Session 1 Education and R&D in University

Nanotechnology Research at Boston University

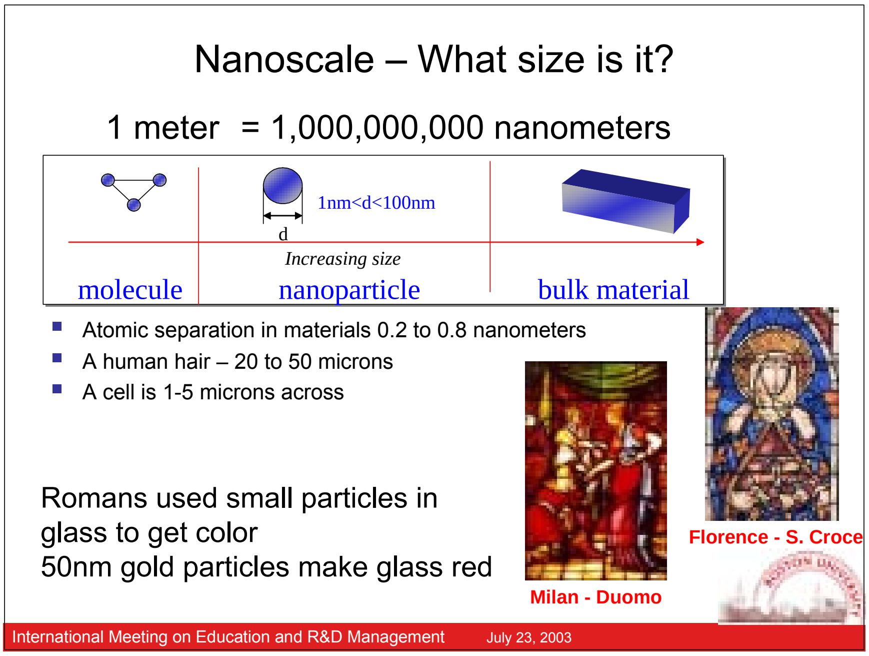
M. Selim Ünlü
Boston University
2003.7.23.

Dr. Yaniv: Mr. Selim Ünlü is working in nanotechnology at Boston University and probably is one of the future contributors to the pocket of Dr. Ronstadt, let us hope. Mr. Ünlü graduated from Ankara University. Then he moved to the United States, where he graduated from the University of Illinois, Urbana-Champaign, and worked in photonics and similar devices. He will present the activities of Boston University in nanotechnology. Mr. Ünlü, thanks.

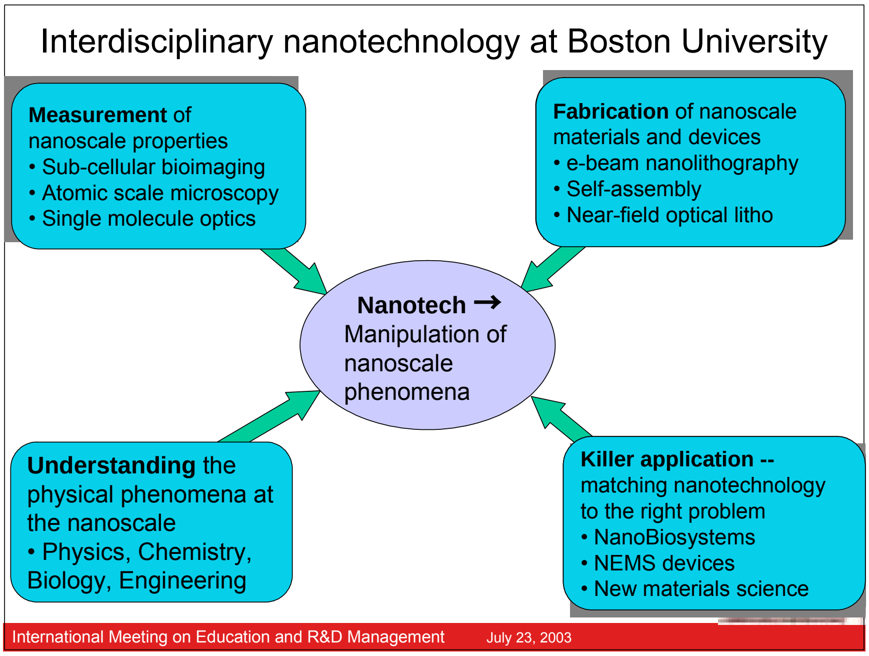
Prof. Ünlü: Well, first of all I would like to thank the organizers for inviting me and giving me this opportunity to speak here.

Boston University has a long tradition. It is a large private university. The university is an urban university with lots students and there has been a recent attempt at the university to build more science and technology and we are trying to lead that effort in terms of building nanotechnology research at Boston University. My name is Selim Ünlü and I am a professor in the electrical engineering department. I also have a joint appointment in the physics department. Dr. Ronstadt mentioned some of the activities and there is a picture of the photonics center from Charles Riverside and that is where my office, classrooms and laboratories are.

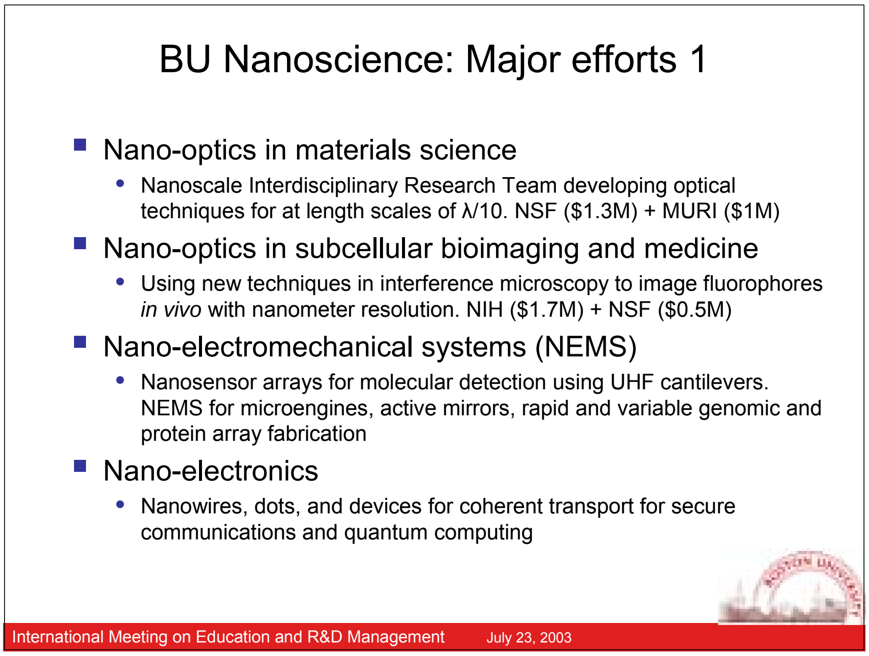
Today I will try to give you a general description of the research activities in nanotechnology, specifically in areas I am involved in personally. I will try to use some examples of graduate students in our program. Instead of giving a very general description of how we handle student education, I would like to go through a couple of examples where we can really pinpoint how success can be achieved in having students involved in technology commercialization. I am going to focus on some of the applications in biology, what we call nano biotechnology, because that is what we have selected as a focus area at Boston University. Now I will mention how we will link things to industry, how we can benefit from technology commercialization, to build our education program. Again Boston University is in the city of Boston, which is a very rich environment, very competitive environment, but we can benefit from that to build our own education and research program.



Since I am the first speaker talking about nanotechnology, maybe I should say a few words about what nanotechnology or what nano scale means. The gist of it, the basic principle of it, is that materials behave differently in the nano scale than they behave either as a bulk material or at the molecular scale. So their behavior is often unpredictable, not well understood, but certainly it goes well back several centuries in terms of its impact and its use. Gold nanoparticles will turn glass red, and in fact if you illuminate from the front or the back you can get different colors using nanoparticles. Although these uses have been known for a long time, the principles of operations have not been understood. Now first of all, I will not be using every slide in your package so do not be alarmed. I will try to use fewer slides.



One of the key points of nanotechnology is it is very interdisciplinary and has several components. First of all, you have to create the material, either using a top-down technology such as in the semiconductor industry, or bottom-up, a self-assembly technology as in chemistry. The second challenge is to measure the nano scale properties or understand how things work, probably more importantly to find the killer application, where nanotechnology is the right solution for the problem. Since nanotechnology is quite unpredictable, oftentimes where the application will be will be unpredictable as well. At Boston University, being a university, obviously we focus on understanding the fundamentals. We also have a strength in metrology, measurements of nano scale properties in biology, also in semiconductor or solid-state systems, and there was a recent attempt in building our capabilities of fabrication and synthesis. We identified as our killer application as a focus area nano biosystems and nano electrical mechanical systems.



