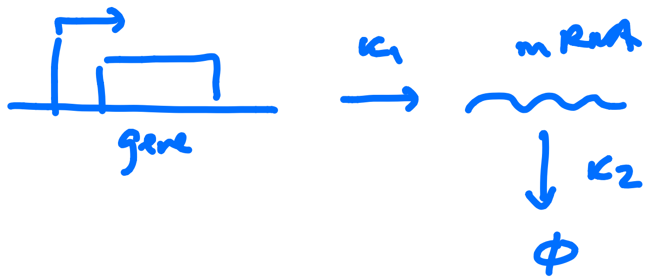
W10 - Molecular dynamics as a Markov process

RNA biosynthesis



$$\phi \xrightarrow{k_1} RNA$$

$$RNA \xrightarrow{k_2} \phi$$

$\longrightarrow$ time $\qquad R_t$ = # number of RNA molecules at t.

$$R_0 \to R_1 \xrightarrow{\Delta t} R_2 \to \cdots \quad R_i \xrightarrow{\Delta t} R_{i+1}$$

$R_i = \{0, 1, 2, \ldots\}$

$P(R \mid t)$ prob of having R molecules at time t

assumptions

i) an RNA mol is produced instantaneously with prob k_1

ii) " destroyed " " " k_2

iii) in a small interval Δt only one of the two possible reactions can happen

Δt

Markov process

$$R_i \xrightarrow{\Delta t} R_{i+1}$$

$$R_i \xrightarrow{k_1 \Delta t} R_{i+1} = R_i + 1 \quad \text{synthesis}$$

$$R_i \xrightarrow{k_2 \Delta t R_i} R_{i+1} = R_i - 1 \quad \text{degradation}$$

$$R_i \xrightarrow{1 - k_1 \Delta t - k_2 R_i \Delta t} R_{i+1} = R_i$$

stochastic process

start R_0

draw $r \in U[0:1]$

if $r < k_1 \Delta t$ add 1 $R_1 = R_0 + 1$

el if $k_1 \Delta t \leq r < k_2 R_0 \Delta t$ remove 1 $R_1 = R_0 - 1$

else $R_1 = R_0$

Master Equation

$$P(R \mid t + \Delta t) = + k_1 \cdot \Delta t \quad P(R-1 \mid t)$$

$$+ k_2 (R+1) \Delta t \quad P(R+1 \mid t)$$

$$+ (1 - k_1 \Delta t - k_2 R \Delta t) \quad P(R \mid t)$$

Δ General expression

$r_1 : \quad \phi \xrightarrow{k_1} R \qquad \eta_{r_1}(R) = +1 = \text{total change}$

$$w_{r_1}(R) = \text{propensity}$$
$$= \text{prob of reaction in } \Delta t$$
$$= k_1$$

$r_2 : \quad R \xrightarrow{k_2} \phi \qquad \eta_{r_2}(R) = -1$

$$w_{r_2}(R) = k_2 \cdot R$$

$$P(R \mid t+\Delta t) = k_1 \Delta t \, P(R-1 \mid t)$$
$$+ k_2 (R+1) \Delta t \, P(R+1 \mid t)$$
$$+ \left[1 - k_1 \Delta t - k_2 (R+1) \Delta t\right] P(R \mid t)$$

$$= \Delta t \, w_1(R+\eta_1) \, P(R+\eta_1 \mid t)$$
$$+ \Delta t \, w_2(R+\eta_2) \, P(R+\eta_2 \mid t)$$
$$+ \left[1 - \Delta t \, w_1(R) - \Delta t \, w_2(R)\right] P(R \mid t)$$

In general

$$\bar{x} = (x_1 \dots x_N)$$

$$\bar{\eta}_r(\bar{x}) = (\eta_r(x_1), \dots, \eta_r(x_N))$$

$$\bar{w}_r(\bar{x}) = (w_r(x_1), \dots, w_r(x_N))$$

$$P(\bar{x} \mid t+\Delta t) = \sum_r \bar{w}_r(\bar{x}+\bar{\eta})\Delta t \, P(\bar{x}+\bar{\eta}_r \mid t)$$

$$+ \left[1 - \sum_r \bar{w}_r(\bar{x})\Delta t\right] P(\bar{x} \mid t)$$

general master equation

Stochastic vs Deterministic solution

Stochastic process - Monte Carlo Simulation

start with R_0

Δt

R_1 draw $r \in U[0:1]$

if $r \le k_1 \Delta t \rightarrow R_1 = R_0 + 1$

elif $r \le k_2 R_0 \Delta t \rightarrow R_1 = R_0 - 1$

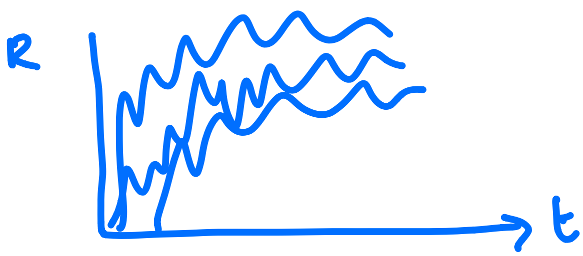
else $R_1 = R_0$

R_1

R_2 draw r in $[0:1]$

⋮

→ class code



Deterministic solution $\Delta t \to 0$

$$P(\bar{x} / t+\Delta t) = \sum_r w_r(\bar{x}+\bar{\eta}_r)\Delta t \, P(\bar{x}+\bar{\eta}_r / t)$$

