Syllabus

(http://www.phy.ntnu.edu.tw/~cchen/class/biophysics/biophysics.html)

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Reference books: (藝軒, 羅斯福路三段316巷３號 台大正對面)
"Cell and Molecular Biology -- Concepts and Experiments" by Karp
"Biophysics -- An Introduction" by Rodney Cotterill

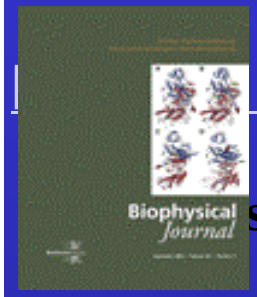
Part I: Introduction to Cell Biology (T.-h. Huang)

9/12	Structures of Cells	Karp Chap.1
9/19	The Chemical Basis of Life	Karp Chap. 2
9/26	Bioenergetics, Enzymes, and Metabolism	Karp Chap. 3
10/3	The Nature of the Gene and the Genome	Karp Chap. 10
10/17	Cellular Reproduction	Karp 14
10/24	The Immune response	Karp Chap. 17
10/31	Quiz (1 hour) Course	

What is biophysics ?

Use of physical methods to investigate biological phenomena.

- Advanced physical techniques – NMR, X-ray crystallography, optical spectroscopy, microscopy, calorimeter etc.
- Advanced physical concepts – Computational techniues, theoretical analysis.



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Contents: Volume 85, Issue 3, September 2003 [Index by Author]

BIOPHYSICAL THEORY AND MODELING:

- Bacterial Flagellar Microhydrodynamics: Laminar Flow over Complex Flagellar Filaments, Analog Archimedean Screws and Cylinders, and Its Perturbations
- Mathematical Model of the Spatio-Temporal Dynamics of Second Messengers in V Transduction
- Molecular Dynamics Simulation of Surfactin Molecules at the Water-Hexane Inte
- A Model of Calcium Waves in Pancreatic and Parotid Acinar Cells
- Concerted Simulations Reveal How Peroxidase Compound III Formation Results in Cellular Oscillations
- Vibrational Frequency Shifts and Relaxation Rates for a Selected Vibrational Mod in Cytochrome c
- Molecular Dynamics Simulation of Bacteriorhodopsin's Photoisomerization Using Ab Initio Forces for the Excited Chromophore.
- Charge Distribution in 7-Methylguanine Regarding Cation- Interaction with Prote Factor eIF4E
- Two-State Folding over a Weak Free-Energy Barrier
- Thermodynamics of - and ß-Structure Formation in Proteins
- Conformational Dynamics of the F_1-ATPase ß-Subunit: A Molecular Dynamics Stud
- A Tree-Based Algorithm for Determining the Effects of Solvation on the Structu of Salivary Gland Tripeptide NH_3^+-D-PHE-D-GLU-GLY-COO^-
- Similarity of Force-Induced Unfolding of Apomyoglobin to Its Chemical-Induced Unfolding: An Atomistic Molecular Dynamics Simulation Approach

What is Life and how do you define a living system ?

1. Self sustain
2. Ability to propagate

- Cell （細胞） is the smallest living system.
- What is Cell
- How does cell function ?
- How does cell propagate ?

1. The Evolution of Cells

生命演化三部曲：

一、化學演化(Chemical Evolution)

原始的地球大氣層促使小型有機分子的誕生，而這些分子的累積，將地表的海洋〝熬〞成一〝營養〞豐富的有機湯(prebiotic soup)**，這進而促使巨型有機聚合物分子的形成。**

- **Reducing atmosphere:** N_2, CO_2, H_2O, H_2, CH_4, NH_3, H_2S

  ➔ amino acids ➔ nucleic acids ➔ proteins ➔ cells

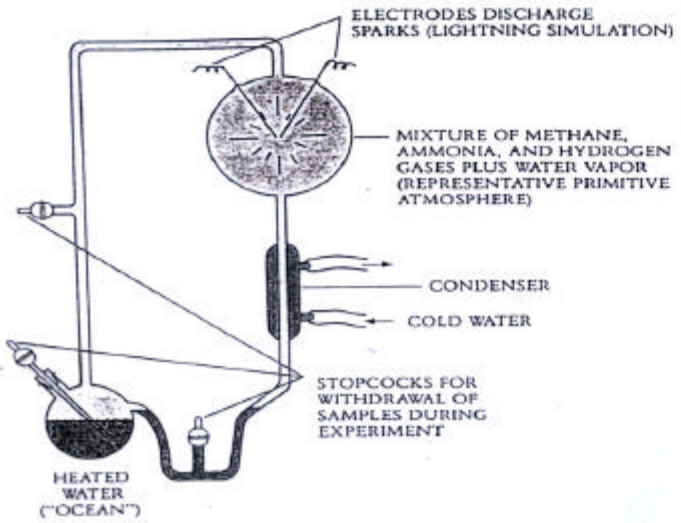
- O_2 appeared in 2.5 billion years ago :

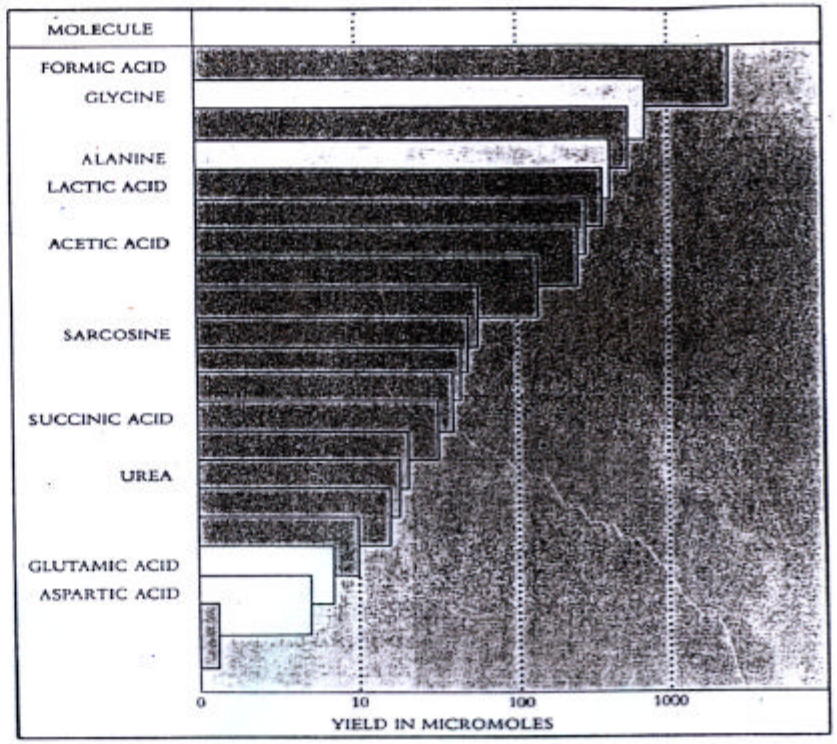
  ➔ Photosynthesis (光合作用)

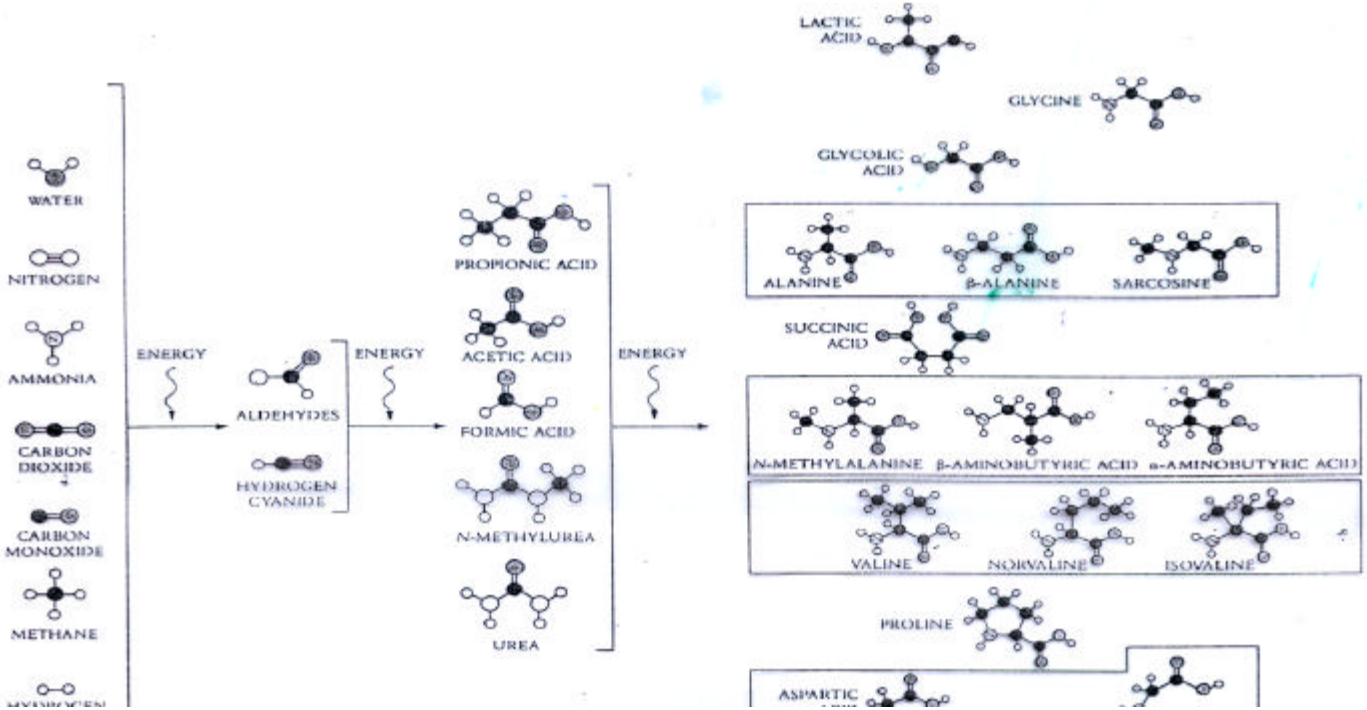
Miller - Urey experiment: Subject above compounds in a right temperatures and lightening conditions to produce:

amino acids (four), urea, HCN and adenine

(Miller - Urey expt.)







生命演化三部曲：

二、自我組織(Self Organization)

巨型有機聚合物分子發展出自我複製的能力為生命體起源的重要關鍵。

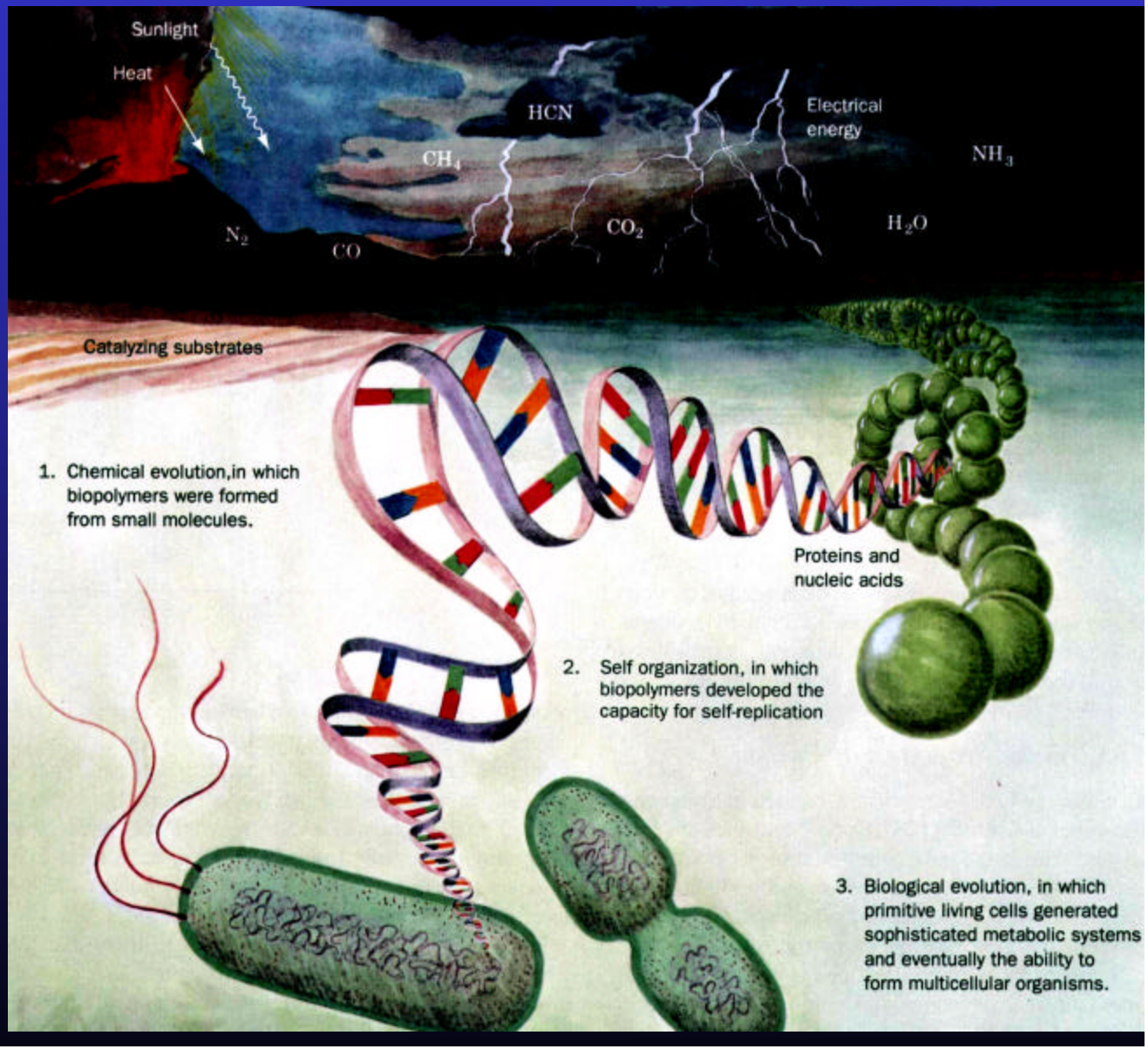
三、生物演化(Biological Evolution)

原始的生命基本單位-細胞的出現，誘發了物質與能源消耗的競爭，於是細胞逐漸演化出繁複的代謝過程以開發擷取不同的來源，這促成多細胞生命的產生。

生命起源的傳奇故事

他們是這麼說的…

1. 簡單生物分子的形成
2. 核甘酸聚合物助長自我的形成
3. 自我複製分子的自然選擇與淘汰
4. 特殊RNA分子催化生化反應
5. 訊息傳遞：由核甘酸聚合物到氨基酸的聚合物
6. 細胞膜的形成：細胞的產生



地球生命史（簡化版）

細胞可分類為原核細胞(prokaryotic cells)與真核細胞(eukaryotic cells)兩種，而原核細胞約比真核細胞早約二十億年即出現於地球上。

四十五億年前 ---- 地球形成

三十五億年前 ---- 原核細胞生物主宰地球

十五億年前 ---- 真核細胞出現

五億年前 ---- 多細胞生物崛起

CELLS

I. DISCOVERY:

■mid-1600's: Robert Hooke (英) observed "cells" in cork.

