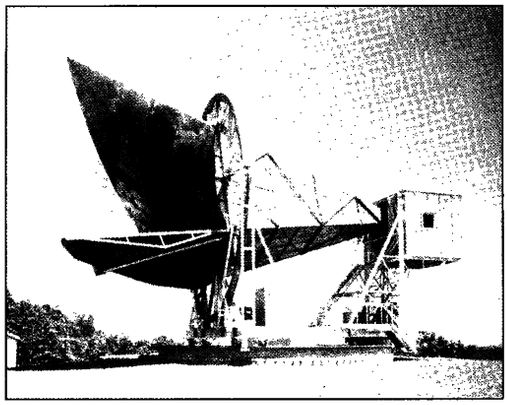

"The Bell Laboratories antenna with which the microwave background was discovered in 1965." [From *Ripples in the Cosmos*]

which they were themselves central, the purpose of which should be to provide the reader with a rip-roaring adventure story, a vicarious immersion into the thrill of doing real science.

By the latter criterion, Smoot provides the more authentic account. He was really there for two major discoveries in 20th-century cosmology: the dipole anisotropy and the ripples. His book is also the better written of the two (perhaps owing to his collaboration with a professional journalist). His "adventures" are more gripping, including the search for a balloon payload lost in the Amazon jungle and, much later in his story, a hastily organized Antarctic expedition to make microwave measurements from the South Pole. His book deserves a place of honor on a short shelf of good science popularizations.

Rowan-Robinson has also made important contributions to cosmology, but of a more arcane character, less easily explained to the lay audience. In the necessary attempt to dramatize, he commits the sin (allowable in specialized forums but unpardonable in popular accounts) of being just too sure of himself. He unwincingly concludes that the universe must consist of 3 percent ordinary matter, 67 percent cold, dark matter, and 30 percent matter in the form of a species of neutrino with a mass of 7 electron volts, and that the total density must add up to exactly the critical cosmological closure density. While such mixed hot-cold cosmologies indeed have some support from some cosmologists, there is still plenty of evidence in apparent contradiction with such models. It is surely misleading to represent the situation as in any sense settled.

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Anatomy of Addiction

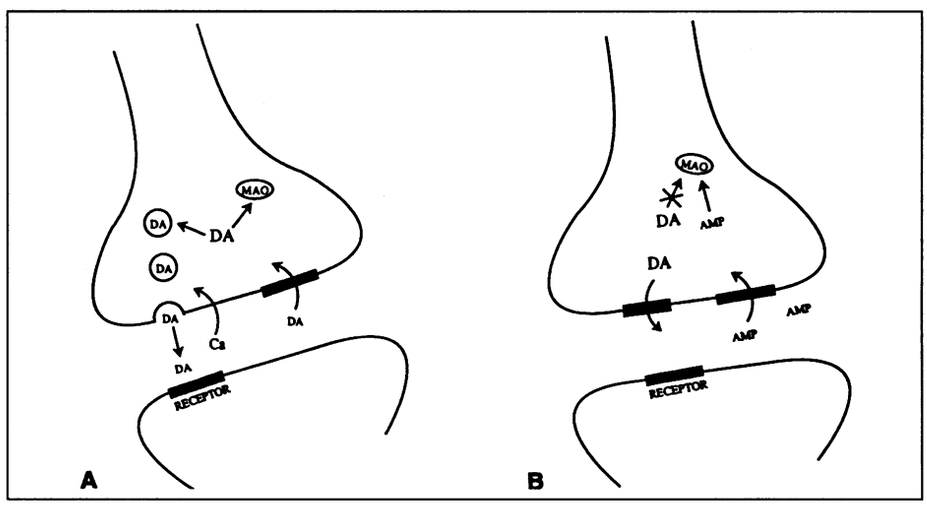
Biological Basis of Substance Abuse. STANLEY G. KORENMAN and JACK D. BARCHAS, Eds. Oxford University Press, New York, 1993. xviii, 516 pp., illus. $75 or £65.

