

Subcellular Biochemistry

Volume 6

Edited by
Donald B. Roodyn

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Aims and Scope

SUBCELLULAR BIOCHEMISTRY aims to bring together work on a wide range of topics in subcellular biology in the hope of stimulating progress towards an integrated view of the cell. In addition to dealing with conventional biochemical studies on isolated organelles, articles published so far and planned for the future consider such matters as the genetics, evolution, and biogenesis of cell structures, bioenergetics, membrane structure and functions, and interactions between cell compartments, particularly between mitochondria and cytoplasm and between nucleus and cytoplasm.

Articles for submission should be sent to Dr. D. B. Roodyn, Department of Biochemistry, University College London, Gower Street, London WC1E 6BT, U.K., and are best sent in the period February to April inclusive of each year. There are no rigid constraints as to the size of the articles and in general they should be between 9,000 and 36,000 words, with an optimum size of about 20,000 words. Although articles may deal with highly specialized topics, authors should try as far as possible to avoid specialist jargon and to make the article as comprehensible as possible to the widest range of biochemists and cell biologists. Full details of the preparation of manuscripts are given in a comprehensive Guide for Contributors which is available from the Editor or Publishers on request.

Preface

This volume continues the tradition of *SUBCELLULAR BIOCHEMISTRY* of trying to break down interdisciplinary barriers in the study of cell function and of bringing the reader's attention to less well studied, but nevertheless useful, biological systems.

We start with an extensive article by T. P. Karpetsky, M. S. Boguski and C. C. Levy on the structure, properties and possible functions of polyadenylic acid. Apart from revealing a general lack of appreciation of many important aspects of the chemical properties of polyadenylic acid, the literature also shows that there is a great gulf between those who study the biological role of polyadenylic acid and those who study its physicochemical properties. The article by Karpetsky and his colleagues is an attempt to overcome this lack of communication and to present an integrated view of the subject. The authors go into the subject in full detail and the more biologically inclined reader may on occasion have to reread his nucleic acid physical chemistry notes! However, the effort is worthwhile and the article is a timely reminder that we cannot treat nucleic acids as mere abstractions, but that they are complex organic macromolecules capable of equally complex, but nevertheless important, interactions.

The next article is by J. Steensgaard and N. P. Hundahl Møller and deals with computer simulation of density gradient centrifugation systems. From the rather early "hit and miss" bulk fractionation schemes, preparative centrifugal fractionation of cell homogenates has now developed into a rigorous and technically sophisticated discipline. The fact that many centrifugation procedures can now be accurately represented by computer models is a great advance. Apart from the convenience it provides of being able to carry out "dummy" runs without actually wasting precious biological material, the fact that the major parameters in the system can be quantified and handled in this way puts centrifugal fractionation on a much more sound theoretical basis. It is to be hoped that Steensgaard and Hundahl Møller's article will stimulate as much as it simulates.

The next article by U. C. Knopf deals with crown-gall tumors in

general as well as the specific role of *Agrobacterium tumefaciens*. From relatively obscure beginnings, the subject is becoming more generally recognized as a most interesting experimental system for studying the induction of tumors. It is also becoming clear that there are some similarities between the processes involved in the action of *Agrobacterium tumefaciens* and of the nitrogen-fixing bacteria, particularly the *Rhizobia*. The famous root nodules of the nitrogen-fixing legumes are in fact "benign" nodules, perhaps different only in degree from the massive crown-galls. We thus have a most interesting comparative system of "benign" and "malignant" growth, and we can only hope, with the author, that the medical implications will not be lost just because the systems are found in plants and not in mice.

We next turn to another system that has only recently achieved the full interest and recognition that it deserves. This is the so-called "petite" mutation in yeast, and it is described in detail by P. A. Whittaker. Although the existence of "petites" was known for years amongst yeast geneticists, it was only with the explosive development of research in mitochondrial biogenesis in the last five years that the full significance of the "petite" mutation became widely appreciated. Mitochondrial genetics has now become a major discipline in its own right, with its own terminology and expertise. It is to be hoped that Whittaker's article will help to guide the reader through some of the intricacies of this new methodology.

The next article by G. Lenaz looks at some fundamental aspects of the role of lipids in cell membranes. In a detailed and extensive article, the author identifies five major roles for lipids in biomembranes. They act as binding surfaces for proteins, they are needed to separate aqueous compartments so as to allow vectorial processes to take place, they provide a hydrophobic milieu for reactions that require one, they are required for the formation of membranes from dissociated subunits, and finally they can act as modulators of membrane-bound enzymes. As with the article by Karpetsky and colleagues, this article delves into fundamental physicochemical aspects of the molecular entities involved and the reader is continually reminded that membranes are not abstractions but are made from very real molecules that have their own inherent chemical properties, a knowledge of which can greatly help in our understanding of the behavior of biological membranous assemblies.

