

Adaptive Optics Revisited

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From the earliest days and nights of telescopic astronomy, atmospheric turbulence has been a serious detriment to optical performance. The new technology of adaptive optics can overcome this problem by compensating for the wavefront distortion that results from turbulence. The result will be large gains in resolving power and limiting magnitude, closely approaching the theoretical limit. In other words, telescopic images will be very significantly sharpened. Rapid and accelerating progress is being made today by several groups. Adaptive optics, together with the closely related technology of active optics, seems certain to be utilized in large astronomical telescopes of the future. This may entail significant changes in telescope design.

AS EVERY TELESCOPIC OBSERVER KNOWS, ATMOSPHERIC turbulence (imperfect "seeing") seriously degrades the images produced by ground-based optical telescopes. The resulting blurred "seeing disk" of a star displays random shifting in position as well as a diameter far larger than the Airy diffraction pattern that a perfect telescope would be capable of producing. The Airy diffraction pattern is a bright spike surrounded by a dark ring of diameter $1.22 \lambda/D$ rad, where λ is the wavelength and D is the diameter of the telescope; additional outlying bright rings are quite faint.

Even at the best observatory sites, the size of the seeing disk, because of time-dependent atmospheric conditions, is found to vary in a range from a few arc seconds down to a few tenths of 1 arc sec. Given a good sky, the quality of the seeing is therefore the most important determinant governing the productivity of a large telescope. This applies forcefully to direct imaging, to spectroscopy, and to photometry. For the past century, it has been recognized at such well-chosen sites as Mount Hamilton (the Lick Observatory) and Mount Wilson that the value of observing time may be said to vary inversely as the square of the diameter of the seeing disk of a star.

A useful measure is the Strehl ratio—the intensity at the centroid of the actual seeing disk divided by the intensity at the peak of the Airy diffraction pattern. At present, practically all observations with large telescopes in the visible region of the spectrum have to be made with a Strehl ratio less than 0.01. It is the ultimate goal of adaptive optics to increase this ratio to approach 1. For direct imaging, the very real advantages of increased resolving power are clear. The concentration of the light of a star into an "Airy spike" means greater contrast with the sky background and a fainter limiting magnitude. For spectrographic observations, adaptive optics will permit a major reduction in slit width and hence in the basic

dimensions of the whole spectrograph. The result will be gains in performance, stability, and operational convenience as well as cost reduction.

Optical Wavefronts

By placing a knife-edge in the focal plane of a telescope to obscure part of the seeing disk, with the eye close behind, one can readily see (or photograph) the primary mirror as illuminated by a star, together with the changing pattern of coherent areas resulting from the distorted wavefronts. Use of a knife-edge in several position angles permits detection of unwanted distortion of the primary mirror due to flexure or thermal effects; it is also the time-honored method of quick and precise focusing.

Four "knife-edge photographs" of the primary mirror of the 200-inch telescope, made by Ira S. Bowen (1) in 1949, are shown in Fig. 1. Bowen used very short exposures for (A) and (B) to illustrate random wavefront distortions due to atmospheric turbulence, whereas (C) and (D), averaged over much longer intervals, show the deviations from perfection of the surface of the mirror at two stages during the course of final optical figuring (on the floor of the dome) by Donald O. Hendrix. Optical figuring, which follows grinding and polishing, is the crucially important procedure by which the optician brings the mirror surface to the desired figure of revolution, with deviations no larger than a small fraction of a wavelength of light.

