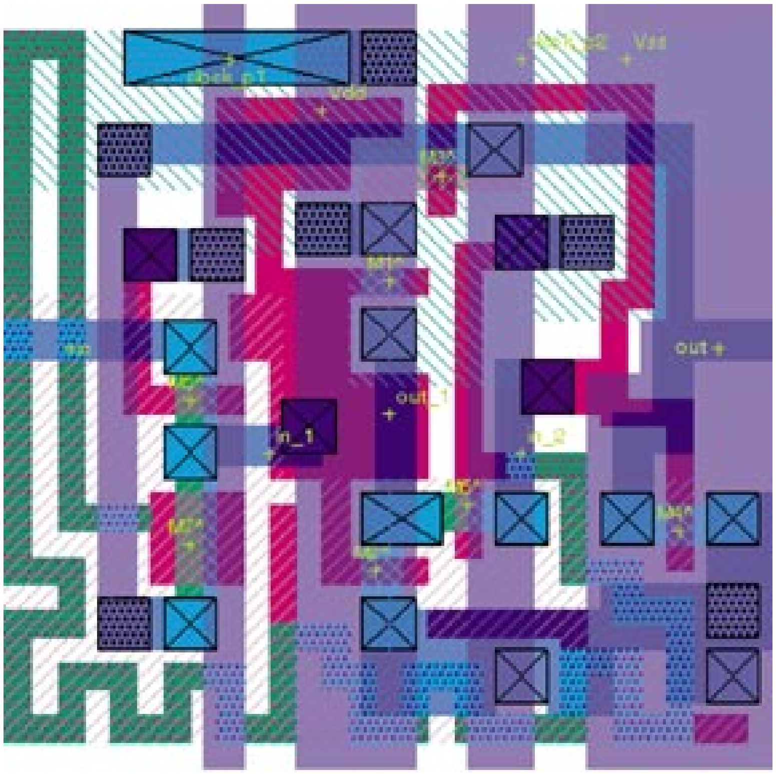
Instrumentation and Measurement Science and Technology

In 1997, ORNL made some exciting advances in the development of instruments. We helped develop the “critters on a chip” technology, a living electronic sensor in which bacteria light up in the presence of specific chemicals, such as pollutants in soil. We have devised a highly sensitive and selective hand-held DNA biochip system that may someday diagnose patients’ diseases rapidly in the doctor’s office. We are developing a chip writing system using electron beams to make faster silicon wafers for computers. Our newly developed “blend-down” monitor is helping to verify that Russian weapons-grade uranium is being converted to reactor-grade uranium fuel, extending energy supplies while cutting back on weapons material.



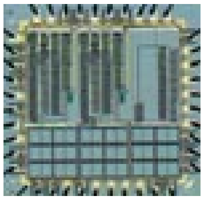
Layout for a logic chip.

To address national needs for improved measurement, monitoring, and control systems, ORNL has broad R&D capabilities in the physical, chemical, electronic, engineering, and computational sciences that can be combined to provide a powerful institutional capability. Our particular strengths include microelectronics and photonics; signal processing and simulation; analytical chemistry and chemical physics; materials characterization; robotics and intelligent systems; and sensors for physical, chemical, biological, and radiological phenomena.

Our activities include fundamental research for elucidating principles that enable novel advances in the measurement sciences; applied research that improves the accuracy, sensitivity, cost-effectiveness, and practicality of advanced techniques and prototype instruments; and design, fabrication, and installation of one-of-a-kind devices and systems. Integration of these capabilities allows the definition, design, and implementation of new instruments and methods for a variety of ORNL activities: energy production and manufacturing processes, environmental characterization and remediation, biotechnology and human health, and national security and forensic science. At the same time, this area of emphasis enhances ORNL’s ability to obtain, process, and analyze the research data needed to support DOE’s science missions.

