1965–1982" (NCHS Advance Data 104, Public Health Service, Hyattsville, MD, 11 February 1985).
9. J. Berent, *Family Planning in Europe and USA in the 1970s* (*Comparative Studies*, no. 20, World Fertility Survey, London, October 1982); United Nations, *Recent Levels and Trends of Contraceptive Use as Assessed in 1983* (United Nations Publication ST/ESA/SER.A/92, New York, 1984.
10. L. Henry, *Eugenics Q.* **8**, 81 (1961). The ten populations judged to have reasonable age reporting were retained in later analyses.
11. J. W. Tukey, *Exploratory Data Analysis* (Addison-Wesley, Reading, 1977), pp. 331–400 and 443–465; A. J. Coale and J. Trussell, *Pop. Index* **40**, 185 (1974).
12. H. J. Page, *Pop. Stud.* **31**, 85 (1977).
13. G. Mineau and J. Trussell, *Demography* **19**, 335 (1982). The Mormon genealogies, collected from surviving kin, may be biased toward high fertility because the more children a couple had, the more likely one or more descendants would be alive to contribute to the family history.
14. These estimated rates by age for females control for the effects of male age and marriage duration. Because older women generally have been married longer and have older husbands, the fertility rates observed for all women decline much more rapidly than these rates.
15. P. Vincent, *Population* **5**, 45 (1950).
16. See Menken and Larsen (*5*) for detailed description of data sources. Between 11 and 35% of women in these populations married after age 30. Two problems, both of which may lead to overestimates of fecundity decline with age, merit attention. For some women the marriage may not be the first, although widow remarriage is uncommon in all of these populations. The proportion infertile of all unions, however, overestimates infertility in first marriages, particularly at the older ages, since some women who have no children in a remarriage will have at least one from an earlier union. Of more concern is premarital pregnancy. Women who married early may have been more fecund and therefore more likely to have an accidental nonmarital pregnancy. The decline with age at marriage in proportions becoming mothers would then be greater than the natural decline in fecundity. When premaritally pregnant women (as determined by a birth within 7 months of marriage) were excluded from the English data, however, the age patterns were virtually unchanged. Data on all women were used for comparability with census tabulations.
17. L. Henry, in *Public Health and Population Change*, M. Sheps and J. C. Ridley, Eds. (Univ. of Pittsburgh Press, Pittsburgh, 1965), pp. 333–350.
18. H. Leridon, *Population* **32**, 231 (1977); J. Barrett, *Demography* **8**, 481 (1971).
19. R. Hatcher, G. K. Stewart, F. Stewart, N. Josephs, J. Dale, *Contraceptive Technology 1982–1983* (Irvington, New York, ed. 11, 1982); R. Kleinman and P. Senanayake, *Handbook on Infertility* (International Planned Parenthood Federation, London, 1979).
20. J. Bongaarts, *Demography* **12**, 645 (1975).
21. J. A. Collins *et al.*, *N. Engl. J. Med.* **309**, 1201 (1983).
22. J. Bongaarts, *Family Planning Perspect.* **14**, 75 (1982).
23. M. P. Vessey, N. H. Wright, K. McPherson, P. Wiggins, *Br. Med. J.* **1-1978**, 265 (4 February 1978). These women may be considered more representative of those who delay childbearing than of all women.
24. R. L. Heuser, *Fertility Tables for Birth Cohorts by Color* [DHEW Publ. (HRA) 76-1152, Government Printing Office, Washington, DC, 1976]; National Center for Health Statistics, *Vital Statistics of the United States* (Government Printing Office, Washington, DC), vol. 1 for various years.
25. J. A. McFalls, *Pop. Bull. 34* (no. 2) (1979), p. 1; ——— and M. H. McFalls, *Disease and Fertility* (Academic Press, New York, 1984).
26. R. B. Jones, B. R. Ardery, S. L. Hui, R. E. Cleary, *Fertil. Steril.* **38**, 553 (1982); J. L. Kane, R. M. Woodland, T. Forsey, S. Darougar, M. G. Elder, *ibid.* **42**, 843 (1984).
27. J. W. Curran, *Am. J. Obstet. Gynecol.* **138**, 848 (1980).
28. S. O. Aral, W. D. Mosher, W. Cates, Jr., *Am. J. Public Health* **75**, 1216 (1985). At each age, the proportion for black women is at least 80% higher than that for white women.
29. L. Westrom, *Am. J. Obstet. Gynecol.* **138**, 880 (1980). Four-hundred-and-fifteen women were examined 9.5 years after initial treatment. The fraction of sterile rose with the number of infections: 12.8% after one infection, 35.5% after two, 75% after three or more. Infecundity from a single episode increased with age and with severity of infection.
30. P. Senanayake and D. G. Kramer, *ibid.*, p. 852; D. W. Cramer *et al.*, *N. Engl. J. Med.* **312**, 941 (1985).
31. K. Ford, "Contraceptive Utilization in the United States: 1973 and 1976" (NCHS Advance Data 36, Public Health Service, Hyattsville, MD, 18 August 1978); W. F. Pratt *et al.*, *Pop. Bull. 39* (no. 5) (1984), p. 1.
32. C. J. R. Hogue, W. Cates, C. Tietze, *Epidemiol. Rev.* **4**, 66 (1982); *Family Planning Perspect.* **15**, 119 (1983).
33. N. B. Ryder and C. F. Westoff, *Reproduction in the United States, 1965* (Princeton Univ. Press, Princeton, 1971); W. Grady, "National Survey of Family Growth, Cycle II: Sample Design, Estimation Procedure, and Variance Estimation" [NCHS Vital and Health Statistics, DHHS Publ. (PHS) 81-1361, series 2, no. 87 (Government Printing Office, Washington, DC, February 1981)]; W. Mosher, C. Bachrach, M. Horn, "National Survey of Family Growth, Cycle III: Sample Design, Weighting, and Variance Estimation" [NCHS Vital and Health Statistics DHHS Publ. (PHS) 85-1372, series 2, no. 98 (Government Printing Office, Washington, DC, September 1985)].
34. W. D. Mosher, "Contraceptive Utilization, United States, 1976" [NCHS Vital and Health Statistics, DHHS Publ. (PHS) 81-1983, Government Printing Office, Washington, DC, March 1981, series 23, no. 2]. Among married women aged 30 to 44, nearly three-fourths of the nonsterilized were contraceptive users.
35. S. Aral and W. Cates, Jr., *J. Am. Med. Assoc.* **250**, 2327 (1983).
36. We thank R. Schofield and J. Knodel for the tabulations of the English and German data, respectively, that appear in Figs. 1 and 2. This research was supported in part by grants to Princeton University: grant HD11720 from the National Institute of Child Health and Human Development and 69006 and 70005 from the Rockefeller Foundation.

The Galactic Center: Is It a Massive Black Hole?

K. Y. Lo

Studies of active galactic nuclei constitute one of the major efforts in astronomy. Massive black holes are the most likely source for the enormous energy radiated from such nuclei. Observations reviewed here suggest unusual activity and the possible existence of a massive black hole in the nucleus of our galaxy. Because of its proximity to Earth, our galactic nucleus can be observed in unsurpassed detail and may serve as the Rosetta stone both for deciphering active galactic nuclei and for confirming the existence of a massive black hole.

THE TERM "BLACK HOLE" IS ONE OF THE MORE POETIC scientific terms and has wide appeal to the imagination of the general public (*1*). It is also a basic consequence of General Relativity and most theories of gravity. Black holes could arise in at least three astronomical settings. (i) Primordial black holes forming out of the ultrarelativistic gas at the early stages of the Big Bang are permissible in principle but very difficult to observe (*2*). (ii) A more realistic stellar black hole may form as the remnant of a supernova explosion at the end of the life of a sufficiently massive star—the outer layers of the star being ejected into interstellar space and the core collapsing into a volume smaller than its event horizon (*2, 3*). (iii) A massive black hole may also form from the coalescence of a star cluster (*4*). Although the detailed mechanisms are not clear, the formation of massive black holes may be an inevitable outcome of the evolution of galactic nuclei (Fig. 1) (*5*). Such massive black holes

The author is a professor in the Department of Astronomy, University of Illinois, Urbana, IL 61801.

have been hypothesized to account for the phenomena observed in active galactic nuclei (*6*).

For over 20 years, active galactic nuclei have been one of the major topics in astronomy and astrophysics. They come in various forms, radio galaxies, quasars, Seyfert galaxies, and BL Lacertid objects, constituting a few percent of the known galaxies (*7*). They are distinguished by several characteristics. They exhibit very energetic activities in the central regions of galaxies. The luminosity L of these active nuclei is extremely high; some can produce $\sim 10^{46}$ erg/sec [$\sim 10^{12}$ the solar luminosity ($L_\odot$), 4×10^{33} erg/sec] of continuum radiation. Such radiation is sometimes found to vary on time scales as short as days, implying that the source is $\lesssim 10^{17}$ cm in extent. Thus, in some cases, as much radiation as is produced by the stars in an entire galaxy [typically 100,000 light-years in diameter (1 light-year = 9.46×10^{17} cm)] is generated within the central light-year. Another common characteristic is the presence of high-density ionized gas moving at speeds sometimes reaching 0.03 c within the central few light-years. The origin of these high velocities is not understood.