A. Leeuwenhoek (荷蘭) observed "bacteria" in pond water

■1838: M. Schleiden (德·科學家) concluded that plants were made of cells and that the plant embryo arose from a single cell.

■1839: Schwann (德國): cells of plants & animals are similar structures and proposed that:

(i) All organisms are composed of one or more cells

(ii) Cell is the structural unit of life

■1855: Virchow demonstrated that

(iii) Cells can arise only by division from a preexisting cell

細胞理論(The Cell Theory)

- 一、 所有的生物有機體(organism)皆為單一或多細胞所組成，其生命過程如代謝(metabolism)與遺傳(heredity)等皆發生於細胞內。
- 二、細胞為最小的生命單位，也是所有有機生命體組成的基本單位。
- 三、細胞皆來自既存細胞的分裂。雖然生命起源論認為早期生命體可由地球環境中演化形成，但是現代的生物學家基本上相信現有的細胞不會再由此類似過程產生。地球上現有的生命體皆為既存細胞的生命延續體。

II. Basic Properties of Cells:

Cells are:

- Highly complex and organized.
- Possess a genetic program and the means to use it.
- Capable of producing more of themselves.
- Acquire and utilize energy.
- Carry out a variety of chemical reactions.
- Engage in numerous mechanical activities.
- Able to respond to stimuli.
- Capable of self-regulations.

→ Cells are the smallest unit to exhibit "life" phenomenon.

→ Immotalized cells (Cell line): Hela cell

Cell （細胞）

1. The Evolution of Cells

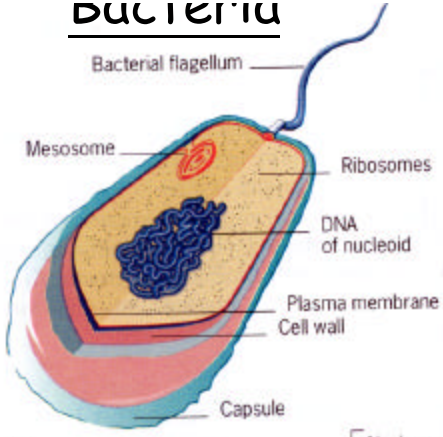
2. Prokaryotes vs. Eukaryotes

2. Prokaryotes
(原核細胞)
vs.
Eukaryotes
(真核細胞)

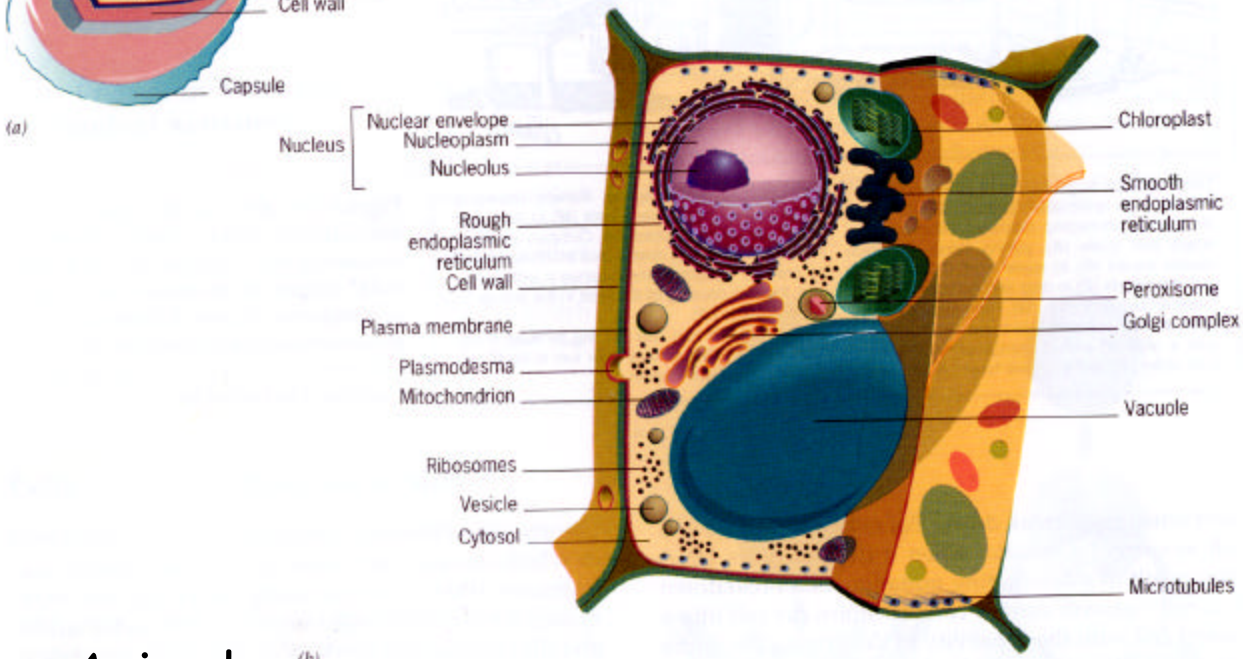
3. Organelles
(胞器)

Bacteria

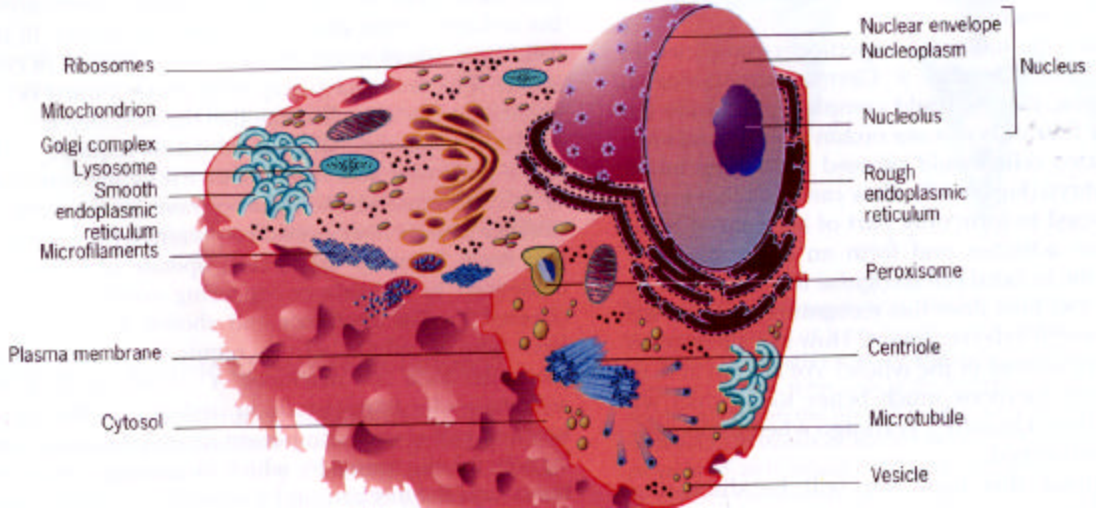
Note: Organelles are not drawn to scale.



Plants



Animals



Different types of human cells

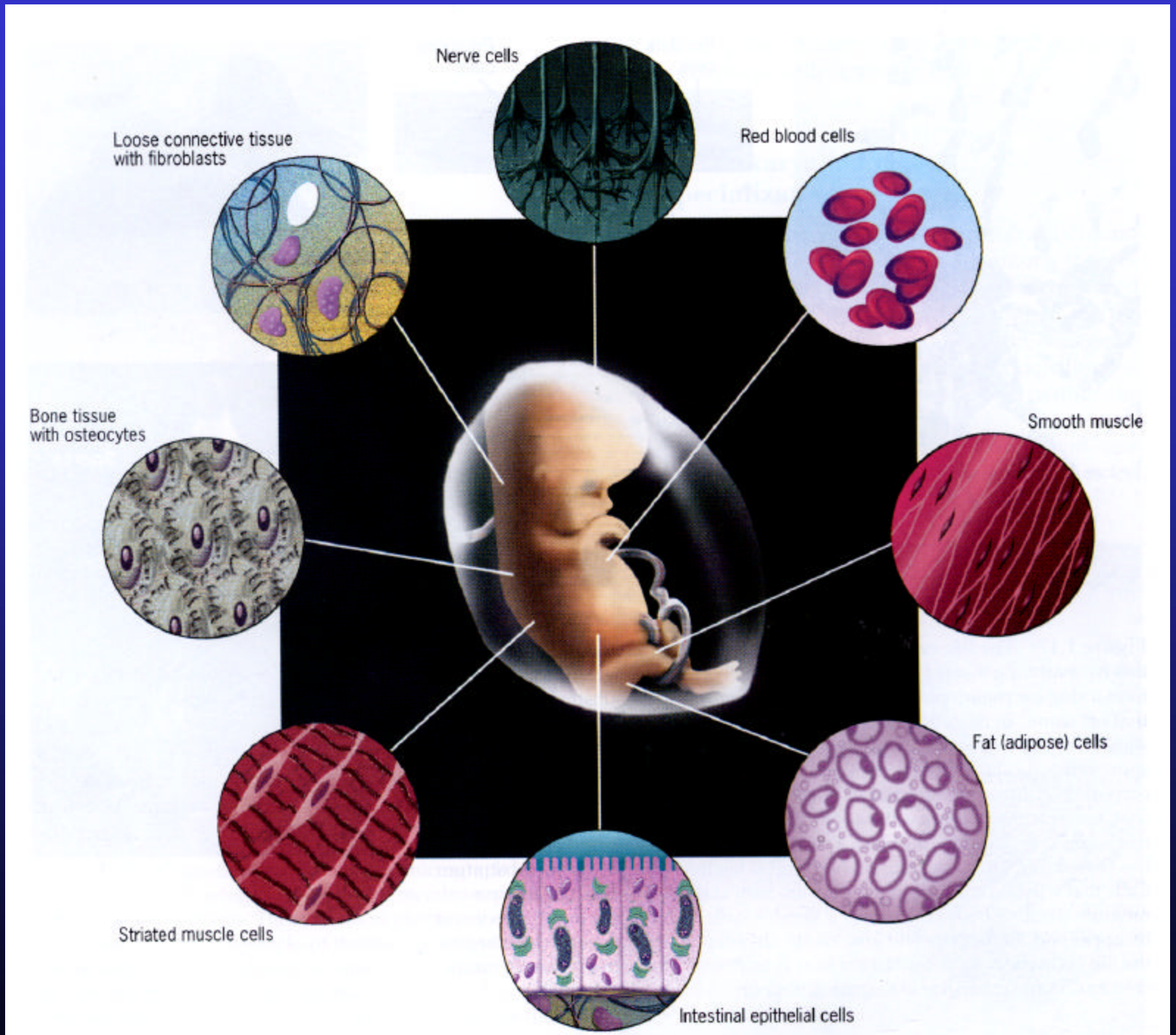
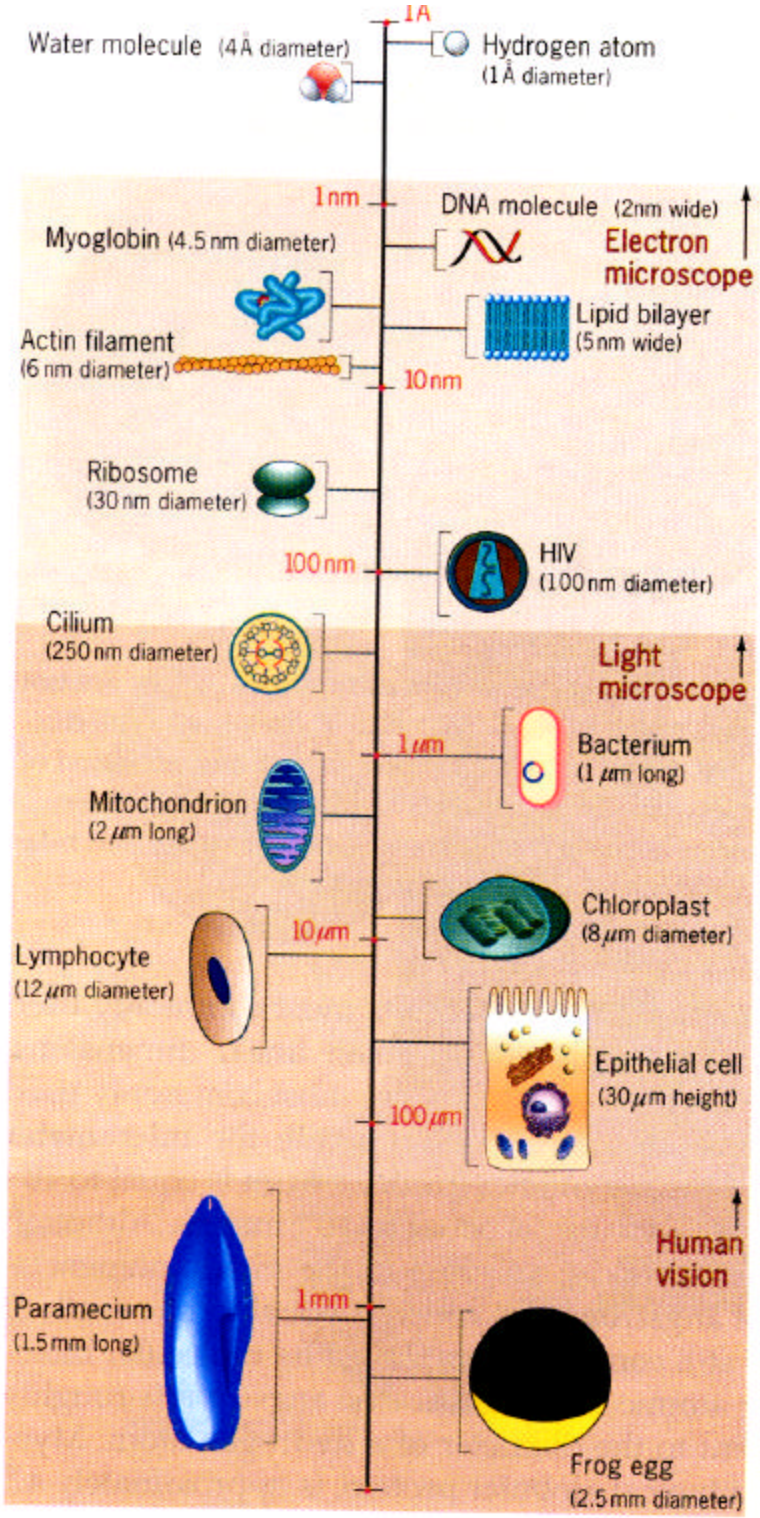
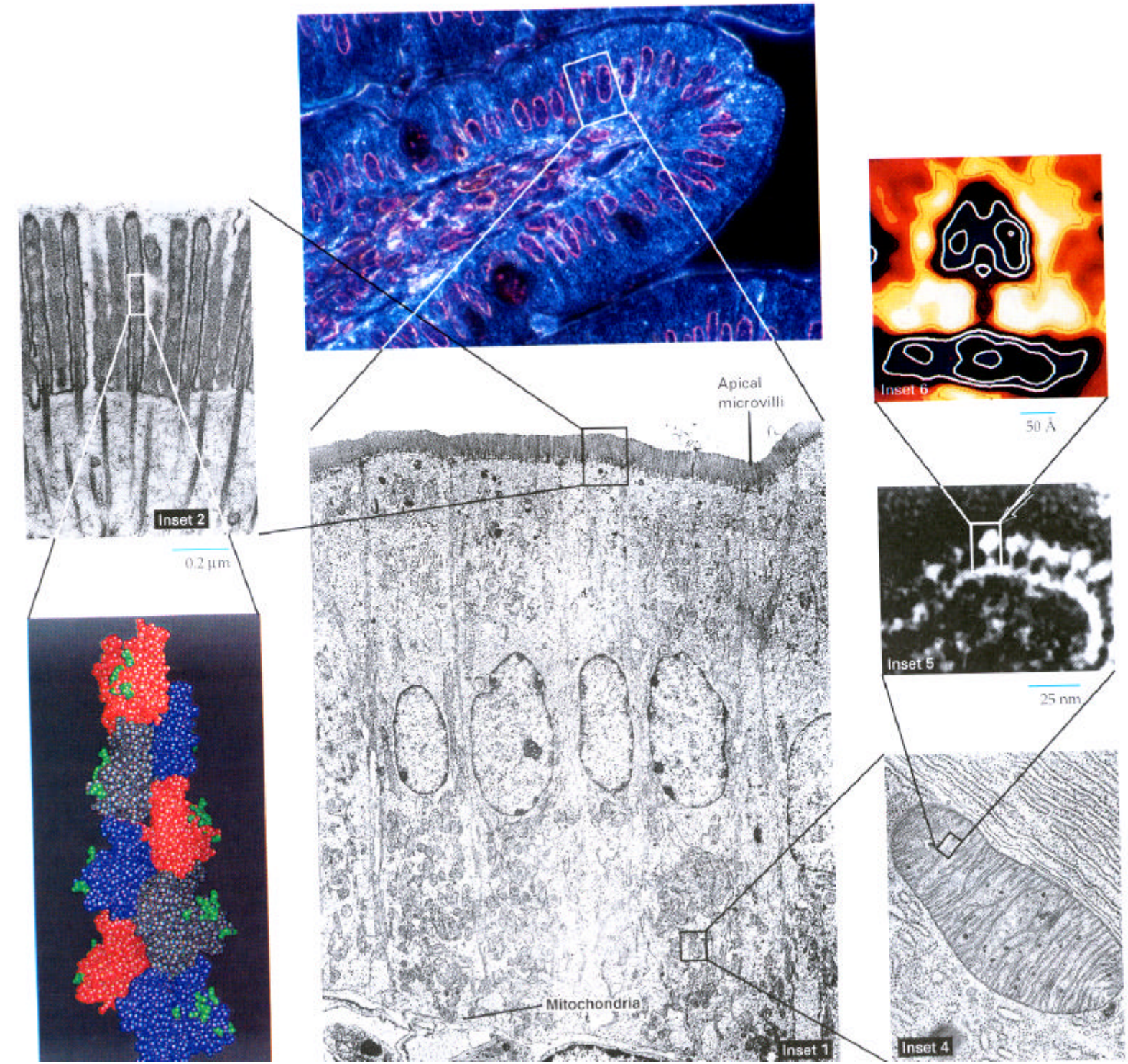


