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University of Minnesota

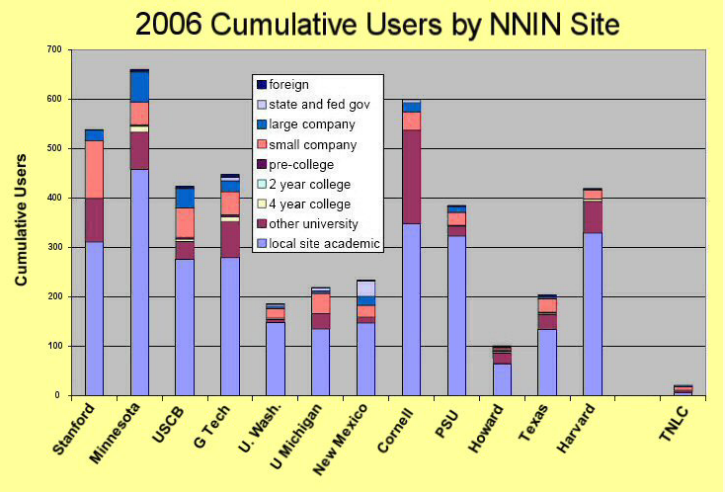
Nanotechnology News from the University of Minnesota

Issue Nine Summer 2007

Welcome to the summer issue of the University of Minnesota's Nano Newsletter. In the winter edition we introduced a new organization on campus, The Center for Nanostructure Applications (CNA), which is working on the application of novel nano materials and structures. Over the next few issues of our newsletter, we will introduce CNA groups working in this area under CNA support. This summer's issue is devoted to the first seed projects which began in 2006 in the area of Nanomedicine under the umbrella, the University of Minnesota NanoBiotechnology Initiative. This effort was very successful, helping to foster several new NIH grants. As always, to learn more about this work, you can go to our website, www.nano.umn.edu and click on the Nanobio link.

New research summaries are also available on the website, so you can get the latest information on nano at the University. We are inaugurating a new web site system which allows visitors to select a research interest area — Nano Medicine, Nano Devices, Nano Energy, or Nano Materials — to see announcements, summaries, and other information prescreened for that specific area.

The Nano Newsletter receives partial support from the National Science Foundation through the National Nano Infrastructure Network, or NNIN. NNIN is a network of university-based facilities that provide open access to all users on an equal basis with the home institution. At the University of Minnesota, NNIN facilities include the Characterization Facility, Nanofabrication Center, and the Particle Technology Lab, the three labs that distribute this newsletter. The graph at the right shows the user statistics for all of the NNIN nodes over the year ending March 1, 2007. The Minnesota node has the largest number of users for any school including the network anchors, Stanford and Cornell. As a result of this intensity of usage, NNIN has increased the Minnesota node support by 25%, effective this year. This will help us provide all of our users with continued improvements in facilities and technical support. For more information about NNIN, you can visit www.nnin.org.



Reminder: If your work uses CharFac, NFC, or PTL, please add the following in the acknowledgements section of any publication: "Parts of this work were carried out in the Minnesota (Characterization Facility, Nanofabrication Center, or Particle Technology Lab) which receives partial support from NSF through the NNIN program."

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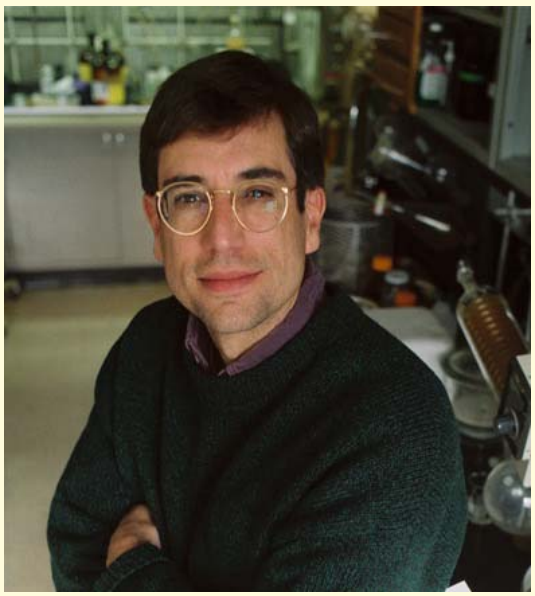
Immunotherapeutic Nanorings

