In this example, that we considered yesterday, let's write down the rate eqns.

$$A \underset{\bar{k}_1}{\overset{k_1}{\rightleftharpoons}} 2A, \qquad 2A \xrightarrow{k_2} B, \qquad B \xrightarrow{k_3} A$$

$$Y = \begin{pmatrix} 1 & 2 & 0 \\ 0 & 0 & 1 \end{pmatrix}$$

$$A = \begin{pmatrix} -k_1 & \bar{k}_1 & k_3 \\ k_1 & -\bar{k}_1 - k_2 & 0 \\ 0 & k_2 & -k_3 \end{pmatrix}$$

$$\Rightarrow \quad YA = \begin{pmatrix} k_1 & -\bar{k}_1 - 2k_2 & k_3 \\ 0 & k_2 & -k_3 \end{pmatrix}$$

$$\Rightarrow \quad \frac{d}{dt}\begin{pmatrix} x_A \\ x_B \end{pmatrix} = \begin{pmatrix} k_1 & -\bar{k}_1 - 2k_2 & k_3 \\ 0 & k_2 & -k_3 \end{pmatrix} \begin{pmatrix} x_A \\ x_A^2 \\ x_B \end{pmatrix}$$

So we get

$$\begin{cases} \dfrac{d}{dt} x_A = k_1 x_A - (\bar{k}_1 + 2k_2) x_A^2 + k_3 x_B \\[2ex] \dfrac{d}{dt} x_B = k_2 x_A^2 - k_3 x_B \end{cases}$$

Compare with "complex-balance" conditions.

Stochastic Modeling

Now $2A \to A$ at $\bar{k}_1 n_A(n_A-1)$

$A \to 2A$ at $k_1 n_A$

$2A \to B$ at $k_2 n_A(n_A-1)$

$B \to A$ at $k_3 n_B$

Master eqn

$$\frac{d}{dt}P(n_A,n_B) = P(n_A+1,n_B)\bar{k}_1 n_A(n_A+1) - \bar{k}_1 n_A(n_A-1)P(n_A,n_B)$$

$$+ P(n_A-1,n_B)k_1(n_A-1) - k_1 n_A P(n_A,n_B)$$

$$+ P(n_A+2,n_B-1)k_2(n_A+2)(n_A+1)$$

$$- P(n_A,n_B)k_2 n_A(n_A-1)$$

$$+ P(n_A-1,n_B+1)k_3(n_B+1) - P(n_A,n_B)k_3 n_B$$

Std st $\Rightarrow$ RHS = 0

Detailed-balance $\Rightarrow$ pair-wise cancellations in RHS.

Similarly, we will see that "complex-balance" gives us some rules for setting RHS = 0 & solving for the prob. distb.

Before solving for the steady-state, let's get the equation for the first moments $\langle n_A \rangle$ & $\langle n_B \rangle$

$$\frac{d}{dt}\langle n_A\rangle = \sum_{n_A,n_B} \bar{k}_1 \left[n_A^2 (n_A+1) P(n_A+1, n_B) - n_A^2 (n_A-1) P(n_A, n_B) \right] \quad (1)$$

$$+ \sum_{n_A,n_B} k_1 \left[n_A (n_A-1) P(n_A-1, n_B) - n_A^2 P(n_A, n_B) \right] \quad (2)$$

$$+ \sum_{n_A n_B} k_2 \left[n_A (n_A+1)(n_A+2) P(n_A+2, n_B-1) - n_A^2 (n_A-1) P(n_A, n_B) \right] \quad (3)$$

$$+ \sum_{n_A n_B} k_3 \left[n_A (n_B+1) P(n_A-1, n_B+1) - n_A n_B P(n_A, n_B) \right] \quad (4)$$

In (1) $\sum_{n_a} \bar{k}_1 \, n_A^2 (n_A+1) P(n_A+1, n_B) \rightarrow \sum_{n_a} \bar{k}_1 (n_A-1)^2 n_A P(n_A, n_B)$

$$\Rightarrow (1) \rightarrow -\bar{k}_1 \langle n_A (n_A-1)\rangle$$

Similarly

$$(2) \rightarrow k_1 \langle n_A \rangle$$

$$(3) \rightarrow -2k_2 \langle n_A (n_A-1)\rangle$$

$$(4) \rightarrow k_3 \langle n_B \rangle$$

$$\Rightarrow \frac{d}{dt}\langle n_A\rangle = k_1 \langle n_A\rangle - (\bar{k}_1 + 2k_2) \langle n_A (n_A-1)\rangle + k_3 \langle n_B \rangle$$

$$\frac{d}{dt}\langle n_B\rangle = k_2 \langle n_A (n_A-1)\rangle - k_3 \langle n_B \rangle$$

This looks pretty close to the equations we get in the deterministic description!