Figure 1.18 Pathways of cell differentiation. A few of the types of differenti-

Relative sizes of cells and cell components



Levels of cellular molecular organization



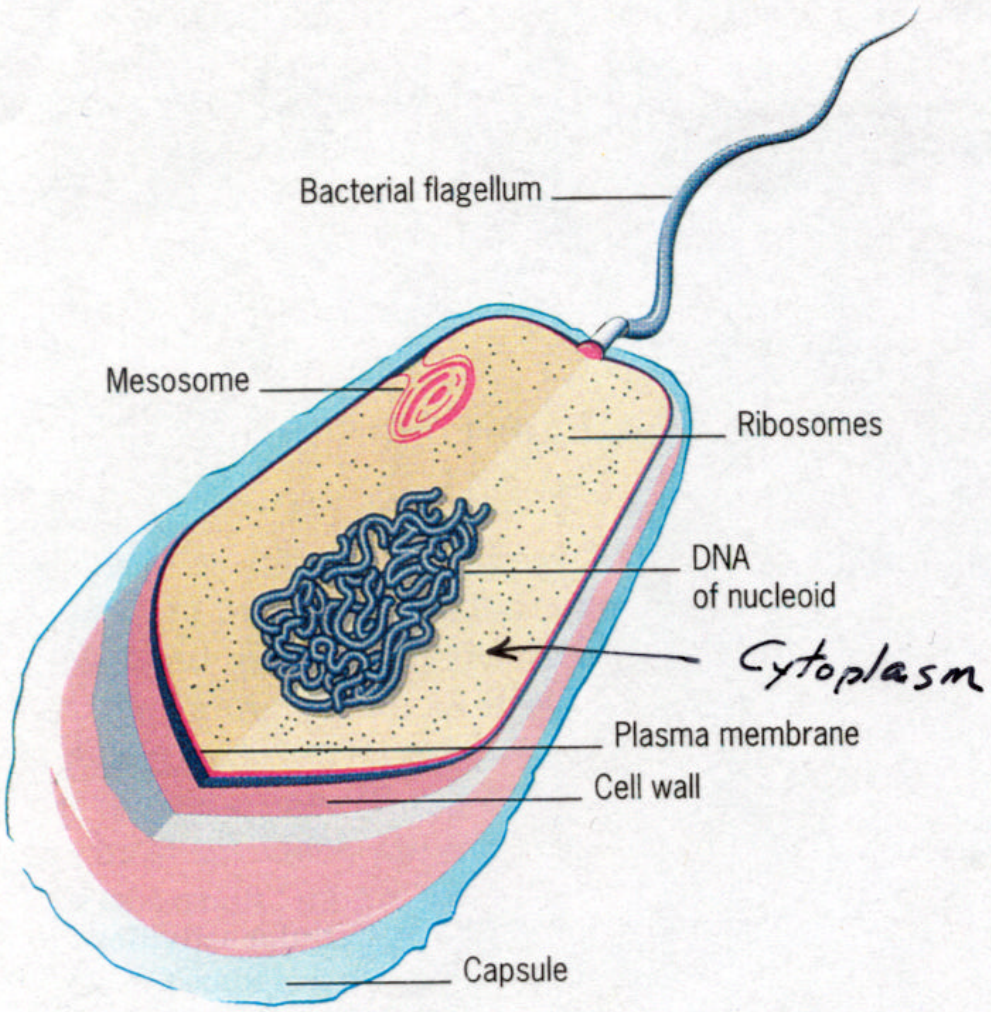
原核細胞(prokaryotic cells)與真核細胞(eukaryotic cells)的比較

原核細胞與真核細胞最明顯的差異在於真核細胞擁有細胞核與為薄膜(membrane)所侷限的細胞器官，而原核細胞沒有。

雖然原核細胞與真核細胞一樣是以DNA為遺傳基礎，也同樣的擁有核醣體(ribosome)、細胞膜與類似的基本代謝過程等。但是，一般而言真核細胞的DNA遠較原核細胞複雜，且平均尺寸也較原核細胞大十倍以上。再則，原核細胞有細胞壁而真核細胞沒有。

結構上原核細胞雖簡單許多，但是其生化組成卻較為多樣性。

(两类不同的细胞)

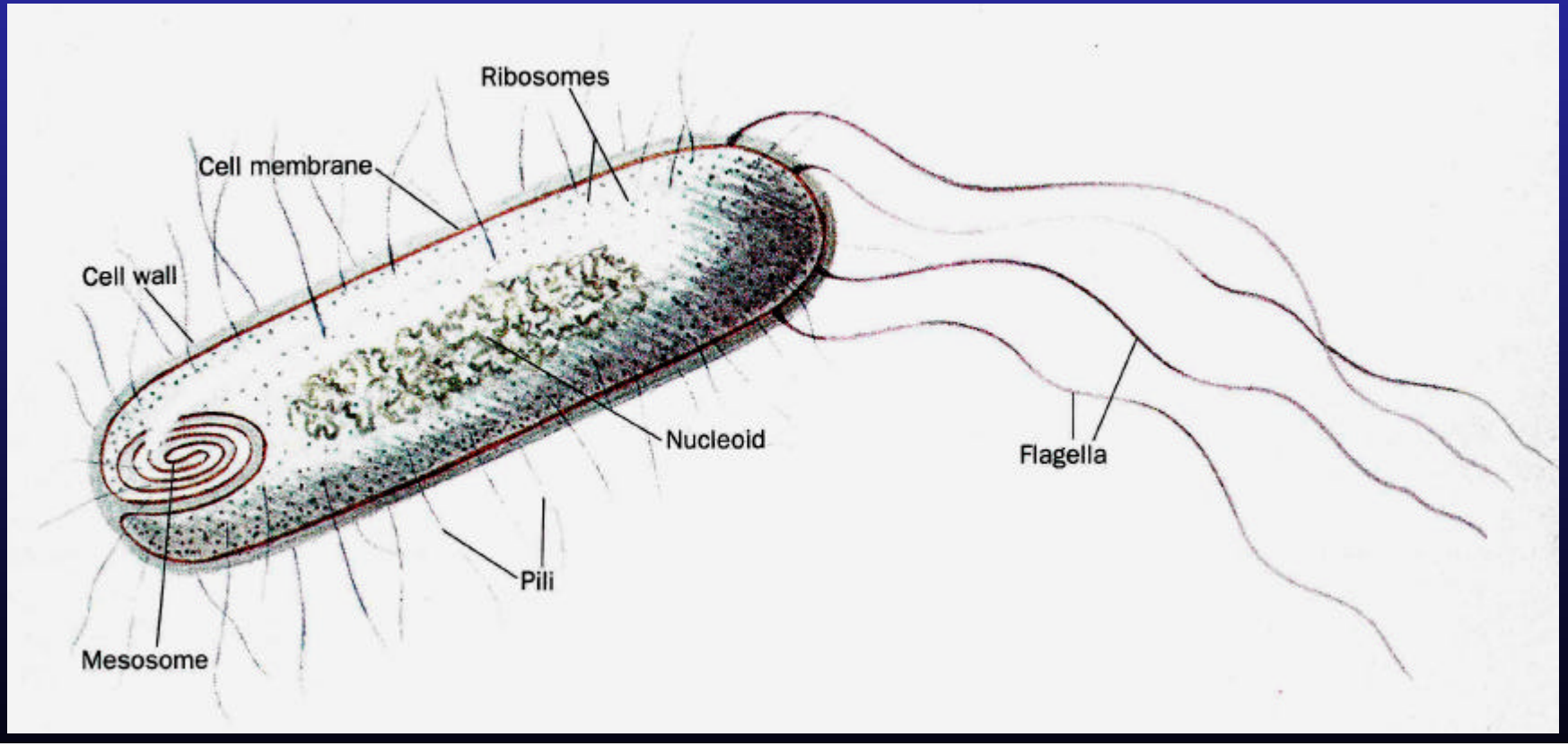


Prokaryotes

FIGURE 1.9 • **The structure of cells.** Schematic diagra
of a "generalized" bacterial (*a*), plant (*b*), and animal (*c*)
Note, organelles are not drawn to scale.

