Fundamental Genetics

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CAMBRIDGE
UNIVERSITY PRESS

PUBLISHED BY THE PRESS SYNDICATE OF THE UNIVERSITY OF CAMBRIDGE
The Pitt Building, Trumpington Street, Cambridge, United Kingdom

CAMBRIDGE UNIVERSITY PRESS
The Edinburgh Building, Cambridge CB2 2RU, UK
40 West 20th Street, New York, NY 10011-4211, USA
477 Williamstown Road, Port Melbourne, VIC 3207, Australia
Ruiz de Alarcón 13, 28014 Madrid, Spain
Dock House, The Waterfront, Cape Town 8001, South Africa

http://www.cambridge.org

First published 2004

Printed in the United States of America

Typeface Swift 10/14 pt. and Gill Sans *System* LaTeX 2_ε [TB]

A catalog record for this book is available from the British Library.

Library of Congress Cataloging in Publication Data

Ringo, John, 1943-

Fundamental genetics / John Ringo.

p. cm.

Includes bibliographical references and index.

ISBN 0-521-80934-7 (hb) – ISBN 0-521-00633-3 (pbk.)

1. Genetics. I. Title.

QH430.R55 2003
576.5–dc21 2003048463

ISBN 0 521 80934 7 hardback
ISBN 0 521 00633 3 paperback

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Chapter 1

Life Forms and Their Origins

Overview

This chapter introduces several basic genetic concepts, without going into detail about any of them. These genetic concepts are as follows:

- life form
- nucleic acid
- gene
- chromosome
- organism
- virus
- semiautonomous organelle

The origin of life and the evolution of the three domains of life are described briefly.

Life Forms Are Genetic Systems

Two essential components of every life form are proteins and nucleic acids. Nucleic acids (DNA and RNA) are thread-like coding molecules, the building material of genes and chromosomes. Genetics is about genes and chromosomes – their structure and function, their behavior and misbehavior, their evolution, and methods of studying them. Because genes are the coding molecules of life, they are complicated and varied. It is difficult to pin down the term "gene" in a simple definition, but, to a first approximation, a gene is a segment of nucleic acid whose immediate function is to encode a piece of RNA (Figure 1.1). The key concepts here are **replication** (copying) of genes and coding. The replication of genes and their coding properties are described in detail in later chapters.

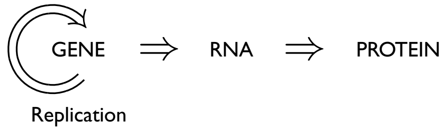


Fig 1.1 Genes replicate and code for RNA. For most genes, the final gene product is protein.

From a genetic point of view, a life form is an assemblage of large molecules capable of reproducing itself and including at least one chromosome. A chromosome is a long, thin thread made of DNA or, in some cases, RNA and may also contain proteins. To qualify as a chromosome, a nucleic acid molecule must contain one or more genes, be replicated faithfully in a regulated manner, and be transmitted from a life form to its descendants in a reproductive cycle. Not every molecule of nucleic acid is a chromosome, even if it contains genes. The nucleic acid part of a life form's set of chromosomes is its **genome**.

All life forms arise from preexisting life forms via a reproductive cycle during which chromosomes are copied and the copies are passed on from parent to progeny (Figure 1.2). According to this broad, genetically based definition, life forms include organisms (cellular forms), viruses, mitochondria, and chloroplasts. This book concentrates on the genetics of organisms.

Organisms

Organisms are made of cells, membrane-bound structures capable of reproduction, growth, and metabolism. The genome of a cell encodes all the proteins required for that cell's survival. Every cell has at least one chromosome, which is made of DNA and proteins. Cells also have many ribosomes, micromachines for synthesizing proteins. A membrane surrounds every cell. In some organisms, the cell envelope includes a cell wall and one or more additional membranes. An organism can be a single cell or many cells joined together.

Organisms comprise three major divisions or domains: Bacteria, Archaea, and Eukarya (Figure 1.3). The compelling genetic evidence for this broad taxonomic division comes from DNA sequences of slowly evolving genes. Despite their genetic and biochemical differences, bacterial and archaeal cells are morphologically similar: they lack nuclei, and they reproduce asexually, by simple cell division. Little is known about the genetics of archaea.

Fig 1.2 Above: Stained chromosomes of a normal female human, from a cell nearing division. Below: The same 46 chromosomes rearranged into numbered pairs, the karyotype. Photograph by Dr. Laurent Beauregard, Genetics Department, Affiliated Laboratory, Inc., Bangor, Maine.

