Molecular Biology Primer

Introduction

Molecular biology is a diverse and constantly evolving field that investigates biological systems at the *molecular* level—the world of chemicals, molecules, and the interactions between them. Although it would be presumptuous to claim that molecular biology is the largest field of biology, its overarching influence makes it one of the central subfields of biology and one of the most popular. In our research in synthetic biology, we are combining the basic tenets of molecular biology with more abstract and generalized formalisms of computer science in order to create a better understanding of the overall architecture of biology. It is therefore imperative to understand the fundamental concepts of molecular biology in order to succeed in this laboratory and many other biology-related fields.

Resources

There are many journal articles and textbooks published in molecular biology and the sheer size of the field makes it intimidating for the beginner. However, there are some time-old classics out there that even blue-collar workers and (dare we say it) humanities people can enjoy.

A very general introductory textbook to biology is:

Campbell, Neil A. and Jane Reece. *Biology*. Benjamin Cummings Publishers.

Typically referred to as "Campbell-Reece," *Biology* is widely used in freshman biology courses and many Advanced Placement courses throughout the United States. Its sections regarding DNA, proteins, and biotechnology are excellent. It is a valuable investment and we suggest you to purchase a personal copy, new or used.

The text this tutorial will take from is another popular, although more detailed, text devoted to molecular biology:

Alberts *et al.* *Molecular Biology of the Cell.* Garland Science Publishers.

Typically referred to as "MBOC," Alberts's text is another ubiquitous reference that is used in many labs and molecular biology courses. Although you may find it useful to purchase it, most of its contents are actually uploaded on NCBI (The National Center for Biotechnology Information, an NIH database that houses much information in molecular biology including gene sequences, protein sequences, and journal articles). The problem with using NCBI, however, is that the information is not laid out in a nice PDF format and you must search for whatever information manually. You can access it through the URL below:

http://www.ncbi.nlm.nih.gov/books/bv.fcgi?call=bv.View..ShowTOC&rid=mboc4.TOC&depth=2

This tutorial will essentially be a "reading list" of sections from the book.

Reading List

** denotes recommended but optional reading*

Part I: Introduction to the Cell*
- Chapter 1: Cells and Genomes
  - -The Universal Features of Cells on Earth
    - All Sections
  - -The Diversity of Genomes and the Tree of Life
    - All Sections starting from "The Tree of Life Has Three Primary Branches"
- Chapter 2: Cell Chemistry and Biosynthesis
  - -The Chemical Components of a Cell
    - All Sections starting from "Cells Contain Four Major Families of Small Organic Molecules"
  - -Catalysis and the Use of Energy by Cells
    - All Sections
- Chapter 3: Proteins
  - -The Shape and Structure of Proteins
    - All Sections
  - -Protein Function
    - "All Proteins Bind to Other Molecules", "The Details of a Protein's Conformation Determine Its Chemistry", "Sequence Comparisons Between Protein Family Members Highlight Crucial Ligand Binding Sites", "Enzymes Are Powerful and Highly Specific Catalysts", "The Catalytic Activities of Enzymes Are Regulated", "Proteins Often Form Large Complexes That Function as Protein Machines", "A Complex Network of Protein Interactions Underlies Cell Function"

Part II: Basic Genetic Mechanisms
- Chapter 4: DNA and Chromosomes
  - -The Structure and Function of DNA
    - All Sections
- Chapter 5: DNA Replication, Repair, and Recombination
  - -DNA Replication Mechanisms
    - All Sections*
  - -DNA Repair
    - All Sections*
  - -Site-Specific Recombination
    - All Sections
- Chapter 6: How Cells Read the Genome: From DNA to Protein
  - -From DNA to RNA
    - All Sections before "Transcription Initiation in Eucaryotes Require Many Proteins"
  - -From RNA to Protein
    - All Sections before "Quality-Control Mechanisms Operate at Many Stages of Translation"; All Other Sections*
- Chapter 7: Control of Gene Expression