(原生细胞)

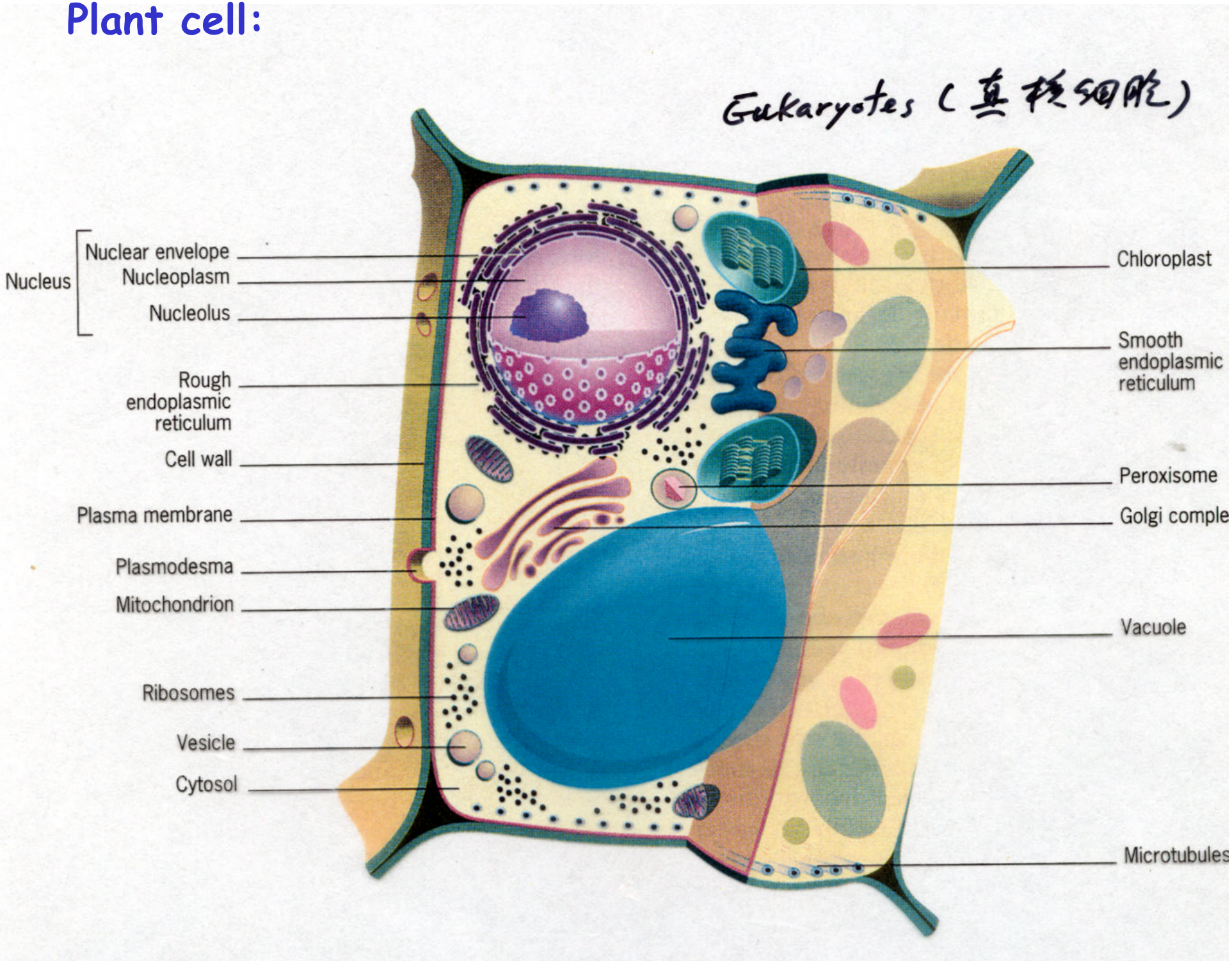
雖然細菌(bacteria)是原核細胞的唯一生命體，然而其種類卻非常的多。Carl Woese提出若由代謝過程來看，細菌應分為Archaebacteria與Eubacteria兩類，他因此提議細胞分類應該分為三大類。

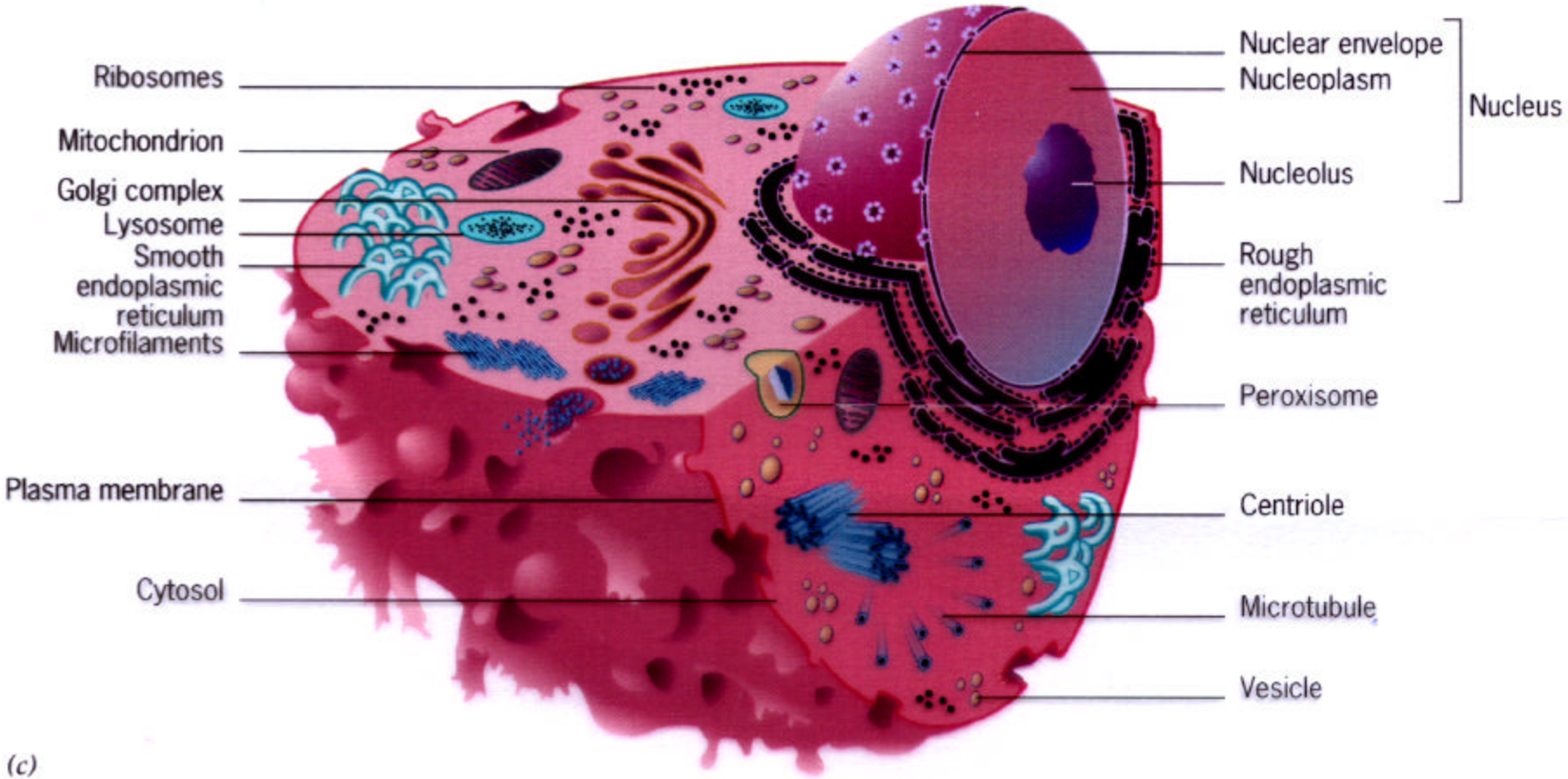


The Structure of Prokaryotic Cells:

1. Cell wall: Made of a single "peptidoglycan".
   - Gram-positive bacteria: Thick cell wall.
   - Gram-negative bacteria: Thin cell wall.
2. Plasma Membrane: Lipid bilayer w/protein embedded.
3. Flagellum: Proteins that allow cells to move around.

Plant cell:


Eukaryotes (真核细胞)
Nucleus
Nuclear envelope
Nucleoplasm
Nucleolus
Rough endoplasmic reticulum
Cell wall
Plasma membrane
Plasmodesma
Mitochondrion
Ribosomes
Vesicle
Cytosol
Chloroplast
Smooth endoplasmic reticulum
Peroxisome
Golgi comple
Vacuole
Microtubules



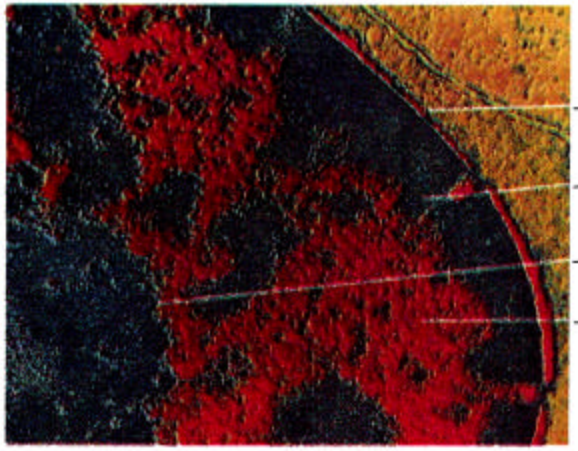
(c)

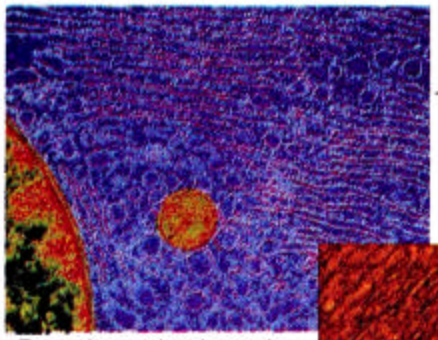
(動物細胞)

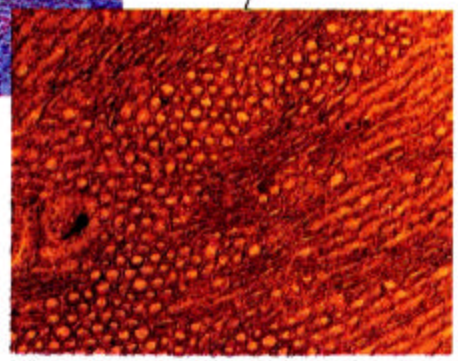
不同細胞內新胞質組成不一 (Brown fat cell 及 plasma

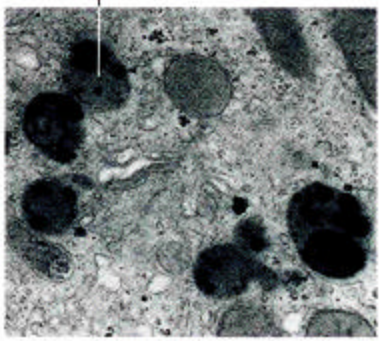
FIGURE 1.9b, c 1

真核細胞(eukaryotic cells)的結構









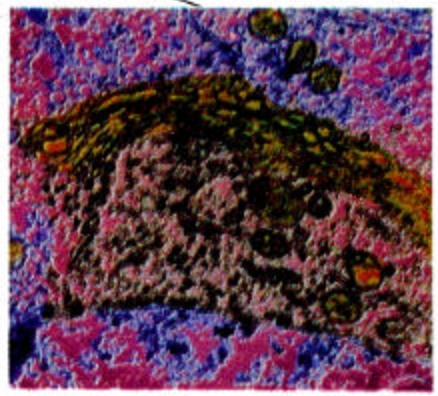
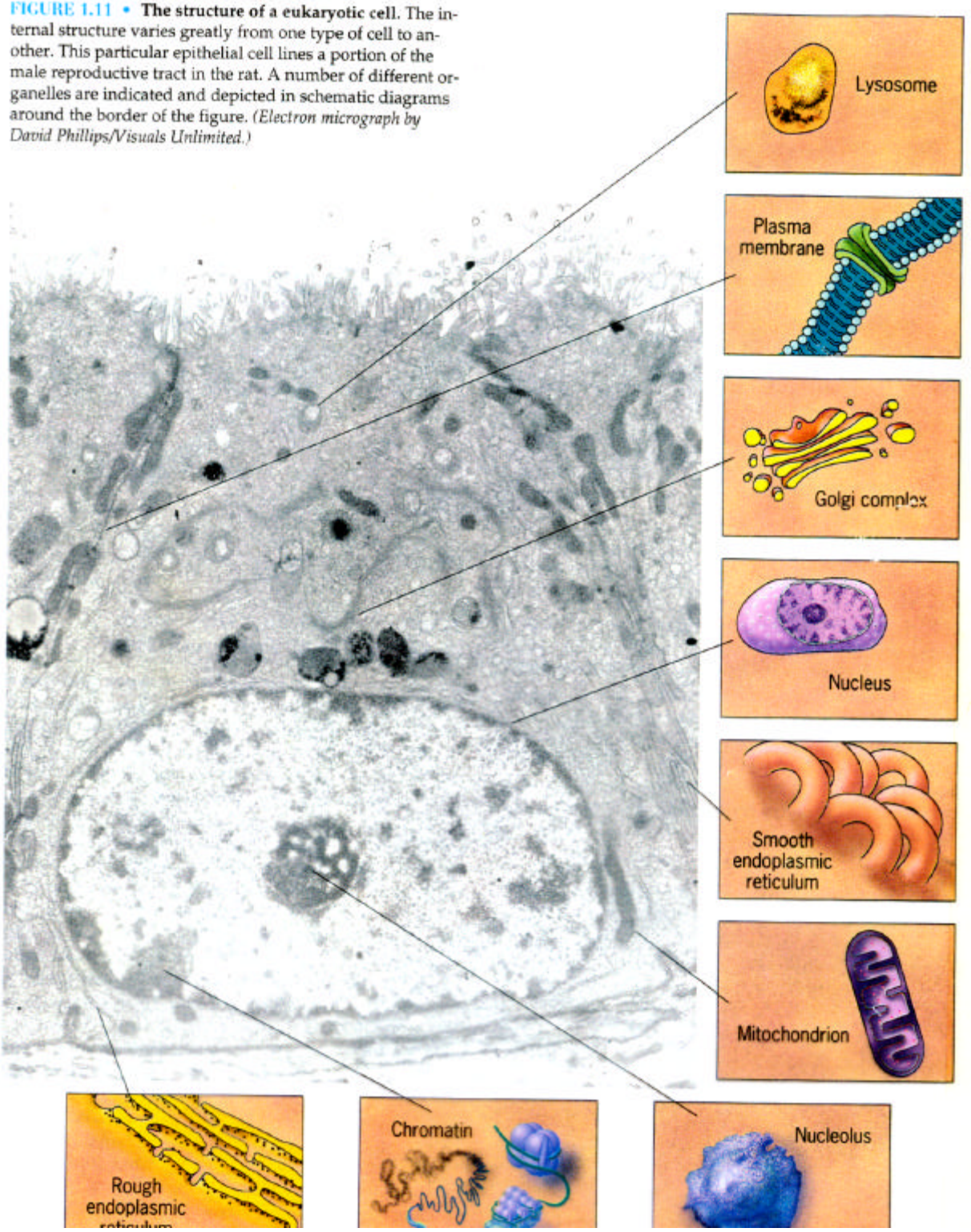


FIGURE 1.11 • **The structure of a eukaryotic cell.** The internal structure varies greatly from one type of cell to another. This particular epithelial cell lines a portion of the male reproductive tract in the rat. A number of different organelles are indicated and depicted in schematic diagrams around the border of the figure. *(Electron micrograph by David Phillips/Visuals Unlimited.)*



The Structure of Eukaryotic Cells:

I. External framework.

1. Plasma membrane:

fluid mosaic model consists of proteins embedded in lipid bilayers. The proteins (peripheral or integral) may have protein, peptide or carbohydrate attached to them.

