## A New Protein Sensor Platform Based on Competitive Protein Adsorption for Thyroglobulin Detection

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We report a new sensing technique of proteins using competitive proteins' displacement reaction on a surface, namely Vroman effect. A target protein displaces a pre-adsorbed weak-affinity protein; however a pre-adsorbed strong affinity protein is not displaced by the target protein. In a microfluidic device, we engineer two gold surfaces covered by two known proteins. The sensor allows selective protein detection by being displaced by a target protein on only one of the surfaces. The SPR (Surface Plasmon Resonance) sensorgrams show that three different human serum proteins, immunoglobulin G (IgG), tyroglobulin (Tg) and fibrinogen (Fib) have different adsorption strengths to the surface and the competitive adsorption of individuals controls the exchange sequence. Based on the exchange reaction, we demonstrate that the sensor has a high selectivity for Tg. Immunosensor techniques have become the dominant test methods in diagnostics, therapeutics and protein research, partially due to the highly selective molecular recognition of antibody and antigen. However, they often suffer from cross-reactivity, non-specific adsorption and lack of antibody diversity. Besides these limitations, integrating antibodies on to a transducer is a time-consuming and labor intensive process and often become the bottle neck of high yield sensors. To date, few alternative platforms for the protein detection have been active in biosensor communities. Here, we report a fundamentally different protein detection method that relies on the competitive nature of protein adsorption onto a surface, namely the Vroman effect. The Vroman effect is governed by thermodynamics as it is more thermodynamically stable in nature. By using the technique, we obviate the need to rely on antibodies and their attachment to transducers. Our approach is that one can engineer two surface pre-absorbed by two known proteins; one is a little smaller and the other is a little bigger molecular weight proteins than the target protein. Then, the pair of the surfaces becomes a highly-selective protein sensor since one is displaced an the other is not displaced by the target protein. In its first implementation, we demonstrate that three human serum proteins, IgG, Tg, and Fib, have different adsorption strengths onto a hydrophobic gold surface. The different strengths induce an exchange reaction among them. The displacement strength is ranked in the following order; Fib (340 kDa) $>$ Tg (660 kDa) $>$ IgG (150 kDa). In other words, fibrinogen can displace all other proteins while Tg only can displace IgG. Based on the results, we can identify specific target proteins without using the conventional immunosensor technique. Our results show how to detect Tg using a pair of surfaces pre-adsorbed by two known-size proteins; IgG in channel 1 and Fib in channel 2. Tg displaces IgG in channel 1 but just flows through the fibrinogen-covered surface in channel 2 without any exchange reaction. The differential measurement of the SPR angle change from channel 1 and 2 allows the detection of Tg and the angle change also indicates how many thyroglobulins replace IgG.

## Innovation in the Product Development Process

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The objective of this study is to show a methodical product development process that is infused with innovative elements in strategic locations, which facilitates product quality, technical breakthroughs, speed to market, and how this method can create a system of development involving all stakeholder groups. This process fosters an understanding of advantageous times for ideation activities and reiteration activities to occur. Due to a lack of industry knowledge and practice regarding design, the subcategorization of steps in this process will lead to understanding of the tasks, costs and timeframes involved in the design phases. The intention of this process definition is also to build an understanding of which functional groups should be involved in research, ideation and design, and develop an understanding of how these groups should collaborate, and which should be responsible for certain product decisions. Although many similarities exist among current development methods, common misconceptions and process deficiencies are prevalent. Innovative aspects of the process are commonly misunderstood, and are often completely lacking or applied at an inefficient juncture of the process. Other times evaluation and research phases are left incomplete, leaping directly to the mechanical development process phase. This causes earlier steps to be done after engineering work is underway, which creates inefficiencies in the process. There is also evidence of a large gap of misunderstanding about what the nature of the design phase really is, which causes it to be left out of the process altogether or ill-applied during the process. We conducted an examination of current studies and process information from medical device companies and evaluated them for the exclusion or placement of key innovative elements. Common similarities were discovered, and a modified development process description was created with the inclusion of elements useful for optimizing innovation and reducing redundancy. Some of the detrimental commonalities include a lack of detail in the research and ideation phases of the process, the tendency for companies to skip around in the process and impeding the ability to hit critical dates, and involving groups and disciplines in the process at incorrect times which stifles innovation and causes bottlenecks. The revised process involves designers in evaluation, research, marketing, engineering, validation and production, finding that it pulls all groups together, linking them to a single process. We found that this model of product development can provide results that will improve performance and acceptance of new medical devices, while increasing innovation and help to uncover breakthrough concepts. Key factors in this process include the practice of planning innovation into the process in the proper places; having a design team involved in all phases to increase product quality; and expending sufficient effort in the highly misunderstood areas of the process. It is also shown that success is achieved if product decisions are made around design criteria derived from the process, with a design team involved in making these decisions. Continued iterations must occur during the appropriate phases, and when the process is followed, bottlenecks are removed, streamlining takes place, innovation can occur, and customer needs are more fully met in the product, increasing overall product quality and launch success.