Lecture 'Simulationstechnik für Master-Studierende A' - Part 3

Intro Lecture Part 3

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Content

- We will discuss different stochastic modeling approaches to describe the dynamics of small chemical reaction networks
- We will derive how these approaches are connected
- **Literature:** Higham (2008). Modeling and Simulating Chemical Reactions. SIAM Rev 50(2), 347-368, 10.1137/060666457 ($\rightarrow$ Ilias)

Learning goals

- Lecture part 3 provides an introduction into stochastic modeling and simulation (exemplified on CRNs)
- You will become familiar how to handle random variables and stochastic processes
- You know standard (stochastic) modeling approaches for CRNs
- This helps you to succeed in other lectures in which stochastic processes / models and concepts from statistics are considered

Stochast. Modeling of Chemical Reaction Networks

Summary

CRN with N molecule types and M reactions with stochastic rate constants c_j, state change vectors $\nu_\mathbf{j}$ and propensities $a_j(\mathbf{X})$ according to the law of mass action

CME: System of linear differential equations, number of equations equals number of microstates of the system, solution $P(\mathbf{x}, \mathbf{t})$ is time-dependent distribution over all microstates

$$\frac{dP(\mathbf{x}, \mathbf{t})}{dt} = \sum_{j=1}^{m} \left(a_j(\mathbf{x} - \nu_\mathbf{j})\mathbf{P}(\mathbf{x} - \nu_\mathbf{j}, \mathbf{t}) - \mathbf{a_j}(\mathbf{x})\mathbf{P}(\mathbf{x}, \mathbf{t})\right) = MP(\mathbf{x}, \mathbf{t})$$

Exact stochastic description for homogeneous reaction systems. Can be solved analytically:

$$P(\mathbf{x}, \mathbf{t}) = \exp\left(\mathbf{Mt}\right)\mathbf{P}(\mathbf{x}, \mathbf{0})$$

Stochast. Modeling of CRNs

Summary

Problem CME: Number of microstates and therefore dimension of CME is huge even for small systems; requires explicit 'listing' of microstates

SSA: Simulates sample paths from CME, avoids explicit listing of microstates

- In microstate $\mathbf{x}^k$, draw waiting time $T \sim \text{Exp}(a_{sum}(\mathbf{x^k}))$ until next event / reaction
- Draw reaction index $J \sim \frac{a_j(\mathbf{x^k})}{a_{sum}(\mathbf{x^k})}$

CME solution can be reconstrcuted by simulation of many sample paths and estimating probabilities $P(\mathbf{x}, \mathbf{t})$ for fixed t with observed relative frequencies

Problem: Computationally intensive if many reactions take place in a given simulation horizon

Stochast. Modeling of CRNs

Summary

τ-**Leaping**: Sets a fixed step size τ in which multiple reactions can happen. Approximation: Propensities $a_j(x)$ are constant in this time interval.

- In state x^k, draw M Poisson-distributed random numbers $p_j \sim Po(a_j(x^k)\tau)$, which determine the number of reactions of type j in the time interval τ
- Update $x(t+\tau) = x^k + \sum_{j=1}^{m} \nu_{\mathbf{j}} \mathbf{p_j}$

Stochast. Modeling of CRNs

Summary

CLE: Approximate Poisson distribution with normal distribution if $a_j(\mathbf{x})\tau \gg \mathbf{1}$ for all j and all 'likely' $\mathbf{x}$. Nonlinear stochastic differential equation system, number of equations equals number of molecule types, solution describes time-dependent molecule amounts in terms of real numbers

$$\mathbf{Y(t+\tau)} = \mathbf{Y(t)} + \tau \sum_{\mathbf{j=1}}^{\mathbf{m}} \nu_{\mathbf{j}} \mathbf{a_j(Y(t))} + \sqrt{\tau} \sum_{\mathbf{j=1}}^{\mathbf{m}} \nu_{\mathbf{j}} \sqrt{\mathbf{a_j(Y(t))}} \mathbf{Z_j}$$

with $Z_j \sim N(0,1)$.

Stochast. Modeling of CRNs

Summary

RRE: Nonlinear system of ordinary differential equations, number of equations equals number of molecule types, solution describes time-dependent concentrations

$$\frac{\mathbf{y(t)}}{dt} = \sum_{j=1}^{m} \nu_{\mathbf{j}} \mathbf{a_j}(\mathbf{y(t)})$$

Examination

- Short oral examinations of $10 - 12$ min
- Dates are organized soon
- Which modeling approaches do exist to describe CRNs?
- On which assumptions are these based?
- How are these approaches related?
- For a given reaction system, describe approach XY. How do the equations look like? How does the simulation look like? How to implement the model? (choose 2 of the four approaches in advance that you should be able to explain in detail)

Questions?