logenetic lineages will harbor genomic architectures that make them much more prone to speciation by genomic rearrangement than others (*6*), but at least one fundamental issue is now a bit clearer. With a rate of origin of duplicate genes on the order of 1% per gene per million years, the segmental duplication-rearrangement process is on a par with adaptive nucleotide changes within genes (genic evolution) as a mechanism for the origin of species incompatibilities. Consider that the average gene contains ~1000 nucleotides, that the mutation rate is ~0.1% per nucleotide per million years, and that the vast majority of mutations are either neutral or deleterious. In this case, the rate of nucleotide sequence changes per gene relevant to reproductive isolation and evolutionary adaptation could easily be less than the rate of gene duplication. Moreover, duplicated segments of DNA, even those not containing functional genes, contribute to chromosomal rearrangements in an indirect way—by serving as sites for nonhomologous recombination, thereby promoting secondary rearrangements (*2, 7*).

The recent observations of genome researchers raise two compelling issues for evolutionary biologists to ponder. First, discriminating between models of speciation that invoke negative epistatic interactions among genomes versus those that invoke microchromosomal rearrangements induced by gene duplication will require attention to the finest of details at scales of less than a few kilobases (the size of a typical rearrangement). Second, although the two big engines of evolution—adaptation and speciation—may be studied in isolation, they both are frequently interconnected through just one mechanism, that of gene duplication.

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PERSPECTIVES: ASTRONOMY

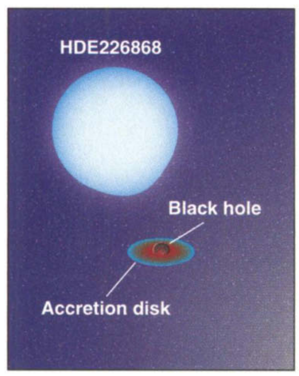
Black Holes Reveal Their Innermost Secrets

A. C. Fabian and J. M. Miller

Black holes can be luminous sources of radiation. During accretion of matter from their surroundings, they release enormous amounts of gravitational energy as gas spirals through an accretion disk into the hole. Recent studies indicate that one component of this emission can provide unprecedented insights into the innermost regions of stellar mass black holes.

The emission spectrum of a black hole is dominated by a broad peak caused by thermal emission within the disk. Emissions extending to hard x-rays, which follow a power law, are produced by interactions between disk photons and hot electrons in a corona above the disk. This type of spectrum is observed for black holes of stellar mass (typically 5 to 15 times the mass of our Sun) in orbit around a normal star. It is also found for supermassive black holes (with typical masses of ~10^7 solar masses) in the nuclei of galaxies. However, the temperatures in a disk around a supermassive black hole are cooler than around one of stellar mass.

A further feature, first clearly seen in the spectra of one class of accreting supermassive black holes, the Seyfert galaxies, is an iron emission line, produced by the irradiation of the disk by the coronal radiation. In its simplest form, it is a fluorescent iron line at 6.4 keV. This line is distorted into a characteristically skewed frequency profile by the combined effects of Doppler shifts, relativistic beaming, and gravitational redshifts. The latter result from the emitting matter that orbits at high velocities deep in the gravitational potential well surrounding the black hole (*1, 2*). Such a line shape was originally used to describe the spectrum of a stellar mass black hole, Cygnus X-1 (see the first figure) (*1, 3*), but was first clearly resolved in the Seyfert galaxy MCG-6-30-15 (*4, 5*).



Artist's impression of the black hole Cygnus X-1 and its stellar companion.

Until recently, evidence for such skewed emission lines from stellar mass black holes was very limited. Stellar mass black holes are much brighter because they are much closer than the supermassive black holes in Seyfert galaxies. But if the disk were highly ionized, little evidence for iron emission would be found. Now, however, the Chandra and XMM-Newton satellites have provided evidence for such lines in data from Cygnus X-1 (*6*) and other stellar mass black holes.

Reanalysis of archival data from recent x-ray satellites such as BeppoSAX (*6–9*) is revealing further evidence for iron lines. Most previous workers misinterpreted these features as breaks in the continuum emission, or had serious problems with the detectors because the sources were too bright. It is of course possible that we are the ones who are misled. But the similarities between the stellar mass black hole lines now found and those from the Seyfert galaxies appear compelling.

Particularly exciting is the extent of the "red" (lower energy) wing on some of the lines, for example, in Cygnus X-1 and XTE J1650-500 (see the second figure). These lines indicate extreme gravitational redshifts, which can only arise when the emitting matter is extremely close [at about one gravitational radius (*10*)] to the black hole's event horizon, from beyond which no information can escape.

The iron lines are the most direct signature from the innermost region around a black hole. The frequency of quasi-periodic oscillations (QPOs) in the x-ray flux from some of these objects (*11*) may be tied to orbital motion and may also point to the inner regions. However, there is no clear consensus on what modulates the QPOs or why high-frequency QPOs are not observed continuously. They therefore do not yet represent as effective a diagnostic probe.

