

Dominant systems for multiscale reaction networks

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We propose a systematic treatment of model reduction of multiscale reaction networks. First, we consider linear kinetic models, which appear as “pseudo-monomolecular” subsystems of multiscale nonlinear reaction networks. For such linear models, we propose a reduction algorithm which is based on a generalized theory of the limiting step developed by Gorban & Radulescu (2008).

For any ordering of reaction rate constants we look for the dominant kinetic system. The dominant system is, by definition, the system that gives us the main asymptotic terms of the stationary state and relaxation in the limit for well separated rate constants. In this limit any two constants are connected by the relation \gg or \ll .

The topology of dominant systems is rather simple; they are those networks which are graphs of discrete dynamical systems on the set of vertices. In such graphs each vertex has no more than one outgoing reaction. This allows us to construct the explicit asymptotics of eigenvectors and eigenvalues. In the limit of well separated constants, the coordinates of eigenvectors for dominant systems can take only three values: ± 1 or 0 . All algorithms are represented topologically by transformation of the graph of reaction (labeled by reaction rate constants). We call these transformations “cycles surgery”, because the main operations are gluing cycles and cutting cycles in graphs of auxiliary discrete dynamical systems.

In the simplest case, the dominant system is determined by the ordering of constants. But for sufficiently complex systems we need to introduce auxiliary elementary reactions. They appear after cycle gluing and have monomial rate constants of the form $k_\zeta = \prod_i k_i^{s_i}$. The dominant system depends on the place of these monomial values among the ordered constants.

Construction of the dominant system clarifies the notion of limiting steps for relaxation. There is an exponential relaxation process that lasts much longer than the others. This is the slowest relaxation and it is controlled by one reaction in the dominant system, the limiting step. The limiting step for relaxation is not the slowest reaction, or the second slowest reaction of the whole network, but the slowest reaction of the dominant system. That limiting step constant is not necessarily a reaction rate constant for the initial system, but can be

represented by a monomial of such constants as well.

The idea of dominant subsystems in asymptotic analysis was proposed by Newton and developed by Kruskal (1963). In our analysis we do not use the powers of small parameters but operate directly with the rate constants ordering.

To develop the idea of systems with well separated constants to the state of a mathematical notion, we introduce multiscale ensembles of constant tuples. This notion allows us to discuss rigorously uniform distributions on infinite space and gives the answers to a question: what does it mean “to pick a multiscale system at random”.

Some of results obtained are rather surprising and unexpected. First of all is the zero-one asymptotic of eigenvectors. Then, the good approximation to eigenvectors does not give approximate eigenvectors (the inverse situation is more common: an approximate eigenvector could be far from the eigenvector). The almost exact lumping analysis provided by the zero-one approximation of eigenvectors has an unexpected property: the lumped groups for different eigenvalues can intersect (compare to the classical results of approximate lumping analysis by Kuo & Wei (1969)). Rather unexpected seems the change of reaction sequence when we construct the dominant systems. And, of course, it was surprising to observe how the dynamics of linear multiscale networks transforms into the dynamics on finite sets of reagent names.

In this work, in addition to our previous research (Gorban & Radulescu (2008)) we

- Construct dominant systems for the reaction network that has a group of constants with comparable values (without relations \gg between them).
- Construct dominant systems for reaction networks with modular structure. We assume that the ratio of any two rate constants inside each module be bounded and separated from zero, but the ratios between modules form a well separated ensemble. We describe all solvable modules such that it is possible to solve the kinetic equation for every module in explicit analytical (algebraic) form with quadratures.

Now we have the complete theory and the exhaustive construction of algorithms for linear reaction networks with well separated rate constants. There are several ways of using the developed theory and algorithms:

1. For direct computation of steady states and relaxation dynamics; this may be useful for complex systems because of the simplicity of the algorithm and resulting formulas and because often we do not know the rate constants for complex networks, and kinetics that is ruled by orderings rather than by exact values of rate constants may be very useful;
2. For planning of experiments and mining the experimental data – the observable kinetics is more sensitive to reactions from the dominant network, and much less sensitive to other reactions, the relaxation spectrum of the dominant network is explicitly connected with the correspondent reaction rate constants, and the eigenvectors (“modes”) are sensitive to the constant ordering, but not to exact values;
3. The steady states and dynamics of the dominant system could serve as a robust first approximation in perturbation theory or as a preconditioning in numerical methods.

The developed methods are computationally cheap, for example, the algorithm for construction of dominant system has linear complexity (\sim number of reactions).

The next step should be construction of dominant systems for nonlinear reaction networks. The first idea here is the representation of a nonlinear reaction as a pseudomonomolecular reaction: if for reaction $A + B \rightarrow \dots$ concentrations c_A and c_B are well separated, say, $c_A \gg c_B$, then we can consider this reaction as $B \rightarrow \dots$ with rate constant dependent on c_A . The relative change of c_A is slow, and we can consider this reaction as pseudomonomolecular until the relation $c_A \gg c_B$ changes to $c_A \sim c_B$. We can assume that in the general case only for small fraction of nonlinear reactions the pseudomonomolecular approach is not applicable, and this set of genuinely nonlinear reactions changes in time, but remains small. First steps of this research program are done in the recent work by Radulescu & Gorban & Zinovyev & Lilienbaum (2008).

Finally, the concept of “limit simplification” will be developed. For multiscale nonlinear reaction networks the expected dynamical behaviour is to be approximated by the system of dominant networks. These networks may change in time but remain small enough. This hypothetical picture should give an answer to a very practical question: how to describe kinetics beyond the standard quasi-steady-state and quasiequilibrium approximations. We guess that the answer has the following form: during almost all time almost everything could be simplified and the whole system behaves as a small one. But this picture is also nonstationary: this small system changes in time. Almost always “something is very small and something is very big”, but due to nonlinearity this ordering can change in time. The whole system walks along small subsystems, and constants of these small subsystems change in time under control of the whole system state. The dynamics of this walk supplements the dynamics of individual small subsystems.

The corresponding structure of fast–slow time separation in phase space is not necessarily a smooth slow invariant manifold, but may be similar to a “crazy quilt” and may consist of fragments of various dimensions that do not join smoothly or even continuously.

References

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