

Integrated Optical Biosensor: Ultrasensitive and Specific Detection of Signature Proteins

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An ultra-sensitive and specific biosensor for the detection and identification of protein toxins has been developed and is being extended to other signature proteins. The integrated optical biosensor mimics nature in two important ways. First, the heart of the sensor is the target of a protein toxin—receptor molecules that decorate the surface of cell membranes. Phospholipid bilayers with optically tagged receptor molecules are directly attached to optical transducers and used to mimic the cell membrane surface. Second, biomolecular recognition is directly coupled to signal transduction and amplification, as they are in many cell signaling processes in nature, by using the protein-receptor binding to trigger proximity-based fluorescence resonant energy transfer (FRET). Protein-receptor recognition that involves two or more receptor molecules (e.g., glycolipids, RNA aptamers) brings multiple optically tagged molecules into close proximity thereby triggering the FRET signal. Using fluid bilayers coated onto glass beads for flow cytometry, sensitivities of < 10 pM (pico Molar) and < 50 pM have been achieved for cholera and avidin respectively. This sensitivity compares favorably with lab-based ELISA methods that are based on immuno assays. In contrast to ELISA, the integrated optical biosensor is fast (minutes), simple (single step with no added reagents), insensitive to temperature variations and is robust owing to the stability of the recognition molecules and membranes.

The integrated optical biosensor, although first demonstrated using flow cytometry, has now been adapted to evanescent wave detection using planar optical waveguides. The advantages of using planar waveguides are multiple: i) ultrasensitive detection of FRET, ii) spatial filtering of non-specific background fluorescence to allow for use of dirty clinical or environmental samples, iii) simple deposition and patterning of recognition molecules for multianalyte detection, iv) sensor elements that are inexpensive, reusable and easy to exchange in the field and v) potential development of fully miniaturized sensor systems using low-cost integrated electro-optical components. Although originally developed for multivalent protein toxins, this approach can be adapted to other signature proteins and envelope viruses. Applications in environmental sensing of toxins and pathogens, low-cost medical diagnostics and early diagnosis of infection will be discussed.