Dynamic Decision Making by Intracellular Kinetics

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Short Abstract —**Decision making in a noisy and dynamically changing environment is a fundamental task for a cell. To choose appropriate decisions over time, a cell must be equipped with intracellular kinetics that can conduct dynamic and efficient decision making. By using the theory of sequential inference, I demonstrate that a dynamic Bayesian decision making can be implemented by an intracellular kinetics. I also clarify that the dynamical properties of the kinetics that dominantly contributes to decision making efficiency, and their underlying statistical principles.**

Keywords — **Bayesian inference, Zero-order ultrasensitivity.**

I. Introduction

Cells are subject to unpredictable environmental changes with regard to the presence of nutrients, toxic molecules, or signaling molecules from other cells. They have developed intracellular kinetics that allows them to actively make a decision by quickly detecting a change of the received signals. Of particular interest is that cells can conduct such decision even with substantial noise in the environment and intracellular reactions[1]. Yet to be revealed, however, is how to implement such efficient decision making dynamics by the intracellular kinetics [2].

II. Modelling

To address this problem, I formulate the decision making dynamics of a cell using sequential Bayesian inference [3]. The simplest decision that a cell makes is whether the environment, $\mathbf{x_t}$, is in a certain state or in another state, denoted here as the **on** state and the **off** state, respectively. Since the environment is not stationary over time, its state changes unpredictably. This random change is statistically modeled by a two-state continuous Markov process in which the transition rate from $\mathbf{x_t}$**=off** to $\mathbf{x_t}$**=on** and from $\mathbf{x_t}$**=on** to $\mathbf{x_t}$**=off** is r_t**=on** and $\mathbf{x_t}$**=off**, respectively. A cell, in general, cannot directly observe the state of the environment. Instead, the state is inferred from noisy reactions of receptors on its membrane. Since the state of each receptor is also binary (i.e., active or inactive), for most situations, the observation via receptors can be represented by a vector of binary variables $\mathbf{s_t}$, where the **i**-th component of $\mathbf{s_t}$ is the state of the **i**-th receptor at time **t**. $\mathbf{s^i_t}$**=1** when state is active, and $\mathbf{s^i_t}$**=0** when state is inactive. The length of the vector, $\mathbf{N_0}$, is the total number of receptors. As the environment changes, the pattern of activation of the receptors also changes dynamically. The information carried by the activation pattern, however, is substantially obscured by the stochastic reactions of the receptors. This erroneous reaction of receptors is modeled by a Poisson point process in which the parameter $\boldsymbol{\lambda_t}$**=** $\boldsymbol{\lambda(x_t)}$ is a function of the state of the environment. Under these settings, I derived the statistically optimal kinetics to infer the state of environment from the noisy observation via receptor activations as

$$\frac{dP}{dt} = F(P,S(t))(1-P) - G(P)P + r_{on}(1-P) - r_{off}P$$

where **P** is the posterior probability that the environment is in the **on** state, $F(P,S(t)) = N_0 P \lambda_r S(t)$, $G(P) = N_0(1-P)\lambda_d$, $\lambda_r = \log \lambda(on)/\lambda(off)$, $\lambda_d = \lambda(on) - \lambda(off)$, **S(t)** is the normalized activities of receptors at **t** If we regard P as the ratio of modified intracellular protein, this kinetics of **P** can be interpreted as a covalent modification reaction of the molecules, which has autoregulatory positive feedbacks described with **F(P,S(t))** and **G(P)**.

III. Results

By numerical simulation, I demonstrate that this kinetics can extract the information of environment from extremely noisy receptor signals. By comparing this kinetics with several other intracellular kinetics including zero-order ultrasensitivity, I also clarify that two dynamical factors dominantly contribute to the decision making efficiency: the combination of linear instantaneous sensitivity and nonlinear stationary sensitivity to the input, and state-dependent sensitivity change. The statistical principles underlying these two factors are further clarified to be log-likelihood-dependent quantification of the input information and uncertainty-dependent sensitivity control[4].

References

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