Some active galactic nuclei are also very powerful radio sources. Such radio sources, by virtue of their nonthermal radiation mechanism (synchrotron radiation), which involves highly relativistic electrons spiraling in magnetic fields, require settings other than ordinary stars for their production. The nuclear component of these radio sources typically has an elongated structure (jet) emanating from a compact core and is exceedingly bright (*8*).

The central question associated with active galactic nuclei is how the enormous amounts of energy are generated at high efficiency within a compact volume. This requirement leads inevitably to gravitation. In the massive black hole model of active galactic nuclei (*6*), energy is derived from the release of gravitational binding energy of matter falling into the black hole. This mechanism is in principle a much more efficient method for generating energy than nuclear fusion and can operate in a very confined space (*9*). However, despite all the advantages of the massive black hole

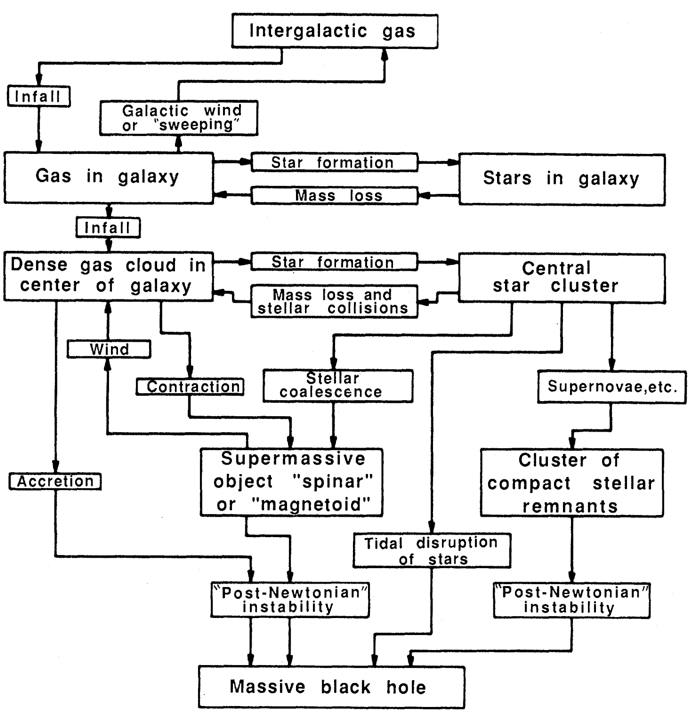

Fig. 1. Flow chart indicating the various processes whereby gas and stars may accumulate at the nucleus of a galaxy. The final result is likely to be the formation of a massive black hole. Adapted from (*5*).

models and despite the dedicated observational efforts of many types of astronomers, direct evidence for massive black holes is lacking, because the angular resolution of the telescopes is insufficient. Conventional ground-based optical and infrared observations are limited to resolutions of $\gtrsim 0.5$ arc sec. For a black hole with a mass of $\sim 3 \times 10^{8}$ solar masses ($M_\odot$) (solar mass = 2×10^{33} g) at a distance from Earth of 300×10^{6} light-years, typical of an extragalactic active nucleus, R_{sc} is 10^{14} cm and subtends an angle of $< 10^{-7}$ arc sec. This is only 10^{-3} of the highest resolution (10^{-4} arc sec) currently achievable with very-long-baseline interferometry (VLBI) techniques (*10*).

The distance to our galactic nucleus is 1/70 of the distance to the nearest extragalactic nucleus. At a distance of about 30,000 light-years, 10^{-4} arc sec corresponds to 1 AU (1 astronomical unit = 1.5×10^{13} cm) or the Schwarzschild radius of a $5 \times 10^{7}\, M_\odot$ black hole. Thus, our galactic nucleus can be observed in great detail. It exhibits phenomena similar to those in other active galactic nuclei (*11*). In particular, within 1 light-year of the peak of the star distribution at the nucleus are found a very compact radio source (diameter <20 AU), which is the best candidate for a massive black hole, a source of luminosity at $\sim 10^{7}\, L_\odot$, and a source of very high velocity ionized gas. This region may also be a copious source of positrons responsible for an extraordinary 0.51-MeV γ-ray line observed toward the center. Finally, there may be dynamical evidence for the existence of a central point mass.

The Galactic Center

Because the sun is located on the outskirts of the plane of our galaxy, the actual galactic center is obscured from view by the large amount of intervening dust (only 10^{-12} of the visible light from the center reaches Earth). As a result, in the study of the galactic center, radio and infrared techniques (5 m $\gtrsim \lambda \gtrsim$ 1 μm) have been used because long wavelength radiation can penetrate the dust. For example, an infrared picture of the inner galaxy made with the Infrared Astronomical Satellite (IRAS) (Fig. 2a) shows the more distant parts of the galaxy compared to the visible-light image (Fig. 2b). In particular, it shows the galactic center as the brightest and warmest bulge.

Although the stars at the center cannot be observed with visible light, they can be traced in the near-infrared (λ = 2 μm) where the radiation is predominantly due to the red giant stars. If the giant stars constitute a constant fraction of all the stars everywhere, the 2-μm light distribution would describe the star distribution. The 2-μm observations suggest that the star distribution in the central region resembles a flattened spheroid in which the density increases inward, roughly as $r^{-1.8}$ where r is the distance to the center (*12*). The central star density is as high as $10^{6}\, M_\odot$ per cubic light-year, about 10^{8} times that in the solar neighborhood.

The first extraterrestrial radio wave detected on Earth was from the powerful radio source at the galactic center—Sagittarius A (Sgr A) (*13*)—which is the strongest radio source associated with our galaxy (Fig. 3) (*14*). Sgr A comprises a mixture of thermal radiation from ionized gas and synchrotron radiation. From the thermal emission, we infer a large ultraviolet (UV) flux which is required to maintain the ionization of the gas; the nonthermal radiation requires sources of relativistic electrons. The mere presence of Sgr A indicates that the central region is more than a quiescent collection of stars.

The discovery in 1951 of the hyperfine structure line (λ = 21 cm) of atomic hydrogen in interstellar space provided a powerful tool with which to probe the interstellar medium (*15*). The penetrating power of this radio frequency line made it possible to demonstrate the large-scale spiral structure of the galaxy (*16*). When similar observations were directed toward the galactic center, the surprising result was that, as far out as 10,000 light-years from the center, the gas is not only rotating but also expanding at high velocity. This was unexpected since, until then, the accepted picture of our galaxy had been that it was a flat, circular, differentially rotating disk. The very large kinetic energy in the expanding motion was taken as evidence for extraordinarily powerful explosions at the nucleus in the past. This was the earliest indication of energetic activities at the center (*17*).

In 1971, Lynden-Bell and Rees analyzed the infrared luminosity and other observations of the central region of our galaxy and proposed that the ultimate energy source is a black hole. They also suggested that a very compact nonthermal radio source might be detected at the center, as one of the critical observations for testing their hypothesis (*18*). In 1974, such a source was unambiguously detected first by Balick and Brown (*19*). The properties of the compact source are similar to those of the extragalactic compact sources found in quasars and radio galaxies. Most importantly, the source is extremely small, imposing a very stringent constraint on models for the source.

At about the same time, observations of the radio recombination lines from Sgr A revealed the presence of ionized gas moving at much greater speeds than the expected thermal motion (*20*). Subsequent higher resolution observations of singly ionized neon suggested that the velocity dispersion of the ionized gas increases toward the center, with radial velocities reaching ±260 km/sec within 0.7 light-year of the center. If the motion of the ionized gas is governed by gravity, then the observed speeds would indicate a highly concentrated mass distribution, and possibly a point mass of $3 \times 10^6 M_\odot$ (*21*).

Until recently, observations of Sgr A have been limited in angular resolution. With the completion of the National Radio Astronomy Observatory's Very Large Array (VLA) in New Mexico, high-sensitivity and high-resolution imaging of radio emission from the galactic center has become possible (*22*). Over the last 5 years, such images have revealed unexpected features and a range of intriguing activities in our galactic center that are observable only because of its proximity. Figure 4a shows such a radio picture of the inner ~0.5° (~300 light-years) of the galaxy, showing Sgr A along with the so-called Arc source (*23*).

