

CenterPiece

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A promising approach for detecting biomolecules using microfabricated cantilevers that hold receptors or other molecules to bind a certain molecule of interest is shown in this artist's representation. The binding causes surface stresses that bend the microcantilever like a diving board. The cantilever's deflection is measured in tens of nanometers by embedding a metal-oxide semiconductor field-effect transistor (MOSFET) into its base and recording decreases in drain current as small as 5 nanometers. This approach offers low noise, high sensitivity, and direct readout. It allows detection of DNA hybridization and protein binding, among other techniques.

This image is from "MOSFET-embedded microcantilevers for measuring deflection in biomolecular sensors" by Gajendra Shekhawat, Soo-Hyun Tark, and Vinayak P. Dravid, *Science* 311:1592-95 (2006).

Developing ultrasensitive technologies

Electronic detection of biomolecular binding

Investigators at Northwestern University Atomic and Nanoscale Characterization Experimental Center (NUANCE) have made a significant step forward in the quest for biochemical sensors that are more practical for research, commercial, and governmental use.

According to NUANCE director Vinayak P. Dravid, "We are excited by the prospect that this approach may open up new vistas in biochemical sensing through high sensitivity electronic detection on computer chips, amenable to large and complex network systems."

—see NUANCE, continued on back cover



Creative collaboration with medical affiliates: Children's Memorial Research Center

The affiliation of the Office for Research with Children's Memorial Research Center (CMRC) brings into Northwestern's research portfolio an outstanding pediatric research organization dedicated to improving the health of children in Chicago and throughout the nation. CMRC, the research arm of Children's Memorial Hospital, Feinberg School of Medicine's pediatric teaching hospital, is one of only a few American institutions dedicated to pediatric research. Researchers at CMRC, who also serve as medical school faculty at Feinberg, conduct clinical and basic science research that they expect will lead to improved treatments, cures, and ultimately prevention of diseases and other health problems that affect children and their families.

Evolution of the Center

CMRC was founded in 1986 and its first director in 1989 was Bernard Mirkin, pediatrics, who remains with CMRC as director of research emeritus. Its first laboratory opened in 1996. There are now more than 500 staff and 200 faculty working at four CMRC locations: the Halsted Street facility in Lincoln Park, the Children's Memorial Hospital (CMH) facility on Fullerton Avenue in Lincoln Park, the Child Health Research Program on Clybourn Avenue in Lincoln Park, and laboratories at the Feinberg School of Medicine.

CMH has just announced that it will break ground for a new hospital near Northwestern's Chicago campus in 2008 to replace the Lincoln Park facility.

The Center's external funding for research has grown enormously since the original laboratory opened, from \$6.4 million in 1996 to almost \$25 million in fiscal year 2005. Nearly two-thirds of that funding comes from the National

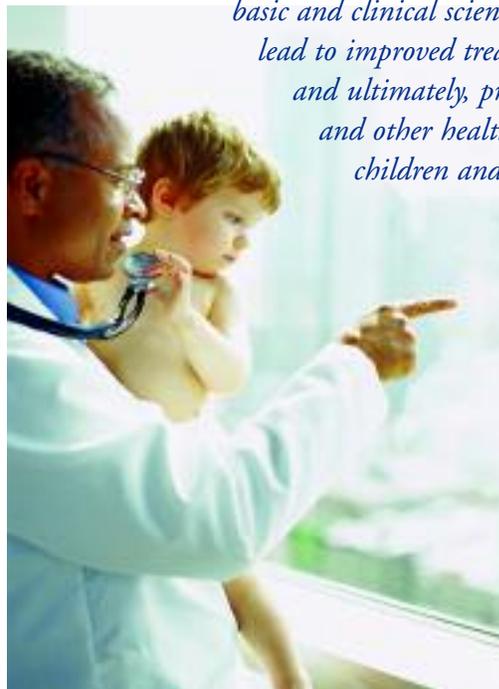
Institutes of Health (NIH) and other federal agencies.

In January 2004, prominent cancer biologist Mary J. C. Hendrix, pediatrics, was appointed president and scientific director. Her laboratory has uncovered key findings on the molecular mechanisms underlying cancer metastasis. She also serves as an energetic advocate for science and science policy nationally and internationally. "Our vision of science and medicine is an exploration through collaboration. We are delighted to be collaborating with Northwestern researchers to advance the discovery, development, and delivery of medical knowledge that can transform health care and improve the lives of children and adults everywhere," says Hendrix.

