ASTROPHYSICS

Young X-ray Satellite Rattles Old Ideas

A year after its launch, Europe's XMM-Newton x-ray satellite is proving its mettle. Last week in Paris, scientists gave a sneak preview of findings that challenged cherished beliefs about what kind of material swarms around supermassive black holes in the middle of active galaxies, and how compact clusters of galaxies chill out. Those results and others, appearing next month as 56 papers in a special issue of the European journal *Astronomy and Astrophysics*, constitute what Roger Bonnet, director of science for the European Space Agency (ESA), describes as "monster astronomy."

Since the mid-1980s, scientists have believed that x-rays they detected in active galactic nuclei were partly absorbed by clouds of warm gas far from the black hole. When XMM-Newton trained its spectrometers on two such nuclei, astronomers expected to see the hallmarks of such a gas shroud: x-ray spectra riddled with gaps where the atoms in the gas absorbed radiation passing through it. But XMM-Newton had other ideas.

"The spectra didn't show the spiky absorption signatures that we expected on the basis of the [warm-absorber] model," says Masao Sako of Columbia University in New York City. Instead, as Sako was the first to realize, the spectra made much more sense if the spectral features originated from very hot gas orbiting extremely close to the black hole. What astronomers were seeing, Sako theorized, were not absorption lines but emission lines, distorted in ways that indicated that the gas must be moving close to the speed of light.

Material far from a black hole could not orbit so swiftly, says Jelle Kaastra of the Space Research Organization Netherlands (SRON) in Utrecht, the project scientist of the XMM-Newton spectrometers. That meant the gas had to be very close to the "edge" or event horizon of the black hole, just a few million kilometers from the center of the hole itself. The results also imply that the black hole is spinning, Kaastra says, because general relativity predicts that there are no stable orbits close to a stationary black hole. Physicists had long sought convincing evidence of such rotating black holes—called Kerr black holes, after the New Zealand physicist who predicted their properties mathematically. Now they have it.

"This is one of the outstanding results of XMM-Newton," says Johan Bleeker of SRON. "For the first time, we're studying emission from the accretion disk itself, very close to the central, rotating black hole." In principle, Bleeker says, observations like these should enable astronomers to derive the geometry, physical properties, dynamics, and chemical composition of the disk.

But Joachim Trümper of the Max Planck Institute for Extraterrestrial Physics in Garching, Germany, says discrepancies in the XMM-Newton data must be resolved before other physicists will accept them as conclusive. "This is certainly not the end for the warm-absorber model," Trümper says.

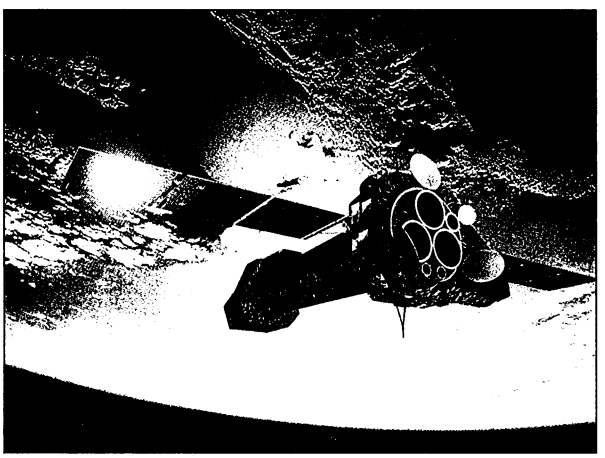
XMM-Newton's second challenge to conventional wisdom targets compact clusters of galaxies—enormous congregations of hundreds or thousands of individual galaxies, generally dominated by a giant elliptical galaxy in the core. Older x-ray observations showed that the space between galaxies in clusters contains hot, x-ray emitting gas. Astronomers have long believed that the hot gas slowly flows into the cluster core, cooling as it goes, says Andrew Fabian of Cambridge University in the United Kingdom, who led one of the groups that proposed the model in 1977. Because the gas in the cluster's core is denser than gas farther out, Fabian explains, it cools more efficiently, radiating its energy away in x-rays. As a result, the pressure near the core drops. Hotter gas from the outskirts of the cluster then starts to flow inward, where it cools in turn.

If the cooling-flow model were correct, XMM-Newton should detect signs of cold gas in the inner parts of the clusters. In particular, astronomers say, its sensitive spectrometers should find the spectral signatures of moderately ionized iron—atoms that have lost just a few of their electrons, an indicator of a low-energy environment. They don't. "The spectra provide us with a very significant [lower] limit on the temperature," says Bleeker. "This puts the cooling-flow model in jeopardy."