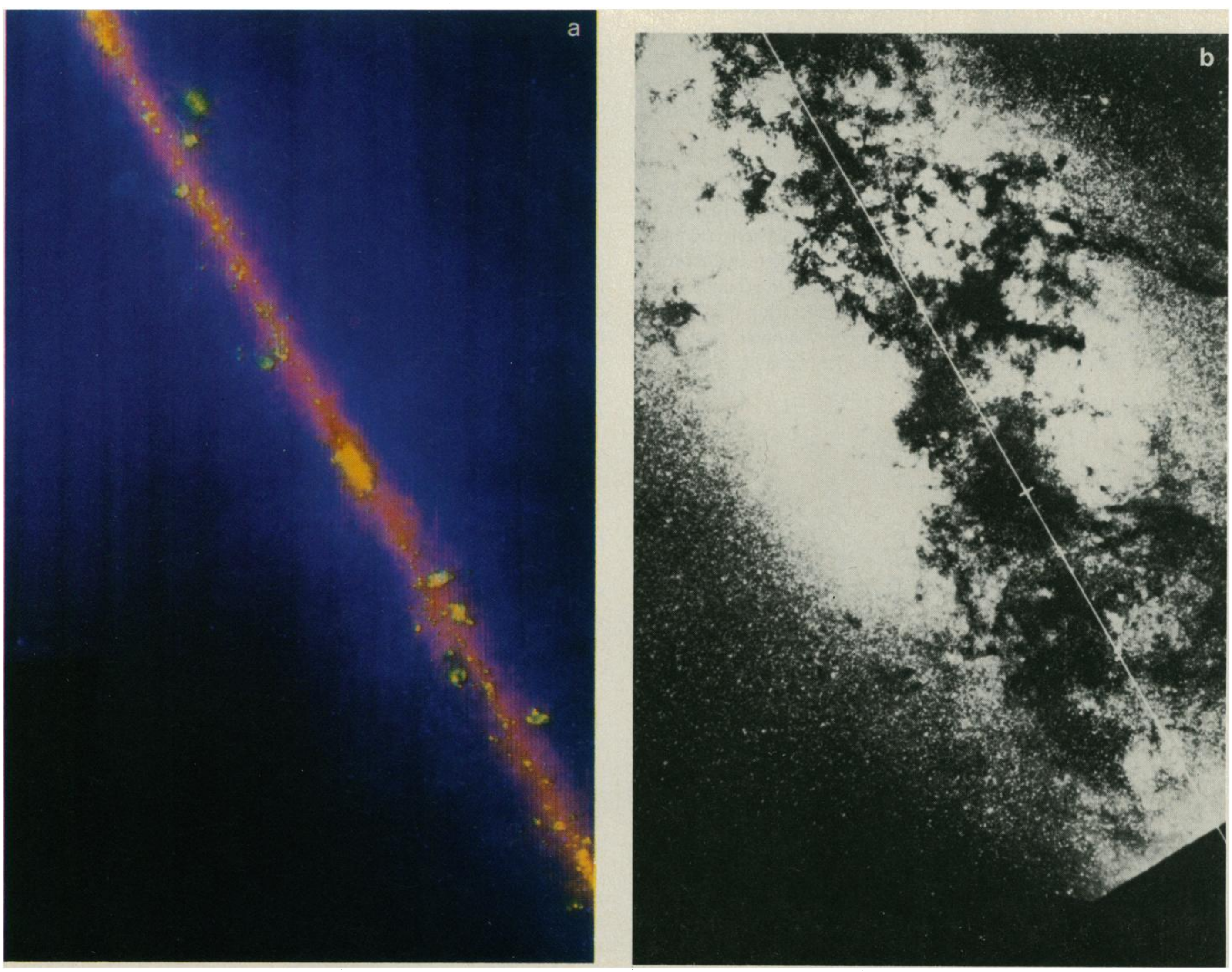

Fig. 2. The same part of the inner galaxy (a) in infrared light (measured with IRAS) and (b) in visible light. North is at the top and east is to the right. In (b), the white line delineates the galactic plane, from galactic longitude 336° (lower right) to 24° (upper left); the cross marks the location of the galactic center at 0°. In (b) the actual center is completely obscured by the foreground dust in the galactic plane. What is seen is dominated by dust and stars fairly close to the sun, within about 3000 light-years. In (a) the infrared emission comes from the more distant parts of the galactic plane where the dust heated by stars produces the bright diagonal band; the galactic center is the yellow bulge near the center of the band. Giant interstellar clouds of gas heated by nearby stars are seen as the bright yellow and green knots scattered along the plane.

The Arc source contains some of the more surprising features uncovered by the VLA images—highly organized, linear structures running perpendicular to the galactic plane. They are strikingly regular, unbroken, and homogeneous in appearance. Each of the filaments is ~100 light-years long and ~3 light-years wide (*23*). Apparently wrapping around the linear features are curved radio emission features that may be connected to Sgr A. Such organized linear structures require a confinement mechanism for the radiating electrons that would otherwise disperse in a very short time. The most natural scheme involves large-scale magnetic fields along the linear structures. This is confirmed by the observations of high intrinsic polarization in the radio emission, indicating synchrotron radiation (*24*). Comparison with larger scale maps (Fig. 4b) (*25*) of the galactic center shows that these linear features are actually enhanced emission at the base of a larger Ω-shaped loop structure extending 600 light-years above the galactic plane. The formation of such highly organized, large-scale magnetic fields perpendicular to the galactic plane and the origin of the high-energy electrons required in the synchrotron radiation are not well understood. The relationship of the galactic center to the Arc source, though unclear, is intriguing.

Extending ~80 light-years and centered on the peak of the central star cluster, Sgr A has a highly disturbed appearance and shows some unusual internal structure. A close-up view (Fig. 5) reveals an oval nonthermal source that may be the remnant of a supernova and an intriguing "spiral" radio source at one edge of it (*26*). The "spiral" structure, called Sgr A West, is thermal radiation from high-density ionized gas. At the centroid of the ionized gas distribution and of Sgr A is the compact nonthermal radio source (Sgr A*).

The actual dynamical center of the galaxy, or the bottom of the

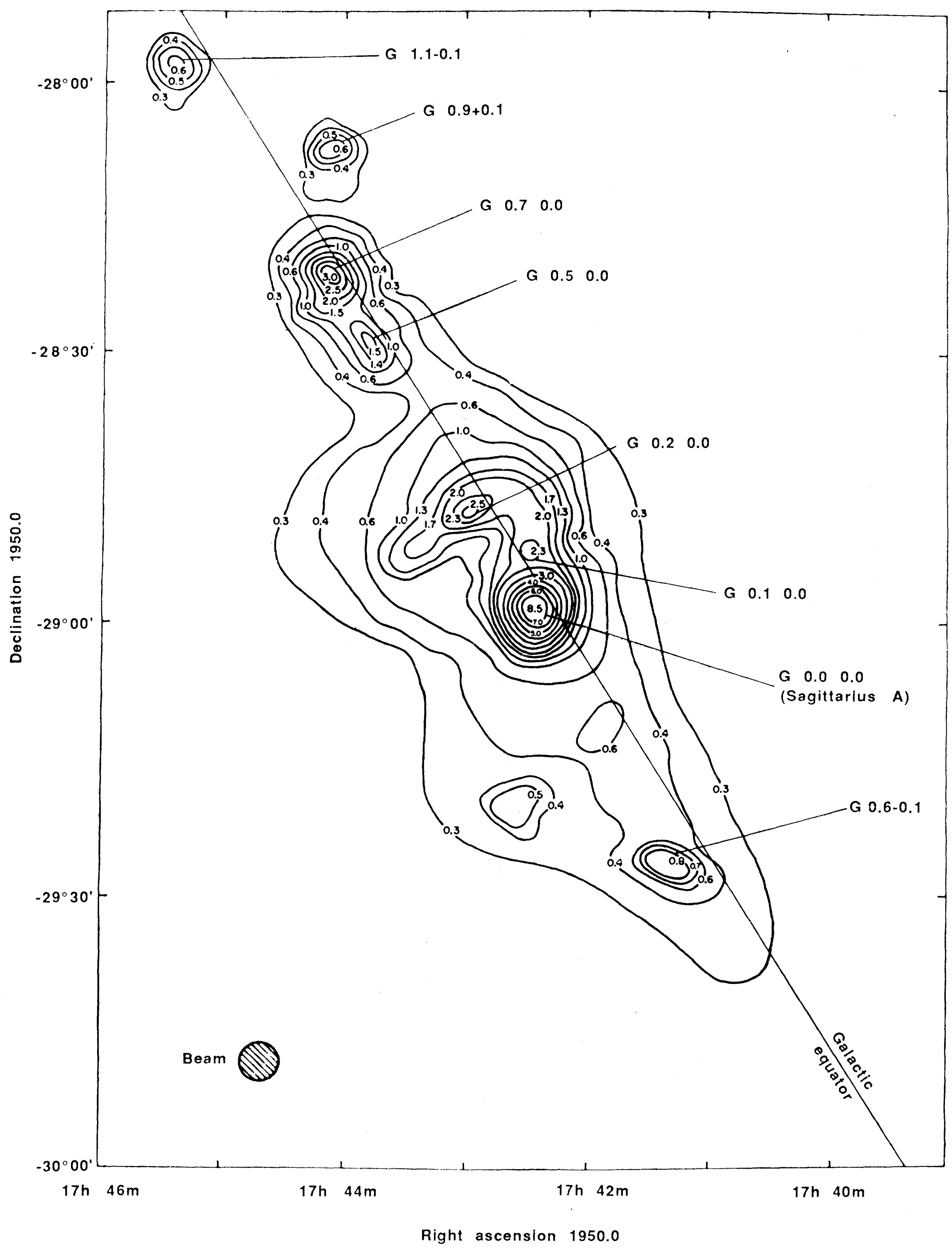

Fig. 3. Map (λ = 3.75 cm) of the central 2° of the galaxy (*14*), showing Sagittarius A (Sgr A), the powerful radio source at the center, and the Arc source (G 0.2 0.0). Detailed structures of these sources are shown in the following figures. Adapted from (*14*).

central potential well, is not well defined on a scale smaller than 0.3 light-year. The most compact object, Sgr A*, is within 0.2 light-year of the 2-μm source, infrared source (IRS) 16, which may be identified with the peak of the underlying star distribution (*14*). A component of IRS 16 has also been suggested as the central luminous source, with a total luminosity of $\sim 10^7\ L_\odot$ (*27, 28*). Within 0.3 light-year of IRS 16, very broad hydrogen and helium emission lines have been detected, with large line widths (~1500 km/sec) typical of the high-speed gas found in active galactic nuclei (*29*).

