Biomaterials and nanostructured surfaces

Projects for MTNANO, TECHNICAL PHYSICS and BIOPHYSICS students

Academic year 2017-18

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PROJECT 1: SU-8 based nanostructures for cell biology research.

In recent years we have been working on development of novel systems for the delivery of bioeffector molecules to cells (celled cell transfection). The delivery platform is based on using high aspect ratio, vertical nanostructures attached to a cell compatible support. Those can be fabricated from epoxy-based resist using electron beam lithography.

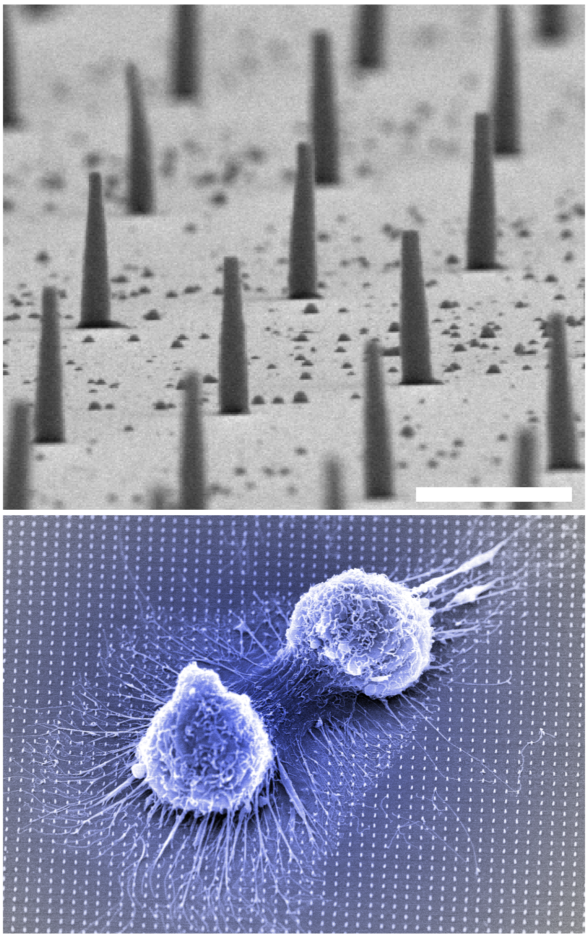

Figure 1: SEM of nanowires fabraicated with electron beam lithography (top) and of cells grown on such nanowire decorated surfaces (bottom). Images: K.Beckwith, NTNU

Controlled perturbation of living cells *in vitro* is a large endeavour in modern cell biology, with a main aim to understand cell function at a molecular level. This is important both from the perspective of fundamental, curiosity driven research, as well as key to understand diseases and to develop new treatments. This controlled perturbation can be achieved by delivery of bioeffector molecules. The project has originally focused on using nanowires as a delivery platform. However, it now includes efforts to understand cell-nanowire interface, as it quickly became apparent that this is essential for design of efficient delivery platform.

The project is closely integrated with the research activities in our group. The exact details will therefore depend on the outcome of the currently ongoing research and on your preferences and interests. It could include a combination of several topics listed below:

- testing of surface functionalization strategies, including development of methods to quantify surface modification.
- integration of electrical contacts into devices to facilitate delivery through electroporation
- development and testing of new fabrication strategies, including novel resists and polymers
- cell experiments and study of cell-nanostructure interactions
- live-cell microscopy to study dynamical process
- optical, fluorescence and electron microscopy, FIB-SEM tomography

We are looking for motivated and dedicated students interested in nanofabrication and bionanotechnology to work in active and multidisciplinary research group. Depending on the exact choice of topic, 20-80% of the project work will be done in the NTNU Nanolab. The project will give you experience with state-of-the-art micro and nanofabrication techniques, and application of those techniques in medical research. The project will provide you with knowledge, experience and hands-on training essential for research and innovation within bionanotechnology, lab on a chip, advanced diagnostics and many other related fields.

Co-supervisors: Dr Kai S. Beckwith (kai.beckwith@ntnu.no). Centre of Molecular Inflammation Research (SFF-CEMIR, DMF) and PhD student Jakob Vinje (Department of Physics)

Journal Publications

Beckwith, Kai Sandvold et al. (2015). "Tunable high aspect ratio polymer nanostructures for cell interfaces". In: *Nanoscale* 7.18, pp. 8438–8450. ISSN: 2040-3364.

Mumm, Florian et al. (2013). "A transparent nanowire-based cell impalement device suitable for detailed cell-nanowire interaction studies." In: *Small* 9.2, pp. 263–72. ISSN: 1613-6829.