But Fabian thinks it's too early to write off the model. In a paper accepted for publication in the *Monthly Notices of the Royal Astronomical Society*, he describes five other possible explanations for XMM-Newton's results. Still, he admits the new observations have made things more complicated.

With so many intriguing clues emerging from just a few months' worth of observations, x-ray astronomers are confident that XMM-Newton will revolutionize the field. "This is not the end of the story," Bonnet says. "I expect the observatory will continue to send back such interesting science results for the next 10 years." **–GOVERT SCHILLING**

Govert Schilling is an astronomy writer in Utrecht, the Netherlands.



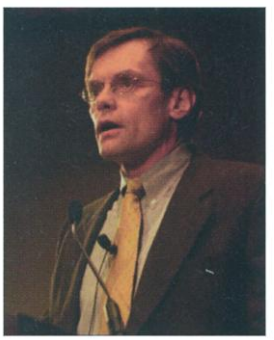
CREDITS (LEFT TO RIGHT): ESA; SAM KITTNER

Astro-monster. The 1-year-old XMM-Newton x-ray satellite is shaking up some of astrophysicists' pet theories.

GENE THERAPY

FDA Moves Against Penn Scientist

The U.S. Food and Drug Administration (FDA) has begun proceedings that could disqualify gene therapy researcher James Wilson of the University of Pennsylvania in Philadelphia from conducting any future clinical trials. Wilson, who is head of the university's Institute for Human Gene Therapy, oversaw the trial in which 18-year-old Jesse Gelsinger died after a genetically altered virus was injected into his liver (*Science*, 17 December 1999, p. 2244).



Under scrutiny. Penn's James Wilson.

Disqualification is the harshest penalty the FDA can impose on an investigator. It bars a researcher from receiving drugs for use in clinical trials—in effect, preventing that investigator from administering experimental drugs to patients. In a 30 November letter to Wilson, the FDA stated that Wilson had "repeatedly or deliberately violated regulations governing the proper conduct of clinical studies." The agency wrote that Wilson and his colleagues enrolled patients who were ineligible for the trial, did not monitor patients properly, did not halt the trial when patients experienced serious side effects, and failed to inform patients that a trial of a similar drug had severely sickened monkeys. The FDA has also issued warning letters to two of Wilson's collaborators in the study—Steven Raper of the Institute for Human Gene Therapy and Mark Batshaw of Children's National Medical Center in Wash-

ington, D.C.

"This is obviously a very serious matter," the university said in a brief statement. "We know that Dr. Wilson understands its importance, is reviewing the letter carefully and intends to respond in a timely way." Wilson has 30 days to reply to the FDA's letter. After reviewing Wilson's response, FDA administrators will make a final decision.

This is a "drastic" step, says Inder Verma of the Salk Institute for Biological Studies in La Jolla, California, who headed a special working group at the National Institutes of Health that investigated the Gelsinger trial. But Savio Woo, a gene therapy researcher at Mount Sinai School of Medicine in New York City and past president of the American Society of Gene Therapy, says that vigorous FDA oversight will strengthen gene therapy research. **–GRETCHEN VOGEL**

NEUROSCIENCE

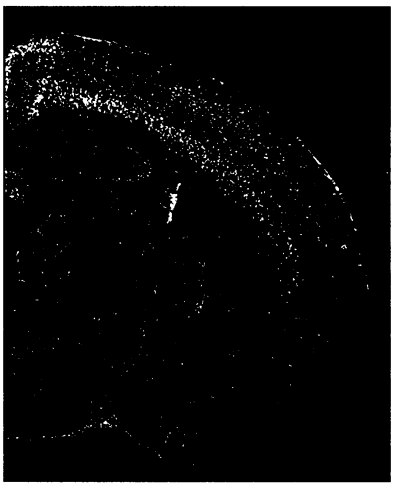
Immune Molecules Prune Neural Links

The developing brain starts off as a tangle of neuronal connections, then activity reinforces some of these connections and causes others to atrophy. Over the past few years, neurobiologists have been on the prowl for molecules that help the nervous system make and break these connections, and they've come up with a few contenders. But now Carla Shatz's team at Harvard Medical School in Boston is proposing an unlikely new candidate: a type of protein previously known for its role in helping the immune system fend off viruses and other foreign invaders.

