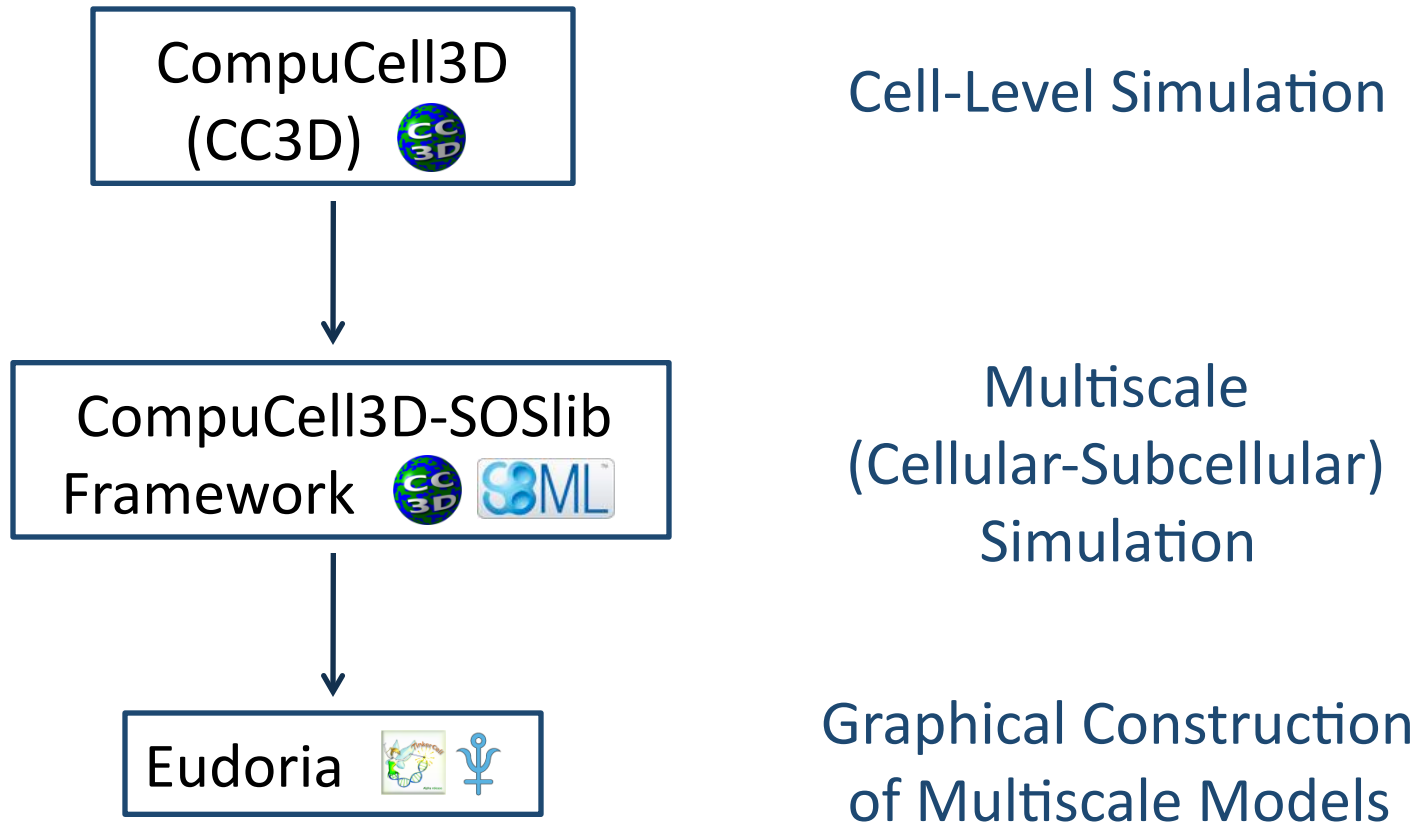# Multiscale Simulation Using CompuCell3D and the SBML ODE Solver Library

Ryan Roper
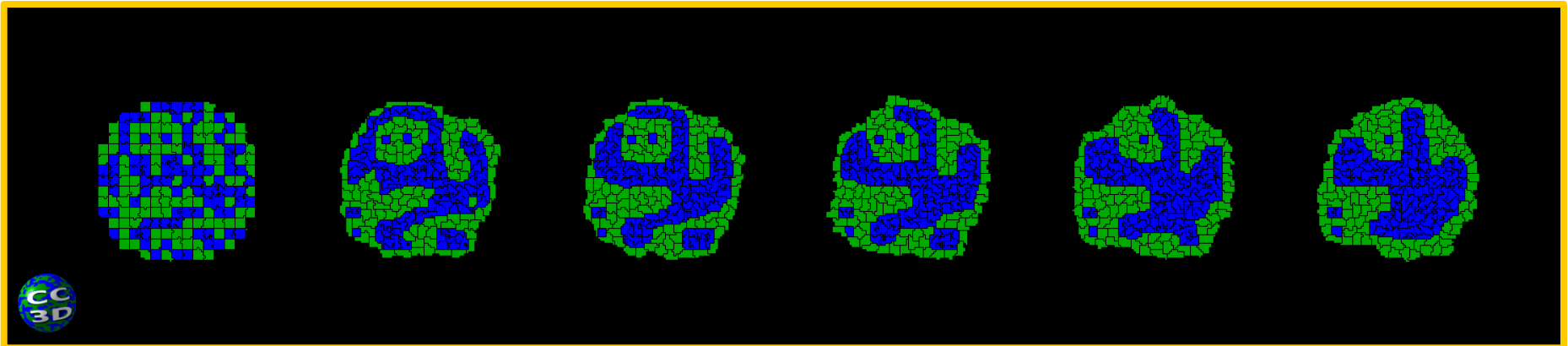University of Washington
Dept of Bioengineering

Sauro Lab

University of Washington

Dept of Bioengineering

Seattle, WA, USA

Glazier Lab

Biocomplexity Institute

Indiana University

Bloomington, IN, USA

Overview

CompuCell3D (CC3D)   Cell-Level Simulation

CompuCell3D-SOSlib Framework   Multiscale (Cellular-Subcellular) Simulation

Eudoria   Graphical Construction of Multiscale Models

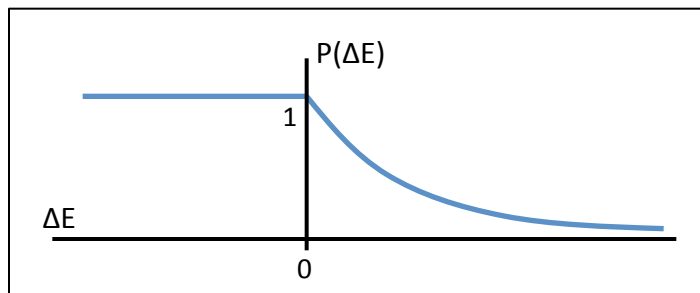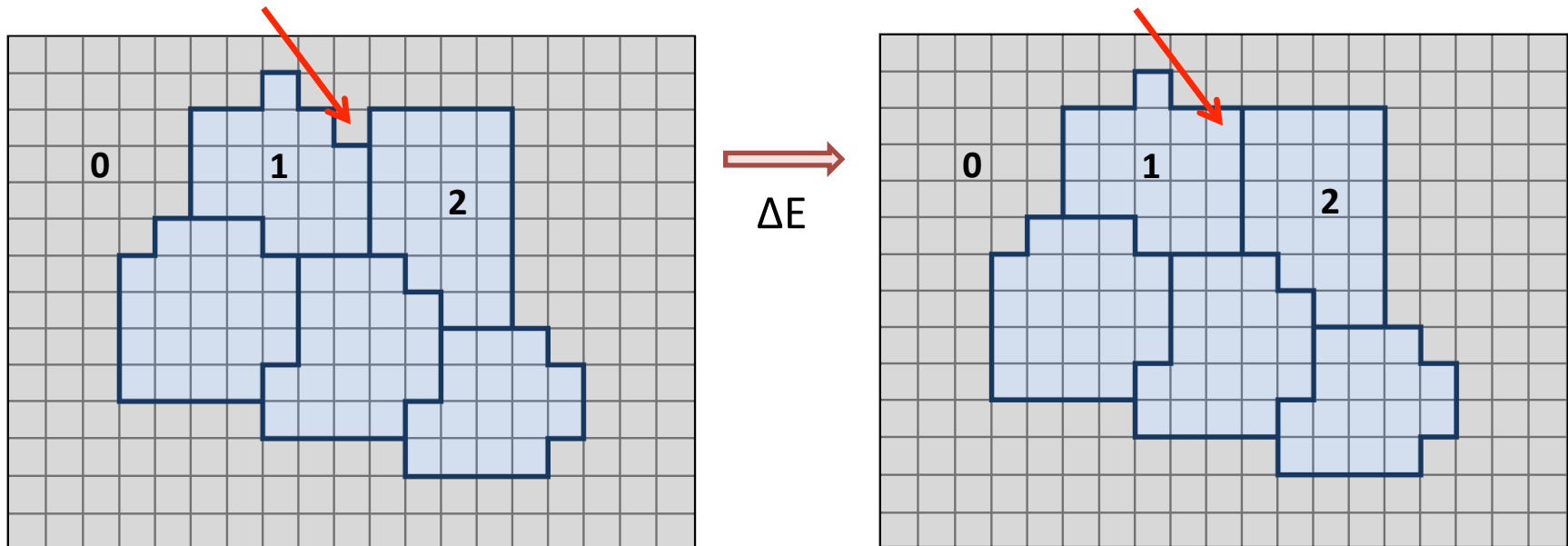# Cell Sorting Simulation using CC3D

