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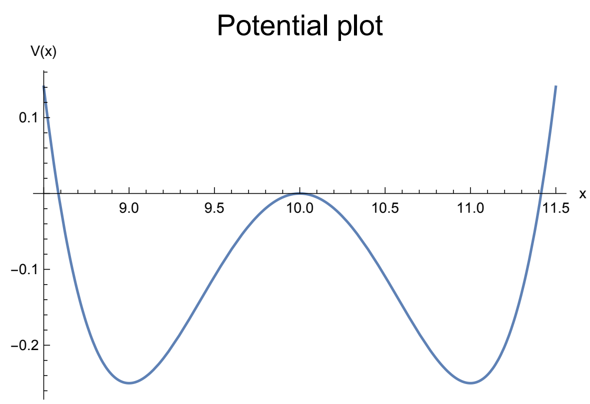
In the standard conceptual picture of the epigenetic landscape, one might imagine a ball rolling around a set of hills and valleys, constantly jostling around with thermal-like motion. This mental picture is misleading; in this note, I will explain why using a simple example.

Imagine a one-dimensional system with two attractors: one corresponds to a steady state with a lower x value, and one corresponds to a steady state with a higher x value. Suppose that the cell sits in the attractor corresponding to the lower x value.

For concreteness' sake, consider a 'Mexican hat'-like potential

$$V(x) = \frac{1}{4}(x-10)^2 - \frac{1}{2}(x-10)^2 \ ,$$

which has a local maximum at $x = 10$ and local minima at $x = 10 \pm 1$.



1 Additive noise

If the system has additive noise, its stochastic dynamics are governed by

$$\dot{x} = -V'(x) + \sigma\eta(t)$$

for some constant $\sigma > 0$. The one-dimensional steady-state Fokker-Planck equation generally reads

$$p' + \frac{2\left[gg' - f\right]}{g^2} p = 0$$

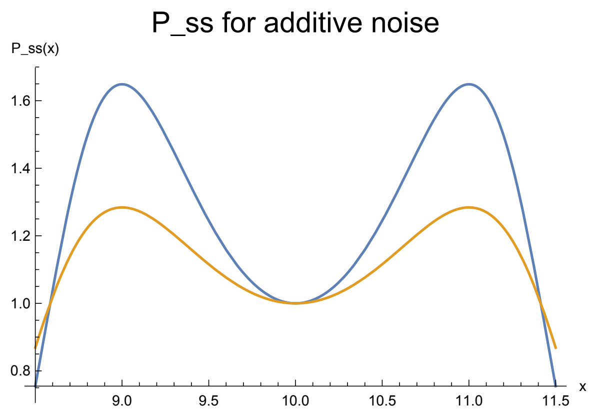
and in this case reads

$$p' + \frac{2\left[V'(x)\right]}{\sigma^2} p = 0 \ .$$

We can easily calculate that the solution is

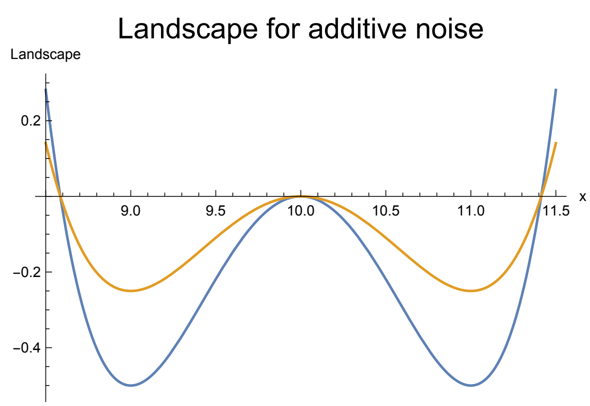
$$p_{ss}(x) = Ne^{-V(x)/(\sigma^2/2)} ,$$

where N is some normalization constant. A graph of this distribution (not normalized) is pictured below for $\sigma = 1$ (blue) and $\sigma = \sqrt{2}$ (orange).



As is plain to see, increasing the additive noise coefficient makes the peaks less sharply defined. One way to think about this is that the probability of being *in between* the attractors goes up; since a ball that jumps the 'hump' between the attractors is overwhelmingly likely to transition, the probability of a transition between attractors goes up.

In terms of the probability landscape ($\phi = -\log p_{ss}$), pictured below, we can see that the p_{ss} with more additive noise (orange) has a lower barrier height, so we imagine transitions to happen more easily.



2 State-dependent noise

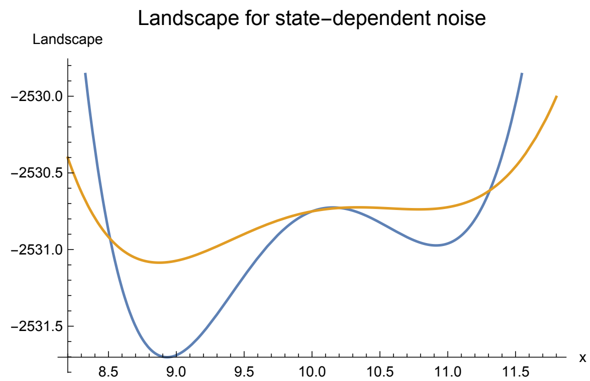
Suppose that the stochastic dynamics of the system are instead governed by

$$\dot{x} = -V'(x) + \epsilon\sqrt{x}\eta(t) ,$$

where $\epsilon > 0$ is small. In this case, our noise is state-*dependent*, so perhaps things will turn out a little differently.

For the choice $\epsilon = 0.6$, the local maxima of p_{ss} turn out to be $x_1 = 8.87458$ and $x_3 = 10.7865$, and the local minimum becomes $x_2 = 10.3389$. Recall that these numbers were $x_1 = 9$, $x_3 = 11$, and $x_2 = 10$ in the additive noise case; the attractors were shifted slightly to the left, and the unstable steady state was shifted slightly to the right.

For the choice $\epsilon = 0.3$, we have $x_1 = 8.93208$, $x_3 = 10.9143$, and $x_2 = 10.1536$. The two probability landscapes are plotted below, with $\epsilon = 0.3$ in blue and $\epsilon = 0.6$ in orange.



As noise (ϵ) is increased (going from blue to orange), the attractor on the right effectively disappears. While it is true that the 'barrier height' decreases, the greater shallowness of the attractor on the right causes transitions to be less and less likely as ϵ increases.

Hence, if the cell starts in the left attractor, and ϵ is increased, the probability of a transition to the right well will actually *decrease!* This fact is not well-represented by imagining a ball with increased thermal motion.