The Medical Research Institute Council (MRIC), principal benefactor of research at CMH, created the Medical Research Institute Council Endowed Chair for the President and Scientific Director at Children's Memorial Research Center. As the recipient of this first endowed chair, Hendrix will expand the Center's recruitment and infrastructure initiatives to pursue new discoveries and innovations in children's health care.

Hendrix also is the recipient of the prestigious MERIT grant award from the National Cancer Institute, and recently

At Children's Memorial Research Center, basic and clinical science studies lead to improved treatments, cures, and ultimately, prevention of diseases and other health problems that affect children and their families.



she received the Henry Gray Award, the highest honor awarded by the American Association of Anatomists. The award recognizes a lifetime of achievement, including unique and meritorious contributions to the field of anatomical science.

Five deputy directors work with Hendrix to carry out CMRC's mission:

- H. William Schnaper, pediatrics: academic development
- Philip V. Spina, chief administrative officer: administration
- Philip M. Iannaccone, pediatrics and pathology: basic research
- Leon Epstein, pediatrics and neurology: clinical research
- Holly Falk-Krzesinski, director, Office for Research Strategic Initiatives: strategic initiatives

As deputy director for strategic initiatives, Falk-Krzesinski acts as liaison between CMRC and Northwestern's Office for Research. Recently, working with Northwestern's budget and general counsel offices she helped develop policy that enables Northwestern graduate students a seamless transition to do their

graduate study at CMRC without loss of compensation, benefits, or seniority.

CMRC programs

As an example of its commitment to exploration through collaboration, the Center's work is organized around seven multidisciplinary research programs that have been established:

- Cancer biology and epigenomics
- Mary Ann and J. Milburn Smith Child Health Research Program
- Developmental biology
- Experimental therapeutics
- Human molecular genetics
- Molecular and cellular pathobiology
- Neurobiology

These programs integrate the research of bench scientists, clinicians, and other CMH health professionals, regardless of physical location. By encouraging synergy among investigators in various disciplines, the Center continues to discover new ways to develop medical advances that can better treat sick children wherever they may be.

A recent example is the success of a team of scientists led by Anne H. Rowley, pediatrics and microbiology/immunology, in identifying a possible viral cause of Kawasaki disease, the most common cause of acquired heart disease in children in developed nations. Since 1967, when Kawasaki disease originally was described, investigators suspected an infectious cause, but until now none had been identified.

An article describing the new findings was published in the November 15, 2005, issue of the *Journal of Infectious Diseases*. Results of the study provide new insights into the cause and course of acute Kawasaki disease.

Rowley's collaborators on this study included Stanford T. Shulman, pediatrics; Susan E. Crawford, pathology; Pauline M. Chou, pathology; and Francesca L. Garcia, research technologist at Feinberg; as well as faculty from the Stritch School of Medicine, Loyola University;

George Washington University School of Medicine, Washington, D.C.; and Toho University School of Medicine, Tokyo.

CANCER BIOLOGY AND EPIGENOMICS

Marcelo B. "Bento" Soares, pediatrics, leads the cancer biology and epigenomics program in its work to uncover molecular mechanisms underlying tumor growth, tumor heterogeneity, and metastasis. Investigators then translate their discoveries to the clinics through integrated basic and clinical research.

Researchers in collaboration with the National Human Genome Research Institute at the NIH have generated molecular classifications of specific tumors and provided new prognostic markers and novel targets for therapeutic intervention.

MARY ANN AND J. MILBURN SMITH CHILD HEALTH RESEARCH PROGRAM

The mission of the Mary Ann and J. Milburn Smith Child Health Research Program, led by Xiaobin Wang, pediatrics, is to better understand the natural history, causes, and psychosocial impacts of common and important child health problems. Specifically, the program engages in both population- and clinical-based research to explore the three key factors in the development of child health problems: environmental factors, genetic susceptibility, and growth and maturation.

Under Wang's direction, the research has recently led to the isolation of a gene responsible for pre-eclampsia, an abnormal condition of pregnancy.

The Smith Child Health Research Program includes five core programs: Biostatistical Research and Consulting program; Child Health Data Laboratory; Center on Obesity Management and Prevention, and Consortium to Lower Obesity in Chicago Children; Pediatric Practice Research Group; and Molecular Epidemiology of Preterm Delivery program.