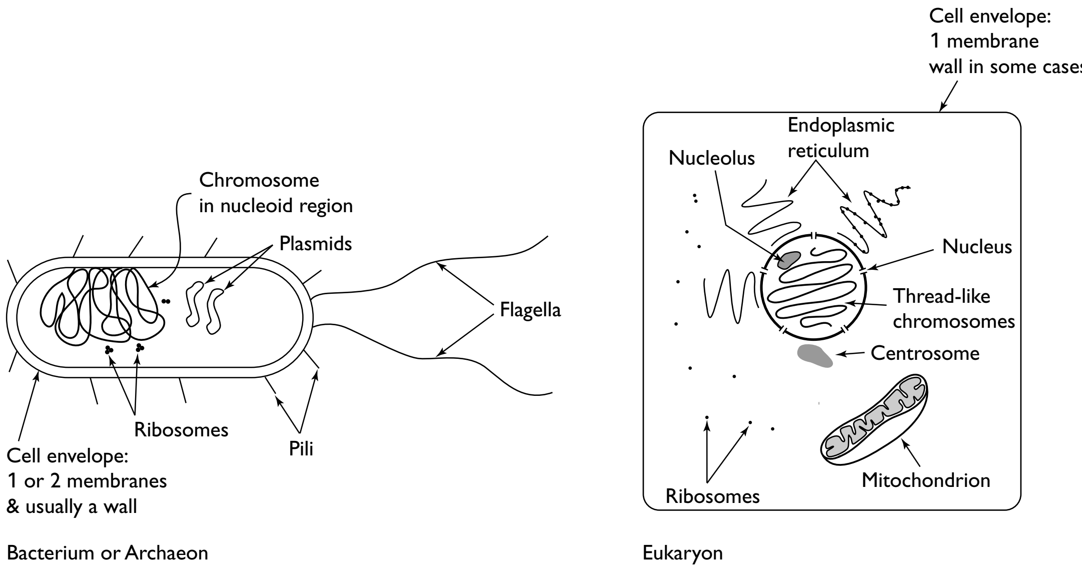


Fig 1.3 A quick look at two kinds of cell.

In contrast to bacteria and archaea, eukaryal cells possess membrane-bound nuclei, an internal system of membranes, and a cytoskeleton made of microtubules.

The Origin of Life

From the time the earth began to form, 4.6×10^9 years (4600 Ma = megaanum, or million years) ago, until it cooled sufficiently for liquid water to exist on its surface, 4400 to 4200 Ma ago, the temperature was too high for life to exist. Meteorites bombarded early earth, and some geophysicists believe these ocean-vaporizing impacts likely did not abate sufficiently for life to emerge until 4200 to 4000 Ma ago (Figure 1.4). The ^{12}C:^{13}C ratio of organic carbon is higher than that of inorganic carbon. This isotopic ratio in fossils of the most ancient sediments known suggests that life was abundant 3900 Ma ago or a bit earlier; sedimentary apatite

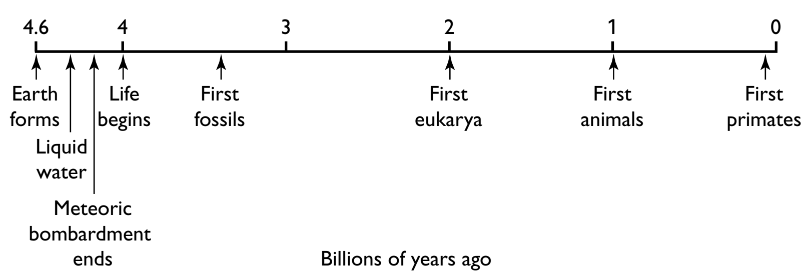


Fig 1.4 Time line of earth's history. The times given for biological "firsts" are very approximate.

(a mineral consisting of calcium phosphates) is a biomarker first appearing in large amounts 3800 Ma ago. The implications are remarkable: life emerged from non-life during a period lasting only 100 to 300 Ma.

Fundamental organic molecules required for life (e.g., amino acids and nucleotides) are thought to have originated through natural chemical reactions starting with simple molecules such as methane, ammonium, phosphate, and water, with the energy for the reactions being heat and electrical discharges in the atmosphere. Modern experiments have shown these reactions to be feasible. Also, under realistic conditions not involving enzymes, amino acids polymerize into polypeptides and nucleotides polymerize into nucleic acids.

