APS Abstract

Pete Rigas, Lambert Lab (Cornell AEP)

November 27, 2020

---

1 Binding Energies of Fn Cas12a

In recent years, CRISPR proteins have attracted much attention due to their use as a DNA binding platform, in which the protein undergoes steps of PAM attachment, crRNA-DNA inspection, and reconfiguration. Thermodynamically, we can model determinants of binding energies for different sites of the genome with a partition function that reflects energetic costs associated with base pair mismatches. From suitably chosen weights that assign higher energetic contributions to base pair mismatches among the first 6 positions of a DNA sequence, appropriate transition probabilities for a random walk X will be defined so as to coincide with base pair mismatches. As X approaches the position of binding, we stipulate that none of the transition probabilities of X from all positions before N vanish. Furthermore, with such a probabilistic approach, we will analyze the energy landscape of Fn Cas12a, leading to a more comprehensive understanding of how the binding energy of a sequence is dependent on individual base pairs. More broadly, this work will also study gRNA and DNA sequences that are conducive to binding in Fn Cas12a.