Few issues, as the editors of this book point out, cross so many disciplines as substance abuse. Long thought of in terms of criminology or as a social phenomenon, drug addiction is now recognized as a category of chronic, biologically based illnesses. Recently, powerful new tools of neurobiology have allowed researchers to begin to unravel the mysteries of the brain mechanisms involved in substance abuse and addiction.

Biological Basis of Substance Abuse conveys the current excitement in drug abuse research. The book reflects the diversity of disciplines encompassed by the field, the changing views and latest theories of addiction, and a wealth of new information from molecular and cellular studies. The observation that different drugs of abuse often have many similar biological effects has led the editors to organize this volume by biological system rather than by pharmacological class of agents: the 30 contributions are arranged under the headings of cell biology, neural systems, neuropharmacology, behavioral mechanisms, and human genetics and pharmacological treatment. Compelling topics addressed include the brain mechanisms responsible for initial drug-induced euphoria, the neuroadaptive changes that occur with repeated drug exposure, and the possibility of a genetic vulnerability to drug addiction.

Central to the theory that substance abuse has a neurological basis is the idea that there exists an endogenous reward center in the brain that mediates all types of reinforcement, including natural reinforcers such as food as well as artificial reinforcers such as drugs. Hence the inherent abuse potential of a given substance is likely to reflect its ability to activate this reward pathway. Some controversy exists as to the precise neuroanatomical site of this reward center. However, the mesolimbic dopamine system together with opioid-releasing neurons is most often implicated; in the book evidence is presented for the ventral tegmental area, the nucleus accumbens, the prefrontal cortex, the lateral hypothalamus, the olfactory tubercle, the hippocampus, and the ventral pallidum as critical areas. Although neurochemical studies have shown that different classes of abused substances produce their initial effects on different neurotransmitter systems (opiates activate opioid receptors, central stimulants potentiate catecholamine neurotransmission), all of these agents interact at some level with the brain's endogenous reward center and thereby become reinforcers. Several excellent chapters discuss the neural circuitry of drug reward and dependence.

The evidence supporting the role of the mesolimbic system in drug reinforcement offers an explanation for the initial euphorigenic nature of many drugs. With repeated exposure to a given drug neuroadaptive changes occur that help maintain normal physiological processes in the pres-



"**A**, Depolarization-induced release of dopamine. The neurotransmitter is stored in vesicles that fuse with the plasma membrane and release their contents by a calcium-dependent process. The cytoplasmic concentration of dopamine (DA) is normally controlled by the uptake into vesicles and by degradation by monoamine oxidase (MAO). **B**, Amphetamine-induced release. Amphetamine (AMP) is taken up into the terminal by the carrier where it inhibits monoamine oxidase and increases cytoplasmic dopamine. The cytoplasmic dopamine is transported out into the synapse by the transporter." [From A. Cho's chapter in *Biological Basis of Substance Abuse*]

ence of that drug. Removal of the drug causes these changes to go unopposed and results in abnormal functioning, which produces withdrawal symptoms such as dysphoria, anhedonia, and drug craving. These symptoms can persist for long periods of time and may contribute to relapse. What are the biological changes that occur over a period of drug abuse, and are they the molecular basis of addiction? Several adaptive processes at the cellular and molecular levels have been documented, including changes in neurotransmitter receptor number, receptor affinity, neuropeptide and transmitter synthesis, autoreceptor sensitivity, neuronal firing rates, protein phosphorylation, and intracellular signal transduction. Expression of immediate early genes such as c-*fos* is regulated in response to both drug administration and drug withdrawal. The question remains, however, whether any or all of these changes are causes or effects of drug addiction.