CompuCell3D (CC3D)

- Implements Cellular Potts Model (CPM)
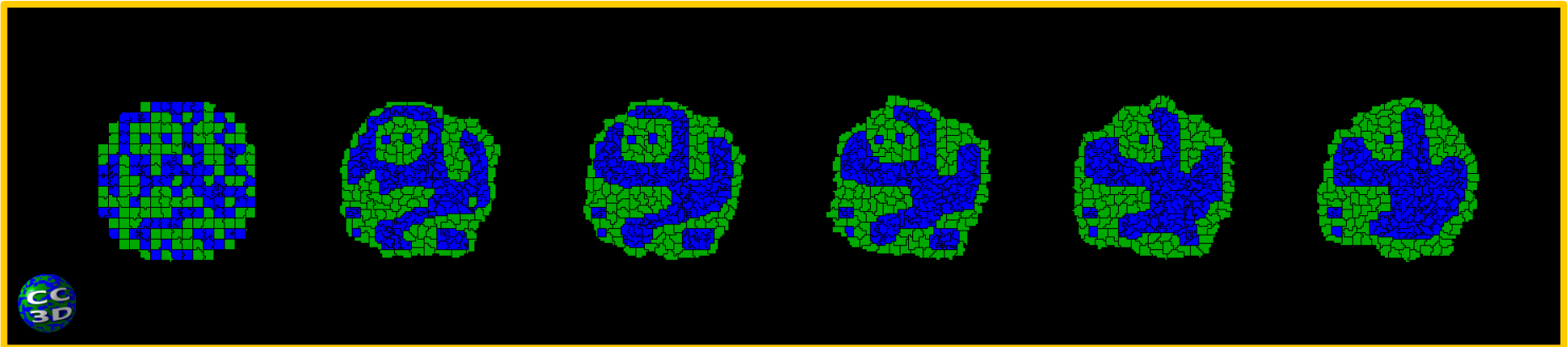- Evolves lattice by Monte Carlo Simulation

Lattice-Based Representation of Cells
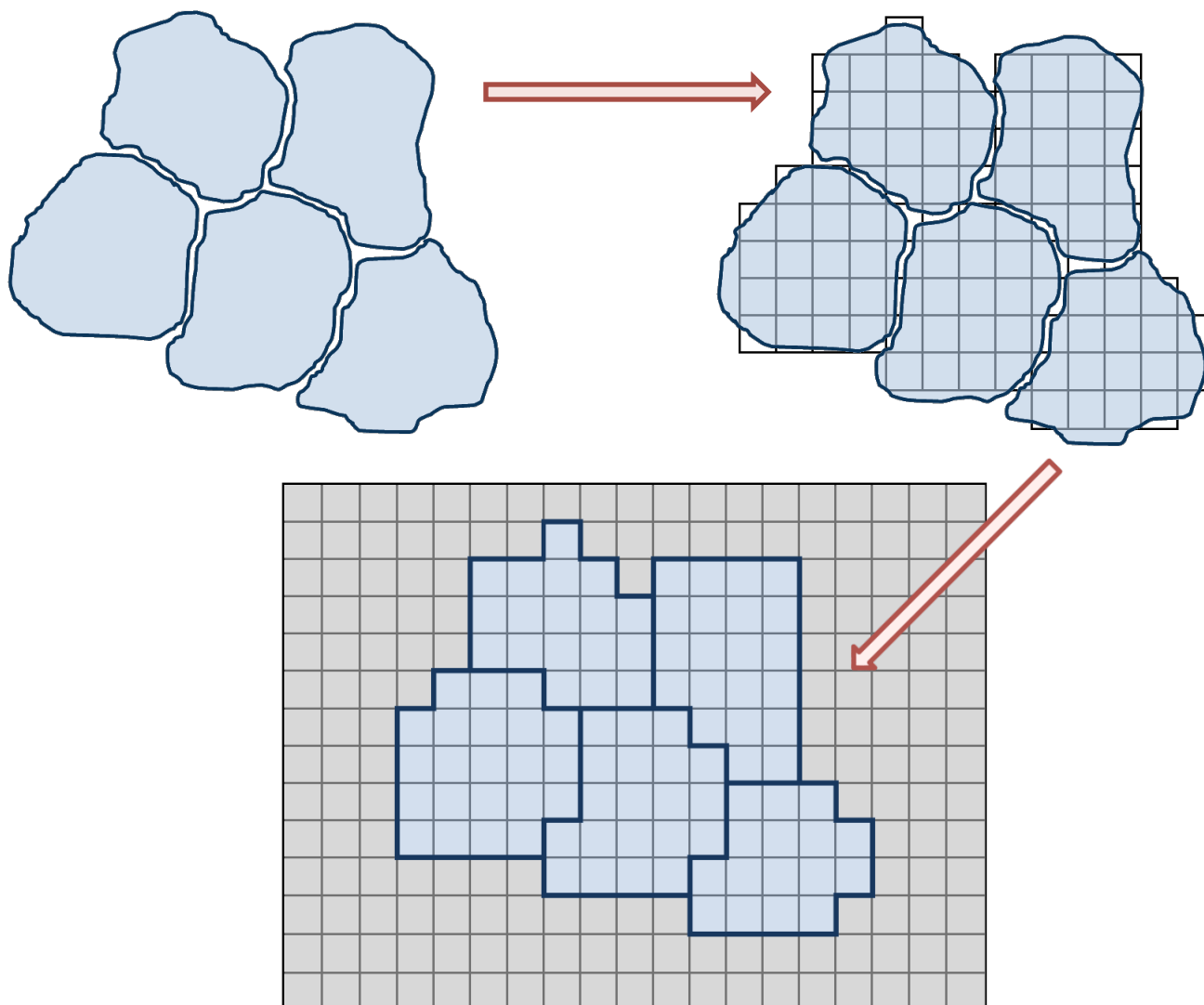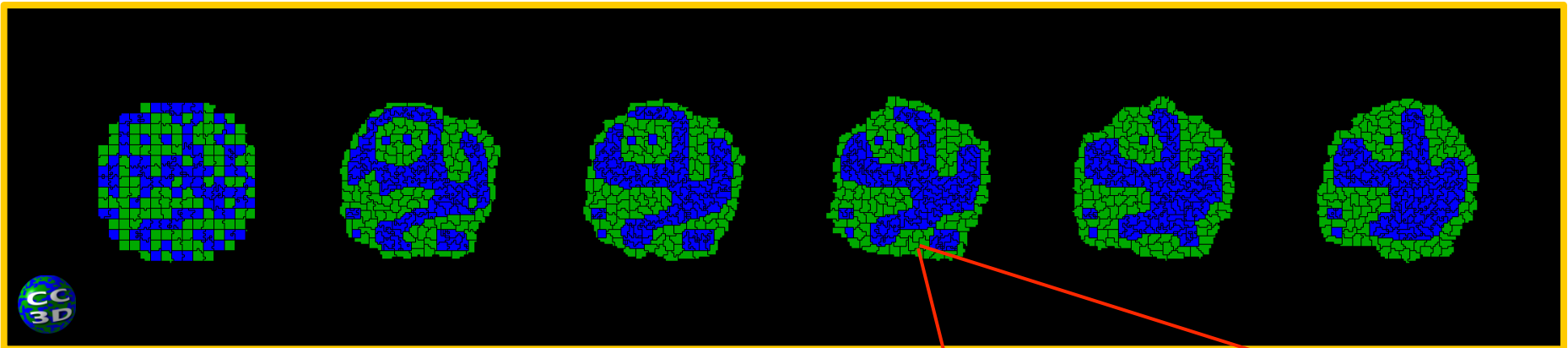
Energy Minimization

