# Fast and slow, large and small

Carsten Wiuf

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I'm genuinely interested in the application of mathematics, probability theory and statistics in the biosciences, and to develop mathematical and statistical theory for biological phenomena. Over the years I have worked in different areas of application, and applied modeling and theory in many different contexts. In recent years my interests have been in systems biology.

One particular focus of systems biology has been to understand the complex dynamical behaviour of cellular systems in living organisms. These systems might play very different biological roles and could be involved in very diverse biological functions, from expression of genes, over maintenance and replication of cells, to ageing and disease progression. Thus, a biologist would think of these as very distinct systems with very different features and functionalities.

However, from a mathematical point of view, cellular systems might all be described within a common mathematical framework, a dynamical system, defined by a labelled graph, also called a reaction network. The edges of the graph are given by (biochemical) reactions between complexes made up of molecular species, such as

$$A + B \xrightarrow{r} C,$$

indicating that the species $A$ and $B$ become $C$ by interaction. The label is the rate of the reaction. The dynamics of a reaction network might be deterministic and modelled by an ODE system, where the variables represent the concentrations of species through time, or stochastic and modelled by a continuous time Markov chain, where the state variable represents the number (counts) of the individual species over time. In either case, the typical modelling regime is mass-action kinetics that gives reaction rates proportional to the product of the concentrations of the reactant species (deterministic), or reaction propensities proportional to the product of the number of reactant species (stochastic).

Over the last, say 10-15, years this area of research has been blessed by the attention of pure mathematicians making it an interesting interdisciplinary research area from a mathematical perspective; drawing on dynamical systems theory, algebraic geometry, probability theory and graph theory.

One particular interest of mine has been scaling properties (or scaling laws) of reaction networks. Real biological networks are generally multi-scaled in time as well as in concentrations (space). From an application point of view it is important to have a representation of the network that is simple to interpret and to work with; and highlights

the scale of interest. The scaling laws come in various forms, for example, in the form of volume scaling, that states a precise mathematical relationship between stochastic and deterministic reaction networks via the abundances of species. As the volume increases, the stochastic system is well approximated by the deterministic system. It is known as Kurtz' theorem and goes back to the early 70ies. Essentially, it is a central limit theorem.

Alternatively, reactions might be scaled in terms of slow and fast reactions, or graded from slow to fast. Going back more than a hundred years to early biochemical pioneers, an ad hoc procedure known as the Quasi-Steady State Approximation was proposed to simplify a reaction network under the assumption of slow and fast reactions. In small examples this procedure is simple to apply (if applicable). The challenge lies in establishing a mathematical theorem that states conditions under which this can be done, but also gives means to determine the (reduced) reaction network and its dynamics that results from the separation of slow and fast reactions.

The ultimate goal is naturally to scale abundances (from low to high, in powers of volume) and reactions (from slow to fast) at the same time; and to have simple tools that determine the reduced reaction network and its dynamics. Without simple tools, this has little applied interest. Ideally, one would like to draw the graph of the reaction network, derive the reduced network from it and state the reduced kinetics without further ado. Together with collaborators we have been able to get some headway with this, stating simple graphical conditions for which reductions can be done under different scaling regimes.