Langevin Dynamic Models for smFRET Dynamic Shift

David L. Frost[1,*], Keisha Cook[1], Hugo Sanabria [2]

[1]*Department of Mathematical and Statistical Sciences, Clemson University, Clemson, SC, 29631*
[2]*Department of Physics, Clemson University, Clemson, SC, 29631*

dlfrost@clemson.edu

In confocal single-molecule FRET experiments, the joint distribution of FRET efficiency and donor lifetime distribution can reveal underlying molecular conformational dynamics via deviation from their theoretical Forster relationship. This shift is referred to as a dynamic shift. In this study, we investigate the influence of the free energy landscape in protein conformational dynamics on the dynamic shift by simulation of the associated continuum reaction coordinate Langevin dynamics, yielding a deeper understanding of the dynamic and structural information in the joint FRET efficiency and donor lifetime distribution. We develop novel Langevin models for the dye linker dynamics, including rotational dynamics, based on first physics principles and proper dye linker chemistry to match accessible volumes predicted by molecular dynamics simulations. By simulating the stochastic translational and rotational dynamics of the dyes, we show that the observed dynamic shift can largely be attributed to the mutual orientational dynamics of the electric dipole moments associated with the dyes and not their accessible volumes.