I will just tell you about some of the recent activities funded by the federal government and other funding agencies in nanotechnology. We do have a strong program in nano optics, which I will give you some examples of that is funded by National Science Foundation (NSF) and the Department of Defense. We also have a sub-cellular imaging project, again funded by the NSF and by the National Institute of Health (NIH). We do have other programs in nanoelectromechanical systems (NEMS) and nano electronics and the funding for these projects is coming from the university in terms of startup funds for new faculty, and those faculties are in fact working hard to secure more funds from the federal government. We also have a large effort in micro and nano biosystems, and this is founded under a Whitaker Foundation Leadership Award at US$14 million and Boston University Master's effort on a one-to-one basis. The basic goal here is applications in drug delivery, self assembly for cellular scaffolding and other applications in nanotechnology in biological areas.

BU Nanoscience: Major efforts 2

- Whitaker Laboratory for Micro and Nano Biosystems ($14M) + BU matching ($14M).
  - Nanotherapeutics: Targeted drug delivery, nanoporous membranes, smart nanoparticles
  - Cellular scaffolding, polymer tethers
  - 3D self assembly,
  - Nanomechanics of biosystems: Individual chemical bonds
- Infrared microscopy to 100nm, femtogram spectroscopy and breast cancer screening using a single strand of hair
- SPR biosensing: Array-based, multichannel sensors

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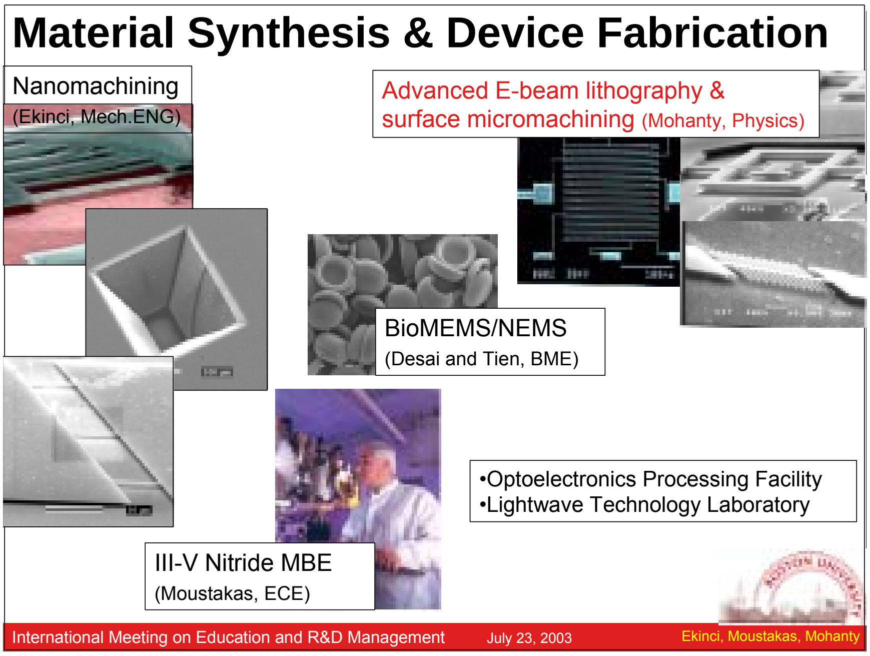
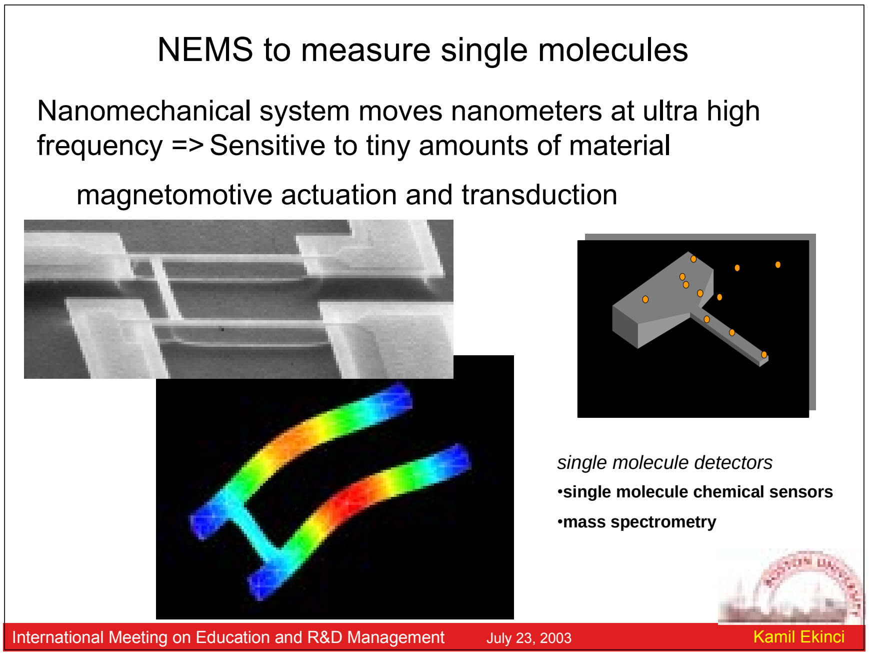
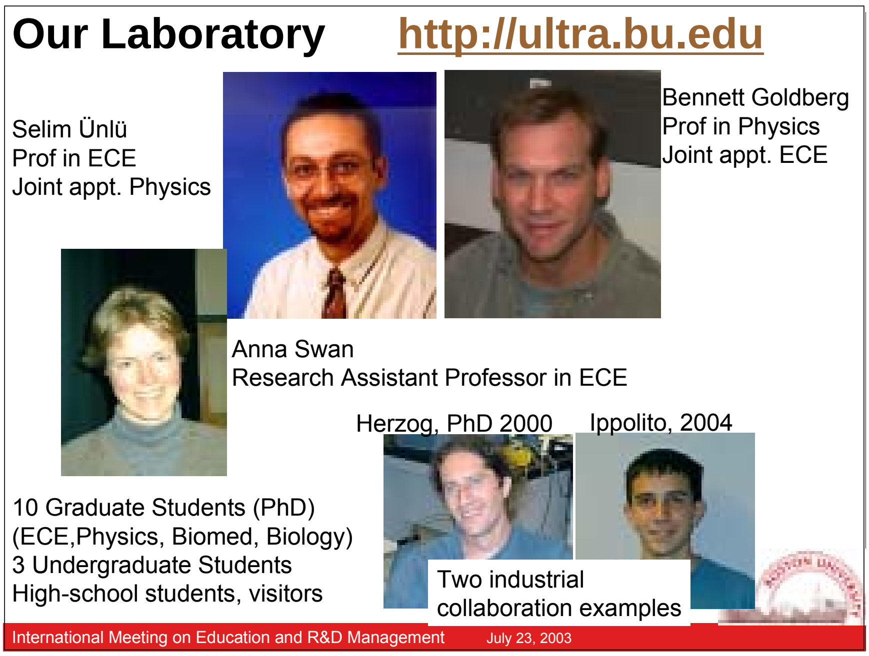


Now as I said, we are making efforts to improve our material synthesis and device fabrication. We have traditional semiconductor growth and fabrication especially in III-V semiconductors and the rest of the examples on this chart are all new for Boston University. We have hired new faculty in the mechanical engineering department related to nano machining and in the physics department, also for surface micro machining and lithography using electron beams. The effort at the Whitaker laboratories in the biomedical engineering department is focusing on the bioMEMS and NEMS. Of course we also have other facilities: a professing facility for optoelectronic devices and we have a unique facility in fiber manufacturing, including a drawing tower inside the photonic center.

