

cipline sponsorship of a 1939 temperature symposium, technical needs evolving in World War II, graduate study with George Gamow, and Edward U. Condon's making two issues of *Reviews of Modern Physics* available to a biophysical study program in 1952. A biological systems group that I started in the 1960s led to a systems science group among colleagues for whom I consulted at the University of Southern California in the 1970s and transformed into a complex systems group at the University of California, Los Angeles, when I moved there in the 1980s. A further extension in the 1970s into social science study has been conducted since the 1980s with a unified, physically oriented social science study group.

Branching from the relatively simpler studies of the engineering physics of fluids (laminar and turbulent flow), these studies—always hierarchical—opened up to the complexity of biological and social physical systems, invariably dynamical, developmental and evolutionary. Technically, they are fluid-plastic-elastic systems composed of units (atomistic components) whose internal processes involve very long time delays and attendant memory function as compared with external interaction time scales between units. Descriptively, we identify them as (or as found in) nature, life, humankind, mind and society.

The general themes common to all these complex systems studies go by the name "homeokinetics" (formally originated in 1965; see, for example, references 2, 5 and 12); they include a set of general principles that apply to complex systems of all types and a set of strategies for studying, describing and analyzing such systems. Homeokinetic strategies are usefully applied to systems too complex to be treated by formal mathematical modeling. Such applications consist mainly of deducing or intelligently guessing from extensive physical background and data the fundamental processes by which the particular system operates at its many and varied temporal and spatial scales and of understanding the interactions among those processes.

Because our studies generally do not fall into standard disciplinary categories and because they generally contain a minimum of formal mathematical modeling (commonly, just a few essential abstracted ideas), they are usually neither written for nor accepted by standard academic disciplinary journals. Our more than 200 papers, reports and book chapters are

thus scattered in many journals, books and government publications. By editorial limitation, I am here allowed to list only about a dozen references. A more complete listing is available on request.

References 1–4 cover biophysical studies. Reference 1, for example, describes the physical-hydrodynamic design of mammals; reference 3 discusses geological-biological evolution. References 5–8 are in the social sciences. Reference 5, for example, presents a description of social operation along combined anthropological and physical lines; reference 7 compares a Marxist and positivist picture of social operation with a physical picture. References 9–12 relate to systems physics, beginning from hydrodynamic flow in tubes and proceeding to general principles and on to self-organization of rivers and societies. Reference 13 offers an interdisciplinary unification of social and biological evolution with Earth's geophysical processes, both internal and external.

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ANDERSON REPLIES: My Reference Frame column of June 1992 was not at all meant to imply that the Santa

Fe Institute either originated complex systems studies or had a monopoly on them. Many previous groups have contributed useful ideas, and many groups work throughout the world in this field. In addition to Arthur Iberall's associates, the "Michigan Mafia" group founded by Walter Reit; the pioneers of artificial intelligence such as Marvin Minsky; Iberall's own teacher Walter McCulloch; Dave Marr and other neural network pioneers; researchers in the extensive field of origin-of-life studies, including Alan Turing, Hans Kuhn, Manfred Eigen and Leslie Orgel; and many others have contributed to the field.

A Reference Frame column is not a review article and need not have any bibliography, much less a complete one. Mine would have included, if it existed, all of the above and more. SFI claims only that it draws together and focuses an extraordinary number of these threads; that wherever possible we draw on people who have contributed solidly in their own fields and on ideas with proven track records; and that we can see, more or less vaguely, certain "integrative themes" (the title of a forthcoming SFI book) emerging.

I freely acknowledge my debt to "Ibby" Iberall, who, with his friend Gene Yates, shared with me their fantastic breadth of knowledge of complex systems from the universe to the cell. Gene and Ibby also introduced me to many of the actors in this world, specifically at a wonderful conference they organized in Dubrovnik in 1980. But even my own background already included the spin glass (in which many simple interacting agents give rise to complex behavior), and my article "More Is Different" dates from 1967.

I am of course glad that Ibby has given us this thumbnail sketch of his ideas. There is much in them that is worth thinking about.

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11/93

Might DNA Shape Tell Proteins How to Fold?

I was fascinated by the well-written article by Hue Sun Chan and Ken A. Dill on the folding structure of globular proteins (February 1993, page 24). The scientific uncertainties expressed in the article are a pleasant departure from the rigid structure of semiconductor physics, with which I was concerned in my career.

I was particularly intrigued by

statements about the complexity of the folding structure. Chan and Dill pointed out that no conceivable supercomputer could begin to explore the free energies of all the possible protein folding structures; then they went on to say that the protein itself does not have the "time" or opportunity to achieve a minimum-free-energy structure. Moreover, only one or at most a few of the possible local structures of a given amino acid chain can be biologically significant.