2. Cytoskeleton:

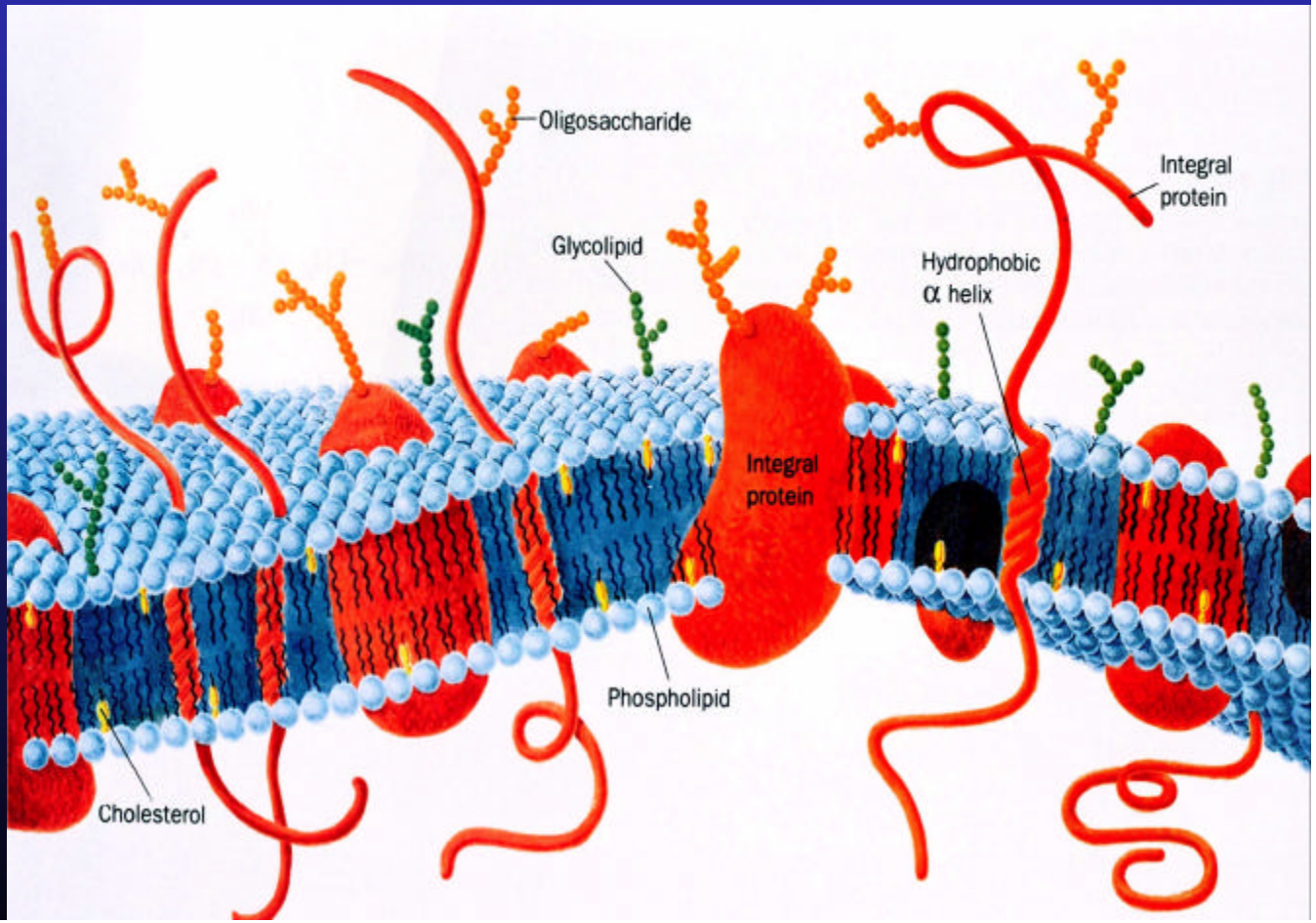
- **Microfilaments:** Thre3ads of 3-6 nm thick that are compound of two proteins, actin and myosin, and are capable of contraction
- **Microtubules:** Cylinders of 15-34 nm thick protein, tubulia, wound in a spiral shape, microtubules radiate outward from a central region in the interior of the cell in three dimension. Microtubules are not stable components, but constantly undergoing assembly and disassembly.

細胞膜(Membranes)

Biological membranes are organized assemblies of *lipids* and *proteins* with small amounts of carbohydrates.

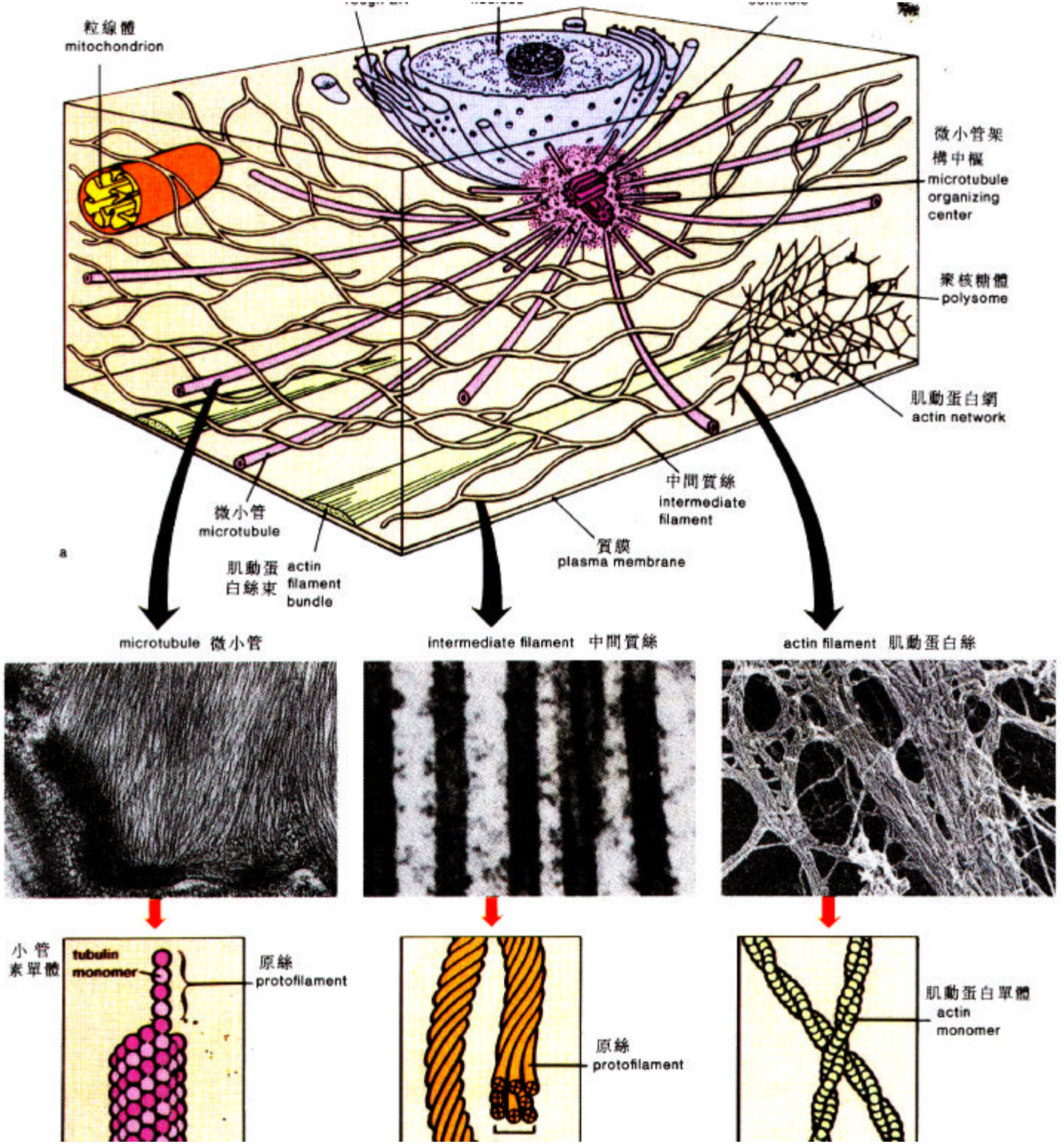
Yet they are not impermeable barriers to the passage of materials.

Rather, they regulate the composition of the intracellular medium by controlling the flow of nutrients, waste products, ions, etc., into and out of the cell.



其他

Skeleton (骨架)



II. Internal Components:

(1). Endoplasmic Reticulum (ER)

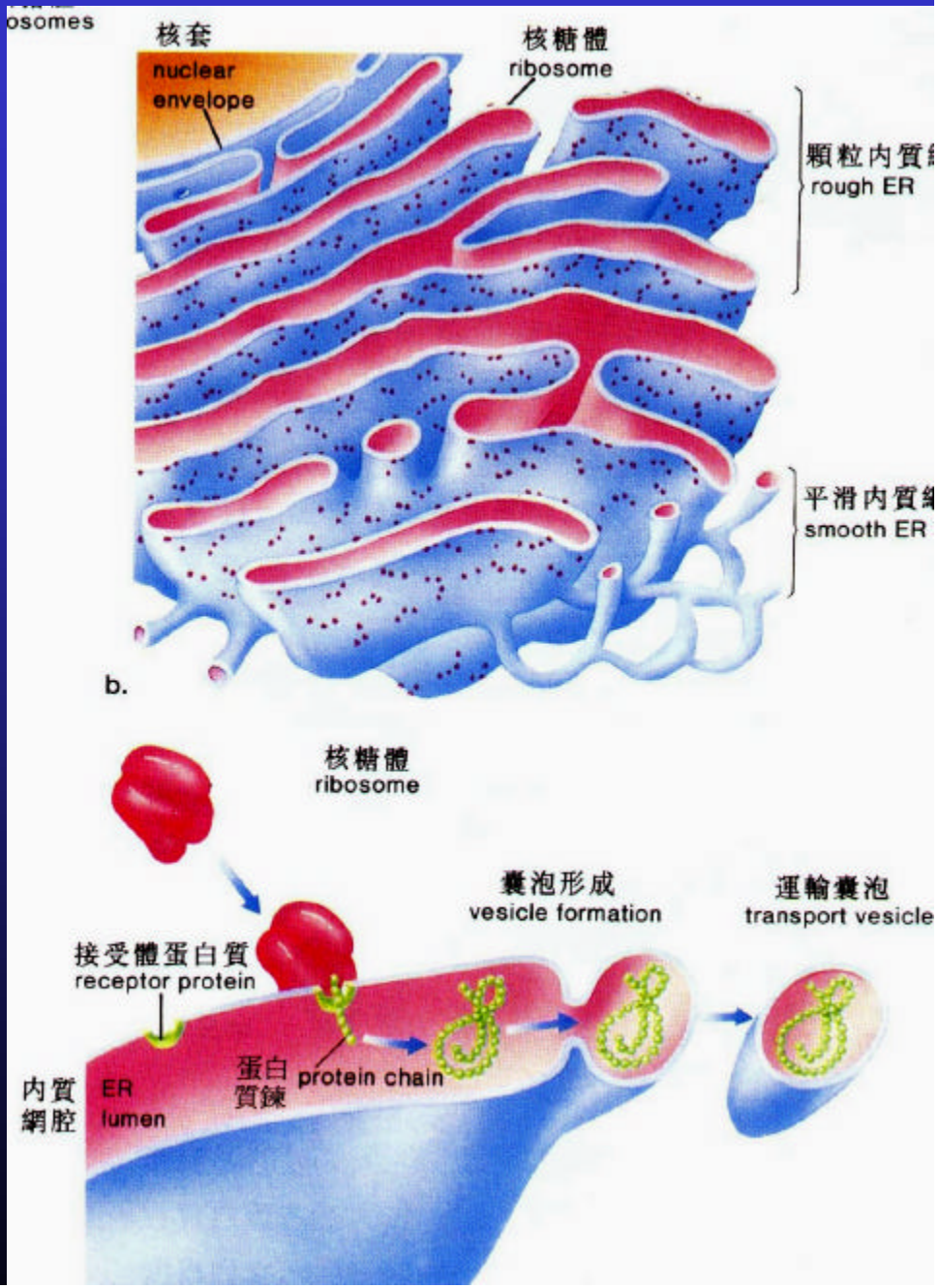
The extensive system of internal membranes that exists within the cells of eukaryotic cells.

- Provide channels through the interior of the cell (Rough ER).
2. Provides a site for enzymes. (Membrane proteins, smooth ER).
3. Creates subcompartment within the cell [Fusion of m.b. to form various cisternae (Vesicles)].