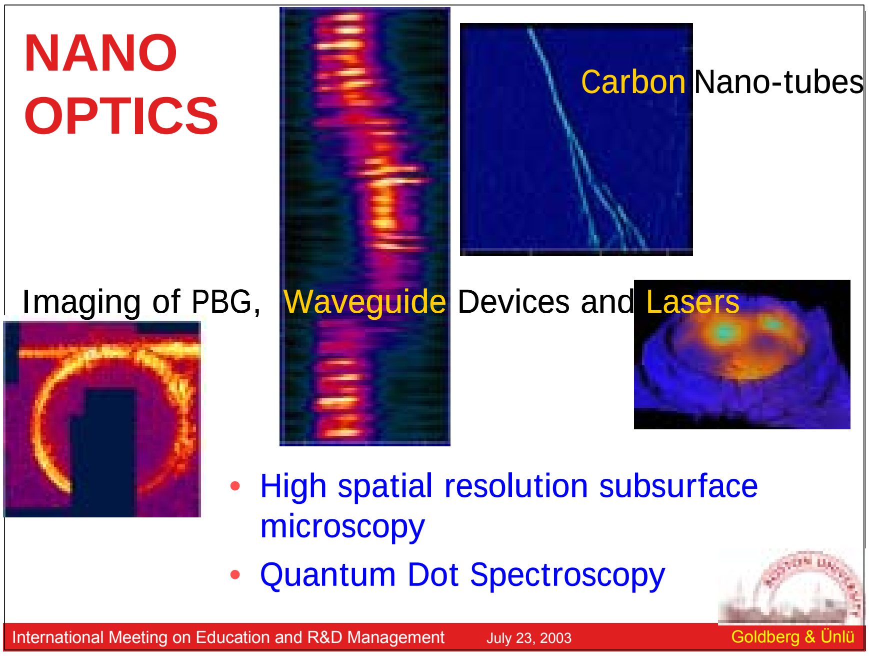


One example of the things we are starting to do is NEMS, and they can be used due to their properties at a very small scale. They can be used for single-molecule deduction. The basic idea here is that since these mechanical resonators are so small, their behavior is influenced by presence of very few molecules, even at the single-molecule level.



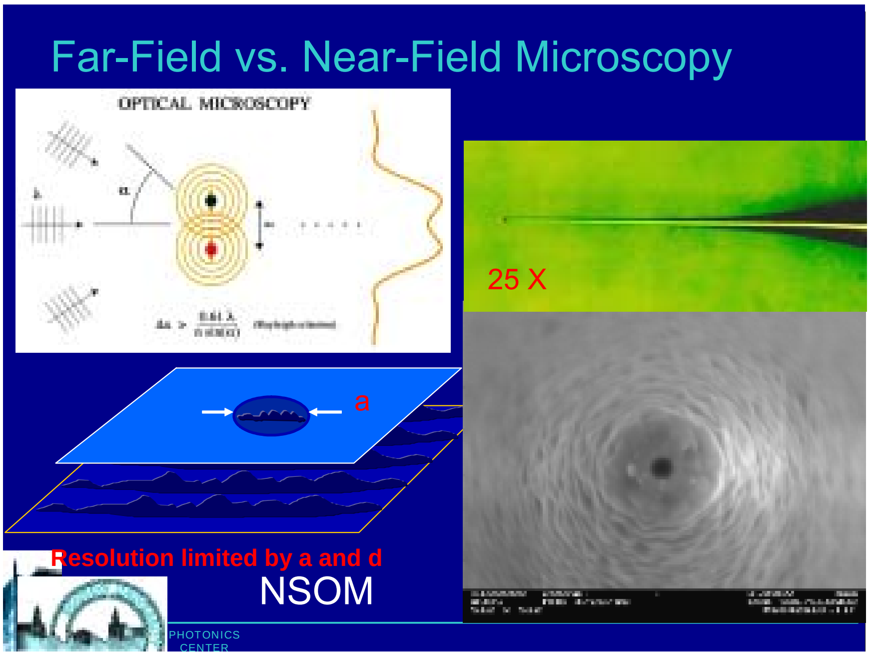
Now I am going to talk about the structure of our laboratory. Our focus is nano optics in our group. This is a fairly unusual setting for a US university, to have professors from different disciplines running the same laboratory together at a peer level as opposed to having a hierarchical level of the director and so on and so forth. I am in electrical engineering as a professor and I have a joint appointment in physics. Prof. Benett Goldberg has his primary appointment in physics and he is also joint in electrical engineering. So we run the laboratory completely together. We have many research funds that we obtained as co-principal investigators. We have students that we supervise together. We have also had a new member in our group the last three, four years, Prof. Ana Suan. She has physics training and she is now a research assistant professor in electrical engineering. So we do have a fairly interdisciplinary laboratory.

At any given time, we have about ten graduate students, they are mostly in the Ph.D. program, doctoral program, and they span different departments from electrical engineering, physics and biomedical engineering to biology. We have typically three or four undergraduate students working in our laboratory and we have high school student visitors which basically results in a completely vertically integrated system, from high school students all the way to the professor interacting on a daily basis. I show two of my students here because those are the examples I will use in terms of how we train the students and how they are involved in relationship with industry as well as technological commercialization. Bill Harizot graduated in 2000, and Steven Nepolito is expected to graduate within the next six months or so.

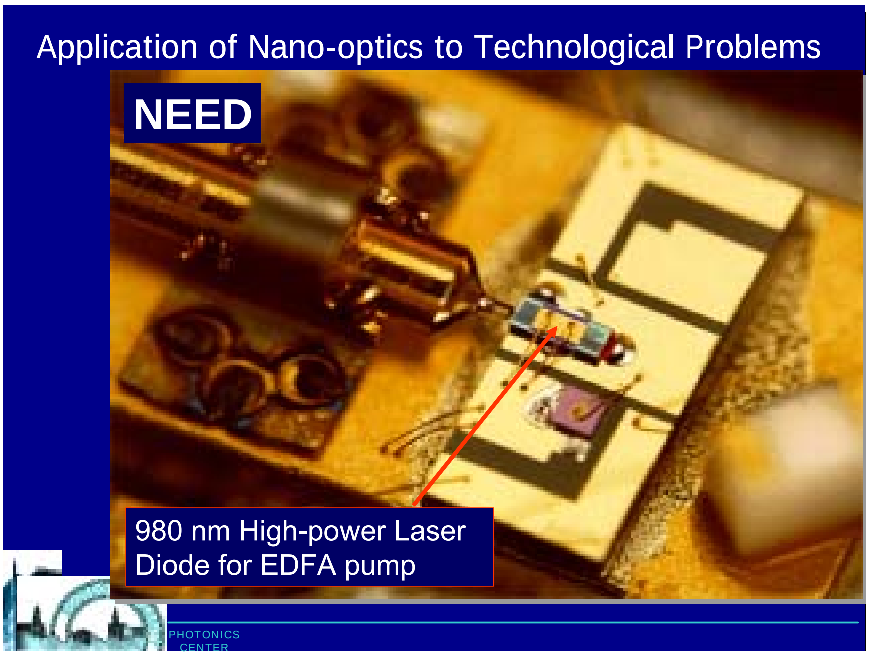


As I said, our group's focus is nano optics. We do quite a bit of very high resolution imaging, all the way from looking at carbon nano tubes to photonic band gap devices, resonators, wave guide devices and semiconductor lasers. We have other efforts in high spatial resolution subsurface microscopy and quantum dot spectroscopy. These are all areas related to being able to measure things at a much smaller scale than otherwise possible by conventional techniques.

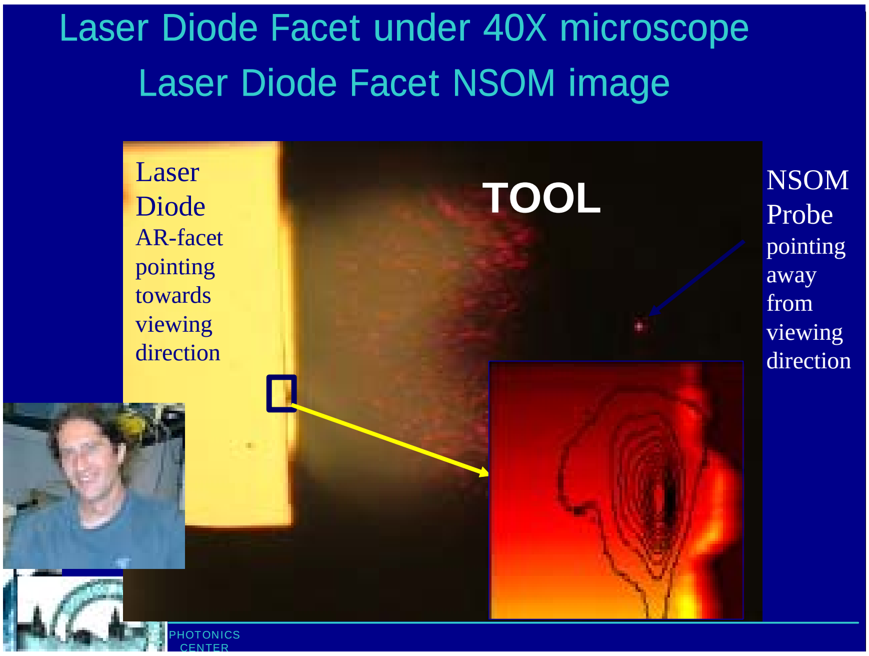
Now as a professor, I feel the urge to lecture and this is part of my technical presentation, some of it. One of the biggest challenges in nanotechnology is being able to measure things, observe things, at a very small scale. You have the limitations of light as an observing technique because using conventional optical microscopy, we cannot resolve objects which are separated less than, typically, a wavelength, or in the case of visible light in the order of a few hundred nanometers. Much of the phenomena happening in the nano scale is happening at smaller scales. Instead of using conventional microscopy, imagine you are looking at the sample through a very small hole kept very close to the sample. In that case, the resolution will be limited by the size of this hole. This idea is called near-field microscopy and this is a very strong research area also in Japan. Basically you form the aperture by using a tapered optical fiber, light is guided through and at the end, you have a small aperture to use as the observation point.



