

I want to investigate the extensive polymorphism at the recognition sites of MHC molecules and its functional consequences in the immune response. There is an interesting interchange between the degree of diversity of MHC molecules and the maintenance of self-tolerance via T cells. Every time a distinct MHC molecule arises (which is often, thanks to frequent gene conversion and highly polymorphic alleles), the T cells that could recognize the self peptide bound to the new MHC molecule must be removed. I could maybe use differential equations such as we did in the lac repressor system to examine the balance between MHC polymorphism (advantageous because it reduces the likelihood that a pathogen will be able to evade immune response) and TCR recognition of foreign peptides bound to self MHC molecules, which is highly specific to a particular composite ligand. Rob's suggestion was to start with simple estimates of the sequence lengths required making high-fidelity decisions about self and non-self peptides.