Beginning about 1936, I have made visually many hundreds of incidental knife-edge observations of primary mirrors in the course of research programs at Mount Hamilton, Mount Locke (McDonald Observatory), Mount Wilson, Palomar Mountain, and Cerro Las Campanas. It is easy to detect the direction and rate of flow of the changing pattern of turbulence as influenced by air movements in the optical path and to estimate the average dimension of the Fried (2) coherence cell size (r_0). Typically r_0 lies in a range from a few centimeters to a few decimeters, but, with the very best natural seeing, in calm conditions at the 100-inch Hooker telescope on Mount Wilson, r_0 has been observed to attain the extraordinary value of 1 m. At such times, which are extremely rare, the boundaries of the coherent areas are of low contrast and they change slowly, on a time scale of several seconds. Coherent patterns of this high quality were correlated with a measured diameter of 0.25 arc sec for the seeing disk at the coudé (250-foot) focus of the 100-inch telescope. The image was not only very small and sharp, but it was remarkably stable. Such superlative seeing has been observed to last for several hours. It can be stated with a high degree of confidence that Mount Wilson offers the best seeing of any North American observatory. The excellent performance of the 60-inch and 100-inch telescopes there not only reflects the quality of the site, but it is also a tribute to the professional skills of George W. Ritchey, who produced the telescope optics. As a dome designer, he also knew

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how to avoid internal degradation of the seeing, a knowledge that has too often been ignored in recent years.

A System for Seeing-Compensation

In 1953 I described (3) a system for the compensation of the wavefront distortion that results from atmospheric turbulence. As proposed then, seeing-compensation can be accomplished in two steps. The first requirement is to remove wandering of the centroid of the seeing disk by introducing two-dimensional (tip-tilt) compensation of the overall wavefront. The second step requires reimaging the primary mirror on a much smaller deformable mirror and photoelectrically sensing the changing slopes of the coherent areas or "subapertures." The resulting flow of information is processed and is continually fed back to control the optical figure of the deformable mirror so as to compensate for wavefront distortion. Response time of the order of a few milliseconds is desirable if the natural seeing is of ordinary quality. Some of the light can be diverted by a partially reflecting or dichroic mirror to be used for observations. The technology described in this paragraph is known today as adaptive optics.

As pointed out in (3), adaptive optical systems are subject to serious limitations. The first is that the reference star must be adequately bright to provide photons at a sufficient rate (100 s^{-1}) from each of the subapertures of the turbulence pattern. The second is that compensation for imperfect seeing is limited to a field of small angular extent (the isoplanatic angle) around the reference star. This angle is generally several arc seconds for visible light, depending on

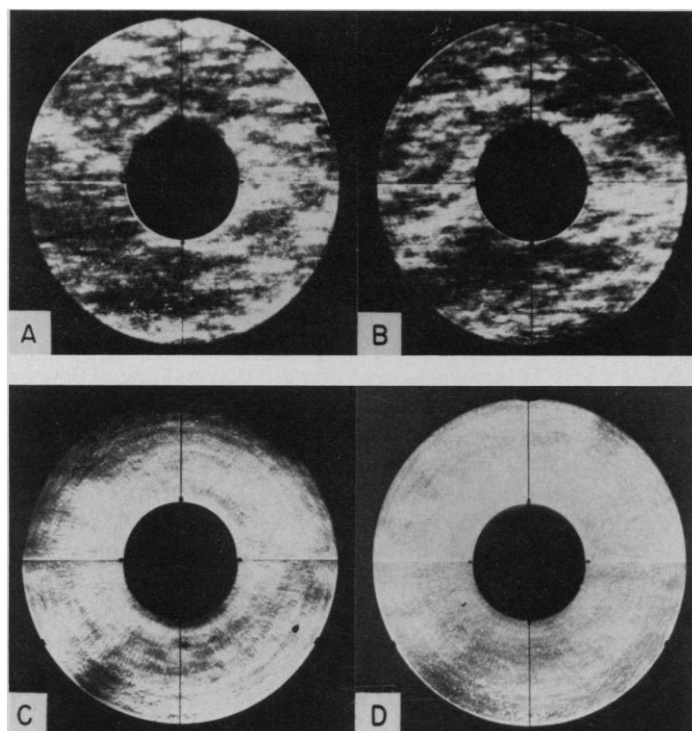
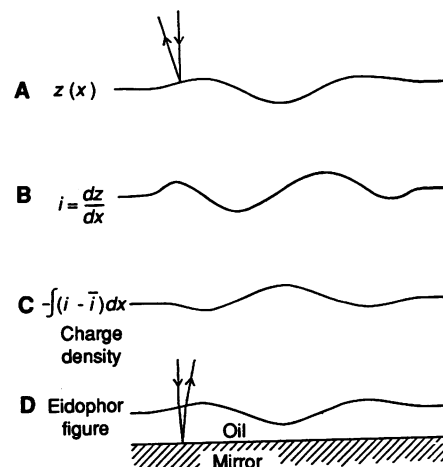


