Delving into Molecular Fingerprints for Biosensing Applications

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Molecularly imprinted polymers (MIPs) have emerged as powerful synthetic recognition elements, yet their broader utility has been hampered by laborious synthesis processes, limited throughput, and insufficient real-time control. Here, we present an advanced microfluidic micro-reactor platform that enables the continuous, in situ generation of trillions of protein-imprinted nanoparticles within an exceptionally short time-span of 5–30 minutes. Leveraging COMSOL Multiphysics simulations, we optimized fluidic parameters to ensure efficient mixing and uniform nanoparticle formation, achieving size control between 52–106 nm. Molecular docking and dynamics simulations provided insight into monomer-template interactions, while principal component analysis (PCA) guided the optimization of critical synthesis parameters, including dispersity and polymer content. The resulting MIPs demonstrated high binding precision (81%), a 4.5-fold enhancement in selectivity, and consistent reusability across multiple cycles. Remarkably, the system achieved synthesis speeds 48–288 times faster than conventional methods, halved reagent consumption, and produced up to 1.5 times more nanoparticles per cycle—all at an estimated cost of ~$10 per unit. Extending this technology, we have also developed a multiplexed nanoplasmonic detection platform for the simultaneous identification of *Escherichia coli* (*E. coli*) and *Staphylococcus aureus (S. aureus*)—two major human pathogens. Bacteria-specific MIPs were functionalized with gold nanoparticles and arrayed in 96-well plates, enabling parallel detection with high throughput. The platform exhibited impressive sensitivity, with detection limits of 4.8×10^4 cfu/mL for *E. coli* and 4.2×10^4 cfu/mL for *S. aureus*, and demonstrated strong selectivity even in the presence of Gram-specific controls. The performance of our platform was further validated in complex biological matrices such as artificial urine and serum. Collectively, this work introduces a versatile and cost-efficient strategy for rapid nanoparticle synthesis and pathogen detection, with significant implications for clinical diagnostics, biosensing, and environmental monitoring.

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