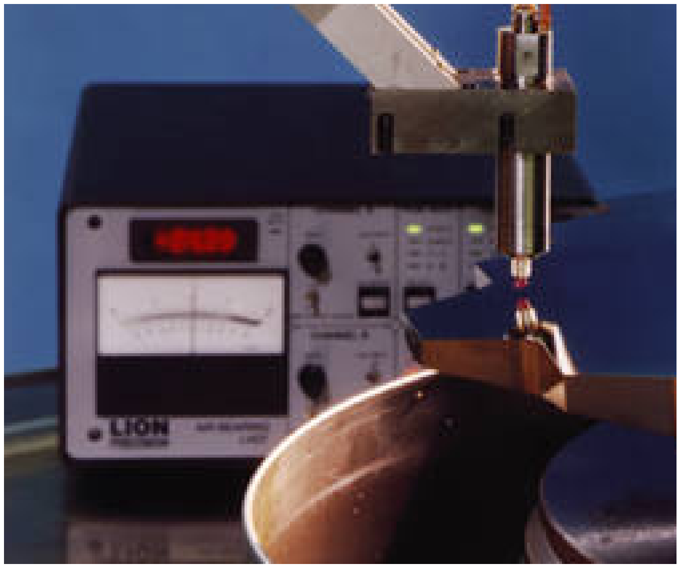
LLNL's 1994 R&D 100 Awards



The Laboratory's six 1994 awards demonstrate once again that research derived from defense concerns can contribute civil applications that advance U.S. economic competitiveness and promise improved human well being.

EACH year *R&D Magazine* selects the 100 most technologically significant products and processes submitted for consideration and honors them with an R&D 100 award. Winners are chosen by the editors of the magazine and a panel of 75 experts in a variety of disciplines. Corporations, government laboratories, private research institutes, and universities throughout the world vie for this "Oscar" of applied research. Past winners include many products that are now a part of everyday life—Polacolor film (1963), the electronic video recorder (1969), antilock brakes (1969), the fax machine (1975), the anticancer drug Taxol (1993). Since the competition began in 1963, the Laboratory has won 50 R&D 100 awards. Among past winners are the process for the diamond turning of optics (1978), the precision-engineering research lathe (1986), ultralow-density silica aerogel (1990), and the hard x-ray lens (1991).

The R&D 100 judges look for products or processes that promise to change people's lives, such as by significantly improving the environment, health care, or security. In 1994, the Laboratory received six R&D 100 awards. Three of them contribute to advances in laser technology:

- Our new multilayer dielectric diffraction gratings free lasers from the limitations imposed on them by conventional metallic gratings currently in use.
- Our methods for rapidly growing high-quality crystals will change the economics of using crystals in lasers of all sizes and powers, especially solid-state, which are especially versatile by virtue of combining high power and small size.
- Our doping of several varieties of apatite crystals with ytterbium has achieved significant increases in the energy storage efficiency of diode lasers.

Each of these three inventions also contributes significantly to research in inertial confinement fusion, which promises someday to be a major source of energy for civil uses.

The other award winners are in the fields of high-precision measurement, silicon microbench technology, and genetic research:

- We have advanced the limits of high-precision metrology by developing an amplifier for use with sensors that measure surface irregularities. This amplifier offers 30 to 40 times better resolution than other high-precision metrology devices using a similar sensor.

- As ever-finer diameters of fibers are used to increase the speed of fiber-optic communication, we have developed a method of achieving the required submicrometer accuracies of component alignment at 10 to 20 times less cost than that of current methods.
- Finally, our chromosome-specific DNA probes allow us to identify chromosomes of the laboratory mouse 60 times faster than the standard chemical staining or banding method. The analysis of "painted" chromosomes does not require highly skilled personnel, so the savings in personnel cost combined with the increased speed yield a 200-fold increase in efficiency. The many applications of chromosome "painting" include several related to cancer and birth defects, gene mapping, and, perhaps most immediately significant, testing new drugs for safety.

Efficient Multilayer Dielectric Gratings

Diffraction gratings have long been used to disperse light into constituent colors, or wavelengths, for spectroscopic applications. These gratings are finding new uses with high-power lasers. Indeed, their dispersive properties are making possible new classes of lasers: because matched grating pairs can stretch or compress a pulse, grating-pair pulse compressors allow pulses of hitherto unsurpassed intensities to be achieved. However, to accomplish this compression, the gratings must be able to withstand high intensities. Traditional reflection gratings use metallic corrugations to form the needed periodic grooves. They achieve a highly reflective surface by means of the high conductivity of the metal. Heating of conduction electrons, however, renders the surface susceptible to damage at fluences of around 0.5 J/cm^2. This low threshold for damage has impeded attempts to develop high-power lasers.

Metallic surfaces are only one means of reflecting light. It has long been known that multiple layers of thin dielectric films act as a highly reflecting structure (because each layer introduces a quarter of a wave of phase retardation). When produced with proper care, these can have high thresholds for laser-induced damage, an order of magnitude higher than those of metallic gratings. In 1991, we proposed that such multilayer dielectric stacks, with a periodic groove structure, could serve as a highly efficient reflection grating. A grating constructed entirely from dielectric material should combine the high damage threshold of transparent material with the high diffraction efficiency hitherto exclusive to metal gratings.

