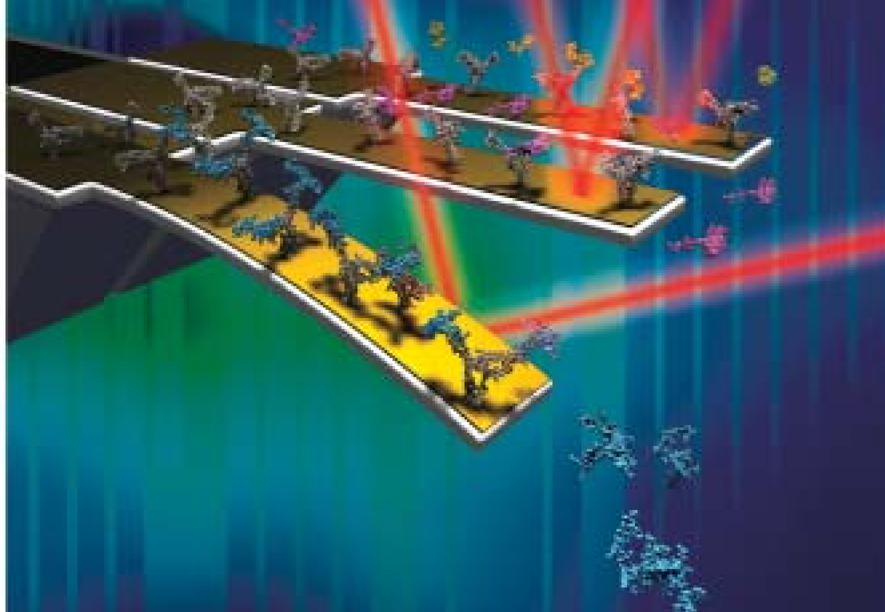
MISSION POSSIBLE

DOE Advanced BIOMEDICAL TECHNOLOGY Research



Office of Science
U.S. DEPARTMENT OF ENERGY
Biological and Environmental Research—BER
December 2002

SHARING THE
POWER OF DOE SCIENCE

"For over 50 years the DOE Office of Science's Biological and Environmental Research Program (BER)* Medical Sciences Division has applied the discoveries of energy-related basic science to advancement in biomedical research. Today, our research projects in advanced biomedical technology truly integrate the amazing progress of DOE physics, chemistry, engineering, mathematics, and genome science. At the core of this progress stands the DOE national laboratory system, well established as an American treasure of unique scientific facilities and expertise. For decades, DOE national laboratories have skillfully balanced the freedom to explore science with disciplined project management. The projects we describe here show the great potential of energy-related research to make life better for all Americans. Ideas that seemed impossible yesterday now emerge as realistic missions—entirely possible in the near future.

Sharing the power of DOE science. Converting energy to biomedical progress. We meet those objectives in the DOE Office of Science, BER Medical Sciences Division."

Michael V. Viola, MD
Director
Medical Sciences
Division, BER

*Before the U.S. Department of Energy was created in 1977, BER existed under different names within other federal agencies.

MISSION POSSIBLE

DOE Advanced BIOMEDICAL TECHNOLOGY Research

December 2002

U.S. Department of Energy—DOE
OFFICE OF SCIENCE

Biological and **E**nvironmental
Research—**BER**

Mission Possible

Artificial Retina

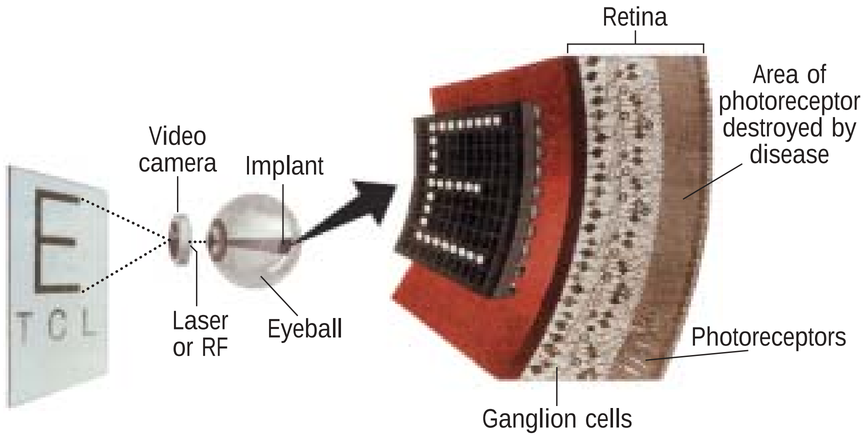
To give doctors a device that restores sight in blind patients with macular degeneration, retinitis pigmentosa, and other eye diseases.