"Critters on a Chip" Detect Pollutants

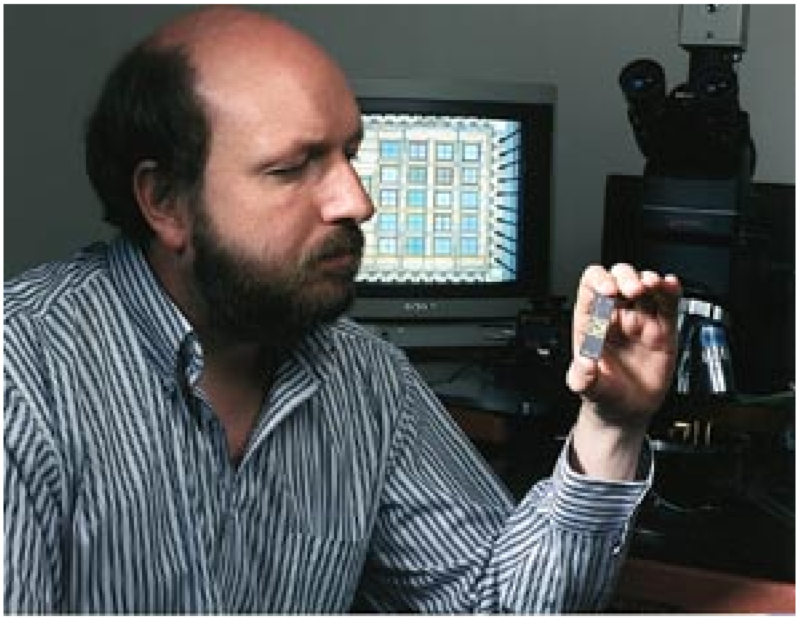
ORNL helped develop a living electronic sensor in which bacteria light up in the presence of specific chemicals.



A silicon chip the size of a match tip is deposited in a contaminated environment. Bioluminescent bacteria intentionally placed on the chip begin to "eat" the pollutant. As the living cells enjoy their feast, they light up. Their photons of blue-green visible light are absorbed by the silicon, creating electrical charges that are fed into processing circuitry on the chip. Signal-processing microelectronics measure the tiny electrical current and sound an alarm. The "critters on a chip," which were genetically engineered to emit light as they eat and digest environmental pollutants, have indeed detected naphthalene and toluene. And the chip electronics linked to these living sensors reveal the concentration of each pollutant, which is related to the amount of electric current produced.

The critters-on-a-chip technology developed at ORNL in 1996 could be used to map soil contamination (by sprinkling a suspect area with the tiny chips). A prototype device was made at ORNL by coupling *Pseudomonas fluorescens* HK44, a novel naphthalene bioreporter microorganism developed by the University of Tennessee Center for Environmental Biotechnology (UT-CEB), to an optical application-specific integrated circuit (OASIC) developed at ORNL. A measured electrical signal was obtained when the device was exposed to moth balls, which are made of naphthalene. A second prototype used the toluene-sensitive *Pseudomonas Putida TVA8*, also developed at UT-CEB.

The combination of the OASIC chip and bacteria engineered to be sensitive to a specific biological or chemical agent could have many applications. The technology could be used to detect specific chemicals in groundwater or soil, including liquid pollutants from fuel spills, toxic metals such as mercury, and explosives such as TNT that may have leaked from land mines. Oil exploration companies might want to use it to detect hydrocarbons that indicate the presence of nearby oil and gas deposits.



Mike Simpson examines the bioluminescent bioreporter chip (magnified on the monitor in the background). Genetically engineered bacteria on the chip emit blue-green light when the pollutant is detected. The chip detects this light. *Photograph by Tom Cerniglio.*

Because of the technology's exciting uses and because of the catchy nickname "critters on a chip" coined by chip developer Mike Simpson of ORNL to better promote the concept, the news media have had a field day with it. It has been featured on television and National Public Radio, and articles on the technology have appeared in *Christian Science Monitor, New Scientist, National Geographic*, and *Business Week*.

As a result of the *Business Week* article, Perkin-Elmer Corporation is developing the chip with ORNL and UT through a $4.05 million cooperative research and development agreement.

The concept sprouted in the summer of 1996 after Simpson heard a seminar on bioremediation given at ORNL by Gary Sayler, UT-CEB director and UT professor of microbiology and ecology. Sayler mentioned successes in incorporating a gene into the bacterial genome that makes the one-celled organism emit visible light during metabolism of its favorite nutrient. One gene (which codes for luciferase) comes from fireflies, and the other gene comes from the bacterial genus *Vibrio*, whose members get protection on a deep-sea fish species in exchange for emitting light the fish needs to attract prey or a mate.

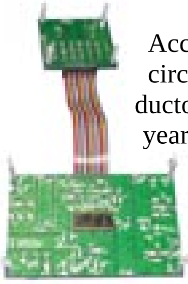
After the talk, Simpson approached Sayler, saying, "You engineer bacteria to emit low levels of light, and I develop optical sensor chips that detect low levels of light. Perhaps we should do a project together."

