Model Reduction in Genetic Control Models

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Although a cell's metabolic and genetic control machinery are chemical in nature, genetic control models present special challenges not seen in "ordinary" chemistry. For example, the time required to transcribe or translate a gene is frequently represented by delayed terms in the differential equations. These delayed terms are an implicit, abstract representation of the very large number of intermediate states of template-polymerase-copy complexes (DNA-RNA polymerase-RNA or RNA-ribosome-protein). The delay-differential equations obtained generally look simpler than would a fully detailed model, which has definite conceptual advantages. Accordingly, most genetic control models which consider the transcription and translation times generally do so through a delay-differential equation representation. However, the computational complexity of these models is roughly as great as that of a fully detailed model due to the necessity to keep track of past states. Moreover, the theoretical treatment is substantially complicated by the fact that delay-differential equations define an evolution on a function space rather than on the more natural state (i.e. concentration) space of the model.

Some time ago, I presented an approximate method for computing state-space manifolds of some systems of delay-differential equations (J. Chem. Phys. 109, 8154, 1998). This method, which is essentially exact for small delays, both reduces the number of equations and eliminates the delayed term(s). However, the method yields only a first-order approximation and cannot be extended to higher orders as the delay increases. In another line of research, we have studied the correspondence between delay-differential equations and models with explicit intermediates (J. Phys. Chem. 100, 8323, 1996; Roussel and Roussel, Physics in Canada 57, 114, 2001). We have found that relatively few intermediates are necessary to recover the behavior of the delayed model semi-quantitatively. This opens an interesting possibility for producing reduced versions of models with delays in two steps: First, replace the delayed terms by appropriately constructed chains of intermediates. Second, apply an invariant manifold construction method such as Fraser's iterated functional mapping. The result should be a small system of ordinary-differential equations which accurately represents the long-time evolution of the original set of delay-differential equations.