The next article is by F. L. Crane, H. Goldenberg, D. J. Morré, and H. Löw and deals with the dehydrogenases of the plasma membrane. As the detailed tables presented by the authors clearly show, there is now overwhelming evidence for the existence of a range of dehydrogenases in plasma membranes isolated from a variety of cell types. Just as it took some time to appreciate the fact that the mitochondrial membrane is not the

only site for linked respiratory activity and the "microsomal" respiratory chain is a complex system in its own right, so we must now generalize the picture even further, and think in terms of other membrane systems having bound respiratory enzymes, performing functions specific to the membrane in which they are found. The authors discuss several interesting ways in which plasma membrane dehydrogenases can act, for example, in redox control of the formation or breakdown of cyclic nucleotides. From primitive views of membrane-bound respiratory enzymes being solely involved in mitochondrial processes, we must now develop much more sophisticated attitudes toward the cellular role of "intrinsic" dehydrogenases, perhaps almost to the point of believing that the mitochondrion is really only a "special case" in which bound redox systems happen to be linked to the production of ATP.

The last article is by N. Lakshminarayanaiah and is entitled "Transport Processes in Membranes: A Consideration of Membrane Potential across Thick and Thin Membranes." Here we are hoping to bridge yet another unfortunate interdisciplinary gap, namely that between biophysicists and biochemists. One of the most important consequences of the famous chemi-osmotic theory of Mitchell is that biochemists have come to realize that the ion transport and membrane potential phenomena studied so eruditely and mathematically by biophysicists are in fact closely interconnected with the respiratory and bioenergetic properties of cell membranes. It is as if there has been a sudden realization that the term "membrane" as used by biophysicists is not some abstract concept or barrier, but refers in reality to *actual* membranes in real cells. Unfortunately, the mathematical rigor of the biophysical approach has not yet fully spilled over into biochemical membranology. Perhaps the phenomena under study are too complex to be represented by formal equations. Nevertheless, any attempt to propagate rigorous attitudes in cell biochemistry is surely to be encouraged, and it is to be hoped that Lakshminarayanaiah's article will demonstrate the remarkable extent to which "classical" physicochemical theory can be applied to the study of biomembranes.

As in previous volumes of *SUBCELLULAR BIOCHEMISTRY* we end with an account of recent books in cell biochemistry and biology. We discuss a number of texts in membrane research, organelle biochemistry, and plant biochemistry as well as some educational texts and once again hope that we are of some use in guiding the reader through the very extensive literature currently published in the overall field of cell biology.

D. B. Roodyn

London

Contents

Chapter 1

Structures, Properties, and Possible Biological Functions of Polyadenylic Acid

Timothy P. Karpetsky, Mark S. Boguski, and Carl C. Levy

1. Introduction	1
2. Isolation and Detection of Poly(A)	2
2.1. Methodology	2
2.2. Determination of the Size of Poly(A) Segments	5
3. Messenger RNA and the 3'-Terminal Poly(A) Sequence	9
3.1. Occurrence of Poly(A) in Living Organisms	9
3.2. Poly(A) Sequences in Prokaryotes	15
3.3. Messenger RNA Lacking Poly(A)	18
3.4. Complexes of Poly(A) with Amino Acids and Proteins ..	24
4. Possible Biological Functions of Poly(A)	24
4.1. Covalent Linkage of Poly(A) RNA	27
4.2. Transport of mRNA from the Nucleus to the Cytoplasm ..	32
4.3. Poly(A) and the Stability of mRNA	40
4.4. Poly(A) Involvement in the Binding of mRNA to Membranes	41
4.5. 3'-Terminal Poly(A) Sequences of mRNA and Protein Synthesis	42
4.6. Summary	43
5. Structure of Poly(A)	43
5.1. Poly(A) at Neutral pH	49
5.2. Acidic Forms of Poly(A)	58
5.3. Effect of Substituents on Poly(A) Structure	64
5.4. Synthesis of Analogues of Poly(A)	66
5.5. Influence of Metal Ions on the Structure of Poly(A)	

6. Interaction of Poly(A) with Monomers and Polymers	72
6.1. Complexes of Low-Molecular-Weight Organic Compounds and Poly(A)	72
6.2. Complexes of Poly(A) and Complementary Monomers ..	80
6.3. Interaction of Poly(A) with Poly(U) and Other Complementary Polynucleotides	83
7. Conclusions	90
8. References	91

