Trade-off between resistance to external and internal fluctuation in biophysical sensing

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***Short Abstract* — Cells must extract relevant information from time-varying external signals while ignoring a sea of other irrelevant fluctuations in those signals. We find that biophysical mechanisms that are most effective at projecting out irrelevant external fluctuations are most vulnerable to the internal noise originated from the mechanisms themselves. We show this trade-off relationship in biochemical receptors that measure ligand concentrations, in regulatory circuits that measure rate of concentration changes and in circadian clocks that measure the phase of the external day-night cycle. We trace this trade-off to a fundamental tension in the length of time used to make a measurement; slow measurements average out external fluctuations but make the system vulnerable to internal fluctuations and vice-versa. We show how such a trade-off emerges in the non-linear dynamical systems that underlie these diverse biological mechanisms.**

***Keywords* — Noise, Dynamical Systems, Computation in Cells, Circadian clocks, Chemosensing, Adaptation**

I. Purpose

Extracting information from a noisy external signal is fundamental to the survival of organisms in dynamic environments [1]. From yeast anticipating the length of starvation and bacteria estimating sugar availability, to dictyostelium counting cAMP pulses, organisms must often filter noisy irregular aspects of the environment while inferring parameters about a regular aspect in order to be well-adapted . However, in addition to external fluctuations, organisms must also deal with internal fluctuations due to finite copy number effects, bursty transcription and other biomolecular fluctuations. While such the impact of noise has been extensively documented, it is not clear whether different sources of noise are equivalent and whether strategies to mitigate them are compatible.

II. Method

We start by analytically showing the trade-off between resistance to external and internal fluctuation in the abstract context of Bayesian estimators – we consider a simple moving average estimator, a slope estimator, and a phase estimator. Then, we use simulations and theory using realistic biophysical mechanisms to show how such trade-offs emerge in non-linear dynamical systems viewed as Bayesian estimators.

III. Result

For all the cases we consider, we found the a trade-off along a Pareto front defined by:

$$\sigma_{int}^2 \sigma_{ext}^2 \sim 1$$

,where σ_{int}^2 and σ_{ext}^2 are the variance of the outputs due to internal and external fluctuation respectively. We arrived at this equation separately from mean estimator, slope estimator, and phase estimator. Here, we also present the simulations of 3 main biological estimators in the push-pull network in chemoreception [3] for moving average estimators, the adaptive network in concentration ramp sensing [2] for slope estimators, and the circadian clock network in [4] for phase estimators.

The universal reasons that the trade-off holds in non-linear biological estimators as well relates to the geometry of the attractor system. To be robust against external fluctuation, the geometry of the estimator's dynamics needs to be flat in the projected dimension of the information in the signal and curved along the direction of the external noise. However, this flat direction makes internal fluctuation diffuse faster, resulting in poor accuracy. Intuitively, the curvature of this flat direction relates to the time scale of the estimator's measurement that trace the performance along the Pareto front. We discuss how result is related to gain-bandwidth trade-offs in some contexts and discuss speed-error trade-offs in these systems. We find that while slow estimators are more accurate when subject to external fluctuations, such a speed-error tradeoff is absent in the context of internal fluctuations – fast estimators are the most accurate estimators.

References

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