Grating-Coupled Fluorescence Plasmonics (GC-FP) Biosensor: Expanding from Protein to Nucleic Acid Detection

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Abstract

Disease diagnosis and biomarker screening require developing highly sensitive and adaptable biosensing platforms. This research focuses on a biosensing platform known as grating-coupled fluorescence plasmonics (GC-FP), which utilizes periodic nanoscale gold gratings to amplify fluorescence emission through surface plasmon-coupled emission (SPCE). When polarized light excites surface plasmons at the metal-dielectric interface, fluorophores near the surface couple their emission into these plasmon modes, resulting in ~100-fold signal enhancement compared to conventional flat-surface fluorescence. This enhancement improves the detection of low-

abundance targets in complex biological samples while maintaining spatial specificity through multiplexed arrays.

GC-FP chips are fabricated at the Albany NanoTech 300 mm wafer cleanroom facility using photolithography, resulting in 500 nm pitch gratings coated with ~70 nm gold and ~3 nm titanium. Biological reagents such as antigens, antibodies, aptamers, or oligonucleotides are deposited using a precision piezo-driven microarrayer (Scienion sciFLEXARRAYER S3) in spatially defined arrays. Samples and reagents are flowed across the chip via automated microfluidics, and fluorescently labeled targets are detected using a Centinela imaging platform (Ciencia, Inc.). We have previously demonstrated GC-FP-based serological detection of Lyme disease and COVID-19 antibodies with excellent sensitivity and specificity [1–4]. Recent developments have translated the platform into point-of-care formats, including dipstick and lateral flow configurations.

Building on this foundation, current work focuses on extending GC-FP to nucleic acid-based detection. Short oligonucleotide probes printed on the grating surface capture complementary DNA or RNA targets through room-temperature hybridization. Preliminary results demonstrate detection of DNA-DNA hybridization events down to 100 pM of the target strands, with specificity confirmed through spatially resolved multiplexing in which only complementary probe regions exhibit fluorescence.

In parallel, we are exploring aptamer-based detection of small molecules such as dopamine using a modular duplex-bubble switch design. A fluorophore-labeled DNA aptamer hybridized to a quencher-bearing displacement strand remains quenched until target binding induces conformational change, increasing fluorophore-quencher separation and generating a SPCE-enhanced fluorescent signal.

We are also investigating switchback DNA strand displacement on the GC-FP platform, tracking fluorescence changes as invading strands displace switchback structures to form conventional duplexes.

Ongoing work focuses on optimizing probe design, surface chemistry, and demonstrating simultaneous detection of nucleic acids and antibodies on a single chip. This versatility positions GC-FP as a promising tool for next-generation diagnostics across laboratory and point-of-care settings.

References

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