elevated $E_1 + E_2$ and prolactin secretion (stimulated by estrogen) are associated with high risk due to family history of breast cancer, particularly of bilateral, premenopausal disease.

This hormonal cluster—depressed thyroid function, low SHBG activity, elevated free estrogen, and elevated prolactin—that may be associated with inherited susceptibility to breast cancer suggests new hormonal-epidemiological studies. For example, Korenman hypothesizes that the duration of periods of estrogen excess, or unopposed estrogen, in a woman's life determines her risk of breast cancer and that conditions such as nonovulatory cycles after menarche, short–luteal-phase cycles, and long–follicular-phase cycles are associated with estrogen excess. He proposes that these conditions, which may occur in cycles of normal total length, be analyzed in young women whose family history puts them at high risk. This is particularly important given the discovery that progesterone deficiency increases subsequent risk of breast cancer (*3*).

Unfortunately, none of the authors reports the effect exogenous estrogens may have on women already at familial high risk of breast cancer. Kelsey, in her otherwise thorough and critical review of epidemiological studies of oral contraceptives, menopausal estrogens, and risk of breast cancer, omits the possibly substantial synergistic effect of inherited susceptibility. By analyzing study subjects at high familial risk separately from other subjects, some of the ambiguity in the published results might be resolved.

A complexity accompanying any analysis of hormonal (or other) possible mechanisms for inherited susceptibility to breast cancer is that even in those families in which susceptibility is most strongly influenced by genetic factors only 50 percent of the daughters of breast cancer patients are, on average, at high risk (*1, 2*). Unfortunately, the high-risk and normal-risk women in such a sample cannot generally be distinguished from one another; such distinctions are one goal of the hormonal analysis. However, as long as statistical analysis is limited to comparisons of mean values of women from high-risk families with mean values of women from normal-risk families, true differences characteristic of the high-risk subset of women may be obscured. More appropriate would be analyses of bimodality in hormone levels within the "high-risk" sample, indicating risk heterogeneity. A simple inspection of Henderson and Pike's $E_1 + E_2$ and prolactin results (p. 117) indicates that perhaps one-third of the daughters of breast cancer patients not selected for bilateral tumors or young age at diagnosis had elevated plasma hormones. Would a larger proportion of the daughters of bilateral, premenopausal patients have elevated levels of $E_1 + E_2$, prolactin, or both?

Integrated endocrinological-epidemiological studies can elucidate still more of the relationship between hormones and breast cancer. One potentially very productive approach would be the concurrent analysis of thyroid function, percentage of free estrogen, length of luteal and follicular phases of cycles, and prolactin level in one group of healthy women from families with high incidence of breast cancer, by means of statistical techniques that do not obscure the heterogeneity of risk within such a population.

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Protein Evolution

The Evolution of Protein Structure and Function. A Symposium in Honor of Professor Emil L. Smith. Los Angeles, June 1979. DAVID S. SIGMAN and MARY A. B. BRAZIER, Eds. Academic Press, New York, 1980. xviii, 350 pp., illus. $25. UCLA Forum in Medical Sciences, No. 21.

Emil L. Smith has long been a towering figure among biochemists. His influence has been felt in a variety of ways, not the least of which is his co-authorship of a long-running and successful textbook. But it is his work on the structure and evolution of proteins that has earned him his enormous reputation. The number of proteins he has worked on is overwhelming: leucine aminopeptidase, papain, subtilisin, cytochrome *c*, histones, and glutamate dehydrogenase, to name the most important. His interest in proteins began more than 40 years ago, at which time biochemical emphasis was on directly relating structure and function. With the introduction of amino acid sequencing techniques in the 1950's, much attention was shifted to the evolution of proteins as a feature relating structure and function. Smith and his colleagues helped pioneer this movement, especially with their studies of cytochrome *c*.