The rest is history. It is now possible to make living sensors using integrated-circuit chips that are small and rugged and require little power. Such wireless chips can be deployed where other devices can't (e.g., groundwater, industrial process vessels, and the battlefield). The key is to place the bioreporter bacteria on a transparent silicon nitride film that protects the etched silicon chip from damage in the presence of hazardous chemicals. To increase the shelf life of the bioreporter chip, the bacteria could be freeze dried, and a micromachine on the chip could activate the living sensors when needed by "dumping" water and nutrients on the dormant bacteria. The chip can be configured to transmit a signal to a receiver linked to a computer. The technical people on the project now call the hybrid, half-living, half-silicon devices "bioluminescent bioreporter integrated circuits," but most folks prefer to call them "critters on a chip."

DOE's Laboratory Technology Research Program helps fund this work.

Digital Electron Beam Technique May Make Faster Silicon Chips

ORNL is developing a chip-writing system using electron beams to make faster silicon wafers for computers.



According to Moore's law, the circuit density on a semiconductor chip doubles every two years and the computing speed resulting from jamming more circuits on each chip doubles every 18 months. To help uphold this law, 10 ORNL electrical engineers and physicists are developing a chip-writing system using electron beams. This system is designed to cram more transistor circuits into the same amount of chip space. By reducing the distances that electrons must travel, this system would make chips that make more calculations faster while using less power—just what the semiconductor industry is seeking. Such chips are needed to speed up computers and other electronic devices.

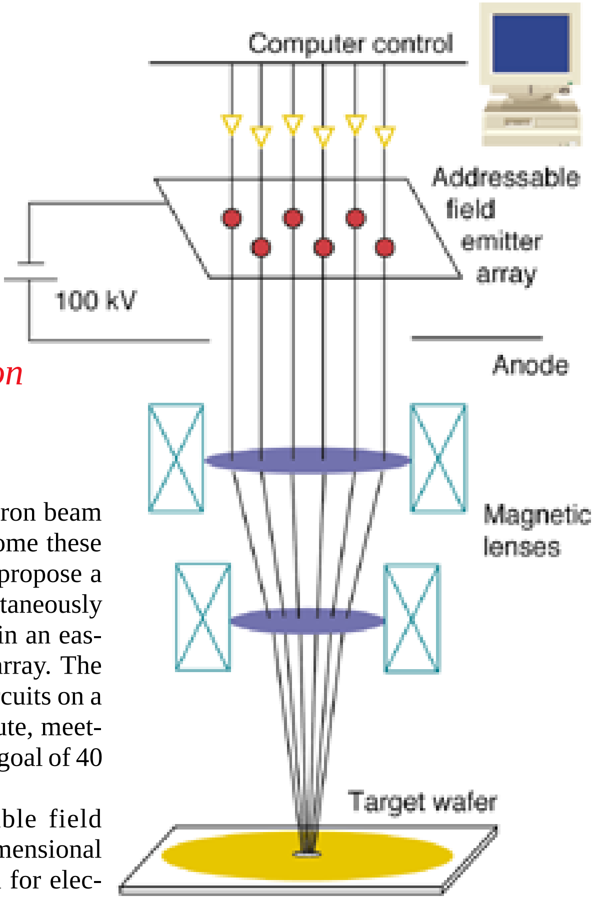
Today's integrated circuits are etched on chips by use of light—optical lithography. A mask containing a circuit pattern is imaged on a silicon chip, and a beam of light exposes the photoresist in the chip part not shielded by the mask. The size of circuits made by optical lithography is limited by the wavelength of light. Because the electron wavelength is so much shorter, an electron beam could carve a much narrower winding path in the chip, creating a finer, more closely packed circuit. Today's state-of-the-art circuits are about 200 nanometers (nm) wide, but ORNL researchers in six divisions, led by C. E. (Tommy) Thomas, think their technique could make a circuit only 100 nm across. They believe that by 2004, they will meet the semiconductor industry's goal of making production chips whose circuits are 8 times denser and up to 16 times faster than chips of the same size currently being etched by optical lithography.

