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Thymic Selection of T-Cell Receptors as an Extreme Value Problem ANDREJ KOSMRLJ, ARUP K. CHAKRABORTY, MEHRAN KARDAR, Massachusetts Institute of Technology, EUGENE I. SHAKHNOVICH, Harvard University — T lymphocytes (T cells) orchestrate adaptive immune responses that clear pathogens from infected hosts. T cells recognize short peptides (p) derived from foreign proteins, which are bound to major histocompatibility complex (MHC) gene products (displayed on antigen-presenting cells). Recognition occurs when T cell receptor (TCR) proteins expressed on T cells bind sufficiently strongly to antigen-derived pMHC complexes on the surface of antigen-presenting cells. A diverse repertoire of self-tolerant TCR sequences is shaped during development of T cells in the thymus by processes called positive and negative selection. We map thymic selection processes to an extreme value problem and provide analytic expression for the amino acid composition of selected TCR sequences (which enable its recognition functions).

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