MAR16-2015-009217

Abstract for an Invited Paper
for the MAR16 Meeting of
the American Physical Society

Collective synchronization of self/non-self discrimination in T cell activation, across multiple spatio-temporal scales

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The immune system is a collection of cells whose function is to eradicate pathogenic infections and malignant tumors while protecting healthy tissues. Recent work has delineated key molecular and cellular mechanisms associated with the ability to discriminate self from non-self agents. For example, structural studies have quantified the biophysical characteristics of antigenic molecules (those prone to trigger lymphocyte activation and a subsequent immune response). However, such molecular mechanisms were found to be highly unreliable at the individual cellular level.We will present recent efforts to build experimentally validated computational models of the immune responses at the collective cell level. Such models have become critical to delineate how higher-level integration through nonlinear amplification in signal transduction, dynamic feedback in lymphocyte differentiation and cell-to-cell communication allows the immune system to enforce reliable self/non-self discrimination at the organism level. In particular, we will present recent results demonstrating how T cells tune their antigen discrimination according to cytokine cues, and how competition for cytokine within polyclonal populations of cells shape the repertoire of responding clones. Additionally, we will present recent theoretical and experimental results demonstrating how competition between diffusion and consumption of cytokines determine the range of cell-cell communications within lymphoid organs. Finally, we will discuss how biochemically explicit models, combined with quantitative experimental validation, unravel the relevance of new feedbacks for immune regulations across multiple spatial and temporal scales.