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Spatially-resolved mathematical modeling of T cell antigen recognition

T cells play a crucial role in the adaptive immune response. Interactions with specific antigens initiate T cell signaling but also ensure that the majority of self-reactive cells are selectively deleted in the thymus during its maturation. However, the underlying mechanisms remain unclear as to why T cells can reliably distinguish cognate antigens from other peptides that have only slightly weaker affinity to the T cell receptor (TCR). Recent data indicate that the clustering of TCRs at the interface of T cell and antigen-presenting cell could be the key to the exquisite ligand recognition specificity. We develop a spatially-resolved mathematical model based on the reaction-diffusion dynamics of individual TCRs. We use stochastic Monte Carlo simulations to analyze the model and its ability to exhibit TCR clustering. The model aims at rationalizing experiments that have demonstrated a sharp affinity threshold for thymic selection. It will help us to identify the role of TCR clustering and the core elements initializing T cell signaling during antigen recognition and will inform new experimental work.