[Talk 20] Heterogeneous Diffusion of a Peripheral Protein on a Lipid Membrane Surface

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Association of peripheral membrane proteins (PMPs) with their target cell membranes plays key roles in many trafficking and signaling events within cell and thus in many diseases. Pleckstrin homology (PH) domains are lipid recognition modules in PMPs. Their major function is to localize PMPs to cell membranes via interactions with phosphatidylinositol phosphates (PIPs). Despite many structural and functional data about the PH domains and related PMPs, it remains challenging to investigate the diffusive behavior of the proteins.

Here we will discuss the diffusive behavior of a PH domain on a lipid membrane surface using molecular dynamics simulations. First we show that the PH domains associate with the PIP molecules in the membrane via a positively charged loop in good agreement with available experimental data [1]. Moreover, we tackle a question of how the protein-lipid interaction affects the diffusion process of the PH domains on the membrane surface. The time-averaged mean square displacement (TAMSD) of the PH domain on the membrane surface exhibits transient subdiffusion. By analyzing the relative standard deviation of the TAMSD we will show that the diffusivity for short-time measurements is intrinsically different from that for long-time measurements. This fluctuating diffusivity results from dynamic changes in interactions between the PH domain and PIP molecules [2,3].

[1]E. Yamamoto, A. C. Kalli, K. Yasuoka, and M. S. P. Sansom, Structure 24, 1421 (2016).

[2]E. Yamamoto, A. C. Kalli, T. Akimoto, K. Yasuoka, and M. S. P. Sansom, Sci. Rep. 5, 18245 (2015).

[3]E. Yamamoto, T. Akimoto, A. C. Kalli, K. Yasuoka, and M. S. P. Sansom, "Dynamic interactions between a membrane binding protein and lipids induce fluctuating diffusivity" submitted.