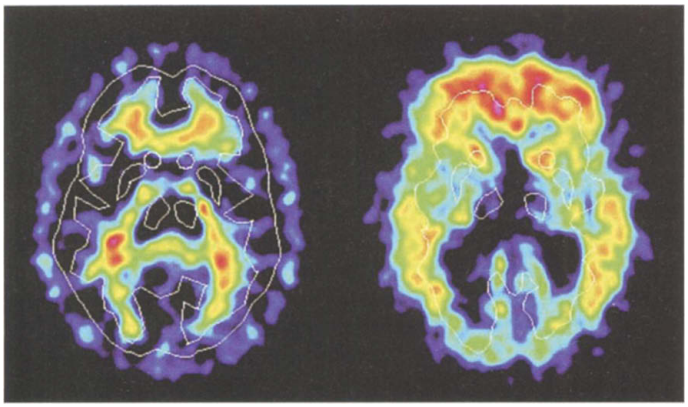
Alzheimer's disease through a process of elimination. Pencil-and-paper tests of memory and problem solving, reports from family members, and standard brain scans suggest that Alzheimer's disease is the culprit, but researchers can't be entirely sure until an autopsy reveals brain tissue riddled with senile plaques and neurofibrillary tangles. The main ingredient in plaques is a protein called β amyloid, which congregates in the brain well before symptoms of dementia appear and is thought to initiate most of the damage.



Aglow with Alzheimer's. The first images of a β-amyloid tracer in humans show an ominous signal in the brains of patients with early symptoms of Alzheimer's disease (right).

CREDIT: W. KLUNK/UNIVERSITY OF PITTSBURGH

Several teams have been racing to find a nonintrusive way to visualize β amyloid in a living brain. William Klunk, Chester Mathis, and colleagues at the University of Pittsburgh spent about 10 years searching for a molecule that fits the bill. Their best candidate, dubbed PIB, crosses the blood-brain barrier, isn't toxic, and can be clipped to a radioactive tag to light up plaques, animal studies have shown.

Starting in February, a group led by Henry Engler of Uppsala University in Sweden injected the molecule into nine people with symptoms of "mild" Alzheimer's disease and five healthy controls and then used a PET scan to see where it went. At the conference, images of the results audibly took the audience's breath away: In healthy people, the marker sailed right through the brain and was well on its way to exiting via the central fluid-filled ventricles. But in people with early Alzheimer's disease, the marker stuck in the cortex, particularly in the frontal lobes and temporal-parietal areas, two of the brain regions most damaged in the disease.

"This is something we've all been waiting for," says Michael Pontecorvo of Mitsubishi Pharma America in Warren, New Jersey. Adds Randy Buckner of Washington University, "this opens a new window on what we think to be the primary marker associated with disease."

β amyloid can be detected in a far more unexpected place, another team reported. Lee Goldstein of Brigham and Women's Hospital in Boston and colleagues have found that the protein also collects in the lens of the eye. What's more, in a postmortem study of eyes from 16 elderly donors, half of whom suffered from Alzheimer's disease, all of the patients had a rare type of cataract on the edges of the lens—apparently caused by β-amyloid deposits. But this doesn't mean that an eye exam for Alzheimer's disease is around the corner, cautions Goldstein, in part because it's not yet clear how early in the disease's progression the protein might become visible in the lens.

Standard brain scans, if analyzed carefully, can also show signs of impending Alzheimer's disease, reported Nick Fox of the National Hospital for Neurology and Neurosurgery in London. By comparing magnetic resonance images taken 1 year apart, Fox and his colleagues found that healthy elderly people lose about 0.2% of their brain volume each year. People who start out with minor memory complaints and progress to Alzheimer's disease, on the other hand, lose about 2.8% a year. This dramatic shrinking is evident in the hippocampus, which helps store memories, and the frontal and temporal lobes.

The technique doesn't provide a quick diagnosis: It takes time to get a clear picture of Alzheimer-like decline. But it could help monitor patients' progress in clinical trials, says Fox. Their performance on tests of memory and problem solving varies a lot from day to day, making it tough to tease out any potential improvements. By providing a more accurate endpoint, he suggests, brain scans might enable researchers to make clinical trials "smaller and faster." –LAURA HELMUTH

ASTROPHYSICS

'Winged' Galaxies Point To Black Hole Mergers

X literally may mark the spot as astrophysicists hunt for colliding black holes. Results of a new mathematical model, published online this week by *Science* (www.sciencemag.org/cgi/content/abstract/1074688), maintain that cross-shaped radio galaxies harbor massive black holes that suddenly flipped their spins, probably by absorbing black holes from other galaxies. When combined with a census of these distinctive galaxies, the model suggests that such titanic encounters happen about once a year in the cosmos.

