Engineered Metallic Nanopores for Biosensing with Cellular Membranes

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Of the top 100 selling pharmaceuticals, almost half of them bind to molecules associated with cellular membranes, such as lipids, proteins and carbohydrates. It is therefore important to be able to assess the binding kinetics and strength of therapeutic agents to constituents of cellular membranes. However, in its standard configuration, the gold-standard method for investigating molecular binding - surface plasmon resonance (SPR) - cannot easily make these measurements. To remedy the shortcomings of traditional SPR, the Oh group has been making nanopore-based SPR sensors that can be functionalized with lipid membranes. The sensors are fabricated in the Nanofabrication Center (NFC) by either focused ion beam milling or template stripping, then coated with a thin layer of SiO₂ by atomic layer deposition, which facilitates the formation of lipid membranes on the sensor surface. In one example, SPR with a free-standing nanoporous gold film was used to investigate the kinetics with which a transmembrane protein called α-hemolysin (α-HL) incorporates into nanopore-spanning lipid membranes. In other work, the Oh group has been collaborating with neurologists at the Mayo Clinic to determine the binding kinetics and affinities of novel natural autoantibodies to cellular membranes. The antibodies discovered by the Mayo Clinic team are potential treatments for multiple sclerosis (MS), and have shown promise in animal models of MS.

Conceptual illustration of cell-mimicking lipid membranes formed on a metallic nanopore biosensor by the rupture of spherical shaped lipid membranes, called lipid vesicles. The nanopore plasmonic biosensor can detect molecular binding to the membrane in real-time to study dynamic interactions between antibodies and lipid membranes.

Reminder: If your work uses the Nanofabrication Center please add the following in the acknowledgements section of any publication: "Parts of this work were carried out in the University of Minnesota Nanofabrication Center which receives partial support from NSF through the NNIN program.”
CHARFAC DIRECTOR’S MESSAGE

CharFac Director,
Greg Haugstad

News in recent months has spanned equipment, staffing and special events.

We are excited to announce the availability of a new X-ray microdiffractometer. Its emphasis is spatially resolved analysis of heterogeneous samples or of tiny volumes as contained in small devices or on odd-shaped objects (e.g., ring below). Specifications include Bruker Hi-Star 2D X-ray detector with 0.04° angular resolution at 15-cm sample-detector distance; Cu-Kα monochromatized X-ray point source collimated to 0.05-0.8 mm spot size; multi-sample x-y-z stage for high throughput and/or programmatic 2D analysis; and video microscope/laser for sample positioning/alignment. Funding derived from a substantial allocation from the University’s Materials Research Science and Engineering Center (MRSEC), plus smaller contributions from faculty members and the CharFac’s capital equipment fund.

We also have news on three systems to be acquired in the first part of 2012: a Laue X-ray diffractometer and two (multi-generation) upgrades to our two Nanoscope/Multimode scanning probe microscopes. Funding derived from two successful grant-in-aid (GIA) proposals from the most recent competition (authors M. Greven, C. Leighton, R. James; and D. Frisbie, C. Macosko, G. Haugstad), and again contributions from MRSEC, CharFac and faculty members, plus the CSE Dean. Laue diffraction is the fastest and most reliable technique to orient and co-mount crystal samples. It will provide our investigators with what is a standard capability at many peer institutions. Our Nanoscope SPMs have served as workhorse instruments for more than two decades, but are in need of modern capabilities; these include high-spatial-density force-distance mapping and 20-fold faster scanning for some applications, together will higher data-density images, faster signal analysis, and upgraded data analysis.

New staff members in the CharFac include postdoc Jake Warner (PhD physics, University of New South Wales), whose emphasis is small-angle X-ray scattering, cryo-scanning electron microscopy and SPM; and Michael DuPont (BS materials science, U of M), whose current emphasis is 120-kV transmission electron microscopy (TEM) and basic X-ray diffractometry training. Please welcome Jake and Mike to the CharFac!