A unique 0.51-MeV γ-ray line was also observed in the general direction of the galactic center (*30*). The line was measured with very high spectral resolution so that its identification with e+e− annihilation and positronium decay seem rather secure (*31*). Because γ-ray observations have very poor angular resolution, the origin of the positrons (e+) is highly uncertain. Most unexpectedly, the line was found to vary with a 6-month time scale (*32*), indicating a compact source for the line and also a single compact source of e+. It has been assumed that this source of e+, with a minimum required production rate of 10^{43} e+ per second, is located at the galactic center (*33*).

The Compact Nonthermal Radio Source (Sgr A*)

The compact nonthermal radio source, located within 0.2 light-year of the dynamical center of the galaxy, may be the key to the activities there. Efforts to determine its structure have continued for many years (*34*). Because of a combination of practical difficulties and the source properties, the structure is still not well known. However, the latest observations set an upper limit of <20 AU for the source diameter. (The source would fit inside the orbit of Saturn.) The observations also reveal an elongation in the source at λ = 3.6 cm, with the position angle of the major axis nearly parallel to the rotation axis of the galaxy (*35*). Whether this reflects the presence of a jet structure is not known. The most recently observed parameters of Sgr A* are summarized in Table 1. Sgr A* has properties very similar to those of extragalactic compact radio sources, except for its much lower luminosity. Unlike the extragalactic case, however, its extremely small dimensions effectively preclude a dense star cluster as a possible energy source and admit only objects with stellar dimensions.

Can this source be powered by a stellar object? Stellar radio sources are known in the form of pulsars (powered by the rotational energy of a neutron star), binary stellar radio sources (powered by accretion onto a white dwarf, neutron stars or even stellar black holes), or very young supernovae. Radio emission associated with stellar atmospheric activities (such as solar flares) is negligibly weak by comparison.

Ordinary pulsars fail to explain Sgr A* because the brightest pulsar known has only 10^{-4} times the radio luminosity of Sgr A*. Although Sgr A* becomes stronger at higher frequency, pulsars have exactly the opposite behavior (indicating a different radiating mechanism). Some binary x-ray sources are also radio sources, but they are characterized by frequent intensity outbursts. Their typical luminosity is 10^{-5} that of Sgr A*, and the brightest one reaches a luminosity that is only 0.1 that of Sgr A* at the peak of an outburst. A young supernova is very compact and could be very bright, but the luminosity decays in a few years as the source expands (*36*), and the supernova remnant expands very rapidly (*37*). Sgr A* is unusually steady and there is a rather stringent limit on the expansion speed, far below what is observed in young supernovae.

A neutron star can supply a total power up to a few times erg/sec (*38*), so that such an object can in principle power the erg/sec of radio luminosity from Sgr A*. The most promising m along such lines is based on an incoherent synchrotron so confined by ram pressure but powered by a pulsar (*39*). Tc confined, the source must move at high velocity through a d interstellar cloud. Recent observational limits on proper motion lack of a high-density cloud around Sgr A*, the new upper lim the source size, and the high turnover frequency all tend to rule such a model (*35*).

On the basis of observational evidence, Sgr A* is a unique r source in the galaxy, and it cannot be accounted for on the bas any known stellar source. Though faint by comparison with extr lactic compact radio sources, Sgr A* is orders of magnitude stro than the typical stellar radio sources. Sgr A* could be due to l level accretion onto a $\sim 10^6\ M_\odot$ black hole (*40*), and it has a consistent with such a black hole ($<10^3$ times R_{sc}). Moreover, A* resembles closely a weaker version of the nuclear radio sourc external galaxies, such as M81 and M104. Such extragalactic nu sources have too large a radio luminosity to be powered by a st object. Nonetheless, although the best explanation for Sgr A* is it is a massive black hole, because of its low luminosity possibility of, for example, a neutron star cannot yet be exclu The mass of Sgr A* needs to be determined.

Mass determination. If there is a supermassive black hole at galactic center, the stars in its immediate vicinity will be moving $1/r$ potential; the closer they are to the center, the larger t velocities will be. Thus, measuring the velocity dispersion of sta varying distances from the center is the best way to probe the ce potential. The stars are ideal gravitational test particles because t motion is unaffected by nongravitational forces such as shocks, pressure, and radiation pressure. Unfortunately, because of the l obscuration toward the center, the central star cluster is not vis and attempts to measure velocity dispersion in the near-infr have not been successful.

There is an indirect way to probe the mass of Sgr A*, vi proper motion. A star found at the bottom of the potential we the central stellar distribution is likely to have a large space velo On the other hand, a supermassive object, because of the equip tion of kinetic energy, would have a small velocity and would s at the bottom of the potential well. Therefore, if Sgr A* is an ol with stellar dimensions, it would have a velocity of ≳150 km/sec possibly a substantial component transverse to the line of sigh transverse motion at 100 km/sec at the galactic center produce angular displacement (proper motion) of 0.002 arc sec/year, w is measurable with present-day techniques. Thus, any measur proper motion would rule out a supermassive black hole mod Sgr A*. The first results of this difficult measurement are consis with the secular parallax expected for an object at rest at the gal center (*41*).

Ionized and Neutral Gas at the Center

Both ionized and neutral gas have strong emission lines in millimeter through infrared wavelength range, thus providing us probes of the central ionizing and heating sources as well as the r distribution. It is important to understand the physical conditio the gas in the central region. The central 10 light-years contai unusual distribution of high-density ionized gas. This gas occup largely evacuated cavity that is bordered by $\gtrsim 10^4\ M_\odot$ of ne material.

Ionized gas. The ionized gas within the central 10 light-yea distributed in an intriguing "spiral" morphology (Fig. 6) (*42*) th

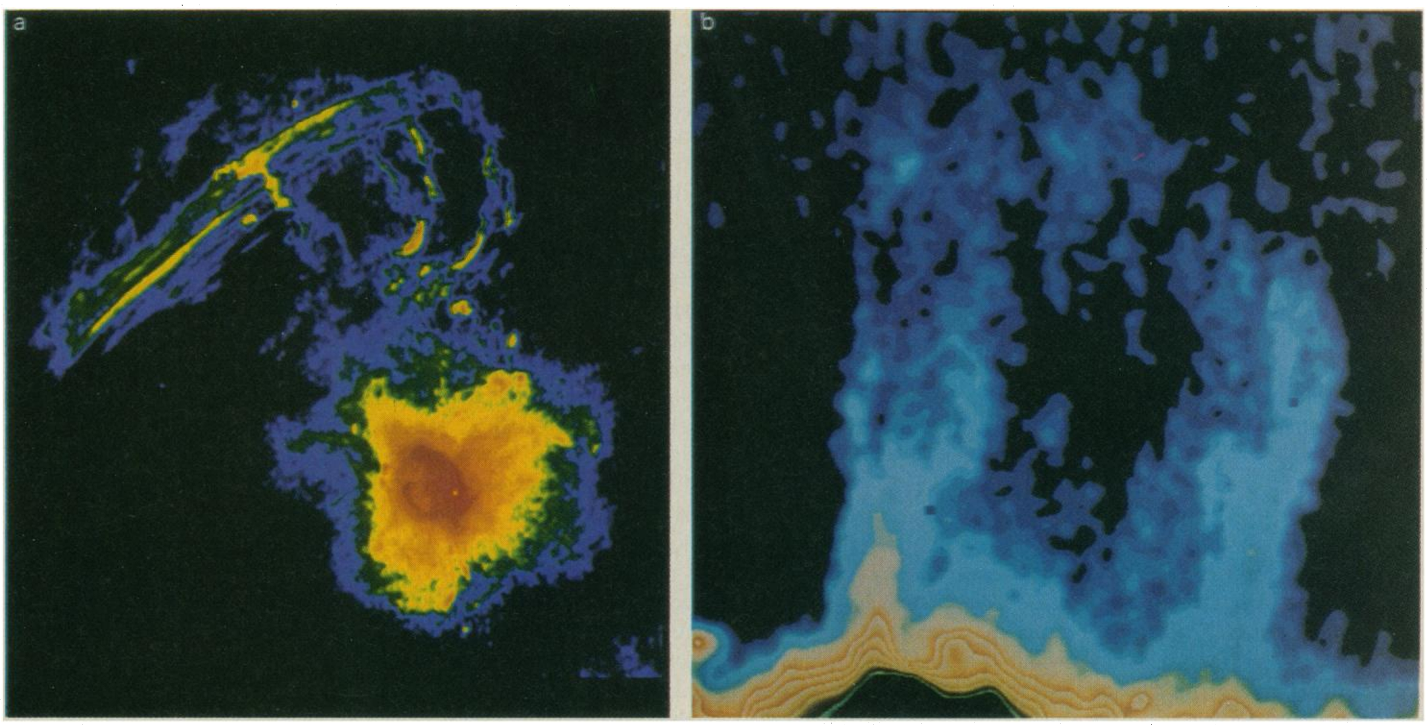

Fig. 4. (a) A radio continuum picture (λ = 20 cm) (~0.5° in extent) of Sgr A plus the Arc source (*23*) (see Fig. 3). Red in the false-color picture represents bright emission, whereas blue represents faint emission. The ~80–light-year halo of Sgr A has a highly disturbed appearance, consisting of the oval-shaped Sgr A East (see Fig. 5) and a number of large-scale protrusions. The yellow dot at the center of Sgr A is the compact nonthermal radio source at the center of the galaxy. An interesting unexpected result is a system of narrow filamentary structures, 100 light-years long, which make up the Arc source, having typical widths of ~3 light-years. North is at the top and east is to the right. (b) A radio continuum (λ = 2.8 cm) large-scale (roughly 1° × 1°) map of the region just above the galactic center (*25*). This picture is oriented differently from the other figures. The galactic plane runs horizontally just below the bottom of the picture. A large Ω-shaped loop of emission extends ~600 light-years above the galactic plane. At the positive longitude (on the left) base of this loop is the Arc source (a) with the system of long filamentary structures (which would run up and down in this map). This Ω-shaped loop is not apparent in Fig. 3 because of the lower sensitivity of the 3.75-cm map.

