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Label-Free Detection, Identification & Quantification of Single Proteins

Proteins play a prominent role in most cellular functions and many biological processes. They are also important as potential therapeutics, drug targets and biomarkers. The size or conformation and subsequent activity of proteins is regulated by both structure and electrostatic properties. Common techniques for measuring the electrostatic properties of proteins have low sensitivity, thus they require large numbers of protein molecules and cannot measure single proteins. Tracking the conformation and mobility change of a single protein can provide insight into the function associated with its structure and electrostatics.

Researchers at the Biodesign Institute of Arizona State University have developed label-free methods for protein analyses, including determination of size, detection of conformational changes, and identification of single proteins. Single proteins are tethered to an indium tin oxide (ITO) chip surface using a flexible polymer linker. The proteins are then oscillated by applying an alternating electrical field to induce an image contrast change which can be measured. From that image, the size and mobility of each protein can simultaneously be obtained and tracked in real-time. Individual proteins can be measured down to 0.25 nm in size and 1.2 electrons in charge, which covers most proteins in nature. Antibody binding to the proteins can also be detected in real time. The charge and size quantification, together with specific antibody binding enable protein identification.

This novel method can determine the charge, size and identity of proteins, analogous to LC, MC and Western Blot techniques, but achieved at the single molecule level, enabling greater capabilities in protein analysis.

Potential Applications

- Protein detection, identification, quantification, size determination, mobility, conformation and analysis of post translational modifications & protein-ligand interactions
  - Diagnostics
  - Therapeutics
  - Drug targets

- Research
- Single cell and single virus analysis

Benefits and Advantages

- Improved detection sensitivity
- Does not require labels
- Fast Fourier Transform is performed on each pixel to remove noise
- Individual proteins can be measured down to 0.25 nm in size and 1.2 electrons in charge, which covers most proteins in nature
- Greater throughput - can measure multiple single protein molecules simultaneously over a much larger surface area
- Both size and mobility (charge) of a single protein can be obtained
- Proteins can be tracked over time to enable ligand binding and dissociation studies

For more information about this opportunity, please see

Ma et al - bioRxiv - 2019

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

Dr. Tao's laboratory webpage