1
Organizzazione, diversità e funzioni cellulari

2
Metodi di studio
e
Sistemi sperimentali

Table 1–1 Historical Landmarks in Determining Cell Structure

1665	Hooke uses a primitive microscope to describe small pores in sections of cork that he calls "**cells**."
1674	Leeuwenhoek reports his discovery of **protozoa**. Nine years later, he sees **bacteria** for the first time.
1833	Brown publishes his microscopic observations of orchids, clearly describing the cell **nucleus**.
1838	Schleiden and Schwann propose the **cell theory**, stating that the nucleated cell is the universal building block of plant and animal tissues.
1857	Kölliker describes **mitochondria** in muscle cells.
1879	Flemming describes with great clarity **chromosome behavior during mitosis** in animal cells.
1881	Cajal and other histologists develop staining methods that reveal the structure of **nerve cells** and the organization of neural tissue.
1898	Golgi first sees, and describes, the **Golgi apparatus** by staining cells with silver nitrate.
1902	Boveri links **chromosomes and heredity** by observing chromosome behavior during sexual reproduction.
1952	Palade, Porter, and Sjöstrand develop methods of **electron microscopy** that enable many intracellular structures to be seen for the first time. In one of the first applications of these techniques, Huxley shows that muscle contains arrays of protein filaments—the first evidence of a **cytoskeleton**.
1957	Robertson describes the bilayer structure of the **cell membrane**, seen for the first time in the electron microscope.
1960	Kendrew describes the first detailed **protein structure** (sperm whale **myoglobin**) to a resolution of 0.2 nm using **X-ray crystallography**. Perutz proposes a lower-resolution structure for **hemoglobin**.
1968	Petran and collaborators make the first **confocal microscope**.
1974	Lazarides and Weber develop the use of **fluorescent antibodies** to stain the cytoskeleton.
1994	Chalfie and collaborators introduce **green fluorescent protein** (GFP) as a marker in microscopy.

- **Tutti gli organismi sono composti da 1 o piu' cellule**
- **La cellula e' l'unita' strutturale della vita**

Cellula: unità fondamentale organismi viventi

Diversità
- forme
- organizzazione
  - unicellulare
  - pluricellulare

Costanza
- funzioni cellulari
- meccanismi molecolari

Cellula: unità fondamentale organismi viventi

Diversità
- **forme**
- **organizzazione**
  - **unicellulare**
  - **pluricellulare**

Costanza
- **funzioni cellulari**
- **meccanismi di base**

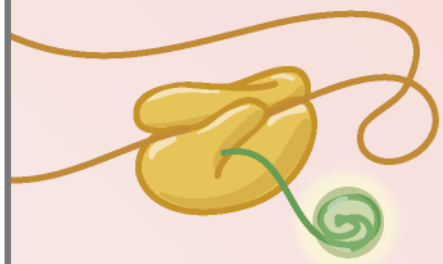
Proprietà essenziali di una cellula

Membrana plasmatica

Separa la cellula dall'ambiente

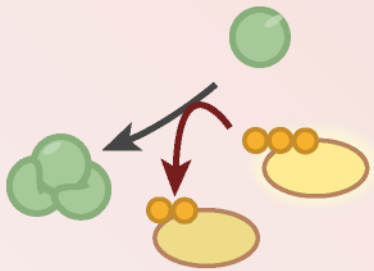
Genoma

Codifica tutte le strutture cellulari



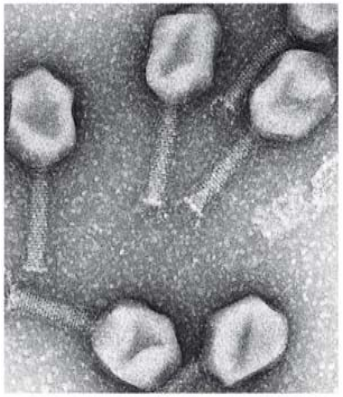
Trasferimento dell'informazione

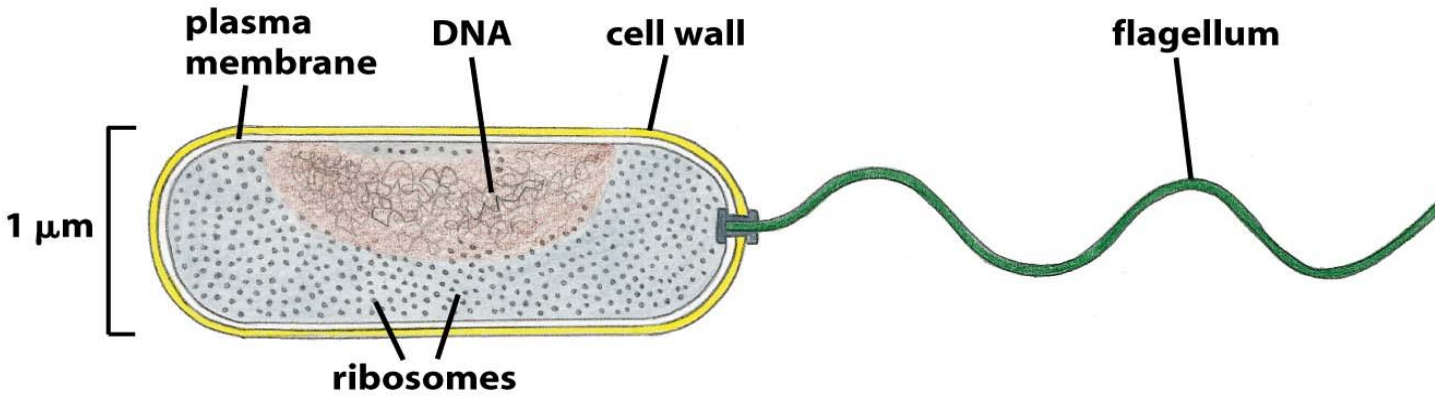
Esprime l'informazione immagazzinata nel codice genetico

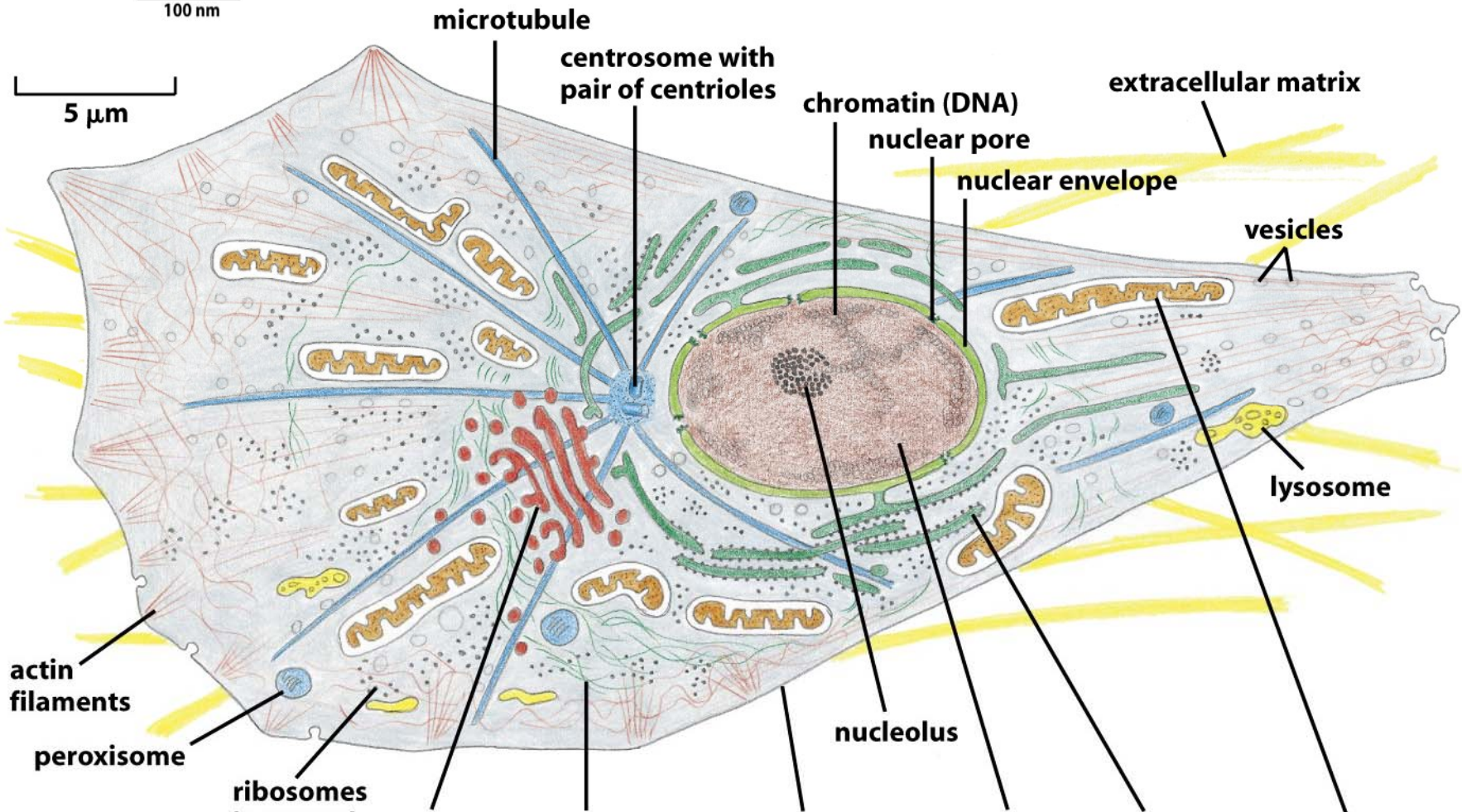


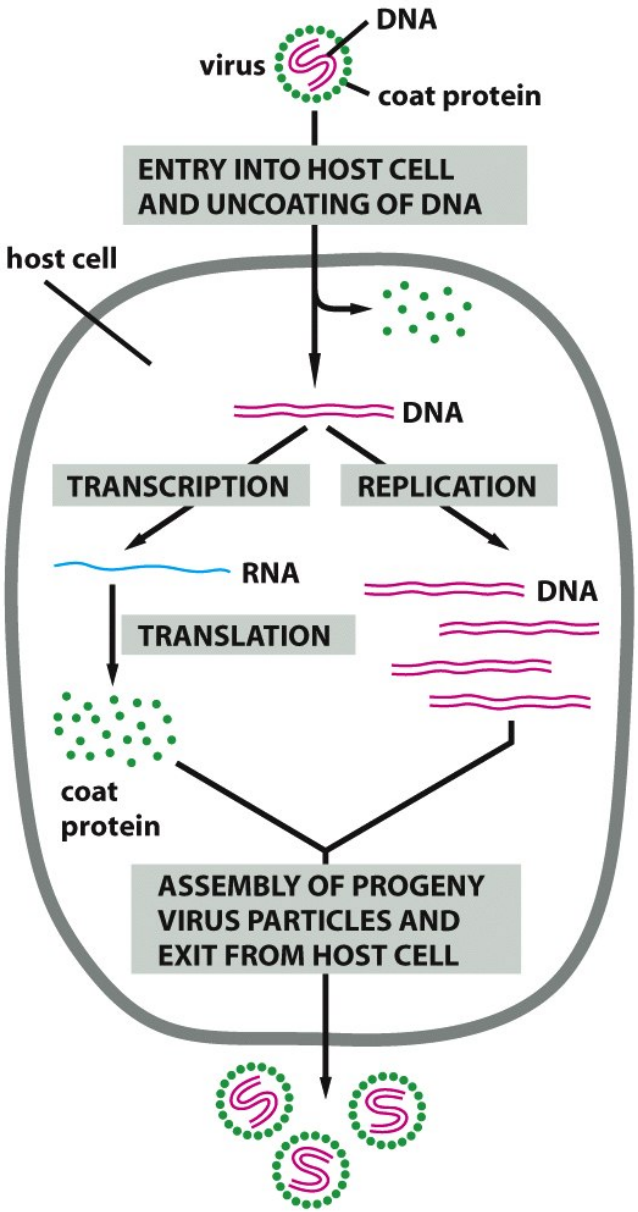
Utilizzazione dell'energia

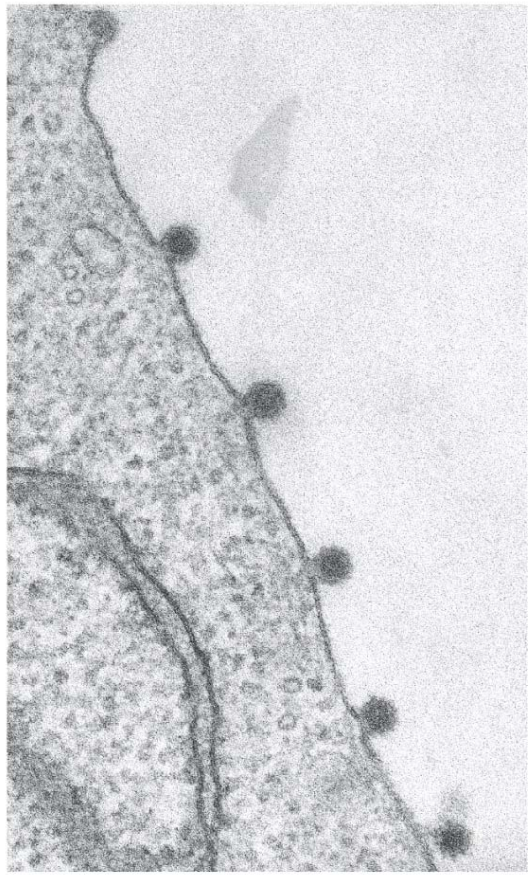
Raccoglie l'energia per formare componenti più complessi

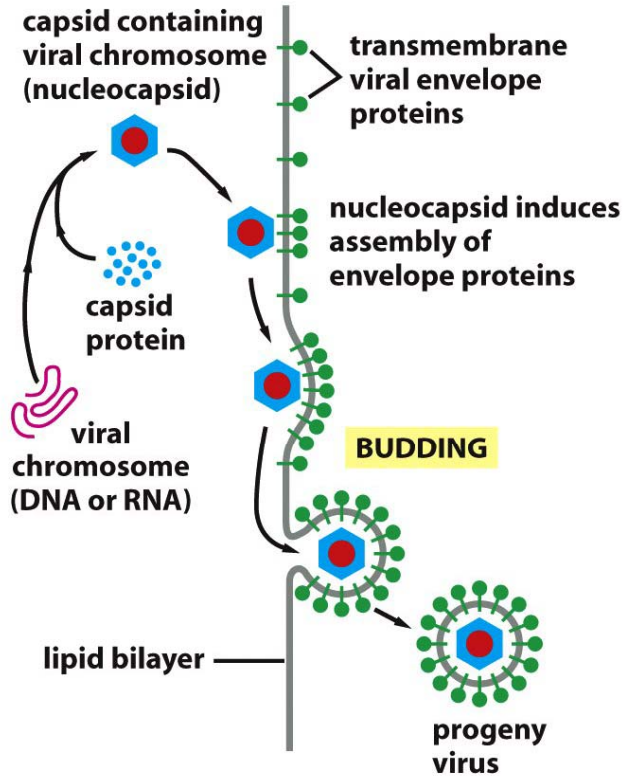

100 nm


plasma membrane
DNA
cell wall
flagellum
1 μm
ribosomes

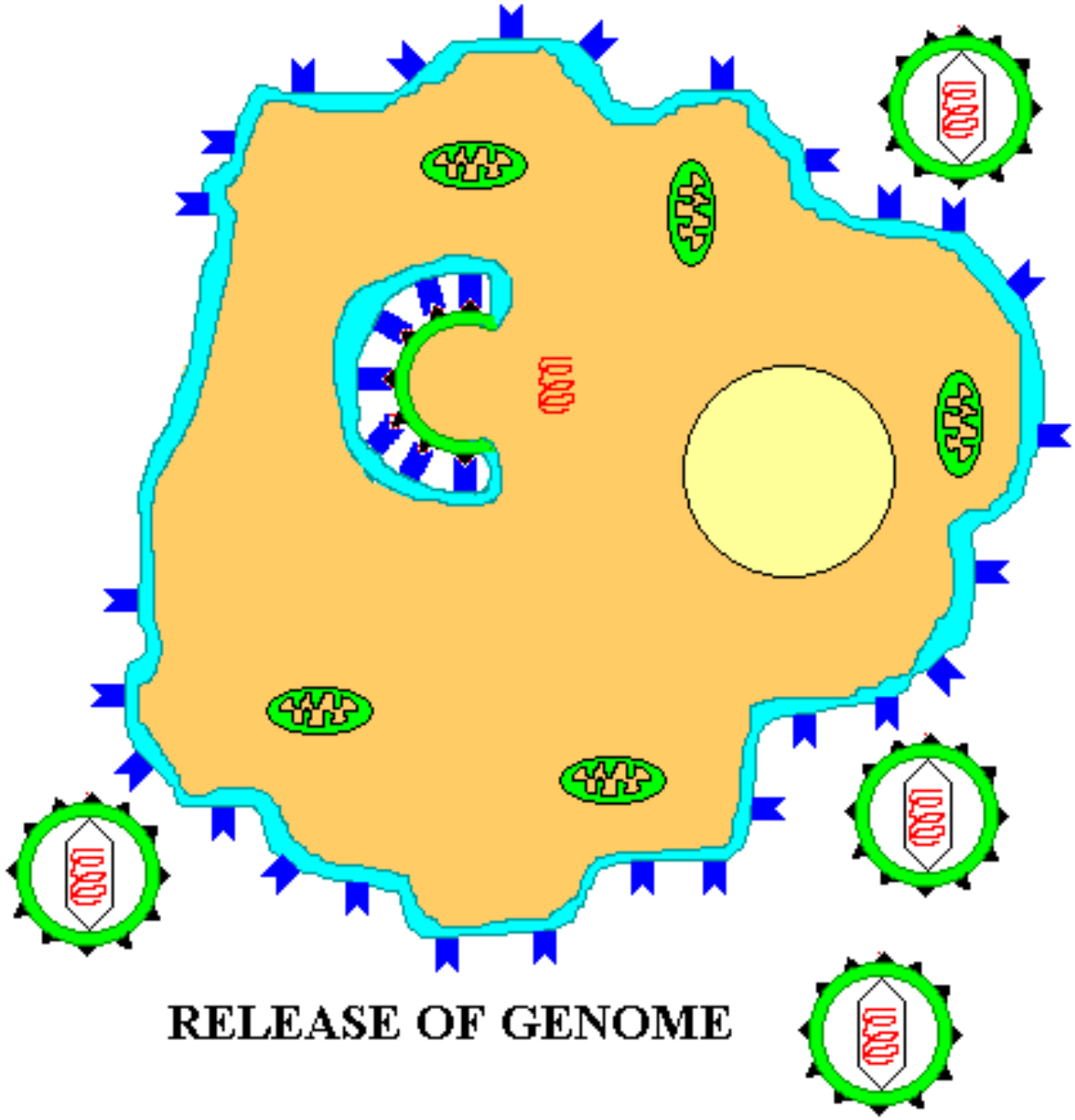

5 μm
microtubule
centrosome with pair of centrioles
chromatin (DNA)
nuclear pore
nuclear envelope
extracellular matrix
vesicles
lysosome
actin filaments
peroxisome
ribosomes
nucleolus


DNA
virus
coat protein
ENTRY INTO HOST CELL
AND UNCOATING OF DNA
host cell
DNA
TRANSCRIPTION
REPLICATION
RNA
DNA
TRANSLATION
coat
protein
ASSEMBLY OF PROGENY
VIRUS PARTICLES AND
EXIT FROM HOST CELL


(A)
100 nm


capsid containing
viral chromosome
(nucleocapsid)
transmembrane
viral envelope
proteins
nucleocapsid induces
assembly of
envelope proteins
capsid
protein
viral
chromosome
(DNA or RNA)
BUDDING
lipid bilayer
progeny
virus
(B)

