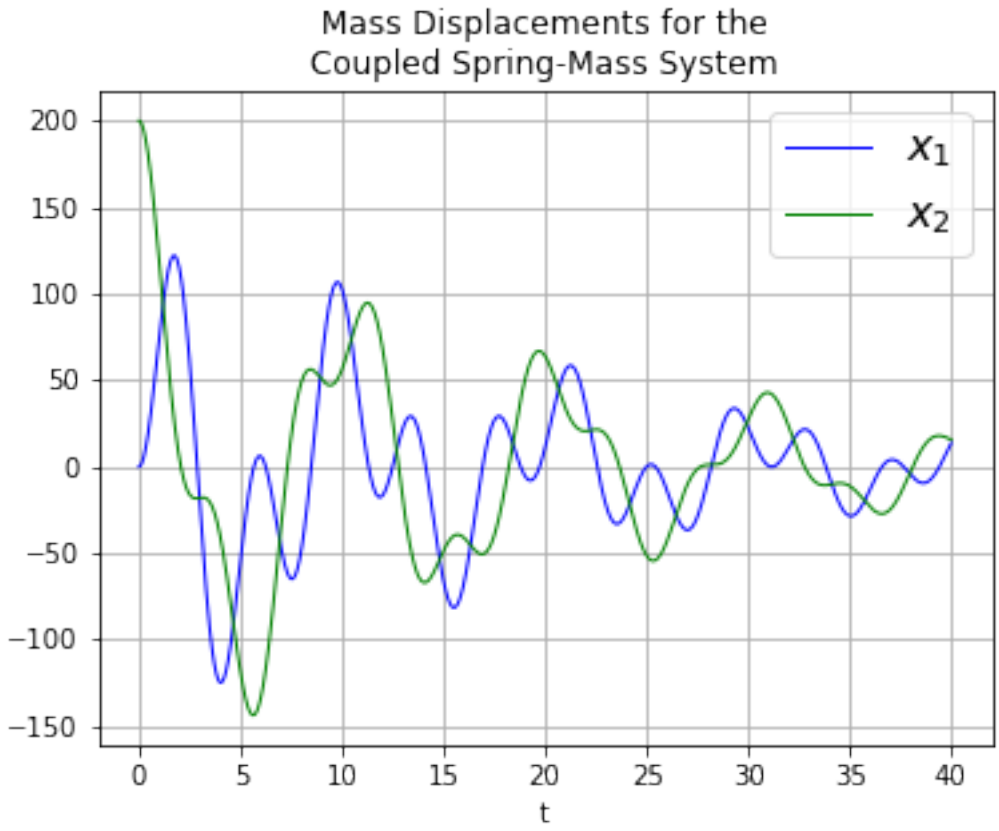
FRET Efficiency Conversion

This model creates a transform that converts FRET efficiency histograms derived from experiment to a distribution of times that a substrate would take going in between individual prions in an aggregate.

We introduce a plane of 3000 x 3000 coupled oscillators that simulate nonradiative resonance transfer between two fluorophores [1].



The FRET efficiency is calculated from each coupled oscillator over the time range with the following equation:

$$E = \frac{1}{\left(1 + \frac{R}{R_0}\right)^6} \quad \ldots 1$$

Where R is the distance between the two oscillators and R_0 is the critical distance at which E = 0.5. R_0 was determined from a paper [4]. An alternative equation to the FRET efficiency is:

$$E = 1 - \frac{t_{DA}}{t_D} \quad \ldots 2$$

Where t_DA is the fluorescence lifetime for the combined oscillator and t_D is the fluorescence lifetime for the donor fluorophore – which from [3] was determined to be 3.3 ns. Rearranging 2 and combining with 1 gives:

$$t_{DA} = \frac{-t_D}{\left(1+\left(\frac{R}{R_0}\right)^6\right)-1} \quad \ldots 3$$

The t_DA was averaged over the time range to account for the multiple bursts. A best-case scenario was taken for substrate movement at 1 angstrom/1ns. A time metric was also created for substrate movement:

$$t_S = \frac{R}{1} \quad \ldots 4$$

This was also averaged over the time range of each coupled oscillator.

