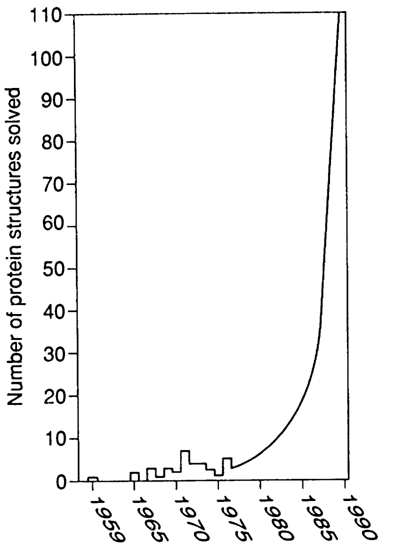

"Annual number of protein structures solved 1959–1990." [From *Protein Structure;* courtesy of Dr. Arthur Lesk]

tor molecules together in the membrane plane, thus signaling to the inside of the cell and stimulating growth patterns. Too recent for inclusion in this book, these findings have had an enormous impact in an already very significant market in therapeutics.

Acknowledging the rapid rate of advance, the book ends with a descriptive list of 25 proteins not discussed in the text whose structures are of clear importance for therapeutic design. The level of excitement in this field is high. Perutz, who had so much to do with the origins of protein-structure determination—indeed, his book begins with a gem, a beautiful 37-page intuitive introduction to protein crystallography and nuclear magnetic resonance—still points the way with adroit perception to the rapidly unfolding future.

Robert M. Stroud
Department of Biochemistry and Biophysics,
University of California,
San Francisco, CA 94134–0448

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Neutron Stars

Isolated Pulsars. K. A. VAN RIPER, R. EPSTEIN, and C. HO, Eds. Cambridge University Press, New York, 1993. xiv, 438 pp., illus. $59.95 or £40. From a workshop, Taos, NM, Feb. 1992.

Although the existence of neutron stars was predicted in 1934, the first successful observation was not until 1967, when Jocelyn Bell noticed "a bit of scruff" in the output of the radio telescope at Cambridge University. Radio pulsars were thus discovered; they were soon shown to be isolated, spinning, magnetic neutron stars. There are now more than 500 known neutron stars. *Isolated Pulsars* brings together work on the theory and observation of these stars from radio waves to gamma rays.

A neutron star has a radius of about 10 km and a mass approximately that of the sun and can spin as rapidly as several hundred revolutions per second. Physical conditions in a neutron star and in nearby space are extreme. The density of material at the center of the star is 10^{14} to 10^{15} g cm^{-3}. The magnetic field at the surface can be 10^{12} gauss, 3×10^6 times stronger than the strongest laboratory field on Earth, and the gravitational field at the surface is 10^{11} times stronger than that on Earth. Tidal forces are strong enough to rip solid objects apart thousands of kilometers above the surface.

The observed signal from most isolated pulsars results from nonthermal radiation generated by a wind of relativistic particles (somehow produced by the rotating star) moving out through the strong embedded magnetic field. As the name "pulsar" implies, radio emission from the spinning object consists of periodic sequences of brief pulses. Masses of a few neutron stars in binary systems have been measured; all are approximately 1.4 times the mass of the sun. Although investigators have not been able to measure other characteristics of pulsars directly, some of the things we would like to know are the radius, the nature of internal material, the interior structure, the nature of the "surface," and the magnetic field strength and morphology.

The brightest pulsars are the youngest, and the brightest by far is the pulsar within the Crab Nebula, which spins at a rate of 30 revolutions per second. Biggs *et al.* show a beautiful light curve (the time history of one cycle of pulsed emission) from the Hubble Space Telescope and use a polar diagram to illustrate small differences between visible observations and ultraviolet data.