Carston (Rick) Wagner (PI), Department of Medicinal Chemistry
Daniel Vallera, Department of Therapeutic Radiology



Carston Wagner is a Professor in the University of Minnesota's Department of MedicinalChemistry

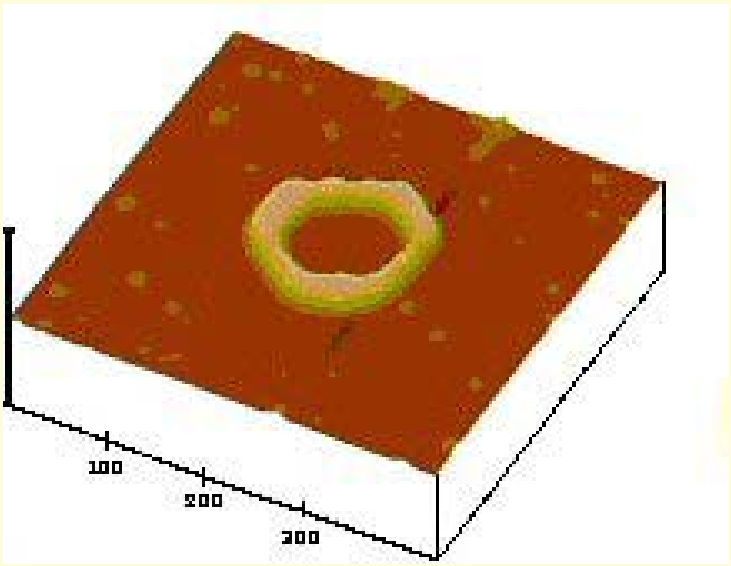
Designing and producing biological based assemblies that can be used for the fabrication of advanced materials is a rapidly advancing area of research. Self-assembling DNA and protein biomolecular building blocks have been used to produce a number of novel nanomaterials that may be applied to microelectronics, tissue engineering and drug delivery. In particular, the design and development of nanodevices capable of functioning both as biosensors and therapeutic agents would revolutionize the treatment of human diseases, such as cancer.

Recently, using the methods of protein engineering and organic chemical synthesis, the Wagner lab has discovered a method for the preparation of stable and homogeneous protein polygons, or nanorings. In particular, dihydrofolate reductase (DHFR) molecules when fused together by a peptide chain of variable length were found by size-exclusion chromatography (SEC), dynamic and static light scattering (DLS and SLS), transmission electron microscopy (TEM) and atomic force microscopy (AFM), to spontaneously self-assemble into protein macrocycles after treatment with a dimeric enzyme inhibitor (MTX^2), that efficiently dimerizes DHFR.[1,2] The size of the nanoring (8-30 nm diameter) was dependent on the length of the linker peptide between the two DHFRs (see Figure 1). Since the amino and carboxy terminus of DHFR are on the opposite face of the MTX binding site, DHFR nanorings afford an excellent scaffold for arraying fusion proteins, such as recombinant single chain antibodies (scFV) and anticancer therapeutics linked to the chemical dimerizer.

