United States to fund the project, which would take an estimated 5 years and cost between $50 million and $90 million.

Malaria researchers say that sequencing the mosquito's genome—which, at 260 million base pairs, is about the size of one large human chromosome—should lead to a better understanding of interactions between the insect and the parasite. "Having the genome sequence would be fantastic," says molecular entomologist Robert Saunders of the University of Dundee in the United Kingdom.

Malaria kills more than 1 million people worldwide each year, and an estimated 86% of those deaths occur in Africa, where it is the second leading cause of mortality after AIDS (*Science*, 14 May, p. 1101). The disease is caused by the protozoan parasite *Plasmodium*, which infects red blood cells and causes them to burst when progeny parasites are released. Since 1995, an international team of researchers has been sequencing the genome of *Plasmodium falciparum*, the species responsible for the most serious form of malaria. The proposed *Anopheles* sequencing project would complement this work.

To enter its human host, *Plasmodium* needs the help of the *Anopheles* mosquito, which injects the parasite into the host's bloodstream while it ingests blood. Some strains of *Anopheles*, however, are resistant to the parasite, mounting an immune response that kills off the protozoan before it can mature. What some researchers call the "Holy Grail" of malaria control would be to create a genetically modified mosquito incapable of transmitting *Plasmodium*, an aim that would be greatly aided by knowing the sequence of the mosquito's genome.

Although the project's supporters have yet to raise the funding, they were encouraged by the fact that the meeting was attended by emissaries from major genome research agencies as well as leading gene sequencing centers. "I'm not really worried" about getting the money, says Fotis Kafatos, director of the European Molecular Biology Laboratory (EMBL) in Heidelberg, Germany, who initiated the project together with *Anopheles* expert Frank Collins of the University of Notre Dame in Indiana. The participants included representatives of NIAID—the infectious disease institute of the U.S. National Institutes of Health (NIH)—and the Wellcome Trust, Britain's mammoth biomedical research charity. Also attending were gene sequencing jockeys from the Wellcome Trust–funded Sanger Centre near Cambridge, France's Genoscope, and The Institute for Genomic Research in the United States.

Kafatos points out that a lot of research has already been done on the *Anopheles* genome, including genetic mapping and preliminary sequencing at Genoscope, EMBL, the University of Iowa, and other centers. "We have really already started, and as the money comes in that will determine how fast we go," Kafatos says. NIH has already said it will consider grants of up to $1.5 million per year for at least the first 2 years of the project. Wellcome director Michael Dexter told *Science* that although there is "excitement" at the trust about the proposal, funding decisions will have to wait until a replacement is found for outgoing Sanger director John Sulston.

Anopheles researchers argue that recent advances in efforts to create transgenic mosquitoes have added urgency to the plan. Mosquitoes have long proved awkward to modify genetically, in part because their eggs are hard and difficult to inject with foreign DNA. Last year, however, two research groups, one led by Collins and the other by Anthony James of the University of California, Irvine, succeeded in injecting foreign genes into embryos of *Aedes aegypti*, the mosquito vector for the viruses that cause yellow fever and dengue fever. This raised the hope that *Anopheles* might be similarly modified. "People will say that it's science fiction until the day you do it," comments Morel. "The human genome is already being sequenced, and so is *Plasmodium*. Once we have *Anopheles*, we will have all three actors in the malaria cycle." —MICHAEL BALTER

IMAGING

X-ray Crystallography Without Crystals

For much of his career, David Sayre has been seeing spots and doing everything he can to get rid of them. Sayre, an x-ray crystallographer now retired from IBM, makes images of materials using x-rays, which can reveal fine detail down to the arrangement of atoms in a molecule. But this ultrahigh-resolution imaging technique only works on crystals, in which many copies of a molecule are lined up in a regular array. When x-rays are targeted at such a crystal, they bounce off the atoms and interact to produce a set of diffraction spots, which researchers can mathematically reconstruct into an image of the molecule. Now Sayre and colleagues in the United States and the United Kingdom have done away with the need to form molecules into a crystal and diffract x-rays into spots. In this week's issue of *Nature* they report creating the first diffraction image from a noncrystalline sample, a feat that could revolutionize the imaging of the vast array of materials that cannot be crystallized, providing ultrahigh-resolution images of everything from cells to individual protein molecules.