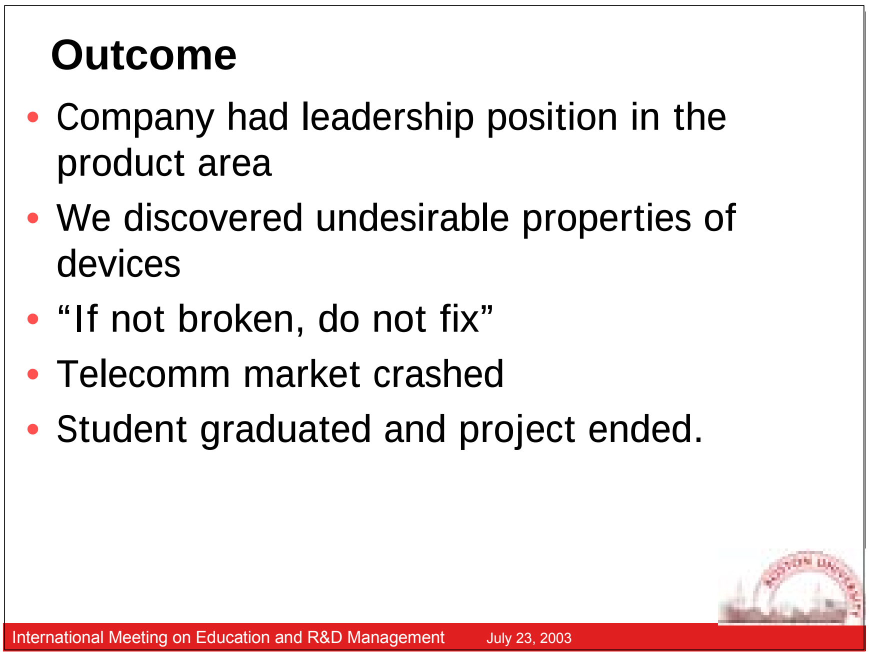
You can see, in a head-on picture of a fiber like this, the dark area in the middle is sub hundred nanometers and that is the aperture, and the outside is coated with metal, typically aluminum.



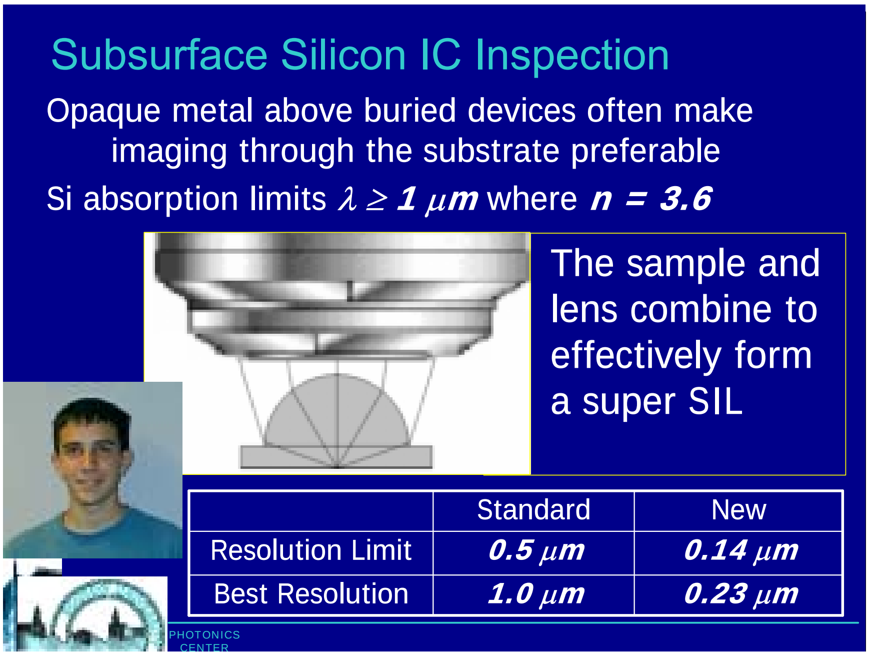
Now I just wanted to go through one application. We work with industry using near-field microscopy, which is a very academic tool, but we were able to use this in an area to benefit industry. The need was an understanding of mode behavior of semiconductor lasers. This is a very large industry, or at least it used to be a very large industry. These high-powered laser diodes are for erbium dope fiber amplifiers. These are for long-distance optical communications. You would like to generate as much light as possible in this laser diode and couple that into this optical fiber. Its modal behavior is very important. Since it is a single mode diode, basically the light emitted from this device is as small as you can see with conventional microscopy. To see the details of that light, you have to use a non-conventional method and there comes near-field microscopy.



Bill Harizot worked on this system in collaboration with a large optoelectronics manufacturer. You can see that when using a conventional microscope, the laser diode is emitting light from this one pixel on the screen. So you cannot see the details of that picture. By using near-field microscopy, you can get a detailed picture of how the light is emitted, what the modal properties are, and what are the physical principals behind it.

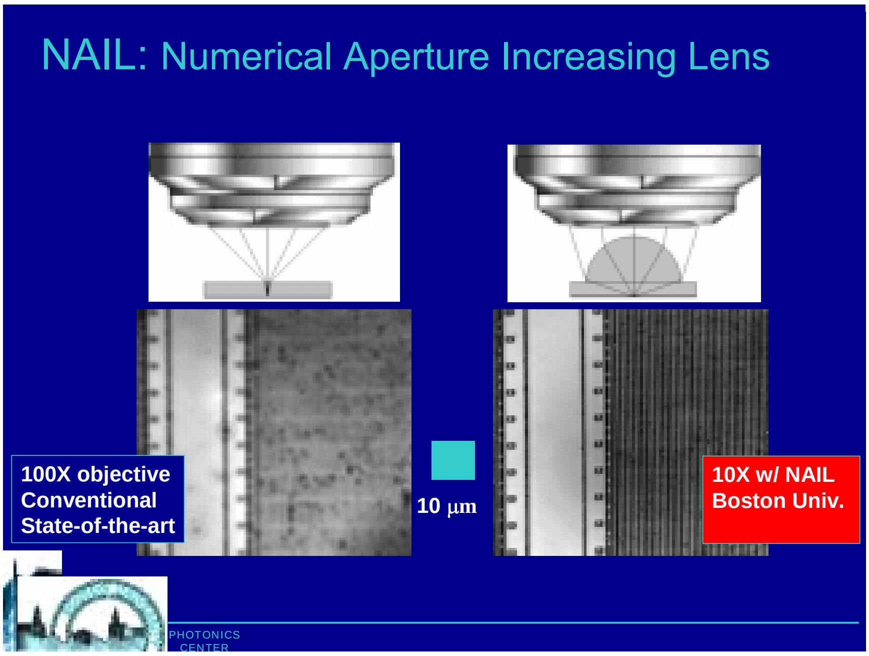


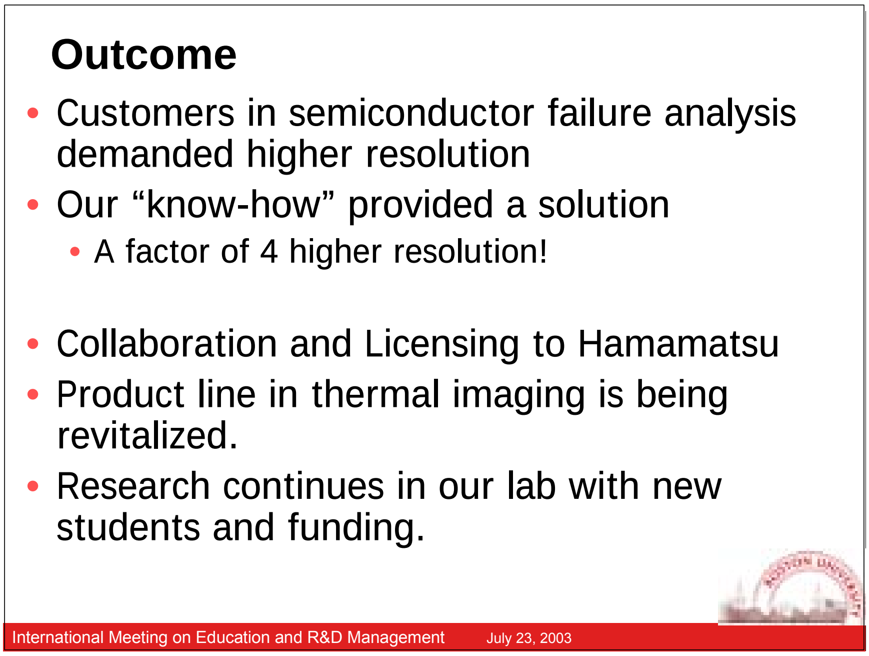
It was very successful. We were able to measure things which were previously not accessible. Here is the outcome. The company we worked with had a leadership position in the product area – this is not in your package, I prepared these things last night. We discovered some undesirable properties of these devises. Unforeseen, the properties we determined using our techniques were not desirable. The company had the policy of if not broken do not fix. They are not interested in finding out the weak sides of their devices. The telecom market crashed, the student graduated (he is now working at Lincoln Laboratories) and the project ended. We did not pursue this project further.