DOE Project Management
Oak Ridge National Laboratory

Other DOE Collaborators
Sandia National Laboratory
Lawrence Livermore National Laboratory
Los Alamos National Laboratory
Argonne National Laboratory

Other Research Collaborators
University of Southern California Doheny Eye Institute
Johns Hopkins University School of Medicine
North Carolina State University
Second Sight, LLC

As a degenerative disease of the retina progresses, the eye loses more photoreceptors, the cells that carry visual signals from the eye to the brain. DOE-funded scientists aim to develop an electronic device, implanted in the eye, that will capture light signals and visual information, bypass damaged photoreceptors, and electrically stimulate viable layers of the retina.

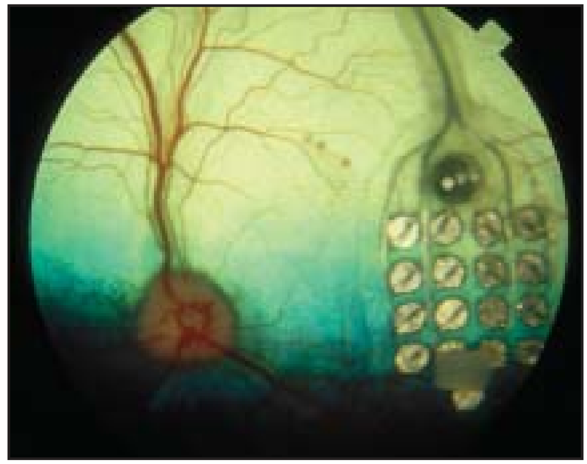


DOE National Laboratories: Forefront of Technologies Converging in Development of Artificial Retina

- Micromachine technology design
- Mathematical modeling of retinal information processing
- Microelectrode arrays designed for retinal tissue stimulation
- Telemetric communications

Wireless Link Between Video Camera Outside the Eye and Electrode Array Inside the Eye

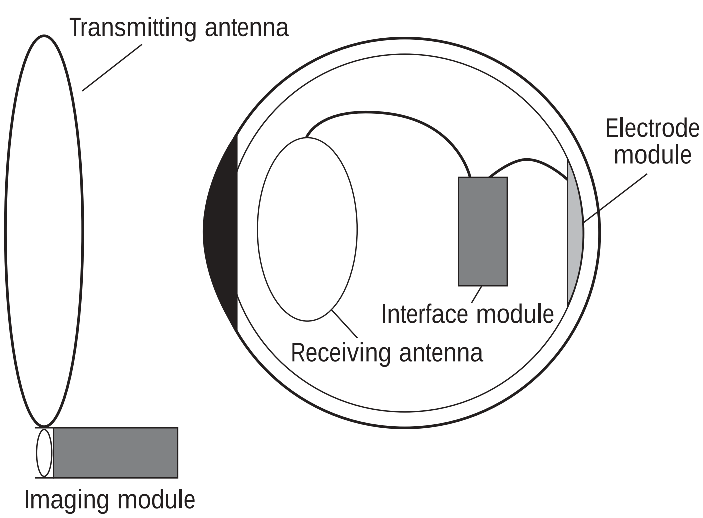
- Transmitting antenna—in a video camera outside the eye, possibly within an eyeglass frame or on a belt pack—to send signals to receiving antenna inside the eye
- Implantable retinal chips—translate signals to viable retinal neurons for simulated sight
- A sensor will provide feedback about the physiology and mechanics of retinal tissue around the implant.
- Stimulation parameters can be adjusted to protect the viable retinal neurons.

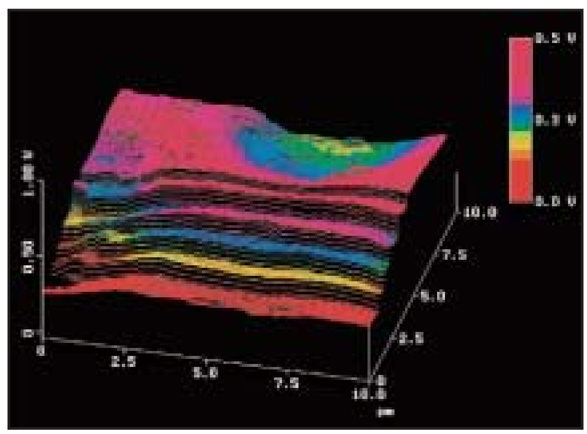


Second Sight implant developed under a bioengineering research partnership (BRP) supported by the National Institutes of Health (NIH) National Eye Institute (NEI)

DOE's Artificial Retina: High-Contrast, High-Resolution Sensors, Enabling the Blind to Read

- DOE goal: To develop a device that mimics (as closely as possible) natural, normal eyesight
- DOE national laboratories contribute unique technology resources and expertise to the development of this advanced device.





