### Chapter 19

# Layer-by-Layer Technology and Its Implications in the Field of Glucose Nanobiosensors

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#### **ABSTRACT**

Diabetes is the seventh leading cause of deaths in the US with almost 439 million people worldwide expected to be diabetic by 2030. The need for continuous, non-invasive monitoring is a top priority. Earlier devices that utilized electroenzymatic sensing technique were minimally invasive and had major pitfalls. Advancements in various non-invasive, especially fluorescence-based, sensing along with developments in LBL assembly have resulted in a new breed of micro/nanosensors that are implantable, reliable, reproducible, mechanically and functionally stable, responsive, and miniaturized. In this chapter, the authors discuss the history of glucose sensors, evolution over the past four decades, methods employed to detect glucose levels in fluorescent biosensors, and assays that can be fabricated on to the sensor membrane, immobilized into the membrane as multilayers, or encapsulated within micro/nanocapsules using LBL assembly technology. The authors briefly review the various materials available and currently implemented for fabrication of glucose biosensors using LBL assembly.

#### INTRODUCTION

What is Layer-by-Layer (LBL) assembly technology? As the name suggests, LBL is a versatile, gentle, easy and inexpensive process for complex multilayer formation with nanoscale precision in a controllable one layer at a time format (Ariga, Hill, & Ji, 2007; Decher, 1997; Love, Estroff, Kriebel, Nuzzo, & Whitesides, 2005; Lvov, Decher, & Mohwald, 1993; M. J. McShane, 2006). In simple terms, this process involves the adsorption technique where in consecutive oppositely charged anionic and cationic layers are alternated to obtain

assembled monolayer (SAM) (Dubois & Nuzzo, 1992; Rudolph, 1994; Wink, van Zuilen, Bult, & van Bennkom, 1997) and the Langmuir-Blodgett (LB) films (Girard-Egrot, Godoy, & Blum, 2005;

thin film morphology (Ariga et al., 2007; Decher, 1997; Lvov et al., 1993). This technique was first

implemented in 1966 using microparticles such

as silica and alumina (Iler, 1966) which was later

modified and established by Decher G. et al.

(Decher & Hong, 1991a, 1991b; Decher, Hong,

Unlike earlier techniques such as the self-

& Schmitt, 1992; Lvov et al., 1993).

Zasadzinski, Viswanathan, Madsen, Garnaes, &

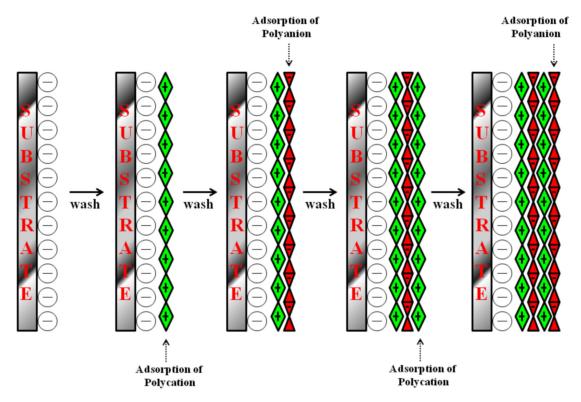
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Schwartz, 1994) which were neither versatile nor simple to construct; LBL assembly paved the way for next generation approach and practical option to achieve multilayer fabrication (Ariga et al., 2007). Of note, the difficulty in establishing robust, thin and well-organized films using LB method resulted in it not gaining much ground over the years. The loss of electrostatic force of attraction after few layers using LB method when compared to LBL technique where in the electro attractive forces are still strong even after 80 layers (Decher, 1997) made it a less feasible option. LBL assembly technique helped to mitigate all the drawbacks with earlier technologies for nanoscale fabrication.

The driving force behind LBL assembly technique is primarily outlined by simple electrostatic attraction between positively charged cations and negatively charged anions (Bernt, Kurihara, &

Kunitake, 1992; Decher, 1997; Decher & Hong, 1991a; Lvov et al., 1993). It constitutes excess adsorption of polycation/polyanion of interest at relatively high concentration resulting in charge neutralization and resaturation bringing about charge reversal (Ariga et al., 2007; Bernt et al., 1992) (Figure 1). Primary advantage of alternating surface charge is the user flexibility and freedom to determine the precise number of layers, definite knowledge over material composition and control over thickness at nanoscale level (M. J. McShane, 2006) resulting from linear growth of bilayers. Other significant advantages include; the absence of covalent bonds, substrate size independence (Lvov et al., 1993) and low cost simplicity of use (Ariga et al., 2007). Hydrogen bonding and metal interactions are also been known to be used for LBL assembly along with various biochemical and physicochemical interactions (Ariga et al., 2007).

Figure 1. Schematic representation of simple layer-by-layer (LBL) assembly technique for adsorption of positively charged cations and negatively charged anions on a substrate of interest (Adapted from (Decher, 1997))



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