Although the structure implied by the interagency task force concept builds on established activities, and recognizes the pluralism of genome research, it leaves unattended some of the worries already expressed. Specifically, as Leroy Hood of the California Institute of Technology notes: "There is still a strong concern about how DOE spends its funds. The national labs have still not got the required skills in molecular biology, and the issue of peer review has not been settled to the satisfaction of many people."

DOE recently made a commitment to submit all such research to peer review, both intramural as well as extramural. Nevertheless, there is still some skepticism about how well this will work.

The third area of concern is that of funding. A frequently expressed sentiment is that, important though the genome project is, it should not bleed other areas of biology in sustaining itself. In fact, this was often used as an argument for having DOE, not NIH, run the projects.

New money, this was what was required. "The difference between old money and new money is not meaningful in the political context," observes Cook-Deegan. "These projects will be funded as line items in the budget year by year, so long as Congress is persuaded they are valuable. You can't insulate budgets into the future, no matter which agency they are in." Researchers have seen biomedical research funds diverted into the AIDS effort, and the same thing is probably inevitable with the genome projects.

Previous estimates on the overall cost of the genome project have varied from $3 billion to several hundred million, depending on assumptions about advances in technology. The OTA report gives estimates for the first 5 years, which begins at $47 million for the first year and rises steadily to $228 million for year five. Unlike the NRC panel, which projected costs over 15 years, the OTA group argued that uncertainties beyond 5 years were just too great to extrapolate further.

The figure of $47 million is, incidentally, very close to independent, approved budget requests by NIH ($28 million) and DOE ($18.5 million). Both agencies are therefore clearly pushing ahead. One difference is that the prime mover behind the project at DOE, DeLisi, has recently left the agency and is yet to be replaced. Meanwhile at NIH the establishment of the Office of Human Genome Research gives that agency a significant boost. No name has yet surfaced as head of the office, but the choice will be crucial if NIH is to establish itself as the de facto if not actual lead agency. ■ ROGER LEWIN

Advances in Measurement Science

Year after year, physicists measure various quantities with increasing accuracy and see various objects in increasing detail. These advances are vital, because science's understanding of the physical world is necessarily limited by the accuracy with which science can measure that world. The Instrument and Measurement Science Topical Group of the American Physical Society sponsored several symposia at the recent APS March meeting in New Orleans that discussed recent advances in measurement and observation.

A New Standard Volt

A new integrated-circuit device is available that will allow scientists to measure voltage with unprecedented accuracy and free laboratories from sending their voltage standards to the National Bureau of Standards (NBS) to be set. Until now, large research labs have used in-house voltage standards called Weston cells to calibrate their voltage meters, but have had to send the Weston cells to the NBS periodically to be checked against the bureau's standard. The new device, in addition to setting the Weston cells more accurately, is sufficiently easy to use that the labs will no longer need to rely on the NBS to set the Weston cells. Richard Kautz of the NBS in Boulder, Colorado, said industrial laboratories are "clamoring" for the $100,000 device.

The U.S. Legal Volt is defined in terms of the voltage generated when microwave radiation is applied to a Josephson junction, which is a simple electronic device consisting of two layers of a superconducting material separated by an insulating layer. The voltage across the Josephson junction depends very precisely on the frequency of the microwave radiation and, since the radiation's frequency can be determined to great accuracy, this provides a handy definition of the volt.

The normal procedure to fix the voltage standard has been to use one or two Josephson junctions driven by microwaves with a frequency of 10 gigahertz, which produces a reference voltage between 5 and 10 millivolts. The small size of this reference voltage made it very difficult to calibrate precisely the 1.018-volt Weston cells that serve as secondary standard. There is now a way around this problem, Kautz said. He and NBS co-workers Clark Hamilton and Frances Lloyd have used photolithography to etch thousands of Josephson junctions onto a single chip, with the junctions arranged in such a way that their individual voltages combine to give a much larger voltage upon exposure to microwave radiation. In 1985, an array of about 2,000 Josephson junctions turned out reference voltages of more than 1 volt, and Kautz said that now an array with 19,000 Josephson junctions exists that puts out reference voltages up to 10 volts.

Not only does this make it easier to set the 1.018-volt Weston cells, but these arrays make it possible to calibrate and check voltmeters with relative ease. Voltmeters can be checked directly, without the step of calibrating Weston cells. And the voltage of the 19,000-junction chip can be varied continuously between 0.1 volt and 12 to 14 volts, making it possible to test the performance of a voltmeter at different voltages, something that has been much harder before.

Even allowing for the inaccuracies of comparing the Josephson standard with the secondary Weston standard, the new standard allows calibration of Weston cells with a precision of three parts in 10^{10}. This is a factor of 100 better than obtainable with the old standard.

Perhaps best of all, the new voltage standard frees labs from the necessity of sending their secondary standards to the NBS location in Gaithersburg, Maryland, for testing, a procedure that can take a month or more. The NBS sells the 19,000-junction chip for $6,000, and a complete voltage standard can be built for about $100,000, Kautz said. Labs that can afford it will be able to have in-house voltage standards against which to test their Weston cells and voltmeters.

Squeezed Light Muffles Background Noise

When scientists who use laser light in such things as measurement or communications try to improve the precision of their work, they come up against a fundamental limit that has nothing to do with the purity of the light or the accuracy of their machines. The limit stems instead from a "background noise" arising from the quantum mechanical nature of light. Recently, researchers at several labs have successfully circumvented that limit by decreasing the background noise in one part of the light at the expense of increasing the noise in another part, and then performing measurements only on the "quiet" part of the signal.

