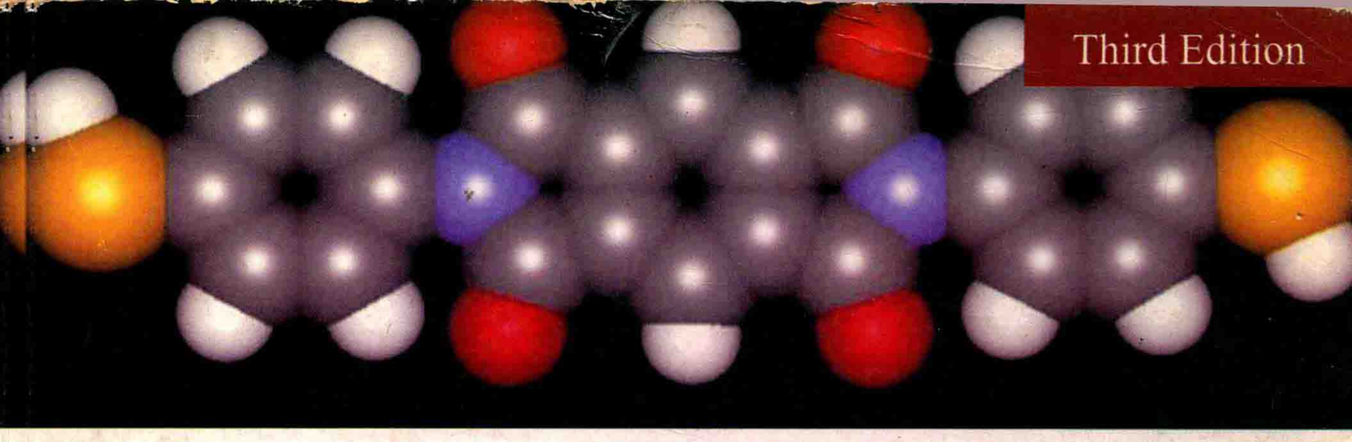
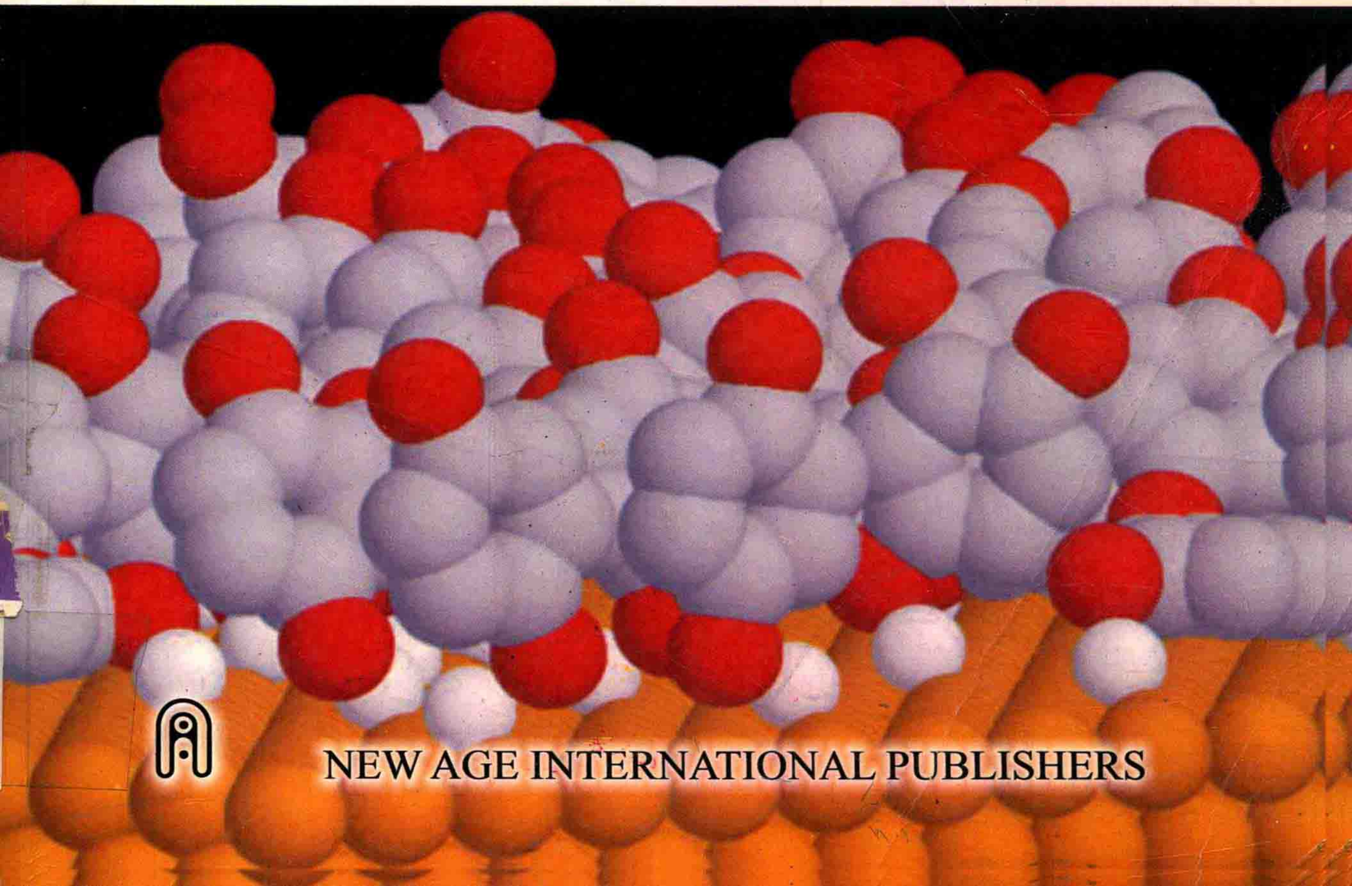