Fig. 1. "Knife-edge photographs" of the primary mirror of the 200-inch telescope of the Palomar Observatory made by Ira S. Bowen (1) in 1949. Short exposures were used for (A) and (B) to show randomly fluctuating wavefront distortions due to atmospheric turbulence. In (C) and (D), averaged over 80-s exposures, are shown the deviations from perfection of the optical figure of the mirror at two stages in the course of figuring by D. O. Hendrix. [Reprinted from (1) with permission of the Astronomical Society of the Pacific]

Fig. 2. Illustration of the principle of wavefront correction by the Eidophor, an early type of deformable mirror developed by Fischer (4, 5). (A) Cross section of corrugations in the effective figure of the telescope objective. (B) Corresponding intensity pattern observed in the knife-edge image. (C) Integrated photoelectric current along trace of raster. (D) Resulting deformation of the Eidophor figure, showing the correction of the deviated ray. [Adapted from figure 2 of (3) with permission of the Astronomical Society of the Pacific]



the altitude of the turbulent layer. These limitations are more serious in the visible spectrum than in the infrared, but, even so, techniques for circumventing them are now being tested by various groups.

In the 1950s, the function of the deformable mirror might have been served by adaptation of the Eidophor, a contemporary device developed by Fischer (4, 5) for the high-intensity projection of television pictures in theaters. Figure 2, reproduced here from (3), shows the operational principle of the Eidophor. A mirror in a vacuum chamber is covered with a thin layer of oil upon which a modulated charge from an electron gun is deposited in a rastered pattern, thereby inducing local forces of surface repulsion that cause transient changes in the slope of the oil film. The wavefront is locally tilted by refraction in traversing the film.

The schematic diagram of the system for seeing-compensation as described (3) in 1953 is reproduced here as Fig. 3. The diagram represents the system to be placed at the focus, F , of a large telescope, with the primary mirror imaged on the Eidophor and on the image tube, which today would be an intensified charge-coupled device (CCD). The knife-edge, K , is rotated rapidly about the optical axis. The first step in seeing-compensation is the detection of any resulting signal modulation at the rotation frequency of the knife-edge; this is amplified to control the two-dimensional tilt of the gimbal-mounted, plane-parallel plate, C , thereby removing wandering of the seeing disk. The second step in compensation is the processing of the data stream from the image tube, taking account of the phase of rotation of the knife-edge, and feeding back this detailed information for real-time deformation of the Eidophor to drive the wavefront distortions toward zero.

Although the Eidophor was central to the system as described in (3), its practical application to astronomy was not attempted as such a large technological effort would have been premature. Today's deformable mirrors are far superior. What was done in 1947 was to implement the first step in seeing-compensation—the two-dimensional tip-tilt correction of the overall wavefront at the coudé focus of the 100-inch telescope (6). The sensor was a rapidly rotating knife-edge followed by a photomultiplier tube. The resulting signal was rectified and applied to relays that pulsed the slow-motion controls of the telescope in right ascension and in declination.