We have demonstrated that such multilayer dielectric gratings can be produced, that they can reflect selected wavelength bands with high efficiency, and that they can be made in large sizes while maintaining high quality wavefronts. The construction of these

Figure 1. A multilayer dielectric diffraction grating designed to reflect yellow light, diffract broadband visible radiation (bottom left), eliminate all green and yellow light in the transmitted diffracted beam (at right), and transmit blue–green light. The grating pictured is 15 ¥ 20 centimeters.

gratings has required that several technologies be integrated in order to create the multilayer dielectric stack, to form a periodic latent image pattern in a two-beam interferometer, and to develop this image and transfer the pattern into a permanent grating.

Multilayer dielectric gratings have several novel properties that offer unique opportunities for new applications:

- With their high damage threshold, our dielectric gratings make possible the construction of grating-pair compressors for kilojoule laser pulses that would destroy metallic gratings.
- For any given wavelength, polarization, and angle of incidence, grating efficiency depends on the phase retardation properties of the multilayer stack, the depth and shape of the grating grooves, and the angle of incidence of the radiation. Adjustments of these properties during manufacture make it possible to control the distribution of energy between reflected, transmitted, and diffracted beams.
- The wavelength discrimination of the multilayer stack makes it possible to build gratings that transmit or reflect light with high efficiency within a narrow optical wavelength bandwidth. A grating can be designed to have nearly any desired efficiency and bandwidth.
- Large, high-efficiency gratings, well beyond the 20 × 30 cm size of conventional metallic gratings, are possible with this new technology. Meter-scale gratings, which are now possible, are a key enabling technology for developing high-energy (l000-TW) picosecond-pulse lasers. The laser program at LLNL is planning to use this technology in constructing the world's first 1000-TW laser.

These highly efficient multilayer dielectric gratings create the opportunity for the development of new products. They may replace the metallic gratings that have become obsolete in many current applications. Broadband solid-state lasers, for example, have become increasingly important devices because their very high output energies make them well suited for compact and reliable systems. However, the full potential of these lasers cannot be realized while they rely on metallic gratings. Dielectric gratings, with their greater threshold for laser-induced damage, will allow the development of high-power tunable narrowband lasers that efficiently extract energy from broadband solid-state materials.

Our new gratings have numerous commercial applications derived from their damage resistance and their ability to act as narrow- or broadband filters or reflectors. When used in commercial laser pulse-compression systems, these designs can substantially reduce grating size over those now used, with proportional cost savings.

The optical selectivity of these gratings will find immediate use in high-contrast spectrometers, which now use multiple conventional gratings to achieve the often-required spectral discrimination to one part per million. Dielectric gratings can be excellent discrimination filters; they can be designed to reflect undesirable narrow-line optical radiation, such as laser radiation, while transmitting most other frequencies. This property may make them valuable on the battlefield, where lasers are increasingly present in weapons and guidance systems. A multilayer grating could transmit visible radiation and diffract unwanted laser radiation with great efficiency.

Because they control distribution of energy between the specularly reflected, transmitted, and diffracted beams (see Figure 1), gratings can act as selective beam splitters in optical switches and distribution systems. The small-scale, high-energy tunable lasers made possible by these gratings should find numerous uses in such areas as remote sensing and biochemical or biomedical diagnostics.

This work was done in cooperation with Hughes Electrooptic Systems in El Segundo, California.

For further information contact Michael D. Perry (510) 423-4915 or Robert Boyd (510) 422-6224.

Growing High-Quality KDP Crystals Quickly

Crystals are essential materials in advanced scientific tools and applications, such as portable, high-power solid-state lasers operating in the visible and ultraviolet spectral regions; remote sensing infrared detection systems; engineered molecules for the pharmaceutical industry; and inertial confinement fusion lasers. High-power lasers for fusion require very large, high-quality crystals of potassium dihydrogen phosphate (KDP) and its deuterated analog DKDP for experiments in fusion.

Conventional techniques for growing crystals from solution are slow and inherently unreliable. (Briefly, crystals are grown from a seed, or "starter," crystal that is submerged in a melt or solution containing the same material; the final growth, having the same atomic structure as the seed, is called the boule.) Growth rates for conventionally grown KDP, for example, are about 1 mm/day. Because of a high density of dislocations, or defects, in the material near the seed crystal in KDP, the quality is low; and because the seed defects propagate into the final boule, a substantial fraction of the boule is of low quality. A large percentage of crystals that have taken a long time to grow are, in the end, useless for their intended purpose.

We have developed a process for growing crystals from solution that is appreciably faster than current commercial processes and produces exceptionally high yields of high-quality crystals. Using our rapid-growth method, we have grown both KDP and DKDP crystals up to 15×15 cm^2 in cross section at rates of 5 to 40 mm/day; that is, 5 to 40 times the rate of conventional methods. Our process uses a small "point" seed and produces only a small number of dislocations. As a result, even material near the seed is of high quality. By saving growth time and reducing waste, our method reduces the cost of crystals. Figure 2 shows two KDP crystals, one grown conventionally in six weeks and the other grown by our process in two and a half days.

Our process relies on pretreatment of solutions using high temperature and ultrafiltration. This process destroys any small crystal nuclei that might be present in the solution and allows it to be highly supersaturated without spontaneous crystallization. We use a crystallizer (the process vessel in which the supersaturated solution is brought to a solid crystal state) that eliminates sources of undesired crystal nuclei (spurious nucleation) during growth. Of secondary importance to the method are the technique for holding the seed, the temperature profile during growth, and the hydrodynamic regime. The two major advantages of this process over conventional growth methods—high growth rate and potentially high yields—dramatically reduce labor costs and therefore total cost.

