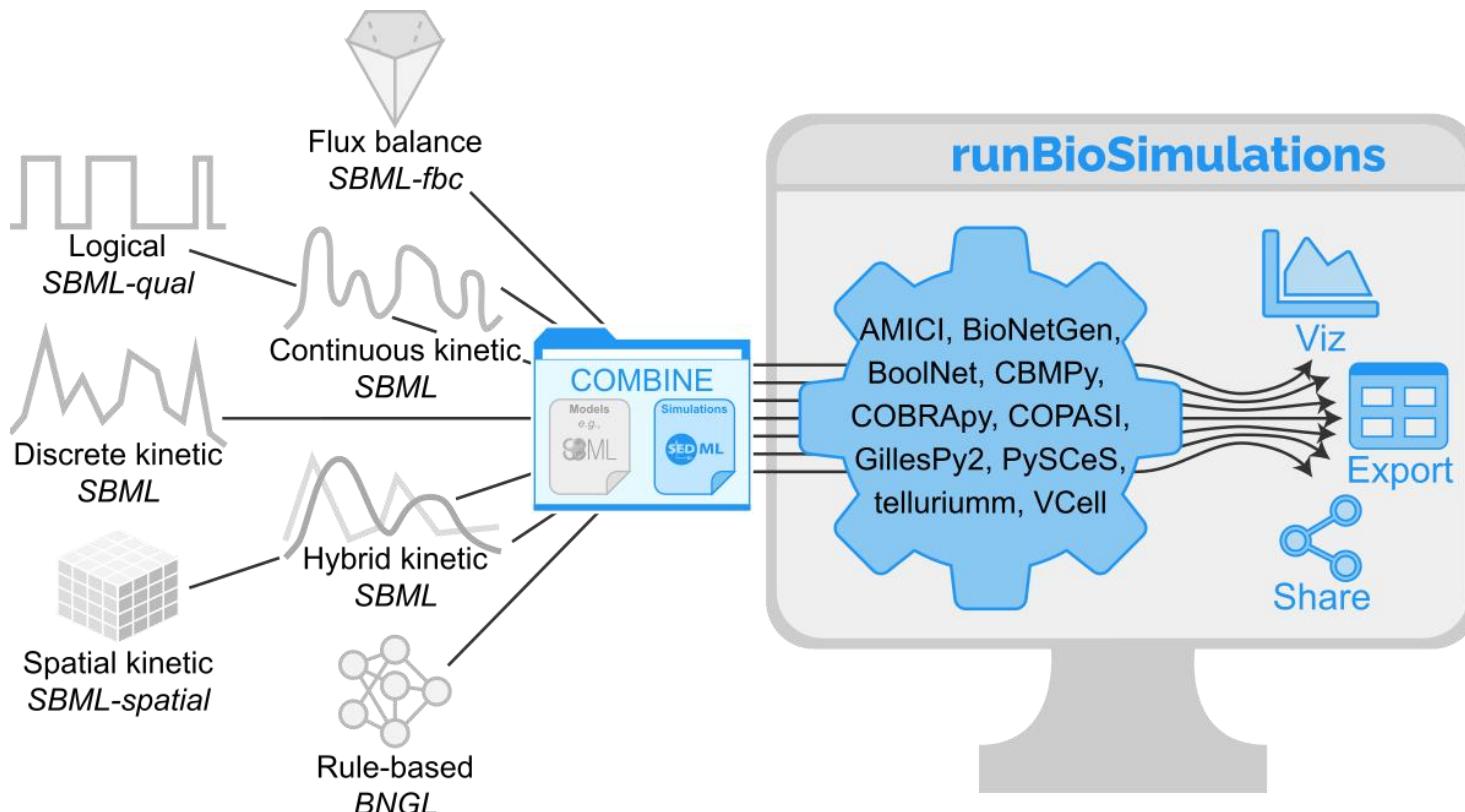
BioSimulations toolkit



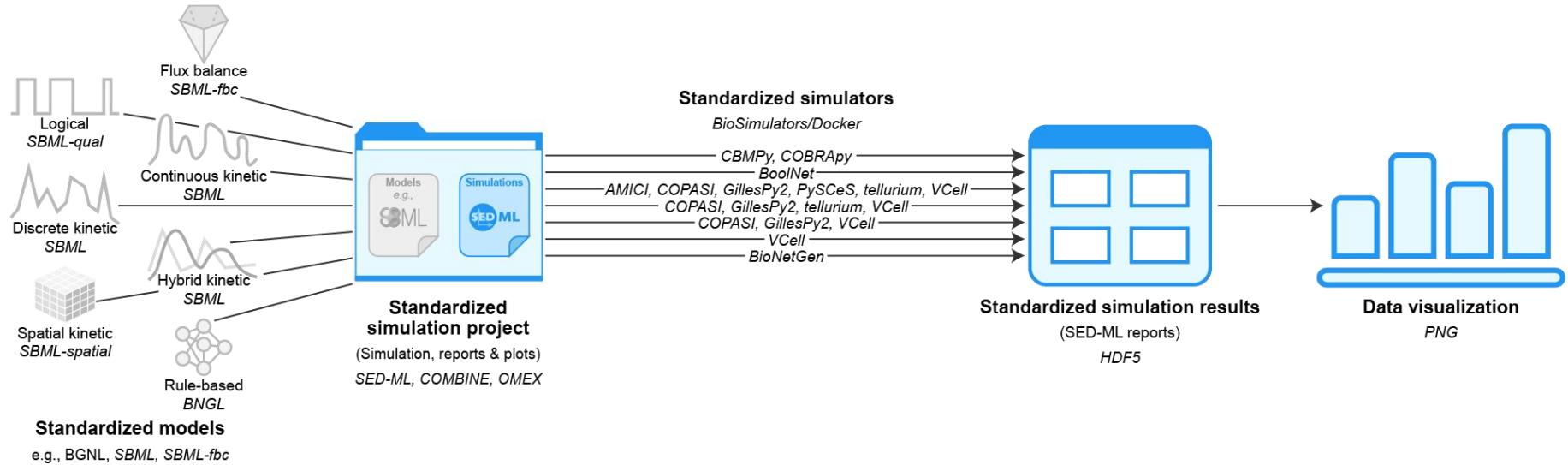
Foundation: common formats and ontologies



Toolkit



Standardized interfaces to simulation tools



Standardized interfaces to simulation tools

```
bionetgen -i study.omex -o results/  
copasi -i study.omex -o results/  
gillespy2 -i study.omex -o results/  
tellurium -i study.omex -o results/  
vcell -i study.omex -o results/
```

HDF5 schema for simulation results

Domain information

COMBINE archive

≥1 SED-ML files

≥ 1 Reports

≥ 1 Data sets

Meta data

Unique id

(Unique) label

Data type

Shape

HDF5

HDF5 file

Group

Data set

Row

Attributes

dataSetIds

dataSetLabels

dataSetDataTypes

dataSetShapes

BioSimulators: registry of simulation tools

The screenshot shows the BioSimulators registry interface. At the top, there's a navigation bar with the BioSimulators logo, a search bar, and links for "Simulators", "Simulator standards", and "Help". Below the navigation bar is a breadcrumb trail: "Home > Simulators". The main area is titled "Simulators" and contains a table of simulation tools. On the left, there's a sidebar with "Controls" (including "Columns", "Filters", and "Search") and a "Filters" dropdown. The table has columns for Name, Frameworks, Algorithms, Model formats, Curation, Run, and Docs. The data in the table is as follows:

Name	Frameworks	Algorithms	Model formats	Curation	Run	Docs
AMICI	non-spatial continuous	CVODES, IDA	SBML	★★★★★	⚙️	📘