START



RELEASE OF GENOME

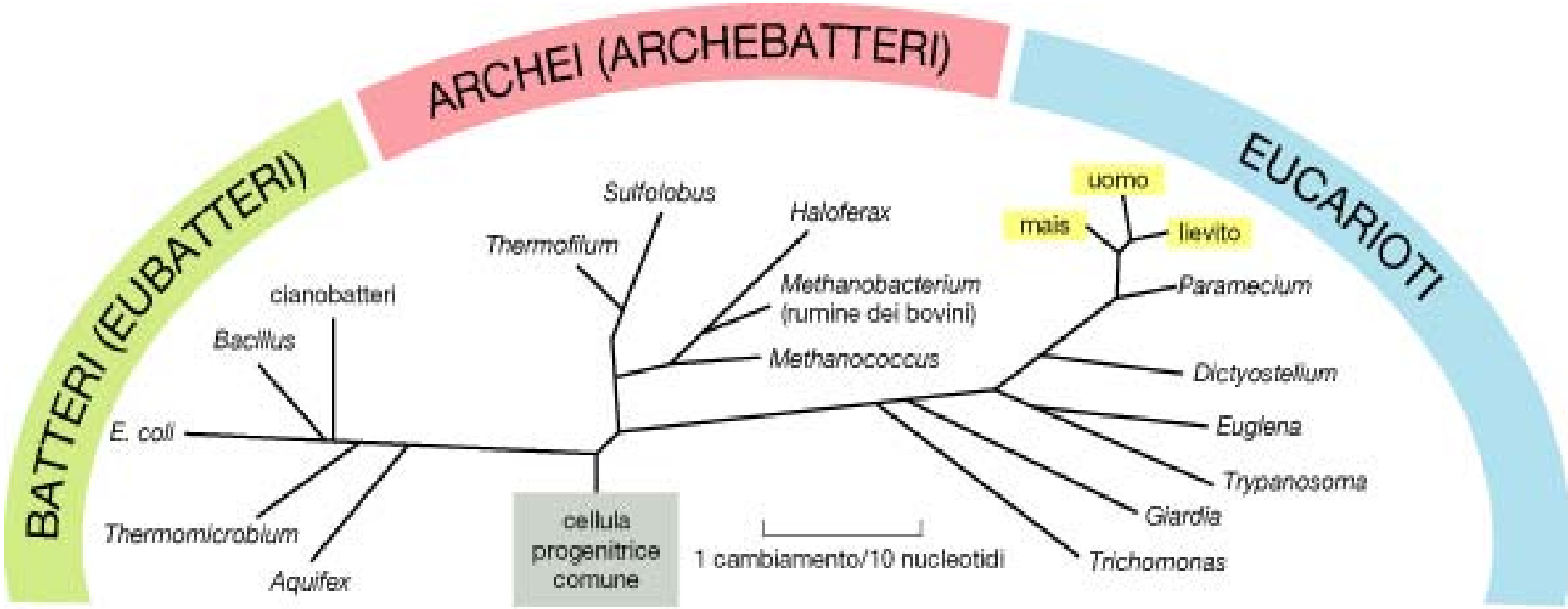
Varietà di forme e di organizzazione

Table 1. The six kingdoms of life and the 34 microbial phyla (based on Cavalier-Smith 1998, 2002*a*, 2003*a*,*b*).

empire PROKARYOTA (Cavalier-Smith 2002*b*)
- **kingdom Bacteria**
  - subkingdom Negibacteria (phyla Eobacteria, Sphingobacteria, Spirochaetae, Proteobacteria, Planctobacteria, Cyanobacteria)
  - subkingdom Unibacteria (phyla Posibacteria, Archaebacteria)

empire EUKARYOTA (Cavalier-Smith 1998)
- **kingdom Protozoa** (Cavalier-Smith 2002*a*, 2003*a*)
  - subkingdom Sarcomastigota (phyla Amoebozoa, Choanozoa)
  - subkingdom Biciliata
    - infrakingdom Rhizaria (phyla Cercozoa, Foraminifera, Radiozoa)
    - infrakingdom Excavata (phyla Loukozoa, Percolozoa, Euglenozoa, Metamonada; the latter now includes Parabasalia and Anaeromonadea; Cavalier-Smith 2003*a*,*b*)
    - infrakingdom Alveolata (phyla Myzozoa (Cavalier-Smith & Chao 2004), Ciliophora)
    - Biciliata incertae sedis: phylum Apusozoa (may be sister to Excavata); phylum Heliozoa[b]
- **kingdom Animalia** (Myxozoa and 21 other[a] phyla) (Cavalier-Smith 1998; Cavalier-Smith & Chao 2003*c*)
- **kingdom Fungi** (phyla Archemycota, Microsporidia, Ascomycota, Basidiomycota) (Cavalier-Smith 2000*b*)
- **kingdom Plantae**
  - subkingdom Biliphyta (phyla Glaucophyta, Rhodophyta)
  - subkingdom Viridaeplantae (Chlorophyta, Bryophyta[a], Tracheophyta[a])
- **kingdom Chromista**
  - subkingdom Cryptista (phylum Cryptista: cryptophytes, goniomonads, katablepharids)
  - subkingdom Chromobiota
    - infrakingdom Heterokonta (phyla Ochrophyta, Pseudofungi, Opalozoa (comprising subphyla Opalinata, Sagenista)
    - infrakingdom Haptista (phylum Haptophyta)

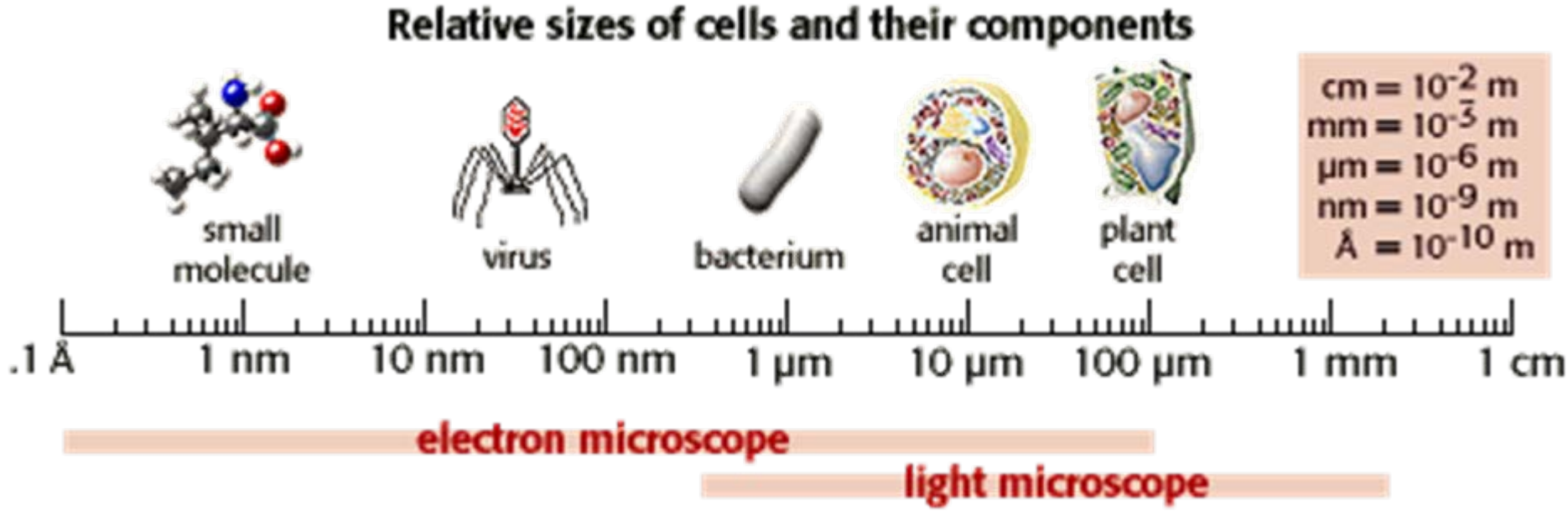
LE TRE PRINCIPALI DIVISIONI DEL MONDO VIVENTE

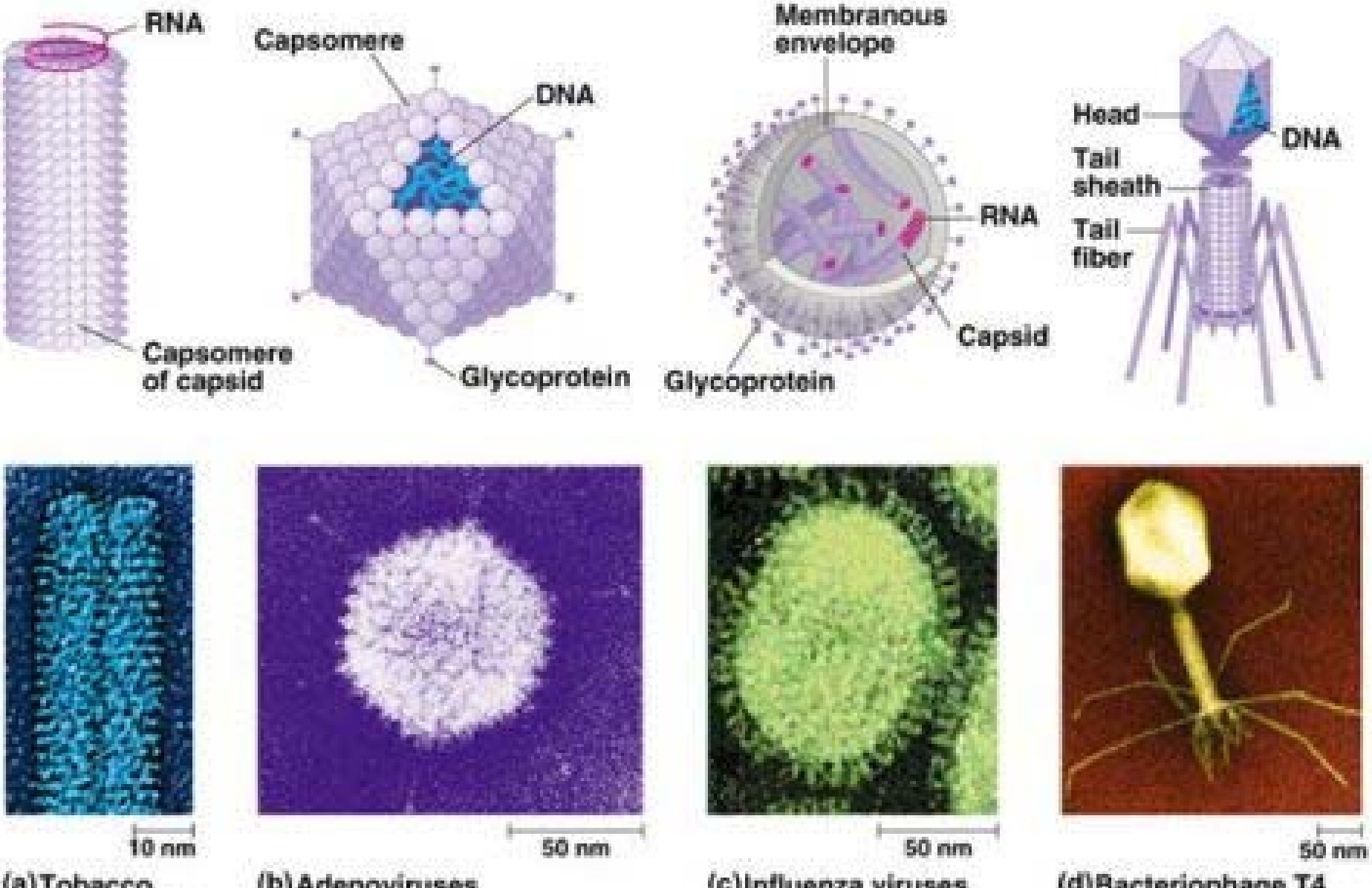


EUCARIOTI= VEGETALI, FUNGHI, ANIMALI

PROCARIOTI= BATTERI E ARCHEI

Dimensioni


Relative sizes of cells and their components
small molecule
virus
bacterium
animal cell
plant cell
cm = 10-2 m
mm = 10-3 m
µm = 10-6 m
nm = 10-9 m
Å = 10-10 m
.1 Å
1 nm
10 nm
100 nm
1 µm
10 µm
100 µm
1 mm
1 cm
electron microscope
light microscope

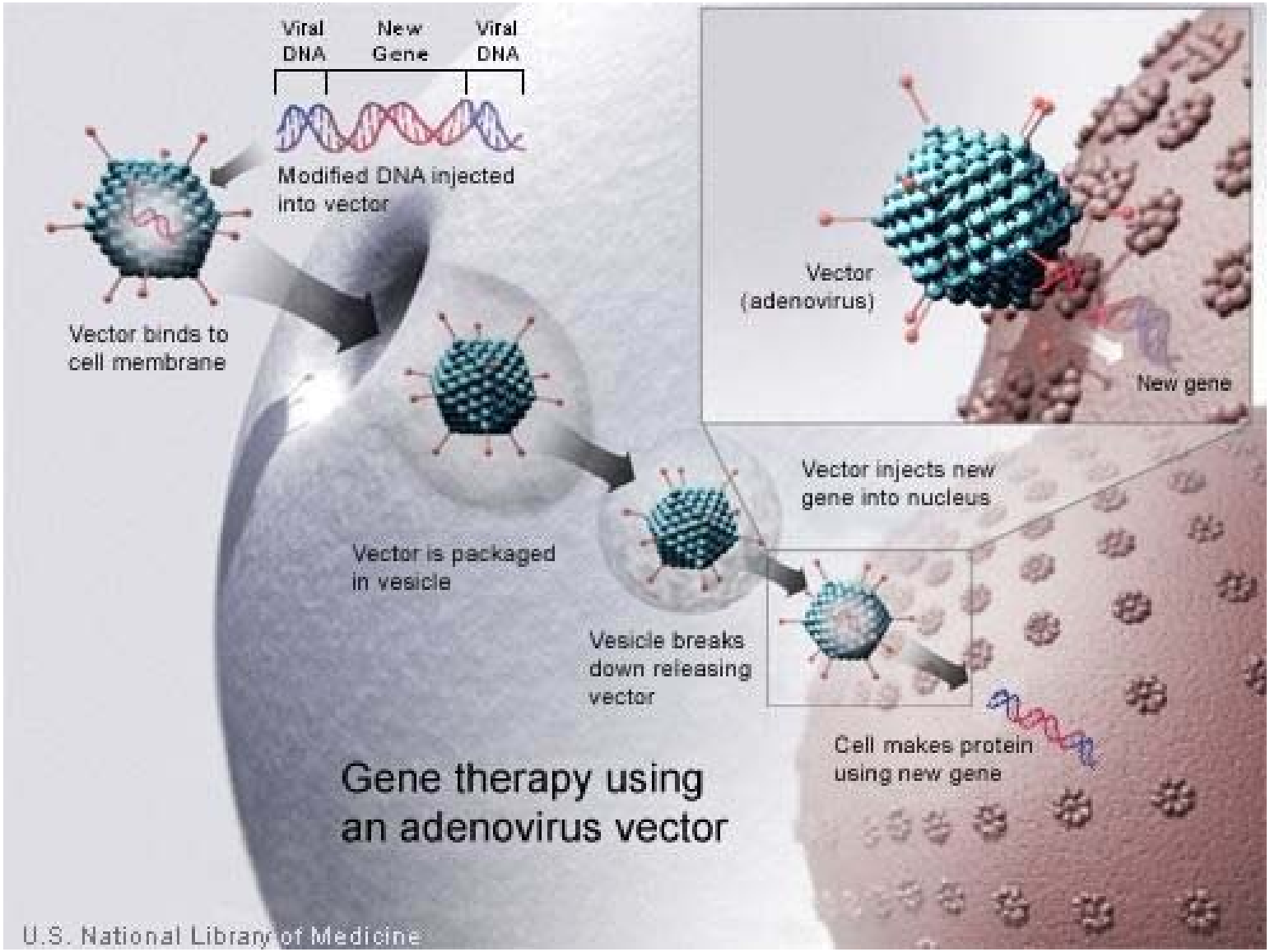


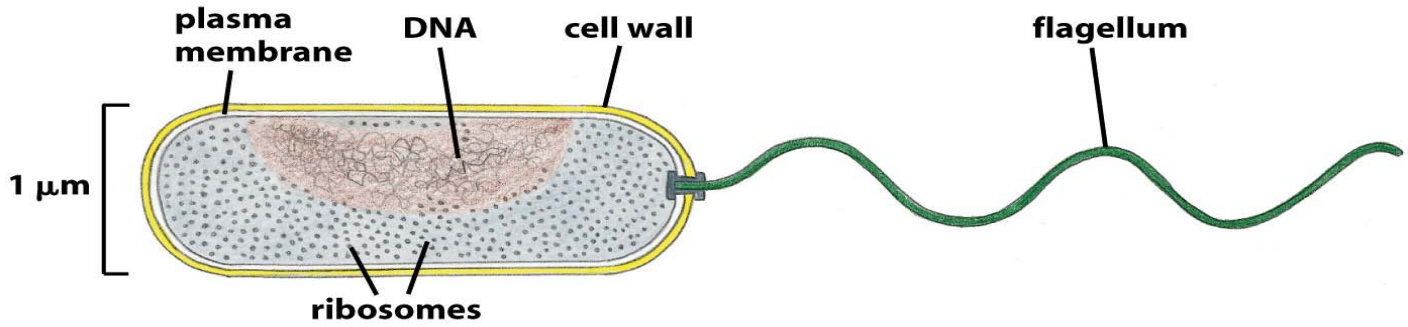
(a) Tobacco mosaic virus

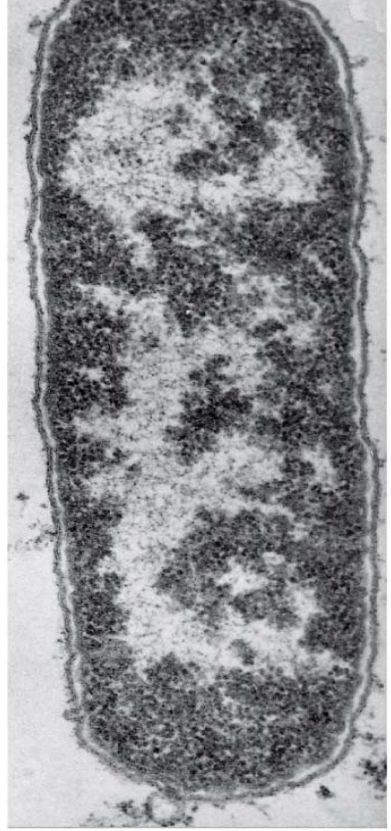
(b) Adenoviruses

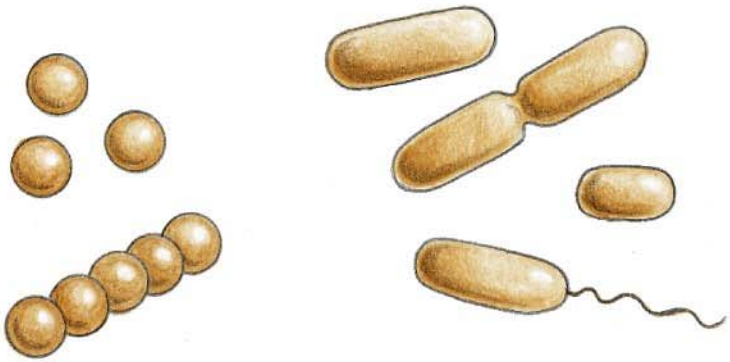
(c) Influenza viruses

(d) Bacteriophage T4


Viral DNA
New Gene
Viral DNA
Modified DNA injected into vector
Vector binds to cell membrane
Vector (adenovirus)
New gene
Vector injects new gene into nucleus
Vector is packaged in vesicle
Vesicle breaks down releasing vector
Cell makes protein using new gene
Gene therapy using an adenovirus vector
U.S. National Library of Medicine



