PERSPECTIVES: ASTRONOMY

Gamma-Ray Astronomy with INTEGRAL

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On 17 October of this year, the European Space Agency (ESA) launched its biggest satellite to date, the International Gamma-Ray Astronomy Laboratory (INTEGRAL) (see the figures). Featuring four telescopes, the satellite is a formidable tool for multiwavelength astronomy. But the real breakthrough is that it enables high-resolution spectroscopy and imaging at high energies—tens of keV to several MeV—characteristic for some of the most energetic processes in space.

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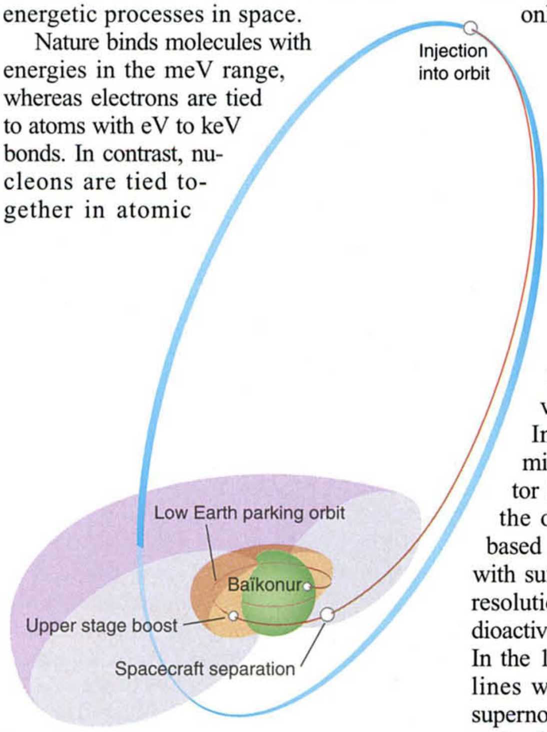
Nature binds molecules with energies in the meV range, whereas electrons are tied to atoms with eV to keV bonds. In contrast, nucleons are tied together in atomic nuclei with MeV energies. Such high energies can now be probed with INTEGRAL, enabling detailed studies, for example, of dense objects like neutron stars and black holes, nucleosynthesis in supernovae, and the enigmatic gamma-ray bursts (GRBs).



Integral into orbit. Both the transfer and the final orbits are shown. The final high ellipticity keeps the mission well away from Earth's radiation belts during most of its lifetime.

From optical to x-ray wavelengths, astronomical spectroscopists from Fraunhofer to Giacconi have provided insight into the chemical composition and dynamics of celestial objects. Gamma-ray spectroscopy, however, is a much tougher nut to crack. First, gamma-ray photons cannot be focused, because their wavelength is smaller than interatomic distances. New tricks must be used to detect source signals against the sky background. Second, no dispersive spectroscopy can yet be done on gamma-ray photons. Thus, to measure precisely the energy of an incoming gamma-ray photon, one must absorb it and accurately gauge the energy it deposits. Third, celestial gamma-ray photons are scarce and do not penetrate Earth's atmosphere. They can therefore only be detected from space.

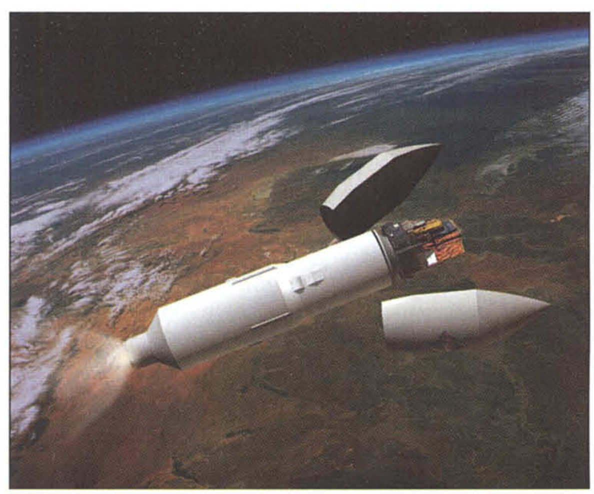
These technical difficulties account for the fact that precious little has been achieved so far in the field of gamma-ray imaging and spectroscopy in the tens of keV to MeV range. Some important observations have, however, been reported. In the late 1970s, NASA's HEAO-3 mission flew the first germanium detector in space (*1*). Such detectors remain the only tool, borrowed from ground-based nuclear spectroscopy, with sufficiently high energy resolution for identifying radioactive decay nuclear lines. In the 1980s, the first Co-Ni lines were detected from a supernova, SN1987A (*2*).