ΔE

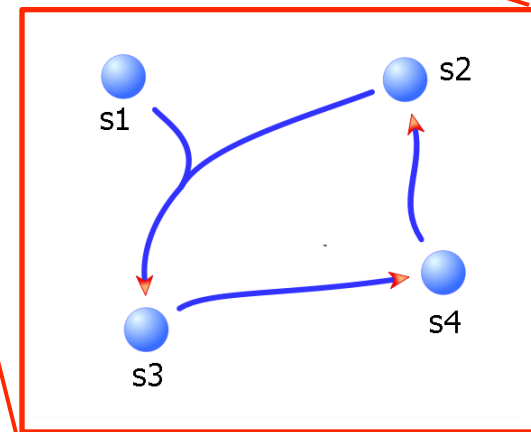# What is Modeled in Cell Sorting Simulation?

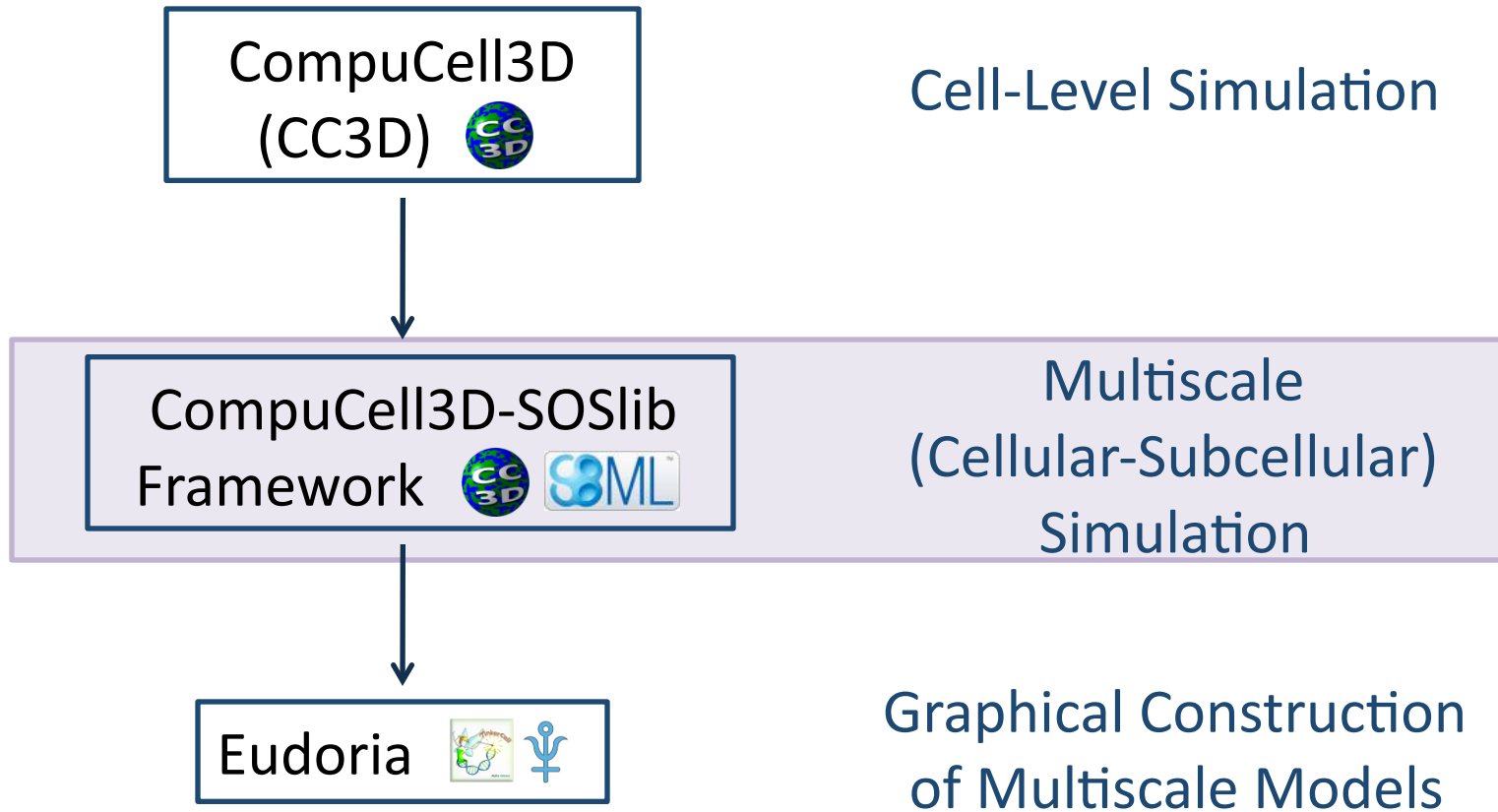Cells are modeled with static physical properties that are independent of intracellular state

Incorporation of Intracellular States

How do we incorporate the intracellular time-evolution of chemical species concentrations?

Overview

CompuCell3D (CC3D) Cell-Level Simulation

CompuCell3D-SOSlib Framework Multiscale (Cellular-Subcellular) Simulation

Eudoria Graphical Construction of Multiscale Models

CC3D-SOSlib Framework for Multiscale Simulation

CompuCell3D (CC3D)