At LLNL we submit crystals to characterization tests while they are growing so that at any stage we know such characteristics as their optical homogeneity, transmitted wavefront distortion, and susceptibility to laser-induced damage. Such methods as x-ray topography and microbeam chemical analysis allow us to trace the optical distortions to structural defects and compositional inhomogeneities. Indeed, atomic force microscopy enables us to observe crystal growth and defect generation at the nanometer level, giving us direct information about how surface morphology during growth depends on growth conditions and the structure of defects. The information provided by these characterization techniques is used to optimize the growth process iteratively.

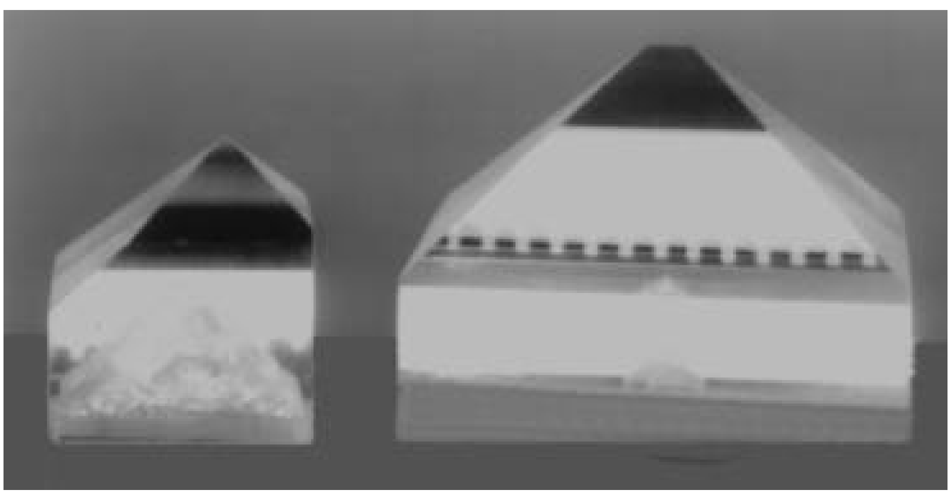


Figure 2. **The KDP crystal on the left took six weeks to grow by a conventional method; the large, high-quality KDP crystal on the right is approximately 10.5 cm on a side and was grown in only two and a half days using our method.**

Having investigated crystals grown by both conventional and rapid-growth methods, we have demonstrated that the quality of the crystals is not a function of growth rate. Rather, it depends on solution purity, hydrodynamics (the flow geometry of the solution), and the conditions during seed regeneration.

Our process is a significant technical advance in the field of crystal growth. Many crystals that are expensive and difficult to grow will soon become readily available as will others that previously could not be grown to usefully large sizes. Extremely large crystals (10,000-100,000 cm^3) for applications such as laser fusion take as long as 2 years to grow and involve great risk of failure. These will be grown in 1 to 2 months and present greater odds of being of sufficient quality. In short, our process is revolutionizing the way solution-based crystals are grown.

Moreover, because it is based on general principles, this technique is applicable to a wide variety of crystal systems. Our process can be used for growing other water-soluble crystals, and we have grown numerous varieties. In all cases, they grow about ten times faster than their conventional counterparts.

The general principles also apply to the stabilization of supersaturated solutions at any temperature or pressure. Modifications of this process should thus be useful with hydrothermally grown crystals, like quartz, and flux-based systems, such as potassium titanyl phosphate (KTP), lithium borate (LBO), and beta beryllium borate (BBO)—three important optical materials whose application has been limited by the size and quality of currently available crystals. Because such crystals are critical to a number of high-power, visible-to-ultraviolet solid-state laser configurations, wide availability of inexpensive, high-quality crystals would make such configurations possible.

Technologies are limited by the quality and capacity of the best available materials. By improving the solutions, our method removes some limitations. As a national laboratory, we are looking for ways to improve the productivity and competitiveness of U.S. businesses. LLNL has a long-standing relationship with U.S. crystal growth companies, and we are formally involved in commercializing this technology for the rapid growth of KDP and its analogs as well as other crystals.

This work was done in cooperation with Moscow State University, Moscow, Russia.

For further information contact James De Yoreo (510) 423-4240.

Ytterbium-Doped Apatite Laser Crystals

We have developed a new class of laser materials whose special properties make them a particularly useful invention at a point when laser diode pump sources are becoming a mature technology. Laser diodes are highly efficient and reliable, are rapidly falling in price, and are, therefore, becoming more common in laser systems. Our challenge was to find new laser materials that could fully exploit the advantages of diode lasers as optical pumps. We thought that special materials like the ytterbium-doped apatites (Yb:apatites) should exist, and we devised the appropriate means of identifying them.

Apatite is a group of phosphate minerals—there are ten species in all. The Yb:apatites are crystals into which approximately 1% Yb is introduced. We have performed this procedure with four apatite species: fluorapatite, $Ca_5(PO_4)_3F$; strontium-fluorapatite, $Sr_5(PO_4)_3F$; a mixture of these two materials $Ca_2Sr_3(PO)_3F$; and strontium fluorovanadate, $Sr_5(VO_4)_3F$. We are the first to grow the last named, and although the other three crystals were known to be growable, we recognized that the Yb dopant gave these materials remarkable laser properties.