Third Edition

Cell Biology

S.C. Rastogi



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Cell Biology

PREFACE TO THE THIRD EDITION

Biologists follow a reductionist approach to the study of cell and its ultrastructure in order to understand the cellular processes. Although the book focuses on biological processes that maintain and extend the life of a cell, it also fires the imagination of the reader that a cell could be visualized as a working model to study its behaviour under everchanging environment. Behaviour of the cell depends upon the signals received from the environment, hence the living cell is a *signal processor*. The cell also responds to signals generated internally. Consequently, a novel concept of E-cell has been evolved, which is used for simulating molecular processes in user definable models, equipped with graphic interfaces that allow observation and interaction. This perspective has to be kept in mind while studying cell biology.

While preparing for the third edition, I referred to the latest syllabi being followed by various universities at undergraduate Hons. and Pass courses. This greatly influenced revision, and updation of the existing material. Besides, three new chapters have been added which include intracellular protein traffic and targeting, cell signaling and apoptosis, i.e. programmed cell death.

New edition of the textbook has been wholly re-set in its new format, and I believe, both students and the teachers will find it more useful and appealing in terms of contents and presentation.

New Delhi

S.C. Rastogi

PREFACE TO THE FIRST EDITION

Cell biology forms an important part of any biology course. It is a specialized branch dealing with the study of the finer structure of the cell, its organelles and their physiology, and the mechanism of cell multiplication, heredity and development. Recently, cell biologists have been mainly concerned with nucleic acids and proteins—the macromolecules that play a primary role in heredity as revealed by molecular biology. It is rather difficult to comprehend the functioning of the whole organism without a good knowledge of the fundamental processes at the cellular level.

Increasing involvement of biochemistry, biophysics, pharmacology and other related areas has widened the scope of cell biology and its applications. The alliance of cell biology with genetics and molecular biology has resulted in the development of new strains of organisms. The new branch of genetic engineering has been carved out of this alliance. Interaction with pathology has helped in discovering the basic causes of diseases and in the development of wonder drugs. A mammoth task at the moment which is yet to be accomplished is the elucidation of the molecular basis of carcinogenesis. A serious environmental problem is encountered resulting from the widespread use of chemicals in controlling noxious insects and plants. Cell biology enables us to study the side effects produced on animals, man and his environment.