DEVELOPMENTAL BIOLOGY

Philip Iannaccone leads the developmental biology program in which researchers strive to understand the genetic mechanisms that underlie pattern formation



Programs at the Center integrate the research of bench scientists, clinicians, and other Children's health professionals, regardless of physical location.

and cell fate specification during human development. The areas of particular interest include signal transduction pathways, stem cell biology, transcription factor networks, and morphogenetic movements. Scientists are uncovering disturbances and disruptions in genes during development that may cause birth defects, cancer, and other childhood diseases.

CMRC investigators use a variety of animal subjects for embryo manipulation, imaging (including live cell imaging with multiphoton laser scanning microscopy), gene expression profiling, genomics, in situ hybridization, in experiments that range from limb regeneration to genetic manipulation to cloning—all in pursuit of new knowledge.

EXPERIMENTAL THERAPEUTICS

Ram Yogev, pediatrics, directs the experimental therapeutics program, which oversees all clinical trials conducted by investigators affiliated with CMRC. Potential sponsors include the NIH, pharmaceutical companies, and philanthropic and other organizations. The primary goal of this program is to expand the breadth of studies conducted at CMRC and to assure the highest scientific standard for all clinical research.

—see CMRC, continued on p. 6

Gautreaux at 40 conference: The legacy and future of landmark public housing decisions

Forty years ago, Dorothy Gautreaux and three other public housing residents filed two class-action lawsuits in Chicago, one of which would make its way to the Supreme Court. The Court's unanimous *Hills v. Gautreaux* decision resulted in a 1976 settlement that set in motion an attempt to end decades of racially discriminatory practices in Chicago public housing—and eventually the nation.

The School of Law and IPR cosponsored the conference.

In tracing the public housing issue from 1966, when it was joined in the courts and the streets through Martin Luther King, Jr.'s march in Chicago for open housing, Rubinowitz marveled, “Who could have imagined that 40 years later several hundred of us would gather to discuss and debate these issues that seem to have no end.”

IPR faculty studies on Gautreaux

James Rosenbaum, human development and social policy, conducted the first studies on Gautreaux I, which helped to lay the foundation for the Moving to Opportunity (MTO) Program implemented by the U.S. Department of Housing and Urban Development (HUD) in 1994.

Rubinowitz and Rosenbaum also documented a truly unusual circumstance—moving poor black families into predominantly middle-class white

suburbs. They recounted the Gautreaux pioneers' complex experiences resulting from racism and harassment to improved life outcomes in their book *Crossing the Class and Color Lines: From Public Housing to White Suburbs* (University of Chicago Press, 2000).

Currently, Greg Duncan, human development and social policy, is leading an evaluation of Gautreaux II families. This second-wave study will provide important qualitative data that could not be gathered from the original Gautreaux research due to limitations in the original program's design.

Gautreaux's legacy: What have we learned?

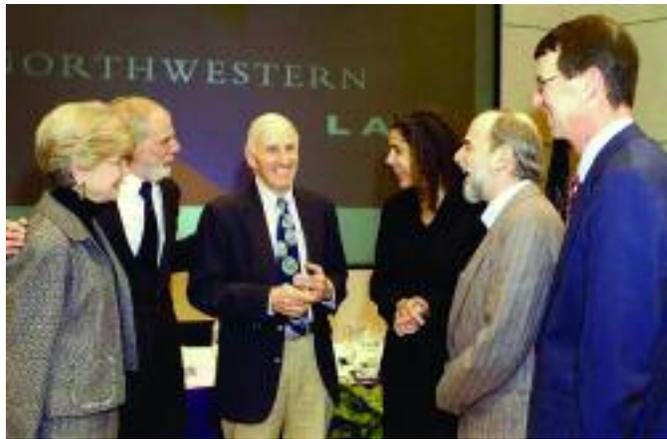
In Duncan's review of Gautreaux I and II and MTO programs, he found mixed

results. Gautreaux I families relocated between 1976 and 1998, with the bulk of moves occurring in the mid-1980s. Once admitted to the program, participants were given Section 8-type vouchers, which subsidize rents for private, market-rate housing based on income. Participants were required to move into neighborhoods with a census tract population that was no more than 30 percent African American.