The shape of the broad iron line allows us to determine the inner radius of the emission and the emission profile on the disk. Sometimes it is steeply peaked inward (*6, 12, 13*), suggesting an additional

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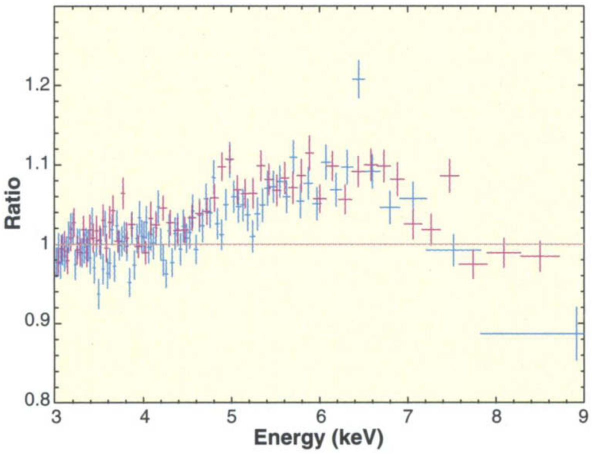

Iron lines in stellar mass black holes. (Red) Ratio of the spectrum of XTE J1650-500 (observed with XMM-Newton) to a simple disk blackbody and power law. (Blue) Same ratio for Cygnus X-1 (from Chandra). Plotting the spectrum in this manner reveals the shape of the iron line, which can be seen as a broad bump between 4 and 7 keV. [Data from (*7*)]

power source; for example, rotational energy may be extracted from a spinning black hole via magnetic connections to the inner accretion disk (*14*).

Spinning (Kerr) black holes have been postulated, but evidence for the spin itself is only now emerging. For several black holes, the inner radius of the disk deduced from the iron line indicates that matter is orbiting much closer than is possible for a nonspinning black hole. The orbit is closer to the stable orbit of a spinning black hole. The hypothesis that the fastest spinning black holes are those with the strongest radio emission remains untested.

A further quantity determined by the profile of the broad iron line is the disk inclination. The Doppler shifts are larger when the disk is seen more edge on, affecting mostly the "blue" (high energy) wing of the line. It is reasonable to suppose that the disk inclination is the same as that of the orbit of the binary companion, in the case of a stellar mass black hole. This has been demonstrated for some systems with optical measurements.

The iron line is a powerful diagnostic of the immediate environment of stellar mass black holes. It will enable us to test strong gravity, catalog black hole spin, and test models for the accretion inflow and jetted outflows from these objects. Further observations with Chandra and XMM-Newton, combined with the Rossi X-ray Timing Explorer (RXTE) (*15*), promise more revelations about stellar mass black holes.

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15. RXTE can measure fast timings and covers a broad spectrum, thereby complementing the high resolution over a narrow spectrum of Chandra and XMM-Newton.

PERSPECTIVES: SIGNAL TRANSDUCTION

History Matters

Nicholas T. Ingolia and Andrew W. Murray

From the swimming of bacteria to communications among scientists, organisms depend on the collection and processing of information from the environment, a process called signal transduction. The simplest signaling pathway is a linear cascade, a collection of unidirectional arrows that connect a stimulus to a response via multiple intermediates. If you lived in this oversimplified world, you would still be staring at the blinding light that illuminated the obstetrician who delivered you from the darkness of the womb, because your visual system would neither have adjusted its threshold to maximize the sensitivity of its response (adaptation), nor returned to its ground state (recovery) once your gaze turned to something else. Properties like adaptation and recovery result from interactions among components of signaling networks. How do these properties reflect the topology of connections within a network, in addition to the detailed properties of the network's biochemical components? On page 1018 of this issue, Bhalla *et al.* (*1*) tackle this question with a combination of theory and experiment. They reveal that the behavior of a common cellular signaling network is history dependent, that is, the network output depends on the recent history of a cell's exposure to the network's activating stimulus.

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Mitogen-activated protein kinase (MAPK) cascades are well-studied signal transduction systems present in a wide variety of eukaryotes. MAPK signaling pathways transduce signals for processes as diverse as mating, cell proliferation, and organ development. Depending on the cellular context, MAPK cascades may provide a switchlike all-or-none decision between two different responses (*2*), or a graded response over a wide range of stimulus strengths (*3*). Bhalla and colleagues present a systems-level analysis of how the MAPK signaling network of cultured mammalian cells processes signals (*1*). They couple computational simulations with pharmacological inhibition of network components, and discover that the network produces two qualitatively different intracellular responses that depend on the cell's prior history.

There is a powerful analogy between biological signal transduction networks and the signal processing systems conceived by engineers. The input of a typical signal transduction system is the concentration of some extracellular stimulus or ligand, whereas the output is the activity of an intracellular factor such as a protein kinase. For Bhalla *et al.*, the concentration of platelet-derived growth factor (PDGF) is the input of the MAPK network, and the activity of MAPK is the output. The amount of MAPK activity is related to the extracellular signals to which the cell is exposed, but this may not be a simple relation. One reason is that the signaling network features feedback regulation, which produces many complex behaviors (see the figure).

Bhalla and co-workers produce a quantitative model of the MAPK network and experimentally test its qualitative predictions. MAPK initiates two feedback loops, one positive and one negative. In simulations and experiments, a 5-minute pulse of PDGF induces MAPK activity that persists for about 30 minutes before slowly declining. Positive feedback results in this bistable (switchlike) behavior, where a brief stimulus flips the system into a state in which a positive-feedback loop sustains the active state. Bistability thus provides a cellular memory, allowing a response to outlast the stimulus that elicited it. Inhibiting either of the two proteins involved in posi-