The Yb:apatite crystals offer laser properties not previously available from an optical material. (See Figure 3.) Most significantly, they store energy substantially more efficiently (2.5 to 5 times) than standard neodymium-doped laser materials, such as yttrium-aluminum-garnet (Nd:YAG), yttrium-lithium-fluoride (Nd:YLF), and glass (Nd:glass). Efficiency is critical to many diode-pumped solid-state lasers used in applications requiring a specified energy output. For example, if the required solid-state laser energy output is 1 J and lasing and pumping efficiency is 20%, the diode output energy must be 5 J in order to serve as the optical driver. Since the laser material is typically pumped for the same amount of time that the energy will be stored, the required diode power is 5 J per unit storage time. It turns out that Nd:YAG requires 21 kW, but Yb:apatite requires only 4 kW.

The greater storage efficiency reduces the needed investment in the most costly part of the laser system—the laser-diode pump source. This cost generally scales in dollars per watt. At the current cost, about $20/W, pump diodes will cost $420,000 for the Nd:YAG system but only $80,000 for the Yb:apatite system. Moreover, laser system cost grows in proportion to output energy (in the millions of dollars for a 10-J system). A 10-J pulse of output energy translates into a diode cost of about $1 million for the Yb:apatite gain medium, less than a third the cost of diode-pumped Nd:glass.

Yb:apatite materials are principally useful for applications requiring a specified energy per pulse from the laser, and especially requiring an energy greater than 1 J. An important example is the printing of circuits by x-ray lithography. Laser x-ray lithography is being developed to support the future productivity and competitiveness of the U.S. electronics industry. Although the methodology has been determined to be viable, the cost of the laser system is a major issue. The laser in current use, a flashlamp-pumped Nd:glass system, is somewhat inefficient and incurs substantial heating, which limits the repetition rate and thus the circuit-production rate. Replacing this laser with a diode-pumped Yb:apatite system will reduce thermal loading by roughly a factor of three and increase overall laser efficiency by a similar factor.

Another application requiring a specified energy per pulse is laser paint stripping (useful for large projects such as bridges, aircraft, and ships). The most common paint-stripping methods are sandblasting and chemical treatment, both of which are expensive and tend to generate substantial pollution. Studies suggest that laser paint stripping is cleaner and more effective—assuming a reliable, efficient, and affordable laser source can be designed and built. A Q-switched diode-pumped Yb:apatite laser may prove useful for this application as well.

Commercial sales of diode-pumped solid-state lasers are modest (approximately $20 million/yr), although the growth rate is a healthy 15%/yr. However, the overall solid-state laser market is considerably larger (about $300 million), and diode-pumped solid-state lasers are likely to replace many of today's flashlamp-pumped systems. Diode-pumped solid-state lasers can serve as enabling technologies, enhancing the total benefits of their deployment far beyond their independent value. The potential impact of x-ray lithography on the multibillion-dollar electronics industry is a prime example.

Yb:apatite lasers could replace diode-pumped Nd-lasers in many current applications. They could be used in scientific research systems, serving, for example, as a laser to pump a tunable titanium-doped sapphire or dye laser. They could be used in compact, efficient systems for marking, remote sensing, and medical applications. In material processing, they could perform cutting, welding, and drilling operations.

A particularly exciting possible application for a diode-pumped Yb:apatite laser could be as a driver for inertial fusion energy. In this application, a certain amount of laser energy (on the order of several megajoules) must arrive at the target to drive it to fusion ignition. Here the storage time has enormous impact on the overall cost of the laser.

This work was done in cooperation with the Center for Research and Education in Optics and Lasers, University of Central Florida, Orlando, Florida.

For further information contact Stephen A. Payne (510) 423-0570.

High-Precision Low-Noise LVDT Amplifier

The precision manufacturing industry requires increased accuracies in measurement in order to lower production costs by reducing the amount of wasted material; increased accuracies can also yield products with improved performance and wear life. Extremely high accuracies require inspection equipment with very fine sensitivities. One type of sensor for measuring surface irregularities is the linear variable differential transformer (LVDT). An LVDT is, briefly, a transformer with a primary and two symmetrically offset secondary windings and a movable magnetic core. A stylus-tipped shaft extends from the core and is held in contact with the part to be measured. Displacements of the stylus move the core, changing the magnetic coupling of primary to secondaries and generating a linearly increasing voltage as the core is displaced from its rest (null) position. An air-bearing LVDT provides the ultimate mechanical configuration; it allows stylus force to be adjusted to minimize part deformation and provides nonstick operation for high precision and resolution.

Through an industrial partnership agreement, LLNL and Lion Precision (St. Paul, Minnesota) jointly developed a precision amplifier for use with the LVDT. This high-gain, low-noise, air-bearing amplifier offers 30 to 40 times better resolution than other high-precision measurement devices using a similar sensor. Contact displacement measurement resolution is near the atomic level: coupled with an air-bearing LVDT, the amplifier's sensitivity and unique circuitry provide resolution to two atomic diameters, or 0.6 nm. Over its range of travel, it rivals the resolution of high-precision displacement-measuring laser interferometers.