Chapter 2

Computer Simulation of Density-Gradient Centrifugation

Jens Steensgaard and Niels Peter Hundahl Møller

1. Introduction	117
2. Some Aspects of the Basic Theory of Gradient Centrifugation	118
3. The Indirect Approach to Simulation of Gradient Centrifugation	122
4. The Compartmental Approach to Simulation of Gradient Centrifugation	127
5. The Analytical Approach to Simulation of Gradient Centrifugation	132
6. General Discussion	138
7. References	139

Chapter 3

Crown-Gall and *Agrobacterium tumefaciens*: Survey of a Plant-Cell-Transformation System of Interest to Medicine and Agriculture

U. C. Knopf

1. Introduction	143
2. Overview of the Process of Plant-Cell Transformation by <i>Agrobacterium tumefaciens</i>	145
3. Conditions for Plant-Cell Transformation by <i>Agrobacterium</i> <i>tumefaciens</i>	145
3.1. Dicotyledonous Host Plants or Gymnosperms	146
3.2. A Temperature below 30°C	146
3.3. A Wound or Wound Stimulus	146
4. Properties and Products of <i>Agrobacterium tumefaciens</i>	149
4.1. Induction of Crown-Galls	149
4.2. General Properties and Classification	150

4.3. Differential Ability to Use Unusual Amino Acids as Sole Nitrogen Source	151
4.4. Production of Plant Growth Substances	152
4.5. Production of Polysaccharides	152
4.6. Production of Vitamins	153
4.7. Production of Antibiotics	153
5. Molecular Components, Genetic Systems, and Search for the Tumor-Inducing Principle (TIP) of <i>Agrobacterium tumefaciens</i>	153
5.1. DNA and DNA Plasmids	153
5.2. An RNA Polymerase and Its Components	157
5.3. RNA	157
5.4. Ribosomes and Their Components	157
5.5. Bacteriophages and Their Components	158
6. Attempts to Define the Crown-Gall Tumor Cell	159
6.1. Transplantability	159
6.2. Presence of Unusual Amino Acids	159
6.3. Autonomy	161
6.4. Accelerated Growth Rate	162
6.5. Limited Capacity for Differentiation	163
7. On the Genetic Basis of the Formation of the Crown-Gall Tumor Cell	163
7.1. Experiments on the Reversion and Suppression of the Tumorous State	163
7.2. Experiments Directed to the Detection of Bacterial and Bacteriophage Genes and Gene Products in Crown-Gall Tumor Cells	164
8. Medical and Agricultural Interest in Crown-Gall/ <i>Agrobacterium</i> Research	166
9. References	168

Chapter 4

The Petite Mutation in Yeast

Peter A. Whittaker

1. Discovery and Initial Characterization	175
1.1. Introduction	175
1.2. Discovery	176
1.3. Genetic and Biochemical Characterization	176
2. Cytology and Ultrastructure of Petite Mutants	182
3. Mitochondrial DNA in Petite Mutants	183
3.1. Grande Yeast Mitochondrial DNA	183

3.2. Petite Yeast Mitochondrial DNA	184
3.3. Mitochondrial DNA Synthesis	188
4. Mitochondrial RNA in Petite Mutants	189
4.1. Grande Yeast Mitochondrial RNA	189
4.2. Petite Yeast Mitochondrial RNA	191
5. Mitochondrial Proteins in Petite Mutants	194
5.1. Synthesis of Mitochondrial Proteins	194
5.2. Tricarboxylic Acid Cycle and Other Enzymes	195
5.3. Respiratory-Chain Components	195
5.4. Mitochondrial Adenosine Triphosphatase	197
5.5. Mitochondrial Transport Systems	198
6. Induction of the Petite Mutation	199
6.1. Temperature and Nutritional Effects	199
6.2. Inhibitors of Mitochondrial Macromolecular Synthesis ..	200
6.3. Miscellaneous Chemical Mutagens	201
6.4. Additional Mutagenic Treatments	202
6.5. Spontaneous Mutation	208
6.6. Antagonists of Petite Mutation	209
7. Petite Mutants and Mitochondrial Genetics	210
7.1. Suppressiveness	210
7.2. Petite Deletion Analysis	212
7.3. Petite Marker Rescue	213
8. Petite-Negative Yeasts	213
9. The Petite Mutation: A Broader View	215
10. Appendix: Abbreviations and Terms	218
11. References	219

Chapter 5

The Role of Lipids in the Structure and Function of Membranes

Giorgio Lenaz

1. Introduction	233
2. Properties of the Lipid Bilayer	235
2.1. Lamellar Systems	235
2.2. Thermotropic Phase Changes and Phase Separations	236
2.3. Lipid Viscosity	239
2.4. Summarizing Concepts	242
3. Lipid-Protein Interactions and Lipid Organization in Membranes	243
3.1. Lipid-Protein Interactions	243
3.2. Asymmetry of Membrane Components	248
3.3. Protein Mobility	252

