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Beyond Limits and Borders

Interdisciplinary team collaborates across scientific disciplines and international borders

By Jonathan Talbot

What would you call an award-winning, collaborative team of researchers and students that works on sensing very small structures at BU's Photonics Center? It's not an idle question.

"We've struggled with the name," says Selim Ünlü, professor in the Electrical and Computer Engineering Department (ECE). For years, entrances to the laboratory space he shares with Bennett Goldberg, professor of physics in the College of Arts and Sciences, boasted different descriptions of their collaborative work. "It changes, but right now the answering machine says, 'the photonics laboratory of Professors Ünlü and Goldberg.'"

Building on nearly a decade of their research in near-field scanning optical microscopy, which moves a tiny aperture over a sample, members of the team now enjoy strong collaboration with faculty from the Departments of Aerospace and Mechanical Engineering, Biomedical Engineering, and Physics, as well researchers beyond Boston University.

"Identifying a particular resource needed, and then the person who has that resource, does not generally work," says Ünlü, who prefers to learn what good potential collaborators are doing and then follow those leads to new research and teaching success. Building on these collaborations across the disciplines and international borders, the team developed capabilities beyond the fundamental limitations of conventional techniques.

The National Science Foundation (NSF) and the National Institutes of Health (NIH) have combined support of $2 million for continuing work on the spectral self-interference fluorescence microscopy pioneered by Ünlü, Goldberg, and Anna Swan, a research assistant professor in ECE, in which instruments image light interference. Some of that light travels directly from a fluorescent molecule, while other light first reflects from a surface placed within several wavelengths of the emitter. The distinct interference pattern reveals the emitter's position within a nanometer. Collaborations with BU's Center for Advanced Biotechnology and professor Clement Karl of ECE, have been an enabling factors in this research.

"I don't know the first thing about how to attach a biological molecule to a surface," Ünlü says. "Interdisciplinary collaborations allow us to identify and address the scientific problems that we cannot solve alone and yield a new modality of doing microscopy."

In partnership with Harvard Medical School and Brigham and Women's Hospital, the lab has also made advances in generating hyperpolarized gases for magnetic resonance imaging. The NSF funds this effort to introduce atoms with controlled spin polarization into the body, rather than imaging protons that are already there. The technology allows for imaging at much lower fields and of previously inaccessible areas when compared with conventional MRIs.

A separate NSF Nanoscale Interdisciplinary Research Team (NIRT) grant of $1.3 million has brought together Ünlü, Goldberg, Swan, and three first-year assistant professors in Physics (Pritiraj Mohanty) and Aerospace and Mechanical Engineering (Todd Murray and Kamil Ekinci), to pursue imaging of quantum dots and nanostructures in semiconductors (see NAIL sidebar). Under the NIRT grant, while Professor Ekinci is pursuing nanoscale structures whose resonance frequencies change when a biological molecule attaches for antibody imaging, Professor Murray is studying the elastic properties of solids, exploring the high-frequency regime of nanoscale stresses for the first time.

Graduate Students Matthew Emsley *(ENG '03, Ph.D.)* and Olufemi Dosunmu *(ENG '04, Ph.D.)* are working on high speed characterization of photodetectors fabricated in collaboration with Prof. Yusuf Leblebici of Swiss Federal Institute. Both students have traveled to Lausanne with funding from NSF International Programs and worked in the clean room facilities for several months.

