

# Elements of Biology

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# General objectives (1)

The objective of this course is to investigate the foundations of modern biology. We shall first identify the basic empirical facts and theoretical concepts on which this science is built, and then attempt to place them in a unifying perspective in relation with other branches of human knowledge.

# General objectives (2)

Historically, four major concepts on which modern biology relies were introduced in the nineteenth century: the theory of evolution, cellular theory, heredity and chirality. The twentieth century brought a deeper understanding of these four concepts, and biological knowledge has now reached a stage where classic biological concepts have an established material basis. The problem of heredity for instance, has been transformed by the discovery of the structure of the genetic material. The polymeric nature of the genetic material implies in turn that issues of genetics must also be understood from the point of view of polymer physics and polymer chemistry. In a broader manner, biological structures and their functional properties, evolution and natural selection, and the role of chance and necessity have to be considered not only from the point of view of physics and chemistry, but also of logic and economy.

# General objectives (3)

The goal of the course is to investigate the foundations of molecular and cellular biology within this unifying framework. In the courses, we shall show that the structure of the genetic material is in a limited sense necessary and not contingent and can be built from basic considerations on living organisms. Through this construction, key concepts of biology can be introduced in an intuitive manner. The following lectures will be then devoted to a general study of biological matter, motion, and the material basis of natural selection.

# A realistic goal?

A very ambitious goal

Requires an in-depth understanding of many disciplines: a major obstacle.

My training in research is in experimental biochemistry, and my knowledge is limited. Ignorance or misunderstanding is to be expected.

Interruptions (questions or comments) are welcome!

# Outline

1. A course on a few basic facts and concepts of Biology
2. Methodology
3. A theoretical construction of the genetic material

# A course on biology

Modern biology is built on four concepts:

- The theory of evolution
- The theory of the cell
- The theory of heredity
- The chiral theory of life

# The theory of evolution (Wallace-Darwin)

Two statements:

- All living organisms descend from a common ancestor.
- The evolution of life is the result of the process of natural selection.

# What is the nature of this theory?

“In biology nothing makes sense except in the light of evolution.” Dobzhansky 1979

—> *A focus on change in biology*

“Evolution is not the key to world understanding:

The experience of science accumulated in her own history has led to the recognition that evolution is far from being the basic principle of the world understanding. It is the end rather than the beginning of an analysis of nature.

Explanation of a phenomenon is to be sought not in its origin but in its immanent law.”

H. Weyl 1949

—> *A focus on invariance in other natural sciences*

# Common descent

Existence of a variety of living organisms,  
such as animals or plants.

- Living organisms have different macroscopic shapes.
  - A classification of living organisms can be made based on morphology.
- Concept of species.

# Common descent (2)

What is the origin of this variety?

- Variety can be obtained artificially, under domestication (cultivated plants and animals), through successive crossings and selection for a desired character. This implies the existence of a biological variability, and the ability to inherit this variability in certain cases.
- The same concepts apply to life in nature. Here a different selection process generates biological diversity.

# Natural selection

Why should there be a selection in nature?

- Existence of a struggle for life:
- It is based on the “Dismal Science” (Economy)

# Natural selection (2)

- Malthus: Human population will grow exponentially (“geometrically”) with time if unconstrained.

However natural resources are limited (Malthus assumes that resources should grow only linearly with time).

Hence the necessity of controlling the growth of human population.

# Natural selection (3)

- In reality, over extended periods of time, natural resources are essentially constant, and (if fluctuations are ignored) the size of the populations of living organisms remain also constant.
- A constant population size implies that there must exist a ferocious struggle for life, both between different species and between various individuals within the same species.

# Natural selection (4)

- Those individuals possessing favorable and inheritable characters in this struggle will reproduce at a faster rate leading gradually to a change in the populations.

→ Concepts of fitness and efficiency

# Universality in biology

The theory of evolution provides a support for inductive reasoning in biology.

When we make an observation for a given living organism, we can use the concept of common descent to try to generalize this observation to all living organisms. This would be much harder otherwise.

Such generalizations are common in **cytology** (the science of the cell) and **biochemistry** (chemistry of life).

Aphorisms on elephants and bacteria:

Kluyvert 1926 "From the elephant to butyric acid bacterium - it is all the same!"

