elaborate procedures by which research is supposedly planned; this ritual of state socialism is not regarded seriously as a means of directing investigations toward worthwhile social or intellectual objectives.

The arbitrary terror of Stalin is now only a bitter memory. In the aftermath, the scientific community recovered sufficient strength and autonomy to protect a few political dissenters. But the era in which liberally inclined scientific notables could apparently act with some independence within the government apparatus is over. In recent years the academic bureaucracy has been more closely geared to the state and party machinery, so that higher degrees and promotion depend upon outward political conformity. By various "administrative" devices, scholarly criteria are overridden, so that only politically reliable people can make their way up to influential scientific positions. The stick of the prison camp for an incautious word is replaced by the carrot of foreign travel as a reward for good behavior.

The fact that many of those now being persecuted as human rights activists are scientists is not without significance but does not mean that all Soviet scientists are of a similar mind. Of course there is always a mutter of unfocused discontent and passive resistance to unpopular official policies, but Medvedev is probably right in suggesting that public dissidence is a trivial factor within the enormous Soviet scientific community. Indeed, in his not altogether sympathetic comments on the disunity of the dissidents in the early 1970's and the current tribulations of the Jewish refuseniks, he probably reflects the point of view of the more thoughtful scientists in Russia on these same issues.

Nevertheless, the emphasis on political conformity is an important factor in Soviet science. In suppressing overt ideological or political dissent, the administrative machine also puts a damper on many other manifestations of independence of mind in the technical intelligentsia. Consider, also, the rigid progression through the hierarchy of advanced degrees and a gerontocratic tradition that leaves energetic old academicians at 70 or 80 in full command of their institutes—and of the scientific theories that may be validated within them. The impression one gets from various instructive episodes in the careers of individual scientists is that everyone is concerned mainly with living quietly, protecting his or her research program from serious disruption, and furthering personal advancement. Unfortunately, science does not progress by technical competence alone: it is driven by obsessional dedication, outrageous ambition, commitment to excellence, and other distinctly idiosyncratic quirks of personality. Those quirks are still to be recognized in individual Soviet scientists, but they don't seem to light up the whole crazy system the way they used to, even in the days when Stalin was knocking them off like ninepins and Hitler's armies were at the gates of Moscow.

That is what it looks like in its more public aspects. But the feature to which Medvedev attaches the greatest weight is the capacity of the Soviet system to concentrate immense resources on particular scientific projects, especially in the military sphere. He refers to immense secret laboratories, staffed by some of the most brilliant graduates and directed by powerful, capable, highly privileged scientists and engineers who never travel abroad and are seldom ever seen or mentioned in public. Out of these hidden technocratic empires have come such triumphs as the Soviet space and nuclear programs, competing successfully with American science and technology at its most advanced and sophisticated.

The history of science has no more bizarre—or frightening—episode than the research and technological development carried out in Stalin's political prisons. Medvedev tells of aircraft designers and nuclear physicists working under the conditions exposed so vividly by Solzhenitsyn in *The First Circle*. This was no aberration, no insignificant tragicomedy, but a major component of the R & D sector of the Soviet economy for a number of years during and after the war. Slave science, almost inconceivable in principle, was a practical reality.

The interesting question is whether the secret research institutions of the modern Soviet Union are more than featherbedded, voluntary variations on the same fundamental theme. Certainly there have been terrible failures as well as achievements: Medvedev gives convincing evidence for the disaster that covered a large region of the South Urals with highly radioactive materials in late 1957 or early 1958. We do not know the real cost of the brute-force approach to nuclear warheads, or space rockets, or sophisticated conventional weapons. There is no proof that Soviet science is more efficient in meeting the demands of the military than is its U.S. counterpart.

Medvedev argues that "scientists in the U.S.S.R are less free to ignore governmental attitudes but more independent of public opinion. The consequences of this in the future are rather clear—research in the U.S.S.R., although a matter of public concern, has more of a chance of proliferating and succeeding than in the democratic countries because it is supported by the government." This instrumental, technocratic view is also widely shared in the West. But it is shortsighted in ignoring factors of morale, of ethics, of values, of human insights and needs, that can come only from public participation in the scientific enterprise and a direct feeling of responsibility on the part of scientists for the benefits they may bring. Without these factors Soviet science is slave science, heading for decadence and sterility. The dissidents and refuseniks have got it right. The only real science in the Soviet Union is in their unofficial seminar, whose members, however persecuted, are free to think and speak their minds.

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## Molecular Interactions

**Cooperative Equilibria in Physical Biochemistry.** D. POLAND. Clarendon (Oxford University Press), New York, 1978. x, 344 pp., illus. $34.95. Monographs on Physical Biochemistry.

This book is a unique and valuable introduction to statistical mechanical methods for analyzing multiple equilibria in general and cooperative equilibria in particular. Multiple equilibria are ubiquitous in molecular biology; every interaction involving biopolymers in solution is a multiple equilibrium. Analysis of these interactions provides information about the magnitudes and chemical nature of the intermolecular forces (noncovalent interactions) responsible for the association equilibria under study, and is a prerequisite for understanding biological processes at a chemical level.

Numerous examples of conformational transitions and ligand binding equilibria are treated at a useful level of detail. In addition, a thorough discussion of various intermolecular forces provides a background for the interpretation of thermodynamic quantities and cooperativity parameters that are extracted from binding isotherms or titration curves. A unifying feature of the author's approach is the use of energy levels and occupational probability distributions over those levels. Parallels are drawn between distributions over energy levels in quantum statistical ensembles, free energy states in simple chemical equilibria, and states of binding in complex multiple equilibria. These distributions are described with the use of the appropriate partition functions, from which averages for the system are evaluated. For multiple equilibria, the appropriate partition function is the molecular grand partition function $\xi$, frequently called the binding polynomial. The mathematical methods that are used to formulate and evaluate the partition function (the matrix method, sequence generating functions, the maximum term method) are developed and applied. The relatively self-contained and practical development of these methods from statistical mechanics is a major strength of the book.