"It's really a brilliant experimental

CONGRESS

U.S. Science Advocate George Brown Dies

Scientists have lost one of their leading advocates in Congress. Representative George E. Brown Jr. (D–CA), the oldest member of the House of Representatives and a leader of its Science Committee, died 15 July of an infection following open heart surgery. The physicist-turned-politician was 79.

Brown studied physics and engineering at the University of California, Los Angeles, in the 1940s and entered politics in 1954, winning a congressional seat in 1962 which he held ever since, except for a 2-year hiatus after losing a Senate race in 1970. He joined the House Science Committee in 1965, rising to chair in 1990. After Republicans won control of the House in 1994, Brown became the committee's senior Democrat. That post is now expected to pass to Representative Ralph Hall (D–TX), a Science Committee veteran and a former chair of its space science subcommittee. Observers say Hall's ascension is not likely to change the committee's direction.

One of the few House members with scientific training, Brown was an outspoken and often wry advocate for government spending on basic research and a booster of crewed and uncrewed space exploration. He was also a force behind the 1976 strengthening of the White House science adviser's office and the 1972 creation of Congress's Office of Technology Assessment, which the Republican leadership disbanded in 1995.

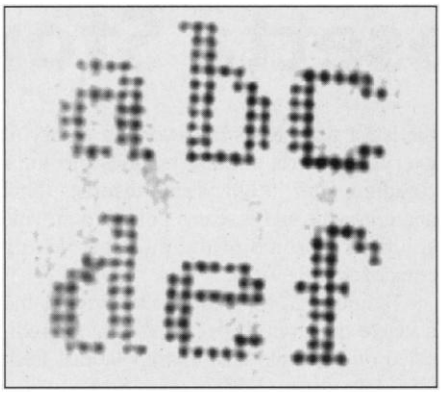
Brown was Congress's "wise man of science," says Rita Colwell, head of the National Science Foundation. "Even after sitting through hundreds of presentations by researchers, George never lost a genuine delight in hearing of new breakthroughs," recalls Representative F. James Sensenbrenner Jr. (R–WI), the current chair of the Science Committee. D. Allan Bromley, dean of engineering at Yale University and a science adviser to several Republican presidents, says Brown "will be very much missed." —DAVID MALAKOFF achievement," says Eaton Lattman, an x-ray crystallographer at The Johns Hopkins University in Baltimore. Sayre and his colleagues—Jianwei Miao and Janos Kirz at the State University of New York (SUNY), Stony Brook, and Pambos Charalambous at Kings College in London—used their new technique to produce images of an array of tiny gold dots with a resolution of 75 nanometers. That doesn't match the resolution available from crystalline samples, which can be hundreds of times finer, but it's already better than the best optical microscopes. And Miao told *Science* the team has already improved the resolution to about 65 nanometers and expects to do considerably better.

The technique is an outgrowth of conventional x-ray diffraction, which requires knowing two properties of the diffracted x-rays to make an image. The first is the intensity of the diffraction spots—easily determined with a photon counter. The second property is the relative timing of the waveforms of the x-rays, known as their phase. Figuring out the phase is more troublesome, traditionally requiring researchers to compare the diffraction pattern from a pure crystal with one from a similar crystal in which heavy metal atoms substitute for some components of the crystal. The signals from the metal atoms provide reference points from which the phase of the other x-rays can be worked out.

That's all well and good for working with orderly crystals. But with noncrystalline samples, x-rays don't produce the clear diffraction patterns studded with sharp and isolated spots. Instead, they generate splotchy patterns. The key is that in these splotches, the intensity varies smoothly from one pixel in the diffraction image to the next in a manner related to the phase. In the early 1980s, other researchers suggested that it might be possible to use that information to work out the phase of x-rays diffracted from such samples. So, the SUNY–Kings College team created an algorithm that is designed to extract an image from this fuzzy diffraction data by first making a wild guess, assessing its accuracy, making adjustments, and then repeatedly trying again.