BioNetGen	non-spatial continuous, non-spatial discrete	CVODE, Gillespie direct algorithm, NFSim agent-based simulation...	BNGL	★★★★★	⚙️	📘
BioUML	flux balance, non-spatial continuous, non-spatial discrete	Dormand-Prince method, Euler forward method, flux balance...	SBML	★★★★★		📘
BoolNet	boolean logical	asynchronous logical model simulation method, probabilistic...	SBML	★★★★★	⚙️	📘
CBMPy	flux balance	flux balance analysis, flux variability analysis, parsimonious enzyme...	SBML	★★★★★	⚙️	📘
CellNetAnalyzer	boolean logical, flux balance	asynchronous logical model simulation method, flux balance...	SBML	★★★★★		📘
COBRA Toolbox	flux balance	ACB flux sampling method, ACHR flux sampling method...	SBML	★★★★★		📘
COBRAPy	flux balance	flux balance analysis, flux variability analysis, geometric flux balance...	SBML	★★★★★	⚙️	📘
COMplex Pathway Simulator	non-spatial continuous, non-spatial discrete	adaptive explicit-implicit tau-leaping method, automatically use...	SBML	★★★★★	⚙️	📘
E-Cell 4	non-spatial discrete, spatial discrete	Elf and Ehrenberg method, enhanced Greens function reaction...	SBML	★★★★★		📘
Escher-FBA	flux balance	flux balance analysis	SBML	★★★★★		📘

BioSimulators: registry of simulation tools

The screenshot shows the BioSimulators registry interface. At the top, there's a navigation bar with links for "Simulators", "Simulator standards", and "Help". Below the navigation bar, the URL "Home > Simulators > tellurium" is visible. The main content area has tabs for "Overview", "Algorithms" (which is selected), "Versions", "Specifications (JSON)", and "Validation test results".