內質網(Endoplasmic Reticulum)

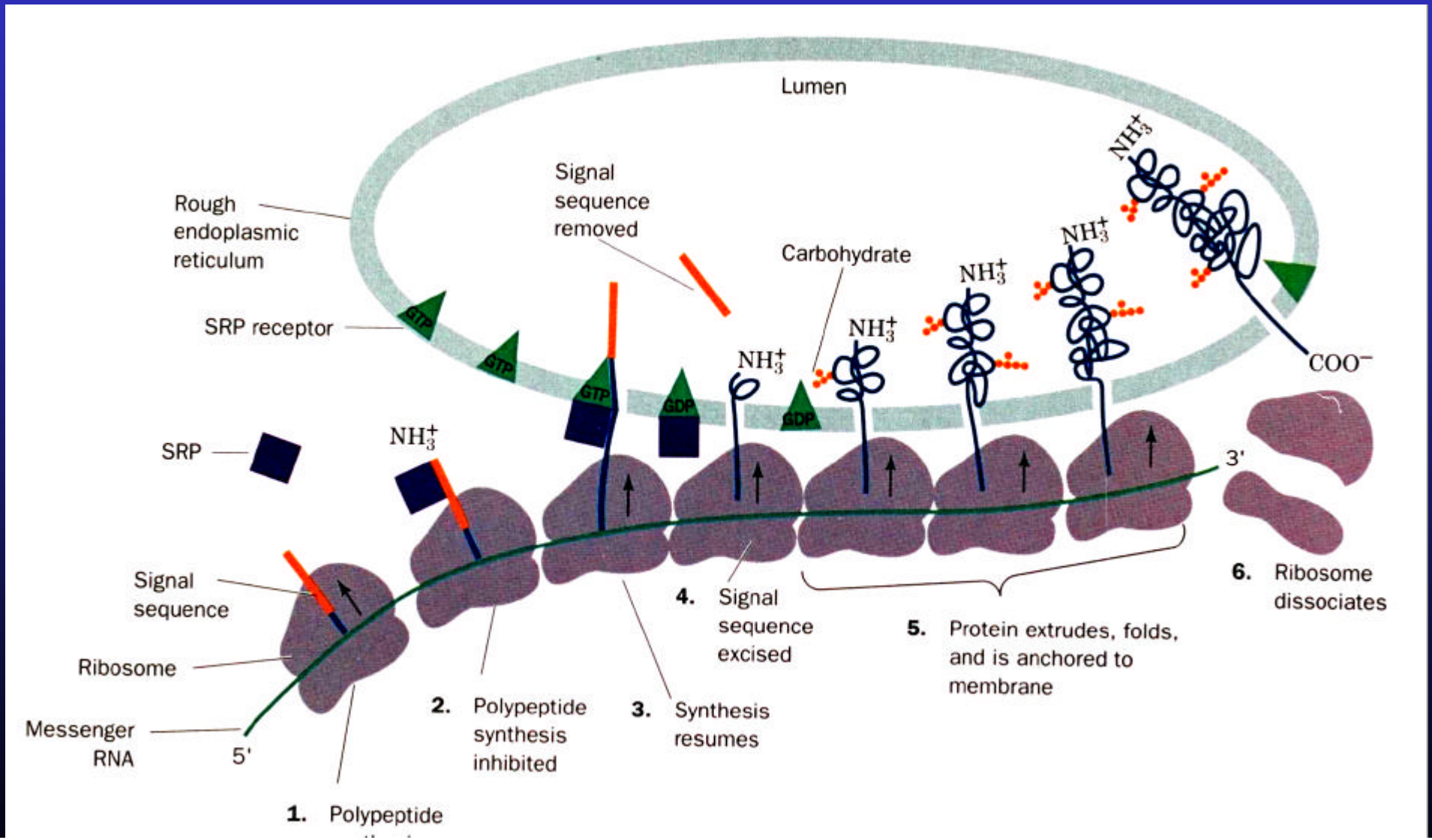
內質網為核套的延伸，其複雜的膜狀管道與囊系與核醣體結合在一起成為顆粒內質網(rough ER)，若缺乏核醣體的結合則為平滑內質網(smooth ER)。

顆粒內質網主要功能為參與蛋白質的合成、特化與傳輸。平滑內質網內含有許多的酵素(enzyme)，其中多數與細胞膜功能有關，主要為特化與傳輸蛋白質



核醣體(Ribosome)

核醣體含有豐富的蛋白質，它能〝讀取〞mRNA以製造所需的蛋白質。每個核醣體參與一種蛋白質製造。



(2). The Nucleus:

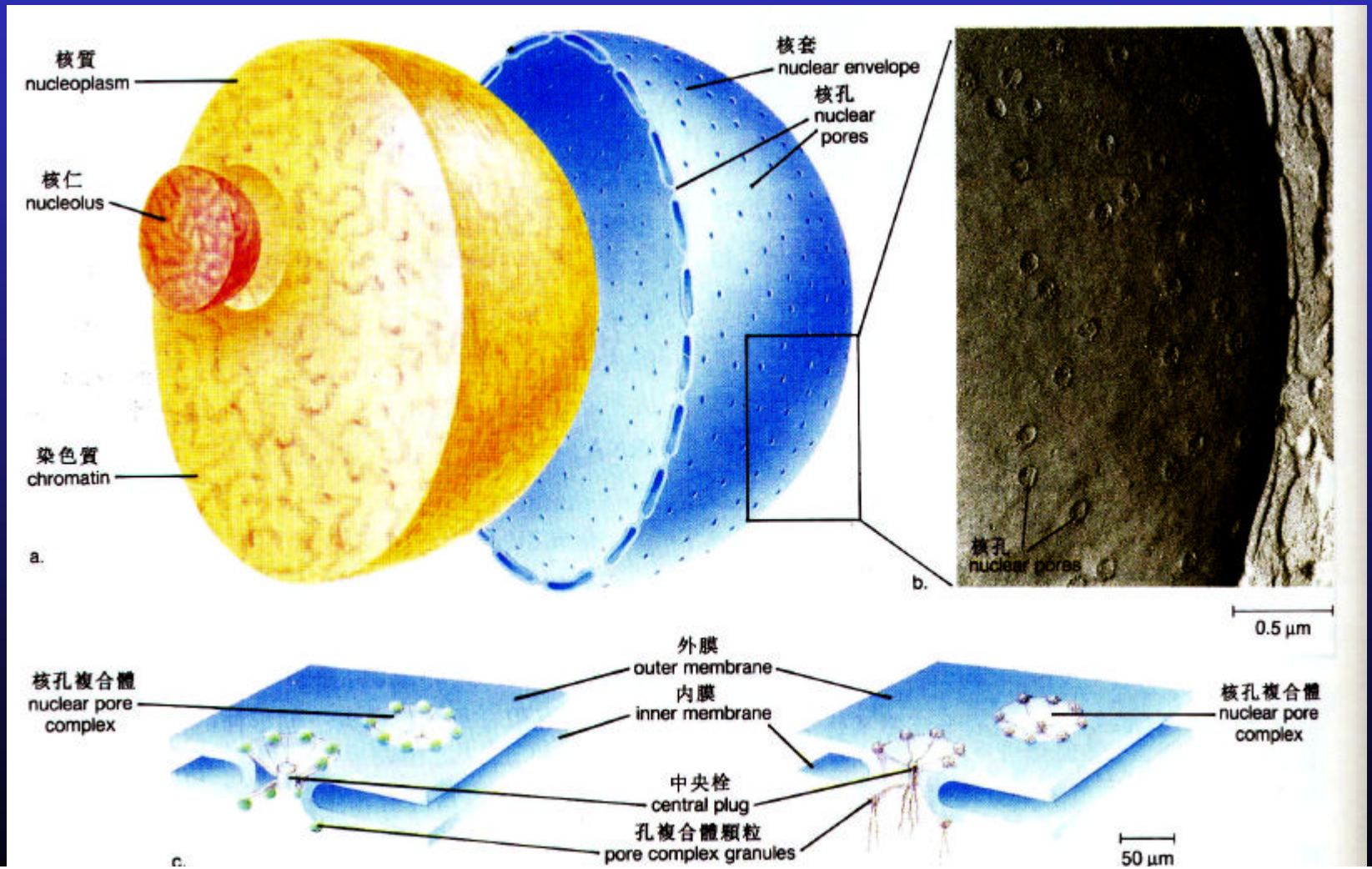
A semipermanent vesicle derived from ER, which contains the cell's hereditary apparatus and isolates it from the rest of the cell. It composes of:

- The Nuclear envelope: An encircling system of double membrane which defines the boundary of the nucleus.
  - Nculear pores: Shallow depressions on the envelope (50-80 nm apart), embedded with protein channels for passage of proteins and RNAs.

2. The nucleoplasm: The cell substance enclosed by thenuclear envelope (contains no ribosomesome)
3. Chromosomes: The DNA of eukaryotic cells are fragmented into several segments, each complexed with proteins.
   - Chromosomes of eukaryotic cells can be condensed into compact rods for ready movement during cell division and later unraveled and can no longer be distinguished individually with a light microscope.
4. Nucleolus: A dark region in the nucleus where very active rRNA (ribosomal synthesis is taking place)

細胞核(Nucleus)

細胞核為細胞的調控中樞，其內部包含攜帶遺傳訊息的DNA，其結構圖大致如下。



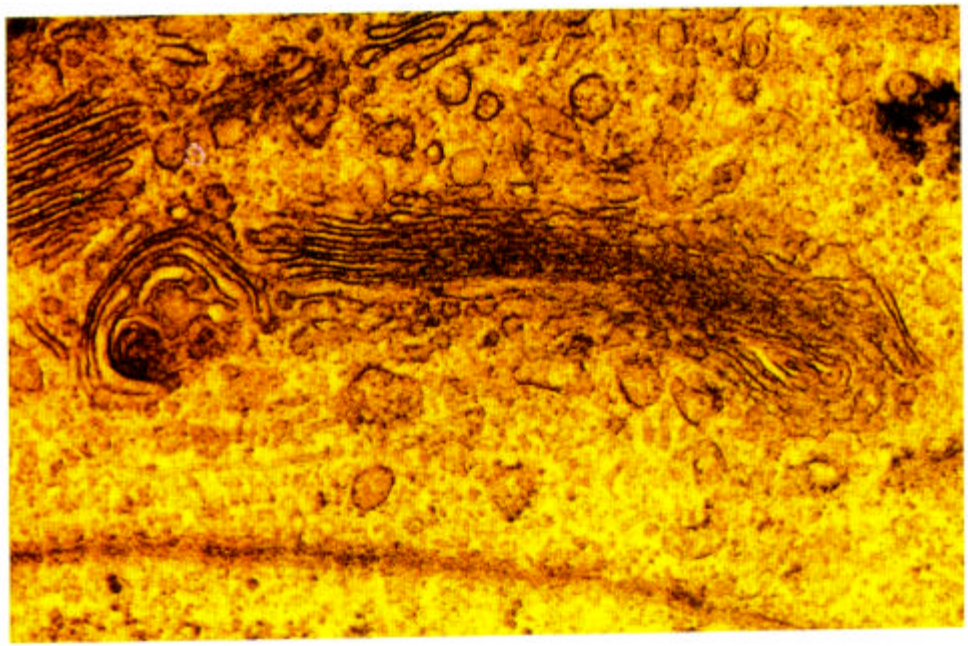
電子顯微鏡下所看到的細胞核，主體為看似細小顆粒狀，其實為線狀物質的染色質(chromatin)，而染色質有時會盤繞成桿狀結構稱為染色體(chromosome)。染色質內主要含有DNA、蛋白質及一些RNA等。

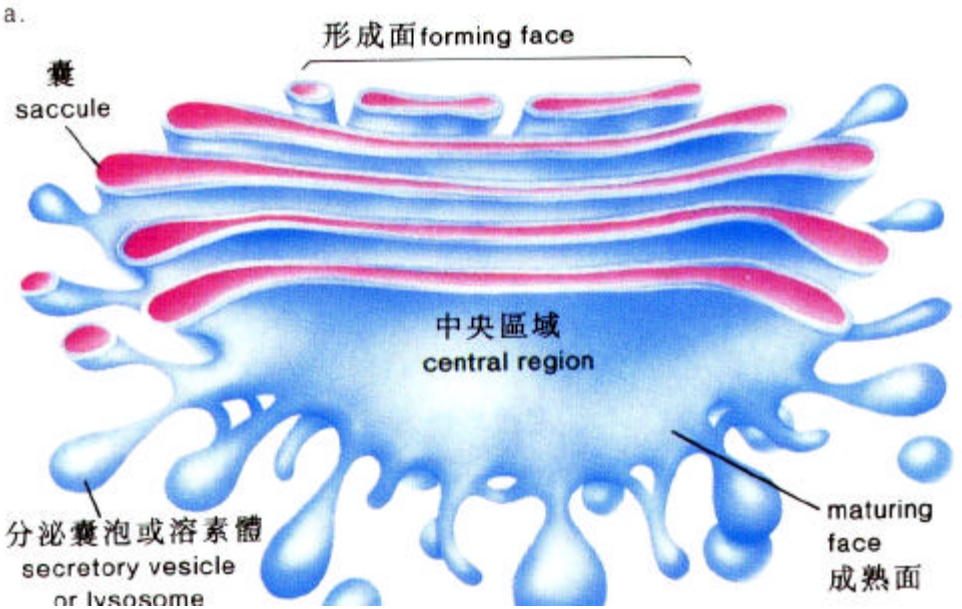
仔細瞧電顯影像時，不難發現會有一或二個顏色較深稱為核仁(nucleoli)的區域。核仁集中的產生另一種不同的RNA (ribosomal RNA or rRNA)，為細胞內核糖體主要的生產中心。

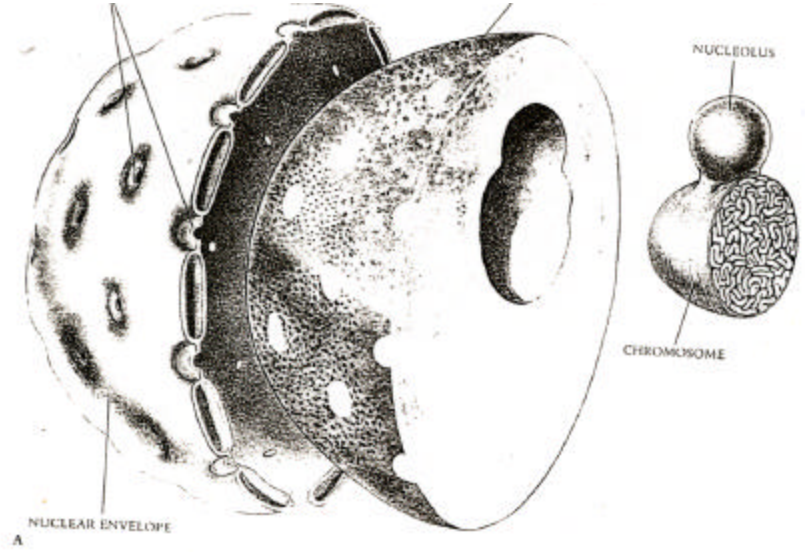
核套(nuclear envelope)區隔了細胞核與細胞質，主要為控管細胞核物質的進出。核套為雙薄膜結構，而其外層膜連接內質網(ER)。核套上有許多大小約50到80nm的孔洞，洞中間填滿了蛋白質以控管出入。其主要管制為允許能形成細胞核結構（或催化其形成）的蛋白質進入，讓已成形的RNA（或含相關蛋白質）出去。

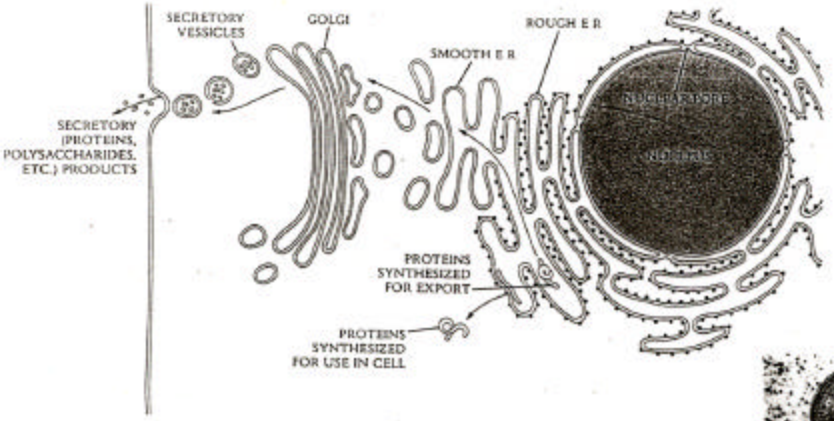
高爾基體(Golgi Appartus)