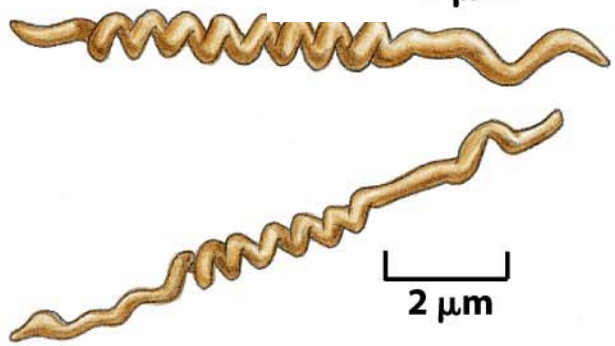




spherical cells
e.g., *Streptococcus*

rod-shaped cells
e.g., *Escherichia coli, Vibrio cholerae*

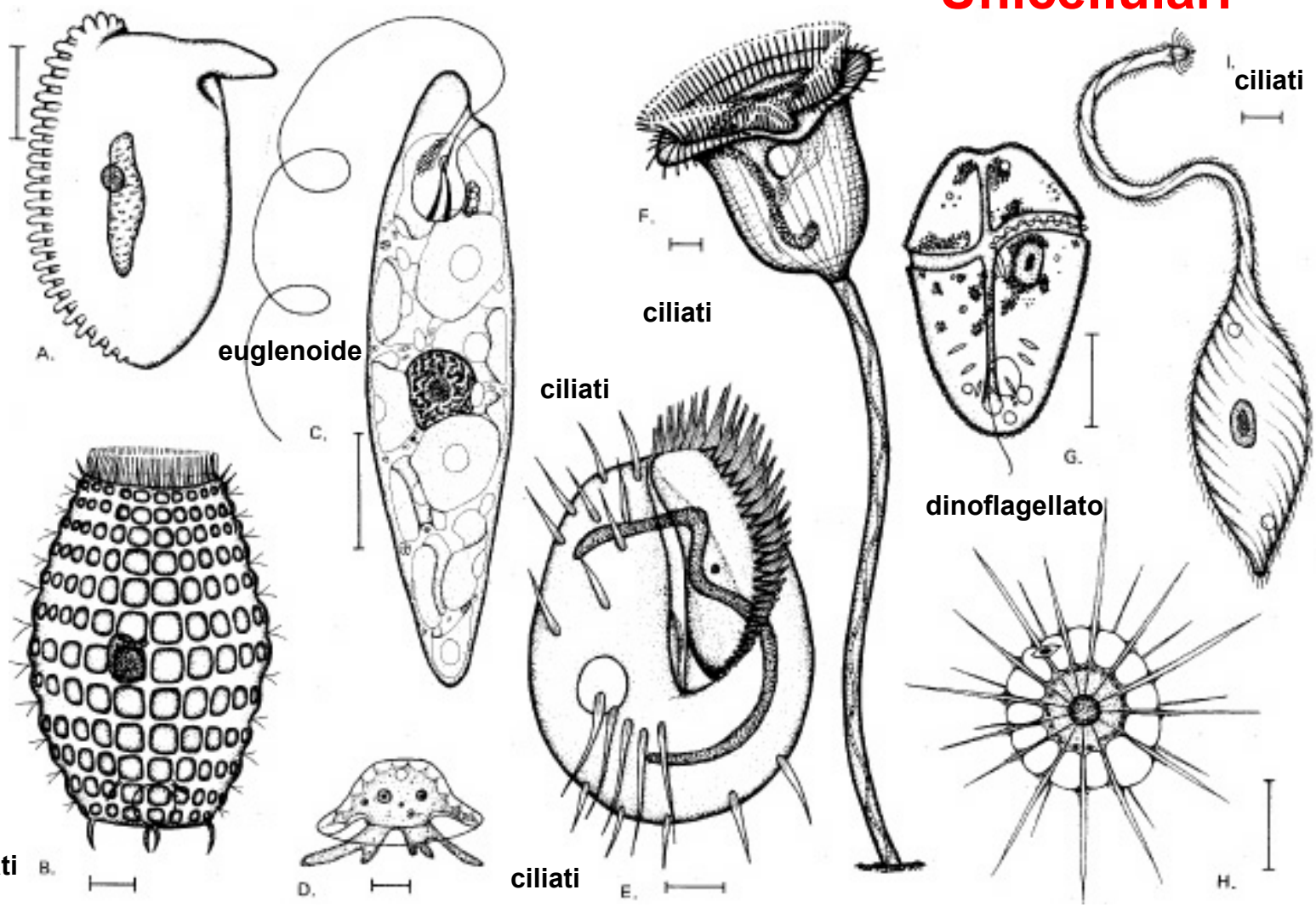
the smallest cells
e.g., *Mycoplasma, Spiroplasma*



spiral cells
e.g., *Treponema pallidum*

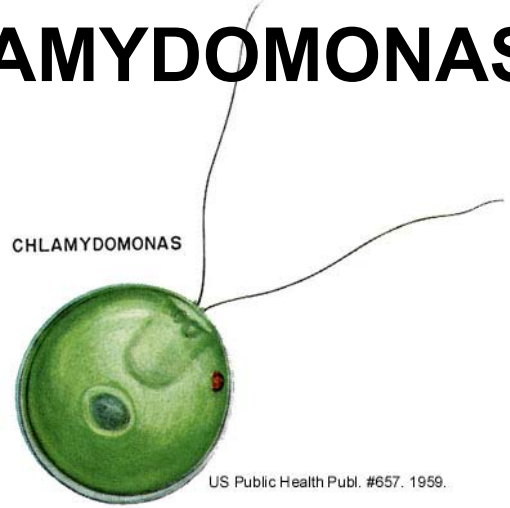
I PROTISTI

Eucarioti Unicellulari

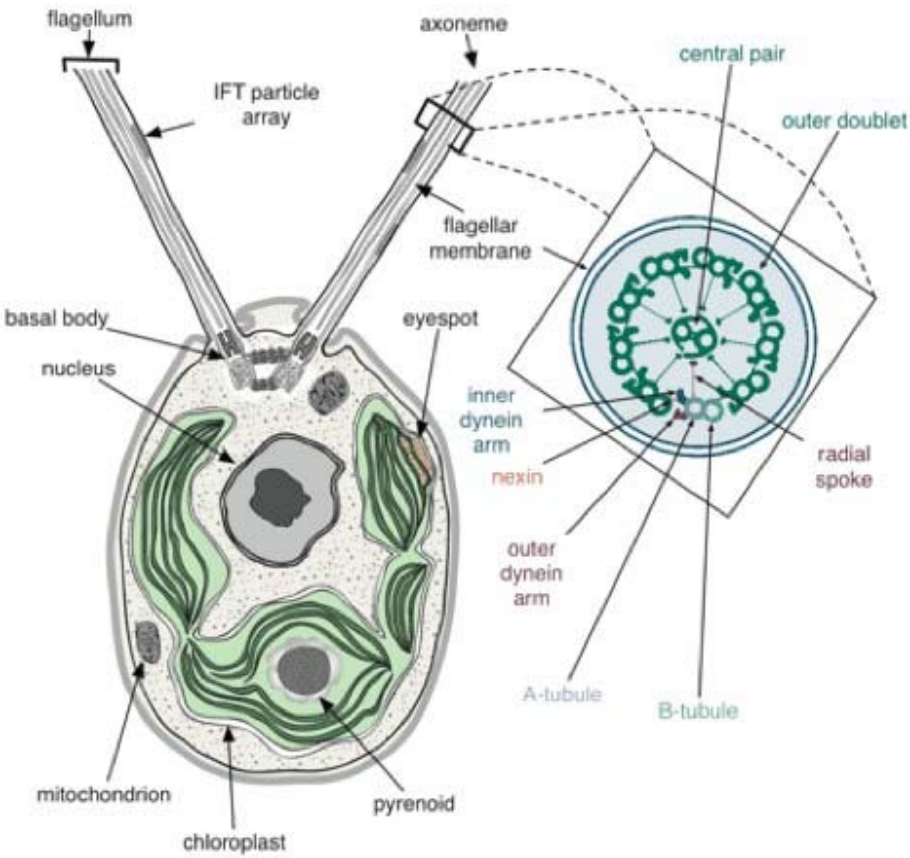


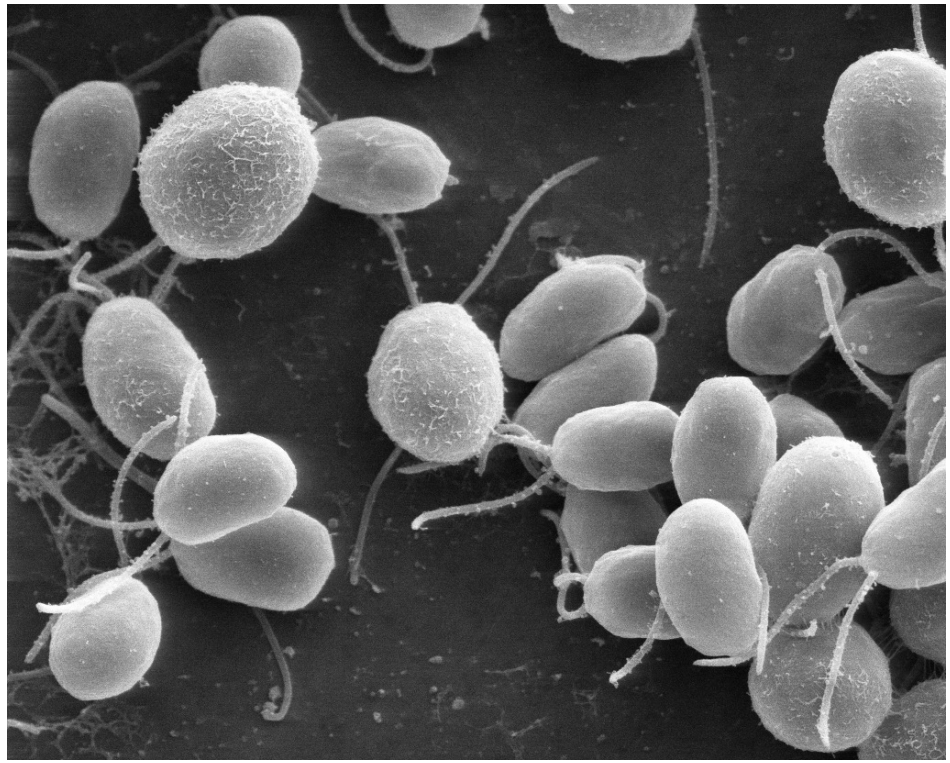
Unicellulari ma presentano specializzazioni del protoplasma in organelli

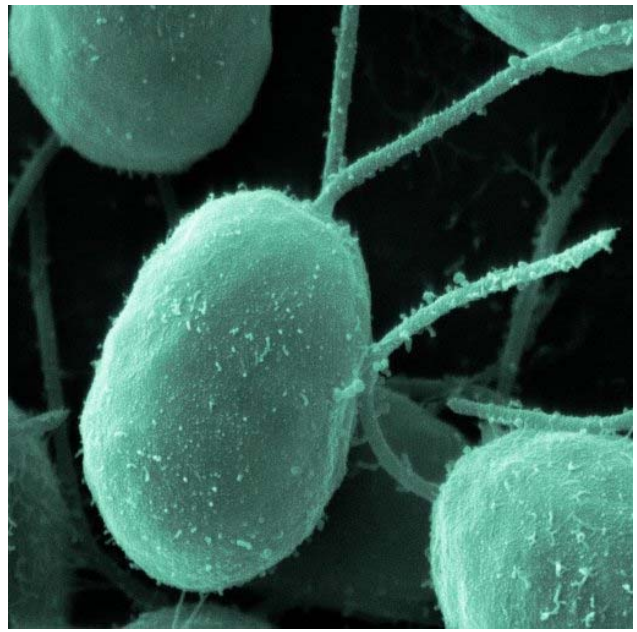
CHLAMYDOMONAS



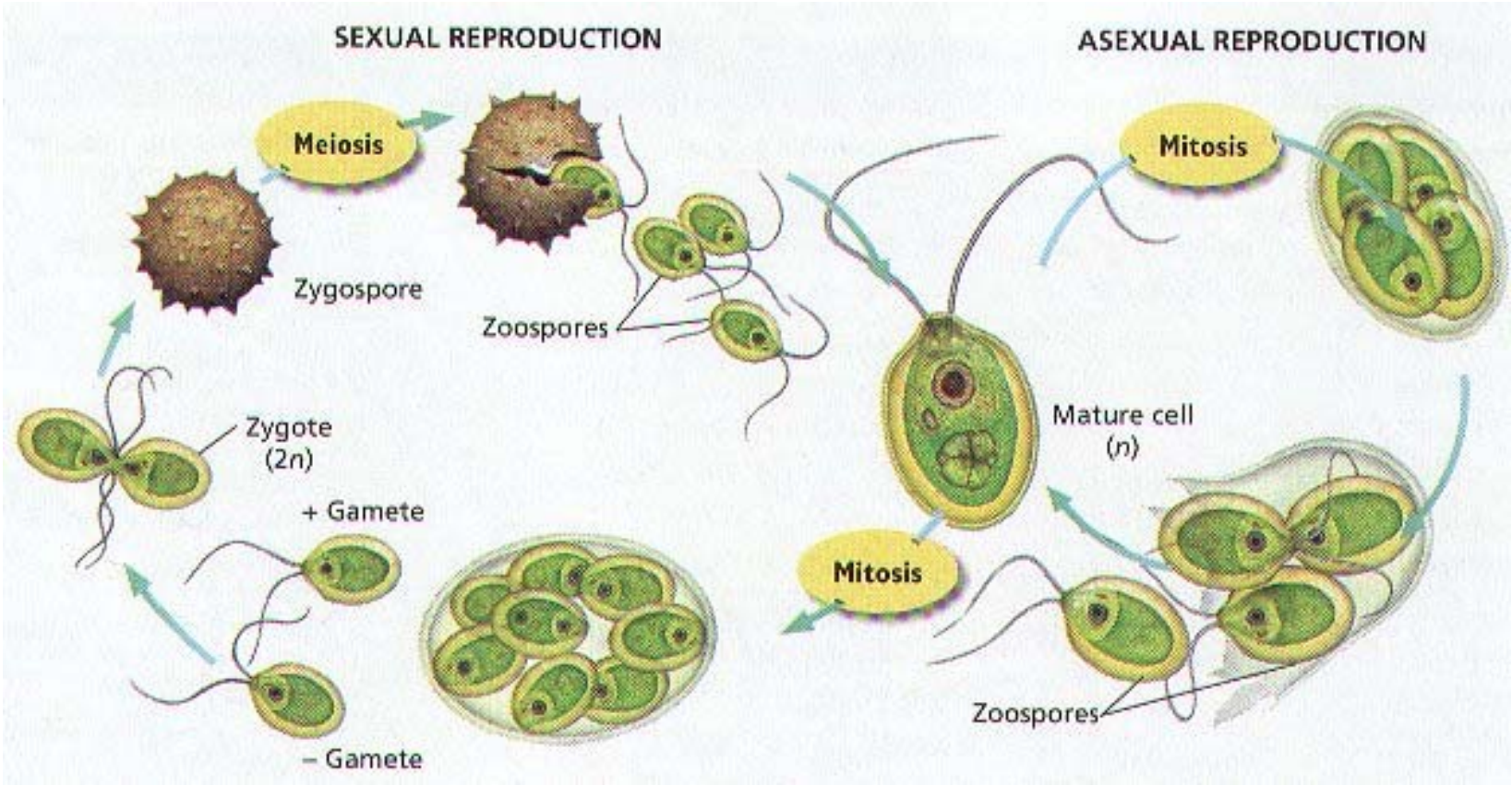
US Public Health Publ. #657. 1959.