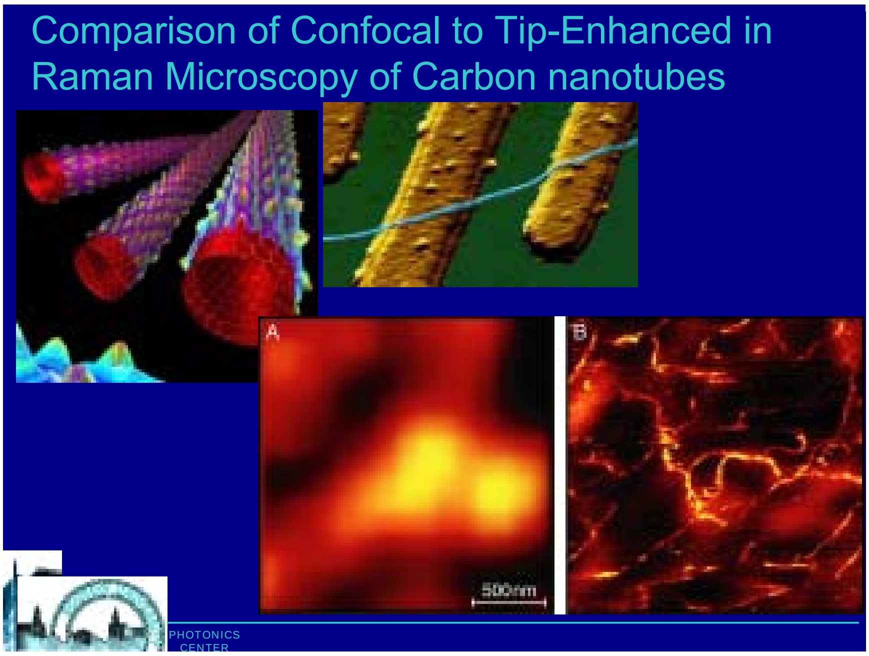
Now we have been working in a different project with a second student I mentioned earlier. This is on subsurface silicon integrated circuit inspection. Typically for silicon-integrated circuits, you write or print the circuit using the top surface where you can use a very short wavelength light and form feature sizes down to 100 nanometers and in fact the next scale is 90 nanometers, and so on and so forth. Since you are using very short wavelength light, it is possible using conventional techniques. However, once you build the variety of layers on top, you can no longer see through these layers and observe the phenomena of the device operation. So typically you look through the substrates. However, substrates are absorbing and you can only look at wavelengths longer than one micron, limiting the resolution to typically ten times the scale of the feature size. So there is not much information you can gain.

Steven Nepolito was the lead inventor on an effort using a solid emerging lens – I do not want to get into the details of this – to look through a silicon substrate and see things at a very small scale at the other end, through the substrate on the other surface, buried under many metal layers from the bottom surface here. In this case the substrate and the micro lens form a super-celled emersion lens and that takes the best resolution you can get in standard microscopy, from one micron, a factor of four, improvement of 200 nanometers. You can see images with state-of-the-art microscopy versus what we were able to achieve in collaboration with Hamamatsu, a Japanese company. In this process we started to work with Hamamatsu very early. Our student has visited the Hamamatsu facilities in Massachusetts and also in Japan. Now, as I speak here, two of my students are working with IBM, a customer of Hamamatsu, in Vermont.

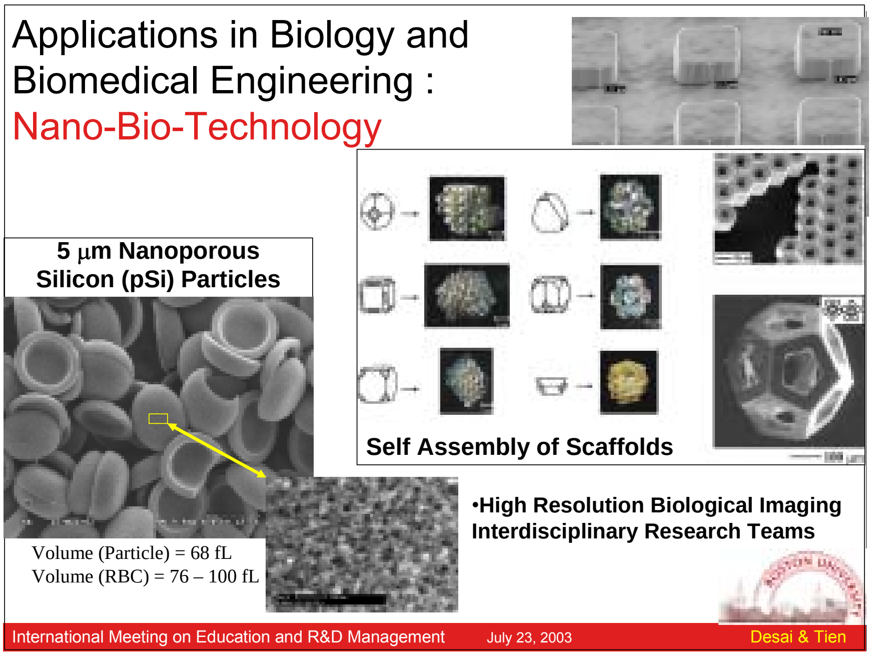




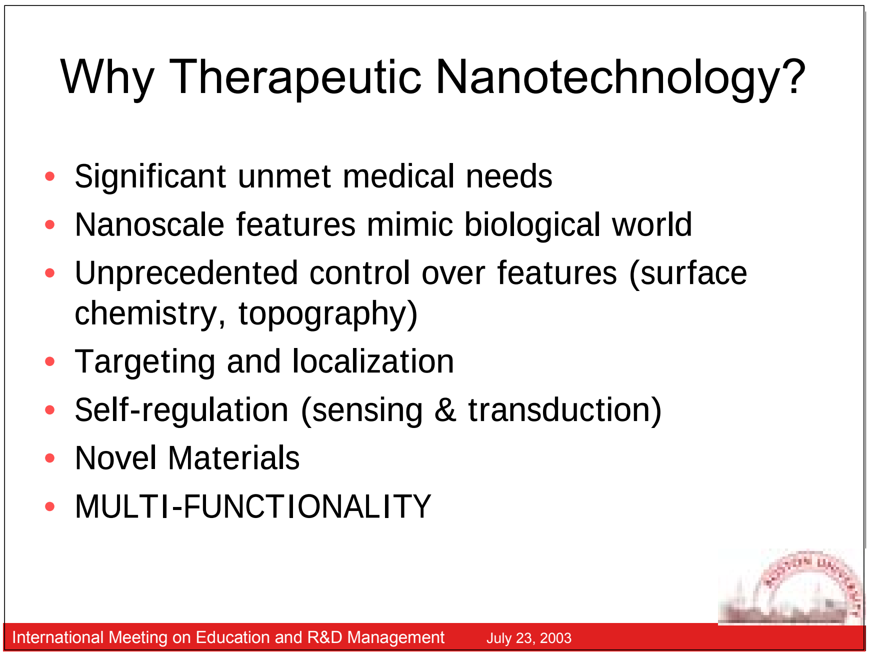
Now the outcome of this project is quite different than the previous project. The customers in semiconductor field analysis demanded higher resolution. Our know-how provided a solution for this, a factor of four better resolution. Then we had collaboration and licensing to Hamamatsu, and as a result, a previously downsized product line in thermal microscopy is being revitalized potentially – this is still in the future – because we were able to deliver a much needed improvement in resolution. Research in our laboratory continues. We have new students and funding. For example, now we are studying, using solid immersion lens microscopy, carbon nanotubes. This is with our collaborators at the University of Rochester.