A much improved two-dimensional guider (7) was developed and put to use in 1953. In this system the function of the rotating knife-edge was served by the edge of a 3-mm steel ball, much larger than the seeing disk of the star, that was caused to revolve at 60 Hz within a nonmagnetic race whose radius was equal to the diameter of the ball; the ball was driven by a revolving magnetic field. The system had as a wavefront corrector a gimbal-mounted, plane-

parallel quartz plate in the converging optical beam ahead of the reflecting jaws of the spectrograph slit; the plate was driven by two low-inertia motors. The working bandwidth was about 10 Hz. For several years this adaptive system was used to real advantage for spectroscopy at the coudé focus of 200-inch Hale telescope of the Palomar Observatory.

Active Optics

Closely related to adaptive optics is a much slower type of system now known as active optics. It may be used for occasional adjustment of the several supports of the primary mirror; through flexure, the adjustments improve the effective optical figure. This procedure, which I also proposed in 1953 (3), may be conducted with any reasonably bright reference star; it does not require rapid response. An active optical system has recently been demonstrated by a group at the European Southern Observatory (8, 9). They have shown that active optics offers such great gains in performance that it seems certain to be utilized in large telescopes of the future.

Recent Developments in Adaptive Optics

In the past 25 years, the possibilities of adaptive optics have inspired work on the theory of atmospheric turbulence as well as research and development on modern systems and components by several groups at observatories, at universities, and in industry. The activity is accelerating.

It is not appropriate or necessary here to attempt a comprehensive review. Numerous reports are to be found in the literature, but many of these may be more widely known among optical engineers than among astronomers. Some of the informative review papers available are the following: "Active optics, a new technology for the control of light" by Hardy (10); "Instrumental limitations in

adaptive optics for astronomy," also by Hardy (11); "Adaptive optics developments at the European Southern Observatory" by Merkle (12); and "Application of adaptive optics to astronomy" by Merkle and Beckers (13). The foregoing references describe a variety of modern components and adaptive optical systems under development.

A striking test has recently been reported by a group of nine from the European Southern Observatory and from French organizations (14, 15). They achieved successful results with an adaptive optical prototype system, using a 1.52-m telescope at the Observatoire de Haute-Provence. The group made observations of bright stars, obtaining images that were diffraction-limited in the infrared ($>3.5 \mu\text{m}$). They remarked (14, p. 4) that adaptive optical systems "will revolutionize the exploitation of the next-generation telescopes . . . and, in many cases, compete with observations carried out by telescopes deployed in space."

In order to provide some examples of the technological progress that is being made, I have rather arbitrarily selected a few essential system components for brief comment below.

The technology of deformable mirrors (DMs) has been advanced through more than a decade of development at Litton-Itek Optical Systems (16). Current models use a thin face sheet of low-expansion glass supported on an array of many small, discrete actuators, each constructed of several stacked and bonded layers of lead-magnesium-niobate (PMN). These electrostrictive actuators, which can be produced in quantity, have excellent dynamic range, insignificant hysteresis, and long life. Customized DMs with hundreds of actuators and the required connectors can be assembled from standard components.

Several types of wavefront sensor have been proposed in the literature. A recent development of the Hartmann-Shack type, with 37 subapertures, has been described by Allen *et al.* (17). An alternative device that senses wavefront curvature has been proposed by Roddier *et al.* (18).

The technology of wavefront reconstruction, that is, real-time processing of data to drive the actuators of the DM, is well advanced. A fundamental treatment of photon noise and atmospheric noise in adaptive systems has been given by Dyson (19).

Artificial Reference Stars for Visible Light

Beckers *et al.* (20) have shown that, although there are in the sky suitably bright reference stars in sufficient number for adaptive optical systems in the infrared ($>4 \mu\text{m}$), there is a marked scarcity of such stars in the visible part of the spectrum. To overcome this lack, Foy and Labeyrie (21) have proposed that artificial, laser-generated reference stars in the earth's upper atmosphere may be useful. Thompson and Gardner (22) have demonstrated at Mauna Kea that pulsed laser beams, tuned to the sodium D_2 resonance line, projected through a telescope, and focused in the Na layer in the mesosphere at an altitude of about 92 km, can produce artificial Na stars by resonance fluorescence. Analyzing the possibilities, they concluded that the use of multiple laser beams to generate several artificial Na reference stars in the field of the telescope will usefully enlarge the isoplanatic angle. They stated that Na lasers of sufficient power and quality are within the reach of current technology.

