Postdoc: Atomic force microscopy of DNA-magnetic nanoparticle hybrid structures for biosensors

Uppsala University is a comprehensive research-intensive university with a strong international standing. Our mission is to pursue top-quality research and education and to interact constructively with society. Our most important assets are all the individuals whose curiosity and dedication make Uppsala University one of Sweden's most exciting workplaces. Uppsala University has 42,000 students, 7,000 employees and a turnover of SEK 6.7 billion.

The position is at the Division of Solid State Physics, Department of Engineering Sciences at the Ångström Laboratory, Uppsala University.

The two-year postdoctoral project aims at using liquid-cell atomic force microscopy (AFM) to gain increased fundamental knowledge on the mechanisms behind a number of optomagnetic biosensor principles using three types of hybrid materials made of magnetic nanoparticles (MNPs) and DNA. These biosensors have important applications relating to e.g. cancer diagnostics, food safety and veterinary medicine. The findings from the project are crucial in order to optimize the performance of these biosensors and are also of high general interest in the research area of nanoparticle-based biosensors.

Background: Magnetic and optomagnetic biosensors offer unique advantages for rapid, sensitive and cost-efficient detection of various pathogens, especially in point-of-care and out-of-lab settings. These biosensors could for instance make use of MNPs functionalized with biomolecular probes. Binding of the target or amplification products thereof to the MNPs gives rise to the formation of DNA-MNP hybrid structures which changes the magnetic or optomagnetic response of the sample, thereby enabling for target quantification. In order to optimize the analytical performance of such biosensors and from a fundamental science perspective it is relevant to obtain detailed structural information of these hybrid structures in their native state. For this liquid-cell AFM is a powerful tool.

Work description: To establish suitable liquid-cell AFM imaging procedures and perform imaging of three kinds of DNA-MNP hybrid structures forming the fundament of three different optomagnetic biosensor principles:

1) Rolling circle amplification (RCA) products with immobilized MNPs. Each RCA product is built up of a random-coil of single-stranded DNA having a repeating sequence. By functionalizing the MNPs with single-stranded DNA probes complementary to the repeating sequence of the RCA-products, MNPs can be hybridized to the RCA-products. This leads to a volume-increase of the MNPs.
2) MNPs with loop-mediated isothermal amplification (LAMP) products on their surface. LAMP is a hypersensitive molecular amplification tools which produces zigzag-shaped DNA-structures of various lengths. These products can bind to MNPs via e.g. biotin-streptavidin interaction which gives rise to a volume increase of the MNPs.
3) Core-satellite magnetic superstructures used for micro-RNA detection. In these satellite MNPs are linked to micrometer-sized magnetic core particles by single-stranded DNA probes complementary to the micro-RNA target. The DNA-probe can either be a short DNA oligonucleotide binding only one MNP or the DNA-probe is produced by RCA giving the possibility to increase the load of satellite MNPs. The micro-RNA target forms a duplex structure with the DNA-probe and the duplex-specific nuclease (DSN) enzyme cleaves this

duplex by hydrolysis while preserving the micro- RNA (target recycling). The DSN-based cleaving reaction releases MNP satellites.

The first half of the project during year 1 will be devoted to establish the liquid-cell AFM imaging methodology including finding optimal imaging and sample preparation conditions. Second half of year 1 will focus on imaging the hybrid structure 1. Second project year will focus on imaging the structures 2 and 3.

Qualifications required: A successful candidate should have received a PhD degree (no later than two years before application of this position is submitted) in applied physics or engineering physics and should have extensive experience of AFM imaging of biological samples. A cross-disciplinary background is meriting as well as practical skills in basic molecular biology work.

Application: Applications should be submitted by e-mail to Klas Gunnarsson (see contact information below). Applications should include a brief description of research interest and previous experiences, publication list, a CV, copies of diplomas and degrees and other relevant documents. Excellent English language skills are required. The candidates are requested to provide letter(s) of recommendation and contact information to reference persons.

Salary: Fixed amount (scholarship).

Application dead-line: 26th of April 2019.

Type of position: Full time position, two years.

For further information about the position please contact Senior Lecturer Klas Gunnarsson, 018-4713136, e-mail klas.gunnarsson@angstrom.uu.se or Associate Professor Mattias Strömberg, 018-4713139, e-mail mattias.stromberg@angstrom.uu.se. Information about the division of Solid State Physics can be found at www.teknik.uu.se/ftf.