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A stochastic T cell response criterion

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Abstract-

The adaptive immune system relies on different cell types to provide fast and coordinated responses, characterized by recognition of pathogenic challenge, extensive cellular proliferation and differentiation, as well as death. T cells are a subset of the adaptive immune cellular pool that recognize immunogenic peptides expressed on the surface of antigenpresenting cells by means of specialized receptors on their membrane. T cell receptor binding to ligand determines T cell responses at different times and locations during the life of a T cell. Current experimental evidence provides support to the following: (i) sufficiently long receptor ligand engagements are required to initiate the T cell signalling cascade that results in productive signal transduction and (ii) counting devices are at work in T cells to allow signal accumulation, decoding and translation into biological responses. In the light of these results, we explore, with mathematical models, the timescales associated with T cell responses. We consider two different criteria: a stochastic one (the mean time it takes to have had N receptor–ligand complexes bound for at least a dwell time, t, each) and one based on equilibrium (the time to reach a threshold number N of receptor–ligand complexes). We have applied mathematical models to previous experiments in the context of thymic negative selection and to recent two-dimensional experiments. Our results indicate that the stochastic criterion provides support to the thymic affinity threshold hypothesis, whereas the equilibrium one does not, and agrees with the ligand hierarchy experimentally established for thymic negative selection.

Index Terms-

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