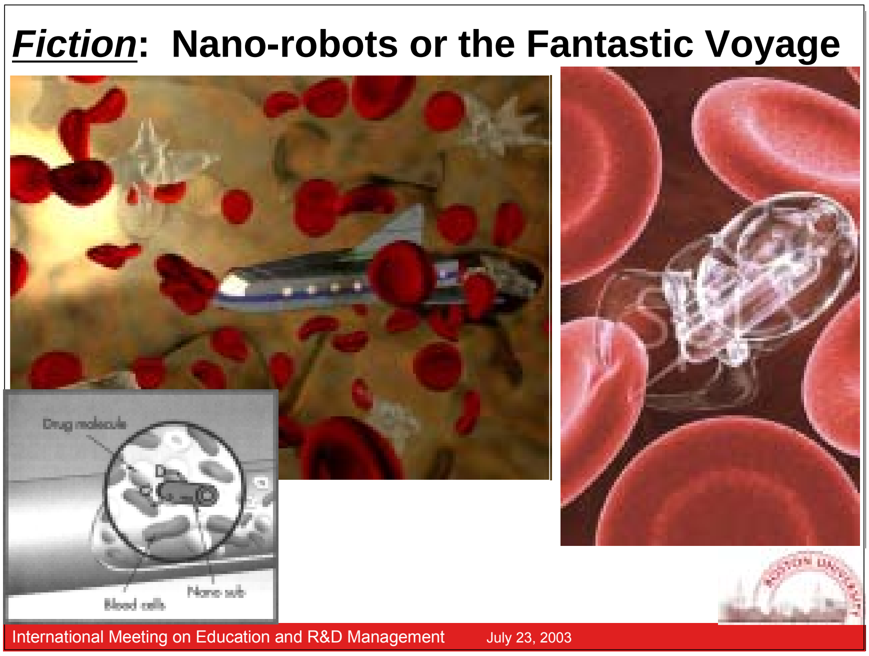


You can see Figure A is with conventional microscopy and Figure B is what we call tip-enhanced microscopy. I am not going to get into technical details but you can see the large contrast in terms of the quality of images one can obtain. If we wanted to work with nano scale, we would have to be able to observe things at the nano scale.

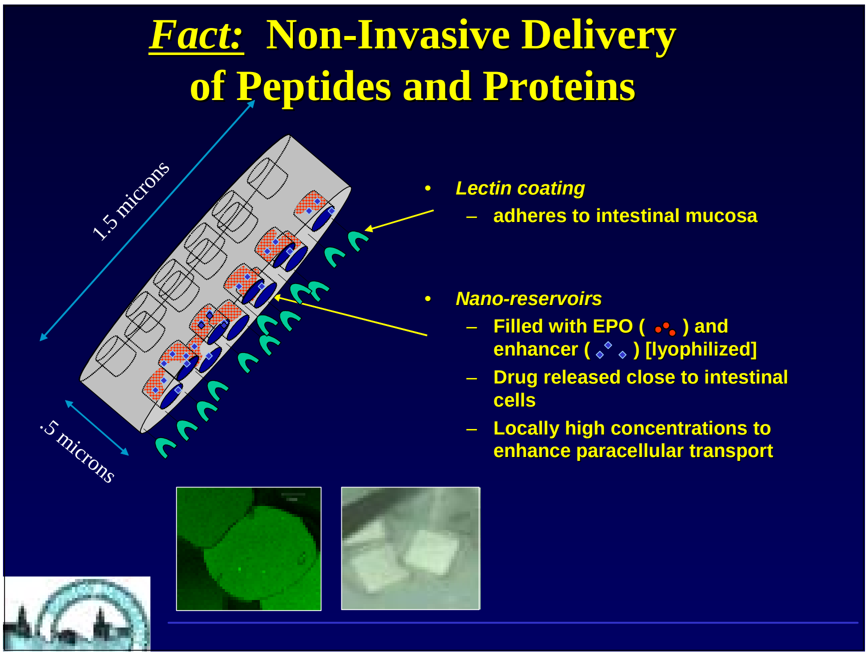


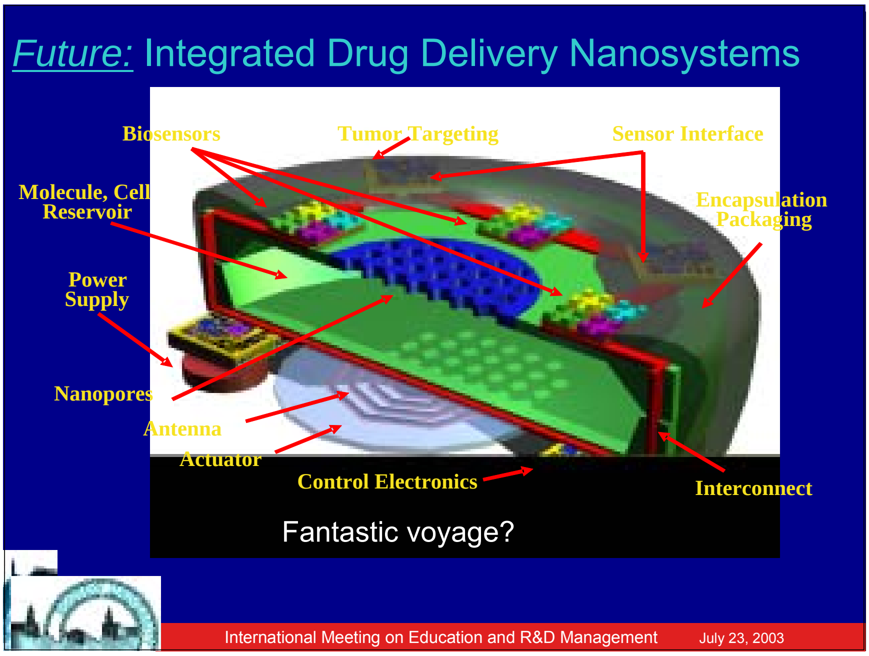
Another focus area, probably the most significant focus area, at Boston University will be in applications in biology and biomedical engineering. In this chart, I show you a couple of examples, one in drug delivery using silicon particles with nano pores on the surface, and the other one is – this is obviously built by top-down technology by taking topography tools and etching tools to generate these structures. This is self assembly to form scaffolds for cellular applications.





Well, first of all, why do we care about therapeutic technology? There are significant unmet medical needs and nano scale features in fact mimic the biological world. You can have a very high level of control, you can target and localize, you can self regulate and have multiple functionality. Here is the glimpse of the future. You have seen the potential in this movie called “The Fantastic Voyage” where you can basically shrink a submarine to a very small scale and go in and fight the bacteria or viruses inside the human bloodstream. This is a picture from Battelle’s annual report showing a very similar thing in a more believable shape. Instead of having humans inside, now you have a nano or micro structure or nano robot doing the direct delivery to an individual cell. The fact is this is not too far away, not necessarily as described in “The Fantastic Voyage,” but in different forms.





There are nanostructures that are used in delivery of peptize and proteins directed to the intestinal mucosa. Basically it is a targeted direct delivery vehicle. In the future, we will probably have self-contained drug delivery options, where you will have power supplies, a reservoir for the drug, you will have control electronics and sensors to determine where the thing is and you will be able to target these individual drug delivery vehicles to the specific points. Well, is it "The Fantastic Voyage?" Probably not yet, but this is an area nanotechnology will have a very strong impact in.

Potential Target Diseases/Therapies

Disease	Drugs	Sales
Chronic hepatitis C	Alpha interferon	$1.5 billion
Anemia	EPO	$4.7 billion
MS	Beta Interferon	$1.6 billion
Neutropenia	G-CSF	$1.9 billion
Psychosis	Anti-psychotics	$4.0 billion
Diabetes	insulin	$4.0 billion
Cancer	chemotherapy	$20 billion

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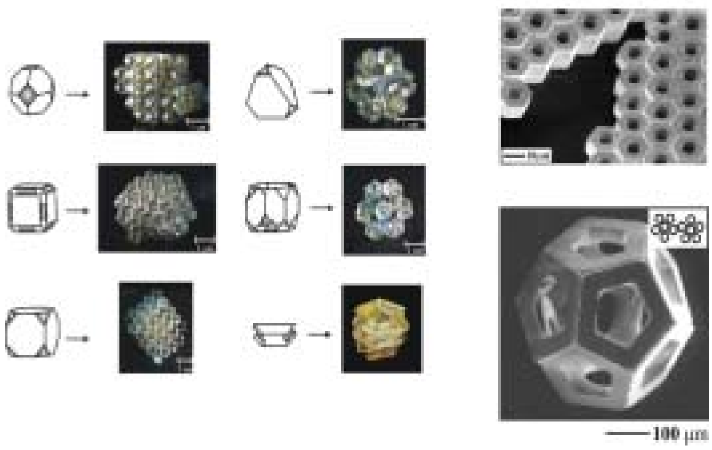
You can see, in terms of numbers, just looking at the two bottom applications in drug delivery: diabetes – delivering insulin. Sufferers of diabetes typically have many puncture wounds because of drug delivery using very archaic technology. And cancer – chemotherapy is US$20 billion a year. So these are areas that can be strongly impacted by the use of nanotechnology in drug delivery.