Observations of the Crab pulsar in the range 0.5 to 10,000 MeV with the four instruments of the Compton Gamma-Ray Observatory are presented by Thompson *et al.*, Busetta *et al.*, Ulmer *et al.*, and Wilson *et al.* Measured light curves from the Crab pulsar, which do not vary much as energy changes, are shown, and some data from the Vela pulsar and from PSR1509-58 are presented. Data for the Crab pulsar are probably definitive, but high-energy observations of other young pulsars are currently under way and available information about these stars will soon be out of date.

Descriptions of the mechanism that produces high-energy radiation in the pulsar magnetosphere are provided by Ho, by Harding and Daugherty, and by Chiang and Romani. Chiang and Romani's contribution contains particularly helpful illustrations. Even after 25 years of study, the pulse generation mechanism of pulsars is not well understood. These papers, together with a group concerning the theory of radio pulses, illustrate that the mechanism for radio emission is believed to be different from that for high-energy emission. Cordes compares radio emission and gamma emission from the Crab pulsar.

The surface of an isolated neutron star is generally believed to have a temperature of about 10^5 K—hot enough to radiate soft x-rays as a black body. Ögelman, Becker, and Finley describe ROSAT detection of such radiation from several young or nearby pulsars. Since neutron stars are probably born hot, cooling with time, the rate of cooling gives information about the conductivity of the interior. Several papers present calculations of cooling curves, which depend on the nature of interior reactions such as the direct Urca process, and compare them with observations. Lai *et al.* discuss the properties of atoms on the surface and the effects produced by extremely strong magnetic fields. Because the magnetic force on the electron is stronger than Coulomb forces, atoms are expected to have a cigar-like structure.

All pulsars, as spinning, magnetized bodies, will slow down with time because of the torque applied by the emitted radiation. Through continuous monitoring of the arrival times of radio pulses and measurement of the pulse period, investigators can readily determine the rate of loss of rotational energy. The steady slowdown of some pulsars, however, is interrupted by glitches—sudden increases in the rotation rate, followed by decay back to a steady slowdown. Observation of the rotation rate just after a glitch can provide valuable information about the interior of the neutron star. Baym, Epstein, Alpar, Link, and Van Riper discuss how behavior during a glitch may be determined by the coupling of superfluid neutrons in the core to the solid crust by the magnetic field.

Other contributions to the volume discuss possibilities for the formation of planets in circular orbits around pulsars, the evolution of spin rates and magnetic fields, and the maximum rotation rate of a neutron star. In "How fast can neutron stars rotate?" Herold *et al.* conclude that a rate of 1800 revolutions per second is possible. They include an interesting illustration showing an observer's view of the surface of a rotating neutron star distorted by general relativistic effects. Overall, this book is a nice collection of the latest observations, calculations, and ideas on isolated pulsars.

Fred Seward
Harvard-Smithsonian Center for Astrophysics, Cambridge, MA 02138

Homeostatic Conditioning

Learning and Physiological Regulation. BARRY R. DWORKIN. University of Chicago Press, Chicago, 1993. xvi, 215 pp., illus. $23.95 or £19.25. John D. and Catherine T. MacArthur Foundation Series on Mental Health and Development.

For a rat, a shot of alcohol is a chilling experience, but only at first. One cubic centimeter of ethanol dilates the rat's blood vessels, increasing thermal conductance between core and periphery, so that in a typical 23°C environment the animal rapidly loses body heat. However, after a few of these chilling experiences, anticipatory thermoregulatory mechanisms kick in when the shot of alcohol seems imminent, generating heat to offset the anticipated loss. Thus the animal's thermal response to alcohol shows what a pharmacologist would call tolerance. The drop in body temperature becomes less pronounced with each successive administration of alcohol.

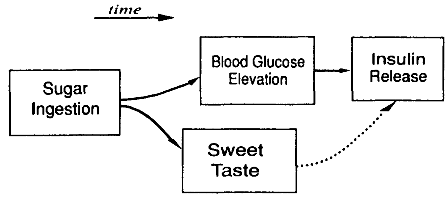
Experiment shows that this tolerance is the result of classical conditioning to stimuli associated with the administration of alcohol. The experimenter first administers alcohol under one set of circumstances and saline solution under different conditions to the same animal and then switches substances. When alcohol is injected under circumstances initially associated with it there is no hypothermic response, indicating tolerance, but when alcohol is injected into the same animal under the circumstances associated with the saline solution, there is a full-blown hypothermic response. Moreover, when the saline solution is injected under circumstances associated with alcohol, there is a strong hyperthermic response. The rat that expects alcohol but gets the saline solution generates heat to offset an anticipated loss that does not materialize.

