nizer Gina Etheredge, a clinical epidemiologist at Tulane University in New Orleans. She eventually recruited outside talent: Christine Bachrach, a demographer at the National Institute of Child Health and Human Development in Bethesda, Maryland. Bachrach said in a phone interview that researchers in her field routinely collect data with a plan to make them public. In Atlanta, she argued that public archiving "reinforces open scientific inquiry," promotes "timely use of information," encourages people to test new analytical methods and ideas, discourages repetition, and creates data sets that can be used for training. Bachrach warned the epidemiologists that, if someone does make a demand through the Freedom of Information Act, "your life is going to be a lot easier if you have put your data in a public archive."

Epidemiologist Manning Feinlieb of Johns Hopkins wasn't convinced. Feinlieb, like Samet, noted that a requirement for more data sharing is a "done deal," but he explained why many of his peers would prefer to share data in other ways. For one, he said, it's "too much trouble" to label and document every scrap of data that is collected in a way that would make sense to a stranger. Nor do epidemiologists want to give away their intellectual property: "They don't want to be scooped" on their work, he said, particularly if they're just beginning to exploit a database that's taken years to build. They're also leery of getting ensnared in long-running squabbles of minor significance—"a big pain"—which they see as more likely to happen if data are dumped onto the Internet. Mandatory data sharing also may mean that more money and time must be spent on paperwork, he argued. And although Feinlieb agreed that public archives would be useful in training Ph.D. candidates, he worried that they might also spawn more secondary analysis and less original field research.

Feinlieb also touched on a related subject—the privacy of medical records—that struck a nerve. Although everyone agrees that personal information should be kept anonymous and encrypted, he said, some panels that review and monitor clinical and epidemiological studies are requiring that individuals who join a study be warned that their privacy cannot be guaranteed. Such warnings and other requests for individual approval could become standard soon: The Department of Health and Human Services has published draft regulations, expected in final form next month, that may require individual consent before data from medical files can be screened and rendered anonymous for use in research.

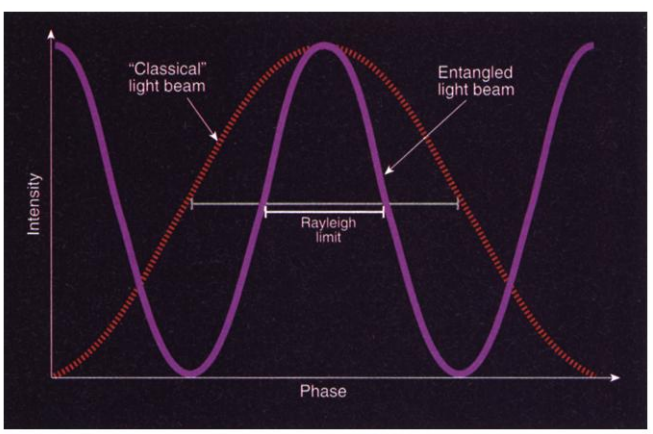
Imagine, said Etheredge, trying to recruit a subject and saying: "Tell me everything about yourself, and I promise to keep it secret—for a while. And then I'll put it on the Internet." Vickie Mays, an epidemiologist at the University of California, Los Angeles, who studies HIV and sexual behavior among African-American gay men, warned: "We're really going to regret" adopting mandatory data release and consent forms with scary warnings about privacy loss.

Observing that information technology is changing everyone's life, Samet said that epidemiologists may experience some especially "painful lessons." **–ELIOT MARSHALL**

PHYSICS

Yoked Photons Break The Light Barrier

It seems to flout the laws of physics, but scientists have found a loophole in the rules that govern diffraction. By exploiting entanglement, the quintessential "spooky" phenomenon in quantum mechanics, physicists at the Jet Propulsion Laboratory in Pasadena, California, have come up with a method for drawing tiny features on a microchip that would be impossible according to the classical theory of light. If it proves practical (always a big "if" where quantum effects are concerned), the technique—described in the 25 September issue of *Physical Review Letters*—could enable chip designers to circumvent the so-called Rayleigh limit, a physical barrier that plagues chip manufacturers much as the sound barrier used to bedevil aerospace engineers. As team member Jonathan Dowling puts it, "Murphy's Law has been repealed, at least in theory."



