Kinetics of reversible reactions in a structured space, at low reactant densities

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We present our recent results on three problems that are related to reaction kinetics in systems where the reactant density is low, and the medium may be inhomogeneous.

The first part is about the effects of confining domains, such as those observed in cell membranes, on the kinetics of reversible reactions in two-dimensions. During the last two decades, single molecule tracking experiments showed that proteins and lipids are temporarily confined in the compartments of a meshwork induced by the actin cytoskeleton (with a typical length scale of 30-300 nm), while diffusing laterally in the plasma membrane. It has been clearly demonstrated that the presence of these compartments significantly hinders the diffusion of membrane molecules. Nevertheless, how confinement affects the interaction between membrane molecules and the regulation of signaling has still not been clarified. Using Monte Carlo simulations and the mathematical theory of diffusion, we showed that the presence of compartments leads to reaction bursts, during which the number of reactions an individual molecule experiences rises sharply, but briefly. Therefore, our results show that the variance of the rate depends strongly on the presence of confinement effects, which turns out to be an indicator of a profound change in the temporal pattern of reaction events: *bursts of reactions instead of constant but low yield*. Surprisingly, we found that the mean reaction rate predicted by this model does not depend on whether compartments exist or not.

In order to investigate the effects of temporary confinement on the statistics of encounter times via an analytically tractable model, we studied first-passage times in finite lattices in one and two-dimensions (1D, 2D). In the second part, we report exact results for the mean and variance of the first-passage time between arbitrary sites in the following: (1) a finite 1D lattice partitioned into temporarily confining domains and (2) a finite 2D lattice with reflecting boundaries, in both cases for a single random walker and an immobile target. In the 1D case, we also present the full first-passage time distribution via numerical inversion of Laplace transforms. Our results showed that the variance of return times in a finite lattice can diverge while its mean stays finite (unchanged).

In the last part, we present an exact solution of the Smoluchowski equation in 2D and calculate the time evolution of the probability of colocalization between two reacting probes, which can be measured in single molecule tracking experiments. Despite the apparent need to study reversible reactions between molecules confined to a 2D space such as the cell membrane, the relevant Green's functions of the Smoluchowski equation have not been reported. We obtained the Green's functions for a Brownian particle reversibly reacting with a fixed reaction center in a finite 2D circular region with reflecting or absorbing boundaries, considering either a spherically symmetric initial distribution or a particle that is initially bound. Furthermore, we showed that Green's function can be used to predict the effect of measurement uncertainties on the outcome of single-particle/molecule-tracking experiments in which molecular interactions are investigated. Hence, we bridge the gap between previously known solutions in 1D (Agmon 1984 *J. Chem. Phys.* **81** 2811) and 3D (Kim and Shin 1999 *Phys. Rev. Lett.* **82** 1578), and provide an example of how the knowledge of Green's function can be used to predict experimentally accessible quantities.