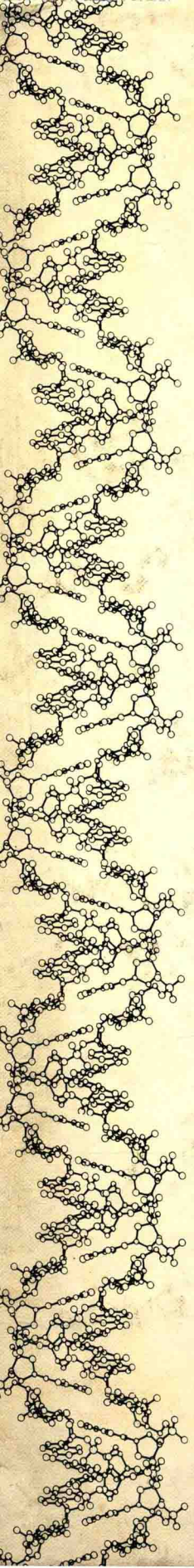


Structure & Dynamics: Nucleic Acids & Proteins



Structure and Dynamics: Nucleic Acids and Proteins

Proceedings of the International Symposium on Structure and Dynamics of Nucleic Acids and Proteins, held at the University of California, San Diego at La Jolla, September 5-9, 1982, under the auspices of the International Society of Quantum Biology.

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Structure and Dynamics Nucleic Acids and Proteins

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Preface

This volume is a collection of contributions to the International Symposium, "Structure and Dynamics of Nucleic Acids and Proteins" held under the auspices of the International Society of Quantum Biology, and organized by Professor Enrico Clementi, the President of the Society. The gathering of so many leading biophysicists and researchers in nucleic acid and protein structural dynamics was made possible by the generous support from a number of national and international sponsors; indeed Adenine Press can offer this volume at about one half the standard cover price, thanks to a subsidy from the symposium's sponsoring organizations.

The pleasant surroundings of the Undergraduate Science Building at the University of California, San Diego contributed most positively to the informal but intellectually very intense atmosphere of the symposium, held during the Labor Day week, September 5-9, 1982. The Program and Collected Abstracts have been published by Adenine Press and these were distributed at the meeting. A few remaining copies of these can be obtained from one of us (EC).

The publication of this volume provides the occasion to thank Professor Berni Alder, University of California, Berkeley, Professor Richard C. Atkinson, University of California, San Diego, Professor Paul J. Flory, Stanford University, Professor Joe O. Hirschfelder, University of Wisconsin, Professor Joseph Mayer, University of California, San Diego, Professor Robert S. Mulliken, University of Chicago, and Professor Linus Pauling, Linus Pauling Institute of Science and Medicine, for kindly accepting to constitute the symposium's Honorary Committee.

We thank Kenichi Fukui for writing the Foreword for the volume, and thank Wilma King Olson and William N. Lipscomb for providing the introductions to Part II (Nucleic Acids) and Part III (Proteins) respectively. We express our appreciation to Mrs. Karen Jones, Ms. Sandra M. Pourquoy and Ms. Karen A. Smith at IBM, Poughkeepsie for patiently feeding the manuscripts through terminals under notable pressure to meet the publication schedule. Most of all we thank and congratulate the various authors of this volume for their full collaboration and for their most notable contributions and Dr. Giorgia Corongiu for proof-reading many articles, and for her help in organizing the La Jolla conference. We are grateful to Struther Arnott and Rengaswami Chandrasekaran for providing the structure of D-DNA, just solved in their laboratory for the cover illustration. One of us (RHS) thanks his friend, wife and scientific associate Dr. Mukti Sarma for her close cooperation and understanding during the tenure of this project on the structural dynamics of nucleic acids and proteins.

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FOREWORD

Really, I did not expect to write the Foreword for this volume, but in view of the kind letter from Dr. Enrico Clementi who has long been one of the best colleagues of mine, I accepted and also with great pleasure since I did participate in that successful meeting of the International Society of Quantum Biology.

Proteins and nucleic acids are the fundamental bricks of life. To model a living body with these bricks—in science—however, is not as easy as making a building. In biological problems, there is a great deal of difficulties in selecting and adopting an appropriate model. In addition, a minute cause or a slight difference in the structure and conformation might seriously influence the physiological action. For instance, the difference between normal and abnormal cells is, at least partly, caused by a minute difference—even one monomeric unit in a polymeric chain composed of thousands of monomeric units—in DNA or proteins.

