

On the Stochastic Modeling of the JAK-STAT Signal Transduction Pathway

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Abstract: At the level of individual cells, signaling is crucial for decisions about division, specialization, death and metabolic control. For more advanced organisms, it controls growth, development, behavior and metabolism; defective signaling is therefore at the origin of many diseases, like cancer, diabetes and developmental illnesses. Here we propose a stochastic framework based on multivariate nonlinear stochastic differential equations to describe the dynamics of the JAK-STAT signal transduction pathway. This signal transduction through the erythropoietin receptor (EpoR) is essential for proliferation and differentiation of erythroid progenitor cells.

Such a stochastic model consists of a known or proposed model structure including stochastic terms which represent disturbances, inputs to the system and unmodelled dynamics of the system. Thus, it is possible to use a priori (biophysical and/or biochemical) knowledge and at the same time to describe the noise in the system by combining a deterministic part with a stochastic one, along with information from data. This makes this approach an attractive tool for modeling the signal transduction dynamics, since the latter are not thoroughly understood or cannot be explicitly modelled deterministically. We consider here stochastic analogs of recent mathematical models of Timmer et al. (PNAS 2003, Int.J.Bif.Chaos 2004) for characterizing the dynamical behavior of the JAK-STAT signaling pathway via differential equations. We analyse our models and estimate the parameters upon using some nonlinear filtering techniques. Moreover, we also consider the case where the noise processes appearing in the observations are correlated.

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