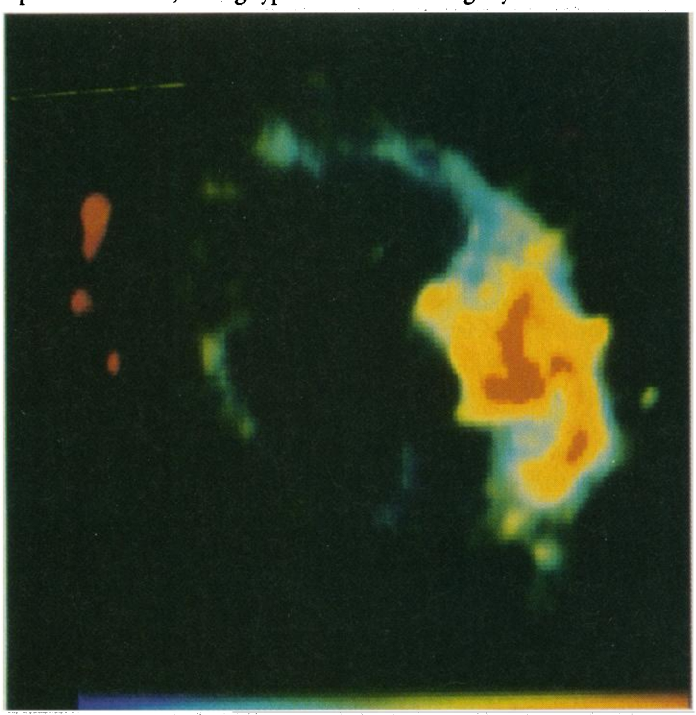

Fig. 5. A close-up view of Sgr A (Fig. 4a) at 8–arc sec resolution, combined from λ = 6 and 20 cm maps (*26*). The false-color coding in this case is used to denote the wavelength dependence of the radio emission, an indicator of the radiation mechanism. The oval-shaped source is Sgr A East, presumably a supernova remnant (the blue-green color indicates synchrotron radiation). The spiral source at the edge of the oval source is Sgr A West [the yellow-red color indicate thermal (bremsstrahlung) radiation from ionized gas]. The three red objects to the east of Sgr A East are due to ionized gas around young hot stars.

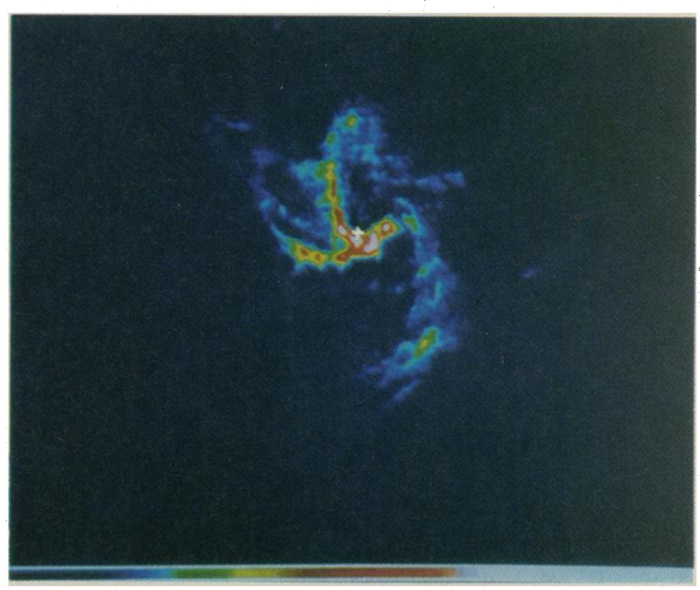

Fig. 6. A radio map (λ = 6 cm) of the central 10 light-years of our galaxy at 1–arc sec resolution (*42*). It shows the "spiral" source, Sgr A West (Fig. 5), in much greater detail. The north-south extent of the radio source is ~60 arc sec (10 light-years). The intense compact radio source at the center has been subtracted from the map and is located at the position marked by the cross. North is at the top and east is to the right. White in this false-color picture denotes bright emission and blue represents faint emission. The brighter emission tends to come from near the center. All the radio emission in this map is thermal radiation from high-density ionized gas, arranged in a unique morphology. Elsewhere in the galaxy, high-density ionized gas is found around young massive stars that ionize all the surroundings gas (out of which they have been formed), in the well-known nebulae such as Orion and Rosette. The unusual filamentary structures shown here reflect the special conditions found at the galactic center.

unique in the galaxy. The ionized gas is clumpy and patchy, with three bright "arms" close to the center. For convenience, they will be termed north, east, and west arms (top, left, and right, respectively, in Fig. 6). Fainter features are found on the periphery of the distribution, such as the arm to the south.

Spectroscopic observations, based on the 12.8-μm line from singly ionized neon and recombination lines of hydrogen, have provided information on the radial motion (*15, 21, 43, 44*). In particular, they show that the radial velocity of the ionized gas varies systematically northward along the arm to the south, past the western arm. Where the south and west arms apparently meet, there is a break; there is also a large difference in the brightness of the two arms. Moreover, there is a velocity discontinuity between the two arms at that point. Together, these data suggest that the south arm is not connected to the western arm but continues northward to the tip of the north arm. The obvious picture of an S-shaped "spiral" is misleading.

The higher surface brightness of the north arm suggests that it is closer to the central ionizing source. The south and the north arms together may form a coherent stream of ionized gas orbiting about and spiraling into the center in a plane whose normal is inclined to the line of sight by ~65° (*42*). Numerical simulations have shown that such a feature can result from a cloud of gas, which, on experiencing drag from the medium it is moving through, spirals inward in a central potential and is stretched out by tidal effects (*45*); according to this hypothesis, the east and west arms are independent streams of ionized gas passing by the center, lying in a different plane from the south and north arms (*42*). An alternate picture is that the south arm is the ionized inner edge of a neutral gas ring

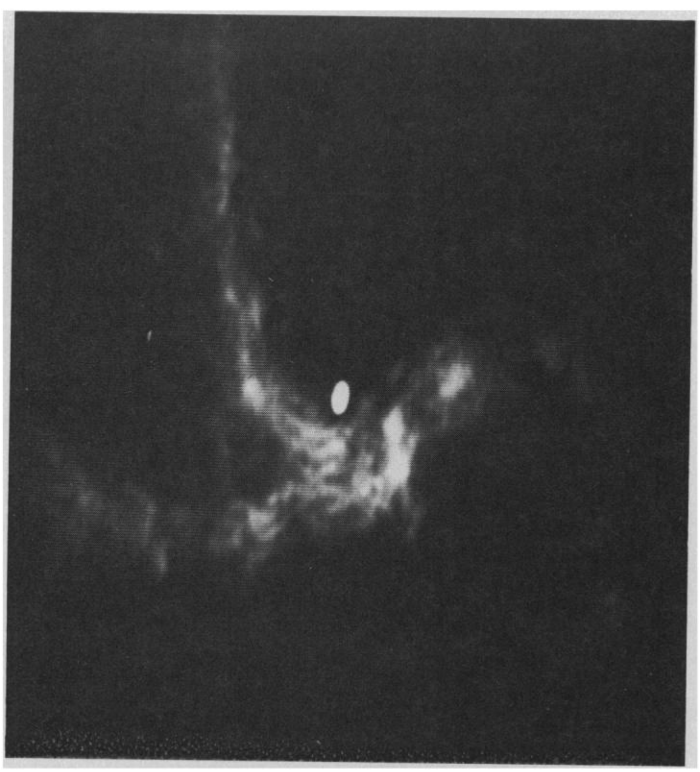

Fig. 7. A radio map (λ = 6 cm) of the central 40" of Sgr A West at 0.3" by 0.6" resolution (*47*), showing the details of the inner bright arms of Sgr A West (Fig. 6). It reveals filamentary structures of very-high-density (~10^5 cm^{-3}) ionized gas within the "arms." The white ellipse at the center represents the compact radio source Sgr A*, which has a size of 0.05 arc sec at this wavelength. The filamentary structures and the absence of many unresolved discrete sources in the ionized gas tend to rule out embedded young stars as the primary ionizing sources.

orbiting about the center, whereas the north arm is ionized gas falling inward along a parabolic orbit (*44*).