Duncan found that 15 years after Gautreaux I's implementation, 67 percent of the mothers placed in the suburbs were still residing in the suburbs. Neighborhood poverty rates were as low as they had been in their placement neighborhoods. More important, children who moved with their mothers and had since become adults were nearly as likely as their mothers to live in the suburbs and in low-poverty neighborhoods. Duncan called it a true story of “inter-generational success.”

Earlier studies by Rosenbaum and others showed that children's attitudes toward school improved and their grades did not drop if they were placed in suburban rather than city neighborhoods. These studies also found the children were more likely to graduate high school, enter college, and enroll in better colleges (four-year versus two-year colleges). They were also more likely to get jobs and to be employed at higher paying jobs.

Unfortunately, preliminary results for Gautreaux II families, who moved between 2002 and 2003, have not been as promising. Families who moved a second time ended up in neighborhoods with higher rates of poverty and percentages of African Americans than Gautreaux I families. These moves seem to be undoing the benefits of the initial move in Gautreaux II, Duncan noted, but the jury is still out on the longer-term fortunes of these families.



IPR faculty participating in the Gautreaux conference with Alexander Polikoff. From left: Fay Lomax Cook, Leonard Rubinowitz, Polikoff, Mary Pattillo, James Rosenbaum, and Greg Duncan.

Thanks to the Gautreaux program that grew out of the settlement, more than 6,000 poor, black Chicago families moved out of their blighted, inner-city housing projects into low-poverty, mostly white suburban neighborhoods. Faculty from Northwestern's Institute for Policy Research (IPR) were among the first to measure and document the successes and failures of residential mobility programs since the 1976 launch of Gautreaux.

The conference “Gautreaux at 40: Race, Class, Housing Mobility, and Neighborhood Revitalization,” organized by Leonard S. Rubinowitz, law, brought together on March 3 more than 400 academics, activists, developers, officials, and public housing residents to discuss and debate the legacy and ongoing impact of these landmark decisions.

In between Gautreaux I and II came MTO. Buoyed by Rosenbaum's Gautreaux documentation and seeking more complete answers to the public housing puzzle, HUD implemented the MTO program in five cities—Baltimore, Boston, Chicago, Los Angeles, and New York—between 1994 and 1998. MTO was designed to fill a research gap in the Gautreaux I program—the absence of control groups. Thus, MTO was a random-assignment program that studied two major groups: a treatment group offered assistance to move to more affluent neighborhoods and a control group that was not offered such assistance. The MTO mandated destination neighborhoods with poverty rates of 10 percent or less, while Gautreaux I only targeted race and Gautreaux II set criteria for both race and poverty.

According to Duncan, MTO's most striking success has been a sharp improvement in the mental health of the mothers who moved, with cases of depression being cut in half. Mothers cited getting away from gang- and drug-ridden neighborhoods as their number one reason for moving.

However, evaluators found that although children of MTO participants attended somewhat higher-achieving schools, these were still underperforming schools, scoring below state achievement levels. Participants also did not experience higher employment, nor less welfare receipt when compared with the control group—though the late 1990s was a time when the control group doubled its employment rate, posing a high standard for the treatment group to exceed.

Rosenbaum explained this might also be due to the fact that when MTO families changed neighborhoods, most of the moves were less than 10 miles away—compared with an average of 25 miles for the Gautreaux participants. This permitted MTO families to move to highly segregated neighborhoods and even allowed their children to remain in the same schools.



James Rosenbaum discusses housing issues with Xavier de Souza Briggs.

Public housing: Where do we go from here?

Highlighting the stigma of subsidized housing that attaches itself to families who move, Xavier de Souza Briggs, Massachusetts Institute of Technology, spoke about how the “politics of property” shapes housing opportunities. There is no evidence to show that Section 8 vouchers or other subsidies “typically” decrease housing values, he noted. In fact, the opposite can be true: Investments in affordable housing can help to revitalize neighborhoods. To improve next-generation housing policies serving the poorest families, including those in public housing, he called for improved mobility counseling and targeting, the use of performance management frameworks, and programs to promote stability and adaptation by relocated families.

Susan J. Popkin (PhD, Northwestern University) of the Urban Institute, a former IPR research associate, underlined the urgent need for a dedicated effort to house the remaining “hard-to-house” families. She spoke about “war-zone” conditions that have damaged some residents to the point where they cannot function in a normal community. “We owe these families, especially the children, a serious effort to try to stabilize their situations and help them to move to better, safer neighborhoods,” she said.