The First Organisms: RNA-Based?

All living organisms have genes made of DNA, which code for RNA. RNA molecules are intermediate coding molecules in the synthesis of proteins, which make important structures of the cell and carry out virtually all the metabolic functions (Figure 1.5). According to one theory, the original life forms used RNA for coding and for metabolic functions. Some RNAs act as enzymes; these are ribozymes. Biochemists are finding many chemical reactions that are catalyzed by RNAs. If ancient proto-organisms possessed RNAs capable of directing the synthesis of more copies of RNA molecules, then both genes and enzymes could have been made of RNA in those ancient times, perhaps between 4000 and 3500 Ma ago. In this "RNA world" RNA served double duty: genes and enzymes.

The ancestral cells or protocells had evolved into bacteria-like cells by 3500 Ma ago; fossil cells that resemble bacteria were very abundant by then. The split between archaea and bacteria occurred between 3500 and 1900 Ma ago, and the eukarya-archaea split probably occurred between 1900 and 1500 Ma ago

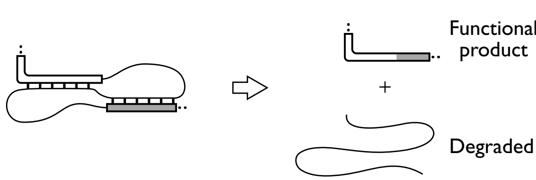
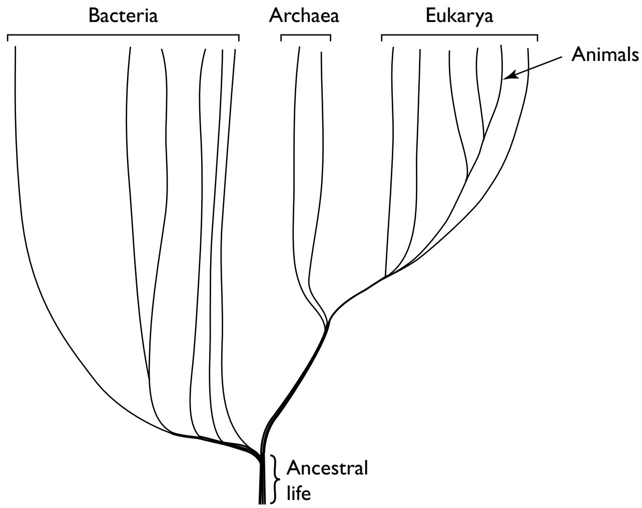


Fig 1.5 Some RNAs can both cut themselves and ligate the pieces.

Fig 1.6 Evolutionary tree of three domains of life. Each line is a major taxonomic lineage.



(Figure 1.6). The eukarya are enormously diverse; taxonomists classify them into a stupefyingly detailed and complex hierarchy of taxa.

Mitochondria and Chloroplasts: Semiautonomous Organelles

Eukaryal cells contain several organelles or "mini-organs" inside the cell. Two important membrane-bound organelles found in many eukarya are the mitochondrion [pl., mitochondria] and the chloroplast. Their main functions are oxidative metabolism (mitochondria) and photosynthesis (chloroplasts). They evolved from purple bacteria and cyanobacteria, respectively (Figure 1.7). The ancestral bacteria became mutualistic endosymbionts in eukaryal

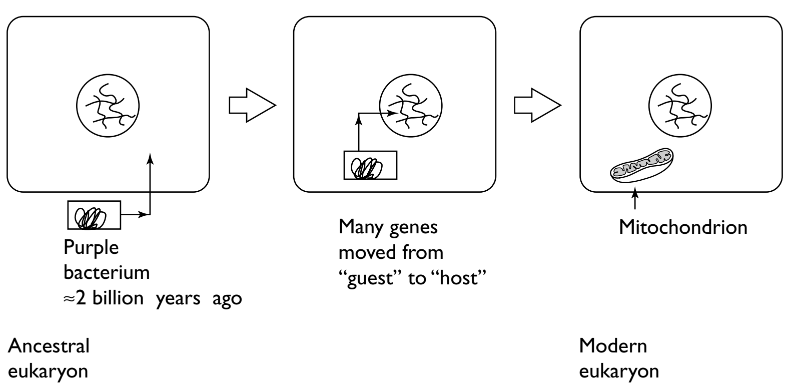


Fig 1.7 Evolution of mitochondria.

