Skysong Innovations
Advancing the Arizona State University Knowledge Enterprise

1475 N. Scottsdale Road, Suite 200
Scottsdale, AZ 85287-3538
Phone: 480 884 1996 Fax: 480 884 1984

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Inventors

Nongjian (nj) Tao

Wenwen Jing

Contact

Jovan Heusser
jovan.heusser@skysonginnovations.com

Time-Resolved Digital Immunoassay

Detection, identification and quantification of molecular biomarkers, such as proteins, peptides, exosomes, hormones, neurotransmitters, metabolites and nucleic acids, are critical to disease diagnosis and progression monitoring. While there are multiple approaches to biomarker analyses, the most validated and well-established is ELISA. Although powerful, the limit of detection (LOD) and time required for testing in ELISA techniques are often insufficient for many clinical applications. Digital immunoassay methods have been developed for single molecule analyses, however, improved detection limits come at the expense of test time (e.g. >1 hr) and dynamic range (e.g. <2 ng/mL), which are critical for disease diagnosis and treatment.

Researchers at the Biodesign Institute of Arizona State University have developed a time-resolved digital immunoassay system that utilizes plasmonic imaging of antibody-conjugated nanoparticles for rapid detection of biomarkers with a wide dynamic range. Plasmonic imaging provides high contrast and fast imaging so that single molecule binding events can be detected. Real-time counting of the nanoparticles as they bind to the biomarkers enables accurate assessment of biomarker concentration without requiring lengthy incubation or additional sample processing. Further, super-localization tracking of each nanoparticle and real-time counting allows two binding events to be detected within a distance smaller than the diffraction limit, enhancing the dynamic range and minimizing counting error.

This novel system is able to rapidly detect and quantify molecular biomarkers with a shortened test time and maximized precision. It could be highly valuable in diagnosing and tracking progression of acute diseases where rapid and precise biomarker quantification is sorely needed.

Potential Applications

- Detection and quantification of molecular biomarkers across a vast concentration rage

o Particular relevance in early detection of acute diseases such as infectious disease and cardiovascular disease

Benefits and Advantages

- Single molecule resolution (protein, peptide, DNA and RNA)
- Limit of detection of ~3 pg/mL, dynamic range of 4-12500 pg/mL, and a total detection time of ~25 mins
- Increased detection precision and speed with higher biomarker concentrations
- High contrast imaging for accurate tracking of each nanoparticle
- Multiple nanoparticle binding events can be resolved in an area within the diffraction limit
  - Highly precise detection of single binding events
  - Wide dynamic range
- Does not require lengthy incubation or additional sample processing steps
  - Can be used on clinical serum or plasma samples
  - Does not require serial dilutions because of the wide range of detection

For more information about this opportunity, please see

Jing et al - ACS Nano - 2019

Jing et al - bioRxiv - 2018

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

Dr. Tao's departmental webpage

Dr. Tao's laboratory webpage