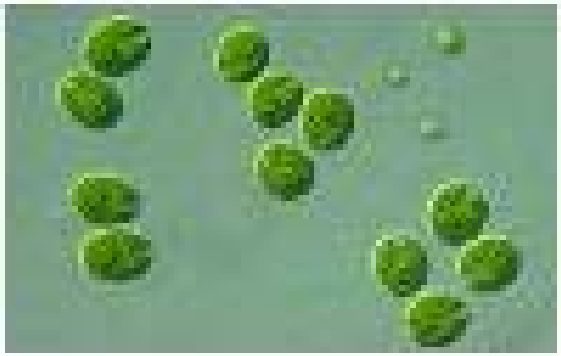




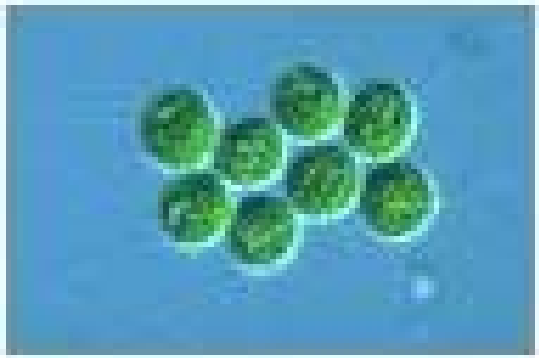


RIPRODUZIONE SIA ASESSUATA CHE SESSUATA

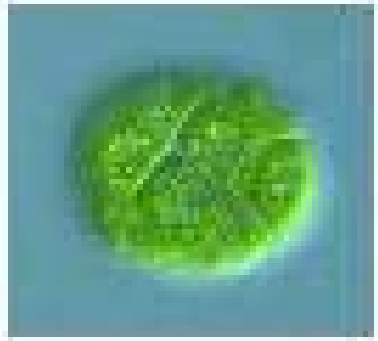




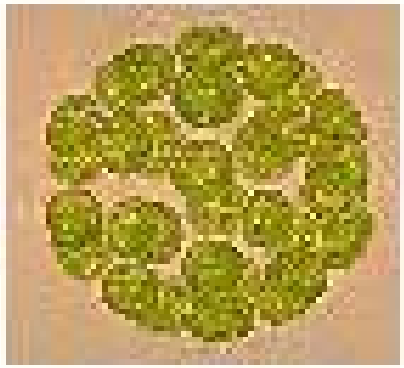
Chlamydomonas



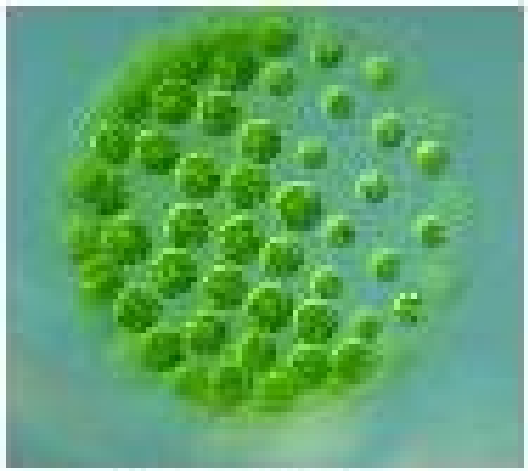
Gonium



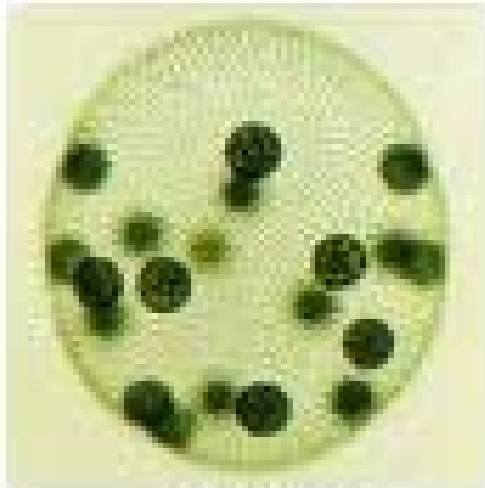
Pandorina



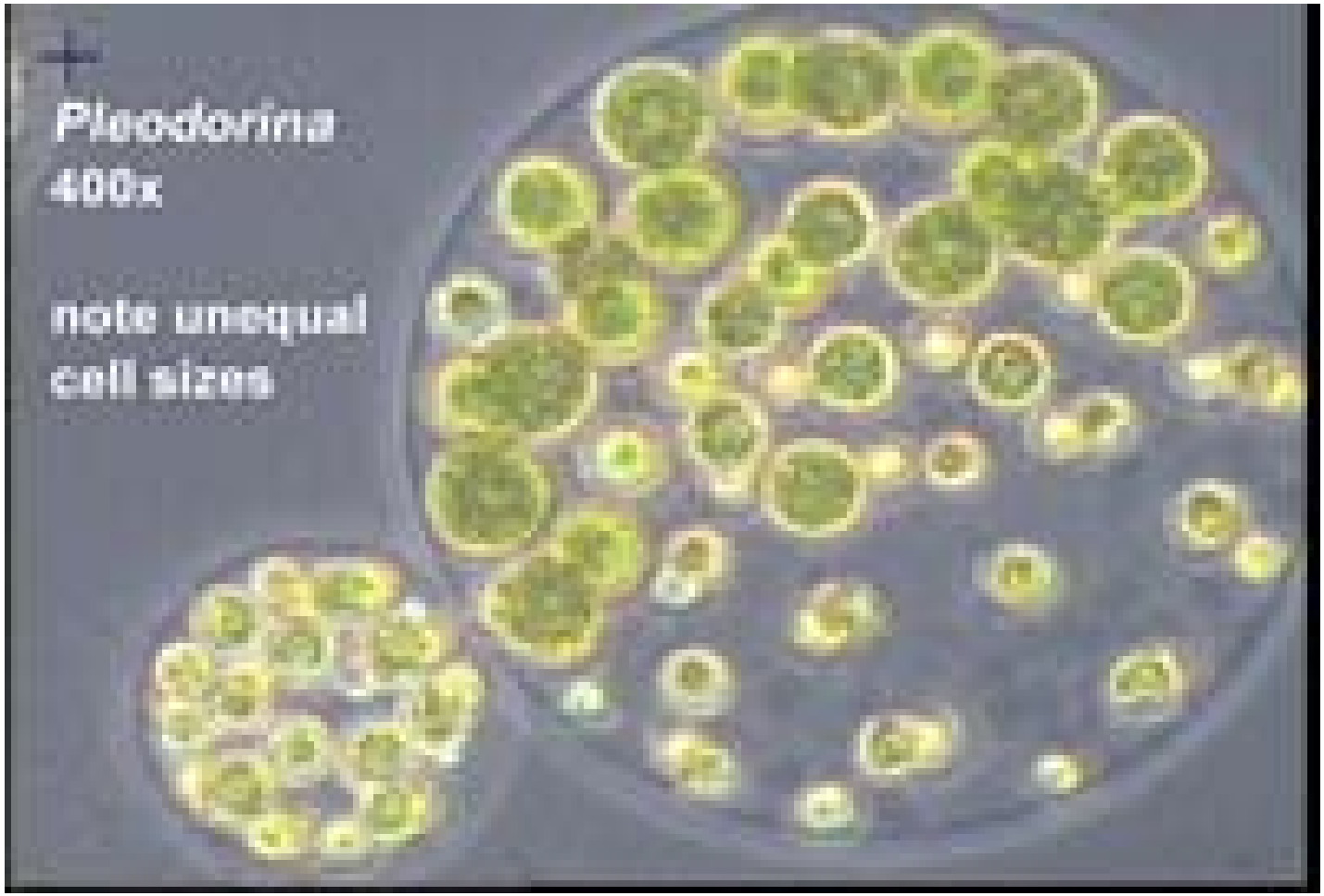
Eudorina

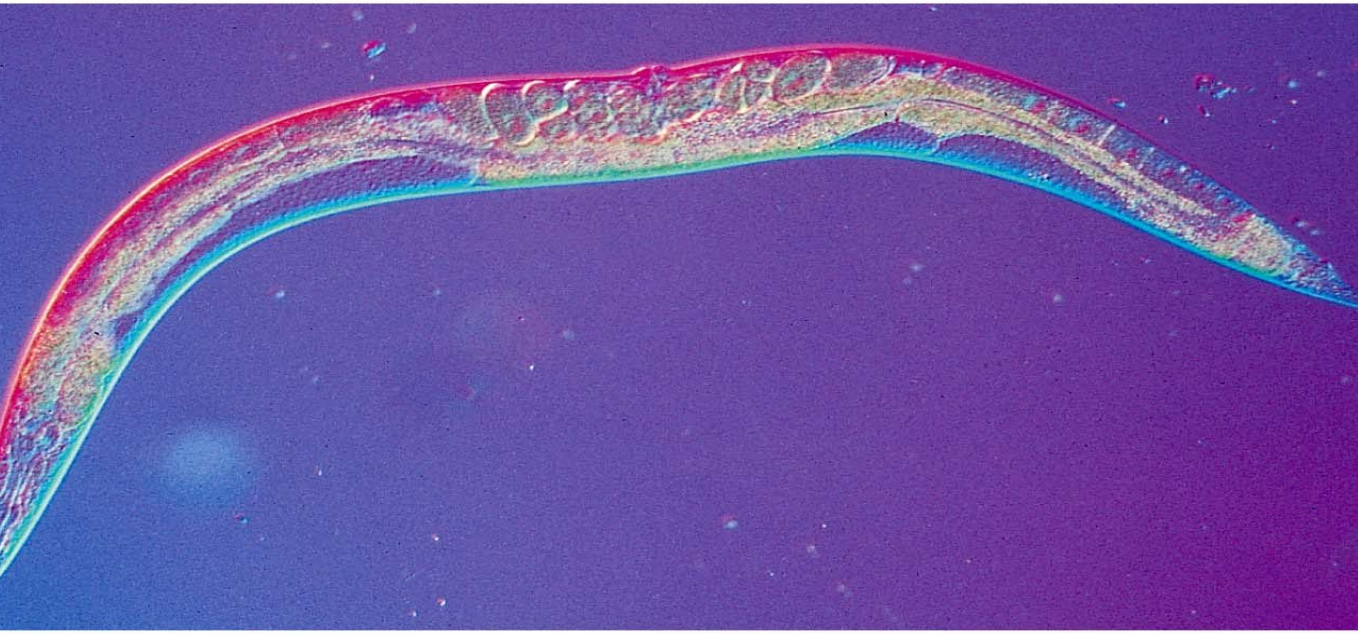


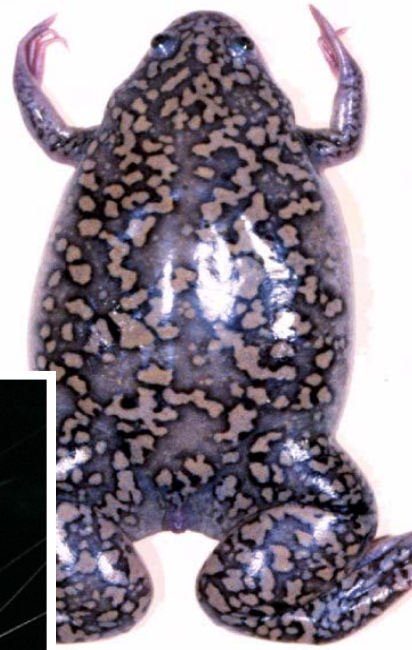
Pleodorina

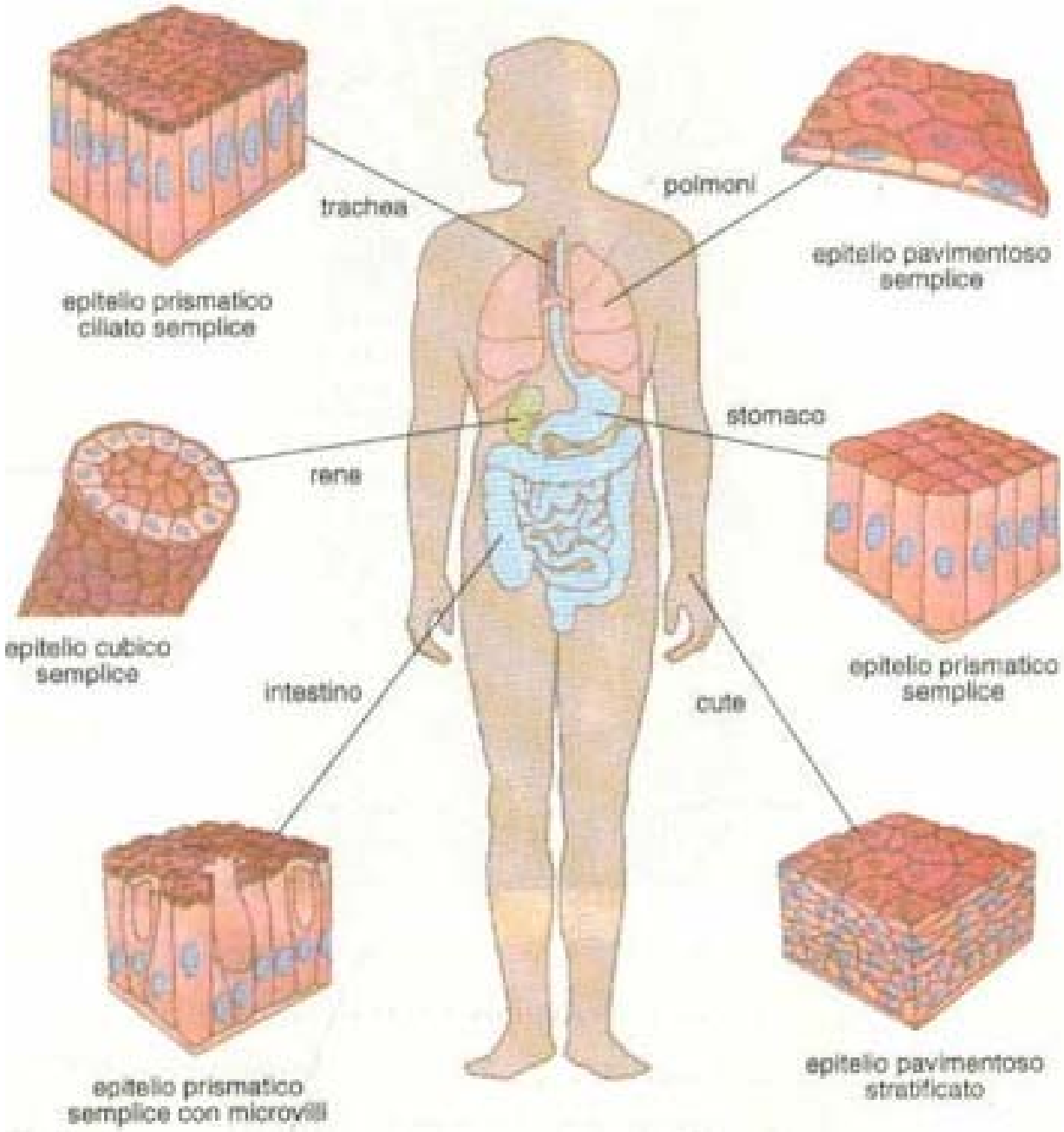


Volvox

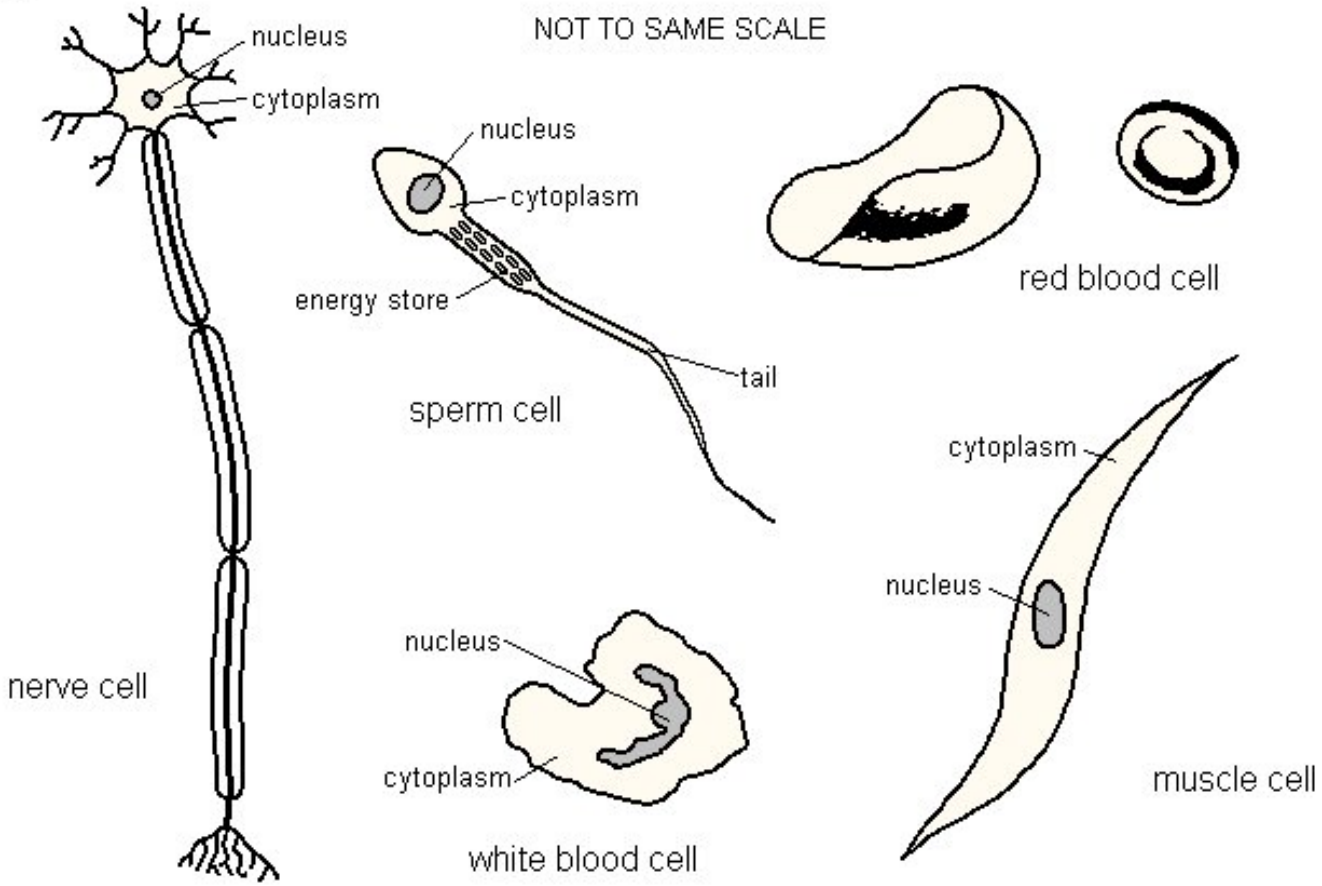

Pleodorina
400x
note unequal
cell sizes


0.2 mm

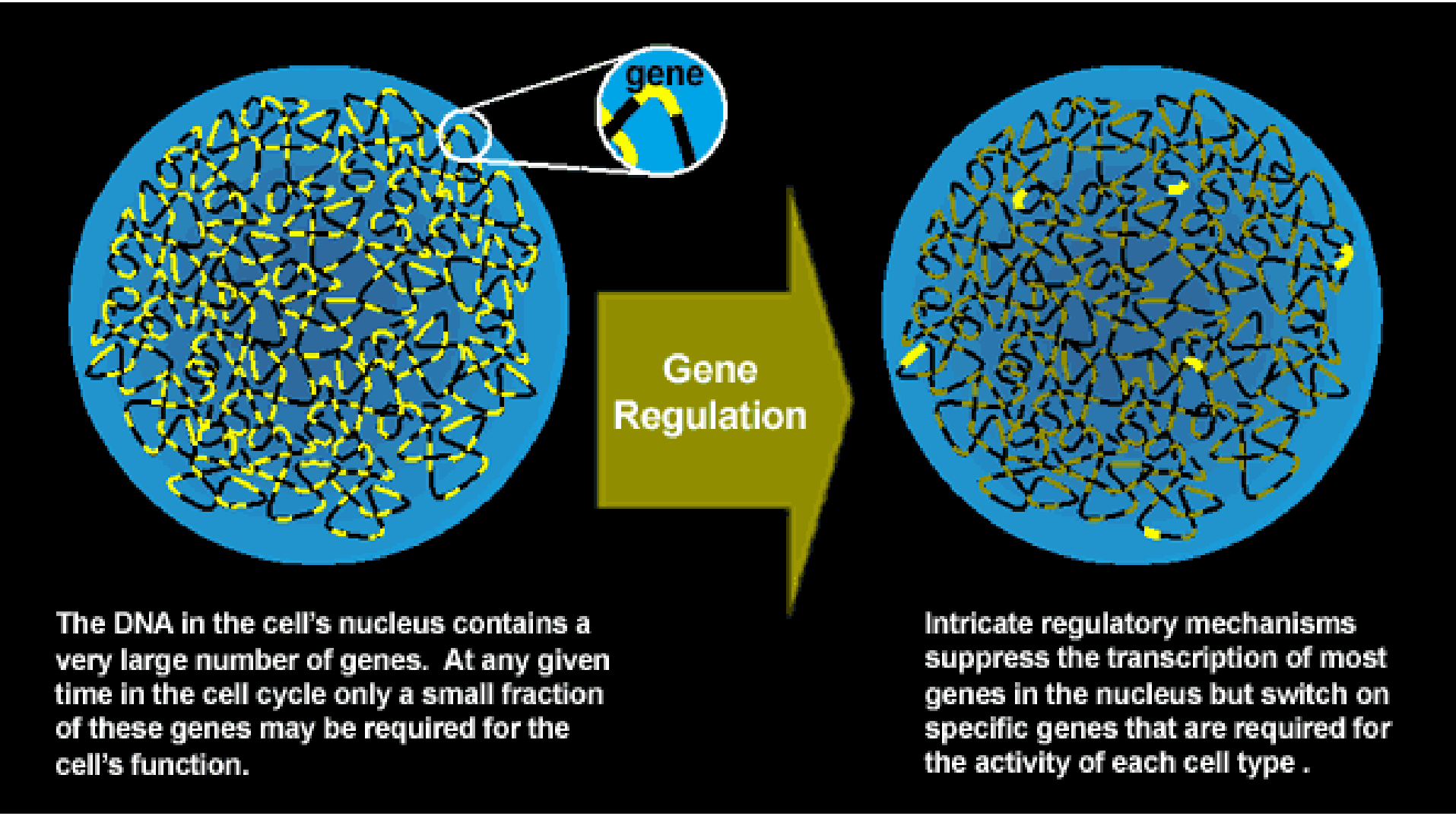



trachea
epitelio prismatico ciliato semplice
polmoni
epitelio pavimentoso semplice
rene
epitelio cubico semplice
stomaco
epitelio prismatico semplice
intestino
epitelio prismatico semplice con microvilli
cute
epitelio pavimentoso stratificato

