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Nth order feedback SDE/Fokker-Planck derivation

List of reactions:

$$
\begin{aligned}
g^0 + p &\xrightarrow{b_{01}} g^1 & \qquad g^0 + p &\xleftarrow{b_{10}} g^1 \\
g^1 + p &\xrightarrow{b_{12}} g^2 & \qquad g^1 + p &\xleftarrow{b_{21}} g^2 \\
g^2 + p &\xrightarrow{b_{23}} g^3 & \qquad g^2 + p &\xleftarrow{b_{32}} g^3 \\
& \cdots \\
g^{N-1} + p &\xrightarrow{b_{N-1,N}} g^N & \qquad g^{N-1} + p &\xleftarrow{b_{N,N-1}} g^N
\end{aligned}
$$

$$
\begin{aligned}
g^0 &\xrightarrow{k_0} g^0 + m \\
g^1 &\xrightarrow{k_1} g^1 + m \\
g^2 &\xrightarrow{k_2} g^2 + m \\
& \cdots \\
g^N &\xrightarrow{k_N} g^N + m \\
m &\xrightarrow{k_p} m + p \\
m &\xrightarrow{d_m} \varnothing \\
p &\xrightarrow{d_p} \varnothing
\end{aligned}
$$

mRNA and protein SDES:

$$
\begin{aligned}
\dot{m} &= \sum_{i=0}^{N} k_i g^i - d_m m + \sqrt{\sum_{i=0}^{N} k_i g^i + d_m m}\ \eta_m(t) \\
\dot{p} &= k_p m - d_p p + \sum_{i=1}^{N} \left[b_{i,i-1} g^i - b_{i-1,i} g^{i-1} p \right] + \sqrt{k_p m + d_p p + \sum_{i=1}^{N} \left[b_{i,i-1} g^i + b_{i-1,i} g^{i-1} p \right]}\ \eta(t)
\end{aligned}
$$

mRNA at QSS forces:

$$
m = \frac{\sum_{i=0}^{N} k_i g^i}{d_m} \ .
$$

Substituting this into the protein SDE yields

$$\dot{p} = \frac{k_p}{d_m} \sum_{i=0}^{N} k_i g^i - d_p p + \sum_{i=1}^{N} \left[b_{i,i-1} g^i - b_{i-1,i} g^{i-1} p \right] + \sqrt{\frac{k_p}{d_m} \sum_{i=0}^{N} k_i g^i + d_p p + \sum_{i=1}^{N} \left[b_{i,i-1} g^i + b_{i-1,i} g^{i-1} p \right]} \; \eta(t) \ .$$

Assuming each binding reaction is at QSS, the protein SDE further reduces to

$$\begin{aligned} \dot{p} &= \frac{k_p}{d_m} \sum_{i=0}^{N} k_i g^i - d_p p + \sqrt{\frac{k_p}{d_m} \sum_{i=0}^{N} k_i g^i + d_p p + \sum_{i=1}^{N} \left[b_{i,i-1} g^i + b_{i-1,i} g^{i-1} p \right]} \; \eta(t) \\ &= \frac{k_p}{d_m} \sum_{i=0}^{N} k_i g^i - d_p p + \sqrt{\frac{k_p}{d_m} \sum_{i=0}^{N} k_i g^i + d_p p + 2 \sum_{i=1}^{N} b_{i,i-1} g^i} \; \eta(t) \ . \end{aligned}$$

Meanwhile, we have that

$$b_{01} g^0 p = b_{10} g^1 \implies g^1 = \frac{b_{01}}{b_{10}} p g^0 \ .$$

Similarly,

$$g^i = \frac{b_{i-1,i}}{b_{i,i-1}} p g^{i-1}$$

for each $i = 1, 2, ..., N$. Defining $B_i := b_{i-1,i}/b_{i,i-1}$ for convenience, it reads

$$g^i = B_i p g^{i-1} \ .$$

Now it is clear that

$$\begin{aligned} g^1 &= B_1 p g^0 \\ g^2 &= B_2 p g^1 = B_1 B_2 p^2 g^0 \\ g^3 &= B_3 p g^2 = B_2 B_3 p^2 g^1 = B_1 B_2 B_3 p^3 g^0 \\ &\vdots \\ g^i &= \left[\prod_{j=1}^{i} B_j \right] p^i g^0 \end{aligned}$$

for each $i = 1, 2, ..., N$. Defining

$$c_i := \begin{cases} \prod_{j=1}^{i} B_j & i = \ 1, 2, ..., N \\ 1 & i = \ 0 \end{cases}$$

for convenience, we have

$$g^i = c_i p^i g^0 \ .$$

Since the total number of gene sites available for transcription is fixed, we have $g^0 + g^1 + \cdots + g^N = G$, where G is the constant total number of gene sites. It should be noted that if $G = 1$, we interpret g^i as the QSS fraction of time that the gene has i protein bound.

Note,

$$\begin{aligned} \sum_{i=0}^{N} g^i &= G \\ \implies \quad g^0 \sum_{i=0}^{N} c_i p^i &= G \\ \implies \quad g^0(p) &= \frac{G}{\sum_{i=0}^{N} c_i p^i} \ . \end{aligned}$$

Then

$$\sum_{i=0}^{N} k_i g^i = \sum_{i=0}^{N} k_i c_i p^i g^0 = \frac{G \sum_{i=0}^{N} k_i c_i p^i}{\sum_{i=0}^{N} c_i p^i} = \frac{G \left[k_0 + k_1 c_1 p + k_2 c_2 p^2 + \cdots + k_N c_N p^N\right]}{1 + c_1 p + c_2 p^2 + \cdots + c_N p^N} \ .$$

Similarly,

$$\sum_{i=1}^{N} b_{i,i-1} g^i = \sum_{i=1}^{N} b_{i,i-1} c_i p^i g^0 = \frac{G \sum_{i=1}^{N} b_{i,i-1} c_i p^i}{\sum_{i=0}^{N} c_i p^i} = \frac{G \left[b_{10} c_1 p + b_{21} c_2 p^2 + \cdots + b_{N,N-1} c_N p^N\right]}{1 + c_1 p + c_2 p^2 + \cdots + c_N p^N} \ .$$

In its final form, the protein SDE reads

$$\begin{aligned} \dot{p} =& \frac{k_p G}{d_m} \ \frac{k_0 + k_1 c_1 p + k_2 c_2 p^2 + \cdots + k_N c_N p^N}{1 + c_1 p + c_2 p^2 + \cdots + c_N p^N} - d_p p \\ &+ \sqrt{\frac{k_p G}{d_m} \ \frac{k_0 + k_1 c_1 p + k_2 c_2 p^2 + \cdots + k_N c_N p^N}{1 + c_1 p + c_2 p^2 + \cdots + c_N p^N} + d_p p + 2G \ \frac{b_{10} c_1 p + b_{21} c_2 p^2 + \cdots + b_{N,N-1} c_N p^N}{1 + c_1 p + c_2 p^2 + \cdots + c_N p^N}} \ \eta(t) \end{aligned}$$