In addition, we can check

$$A \underset{\bar{k}_1}{\overset{k_1}{\rightleftharpoons}} 2A, \quad 2A \xrightarrow{k_2} B, \quad B \xrightarrow{k_3} A$$

$$\frac{d}{dt}\begin{bmatrix} \langle n_A \rangle \\ \langle n_B \rangle \end{bmatrix} = YA \begin{bmatrix} \langle n_A \rangle \\ \langle n_A(n_A-1) \rangle \\ \langle n_B \rangle \end{bmatrix}$$

$$= \begin{bmatrix} 1 & 2 & 0 \\ 0 & 0 & 1 \end{bmatrix} \begin{bmatrix} -k_1 & \bar{k}_1 & k_3 \\ k_1 & -\bar{k}_1 - k_2 & 0 \\ 0 & k_2 & -k_3 \end{bmatrix} \begin{bmatrix} \langle n_A \rangle \\ \langle n_A(n_A-1) \rangle \\ \langle n_B \rangle \end{bmatrix}$$

So the rate eqns we got before look like the eqns. for the 1^{st} moment.

ACK showed that the steady-state prob. distb. can be obtained by "complex-balancing" the probabilities

(1) $P(n_A+1, n_B)\bar{k}_1 n_A(n_A+1) - k_1 n_A P(n_A, n_B) + k_3(n_B+1)P(n_A-1, n_B+1) = 0$

(2) $k_1(n_A-1)P(n_A-1, n_B) - k_2 n_A(n_A-1)P(n_A, n_B) - \bar{k}_1 n_A(n_A-1)P(n_A, n_B) = 0$

(3) $k_2(n_A+1)(n_A+2)P(n_A+2, n_B-1) - k_3 n_B P(n_A, n_B) = 0$

& that a product of Poissons solves these eqns [& by Perron-Frobenius, this is guaranteed to be the soln.]

$$P(n_A, n_B) = \frac{(x_A)^{n_A}}{n_A!} e^{-x_A} \cdot \frac{(x_B)^{n_B}}{n_B!} e^{-x_B} \qquad x_A = \langle n_A \rangle, \quad x_B = \langle n_B \rangle$$

(1) $\Rightarrow$ $\bar{k}_1 x_A^2 - k_1 x_A + k_3 x_B = 0$

(2) $\Rightarrow$ $k_1 - (k_2 + \bar{k}_1)x_A = 0$

(3) $\Rightarrow$ $k_2 x_A^2 - k_3 x_B = 0$

exactly what we got before for the deterministic system!

Anderson-Craciun-Kurtz (ACK) Theorem

Theorem

If a CRN modeled deterministically is complex balanced with a complex balanced fixed point, then the stochastically modeled (mass action) system has a product-form stationary distribution.

Anderson, Craciun and Kurtz, *Bull. Math. Biol.* 72,1947, 2010

$$\mathbf{E+S} \underset{k_1}{\overset{\bar{k}_1}{\rightleftharpoons}} \mathbf{ES} \underset{k_2}{\overset{\bar{k}_2}{\leftrightharpoons}} \mathbf{E+P}$$

$$\mathbf{E} \underset{\bar{k}_3}{\overset{k_3}{\rightleftharpoons}} \mathbf{0}$$

$$\rho = e^{-c_1} \frac{c_1^{n_1}}{n_1!} (N!) \frac{c_2^{n_2}}{n_2!} \frac{c_3^{n_3}}{n_3!} \frac{c_4^{n_4}}{n_4!}$$

$$c_2 + c_3 + c_4 = 1$$

$$n_2 + n_3 + n_4 = N$$

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If a CRN modeled deterministically is complex balanced with a complex balanced fixed point, then the stochastically modeled (mass action) system has a product-form stationary distribution.

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$$\mathbf{E+S} \underset{k_1}{\overset{\bar{k}_1}{\rightleftarrows}} \mathbf{ES} \underset{k_2}{\overset{\bar{k}_2}{\leftrightarrows}} \mathbf{E+P}$$

$$\mathbf{E} \underset{\bar{k}_3}{\overset{k_3}{\rightleftarrows}} \mathbf{0} \underset{\bar{k}_4}{\overset{k_4}{\rightleftarrows}} \mathbf{S}$$

$$\rho(n_1, n_2, n_3, n_4) = \Pi_i e^{-c_i} \frac{c_i^{n_i}}{n_i!}$$

Ex

$$E+S \underset{\bar{k}_1}{\overset{k_1}{\rightleftharpoons}} ES \underset{k_2}{\overset{\bar{k}_2}{\rightleftharpoons}} E+P$$
$$E \underset{k_3}{\overset{k_3}{\rightleftharpoons}} \phi \underset{k_4}{\overset{k_4}{\rightleftharpoons}} S$$

$$P(n_E, n_S, n_{ES}, n_p) = \frac{(x_E)^{n_E}}{n_E!} e^{-x_E} \frac{(x_S)^{n_S}}{n_S!} e^{-x_S} \frac{(x_{ES})^{n_{ES}}}{n_{ES}!} e^{-x_{ES}} \frac{(x_p)^{n_p}}{n_p!} e^{-x_p}$$