Although electron beam technology has long been a strong candidate for chip lithography, writing with a single electron beam is slow and expensive. To overcome these deficiencies, ORNL researchers propose a maskless system that writes simultaneously with millions of electron beams in an easily programmable field emitter array. The system should be able to write circuits on a 300-cm^2 (8-inch) wafer in a minute, meeting the semiconductor industry's goal of 40 to 80 wafers an hour.

ORNL's proposed addressable field emitter array (AFEA) is a two-dimensional array of miniature cathodes used for electron beam sources. The proof-of-principle AFEA chips developed at ORNL have 5-micron cathodes 300 microns apart, but the researchers believe that, with the aid of an industrial partner, 200-nm cathodes can be made for chip writing (250-nm circuits are present on Intel's fastest Pentium chips). ORNL's goal is an array of 6.25 million (2500 × 2500) 200-nm cathodes on a 1-cm chip.

Using laser ablation, ORNL solid-state physicists have formed cathodes from amorphous diamond deposited on the array. When a computer-controlled bias grid places a cathode under a voltage, it emits electrons, which are accelerated to 100 kilovolts to avoid aberrations caused by stray magnetic fields. When the voltage is dropped to zero, the cathode stops emitting electrons.

Each cathode is addressable by a computer, enabling the programming into the AFEA of the desired circuit patterns to be written onto the target chip. The chip-writing program will be allocated to a network of 100 parallel computers (taking up the space of an office desk), which will send turn-on and turn-off signals to the AFEA logic and memory circuits connecting the cathodes. This digital "mask" can be reprogrammed to create different circuits on new layers within milliseconds.