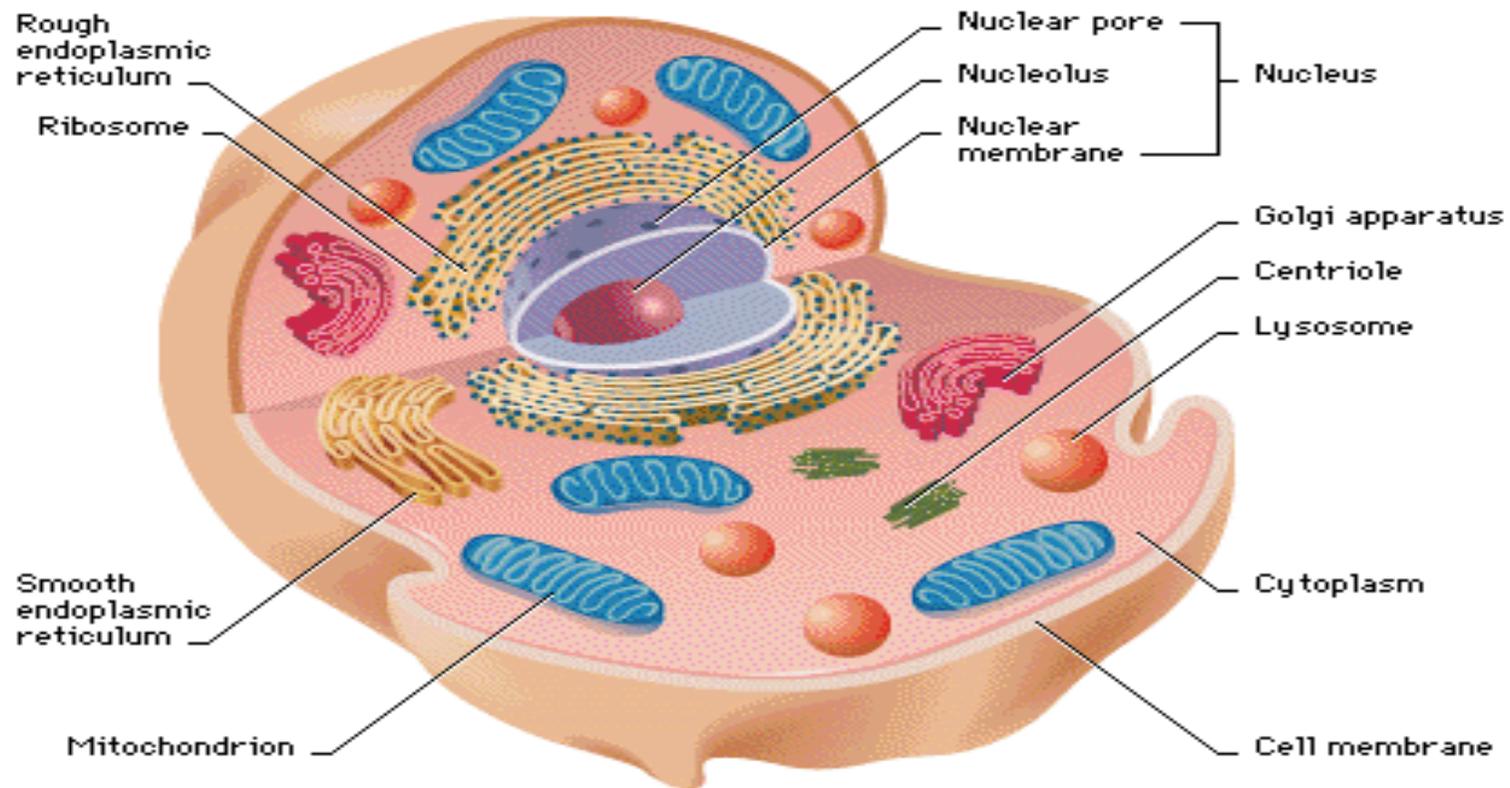
Monod & Jacob 1961 "What is true for bacteria is also true for elephants"

# The cell

A universal feature of life:

- All living organisms are made of cells
- The process of cell division (called mitosis) is universal among living organisms.
- The cell is an element of life (it is the simplest structure in which the process of cell division can be observed).
- All cells come from a previous cell.

