Self-organization mechanism affects the time dependency of molecular diffusion

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***Short Abstract* — Intracellular heterogeneity exists to space, time, energy and force. These heterogeneity occurs by fluctuation of reactions which consists of small number of reaction species. At the same time, these elements are not independent each other, moreover affect each others. In this article, we focused the effect of organization mechanism of intracellular structures, which produce spatial heterogeneity and time dependency of molecular diffusion. By investigating spatial characteristics and the time dependent mean square displacement of mobile particles, we conclude that the history of the organization mechanisms of intracellular environment induces time-dependent behavior of mobile particles in the environment.**

***Keywords* — fractal dimension, spatial entropy, molecular crowding, anomalous diffusion**

I. Introduction

INTRACELLULAR environment is crowded with macromolecules [1]. The molecular crowding brings about 50 times higher viscosity to cytoplasm than water [2]. Such environment can result trapping the signaling molecules in cytoplasm. However, actual *in vivo* environment does not prevent molecular transferring from cell surface to nucleus. In order to realize such movement under the condition, heterogeneity of the intracellular environment is significant as once signaling molecules had been trapped, they can be released later. This type of diffusion manner is named continuous time random walk [3]. By considering the process to produce this type of molecular behaviour, the distribution pattern of the cause of viscosity is effective. That means the rules or mechanisms, which decide the distribution of macromolecular structures in a cell may be dominant to control the fate of molecular behaviors *in vivo*.

In this study, we investigated the organization mechanisms of structures of reaction space, which changes the final distribution pattern of structural obstacles. We classified the organization mechanisms into diffusion-limited or reaction-limited. We chose spatial parameters to investigate the characteristics of models and cell images and compared which organization mechanism is more plausible, and estimated the further affect of the difference on mobile particle in the reaction spaces.

II. Results

We constructed 3D volumes of intracellular environment based on transmission electron microscopy (TEM) images. We constructed additional 6 structural models of simply random model, diffusion limited aggregation model, cluster-cluster aggregation model (diffusion-limited models), modified DLA model, Eden model, and modified Eden model (reaction-limited models). We used these 3D volumes to compare the spatial characteristics to know which model could give better explanation of the self-organization mechanisms of intracellular structures.

A. Parameters to describe the spatial characteristics

We analysed 3D fractal dimension, spatial entropy, surface/volume ratio of free mobile space, the volume distribution of restricted volume, and the size of circling space. All these parameters indicated that reaction-limited models keep similar characteristics with TEM 3D image.

B. Comparison of Mean Square Displacement of a free mobile particle in the 3D spaces

We compared the anomalous characteristics of a mobile particle in the 6 simulation spaces. The anomalous diffusion constant of a particle in reaction-limited models showed the similar value with a particle in TEM 3D image.

C. Confirmation of the components of structures and the actual diffusion manner with experiments

We investigated the candidates of the cluster-like structures in 3D simulation spaces by immunocytochemistry. The protein-membrane complexes had the same range of their size with the clusters. Single particle tracking showed that the environment we prepared for the investigation also produced the same anomalous diffusion of a mobile particle.

III. Conclusion

Our results suggest that the heterogeneity to time of molecular diffusion depends on the organization mechanisms of environmental structures.

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