Electrostatic potential map of nickel electrodes embedded in glass

Converting ENERGY to Biomedical Progress
BER

Mission Possible

Adaptive Optics

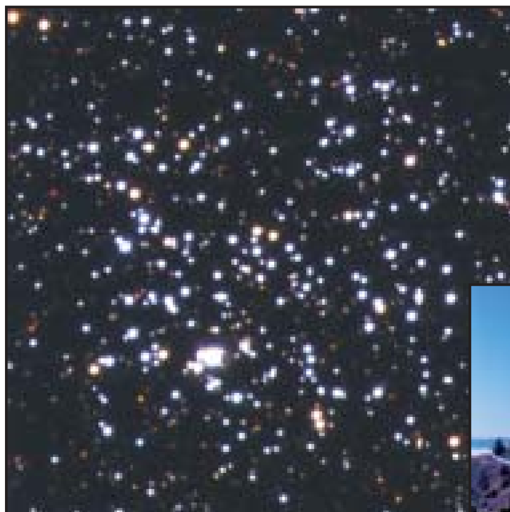
To give doctors space-age "telescopes" for eye exams.
To restore sight, improve vision.
To learn more about early stages of eye diseases and blindness.

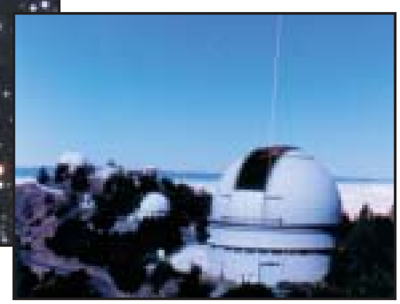
DOE Project Management
Lawrence Livermore National Laboratory

Other DOE Collaborators
Sandia National Laboratory

Other Research Collaborators
University of Rochester
University of Southern California Doheny Eye Institute
U.S. Army Aeromedical Research Laboratory
Bausch & Lomb
University of California, Berkeley

Astronomers use "adaptive optics" to straighten out starlight that bends and distorts as it travels through the atmosphere. This effect of air turbulence on light makes us see the twinkling in stars. In the human eye, disease and vision problems also cause light rays to distort, resulting in blurred vision. DOE-funded scientists are developing miniature versions of adaptive optics systems used in observatories so eye doctors can use this technology to improve patient care.