Unfortunately, the lack of a general overview of methods of analysis of complex multiple equilibria, coupled with the lack of a general discussion of the origins and implications of cooperativity in the interactions of biological molecules, may reduce the potential impact of the book. Various methods of analysis of these systems are available. The statistical mechanical approach described by Poland has been principally applied to highly cooperative conformational transitions of polypeptides and nucleic acids. A related but distinct statistical thermodynamic treatment using the concepts of binding potentials, binding polynomials, and linked function analysis (developed to analyze cooperative ligand binding to hemoglobin) has been extensively applied to the analysis of macromolecular binding. Thermodynamic analysis (using free energy level diagrams) and conditional probability theory have also been applied to cooperative ligand-binding equilibria. Reference to these and other numerical methods would be appropriate. Another omission of note occurs in the discussion of intermolecular interactions. The book is primarily devoted to a quantitative description of the energetics of various direct interactions between charged species, neutral species, or both. However, a large number of noncovalent association reactions involving biological molecules are entropy-driven processes occurring in aqueous solution as a result either of the release of structured water in the association of hydrophobic surfaces or of the release of counterions in the association of oppositely charged polyelectrolytes.

These omissions result in part from the difficulty of covering in one book a broad and active field (work more recent than 1974 is not covered in the book); they do not detract from the strength of the book as a clearly written introduction for the experimentalist to a complex but increasingly essential body of knowledge. The uninitiated reader should be forewarned, however, that there are a number of minor errors (typographical errors, problems with significant figures, notation, and legends to figures or tables) in the book.

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## Neuroendocrinology

**The Hypothalamus.** SEYMOUR REICHLIN, ROSS J. BALDESSARINI, and JOSEPH B. MARTIN, Eds. Raven, New York, 1978. xiv, 490 pp., illus. $35. Research Publications: Association for Research in Nervous and Mental Disease, vol. 56.

This book focuses primarily on aspects of the hypothalamus that are related to the regulation of secretion of anterior and posterior pituitary hormones. The extent of the progress being made in the field can be gauged by comparing the current volume with a 1940 book, *Hypothalamus and Central Levels of Autonomic Function*, also published under the sponsorship of the Association for Research in Nervous and Mental Disease. In the 1940 volume, Ernst and Berta Scharrer summarized their then controversial hypothesis that neurons in the supraoptic and paraventricular nuclei had a neurosecretory function, that is, secreted hormones into the general circulation. This hypothesis was based entirely on histological studies indicating the similarities between these cells and known endocrine cells. No evidence was available at that time concerning the nature of the proposed secretory material except that it seemed to be proteinaceous. Furthermore, it was not known from what site the material was secreted.

On the basis of a large body of data, which is summarized in chapters by Hökfelt *et al.*, Defendini and Zimmerman, McKelvy and Epelbaum, and Renaud, we now know that these neurons synthesize vasopressin or oxytocin, two nonapeptides. The hormones are then transported to the terminals of these neurons in the posterior pituitary by rapid axonal transport and secreted when the neurons fire in response to certain physiological stimuli (for example, high plasma osmolarity for the vasopressin neurons and suckling for the oxytocin neurons). Renaud refers to an elegant series of studies by Lincoln and Wakerley in which bursts of firing in neurons of the paraventricular and supraoptic nuclei were correlated temporarily with brief rises in intramammary pressure (presumably caused by release of oxytocin) in lactating rats with suckling pups.

A second, originally controversial, hypothesis vital to the book was not yet formulated when the 1940 book was published. This hypothesis, proposed by G. W. Harris, is that secretion of tropic hormones by cells in the anterior pituitary gland is itself regulated by hormones secreted by neurons in the hypothalamus. Harris proposed that these hypothalamic hormones were secreted into a portal circulation that connected the median eminence, an area at the base of the hypothalamus, with the anterior pituitary gland. The history of the isolation, structural analysis, and synthesis of three such hypothalamic hormones, thyrotropin-releasing hormone (TRH), luteinizing-hormone–releasing hormone (LHRH), and growth-hormone–release–inhibiting hormone (somatostatin) by Guillemin, Schally, and their co-workers is well known to readers of *Science*. One of the more unpredictable outcomes of studies of these hormones, which is discussed in various chapters in this book, is that they may have a much broader function than was previously imagined. Take TRH for instance. When antibodies against this tripeptide were prepared and immunohistochemical studies performed, heavily stained processes were found in the external layer of the median eminence as one might predict. However, processes were also found in other areas of the hypothalamus and in a number of extrahypothalamic sites such as the ventral horn of the spinal cord. Furthermore, TRH, at least as measured by radioimmunoassay, has a wide phylogenetic distribution including species in which it does not affect thyrotropin secretion by the pituitary and species that have no pituitary. Finally, iontophoretic studies have indicated that TRH depresses the firing rates of neurons in many areas of the brain. As discussed below, it has been proposed that TRH may function as a neurotransmitter at certain central synapses. Perhaps the situation is as though dopamine—considered by some to be a prolactin-release–inhibiting factor—had first been characterized by this activity rather than by its concentration in neurons in certain extrapyramidal regions of the brain.

Even the exact neuroendocrine function of TRH (and of other hypothalamic hormones) is unclear. For instance, TRH releases prolactin as well as thyrotropin. Furthermore, Knigge and others in this volume discuss the hypothesis that hypothalamic hormones are secreted not