Algorithms section:

- CVODE
- explicit fourth-order Runge-Kutta method
- Fehlberg method
- Gillespie direct algorithm
- Newton-type method

CVODE (KISAO_0000019) detail view:

Description: The CVODE is a package written in C that solves ODE initial value problems, in real N-space, written as $y' = f(t,y)$, $y(t_0) = y_0$. It is capable for stiff and non-stiff systems and uses two different linear multi-step methods, namely the Adam-Moulton method and the backward differentiation formula.

Modeling frameworks: non-spatial continuous framework

Model formats: SBML L3v2: Information about which features this algorithm supports is not available.

Simulation formats: SED-ML L1v3: Information about which features this algorithm supports is not available.

Archive formats: COMBINE OMEX 1: Information about which features this algorithm supports is not available.

Parameters table:

Name	Type	Default	Recommended range	Availability	KISAO id
absolute tolerance	float	1e-12		BioSimulators Docker..	KISAO_0000211
ER-leap initial leap	float			BioSimulators Docker..	KISAO_0000332
maximum Adams order	integer	12		BioSimulators Docker..	KISAO_0000219
maximum BDF order	integer	5		BioSimulators Docker..	KISAO_0000220
maximum number of steps	integer	2e4		BioSimulators Docker..	KISAO_0000415
maximum step size	float			BioSimulators Docker..	KISAO_0000467
minimum step size	float			BioSimulators Docker..	KISAO_0000485
progression with adaptive time step	boolean	false		BioSimulators Docker..	KISAO_0000107
relative tolerance	float	1e-6		BioSimulators Docker..	KISAO_0000209

Dependent dimensions: time instant (SIO_000418)

Dependent variables table:

Description	Target pattern
parameter values	/sbml:sbml/sbml:model:sbml:listOfParameters:sbml:parameter/@value
species concentrations	/sbml:sbml/sbml:model:sbml:listOfSpecies:sbml:species

Standardized fetching of simulation tools

```
docker pull ghcr.io/biosimulators/copasi
docker pull ghcr.io/biosimulators/copasi:latest
docker pull ghcr.io/biosimulators/copasi:4.29.228
```

Registered simulation methods and tools

Simulator	Ref.	Modeling framework								Modeling format			Other formats						
		Logical	Flux balance	Kinetic, DAE	Kinetic, ODE/PDE	Kinetic, SDE	Kinetic, discrete	Kinetic, hybrid	Kinetic, spatial	Kinetic, steady-state	BNGL (1)	SBML (2)	SBML-fbc(4)	SBML-qual(5)	SBML-spatial	SBML-comp(3)	SBML-dFBA (6)	SED-ML (10)	HDF5(11)
AMICI	13				✓						✓						✓	✓	✓
BioNetGen	14, 15			✓		✓											✓	✓	✓
BoolNet	16	✓									✓	✓					✓	✓	✓
CBMPy	17		✓										✓				✓	✓	✓
COBRApy	18		✓										✓				✓	✓	✓
COPASI	19			✓	✓	✓	✓					✓				✓	✓	✓	✓
GillesPy2	20			✓		✓		✓				✓				✓	✓	✓	✓
iBioSim	21			✓		✓						✓				✓	✓	✓	✓
PySCeS	22			✓								✓				✓	✓	✓	✓
tellurium	23			✓		✓		✓		✓		✓				✓	✓	✓	✓
VCell	15, 24		✓	✓		✓	✓	✓	✓		✓	✓			✓		✓	✓	✓

runBioSimulations: web app for running simulations

The screenshot shows the 'Run a simulation project' page of the runBioSimulations web application. At the top, there is a navigation bar with the runBioSimulations logo, a menu icon, and links for 'Run a simulation', 'Your simulations', and 'Help'. Below the navigation bar, the URL 'Home > Run' is visible.