- Implements Cellular Potts Model (CPM)
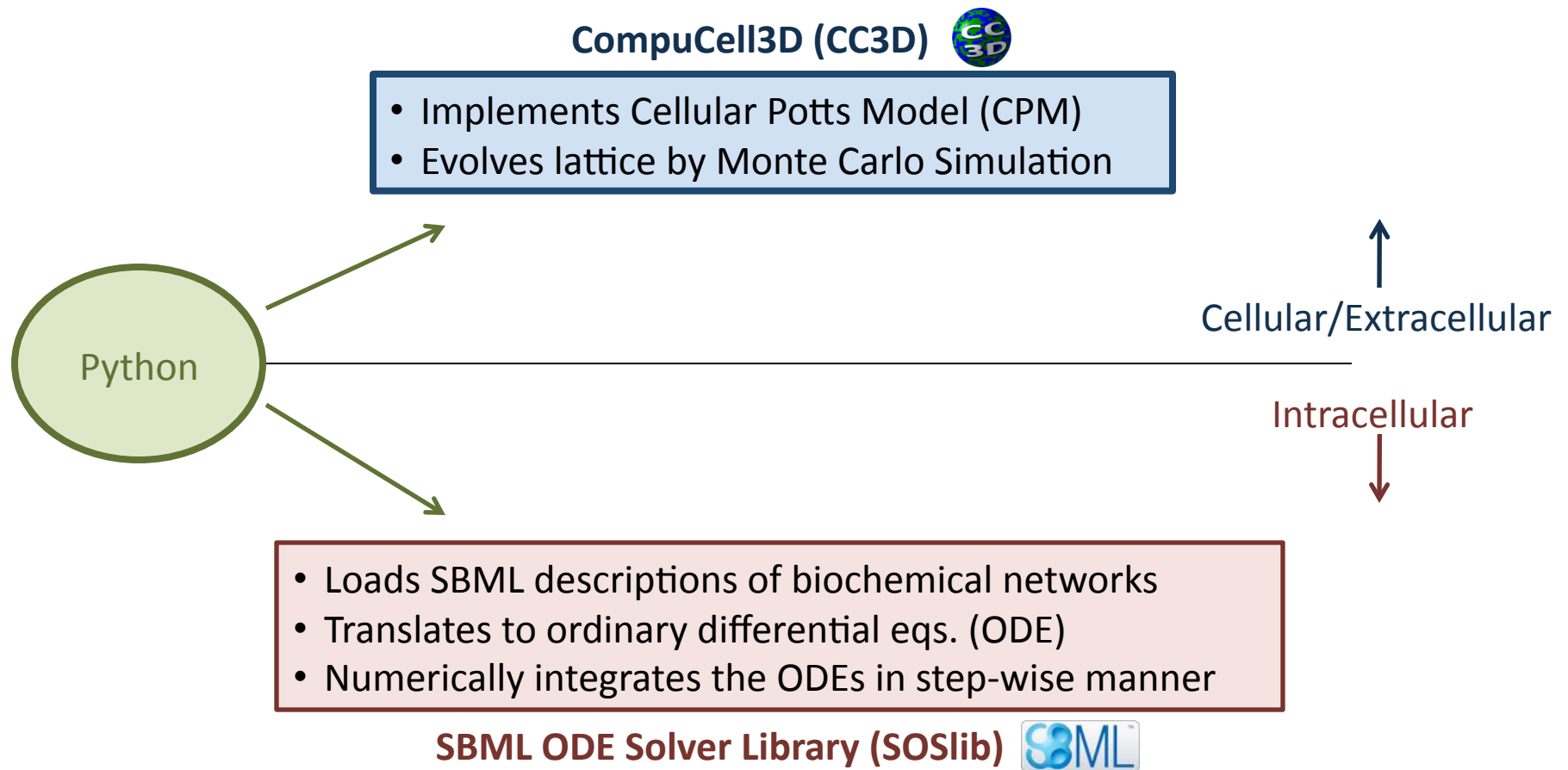- Evolves lattice by Monte Carlo Simulation

Cellular/Extracellular

Intracellular

- Loads SBML descriptions of biochemical networks
- Translates to ordinary differential eqs. (ODE)
- Numerically integrates the ODEs in step-wise manner

SBML ODE Solver Library (SOSlib)

CC3D-SOSlib Framework for Multiscale Simulation

CompuCell3D (CC3D)

- Implements Cellular Potts Model (CPM)
