Gain control in molecular information processing

Ilya Nemenman[1]

***Short Abstract* — Statistical properties of environments experienced by biological signaling systems in the real world change, which necessitates adaptive responses to achieve high fidelity information transmission. One form of such response is gain control. Here we argue that a certain simple, *non-adaptive* mechanism of gain control, understood well in the context of systems neuroscience, translates to molecular signaling as well. The mechanism allows to transmit more than one bit (*on* or *off*) of information about the signal independently of the signal variance. It does not require additional molecular circuitry beyond that already present in many molecular systems, and, in particular, it does not depend on existence of feedback loops. The mechanism provides a potential explanation for certain aspects of structural organization of biological regulatory networks.**

***Keywords* — Adaptation, information, signaling.**

I. Purpose

In molecular signaling systems, the response $r(t)$ is produced from the signal $s(t)$ by some (possibly nonlinear and noisy) dynamics. For example, in a simple deterministic molecular circuit, we may have $dr/dt = f(s(t)) - kr$, where f is the synthesis rate of the response molecule, which depends on the current value of the signal, and k is the rate of the first-order degradation of the molecule.

The distribution of the signal, $P[s(t)]$, places severe constraints on f. For example, for quasi-stationary signals, we can write the steady state dose-response curve $r_{ss}=f(s)/k$. A typical monotonic, sigmoidal f is characterized by only a few large-scale parameters: the range, f_{min} and f_{max}; the mid-point $s_{1/2}$; and the width of the transition region, Δs (see Fig. 1). The mean of the signal, μ, and its standard deviation, σ, must match $s_{1/2}$ and Δs for the information transmitted by this molecular system to be large [1]. Multiple adaptive feedback mechanisms have been explored to match the mean and the mid-point [2], but a lot less is known about the gain control, that is, matching Δs to σ.

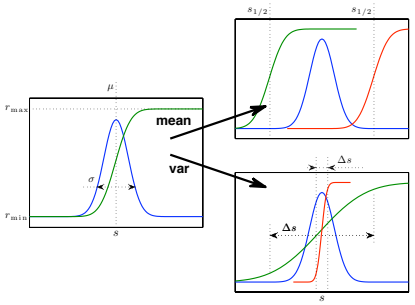

Fig 1. Characterizing a response. Left: the probability distribution of the signal, $P(s)$ (blue), and the best-matched steady state response curve r_{ss} (green). Top right: if the mid-point of r_{ss} is far away from the signal mean, a typical response will be extremal. Bottom right: if the width of r_{ss} doesn't match the signal standard deviation, then the typical response is either extremal, or near the middle. These mismatches lower the information the response conveys about the signal.

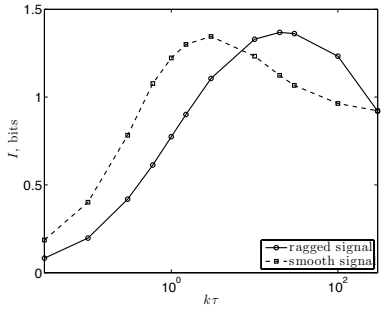

Fig. 2. The signal-response mutual information for different signal distributions and for various response degradation rates.

II. Results

Following similar analysis in the context of signal processing in neural systems [3], we see that, for a step-like f, temporal dynamics of the stimulus can be used to make the response insensitive to the signal variance. Specifically, the value of s/σ, but not s itself, is correlated with how long the signal has stayed positive, and hence with the duration of the increase in the response, and, finally, with its value. This happens without any additional molecular circuitry and, in particular, without feedback-driven adaptation common to the mean/mid-point of response matching.

We analyze the dependence of this observation on the details of the synthesis/degradation functions and on the temporal properties of the signal, see Fig. 2. We find our conclusions to be robust to these variations, and, in particular, we show that such signaling systems can communicate more than one bit of information in a gain-independent fashion, even when the synthesis function f is binary (step-like).

[1]Departments of Physics and Biology, and Computational and Life Sciences University Strategic Initiative, Emory University, Atlanta, GA 30322, USA. E-mail: ilya.nemenman@emory.edu

References

[1] Laughlin S, *Z. Naturforsch*. **36**, 910 (1981).
[2] Berg H, *E. coli in motion* (Springer-Verlag, New York, 2003).
[3] Borst A, Flanagin A, and Sompolinsky H, *Proc. Natl. Acad. Sci. (USA)* **102**, 6172 (2005).