The main form has several input fields:

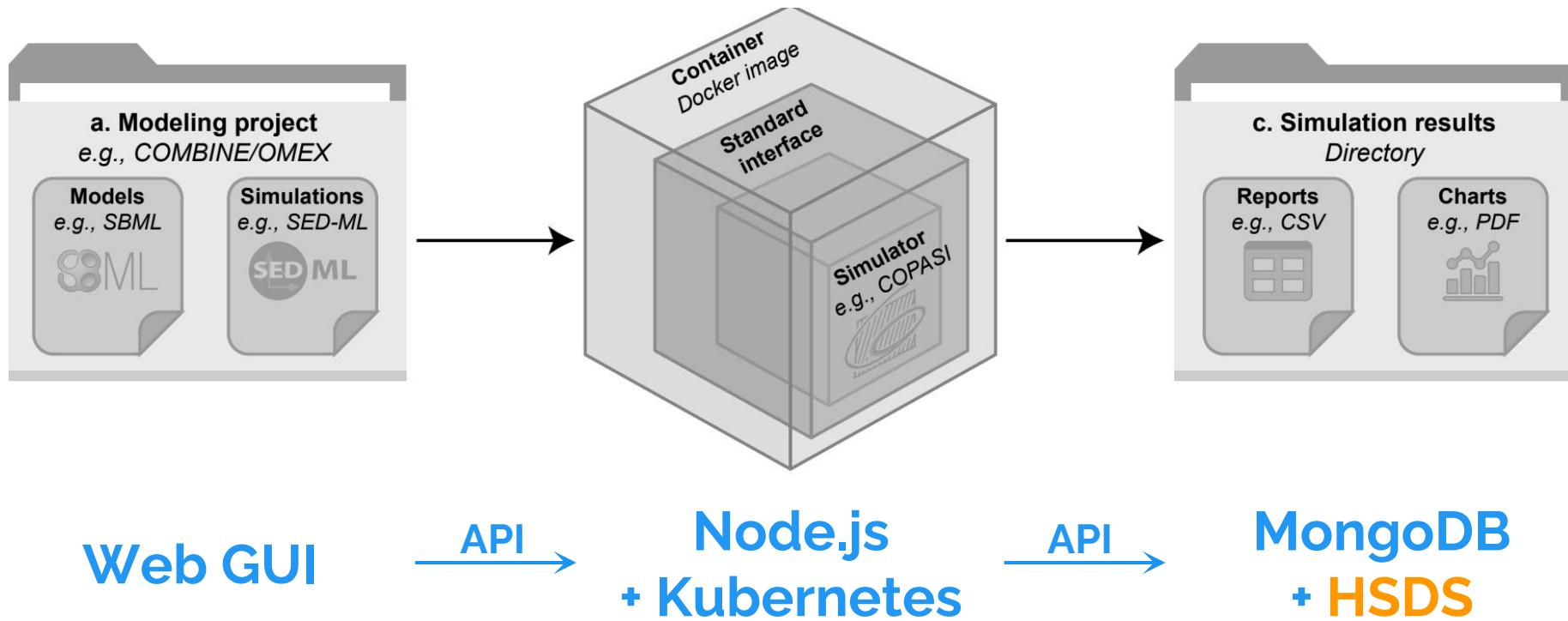
- Select a method for providing a simulation project (COMBINE/OMEX file) ***:
This field includes a dropdown menu with options like 'Select a local file' and 'Upload a local file'. A note below says: 'Select a method for providing a COMBINE/OMEX archive. COMBINE/OMEX files can either be uploaded for your local computer or loaded from a publicly-accessible URL.'
- Select a simulation project (COMBINE/OMEX file) ***:
This field shows a file selection dialog with the placeholder 'Select a simulation project (COMBINE/OMEX file) *'. Below it, notes say: 'Select a COMBINE/OMEX archive file which describes one or more simulations (e.g., in SED-ML format) of one or more models (e.g., in BNGL, SBML, formats). An example archive which can be executed by VCell is available here. Additional examples are available in the BioSimulators test suite. More information about COMBINE/OMEX archives is available at <https://combinarchive.org>'.
- Select a simulation tool ***:
This field shows a dropdown menu with the placeholder 'Select a simulation tool *'. Below it, notes say: 'Select a simulation tool which is capable of executing your archive. This tool must support all of the modeling frameworks (e.g., logical, FBA, kinetic), simulation algorithms (e.g., ODE, SSA), and model formats (e.g., BNGL, SED-ML) involved in your archive. Note: because each tool supports a different set of frameworks, algorithms, and formats, your archive is likely only compatible with a subset of the available simulation tools. The README for the BioSimulators test suite outlines the simulator compatibility of several of the example archives in the test suite. BioSimulators describes the modeling frameworks (e.g., logical, FBA, kinetic), simulation algorithms (e.g., ODE, SSA), and modeling formats (e.g., COMBINE/OMEX, SBML, SED-ML) that each simulation tool supports. We recommend using BioSimulators to determine which tools are capable of executing your archive.'
- Select a version of the simulation tool**:
This field shows a dropdown menu with the placeholder 'Select a version of the simulation tool'. Below it, notes say: 'See BioSimulators for information about each version of each simulation tool.'
- Enter a descriptive name to help you recall this project ***:
This field shows an input field with a placeholder 'Enter a descriptive name to help you recall this project *'. Below it, notes say: 'Provide a name for your modeling project. If you execute multiple projects, this name will help you identify this project among all of your projects.'
- Enter your email address**:
This field shows an input field with a placeholder 'Enter your email address'. Below it, notes say: 'Optionally, enter your email address to receive notification of the completion of your simulation. After submitting your simulation, you will also receive a URL where you will be able to check the status of your simulation and retrieve its results.'