Theory is the human way to organize concepts and to make plans for action. During these years biology has continued to provide theoreticians with a stage on which the use of quantum mechanics would display its strength. The choice and adoption of a suitable model on the basis of which calculations were carried out is, therefore, a particularly important idea.

In theoretical studies of biological systems, in addition to nonequilibrium and dynamic phenomena, cooperative phenomena may also be involved. The theoretical study for macromolecular interactions of higher orders may be a clue to approach these problems.

Today experiments can be performed even at the computers, if the model is adequate; we are not limited to laboratory experiments, the traditional way. This new way will continue to possess a significance in particular in the phenomena which are not easily accessible for traditional means of experiments.

In this context it is nice and fortunate to have this volume which contains excellent contributions from leaders in theory and in laboratory and computer experiments. The volume starts with an illuminating discussion of conceptual and theoretical background, and then proceeds to the structural dynamics of nucleic acids and proteins. The volume is a frontier publication in that it provides a unification between theory and experiment, between

Physics, Chemistry and Biology, and indeed discusses extensively, unbiased, the concept of solitons and its relevance in biology. I trust that the book will be very useful for both theoreticians and experimentalists.

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Introduction to Part I: Conceptual and Theoretical Background

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The first part of this volume deals with view-points relevant not only to nucleic acids and proteins, but—in general—to matter when it is those states and structures pragmatically and traditionally referred to as living matter. One after the other, these chapters recall the many facets of contemporary research in living matter: a moment of reflection and meditation, an enthusiastic proclamation of a formal design to model matter from the electron's gas to biological systems, a didactical and a pedagogical introduction to old-new concepts, first on mathematical, then on physical terms, an awakening to reality by recalling long standing difficulties in solving much "simplier" and "confined" aspects of the overall problem, a reminder of different models and view-points—where order and chaos are confronted—and finally, a schematization, which could be used as alternative indexing scheme for this volume, and where water—as solvent—is seen as the unifying aspect of biological systems. But let us proceed in more detail.

The volume opens with Careri and the terms "structure" and "dynamics" are analyzed at the conceptual and semantic level—as seen by a physicist—in the context of biophysical models and experiments. A less articulated but somewhat complementary view-point is often tacitly adopted by chemists, with much attention to detailed local aspects at the expense of the collective characterizations. Clearly, interdisciplinary cross-fertilization, one of the main aims of our International Symposium and of this Volume remain a perennial goal.

Löwdin presents a theoretical formulation, based on density matrices and system operators, which is capable to model systems from electron's gas to biology. Entropy enters the formulation as a convex functional, and time evolution is present in the microscopic systems, which do satisfy a Liouville equation of time. The emphasis being on concepts, expressed with a powerful algebraic notation, problems related to the theory's applicability and numerical evaluation are not stressed. Adenine Press has made a special effort to reproduce Löwdin's calligraphy in this chapter's mathematical notation: a tribute to Professor Löwdin who retires from the University of Uppsala this year.

An increasingly familiar concept and model in quantum-mechanical application is one of solitary waves or solitons. These highly non-linear and local excitations can be easily “misused” either by adopting the concepts in a semantically incorrect context, or by somewhat stubbornly refusing to use the solitons formalism even when the correct conditions are satisfied. Professor McLaughlin’s clear introductory exposition on the mathematical constraints associated with the soliton concept should be most useful in preventing such errors. In the next paper Professor Krumhansl further elucidates the solitons concept with attention to biophysical applications in general, and to nucleic acids in particular. These papers are excellent introductions to the detailed applications we shall find in Part III, specifically in the chapters by Professor Scott—where experimental evidences are advanced in support of the classical model of muscle contraction—discussed by Professor A. Davydov in his chapter. Professor Davydov’s last moment inability to be present at the meeting has not prevented him from sending us his manuscript; in thanking Professor Alexander Sergeevich Davydov, we wish him our best for his seventieth birthday, (December 26, 1912).

A basic problem—namely the often limited applicability of otherwise beautiful models—because of numerical or analytical difficulties—is rather abruptly introduced with two contributions, one by Professor van Duijnen and coworkers, and one by Professor Finney and coworkers. These contributions show that the “resolution power” does limit not only laboratory, but also computer experiments. In Professor van Duijnen’s work, a number of approximations are proposed to represent the electric field generated at an enzyme active site by the distant atoms of the enzyme and of the substrate: the practical impossibility of a direct quantum chemical approach is at the base of these approximations. The contribution by Professor Finney is representative of one among the different and contemporary view-points on the prediction of reliable intermolecular forces and atom-atom potentials, the necessary input for Molecular Dynamics and Monte Carlo statistical mechanical treatment of biosystems, in this case small molecules as solute and water molecules as a solvent. For the very specific aspect concerning hydrophobic interactions—a problem of importance in proteins—an interesting note is given by Professor Beveridge in Part III.