Two critical issues in addiction research—addressed in this volume at the cellular, behavioral, and clinical levels of investigation—are the phenomena of altered drug sensitivity which occurs with multiple drug exposures over a period of time, and residual drug-induced changes which can persist even after long periods of abstinence and may be the basis of drug craving. It has long been known that repeated administration of a drug can produce tolerance—that is, a situation in which increasing doses are required to produce the same effect. The opposite can also occur: some effects of drugs intensify with repeated administration. This is termed sensitization, or reverse tolerance. Both tolerance- and sensitization-related changes in behavior and physiology can be persistent, with some changes lasting indefinitely. The molecular bases of the changes in drug sensitivity and their role in addiction are currently under intense investigation. Robinson argues that sensitization may play a major role in the development of addiction as well as in relapse, of which there is a high rate even after long periods of abstinence. Although sensitization is most frequently associated with psychomotor stimulants such as amphetamine and cocaine, animal studies have shown that it can also occur with other drugs of abuse such as opiates and PCP. The underlying mechanisms have not been fully elucidated, but dopaminergic systems are clearly involved. Repeated administration of a variety of addictive substances produces a hyperresponsiveness of mesostriatal dopamine neurons to stimuli that increase dopamine neurotransmission. Other systems, such as glutamate and GABA (γ-aminobutyric acid), may also be involved. Sensitization develops not only to the psychomotor effects of drugs but also to their incentive-rewarding properties. This may underlie the persistence of craving and help explain why drug-seeking and drug-taking behaviors become more and more compulsive over time.

Several recent molecular advances, highlighted in this book, have provided the tools needed to identify specific sites and mechanisms of drug actions. An example is the recent cloning of the THC (tetrahydrocannabinol) receptor. Sequence analysis of the cloned THC receptor confirmed that it is a member of the family of G protein (guanine-nucleotide binding protein)–coupled receptors, which includes such other receptors as the beta-adrenergic, muscarinic acetylcholine, serotonin, substance K, dopamine, and opioid receptors. Each G protein–coupled receptor is a single polypeptide molecule containing seven hydrophobic, presumably membrane-spanning, domains. These receptors interact with G proteins to initiate various cellular responses such as regulation of adenylyl cyclase activity (activation of the THC receptor inhibits adenylyl cyclase activity), phosphodiesterase, phospholipase C, and ion channels. The cloning of the THC receptor has opened the door to a better understanding of the actions of cannabinoids and their receptors. Probes are now available that make it possible to identify neurons in the cerebellum, caudate putamen, hippocampus, lateral olfactory tract, and cerebral cortex that contain the gene encoding this receptor. The large number of THC receptors found in several specific brain regions implies that these receptors have an important role in normal brain processes such as those involved in cognition, memory, movement, and reward. Important molecular discoveries have continued; within the past year, the genes for the opioid receptors have been cloned and an endogenous ligand for the THC receptor has been isolated. These findings were too recent to be included in this volume.

Research on basic biological mechanisms of pleasure and pain have resulted in better pharmacological and psychotherapeutic approaches to the management of addictive disease. Several chapters describe new and innovative approaches to the treatment of substance abuse that have grown out of data derived from basic animal studies. Also discussed in this context is the possibility of a genetic basis of vulnerability to substance abuse and addiction.

The editors of this book have done an excellent job of bringing together work from a wide variety of disciplines. The individual chapters are well written, with good overview sections for the less informed reader and plenty of data for the specialist. Recent advances and promising new techniques are highlighted with appropriate enthusiasm. *Biological Basis of Substance Abuse* will be a valuable resource for both new and seasoned researchers in the field, as well as for anyone else with an interest in addiction or neuropharmacology.

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Vignettes: Advances in Sci-Fi

I believe that present-day philosophers and science fiction writers are going to have to become knowledgeable about the new work by physicists on time travel. It simply won't do any longer for Philosophy Professor X to invoke the grandfather paradox during a discussion of causality and free will and airily to declare them to be "obviously" incompatible with time travel to the past. And it simply won't do any longer for Famous S-F Writer Y to send his hero into the past to kill Hitler as a baby, and thereby change recorded history. . . . The principle of self-consistency around closed timelike curves is going to have to become as much a part of the science fiction writer's craft . . . as it will have to become part of the fundamental philosophical axioms.

—*Paul J. Nahin*, in *Time Machines: Time Travel in Physics, Metaphysics, and Science Fiction* (American Institute of Physics)

I wish science fiction were not as male as it is, but it isn't as male as it was, not by a long shot. . . . We have regendered a field that was, to begin with, practically solid testosterone.

Ursula K. Le Guin, in *The Norton Book of Science Fiction: North American Science Fiction, 1960–1990* (Ursula K. Le Guin and Brian Attebery, Eds., Norton)