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Competitive localization of molecules in mass-conserved systems

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Localization of molecules in a site of the system is often observed and plays crucial role in biological systems. As a typical example, localization of various kinds of molecules determines the polarity of a cell. In such case, localization should occur only at one site. If there are two or more localized sites, they compete with each other and only one of them survives, which determine head of the cell. Because many kinds of molecules are related with cell polarization, interactions between molecules are important for spatial regulation of localized processes. So far, some theoretical models were proposed for the regulation of the localization. Here we give a novel mechanism, in which mass conservation of chemical component(s) with multiple states leads to the localization and competence. Such situations naturally arise in many biological models (and has been proposed). For example, an enzyme takes active and inactive states and diffuses in cell, and total mass of the enzyme is regarded as conserved quantity within a certain time scale. We show theoretically that the localization and competence are valid for wide variety of mass-conserved systems, not limited in a specific model, and thus is applicable to many biological systems.

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Solving the shortest path problem by Physarum solver - Modeling of the Adaptive Network of True Slime Mold

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We describe here a mathematical model of the adaptive dynamics of a transport network of the true slime mold *Physarum polycephalum*, an amoeboid organism that exhibits path-finding behavior in a maze. This organism possesses a network of tubular elements, by means of which nutrients and signals circulate through the plasmodium. When the organism is put in a maze, the network changes its shape to connect two exits by the shortest path. By reproducing this phenomenon we introduce new method to solve shortest path problem.

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Emergence of Morphological Order in the Network Formation of *Physarum Plasmodium*

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Emergence is the notion to describe the generation of complex order in a system through the interactions of the system's elements. Biological entities are often referred as the most dramatic illustrations of emergent phenomena. It is unclear, however, in what kind of organization of a biological system emergence can be found. Thus we began with an experimental observation of the phenomena, using the plasmodium of *Physarum polycephalum*. *Physarum* plasmodium is a giant unicellular, multinuclear amoeboid organism. For separate food sources, the plasmodium connects each food source forming a cellular tube, providing a mathematical solution for an efficient network. In our experiment, the plasmodium was set to spread uniformly into a circular field. We then applied three food sources to the field, so that they formed an equilateral triangle at the edge of the circle. The plasmodium was stayed still until it formed a tubular network. In the second experiment, all the conditions were the same except that a pair of the circles was connected with a narrow path. Both experiments had the same condition within a circle, though only in the latter one, the plasmodium networks were given a chance to interact with each other. In the latter experiment, the pair of the networks showed a morphological homology. This suggests that the parts of the plasmodium refer to the other parts to form a global order in a system, and that we successfully observed an emergent phenomenon generated by the local interactions in the cellular system.

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Predicting regulation of the phosphorylation cycle of KaiC clock protein using mathematical models

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The cyanobacterial clock protein KaiC show circadian cycling of phosphorylation even under *in vitro* transcription-less conditions. Using mathematical models, we investigated the mechanism for the transcription-less KaiC phosphorylation cycle. We developed a simple model based on the possible KaiC behavior, which is suggested by previous experimental studies. The KaiC-KaiA complex formation causing decrease in free KaiA may attenuate KaiC phosphorylation rate, and it acts as negative feedback. However, analysis proved that simple dynamics based on the model never show the phosphorylation cycle. Then we developed generalized models and determined the necessary condition to generate the cycle. Analysis revealed that oscillations can occur when the distance of feedback between the recipient reaction and the effector is far enough. Further, we found that the negative feedback regulations in closed systems can be classified into two types: "destabilizing" and "stabilizing inhibition". Based on this result, we predicted that, in addition to identified states of KaiC, another unknown state must be present between KaiC phosphorylation and complex formation. By incorporating the state, we realized the periodic pattern reminiscent of KaiC phosphorylation cycle. This result implies that KaiC-KaiA complex formation requires more than one step of posttranslational modification including phosphorylation change of KaiC. Takigawa-Imamura, H. and Mochizuki, *Journal of Biological Rhythms* In Press (2006)