Multi-phenotypic Cellular Arrays for Biosensing

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5.1. INTRODUCTION

The term “biosensor” is a broad based term referring to a sensor that uses a biological molecule as the sensing element. A “cell-based” biosensor, then, would utilize a prokaryotic or eukaryotic cell or cell line as the sensing agent (Figure 5.1). Single phenotype biosensors use one type prokaryotic or eukaryotic cell line as the sensing elements, which are contrasted to single-cell biosensors that may use, as the name implies, one cell as the sensing element. Though many methods have measured chemical toxins have utilized chemical, nucleic acid, and antibody approaches [1], sensing technology as a whole would be improved through the introduction of whole cell based biosensors. Whole cell-biosensors have several inherent advantages over DNA, RNA, and protein arrays. Foremost, a whole cell biosensor can offer functional information, i.e., information about the effect of a stimulus on a living system [2]. Functional information includes the effects of stimuli on cell health (toxicity) as well as cell function. Secondly, the use of cell-based biosensors eliminates the need for costly purification steps, such as the isolation and retrieval of RNA and DNA. A cell based biosensor also provides natural signal amplification of a response through cellular pathways and cellular cascades [3].

The use of cell-based biosensors has rapidly advanced in the last decade for environmental monitoring, sensing for chemical and biological warfare agents, and high-throughput
drug screening. Of particular importance is the application of cell-based systems to drug discovery, because cells represent the ultimate target for pharmaceuticals. In this instance, a multi-phenotypic biosensor would allow systemic information to be obtained for a drug candidate in a one-pass system. For example, a drug candidate could be tested on hepatocytic and macrophagic cells simultaneously to gauge that candidates affect on liver function and immune response in a single assay step.

Additionally, with the increasing number of drug candidates available in the recent years, the demands for high-throughput drug screening system with lowered costs [4] have stimulated development of assay miniaturization [5–7]. To move towards assay miniaturization, significant efforts have focused on the fabrication of microarrays of living cells using a variety of cell patterning techniques. Cellular arrays are being coupled with fluorescence technology (either whole cell fluorescence or green-fluorescent protein transfected cells) and incorporated into microfluidic devices to optically detect the physiological changes of cells by drug candidates. As an alternative to measuring the optical properties of fluorescent cells, sensors can utilize the electrochemical properties of cells. Changes in the electrical properties of neural, cardiac, or pancreatic beta cells can be directly measured in response to changes in external environment [3].

In order to become a widely used sensing tool, multi-phenotypic biosensors must meet several technical criteria. First, the fabrication of cellular arrays must be relatively easy, inexpensive, and non-toxic. These fabrication methods should be conducive to storage of