The explanation that the arms are ejecta in two opposite directions from a precessing twin-jet (*46*) appears untenable, because a natural consequence of such a mechanism—point reflection symmetry in the paths of the ejecta—is not observed. Sgr A*, the natural choice for the source of ejection, is clearly displaced from the ionized gas (Fig. 7) (*47*). Also, there is no obvious point of divergence in the ionized gas near the center, so that it is difficult to invoke ejection from a common point. Furthermore, there is ~10^4 $M_\odot$ of neutral gas physically associated with the ionized gas. It is difficult to think of an ejection mechanism that would account for both the ionized and the neutral gas.

Without a sustained source of UV photons, the electrons and ions in Sgr A West will recombine and become neutral in less than 10 years, a time that is inversely proportional to the ionized gas density. Elsewhere in the galaxy, such high-density ionized gas is found around young massive stars. If the gas in Sgr A West is similarly ionized by embedded hot stars, a very unusual arrangement of young massive stars in the form of the ionized gas would be required. The gas can be ionized by external sources, but this would require that the space between the source and the ionized gas be largely empty, so that the UV photons can propagate without being absorbed. In fact, far-infrared observations of dust emission indicate that the central region is largely devoid of neutral matter (*28*). The radio emission from the ionized gas is brighter closer to the center, requiring that either the ionizing flux or the gas density increases toward the center. Since the neutral gas density at the periphery of Sgr A West is as high as the ionized gas density close to the center, a central ionizing source is implied. Whether the source is a compact cluster of young hot stars or a single object is, however, not yet certain.

Neutral gas. The spatial resolution of observations of the neutral gas near the center is limited, and the distribution of this gas is not nearly as well delineated as that of the ionized gas. The first clear idea of the overall distribution of the neutral gas within the central 30 light-years came from observations of dust emission in the far-infrared (*28*). The 50- to 100-μm dust continuum is concentrated in two lobes just outside the ionized gas region of Sgr A West (see Fig. 8), but the dust temperature is centrally peaked. This implies that the central few light-years of the galaxy are largely empty of dust and neutral gas and are surrounded by neutral material.

Subsequent far-infrared spectroscopic observations show that the gas motion can be interpreted as rotation about the center. A rotating ring of gas has become a convenient picture of how the neutral gas is distributed just outside the ionized gas (*48*). More extensive observations of the rotational transition of CO $J = 2$ to $J = 1$ (where J is the angular momentum quantum number (*49*) have shown that the molecular gas is more extended and asymmetrically placed about Sgr A West than the far-infrared emission (Fig. 8). This result suggests that the far-infrared emission arises predominantly from the neutral interface between the ionized interior (Sgr A West) and a more extensively distributed cooler molecular gas (*48*). Although the bulk of the neutral gas is orbiting about the center in the normal sense of galactic rotation, the actual spatial distribution and motions are likely to be more complicated than those of a circularly rotating ring. In particular, a substantial amount of the gas displays noncircular motion.

Gas distribution in the galactic center. The central 10 light-years, in addition to having a very high concentration of stars, is largely devoid of gas and dust. It is, however, surrounded by $\gtrsim 10^4$ $M_\odot$ of neutral gas orbiting the center. The central cavity is threaded by filaments or streams of high-density ionized gas moving at speeds up to 300 km/sec. These streams occupy only a few percent of the cavity volume and amount to less than 100 $M_\odot$ of ionized gas. This ionized gas most likely originates outside the central 10 light-years, where there is a substantial reservoir of neutral gas. Clumps of molecular gas with low angular momentum fall in toward the bottom of the potential well. As they fall inward, they become tidally stretched into filaments and ionized by the central ionizing source.

The limited extent and the high speed of the ionized gas imply that these filaments are very short-lived structures. In another 10^4 years, the ionized gas will have a very different appearance. The transient nature of the ionized gas filaments suggests that the phenomena at the center are not in a steady state. For instance, events must have taken place $\gtrsim 10^4$ years ago to evacuate the central region and to initiate the formation of the ionized gas filaments.

Mass Determination from Motions of Gas

Crawford *et al.* (*50*) have collated the body of velocity measurements of ionized and neutral gas at various radii from the center. By making the simplifying assumption that the gas velocities represent equilibrium circular motion about a spherically symmetric mass distribution, they infer that the mass density of the galactic center varies radially as $r^{-2.7}$ between $r = 0.3$ and 30 light-years. They argue that such a mass distribution is much more centrally peaked than the star distribution inferred from the 2-μm observations and therefore suggests a central point mass.

The inferred rapid decrease of mass density between $r \sim 5$ and 30 light-years is based on low-resolution far-infrared observations of the velocity drop-off in the warm interface gas surrounding Sgr A West (*50*). However, this drop-off is not seen in observations of the cooler molecular gas that extends farther from the center (*49*), and the distribution of the neutral gas appears to be more complicated than the simple model of a rotating ring. Until higher resolution observations permit clarification, inferences on the mass distribution based on the neutral gas velocities are ambiguous.

The ionized gas at the center is most likely falling into the central potential well. In this case, the motion is dominated by gravity and, in the absence of stellar velocity dispersion data, provides the best estimate of the mass distribution within the central 5 light-years. In particular, the presence of ionized gas at ± 300 km/sec within 0.75 light-year of the center suggests a highly concentrated mass distribution, unless this high-velocity gas is expelled by a nongravitational mechanism.

The best way of confirming the presence of a point mass is to demonstrate the Keplerian dependence of velocities at distances as close to R_{sc} as possible. The probe closest to the center is currently provided by the broad hydrogen and helium lines that are found within $r \sim 0.3$ light-year of the center. But, since neither the extent nor the velocity field of this high-speed gas has yet been well established, the implication for the central mass is unclear. If the line width is due to an outflow driven by radiation pressure, the observed total luminosity of 10^7 $L_\odot$ from the center would imply a central mass of only ~300 $M_\odot$ (*51*).

Until the distribution and motions of the gas at the center is more completely understood, the central mass distribution cannot be conclusively determined from the present observations of the gas velocities.

Table 1. Observed properties of Sgr A*.

Measure	Value
Source size	<20 AU (~3 × 10^{14} cm)
Wavelength dependence of size	$\lambda^{2.0}$ ($\lambda \geq 1.35$ cm)
Position angle of elongation	98° ± 15° ($\lambda = 3.6$ cm)
Axial ratio	0.55 ± 0.25 ($\lambda = 3.6$ cm)
Upper limit to source expansion	≲16 km/sec
Flux density variability ($\Delta S/2S$)†	≲0.2 (1975–1983)
Spectral index‡	~0.25
Turnover frequency‡	≳89 GHz
Radio luminosity	~2 × 10^{34} erg/sec
Brightness temperature	>7 × 10^8 K ($\lambda = 1.35$ cm)

†ΔS, peak-to-peak variation; S, mean flux density (*53*). ‡From (*54*).

Conclusions

The compact nonthermal radio source Sgr A* is unique in our galaxy. Its extremely small size admits only objects with stellar

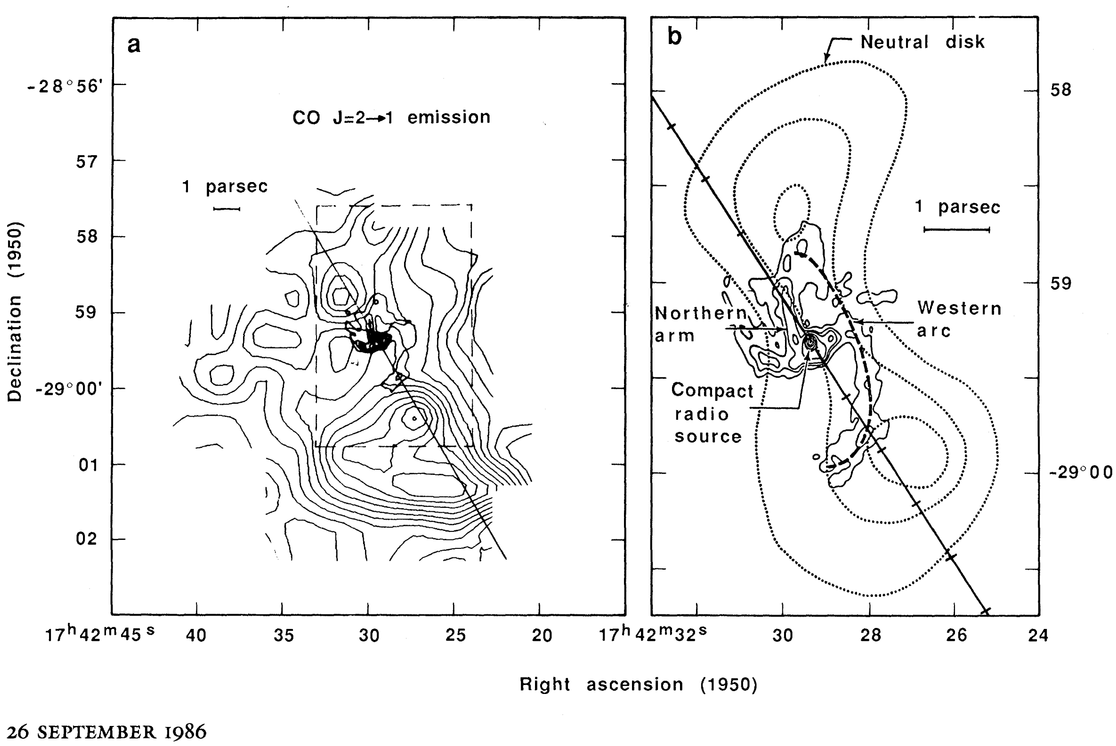

Fig. 8. (a) The integrated intensity of the $J = 2 \rightarrow 1$ transition of CO ($\lambda = 1.3$ mm) at an absolute velocity of >80 km/sec from the central 4 arc min (*49*). The contours roughly correspond to the minimum column density of the molecular gas within the central 40 light-years. The radio source Sgr A West, representing the ionized gas in the central 10 light-years, is superposed on the contours. (b) An expanded view corresponding to the dashed rectangle in (a). The dotted contours represent 63-μm continuum emission from warm dust adjacent to the ionized gas (*50*). The diagonal solid line is parallel to the galactic plane; 1 parsec = 3.27 light-years.

