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A novel estimation method for diffusion in biological membranes

Random walk of lipids and other molecules present in biological membranes is of great relevance in biology and medicine. The distance travelled by walking molecule depends on the geometrical characteristics of the trajectory. At the beginning of Brownian movement, the molecule performs ballistic motion within one step, which is a rectilinear segment. Then the character of motion evolves to diffusive and the trajectory becomes a self-intersecting polygonal chain with the increase of number of steps.

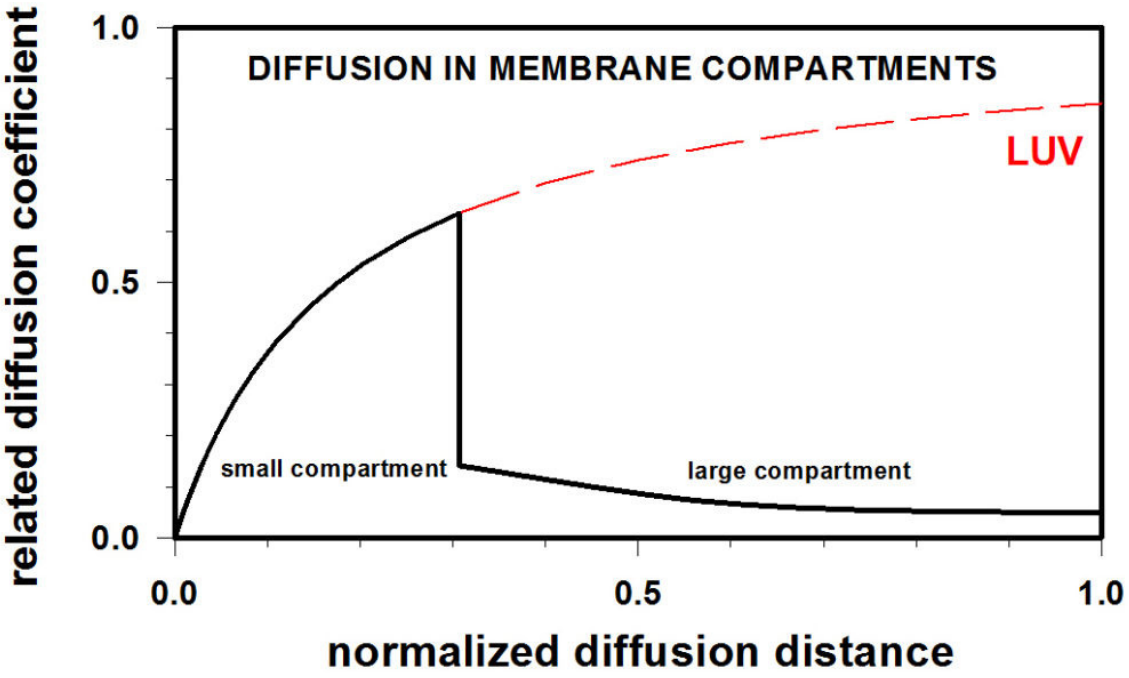

Fig. 1. Fractal description of the Brownian trajectory gives the quantitatively description of the trajectory character evolution from the ballistic to the diffusive one. This results in the dependence of the diffusion coefficient on the molecule displacement related to the length of the Brownian step. Knowing the length of the Brownian step, it is possible to describe the diffusion coefficient as a function of the diffusion distance related to the size of large compartment. The figure presents the evolution of diffusion coefficient in compartments related to that measured in large unilamellar vesicles (LUV) which are not compartmentalized. At the distance of the large compartment size, the diffusion coefficient approaches a constant low value whereas free diffusion coefficient is still approaching the asymptotic one.

The structure of compartmentalized cell membrane and existing interactions in this crowded environment, cause specific mobility of the molecule. The steps performed by a biomolecule are much longer than it would be without interactions. Small size of the compartment as compared to the Brownian step length causes that there is no space sufficient to achieve the fully developed diffusive regime. Additionally, after the molecule displacement becomes comparable to the compartment size, the molecule performs the steps longer without increment of the distance, which causes the decrease of achieved previously diffusion coefficient. At a longer

time, the sub-diffusion is observed due to multiple visits in the compartments, more frequent than for pure random walk. All the phenomena cause the molecule displacement is reduced.

The diffusion coefficient is determined by the square of diffusion distance divided by the fourfold time of the movement. If the membrane is double compartmentalized, it increases in the range where the diffusion distance is less than compartment size and then decreases when the distance is temporarily unchanged. After the molecule leaves the compartment, hoping to an adjacent one, the diffusion coefficient is further reduced because of multiple visits of diffusing molecule in small compartments. Frequent visits result in more time necessary to achieve a given distance as compared to a random walk.

To support the above theoretical considerations, the experimental data were analyzed of the molecular movement of 1,2-dioleoyl-*sn*-glycero-3-phosphoethanolamine (DOPE), tagged with Cy3 in the head group region, in the cell membrane of normal rat kidney (NRK) fibroblast cells (Fujiwara et al. 2002, J Cell Biol 157(6):1071–1082). The membrane consisted of small compartments od the size of 0.23 μm formed within larger ones of the size of 0.75 μm.

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