Susan Popkin, senior research associate at the Urban Institute addresses the conference.

Duncan proposed that residential mobility programs should be examined in the wider context of programs that might help low-income families. He gave the example of Milwaukee's successful New Hope work-support program. New Hope offers a cafeteria-style program of benefits, including child-care and income supports, providing the working poor with the same opportunity as the middle class to balance the demands of work and family, Duncan said.

Perhaps the most radical proposal for “dismantling the black ghetto” came from Alexander Polikoff, lead counsel in the *Gautreaux* lawsuits. He presented his idea for a national Gautreaux program under which a portion of existing housing vouchers would be “recycled” and offered to 50,000 black families each year. Polikoff explained why he thought such a program



Alexander Polikoff receives a framed print of the cover of his recently released book, *Waiting for Gautreaux: A Story of Segregation, Housing, and the Black Ghetto* (Northwestern University Press, 2006).

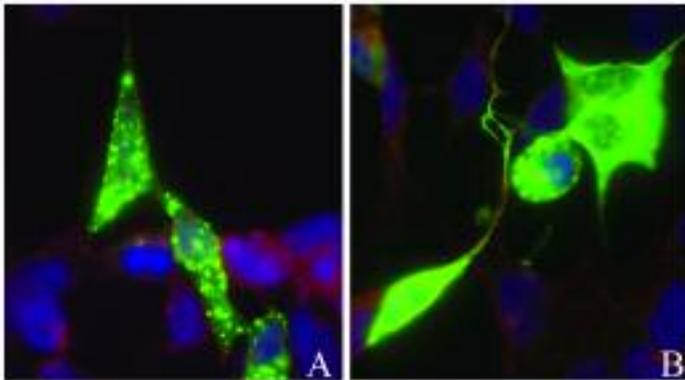
would be fiscally and programmatically feasible and, in a decade, would enable half of the resident black families to leave their ghettos. Polikoff believes this would trigger redevelopment that would end black ghettos as we know them.

The public housing debate has gained new strength and relevance in the wake of Hurricane Katrina. But it involves

—see *Gautreaux*, continued on p. 7

—CMRC, continued from p. 3

As scientists reveal new information leading to innovations in detecting and treating diseases ranging from cancer to cerebral palsy, CMRC investigators will be able to test promising new treatments and devices to ensure that they reach those who most need them. A program in pediatric experimental therapeutics is offered to train investigators in experimental and biostatistical methodology for the design, conduct, and analysis of therapeutic trials related to pediatric disorders. The program also emphasizes research ethics and the protection of human subjects.



Expression of a schizophrenia susceptibility gene, DISC1, in a neuronal cell line. **A.** Wild-type DISC1 (green); **B.** Mutated DISC1 (green). This image is from the research of Jill A. Morris, pediatrics. Morris and her group at CMRC study the molecular basis of schizophrenia. Go to www.childrensmrc.org/morris for more information about their research.

HUMAN MOLECULAR GENETICS

Program director Ann Harris, pediatrics, is building a world-class center of translational genetic medicine. Current faculty members are working on projects that explore aspects of neurological genetic disease, spinal muscular atrophy, autism, schizophrenia, and the molecular basis of cystic fibrosis.

MOLECULAR AND CELLULAR PATHOBIOLOGY

Program director Lauren M. Pachman, pediatrics, works to bring together the research of clinician-scientists who study mechanisms that alter diseases, susceptibility, and response. These studies include immune recognition and regulation, injury to the gastrointestinal tract in

newborns, single-cell transplantation approaches to liver diseases, angiogenesis and the regulation of vascular tone, in addition to the mechanisms of drug resistance.

NEUROBIOLOGY

Working together under the leadership of Martha C. Bohn, pediatrics and molecular pharmacology and biological chemistry, are neuroscience faculty, graduate students, postdoctoral fellows, and research associates using cutting-edge technologies in imaging and gene profiling to define molecular processes critical to development, degeneration, and regeneration of cells in the brain.

Their research represents several emerging areas in the field of neuroscience, including how stem cells in the brain respond to injury, virus-based gene therapy as a means for delivering molecular therapies to the diseased and injured brain, gene profiling of pediatric and adult brain tumors as a way to identify therapeutic targets for brain cancers, molecular mechanisms involved in the death of cells that further understanding of cancer and neurodegenerative diseases, and RNA

interference for gene silencing. The program emphasizes the extrapolation of laboratory findings to the development of molecular cures for diseases and injuries of the human nervous system.