runBioSimulations: web app for running simulations

The screenshot shows the 'Your simulations' page of the runBioSimulations web application. At the top, there's a navigation bar with the runBioSimulations logo, a 'Run a simulation' button, a 'Your simulations' link, and a 'Help' link. Below the navigation is a breadcrumb trail: 'Home > Your simulations'. The main area is titled 'Your simulations' and includes a sub-instruction: 'Click here to try a set of example simulations'. On the left, there's a sidebar with 'Controls' for filtering simulations based on 'Name', 'Simulator' (with options like amici 0.11.11, bionetgen 2.5.2, booleNet 2.1.5, cbmpy 0.725, cobrapy 0.20.0, copasi 4.30.233, gillespy2 1.57, pycses 0.9.9, tellurium 2.2.0, vcell 7.3.0.06), 'Status' (Submitted, Last updated, Submitted locally), and a search bar.

Id	Name	Status	Submitted	Viz	Export	Log	Share	Trash
6042a5fd39e3d05bagb658...	BioNetGen example...	succeeded	2021-03-05 16:43:25					
603d35ff5d7123009gedd13...	bmtest	succeeded	2021-03-01 13:44:15					
6037ee386e279f70b395461c...	Caravagna 2010: tumor-...	succeeded	2021-02-25 13:36:38					
6037ee376e279f603595461e...	Caravagna 2010: tumor-...	succeeded	2021-02-25 13:36:39					
6037ee376e279f600995462...	Caravagna 2010: tumor-...	succeeded	2021-02-25 13:36:39					
6037ee386e279f4436954622...	Chauviya et al. BMC...	succeeded	2021-02-25 13:36:40					
6037ee386e279fb0395462...	Ciliberto 2003...	succeeded	2021-02-25 13:36:40					
6037ee396e279fdd6f54626...	Ciliberto 2003...	succeeded	2021-02-25 13:36:41					
6037ee396e279ff548954628...	Ciliberto 2003...	succeeded	2021-02-25 13:36:41					
6037ee3c6e279foc4795462e...	Escherichia coli core...	succeeded	2021-02-25 13:36:44					
6042aabe39e3d0366bb658...	Escherichia coli core...	succeeded	2021-03-05 16:38:06					
6037ee3c6e279f5d7d95463...	Escherichia coli core...	succeeded	2021-02-25 13:36:44					
6042aa4939e3d0505cb658...	Escherichia coli core...	succeeded	2021-03-05 16:37:45					
6037ee3d6e279f856695463...	Parmar 2017: iron...	succeeded	2021-02-25 13:36:45					
6037ee3a6e279f571295462...	Parmar 2017: iron...	succeeded	2021-02-25 13:36:42					
6037ee3d6e279f39ab95463...	Parmar 2017: iron...	succeeded	2021-02-25 13:36:45					
6037ee3e6e279f32f8954636...	Parmar 2017: iron...	succeeded	2021-02-25 13:36:46					
6037ee3e6e279f3acce954638...	Szymanska 2009: HSP...	succeeded	2021-02-25 13:36:46					
6037ee406e279f2a8b95464...	Tomida 2003: NFAT...	succeeded	2021-02-25 13:36:48					
6037ee406e279f70b395464...	Varusai 2018: mTOR...	succeeded	2021-02-25 13:36:48					
6037ee416e279fc246954646...	Vilar 2002: circadian...	succeeded	2021-02-25 13:36:49					

