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Asymmetric noise without deterministic asymmetry

Given that slight noise asymmetries can create interesting system asymmetries (for example, in state occupancy bias) even without any deterministic asymmetry, one faces a natural question: how can one rig up a system with no deterministic asymmetry, but a little noise asymmetry?

From the point of view of Gillespie's derivation of the chemical Langevin equation, the problem might at first seem impossible. Supposing the concentration of a species x is affected by reactions with propensities $a_1(x)$, $a_2(x)$, and $a_3(x)$ (with species change numbers $\nu_1, \nu_2, \nu_3 \in \{+1, -1\}$), the chemical Langevin equation reads

$$dx = \left[\nu_1 a_1(x) + \nu_2 a_2(x) + \nu_3 a_3(x)\right] dt + \sqrt{a_1(x) + a_2(x) + a_3(x)} dW \ ,$$

where W is a Wiener process. Naively, one expects that whatever terms show up in the deterministic part must show up in the noise part as well.

But with just a little more thinking, we can realize that terms can *cancel* in the deterministic part, but remain in the noise part. For example, suppose that $\nu_1 = 1$, $\nu_2 = 1$, and $\nu_3 = -1$. Then we have

$$dx = \left[a_1(x) + a_2(x) - a_3(x)\right] dt + \sqrt{a_1(x) + a_2(x) + a_3(x)} dW \ .$$

If the reactions associated with $a_2(x)$ and $a_3(x)$ are in equilibrium (so that $a_2(x) = a_3(x)$), then we have

$$dx = \left[a_1(x)\right] dt + \sqrt{a_1(x) + a_2(x) + a_3(x)} dW \ .$$

In other words, the reactions $a_2(x)$ and $a_3(x)$ no longer affect what happens on average, but *do* affect the noise about the mean. In general, one can imagine many reactions roughly at equilibrium contributing mostly to a system's noise.

Let's consider a specific example: a gene that regulates itself (via first-order binding). The associated reactions are

$$\begin{aligned}
g_0 &\xrightarrow{k_m^0} g_0 + m \\
g_1 &\xrightarrow{k_m^1} g_1 + m \\
m &\xrightarrow{k_p} m + p \\
m &\xrightarrow{d_m} \varnothing \\
p &\xrightarrow{d_p} \varnothing \\
g_0 + p &\xrightarrow{b_{01}} g_1 \\
g_1 &\xrightarrow{b_{10}} g_0 + p \ .
\end{aligned}$$

The protein concentration p changes according to

$$dp = [k_p m - d_p p - b_{01} g_0 p + b_{10} g_1] + \sqrt{k_p m + d_p p + b_{01} g_0 p + b_{10} g_1} dW \ .$$

If the self-binding is at equilibrium (and there are $G = g_0 + g_1$ total available gene sites), then

$$\begin{aligned} & b_{01} g_0 p = b_{10} g_1 \\ \implies \ & b_{01} g_0 p = b_{10}(G - g_0) \\ \implies \ & b_{01} g_0 p = b_{10} G - b_{10} g_0 \\ \implies \ & g_0 = \frac{b_{10} G}{b_{01} p + b_{10} g_0} \ , \end{aligned}$$

so that the amount of g_0 changes approximately instantaneously as the protein concentration p changes. Our SDE reads

$$dp = [k_p m - d_p p] + \sqrt{k_p m + d_p p + b_{01} g_0 p + b_{10} g_1} dW \ .$$

The parameters b_{01} and b_{10}, on which there are no restrictions, now tune how much *extra noise* there is.

