Robust Statistics and Deep Learning Assisted Analysis of Single Molecule Imaging Data

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Single-molecule imaging and spectroscopy have revolutionized how we investigate the mechanism of processes at the nanometer scale. In particular, Single-molecule Förster resonance energy transfer (smFRET) allows investigation of the dynamics of single biomolecules in cells, membranes and solution. using two-color single-molecule microscopy (Fig. 1). smFRET probes distances on the nanometer scale (2.5-10 nm) one molecule at a time on the timescale of seconds to minutes. Its ability to measure accurate distances and kinetics has turned smFRET into a powerful tool for deciphering molecular interaction mechanisms and structures of biomolecules.

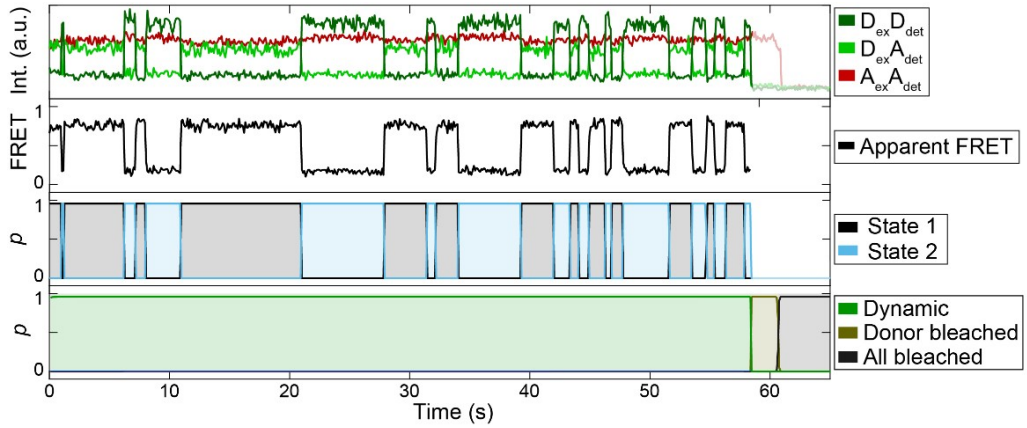

Fig. 1. Top: Two-color single-molecule time trajectory and FRET quantification. Botton: modelling and analysis

Quantitative smFRET data analysis is strongly hampered due to low statistics, low signal-to-noise ratio (SNR), and photophysics. Overcoming these limitations requires large data volumes as very few molecules contain the desired information with suitable quality. Various approaches have been developed, conventionally employing user-defined thresholds. However, depending on the user, data evaluation is prone to cognitive biases and poses a challenge to reproducible analysis results. Recently, **robust statistics and deep learning assisted analysis** have been demonstrated to rapidly automate trace classification and keep user bias to a minimum.

In this project, the student will get familiar with **Single-Molecule Imaging and Spectroscopy Techniques for data acquisition and analysis based on robust statistics and deep learning**. The main **objective** of the project is to implement robust statistics through Hidden Markov Modelling Analysis and compare it against Deep-Learning Assisted approaches for Single-Molecule FRET data.