HSDS database for simulation results



BioSimulations: platform for sharing simulations

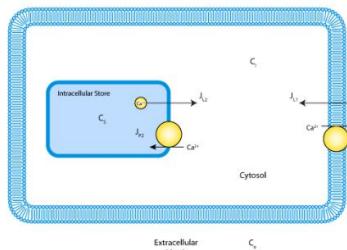


Simulation projects Utilities Conventions Help

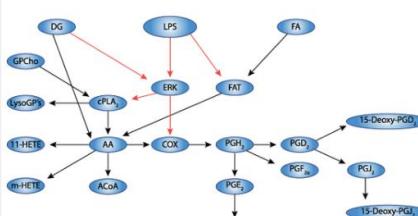
Home » Simulation projects » Browse

Search & filter

iCa₂₊ oscillations in sympathetic neurons: an experimental test of a theoretical model



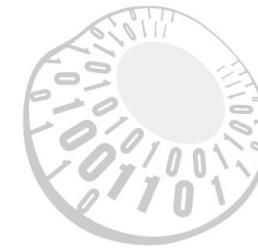
3fd



A oD model of the Heart



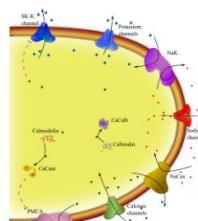
A computational model of a small DRG neuron to explore pain (Verma et al. 2019, 2020)



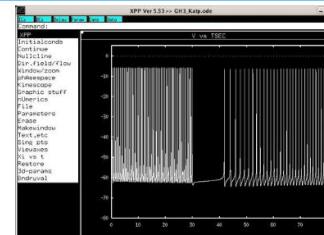
A mathematical model of evoked calcium dynamics in astrocytes (Handy et al 2017)



A model for pacemaking in substantia nigra neurons (A simple model based on a spherical...



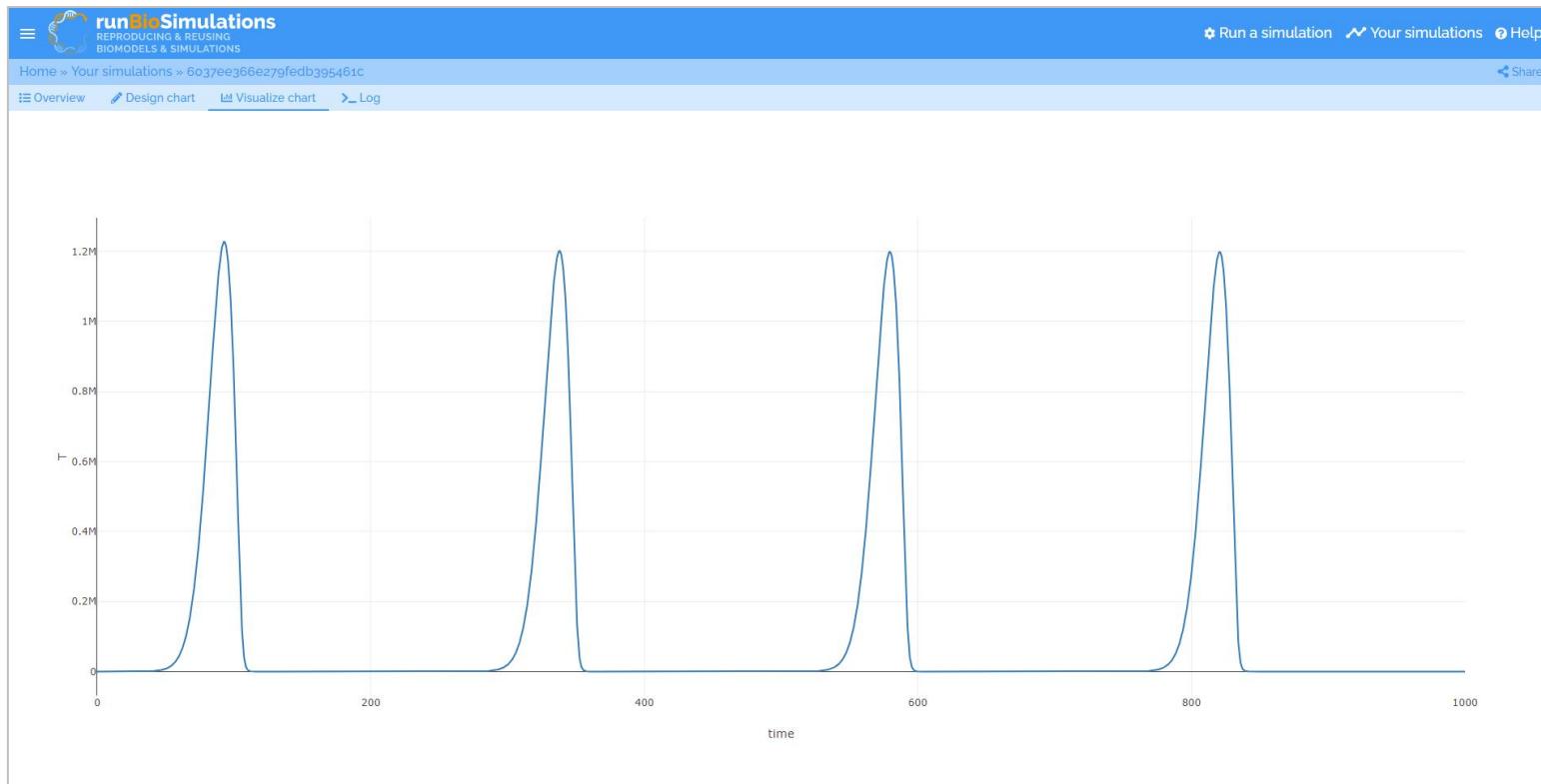
A model for pituitary GH(3) lactotroph (Wu and Chang 2005)



