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Biological System Imaging and Analysis Portfolio

Professor Steve Presse, at Arizona State University, and various collaborators at both ASU and other institutions, have developed a novel portfolio of technologies in the biological system imaging and analysis space. These technologies help to understand the complex dynamics of living systems from single molecules to whole cells by utilizing computational tools to analyze biophysical spectroscopic and imaging data.

M23-107L: Gene Network Inference. Gene networks, their connectivity and associated rates are encoded in single molecule Fluorescence In Situ Hybridization (smFISH) snapshot data, however extracting that information is challenging. Prof. Presse and collaborators at both ASU and St. Jude developed a novel tool to find the number of transcriptional modes of a gene alongside quantification of their levels of gene expression to enable inference of the number of gene states. This makes learning gene expression models possible from snapshots of RNA counts in collections of cells across time.

M23-108L: Particle Tracking System. While 3D particle tracking and localization enable direct monitoring of biomolecular processes within nanoscale environments, optical aberrations due to inhomogeneous refractive indices present challenges to probing these processes in situ. Prof. Presse and collaborators at both ASU and St. Jude have developed a novel method for 3D particle tracking and localization, in vivo, using 3D fluorescent microscopy techniques. This framework is capable of simultaneous particle tracking, phase retrieval and point spread function learning. It corrects for optical aberrations without using outside calibration techniques so that the 3D tracking is quantitative.

M23-110L: Single Molecule FRET Analysis. The goal of smFRET is to capture in progress changes of the macromolecular system in distance. Unfortunately, multiple sources of stochasticity obscure direct interpretation and contribute to uncertainty in the number of distinct system states visited by a labeled system. Prof. Presse and collaborators from both ASU and University of Tennessee developed a novel method for analyzing single photon single molecule FRET data. This method uses an adapted Bayesian nonparametrics framework to overcome the model selection problem and provide more accurate results in a more transparent fashion.

M23-286L: Potential Energy Landscapes from FRET. Single molecule FRET encodes information on potential energy landscapes from biological systems which are useful models for describing events such as protein folding and binding. However, current methods for decoding smFRET data to these landscapes assumes that the system probed evolves in discretized state-space, which is not appropriate for dynamics that occur along a continuous reaction coordinate. Prof. Presse and an ASU colleague have developed a novel method to decode a continuous potential from smFRET data without resorting to discrete state-space assumptions. This method unveils the full potential energy landscape, including barrier heights and friction coefficients all with reduce computational cost.

Potential Applications

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- Learning gene expression models to assist in targeted gene therapies, bacterial chemical manufacturing, bioengineering to target gene expression and more

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- Analysis software package to track particles and monitor details within nano-scale environments having inhomogeneous optical properties

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- Studying intra- and intermolecular dynamics of proteins, nucleic acids and their interactions using single molecule FRET (protein folding/misfolding/refolding, protein-protein interactions, disordered proteins, and more)

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- Inferring potential energy landscapes to unravel key biophysical phenomena including protein folding, binding, and the dynamics of molecular motors

Benefits and Advantages

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- Enables empirical quantification of any gene’s expression
- The sampling techniques used provide increased efficiency, critical for estimating network node numbers and rates simultaneously and self-consistently
- Able to simultaneously learn the number of modes of gene expression and