Cellule specializzate provenienti da diversi tessuti

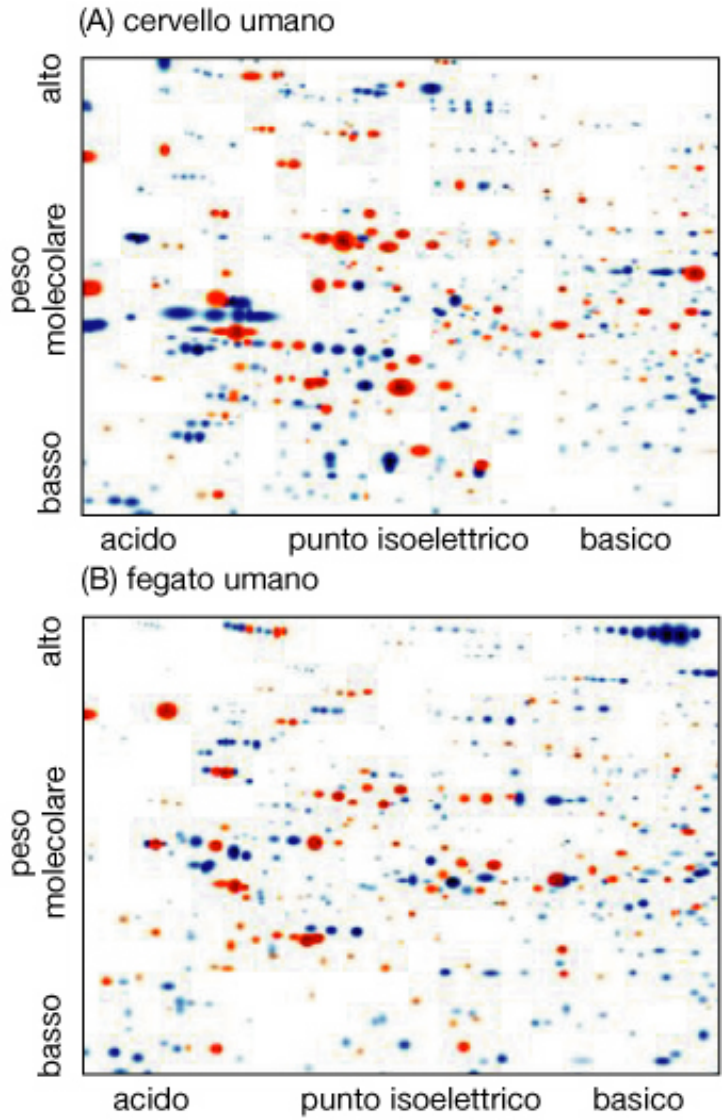


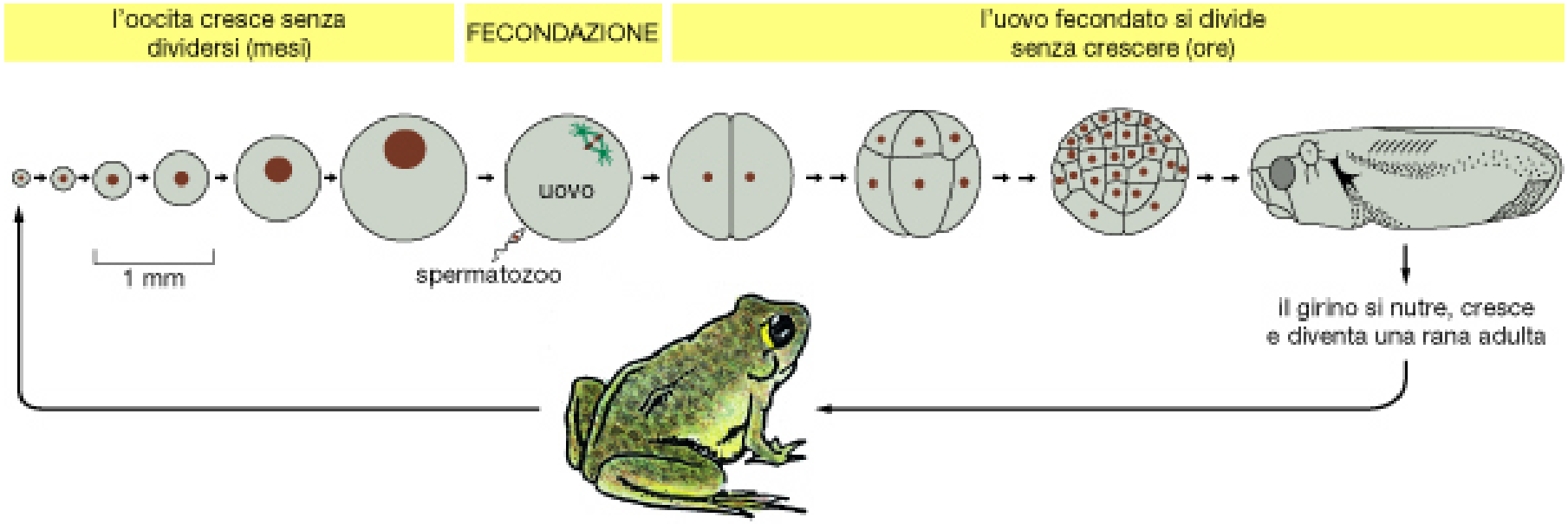
DIFFERENZIAMENTO CELLULARE



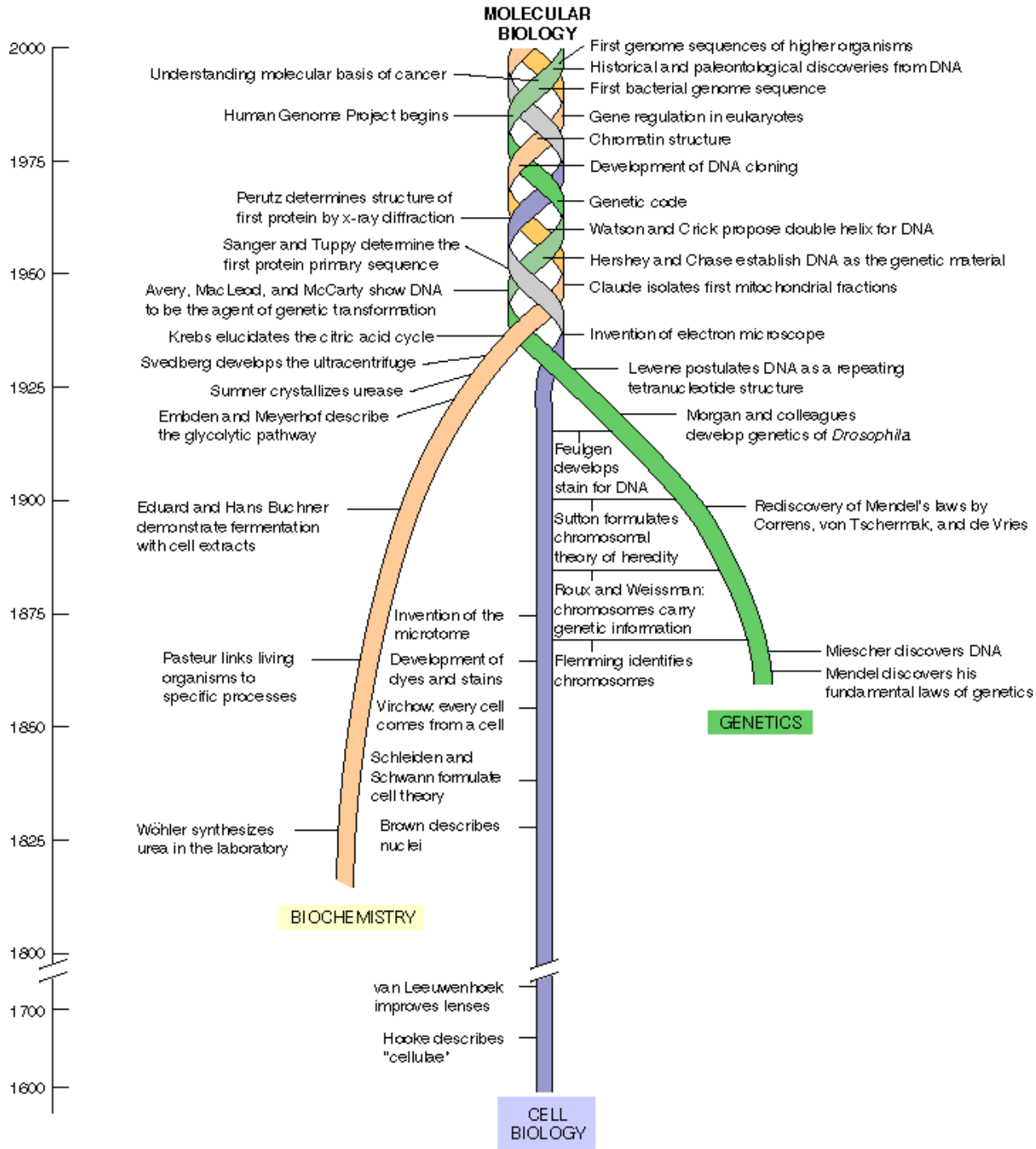
Elettroforesi bidimensionali di estratti proteici

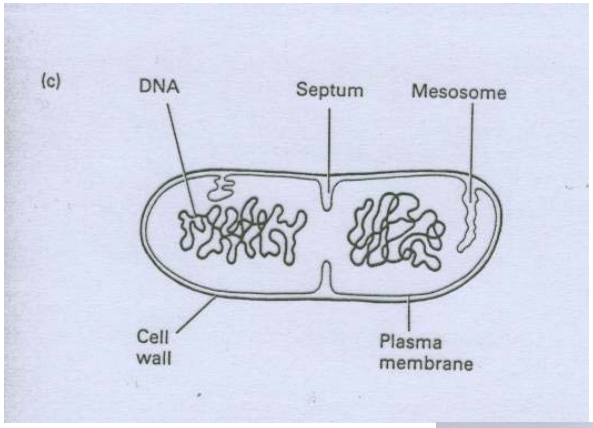
- proteine comuni
- proteine specifiche

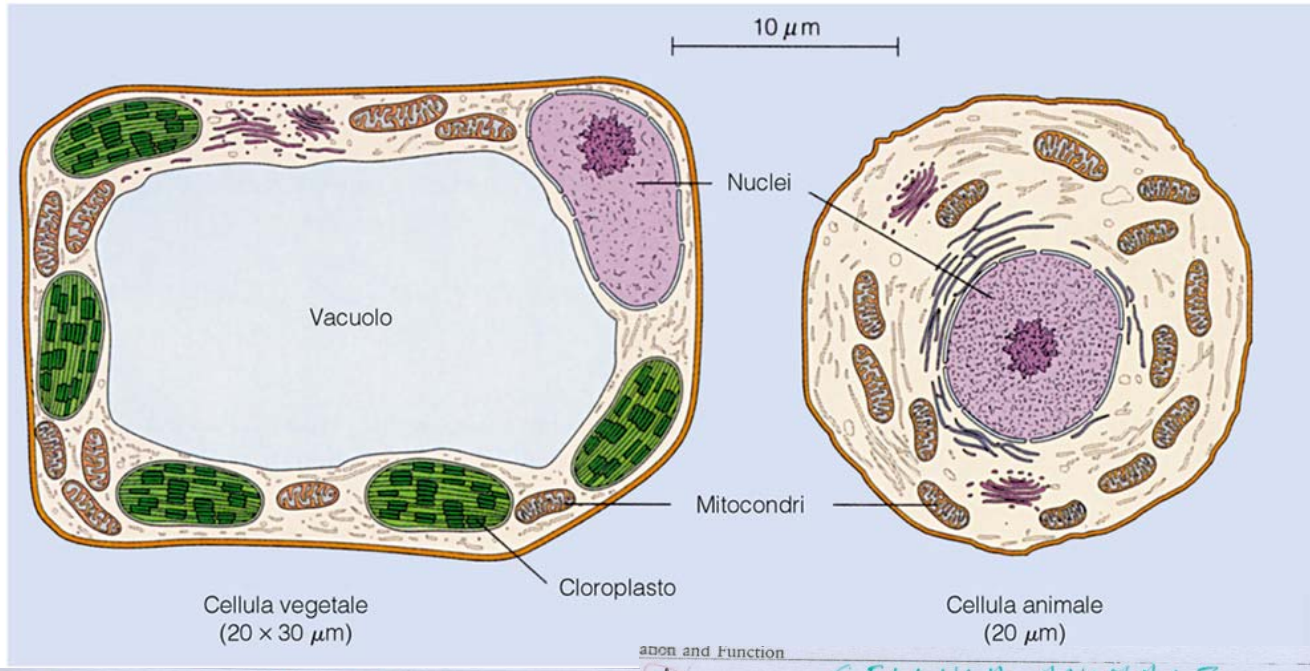


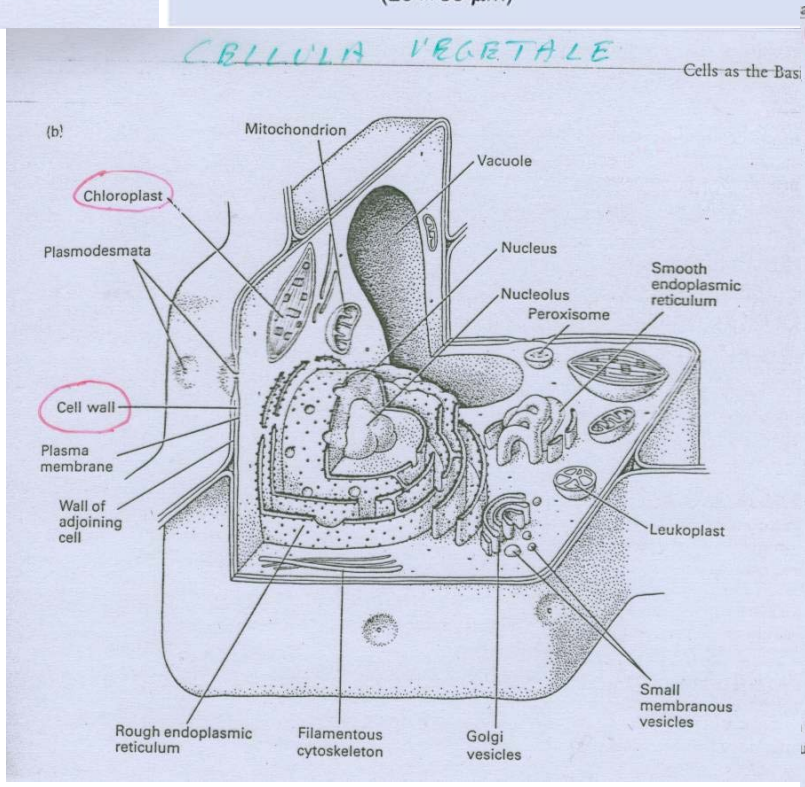


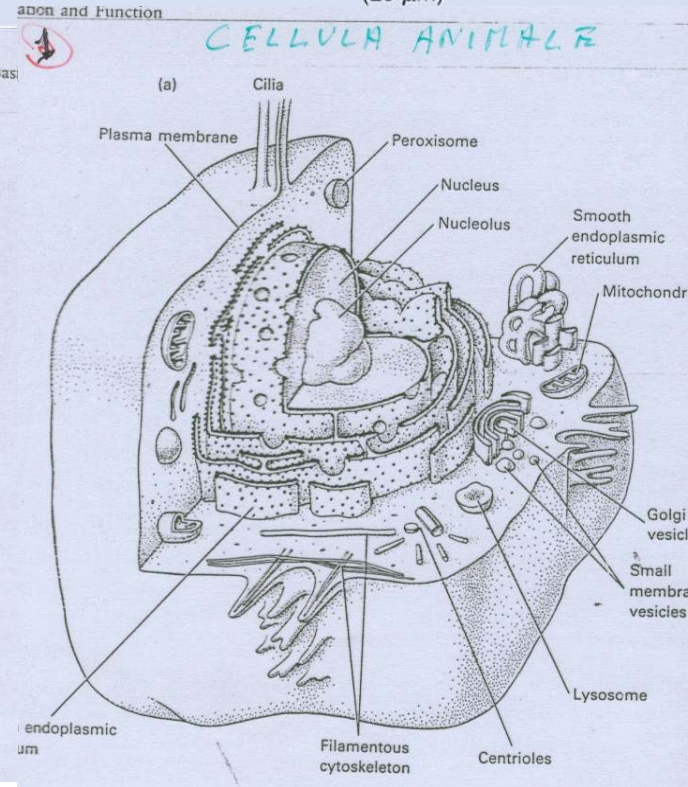
Uovo maturo, pronto per la fecondazione


MOLECULAR BIOLOGY
2000
1975
1950
1925
1900
1875
1850
1825
1800
1700
1600
First genome sequences of higher organisms
Historical and paleontological discoveries from DNA
First bacterial genome sequence
Gene regulation in eukaryotes
Chromatin structure
Development of DNA cloning
Genetic code
Watson and Crick propose double helix for DNA
Hershey and Chase establish DNA as the genetic material
Claude isolates first mitochondrial fractions
Invention of electron microscope
Levene postulates DNA as a repeating tetranucleotide structure
Morgan and colleagues develop genetics of Drosophila
Rediscovery of Mendel's laws by Correns, von Tschermak, and de Vries
Miescher discovers DNA
Mendel discovers his fundamental laws of genetics
GENETICS
Understanding molecular basis of cancer
Human Genome Project begins
Perutz determines structure of first protein by x-ray diffraction
Sanger and Tuppy determine the first protein primary sequence
Avery, MacLeod, and McCarty show DNA to be the agent of genetic transformation
Krebs elucidates the citric acid cycle
Svedberg develops the ultracentrifuge
Sumner crystallizes urease
Embden and Meyerhof describe the glycolytic pathway
Eduard and Hans Buchner demonstrate fermentation with cell extracts
Pasteur links living organisms to specific processes
Wöhler synthesizes urea in the laboratory
BIOCHEMISTRY
Feulgen develops stain for DNA
Sutton formulates chromosomal theory of heredity
Roux and Weissman: chromosomes carry genetic information
Flemming identifies chromosomes
Invention of the microtome
Development of dyes and stains
Virchow: every cell comes from a cell
Schleiden and Schwann formulate cell theory
Brown describes nuclei
van Leeuwenhoek improves lenses
Hooke describes "cellulae"
CELL BIOLOGY


(c)
DNA
Septum
Mesosome
Cell wall
Plasma membrane

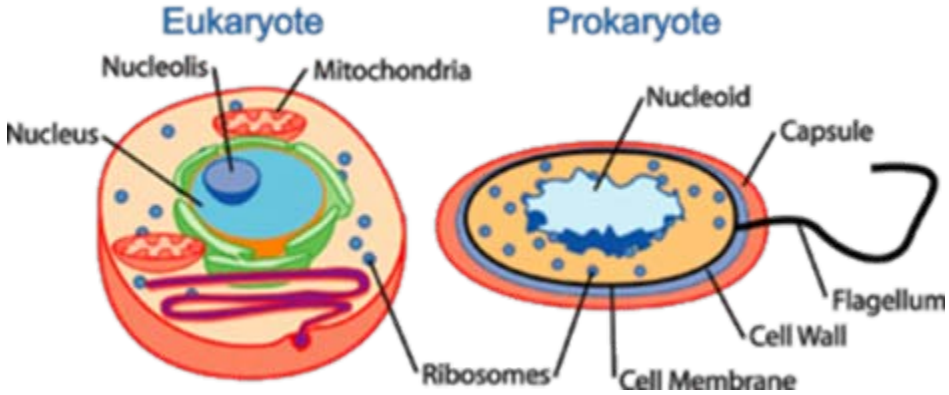

10 μm
Nuclei
Vacuolo
Mitocondri
Cloroplasto
Cellula vegetale
(20 × 30 μm)
Cellula animale
(20 μm)


CELLULA VEGETALE
Cells as the Bas
(b)
Mitochondrion
Vacuole
Chloroplast
Plasmodesmata
Nucleus
Nucleolus
Peroxisome
Smooth endoplasmic reticulum
Cell wall
Plasma membrane
Wall of adjoining cell
Leukoplast
Small membranous vesicles
Rough endoplasmic reticulum
Filamentous cytoskeleton
Golgi vesicles


apon and Function
CELLULA ANIMALE
(a)
Cilia
Plasma membrane
Peroxisome
Nucleus
Nucleolus
Smooth endoplasmic reticulum
Mitochondr
Golgi vesicl
Small membra vesicles
Lysosome
Centrioles
Filamentous cytoskeleton

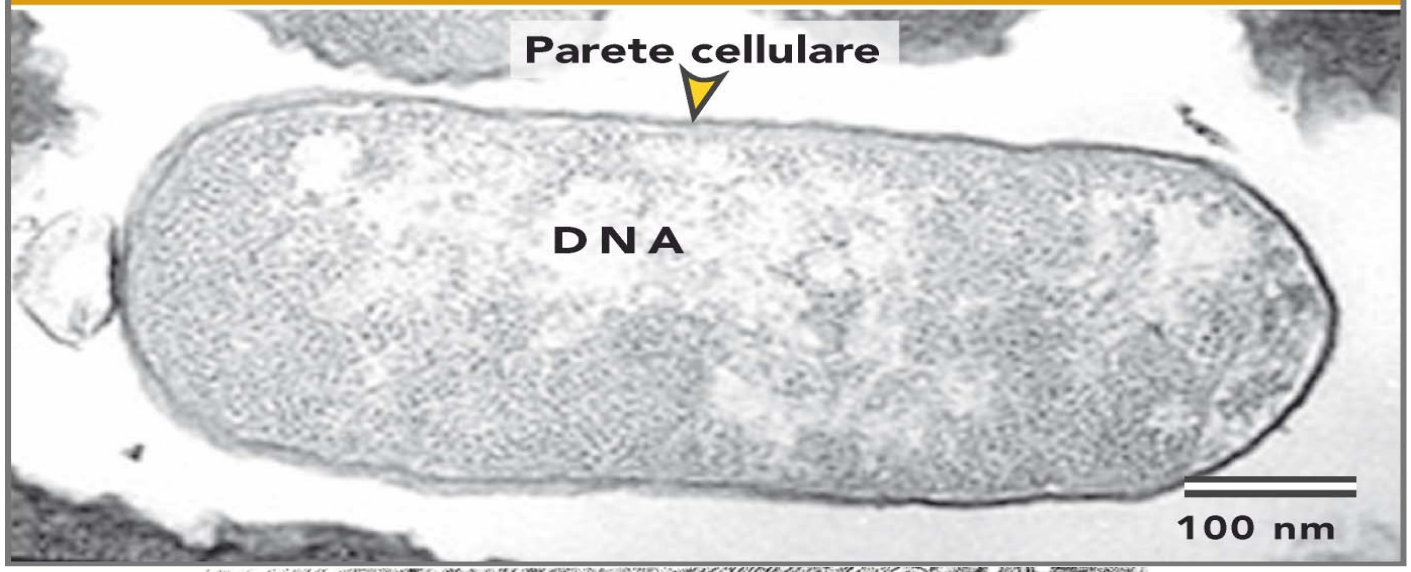
CELLULE PROCARIOTICHE/EUCARIOTICHE MESSE A CONFRONTO