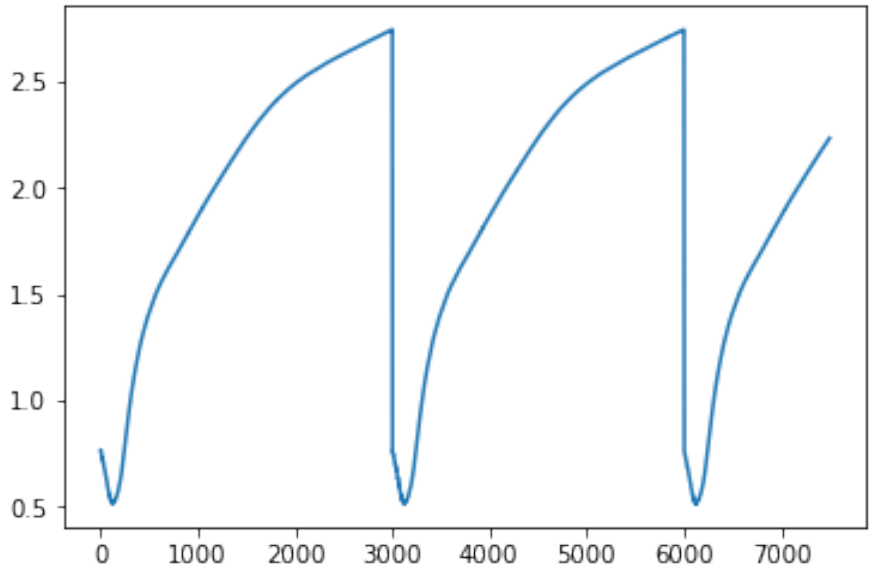


Figure 1 Resonance Transfer Times

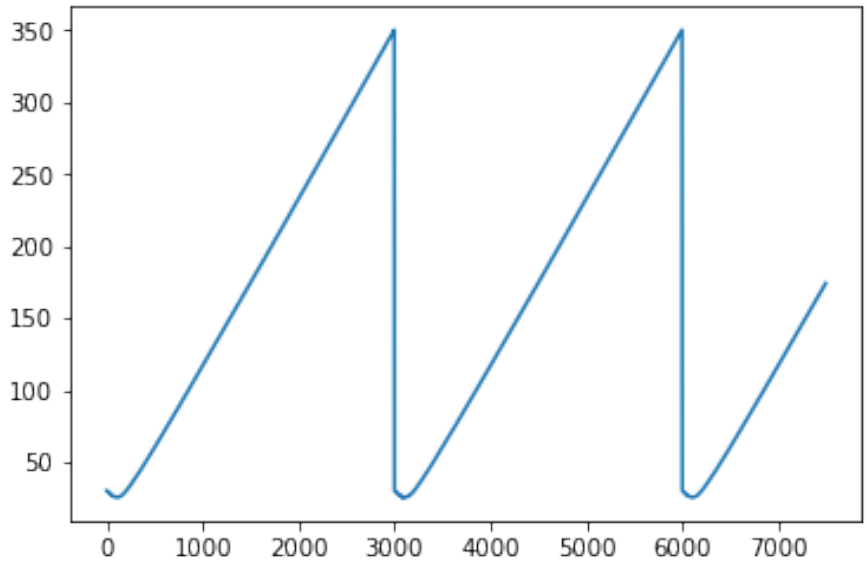


Figure 2 Substrate Times

If we analyze the plots for the resonance transfer and the substrate movement, we see that the resonance transfer trend is a nonlinear variation of the substrate one. In other words, the substrate channeling can be modelled by taking the first peak in the power spectrum of the resonance transfer.

