ELOBIS—Elasto-optical Biosensor Based on Nanostructures

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Cross-links:

Functional Peptides

Nanoparticle Technology

Thin Adaptive Films

Modeling and Simulation

Bioanalytics, and in particular biosensorics, is one of the most rapidly progressing fields in biotechnology, providing a variety of methods for the detection of biomolecules, such as DNA, RNA, or proteins in medical diagnostics or quality control in the food industry. In the feasibility study reported here, we focus on the development of a new optical method for the detection of analyte molecules that specifically bind known ligands. The method is designed to function without amplification and without the necessity to label the analyte. The principle used is based on the distance dependence of the Fluorescence Resonant Energy Transfer (FRET) within an elastic capture molecule attached to a nanostructured surface or nanoparticle. By applying a global mechanical excitation using either periodic or aperiodic mechanical, electrical, or magnetic forces, the distance between the two fluorophors within the elastic capture molecule changes and thus the individual emittance of the two optical active centers will vary due to the changed FRET. As a counter force against the global excitation, entropic elasticity will drive the polymer chain back to a mean reference elongation state. However, if the capture molecule binds to an analyte molecule (Fig. 1), the amplitude of the mechanical excitation will change, and the corresponding change in FRET between the two fluorophors will allow to detect the binding event. The capture molecules are developed and synthesized by the project partners, whereas the task of caesar is the development of the measurement method. This development involves an interdisciplinary effort comprising mathematical modeling for the determination of promising experimental parameters, nanostructuring of active biosensor surfaces, construction of fluid cells and of the actual measurement apparatus. In the following we highlight a few results from this work.

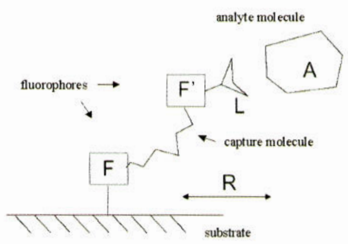

Figure 1: Schematic of the detection principle.

In order to optimize fluidic parameters close to the active surface of the sensor, we have used finite-Element calculations to obtain detailed information about flow profiles along 3-dimensional structures (Fig. 2). The modeled surfaces have been realized as gold islands by means of nanosphere lithography (Fig. 3).

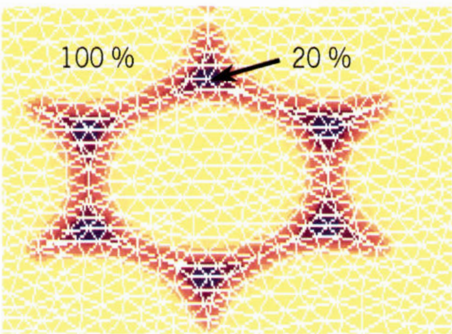

Figure 2: Modeling results for nanoisland flow profiles—color coded for flow velocity.

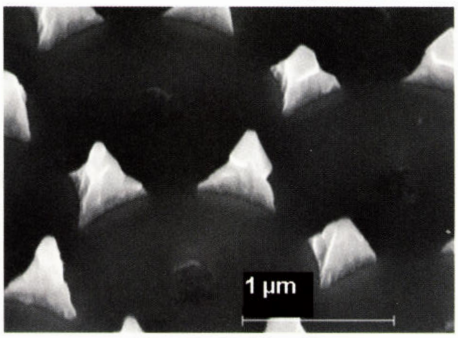

Figure 3: Gold nanoislands on glass substrate.

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The nanostructured surface together with capture molecules immobilized at the tips of the islands form the basis of a chip that implements the sensor principle sketched above. The chip can be mounted in a suitable transparent fluid cell (Fig. 4) that is placed into an optical microscope with an optical spectrometer attached.

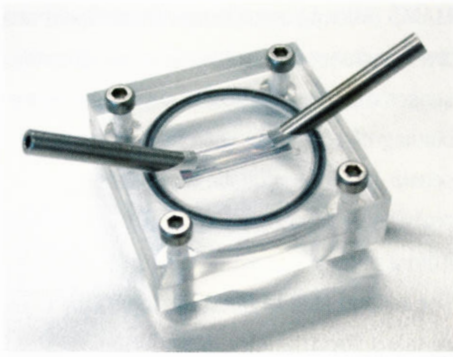

Figure 4: Fluid cell setup for FRET detection.

Cooperation:

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Different mechanical excitation principles have been analyzed, several of which have turned out to be unsuitable for application. The main reasons for these limitations are the nanometer size effects in a fluid. Atomistically, near a surface the fluid molecules behave differently compared to bulk water; they are trapped in a zone of decreased mobility, decaying with 1/distance from the surface. Therefore the elastic polymer can only be stretched by large shear forces within the fluid. Mechanical ultrasound vibration for example does not provide large enough shear amplitudes. Static and dynamic electrical fields are shielded by the polarization of the water solvent. Electro-osmosis on the other hand does not provide large enough shear velocities.
A promising route currently under investigation is the use of magnetic nanoparticles or capsules. Fig. 5 shows an experimental setup of an integrated coil system within a fluid capillary. Using high frequency magnetic excitation, the magnetic particles are expected to rotate and stretch the elastic polymer. Using pulsed excitation should further improve the signal to noise ratio via lock-in techniques.

The unique combination of properties, i.e. label free optical detection with the potential of single molecule analytics makes ELOBIS an attractive method for many applications. Once established, the measurement system is expected to have a long term impact on 'high-end' bioanalytics, with customers in the biotech, pharma and food industry.

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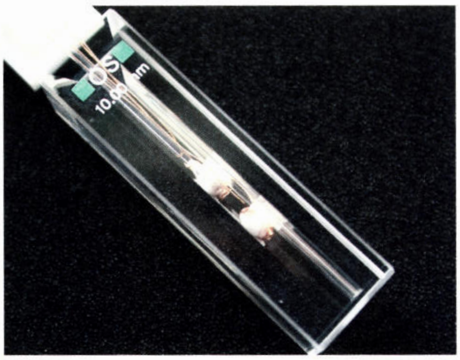

Figure 5: Optical measurement cell with incorporated magnetic coil system.