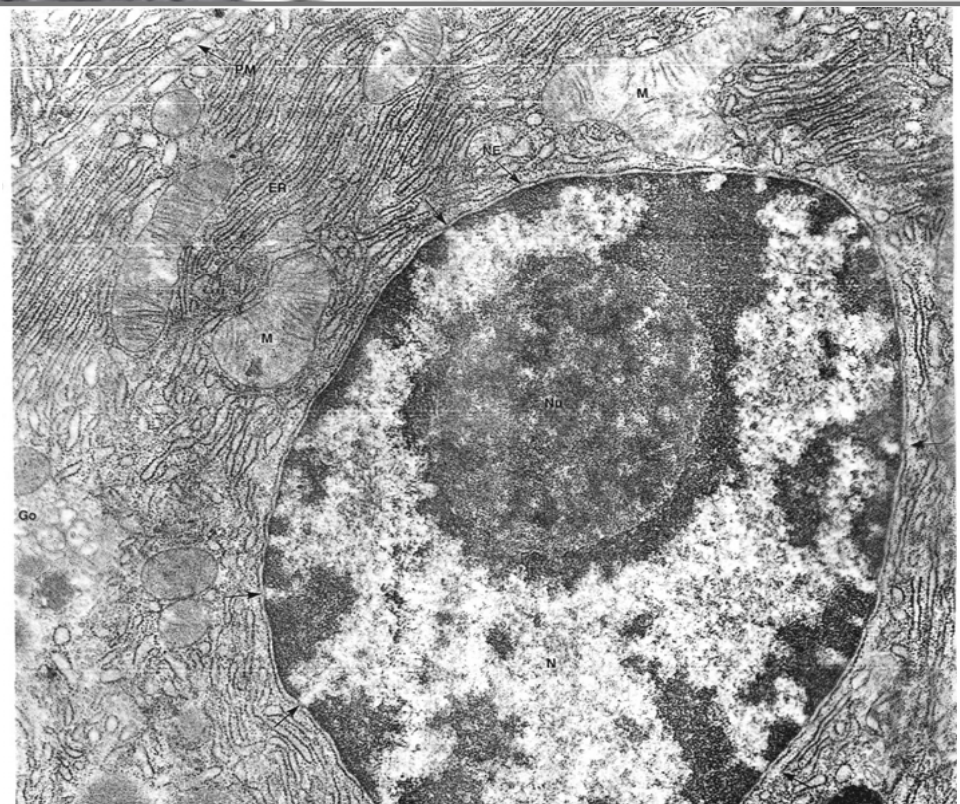
A livello morfologico…….



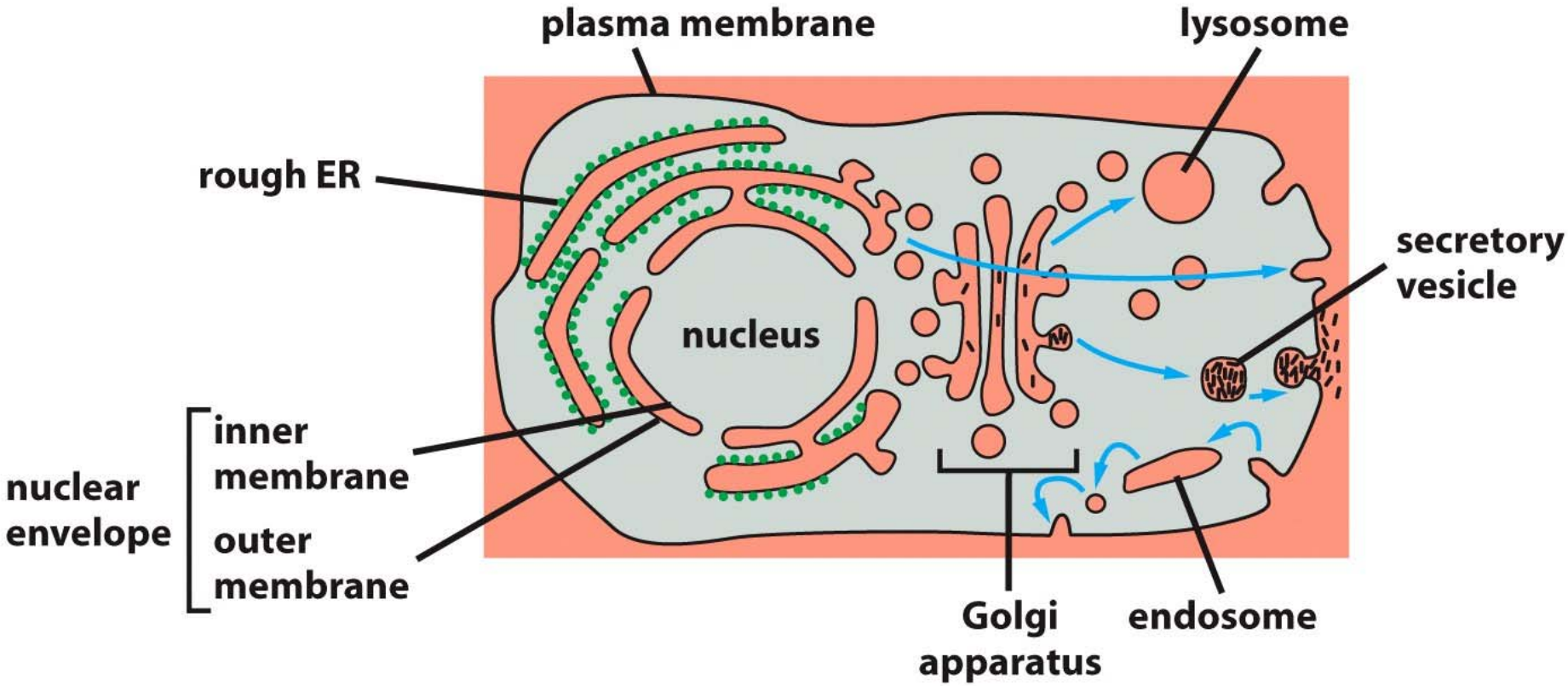
CHARACTERISTIC	PROCARYOTIC CELLS	EUCARYOTIC CELLS
Size	1–10 μm	10–100 μm
Nuclear envelope	Absent	Present
Chromosomes	Single, circular, with no nucleosomes	Multiple, linear, wound on nucleosomes
Golgi apparatus	Absent	Present[a]
Endoplasmic reticulum, lysosomes, peroxisomes	Absent	Present[a]
Mitochondria	Absent	Present[a]
Chlorophyll	Not in chloroplasts	In chloroplasts
Ribosomes	Relatively small	Relatively large
Microtubules, intermediate filaments, microfilaments	Absent	Present
Flagella	Lack microtubules	Contain microtubules

Un batterio ha un unico compartimento





Specializzazione

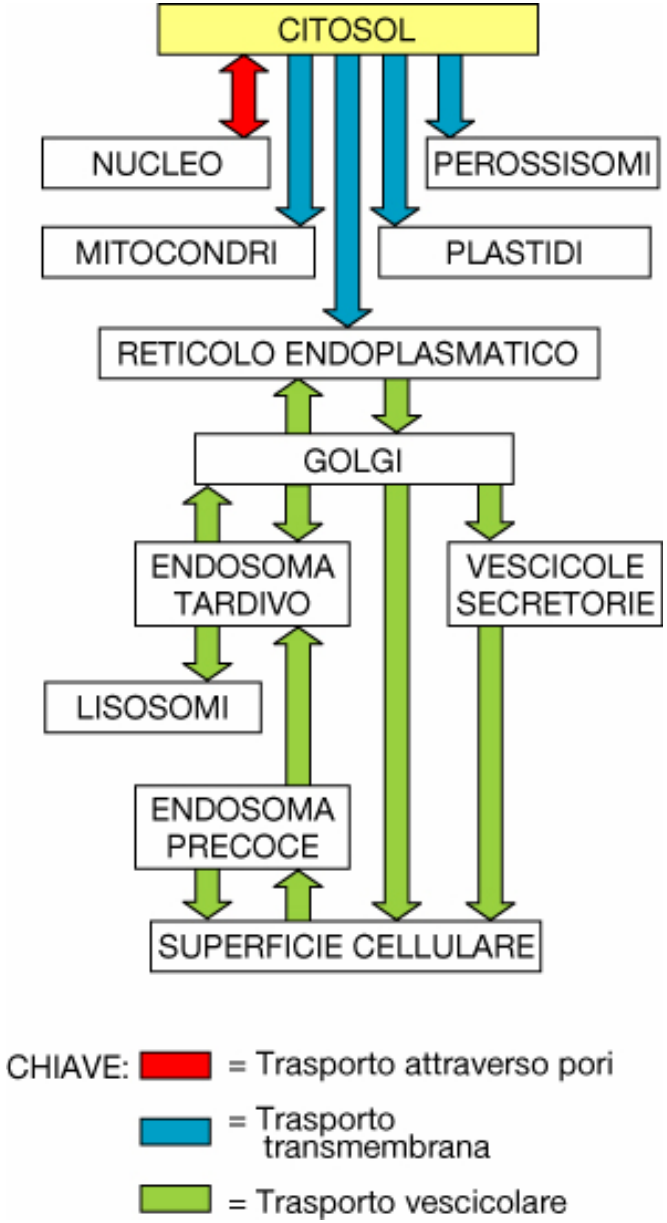


I compartimenti cellulari sono una separazione topologica dell'area intracellulare ma sono anche strutture funzionali e per questo sono anche chiamati organelli

Ogni organello ha una funzione distinta	
ORGANELLO	**FUNZIONE**
Nucleo	Espressione genica per le proteine da esportare e importare; esportazione di RNA
Reticolo endoplasmatico	Modificazione delle proteine; proteine importate per traslocazione cotraduzionale
Apparato di Golgi	Modificazione delle proteine; le proteine vi accedono dall'RE
Endosoma Endosoma primario Endosoma tardivo	Smistamento delle proteine internalizzate per il trasporto ad altri compartimenti; le proteine negli endosomi sono indirizzate dalla via secretoria
Lisosoma	Degradazione di proteine internalizzate; degradazione di proteine del citosol in cellule danneggiate; le proteine che agiscono nei lisosomi sono marcate dalla rete *trans*-Golgi
Mitocondrio	Gestione dell'energia; proteine importate dal citosol; alcune proteine sintetizzate negli organelli
Perossisoma	Processi ossidativi; proteine importate dal citosol

Table 12–1 Relative Volumes Occupied by the Major Intracellular Compartments in a Liver Cell (Hepatocyte)

INTRACELLULAR COMPARTMENT	PERCENTAGE OF TOTAL CELL VOLUME
Cytosol	54
Mitochondria	22
Rough ER cisternae	9
Smooth ER cisternae plus Golgi cisternae	6
Nucleus	6
Peroxisomes	1
Lysosomes	1
Endosomes	1


CITOSOL
NUCLEO
PEROSSISOMI
MITOCONDRI
PLASTIDI
RETICOLO ENDOPLASMATICO
GOLGI
ENDOSOMA TARDIVO
VESCICOLE SECRETORIE
LISOSOMI
ENDOSOMA PRECOCE
SUPERFICIE CELLULARE
CHIAVE:
= Trasporto attraverso pori
= Trasporto transmembrana
= Trasporto vescicolare

Sequenze segnale: importazione nucleo
mitocondri
perossisomi
ER
ritorno a ER

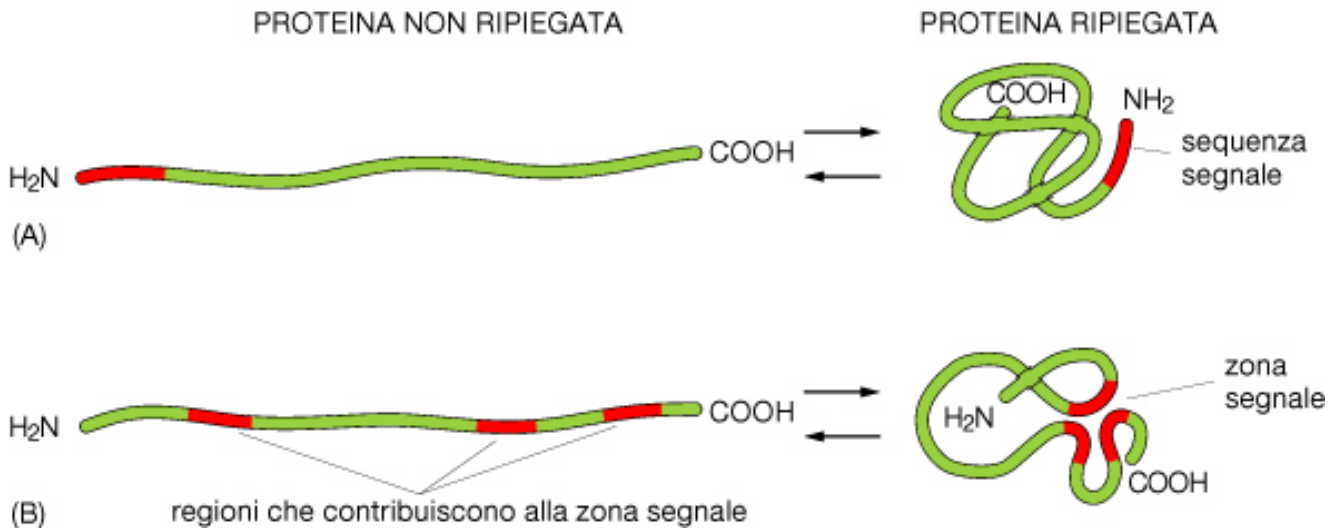


Table 12–3 Some Typical Signal Sequences

FUNCTION OF SIGNAL SEQUENCE	EXAMPLE OF SIGNAL SEQUENCE
Import into nucleus	-Pro-Pro-Lys-Lys-Lys-Arg-Lys-Val-
Export from nucleus	-Leu-Ala-Leu-Lys-Leu-Ala-Gly-Leu-Asp-Ile-
Import into mitochondria	$^{+}H_3N$-Met-Leu-Ser-Leu-Arg-Gln-Ser-Ile-Arg-Phe-Phe-Lys-Pro-Ala-Thr-Arg-Thr-Leu-Cys-Ser-Ser-Arg-Tyr-Leu-Leu-
Import into plastid	$^{+}H_3N$-Met-Val-Ala-Met-Ala-Met-Ala-Ser-Leu-Gln-Ser-Ser-Met-Ser-Ser-Leu-Ser-Leu-Ser-Ser-Asn-Ser-Phe-Leu-Gly-Gln-Pro-Leu-Ser-Pro-Ile-Thr-Leu-Ser-Pro-Phe-Leu-Gln-Gly-
Import into peroxisomes	-Ser-Lys-Leu-COO^{-}
Import into ER	$^{+}H_3N$-Met-Met-Ser-Phe-Val-Ser-Leu-Leu-Leu-Val-Gly-Ile-Leu-Phe-Trp-Ala-Thr-Glu-Ala-Glu-Gln-Leu-Thr-Lys-Cys-Glu-Val-Phe-Gln-
Return to ER	-Lys-Asp-Glu-Leu-COO^{-}

Some characteristic features of the different classes of signal sequences are highlighted in color. Where they are known to be important for the function of the signal sequence, positively charged amino acids are shown in *red* and negatively charged amino acids are shown in *green*. Similarly, important hydrophobic amino acids are shown in *white* and hydroxylated amino acids are shown in *blue*. $^{+}H_3N$ indicates the N-terminus of a protein; COO^{-} indicates the C-terminus.

Cellula: unità fondamentale organismi viventi

Diversità
- forme
- organizzazione
  - unicellulare
  - pluricellulare

Costanza
- funzioni cellulari
- meccanismi molecolari

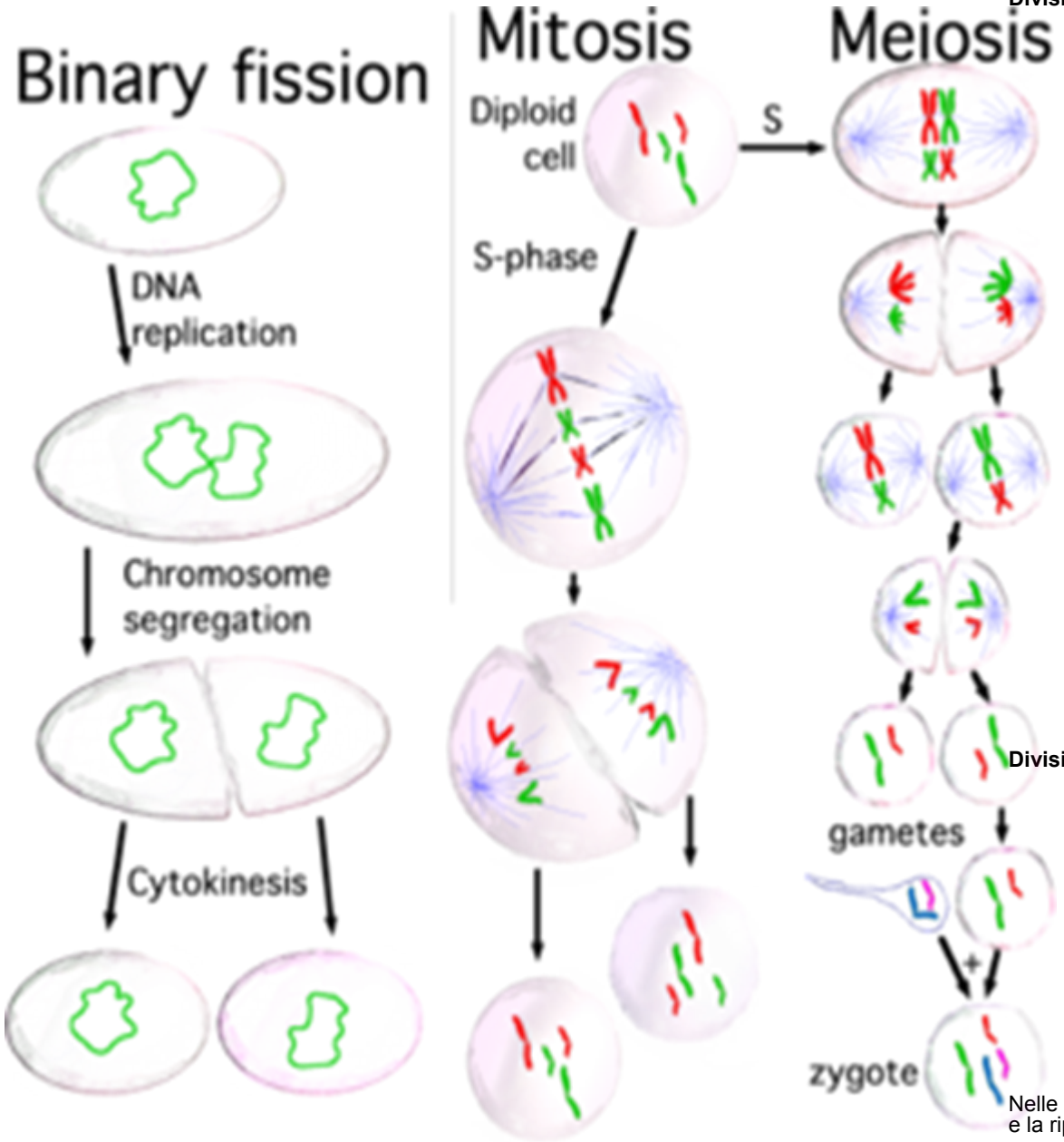
Definizione organismo vivente

- automantenimento: costanza forma e dimensioni
- autoriproduzione

Funzioni cellulari

- Riproduzione: formazione progenie
  mantenimento forma e dimensioni
- Ricezione e risposta a segnali
- Motilità
- Specializzazione