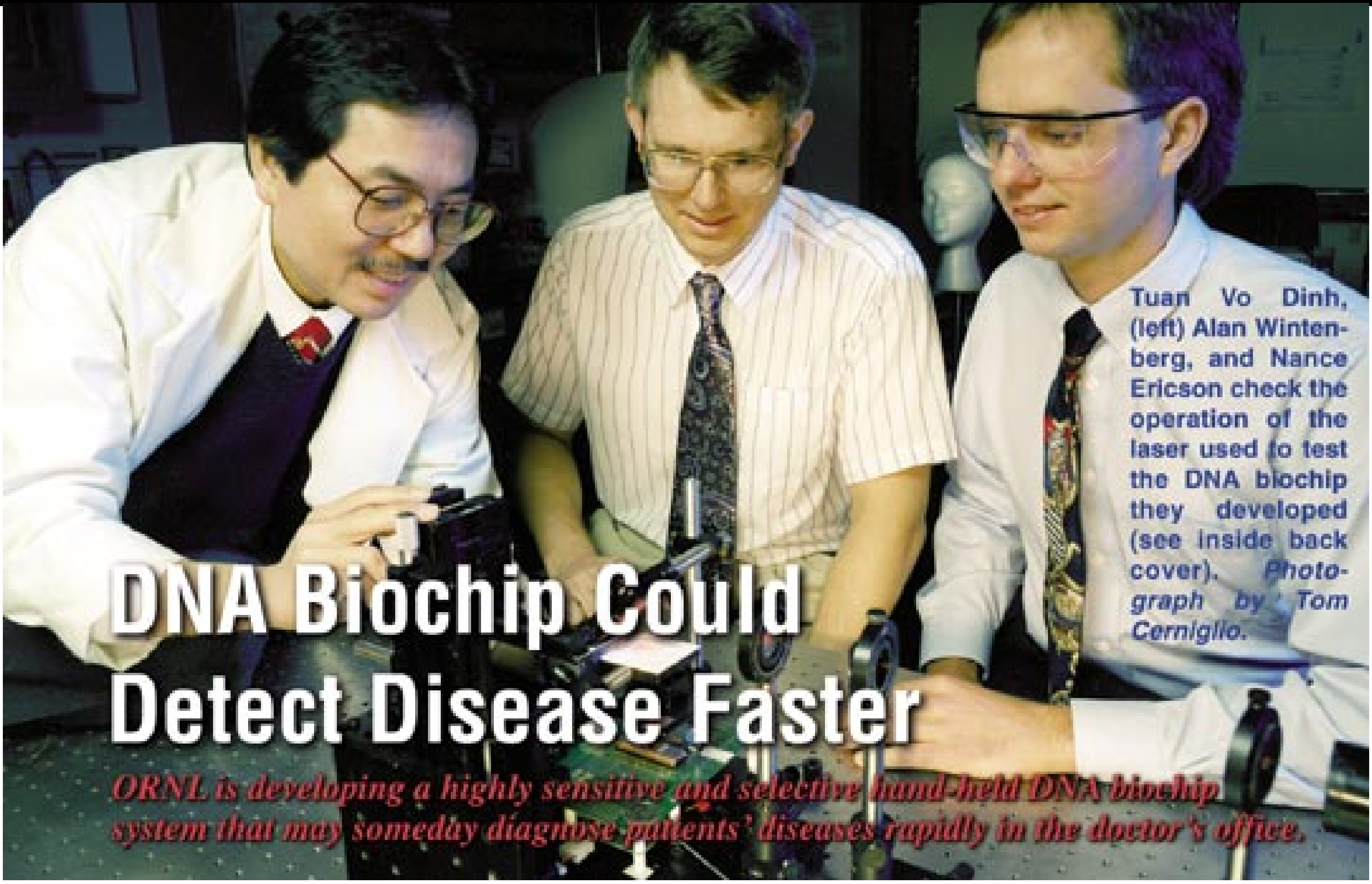


Schematic of ORNL's proposed chip-writing system.

Because ORNL researchers are facing competition from other techniques being developed (which use extreme ultraviolet light, laser light, X rays, or electron beams using masks), they are working vigorously to tackle various technical issues to make the system work. They will determine if amorphous diamond nanocathodes are reproducible and if they can be made stable and reliable enough to operate for months at a time. They will try to scale up the magnetic lens to focus into a "writing" beam the individual beams of electrons in a much larger array than is currently being handled by the best electron microscopes.

ORNL's proof-of-principle AFEA chips are assembled by IntraSpec of Oak Ridge. In 1998 the researchers will test many 2-millimeter chips, each with an array of 25 amorphous diamond cathodes (5 × 5). It may be the start of the chip-writing system of the future for the semiconductor industry, one that would show that Moore's law still holds true.

The development is being supported by the U.S. Defense Advanced Research Projects Agency.



DNA Biochip Could Detect Disease Faster

ORNL is developing a highly sensitive and selective hand-held DNA biochip system that may someday diagnose patients' diseases rapidly in the doctor's office.

Tuan Vo Dinh, (left) Alan Wintenberg, and Nance Ericson check the operation of the laser used to test the DNA biochip they developed (see inside back cover). *Photograph by Tom Cerniglio.*

You're coughing and feeling weak. You make an appointment with your doctor. A nurse greets you in the office waiting room, takes a drop of blood from your finger, and injects the blood into an instrument that fits in the palm of her hand. When you see the doctor ten minutes later, you learn the results. You don't have tuberculosis (TB) or the AIDS virus or any signs of genetic predisposition to cancer. You just have a bad case of the flu.

In two or three years, physicians may be making rapid diagnoses of patients' conditions using a small instrument containing a DNA biochip like the one being developed at ORNL by Tuan Vo-Dinh, Alan Wintenberg, and Nance Ericson. A DNA biochip mimics a living system's sophisticated recognition capability, making it highly selective and sensitive; it is able to distinguish between, for example, a bacterium and a virus or between a chemical and a biological organism.

The DNA biochip developed at ORNL will provide results in minutes instead of a few days, as is commonly the case when blood samples are sent to the laboratory for analysis by gel electrophoresis. In addition, a DNA biochip requires less blood for analysis. Unlike gel electrophoresis, the DNA biochip system uses no radioactive substances. Thus, it does not pose potential health risks for technicians handling samples, use materials that have a short shelf life, or have high disposal costs.

ORNL researchers have demonstrated the concept of a miniaturized DNA biochip system using a laser, an electric-optic integrated-circuit chip, an amplifier, and other electronics. Aided by Jean Pierre Alarie, Narayan Isola, and David Landis, Vo-Dinh showed that the concept works on a synthetic gene fragment of the AIDS virus. Other probes they designed for testing are a synthetic TB bacterium and cancer genes.

ORNL's thumbnail-size biochip will contain a membrane on which are bound up to 100 different DNA fragments. Each fragment consists of a characteristic order of chemical bases, or "letters," that spell out part of a gene [adenine (A), thymine (T), guanine (G), cytosine (C)]. Some of these bound fragments may be "detected" by free DNA probes that are introduced to the membrane. Because base A always pairs with base T and base G always pairs with base C in opposite strands of DNA (e.g., AACCT pairs with TTGGA), the free DNA probe will attach, or hybridize, itself to the bound DNA fragment that has the right opposite bases in the same sequence. The two strands are said to be complementary to each other.