Self Assembly of Scaffolds



Self-assembled, 3D scaffolds for tissue engineering and for advanced biomaterials, sensors, reactors, and composites

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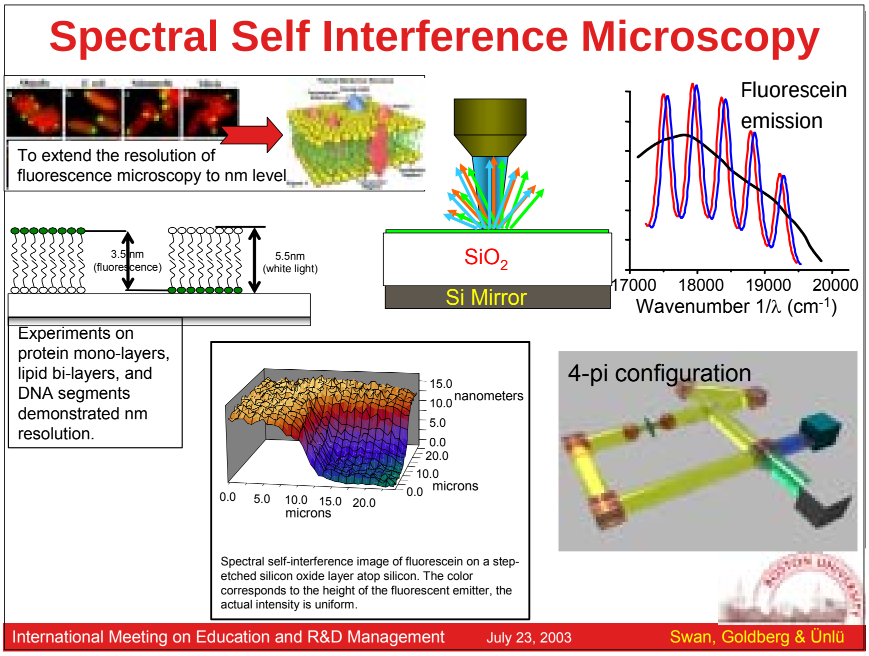
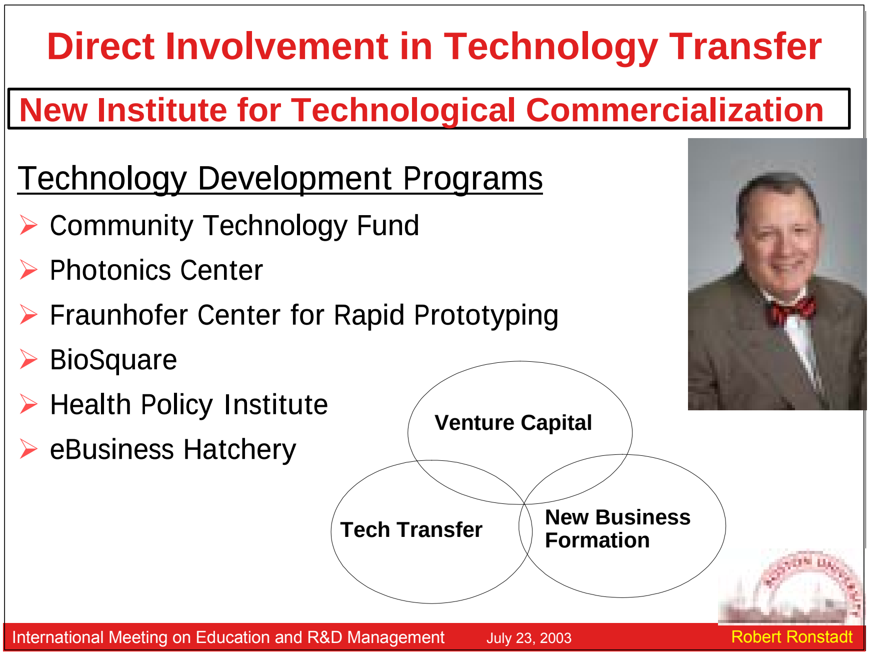
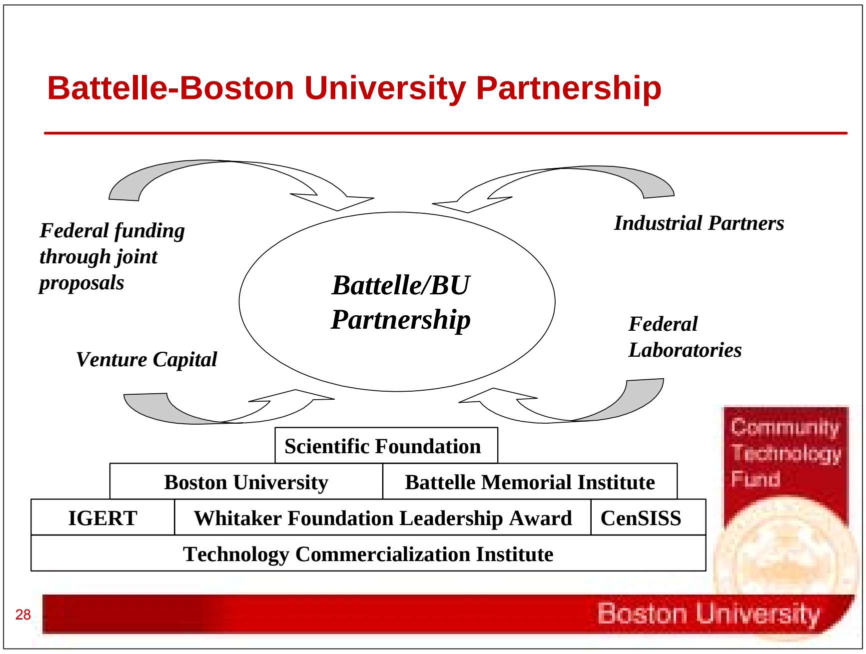
Another area is obviously in self-assembly. You can build structures mimicking the biological systems that will allow you to have a scaffold similar to cellular scaffolding to enhance tissue growth.



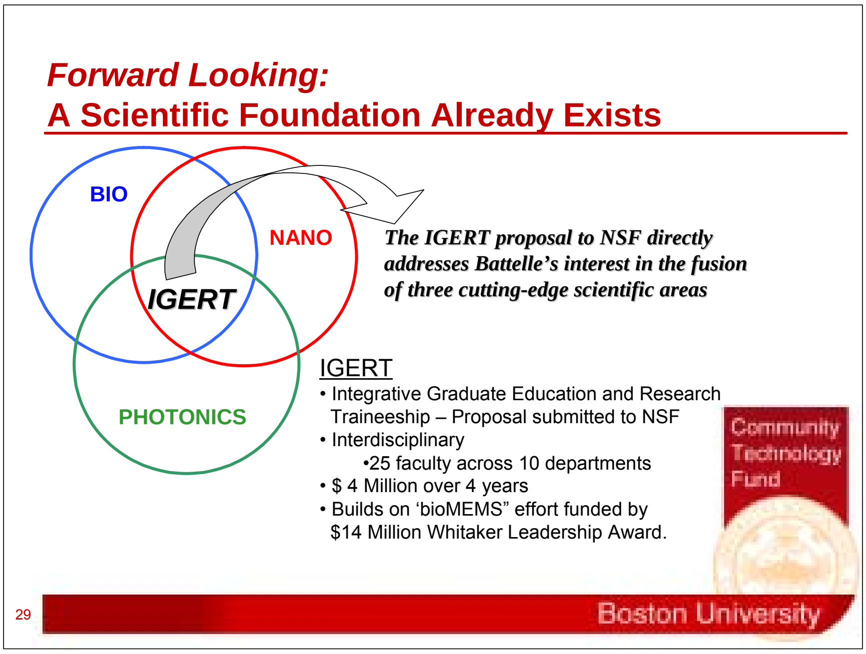
We are also working in microscopy of biological systems. Typical florescence microscopy can only tell you very rough information about sub-cellular processes. The idea is to take this resolution capability from about half a micron down to the cellular level. This is a cell wall, a bi-layer lipid structure, which has about a five-nanometer thickness. What we have used is our know-how in semiconductor devices and spectroscopy, and built systems – what we call spectral self-interference microscopy, which can determine the position of fluorophores with nanometer precision. We are building a new microscope systems founded by NIH.