- Evolves lattice by Monte Carlo Simulation

Python

Cellular/Extracellular

Intracellular

- Loads SBML descriptions of biochemical networks
- Translates to ordinary differential eqs. (ODE)
- Numerically integrates the ODEs in step-wise manner
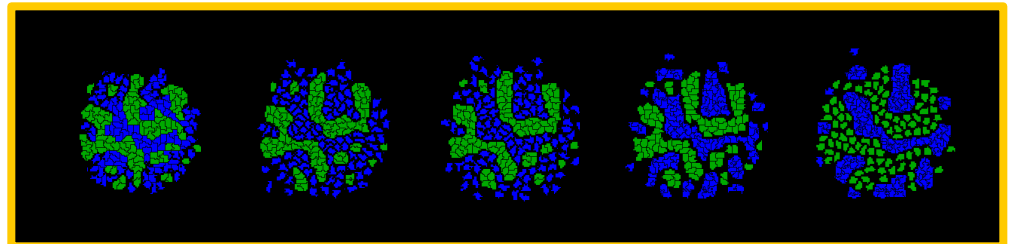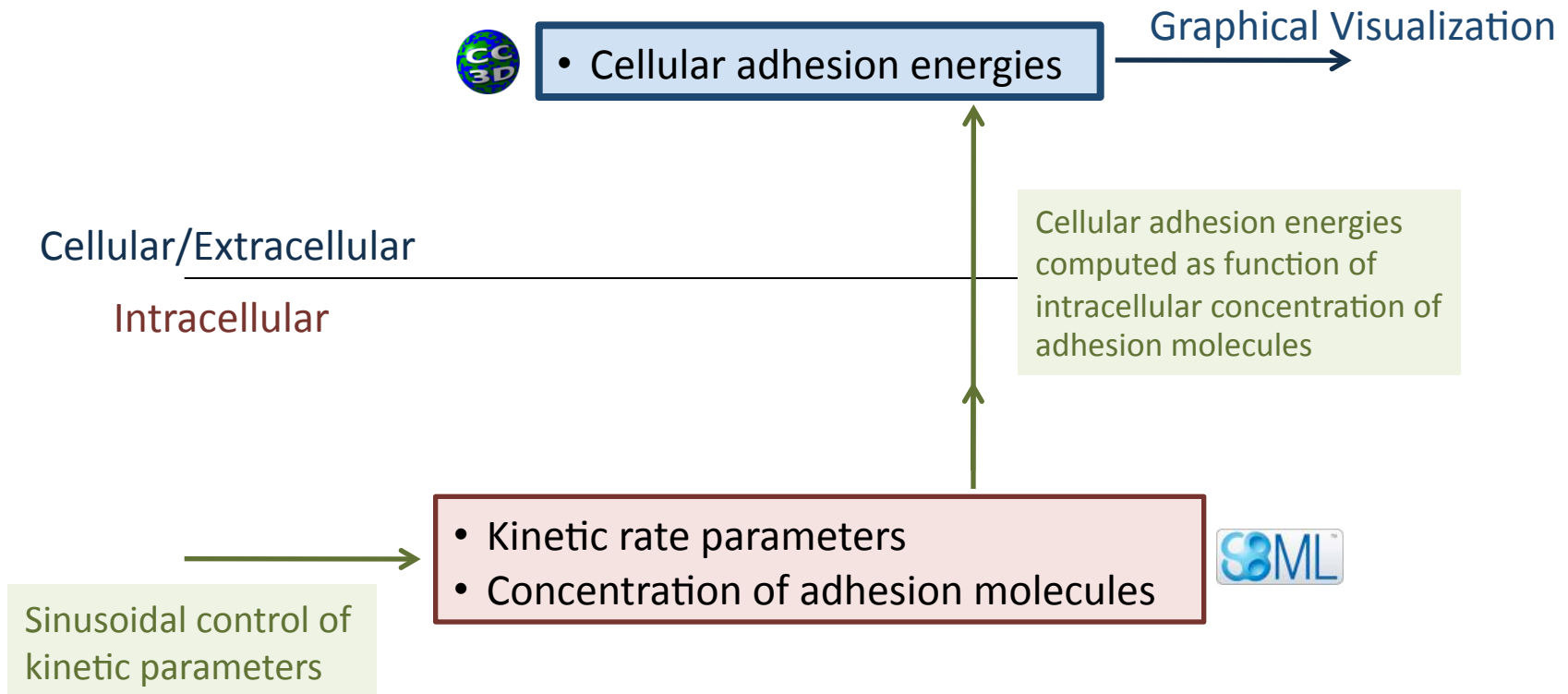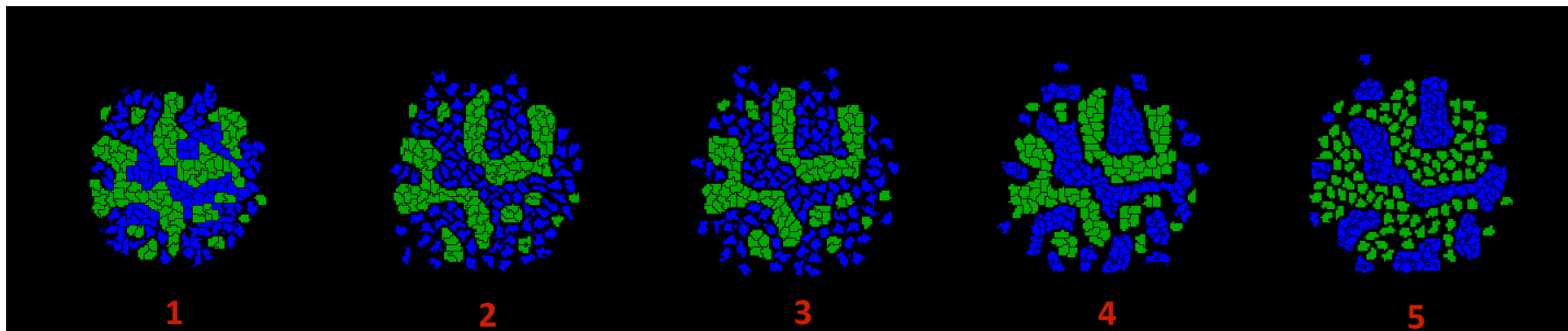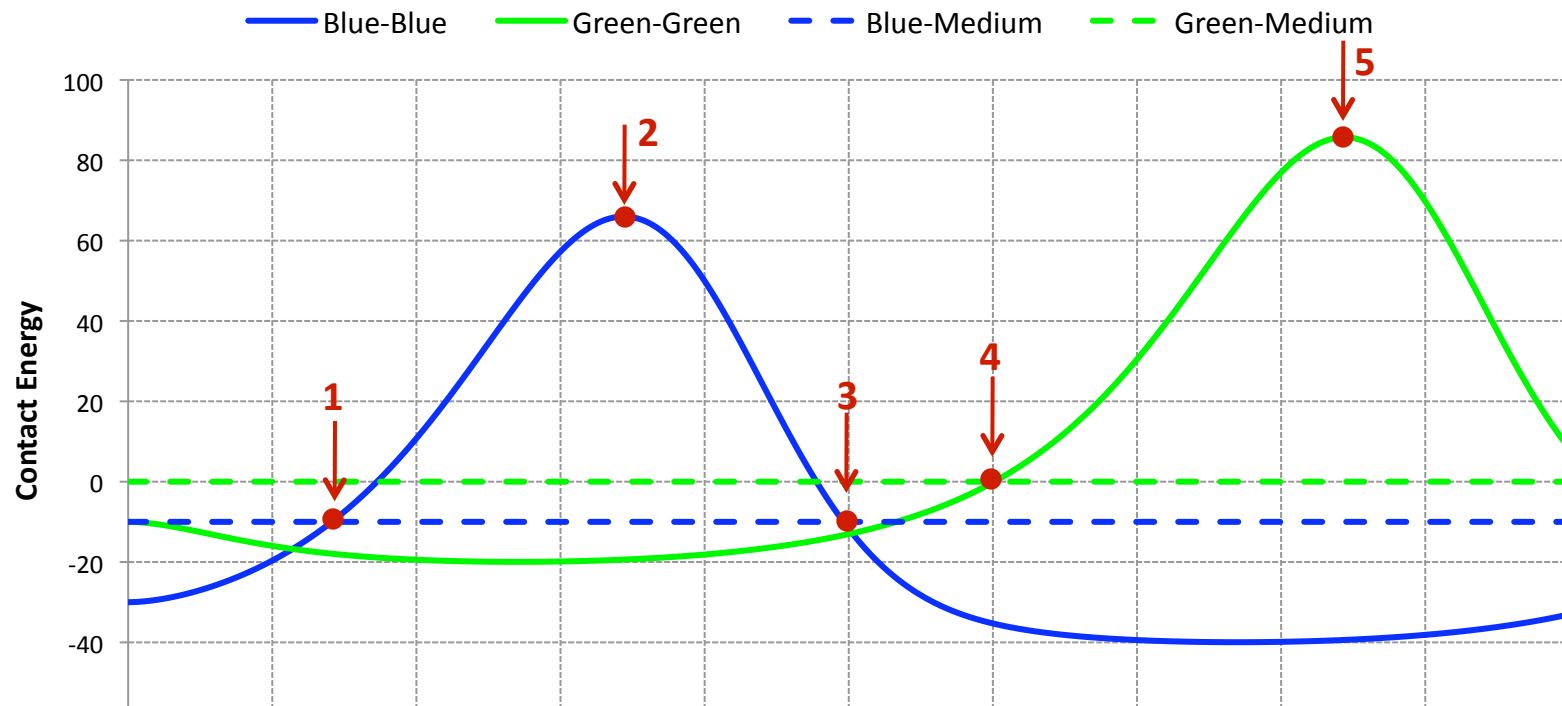
SBML ODE Solver Library (SOSlib)

