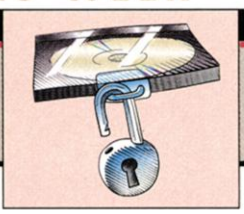
THIS WEEK

NEWS



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Locking up freedom of expression?

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Scrapie-BSE link strengthened

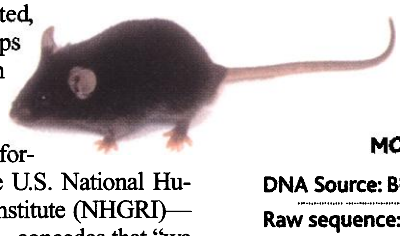
GENOME SEQUENCING

Celera Assembles Mouse Genome; Public Labs Plan New Strategy

DNA sequencers celebrated after they created a draft of the human genome sequence last year. But there's been hardly a triumphant peep, or squeak, over another much-anticipated event this spring—the completion of two draft sequences of the mouse genome, one by a public-private consortium and the other by a private company. The reason: Neither group has produced data that are both free and user-friendly. Biomedical scientists, eager to get their hands on the mouse genome sequence, are beginning to champ at the bit.

The public-oriented mouse team, called the Mouse Sequencing Consortium (MSC), has been making its raw data freely available (*Science*, 13 October 2000, p. 242). Its 6-month, $58 million effort, according to a press release last October, was designed to "decipher the mouse genetic code" and "produce a high quality genome sequence" to help analyze human DNA. The effort ends this week. But if users thought the MSC would produce an assembled mouse genome sequence, they will be disappointed.

The consortium chopped up DNA from the black 6 mouse into millions of overlapping pieces and sequenced them to provide an average of threefold coverage of the entire genome. Users are grumbling that the DNA collection is so fragmented, unordered, and full of gaps that it doesn't enable them to study the structure or function of genes. Mark Guyer, scientific information coordinator at the U.S. National Human Genome Research Institute (NHGRI)—the MSC's largest backer—concedes that "we weren't as clear as we might have been" last fall that the consortium would not produce an assembled genome sequence. He says U.S.-funded labs in the consortium are preparing to shift gears and complete the sequence using a new strategy.



In contrast, a private company—Celera Genomics of Rockville, Maryland—claimed last week to have assembled a mouse genome sequence of about 2.6 billion bases. Celera says it sequenced DNA from three strains (129X1/SvJ, DBA/2J, and A/J) to provide sixfold coverage—enough redundancy to assemble and order the fragments into a rough draft of the genome. "It came together quite nicely—without relying on public data," says Celera scientist Mark Adams. Celera president J. Craig Venter has announced that he will "self-publish" a paper on how this was done. But anyone who wants to see the results will have to pay for access to Celera's database: The company had said from the start that it would charge users for access, and even current subscribers will have to pay extra for the assembled mouse genome sequence.

CELERA GENOMICS

DNA Source: 3 mouse strains—129X1/SvJ, DBA/2J, A/J

Raw sequence: 15.9 billion base pairs

Genome Coverage: 99%

DNA redundancy: Sixfold

Assembled genome: 2.6 billion base pairs

Contiguity: 80% in segments of 1 million base pairs

Ref: (www.applera.com/press/prccorp042701.html)

One problem with the unassembled data from the MSC is that the sequences are typically no more than 500 bases long. That's much shorter than a single gene. These fragments can be very useful, says Maja Bucan, a geneticist at the University of Pennsylvania in Philadelphia. Search engines can detect patterns among them and sometimes find genes, says Bucan, but it is practically "impossible" to use the data to examine the structure and function of genes. So Bucan and others have made a pitch to NHGRI to produce "intermediate" forms of data that are more useful, but less expensive than a "finished" genome sequence.