The amplifier also provides very high gain, or increase, in signal power—100 to 1000 times that of competitors—while requiring 5 to 10 times less excitation of the sensor than competitive products. Minimizing sensor excitation reduces LVDT heating, decreasing thermal distortion of the part being measured, thus providing higher precision and repeatability. The amplifier provides a fixed-frequency, highly stable primary excitation signal. The secondary signal is amplitude modulated by the core position

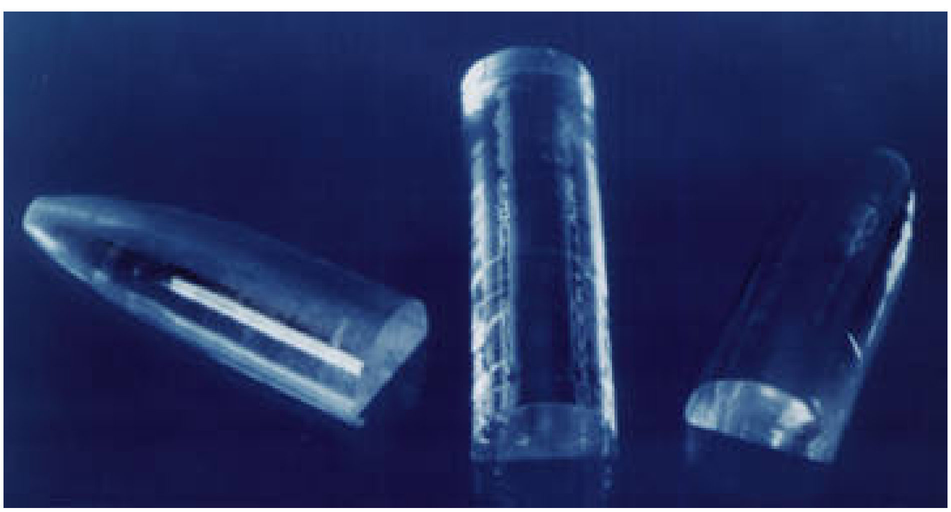


Figure 3. **Several crystals of Yb:apatite, showing that they can be grown in large sizes (7.5–9 ¥ 2 cm) and with high optical quality.**

(dictated by the displacement of the stylus). A phase-sensitive detector demodulates position information returned from the LVDT secondaries. Resolution is almost infinite and depends on the signal-to-noise ratio of the signal-conditioning electronics. By providing constant current excitation of the LVDT, our amplifier provides the same level of coupling to the secondaries even if coil resistance changes because of temperature changes.

The LVDT signal has one desired component (the displacement signal) and one undesired. The amplifier has a circuit to handle each: one circuit maximizes the desired signal amplitude; the other cancels the undesired signal before it can saturate any predetector amplifiers. Predetector gain is maximized and postdetector gain minimized. Cancellation of the undesired signal is one of the reasons this amplifier easily outperforms the resolution of the next-best amplifiers. Resolution better than 2.5 nm is possible with a 100-Hz bandwidth, and 0.6 nm with a 2.5-Hz bandwidth.

Machine tool builders, metrologists, and quality inspection departments can now measure surface irregularities as tiny as 1/120,000 the width of a human hair. Indeed, principal applications include machine tool metrology, coordinate measuring machines, diamond-turning machines, roundness gauges, and precision manufacturing. Parts made at LLNL by machines such as the Large Optics Diamond Turning Machine—the world's most accurate diamond turning machine—typically require that the part be measured to better than 2.5 nm and part surface finishes to better than 12.5 nm. This amplifier can immediately improve measurement resolution of inspection machines.

The amplifier can replace signal-conditioning electronics for any sensors using LVDT technology, such as load cells for measuring force or torque, pressure measurement sensors, accelerometers, and inclinometers. Future applications include metallurgical research and use by the semiconductor industry to measure the thickness of thin-film deposits on microelectronic components.

This amplifier advances contact displacement measurement to the same accuracy and resolution commercially available until now only from noncontact displacement measuring systems, such as capacitance gauges and interferometers. For many tasks, such as measuring small objects that are nonconducting or are not completely free of oil or coolant, capacitance technology is inappropriate. Although capacitance gauges measure contour figure with high resolution, they provide poor spatial resolution and therefore cannot measure part surface finish. Laser interferometers require a reflective mirror surface to return the beam, so direct part measurement is normally not possible. Moreover, interferometer systems are more complex, larger, and more costly to use than the LVDT amplifier. (The amplifier can also be configured for noncontact displacement measurement. Resolution is at the atomic diameter level.) Thus, this amplifier breaks new ground in defining the state of the art in contact displacement measurement.

This work was performed under a cooperative research and development agreement (CRADA) with Lion Precision, St. Paul, Minnesota.

For further information contact David Hopkins (510) 423-6134.

Figure 4. **The amplifier (left), shown next to a part under inspection; the LVDT probe extends from the tool bar of the Large Optics Diamond Turning Machine. The part under inspection is the Keck II secondary mirror for the Keck Observatory in Hawaii.**

Silicon Microbench Technology

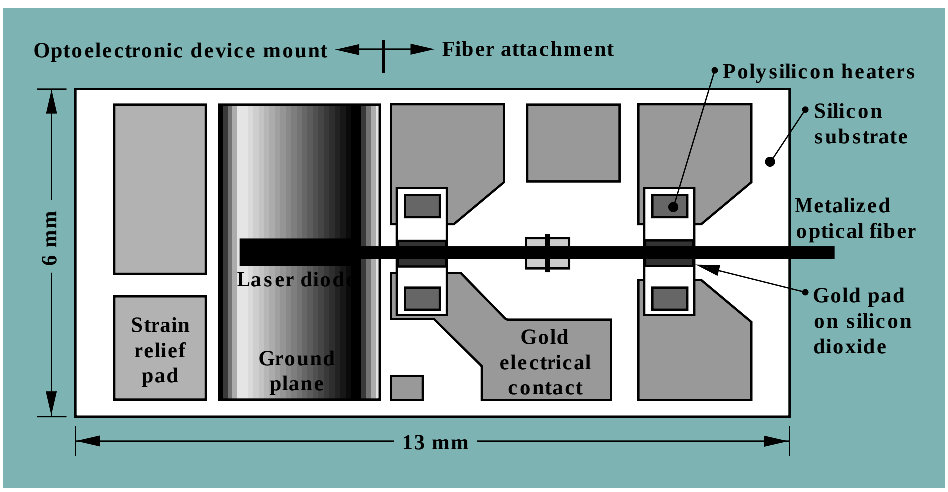
Most fiber optic communication is now done at rates below 1 gigabit (1 billion bits) per second (Gb/s). The dimensions of the multimode fibers used at these rates allow component-alignment tolerances of several tens of micrometers. New communications standards are designed for operation well above 1 Gb/s. Such high speeds require that much finer single-mode optical fiber be used. This fiber must be aligned to single-mode optoelectronic components at submicrometer tolerances. Achieving these tight tolerances using current cumbersome manual alignment and attachment (pigtailing) techniques takes extraordinarily long times. These times drive up the costs of packaging, which can account for as much as 95% of the cost of optoelectronic devices. The most time-consuming and, therefore, most expensive part of the packaging is the alignment and attachment of the fiber. Today, each single-mode packaged device typically costs several thousand dollars.

