

Anomalous diffusion in membranes and cytoplasm of biological cells

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Lipid molecules are amphiphilic molecules with a hydrophilic head group and two hydrophobic tail groups. In water the lipids self-organise into micelles or bilayer sheets in order to avoid contact between the tail groups and the water molecules. Such bilayers form the basis of all biological membranes in living cells, and they are also at the heart of bio-compatible containers envisaged in drug delivery into biological cells.

This talk will focus on the dynamics of lipid molecules in lipid bilayer membrane systems as well as that of proteins embedded in the bilayer. It combines information from extensive all atom and coarse grained Molecular Dynamics simulations as well as single potassium channel trajectories measured in the membranes of living human cells. Particular focus is laid on deviations of the lipid and protein motion from normal diffusion. Such anomalous diffusion, characterised by a non-linear power-law scaling of the mean squared displacement will be demonstrated to characterise both lipids and proteins. While in a pure lipid system at room temperature this anomalous diffusion crosses over to normal diffusion at around 10 nanoseconds, it will be shown that the addition of disorder in the form of membrane-embedded cholesterol or protein molecules extends the range of the anomalous diffusion regime by several orders of magnitude. In the case of the membrane of the living cell, the anomalous diffusion reaches macroscopic time scales, at least of the order of hundreds of seconds. The stochastic motion of both lipids and proteins corresponds has its origin in the viscoelastic nature of the lipid bilayer-protein system, similar to the motion of a monomer in a Rouse chain.

When the concentration of proteins in the lipid bilayer becomes appreciable (protein crowding) it will be shown that the previously Gaussian nature of the probability density function of the particles is replaced by a stretched Gaussian form. This is shown to be connected with strongly varying mobilities in the system. Remarkably, very similar features are observed in a simple two dimensional argon systems, and thus a major contribution of the complexity of the motion is due to geometric constraints. In the protein motion in the living cell, the anomalous diffusion is dominated by waiting time motion with diverging time scale, and thus the motion becomes both ageing and non-ergodic.

[1] R. Metzler et al, BBA - Biomembranes **1858**, 2451 (2016).

[2] K. Norregaard et al, Chem. Rev. **117**, 4342 (2017).

[3] J.-H. Jeon et al, Phys. Rev. Lett. **109**, 188103 (2012).

[4] J.-H. Jeon et al, Phys. Rev. X **6**, 021006 (2016).