MOUSE SEQUENCING CONSORTIUM

DNA Source: Black 6 strain—C57BL6/J

Raw sequence: 14.9 million reads of about 500 bases each

Genome coverage: 90%

DNA redundancy: Threefold

Assembled genome: —

Contiguity: 8.6% in segments of 1 million base pairs

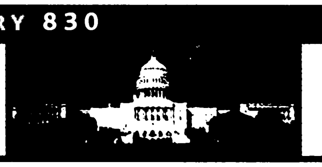
Ref: (www.ncbi.nlm.nih.gov/genome/seq/MmProgress.shtml)

Guyer says the institute intends to do just that. To finish the job, the NHGRI-funded labs will switch from whole-genome shotgunning—the approach used so far by the MSC—to a more deliberate process in which stretches of DNA cloned in bacterial artificial chromosomes (BACs) are mapped to specific points on the genome before being sequenced. The NHGRI work will involve the two U.S. labs that participated in the MSC—the Whitehead Institute/Massachusetts Institute of Technology (MIT) Genome Sequencing Project in Cambridge, Massachusetts, and the Washington University Genome Center in St. Louis. (The MSC's third lab was the Sanger Centre in Hinxton, U.K.) The center directors leading this effort, Eric Lander at MIT and Robert Waterston at Washington University, have not settled on the exact mix of whole-genome shotgun data and BAC data but will publish a strategy soon, says Waterston. Marco Marra of the University of British Columbia in Vancouver, Canada, has already fingerprinted 300,000 BAC clones and lined up 9000 mapped clusters for sequencing.

If all goes well, the labs will begin to "burn through" the mouse BACs this June, says Guyer. But first, he adds, they must finish some important gap-filling work on the human genome sequence, and they must figure out how much funding remains available from that project to redirect to mouse sequencing. "If everything works as well as it possibly could," Guyer says, a high-quality draft mouse genome sequence might be assembled in 2003. The final version isn't expected until 2005.

In the interim, researchers at the Sanger Centre and the European Bioinformatics Institute led by Ewan Birney have begun to display raw mouse DNA sequence in a more user-friendly format by aligning trace data

CREDIT: THE JACKSON LABORATORY (MOUSE)

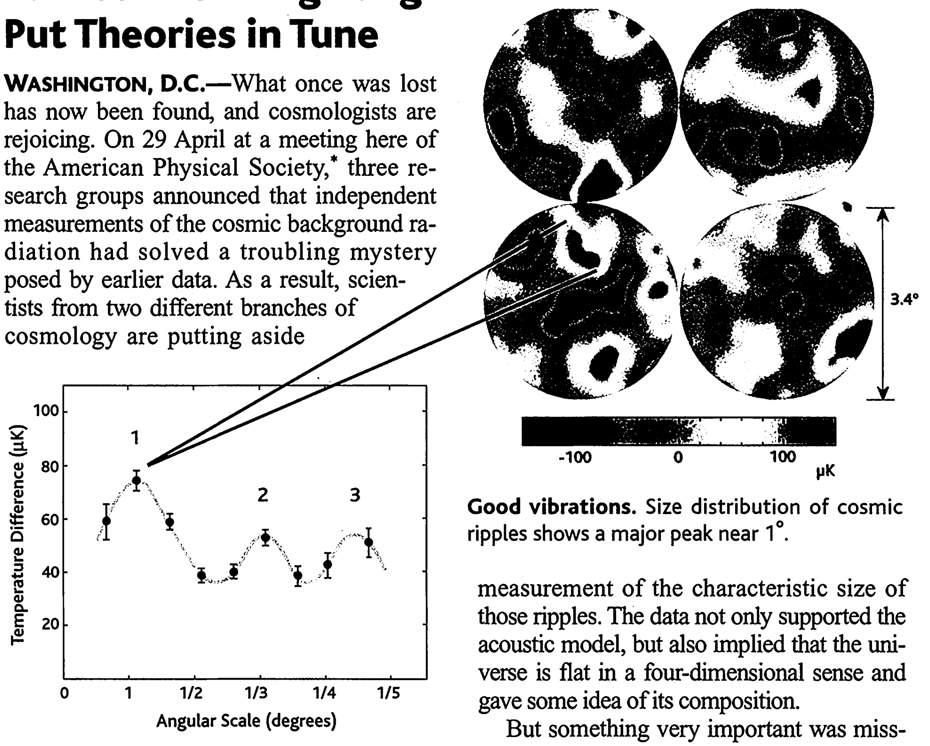


with the draft human genome sequence (www.ensembl.org). NHGRI is encouraging a bioinformatics group led by David Haussler and Jim Kent at the University of California, Santa Cruz, to do the same on their Web site (genome.ucsc.edu). "I can't give you a timetable for completion" of this work, says Haussler, but "people in the mouse community should stay tuned." **–ELIOT MARSHALL**