The need for such quiet light arises in a number of applications. Interferometers, for instance, use the interference between two beams of laser light to measure distances, and quieter light means more sensitive measurements. Astronomers who use interferometers in gravity wave detectors in order to observe such events as supernova explosions already have reached the limit of their precision unless they can get around the background noise of the laser light.

Richard E. Slusher of AT&T Bell Labs in Murray Hill, New Jersey, said several labs, including his, have demonstrated laser light that is more silent than ideal laser light. Such "squeezed light"—so called because the noise is squeezed out of one part into another—has been generated that has only one-half to one-third the background noise of normal light, he said, and a reduction of at least 90% should be possible.

The noise these researchers are muffling is tiny, random fluctuations in the oscillating electromagnetic field that is laser light. Electromagnetic radiation is wavelike, and if laser light is pictured as a wave moving across the surface of a pond, then the noise is analogous to the little surface disturbances all along the wave. Even if no wave exists, the surface of the pond will not be completely flat—tiny, random movements will appear here and there—and similarly there are quantum fluctuations even in the absence of light. Just as the pond's surface fluctuations will prevent an exact measurement of the wave, quantum fluctuations introduce an uncertainty into laser light.

Researchers have found that this uncertainty can be manipulated. In the pond analogy, the surface fluctuations along one part of the wave can be smoothed out at the expense of increasing the fluctuations at another part. To do this, the laser light is put in a reflecting cavity where it bounces back and forth between two mirrors. In the cavity is a nonlinear optical material—a gaseous, liquid, or solid substance whose optical properties vary depending on the amount of light passing through it. The apparatus includes a second laser shining on this material, so that this laser modifies the passage of the light from the first.

In this way, the noise of certain parts of the laser light is increased, while it is quieted in other parts. By looking at just the part of the light where the noise has been decreased, researchers have reduced the background noise by a factor of 2 to 3, Slusher said.

The ultimate payoff should be greatly increased precision in many laser applications. Slusher said that two types of interferometers already have shown increased sensitivity by using squeezed light. Possible future applications include spectroscopy, where background noise limits accuracy, and optical communications and computing, where background noise limits have not yet been reached.

Novel Types of Microscopes

Ever since Anton van Leeuwenhoek gazed through the lenses of the first microscope some three centuries ago, scientists have searched for ways to see things that are invisible to the naked eye. When visible light proved too limiting, microscopists turned to other forms of radiation, such as x-rays, and even fundamental particles such as electrons. The past few years have seen a tremendous flowering of microscopy as scientists have developed several novel ways of "seeing" samples, and one symposium at the annual meeting of the APS was devoted to new types of microscopes.

The best known of this new generation of microscopes is the scanning tunneling microscope, or STM. The STM traces out a topographic map of a microscopic sample in much the same way as a blind person uses a cane to detect the dips and rises in the ground in front of him. A tiny metal tip is played across the surface of the sample at a constant height of a few angstroms, and, by recording the raising and lowering of the tip, the STM generates an image of the surface's hills and valleys. The machine keeps the tip at a constant distance from the surface by placing a voltage between the tip and the sample and observing the resulting quantum tunneling current. This current depends sensitively on the distance between tip and surface; keeping the current constant assures the distance remains constant.

Recently, the STM has been used to image biological molecules submerged in water, which is an important step toward viewing such molecules reacting with each other in their natural state. Stuart Lindsay of the Arizona State University physics department reported he has been able to form images of DNA molecules packed on a gold substrate under water. Although he does not get atomic resolution, he said that the resolution is good enough to follow the contours of the molecule. Since a single strand of DNA consists of just four basic molecules lined up, it should be possible to sequence the DNA by looking at how it bends, Lindsay said. "I think we can start doing some biology with this thing," he said.

H. Kumar Wickramasinghe of the IBM Watson Research Center in Yorktown Heights, New York, described a variation on the STM that can map various physical and electromagnetic properties of a sample. This force microscope uses a tiny tip that is vibrated at near its resonance frequency. As the tip approaches the sample, the force of the interaction between tip and sample alters the resonance frequency of the tip. A sensitive mechanism detects these changes and moves the tip up or down to keep it at a constant distance from the surface.

Using different types of tips, Wickramasinghe is able to map various properties of the surface. With an alternating current through the tip, he can measure electrostatic forces between the surface and the probe, mapping the charge distribution along the surface. With a magnetic tip he images magnetic properties of a sample. And with a thermal probe coupled with a heat source that warms the surface, he determines the thermal absorption properties of the sample. It is, he said, "the world's smallest thermometer." Resolution is about 1000 angstroms, compared to just a few for the STM.

In addition to this family of scanning probe microscopes, new ways of using old-fashioned visible light have been developed. Standard light microscopes cannot make out details any smaller than the wavelength of visible light, which is between 4000 and 7500 A. However, a recently developed technique called near-field optical microscopy or optical stethoscopy achieves a resolution of one-tenth of a wavelength. Michael Isaacson of Cornell University said he shines a bright light through a tiny (about 500 A) hole in an opaque screen and then through the sample, detecting the light that is transmitted through the sample. The name "optical stethoscopy" refers to the standard doctor's stethoscope whose size is only a fraction of the wavelength of the bodily sounds it detects. The resolution that optical stethoscopy gives is nearly as good as an electron microscope, and it does not damage the sample and can be used in air, Isaacson said. Since it can be used in water, it may be useful in seeing details in biological samples in their natural environment.

The quest for novel types of microscopes is driven not merely by the desire to see smaller and smaller details. James Matey of the Sarnoff Research Center, who organized the session on microscopy at the meeting, noted the different devices each give different information about a sample, and one may be able to see details that another couldn't. ■ ROBERT POOL

Robert Pool is a writer based in Beaumont, Texas.