In recent years spectacular advances have been made in the field of cell and molecular biology and, therefore, it is immensely important that a suitable course is devised and offered at an appropriate level. The present text is designed for students who are already familiar with the elementary courses in biology. For quite some time I have felt the need for a book that presents not only the fundamental concepts but also describes an interdisciplinary approach to the subject in a comprehensive manner. Though it is an arduous task to include many advances made in the field, yet I have tried to include the multitude of complex and diverse information to make this text innovative, stimulating and useful. Thus it bridges the gap between elementary texts and advanced works in the area. I sincerely feel that this book will serve the vast majority of the student population both at the undergraduate and graduate levels.

A living cell is the locus of behaviour and that this behaviour has a structural basis is the central theme of the book. The book gives an indepth treatment of cell structure, organelles, related biochemistry and functions. Certain application-oriented topics are also included.

The book is organized into 25 chapters that have been grouped into five parts, each presenting a specific aspect of the life of the cell. Part I deals with the organization of life. The first chapter surveys the origin of life, gives an overview of the evolution of cell-free systems, and the cell. Chapters 2 to 8 cover subjects that are basic to the understanding of the cell, viz. various cell forms, biochemical components and the ultrastructure of cell organelles.

Part II describes various functions of life. Chapters 9 to 14 of Part II are devoted to the metabolic functions of the cell, such as biological catalysis, photosynthesis, DNA replication and the mechanisms by which the cells reproduce. It is emphasized here that these specialized functions are segregated into discrete regions which are often delimited from the rest of the cell by membranes. The cell's organelles reflect this segregation.

Part III (Chapters 15 to 19) preents genetic control mechanisms that are essential not only for the survival of the cell but also for its differentiation and perpetuation. The next part dealing with the molecular mechanisms surveys modes of transport and the processes that allow contractile movements and impulse conduction. The last part covers special topics on cell ageing, cancer and cells, and genetic engineering which are emerging areas of cell biology. At the end of each chapter a list of references and suggested readings have been given to help both the novice and the professional interested in this rapidly growing field. Review questions at the end of each chapter will prove to be of great use to the student for the purpose of self-testing.

I take full responsibility for any factual errors, which appear in the book, I shall, however, welcome comments and criticism from the readers for improvement in the next edition.

S.C. Rastogi

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Many persons have helped in the preparation of this book. I am most grateful to Dr. C.R. Mitra, Director BITS, for the ample encouragement that I received. I am also indebted to many of my colleagues in the department for fruitful discussions on the organization of the book. My special thanks are due to Dr. B.D. Deshpande for his constructive suggestions, and to Dr. V.N. Sharma for supporting material and some microphotographs used in the book. I have been greatly benefitted from their rich experience. I have great pleasure in expressing my profound appreciation to my wife Sarala who has been a constant source of encouragement and who patiently endured my busy shcedule of writing. My appreciation is also due to my son Parag for his assistance, and to my daughters Smita and Namita for their understanding and interest in the venture. Typing assistance from Mr. Ramakant Prasad is gratefully acknowledged.

S.C. Rastogi

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Origin of Life : An Overview

Ever since man became aware of his environment, his curiosity began in acquiring knowledge about life, its origin and form. The eternal unsolved question, whether egg came first or the chicken, remains an enigma for ever. The quest is still continuing. It has been estimated that life began on our planet about two and a half billion years ago. But the question arises, in what form? We might presuppose that life began by transformation of matter, non-living matter into living matter. We might now ask, what is matter?

1.1 MATTER, ENERGY AND LIFE

The earth's crust is composed of matter which exists in three physical states: solid, liquid and gas. In chemical terms we define matter that occupies space and has mass. We often use four words– time, space, energy and matter, which are hard to define but are rather understood on usage. When the changes do not alter the chemical bonds of a substance, we refer them as physical changes. Chemical changes bring about a change in the composition of substances, chemical bonds and rearrangement of molecules to form new substances.

