
Preface

Molecular genetics, born in the middle of the twentieth century, advanced immensely during the following decades. The basic questions about organization of life on the molecular level were nearly resolved. Genomes of many species have been sequenced and opportunities for new discoveries look great. This spectacular progress in unraveling the most fundamental principles of living matter led to an array of practical applications in medicine, numerous industries, and agriculture. Intellectual power produced by this impressive development seems unlimited and further advances follow with unprecedented speed. Rightly or wrongly, human reaction to these developments varies from admiration to rejection. Expressions like "genetics plays god" have become common and some countries have introduced laws prohibiting use of a wide range of molecular genetic technologies.

Neither science nor society had enough time to fully comprehend the scale of new biological revolution, and deep considerations of this new paradigm are still emerging. In some ways there are similarities between the current situation in genetics and the circumstances in theoretical physics about seventy years ago. In both cases science has reached certain limits and faced an unfamiliar world, sometimes beyond its grasp.

A significant degree of randomness typical of life has been known for a long time. Brilliant scientist and Nobel Prize laureate J. Monod wrote in his book *Chance and Necessity* more than thirty-five years ago: "Randomness caught on the wing, preserved, reproduced by the machinery of invariance and thus converted into order, rule, necessity." Similar understanding of the essence of life and evolution can be found in other publications. The origin of such views can ultimately be found in the Darwinian system where random hereditary changes are considered as fundamental elements of biological evolution. In this book we attempt consideration of randomness in major genetic processes and events.

Chapter 1 is an introduction to the problem and it summarizes the major ideas relevant to uncertainty and randomness in physics and mathematics. It is crucial to realize that randomness is universal and a very basic phenomenon that has few different physical sources as well as some

roots in logic. Not surprisingly biology provides countless evidence of randomness, which can be observed on all levels of biological organization, including genes and cells, organisms, populations and the evolutionary process as a whole. In this book we are going to explore the nature of genetic uncertainty from different points of view and at different levels. Chapter 2 is devoted to mutations. The proposal that many mutations are spontaneous and probably related to or even caused by subatomic randomness became popular among a group of physicists, including E. Schrödinger and M. Delbrück, well before the discovery of DNA structure. Here we shall discuss this fundamental problem again in order to trace the genesis of these ideas and also the deep links between subatomic fluctuations and long-term macroscopic changes in living organisms. Such understanding of the nature of mutations was strongly confirmed by numerous investigations and now can be found in textbooks.

Chapter 3 considers recombination events as the second layer of randomness that contributes greatly to genetic variability. The number of combinations resulting from constantly ongoing recombination processes is huge. This provides a practically inexhaustible source of new genetic variations. A multitude of random events that occur during development is the subject of Chapter 4. One of the reasons for the vast gap between phenotype and genotype is developmental randomness. Filtering and utilization of this type of randomness is essential in the process of adaptations building. Even more than that, randomness became a core phenomenon in immune response at least in high vertebrates. An ability to generate randomness on a grand scale becomes a matter of life and death. One can speak in this case about "promoted" randomness.

Chapter 5 concentrates on segregation, another level of genetic processes found in diploid organisms. Here randomness is completely organized and reaches a maximum degree of uncertainty. A chance for nearly each allele to be transmitted to a particular gamete is about 50%. Only in very rare situations can specific genes and chromosome structures cheat the mechanism of equal segregation and thus lead to segregation distortions. As Chapter 6 shows, the majority of if not all population processes include a significant degree of randomness. This was clearly understood by the founders of population genetics and became an even more prominent part of the theoretical framework in the last decades. The cornerstones of evolutionary process, genetic drift and fluctuating natural selection, are the best demonstrations of randomness at this level of biological organization.

The major aim of science is finding general principles, laws, and mechanisms, as well as regular and predictable events. Randomness, at first glance, is the alternative to all of these and may as appear to be an annoying nuisance that limits science and prevents generalizations. Such a deterministic and outdated understanding of science is steadily

being replaced by the probabilistic view which became so typical for genetics. All these issues are discussed in Chapter 7. Hopefully this book will be helpful in the consolidation and propagation of this probabilistic understanding of life.

It is my pleasant duty to acknowledge the great support I have received from the University of New England, Australia. This book would hardly have been written without the generous sabbatical and other help provided by the university. I am also in debt to many colleagues and friends with whom I discussed different aspects of randomness over the years. I am grateful to Brian Kinghorn for discussions and his comments on the manuscript. Certainly, warm thanks go to my family for the constant help.

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