A first attempt on spatial modeling of germinal center reactions

Can Keşmir and Rob J. De Boer

Theoretical Biology group, Utrecht University, Padualaan 8, 3584-CH Utrecht, The Netherlands.

Abstract

Affinity maturation during immune responses to T-dependent antigens occurs in germinal centers, at least under physiologically normal conditions. Following somatic hypermutation, a strong selection is necessary for efficient affinity maturation. This presumably takes place on the surface of antigen presenting cells (mainly follicular dendritic cells, FDC).

We study FDC-B cell interactions and competition between B cells on FDC surface, by a model based on a special cellular automata (CA) model-formalism developed by Glazier & Graner [1]. The advantage of this formalism is that there is true spatial competition on FDC surface. Cells have certain size and shape, instead of being simple points in the CA space. The movements of the cells and their growth in the 2D space are determined by an adhesion energy that is calculated on the borders of the cells. Updating is based on a Boltzmann energy rule involving i) chemotactic signals, ii) free energy bonds between cells, iii) affinity to the antigen when in contact with FDC, and iv) volume constraints. This model has an additional advantage of being stochastic into the affinity maturation process. Earlier it was suggested that the observed waiting time for key mutations can only be explained by stochastic effects [2].

I will present preliminary results of this model with special emphasis on effects of recycling (i.e. centrocyte to centroblast conversion) and chemotaxis on dynamics of germinal center reactions and affinity maturation.

References

[1] Graner, F. and J. A. Glazier. 1992. Simulation of biological cell sorting using a two-dimensional extended Potts model. *PHYSICAL. REVIEW. LETTERS. 69*:2013.

[2] Radmacher, M. D., G. Kelsoe, and T. B. Kepler. 1998. Predicted and inferred waiting times for key mutations in the germinal centre reaction: evidence for stochasticity in selection. *Immunol. Cell. Biol. 76*:373.