Abstract

Förster resonance energy transfer (FRET) is a photophysical process in which an electronically excited chromophore spontaneously transfers energy to another molecule by a non-radiative dipole-dipole interaction. While this occurs naturally in processes such as light harvesting in photosynthetic organisms, it is now commonly used as a tool in molecular biophysics to examine the proximity and structure of biological macromolecules and to report on biochemical events. One of the features making FRET so widely used is the strong dependence of transfer on the distance between the participating molecules. Due to this, it has been termed a 'spectroscopic ruler' enabling the measurement of intermolecular distances and conformations of proteins and nucleic acids.

Although the utility of this method is now well appreciated, many di culties arise in interpreting FRET experiments to gain detailed quantitative information.One complication is that the chance of transfer taking place is dependent on the orientation of the participating molecules, something that is di cult (if not impossible) to measure. Another di culty comes from the fact that the commonly used uorescent dyes are characterised by high conformational exibility, which allows them to sample substantial space around the point of attachment introducing further uncertainty to the distance measurements. Moreover, the range of possible application of FRET as a spectroscopic ruler is limited to 10 nm, whereas many of biological events that could potentially be signalled by FRET occur on larger distances.

In my work, I aim to use computational techniques to address these di culties, by developing tools that can be used to better interpret the results of FRET experiments and to contribute to the design of new experiments employing FRET.

This thesis are comprised of published articles with an introduction and conclusion drawing together the published papers in a cohesive manner. Due to the dual-award form of this thesis that need to compromise both Polish and Australian law, the introduction contain also two unpublished chapters that describe our plans for future research.