In work described on page 2155, Shatz and her colleagues suggest that the class I major histocompatibility complex (MHC) proteins are necessary for the formation of normal neuronal connections in a visual area of the brain during development. Later in life, they're called into play in the hippocampus, a brain area involved in memory and learning. The work shows "a completely unexpected function for the molecules," says neurobiologist Marc Tessier-Lavigne of the University of California, San Francisco.

The current results are an outgrowth of observations that Shatz's team, then at the University of California, Berkeley, reported 2 years ago. While examining how gene expression patterns in the brain react to changes in retinal activity, the researchers found, to their surprise, that the genes encoding class I MHC proteins are active in the developing brain. To explore what these seemingly alien molecules were doing there, Gene Huh, a postdoc in the Shatz lab, turned to three strains of mice that had been genetically altered. Two of these strains lacked the ability to display class I MHC proteins in their normal location on the cell surface; the third lacked part of a receptor that T cells use to respond to class I MHC proteins. In the first phase of their work, Huh and his colleagues tested how these gene knockouts affected the development of the animals' visual systems.

Like many animals, mice aren't born with the ability to see. The visual system matures only when neural signals, originating either from spontaneous neural firing in the retina before the eyes open or from looking around afterward, help organize the parts of the brain that receive and process visual information. Huh found that this process, which involves both strengthening frequently used connections and pruning useless ones, is disrupted in all three knockout mice.



CREDIT: G. HUH ET AL.

Sort it out. As indicated by the colored staining patterns, different class I MHC genes are expressed in different brain areas.

The visual signal's first stop after the eye is the lateral geniculate nucleus (LGN). There, neuronal projections from the retina normally form what Huh describes as a "big misshapen doughnut." The doughnut itself, occupying most of the LGN, receives input from the eye on the opposite side of the body, while a small "doughnut hole" in the middle of the LGN gets projections from the same-side eye. But in the knockout mice the doughnut hole is much larger, implying that the inputs from the two eyes overlap. The finding suggests that in the absence of functioning class I MHC proteins, the normal pruning of connections that should have occurred in the LGN is defective.

Similar strengthening and weakening of neuronal connections is thought to occur during memory formation in the adult hippocampus. So Shatz and her colleagues next looked at synapses in that brain region, where their earlier work had shown that the class I MHC genes are also active.

When postdoc Lisa Boulanger stimulated the hippocampal neurons, she found that neurons in the knockout mice reacted strangely. Long-term potentiation (LTP), the strengthening of signals with stimulation, was enhanced: Hippocampal neurons in the knockout mice responded more dramatically than did those in normal mice to a high-frequency stimulus that can evoke LTP. And when she applied low-frequency stimulation, which causes the synapse weakening known as long-term depression, neurons in the knockout mice failed to rein in their signals as they should have. "To us," says Shatz, "the results imply that there may be a commonality of cellular and molecular mechanisms" in how neurons in the hippocampus and the developing nervous system respond to activity.

Huh and Shatz suspect that the class I MHC proteins also help neurons tune their connections in other areas of the brain. The mouse carries about 30 different varieties of the protein. When Huh tested where four of the genes are expressed, he found that different ones are active in different places in the brain (see figure), possibly tailoring nearby neurons to fit into the correct neural pathways.

Despite the evidence indicating that the class I MHC proteins are somehow involved in refining neuronal connections in the brain, researchers don't yet know how the molecules are acting. Immunologist Hidde Ploegh of Harvard says he's "intrigued by the possible role of [these molecules] in something that appears to have no immunological correlate." But he awaits the details of how they might be helping the nervous system figure out which connections should atrophy.

–LAURA HELMUTH

NEUROPSYCHOLOGY

Language Affects Sound Perception

NEWPORT BEACH, CALIFORNIA—Neuropsychologists may owe a debt to the devil. At the 140th meeting of the Acoustical Society of America here last week, University of California, San Diego, psychologist Diana Deutsch demonstrated that an auditory illusion based on the tritone—also known as the "devil in music"—is perceived differently by listeners with different linguistic histories. And those perceptions might help psychologists understand how the brain rewires itself during childhood.

Played together, two notes a half-octave apart (such as C and F sharp) sound jarring; medieval musicians considered this combination, a tritone, so discordant that they dubbed it the "diabolus in musica." But a tritone is music to Deutsch's ears. For more than a decade, she has been studying an auditory illusion—the acoustical equivalent of an optical illusion—based upon the tritone.

With a computer, Deutsch created am-