Models for Diffusion Processes in Complex Media with Applications to Biological Systems

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Transport of molecules in a cellular environment regulates many processes underlying biological functions. With the current experimental techniques, it is possible to perform single particle tracking (SPT) of long single-molecule trajectories in living cells. These experiments revealed very complex diffusion patterns, often showing anomalous subdiffusion and ergodicity breaking. We will discuss an example of such behavior, observed by recent SPT experiments in the motion of molecules in living-cell membranes [1]. These data seem to exclude conventional explanations for ergodicity breaking, based on continuous-time random walks with transient trapping. Thus the underlying microscopic mechanism for the nonergodic subdiffusion of the molecules is unclear.

In this scenario, we will discuss two stochastic models that provide a description compatible with the observation of such experiments. We will first discuss models of a particle diffusing in a disordered medium, in which particles' diffusivities vary either in time or space, reproducing the heterogeneous dynamics - characterized by frequent changes of diffusivity - revealed by the experiments [2]. Second, we will discuss a model in which a particle performs continuous Brownian motion with changes of diffusion coefficients induced by transient molecular interactions with diffusive binding partners [3].

From the biophysical point of view, the latter model reflects the scenario of a diffusing molecule which, upon interaction with another molecule, undergoes a transient change of diffusivity for the time the interaction takes place. An important feature of the model is the possibility of being experimentally tested by means of current multicolor single particle tracking techniques. As an example, in a dual color single particle tracking (DCSPT) experiment it is possible to simultaneoulsy follow the motion of two closely spaced particles with high time and relative-distance resolution. In addition, DCSPT make it possible to experimentally verify the occurrence of interactions between diffusing species, measure the duration of such events, and check whether they affect the diffusivity of the particles involved.

Once the occurrence of the interaction mechanism in a specific system is proven, the model allows to directly calculate microscopic parameters of the system. In particular, the scaling exponent of the eMSD is a proxy for the degree of heterogenity of the environment. But even more importantly, the timescale for the onset of subdiffusion in the eMSD curve provides an estimation of the average density of interacting particles. In Fig. 1 we show a collection of eMSD curves obtained for different densities of particles $\rho = N/L$, with L being a characteristic size of the system (length in 1D). The degree of disorder is characterized by the asymptotic value of the exponent α, and does not depend on the density (for all curves here $\alpha = 0.2$). In

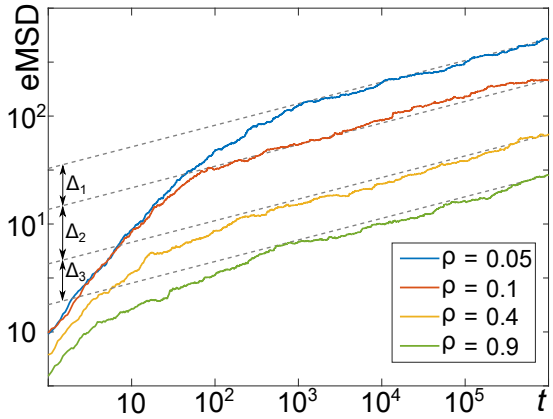

Figure 1: Evolution of the mean squared displacement (eMSD). The eMSD is obtained as an ensemble average, i.e., over many trajectories of different particles. The long-time scaling exponent of the eMSD is independent of the density ρ and corresponds to a subdiffusive motion ($\alpha = 0.2 < 1$). In the asymptotic regime, curves obtained for different densities are separated by a distance Δ, which is related to the different densities.

contrast, the onset of subdiffusion occurs at later times for more dilute systems. This corresponds to a separation Δ between two curves for different densities. This separation can be expressed in terms of the densities of the corresponding curves. For the same system size and for dilute systems, $\Delta = \log(N_j/N_i)$, $N_{j(i)}$ being the number of particles of the denser (more dilute) system.

In conclusion, both models offer a plausible and experimentally-verifiable explanation for the nonergodic subdiffusion of molecules in cellular environments. In addition, the generality of these theoretical frameworks allows them to be applied to a wider range of complex systems showing diffusion heterogeneity, such as those found in ecology, geology or soft condensed matter. As an outlook, we plan to include the coupling of the particle to a system of Ising spins, and solve with a quantum kinetic Ising Hamiltonian approach [4].

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