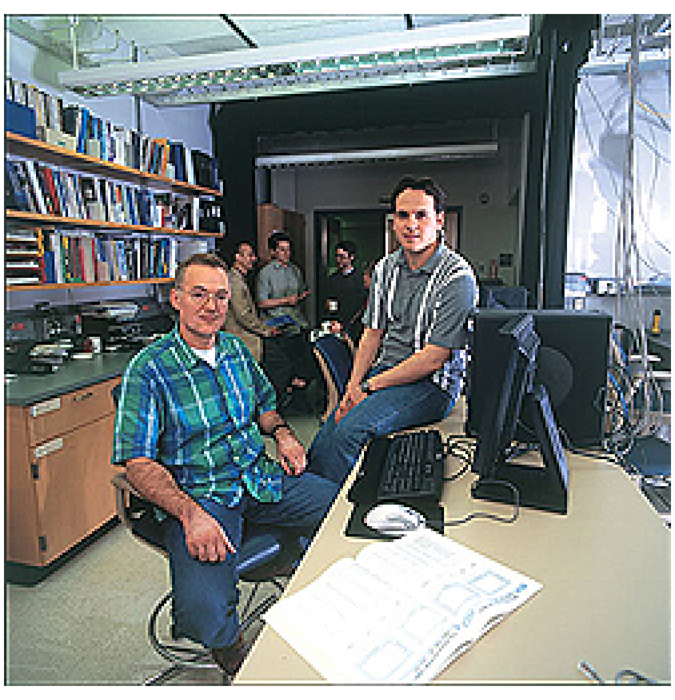
The group is also collaborating with the Institute of Optics at the University of Rochester in developing solid immersion microscopy techniques combined with metal tips to provide unprecedented resolution for spectroscopy of semiconductor systems. The ultimate goal of the proposed program is to develop robust and efficient optical techniques at a spatial resolution on the order of 10 nm. This collaboration is further fortified with a recent Multidisciplinary University Research Initiative (MURI) grant on nanoprobes. On the international front, an Austrian nanofabrication facility grows quantum dots on reflective substrates used for Ünlü's research in resonant cavity enhanced photodetectors, while BU graduate students working at a Swiss clean room facility fabricate high-speed photodetectors and arrays. A small company in Zurich packages those devices with optical amplifiers to test the BU lab's innovations. The United States Army Research Lab funds the photodetector work through a grant to the Photonics Center.

The lab is building on these already impressive collaborations and looks to closer partnerships with the BU Medical Campus; universities in Japan, Germany, and Australia; and Boston University's brand-new Institute for Technology Commercialization. The group already collaborates with a U.S. waveguide manufacturer to develop biosensors to detect single biomolecules of interest, for which Tejal Desai, associate professor in the Biomedical Engineering Department, is preparing binding sites (see nanobiotechnology sidebar).

The dozen or so graduate students in the Ünlü-Goldberg group benefit from its multidisciplinary, international nature while contributing to its success. "We are able to train students in a very broad knowledge base," says Ünlü. Students are also in the thick of communications with private companies, learning to pursue collaborations, understand state-of-the-art technology, and test commercial products.

Ünlü, Goldberg, and Swan act as co-advisors to several graduate students, and draw students from different BU departments for research projects. "We might have several students on a joint grant," says Ünlü, and "the decision on which of the professors would serve as the first reader for a thesis is made well after a student joins our group." An electrical engineer by training, Ünlü has acted as the primary adviser for physics students, and Goldberg, a physicist, has played that role for electrical engineering students.

For Lev Moiseev, Ph.D. '03 in molecular biology, Ünlü, Goldberg, and Swan acted as co-advisers, while Charles Cantor of the Center for Advanced Biotechnology (CAB) acted as primary adviser. "It was unusual," says Ünlü. "He had a thesis committee of biomedical engineering, physics, and electrical engineering."



Graduate student Mehmet Dogan *(ENG '05, Ph.D.)* working with Professor Isradi Aksun on electromagnetic modeling of fluorescent emission on reflecting surfaces during Aksun's visit to BU.

Weekly meetings allow students and researchers to present current work to the others in the group in a way that will interest a general scientific audience. As with other aspects of the program, Ünlü says that distinctions between faculty and students are forgotten during critiques. "Students learn from giving even bad presentations," says Ünlü, adding, "It is best to learn from mistakes in this informal environment rather than at a major international conference." Recently, students on the NIRT grant teams have begun to attend the meetings even in the absence of faculty, bringing the attendance to more than 25, even in the summer.

Traveling, living and working internationally, and interacting with visiting researchers from around the world further motivates already hard-working students, says Ünlü, by offering opportunities to work in different cultural and institutional contexts. Doctoral student Mehmet Dogan, for example, has traveled twice to Turkey to work with Irsadi Aksun, professor of electrical engineering at Koc University in Istanbul, Turkey. For many years, several former Ph.D. students worked at facilities at Bilkent University, in collaboration with Ekmel Ozbay, professor of physics in Ankara, Turkey. But the students are motivated to cross boundaries in other ways as well.

