Catch bonds at T cell interfaces

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Membrane-associated proteins experience a variety of forces at the interface between interacting cells. The forces can arise from sources including membrane undulations, cell motion, and active cytoskeletal processes. Catch bonds are an interesting class of protein-protein bonds that have average lifetimes that initially increase with an increasing tensile force. Recently, catch bonds have been implicated in T cell activation, where potentially small numbers of receptor-ligand bonds at a cell-cell interface control the decision to activate. An outstanding problem in immunology is how T cells discriminate between self and foreign ligands while being sensitive to even a single antigenic ligand. Here, we use hybrid computational methods to investigate small numbers of bonds at the interface between two membranes, accounting for the dynamical changes in membrane shape and the organization of other surface molecules in response to bond formation. We characterize the time-dependent forces experienced by the bonds and determine the distribution of bond lifetimes using recent experimental data for the force-dependent lifetimes of T cell receptors (TCRs). We find that strong agonists, which exhibit catch-bond behavior, are markedly more likely to remain intact than an antagonist, which does not exhibit catch bond behavior. Thermal fluctuations of the membrane shape promote the equilibration of the intermembrane junction but also lead to force fluctuations on bonds, which can promote their rupture. When more than one bond is present, collective effects modulate the average force on the bonds, leading to changes in lifetime distributions. Our results highlight the importance of force-dependent binding kinetics when a bond experiences a time-dependent and fluctuating force, as well as potential consequences of collective bond behavior. We conclude by discussing our results in the context of antigen discrimination by T cells.