Exchange of Biological Information within the CC3D-SOSlib Framework

CompuCell3D (CC3D)

- Cellular adhesion energies, volumes, surface areas, positions
- Extracellular concentrations

Cellular/Extracellular

Intracellular

- Amounts/concentrations of biochemical species and macromolecules
- Kinetic rate parameters
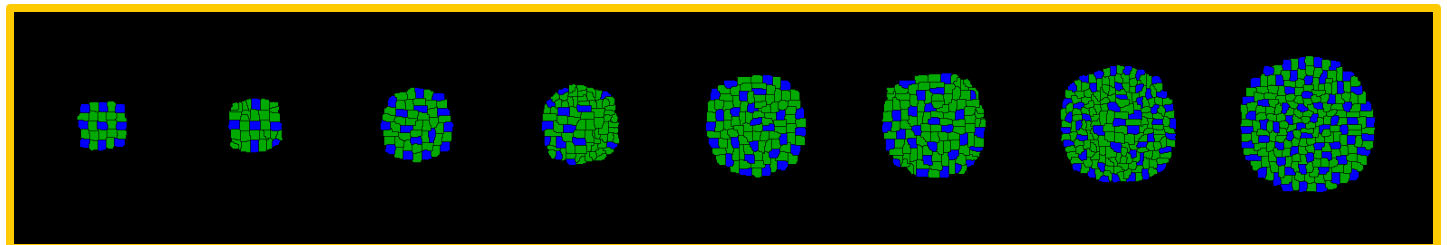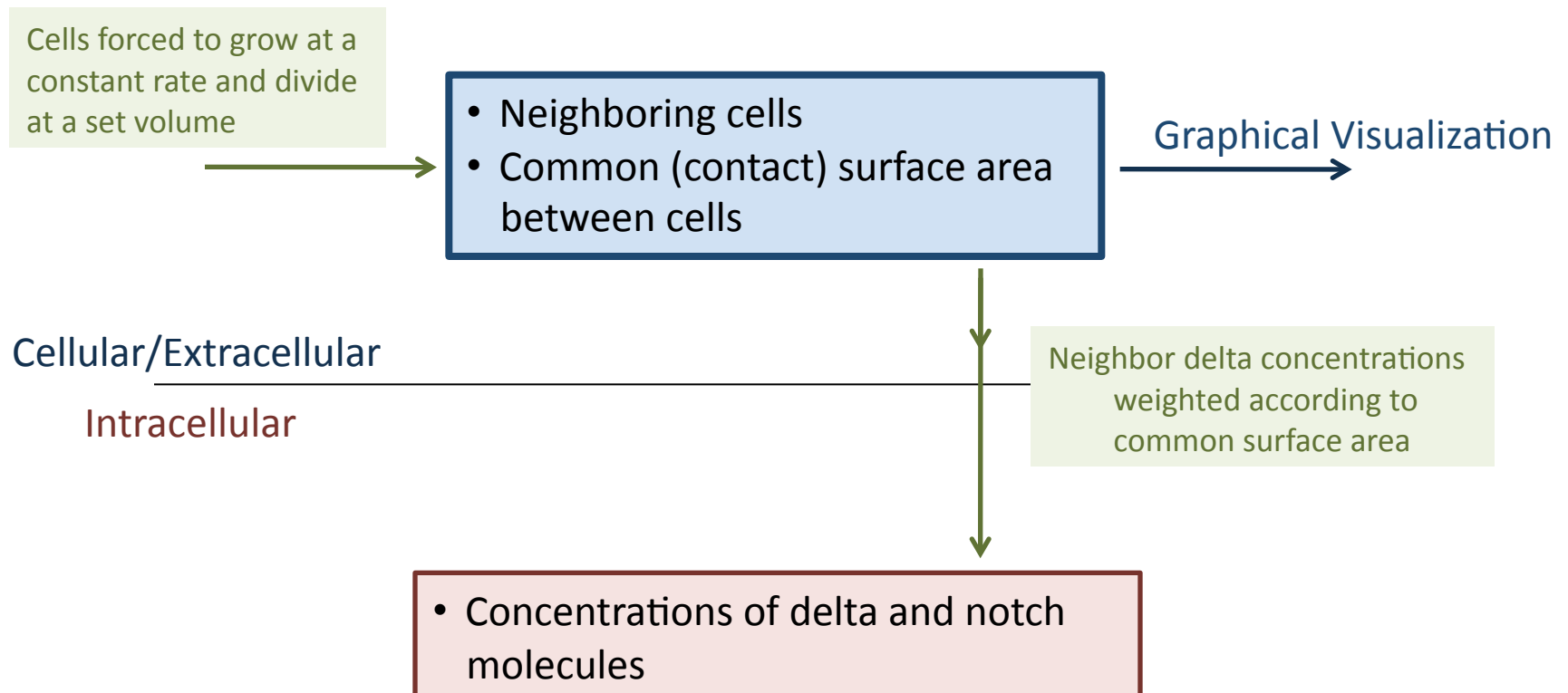
SBML ODE Solver Library (SOSlib)
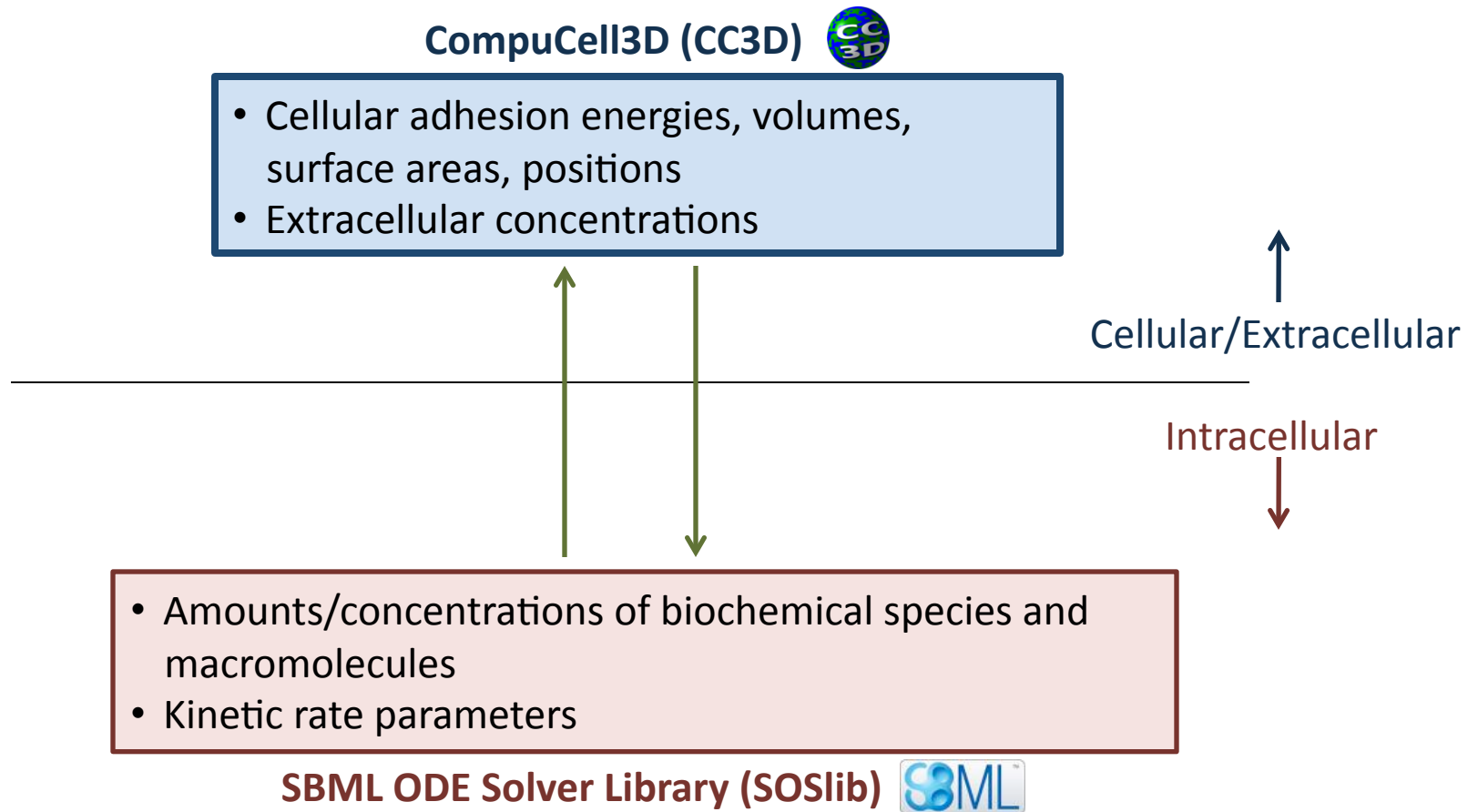
Changing Adhesion Energy Simulation

Changing Adhesion Energy Simulation

Delta-Notch Simulation with Cell Growth

Cells forced to grow at a
constant rate and divide
at a set volume

- Neighboring cells
- Common (contact) surface area
  between cells

Graphical Visualization

Cellular/Extracellular

Intracellular

Neighbor delta concentrations
weighted according to
common surface area

- Concentrations of delta and notch
  molecules

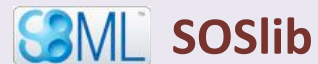# Delta-Notch Simulation with Cell Growth
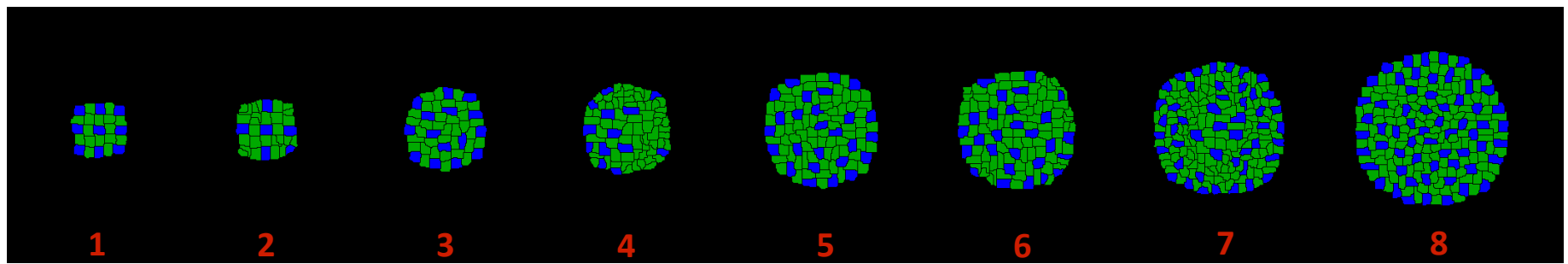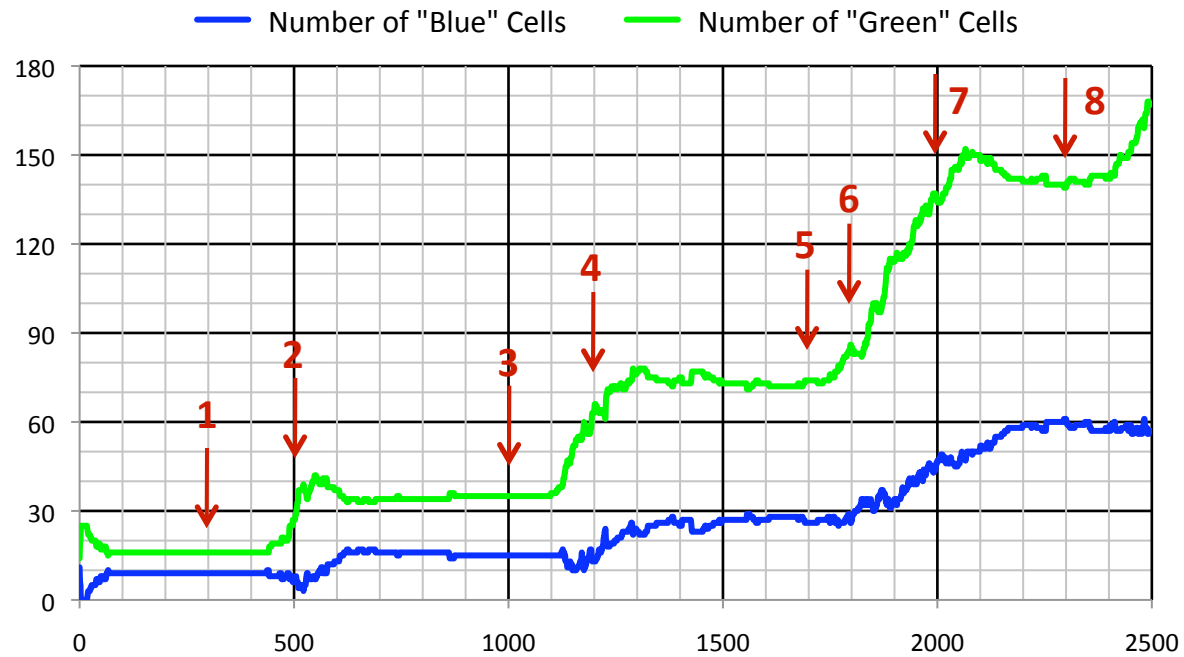
Files for Multiscale Simulation