# A typical animal cell



# Cytology and the theory of evolution

Darwin (and Wallace) focus exclusively on macroscopic organisms, and say nothing of cells.

Combining both theories, one can conclude that the last common ancestor was a unicellular organism.

# History of cell research

Based on the invention of the microscope during the seventeenth century

- Hooke (from Hooke's law) observed a slice of cork *cella* = small room, cubicle
- Leeuwenhoeke (discovered unicellular organisms).
- Cell theory: Schleiden & Schwann (1839), Virchow (1858) *Omnis cellula e cellula*
- Cell division: Flemming (1882 in plants)

# Variety of cells

- Animal cells
- Plant cells

With or without nucleus (a term due to Robert Brown)

- Eukaryotes
- Prokaryotes

# Cell motility

- Biological macroscopic motion: distinction of animals and plants (however, the movement of plants can be observed on longer time scales).
- Microscopic motion of cells (requires a microscope)
- Subcellular movements: for instance in large (plant) cells, during interphase (cytoplasmic streaming) or cell division

# Motility of *E. coli* (H.C. Berg)

Bacterial cells  
swimming near a  
glass surface, then  
above the surface

# Mitosis in a plant cell (Bajer)

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# Heredity

- The phenomenon of biological heredity, the transmission of certain characters by their parents to their offspring, has been known since the beginning of history.
- A main feature of this phenomenon is that of invariance: the characters remain the same through the transmission process.

# The theory of heredity (1)

- Experiments of Mendel on peas (1866): Mendel studies the phenomenon of heredity from a logical point of view.
- The application of elemental analysis to the complex phenomenon of heredity leads to the concept of the unit of heredity, an “element” in the language of Mendel, later called *gene* by Johannsen (1909).
- Such “elements” control the presence of an observable character (*phenotype* in the language of Johannsen). As an example of such units of heredity we can cite the round or wrinkled character of peas studied by Mendel.

# The theory of heredity (2)

- The observable characters that Mendel chose to study could be described in a qualitative manner (presence of absence). The concept of recessive/dominant “elements” or genes was introduced to account for the observed transmission of such elements. Truth tables were built to explain the character displayed by the plant in terms of its controlling elements ( $AA \rightarrow A$ ,  $Aa \rightarrow A$ ,  $aa \rightarrow a$ ).
- A *statistical calculus* based on the theory of *probability* was used to predict the frequency of dominant and recessive characters in a large population of plants (crossing of  $aa \times AA$ , frequency of 3:1 in the F2)

# Genes from matter?

- The concept of the gene emerged from such studies as a formal one. It can be viewed as a “black box” and considered solely as an *information* containing device, to be treated exclusively from a logical point of view. This provides the foundation of formal genetics, and needs not take into consideration the existence of a possible material support.
- The logical approach independent of any material support is not satisfactory. Indeed, the transmission of hereditary information is associated with a *spatial segregation*. Fundamental biological knowledge on living matter therefore calls for further conceptual developments.

# Genetic information today

Genetic information has a material basis, a heteropolymer known as DNA

# The flow of genetic information (1)

DNA → DNA Replication

DNA → RNA Transcription

(RNA → DNA Reverse Transcription)

RNA → Protein Translation

(with ribosomes)

# The flow of genetic information (2)

RNA → Protein Translation

Uses the genetic code which relates triplets of bases to amino acids and stop codons

$4^3 = 64$  triplets, coding for 20 amino acids and three stop codons

The genetic code is *not* universal

# Chirality and life

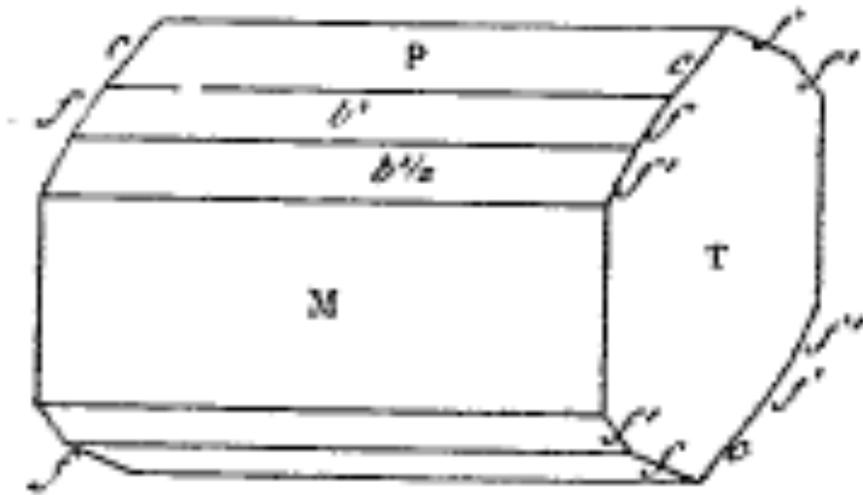
Two statements:

- Living organisms contain chiral compounds
- Living organisms contain chiral catalysts (called enzymes when the catalysts are proteins).
- A universal property of living organisms

# Chirality and life (2)

- Pasteur's discovery of chemical chirality (molecular dissymmetry).
- Pasteur's discovery of the chirality of life
- Chirality of biological compounds (e.g. amino acids and sugars).
- Chiral catalysis

# Molecular chirality



Pasteur  
1848



van't Hoff  
1875

<http://www.museumboerhaave.nl/>

# I. Pasteur's work on tartaric acid (1848)

- Tartar is a by-product of the fermentation of grapes. From tartar one can prepare tartaric acid and also another compound called paratartaric acid or racemic tartaric acid.
- Tartrates and racemates have the same molecular weight and the same composition: they are *isomers*.
- Molecular formula  $C_4H_6O_6$

Pasteur's writings: 1848, 1860 and 1883. <http://gallica.bnf.fr/>

John Desmond Bernal. *Molecular Asymmetry in Science and Industry in the Nineteenth Century*. Routledge and Kegan, London 1953, pp. 181-219.

# Mitscherlich's puzzle

Mitscherlich's work on tartrates and tartrate racemates (done in 1830, published in 1844):

- The two salts appear to have the same crystalline form.
- However, when dissolved in water, the tartrate rotates the plane of polarized light, but the paratartrate does not.

# Pasteur's solution (1)

0) Minute examination of the crystalline forms of the tartrates: they are “hemihedric” (chiral), with “the small facets always on the left” (already known to Hankel in 1843).

*Is this true of crystals of paratartrates?*

1) Minute examination of the crystalline forms of the paratartrates “The crystals of paratartrates are often hemihedral to the left, often to the right, that is the difference between the two salts.”

*This discovery solves the crystallographic problem, but the optical problem remains.*

# Pasteur's solution (2)

2) Pasteur separates and dissolves 8 grams of the right-hemihedral crystals of paratartrates: the solution deviates polarized light to the left.

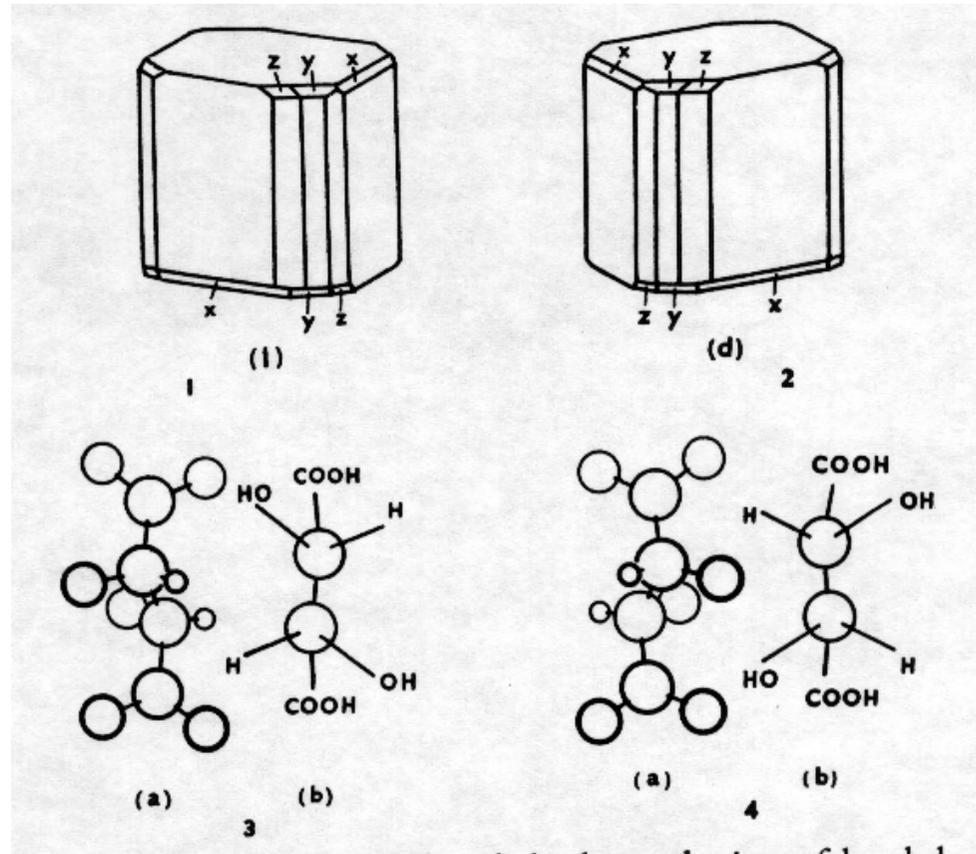
In a control experiment, Pasteur dissolves 8 grams of tartrate: it deviates polarized light to the right (and the absolute value of the deviation is close to the one obtained with right-hemihedral crystals of paratartrate) .

