Surface Acoustic Wave (SAW)-Induced Mixing Enhances Biomolecules Kinetics in a Novel Phase-Interrogation Surface Plasmon Resonance (SPR) Microfluidic Biosensor

Authors : M. Agostini, A. Sonato, G. Greco, M. Travagliati, G. Ruffato, E. Gazzola, D. Liuni, F. Romanato, M. Cecchini Abstract : Since their first demonstration in the early 1980s, surface plasmon resonance (SPR) sensors have been widely recognized as useful tools for detecting chemical and biological species, and the interest of the scientific community toward this technology has known a rapid growth in the past two decades owing to their high sensitivity, label-free operation and possibility of real-time detection. Recent works have suggested that a turning point in SPR sensor research would be the combination of SPR strategies with other technologies in order to reduce human handling of samples, improve integration and plasmonic sensitivity. In this light, microfluidics has been attracting growing interest. By properly designing microfluidic biochips it is possible to miniaturize the analyte-sensitive areas with an overall reduction of the chip dimension, reduce the liquid reagents and sample volume, improve automation, and increase the number of experiments in a single biochip by multiplexing approaches. However, as the fluidic channel dimensions approach the micron scale, laminar flows become dominant owing to the low Reynolds numbers that typically characterize microfluidics. In these environments mixing times are usually dominated by diffusion, which can be prohibitively long and lead to long-lasting biochemistry experiments. An elegant method to overcome these issues is to actively perturb the liquid laminar flow by exploiting surface acoustic waves (SAWs). With this work, we demonstrate a new approach for SPR biosensing based on the combination of microfluidics, SAW-induced mixing and the real-time phase-interrogation grating-coupling SPR technology. On a single lithium niobate (LN) substrate the nanostructured SPR sensing areas, interdigital transducer (IDT) for SAW generation and polydimethylsiloxane (PDMS) microfluidic chambers were fabricated. SAWs, impinging on the microfluidic chamber, generate acoustic streaming inside the fluid, leading to chaotic advection and thus improved fluid mixing, whilst analytes binding detection is made via SPR method based on SPP excitation via gold metallic grating upon azimuthal orientation and phase interrogation. Our device has been fully characterized in order to separate for the very first time the unwanted SAW heating effect with respect to the fluid stirring inside the microchamber that affect the molecules binding dynamics. Avidin/biotin assay and thiol-polyethylene glycol (bPEG-SH) were exploited as model biological interaction and non-fouling layer respectively. Biosensing kinetics time reduction with SAW-enhanced mixing resulted in a \approx 82% improvement for bPEG-SH adsorption onto gold and \approx 24% for avidin/biotin binding—≈ 50% and 18% respectively compared to the heating only condition. These results demonstrate that our biochip can significantly reduce the duration of bioreactions that usually require long times (e.g., PEG-based sensing layer, low concentration analyte detection). The sensing architecture here proposed represents a new promising technology satisfying the major biosensing requirements: scalability and high throughput capabilities. The detection system size and biochip dimension could be further reduced and integrated; in addition, the possibility of reducing biological experiment duration via SAW-driven active mixing and developing multiplexing platforms for parallel real-time sensing could be easily combined. In general, the technology reported in this study can be straightforwardly adapted to a great number of biological system and sensing geometry.

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