CC3D

- CC3D XML Input File
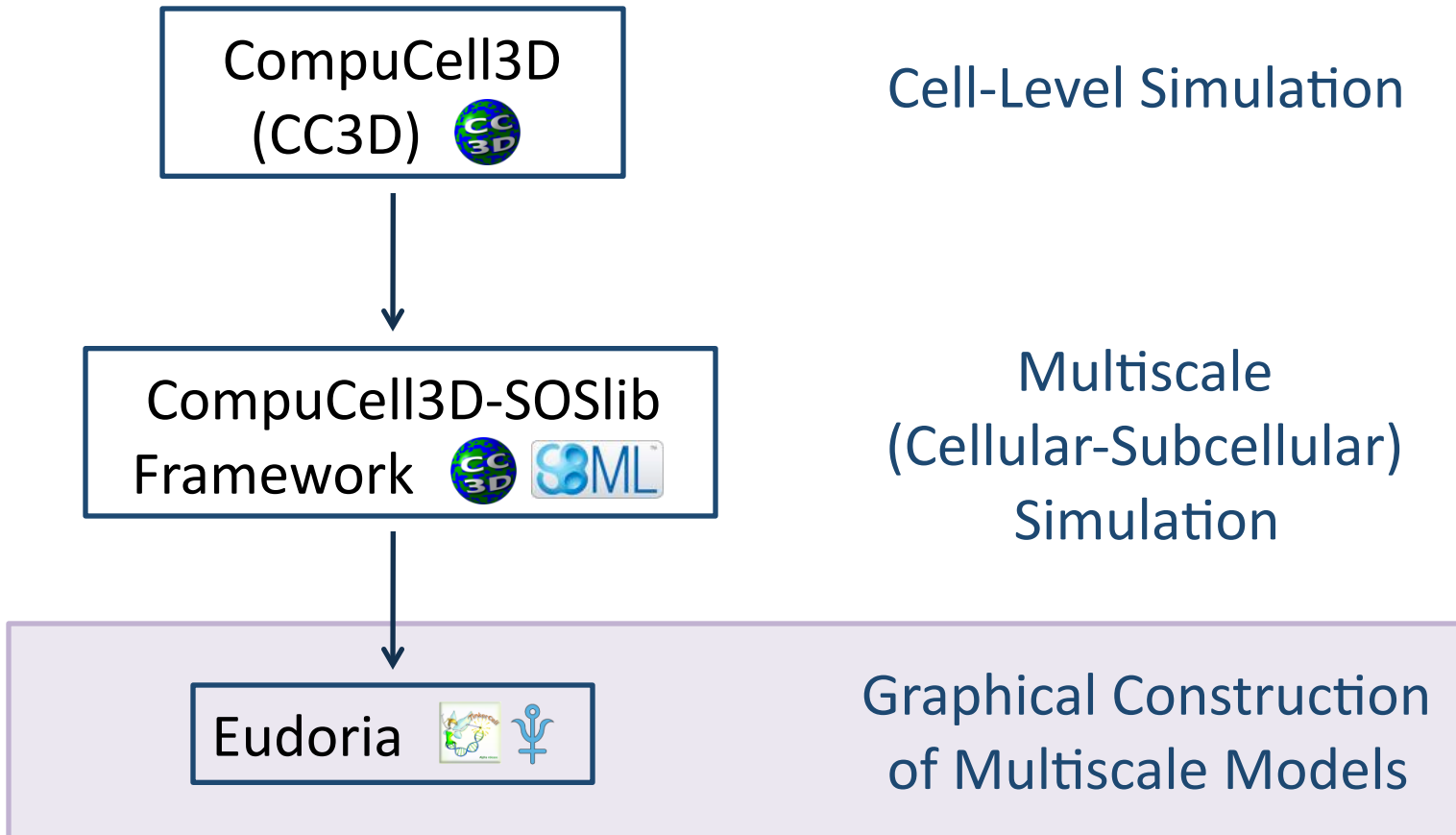- PIF file for cell positions and shapes