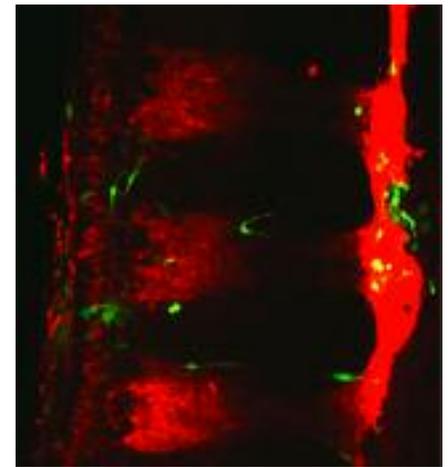
CMRC discovery, technology transfer, and investment

The Center's growing technology transfer program pursues patents for discoveries and inventions made by its investigators—discoveries that will be of interest to commercial and venture capital firms that sponsor research. By identifying commercial partners with the resources and experience to market its research, CMRC has a greater potential to contribute new technologies that will benefit patient healthcare.

Through transfer partnerships, new drugs, devices, diagnostics, and therapies developed at CMRC can make an impact on the greatest number of children. These partnerships also provide the means to reinvest in additional research programs.

Contact Holly Falk-Krzesinski at h-falk@northwestern.edu or 773-755-6583 for more information about the research enterprise at CMRC.

The Center's web site can be found at www.childrensmrc.org.



Human metastatic melanoma cells transplanted into the chick trunk neural tube migrate to dorsal root and sympathetic ganglia sites similar to chick neural crest cells. The image is a sectional view through a typical chick embryo in a region where adult human melanoma cells labeled with green fluorescent dye have been transplanted. The background is stained red and shows the host chick neural crest cells migrating through specific sections of the tissue. The melanoma cells (green) appear to co-localize with the chick neural crest cells and migrate to the same regions, but they do not form tumors. Essentially, the melanoma cells have reverted to their ancestral cell type of origin, the neural crest cell which gives rise to the melanocyte ["Reprogramming metastatic melanoma cells to assume a neural crest cell-like phenotype in an embryonic environment." P.M. Kulesa, J.C. Kasemeier, J.M. Teddy, N.V. Margaryan, E.A. SefTOR, R.E.B. SefTOR, and M.J.C. Hendrix. *Proceedings of the National Academy of Sciences*, 103:3752–57 (2006)].

This image shows research from the group headed by Mary J.C. Hendrix, CMRC president and scientific director. Their research involves examining the epigenetic role of the micro-environment in determining cell plasticity.

For more information about this group's research, go to www.childrensmrc.org/hendrix.

—Gautreaux, continued from p. 5

a complex set of issues, actors, and competing interests, compounded by too little understanding of what public housing residents want themselves. While some evidence indicates that by moving, such residents can do better, the conference also showed that poorly designed interventions and insufficient resources mean they can also do the same or worse. A group of public housing residents who attended the conference made it perfectly clear that they are not happy about being forced to leave their communities and social networks behind. “These are our homes you are talking about,” one argued.

For a complete bibliography of Gautreaux research by IPR faculty, please go to www.northwestern.edu/ipr/publications/Gautreaux.html. Conference papers will be published online this summer in the newly launched *Northwestern Journal of Law and Social Policy*. The complete conference program can be viewed at www.law.northwestern.edu/faculty/conferences/research/gautreaux.html.

CenterPiece

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C. Bradley Moore, vice president for research

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Kathleen P. Mandell, senior editor

To submit center news or request copies of *CenterPiece*, contact Kathleen Mandell at 847/491-3880 or by e-mail at kathym@northwestern.edu.