This is the second discovery in the same day!

# Crystals and molecules

Top: idealized representations of the crystals of paratartrates: they are mirror images of one another.

Bottom: absolute configurations of the corresponding molecules (Bijvoet, Nature **1951**)



# Names: dissymmetry, asymmetry and chirality

- Pasteur uses the name “dissymétrie” (the Greek dys means ill or imperfect). Dissymmetry in modern English would correspond to symmetry breaking or broken symmetry. The word “dissymétrie” is usually translated as “asymmetry”.
- “Asymmetry” focuses on a lack of symmetry.
- Chirality (Kelvin, 1893) is the nonidentity of an object with its mirror image. This term is used universally today in this context.

# Historical background: multidisciplinarity at work

- **Cristallography:**  
Haüy (1810) hemihedry of the quartz.
- **Optics:**  
Malus (1808) discovery of polarized light (in Iceland spar).
- **Cristallography + optics:**  
Arago (1811) discovery of the rotation of the plane of polarization by quartz; Herschel (1820) discovery of a correlation between hemihedry in quartz crystals and their optical rotation.
- **Chemistry:**  
Biot (1815) discovery of the rotation of the plane of polarization by certain organic solutions, including tartaric acid and its salts. Berzelius(1830) shows that paratartaric acid (described by Gay-Lussac in 1826) and tartaric acid have the same atomic weight and the same composition (isomers) .



# Asymmetry and life

## Pasteur, CRAS, 78, 1515, 1874

de corps actifs dissymétriques. Le rôle de la dissymétrie moléculaire a été introduit également comme facteur des phénomènes de la vie, le jour où il a été constaté qu'un ferment organisé vivant faisait fermenter facilement l'acide tartrique droit et non son inverse l'acide tartrique gauche, et que des êtres vivants empruntaient à l'acide tartrique droit le carbone nécessaire à leur nutrition, de préférence au carbone de l'acide tartrique gauche. Dès lors, puisqu'il y a dissymétrie dans les principes immédiats naturels, notamment dans ceux qu'on pourrait considérer comme primordiaux, c'est-à-dire dans les principes immédiats constitutifs de la cellule vivante; puisque les végétaux produisent des substances dissymétriques simples à l'exclusion de leurs inverses; puisque, contrairement à ce qui a lieu dans les réactions de nos laboratoires, le règne végétal ne forme pas exclusivement des paratartriques ou des inactifs simples, et que probablement même il ne forme de ces derniers produits que par des actions oxydantes ou réductrices secondaires, de l'ordre de celles de la chimie minérale, témoins les acides oxalique ou acétique naturels, je conclus qu'il faut de toute nécessité que des actions dissymétriques président pendant la vie à l'élaboration des vrais principes immédiats naturels dissymétriques.