Riproduzione: formazione progenie



Divisione asessuata o per via vegetativa

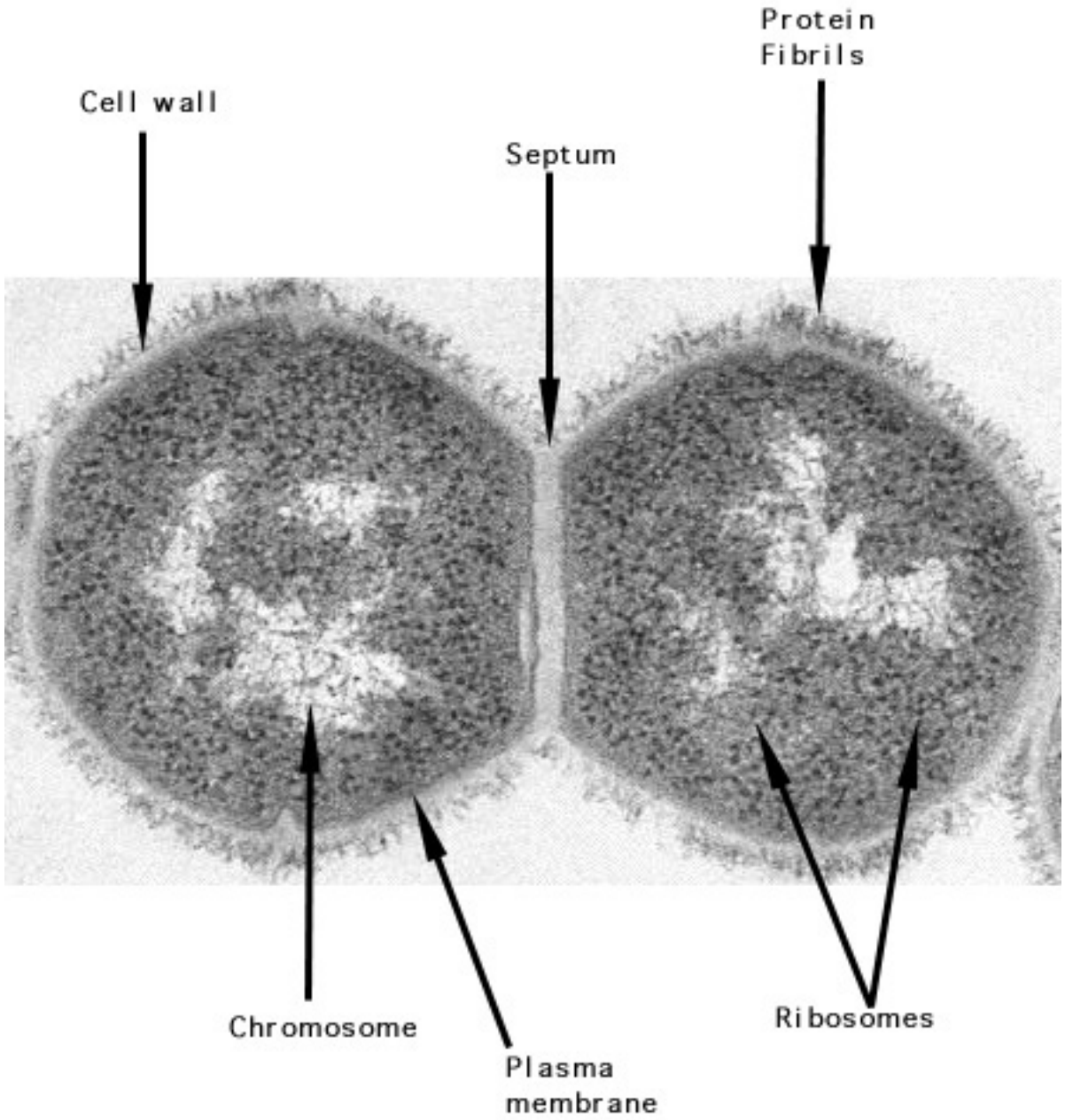
- fissione binaria ovvero la forma di riproduzione usata dagli organismi procarioti. Questo processo esita nella formazione di due parti, ognuna delle quali ha il potenziale di crescere fino alle dimensioni della cellula originale. Ed ognuna delle parti è un organismo completo.
- mitosi: ovvero divisione del nucleo genitore (in inglese *parent nucleo*) in due nuclei figli (inglese *daughter nucleus*), ognuno dei quali contiene un genoma identico al genoma genitoriale.
- divisione multipla
- gemmazione
- frammentazione
- rigenerazione
- clonazione
- poliembrionia
- sporulazione

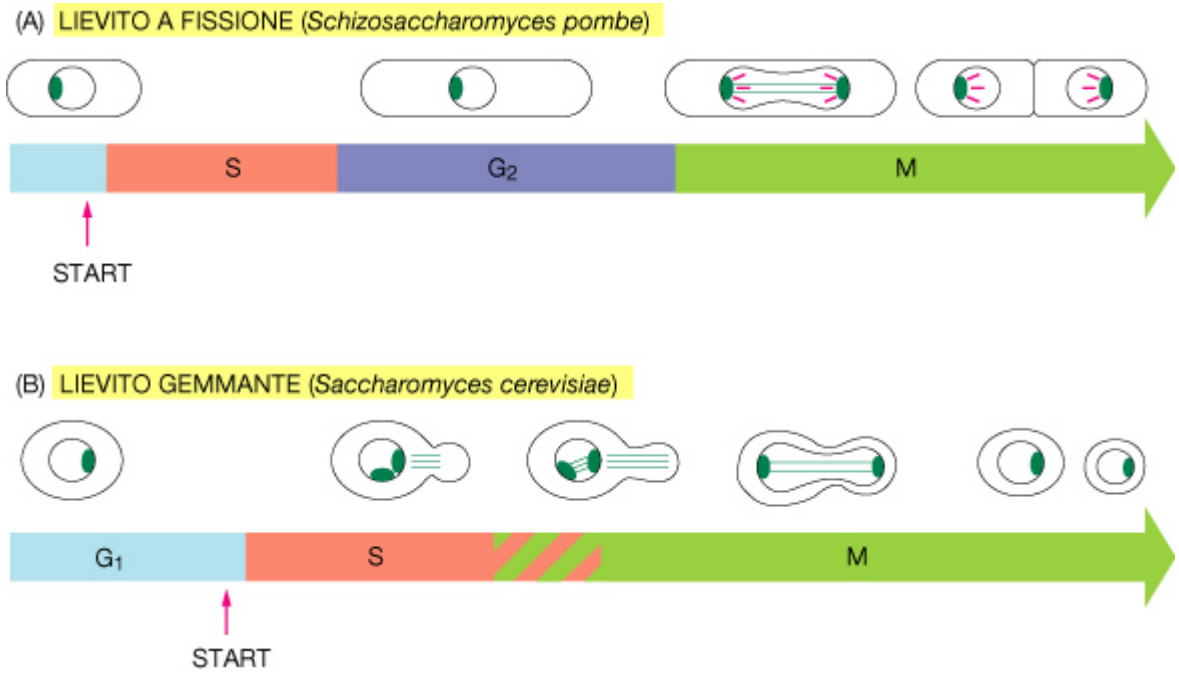
Divisione sessuata

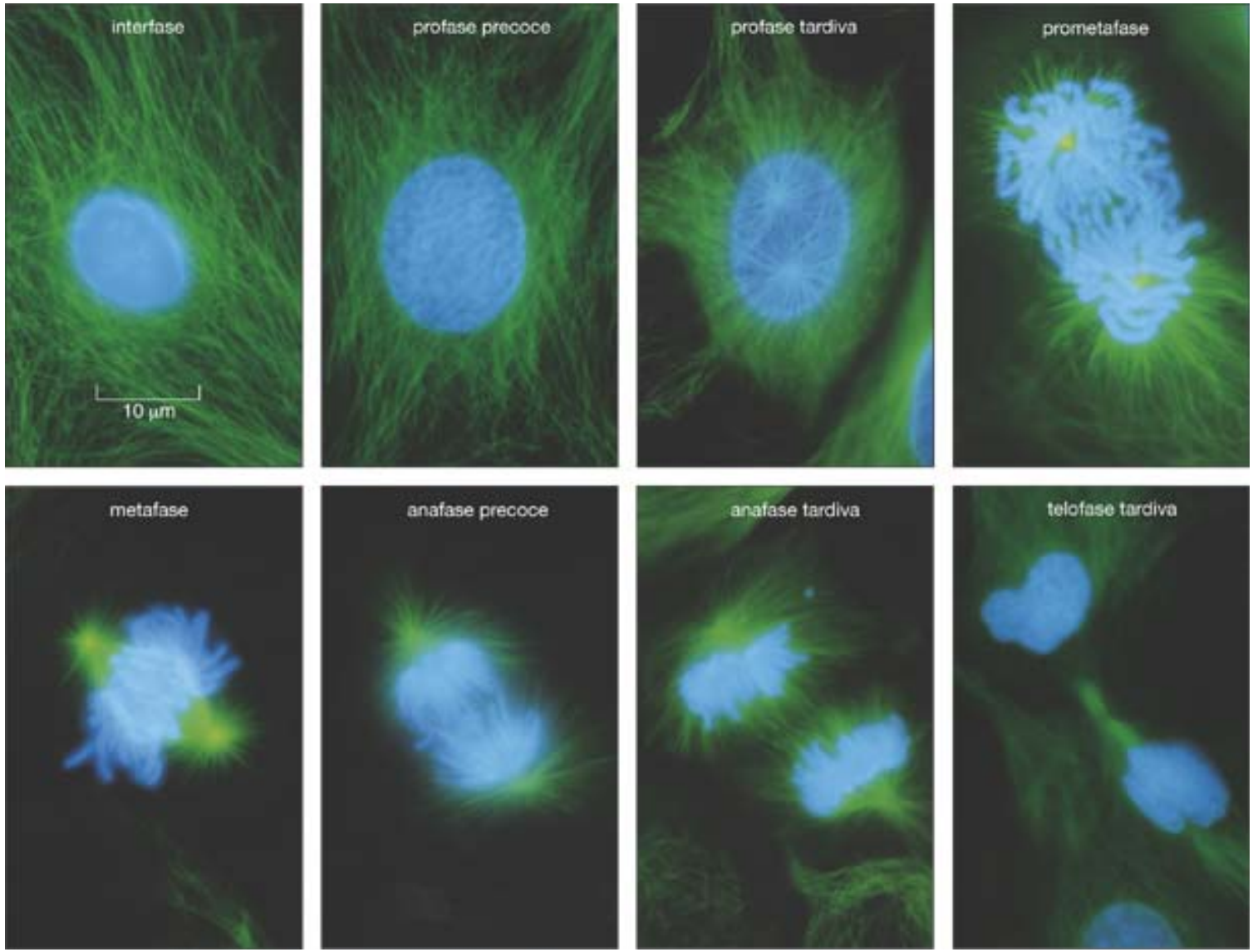
- mitosi: ovvero divisione del nucleo genitore (in inglese *parent nucleo*) in due nuclei figli (inglese *daughter nucleus*), ognuno dei quali contiene un genoma identico al genoma genitoriale.
- meiosi: ovvero la divisione del nucleo in cellule sessuali, le quali riducono il numero diploide di cromosomi ad un numero aploide.

Nelle cellule eucariote multicellulari la mitosi permette la crescita e la riparazione cellulare.

Streptococco



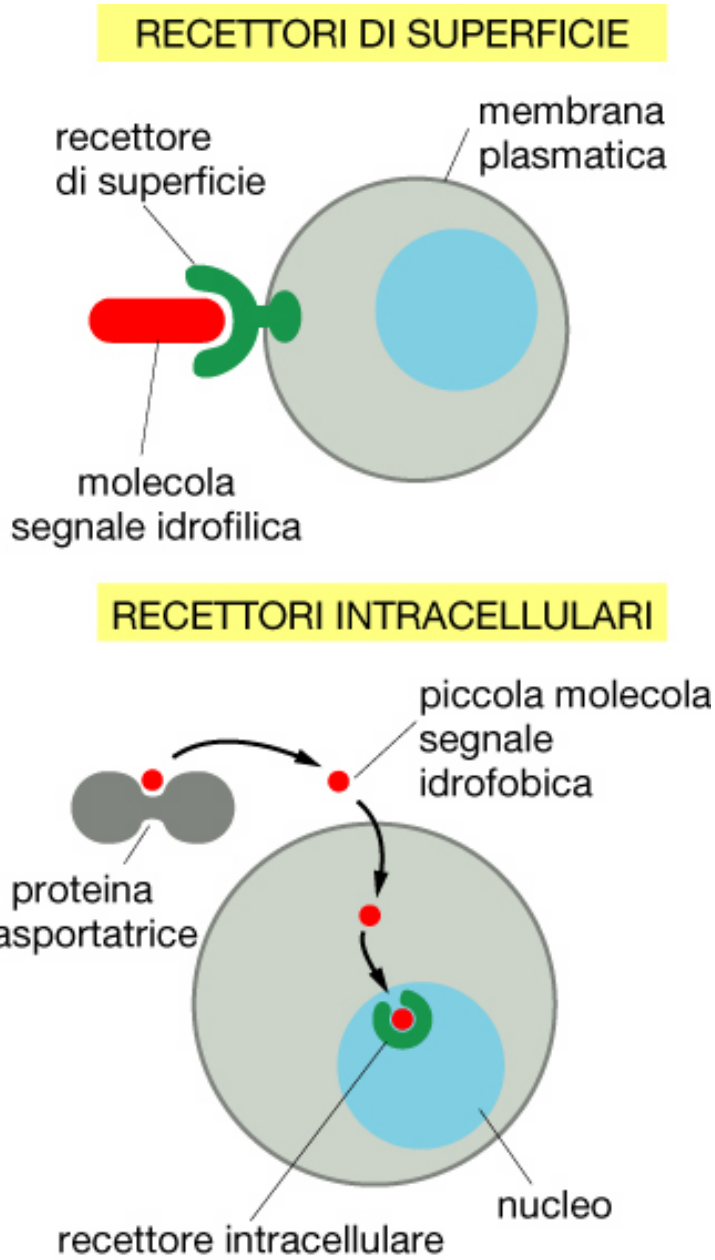

(A) LIEVITO A FISSIONE (Schizosaccharomyces pombe)
S
G2
M
START
(B) LIEVITO GEMMANTE (Saccharomyces cerevisiae)
G1
S
M
START


interfase
10 µm
profase precoce
profase tardiva
prometafase
metafase
anafase precoce
anafase tardiva
telofase tardiva