We are developing automated alignment and attachment techniques to reduce the cost of packaged opto-electronic devices. Our mounts provide the stability and localized heating to achieve the tight tolerances while simplifying assembly and allowing relatively inexpensive mass production. Volume production is the key to reducing costs 10 to 20 times, to less than $10 a device for the packaging cost.

The key to mass production is to reduce the time per “pigtail”—the packaging operation of joining an optical fiber to an optoelectronic device, such as a laser. We are building a fiber pigtailing machine that will automatically align a fiber to a laser diode or to a lithium niobate modulator with submicrometer accuracy in less than 5 minutes. (At volumes of several thousand pigtails per year, the cost per manual pigtail approaches $100, whereas at volumes of several tens of thousands per year, the cost per automated pigtail is less than $10.) We designed and built silicon substrates with geometries that are compatible with the automated processes and have the stability required to maintain the submicrometer alignment tolerances necessary for single-mode operation. These substrates are the key part of an automatic alignment package.

We have designed our mounts with discrete areas for optoelectronic device attachment and areas for fiber attachment. For example, the 13- × 6-mm mount shown in Figure 5 is for packaging a 1550-nm distributed feedback laser. On the left half, gold pads provide a ground plane for the laser and stress relief for the wire bonds. To attach the fiber on the right half of the mount, two polysilicon heating elements are connected to gold bonding pads for electrical contact. In the center of each heater, a 1- × 0.5-mm gold solder attachment base (on a layer of silicon dioxide for electrical isolation from the polysilicon heater) is large enough for a 125-µm-diameter

(a)



(b)

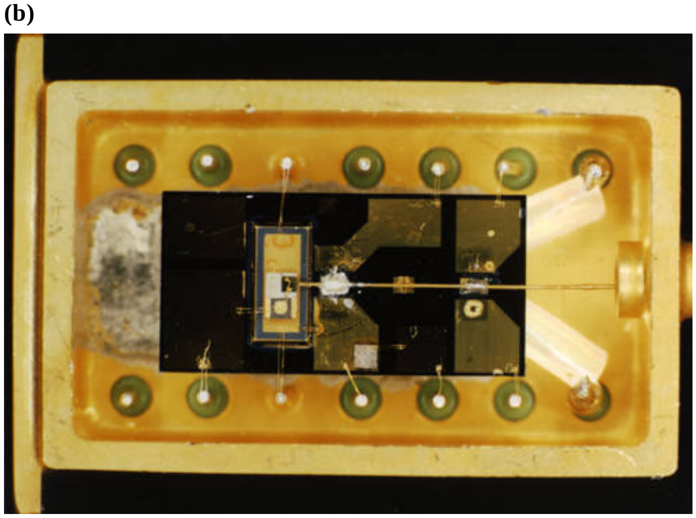


Figure 5. (a) Sketch of silicon mounts showing the location of the components and heaters. (b) Photomicrograph of a silicon mount inside a standard gold-plated metal package with a laser diode. A metalized optical fiber is mounted and aligned to the diode. The silicon mount is 6 ¥ 13 millimeters.

fiber to be soldered to it. We use either 100-μm-diameter solder balls or solder paste to attach the metalized fiber.

A simple power supply and a timed switch allow us to control accurately the magnitude and time of the applied current, giving our prototype very reproducible performance. We use active feedback to align the fiber to submicrometer accuracies. While the fiber is held in the position that maximizes the optical coupling, current is passed through the heater to reflow the solder, which wicks around the metalized fiber without disturbing the automatic submicrometer optical alignment. Conventional techniques for melting solder heat the entire substrate, creating considerable difficulty with drift of the alignment after the solder has cooled and requiring such corrective measures as preshifting the fiber so that after cooling the thermal shifts will tend to bring the fiber into alignment. By providing only the small amount of heat needed to melt the solder locally, we avoid these thermal shifts and greatly simplify the alignment process. We observe no decrease in the light coupled from a 800-nm laser diode into the single-mode fiber after the solder has cooled.

Silicon mounts offer the additional benefit of allowing us to use standard, low-cost silicon etching techniques to bring the optical axis of different components in approximately the same line vertically (see Figure 6), minimizing the solder thickness and therefore thermal drifts and long-term creep that are problems with other packages that use thick solder or metal "shims" to bring the optical axis in alignment.

