laboratory procedures." They also had to bring in the informaticists to produce a system for tracking and integrating the vast amount of data produced.

The genome community is also pleased, partly because the new map fills in some serious gaps. Even though researchers are producing STS-based maps of individual chromosomes, together these account for only about one third of the genome, says Eric Green of the NCHGR, whose team is mapping chromosome 7. The new map, he notes, "is a good start on the rest of the genome, which everyone was afraid would be incompletely covered."

Researchers are also more confident that the markers are arranged correctly. "Previous maps were very good at having clone coverage," says molecular geneticist David Cox of Stanford University. "We had YACs and some idea of how these YACs went together, but we weren't so comfortable about the order of the markers." Here, he adds, they are "really delineating the position of these unique markers and delineating them in a way that is easy to use."

The STS sequences, after all, allow the map to be made available to anyone who wants to use it, because they can be maintained as a database rather than as clones in a freezer. What's more, says Olson, "this whole map, because it is STS-based, can be put up on the World Wide Web." In fact, the Whitehead team has been putting the data on the Web from the start (http://www-genome.wi.mit.edu). "They've been very good about that, and they should be commended," says Peter Goodfellow of the University of Cambridge, U.K., who provided the cell lines used to make the radiation hybrid map. In fact, people trying to find disease or other genes were using the data even before the map coalesced. Says Collins, "You can't find anyone who is hunting genes who doesn't know the Whitehead World Wide Web address by heart."

And the map should remain useful even as genome technology changes. Because STS markers are sequences, they can be used to orient gene searchers or sequencers no matter what type of DNA clones they are working with. "The neat thing about STSs is the universality of the landmarks. You can move quickly from one mapping resource to another," Green says. That's important, because even though YACs have proved very useful for map-building, they are not likely to be used for the eventual sequencing effort, because the DNA they contain sometimes gets rearranged so that it doesn't accurately reflect what's in the genome. Researchers will instead use smaller, more stable forms of cloned DNA such as that made in cosmids or bacterial artificial chromosomes.

For all its advantages, Collins and others, including the Whitehead team members themselves, note that the map does not yet provide dense enough coverage of the genome to finish the project. The average distance between the markers is now about 200 kilobases, and Collins says "to finish [sequencing] we really need [marker] spacing of 100 kilobases, or better yet 50 or 30 kilobases." Lander predicts, however, that the combined effort of his lab and others ought to bring the project up to the 100-kilobase target sometime next year. The genome mappers, it seems, will soon have the detailed map they need to guide them to the end of their long and winding road.

–Jean Marx

MICROSCOPY

Making a New Ruler for the Nanoworld

GAITHERSBURG, MD—A good machinist needs precise measuring tools, and so do craftspeople whose wares are very, very small. The etched circuits on a computer chip, for example, won't function well unless their height, width, and smoothness fall within tight tolerances. And those tolerances are getting even tighter, as devices shrink to the nanometer (a billionth of a meter) scale. But the rulers used to measure these minute features and the distances between them aren't keeping pace. "We're getting to a situation where we have a capability to manufacture smaller dimensions than we can accurately measure and certify," says James Greed, president of VLSI Standards Inc., a company in San Jose, California, that makes grids used to calibrate a cutting-edge measuring device, the scanning tunneling microscope (STM).

Last week, however, researchers at the National Institute of Standards and Technology (NIST) in Gaithersburg unveiled a ruler that can measure the width of a circuit feature to within a few tens of nanometers and tell you how far that feature is from another one, which can be millions of nanometers away. That's comparable to combining a microscope that can size up a ladybird on one hilltop with a telescope that can measure the distance to the next hilltop with almost the same precision. The device, called the "molecular measuring machine," or M^3, combines a probe that senses atomic contours with a precise system for tracking that probe. In the nanoworld, says metrologist Joe Griffith of AT&T Bell Labs in Murray Hill, New Jersey, "there is no machine in existence now that has higher precision over those distances."

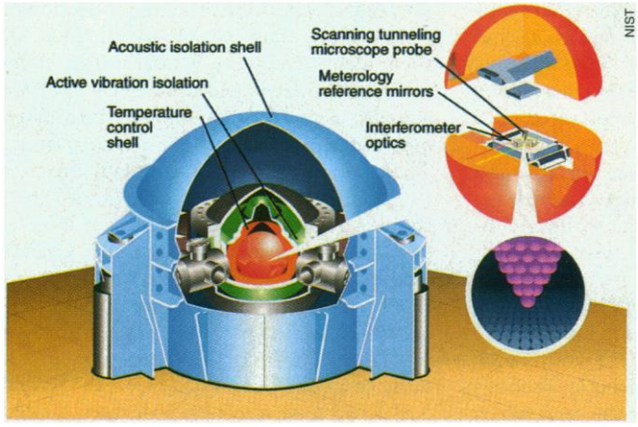
The present nanochampion, the STM, works by moving a tip over a sample, maintaining a slight but constant electrical current between the tip and the sample surface. This constancy requires the tip to move up and down as it encounters atomic hills and valleys, allowing it to pick out and measure atomic-scale features. But the microscope isn't designed to measure precise distances between such features when they are farther than 100 micrometers apart.

So physicist Clayton Teague of NIST designed a machine that combines an STM with a technique for tracking the position of the STM tip over relatively vast distances: laser interferometry. By training a laser on the STM tip as it moves across a vaster landscape, M^3 can measure small features and indicate just how far apart those features are.

To date, M^3 can measure the distance between points 1 millimeter apart to within 20 to 40 nanometers. Teague's team is now shooting for an accuracy of one nanometer over 50 millimeters. Alignment problems between the interferometer and the STM, and errors that arise because mirrors that channel the laser don't move exactly in sync with the STM tip, are currently preventing this. The researchers believe they can solve these problems within 2 to 3 years.

Still, the M^3 can already do something a standard STM can't: measure the accuracy of the 600-micrometer grids, divided into 1.8 micrometer squares, that are used by semiconductor manufacturers to calibrate their own STMs and other microscopes. And that's no small achievement.

–Jocelyn Kaiser



Multipurpose tool. The "molecular measuring machine" can measure atom-scale features and vast distances between them.