$\{x_E, x_S, x_{ES}, x_p\}$ are obtained from the deterministic description

① $(n_E n_S) k_1 \, P(n_E, n_S, n_{ES}, n_p) = \bar{k}_1 \, P(n_E-1, n_S-1, n_{ES}+1, n_p)(n_{ES}+1)$

This gives $k_1 x_E x_S = \bar{k}_1 x_{ES}$

② $\bar{k}_1 n_{ES} \, P(n_E, n_S, n_{ES}, n_p) = k_1 \, P(n_E+1, n_S+1, n_{ES}-1, n_p)(n_E+1)(n_S+1)$

which gives the same condition

Here complex balance is infact detail balanced.

So the ~~pop~~ factorised distribution holds

if we can solve for the $\{x_E, x_S, x_{ES}, x_p\}$.

But from the $\delta = 0$ theorem, we know we can do that. So the ACK theorem holds.

Ex

$$E+S \underset{\bar{k}_1}{\overset{k_1}{\rightleftharpoons}} ES \underset{k_2}{\overset{\bar{k}_2}{\rightleftharpoons}} E+P$$
$$\phi \underset{\bar{k}_3}{\overset{k_3}{\rightleftharpoons}} E$$

$(N_S + N_{ES} + N_p = N \text{ (conserved)})$

$$A \rightarrow \begin{array}{ccccc} \phi & E & E+S & ES & E+P \end{array}$$
$$\begin{bmatrix} -k_3 & \bar{k}_3 & 0 & 0 & 0 \\ k_3 & -\bar{k}_3 & 0 & 0 & 0 \\ 0 & 0 & -k_1 & -\bar{k}_1 & 0 \\ 0 & 0 & k_1 & -\bar{k}_2+\bar{k}_1 & k_2 \\ 0 & 0 & 0 & \bar{k}_2 & -k_2 \end{bmatrix}$$

"complex balance" gives

① $k_3 \, P(n_E-1, n_s, n_{ES}, n_p) = \bar{k_3} \, n_E \, P(n_E, n_s, n_{ES}, n_p)$

② $\bar{k_1} \, P(n_E-1, n_s-1, n_{ES}+1, n_p) \, (n_{ES}+1) = k_1 n_E n_s \, P(n_E, n_s, n_{ES}, n_p)$

$= (\bar{k_1} + \bar{k_2}) \, n_{ES} \, P(n_E, n_s, n_{ES}, n_p)$

③ $\begin{cases} k_1 (n_E+1)(n_s+1) P(n_E+1, n_s+1, n_{ES}-1, n_p) \\ \quad + k_2 P(n_E+1, n_s, n_{ES}-1, n_p+1) (n_E+1)(n_p+1) \end{cases}$

If we put our ansatz

$$P(n_E, n_s, n_{ES}, n_p) \sim \frac{(x_E)^{n_E}}{n_E!} \frac{(x_s)^{n_s}}{n_s!} \frac{(x_p)^{n_p}}{n_p!} \frac{(x_{ES})^{n_{ES}}}{n_{ES}!} \, \text{Norm}$$

we get

$$\left.\begin{aligned} &① \quad \bar{k_3} x_E = k_3 \\ &② \quad k_1 x_E x_s = \bar{k_1} x_{ES} \\ &③ \quad (\bar{k_1} + \bar{k_2}) x_{ES} = k_1 x_E x_s + k_2 x_E x_p \end{aligned}\right\}$$

the same eqns we got before!

$x_s + x_p + x_{ES} = N$

So $P(n_E, n_s, n_{ES}, n_p) = e^{-x_E} \frac{(x_E)^{n_E}}{n_E!} \left(\frac{N!}{n_s! \, n_p! \, n_{ES}!} \right) (c_s)^{n_s} (c_p)^{n_p} (c_{ES})^{n_{ES}}$

$c_s + c_p + c_{ES} = 1 \quad \left(= \frac{x_s + x_p + x_{ES}}{N} \right)$

$$\text{Norm} = \frac{N!}{N^N}$$