

# Mathematical Modeling for Cell Biology

CellBio 24 workshop

Sunday, December 15<sup>th</sup>

In order of appearance: Stefan Hoops, Leslie Loew, Michael Blinov, Ann Cowan

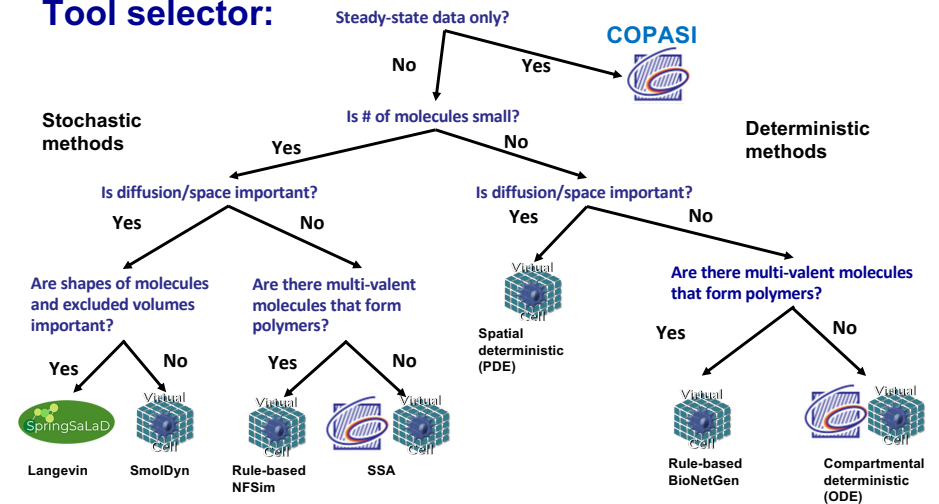
Introduce kinetic simulations, steady state analysis, parameter estimation, spatial modeling, rule-based models, demonstrating them using two modeling and simulation tools:

COPASI (<http://copasi.org>) and Virtual Cell (<http://vcell.org>).

This handout is available at: <https://compcellbio.org/assets/ASCB2024.pdf>

See also: <https://compcellbio.org/>

## Tool selector:



## Capabilities of our modeling tools:

METHODS	COPASI	VCell
Compartmental deterministic modeling (ODE)	✓	✓
Stochastic compartmental modeling (SSA)	✓	✓
Spatial deterministic modeling (PDE)		✓
Steady-state modeling	✓	
Stochastic differential equations (SDE)	✓	
Parameter fitting	✓	✓ (COPASI)
Compartmental rule-based modeling of multi-component molecules		✓ (BioNetGen)
Compartmental agent-based modeling of multi-component molecules		✓ (NFSim)
Spatial stochastic modeling		✓ (SmolDyn)
Spatial stochastic modeling accounting for volumes		✓ (SpringSalad)

## Example models for today's workshop

1. **Steady-State, Time Course, and Parameter Fitting with COPASI** ([Negative feedback and ultrasensitivity can bring about oscillations in the mitogen-activated protein kinase cascades](#)) - presented by Stefan Hoops ([Biomodels Database: BIOMD0000000010](#))
2. **Using PDEs to simulate FRAP of a biomolecular condensate** (Cowan and Loew, Biophys. J. 2023, [PUBMED: 37353932](#) - presented by Leslie Loew (<http://vcell.org/biomodel-255507058>))
3. **Using ImageJ to define initial concentration distribution in reaction-diffusion simulations** (Ding et al., 2020; Current Biology; [PUBMED:32155414](#)) - presented by Michael Blinov (<https://vcell.org/biomodel-169993006>)
4. **Rule-based modeling defining molecules and multi-molecular species** (Nosbisch et al., 2022, JBC; [PUBMED:35367415](#)) - presented by Michael Blinov (<https://vcell.org/biomodel-232498815>)

## Learning resources

This presentation: <https://compcellbio.org/assets/ASCB2024.pdf>

COPASI: <http://copasi.org>

<https://vcell.org/support>

Multiple Tutorials (including FRAP and Rule-based)  
Links to YouTube channel, CompCellBio lecture videos

Computational Cell Biology Courses

Online Feb 24-28, 2025 <https://compcellbio.org/ccbworkshop>  
In person CCB Workshop, Summer 2025.

## CompCellBio workshops

<https://compcellbio.org/ccbworkshop>



## COPASI Capabilities

- Time course (deterministic, stochastic, and hybrid algorithm)
- Steady state
- Stoichiometric analysis of the reaction network, including mass conservation analysis and elementary flux modes.
- Optimization of arbitrary components of the model using a range of diverse algorithms.
- Parameter estimation using a range of diverse optimization algorithms. This can be done over several different experiments simultaneously, including mixtures of steady-state and time course experiments.
- Local sensitivity analysis.
- Metabolic control analysis (a special form of sensitivity analysis).
- Time scale separation analysis; this allows definition of fast and slow components of the model, in a time-dependent way.
- Analysis of stochasticity using the linear noise approximation (allows estimating variances and co-variances even in the presence of large numbers of particles).
- Cross sections, which allow to characterize non-linear dynamics properties, such as oscillations and chaos.
- Lyapunov exponents, which allows to establish if the system dynamics are chaotic.