Thompson and Gardner (23) and Gardner *et al.* (24) discuss the design requirements of a laser-guided adaptive telescope, together with expected imaging performance. They consider two types of laser-generated reference star: (i) Na stars excited by resonance fluorescence in the mesospheric Na layer at an altitude of about 92 km and (ii) Rayleigh back-scattering by air molecules from a laser beam in the stratosphere. Advantages and disadvantages of each

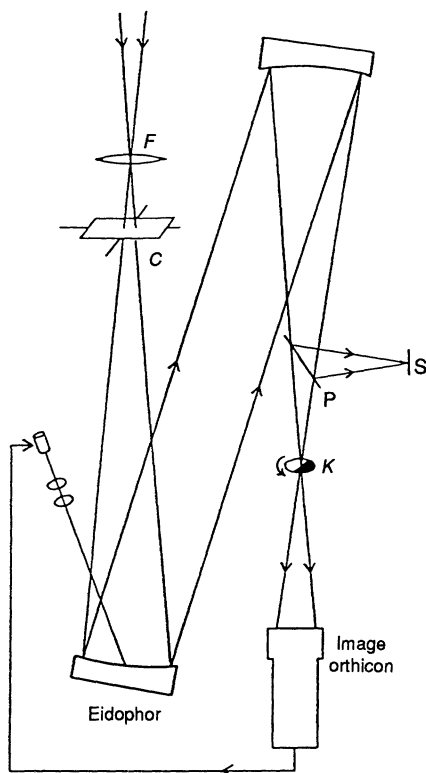


Fig. 3. Schematic diagram of the seeing compensator described (3) in 1953. The device is to be placed at the focus of a large astronomical telescope. A "knife-edge image" of the telescope objective, showing the random distortion of the wavefronts, is formed on the image tube. After processing with reference to the phase of rotation of the knife-edge, *K*, the pattern is projected by an electron gun onto the oil film of the Eidophor mirror. This results in the correction of the wavefront distortion. *F* is a field lens; *C* is a fast guider for centering the reference star on the knife-edge; *P* designates a dichroic pellicle; *S* is the focal plane (star image). [Adapted from figure 1 of (3) with permission of the Astronomical Society of the Pacific]

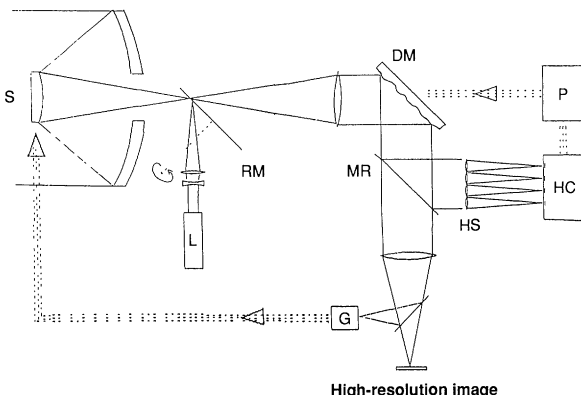


Fig. 4. Adaptive optics for a large telescope. A pulsed Na laser projects spots focused by the full aperture into the Na layer at an altitude of about 92 km. Multiple laser spots may be used as proposed by Foy and Labeyrie (21). A rotating mirror-shutter RM is synchronized with the laser pulses. DM is the deformable mirror. A dichroic reflector MR diverts the Na light to the Hartmann screen HS, consisting of a two-dimensional array of lenslets. HC is the Hartmann camera with an intensified CCD; in effect, it provides a quadrant detector for each lenslet. The output of HC, through the processor P, drives the deformable mirror DM to remove higher frequency wavefront distortion. Lower frequency wavefront distortion, in the form of overall tilt that spans the telescope aperture, is sensed by the guider G using a single natural star and is compensated by a tip-tilt mirror, which may be the secondary mirror of the telescope.

type are discussed. Here only Na reference stars will be considered; for these, the required pulsed-laser power is predicted to be on the order of 6 W at the zenith if r_0 is 20 cm.

