On the Connection between Computational and Biochemical Measurement

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***Short Abstract* — Cells use readout molecules to record the state of cell-surface receptors, apparently analogously to computational measurements. But at what level does this analogy hold? Do living cells operate at the thermodynamic limits of efficiency? We consider a canonical biochemical network for receptor readout and map it onto a typical idealized computational measurement protocol. The biochemical network does not achieve thermodynamic limits of efficiency, facing a tradeoff between dissipation and accuracy of measurement that is more severe than and qualitatively distinct from that required thermodynamically. Biomolecules can, however, perform optimal measurements when the concentrations of ATP and ADP are externally manipulated.**

***Keywords* — Cellular sensing, computation, biochemical networks, non-equilibrium thermodynamics.**

I. Introduction

From the literature on computation developed in the 20th century, and particularly in the wake of Maxwell's demon, much is known about the thermodynamics of taking a measurement or copying a system's state into a memory device. If it were possible to perform many measurements using a single bit of memory without putting in work, Maxwell's demon would be able to violate the second law of thermodynamics. It has been argued, however, that this is impossible, and the necessity of work in the measurement cycle has been demonstrated in a range of physical models [1-3]. The Landauer bound of kTln2 sets the minimum amount of work that is required to perform a copy if it is perfectly accurate and has a 50/50 outcome [1,3].

At least superficially, many biological processes appear to perform computational copies [1]. Perhaps the most tantalising analogy is in the context of cellular sensing of external ligand concentrations. In 1977, Berg and Purcell suggested remarkable accuracy can be achieved in spite of the noisy signal from a single receptor by averaging the receptor signal over time [4]. It has since been argued that downstream signaling networks can achieve this by taking multiple measurements of the same receptor, essentially copying the receptor's state into memory [5-7]. Currently, however, the analogy between computational and biological systems is qualitative, rather than quantitative. How efficient are biological networks at performing copies, and can they reach the Landauer bound? Can the action of biological networks be understood in terms of typical idealised computational protocols?

In this work we formally describe a steady-state receptor-readout network as a process that performs copies at a certain rate and with a certain accuracy. We relate the network directly to typical idealized protocols from the computational literature, highlighting the limitations placed on the biochemical network. We find that the biochemical network does not reach the limits of thermodynamic efficiency, with a cost per copy that diverges logarithmically as the system approaches 100% accuracy. This deviation is qualitative as well as quantitative, and optimal behaviour cannot be achieved simply by reducing copying speed. The biochemical network, however, is more adaptive than standard thermodynamically optimal protocols. Biased measurement outcomes (i.e., not 50:50) have a lower minimal cost per measurement [3], but achieving this limit requires a distinct ideal protocol for each bias. By contrast, the biochemical network automatically adapts to dissipate less when the measurement outcome is biased.

Fundamentally, the biochemical network has a constant thermodynamic drive set by the free energy stored in fuel molecules such as ATP, whereas optimally efficient computational protocols involve quasistatic manipulation of biasing potentials. We conclude by demonstrating that this difference can be overcome through exogeneous manipulation of ATP and ADP concentrations. This approach enables the design of biochemical protocols that reach the optimal Landauer bound. Our proposed system suggests a novel setting for the experimental investigation of non-equilibrium and computational thermodynamics.

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