Observations of galactic cores, including

ScienceScope

Trickle-Down The global economic slump could delay construction of the world's most powerful particle accelerator now that a key parts supplier has gone bust. Babcock Noell Nuclear in Würzburg, Germany, is supposed to supply one-third of the 1236 superconducting magnets needed for the Large Hadron Collider (LHC), being built at the European particle physics laboratory CERN near Geneva. But on 4 July, Noell's parent company, the industrial giant Babcock Borsig AG, declared bankruptcy. Noell is now in the hands of receivers—and physicists are wondering if they'll get their magnets on time.

The bankruptcy "came as a real surprise," says LHC director Lyndon Evans, and it threatens to add to LHC's woes. The project is already $300 million over its original $1.6 billion budget and 2 years behind schedule, with completion now slated for 2007 (*Science*, 28 June, p. 2317).

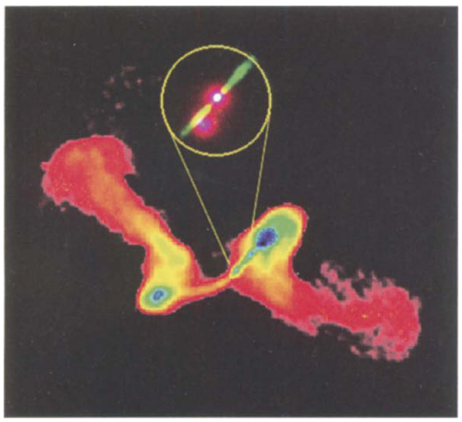
Noell executives say the company remains profitable despite the parent company's troubles, and they plan on finishing CERN's magnets. If they can't, two other magnet suppliers—Italy's Ansaldo and France's Alstom-Jeumont—will scramble to meet LHC's needs.

Dependence Day Greater autonomy and a $3.5 million annual bank account might sound like a pretty good deal to most people—but not to the National Science Board, the presidentially appointed oversight body for the National Science Foundation (NSF).

Last week the Senate Appropriations Committee created a separate account for the 24-member board in its proposed 2003 budget for NSF (see p. 755). It argues that the board—which oversees the $5-billion-plus agency and advises the nation on scientific issues—should be financially and operationally independent of NSF. But board chair Warren Washington says he prefers the status quo, under which the board's staff members are NSF employees and the board gets its resources from the agency. Washington also says that borrowing NSF employees as needed gives the board greater flexibility than hiring a permanent staff.

The board is expected to discuss the idea at its meeting 14 to 15 August. Legislators will also get another crack at it as the spending bill moves through Congress.

Contributors: Adam Bostanci, Charles Seife, Adrian Cho, Jeffrey Mervis



Crossing pattern. A jet (*inset*) at the core of the merging galaxy system NGC 326 might have flipped direction when two giant black holes combined.

the center of our Milky Way, have revealed that most galaxies host supermassive black holes with millions or billions of times the mass of the sun. In active galaxies—those that spew enormous fountains of energy into space—theory holds that these vortexes spin at awesome rates as they devour gas and stars. The incoming matter spirals into a raging disk, which shoots jets into space at nearly the speed of light. Astrophysicists don't yet understand this process, but they assume that the jets mark a black hole's spin axis.

Previous surveys showed that about 7% of active radio galaxies have X-shaped, or "winged," jets ranging in shape from narrow beams to cones. Astronomers thought these features pointed to a precession of the central black hole, much as Earth's spin axis wobbles over time. However, recent high-resolution radio images of some winged galaxies show sharp breaks where a pair of jets angles off into a new direction, rather than sweeping out gradual curves (see figure, above). "That's clearly not precession," says astrophysicist David Merritt of Rutgers University, Piscataway, New Jersey. "It has to flip over."

The likeliest mechanism is the arrival of a second massive black hole during a galaxy collision, say Merritt and his colleague, radio astronomer Ron Ekers of the Australia Telescope National Facility in Sydney. According to their model, an incoming black hole with at least 20% of the mass of its partner will knock the main black hole off kilter, no matter how rapidly it spins.

The calculation agrees with an independent analysis of black hole mergers using Einstein's theory of general relativity, says astrophysicist Scott Hughes of the University of California, Santa Barbara. "It's really hard to torque a black hole around by a large amount without having something as massive as another black hole slam into it," Hughes says. He and astrophysicist Roger Blandford of the California Institute of Technology in Pasadena are preparing their work for publication.