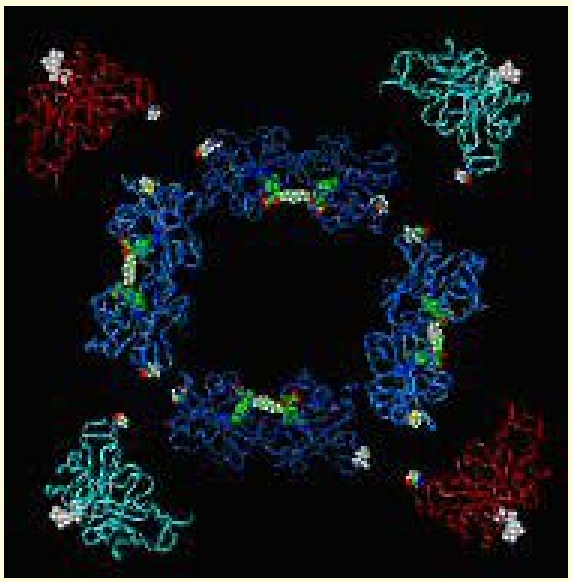
Currently, in addition to traditional chemotherapeutic approaches to the treatment of cancer, monoclonal and recombinant antibodies have been deployed as anticancer agents. Antibodies have a distinct advantage over typical drug therapies, since they can be engineered to be highly specific for the cancer tissue, and are thus less likely to be associated with the toxic side effects of anticancer drugs. Because of their specificity, antibodies can also be used to deliver drugs to cancer tissues. Radionuclide antibody conjugates in particular have proven to be effective at destroying tumors, particularly those that do not respond to drug therapy or have become drug resistant. In addition, the ability to use antitumor based radiotherapeutics to locate and image tumors is a significant advantage over methods focusing on just the delivery of toxins and drugs. Nevertheless, despite their preclinical and clinical success, the development of monoclonal antibody radionuclide conjugates suffers from a number of problems, such as, complex methods of production, reduced imaging capability due to low renal clearance, toxic radionuclide bone and kidney accumulation, restricted binding affinity, and potential immunogenicity. In theory, these concerns could be addressed if a method for the preparation of antibody-nanostructures existed that allowed

Figure 1.

A) AFM of DHFR Nanoring



B) Protein-Antibody Nanoring



for; 1) radionuclide labeling, 2) the use of small engineered antibodies, and 3) temporally controlled elimination of the nanostructures and radionuclide from the body.

To accomplish this goal, we are taking advantage of the Wagner lab's recent discovery of how to construct discrete chemically induced and highly stable protein nanorings that can be disassembled in the presence of a non-toxic drug and the Vallera lab's development of anti-B-cell leukemia single-chain antibodies and radiolabeled antibodies.[3] Recently, we have made major strides toward accomplishing our goal, by developing an efficient method for the expression and purification of DHFR-scFv fusion proteins and demonstrating that they can indeed form biologically active antibody-nanorings. Studies of their biological and therapeutic utility are currently underway.

1. Jonathan C. T. Carlson, Aaron Kanter, Guruvasuthevan R. Thuduppathy, Vivian Cody, Pamela E. Pineda, R. Scott McIvor, and Carston R. Wagner, *J. Am. Chem. Soc.*, **2003**, 125, 1501-1507.
2. Jonathan C. T. Carlson, Sidhartha S. Jena, Michelle Flenniken, Tsui-fen Chou, Ronald A. Siegel, and Carston R. Wagner, *J. Am. Chem. Soc.*, **2006**, 128, 7630-7638.
3. Daniel A. Vallera, D. T., David W. Kuroki, Yanqun Shu, Andy Sicheneder, and V. D. V. Angela Panoskaltsis-Mortari, Hua Chen, *Leukemia Research*, **2005**, 29, 331-341.

Nanostructured Contrast Agent for Imaging Breast Tumors

Allison Hubel[(1)], Uwe Kortshagen[(1)], Chun Wang[(2)], Doug Yee[(2)]
[(1)]Department of Mechanical Engineering, [(2)]Department of Biomedical Engineering,
[(3)]University of Minnesota Comprehensive Cancer Center

Breast cancer is the most common malignancy. Despite the large number of women diagnosed with breast cancer every year, mortality continues to fall. Falling breast cancer mortality rates have been attributed to population-based screening mammography programs and a wider use of systemic chemo- and hormonal therapy after primary breast surgery. Since breast cancer is a heterogeneous disease, a single form of therapy is unlikely to be effective for all women. If methods existed that could predict response to individual agents, then women could be spared exposure to ineffective therapies. Advances in tumor cell biology have fueled the development of new therapies for breast cancer. For example, identification of human epidermal growth factor receptor-2 (HER2) gene amplification in breast cancer provided important clues to the origin of some breast cancers. An antibody for this growth factor receptor has proven to be an effective therapeutic alone or in combination with chemotherapy. Existing methods of detecting the specific biology of the tumor are not adequate and prevent us from designing more effective treatment programs for those diagnosed with breast cancer.

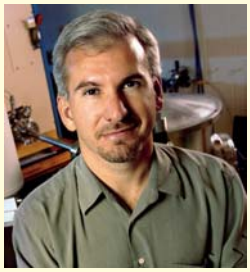
Allison Hubel is an Associate Professor in the University of Minnesota's Department of Mechanical Engineering.

