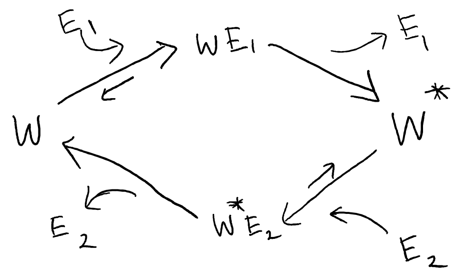
Ultra-sensitivity through opposing forces

Ph 409, Arvind Murugan. Assigned Oct 10, 2015. Due Oct 19, 2015.

Ultra-sensitivity is the sharp response of the state of a system (e.g., rotation of the E Coli flagella motor) to a small change in the concentration of a signaling molecule (e.g., CheY-P). Ultra-sensitivity can be quantified by the Hill coefficient n which is the slope of output plotted against log(input).

In equilibrium systems, achieving $n > 1$ requires n binding sites and cooperativity in some form (e.g., the Monod-Wyman-Changeaux (MWC) model). In contrast, non-equilibrium driving by opposing forces can achieve arbitrary n with simple reaction networks.

The Koshland-Goldbetter mechanism is the earliest of such examples:

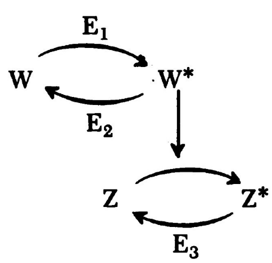


Assume all reactions to be first-order with arbitrary kinetic constants. For e.g., the equation for W would read,

$$\frac{d[\mathrm{W}]}{dt} = -a_1[\mathrm{W}][\mathrm{E}_1] + d_1[\mathrm{WE}_1] + k_2[\mathrm{W^*E}_2]$$

By solving all the equations for steady-state, find the parameter regime in which $[W^*]/[W]$ is ultra-sensitive to the value of $[E1]_{total}/[E2]_{total}$. What is the Hill coefficient?

Without doing any complex calculations, figure out what the Hill coefficient when you cascade two such loops:



Both clippings taken from Goldbetter, Koshland PNAS Nov 1981, Vol 78, No 11. You can consult the paper for help, provided you understand what you are doing.