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Dynamics of ligand-receptor binding in microfluidic chips

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Abstract:

Dynamical behavior of a ligand-receptor system has been studied in a polystyrene microfluidic device. A seven channel microchip has been constructed by micromilling and high temperature assembling. The main characteristics of the chip are low consumption of bioanalytes and fast performance of the bioassay. Protein A (PA, a cell wall protein deriving from *Staphylococcus aureus*) immobilized by the passive sorption on microchannel walls has been used as a receptor for the quantification of human immunoglobulin G (hIgG). Two bio-affinity formats have been carried out in the microchip: a) PA as a receptor and fluorescently labeled FITC-hIgG as a quantified ligand in the one-step assay and b) PA as a receptor, hIgG as a quantified ligand and fluorescently labeled goat anti-human IgG (FITC-gIgG) as a secondary ligand in the two-step assay. Pressure driven transport for dosing of all analytes has been used. Fluorescence microscope and digital camera have been used as the optical detection system of the formed ligand-receptor complexes.

A mathematical model describing the formation of the PA-FITC-hIgG complex has been constructed. The model is based on reaction-transport equations, i.e. the equation of diffusion transport of antibody in the microchannel and the kinetic equation of ligand-receptor binding. Dynamics of formation of the complex has been studied in the space of parameters: the kinetic constant of the PA-FITC-hIgG binding k_{on} and the equilibrium dissociation constant of formed complex K_d . The calibration curves of concentration of the formed complex on the antibody concentration in the sample at the time 5 minutes after the start of simulations have been computed. The values of the kinetic constant $k_{on} = 5.5 \text{ m}^3\text{mol}^{-1}\text{s}^{-1}$ and the equilibrium dissociation constant $K_d \leq 3 \times 10^{-6} \text{ mol m}^{-3}$ were obtained by an optimization technique.

The proposed microfluidic device enables fast evaluation of the kinetic and the equilibrium constants of ligand-receptor bio-affinity pairs and the ligand quantification.