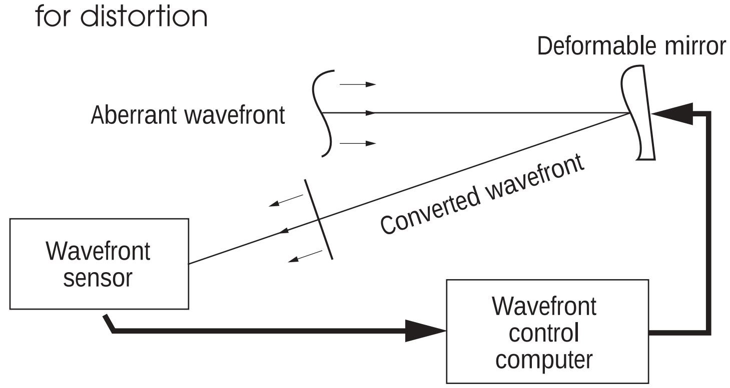




University of California's Lick Observatory

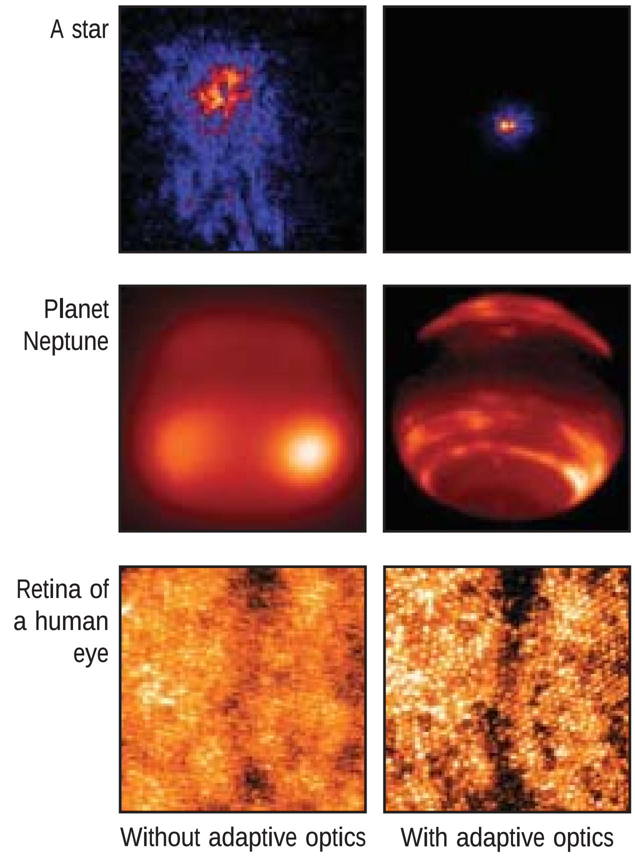
Adaptive Optics in Astronomy

- Wavefront sensor—analyzes how light from stars has been distorted by atmospheric turbulence
- Deformable mirror—flexible (like a fun-house mirror) to reflect light rays at angles that correct for distortion



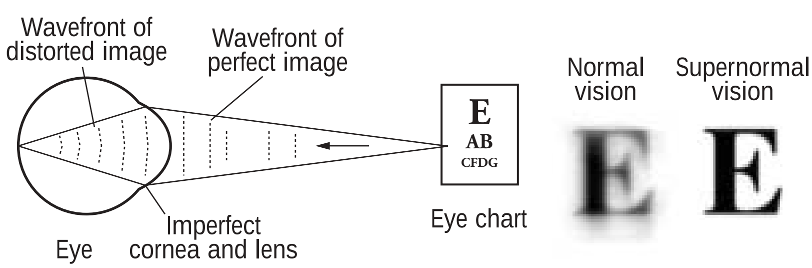
Future of Adaptive Optics: Advancing Ophthalmology

- Wavefront control system using micro-electro-mechanical system (MEMS) deformable mirrors
- Enhanced functional capabilities of instruments now used by ophthalmologists (e.g., fundus cameras, surgical microscopes, phoroptors)
- Better vision correction from eyeglasses, contact lenses, and laser surgery. Vision could improve from normal 20/20 to "supernormal" 20/8.
- Improved techniques for diagnosing and possibly treating macular degeneration, glaucoma, diabetic retinopathy, retinitis pigmentosa, and eye cancer



DOE Scientists Collaborate with NSF Center for Adaptive Optics: Leading the Revolution

- This DOE research grew out of collaborations started at the National Science Foundation's Center for Adaptive Optics, founded in 1999.
- The Center's goal: "To lead the revolution in adaptive optics..., catalyzing advances nationwide."



Mission Possible

Faster Test for TB

To give doctors a more rapid, sensitive, and specific tool for detecting tuberculosis. To reduce the spread of TB and fight the global TB epidemic.

DOE Project Management

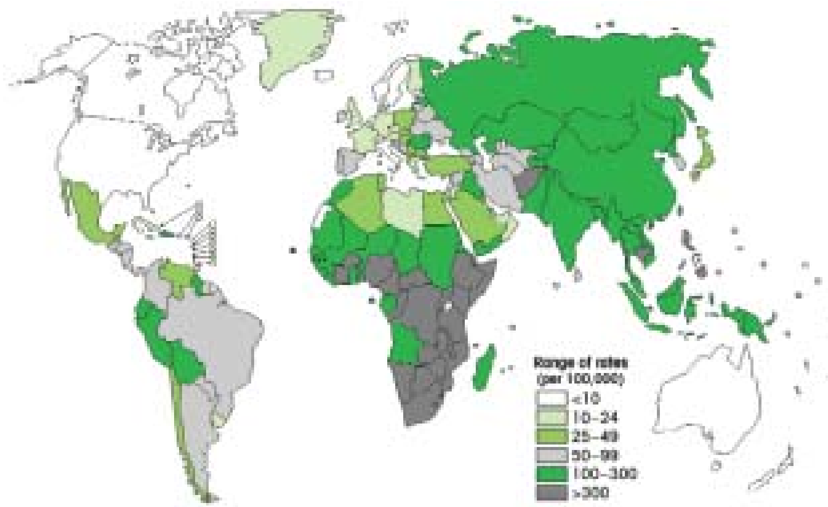
Los Alamos National Laboratory

Other Research Collaborators

Johns Hopkins University
Center for Tuberculosis Research

National Institute of Allergy and Infectious Diseases

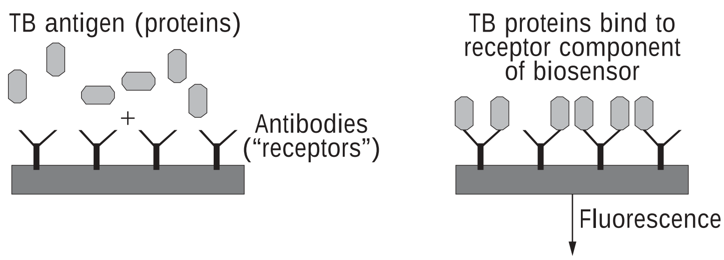
The World Health Organization has declared tuberculosis (TB) a global emergency. TB kills 2 million people a year. Over the next 20 years, TB could infect 1 billion people and kill 35 million. TB infection also hastens the progression of HIV/AIDS. DOE-funded scientists are developing an “optical biosensor” for early and rapid TB detection, particularly needed in developing countries.



