Using Ordinary/Stochastic Differential Equations and Probabilistic Methods to Model Biological Processes

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Abstract

Agent-based models are used for simulating cellular and subcellular processes because they are straightforward to visualize and use and easily extensible. BioLogic is an agent-based simulator of cells, which adapts to the high variability of experimental data by simple logical variables such as high, low, or none. Extensions were added to the simulator to be able to simulate reactions using 1) probabilistic models, when the number of agents is small 2) stochastic differential equations, when the number of agents is moderate and 3) ordinary differential equations when the number of agents is large. Ideally, the algorithm should use a combination of the three methods for maximal efficiency. In the probabilistic model we calculate probabilities for reactions based on rate constants and the law of mass action. Both the stochastic differential equations as well as the ordinary differential equations models use Euler's method to approximate the solution. The software uses as input descriptive XML files to represent the hierarchy of structures within the simulation environment and regular text files to define the reaction rates.

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Probabilistic Method

Small Population Size

Quantities are
Discrete

Stochastic

- Compute timestep size so it is very likely that at most one reaction happens
- Probability of a reaction occurring depending on the current rate multiplied by the timestep

Simulation Step

The new number of molecules is changed by the amount specified in one reaction according to the probability of a reaction occurring in the timestep.

Stochastic Differential Equations

Medium Population Size

Quantities are
Continuous

Stochastic

- Timestep is calculated such that many reactions occur
- Number of reactions that occur during each timestep is approximated by a normal random variable

Simulation Step

The new number of molecules is the current number of molecules plus a normal random variable with mean and variance the timestep multiplied by the current rate.

Ordinary Differential Equations

Large Population Size

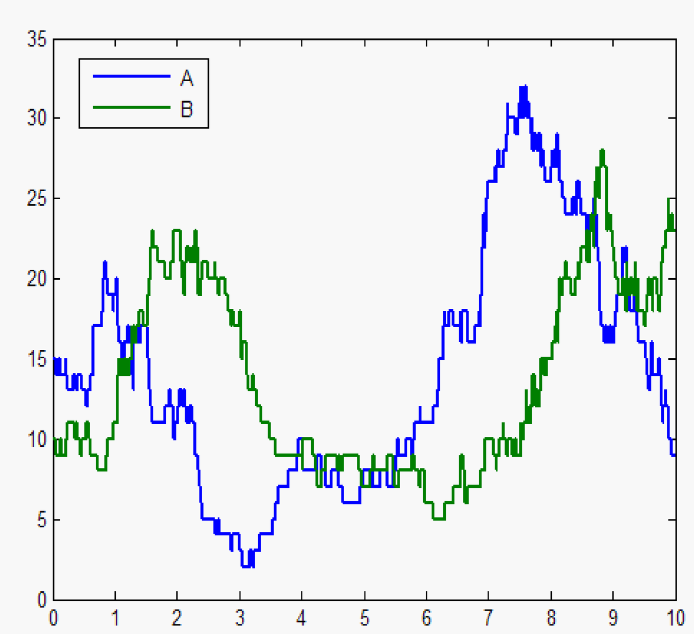
Quantities are
Continuous

Deterministic

- Reaction rates are transformed into differential equations based on rate constant and concentrations
- Uses Euler's Method to approximate solutions.

Simulation Step

The new concentration is the current concentration plus the timestep multiplied by the current rate.

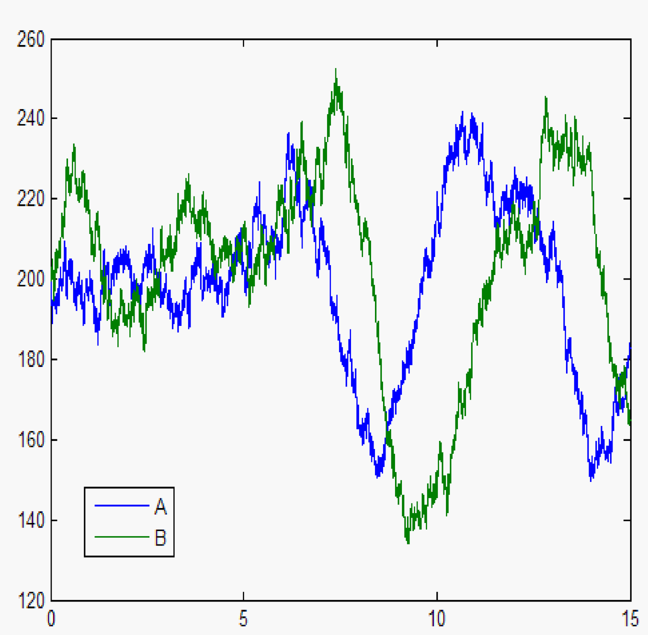


X+A->2A rate: k1
A+B->2B rate: k2
B->Y rate: k3

k1 = 0.5
k2 = 0.01
k3 = 0.2

Initial Conditions:
A=15
B=10

Lotka Volterra Model of Predator and Prey – Probabilistic Version
Small Population

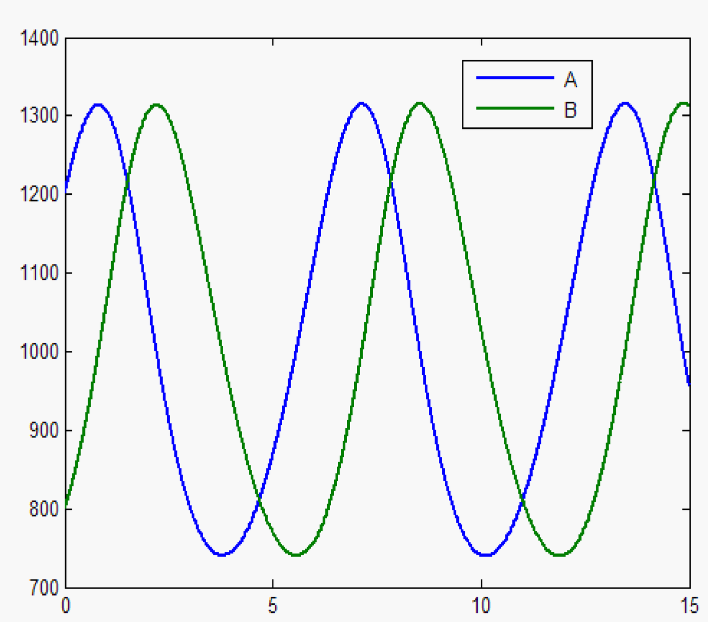


X+A->2A rate: k1
A+B->2B rate: k2
B->Y rate: k3

k1 = 1
k2 = 0.005
k3 = .6

Initial Conditions:
A=190
B=200

Lotka Volterra Model of Predator and Prey – SDE Version
Medium Population



X+A->2A rate: k1
A+B->2B rate: k2
B->Y rate: k3

k1 = 1
k2 = 0.1
k3 = 3

Initial Conditions:
A=1200
B=800

Lotka Volterra Model of Predator and Prey – ODE Version
Large Population