Figure 4 is a diagram of an adaptive optical telescope that uses laser-generated Na reference stars, a Hartmann wavefront sensor controlling a deformable mirror, and a guider. Each outgoing laser pulse returns from the 92-km Na layer, retracing its detailed path, in about 700 μ s. Such a system should be capable of compensating higher frequency wavefront distortions. This will result in sharp images having a much improved Strehl ratio. But the field of natural stars will wander as a unit if affected by low-frequency wavefront distortions that span the telescope aperture (24). This low-frequency wandering can be sensed by a guider that responds to any displacement of a single natural guide star in the isoplanatic field and can be corrected by means of a tip-tilt mirror in the system (3).

Because the whole wavefront is sensed, this natural guide star can be much fainter than a star that is bright enough for correcting the slopes of single subapertures of the Hartmann detector; this advantage increases for larger telescopes. Also, as Valley (25) has shown, the isoplanatic angle for low-order wavefront effects is larger than that for high-order wavefront distortions. For the correction of low-order turbulence, there are, distributed over the sky, sufficient natural guide stars in visible wavelengths to permit nearly unrestricted sky coverage for adaptive optical telescopes.

Expected Performance

Gardner *et al.* (24) calculate that a 2-m, ground-based, laser-referenced adaptive optical telescope should be able to achieve near diffraction-limited imaging with a Strehl ratio of about 0.73 and an angular resolution of approximately 0.07 arc sec for an observation wavelength of 0.5 μ m. This imaging performance at visible wavelengths nearly matches that of the Hubble Space Telescope (HST). For comparison, the HST is reported by Glenn (26) to have a wavefront error of $\lambda/21.4$ at 0.63 μ m, which corresponds to a Strehl ratio of 0.92.

Research and Development for the Future

We have seen that the value of active optics has been proven at the European Southern Observatory and that a prototype adaptive optical telescope working in the infrared has been demonstrated at the Observatoire de Haute-Provence. Although full-scale implementation of adaptive optics for routine use remains a major technological challenge, good progress is being made on many fronts today. The gains to be realized for astronomy fully justify the effort—indeed, an expanded effort—but they suggest that coordination may become increasingly useful in ensuring convergence toward a small number of system types. Some of the issues are summed up below.

Spectral region. The design of adaptive telescope systems for both the infrared and the visible regions will undoubtedly continue to move ahead. A highly significant difference is in the resolution that can be delivered. As discussed in (24), the diffraction limit for a 4-m telescope operated at 5 μ m is 0.32 arc sec whereas in visible light it is 0.03 arc sec. Adaptive telescopes in the infrared will not match the resolution of the HST, but in the visible they may exceed it. This alone will provide a strong incentive to proceed if at all possible with the development of adaptive systems for visible light. Research problems in abundance demand high resolution. One need only mention the fine structure of quasars and their surroundings.

Systems engineering. Several very large telescopes are in the planning or design stages today. It follows that there is interest in predicting the parameters of future adaptive optical systems, especially with reference to the size and disposition of components, so that reasonable provision can be made to accommodate such systems with adequate flexibility.

Quality of artificial stars. Artificial reference stars are degraded rather rapidly with increasing zenith angle (24, figures 29 through 31), especially when this angle becomes greater than about 30°. It follows that, when realizing the advantages of adaptive optics, telescopes of the future may be considerably restricted as to zenith angle. This fact supports the choice of an equatorial mounting for a telescope as contrasted to an alt-azimuth (27). The alt-azimuth not only has an inaccessible zone at the zenith, but its "carousel effect" may present problems. Quite apart from adaptive optics, the equatorially mounted telescope, with its absence of field rotation, is generally better suited for observing near the zenith, the region of the sky that offers superior seeing and transparency with minimal atmospheric dispersion.