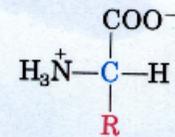
Quelle peut être la nature de ces actions dissymétriques? Je pense, quant à moi, qu'elles sont d'ordre cosmique. L'univers est un ensemble dissymétrique, et je suis persuadé que la vie, telle qu'elle se manifeste à nous, est fonction de la dissymétrie de l'univers ou des conséquences qu'elle entraîne. L'univers est dissymétrique, car on placerait devant une glace l'ensemble des corps qui composent le système solaire, se mouvant de leurs mouvements propres, qu'on aurait dans la glace une image non superposable à la réalité. Le mouvement de la lumière

# Chemistry of life

- Chiral compounds: amino acids, sugars
- Chiral catalysts

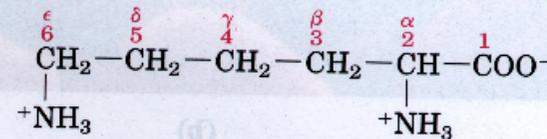
# Chirality of biological compounds: amino acids (1)

The amino acids found in proteins (except glycine which is a prochiral compound) are chiral: the  $\alpha$  carbon atom (bonded to 4 different groups) is always in the same absolute configuration.



**figure 5-2**

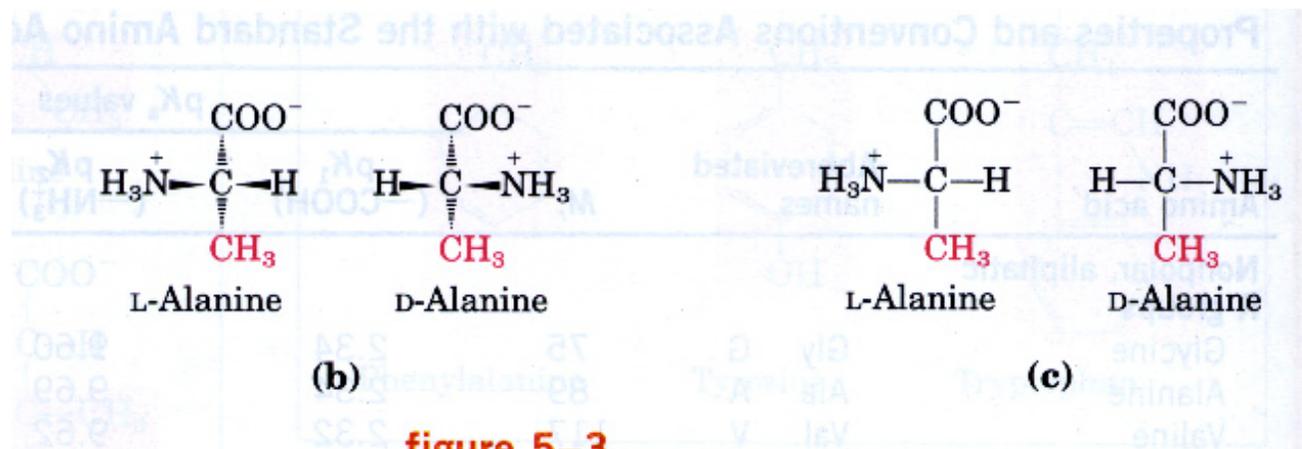
**General structure of an amino acid.** This structure is common to all but one of the  $\alpha$ -amino acids. (Proline, a cyclic amino acid, is the exception.) The R group or side chain (red) attached to the  $\alpha$  carbon (blue) is different in each amino acid.