Sharper image. By halving photons' effective wavelengths, quantum entanglement may enable chipmakers to etch much smaller transistors.

If so, the reprieve comes in the nick of time. Although computer chips are growing ever smaller and more powerful—doubling in speed and halving in cost every 18 months or so—it's getting harder and harder to manufacture those chips. One reason is that most chips are made by photolithography, a process in which the manufacturer shines light through a patterned "mask" onto a chip slathered with a light-sensitive coating called photoresist. The light toughens the coating, allowing the manufacturer to etch away unexposed parts of the chip.

Unfortunately, as microcircuitry grows ever finer, chipmakers run smack into the Rayleigh limit, which dictates that the smallest feature a light beam can write on a chip is half the wavelength of the light. To etch smaller and smaller transistors, manufacturers must resort to shorter and shorter wavelengths—moving from red to blue to ultraviolet to extreme ultraviolet to x-rays. Short wavelengths, however, are both hard to control and tough on chips. The Rayleigh limit ensures that manufacturers pay dearly for smaller transistors.

To smash the barrier, Dowling and colleagues imagine "entangling" two photons so that when they are shot at a beam splitter from opposite directions, they will always wind up moving together in lockstep. Thus yoked, the photons will remain inseparable until they strike a target—in this case, the chip-in-progress. "This strange quantum-mechanical disembodiment allows them to conspire to arrive at the same atom at the same time," Dowling says.

If the entangled photons are made out of red light, the optics will bend them just as they bend red light, Dowling says. But when the two photons hit the target together, their combined energy might equal that of a single ultraviolet photon—a particle with a shorter wavelength. "It acts like UV for all intents and purposes," says Dowling. In fact, if you set up an interferometer, the interference pattern would look like one for ultraviolet photons rather than red ones: The fringes are twice as fine. That should make it possible to etch transistors twice as finely as the Rayleigh limit allows, Dowling says, provided that chipmakers can find photoresist that still hardens well when struck by photons with twice the usual angular momentum.

"Dowling had a very brilliant idea to use this for lithography," says Yan-hua Shih, an experimentalist at the University of Maryland, Baltimore County, who is trying to put the scheme into effect. Photoresist is his current stumbling block, he says. "Two-photon absorbing materials are not very sensitive; we're looking for a much better material."

Other scientists, however, think it will

take more than tinkering to rout Rayleigh. Paul Kwiat, a physicist at Los Alamos National Laboratory in New Mexico, suspects that the difficulty of creating bright beams of entangled light will limit the usefulness of the technique. "But it's good to have people think about these things," he adds.

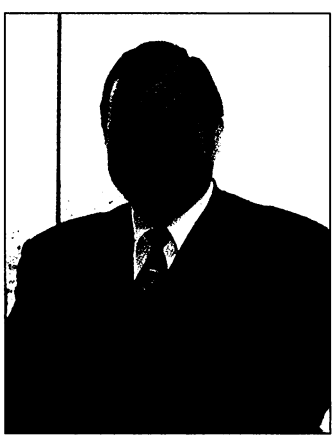
–CHARLES SEIFE

POPULATION GENETICS

Estonia Prepares for National DNA Database

TARTU, ESTONIA—If a nation's most valuable resource is its people, then how precious are its people's genes? For this tiny Baltic state, the opening bid lies somewhere between $100 million and $150 million. That's how much money Estonia expects to raise for a project, set to begin next year, that would compile DNA profiles and health information on 75% of the country's 1.4 million citizens. Officials hope that the database will not only allow researchers to track down disease genes and improve health care but also boost Estonia's budding biotechnology sector.

Last month the Estonian parliament began considering a bill to regulate the collection of genetic information and database research, and observers predict quick passage. "I expect the final approval before Christmas," says Minister of Social Affairs Eiki Nestor. The next step would be a $1 million test of the concept on 10,000 volunteers.



Booster. Andres Metspalu sees databases as a boon to research.

CREDIT: TARTU UNIVERSITY

With a pilot project possibly only a few months away, scientists held a meeting here last month for a global audience of colleagues and venture capitalists. "At this point we are interested in ideas and perspectives," says Jaanus Pikani, chair of the Estonian Genome Foundation (EGF), which began organizing the project last year (*Science*, 12 November 1999, p. 1262). Prospective investors who attended the meeting think that Estonia should have little trouble finding backers. "Once a legal structure is in place," says Todd Morrill of Venture Merchant Group in Walnut Creek, California, "success [will depend] on getting the pilot project under way."