The anticipatory thermoregulatory response illustrates the thesis of Barry Dworkin in *Learning and Physiological Regulation*, in which he brings together two historically disparate experimental and theoretical traditions—the study of learning and the study of regulatory mechanisms. His goal is to get students of learning to think about classical and instrumental conditioning in a regulatory context and to get students of regulatory mechanisms to appreciate the large role that learning plays in regulation. In the process, he gives a sympathetic review of the often ignored Russian work on the conditioning of interoceptive reflexes.

Dworkin brings into sharp focus a major unsolved problem in regulatory physiology: how the brain achieves accurate long-term regulation of the physiological state in the apparent absence of transducers capable of a prolonged steady-state response. Many physiological variables are held within narrow limits for most of an animal's lifetime. To hold constant such vital internal factors as blood pressure, body temperature, pH, carbon dioxide concentration, salinity, nutrient levels, and so on, the neuroendocrine system receives signals from specialized interoceptive sensors. Many such interoceptors have been identified and studied experimentally. Without fail—as Dworkin goes to some lengths to document—they have one serious shortcoming: they cannot signal drift (slow change). They adapt so rapidly that within a few seconds to, at most, a few minutes after a step change in the value of the sensed variable, the signal from the transducer is essentially zero. Imagine trying to design an effective heating and air-conditioning system when all available thermometers read zero regardless of the actual temperature, provided only that the actual temperature has remained steady for the last few minutes.

Dworkin thinks that instrumental conditioning mechanisms may offer a solution to the problem of how regulatory mechanisms cope with this serious shortcoming in transducer characteristics. The idea is that all the transducers need to do is signal "mistakes" in the patterns of efferent regulatory neural signals. Mistakes are efferent patterns that drive regulated variables outside the bounds of what local buffer-like, non-neural tissue reactions can manage. The mistake signals act the way punishers in instrumental conditioning do; they decrease the frequency of the kinds of outputs that generate them (according to the law of effect, as it applies to punishers). These ideas are developed only in schematic form in the final chapter of the book. It is hard to judge whether they offer serious prospects for resolving the paradox posed by adapting transducers in regulatory pathways.

In contrast, Dworkin devotes two earlier chapters to a more rigorous, mathematical development of the idea that classical conditioning endows regulatory systems with what amounts to anticipatory control. Anticipatory control is a much more sophisticated form of control than that provided by the simple servomechanisms taught in introductory courses in regulatory physiology. Anticipatory regulators extrapolate future challenges and take countermeasures before those challenges materialize. Yet Dworkin's development of this concept is awkward, relying on unconventional discrete time-bin mathematics and equally unconventional diagrams intended to illustrate his arguably more intuitive but certainly less mathematically felicitous approach to the problem of mathematically characterizing the behavior of mechanisms whose outputs and inputs are both continuous functions of time.



"Conditioned insulin release. The act of eating candy is a common example of this paradigm. Candy contains sucrose, which tastes sweet and when digested and absorbed raises blood glucose, eventually releasing insulin. It goes first into the mouth and from there into the stomach; so the sensory stimulus of a sweet taste automatically precedes the physiological stimulus of elevated blood glucose. After consuming many pieces of candy, a sweet taste alone will release insulin." [From *Learning and Physiological Regulation*]

Serious students of regulatory physiology will want to read this book. Students of conditioning may also find it thought-provoking, despite what many will think a dated and simplistic treatment of classical and instrumental conditioning.

C. R. Gallistel
Department of Psychology, University of California, Los Angeles, CA 90024–1563

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