Matter and Energy

The matter (non-living state) exists on earth in a state whose mass remains constant. The transformation of this matter into living state must have been a *chance event*, caused by interaction between matter and energy. Energy is a measurable quantity and hence its concept is important in biology and chemistry. Energy is defined as the *capacity to do work*, which can be measured in terms of mechanical quantity. This energy could be either *kinetic or potential.* Kinetic energy is intrinsic in an object that has motion. Potential energy is stored energy intrinsic in an object because of its position with respect to other objects. Several forms of energy exist, mechanical, electrical, thermal, radiant etc.

Before we discuss more about energy, let us introduce three more terms: system, state and state function. A system is a conglomerate of a number of conditions including the surroundings in which an actual event is studied. A system may be isolated or part of a bigger system. The state is definable in more precise terms, like liquid, solid and gas. Any term used in describing the state is called a *state function*. Energy is a state function as also are the temperature and pressure. An important attribute to state function is that it can be made to change without regard to the method or pathway by which this change is achieved.

The total energy of a system is distributed partly as kinetic energy and partly as potential energy. Other familiar forms of both kinetic and potential energies are heat, light, sound, electric and chemical energy, which can be transformed into each other. The transformation can actually be observed, during which process the total energy content remains the same.

Chemical reaction is transformation of one substance into another involving a change in the potential energy of the matter. This change appears as a liberation or absorption of kinetic energy in the form of heat. If heat is liberated into the environment, the reaction is said to be *exothermic*; if heat is absorbed in the reaction, it is *endothermic*.

Conservation of Energy and First Law of Thermodynamics

Like the concept of conservation of mass, the idea of conservation of energy is also applicable to all chemical reactions. The concept of conservation of energy is applied to study the energy bonds, stability of chemical bonds and the tendency of the occurrence of chemical reactions. This may be studied from the point of view of thermodynamics. All forms of energy are equivalent to each other, and that in all physical and chemical changes, energy is conserved. The first law of thermodynamics states that the amount of work done by a physical or chemical process involves certain amount of thermal energy evolved or absorbed. A system that absorbs some amount of heat is said to undergo a change in its internal energy, thus a change in *enthalpy* follows. We may define enthalpy of a system as the heat content of a system. A knowledge of enthalpy change, ΔH, gives an insight into the nature of a chemical reaction because it is the dominant change.

1.2 LIVING STATE AND SECOND LAW OF THERMODYNAMICS

What is life? This is an intriguing question, difficult to answer. Perhaps, the non-living matter has given rise to living matter. Our knowledge of the process is far from satisfactory to explain this transformation. What stage was set and what conditions were necessary to bring about this transformation are a matter of speculation only.

A living state is distinguishable from the non-living by a set of unique criteria. The dynamism of the living state is maintained at the cost of some essential elements found on the earth's crust. There are some 20-odd elements which are used to maintain the intricate fabric of the living cell in different permutations and combinations. What is the criterion for selecting some twenty elements out of 107 present on the earth? It has been suggested that the functions expected from such a selection of elements from the basis of this selective process. These are:

1. Interactions of atoms with water.
2. Capability of carbon to bear both hydrophobic and hydrophilic groups.
3. Amenability to modification of functional groups to form various conformations.
4. Capacity to form multiple bonding and to hybridize.

The basis of living state is the *protoplasm*, which is capable of evolving and maintaining a tremendous degree of organisation at the expense of energy and matter, that it exchanges with the environment. A living state then would require a system that is open, capable of self-organising and possessing an organised oscillating system needed for channelling matter and energy. We shall now see whether the second law of thermodynamics is applicable to such a state.

Everyday experience tells us that a physical system would tend toward a state of lower energy, that is the system tends to become disordered. This disorder is described in terms of a property or state function, called *entropy*. To make the point clear, a specific example may be cited. Water in the form of liquid has a higher entropy because of random molecular arrangement than that of the ice due to ordered arrangement of molecules. Since living systems are isothermal, a change will occur at a fixed temperature. The quantitative interplay of free energy and entropy can be described by the equation:

$$\Delta G = \Delta H - T\Delta S$$

Where ΔG is the change in free energy, ΔH is the change in the heat content, T is the absolute temperature and ΔS is the change in enthalpy.