World Health Organization. Global Tuberculosis Control. WHO Report 2001. Geneva, Switzerland, WHO/CDS/TB/2001.287

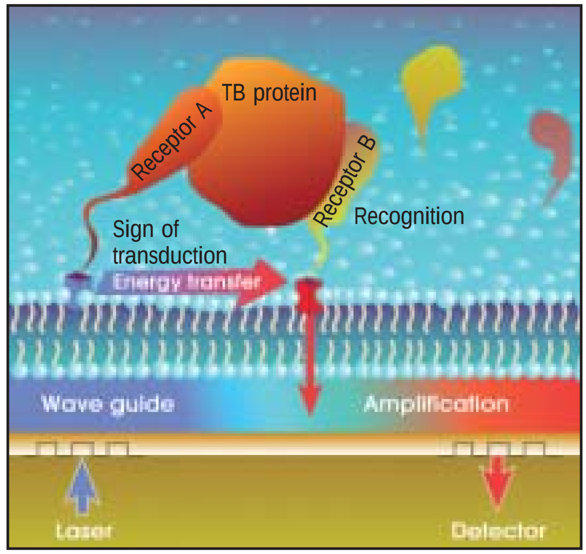
Optical Biosensor

- Optical biosensor—man-made hybrid of a
  - biological component (e.g., an antibody or receptor) that recognizes a specific protein
  - physics component (transducer) that sends a light signal when targeted protein binds to biosensor
- Los Alamos TB optical biosensor—embedded in a disposable strip, will detect TB infection in sputum or blood serum samples



DOE National Labs: Leaders at Frontier of Advanced Biosensor Technology for Medical Applications

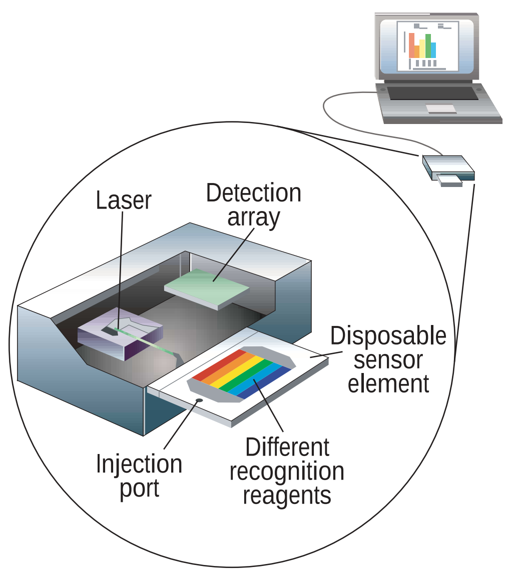
- DOE research provides the scientific world with a vast body of knowledge on biosensors.
- Biosensors are like "bionic" cell fragments rigged with burglar alarms.
- A targeted toxin or protein binds to the sensor, designed to mimic a biochemical event in the human body, and triggers a signal.
- In addition to diagnostic tests (e.g., blood glucose home monitors), biosensors can also monitor environmental pollution, food quality, and exposure to biological or chemical agents.



Receptor-protein recognition triggers proximity-based fluorescence change

Los Alamos Optical Biosensor for TB Detection: Faster and Simpler than Getting a Culture

- Today, it takes about 4 weeks to get results from a bacterial culture to diagnose TB, delaying treatment as the patient exposes others to this contagious disease.
- Most developing countries lack sufficient lab facilities and technical skills needed for wide use of cultures to diagnose infectious diseases.
- The Los Alamos team aims to develop a TB optical biosensor system that provides accurate and rapid results—in just minutes or hours, while the patient waits in the clinic.
- The biosensor system should be portable, inexpensive, and simple to use by healthcare workers with minimal technical expertise.



Schematic of portable TB sensor system for use in the field

Converting ENERGY to Biomedical Progress
BER

Mission Possible

Micro Blood Flow Monitor

To give doctors realtime, “wireless” blood flow and oxygen measurements around microscopic blood vessels. To improve wound healing after surgery. To better monitor patients in emergency rooms and intensive care units. To help prevent organ failure and death in hospital patients.