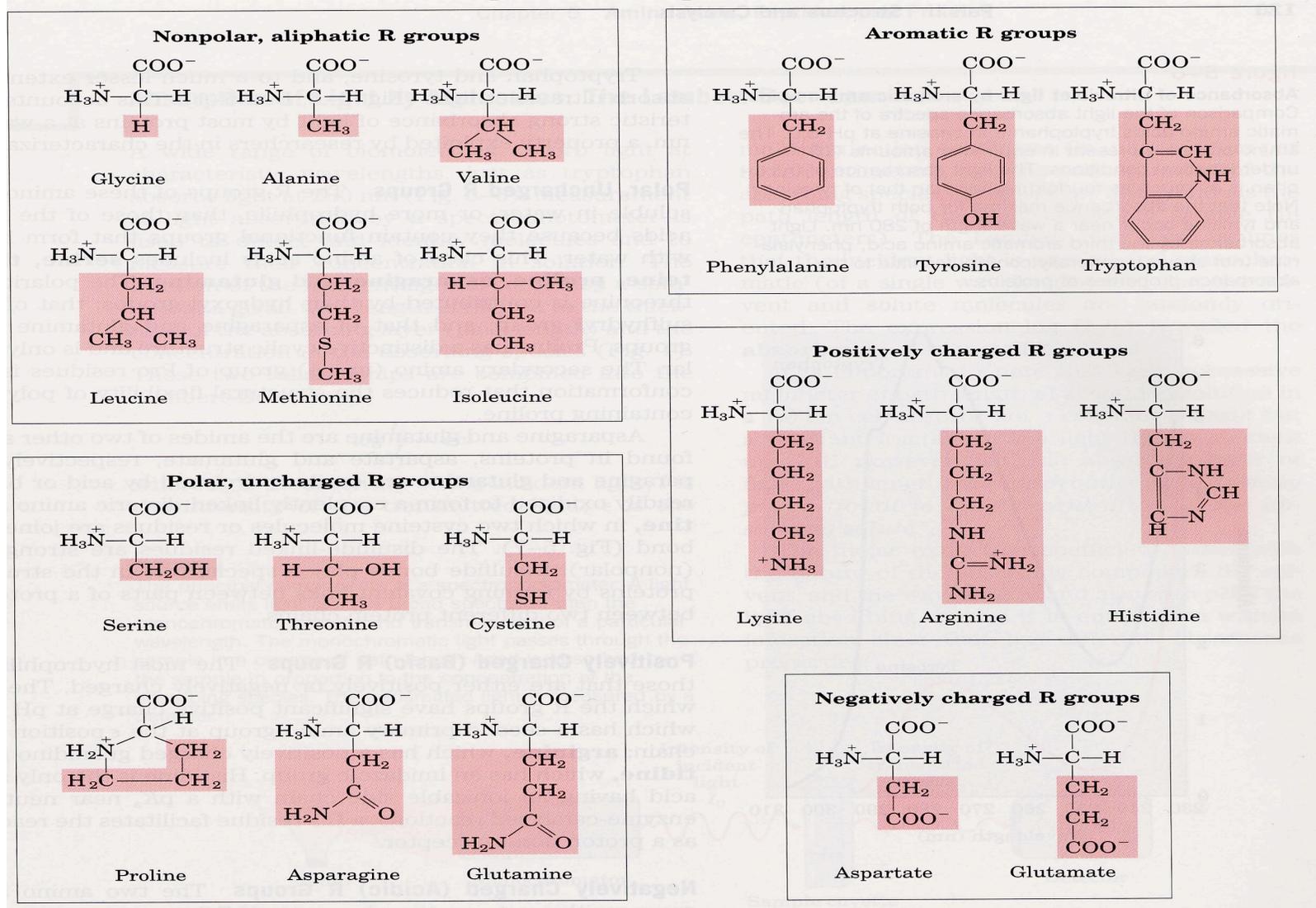
Lysine

# Chirality of biological compounds: amino acids (2)

Amino acid residues in proteins are all L stereoisomers (except glycine):



# The 20 standard amino acids





# Chemistry of life: chiral catalysis

Living organisms can perform chiral chemical reactions (Pasteur)

- “Lock and key” (Fischer)
- The efficiency of chiral catalysis (Ogston)

# Lock and key (1894)

- “To take an image, I claim that the enzyme and the glucoside have to be put together as the lock and the key (Schloss und Schlüssel) in order to effect a mutual chemical action.”

→ Concept of complementary recognition

“Enzyme efficiency is to a high degree determined by molecular geometry.”

# Efficiency of chiral catalysis

- Is it possible for a chiral catalyst to distinguish between the identical groups of a symmetrical compound?

Yes: Ogston (1948): a chiral catalyst can distinguish between the identical groups of a prochiral compound, and produce a chiral compound with a yield of 100%.

# Nature of the four theories

- Evolution: macroscopic world with a role of history (and a material basis).
- Cell: microscopic world, accessible through optics, with a material basis.
- Heredity: macroscopic world, a logical theory focusing on the transmission of information.
- Chirality: “nanoscopic” world, a chemical theory with a material basis.