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University research centers

Center for Applied Psychological and Family Studies

William M. Pinsof, director | e-mail: family-institute@northwestern.edu

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Materials Research Institute

R.P.H. Chang, director | <http://materialsresearchinstitute.northwestern.edu>

Northwestern Institute on Complex Systems

Daniel A. Diermeier and William L. Kath, codirectors
www.northwestern.edu/research/nico

Northwestern Synchrotron Research Center

Wayne F. Anderson and Michael J. Bedzyk, codirectors
www.dnd.aps.anl.gov

Northwestern University Atomic and Nanoscale Characterization Experimental (NUANCE) Center

Vinayak P. Dravid, director | www.nuance.northwestern.edu

Program of African Studies

Richard A. Joseph, director | www.northwestern.edu/african-studies

NUANCE investigators, led by Gajendra S. Shekhawat, recently introduced an innovative detection approach for biochemical binding using a microcantilever in which a MOFSET (metal-oxide-semiconductor field-effect transistor) has been embedded. This approach requires neither electronic labels nor optics (see image on front cover). Their ongoing research promises progress in the use of this biochemical technology for a wide variety of sensing mechanisms (for instance, detection of viral and other harmful pathogens, biochemical warfare agents, or toxic gases) and diagnostics (such as proteomics studies, DNA analysis, and inhibition studies in drug discovery).

Seeing the invisible

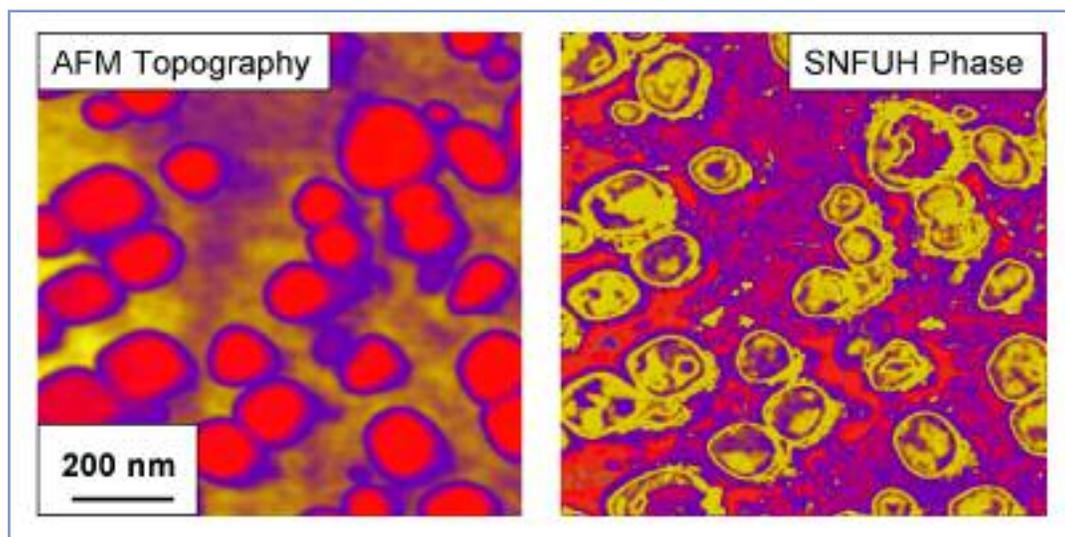
Members of the Nanoscale Integrated Fabrication, Testing, and Instrumentation Center (NIFTI) at NUANCE developed a unique and exciting method for real-time, noninvasive imaging using Scanning Near-Field Ultrasound Holography (SNFUH).

The new technique combines the nondestructive nature of acoustic waves for depth information, high-lateral spatial resolution of near-field scanning probe microscopy (SPM), and a holograph model for phase-sensitive detection. The results were published in “Nanoscale imaging of buried structures via scanning near-field ultrasound holography” by Gajendra S. Shekhawat and Vinayak P. Dravid, *Science* 310: 89–92 (2005).

NIFTI researchers demonstrated the efficiency of SNFUH with various studies—from finding buried nanostructures and subsurface measurement problems in microelectronics to noninvasive, high-resolution imaging of malaria parasite infection in red blood cells.

SNFUH bridges the noninvasive imaging gap at the critical length scale of 10 to 100 nanometers. The technique provides nondestructive measurement of structures and devices, therefore it may be applied to numerous physical and life science investigations, as well as to analyses of engineered systems. The effectiveness of SNFUH in biological material is shown in the image below.

Visit www.nuance.northwestern.edu/index.htm for more information about these and other innovative developments at NUANCE. 



Liposomes contain trapped air bubbles that provide high contrast in sonography imaging. The atomic force microscopy (AFM) topographic image (left) shows only the outline of liposomes, while the SNFUH phase image (right) reveals the inside of the liposomes. Liposome specimens courtesy of Robert C. MacDonald, biochemistry, molecular biology, and cell biology.

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Office for Research
Northwestern University
633 Clark Street
Evanston, Illinois 60208-1108