

A Study of Spatial Formation of Immune Cells

Shin I. Nishimura

shin-nishimura@aist.go.jp

Computational Biology Research Center (CBRC), National Institute of Advanced Industrial Science and Technology (AIST), 2-41-6 Aomi, Koto-Ku, Tokyo 135-0064, JAPAN

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1 Introduction

Immune system is a network that recognized viruses and bacteria and destroys those. Two groups of proteins called complement and antibody recognizing those, then cells named phagocyte “eat” those [1]. If each bacteria stays at the same place, all phagocytes have to do is to approach bacteria marked by complements or antibodies, then destroy those. However, bacteria usually can move. It is expected that phagocyte effectively make a spatial formation in order not to bacteria get away. It is also expected that signal molecules, cytokines control a spatial formation of phagocyte with other immune cells. There are a few mathematical or computational studies of this concern [2]. However, models of those studies were too simple to discuss so complex immune system. In this paper, I give a model that can treats more complex interaction among cells, movement of cells as well. Genetic algorithm (GA) selects the best set of parameters for cells to catch bacteria.

2 Method and Results

2.1 Method

It is assumed that any “cell” (including immune cell and bacterium) moves around a two-dimensional space in my model. The space and time are discrete in order to reduce costs of computation. The space is interpreted by hexagonal lattice. Therefore, cells can move to six directions. Each cell has its internal discrete state. Therefore, the i th cell has the lattice position p_i and the internal state s_i . The cell is indicated by $cell(p_i, s_i)$. Not only cells but also “cytokines” (including chemokines) are assumed. Density of cytokines is defined at all lattice positions. We denote the density of j th cytokine at the position p as $d_j(p)$.

How to change the cell’s position and internal state depends on densities and gradients of cytokines and its current internal state. Formally, we can write it as follows:

$$cell(p_i(t+1), s_i(t+1)) = F(d_1(p_i), d_2(p_i), \dots, g_1(p_i), g_2(p_i), \dots, s_i), \quad (1)$$

where $g_1(p_i), g_2(p_i), \dots$, are gradients of cytokines. We will select map F suitable to given conditions. Since it is impossible to search all possible maps, we have to limit space of maps. First, a cell can only move to neighboring six lattice positions per a time step. Second, a cell can only detect whether cytokines are over a given threshold value. Finally, a cell can only a gradient of a cytokine at a time step and move to the largest gradient direction, which simulate chemotaxis of immune cells.

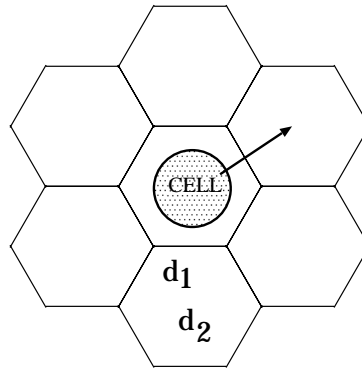


Figure 1: A cell is placed at a hexagonal lattice point. Hence it can move to six directions. d_1 and d_2 written in the hexagon under the cell indicate densities of cytokines at the lattice.

A cell can release cytokines. We restrict a cell to release only one cytokine at a time step. Which cytokine a cell drops depends on its internal state:

$$j = Z(s_i), \quad (2)$$

where j means that the i th cell drop the j th cytokine. Z is a given map that should also selected suitable to given conditions.

Both maps F and Z are selected by genetic algorithm (GA). Since both maps are not continuous but discrete, both can be written as maps from an integer to an integer:

$$n_1, n_2, n_3, \dots, n_m \in N, \quad (3)$$

where N is the set of natural numbers. GA method selects above arranged numbers.

2.2 Results

In order to test this model, assume that the immune cells have three internal states, and emit three cytokines. Bacteria cells are also introduced, moving randomly on the space. Bacteria emit a sort of substance, like fMLP. GA tries to select systems that kill bacteria as many as possible.

GA seems to select cells having following features: immune cells get together using cytokines. Then, they search bacteria moving randomly. This test makes us expect that this model describes more complex interaction between cells since only introducing three internal states and three cytokines leads to organized behavior.

3 Discussion

Although this paper is not directly related to genome informatics, it is anticipated that simulation technique of multi-cellular system is important to investigate genome in future since many genes are related to interaction between cells.

References

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