This collection of essays in honor of Smith is divided into sections dealing with enzymology, protein structure and function, and evolution, but the theme of evolution of structure and function runs throughout. Some of the most enjoyable chapters intertwine some personal history with a review of a subject. The opening chapter, by Stanford Moore, is a charming memoir of how he and Smith began studies of proteins with Max Bergmann at the Rockefeller Institute, after Smith had finished his Ph.D. with Selig Hecht at New York University. Moore deftly captures the spirit of the times and the technological developments that were required for progress in understanding the chemistry of proteins and how these influenced the choice of problems. James Bonner also manages to intercalate a good deal of reminiscing when chronicling the birth of chemical studies of chromosomal proteins. These two chapters alone would make the book worth owning for any protein chemist with a sense of history.

But the fact is that all the chapters are interesting. There is a cluster of chapters on bacterial enzymes, including one on *recA* protein by I. Robert Lehman, another on in vitro enzyme evolution studies by Brian S. Hartley, and a splendid one on virtually every structural feature of β-galactosidase by Irving Zabin. From that point on the titles are mostly up-to-date echoes and reminders of subjects that Smith himself worked on: metalloenzymes (Bo G. Malmström), glycoprotein hormones (John G. Pierce and Thomas F. Parsons), histones (R. J. De Lange), and cytochrome *c* (E. Margoliash). The authors seem to have made distinct efforts to keep their contributions novel, not simply to reprint previously published material. Other chapters include an insightful approach to analyzing those aspects of protein structure that lead to thermal stability (Patrick Argos *et al.*) and a reiteration of the neutral mutation concept (Thomas H. Jukes). Richard E. Dickerson persuasively makes the case that we have all descended from a defective photosynthetic bacterium.

By and large this is a very enjoyable compendium. All protein chemists will want to own it for its reflection of an age, and all biochemists can read it with profit

and will gain an appreciation of how much we have learned in a relatively short period about living creatures from the study of their proteins. Emil Smith can proudly stack the volume next to the six enormous editions of *The Principles of Biochemistry* that he helped issue over the years.

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Aqueous Solutions

Ionic Liquids. Papers from a conference, Oxford, England, July 1978. DOUGLAS INMAN and DAVID G. LOVERING, Eds. Plenum, New York, 1981. x, 450 pp., illus. $49.50.

This book of papers on highly concentrated aqueous solutions and molten salts covers experimental data on spectroscopic, transport, and thermodynamic properties; computer simulations; alternative macroscopic properties; applications to industrial electrochemistry; acid-base phenomena; and purification of materials.

In the last 60 years, following the development of the Debye-Hückel theory, the study of electrolytes has primarily been devoted to dilute aqueous solutions. Only in the last 20 years has there been a resurgence of interest in concentrated solutions. The subject is of interest to the geosciences community because of its increasing applications to the understanding of oil and ore formation and of hydrothermal and diagenetic processes.

Industrial applications mostly involve solutions or molten salt systems that are outside the region of validity of most microscopic theories. Consequently, much of the description of such systems is macroscopic or semi-empirical. Clearly much more experimental work needs to be done to aid future theoretical development. Many of the papers in the book describe the connections and analogies between concentrated aqueous solutions and molten salts. These connections and analogies will be the path of theoretical development over the next few years, and numerous new and old ideas are suggested for consideration by the various authors.

One that is of interest is the use of computer simulations (molecular dynamics) to explore the impact of various potentials and to isolate the most significant theoretical factors (Adams and Hills). However, it will be some time before real systems will be accurately modeled. Another example is the comparison of a given macroscopic transport property for concentrated solutions, molten salts, and even ionic solids (Richter) to exploit or verify the prediction abilities of the various models such as free volume, lattice, and configurational entropy. Such comparisons are best made by using general macroscopic formulations like the Onsager l_{ij} or R_{ij} of irreversible thermodynamics or velocity correlation coefficients (Richter; Spiro and King). A third example is the empirical correlation between optical basicity parameters from absorption spectra and acid strength (Duffy and Ingram), although complex ion formation (for example, in $ZnCl_2$) does not seem to have been considered. A last example is the interesting linear correlations over quite substantial concentration ranges of charge-transfer-to-solvent spectral shifts with activity coefficients and with lattice-model Madelung constants (Griffiths and Wijayanayake).

Although the papers vary in quality and generality, overall the book is a rather nice survey of a field of growing importance and contains enough interesting and controversial ideas to be worth perusing.

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