This is an important equation because it explains that at constant temperature and pressure, a process can occur spontaneously only if there is a decrease in free energy. Thus in a spontaneous process ΔG must be negative. A negative ΔG can result either from a decrease in heat content or an increase in entropy.

Most important postulate of the second law of thermodynamics is that 'a system when left to itself will tend to increase its disorderlines', that is decrease in its state of organisation. Nevertheless, the same system will allow increase in its organisation when free energy is supplied to the system. The living state exhibits this property. The system maintains a high degree of organisation at the cost of a continuous supply of free energy. Since a living system is open, both matter and energy freely flow in and out to maintain the organisation in a *steady state*. When the supply of free energy is discontinued, the state of organisation tends to be disordered and ultimately death follows. The steady state condition of the living state is far from the condition of equilibrium, because at equilibrium the system has the lowest possible free energy and the highest disorderliness.

At absolute zero temperature, the entropy of a system is also zero. Thus a constant supply of free energy is an essential requirement for maintenance of a steady state, and to utilise this free flow of energy the living system requires an elaborate machinery. Biologists believe that the matter existing in the physical world got transformed in a state that could use free energy.This might have been a chance event. Tiny systems must have evolved with a minimum organisation, capable of absorbing and utilising radiant energy. Then the primordial system must have evolved through natural selection, to attain greater complexity of organisation. How this might have happened?

1.3 ORIGIN OF LIFE

Origin of life is one of the most interesting topics that has occupied the attention of mankind since antiquity. Emergence of a highly ordered self-organising system capable of self-adjustment and self-perpetuation may be considered a miraculous feat of nature. How and when was this accomplished? Can we describe this as a spontaneous process? To answer these questions we have to trace the early chemical history of the earth and the conditions necessary for the formation of organic compounds which might have given a start to the evolution of life.

Primeval Earth

The origin of life or *biopoiesis* cannot be explained unless we trace the geological history of the earth. According to a reliable estimate (Urey, 1952), the earth is believed to be formed about 4.5 billion years ago. Tremendous heat was generated in the earth and the atmosphere consisted of many lighter elements in a gaseous state. The earliest atmosphere of the earth probably consisted of water, ammonia, methane, hydrogen sulphide, hydrogen, nitrogen and carbon dioxide. As the earth gradually cooled, most of these lighter elements (hydrogen, ammonia and methane) eventually got lost.

The upper crust of the earth became hard and rocky, but below the surface the trapped hydrogen and oxygen were subjected to great pressure and heat, which eventually condensed into water. This water escaped from the earth and formed an atmosphere of vapour. Gradually the earth's surface got further cooled, condensing the vapour into water which poured down in the form of rains. The rains continued incessantly for thousands of years. This continuous downpour resulted in erosion of rocks on the earth, forming vast oceans carrying dissolved minerals in it. Most of the minerals commonly found in the oceans (oxides and sulphates were however not formed then) formed a *prebiotic soup*.

There is an irresistible argument that the primitive forms of life must have depended on some kind of energy, as the present forms do. This suggests many possibilities. The sunlight, ultraviolet radiations, electric discharges and heat must have been the agents responsible for catalytic reactions in the prebiotic earth. Electric discharges catalyse reactions to synthesise molecules, a phenomenon that has been experimentally proved. Sunlight can produce large amount of oxygen by splitting water and producing simultaneously hydrogen, which is capable of enhancing the reducing power of the atmosphere. Haldane long ago suggested that in the prebiological earth ultraviolet radiations were responsible for generation of complex molecules. The reactions of this type do exist, as evidenced by the presence of formaldehyde and glyoxal in *mixtures irradiated* with ultraviolet rays.

Setting Stage for Chemical Evolution

Chemical evolution of the earth has been much debated by Haldane (1954), Oparin (1953), Bernal (1965) and Pringle (1953). The early earth probably contained little oxygen,