DOCTORAL DEFENSE

Physical Limits to Cellular Sensing of the Environment

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Abstract: Cells must accurately sense various aspects of their environment for survival. In 1977, Berg and Purcell initiated a line of work placing physical limits on cell sensing. The work herein is a continuation of this tradition. In our first project, we studied the effect of critical biochemical feedback on cell sensing. Using a concrete model, we weighed the trade-offs between high susceptibility, long-range correlations and critical slowing down. We found that the critical system could have high steady state mutual information between a ligand and an internal readout molecule if the ligand dynamics are sufficiently slower than the intracellular dynamics. However, the information rate is always minimized at the critical point due to critical slowing down. Our second and third projects involved deriving lower bounds on signal-to-noise ratios for environmental variables, much like the initial work of Berg and Purcell. The novelty is that the sensed quantities are fluid flow direction and temperature. These extend the range of their work, as these are non-chemical cues, however, they are sensed using molecules. Our work on flow sensing was motivated by studies on metastatic cancer cells that showed they could detect the direction of fluid flow. They do so by secreting molecules that are pushed by the flow and return to the surface anisotropically. We compared two different strategies for signal transduction: endocytosis and reversible binding. We found that reversible binding admits a lower relative error than endocytosis. The endocytosis model has an optimal absorption rate. We use experimental data to argue that the endocytosis rate is far from the optimum, supporting the possibility that receptor binding transduces the information. In our third project, we started by computing the relative error in temperature sensing arising from its own fluctuations. We found that it was too low to be limiting. Temperature sensing is indirect, it is transduced from molecular conformations, changing reaction rates, or various mechanical properties. Turning to a biochemical model based on the canonical protein thermometer TlpA, we found that the error arising from the biochemical reactions dominated the system. We discuss the connection to existing experimental data.