DOE Project Management
Oak Ridge National Laboratory

Other Research Collaborators
Texas A&M University
University of Pittsburgh

Lack of sufficient blood flow causes many diseases and health problems. Medical technology today does a decent job evaluating the clogged and constricted arteries that lead to heart attack and stroke. But zoom in for a closer look at the microcirculatory system, the networks of capillaries that feed small millimeter-sized regions of organs and muscle. Here, it’s very difficult to know if regional blood flow is normal, or if blood is delivering enough oxygen to surrounding tissues. DOE-funded scientists are developing a miniature, wireless implant that would send early warning signals of potential tissue damage, wound-healing problems, and organ failure.

Micro network of blood vessels, courtesy of Frederick Miller, PhD, Department of Physiology and Biophysics, University of Louisville

Biocompatible Implant: Optical Biosensor, Specialized Integrated Circuit Chips, Radiofrequency Telemetry

- Micro blood flow monitor—designed as a long-term biocompatible implant with highly specialized sensor and microelectronics
- Optical biosensor—detects changes in blood flow and tissue oxygen levels
- Miniaturized integrated circuits—control sensor data digitization, digital signal processing, and radio transmission of signals to a remote receiver

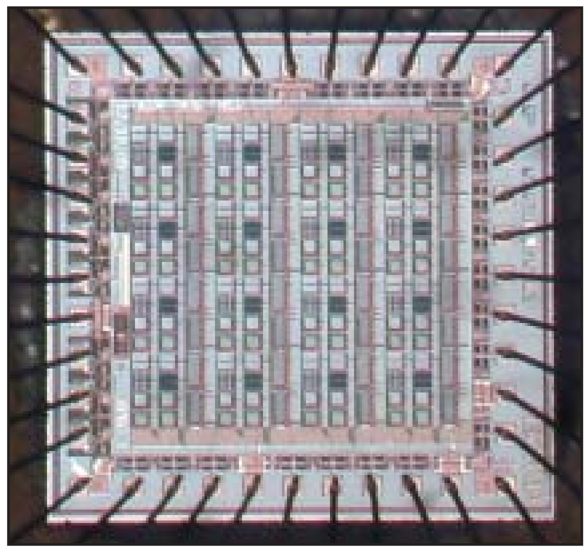
Oak Ridge National Lab: Experts in Designing Micro Integrated Circuits and Sensors for Potential Use in Advanced Medical Technology

- Scientists and engineers who research sensors, software, optics, semiconductors, chips, microelectronics, and systems for measuring various phenomena in physics
- Equipped to create and analyze microscopic structures potentially useful in healthcare

Microcirculation with capillary bed, courtesy of Frederick Miller, PhD, Department of Physiology and Biophysics, University of Louisville

DOE Micro Blood Flow Monitor Could Solve Unmet Needs for Hospital Patients and Surgeons

- Today, hospitals have no reliable methods for routinely monitoring organ-specific or local regional blood flow.
- Impaired tissue blood flow can lead to organ failure, the most common cause of death in critically ill hospital patients.
- The implanted DOE micro blood flow monitor would act as a "sentry" at the site of potential tissue damage, and "radio for help" when it detects a reduction in blood or oxygen levels.
- This device could
  - alert surgeons to blood flow problems that might affect wound healing, tissue grafts, and organ transplants.
  - help ER doctors evaluate traumatic injuries.
  - monitor ICU patients at risk for kidney failure, multiple organ failure, and death.



Integrated circuit with photodetector array, built at Oak Ridge National Laboratory

Mission Achieved

Better Cancer Care

Two research projects started in the mid-1990s have met their research goals. These advanced biomedical technologies are now moving out of DOE and into the private sector.

Both of these success stories show the real-world results that DOE science can achieve with disciplined project management. They demonstrate how sharing the power of DOE science can benefit millions of Americans.

Peregrine™ System Helps Oncologists Target Tumors More Precisely with Radiation Therapy