Special events since November have included an FT-IR microscopy workshop held in collaboration with ThermoScientific; (an open house for the recently installed FEI Tecnai Spirit Bio-Twin TEM (see past two newsletters); a poster session in collaboration with the Minnesota Microscopy Society; and participation (of G. Haugstad and W. Zhang) in a national workshop of the Materials Research Facilities Network (MRSEC affiliated) at Northwestern University. A formal report is being drafted from the latter event, addressing issues of facility funding, user training, maintenance, remote access and more.
I would like to alert you to three new pieces of equipment that will be arriving in NFC during the winter of 2012. We just received three large crates containing our new Heidelberg mask maker. This system will allow us to make masks with much smaller and smoother features, even curved features. It will also allow 3D optical lithography and direct write optical lithography, capabilities we have not had. Unfortunately, one of the crates was damaged during shipping. I cannot yet say when the system will be available. Supporting the e-beam lithography system, we will also be receiving a refurbished field emission scanning electron microscope. With a resolution of just over 1 nm, the system will allow us to inspect patterns written on the Vistec for process optimization. It should be here in mid-February. Finally, I am pleased to announce that we have just agreed to purchase an advanced Oxford etch system to replace the old Trion etch system. This will be a major upgrade to our etching capabilities. This refurbished unit provides inductively coupled plasma etching, a turbo pumped load lock and a chemically resistant primary turbo. It comes configured for BCl3, SiCl4, HBr, CF4, Ar, O2, SF6, Cl2, H2, CH4, NH3. While we will not hook up all of these gasses immediately, the tool will give us a very wide range of process options, especially for anisotropically etching semiconductors with high selectivity. We look for this tool to be operational by late March.

The construction of the new building is also continuing. The construction documents will be finalized at the end of January. The crew is currently drilling the piers which will support the building. As this work proceeds you will find a very high density of these piers on the west side of the site. These will provide low vibration support to the clean room floor. The College has set up a webcam. If you want to inspect the site from your desk go to: http://cse.umn.edu/pnwebcam. Finally, the Office of the Vice President for Research has produced a very nice two-minute promotional video for NFC. If you are interested, you can see it here: http://www.youtube.com/watch?v=1gZlZmzlCp4. Stay warm.

**THIN FILM DEPOSITION TECHNIQUES**

An important aspect of many micro- and nanofabrication processing sequences is the deposition of thin films. The films may be conductors, insulators, semiconductors or magnetic materials. At the Nanofabrication Center we have several different process tools for deposition of a wide variety of thin films using the techniques of evaporation and sputtering. We currently have 3 different electron beam evaporation systems in our facility. Two of these evaporators, the CHA system and the Temescal system, are inside the cleanroom. The CHA is a newer tool with complete automation capability, a six pocket gun, fixturing for both planetary and lift-off deposition, and heated deposition capability. The Temescal is an older, manual operation system with a four pocket gun and lift-off fixturing. Both systems can support four to six inch wafers and smaller. Commonly deposited films include Cr, Ti, Ni, Al, Au, Pt, Pd, Ag, Mo, Cu, and Ge. NFC sputtering capabilities are centered around two AJA International systems. These tools have both RF and DC guns (2 each), load lock loading, single wafer deposition up to 8 inch diameter, and heated deposition. Common materials include Al, Al2O3, Au, Cr, Cu, Ge, ITO, Ni, SiO2, Ta, Ti and W. If thin film deposition is needed for your project, consider having the work done at NFC on these excellent systems.
Center for Nanostructure Applications

The primary mission of the Center for Nanostructure Applications is to seed interdisciplinary nano research projects that will go on to attract external support. Active nanostructures include applications of nano as diverse as energy conservation and production, large area displays and lighting, printed electronics, smart fabrics, electronic noses, drug delivery, cancer therapy, and new types of medical imaging.

These applications often require significant participation across traditional disciplines and the Center is designed to foster the cross-disciplinary research necessary to bolster the nano applications area at the University.

The Center also organizes workshops, speaker series, and short courses, as well as serving as a focal point for nano at the University.

For more information, visit http://www.nano.umn.edu/

The National Nanotechnology Infrastructure Network

The National Nanotechnology Infrastructure Network (NNIN) is an integrated networked partnership of user facilities, supported by the National Science Foundation, serving the needs of nanoscale science, engineering and technology. The mission of the NNIN is to enable rapid advancements at the nano-scale by efficient access to nanotechnology infrastructure. The NNIN supports the Nanofabrication Center at the University of Minnesota. As a node in NSF’s National Nanotechnology Infrastructure Network (NNIN), the NFC provides access to advanced multi-user facilities to both industry and academic researchers, the latter at a subsidized rate.

For more information, visit www.nnin.org