



Adding dynamics to structural biology - Easy-to-use single-molecule fluorescence tools to bring static biomolecular structures to life.

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Structural biology methods like cryo-electron microscopy and X-ray crystallography are enormously powerful tools to unravel biomolecular mechanisms of action. More recently, Artificial Intelligence and other computational approaches have opened new frontiers in protein design and structure determination. However, due to the largely static nature of their outputs, both types of approaches are typically unable to **provide insights into the dynamics of biomolecular complexes, such as temporal conformational changes, binding kinetics and diffusion properties**. Dynamic single-molecule techniques, such as Förster Resonance Energy Transfer (smFRET) and Fluorescence Correlation Spectroscopy (FCS) fill this gap. By revealing transient states and heterogeneous populations in real time, these approaches bridge the gap between high-resolution structures and functional dynamics, enabling a comprehensive understanding of biomolecular mechanisms. Unfortunately, so far, these methods have been inaccessible to the broader life science and drug development community.

Here, **we introduce the EI-FLEX, a novel benchtop instrument designed for seamless smFRET and FCS measurements, democratizing access to these powerful techniques**. Its compact, user-friendly design requires minimal setup and no specialized expertise, allowing researchers in standard laboratory environments to perform experiments effortlessly, at high throughput. Ease-of-use is achieved through integrated calibration and correction routines and automated sample handling, supporting rapid screening of multiwell plates as well as individual samples with sub-millisecond and sub-nm spatio-temporal resolution and single molecule sensitivity. Data analysis is streamlined via intuitive software featuring automated fitting algorithms, real-time visualization, and exportable reports, minimizing post-processing time and errors. The EI-FLEX empowers structural biologists, biochemists and drug developers to finally incorporate dynamic data on the level of individual biomolecular complexes into their workflows. It enables them to truly unravel and quantify drug-target interactions, complex formation and biomolecular conformational changes at unprecedented spatio-temporal resolution. By lowering barriers to entry, it propels the field toward faster, more complete discoveries in complex biomolecular systems.

In this seminar, we will cover applications of our instrument in a broad range of topics, such as **disordered proteins, phase separation and aggregation, membrane proteins, ternary complexes, membrane proteins, antibody development and virology**.

Afterwards, there will be the opportunity for in-depth 1:1 discussions to elaborate on specific project ideas and to prepare/design experiments for the upcoming test of the tool, planned for March. Please reach out to roman.renger@excitinginstruments.com or Angelica Struve Garcia (angelica.struve@embl-hamburg.de) to reserve a time slot to chat with Tim Craggs.