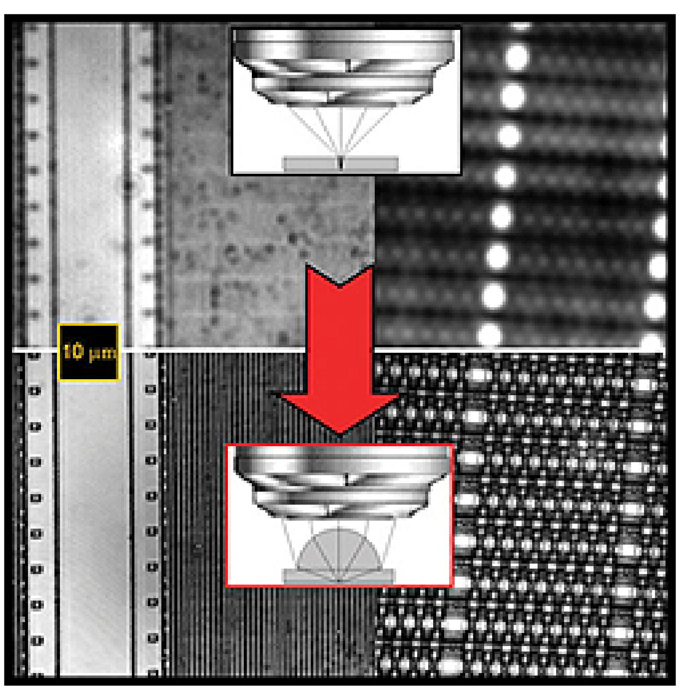
"When I became involved, Professors Goldberg and Ünlü were looking to implement joint projects that required the input of physicists, engineers, and biologists, Moiseev says. "At the time, I was a graduate student in biology and came on board to work solely on biological problems." After some changes in the research staff, Moiseev realized learning physics would help the team further their goals. "No one pressured me to do this," he stresses, "but I ended up learning physics, optics, and computer programming." Moiseev credits the multidisciplinary environment with helping him discover some hidden talents that otherwise may have never been found. Today, he combines these areas as a research associate at the CAB as he continues to work with Ünlü's group.

A master's degree in photonics, new in 2002, is attracting new students now able to take exclusively photonics courses. A Combined Research and Curriculum Development (CRCD) grant from the NSF, combined with matching funds from the University, provided about $400,000 to build a Photonics Education Lab that now supports experiments for the photonics courses. Ünlü has won awards from the University for innovative teaching, and BU's Science and Technology Day has recognized many of the group's students for doing some of the best student research at the University. In fact, over the past decade, about ten students from this group have won awards from BU.

While the name for their group may be in question, one thing is certain: Professor Ünlü and his collaborative efforts are helping the world to see the very small in a whole new light.

Sharper Focus with NAIL Technique

Although Moore's Law has successfully predicted for decades that the number of transistors on a microprocessor will double every eighteen months, desire to make transistors ever smaller has outpaced the ability to analyze why those transistors can fail.



Semiconductor manufacturers use short-wavelength ultraviolet light to print fine structures on individual layers of silicon, metals, and dielectrics. In finished chips, multiple device layers are capped with opaque metal. To determine where a circuit overheated and failed, engineers must image through the silicon substrate, which is opaque to the wavelength used to pattern it but transparent to near infrared light with longer than one-micron wavelength.

The need to image with longer-wavelength light has traditionally limited the spatial resolution possible with far-field microscopy because spatial resolution scales with wavelength. "You are writing with UV light," explains Selim Ünlü, "but reading with three times the wavelength, and your resolution is proportionally worse."

The group has developed a novel solution, known as the Numerical Aperture Increasing Lens, or NAIL as coined by the ECE doctoral student Stephen Ippolito (ENG'04). By placing a hemispheric lens made of similar or the same materials as the substrate, light exiting the wafer and entering the polished planar surface of the lens does not refract. The light exiting the curved surface of the NAIL does refract before traveling through air to a far-field microscope lens, but the oblique angle at which it exits the NAIL improves the collection angle of the system, for a net increase in resolution.