In the 1990s, the Franco-Soviet mission SIGMA, with a new trick for gamma-ray imaging, the coded-mask technique, discovered a variable microquasar (*3*) close to the center of our Galaxy. SIGMA also observed a redshifted electron-positron annihilation line from a nova in the Musca constellation (*4*). In the same decade, NASA's Gamma Ray Observatory (GRO) yielded the first image of our Galaxy at 1.8 MeV (the aluminum-26 line, a fingerprint of star formation) and provided evidence for abundant matter-antimatter annihilation close to the galactic center (an indication of a black hole) (*5*).

INTEGRAL is more powerful than all these preceding missions. It combines the sub–arc minute spatial resolution of its coded mask imager, IBIS (*6*), with the keV spectral resolution of its germanium spectrometer, SPI (*7*). It has the further advantages of coaxial x-ray and optical monitors. Its launch comes 70 years after Anderson, Blackett, and Occhialini took the first pictures of antimatter (in the form of Dirac's positive electron) and Chadwick pioneered the understanding of nuclear structure. INTEGRAL also comes 30 years after the first images of the gamma-ray sky from NASA's SAS-2.

Which insights into astrophysics may be expected from INTEGRAL? In our Galaxy, SPI will look at gamma-ray lines such as Al^{26} (1.8 MeV), Ti^{44} (1.1 MeV), and Na^{22} (1.2 MeV), which serve as tracers for nucleosynthesis either in the stars' nuclear furnaces or in their violent deaths. Despite their elusiveness, gamma-ray lines have two useful properties: They are not absorbed by the interstellar medium, and they come from nuclei with a well-known lifetime. Hence, we can trace recent star formation throughout the galactic disk by mapping Al^{26} (which has a lifetime of 1,000,000 years). Doppler broadening of the line will reveal how the regions under study are moving in the context of galactic rotation.

INTEGRAL may also shed light on the "missing supernova mystery." The last known galactic supernova event was reported by none less than Kepler and Galileo in 1606—yet it is easy to show that they should occur roughly every 50 years. If modern supernova remnants are



Integral on the proton. The Proton rocket, Russia's largest operational launch vehicle, is needed to put the heavy spacecraft into its unusually high Earth orbit, which is crucial for the scientific success of the mission.

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lurking unseen somewhere in the galactic disk, they should be observable through the "young isotope" gamma-ray light of Ti^{44} and Na^{22} (with lifetimes of 89 and 4 years, respectively), both created by the explosive process. If none are discovered, then the true galactic SN rate must be longer than previously assumed.

Barring the unexpected, SPI will be a long-distance runner: Its combined survey and in-flight calibration should yield their best results a few years into the mission. IBIS, on the other hand, will be a sprinter: Its wide field-of-view should yield a bounty of new, well-defined celestial sources, starting with a map of the center of our Galaxy. It will also provide important data on objects outside our Galaxy, especially active galactic nuclei (AGNs).

AGNs were first seen as 100-MeV gamma-ray sources by ESA's COS-B satellite in the 1970s (*8*) and then by GRO in the 1990s (*9*). The available evidence indicates that they are powered by central, massive black holes, with a peak energy output in the MeV region. Together with INTEGRAL's x-ray detector and optical monitor, IBIS will further explore AGNs at multiple wavelengths, continuing on from GRO and, more recently, the BeppoSAX satellite.

BeppoSAX also blazed the trail to identifying gamma-ray bursts with massive cosmological explosions (*10*). INTEGRAL will observe tens of bursts per year, performing germanium-resolution spectroscopy on them for the first time. NASA's SWIFT, dedicated to "catching GRBs on the fly," will be in orbit in 2003 (*11*). In 2004, the Italian mission AGILE (*12*) will provide the high-energy (>100 MeV) complement to INTEGRAL. The even more powerful GLAST should be launched by NASA a few years later.

