

Feedback

Q1: DSSA: How to update the latest reaction?

A1: The DSSA updates non-delayed reactions in the same way as the SSA, instantaneously. Non-consuming delayed reactions are updated when they are due (after the delay is “run down”). However, for consuming delayed reactions we update twice, when the reaction is chosen we update the reactants that are consumed and when the delayed reaction is due we update the products.

Q2: What is the importance of revealing oscillatory behaviour?

A2: Oscillatory behaviour is a very common dynamics in (cell) biology and seems to be very important for organisms to run. Clocks and oscillators are considered to control growth rate, to adapt to periodically varying environmental conditions, control information flow, etc. So finding that something oscillates is interesting per se. Comparing this with other oscillatory systems one might find common patterns and mechanisms and can understand how oscillation is generated.

Feedback

Q3: Introducing stochasticity into simulations means that each run of the simulation gives different results. Does this mean that simulations must be run repeatedly to yield reliable results? Or can you just increase the number of particles to reduce the variability?

A3: Indeed. A single run gives us only limited information (however, it can still give us new insights). Therefore, we usually do multiple runs, compute many ensembles and compute statistics. In the limit, the probabilities for the system to be in a particular state at a given time converge to the CME. This is not the same than increasing the number of particles!

Feedback

Q4: Do we biologically need delay in the transcription process? What biological advantages are there to the delay?

A4: The delay is inherent in the transcription and translation process in eukaryotes. It is partly because of the compartmentalization (nucleus / cytoplasm; translocation time). One might argue that the invention of the nucleus during evolution increased the “regulatory power” (complexity) by adding a variety of new mechanisms that could generate diverse dynamic behaviour – one of these mechanisms is time delay (?).

Q5: How do we analyse the noise? Is there any specific tool or method?

A5: In general, there is a variety of methods and algorithms to detect and analyse noise in complex systems (coming from various fields such as electrical engineering, telecommunications, etc.).

Feedback

Q5: Is it possible to avoid delays in biological system modelling?

A5: Yes! As for transcriptional and translational delay, remember where these delays come from. We have to consider time delays because we do not model these processes in detail, that is, our model is very coarse (e.g. it does not include any spatial information).

Q6: Is the propensity the most granular time period that would encapsulate the chance of only one reaction occurring (if it does occur)?

A6: No, the propensity a_j (of a specific reaction channel R_j !) is a function depending on the current state x (at time t) and $a_j(x) dt$ is the **probability** that the reaction occurs within $[t, t+dt)$.

With this definition we obtain the so-called next-reaction density function:

$$P(\tau, j) = P(\tau, j | x, t) = a_j(x) \exp(-a_0(x)\tau)$$

This is the probability that given x , the next reaction will occur in $[t+\tau, t+\tau+dt)$ and will be reaction R_j .

Feedback

Q7: When is the continuous-stochastic approach applicable?

A7: Under certain conditions the CME can be approximated by SDEs. It is valid to use this approach if the system possesses a “macroscopically infinitesimal time scale”, so that during any dt on that scale all of the reaction channels fire many more times than once yet none of the propensity functions change appreciably.

Q8: Jump Markov Processes – What does “jump” means?

A8: A discrete Markov process (discrete state space) is also called a jump Markov process. The described system “jumps” stochastically from one discrete state into another.

Supplement – SSA: First Reaction Method

In contrast to the SSA **Direct Method** (where we create only 2 random numbers) the **First Reaction Method** draws M random numbers, one for each reaction channel R_j :

- Draw M independent samples r_j ($j = 1, \dots, M$) of $U(0,1)$
- Calculate the M tentative reaction times for each reaction channel R_j :

$$\tau_j = \frac{1}{a_j(X(t))} \ln\left(\frac{1}{r_j}\right)$$

- Let τ_l be the smallest of $\{\tau_1, \dots, \tau_M\}$.

Update:

$$X(t+\tau) = X(t) + \nu_l$$