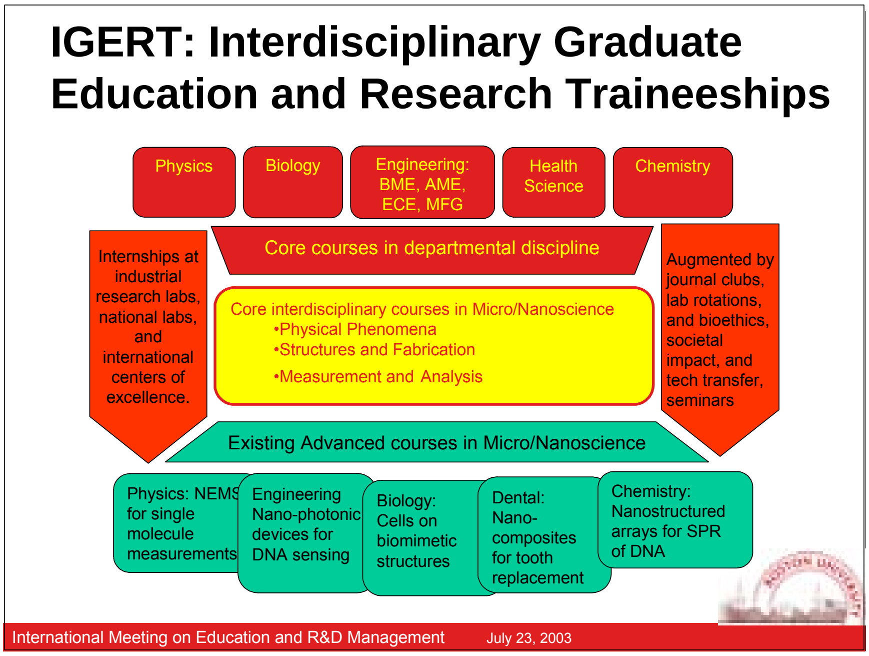
Prof. Ronstadt mentioned efforts in technology commercialization and this is a very important thing for Boston University to combine some of our efforts towards a common goal.



I wanted to say a few things about a recent industry relationship we have that is with Battelle, which has 16,000 researchers and about US$2-3 billion in revenue per year. It is a non-profit organization. Basically, we wanted to build on the scientific foundation from Boston University and Battelle and form this partnership where we can do joint R&D and commercialization. We wanted to start slowly and continue on at a phased structure.



One of the interesting things that came out of meetings with Battelle is that they wanted to cover several key research areas, and they were biology, nanostructures and photonics. Basically, it was a coincidence that we had already been considering these areas as an important target area and a combination of these as the important growth area for our university's education and research, and we have already applied to the NSF for an integrative graduate education and research traineeships program. It is a US$4-million program for four years to support about a dozen students.



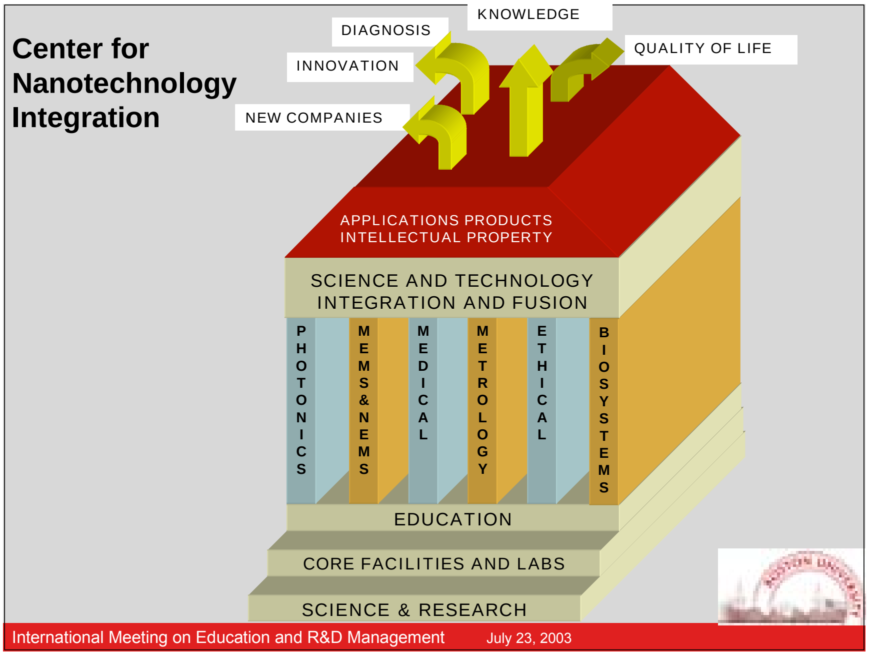
The structure will be as follows: we do already have many courses from different disciplines which are related to micro and nano science. We want to complement these with new courses or core courses from different disciplines – physics, biology, engineering, health science and chemistry – but also create new courses in the core interdisciplinary micro and nano science. Other key points of a program like this will be augmenting the formal education within the university with discussion groups, lab rotations, and more importantly things related to the society – the ethics, the societal impact, technical transfer.

And we do benefit from the fact that Boston University is in Boston and we can have many industrial collaborations, where we send our students to research laboratories and industrial collaborators.

Just to give you a couple of examples, there is a new Massachusetts Nanotechnology Initiative, and since we are in Boston, we belong to this Initiative, and Prof. Goldberg is on the steering committee. The fields which are related to medicine are also shifting towards nanotechnology.

For example, there is a Center for Integration of Medicine & Innovative Technology (CIMIT). They organize forums to discuss important research topics, and for this year they have selected nanotechnology and medicine as the core topic to be discussed. We do participate in these. One of our professors in biomedical engineering is giving one of the presentations, and this is sponsored by the Harvard Medical School and other institutions in the Boston area.

Now in terms of conclusions and the future, and I believe I am almost on time, Boston University has developed a significant expertise and infrastructure in nanotechnology and we are continuing to invest in this area. We are now building an interdisciplinary curriculum and a graduate student training program. Now, in US institutions, the graduate students are almost always supported under fellowships, either research fellowships, assistantships, teaching assistantships or government fellowships. A program like this will be putting in more students in our program, about a dozen students supported by a national fellowship program, and that will certainly increase our visibility and our capability to perform research at a higher level and training at a higher level. We are now contemplating starting a new nanotechnology center to include research, education and, probably as important, technology commercialization.



As our last view graph, I would like to put this up so we can open for questions. We do have science and research, facilities and education programs. We want to build in areas of our strength: photonics, MEMS and things related to society in general. Then, put on top of this the science and technology integration and fusion with help from offices such as Dr. Ronstadt's office. The goal is to have applications, product and intellectual property. Our students are involved at a very early level in intellectual property creation. They do get royalties from patents that are licensed. Universities create knowledge, but we want to go beyond this and have innovation out of this, new companies with the ultimate goal of improving the quality of life. Thank you for your attention.

Dr. Yaniv: Some questions, please. We have time, like three minutes, for questions. Please.

Mr. Konagai: I am very interested in this slide. Yes, when we carry out education for interdisciplinary areas, we were discussing whether we should divide the organization for education and also for research.

But according to this slide, it seems that education as well as research is carried out in the same organization. Is that correct?

Prof. Ünlü: Education and research is within the academic departments of our university. For our doctoral students that are working on research programs, then that is part of their education.

Mr. Konagai: For example, when it comes to students studying electrical engineering, when they study nanotechnology, my image is that they would go to the Center to study that, so that is why we say that research and education should be divided. But according to this example, it seems that the students will study all of these disciplines, right? So it is not that the electrical engineering students study nano, but actually the nano students study nano in a wider definition, correct?

Prof. Ünlü: Now I understand your question. Basically, it is very difficult at a university such as Boston University to create a new degree program, and that will take years. So if we eventually have a degree program in nanotechnology, it will have to be a separate entity. But as an initial starting point, we can only have a certificate program in which students come from a variety of different disciplines. A student can be an electrical engineering student, and they are required to take certain core courses. In addition to these core courses, they will be required to take additional courses in nanotechnology. Electrical engineering students will be asked to take courses in biology if they are in this program. Biology students will be asked to take courses in semiconductor processing, so we will not create a new interdisciplinary program immediately. But what we will do is take individual students from individual departments where they are governed by the requirements of the department, but put on them more load in terms of learning. But we are also working with departments to reduce the existing core requirements, so that students will have the time and the energy to take these courses in nanotechnology.