Chapter 35
Quantitative Modeling of Neuronal Polarization

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ABSTRACT

Biological phenomena are systematically controlled by various components. In addition to biological molecules, physical components such as length and force must play an important role, especially in the cellular morphogenesis. Although a quantitative mathematical model is useful for understanding the underlying mechanism of biological phenomena, a model including the physical components is likely to become too complex to be designed mathematically. In the authors' previous work, they proposed a quantitative mathematical model of neuronal polarization that is described by several simple equations and can reproduce a number of experimental observations. Based on that work, this chapter explains how the authors obtained a simple quantitative model from the complex processes of neuronal polarization.

INTRODUCTION AND BACKGROUND

Mathematical Model in Biology

A mathematical model based on quantitative data was first developed in neuroscience. Hodgkin and Huxley (HH) compiled their findings into a quantitative mathematical model (HH model) that reproduced the membrane action potential of neurons (Hodgkin & Huxley, 1952). In the HH model, nonlinear functions are used as model components, which express the state transition rates of the ionic channel (open and closed states) based on the Boltzmann transport equation. Although these nonlinear equations were simplified assumptions of the real processes that ignored the detailed mechanisms, Hodgkin and Huxley verified that the component equations could reproduce the experimental data quantitatively; this verification guarantees reliable validation of the model that is composed of these components. The model has been validated by a number of agreements between the model prediction and experimental data. During the last 60 years, the HH model has

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been applied to many fields within computational neuroscience and has been used as the fundamental equation in simulation platforms (Bower & Beeman, 1998; Carnevale & Hines, 2006) and in a large-scale simulation project (Markram, 2005).

Recently, researchers who study systems biology constructed mathematical models of biochemical reaction interactions to reproduce biological phenomena such as a bistable response of mitogen-activated protein (MAP) kinase (Angeli, Ferrell, & Sontag, 2004; Brandman, Ferrell, Li, & Meyer, 2005; Ferrell, 2002; Ferrell & Machleder, 1998; Ferrell, et al., 2009). Although each of the primary reactions was also modeled as an approximated equation based on biochemical kinetics, the model reaction showed the quantitative reproducibility of a real reaction by fitting the model parameters to experimental data. The model of the reaction network could reproduce target experimental data by integrating the quantitatively verified equations. In systems biology, various simulation platforms for large-scale interactions have also been developed (Bhalla, 1995; Kitano, 2005; Tomita, 1996).

Quantitativity and Multimodality

The HH model and the biochemical reaction models described above take an orthodox and important methodology for modeling scientific targets. Detailed processes in a component are modeled as a simple quantitative equation with parameters that are based on experimental data, although the equations contain some assumptions. In contrast, the entire model is the integration of quantitatively verified components; this quantitativity is critical for verifying a model component. Even in the era of Hodgkin and Huxley, researchers could formulate a beautiful quantitative mathematical model based on experimental data. Recent advantage in experimental technology has enabled us to quantify various features of biological targets. Thus, it becomes more feasible to construct mathematical modeling based on the experiments, and this quantitative approach has attracted theoretical researchers (q-bio, 2007).

A recent hot topic is the multimodality of biological model components. In addition to molecular concentration, a biological system often uses physical components such as force (Chan & Odde, 2008; Giannone, et al., 2007; Iwadate & Yumura, 2008; Lamoureux, Ruthel, Buxbaum, & Heidemann, 2002; Munevar, Wang, & Dembo, 2004; Shimada, et al., 2008), voltage (Bedlack, Wei, & Loew, 1992; Cohan & Kater, 1986; Nishiyama, von Schimmelmann, Togashi, Findley, & Hong, 2008; Wang & Poo, 2005), and space (Naoki, Sakumura, & Ishii, 2005; Seetapun & Odde, 2010; Toriyama, et al., 2006). Cellular morphogenesis is a popular issue in biology (Arrieumerlou & Meyer, 2005; Machacek, et al., 2009; Pollard & Borisy, 2003; Ponti, et al., 2005) and is regulated by multimodal components such as molecules, space and force. Taken together, quantitativity and multimodality are necessary to model cellular morphogenesis. Current experimental techniques enable us to quantify the features of a target phenomenon.

MODELING OF NEURONAL POLARIZATION

We previously proposed a quantitative mathematical model of neuronal polarization by integrating the multimodal interactions among molecular concentration, force, and protrusion length (Inagaki, Toriyama, & Sakumura, 2011; Toriyama, Sakumura, Shimada, Ishii, & Inagaki, 2010). A developing neuron initially extends several protrusions called neurites, which are all similar in length. Subsequently, the neuron selects a single neurite that elongates much more than the other neurites and becomes an axon, while the other shorter neurites become dendrites (Craig & Banker, 1994; Dotti & Banker, 1987). This morphological polarization is important for the

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