The potential market is enormous. As fiber communication products become more prevalent, one can envision these packages used at either end of every fiber for transmitters and receivers of high-speed optical signals. At sufficiently low production costs, the market is potentially many millions to billions of devices in a multitude of applications, ranging from single-mode fiber-optic communication products and laser-diode transmitters, to the assembly of hybrid optoelectronic multichip modules and fiber arrays, semiconductor optical amplifiers, fiber-optic gyroscopes, optical interconnects for computer backplanes, asynchronous transfer mode (ATM) switches, all optical switches, and optical modulator arrays.

Our mount geometries with on-board heaters allow rapid attachment of not only the fiber but other components as well. Using solders with different melting temperatures and attaching components farthest from heaters first allow sequential mounting of several components on the same silicon mount without melting solder and disturbing the alignment of previously attached components. Since many components do not require submicrometer alignment, we envision that an automated system could place and solder them onto the mounts in only a few seconds.

On-board heaters can be used in applications other than packaging laser diodes. For example, we are designing a longer mount with heaters at each end to pigtail both ends of a semiconductor optical amplifier. We are also investigating geometries compatible with high-speed applications in which on-board transmission lines will be needed to provide sufficient electrical bandwidth for the very high-speed optoelectronic devices.

For further information contact Michael Pocha (510) 422-8664.

Chromosome-Specific DNA Probes for the Mouse

We have developed DNA reagents, or probes, that color or "paint" chromosomes of the laboratory mouse to make them instantly identifiable. Chromosomes are made up of complex folded strands of DNA that contain the genetic information (genes) inside each cell of an organism. Our DNA

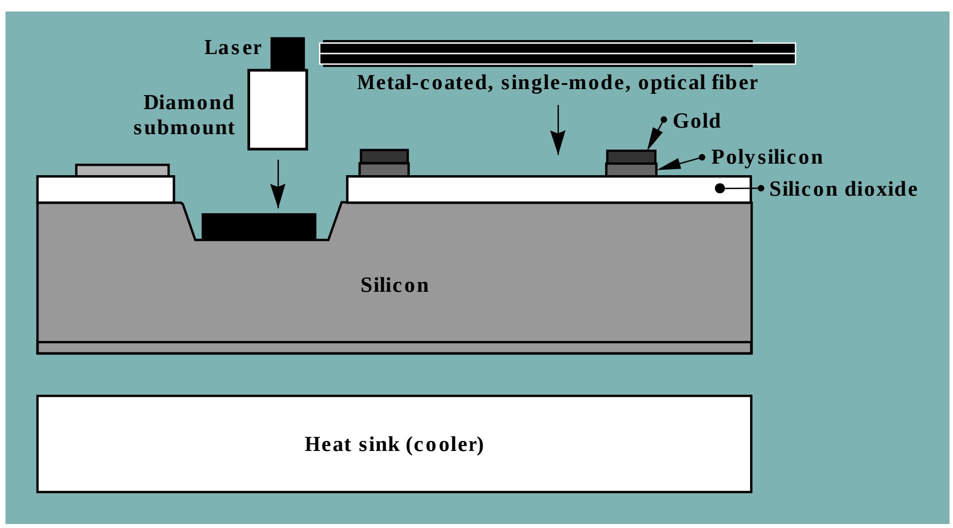


Figure 6. Cross section of a mount showing precision-etched well for laser diode to help vertically align the optical axis.

probes can clearly and distinctly identify one or more of the 20 pairs of chromosomes that are normally found in mouse cells. Figure 7 shows painted mouse chromosomes and a similar cell stained by the old method of chemical staining or banding. Painting clearly identifies eight of the 40 chromosomes, permitting several chromosomes from each cell to be rapidly and distinctly identified, even by a novice investigator. Identifying them by the old method is difficult, even for someone highly trained, because of the similarity in size of chromosomes from the mouse.

Each probe is a mixture of thousands of different DNA sequences, each present in thousands of copies. The probes are mixed in solution and placed on a microscope slide over the area to be stained so that the probes anneal, or stick, to the target chromosomes. For painting to be specific to a single chromosome type, all the DNA in a probe must be derived from only that designated chromosome.

Painting probes are commonly used to detect chromosome rearrangements, and this method is more than 60 times faster than the standard chemical staining or banding method. Painted chromosomes are so simple to analyze that we have taught this method to new people in 2 hours. With chemical staining, highly skilled personnel must be employed. Thus, when cost and speed are both considered, painting is up to 200 times more efficient than banding.

The DNA probes we developed for the mouse have numerous applications, many of which relate to cancer and birth defects.

Toxicology. We developed our probes to apply chromosome painting to toxicology. We are using them to evaluate two cancer-causing chemicals found in food and will soon evaluate two more cancer-causing chemicals found in drinking water. We are also painting cells from mice exposed to ionizing radiation, which also causes cancer. For each study, we screen cells like those in Figure 7 for rearrangements between painted and unpainted chromosomes. Rearranged chromosomes appear bicolored, for example, red at one end and yellow at the other.

These probes make it easy to detect a class of chromosome rearrangements called translocations. Unlike other rearrangements, translocations are stable through cell division; thus, their frequency does not diminish with time, they accumulate for as long as exposure to chemicals or radiation continues, and they persist after exposure terminates. Translocations do not always change the length of a chromosome and thus are difficult to detect. As a result, before the advent of painting, toxicologists performing chromosome analyses generally did not consider translocations. Virtually all humans experience long-term adverse environmental exposure—DNA-damaging chemicals are found in cooked food, diesel exhaust, and some drinking water, to name just a few sources. Natural background radiation is also ubiquitous; one example is radon. Until now, the understanding of how chronic exposure to these and other agents affects human health has been limited. These mouse-painting probes permit the development of an animal model to test the effects of these exposures.