ASTROPHYSICS

Echoes of the Big Bang Put Theories in Tune

WASHINGTON, D.C.—What once was lost has now been found, and cosmologists are rejoicing. On 29 April at a meeting here of the American Physical Society,* three research groups announced that independent measurements of the cosmic background radiation had solved a troubling mystery posed by earlier data. As a result, scientists from two different branches of cosmology are putting aside their differences and are coming to a long-anticipated concord on a model of the early cosmos and the fraction of "ordinary" matter the universe contains.



Good vibrations. Size distribution of cosmic ripples shows a major peak near 1°.

"This weekend, I think, is going to be a benchmark that's going to be remembered for a long time in this field," says Andrew Lange, a physicist at the California Institute of Technology in Pasadena. Physicist Max Tegmark of the University of Pennsylvania in Philadelphia agrees. "This is like Santa Claus is arriving," he says.

What has everyone so excited is a follow-up to arguably the biggest physics story of 2000: preliminary results from BOOMERANG, a balloon-borne instrument tuned to listen for the microwave whispers from the early universe (*Science*, 28 April 2000, p. 595). Until about 300,000 years after the big bang, the universe was a roiling blob of plasma, ringing with pressure waves from the cataclysm that created it. According to the reigning acoustic model of the early cosmos, those waves caused density fluctuations in the plasma—fluctuations that now show up as ripples in the microwave background radiation that bombards us from every direction. Last year, BOOMERANG made a celebrated measurement of the characteristic size of those ripples. The data not only supported the acoustic model, but also implied that the universe is flat in a four-dimensional sense and gave some idea of its composition.

But something very important was missing. The acoustic model also predicts that overtones from the big bang should have produced smaller ripples—relatively faint second and higher peaks in the microwave spectrum. BOOMERANG heard the fundamental note loud and clear, but where scientists expected to hear overtones, there was merely an awkward silence. Although a ground-based telescope heard hints of an overtone (*Science*, 19 January 2001, p. 414), the missing second peak posed a potentially huge problem for the acoustic model.

No longer. At the meeting, BOOMERANG researchers presented their analysis of 14 times the amount of data that went into last year's result. "We see the first peak very well again, and we do see two more bumps and wiggles out here that indicate the acoustic oscillation of the early universe," said team member John Ruhl, a physicist at the University of California, Santa Barbara. At the same session, John Carlstrom of the University of Chicago presented the first results from the Degree Angular Scale Interferometer, an Antarctic telescope that uses an entirely different technique to measure the microwave background. "We see the first peak, see the second peak, and it strongly suggests a third peak," Carlstrom said. Yet another project, MAXIMA, a balloon-borne experiment similar to BOOMERANG, also sees evidence of a third peak.

"This is a really great party," beams University of Chicago physicist Mike Turner, who says that the acoustic theory has just "passed a very important test."

The new results also iron out a nagging disagreement about how much of the universe consists of so-called baryonic matter, the familiar stuff of atoms, stars, and people. Measurements of the relative abundance of various atoms in the universe give a figure of about 4% of all the mass and energy that scientists think is out there. Until this weekend, cosmic background experiments put the total at 5%—a statistically significant difference. The new, more precise cosmic background measurements bring the two methods into agreement. "The whole controversy business about baryon fraction? Forget about it," says Tegmark.

These results are just the beginning; several experiments were gathering data even as the meeting was going on. Within a year or two, scientists expect to see measurements of the polarization of the background radiation, which carries previously inaccessible information about the early universe, as well as even more precise data from the entire sky. Theorists are worried, Turner jokes. "Now our ideas get tested as soon as we write them down," he says. "We're living dangerously." **–CHARLES SEIFE**

QUANTUM PHYSICS

Loopy Electron Model Solves Ion Mystery

Newton's laws usually fly out the window in the subatomic realm. Unlike planets around a star, electrons don't loop around their nuclei in nice, elliptical orbits—at least according to the traditional interpretation of quantum theory. But now, an international team of scientists has shown that a nearly Newtonian set of electron orbits can explain

CREDITS: DASI

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* 28 April–1 May.