Stochastic simulation - Gillespie's algorithm

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3.12.2007

The problem

- fixed volume V
- N chemical species (spatially uniform distribution)
- M possible reactions
- given $X_1(t), X_2(t), \ldots, X_N(t)$

$X_1(t+\tau), \ldots, X_N(t+\tau) =?$

Continuous + deterministic x Discrete + stochastic

Collision rate x Collision probability in unit time

Problems as $\delta t \rightarrow 0$

c_μ is stochastic reaction constant

$c_1 dt$ = average probability that particular combination of S_1, S_2 molecules will react due to R_1 in the next infinitisemal interval $(t, t + dt)$

h_μ is function of $X_1(t), \ldots, X_N(t)$, number of all possible reactant combinations for reaction R_μ

$h_\mu c_\mu dt$ = probability of reaction R_μ occuring in the interval $(t, t + dt)$

fundamental hypothesis the existence of such constants c_μ (well-stirred system)

$P(X_1, \ldots, X_N; t)$ is the probability that in time t there are X_i molecules of species S_i.

k^{th} **moment of P with respect to X_i**

$$X_i^{(k)}(t) = \sum_{X_1=0}^{\infty} \cdots \sum_{X_N=0}^{\infty} X_i^k P(X_1, \ldots, X_N)$$

$X_i^{(1)}, X_i^{(2)}$ **are useful**

$$\Delta_i(t) = \left(X_i^{(2)}(t) - (X_i^{(1)}(t))^2 \right)^{\frac{1}{2}}$$

$$[X_i^{(1)}(t) - \Delta_i(t),\ X_i^{(1)}(t) + \Delta_i(t)]$$

$a_\mu dt$ = probability that R_μ will occur in time interval $(t, t+dt)$ given the values $(X_1, \ldots, X_N)$ at time t

$$a_\mu = h_\mu c_\mu$$

$B_\mu dt$ = probability that system is at t in the state "$(X_1, \ldots, X_N)$ with one R_μ undone" and R_μ occures in $(t, t+dt)$

$$P(X_1, \ldots, X_N, t+dt) = P(X_1, \ldots, X_N, t)(1 - \sum_{\mu=1}^{M} a_\mu dt) + \sum_{\mu=1}^{M} B_\mu dt$$

$$\frac{\partial}{\partial t} P(X_1, \ldots, X_N, t) = \sum_{\mu=1}^{M} (B_\mu - a_\mu P(X_1, \ldots, X_N, t))$$

Simulation - what do we need to know

- when will the next reaction occur?

- what reaction it will be?

The reaction probability density function $P(\tau, \mu)$

$P(\tau, \mu)d\tau$ = probability that, given the state $(X_1, \ldots, X_N)$ at time t, the next reaction in V will be R_μ and will occur in the infinitesimal time interval $(t + \tau, t + \tau + d\tau)$

Determining the probability density function

$$P(\tau, \mu)d\tau = P_0(\tau)a_\mu d\tau$$

$$P_0(\tau) = e^{-\sum_{\nu=1}^{M} a_\nu \tau}$$

$$P(\tau, \mu) = \begin{cases} a_\mu e^{-a_0 \tau} & \text{if } 0 \leq \tau < \infty \text{ and } \mu = 1, \ldots, M \\ 0 & \text{otherwise} \end{cases}$$

where $a_\mu = h_\mu c_\mu$ and a_0 denotes $\sum_{\nu=1}^{M} a_\nu$

Simulation - random number generator

unit interval uniform random number generator (UNR)

r_1, r_2 random numbers generated by UNR

$$\tau = \frac{1}{a_0} ln(\frac{1}{r_1})$$

$$\sum_{\nu=1}^{\mu-1} a_\nu < r_2 a_0 \leq \sum_{\nu=1}^{\mu} a_\nu$$

$$P_1(\tau) = a_0 e^{-a_0 \tau}$$

$$P_2(\mu) = \frac{a_\mu}{a_0}$$

$$P_1(\tau) P_2(\mu) = P(\tau, \mu)$$

Algorithm

Step 0.

. Read $c_1, \ldots, c_M$,$X_1, \ldots, X_N$ from input.

. $t \leftarrow 0, n \leftarrow 0$

. Initialize the URN generator.

Step 1.

. $a_1 \leftarrow h_1 c_1, \ldots, a_M \leftarrow h_M c_M$

. $a_0 = \sum_{\nu=1}^{M} a_\nu$

Step 2.

. Generate r_1, r_2.

. Compute τ, μ.

Step 3.

. $t \leftarrow t + \tau$

. Change the X_i values by "performing R_μ".

. $n \leftarrow n + 1$

. Repeat the algorithm from step **1**.