dimensions as the underlying energy source, but it cannot be accounted for by any known stellar object. It is best explained as due to a massive black hole. The lack of measurable proper motion would also argue for a massive object. The only factor contributing to a lingering doubt is its low luminosity. Although this source can be powered by a neutron star in principle, there is no convincing model involving pulsars that can account for its observed properties. Furthermore, any such model would also have to explain why radio sources such as Sgr A* are not found elsewhere in the galaxy, since pulsars are distributed throughout. Sgr A* is the best candidate for a massive black hole.

Further progress on understanding the radio source itself must await a proper map showing the details of its intrinsic structure. In the preparation of this map, it will be necessary to use the shortest possible wavelength. Given the transient nature of various phenomena at the center, it is not impossible that the radio source undergoes outbursts in which the peak luminosity exceeds that available from a star. Observations of such an outburst would eliminate the alternative of a stellar energy source.

The central few light-years of the galactic center have all the ingredients of an active galactic nucleus, albeit at a very modest level. The proximity of the galactic center to Earth has enabled us to delineate the complicated structure of the ionized gas in the central 10 light-years and to view directly the paths of accretion of interstellar gas by our galactic nucleus. Sgr A West serves as a valuable illustration of the possible structure of the ionized gas in active galactic nuclei and of the way in which interstellar gas might be accreted by a massive black hole.

The high obscuration of the center has prevented observers from obtaining a clear picture of how the stars are distributed relative to the compact radio source. The question of whether the compact radio source, if it has a large mass, has attracted a cusp of stars around it is not satisfactorily resolved (*52*). The structure of the central 0.5 light-year—the identification of the peak of the central star cluster (the dynamical center) and the source of the broad hydrogen and helium emission lines—remains to be clarified. High-resolution γ-ray imaging is also needed to identify the extraordinary source of positrons.

From the conservative but prudent scientific viewpoint, there is no conclusive evidence for a massive black hole at the galactic center. On the other hand, the extraordinary phenomena within the central 1 light-year of the galaxy definitely call for something unusual. With the rapid development of novel techniques and the completion of various new space and ground-based telescopes, the next few years will be exciting times for understanding the intriguing center of our galaxy and for establishing whether a massive black hole is present.

REFERENCES AND NOTES

1. J. A. Wheeler, *Am. Sci.* **56**, 1 (1968). "Black hole" refers to a region of space-time from which there is no escape to infinity. It has a boundary called the event horizon with a radius called the Schwarzschild radius, $R_{sc} = 2GM/c^2$, where M is the mass of the black hole, G is the gravitational constant, and c is the speed of light. The Schwarzschild radius of a 1 $M_\odot$ (solar mass = 2×10^{33} g) black hole is 3 km. Outside its event horizon, a black hole is invisible and is characterized only by its mass, spin, and charge. However, it is possible to identify the presence of a black hole via its influence on the immediate surroundings.
2. I. D. Novikov and K. S. Thorne, in *Black Holes*, C. DeWitt and B. DeWitt, Eds. (Gordon and Breach, New York, 1973), pp. 345–450.
3. The best candidates for a stellar black hole are found in the binary x-ray sources Cygnus X-1 and LMC X-3. See, for example, J. Frank, A. R. King, D. J. Raine, *Accretion Power in Astrophysics* (Cambridge Univ. Press, Cambridge, 1985).
4. S. L. Shapiro, in *Dynamics of Star Clusters*, J. Goodman and P. Hut, Eds. (International Astronomical Union Symposium 113, Reidel, Dordrecht, Holland, 1985), p. 373.
5. M. C. Begelman, R. D. Blandford, M. J. Rees, *Rev. Mod. Phys.* **56**, 225 (1984).
6. E. E. Salpeter, *Astrophys. J.* **140**, 796 (1964); Y. B. Zeldovich and I. D. Novikov, *Dokl. Acad. Nauk. SSSR* **158**, 811 (1964).
7. D. E. Osterbrock, in *Active Galactic Nuclei*, C. Hazard and S. Mitton, Eds. (Cambridge Univ. Press, Cambridge, 1977), p. 25; S. L. O'Dell, *ibid.*, p. 95; I. Robinson, A. Schild, E. L. Schucking, Eds., *Quasi-Stellar Sources and Gravitational Collapse* (Univ. of Chicago Press, Chicago, 1965).
8. K. I. Kellermann and I. Pauliny-Toth, *Annu. Rev. Astron. Astrophys.* **19**, 373 (1981).
9. The gravitational binding energy released by a mass Δm falling onto the surface of a body of mass M and radius R is $GM\Delta m/R = (R_{sc}/2R)\Delta mc^2$. For a neutron star, $(R_{sc}/2R) \sim 0.15$, which is the ratio of the binding energy released per unit rest mass energy. For a stationary black hole this ratio is 0.057, whereas for a maximally rotating black hole it is 0.42 (*5*). For nuclear fusion, the maximum ratio obtainable (converting hydrogen to iron, the most tightly bound nucleus) is 0.009.
10. M. H. Cohen, *Annu. Rev. Astron. Astrophys.* **7**, 619 (1969). The current resolution of VLBI is essentially limited by the size of Earth.
11. R. L. Brown and H. Liszt, *ibid.* **22**, 223 (1984); J. H. Oort, *ibid.* **15**, 295 (1977).
12. M. E. Bailey, *Mon. Not. R. Astron. Soc.* **190**, 217 (1980); D. A. Allen, A. R. Hyland, T. J. Jones, *ibid.* **204**, 1145 (1984).
13. K. G. Jansky, *Proc. Inst. Radio Eng.* **20**, 1920 (1932); *ibid.* **21**, 1387 (1933); *ibid.* **23**, 1158 (1935).
14. D. Downes and A. Maxwell, *Astrophys. J.* **146**, 653 (1966).
15. H. I. Ewen and E. M. Purcell, *Nature (London)* **168**, 356 (1951). A spectral line provides, among other information, a measurement of the "radial velocity" (the velocity component along the line of sight) of the source via the Doppler effect. The frequency or wavelength shift of the line relative to the laboratory value is directly proportional to the radial velocity. Hence in astronomy, line frequencies and line widths are often in units of kilometers per second. Positive values correspond to radial motions away from Earth.
16. F. J. Kerr and G. Westerhout, in *Galactic Structure*, A. Blaauw and M. Schmidt, Eds. (Univ. of Chicago Press, Chicago, 1965), p. 167.
17. G. W. Rougoor and J. H. Oort, *Proc. Natl. Acad. Sci. U.S.A.* **46**, 1 (1960). Such expanding motions were also observed in subsequent observations of molecular gas, for example, by N. Z. Scoville [*Astrophys. J.* **175**, L127 (1972)]. More recent observations of the atomic and molecular gas present toward the galactic center suggest that much of the large-scale motion may be due to noncircular motion in a bar potential, although not all the expanding features are explainable in this way. For more details, see (*11*).
18. D. Lynden-Bell and M. J. Rees, *Mon. Not. R. Astron. Soc.* **152**, 461 (1971).
19. B. Balick and R. L. Brown, *Astrophys. J.* **194**, 265 (1974).
20. T. Pauls, P. G. Mezger, E. Churchwell, *Astron. Astrophys.* **34**, 327 (1974).
21. J. H. Lacy, C. H. Townes, T. R. Geballe, D. J. Hollenbach, *Astrophys. J.* **241**, 132 (1980).
22. The VLA, consisting of 27 25-m radio telescopes located in the plain of San Augustin in New Mexico, is operated by the National Radio Astronomy Observatory (NRAO) under contract with the National Science Foundation. A. R. Thompson, B. G. Clark, C. M. Wade, P. J. Napier, *Astrophys. J. Suppl. Ser.* **44**, 151 (1980). The VLA actually measures the spatial correlation of the radiation from the source, which is the Fourier transform of the source brightness distribution (that is, the image). This Fourier transform relation is the spatial analog of a similar relation between the temporal correlation of a wave and its power spectrum. Thus, the VLA maps typically require substantial efforts of computerized image processing after the observations which are made relatively quickly.
23. F. Yusef-Zadeh, M. Morris, D. Chance, *Nature (London)* **310**, 557 (1984).
24. M. Tsuboi *et al.*, *Publ. Astron. Soc. Jpn.* **37**, 359 (1985).
25. Y. Sofue and T. Handa, *Nature (London)* **310**, 568 (1984).
26. R. D. Ekers, J. H. van Gorkom, U. J. Schwarz, W. M. Goss, *Astron. Astrophys.* **122**, 143 (1983).
27. J. P. Henry, D. L. DePoy, E. E. Becklin, *Astrophys. J.* **285**, L27 (1984).
28. E. E. Becklin, I. Gatley, M. W. Werner, *ibid.* **258**, 135 (1982).
29. D. N. B. Hall, S. G. Kleinmann, N. Z. Scoville, *Astrophys. J.* **260**, L64 (1982); T. R. Geballe *et al.*, *ibid.* **284**, 118 (1984).
30. W. N. Johnson, F. R. Hamden, R. C. Haymes, *ibid.* **172**, L1 (1972).
31. M. Levanthal, C. J. MacCallum, P. D. Stang, *ibid.* **225**, L11 (1978).
32. G. R. Riegler *et al.*, *ibid.* **248**, L13 (1981).
33. R. E. Lingenfelter and R. Ramaty, in *The Galactic Center*, G. R. Riegler and R. D. Blandford, Eds. (AIP Conference Proceedings No. 83, American Institute of Physics, New York, 1982), vol. 83, p. 166.
34. K. Y. Lo, M. H. Cohen, A. C. S. Readhead, D. C. Backer, *Astrophys. J.* **249**, 504 (1981).
35. K. Y. Lo *et al.*, *Nature (London)* **315**, 124 (1985).
36. P. P. Kronberg and R. A. Sramek, *Science* **227**, 28 (1985).
37. N. Bartel *et al.*, *Nature (London)* **318**, 25 (1985).
38. The power available from accretion of matter onto a neutron star is essentially limited to the Eddington luminosity at which the radiation pressure will balance the gravity on the accreting gas. For a 1 $M_\odot$ object, this is 1.6×10^{38} erg/sec. The power available from the rotation of a neutron star may be inferred from the total luminosity of the Crab Nebula, which is powered by a pulsar, of $\sim 10^{38}$ erg/sec. The total radio luminosity from the Crab Nebula is $\sim 10^{37}$ erg/sec.
39. S. P. Reynolds and C. F. McKee, *Astrophys. J.* **239**, 893 (1980).
40. M. J. Rees, in *The Galactic Center*, G. R. Riegler and R. D. Blandford, Eds. (American Institute of Physics Conference Proceedings 83, American Institute of Physics, New York, 1982), p. 166.
41. D. C. Backer and R. A. Sramek, *Astrophys. J.* **260**, 512 (1982).
42. K. Y. Lo and M. J. Claussen, *Nature (London)* **306**, 647 (1983).
43. J. van Gorkom, U. J. Schwarz, J. D. Bregman, in *The Milky Way Galaxy*, H. van Woerden, R. J. Allen, W. B. Burton, Eds. (International Astronomical Union Symposium 106, Reidel, Dordrecht, Holland, 1985), p. 371.
44. G. Serabyn and J. H. Lacy, *Astrophys. J.* **293**, 445 (1985).
45. P. Quinn and G. Sussman, *ibid.* **288**, 377 (1985).
46. R. L. Brown, *ibid.* **262**, 110 (1982).
47. K. Y. Lo, M. J. Claussen, C. Wilson, M. Herant, in preparation.
48. R. Genzel, D. Watson, M. K. Crawford, C. H. Townes, *Astrophys. J.* **297**, 766 (1985).
49. K. Y. Lo, E. Sutton, C. R. Masson, T. G. Phillips, A. I. Sargent, in preparation.
50. M. Crawford *et al.*, *Nature (London)* **315**, 467 (1985).
51. L. Ozernoy, personal communication. $10^7 L_\odot$ is the Eddington luminosity of a 300 $M_\odot$ solar source.

