

Stochastic Dynamical Systems: Spectral Methods for the Analysis of Dynamics and Predictability

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Summary

To enable analysis of stochastic dynamical systems, e.g. stochastic reaction network models of gene regulatory networks, we developed spectral stochastic methods for sensitivity analysis and reduced order modeling. These methods allow a more fundamental understanding of these systems and provide insight into the dominant reactions that drive their observed dynamics.

Given recent advances in nanotechnology and biophysics, many nanoscale phenomena can now be studied quantitatively on a molecular level. At this scale, stochastic effects often play a dominant role in system behavior and function. In particular, random noise plays an important role in the dynamical behavior, such as switching between different branches, of gene regulatory networks in biological cells. Stochastic dynamics are also of importance in the surface catalytic reactions taking place in fuel cells.

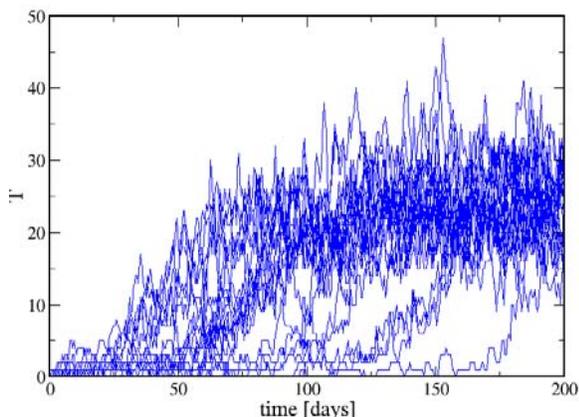


Figure 1. Sampling of simulated trajectories of a stochastic viral kinetics model.

Fig. 1 shows an example of the behavior of a stochastic dynamical system, namely a stochastic reaction network model for the intracellular kinetics of a non-lytic virus [1]. Individual realizations of the population of the template species (T) exhibit significant variability, with some infections taking off rapidly, while others are delayed or die off.

In order to properly understand the dynamics and function of such systems, new analysis tools need to be developed for stochastic dynamical systems. Over the past year, we have developed methods for local sensitivity analysis as well as reduced order modeling, using spectral expansions for representing random variables and stochastic processes. Our advances in both of these areas are summarized below.

Sensitivity analysis is concerned with the assessment of the relative contribution of each of the parameters of a computational model on the observables of interest. In our work, sensitivity analysis is performed by assigning properly chosen perturbations to the parameters of interest. Those perturbations are represented with spectral polynomial chaos expansions (PCEs), which

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are propagated through the dynamical system using non-intrusive spectral projection methods to obtain their effect on the observables of interest. The result is a response surface from which the sensitivities are derived. Quadrature-based sampling methods are used for efficiency.

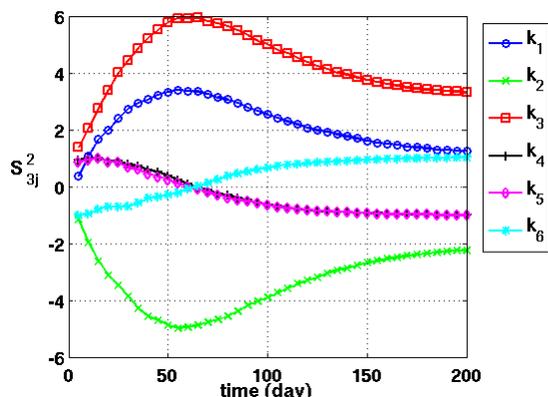


Figure 2. Sensitivity of viral production rate with respect to the 6 model parameters

Fig. 2 shows the sensitivity of the expected viral production rate with respect to each of the rate constants in the above viral kinetics model. It is clear that the 2nd and 3rd rate constant have the dominant effect, which points at the relevance of the template decay and genome production reactions. For further detail, see Kim *et al.*, 2006 [2]

In the second part of this work, we used Karhunen-Loève (KL) decompositions for reduced order modeling of stochastic dynamical systems. This method represents the system as a sum of eigenmodes that are multiplied with associated random variables. While a very large number of KL modes would be required to replicate the *full* dynamics of the original system, we have shown that a relatively small number (10) is sufficient for capturing the large scale dynamics of interest.

The modes in the KL decomposition can be also used to further analyze the dynamics of the system. In a bi-stable system, the first

mode is much larger than the others, and the sign of the associated bimodal random variable indicates which branch the system state is in. For the same system, but with larger stochastic noise levels, the system moves back and forth between the two branches. The corresponding modes are much closer in magnitude and have associated unimodal random variables.

We plan to expand this work to include predictability analysis, while also improving the generality and robustness of these methods, to make them more widely applicable on larger-scale systems with both parametric and inherent uncertainties.

Our application of spectral expansions to stochastic dynamical systems enables their detailed analysis. This capability therefore allows a more fundamental understanding of these systems, provides insight into dominant reactions that drive their observed dynamics, and can facilitate design of strategies for manipulation of these systems. When applied to biosystems, for example, this analysis could indicate what causes an organism to go from a healthy to a diseased state, and which reaction mechanisms would need to be targeted with drugs to bring the organism back to health.

References

- [1] Srivastava, R. *et al.*, J. Theoretical Biology, 218:309-321, 2002.
- [2] Kim, D., Debusschere, B., and Najm, H., “Spectral methods for parametric sensitivity analysis in stochastic dynamical systems”, under revision for the Biophysical Journal, 2006.

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