Is it possible that as amino acid chains are replicated from a given RNA template, they do indeed form all or a great deal of the false structures? Perhaps only one in a million or even a billion of the chains that are formed are biologically active. Chan and Dill do indeed point out that chain formation would have to occur on a nanosecond time scale for a biologically significant number of active proteins to form. This would seem to require a violation of the diffusion laws that are normally associated with molecules in solution.

I had another thought on the complexity of the RNA and DNA templates. Since the discoveries of Francis Crick and James Watson, for heuristic purposes DNA has always been represented by a geometrically simple helical pattern. However, it must be that DNA and hence RNA have complex folded patterns that are "inherited" as these molecules are replicated. Perhaps a given protein's folding pattern is determined by that of the RNA that generated the protein, and the ensemble of such folding patterns is passed on, perhaps with slight mutations, from individual to individual of a species. Maybe the DNA genetic code itself is not sufficient to describe the molecule, and the DNA's folding and unfolding pattern as well is an essential part of the description. These patterns may determine "forever" the observed folded forms of the globular proteins.

RNA is generally depicted as splitting from the DNA parent in a regular fashion, like a zipper unzipping. Suppose that the DNA is folded and that the unzipping begins at many points on the molecular surface, much as happens with a damaged mechanical zipper. Suppose further that protein formation does not await the complete separation of the RNA half. This then might be a mechanism for replicating a folded structure from a folded template.

Doubtless by this time the reader can guess that I was not trained as a physicist. My first love was biology, and my training was in chemistry. Chan and Dill's quest for free

energy minima seems a bit mechanistic to me, although I freely grant the usefulness and even the necessity of statistical mechanics as one approach to the subject. On the other hand, I am enough of a scientist to be a bit uncomfortable with the mystical elements that could be read into some of my thinking. The combination of the genetic code and the folding structure could be interpreted as a "life force," a concept that Friedrich Wöhler refuted by his synthesis of urea. Let us spare ourselves metaphysical speculations concerning the "first" biologically active DNA molecule and get on with the fine work described in Chan and Dill's article.

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5/93

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CHAN AND DILL REPLY: A number of experiments show that the RNA or DNA templates cannot be imparting structure to proteins. Proteins are routinely "refolded," that is, put into denaturing conditions and then renatured *in vitro* in the absence of any other biological agents. Remarkably, the proteins return to their original active native structures, often in quite high yields. Hence the encoding of the protein structure must fully reside within the amino acid sequence.

The nanosecond time scale we mentioned applies to the current *computational* limit of molecular dynamics methods. The time scale for protein folding is nearer to milliseconds to seconds, which does not exceed diffusion limits. It follows that current molecular dynamics techniques cannot simulate the entire folding process and that many real proteins—at least those that are small and have globular native states—are able to fold to their global free-energy-minimum structures within milliseconds to seconds.

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11/93

A Woman Who Ran Los Alamos's Weapons Work

The August 1993 Washington Reports (page 41) states that Martha Krebs, as the Lawrence Berkeley Laboratory associate director for planning and development, was the "first woman associate director in the whole DOE national laboratory system." Back before people kept track of that sort of thing, before DOE swallowed the Energy Research and Development Administration and the

Atomic Energy Commission, and before assistant directors became associate directors at Los Alamos and some other national labs, Jane Hall ran the nuclear weapons program at Los Alamos Scientific (now National) Laboratory as the assistant director for weapons from 1958 to 1970.

Hall commanded respect and was seen as discharging her responsibilities with strength and careful judgment. Looking back, I wonder if she would have been as professionally respected had she been seen as a "first woman" rather than being recognized for her abilities. Similarly, I wonder if Krebs might find it easier to be regarded on the basis of her abilities by PHYSICS TODAY and the public she will deal with, rather than as a "first woman." Does PHYSICS TODAY do Krebs a disservice by falling into the politically correct rhetoric of today?

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9/93

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What Today's Physicists Really Need to Learn

Physicists must abandon their "welfare mentality" and stop complaining. The world does not owe us a living. Unemployment is an essential mechanism of the free-market economy that cleanses the labor force of those who are unfit or unwilling to adapt themselves to market forces. Physicists need only learn to supply what the free market demands. We must strive to acquire the new skills that we need to compete in the global economy. Physics curriculums and indeed the whole of physics education need to be completely restructured. What skills does the modern physicist need?

The professional physicist spends a considerable amount of time writing research proposals and making presentations. It is not enough merely to communicate knowledge; you must impress the audience—especially those who allocate funds. As much as possible the message should be conveyed pictorially, since few executives have time to read anything. For this purpose good color graphics are absolutely indispensable: One picture is worth a million dollars. The modern physics curriculum should include courses in the graphic arts, including data visualization—preferably oriented toward advertising.

If you actually do find a job, more time than you realize will be devoted to advertising your skills and marketing your achievements, so you might as well take a couple of courses on advertising and marketing. The importance of good demonstrations