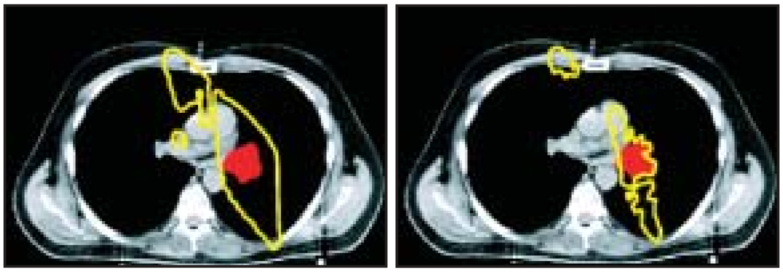
- 1 in 5 Americans receive radiation therapy in lifetime.
- Radiation therapy fails to eradicate 1 in 3 primary tumors.
- Peregrine: Highly sophisticated dose calculation system; accurately models radiation beam delivery
  - Applies mathematical technique—3-dimensional Monte Carlo transport—to simulate the trillions of radiation particles that enter the body during a treatment procedure
  - Makes use of extensive databases on nuclear and atomic interactions, compiled at Lawrence Livermore National Laboratory
  - Calculates dose by modeling how the radiation interacts with muscle, bone, organs, and other tissues in its path toward the tumor
  - Received FDA clearance in October 2000; produced and marketed by NOMOS Corp., of Sewickly, Pennsylvania

DOE Project Management

Lawrence Livermore National Laboratory

Other Research Collaborators

University of California, San Francisco



Planned radiation treatment (left). Peregrine calculation (right) indicates that radiation (within yellow boundaries) will actually hit a smaller area around the lung tumor (red) than the planned prescribed dose.

PSA Microcantilever "Diving Board" Optical Biosensor Provides More Sensitive Test for Prostate Cancer Marker

- Prostate cancer—most prevalent cancer in men, 2nd-leading cause of cancer death in men
- Prostate-specific antigen (PSA)—blood-serum marker for detecting prostate cancer and monitoring therapy
- Standard PSA test—ELISA assay
- PSA microcantilever—20 times more sensitive than conventional ELISA assay for PSA
  - Silicon chip "diving board" the size of a hair, coated with prostate-specific antibodies
  - Microcantilever biosensors—capable of detecting protein markers for many other diseases, from breast cancer to AIDS

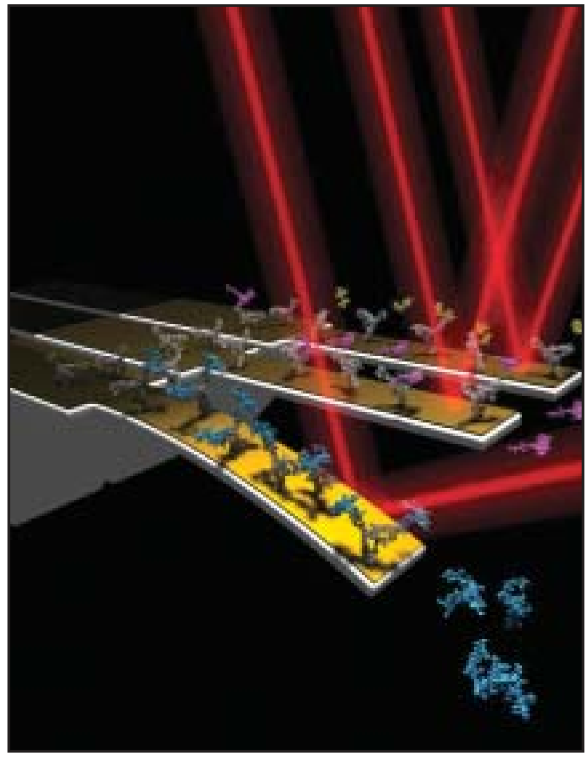
DOE Project Management

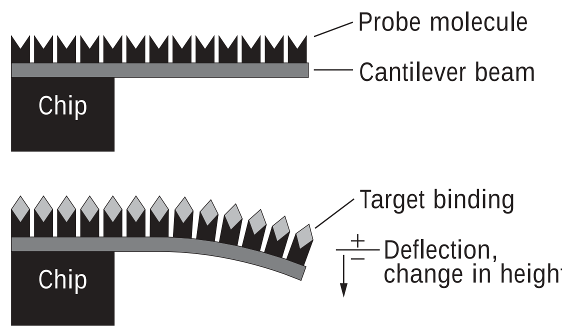
Oak Ridge National Laboratory

Other Research Collaborators

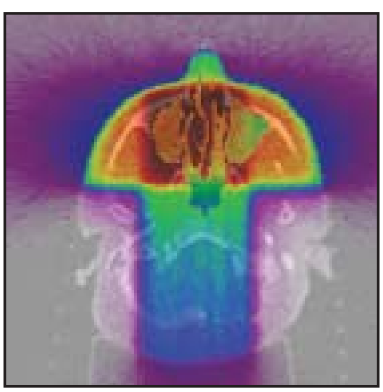
University of California, Berkeley

University of Southern California





When PSA binds to antibodies on the silicon chip, the microcantilever moves about 10 to 20 nanometers. Lasers can detect deflections as small as 1 nanometer, as sensitive as detecting a 1-inch movement in a cantilever the length of a football field. Courtesy of Kenneth Hsu, University of California, Berkeley, and the Protein Data Bank.



