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Mathematical modeling of gene interactions associated with Wnt signaling pathway in colorectal carcinoma
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Colorectal carcinoma (CRC) is one of the most common causes of cancer death in Europe and the United States. In Japan, according to dietary habit change to Western style food, CRC is expected to increase in the future. In cancer cells of CRC, beta-catenin is known to accumulate in nucleus and cytoplasm because of aberration of Wnt signaling pathway. The well-known target genes of beta-catenin are cyclin D1 and c-myc; the former is a cell cycle-related gene, the latter is an oncogene which controls cell proliferation and apoptosis. Expression levels of these genes are upregulated by accumulation of beta-catenin. Thus, beta-catenin is one of the most important molecules of Wnt signaling. In this research, we developed mathematical model about the relation of selected genes in Wnt signaling pathway. Using genes such as APC, Axin, and CTNNB1 (encoding beta-catenin) associated with Wnt signaling pathway, we expressed interactions among these components with differential equations based on reaction kinetics. We studied the behavior of the model by simulations as well as by mathematical analysis.

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A Mathematical Model of Cell Size Homeostasis
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In order to sustain size homeostasis over successive generations, living cells must control their size before dividing which requires a tight coordination between growth and division processes. Failures of such control give rise to progressively smaller or larger, eventually unviable cells. Thus, a main feature of cell size control is the existence of a critical cell size in spite of random variations of birth cell size. Furthermore this critical cell size is not rigidly programmed but it can vary according to external nutrient conditions. The issue of cell size control is addressed using a theoretical framework. A minimal model of a cellular biochemical network is designed where the growth and division catalytic processes, through the dynamics of ribosomal proteins and cyclin family proteins, are differentiated but coupled. Combining analytical and numerical approaches, we have investigated how the non-linear dynamics of this model efficiently alleviates the effects of intrinsic random fluctuations but adapt to significant changes of the external nutrient level.

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Mathematical modeling for pattern formation of dendrite
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Dendrite is a neuronal process, which is specialized for receiving and processing synaptic or sensory inputs. Morphologies of dendritic trees are highly variable from one neuronal type to another and this diversity contributes to differential processing of information in each type of neurons. For instance, retinal ganglion cells and Drosophila class IV da neurons elaborate dendrites that uniformly cover their receptive field (this complete but non-redundant coverage is called "Tiling"). We previously showed that tiled da neurons regenerate space-filling patterns after severing branches (1, 2). This and other experimental data suggested that self-organization machinery controls development of "space-filling" dendrites. Our reaction-diffusion model that includes a cellular structure develops dendritic patterns autonomously. In addition the model also manifests the distinctive two feature of spatial regulation of neurons: tiling and regeneration. By the numerical analysis of the model we determined generalized conditions for branching. We also found that the spatial property of obtained patterns can be characterized by a statistic, "branch alignment". Our preliminary analysis showed that the statistic reflects the distribution of activator inside of the cell. Therefore we may able to characterize neurons by the statistics and to predict internal distribution of activator from the external feature of neuronal branches.1. Sugimura et al. Neuron (2004). 2. Sugimura et al. JNS (2003).

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Neural Circuit and Behavioral Criteria of C. elegans
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Introduction: The Caenorhabditis elegans has 302 neurons whose synaptic connectivity is entirely determined. When behavior of C. elegans is numerically studied, nevertheless, a closed partial neural circuit is employed to reduce the degree of freedom. Only the associated neurons are taken into account in the partial neural circuit. The influence of the remaining neurons is completely neglected. In the previous study (Iwasaki and Gomi, 2004), a problem in such the condition is shown and a stochastic formulation for the McCulloch-Pitts model is presented to solve the problem. In this study, a formulation for physiologically relevant models is presented.

Method: Dynamical mean-field approximation is used to evaluate the influence of the remaining neurons. This formulation provides the close equations of motion of the neuron states in the partial neural circuit and the means and the variances of the remaining neuron states. A statistical property of the remaining neurons is extracted in the global variables such as the means and the variances.

Result: In C. elegans, the synaptic polarities, that is, whether chemical synapses are excitatory or inhibitory, are not fully determined. Therefore, the presented formulation is applied to predict the synaptic polarities. Dynamics of the neurons is simulated for all possible polarity configurations and functional configurations are singled out to satisfy certain behavioral criteria. The predicted polarities well explain the behavior of the real C. elegans.

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