

stem cell, and their growth and differentiation are regulated to keep the number distribution of each cell to achieve homeostasis of the hematopoietic system. In this case, in addition to the proportion regulation, the absolute size of stem cells is also important because all the hematopoietic cells will ultimately die out without their existence. Indeed, regulation of the numbers of each cell type is rather common in multicellular organisms. As the distribution of each cell type is a property of an ensemble of cells, cell-cell interactions should be essential for such regulation.

There are several theoretical studies discussing the importance of cell-cell interactions. By considering an ensemble of cells with intra-cellular genetic (or chemical) networks and intercellular interactions, synchronization of oscillation (García-Ojalvo et al., 2004; McMillen et al., 2002) or dynamical clusterings (Kaneko and Yomo, 1994; Mizuguchi and Sano, 1995; Kaneko and Yomo, 1997; Furusawa and Kaneko, 1998; Ullner et al., 2007; Koseska et al., 2007) are observed. Cell states distinguishable from those of a single-cellular dynamics are generated, providing a basis for functional differentiation for multicellularity. The preservation of the proportion of different cell types is realized by taking advantage of Turing instability (Mizuguchi and Sano, 1995), while the robustness in the number distribution of different cell types is discovered in reaction network models (Kaneko and Yomo, 1994; Furusawa and Kaneko, 1998; Kaneko and Yomo, 1999). Nevertheless, regulatory mechanisms for cell type populations are not elucidated in terms of dynamical systems because of the high dimensionality of the models.

In the present paper, we propose a regulatory mechanism of cell differentiation based on dynamical systems theory by taking simple cell models with biological gene regulation dynamics. Specifically, we study how cell states are differentiated with the change in the total cell number following cell-cell interactions. By incorporating different interaction kinetics, we show how simple functional modules generate specific cellular behaviors such as a cell fate switching, size regulation of each cell type, and preservation of the number ratio of each cell type.