4. Effects of Lipids and Their Physical State on the Properties of Biomembranes	256
4.1. Means Employed to Investigate the Effects of Lipids in Membrane Functions	256
4.2. Permeability and Transport	258
4.3. Lipids and Enzyme Activity	264
4.4. Effects of Lipids on Hormonal Response	280
4.5. Lipids and Other Membrane Properties	283
4.6. Coenzymatic Function of Lipids	283
5. Roles of Lipids in Membrane Functions	285
5.1. Lipids Represent a Binding Surface for Proteins	286
5.2. Latency and Compartmentation	288
5.3. Lipids Provide a Hydrophobic Medium or a Binding Interface	292
5.4. Molecularization and Membrane Formation	299
5.5. Conformational Role of Lipids	301
6. Summary	315
7. References	317

Chapter 6

Dehydrogenases of the Plasma Membrane

Frederick L. Crane, Hans Goldenberg, D. James Morré, and
Hans Löw

1. Introduction	345
2. Extrinsic Dehydrogenases	347
2.1. Glyceraldehyde-3-phosphate Dehydrogenase	348
2.2. Lactic Dehydrogenase	349
2.3. Other Dehydrogenases	351
3. Intrinsic Dehydrogenases	352
3.1. NADH Dehydrogenases	352
3.2. Selective Inhibition of Plasma Membrane NADH Dehydrogenase	365
3.3. NADPH Dehydrogenases	367
3.4. Xanthine Oxidase	369
3.5. Other Dehydrogenases	371
4. Relationship of Dehydrogenases to Membrane Function	372
4.1. Energy-Linked Transport	372
4.2. Metabolic Conversions	375
4.3. Peroxide or Superoxide Generation	375
4.4. Redox Control of Plasma Membrane Functions	376
5. Conclusions	381
6. References	382

*Chapter 7***Transport Processes in Membranes: A Consideration of Membrane Potential across Thick and Thin Membranes**

N. Lakshminarayanaiah

1. Introduction	401
2. Biological and Lipid Bilayer Membranes	403
2.1. Chemical Constituents and Physical Structure	403
2.2. Properties of "Undoped" Bilayer Membranes and Biomembranes	410
2.3. Properties of "Doped" Bilayer Membranes and Biomembranes	418
3. Membrane Potential	427
3.1. Donnan Potential	428
3.2. Diffusion Potential	429
3.3. Theories of Membrane Potential	430
3.4. Distribution, Surface, or Interfacial Potentials	439
3.5. Applications of the Gouy–Chapman Double-Layer Theory	449
3.6. Adsorption Approach to Membrane Potential	463
4. Summary	468
5. Appendix: Mathematical and Electrochemical Terms and Symbols	471
6. References	474
 Some Recent Books in Cell Biochemistry and Biology	 495
1. Molecular Biology and Cell Organelles	496
2. Membrane Research	500
3. Plant Biochemistry and Morphology	505
4. Educational Texts	506
 Index	 511

Chapter 1

Structures, Properties, and Possible Biologic Functions of Polyadenylic Acid

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1. INTRODUCTION

Our original interest in preparing this review lay in the fact that no one had presented a thorough examination of the topic, with particular attention to the *several* possible biological functions of polyadenylic acid [poly(A)]. However, as we scrutinized the literature, one point cropped up repeatedly: those engaged in research efforts aimed at clarifying the physiological significance of poly(A) did not make full use of the current body of knowledge concerning the chemical properties of the homopolymer. Similarly, results of experiments that clarify aspects of the physical nature of poly(A) were never interpreted in terms of intracellular functions. Thus, two vast bodies of literature exist in roughly equal proportions, one con-

The MEDLINE computer service of the National Library of Medicine, Bethesda, Maryland, and the CHEMCON data base (BRS, Inc., Schenectady, New York) were utilized to compile the initial bibliography on poly(A), consisting of articles published between 1966 and February 1977. The literature survey for this review was completed in July 1977.

Abbreviations used in this chapter: (CD) circular dichroism; (cDNA) complementary DNA; (DEAE) diethylaminoethyl; (DMSO) dimethylsulfoxide; (ESR) electron spin resonance; (HnRNA) nuclear heterogeneous RNA; (mRNA) messenger RNA; (mRNP) ribonucleoprotein complex; (NMR) nuclear magnetic resonance; [oligo(dT)] oligodeoxythymidylic acid; (ORD) optical rotatory dispersion; [poly(A)] polyadenylic acid; [poly(C)] polycytidylic acid; [poly(dT)] polydeoxythymidylic acid; [poly(G)] polyguanylic acid; [poly(U)] polyuridylic acid; (rRNA) ribosomal RNA; (SDS) sodium dodecyl sulfate; (tRNA) transfer RNA.