-An Overview of Gene Control
All Sections
-How Genetic Switches Work
"The Tryptophan Repressor Is a Simple Switch That Turns Genes On and Off in Bacteria", "Transcriptional Activators Turn Genes On", "A Transcriptional Activator and a Transcriptional Repressor Control the *lac* Operon", "Bacteria Use Interchangeable RNA Polymerase Subunits to Help Regulate Gene Transcription"; "Gene Switches Have Gradually Evolved"*
-The Molecular Genetic Mechanisms that Create Specialized Cell Types
"Gene Regulatory Circuits Can Be Used to Make Memory Devices as Well as Oscillators", "The Expression of Different Genes Can Be Coordinated by a Single Protein", "Expression of a Critical Gene Regulatory Protein Can Trigger Expression of a Whole battery of Downstream Genes"
-Posttranscriptional Controls
"Alternative RNA Splicing Can Produce Different Forms of a Protein From the Same Gene", "The Definition of a Gene Has Had to Be Modified Since the Discovery of Alternative RNA Splicing", "RNA Editing Can Change the Meaning of the RNA Message"; "RNA Interference Is Used by Cells to Silence Gene Expression"*

Part III: Methods
Chapter 8: Manipulating Proteins, DNA, and RNA
-Isolating, Cloning, and Sequencing DNA
All Sections
-Analyzing Protein Structure and Function
All Sections*
-Studying Gene Expression and Function
All Sections

Study Guide

The following is more of a set of suggestions than a detailed outline. It is intended to help you place the vast amount of information above into the context of our project.

Reading Sequence

Although you may read the above in any order you want, we warn you that this is very heavy reading that comprises hundreds of pages. In order to facilitate your familiarity with the subject, we suggest that you first start with Part III so that you are familiar with the basic lab techniques in molecular biology. We understand that it is incomplete as it is not intended to be a catalogue, so any further information should be consulted via internet or other lab members.

We will assume that you have a basic knowledge of DNA and proteins, so we have made the introductory sections to the cell optional. If, however, you feel that your background is

lacking, please refer to Part I as it is essential that you can thoroughly understand and synthesize the information from it.

In order to talk intelligently about molecular biology, you will have to master the information presented in Part II. The information presented in these sections compromise what is known as the "Central Dogma of Molecular Biology," which relates each level or module of information to other levels. Understanding the Central Dogma is crucial to integrating molecular biology with computer science, as it is analogous to modular categorizations known as "hierarchy of abstraction." We understand that many come to labs for practical experience and we hope to provide much of it. However, without a driving theory or hypothesis, labwork is essentially aimless grunting, producing commodities that have no demand.

Note-Taking

Although we are not instructors in the strictest sense, we still strongly recommend that you take notes while going through the primer. You do not need a formal outline of each section, but we suggest that you take notes as you would while studying for a class for easy reference. Please invest in a notebook separate from the lab notebook you will be using to record your results and experiments. However, when you have an idea that you would like to play with in the lab—experimental or theoretical—record them in your lab notebook as a record of your work. The same goes for specific procedures you will personally use in the lab.

General Questions to Keep in Mind while Drudging through the Text

-What is biological information and how can we relate it to other systems such as computers and machines?

-What are the various organizational systems of biological organism and how can we synthesize an efficient structure to utilize in constructing synthetic biological systems?

-Given the complexity of biological systems, how can we simplify them to create more efficient and minimize various types of error?

-How can we modify biological systems to produce maximum flexibility in engineering them?

-Is life truly programmable or is just an idle illusion of various computer scientists and physicists who want in on the large funding disbursed to biological research?

-What is the meaning of life? Semantic and/or existential?

-Do we have the foggiest idea of what the hell we're doing?

Conclusion

Here be a very simple and very general introduction of molecular biology. We hope you find it useful both for this project and future projects. May the sauce be with you.