Silicon quantum dots with the room light on (left) and room light off and irradiated with a UV lamp.

One potential tool for detection of cancer is semiconductor nanoparticles, more commonly known as quantum dots (Qdots). Qdots have physical dimensions comparable to many biological molecules, high quantum yields, narrow fluorescence emission bands and other traits that make them attractive for use in cancer detection. Several issues including potential toxicity (conventional quantum dots contain heavy metals) and high cost (principally associated with the challenges of synthesis) represent significant hurdles to commercial and clinical application of this technology. Recently, we developed a new method of synthesis for silicon quantum dots (Si-QD), which enables the synthesis of macroscopic quantities of Si-QDs. New methods of surface passivation have resulted in improved optical properties. These nontoxic and highly efficient Si-QDs may facilitate the development of inexpensive, rapid breast cancer detection using light.

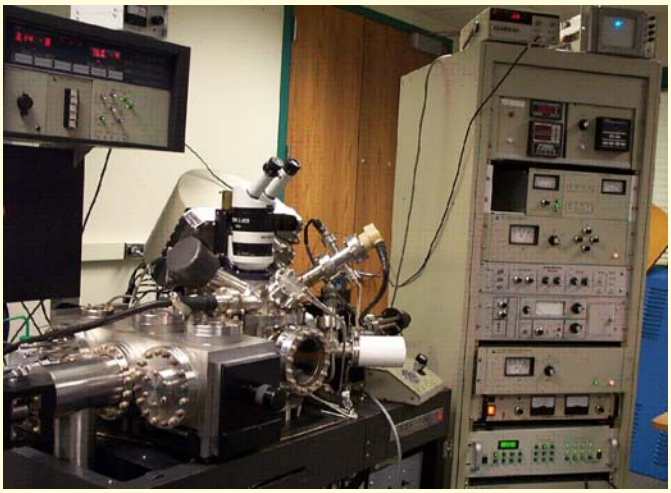
Characterization Facility News

CharFac Director's Message



CharFac Director, Greg Haugstad

Instrument acquisitions continue to dominate news in the CharFac. An SSX-100 X-ray photoelectron spectrometer (XPS) is operational, purchased from the University of Washington's core surface analytical facility via a grant-in-aid from the Graduate School augmented by funds from the Dean of the Institute of Technology (IT). This system, pictured below, provides much more modern XPS capabilities than previously available on campus. Most notably the system includes a high throughput bent quartz crystal monochromator



to sharpen the Al K x-ray source line. This provides greatly improved spectral resolution, meaning certain resolvable chemical shifts where previously only line broadening would be observed using older systems. The instrument also provides a variable X-ray spot size down to 50 microns and angle-resolved measurements. Other XPS (and Auger) systems will continue to be available for applications not requiring the newer features. Staff members Drs. John Thomas and Bing Luo preside over these instruments and are available for research discussion, specimen analysis, training and assistance. XPS, Auger, time-of-flight secondary ion mass spectrometry and Rutherford backscattering, will be featured in the upcoming Surface and Thin Film Characterization Master Class on May 31-June 1, during the IPRIME Annual Meeting (http://www.iprime.umn.edu/annual_mtg.htm).

A second recent major acquisition is a new FEI Tecnai 300-kV transmission electron microscope for cryogenic and energy filtered (Gatan) applications as well as tomography. This next-generation system is primarily intended for biological as well as soft material systems such as block copolymer nanostructures. The installation and configuration process began in mid April and a fully configured system is expected by mid summer. The instrument required an oversized laboratory not previously available in the CharFac. Funding to move walls and reconstruct a room in the Nils Hasselmo Hall CharFac site (where cryo SEM labs reside) was made available by the offices of the VP for Research, the Senior VP of the Academic Health Center, and the Dean of IT, which together paid for the instrument. Ongoing financial support will be provided by the deans of IT, Medical and Dental Schools. Near term staffing will draw from current personnel active in TEM, cryo and bio, while a strategic search continues for an expert microscopist in cryo-bio TEM as well as a new faculty expert within the Academic Health Center.