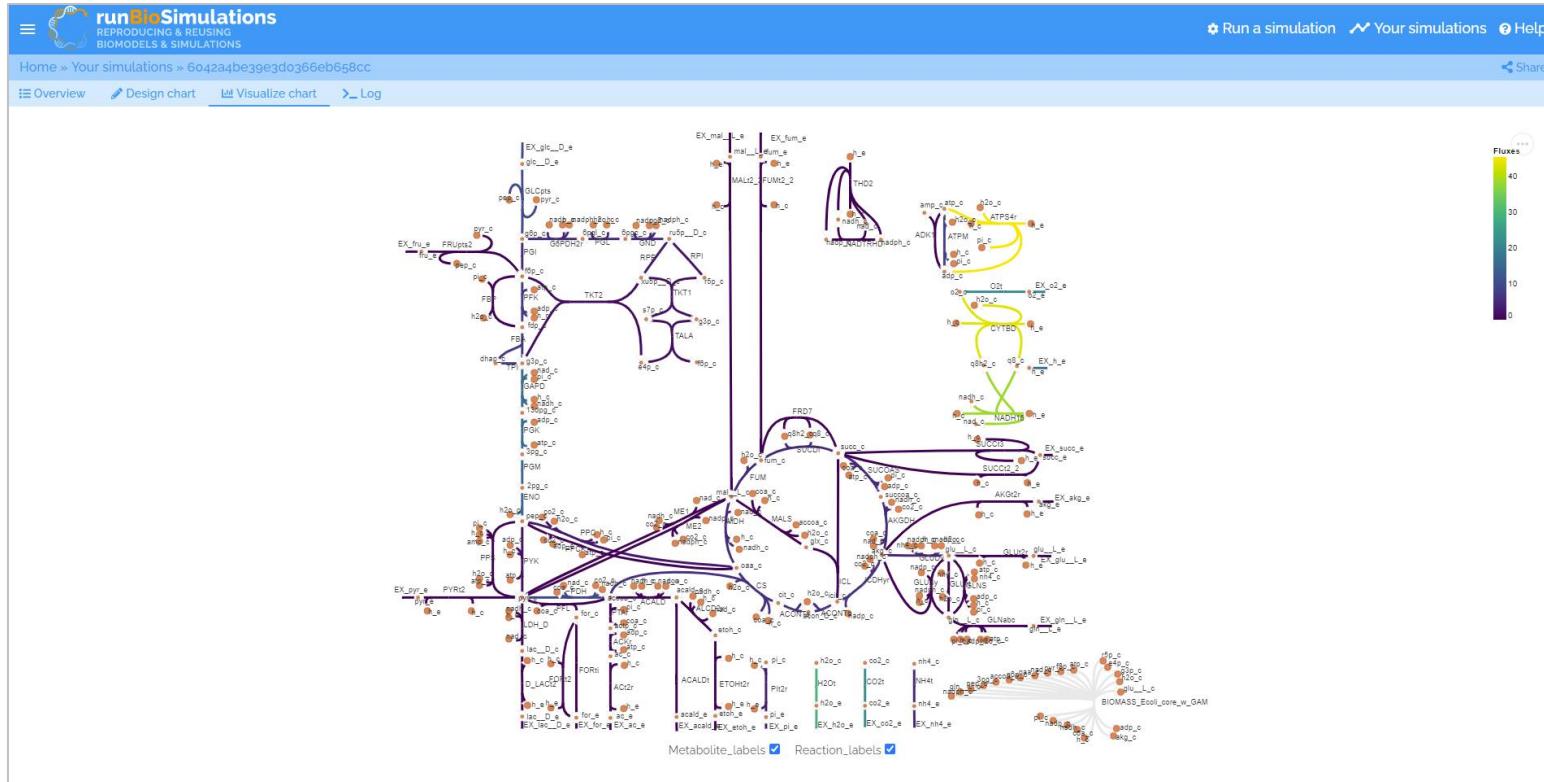
A model of intracellular pH control



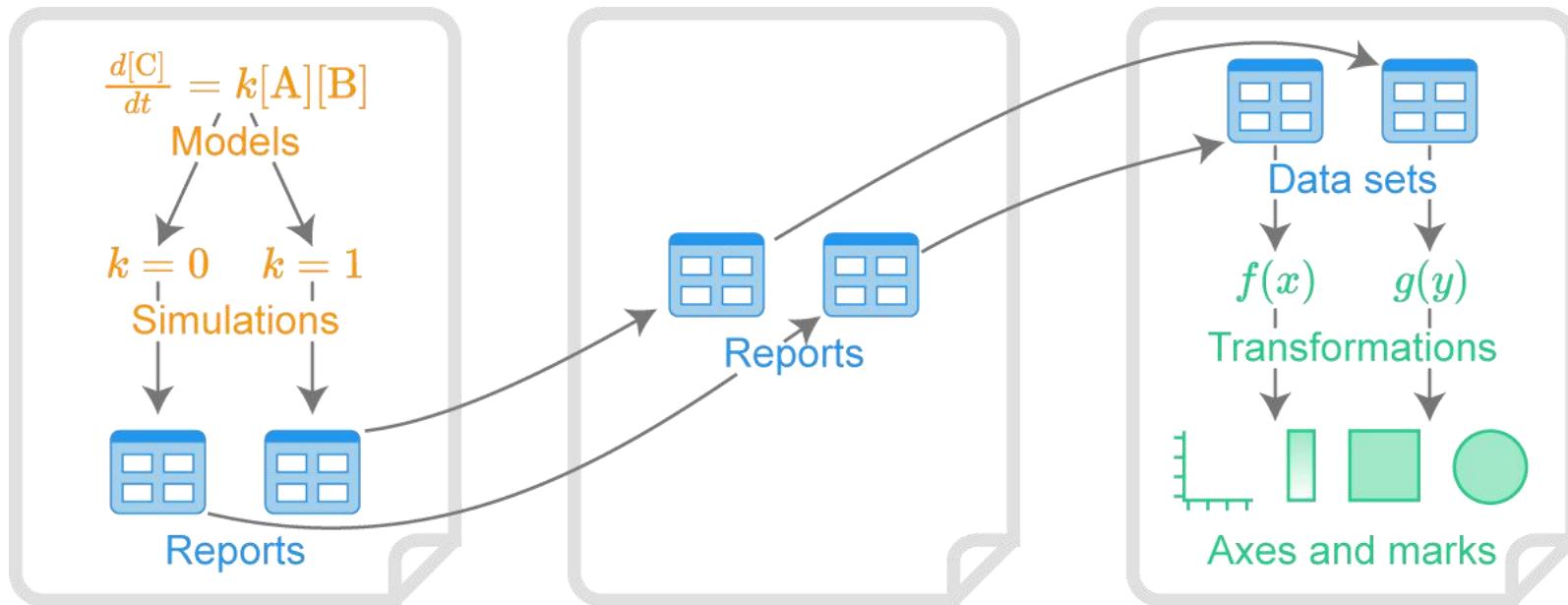
Data visualizations combine HS DS with Vega



Data visualizations combine HSDS with Vega



Visualizations: Vega



Simulation expts.

SED-ML

Simulation results

HDF5

Visual diagrams

Vega

Availability

BioSimulations

<https://biosimulations.org>

runBioSimulations

<https://run.biosimulations.org>

BioSimulators

<https://biosimulators.org>

Acknowledgements

Core team

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COPASI: Frank Bergmann, Stefan Hoops, Pedro Mendes

EDAM: Jon Ison, Matúš Kalaš

GillesPy2: Brian Drawert, Linda Petzold

iBioSim: Chris Myers, Payton Thomas

jNeuroML, PyNeuroML: Padraig Gleeson

KiSAO: Anna Zhukova

OpenCOR: Alan Garny

PySCeS: Brett Olivier, Johan Rohwer

SED-ML: Mattias König, David Nickerson, Lucian Smith

SIO: Michel Dumontier

tellurium: Kiri Choi, Kyle Medley, Herbert Sauro

VCell: Dan Vasilescu