Site selection. It is clear that the demands placed on a complete adaptive system for use at the telescope increase enormously as the quality of the natural seeing deteriorates, that is, when r_0 becomes small and the wind speed increases. But at those times when the natural seeing is good—better than 1 arc sec—the technology becomes far more tractable. Few, if any, observatory sites offer proven natural seeing of 0.5-arc sec quality for more than a small fraction of the time. This fact places an even greater premium on care in the selection of sites (28). It should also be noted that instrumental compensation for imperfect seeing, even when only partially achieved, may nevertheless produce a very significant improvement in the Strehl ratio and may therefore be highly rewarding.

REFERENCES AND NOTES

1. I. S. Bowen, *Publ. Astron. Soc. Pac.* **62**, 91 (1950).
2. D. L. Fried, *J. Opt. Soc. Am.* **56**, 1372 (1966).
3. H. W. Babcock, *Publ. Astron. Soc. Pac.* **65**, 229 (1953).
4. F. Fischer and H. Thiemann, *Arch. Angew. Wiss. Tech.* **7**, Nos. 1, 2, 11, 12 (1941); *ibid.* **8**, Nos. 5, 6, 7, 10 (1942).
5. E. Baumann, *J. Br. Inst. Radio Eng.* **12** (New Series), No. 2 (1952).
6. H. W. Babcock, *Astrophys. J.* **107**, 73 (1948).
7. B. H. Rule, J. B. Fassero, *Publ. Astron. Soc. Pac.* **68**, 256 (1956).
8. R. N. Wilson, F. Franza, P. Giordano, L. Noethe, M. Tarenghi, *ESO (Eur. South. Obs.) Messenger No. 53* (September 1988).

9. R. Wilson, *ESO Messenger* No. 56 (June 1989).
10. J. W. Hardy, *Proc. IEEE (Inst. Elec. Electron. Eng.)* **66**, 651 (1978).
11. ———, *Proc. SPIE (Int. Soc. Opt. Eng.)* **1114**, 2 (1989).
12. F. Merkle, in *Proceedings of the European Southern Observatory Conference on Very Large Telescopes*, M.-H. Ulrich, Ed. (European Southern Observatory, Garching bei Munchen, 1988), vol. 2, pp. 639–656.
13. ——— and J. M. Beckers, *Proc. SPIE* **1114**, 36 (1989).
14. F. Merkle *et al.*, *ESO Messenger* No. 58 (December 1989).
15. S. Dickman, *Nature* **341**, 675 (1989).
16. M. A. Ealey and C. E. Wheeler, *Proc. SPIE* **1114**, 122 (1989); *ibid.*, p. 134.
17. J. G. Allen, A. Jankevics, D. Wormell, L. Schmutz, *ibid.* **739**, 124 (1987).
18. F. Roddier, C. Roddier, W. Roddier, *ibid.* **976**, 203 (1988).
19. F. J. Dyson, *J. Opt. Soc. Am.* **65**, 551 (1975).
20. J. M. Beckers, P. J. Roddier, P. R. Eisenhardt, L. E. Goad, K.-L. Shu, *Proc. SPIE* **628**, 290 (1986).
21. R. Foy and A. Labeyrie, *Astron. Astrophys.* **152**, L29 (1985).
22. L. A. Thompson and C. S. Gardner, *Nature* **329**, 229 (1987).
23. ———, in *Instrumentation for Ground-Based Astronomy*, L. B. Robinson, Ed. (Springer-Verlag, New York, 1988), pp. 337–344.
24. C. S. Gardner, B. M. Welsh, L. A. Thompson, *Proc. IEEE*, in press.
25. G. C. Valley, *Appl. Opt.* **19**, 574 (1980).
26. P. Glenn, *Opt. Eng.* **25**, 1026 (1986); *ibid.* **27**, 922 (1988).
27. H. W. Babcock, in *Proceedings of the European Southern Observatory Conference on Very Large Telescopes*, M.-H. Ulrich, Ed. (European Southern Observatory, Garching bei Munchen, 1988), vol. 1, pp. 99–110. Preprints of a significantly improved and updated version of this paper, which describes the design of an 8-m pneumatic telescope, may be made available upon request to the author.
28. H. W. Babcock and J. B. Irwin, “Carnegie Institution of Washington Southern Observatory (CARSO) site survey, 1963–1968”; in *Proceedings of an International Conference on Telescope Sites*, R. L. Millis and H. D. Ables, Eds. (U.S. Naval Observatory, Washington, DC, 1986), pp. 99–102.
29. I am grateful to C. S. Gardner, B. M. Welsh, and L. A. Thompson for providing me with a preprint of their paper (24).