Can we use this to rig up a bistable switch with asymmetric noise, but symmetric deterministic terms? I think so. Here's a list of reactions analogous to the list above, for two genes that inhibit each other's transcription:

$$
\begin{aligned}
g_x^0 &\xrightarrow{k_m^0} g_x^0 + m_x \\
g_x^1 &\xrightarrow{k_m^1} g_x^1 + m_x \\
m_x &\xrightarrow{k_p} m_x + p_x \\
m_x &\xrightarrow{d_m} \varnothing \\
p_x &\xrightarrow{d_p} \varnothing \\
g_x^0 + p_y &\xrightarrow{b_{01}^x} g_x^1 \\
g_x^1 &\xrightarrow{b_{10}^x} g_x^0 + p_y \\
g_y^0 &\xrightarrow{k_m^0} g_y^0 + m_y \\
g_y^1 &\xrightarrow{k_m^1} g_y^1 + m_y \\
m_y &\xrightarrow{k_p} m_y + p_y \\
m_y &\xrightarrow{d_m} \varnothing \\
p_y &\xrightarrow{d_p} \varnothing \\
g_y^0 + p_x &\xrightarrow{b_{01}^y} g_y^1 \\
g_y^1 &\xrightarrow{b_{10}^y} g_y^0 + p_x \ .
\end{aligned}
$$

As you can see, all of the transcription, translation, and degradation parameters are symmetric. What is *not* symmetric are the binding parameters. Assuming as before that binding is at quasi-equilibrium, the protein concentration SDEs read

$$
\begin{aligned}
dp_x &= [k_p m_x - d_p p_x] + \sqrt{k_p m_x + d_p p_x + b_{01}^x g_x^0 p + b_{10}^x g_x^1} dW_x \\
dp_y &= [k_p m_y - d_p p_y] + \sqrt{k_p m_y + d_p p_y + b_{01}^y g_y^0 p + b_{10}^y g_y^1} dW_y \ ,
\end{aligned}
$$

which look pretty symmetric.

Of course, it turns out that we are cheating a little. m_x and m_y follow slightly different dynamics, because they depend on g_x^0/g_x^1 and g_y^0/g_y^1, respectively (which depend on the binding parameters).

We can construct a purer example. Take the previous mutual inhibition system, and make the binding parameters *exactly* the same, so that the system is *completely* symmetric. But now suppose that species y binds reversibly to species z, and that this binding is at quasi-equilibrium. The list of reactions is almost the same as before, but now we add the extra binding:

$$
\begin{aligned}
g_x^0 &\xrightarrow{k_m^0} g_x^0 + m_x \\
g_x^1 &\xrightarrow{k_m^1} g_x^1 + m_x \\
m_x &\xrightarrow{k_p} m_x + p_x \\
m_x &\xrightarrow{d_m} \varnothing \\
p_x &\xrightarrow{d_p} \varnothing \\
g_x^0 + p_y &\xrightarrow{b_{01}} g_x^1 \\
g_x^1 &\xrightarrow{b_{10}} g_x^0 + p_y \\
g_y^0 &\xrightarrow{k_m^0} g_y^0 + m_y \\
g_y^1 &\xrightarrow{k_m^1} g_y^1 + m_y \\
m_y &\xrightarrow{k_p} m_y + p_y \\
m_y &\xrightarrow{d_m} \varnothing \\
p_y &\xrightarrow{d_p} \varnothing \\
g_y^0 + p_x &\xrightarrow{b_{01}} g_y^1 \\
g_y^1 &\xrightarrow{b_{10}} g_y^0 + p_x \\
z + p_y &\xrightarrow{b_{zf}} zp_y \\
zp_y &\xrightarrow{b_{zr}} z + p_y \ .
\end{aligned}
$$

The protein concentration SDEs are

$$
\begin{aligned}
dp_x &= [k_p m_x - d_p p_x] + \sqrt{k_p m_x + d_p p_x + b_{01} g_x^0 p + b_{10} g_x^1} dW_x \\
dp_y &= [k_p m_y - d_p p_y] + \sqrt{k_p m_y + d_p p_y + b_{01} g_y^0 p + b_{10} g_y^1 + b_{zf} z p_y + b_{zr}(z_{tot} - z)} dW_y \ ,
\end{aligned}
$$

which now *only* differ in the additional noise terms.

In short, we *can* obtain asymmetric noise without deterministic noise. This can be achieved by tweaking binding parameters (although this does not leave the deterministic parts *completely* symmetric), and by having one species experience a reversible reaction in quasi-equilibrium that the other does not experience.