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10/30/18

For a single gene with Nth order self-regulation, the Gillespie noise prescription yields the SDE

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

1 Basic idea behind additive/multiplicative noise approximation

The noise term in the SDE above is

$$\sigma(p) := \sqrt{\frac{k_p G}{d_m}\ \frac{k_0 + k_1 c_1 p + k_2 c_2 p^2 + \cdots + k_N c_N p^N}{1 + c_1 p + c_2 p^2 + \cdots + c_N p^N} + d_p p + 2G\ \frac{b_{10} c_1 p + b_{21} c_2 p^2 + \cdots + b_{N,N-1} c_N p^N}{1 + c_1 p + c_2 p^2 + \cdots + c_N p^N}}\ ,$$

which is somewhat complicated. In many theoretical studies of stochastic gene regulation, it is assumed that the noise term $\sigma(p)$ can be approximated as either

$$\sigma(p) \approx \sigma_a$$

for some constant $\sigma_a > 0$, or

$$\sigma(p) \approx \sigma_m p$$

for some constant $\sigma_m > 0$. The first kind of approximation is called the *additive noise* approximation, and the second kind of approximation is called the *linear multiplicative noise* (or just multiplicative noise) approximation. It can also be useful to consider an approximation that combines the two:

$$\sigma(p) \approx \sigma_a + \sigma_m p\ .$$

Usually these approximations are made without rigorous justification. In this note, we will attempt to justify them by expanding $\sigma(p)$ about p_{ss}, assuming that p is not far from p_{ss}.

2 No regulation

Our Langevin equation reads

$$\dot{p} = \frac{k_p G k_0}{d_m} - d_p p + \sqrt{\frac{k_p G k_0}{d_m} + d_p p}\ \eta(t)\ ,$$

so

$$\sigma(p) = \sqrt{\frac{k_p G k_0}{d_m} + d_p p} \ .$$

By setting $\dot{p} = 0$, we can find that there is just one steady state at

$$p_{ss} = \frac{k_p G k_0}{d_m d_p} \ .$$

Most of the time—especially if our steady state probability distribution is sharply peaked—the protein number p will be near p_{ss}. This means that

$$\epsilon := \frac{p - p_{ss}}{p_{ss}}$$

is small. Now we can write

$$\begin{aligned}
\sigma(p) &= \sqrt{\frac{k_p G k_0}{d_m} + d_p p_{ss}\,(1+\epsilon)} \\
&= \sqrt{d_p p_{ss} + d_p p_{ss}\,(1+\epsilon)} \\
&= \sqrt{2 d_p p_{ss}}\sqrt{1 + \frac{\epsilon}{2}} \ .
\end{aligned}$$

Using the fact that

$$\sqrt{1+x} = 1 + \frac{1}{2}x + \mathcal{O}(x^2)$$

for $x \ll 1$, we can write

$$\begin{aligned}
\sigma(p) &\approx \sqrt{2 d_p p_{ss}}\left[1 + \frac{\epsilon}{4}\right] \\
&= \sqrt{2 d_p p_{ss}}\left[1 + \frac{p - p_{ss}}{4 p_{ss}}\right] \\
&= \sqrt{2 d_p p_{ss}}\left[\frac{3}{4} + \frac{p}{4 p_{ss}}\right] \\
&= \frac{3}{4}\sqrt{2 d_p p_{ss}} + \frac{\sqrt{2 d_p p_{ss}}}{4 p_{ss}} p \\
&= \sqrt{\frac{9}{8}\frac{k_p G k_0}{d_m}} + \sqrt{\frac{d_p^2 d_m}{8 k_p G k_0}} p \ .
\end{aligned}$$

Hence, we can justify approximating $\sigma(p)$ as $\sigma(p) \approx \sigma_a + \sigma_m p$, where

$$\begin{aligned}
\sigma_a &:= \sqrt{\frac{9}{8}\frac{k_p G k_0}{d_m}} \\
\sigma_m &:= \sqrt{\frac{d_p^2 d_m}{8 k_p G k_0}} \ .
\end{aligned}$$

What if we want to approximate $\sigma(p)$ as *only* additive or multiplicative? To approximate $\sigma(p)$ as additive, we can use the same expansion, and just assume that $p = p_{ss}$ (if you had to choose *one* number for p to be, that seems like the most reasonable choice):

$$\begin{aligned}\sigma(p) &\approx \sqrt{2d_p p_{ss}} \left[1 + \frac{p - p_{ss}}{4p_{ss}}\right] \\ &\approx \sqrt{2d_p p_{ss}} \left[1 + \frac{p_{ss} - p_{ss}}{4p_{ss}}\right] \\ &= \sqrt{2d_p p_{ss}} \\ &= \sqrt{2\frac{k_p G k_0}{d_m}} \ .\end{aligned}$$

To approximate $\sigma(p)$ as multiplicative, we can use the fact that $p \approx p_{ss}$, so we can 'multiply by 1':

$$\begin{aligned}\sigma(p) &\approx \frac{3}{4}\sqrt{2d_p p_{ss}} + \frac{\sqrt{2d_p p_{ss}}}{4p_{ss}} p \\ &\approx \frac{3}{4}\sqrt{2d_p p_{ss}} \frac{p}{p_{ss}} + \frac{\sqrt{2d_p p_{ss}}}{4p_{ss}} p \\ &= \sqrt{2d_p p_{ss}} \frac{p}{p_{ss}} \\ &= \sqrt{\frac{2d_p^2 d_m}{k_p G k_0}} \ p \ .\end{aligned}$$

3 First-order feedback

Our Langevin equation reads

$$\dot{p} = \frac{k_p G}{d_m} \ \frac{k_0 + k_1 c_1 p}{1 + c_1 p} - d_p p + \sqrt{\frac{k_p G}{d_m} \ \frac{k_0 + k_1 c_1 p}{1 + c_1 p} + d_p p + 2G \ \frac{b_{10} c_1 p}{1 + c_1 p}} \ \eta(t) \ ,$$

so

$$\sigma(p) = \sqrt{\frac{k_p G}{d_m} \ \frac{k_0 + k_1 c_1 p}{1 + c_1 p} + d_p p + 2G \ \frac{b_{10} c_1 p}{1 + c_1 p}} \ .$$

4 Second-order feedback

Our Langevin equation reads

$$\dot{p} = \frac{k_p G}{d_m} \ \frac{k_0 + k_1 c_1 p + k_2 c_2 p^2}{1 + c_1 p + c_2 p^2} - d_p p + \sigma \ \eta(t) \ ,$$

so

$$f(p) = \frac{k_p G}{d_m} \; \frac{k_0 + k_1 c_1 p + k_2 c_2 p^2}{1 + c_1 p + c_2 p^2} - d_p p \; .$$