

Fisher information analysis for first passage time distributions of stochastic biochemical reaction networks

Zachary R Fox

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Abstract

First passage time dynamics are useful for studying when an event can be expected to happen. In biochemical reaction networks, they have been analyzed in a variety of contexts [? ? ?] to understand not just when biochemical events are likely to happen but with what variability one can expect. In this study, we develop a form of the Fisher information matrix to understand how sensitive the first passage time may be to different relevant quantities for biochemical systems, such as thresholds of molecule counts [? ?], biochemical reaction rates (i.e. protein decay rates), and more.

The chemical master equation [?] is the workhorse of stochastic biochemical reaction networks, with bleh blah blehh blah. This set of ODE's can be compactly written as $\frac{d\mathbf{p}}{dt} = \mathbf{A}\mathbf{p}$. The finite state projection approach truncates this infinite set of ODE's into a finite subset which, when \mathbf{A} is not time-varying, leads to the creation of a set of ODEs which has the solution

$$\mathbf{p}(x, t; \boldsymbol{\theta}) = \exp(\mathbf{A}(\boldsymbol{\theta})t)\mathbf{p}_0. \quad (1)$$

Using the FSP, one can easily find a first-passage time distribution by noting that the exit of probability from the state space into the FSP sink $g(t)$ is simply $\frac{dg}{dt} = -\mathbf{1}\mathbf{A}_{JJ}\mathbf{p}(t)$. Therefore, the equation $g(t)$ is the cumulative density of the first passage time distribution,

$$F(t) = 1 - \mathbf{1}^T \exp(\mathbf{A}_{JJ}t)\mathbf{p}_0 \quad (2)$$

and the first passage time distribution is $f(t) = \frac{\partial F(t)}{\partial t}$,

$$f(t) = -\mathbf{1}^T \mathbf{A}_{JJ} \exp(\mathbf{A}_{JJ}t)\mathbf{p}_0. \quad (3)$$

The moments of this distribution are

$$\mathbf{E}[t^n] = (-1)^n n! \mathbf{1}^T \mathbf{A}_{JJ}^{-n} \mathbf{p}_0. \quad (4)$$

The Fisher information matrix has recently been used to analyze stochastic biochemical reaction dynamics [?] in terms of model and parameter identifiability and experiment design. So far, these approaches rely on measuring molecular species over time, and using directly the molecular abundances or their moments to construct the FIM,

$$\mathcal{I} = xx \quad (5)$$

While previous