cells, meaning that both the host cell and the life form that living inside it benefited. Mutualistic endosymbiosis is not rare. However, in these cases, the now-organelles have clearly lost their status as bacterial cells, for genes in the "host" eukaryon's nucleus encode many proteins of these organelles. Mitochondria and chloroplasts are therefore genetically parasitic. On the other hand, every mitochondrion and every chloroplast has its own chromosome and its own protein-coding machinery. Furthermore, mitochondria and plastids (chloroplasts and related organelles) are unlike any other membrane-bound organelle, such as the nucleus: mitochondria and chloroplasts are never disassembled and reassembled; instead, they reproduce by division, as did their ancestral bacteria.

Viruses, the Completely Acellular Life Forms

Viruses are acellular life forms: obligate intracellular parasites possessing one or more chromosomes. During the infectious stage of a virus's life cycle, the virus is a virion – the viral genome encapsulated in a structure made of protein. Sometimes the virion includes a membrane envelope stolen from the host's cytoplasmic membrane (Figure 1.8). Most viruses are genetically parasitic, relying on its host for enzymes used in genetic processes. Only viruses with relatively large genomes code for many of the proteins required for their own reproduction. Viruses infect all three domains of life and may be classified according to host, genetic material, or phylogeny. An overall phylogeny of viruses is not appropriate, for viruses appear to have evolved independently many times. Any phylogeny of viruses, except for closely related ones, is difficult to establish, owing to rapid evolution and the tendency of viruses to acquire cellular genes. The going theory is

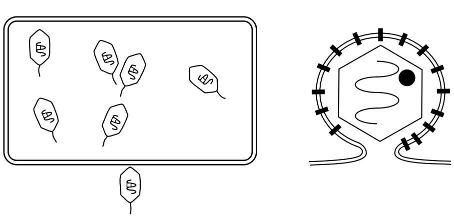


Fig 1.8 Some infectious virus particles.

that virus genomes evolved from bits and pieces of their hosts' genomes.

A Few Odd Forms

Plasmids are small, nonessential, "extra" chromosomes of cells. Plasmids code for proteins, including proteins useful to the cell (e.g., genes conferring antibiotic resistance). Some plasmids move between cells and may have genes encoding the machinery for intercellular movement. Are plasmids life forms? Some say yes, because plasmids are parasite-like, but I opt for the idea that plasmids are merely small, inessential chromosomes. Another category of DNA molecule with some of the basic properties of a life form is the **transposon**. Transposons are sequences of DNA that can move about the genome, within or between chromosomes; transposons code for proteins that help them to move.

There are nucleic acid molecules that do not qualify as life forms by the definition offered here but that some biologists do consider living, or at least lifelike. These are **viroids** and **virusoids**, small circular RNA molecules that do not code for protein. Viroids are parasites of plants and cause significant economic damage. Virusoids are parasites of viruses.

The strangest of all life-oid things is the **prion**, an infectious protein that can cause the modification of similar proteins in a cell, ultimately leading to the cell's death. Prions cause certain slow, infectious, neurological diseases, including bovine spongiform encephalopathy ("mad cow disease").

Most of Genetics Is Based on a Restricted Sample of Organisms

There are over 10 million species in the three domains of life. Much of what is known about the genetics of cellular organisms has been learned from intensive study of a limited sample of species clustered in a few branches of the evolutionary tree of organisms, most prominently two bacteria (*Escherichia coli* and *Bacillus subtilis*), a few fungi (notably the mold *Neurospora crassa* and the bread yeast *Saccharomyces cervisiae*), two flowering plants (*Zea mays* and *Arabidopsis thaliana*), and four animals (the fruit fly *Drosophila* *melanogaster*, the nematode *Caenorhabditis elegans*, the mouse *Mus musculus*, and *Homo sapiens*). Important genetic phenomena have been substantially investigated in hundreds of other species of bacteria, fungi, plants, animals, and ciliates, as well as in many viruses – only viral species, though, that infect bacteria or multicellular/multinucleate eukarya. The most conspicuous and troubling gaps in knowledge of basic genetics occur in the archaea and in the early-branching taxa of eukarya – troubling, because we have no idea how large those gaps may be. Fortunately, straightforward analysis of DNA sequences is beginning to allow us to infer a great deal about the genetics of these organisms.

Further Reading

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