52. D. A. Allen and R. H. Sanders, *Nature (London)* **319**, 191 (1986).
53. R. L. Brown and K. Y. Lo, *Astrophys. J.* **253**, 108 (1982); J. van Gorkom, K. Y. Lo, M. J. Claussen, unpublished result.
54. D. C. Backer, in *Extragalactic Radio Sources*, D. S. Heeschen and C. Wade, Eds. (International Astronomical Union Symposium 97, Reidel, Dordrecht, Holland, 1982), p. 389.
55. This research is supported by the NSF. I am grateful to Y. Sofue, T. Soifer, and M. Weems for providing some of the images used in this article; to R. Blandford for permission to reproduce his diagram for Fig. 1; and to D. Watson for help in preparing Fig. 8. I thank A. Readhead and C. Wilson who read a draft of the manuscript and made helpful suggestions for improving the article. I also thank the large number of collaborators who have made much of the work reviewed here possible. The article was prepared at the Department of Astronomy, California Institute of Technology.

Research Article

A Genetic Approach to Analyzing Membrane Protein Topology

COLIN MANOIL* AND JON BECKWITH

Fusions of the secreted protein alkaline phosphatase to an integral cytoplasmic membrane protein of *Escherichia coli* showed different activities depending on where in the membrane protein the alkaline phosphatase was fused. Fusions to positions in or near the periplasmic domain led to high alkaline phosphatase activity, whereas those to positions in the cytoplasmic domain gave low activity. Analysis of alkaline phosphatase fusions to membrane proteins of unknown structure may thus be generally useful in determining their membrane topologies.

THE AMINO ACID SEQUENCE OF A PROTEIN IS FREQUENTLY known with little or no additional information available about how the sequence is folded in its normal three-dimensional structure. The situation can be less grim if the sequence is that of an integral membrane protein rather than that of a cytoplasmic protein, because of the common occurrence in such membrane proteins of easily identified long contiguous stretches of hydrophobic amino acids. High resolution structural analyses of bacteriorhodopsin and the *Rhodopseudomonas viridis* photosynthetic reaction center polypeptides have shown that such long hydrophobic sequences generally correspond to transmembrane alpha-helical stretches of a membrane protein (*1, 2*). Armed with this fact, and with a plot of the average hydrophobicity along the sequence of a membrane protein (*3*), possible two-dimensional membrane topologies for the polypeptide can be drawn, with each long hydrophobic sequence corresponding to a transmembrane alpha helix. Such a protocol appears to have correctly predicted the transmembrane segments of reaction center polypeptides before the high resolution structures were determined (*2, 4*).

How can models for the membrane topology of a protein be tested in the absence of diffraction analysis? There are a number of ways to determine elements of membrane protein structure. Identifying sites of a membrane protein that interact naturally with other proteins of known cellular location, such as modifying enzymes (*5, 6*) or binding proteins (*7*), position the sites relative to the membrane. Sites can also be positioned by their reaction with membrane-impermeant small molecules, proteases, or antibodies added from one side or other of the membrane (*8*). Reagents that react from within the lipid bilayer can directly identify membrane-spanning sequences (*9*). Spectroscopic analysis of purified membrane proteins can provide an overall measure of their secondary structures, which includes that of their membrane-spanning sequences (*10*).

In this article, we describe a genetic method to help determine membrane protein topology. This approach offers the advantage that it does not depend directly on the exposure and reactivity of amino acid side chains of the polypeptide, and should be a useful complement to the approaches which do.

Rationale of the method. A protein spanning the cytoplasmic membrane of *Escherichia coli* will have different domains exposed to the cytoplasm and periplasm. Using fusions of such a membrane protein to alkaline phosphatase we have sought to distinguish these domains. Alkaline phosphatase appears to require export to the periplasm to show enzymatic activity (*11*). The idea underlying this approach is illustrated in Fig. 1 for a hypothetical membrane protein whose polypeptide chain crosses the membrane six times. If alkaline phosphatase were fused to a site normally facing the periplasm (fusion 1), it is possible that the alkaline phosphatase moiety would be exported to the periplasm and show enzymatic activity. Alternatively, if it were fused to a part of the protein facing the cytoplasm (fusion 2), the alkaline phosphatase moiety would remain cytoplasmic and inactive. Thus, the activities of fusions at different positions would reflect the normal membrane topology of the protein.

Tsr protein fusions. To test the scheme illustrated in Fig. 1, we have analyzed fusions to the *E. coli* Tsr protein, one of a set of four related proteins involved in chemotaxis as chemoreceptors. These proteins appear to exist as tetramers of a simple transmembrane structure in which each polypeptide chain crosses the membrane twice (Fig. 2a). Each polypeptide is divided into a periplasmic domain between the two transmembrane sequences, and a large cytoplasmic domain at the carboxyl terminus of the protein (Fig. 2a). This structure is derived from the amino acid sequences of the proteins (*12, 13*), the properties of proteolytic fragments of one of them (*14*), the sites of covalent modification of one of the proteins

The authors are in the Department of Microbiology and Molecular Genetics, Harvard Medical School, Boston, MA 02115.

*Present address: Department of Genetics, University of Washington, Seattle, WA 98195.