Birth Defects. DNA probes for the mouse will also aid studies of factors that cause sperm to have the wrong number of chromosomes, which leads to birth defects.

(a) (b)

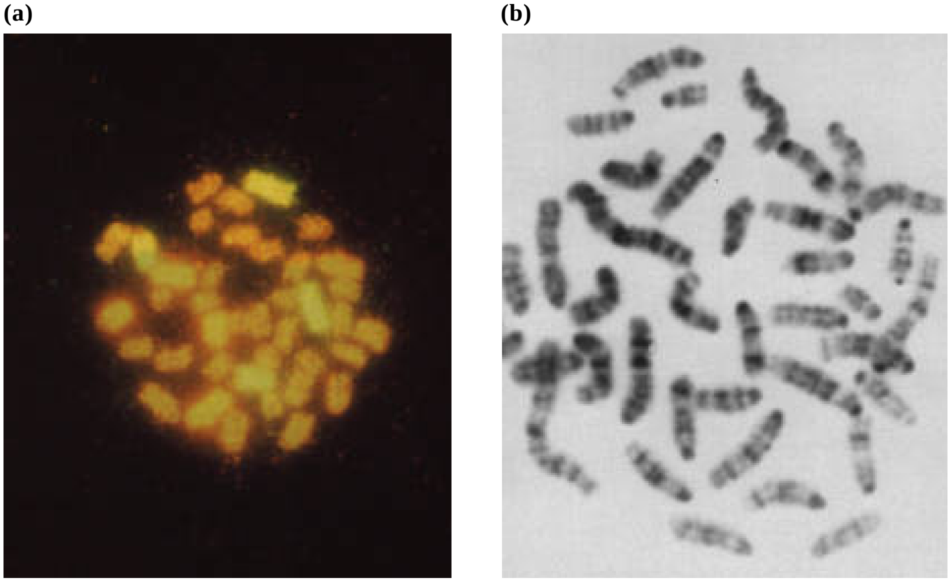


Figure 7. (a) Mouse chromosomes, from a single cell, painted with DNA probes for chromosomes 2 and 8 (red) and chromosomes 1 and 3 (yellow). These chromosomes are distinguished from the others by their color. (b) Mouse chromosomes from a single cell stained by the chemical staining or banding method. The black and white bands are used to distinguish one chromosome from another.

Tumor Research. Tumor cells typically have alterations in chromosome number and size, and these abnormalities are notoriously difficult to evaluate with standard banding methods. Chromosome painting can be used to solve this important problem.

Mouse Genome Project. The goals of the mouse genome project include identifying, locating, and characterizing each of the 50,000 to 100,000 genes in the mouse. More is known about the genetics of the mouse than any mammal except the human, and discoveries in the mouse frequently lead to an improved understanding of human biology. Genes found in one species frequently have a counterpart in the other, and the identification of a gene in the mouse greatly simplifies the process of locating the corresponding human gene. Our probes have been made available to one of the leading laboratories working on this project.

Genetic Research. Gene mapping, or locating a gene on a chromosome, is frequently an important step in the process of obtaining and cloning a new gene. We have used our probes to map a gene onto a mouse chromosome by performing dual-color hybridizations. We labeled the DNA for the gene in yellow and DNA for the chromosome painting probe in red. The chromosome bearing the gene was identified by a yellow hybridization signal on an otherwise red chromosome. The simplicity of this method suggests that it will be used more widely by ourselves and others in the future.

Pharmaceutical Research. The most significant potential application of these mouse chromosome painting probes is their use by pharmaceutical companies, which must assure the Food and Drug Administration that new drugs are safe to market. The battery of tests include genetic assays designed to determine whether the compound breaks chromosomes. If it does, it is very unlikely to be approved for clinical use, because chromosome breakage is associated with cancer and birth defects.

In many chromosome breakage assays, mice are given a single exposure to a drug at a much higher dose than people would normally be given, and their chromosomes are examined a day or so later. This exposure method is unrealistic because most drugs are taken by people at low doses over a period of days, weeks, or even years. Indeed, toxicology assays that involve lower, more realistic, doses are also performed on mice. However, testing for chromosome damage as part of these protocols is difficult because a good method of quantifying stable translocations from a large number of cells has been lacking. The tremendous sensitivity of our mouse probes has enabled us to quantify stable genetic damage following chronic exposure at lower doses. Mouse chromosome painting for translocation analysis could be coupled with existing drug testing protocols to provide improved estimates of chromosome damage under realistic exposure scenarios.

The development of chromosome-specific composite DNA probes for the mouse promise a significant impact on human health with long-term benefits. The primary benefits include:

- An improved understanding of how chronic exposure to chemicals and radiation affects human health.
- The genetic testing of potential pharmaceutical drugs at realistic exposure levels.
- An improved ability to use the mouse for mapping and cloning important new genes.
- An improved understanding of the chromosomal changes involved in tumor formation.

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Summary

R&D 100 awards are given for processes and products that the panel of judges considers to promise significant contributions to the quality of life in the United States and throughout the world. Past award winners have indeed improved the ways people do such things as communicate, transact business, spend their leisure time, maintain health, and fight disease. We at Lawrence Livermore National Laboratory are gratified that in the 30-odd years that the award has been given, we have won 50, six of them in the last year alone. These awards signify that the Lab's work has been valuable not only for maintaining national security in the past, when defense research was necessarily the largest single component, but for advancing it now, when the mandates of economic competitiveness—speed, efficiency, and quality—give urgency to our work.