PROJECT 2: Mineralized, hydrogel-based materials for tissue engineering applications

Bone tissue is a composite material mainly consisting of a calcium phosphate mineral (hydroxyapatite, HAp) and collagen. A complex, hierarchical design, combining the stiffness of the brittle mineral crystals and the toughness of the soft organic matrix, is responsible for the high mechanical properties of bone. Bone tissue engineering aims to stimulate natural regeneration of bone through bioactive materials, or even create a synthetic implant with similar properties of bone. Our group is focusing on development of composite materials based on alginate hydrogels and calcium phosphate ceramics. Understanding of the mineralization process is the key aspect of our research. To meet this goal, we have developed an experimental toolbox to study gelling kinetics of alginate upon crosslinking with calcium ions, and to investigate mineralisation with spatial and temporal resolution and in a correlative manner. Our system allows study of mineralization with a range of experimental techniques, including advanced optical microscopy, Raman microspectroscopy and electron microscopy. Established models system allows for experimental data to be used to develop numerical models, providing quantitative description of physical processes taking place during the gel formation process and during mineralization.

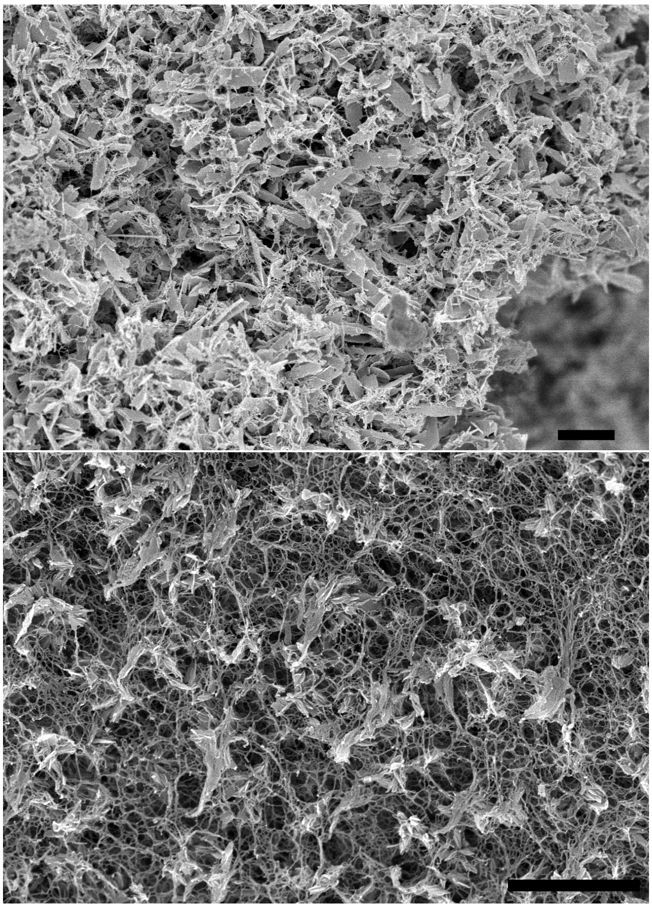

Figure 2: SEM micrograph of a mineralized hydrogel (images: S.H. Bjrny, NTNU). Scale bar represents 1μm

Several research topics related to this class of composite materials can form a basis for an experimental research project. This includes:

- development of spin coating, cell compatible method to make layered, mineralized hydrogel composites with different properties
- FIB-SEM analysis of hydrogels
- use of Raman and confocal microscopy for *in situ* studies of the mineralization process.
- applications of mineralisation methods to different hydrogel systems, for example to collagen and alginate/collagen gels.
- biological effects of calcium phosphate minerals on cells

We are looking for motivated and dedicated students interested in micro- and nanofabrication, nanometarials or/and and bionanotechnology to work in active and multidisciplinary research group. Depending on the exact choice of topic, 20-80% of the project work will be done in the NTNU Nanolab. The project will give you a good insight into the field of biomaterials and micro and nanotechnology for study of biomaterials and biological systems.

Journal Publications

Bassett, David C. et al. (2016). "Competitive ligand exchange of crosslinking ions for ionotropic hydrogel formation". In: *J. Mater. Chem. B* 4.37, pp. 6175–6182. ISSN: 2050-750X.

Bjørnøy, Sindre H. et al. (2016a). "A correlative spatiotemporal microscale study of calcium phosphate formation and transformation within an alginate hydrogel matrix". In: *Acta Biomater.* 44, pp. 254–266. ISSN: 17427061.

Bjørnøy, Sindre H et al. (2016b). "Controlled mineralisation and recrystallisation of brushite within alginate hydrogels." en. In: *Biomed. Mater.* 11.1, p. 015013. ISSN: 1748-605X.

Bjørnøy, Sindre H. et al. (2016c). "Gelling kinetics and in situ mineralization of alginate hydrogels: A correlative spatiotemporal characterization toolbox". In: *Acta Biomater.* 44, pp. 243–253. ISSN: 17427061.

PROJECT 3:

New topics related to study of cementation process on the grain scale in connection to newly funded project "Systems analysis and fundamental control of bacterial processes in the production of bio-concrete for construction purposes" will also be available in 2017/18.