$$+ \left[1 - \sum_r w_r(\bar{x})\Delta t\right] P(\bar{x} | t)$$

$$\frac{P(\bar{x} | t+\Delta t) - P(\bar{x}|t)}{\Delta t} = \sum_r w_r(\bar{x}+\bar{\eta}_r) P(\bar{x}+\bar{\eta}_r | t)$$

$$- \sum_r w_r(\bar{x}) P(\bar{x}|t)$$

$$\frac{dP(\bar{x}|t)}{dt} = \sum_r w_r(\bar{x}+\bar{\eta}_r) P(\bar{x}+\bar{\eta}_r | t) - \sum_r w_r(\bar{x}) P(\bar{x}|t)$$

continuous time master equation

For RNA synthesis/degradation

$$\frac{dP(R|t)}{dt} = k_1 P(R-1|t) + k_2(R+1) P(R+1|t) - (k_1 + k_2 R) P(R|t)$$

Now, let's take averages

$$\sum_R R \frac{dP(R|t)}{dt} = k_1 \sum_R R\, P(R-1|t)$$
$$+ k_2 \sum_R R(R+1)\, P(R+1|t)$$
$$- k_1 \sum_R R\, P(R|t) - k_2 \sum_R R^2\, P(R|t)$$

$$= k_1 \sum_R (R+1)\, P(R|t)$$
$$+ k_2 \sum_R (R-1) R\, P(R|t)$$
$$- k_1 \sum_R R\, P(R|t)$$
$$- k_2 \sum_R R^2\, P(R|t)$$

$$= k_1 \sum_R P(R|t)$$
$$- k_2 \sum_R R\, P(R|t)$$

$$\langle R \rangle_t = \sum_R R\, P(R|t)$$

$$\boxed{\frac{d\langle R \rangle_t}{dt} = k_1 - k_2 \langle R \rangle_t}$$

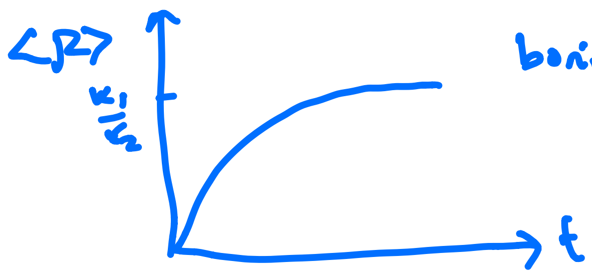
deterministic eq. on averages

Deterministic solution

$$\frac{d\langle R\rangle_t}{dt} = k_1 - k_2 \langle R\rangle_t$$

$$\langle R\rangle_t = \langle R\rangle_0 e^{-k_2 t} + \frac{k_1}{k_2}\left(1 - e^{-k_2 t}\right)$$

$$= \frac{k_1}{k_2}\left(1 - e^{-k_2 t}\right)$$



boring!

$$\lim_{t\to\infty} \langle R\rangle_t = k_1/k_2$$

Stochastic Simulations – The Gillespie Algorithm

Alternative to the "brute force" Monte Carlo simulations that we introduced before.

The Gillespie algorithm relies on calculating the time there is no change in the system. $\equiv$ the dwell time.

The result is

$$\boxed{P(\text{dwell time} = \tau) = w_R\, e^{-w_R t}}$$

where $w_R = \sum_r w_r$ the propensities for all reactions

Then the simulation goes as this:

i) start at t_0, $R = R_0$

ii) sample τ from $P(\tau) = w_R\, e^{-w_R \tau}$

where $w_R = k_1 + k_2 R_0$

$t_1 = t_0 + \tau$

iii) sample $r \in U[0:1]$

if $r < k_1$ $R_1 = R_0 + 1$
elif $r < k_2 R_{''}$ $R_1 = R_0 - 1$
elif $R_1 = R_0$

The dwell time

$$\underline{P(\tau) = W_R\, e^{-W_R \tau}}$$

$$P(\tau) \propto P(x, t+\tau \,/\, x, t)$$

$$= P(x, t+\tau / x, t+\tau-\Delta t)$$

$$P(x, t+\tau-\Delta t \,|\, x, t+\tau-2\Delta t)$$

$$\vdots$$

$\tau = m\Delta t$

$$P(x, t+\Delta t \,|\, x, t)$$

$$= \left(1 - \sum_r w_r(x) \cdot \Delta t\right)^m$$

$$= \left(1 - \sum_r w_r(x) \frac{\tau}{m}\right)^m$$

$$\lim_{m \to \infty} = e^{-W_R(x) \cdot \tau}$$

Then

$$P(\tau) = P(\text{there is a instantaneous change}) \cdot e^{-W_R(x) \cdot \tau}$$

$$\boxed{P(\tau) = W_R(x)\, e^{-W_R(x) \cdot \tau}}$$