Estonia hopes to chart a course different from that of a similar, but controversial, Icelandic project (*Science*, 30 October 1998, p. 859). In January, Reykjavík-based deCODE Genetics received an exclusive license to run Iceland's health-sector database for 12 years, a proprietary lock on the country's health records that allowed deCODE to raise nearly $160 million in a stock offering last July. Critics have complained, however, that the project requires individuals to opt out rather than making the company obtain informed consent ahead of time for health profiles. DeCODE is now negotiating the issue with the Icelandic Medical Association.

Another issue involves the use of the databases. The information in the Icelandic project will be maintained anonymously, meaning that donors will not have access to their own information. By contrast, data and DNA samples in the Estonian project will be identifiable through a coded system. But it will belong to a nonprofit state-controlled foundation, and donors must give their informed consent for its use. If donors change their minds and want out of the database, their samples can be destroyed.

"Valuable lessons from the well-known Icelandic project have been learned," says University of Montreal law professor Bartha Maria Knoppers, chair of the Human Genome Organization's International Ethics Committee. She believes that the Estonian effort is "the more responsible approach, because it allows citizens to see what research is done with the information they donate. People want to know." She says it's also important that the project educate the public on the information that is available after health data and DNA are analyzed.

Estonia's decision to make the genetic data accessible to donors themselves means that donors someday may be able to take preventive measures against diseases to which their DNA places them at risk, or receive medical treatments tailored to genetic deficiencies. "The potential for a return for the health care system is substantial," says Thomas Caskey, CEO of Cogene BioTech Ventures in Houston, Texas, and former president of the Merck Genome Research Institute.

Participants in the pilot project will fill out extensive health questionnaires and give blood for genotyping. If all goes well, says Pikani, "we can move on to the major effort within a year." Genotyping would be done on 1 million people over 5 years, using single-nucleotide polymorphism markers, and medical information would be updated continually.

That prospect makes disease gene–hunters salivate. Topping the most wanted list are genes that contribute to major killers such as diabetes, heart disease, and Alzheimer's. The large sample size may allow scientists to home in on genes involved in diseases triggered by the interplay of genetics and the environment, says Max Baur, a medical statistician at Bonn University. "The success of the Estonian project," he says, "hinges on high-quality medical data, good genotyping, and good data handling."

Companies are now talking with the Estonian government about how they might support—and profit from—a government-owned venture. Although the database will belong to a nonprofit foundation formed by the EGF and the Ministry of Health, a for-profit subsidiary will have the right to sell access and information. "I believe there will be interest, but investors will have to know exactly what they [are] buy[ing] into," says Greg Lennon of Veragene, a genomics consulting firm in Maryland. Estonia plans to strike limited, nonexclusive deals that would, for example, allow a company to mine the database for clues to one or more diseases and receive intellectual property rights to treatments derived from its research. Access to data would be given to public researchers at no cost or for a handling fee. Estonian Prime Minister Maart Laar, a big supporter, is aiming for a balance between private and public involvement. "The important thing is that ownership [be] properly regulated," he says.

Estonian scientists predict that the project will be a boon to the country's embryonic biotech industry. Much of the massive genotyping, for instance, must be done in Estonia, as DNA samples cannot be exported without a special license from the Ministry of Health and Social Affairs. At the same time, "the database will boost research and make it possible for local scientists to attract funds from outside," says Andres Metspalu, head of molecular diagnostics at Tartu University, who came up with the initial concept.

The idea of collecting and storing a nation's health data and genetic profiles has sparked surprisingly little discussion in Estonia. "It has been hard to have a debate with no real opposition around," observes science editor Tiit Kändler of *The Estonian Daily*. One reason, he and others suggest, is the country's eagerness to become a player in the world economy and to wipe away all vestiges of its Soviet past. There is much talk that the country needs to find its own Nokia, the phenomenally successful telecommunications giant that lifted the Finnish economy. Says Andrus Kaldalu of Tartu's Asper Biotech, "There is a feeling that biotech could be it."

–LONE FRANK

Lone Frank is a writer in Copenhagen, Denmark.