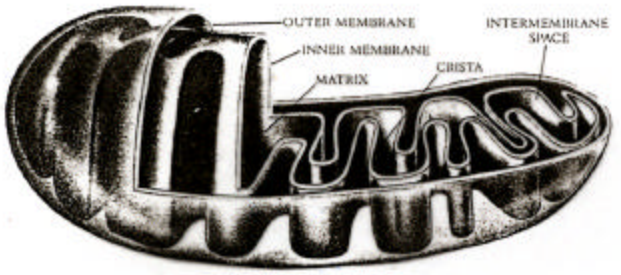
高爾基體的外觀類似一層層疊在一起的燒餅，於其囊系末端存有許多囊泡。高爾基體為細胞內分泌系統的一環，主要的功能在於加工分子，並予以包裝運輸到所需的地點。植物細胞的高爾基體提供物質，在細胞分裂時形成新的細胞壁與細胞膜。

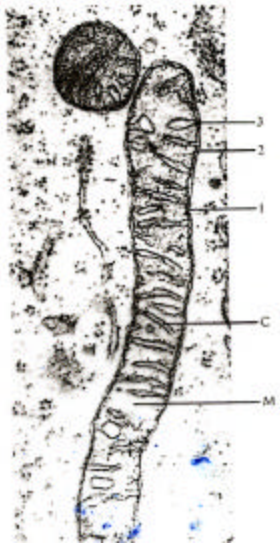





NUCLEOLUS
CHROMOSOME
NUCLEAR ENVELOPE
A


SECRETORY VESICLES
GOLGI
ROUGH E R
SMOOTH E R
SECRETORY (PROTEINS, POLYSACCHARIDES, ETC.) PRODUCTS
PROTEINS SYNTHESIZED FOR EXPORT
PROTEINS SYNTHESIZED FOR USE IN CELL


OUTER MEMBRANE
INNER MEMBRANE
MATRIX
CRISTA
INTERMEMBRANE SPACE


3
2
1
C
M

(3). The Golgi Complex (Aparatus) :

A collection of Golgi bodies which are flattened stacks of membrane derived from E.R.

- Function in the collection, packaging, and distribution of molecules synthesized elsewhere in the cell (Cell delivery system).

Advantages:

- They provide exist for the cells.
- They facilitate growth of the cell
- They isolate certain enzymes within cacs (microbodies).

(4) Microbodies:

(1). Lysosomes: Vesicles that contain in a concentrates mixture digestive enzymes of the cell. (lipases, proteases, lysozymes, nucleases)

(2). Peroxisome: Vesicles containing oxidative enzymes.

(3). Glyoxysomes: Vesicles containing enzymes for converting fat into carbohydrates, present only in plants

溶素體(Lysosome)

溶素體為由高爾基體製造的覆膜囊泡，內含水解消化酵素。

有時巨型分子藉由質膜所形成囊泡進入細胞時，溶素體能與這些囊泡融合，利用其酵素將之消化成較簡單的次單元。

(5). Relict Symbions: :

(1). Mitochondria Microbodies (Not derived from ER):

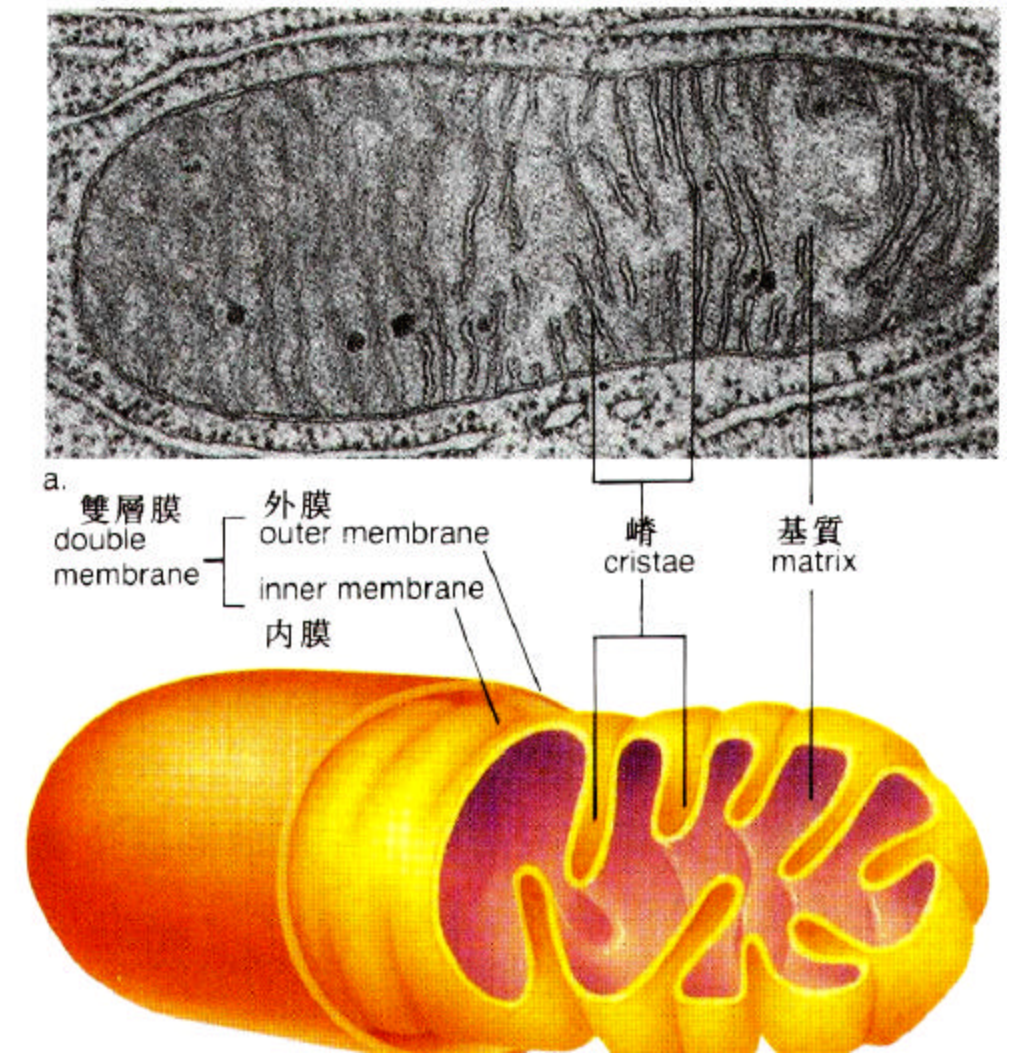
1. Long tubular shape of 1-3 microns.
2. Bounded by two membrane, the outer m.b. is similar to plasma m.b., the inner m.b. folds into lamellae which partition the mitochondria into "Cristae',
3. Mitochondria is cell "Power plant" and is the site of aerobic respiration (Oxidative phosphorylation) to produce ATP.
4. It maintains a circular DNA, encoding proteins and small RNA and robosomal components for producing essential proteins.
5. Mitochondria is capable of undergo division to produce new mictochondria. Most of the components required to assemble a new mitochondria are encoded as genes within the eukaryotic nucleus.

(2). Chloroplasts (葉綠體): The plant equivalent of mitochondria. It contains chlorophyl (葉綠素).

粒線體(Mitochondria)

粒線體為細胞行有養呼吸的地方，為細胞最主要的能量製造產生中心。相當於植物體的葉綠體(chloroplasts)。

粒線體為雙層膜包覆體，直徑約在0.5-1.0μm之間，長度約為7 μm。由於原始真核細胞並無與能量相關的胞器，故有學說認為粒線體為原核生物的子孫，它們與真核細胞形成共生的關係。



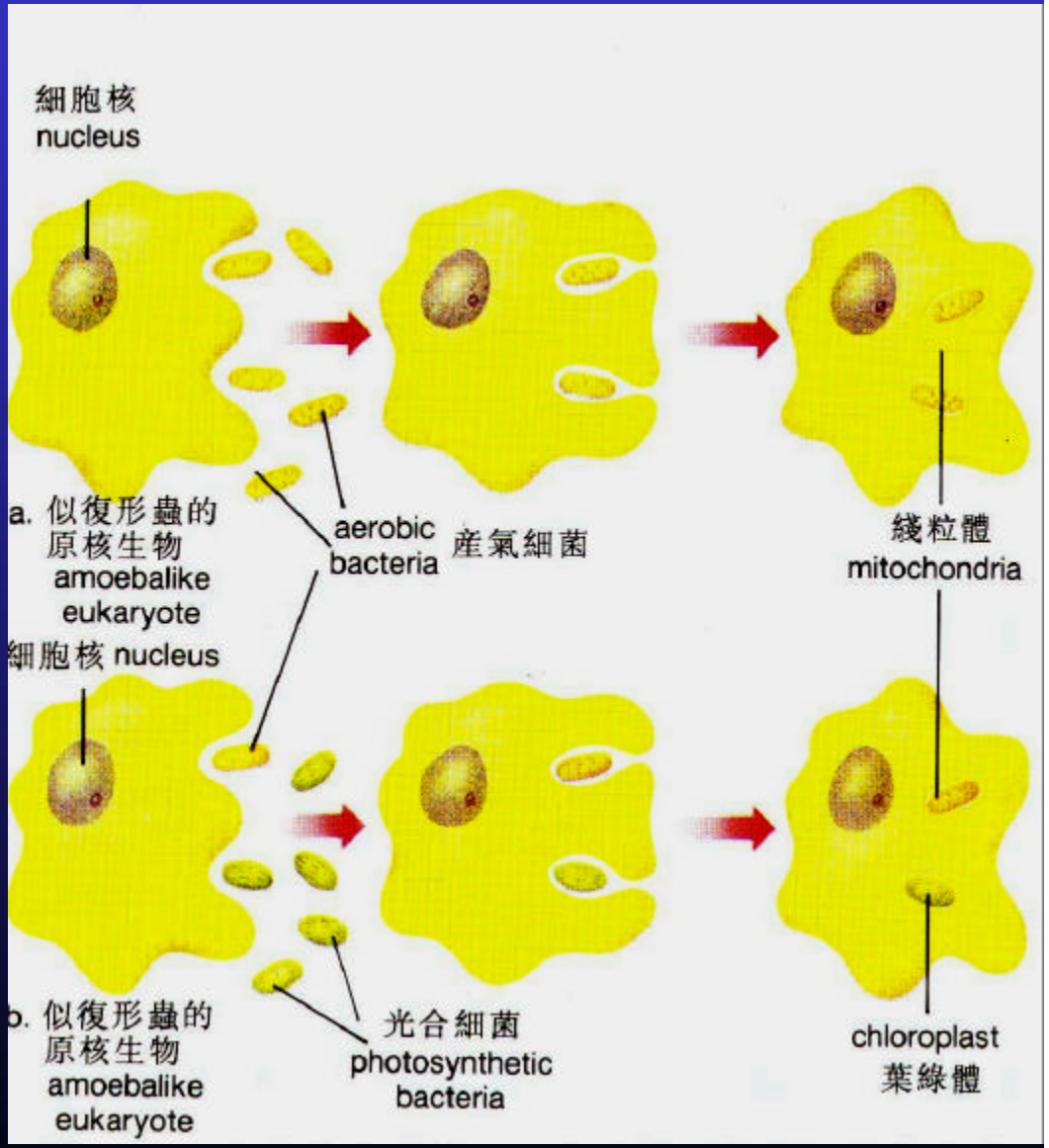
粒線體與真核細胞共生學說所依據的主要證據為

一、其大小與細菌類似

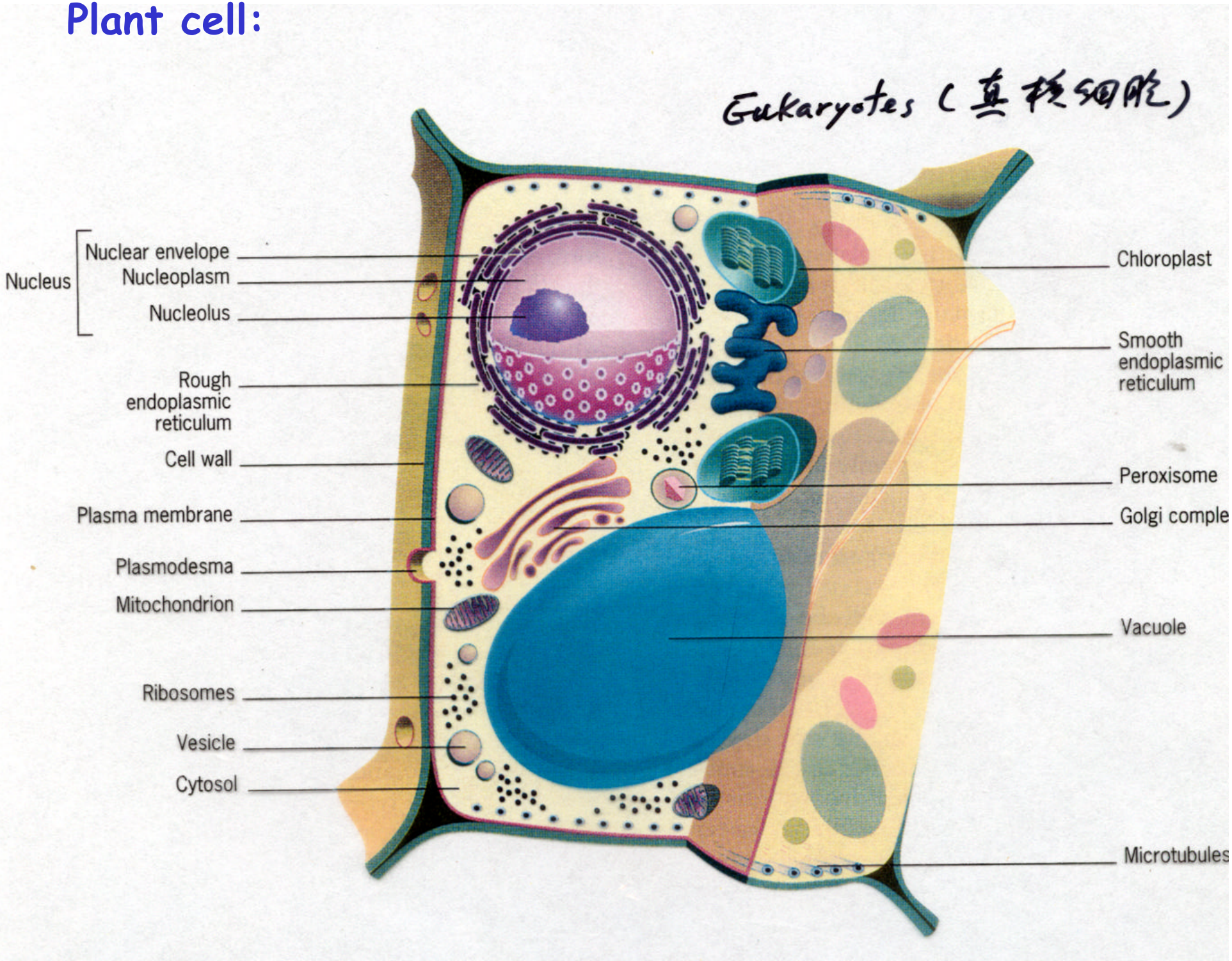
二、雙層膜結構：外膜可能源自吞食之包囊。

三、具自我再生能力：粒線體含有有限量的基因物質，其DNA與細菌類似.