Right now, two major x-ray observatories, NASA's Chandra and ESA's Newton, are in orbit, ready to start formation flight with INTEGRAL, providing simultaneous data at different wavelengths. Astronomers eagerly await the first data from this exciting mission. But even before take-off, INTEGRAL had bagged a result: technological innovation. In the best tradition of high-energy astrophysics, germanium spectrometers and CsI imagers, like Geiger counters or spark chambers, bring into space ideas developed for laboratory physics. In turn, space hones ground-based technology to a new sharpness, a cross-fertilization that makes both fields grow.

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PERSPECTIVES: ANALYTICAL CHEMISTRY

Analytes Ante Portas

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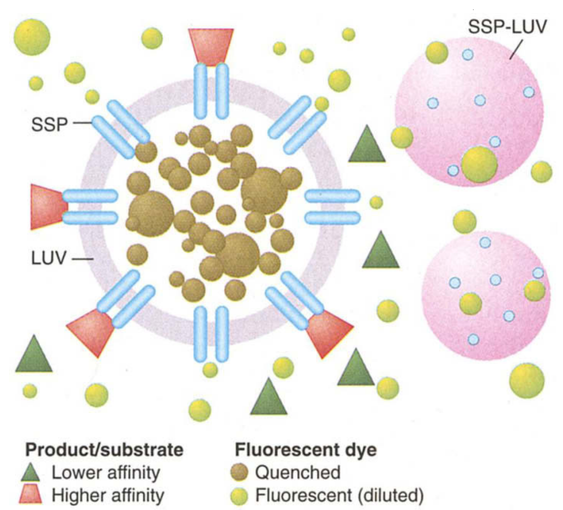
From genomics to proteomics and drug discovery, the demand for analytical tools enabling easy, reliable, and rapid screening of large numbers of samples is increasing constantly. On page 1600 of this issue, Das *et al.* (*1*) present a surprisingly simple but nonetheless effective and flexible method with potential applications in high-throughput screening.

In genomics, the main analytical task is to check for the presence or absence of specific DNA or RNA sequences. State-of-the-art assays make use of hybridization of complementary strains labeled with enzymes, fluorescent dyes, or nanoparticles. In proteomics, the analytical tasks are much more diverse. A specific marker is required to detect and quantify the activity of an enzyme. The selectivity of antibodies remains unchallenged, but it takes several weeks to get an antibody for a new target. Even minor changes in the chemical structure of the substrate require the same lengthy procedure. Modified enzyme substrates carrying a marker may be used, but they must also be synthesized in advance, limiting the flexibility of this technique.

The system introduced by Das *et al.* (*1*) should be particularly applicable to proteomics screening. The authors use large unilamellar vesicles (LUVs) containing a fluorescent dye. Self-assembling supramolecular pores (SSPs) span the LUV membrane (see the figure), defining the only spots where low molecular weight compounds like the fluorescent dye can diffuse from within the LUV to the outer medium. Binding of a compound inside the pore suppresses the diffusion of the fluorescent dye.



Pore control. SSP-LUVs containing fluorescent dye at self-quenching concentrations are added to an analyte solution. The dye can only diffuse through the SSP channels. When a SSP is blocked either by the substrate or by the product of an enzymatic reaction, the release rate decreases. The enzyme activity is measured as the ratio between blocking and non-blocking substrate/product.

The chemical building blocks of the SSPs can be easily modified. Octaphenyl groups determine the length of the pore spanning the LUV membrane. The eight phenyls in each octaphenyl chain do not form a planar structure; rather, every second one is oriented perpendicular to the plane of the others. Short peptides are attached to each phenyl group. According to the orientation of the phenyl rings, every second peptide chain is oriented perpendicular to the other side chains. Because the peptide side chains of one octaphenyl group interdigitate with those of the next, β-sheet structures are formed and a barrel-shaped pore is obtained.

The outer surface of the SSPs is designed to incorporate them into the lipid bilayer of the LUVs. Das *et al.* chose leucine residues for this purpose. The inner surface of the pores can be functionalized by introducing different amino acid residues. Depending on their size and charge, molecules may bind to the inside of the pore and block the pore cavity. If two different molecules with different affinities to the SSPs—such as

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