O-27.5 Short talk

Programmable DNA-origami-based platform for label-free protein profiling

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High-resolution protein detection is vital for early diagnosis and proteomics, yet conventional methods often rely on labeling, sample processing, or complex instrumentation, limiting real-time analysis and detection in biological media. Here, we introduce a modular DNA origami-based dynamic mass photometry (MP) platform that enables label-free, single-molecule, and multiplexed protein detection in buffer and complex biological media. Our system uses programmable DNA nanostructures with distinct mass and diffusion properties on a supported lipid bilayer, each selectively functionalized with an antibody for a specific biomarker (CA-125, transferrin, HER2, AFP, EGFR, or Rb). By combining mass and diffusion multiplexing, we link each complex's unique signature to its biomarker, enabling real-time detection and monitoring of interactions- including oligomerization events- while internal controls rule out nonspecific interactions. We demonstrate rapid detection and multiplexed profiling of native protein biomarkers in diverse cell lysates and plasma, highlighting the platform's sensitivity and adaptability. Its programmability extends its scope to diverse targets, enabling personalized diagnostics and improving early detection. By uniting programmability, scalability, and robustness, this approach offers a powerful tool for high-precision proteomic research and advanced diagnostics.