Python Scripts

SBML specification of intracellular models

SOSlib

Overview

CompuCell3D (CC3D)   Cell-Level Simulation

CompuCell3D-SOSlib Framework   Multiscale (Cellular-Subcellular) Simulation

Eudoria   Graphical Construction of Multiscale Models

Tinkercell for Biochemical Network Design

Graphical construction of biochemical networks

Tools for Biochemical Network Analysis

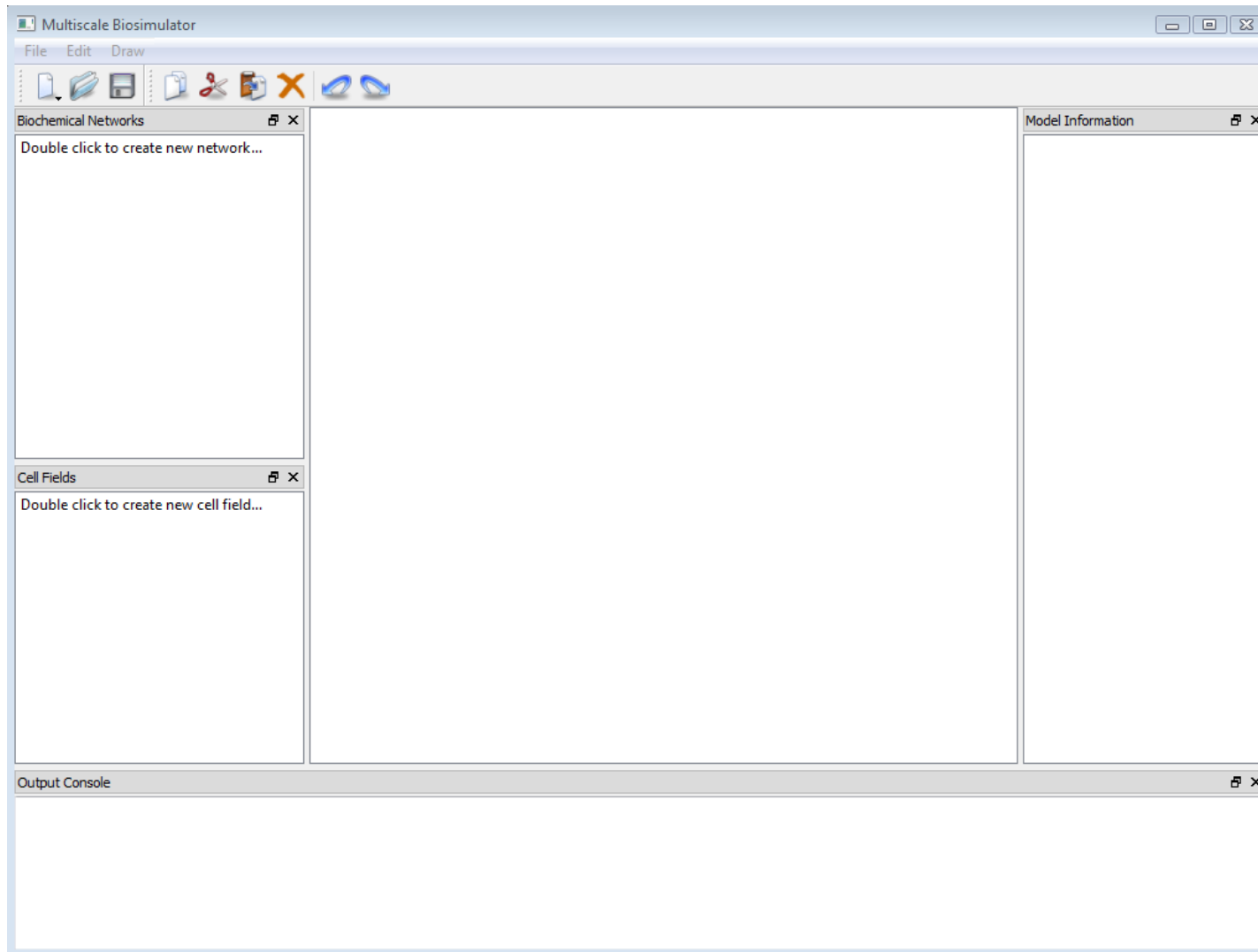# Eudoria for Multiscale Cellular Systems Design
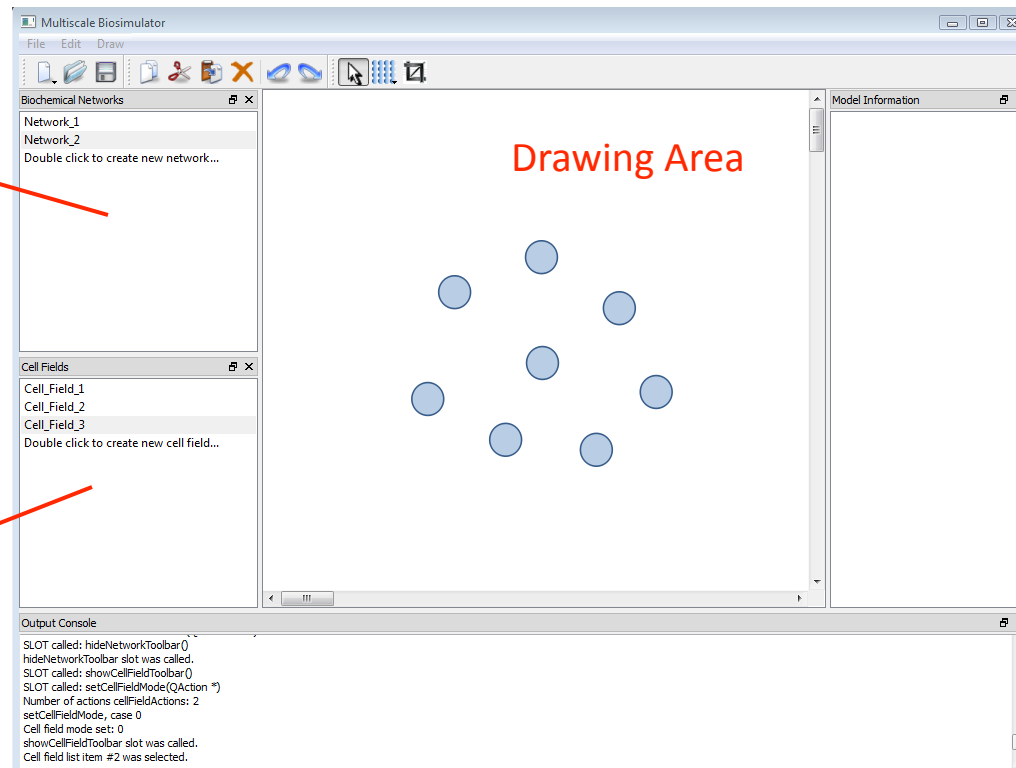
Eudoria with CompuCell3D

Eudoria in the Short Term

- ## PIF file generation:
    Specify cell types, sizes and locations

- ## CC3D XML generation:
    Specify Potts parameters, contact energies, volume and surface area plugins, etc.

- ## Python script template generation:
    Extend basic capabilities of CC3D and allow customization by modelers
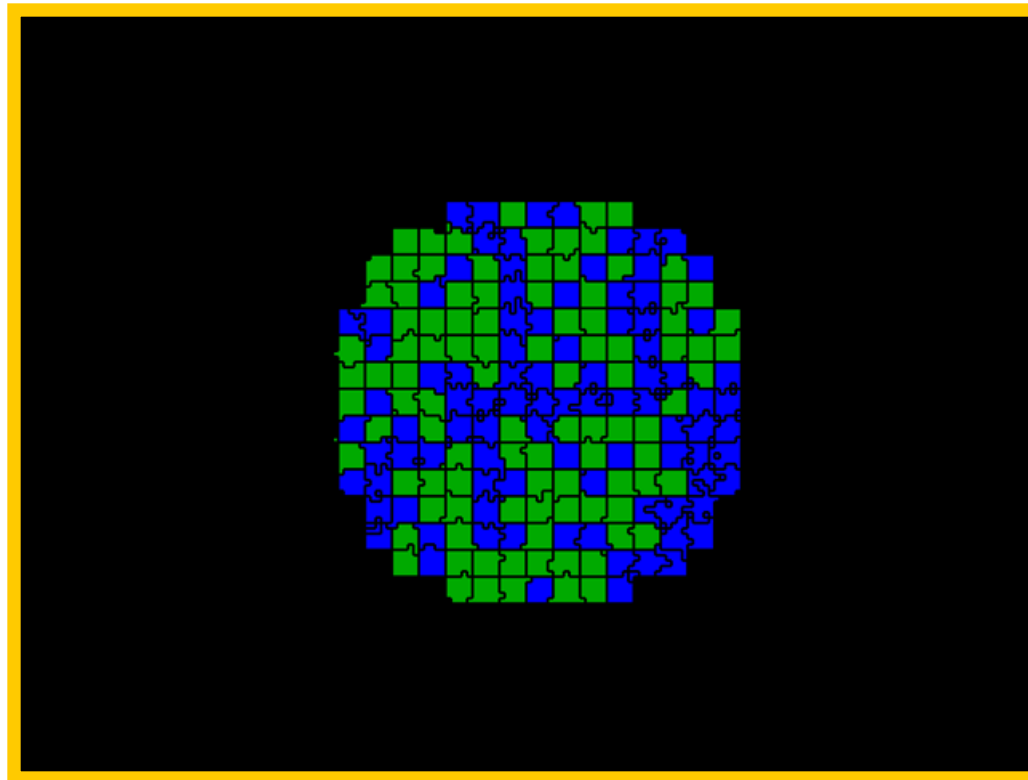
- ## SBML generation

Eudoria in the Long Term

- Move from only model-building and CC3D file-generation to multi-methodology simulation
  - Lattice-based simulation (CPM)
  - Lattice-free simulation
  - Hybrid simulation

- Conform, internally, to methodology-independent model specifications (CBO and SBO)

- Generate model specification files in relevant markup languages (e.g. Cell Behavior Markup Language, when it exists)

Acknowledgments

Changing Adhesion Energy Simulation

Delta-Notch Simulation with Cell Growth