Diversity of *Conus* Neuropeptides

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Conus venoms contain a remarkable diversity of pharmacologically active small peptides. Their targets are ion channels and receptors in the neuromuscular system. The venom of *Conus geographus* contains high-affinity peptides that act on voltage-sensitive calcium channels, sodium channels, N-methyl-D-aspartate (NMDA) receptors, acetylcholine receptors, and vasopressin receptors; many more peptides with still uncharacterized receptor targets are present in this venom. It now seems that the *Conus* species (approximately 500 in number) will each use a distinctive assortment of peptides and that the pharmacological diversity in *Conus* venoms may be ultimately comparable to that of plant alkaloids or secondary metabolites of microorganisms. The cone snails may generate this diverse spectrum of venom peptides by a “fold-lock-cut” synthetic pathway. These peptides are specific enough to discriminate effectively between closely related receptor subtypes and can be used for structure-function correlations.

CERTAIN TAXONOMIC GROUPS HAVE DEVELOPED CHARACTERISTIC chemical strategies for interacting with other organisms in their environment. Thus, higher plants have evolved alkaloids, presumably as a defense against animals, and microorganisms (such as the *Streptomyces*) have many secondary metabolites, including antibiotics. These compounds have provided a major source of raw materials for drug development. In these two

cases, the agents used by the organisms constitute a large and varied set of molecules that are a characteristic biochemical specialization of the group.

Few interactions between organisms are more striking than those between a venomous animal and its envenomated victim. Venom may be used as a primary weapon to capture prey or as a defense mechanism (1). Venoms disrupt essential organ systems in the envenomated animal: many venoms contain molecules directed to receptors and ion channels of neuromuscular systems.

The predatory cone snails (*Conus*) have developed a unique biological strategy. Their venom contains small peptides that are targeted to various neuromuscular receptors and may be equivalent in their pharmacological diversity to the alkaloids of plants or secondary metabolites of microorganisms. These peptides are among the smallest nucleic acid-encoded translation products with defined conformations. Peptides in this size range normally equilibrate among many conformations (in order to have a fixed conformation, proteins generally have to be much larger).

Biology of *Conus*

The cone snails that produce these toxic peptides are a large genus of venomous gastropods comprising approximately 500 species (2). Since living *Conus* have inflicted stings fatal to humans, both the popular and scientific literature have alluded to the “beautiful but deadly cones” (3). Many times humans have been stung when, as collectors, they picked up cone snails for their striking shells; rarer varieties such as the glory-of-the-sea cone (*Conus gloriamaris*) and the matchless cone (*Conus cedonulli*) were once so highly prized that they were routinely listed at auctions with paintings by the Old Masters (4) (Fig. 1).

All cone snail species are predators that inject venom to capture prey. The spectrum of animals that the genus as a whole can envenomate is broad; in addition, a wide variety of hunting strategies is used. However, every *Conus* species uses fundamentally the same basic pattern of envenomation. The prey is harpooned with a dispos-

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