

Simulations of Lateral Flow and Vertical Flow Microarray Assays for Point of Care Diagnostics

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Abstract

Paper based lateral flow assays are widely used as point of care devices for disease diagnostics in low- as well as high resource areas, due to their low cost, short run time and ease of use. Binder molecules specific for certain molecular biomarkers of interest are typically deposited as dots or lines on paper strips, whereupon sample can be flowed through the paper strip via capillary forces in order to measure the concentration of the target analytes in the sample. In an alternative setup, sample may be applied in a cross flow fashion using a cartridge holder for the affinity-labelled membrane. In our lab we have combined such paper-based assays with highly multiplexed protein microarrays to enable rapid affinity proteomic analysis, with such applications as infection diagnostics, autoimmune and allergy profiling.

In a variation of the vertical flow assay that is being developed in our lab, we immobilize beads on the paper surface in order to achieve an extremely multiplexed (100.000 targets) paper based planar bead array, where affinity binders are attached to the beads rather than to the paper surface. To achieve a systematic development and application of our lateral flow and vertical flow assays it is of interest for us to model both lateral and vertical flow assay setups in COMSOL Multiphysics® software, with the aim to predict the effect on the assay performance from various parameters such as geometry, flow rate, analyte concentration, binder concentration and affinity rate constants.

Models of the lateral and vertical assay setups have been created in COMSOL Multiphysics® (Figure 1). An initial concentration of binder is assigned to the spots and the beads, and analyte is transported to the reaction surfaces due to convection. As the analytes reach the binder surface, the analyte binds reversibly to the binder with a given association rate and the binder-analyte complex dissociates with a given dissociation rate. All these parameters can be easily modified in order to observe how the systems behave under different realistic conditions.

For the lateral flow model we have investigated how the concentration distribution of binder-analyte complex over a spot is affected by changing the kinetic parameters of the binding reaction (Figure 2). For the vertical flow model we have investigated how the analyte is distributed over the surface of the spheres (Figure 3), as well as how long it takes for the surface of the spheres to reach a steady state concentration of analyte (Figure 4).

Using COMSOL Multiphysics® models of our molecular diagnostic assays, it is possible to

better understand how various parameters such as flow rate, binder concentration and analyte concentration may affect the system performance which limits the amount of practical optimization work. Using these models will therefore likely save us both time and resources in our work to further develop, improve and apply the presented tests.

Figures used in the abstract

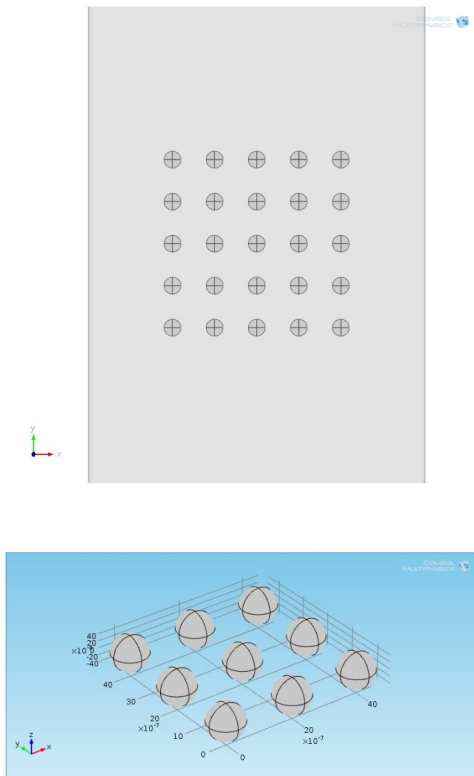


Figure 1: Overall geometry of the lateral flow and vertical flow models. In the lateral flow model, binders are placed in circles on the surface of a rectangular block through which the analyte flows. In the vertical flow model, binders are placed on the surface of spheres and analyte flows in from above.

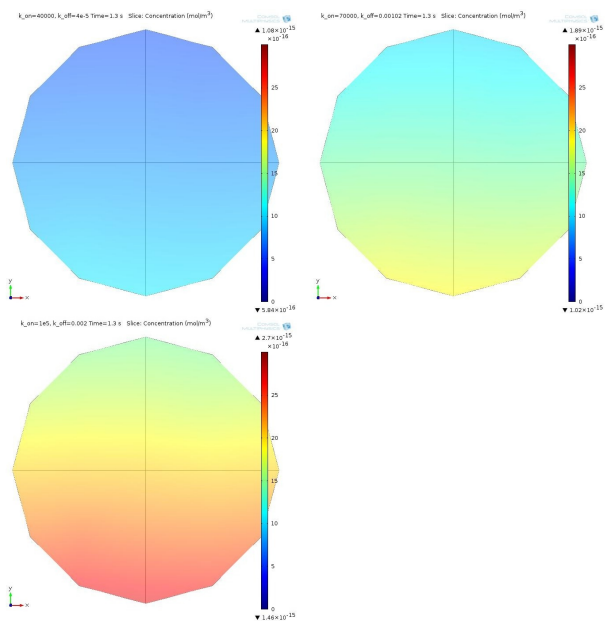


Figure 2: A comparison of analyte concentration distribution over a spot in the lateral flow microarray at a given point in time when the binding reaction occurs with three different sets of on and off rates.

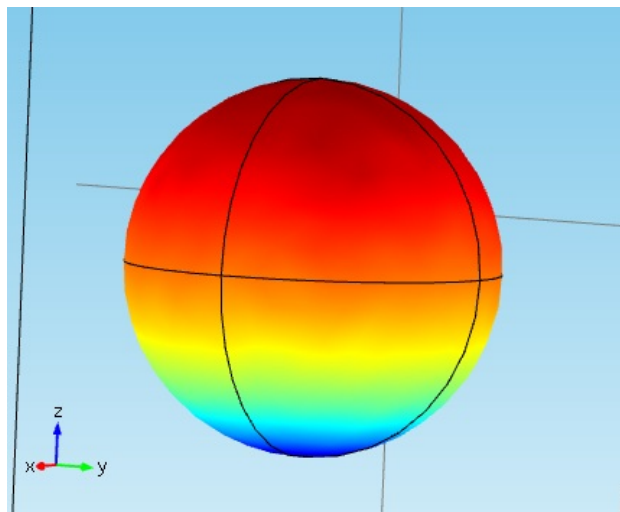


Figure 3: Analyte concentration distribution over the surface of a bead in the vertical flow model. Analyte flows in from above the sphere, hence the analyte concentration is higher on the top of the sphere compared to the bottom.

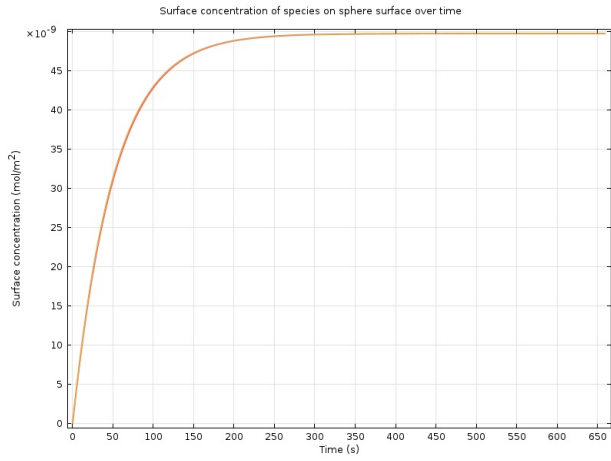


Figure 4: Surface concentration of analyte over time in a specific point on the surface of a bead in the vertical flow model.