"Even if you use a much lower magnification objective lens in the far-field optics, you can resolve much greater detail with a NAIL lens on the sample," says Ünlü.
He envisions NAIL microscopy becoming as inexpensive as atomic force microscopy, which can be found in any research facility, with its variety of available lenses costing just a few dollars each. The NAIL technique has also been extended to thermal imaging, providing record resolution. This form of microscopy for examining quantum dots and nanoscale structures on semiconductors can improve resolution by a factor of as much as five, but that was not good enough for this team.

Researchers knew that light shone at an oblique angle to a nanoscale metal tip focuses that light at the end of the tip. That tip, however, suspended in nothing but air, has tended to come into contact with samples and bend, rendering it useless. Besides, there is a large background of light in addition to the tightly focused spot around the tip. Calculations suggested that placing the metal tip at the focal point of the NAIL would likely enhance its resolution even more, but placing a tapered nanoscale tip inside a solid lens was a baffling prospect.

Physics professor Pritiraj Mohanty at BU and Lukas Novotny, professor at the University of Rochester, are working on nanofabrication techniques to build a metal tip on the outside of the NAIL. One potential method is to fabricate nanoscale metal pillars and then add a layer of the same material used in manufacturing the NAIL to surround and support the ultrafine metal whisker. Encasing the metal pillar provides a robust probe while limiting background light and improving resolution.

Ünlü believes that the tip-enhanced NAIL will eventually improve the resolution to better than 20 nanometers. "We haven't done that yet," says Ünlü, "but there is evidence it can be done, and when we can demonstrate that, with high collection efficiency, that will have tremendous impact. It will be a new and unique tool."
Research into the innovative solid-immersion lens with enhanced tip microscopy is supported by the MURI and NIRT grants, and supports work by professors Todd Murray and Kamil Ekinci of the Department of Aerospace and Mechanical Engineering at the College, as well as Mohanty.

When Bio Goes Nano

The research community is becoming increasingly interested in accessing the nanoscale world of biological systems for applications ranging from nanofabrication to drug delivery and bio-terrorism detection.

"Lots of institutions look at nanostructures and semiconductors," says Selim Ünlü. "When Bennett Goldberg and I spoke with Tejal Desai, we hit upon nanobiotechnology as a field in which BU could really distinguish itself."

In 2002, ENG recruited Desai, associate professor in the Biomedical Engineering Department, to its Micro and Nano Biosystems Facility, dedicated that year. Funded in part by the University's 2001 Whitaker Foundation Leadership Award, Desai focuses on micro- and nano-technology for biomedical applications, including in vivo biosensor membranes and bioMEMs (biomechanoelectric machines).
It didn't take long for the group to realize the potential for collaboration with Desai. "There's nothing like having new smart people with complementary expertise put into the same environment with you, who are willing to work with you," says Ünlü.

One of Desai's collaborative projects has been the engineering of waveguide bio-sensors. A dielectric waveguide confines and guides light similar to a fiber-optic cable. Most of the light is inside the guiding layer, and typically, a small portion travels along the outside, interacting with the environment and thus allowing for sensor applications.

Desai has expertise in attaching binding sites for target biomolecules to the exterior glass surface of the waveguide. Target molecules such as proteins stick to those binding sites. The protrusion of even a single target molecule into the flow of waves through the waveguide modifies the field properties, signaling the presence of the molecule of concern.

In efforts to develop waveguide biosensors, in which a molecule of interest would bind to a site on the surface of a waveguide, disrupting the field within, uninteresting small particles will also be collected on the surface. The technology, which is sensitive enough to detect a single particle, would be rendered blind by the clutter. By controlling the thickness of the waveguide and utilizing different polarizations of light, BU researchers devised a technique that is insensitive to the immediate surface and applied for a patent on "surface desensitization" of biosensors. This kind of innovation and a broad base of expertise attract industrial partners to work with the group.

The industrial partner they are collaborating with brings to the table state-of-the-art technology in telecom devices looking for an application in biotechnology. As an indication of how they build partnerships, not surprisingly, Ünlü and Goldberg have a history of successful collaboration with the same researchers on waveguide devices prior to commercialization of their technology.

Desai is also working with Ünlü and Goldberg on establishing an interdisciplinary graduate education research traineeship. The proposed $3.7 million program would emphasize close ties to the Boston University Medical School and strong industrial and international collaborations.