Constructive role of noise in self-organized pattern formation in social amoeba

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***Short Abstract* —To understand constructive role of noise in biological pattern formation, we investigated self-organized aggregation of social amoeba. To correlate cellular activity to whole system dynamics, we conducted live cell calcium imaging in the population of 100,000-cells with single-cell resolution. In addition to the propagating circular/spiral waves, we successfully detected non-propagating calcium spikes in few 10s of cells, which would reflect stochastic cAMP release. Incorporating observed frequency or amplitude of these spikes, our stochastic simulation with typical reaction-diffusion scheme well explains essential features of wave dynamics, suggesting that biological noise is indispensable for *Dictyostelium* pattern formation.**

Keywords —Noise, Reaction-Diffusion system, *Dictyostelium*, Calcium imaging.

I. Purpose

NOISE has been believed to have negative impacts on system performance. Thus it is quite natural to ask how dynamical systems in nature operates robustly even in the presence of noise. Much attention has been paid to qualitatively or quantitatively measure the biological noise. Analysis to elucidate underlying mechanism of biological robustness has been also active [1]. Interestingly, recent theoretical studies suggest that noise can play constructive roles in the system operation[2], although experimental analysis has been largely lacking. To better understand constructive role of noise in biological system, we focused on the self organized pattern formation in dictyostelium development, being one of the best studied living excitable medium. During their development, 100,000 of dictyostelium cells aggregate in the form of circular or spiral waves, supported by chemotactic signaling relay. Two-dimensional wave dynamics has been extensively analyzed by the use of indirect observation such as an optical density recording and image enhancement techniques. However, these analyses only allowed us to make a macroscopic observation with quite low spatio-temporal resolutions. To correctly understand signaling relay dynamics, we tried to develop fine resolution imaging-based analysis then obtained data were subjected for stochastic simulations. Significance of noise in self organized pattern formation will be discussed.

II. Result

First, we developed new FRET-based calcium indicator with highest sensitivity (Kd=30nM) reported so far [3]. This allowed us to directly visualize the signaling relay pattern with high S/N ratio and single cellular resolution even at 100,000 cell scale, which had not been possible without this sensor.

Next, we conducted systematical measurement of signaling relay pattern by live cell calcium imaging. Of course, expected circular and spiral waves are reproducibly visualized, non propagating localized calcium spikes are also identified unexpectedly[4].

Third, we carried out stochastic simulations to reproduce both expected and unexpected intercellular signaling activities. From a line of numerical experiments, we obtained several interesting predictions about the relationship between noise strength and system outputs.

Finally, theoretical predictions were experimentally validated by perturbation analysis utilizing some mutant strains or pharmacological treatment. Obtained results strongly suggest constructive role of noise in pattern formation of dictyostelium population.

III. Conclusion

In addition to the expected cAMP relay, spontaneous cAMP release was detected as traveling calcium wave and localized calcium spikes, respectively. Quantitative analysis and stochastic simulation demonstrate that; 1) at the microscopic scale, spontaneous cAMP release would originate from stochastic regulation of cAMP synthesis. 2) Noise-driven cAMP release, in turn, triggers wave propagation at the macroscopic level. These results clearly indicate that pattern formation in Dictyostelium cannot be achieved in the absence of noise.

References

[1] Horikawa K, Ishimatsu K, Yoshimoto Y, Kondo S and Takeda H (2005) "Noise resistant and synchronized oscillation of the segmentation clock" Nature 441 719-723

[2] Muratov CB, Eilnden E, Weimann E (2007) *"Noise can play an organizing role for the recurrent dynamics in excitable media" PNAS 104. 702-707*

[3] Horikawa K, Nagai T. "Development ultrasensitive calcium sensor" in preparation.

[4] Horikawa K, Nagai T. "Constructive role of noise in self-organized pattern formation in social amoeba" in preparation.

Acknowledgements: This work was funded by JST grant for PREST

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