四、雖然多數的粒線體蛋白質為宿主所提供，但是它具有自己能製造蛋白質的核醣體。



Plant cell:


Eukaryotes (真核细胞)
Nucleus
Nuclear envelope
Nucleoplasm
Nucleolus
Rough endoplasmic reticulum
Cell wall
Plasma membrane
Plasmodesma
Mitochondrion
Ribosomes
Vesicle
Cytosol
Chloroplast
Smooth endoplasmic reticulum
Peroxisome
Golgi comple
Vacuole
Microtubules

A comparison of prokaryotic and Eukaryotic Cells:

(1). Features held in common by the two types of cell:

1. Plasma membrnane of similar construction.
2. Genetic information encoded in DNA using identical genetic code.
3. Similar mechanisms for transcription and translation of genetic information, including similar ribosomes.
4. Shared apparatus for conservation of chemical energy as ATP (located in plasma membrane of prokaryotes and the mitochondria membrane of eukaryotes).
5. Similar mechanism for synthesizing and inserting membrane proteins.
6. Proteosomes (protein digesting structures) of similar construction (between archaebacteria and eukaryotes)

(2). Features of eukaryotic cells not found in prokaryotes:

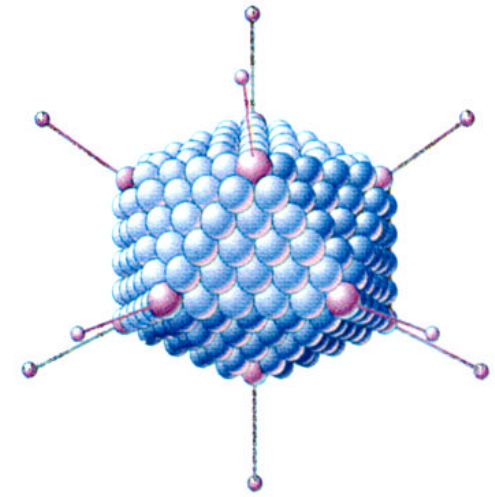
1. Division of cells into nucleus and cytoplasm, separated by a nuclear envelope containing complex pore structures.
2. Complex chromosomes composed of DNA and associated proteins that are capable of compacting into mitotic structure
3. Complex membraneous cytoplasmic organelles (includes endoplasmic reticulum, Golgi complex ….. Etc).
4. Specialized cytoplasmic organelles for aerobic respiration (mitochondria) and photosynthesis (Chloroplasts).
5. Complex cytoskeletal system.
6. Complex flagella and cilia.
7. Capable of ingesting fluid and particulate material by enclosu within plasma membrane vesicles (endocytosis and phagocytosi
8. Cellulose-containing fluid walls (in plant).
9. Cell division utilizing a microtubule-containing mitotic spindle that separate chromosomes.
10. Presence of two copies of genes per cell (diploidy), one from each parent.
11. Sexual reproduction requiring meiotic and fertilization.

Virus: Small oblitory intracellular parasites which cannot reproduce by themselves unless present within the host cells, which, depending on the specific virus, may be a plant, animal Or bacteriz cells.

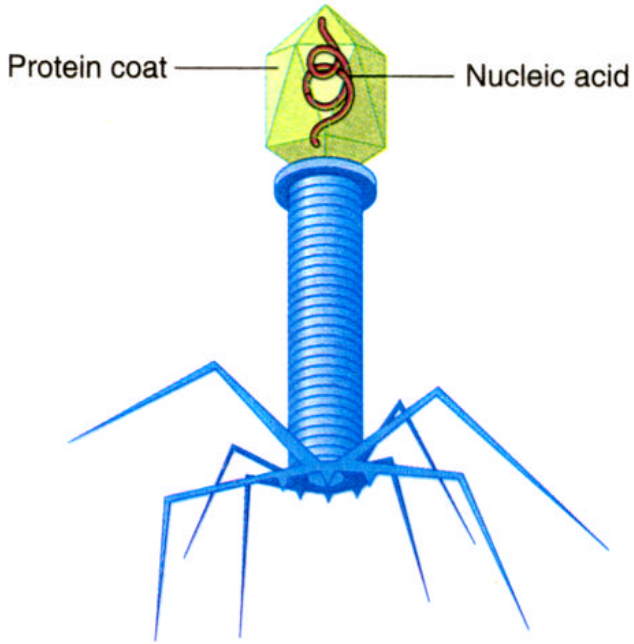
1. Outside the cell viruses exist as "virions".
2. Virions contain a small amount of genetic material which can be DNA (single or double stranded) or RNA.
3. The virion DNA or RNA may code for few to few hundreds of proteins.
4. The genetic material is surrounded by a protein capsule, or "capsid", which is generally made up of a specificc number of subunits organized into a polyhedron.
5. Virions are molecular aggregates which by themselves are unable to reproduce, metobolize or carry out activities associated with life.
6. Most virus infect only specific types of hosts.
7. Modes of infections: (i) Taken over the host cell machinery leading to the death of host cell: (ii) Insert its DNA into host cell chromosomal DNA to become provius.

Viroid: The simplest pathogents consisting of small circular RNA molecul that totally lack a protein coat.

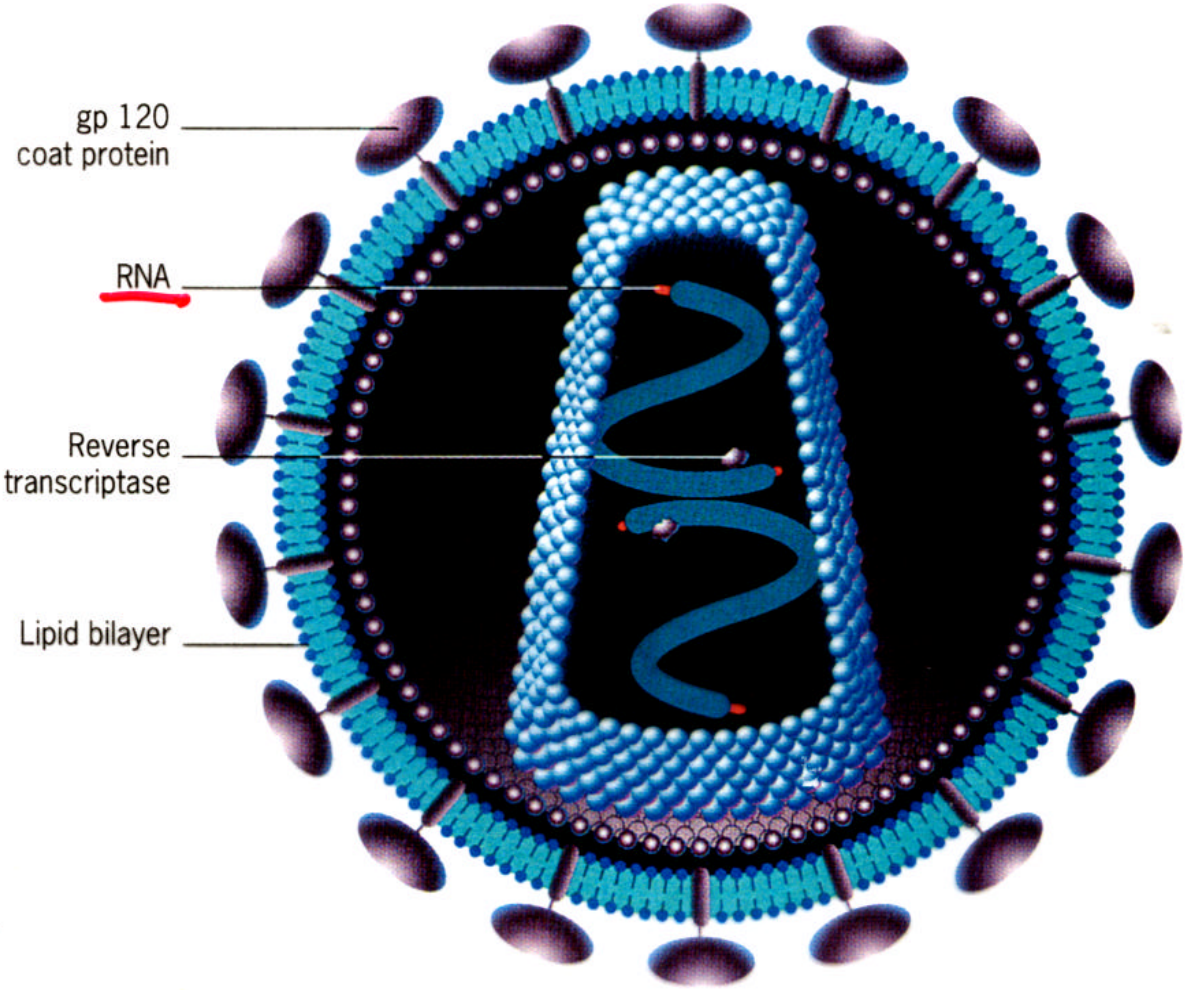
AIDS



(a)



(c)



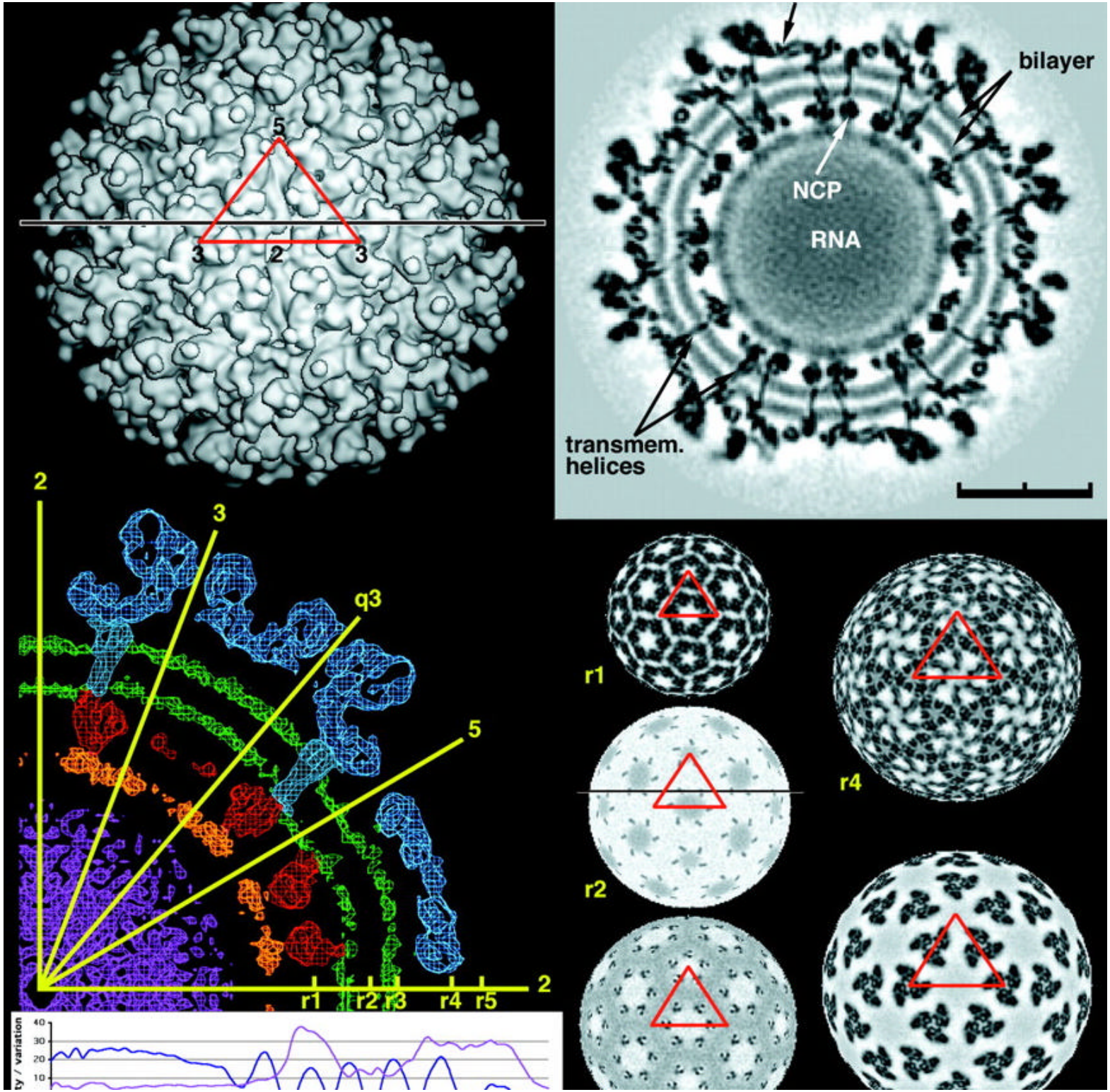
(b)

FIGURE 1.21 • **Virus diversity.** The structures of *(a)* an adenovirus, *(b)* a human immunodeficiency virus (HIV), and *(c)* a T-even bacteriophage.

AIDS !

感冒

SARS


5
3
2
3
bilayer
NCP
RNA
transmem.
helices
2
3
q3
5
2
r1
r2
r3
r4
r5
r1
r4
r2