From estimates of how long the X-shaped radio lobes persist, Merritt and Ekers deduce that a typical large galaxy will undergo a black hole–tilting crash once every billion years. That's enough for one such event to pop off somewhere in the universe each year. The result bodes well for astrophysicists who hope to observe the intense ripples in spacetime, called gravitational waves, that should cascade from such mergers.

The research should spur theorists to figure out how gigantic black holes manage to merge—instead of forming binaries that waltz for billions of years, as most models hold. "This suggests that nature does find a way to bring some black holes together," Merritt says. "We're just not sure how."

–ROBERT IRION

EUROPEAN PATENTS

Tough Stance on Stem Cell, DNA Claims

BERLIN—Biotech players hoping to stake claims on human stem cells or DNA sequences in Europe saw a couple of warning shots whiz across their bows last week. On 24 July, the European Patent Office (EPO) strongly limited a controversial patent covering stem cell technology, striking out all references to human or animal embryonic stem (ES) cells. And the influential Nuffield Council on Bioethics, a British think tank, called on patent offices around the world to refrain from awarding patents on DNA sequences.

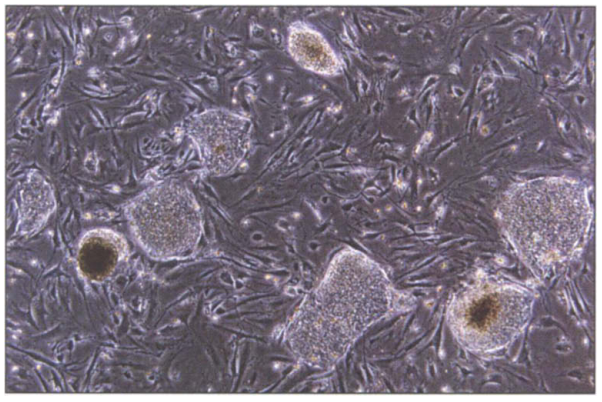
EPO cautioned against reading too much into a single decision in the rapidly developing field of stem cell research. "One could not possibly deduce a patent policy from a single case," says EPO spokesperson Rainer Osterwalder. Nevertheless, EPO's stance contrasts sharply with policies at the U.S. Patent and Trademark Office (USPTO), which has granted half a dozen patents involving human ES cells, including a broad patent on the technique used to derive cell lines. That patent's owner, the Wisconsin Alumni Research Foundation, claims that its patent covers all import and use of human ES cells in the United States. Its application for a similar patent in Europe is under review at EPO.

Last week's EPO ruling concerned the so-called Edinburgh patent, which covers techniques for using molecular markers to identify stem cells. Granted in 1999 to developmental geneticist Austin Smith of the University of Edinburgh and Peter Mountford of Stem Cell Sciences in Melbourne, Australia, the patent generated controversy 2 years ago when Greenpeace charged that its transgenic animals claims could be construed as covering the creation of transgenic humans (*Science*, 3 March 2000, p. 1567).

EPO admitted that it had erred in allowing that claim, explaining that the examiner had simply overlooked the possibility that the patent might cover the creation of human beings. And the patent holders said they never intended to conduct such experiments. Indeed, when the storm broke they proposed modifying their claim accordingly. But before they could do so, 14 parties, including Greenpeace and the governments of Italy, Germany, and the Netherlands, filed opposition petitions.

After 3 days of hearings, an EPO review panel concluded that the patent conflicted with the European Patent Convention, which governs EPO, on two grounds: The convention prohibits patents involving the use of human embryos for industrial or commercial purposes, and it requires that work described in a patent be specific enough to be repeated by an expert in the field. The claims involving ES cells were too vague, the panel said, in part because the patent application was filed in 1994, several years before scientists first reported isolating human ES cells. Faced with that ruling, the patent holders agreed to strike all references to ES cells, leaving only claims dealing with stem cells derived from adults or fetal tissue. The panel allowed the narrower patent to stand and will issue a written decision within several months, after which either side can appeal.

Some experts argue that the ruling does not preclude future patents on the use of human ES cells. According to George Schlich, a patent attorney for the University of Edinburgh and Stem Cell Sciences, researchers might still be able to win European patents on processes involving differentiation of human ES cells into tissues that could be used to treat diseases such as diabetes or heart disease. The key, he says, would be to focus



Ruled out. The European Patent Office has struck down patent claims covering human embryonic stem cells.

CREDITS: (TOP) M. MURGIA *ET AL*./NRAO/VLA; (INSET) STSCI; (BOTTOM) UNIVERSITY OF WISCONSIN, MADISON