Peregrine: Computer-generated model of patient anatomy and tumor with simulated tracking of more than 100 million radiation particles, simulating radiation treatment for accurate dose calculation.

Mission Possible

Advances in Imaging

Four projects related to advancing nuclear medicine imaging are at the early stages of research. Today, hospitals and clinics perform about 13 million nuclear medicine procedures on patients each year (about 35,000 every day) in the United States. These procedures depend on radiolabeled tracers and sophisticated scanners.

To Better Study Normal Physiology, Disease, and Effects of New Drugs in Mice and Other Small Lab Animals

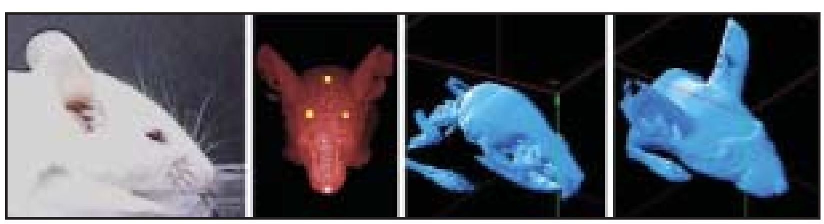
- Adapt recent breakthroughs in gamma-ray astronomy to improve resolution in small scanners that image mice repeatedly
- Reduce need to sacrifice lab animals when studying organs and other internal structures

DOE Project Management
Lawrence Livermore National Laboratory

Other DOE and Research Collaborators
Lawrence Berkeley National Laboratory
University of California, San Francisco
University of California, Berkeley

To Develop a Miniature, High-Resolution, High-Sensitivity SPECT System to Image Unrestrained Mice Without Anesthesia, Using CT Images and Surface Maps to Correct for Movement

- Biological effects of restraints and anesthesia can disrupt physiological and neurological processes studied in laboratory animals.
- Infrared laser tracking system with software to produce a 3-dimensional surface map, indicating the animal's position and motion
- Single-photon emission computed tomography (SPECT) images coregistered with surface maps and anatomic X-ray computed tomography (CT) images to correlate anatomic and functional information



DOE Project Management
Thomas Jefferson National Accelerator Facility

Other DOE and Research Collaborators
Oak Ridge National Laboratory
Johns Hopkins School of Medicine

To Develop a Miniature Mobile PET camera and MRI Scanning Techniques for Brain Imaging in Mice/Rats Without Anesthesia

- Brain imaging research with positron emission tomography (PET) and magnetic resonance imaging (MRI)—essential to study neurological and psychiatric diseases and potential drug therapies
- Animals usually anesthetized to reduce motion
- However, anesthesia creates "artificial coma" that may change brain chemistry and interfere with accurate results.

DOE Project Management
Brookhaven National Laboratory

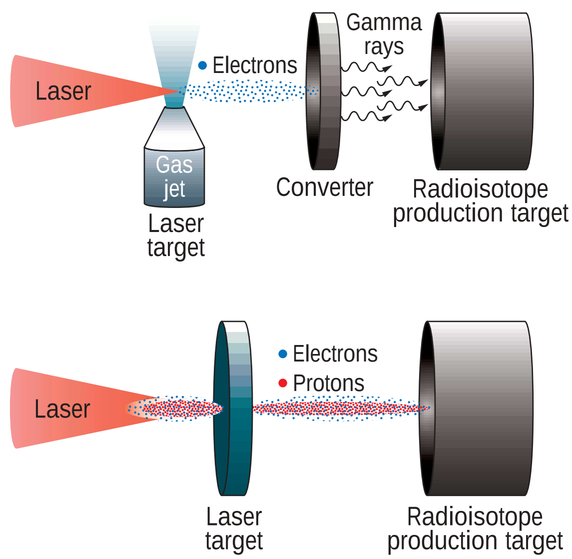
Other DOE and Research Collaborators
Lawrence Berkeley National Laboratory
State University of New York, Stony Brook

To Develop a New Type of Accelerator, Small Enough to Fit Next to Hospital or Clinic Scanners, to Create Radionuclides for Nuclear Medicine Imaging

- Accelerator-produced radionuclides—usually produced offsite or in large, expensive hospital cyclotrons for nuclear medicine facilities
- New method—advanced laser technology and plasmas—could accelerate electrons and protons at targets just a few millimeters away.
- Laser-based system could cost less than a cyclotron.

DOE Project Management
Lawrence Berkeley National Laboratory

Other Research Collaborators
University of California, San Francisco



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Research

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