For example, here's how the biochip could determine if a patient has the AIDS virus. DNA fragments isolated from a patient's blood are bound chemically on the biochip's membrane. DNA probes tagged with a fluorescent dye that are complementary to pieces of the AIDS virus DNA are introduced, and, following an amplification process, the tagged DNA attaches to any DNA present on the membrane to which it is complementary. The unattached free DNA is washed off. A laser light illuminates the membrane, causing the attached tagged DNA to give off light, which is captured by detectors below the membrane and turned into electrical signals that provide the diagnosis to the doctor.

Following system packaging, clinical trials could begin to test the device for biomedical applications. If everything goes smoothly, in about two or three years, the DNA biochip system could be in use to give patients and doctors results in only a few minutes. Such a device could help doctors diagnose important diseases earlier, cutting health care costs.

ORNL's Laboratory Directed Research and Development Program and DOE's Office of Biological and Environmental Research sponsored this work.

Confirming Conversions of Weapon Materials to Reactor Fuels

An ORNL-developed instrument is helping to verify that Russian weapons-grade uranium is being converted to reactor-grade uranium fuel.

Reducing the number of nuclear weapons in the world is one of President Clinton's chief foreign affairs goals. One step toward achieving that goal is the U.S. purchase of 500 metric tons of highly enriched uranium (HEU) from the Russian Federation over the next 20 years at a cost of $12 billion. The HEU extracted from nuclear weapons is being diluted, or blended down, in Russia to produce low-enriched uranium (LEU) for use as fuel for nuclear reactors that generate electricity. In this way, the uranium in weapons cannot be recycled to make other weapons, but it can be used to extend each nation's uranium supplies for energy production. An instrument developed at ORNL will be one of two used to verify that the Russians have properly blended down the 500 metric tons HEU purchased by the United States.

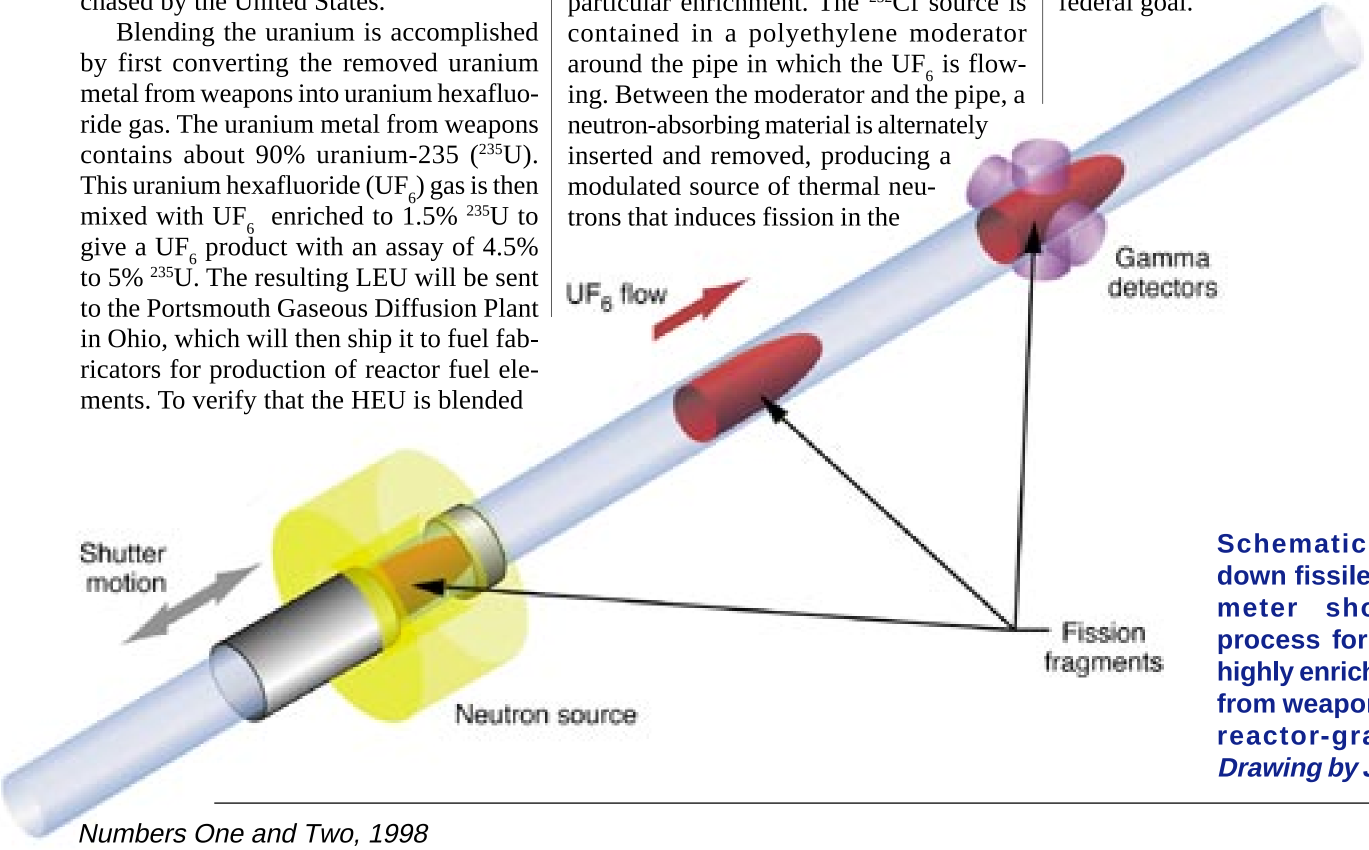
Blending the uranium is accomplished by first converting the removed uranium metal from weapons into uranium hexafluoride gas. The uranium metal from weapons contains about 90% uranium-235 (^{235}U). This uranium hexafluoride (UF_6) gas is then mixed with UF_6 enriched to 1.5% ^{235}U to give a UF_6 product with an assay of 4.5% to 5% ^{235}U. The resulting LEU will be sent to the Portsmouth Gaseous Diffusion Plant in Ohio, which will then ship it to fuel fabricators for production of reactor fuel elements. To verify that the HEU is blended down, a special measurement system that could be deployed without cutting pipes was needed.

