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Tracking Single Molecule Interactions and Dynamics

Single molecule tracking is critical to understanding molecular heterogeneity, interactions and intracellular processes which are important in disease diagnoses as well as progression monitoring. Most 3D tracking techniques lack precision for measuring biomolecular dynamics with the spatial scale of several nanometers, which includes DNA and proteins. Single molecule fluorescence is the most commonly used technique for tracking, however, photobleaching and the limited number of photons emitted from a single molecule compromise temporal resolution, precision and duration. Nanoparticle labels can overcome some of these limitations, but there are still challenges with achieving sub-nanometer resolution. A simple yet precise 3D tracking technique is needed for measuring single molecule dynamics.

Researchers at the Biodesign Institute of Arizona State University have developed a novel surface plasmon resonance microscopy (SPRM) technique which can track the motion of tethered nanoparticles in 3D. This method has been used to track 100 particles simultaneously in three dimensions with millisecond time resolution. Further, no additional optical components for determining axial displacement are required. This technique has been used to study the dynamics of short DNA and its interaction with helicase, as well as differentiation of specific and non-specific binding of antibodies.

This multiplexed 3D single-particle SPRM tracking technique will provide unprecedented insight into understanding single-molecule dynamics and biosensing.

Potential Applications

- Studying the details of molecular binding events at the single molecule level
  - Particle based detection of antibody-antigen binding and discriminate between specific and non-specific binding events
  - Determine the unwinding rate of DNA and the rotation angle of bound helicase
  - Investigate protein conformation change & single base pair change in DNA
  - Diagnostics/immunoassays with improved sensitivity and specificity

Benefits and Advantages

- Can precisely image 100 single tethered molecules in 3D simultaneously
- Takes advantage of the high sensitivity in the axial direction for sub-nanometer precision
- Temporal resolution of up to 1000 fps – can be improved by increasing the incident light intensity
  - ~1 nm precision in xy and ~0.1 nm precision in z can be readily achieved with a 15 mW SLED light source
- Processes multiple signals at once
- Can separate specific from non-specific binding events for accurate diagnostic analyses
- Analysis of molecular binding events and kinetics that were previously not possible with existing techniques can be achieved

For more information about this opportunity, please see

Ma et al - ACS Sens - 2021

For more information about the inventor(s) and their research, please see

Dr. Wang's departmental webpage

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