In the last two papers of Part I we return to more general problems. Professor R. Lefever discusses the consequences of perturbing a system with random noise from an external source; the possibility of ordered structures emerging from white noise perturbation, is one more application to biophysical problems of the formalisms from the well known Prigogine’s school. In this context, I cannot refrain to recall with curiosity a diffuse mythological tradition, where order arised from chaos. Part I is then concluded with Professor Palma’s chapter, where the paramount importance of water in biological systems is logically organized and categorized in a table, which not only provides an excellent overview, but could have been used as an alternative indexing scheme for this volume.

As a closing note, we recall that there are several theoretical contributions to this volume not included in Part I, whenever either nucleic acids or proteins, the specific subjects for Part II and Part III respectively, were the main focus of the chapter.

Structure and Dynamics of Biomolecules Viewpoint from Physics

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Introduction

Biological macromolecules are physical objects of biological significance; therefore it seems sound to ask ourselves if “structure” and “dynamics” are appropriate as terms for their physical description. To this end we shall first recall the problem of describing complex physical objects, and then reconsider the nature of the entities that both physics and biology can describe. These two introductory sections will be followed by a discussion of the description levels of biomolecules with some reference to current work in this area of research.

Being the last speaker at this Conference, I have been asked to contribute a paper of a somewhat critical and philosophical character. According to Whitehead¹ “the world around us is complex, composed of details. We have to settle upon the primary types of detail in terms of which we endeavor to express our understanding of nature. We have to analyze and to abstract, and to understand the natural status of our abstractions.” Therefore our philosophical question can be better reformulated as follows: what structural and dynamical details of biomolecules are truly primary, and after analyzing them properly, what kind of abstract description are we going to express?

Description Levels of Complex Physical Systems

The problem of levels (or scales) of description is often encountered in physics, because systems of interest vary from quarks to atoms, from electrons to galaxies. Usually, description in a certain level means description which employs only certain concepts and some laws which relate these concepts to others, and it is found that these various levels possess a surprising degree of autonomy. One typical example is the “classical hydrodynamical level,” where the quantities involved are density, local velocity, local pressure and local temperature, and the relevant laws are those of classical continuum mechanics and classical thermodynamics. However, another possible level is the “kinetic or molecular level” where the entities are molecular parameters and their interactions, and the laws are those of classical

particle mechanics. The general relationship between micro- and macroscopic description levels is the subject of classical statistical mechanics, and in view of its relevance here, it shall be recalled below.

Following Uhlenbeck,² the scale description of statistical mechanics develops according to the following procedure.

- (a) The starting point is an underlying *microscopic dynamics*, described in terms of variables x , so that any set $x_1...x_N$ of these variables gives a complete specification of the microscopic state.
- (b) The next point is the introduction of macroscopic variables y such that

$$y_i = f_i(x_1...x_N) \quad i = 1...S \quad (1)$$

where $S \ll N$. We also note that

$$\begin{array}{l} x \rightarrow y \\ y \not\rightarrow x \end{array} \quad (2)$$

It is implied that the y description is less detailed than the x description, and if x and y are real variables, this requires that the number of y be much lower than the number of x variables. For this reason, such a description is called a *contracted description*.

- (c) A macroscopic or contracted description is called a *macroscopic level* or *scale* if the description is *both closed and causal*. The closure refers to the fact that the y description involves only the y variables, and the causality asserts that the specification of initial data on the y level is sufficient to determine the y variables at a later time.
- (d) Finally, the macroscopic variable y must be a *secular* variable. This means that y changes very little in comparison to the change in the x variable, namely $y(t)$ is a slow variation on the time scale of $x(t)$.

Inasmuch as the contracted description is incomplete relative to the microscopic description, it follows that a contracted description must contain *stochastic* elements. In general $\overline{y^2} \neq (\overline{y})^2$, there are fluctuations, but in macroscopic systems the fluctuations are small. A different way of phrasing the condition of closure of a level is that the average fluctuations in the measured variables of that level shall be less than the experimental accuracy. Therefore, we note that the closure of a level also depends on the type of experiments to which the system is subjected.

Usually a macroscopic level is identified from macroscopic experiments, and in practice first macroscopic laws are found empirically at a macroscopic level and then suitable procedures are worked out to deduce them from a more basic micro-