Four other equipment additions derive from successful grant-in-aid proposals. (1) a new Woollam VASE spectroscopic ellipsometer (delivery mid June); (2) a new metallographic specimen polisher for TEM (particularly important for heterostructure cross sections); (3) new cryo-microtome for Nils Hasselmo Hall CharFac; (4) second cryo specimen holder for the new cryo-bio TEM.

Staffing news: Jingshan (Sam) Dong (PhD, Chemical Engineering, UMN, 2006) has a 60% appointment in the CharFac concentrating on cryo-TEM and microtomy in Shepherd Labs, generalizing to cryo-TEM effort in both sites this summer. John Schafer is working 50% time in the CharFac as web master and in other information technology support roles. Constance Sorensen is sharing front desk duties with Lora Witte. Undergraduates Andrew Waytulonis, Maro Andaya, Krystal Haley and Angela Schroeder are working in technical support roles in Shepherd Labs or Nils Hasselmo Hall.

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Greg Haugstad, Director
Mike Boucher, Lab Manager

Nanofabrication Center News

NFC Director's Message

NFC Director, Steve Campbell

The Nanofabrication Center has several new systems to offer our users. In our last newsletter issue, I discussed the Atomic Layer Deposition (ALD) System which allows us digital control for coating, even highly nonplanar materials. Furthermore the deposition temperature is very low, allowing conformal coating of even organic materials in some cases. The system has been installed and is now capable of running HfO_2 and Al_2O_3. Recipes exist for many other materials, and the system will ultimately be capable of running elemental metals and metal nitrides. Contact us if you have an interest in using the system.

The heavy lab usage mentioned on the front cover of this issue has come at a time when our internal staffing is down two people. My personal thanks go to the NFC staff for maintaining a high level of user support even as positions were lost. We will be using some of the increased support from NNIN to hire an additional person to better support your needs. I hope that this person will be on board by early summer.

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Steve Campbell, Director
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Processing Capability Chemical Vapor Deposition (CVD) Techniques

An important aspect of many micro- and nanofabrication processing sequences is the deposition of thin films. Chemical vapor deposition techniques make use of gases and a chemical process, such as a decomposition or reaction, to generate the material to be deposited. For example, silane (SiH_4) is a common source for silicon in CVD systems. At sub-atmospheric pressures and elevated temperatures (620°C is common), silane chemically breaks down, resulting in silicon deposition. NFC currently has two different CVD systems. The low pressure CVD (LPCVD) system uses high temperatures (400 to 850°C) to drive the chemical processes to deposit films such as polysilicon, silicon nitride and silicon dioxide. The polysilicon films can be doped with phosphorus to increase the conductivity of the resulting film, and the SiO_2 films can be doped with phosphorus and/or boron. Silicon nitride also comes in two varieties: standard stoichiometric Si_3N_4, and more silicon rich films commonly known as low stress silicon nitride. The low stress silicon nitride films can be deposited to thicknesses of over 2um, and can be used to form freestanding cantilever beams and thin membranes as is often seen in MEMS devices. Plasma-enhanced CVD (PECVD) operates at lower temperatures (100 to 350°C), and hence is compatible with aluminum metallization. NFC can deposit silicon dioxide, silicon nitride and amorphous silicon by PECVD.

If you are interested in knowing more about these materials and CVD, please contact NFC at nfc@umn.edu.

Safety Training

NFC is offering safety training for new users twice each month. On the first Thursday of every month, the training sessions begin at 1:30PM, and on the third Thursday of the month sessions begin at 10:00AM. The training includes watching our safety video and taking a brief quiz. Also, a NFC staff member provides a tour showing some of the safety related equipment and the gowning process used for the NFC cleanroom. Finally, there is training on using the Coral lab software. The safety training takes about two hours to complete, and must be done before users will be granted access to NFC facilities.

PARTICLE TECHNOLOGY LAB NEWS

PTL DIRECTOR'S MESSAGE

Distinguished McKnight University Professor, David Y.H. Pui

The Center for Filtration Research (CFR) is a component of the Particle Technology Laboratory. We currently have seven industry members (3M, Cummins, Donaldson, DuPont, W.L. Gore, Samsung, and TSI) plus a government agency, National Institute for Occupational Safety and Health (NIOSH). The seven companies have an estimated $6-8 billion in annual sales in a variety of filtration products, ranging from filters for computer disk drives to Diesel soot collectors, and respirator filters for personal protection.

