Mechanical modulation of receptor-ligand bonds at cell-cell interfaces

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Receptors, molecules on the surface of living cells, initiate many biological signals. An important class of receptors, including T-cell receptors, bind to molecules that are anchored to other cells or surfaces, and remain poorly understood. The T-cell receptor complex spans 15 nanometers, while other interacting molecules such as the phosphatase span 40 nanometers. This has been proposed to lead to size-based segregation that triggers signaling, but it is unclear whether the physics supports such small-scale segregation. I will present a nanometer-scale quantitative model that couples membrane elasticity with compressional resistance and lateral mobility of phosphatase. We find robust supradiffusive segregation of phosphatase from a single receptor-ligand complex. The model predicts a time-dependent tension on the complex leading to a nonlinear relationship between stressed and unstressed bond lifetimes, which could enhance the receptor’s ability to discriminate between similar ligands, provides a mechanical source of ligand sensitivity, in contrast to biochemical sources of sensitivity that have been proposed previously. In addition, we have developed a novel combined experimental-theoretical method based on Forster resonance energy transfer that allows estimation of mechanical properties of surface molecules that have implications for cell-cell mechanical interactions in general.

Friday, August 2
11:30AM
Dunn 101