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System for Single Protein Imaging and Analysis

The ability to determine molecular binding is crucial in drug screening, biomarker detection, and understanding biological processes at the molecular level. Many methods for looking at binding kinetics, such as liquid chromatography, mass spectrometry, western blot, etc., are time consuming, cause protein fragmentation/denaturation and do not allow for single molecule analyses.

Current optical detection technologies fall into two categories, label-based and label-free. Label-based approaches can detect molecules before and after molecular binding occurrences. While specific, they lack kinetic information. Label-free approaches can provide information about molecular binding kinetics, however, sensitivity diminishes with small or single molecules.

Researchers at the Biodesign Institute of Arizona State University have developed a novel surface plasmon resonance (SPR) scattering optical imaging system, including image processing algorithms, to image and analyze binding kinetics as well as other characteristics of single molecules. Because detection of reflected light produces a strong background that can overwhelm signals from single molecules, this system, instead, detects light scattered from the sample molecules and sensor surface.

By coupling the detection of scattered light from the molecules and sensor surface with novel image processing algorithms, this system is able to effectively image and analyze single molecules and their binding kinetics.

Potential Applications

- Biomarker detection
- Drug screening
- Analyzing molecular binding kinetics of single molecules
  - Quantify molecular interaction kinetics of proteins at single molecule level
  - Quantifies protein expression levels and differentiates binding of impurity molecules from that of the target protein
  - Monitor/analyze heterogeneity of proteins

Benefits and Advantages

- Label free
- Size and number of individual molecules can be measured simultaneously
- Proteins or other molecules do not need to be separated prior to detection
- Collects only light scattered from the samples and sensor surface for improved photon collection efficiency
- Overcomes problems with rapid signal decay in conventional dark field microscopy by interferometry scattering effect
- Novel image processing algorithms
  - Subtract background noise
  - Correct mechanical or thermal drift
- Allows for monitoring of heterogeneity of proteins
- Retain the capabilities of traditional SPR

For more information about this opportunity, please see

Zhang et al - Nature Methods - 2020

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

Dr. Wang's departmental webpage