

Organization: Purdue University



Title: Optimizing the Immuno-Surface Characteristics for Biosensors and Filters through Modeling and Experiments

MTO Simbiosys

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Project Goals

The goal of this project is the development of a mathematical model of antigen capture efficiency as a function of immuno-surface properties: flexibility, hydrophobic nature, surface charge, antibody density, and antibody extension. Analytical determination of the optimal immuno-surface configuration for a specified target antigen.

Technical Approach

- The scope of this work encompasses and integrates experimental exploration with model development, validation, and optimization studies for determining the best configuration and composition of immuno-surfaces.
- The majority of the experiments are conducted in a flow-through chamber fitted with an immuno-surface exhibiting the explored properties. The antigenic particles are 1 μ m fluorescent beads with attached DNP epitopes. These experiments are supplemented with BIACORE experiments exploring the binding dynamics of multivalent DNP-BSA with anti-DNP IgG. The experiments quantify the antigen capture efficiency and assist the modeling by providing data to extract the association rates, dissociation rates, and a relative measure of the bond strength.
- The model is composed of differential equations that reflect the antigen capture. The epitope-antibody association and dissociation rates incorporate the influence of the membrane and antibody properties.
- The model derived will be subjected to multivariable optimization techniques. The optimization search will be performed to maximize the antigen capture efficiency as a function of the immuno-surface parameters. Given the nominal affinity of the associated antibodies and the target antigen epitope density, the optimization will determine the best configuration of the immuno-surface.

Recent Accomplishments

- Controlled oriented antibody surface density using protein-A.
- Initiated studies to compensate for non-uniform antibody surface density.
- Investigated fabricated DNP-MS epitope distribution and density.
- Initiated DNP-BSA BIACORE experiments.
- Constructed simplified two-compartment model reflecting kinetics of antigen capture.
- Explored methods to obtain the dominant rate parameters.

Six-Month Milestones

- Quantify antibody attachment to solid support immuno-surfaces.
- Control or compensate for a non-uniform immuno-surface.
- Fabricate and characterize the antigen particles of differing valency from microspheres.
- Model antigen capture efficiency for solid support immuno-surfaces for antigen of different valencies.
- Predict and demonstrate the best antibody surface density for capturing antigen of various valencies.

Team Member Organizations

Department of Biomedical Engineering and the Veterinary School at Purdue University

Purdue University
Optimizing The Immuno-Surface Characteristics For Biosensors And Filters
Through Modeling And Experiments

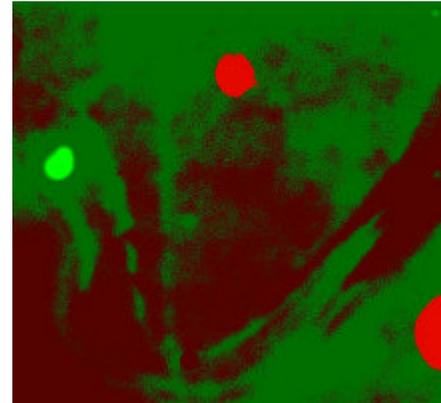
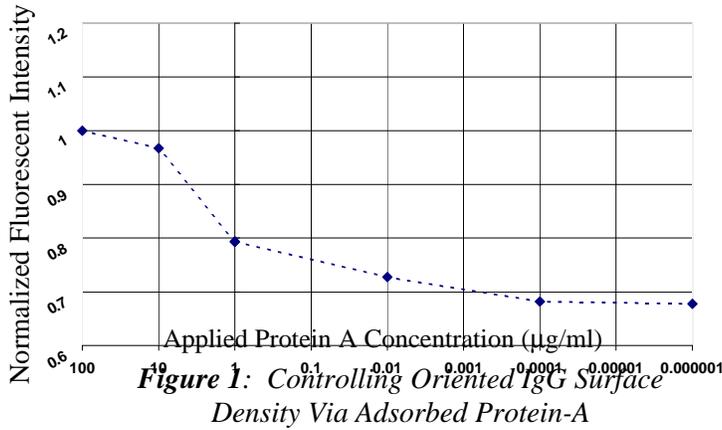


Figure 2: Investigations into Uniformity Compensation using Dual Wavelength Experiments (FITC Fab2 and TRITC MS images @ 10ng/mL IgG, 20x)

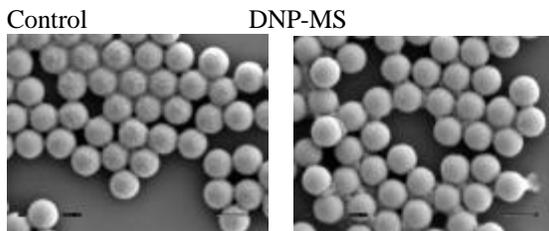


Figure 3: SEM images of microspheres plain and coated with DNP epitopes.

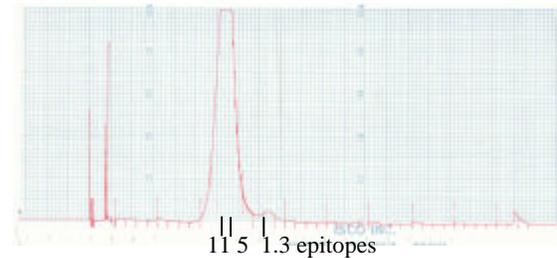


Figure 4: Distribution of Valency of DNP-BSA.

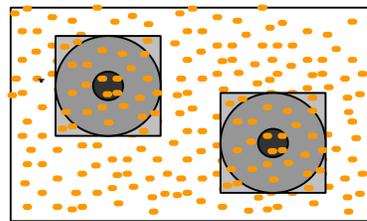
Modified Two-Compartment Model

$$\frac{V_1}{S} \cdot \frac{dC_1}{dt} = -(k_m(C_1 - x_0) + k_g C_1)$$

$$\frac{V_2}{S} \cdot \frac{dx_0}{dt} = -k_a x_0 R_f + k_d x_b + (k_m(C_1 - x_0) + k_g C_1)$$

$$\frac{dx_b}{dt} = k_a x_0 R_f - k_d x_b$$

$$R_f = R(1 - N_a x_b D^2)$$



- Antibody ● Antigen
- Contact area (Binding area) □ Exclusion area