During the past five years, we have been applying nanoscale science and engineering in modeling and designing modern filters. Filters are used to protect workers and to recover nanoparticle products in reactors. Three years ago, two European research groups published results showing nanoparticles smaller than 20 nm may bounce through the filters due to their high thermal speed. There are health and environmental consequences with these observations.

At the request of our CFR members and NIOSH, we have conducted comprehensive experimental evaluations and modeling studies. Our results, published recently in *Journal of Nanoparticle Research*, clearly show that there is no evidence of particle bounce down to 3 nm under room temperature.

(continued, top right)

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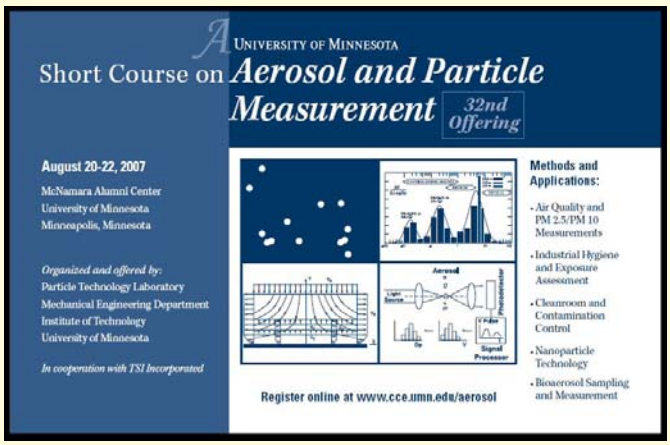
David Y.H. Pui, Director
Mark Stolzenburg, Lab Manager

A second research topic involves modeling and evaluating nanofiber filters. Nanofibers with diameters smaller than 100 nm are now incorporated in many modern filters. They help to increase the filter efficiency under the same pressure drop condition. Additionally, it enables easy cleaning of bag house and cartridge filters in recovering nanoparticle products. To successfully model the nanofiber filters, we need to incorporate slip condition for the flow around the fibers, which is not available in commercial filtration software. We have successfully developed such software that is validated with experiments.

Other topics under investigation include Bioaerosol Filtration, Nanoparticle Soot and Agglomerate Filtration, Filter Loading, and Filtration of Highway Nanoparticles by Cabin Air Filters. At our semi-annual review meeting, over 90 attendees from our CFR member companies attended with great interest. If you would like to receive more information about CFR or find in-house facilities that may be used under NNIN, please contact Dr. Jing Wang at wangj@aem.umn.edu.



We are pleased that our popular **Short Course on Aerosol and Particle Measurement** will be offered for the 32nd time this summer, August 20-22, 2007. During the past 31 offerings, over 1,850 registrants attended the course, most of them from industry. It is the first and the longest running aerosol short course in the U.S. It covers topics on sampling methods of PM2.5/PM10 standards, air quality and pollution control, cleanroom technology, nanoparticle technology, bioaerosol sampling and measurement, and industrial hygiene. We have added more lectures and lab demonstrations on the topics of Bioaerosols, Single Particle Mass Spectrometry, and Nanoparticles. Twelve internationally renowned professionals will give lectures and conduct laboratory experiments for this popular short course. Please check the following website for more information and for on-line registration: http://www.cce.umn.edu/aerosol.

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 Minnesota Nanotechnology Cluster

MiNTeC is an umbrella organization of three labs at the University of Minnesota that support the development of nano technology: the Characterization Facility, Nanofabrication Center, and Particle Technology Lab. As a node in NSF's National Nanotechnology Infrastructure Network (NNIN), MiNTeC provides access to advanced multi-user facilities to both industry and academic researchers, the latter at a subsidized rate. The MiNTeC facilities are at the University of Minnesota's Minneapolis campus, about 2 miles east of downtown.

For more information, visit http://www.mintec.umn.edu/ and www.nnin.org

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Comments and suggestions are welcome! Would you like to be added to or removed from our distribution?
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