To meet this requirement, an ORNL team led by John Mihalczo, Jim Mullens, and Jose March-Leuba developed, tested, demonstrated, and implemented the blend-down fissile mass flowmeter. A prototype was demonstrated to DOE and the Department of State and to representatives of the Russian Ministry of Atomic Energy. The United States has negotiated the installation of this equipment in Russian facilities involved in the blend-down of HEU as a way to provide confidence that the Russian Federation is abiding by terms of the agreement.

The flowmeter contains a californium-252 (^{252}Cf) source that introduces neutrons periodically into the pipe carrying UF_6 of a particular enrichment. The ^{252}Cf source is contained in a polyethylene moderator around the pipe in which the UF_6 is flowing. Between the moderator and the pipe, a neutron-absorbing material is alternately inserted and removed, producing a modulated source of thermal neutrons that induces fission in the UF_6 gas, producing waves of activation (delayed gamma ray emissions by uranium atoms in the gas along the pipe) that are detected downstream. The time delay between the activation and the detection downstream, and the distance between the source and detectors, allows measurement of the gas flow velocity. The amount of the signal downstream at the detector is proportional to the concentration of ^{235}U in the gas. (The more uranium, the more gamma rays in the signal.) From these two quantities, the fissile mass flow is obtained.

The blend-down fissile mass flowmeter is undergoing calibration and verification demonstrations with 1.5 wt % ^{235}U-enriched gas at the Paducah Gaseous Diffusion Plant. It will be installed in Russia to monitor blend-down of the U.S.-purchased uranium. The flowmeter has been demonstrated to Russians as part of their training so that they can safely install and operate it at the Russian blend-down facilities. Jim McEvers and William H. Sides are project managers for the fabrication and installation of the flowmeter in Russia.

This program has brought international recognition to ORNL. The Laboratory received a substantial amount of funding for the development of this instrument for use in the Russian blend-down facilities. While reducing nuclear weapons-grade uranium, the ORNL instrument is helping the United States extend its supplies of nuclear fuel for power production, helping meet yet another federal goal.



Schematic of blend-down fissile mass flowmeter showing the process for converting highly enriched uranium from weapons-grade to reactor-grade fuel. ***Drawing by Judy Neeley.***