The program starts with the intensity data in the splotchy diffraction pattern and combines this with random phase information generated by the computer to churn out an approximate image of the target responsible for the diffraction. It then adjusts this image by comparing it to a set of known mathematical constraints. Next, it reconverts the revised image back into the corresponding diffraction intensity data and phase information. It combines the new phase information with the original intensity data to generate a new picture. Repeating this cycle about 1000 times, the computer homes in on a final image.

The new algorithm is designed to work with low-energy, "soft" x-rays, which are ideal for imaging biological materials. Such samples vary greatly in the amount of soft x-ray photons they diffract at different wavelengths, says Ian Robinson, a physicist at the University of Illinois, Urbana-Champaign. So, researchers should be able to create high-resolution, high-contrast composite images of cells by combining separate images taken at different soft x-ray wavelengths, he says. Down the road, adds Louise Johnson, a biochemist at Oxford University, the technique could make it possible to image single protein molecules, eliminating the need to crystallize them first, often a major hurdle for protein crystallographers. But generating enough diffraction data from a single molecule will require new x-ray sources billions of times brighter than today's.



Letter perfect. Micrometer-sized letters, formed from gold dots imaged with x-ray diffraction.

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–ROBERT F. SERVICE

DATA DISCLOSURE

Congress Votes Down Delay in Access Law

Congress last week rejected a proposal to overturn a controversial new law that would force the release of scientific data from federally funded research. Universities and other scientific groups concerned about the impact of the legislation are now shifting their focus to a statement due out shortly from the White House Office of Management and Budget (OMB) on how it plans to implement the law, which is expected to go into effect this fall.

The law requires "all data" funded by federal grants to be subject to the Freedom of Information Act (FOIA), which gives the public access to government documents. It was tucked into last fall's omnibus appropriations bill by Senator Richard Shelby (R–AL), who argued that the raw data underlying regulations—such as recent new air pollution rules—should be publicly available. Scientific and university organizations have weighed in heavily against it, saying the new law would harass researchers, violate confidentiality agreements, and hinder the conduct of science (*Science*, 12 February, p. 914).

Legislators who had hoped to block the law suffered a major blow on 13 July, when the House Appropriations Committee voted 33 to 25 to reject an amendment to a bill funding OMB that would have delayed implementing the legislation for 1 year pending a study. The amendment was sponsored by James Walsh (R–NY) and David Price (D–NC). Two days later, National Institutes of Health director Harold Varmus and National Academy of Sciences president Bruce Alberts testified before another House panel on another bill to repeal the law. "We should go back to ground zero and ask, 'What is it we're trying to solve?' " Varmus said about the bill, sponsored by Representative George Brown (D–CA), who died last week (see p. 509). But with the defeat of the Walsh-Price amendment, supporters of Brown's bill say its chances of passage appear slim.

The vote shifted attention to OMB, which is expected to issue within a few days a second version of a proposal released in February that drew more than 9000 comments. An unofficial copy circulating in Washington has eased the concerns of some who felt FOIA's exemptions for intellectual property rights and medical privacy weren't sufficient and that experimental results might be released before they had even been published. For example, the draft OMB document defines "data" as "any raw underlying information necessary to validate [research] findings, but not information that would violate the privacy rights of research subjects or the intellectual property rights of researchers." The draft also restricts the law's reach to data "published in a peer-reviewed journal" or when cited "in a proposed rule." Says Nils Hasselmo, president of the Association of American Universities: "It does address some of the critical issues that the scientific community had raised."

It was unclear as *Science* went to press whether OMB will tinker further with this version before publishing it. Shelby's staff declined to comment until it appears in the *Federal Register*. Louis Renjel of the U.S. Chamber of Commerce—a strong supporter of the law—said the chamber believes OMB should apply the law not just to major rules but also to things like risk assessments. Right now, the draft defines "rule" as "an agency statement … intend[ed] to have the force and effect of law … designed to implement, interpret or prescribe law or policy. …"

Whatever it decides, OMB faces a tight schedule. The agency will allow for another 30-day comment period before issuing a final rule by 30 September.

–JOCELYN KAISER