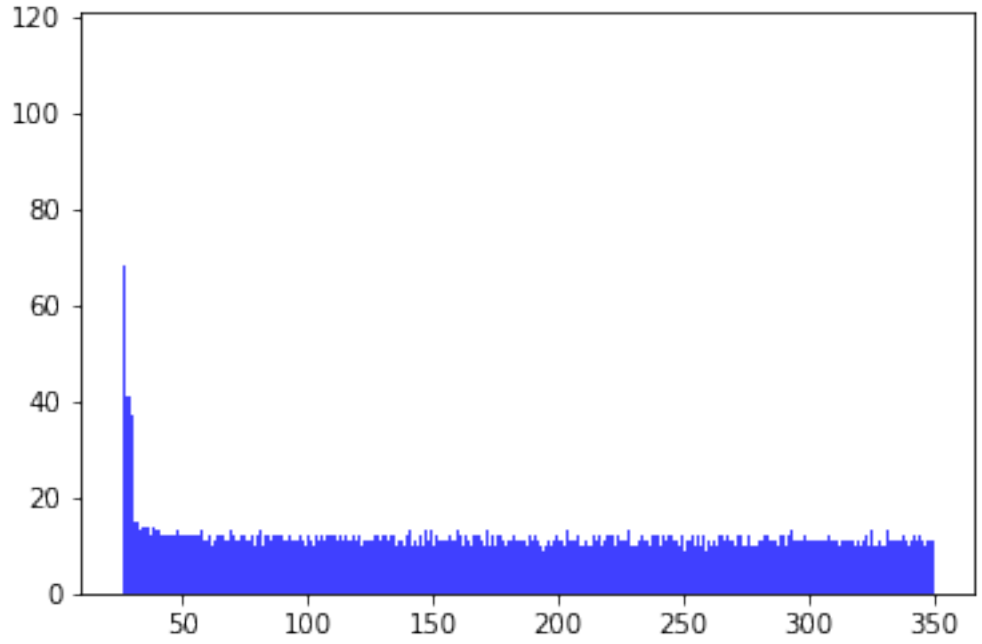


Figure 3 Substrate Time Distributions

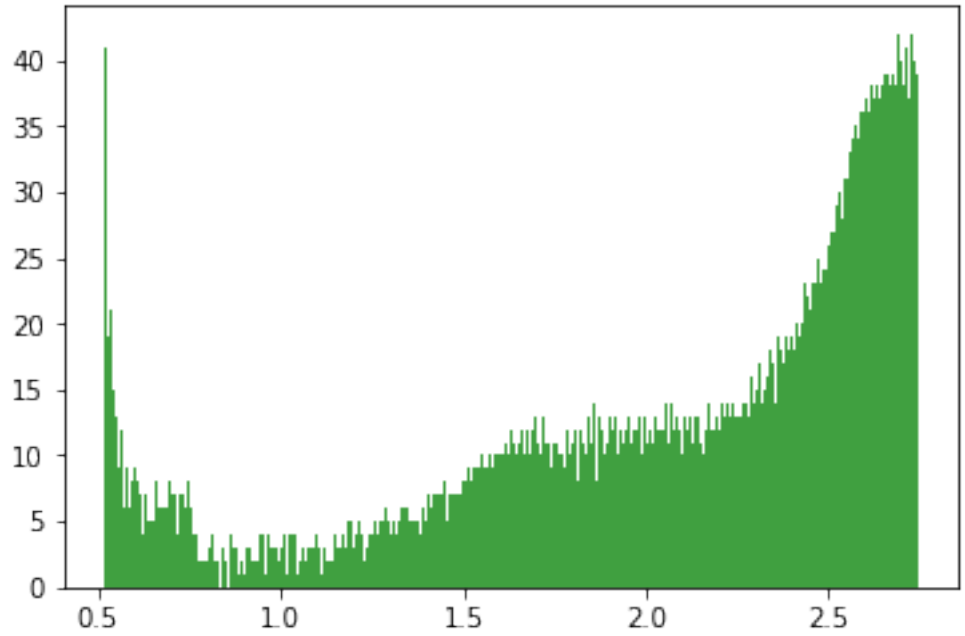


Figure 4 Resonance Transfer Distributions

Coming back to distributions that the FRET machine can provide, we deconvolve the resonance transfer signal from the substrate movement signal. The result can be convolved with experimental FRET results to obtain distributions of times [5].

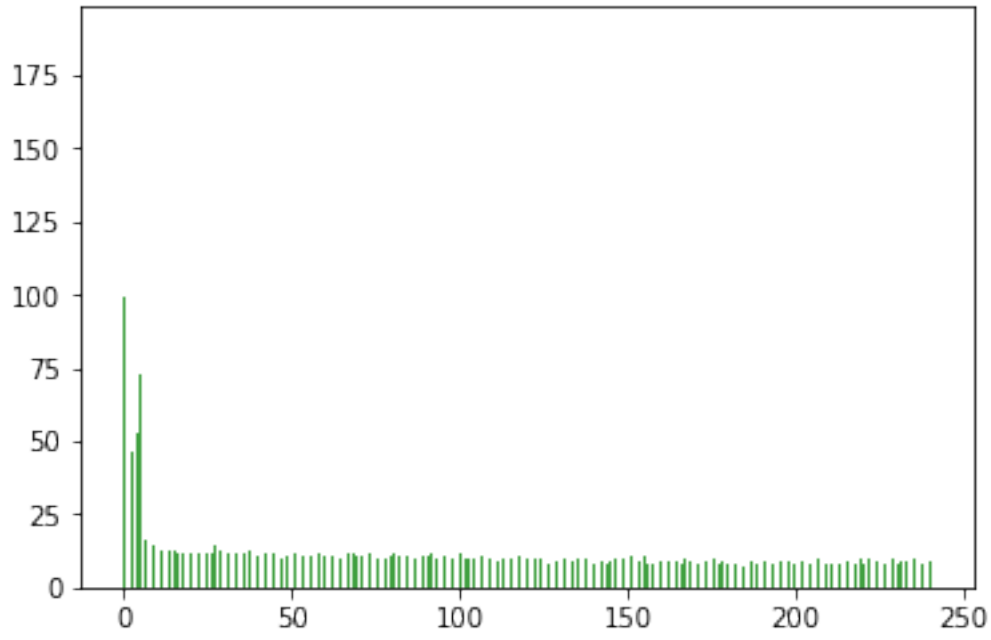


Figure 5 Representative Distribution of Transform

References

[1] https://arxiv.org/ftp/arxiv/papers/0908/0908.1815.pdf

[2] On Resonance Transfer of Excitation Energy Between Aromatic Aminoacids in Proteins - George Karreman, Richard H. Steele and Albert Szent-Gyorgyi

[2] https://www.jstor.org/stable/89418?seq=3#page_scan_tab_contents

[3] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1300756/

[4] http://www.jbc.org/content/282/49/35440.long

[5] http://www.math.drexel.edu/~tolya/Aronszajn_RKHS.pdf