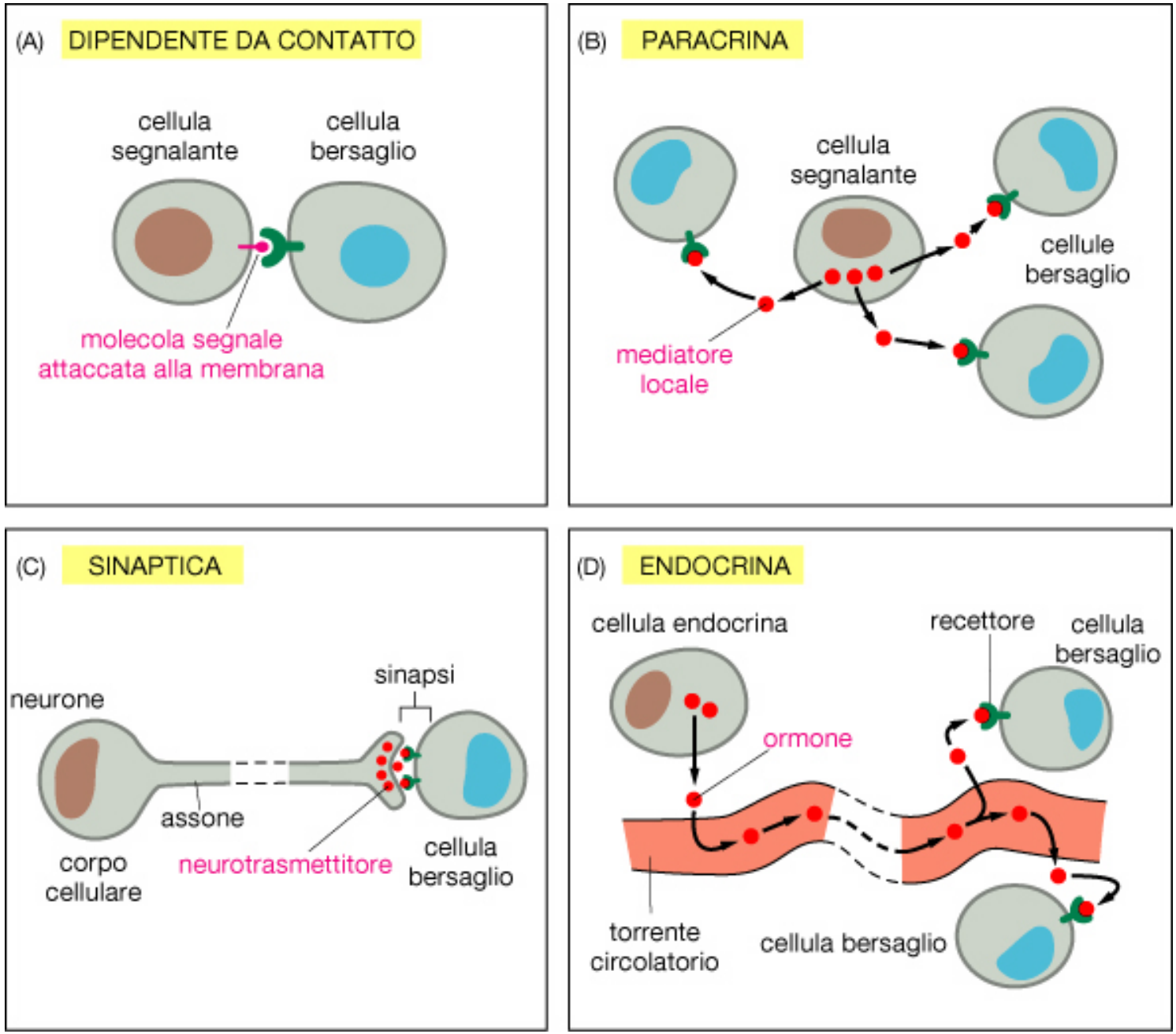
- Ricezione e risposta a segnali

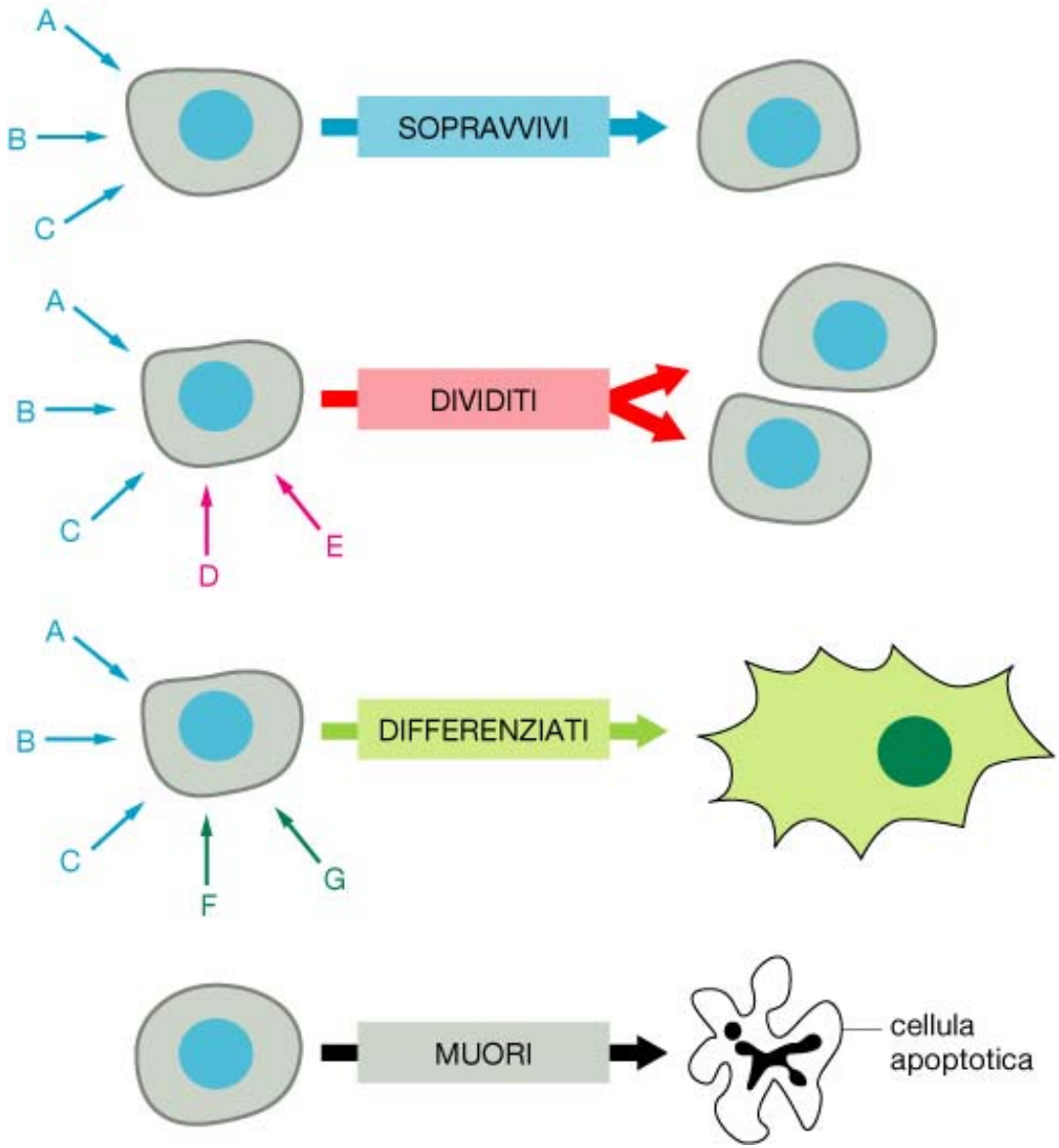
Alta specificità

Bassa concentrazione ligando necessaria

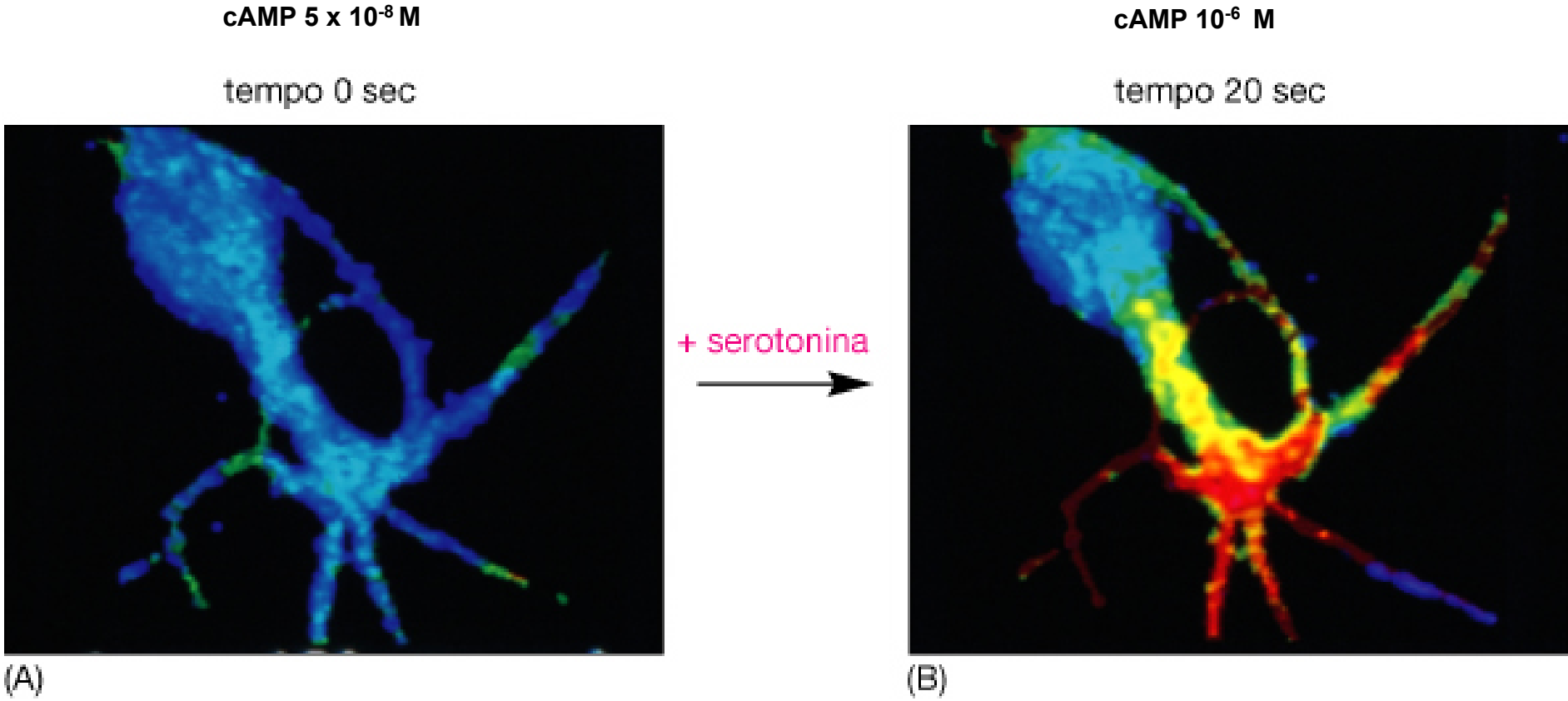


Risposta immunitaria

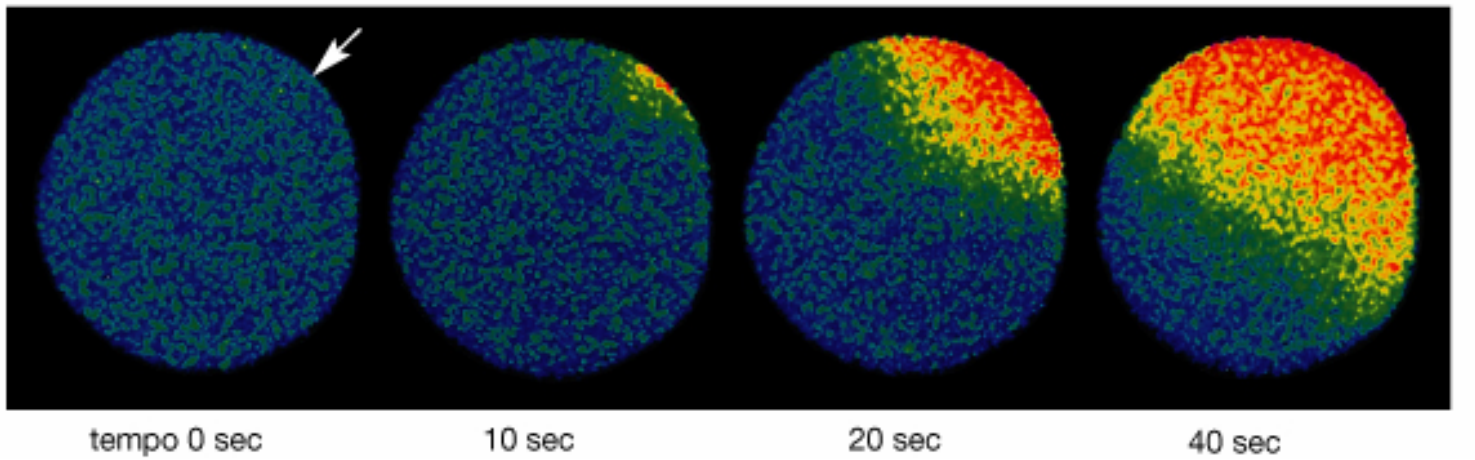



A
B
C
SOPRAVVIVI
A
B
C
D
E
DIVIDITI
A
B
C
F
G
DIFFERENZIATI
MUORI
cellula
apoptotica

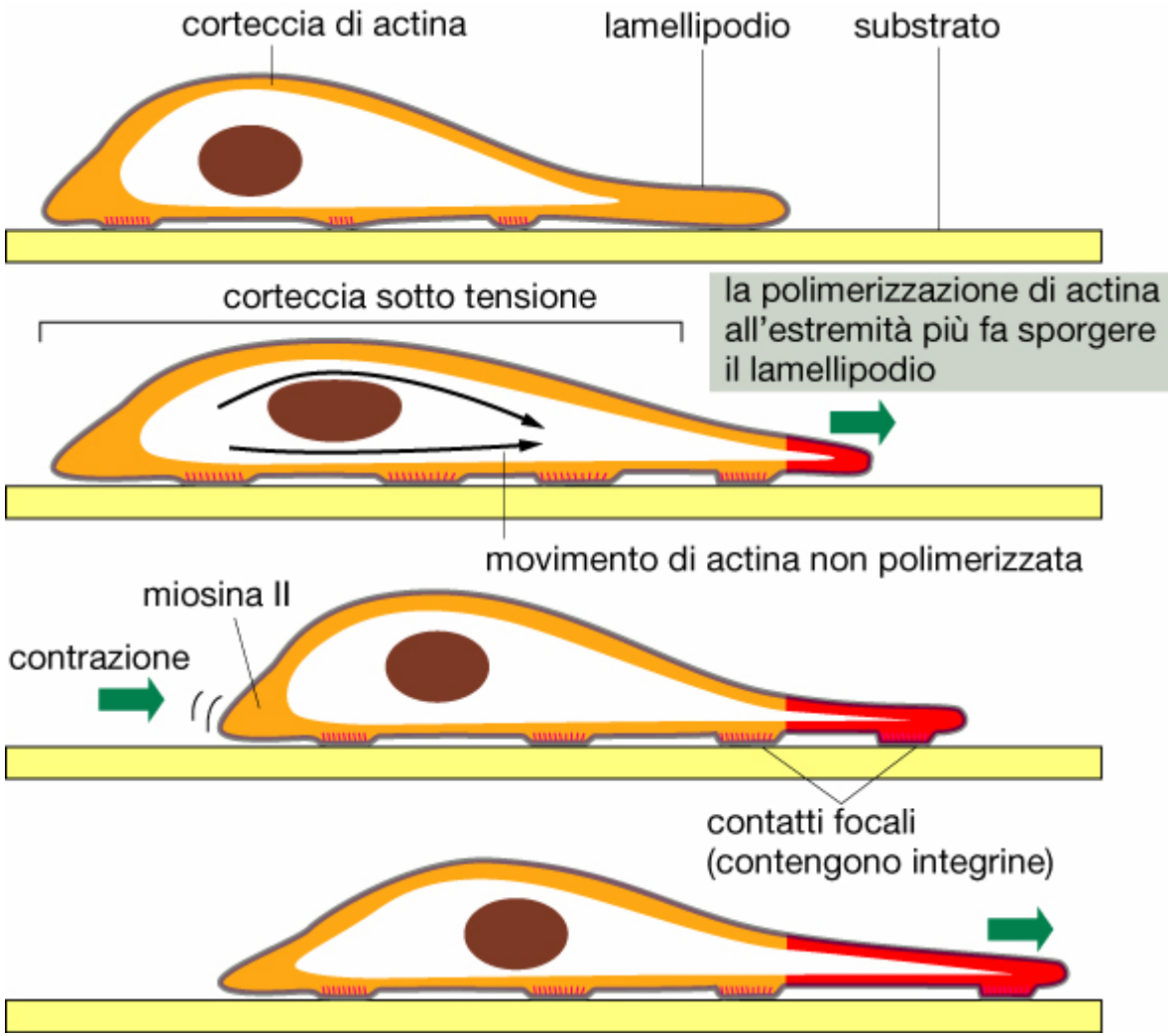
Livelli intracellulari di cAMP in risposta a stimolazione da serotonina



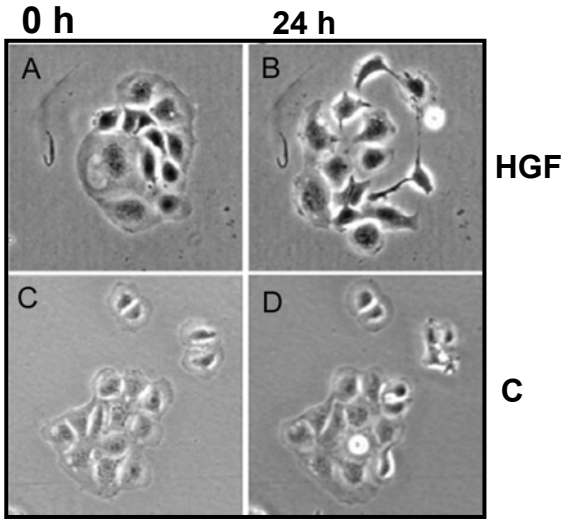
Onda di Ca^{2+} fecondazione

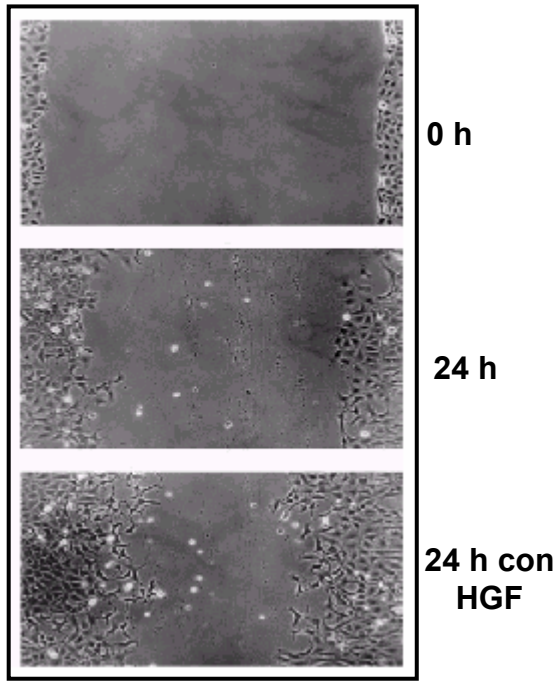


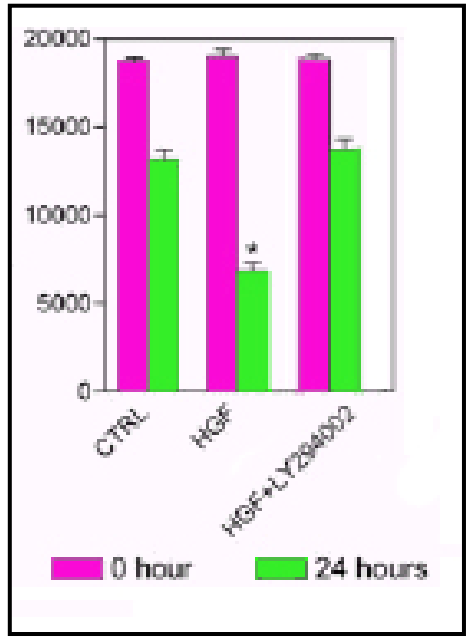
Motilita’


corteccia di actina
lamellipodio
substrato
corteccia sotto tensione
la polimerizzazione di actina all'estremità più fa sporgere il lamellipodio
movimento di actina non polimerizzata
miosina II
contrazione
contatti focali
(contengono integrine)

MOTILITA' CELLULARE INDOTTA DA HGF NELLE CELLULE ST14A





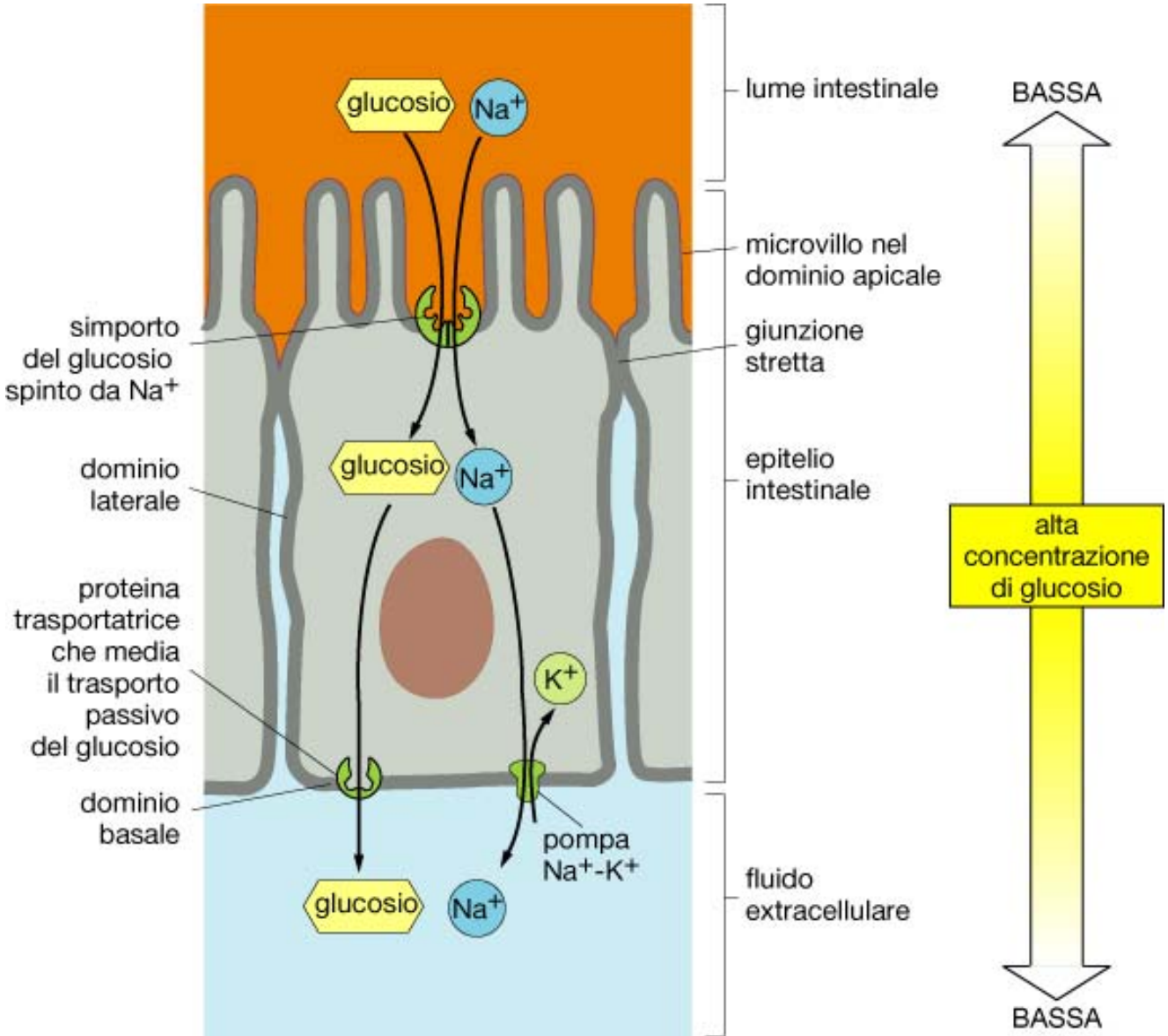


LE CELLULE ST14A POSSIEDONO IL RECETTORE MET E LA RISPOSTA MOTOGENA ALL'HGF E' REGOLATA DALLA VIA PI3K

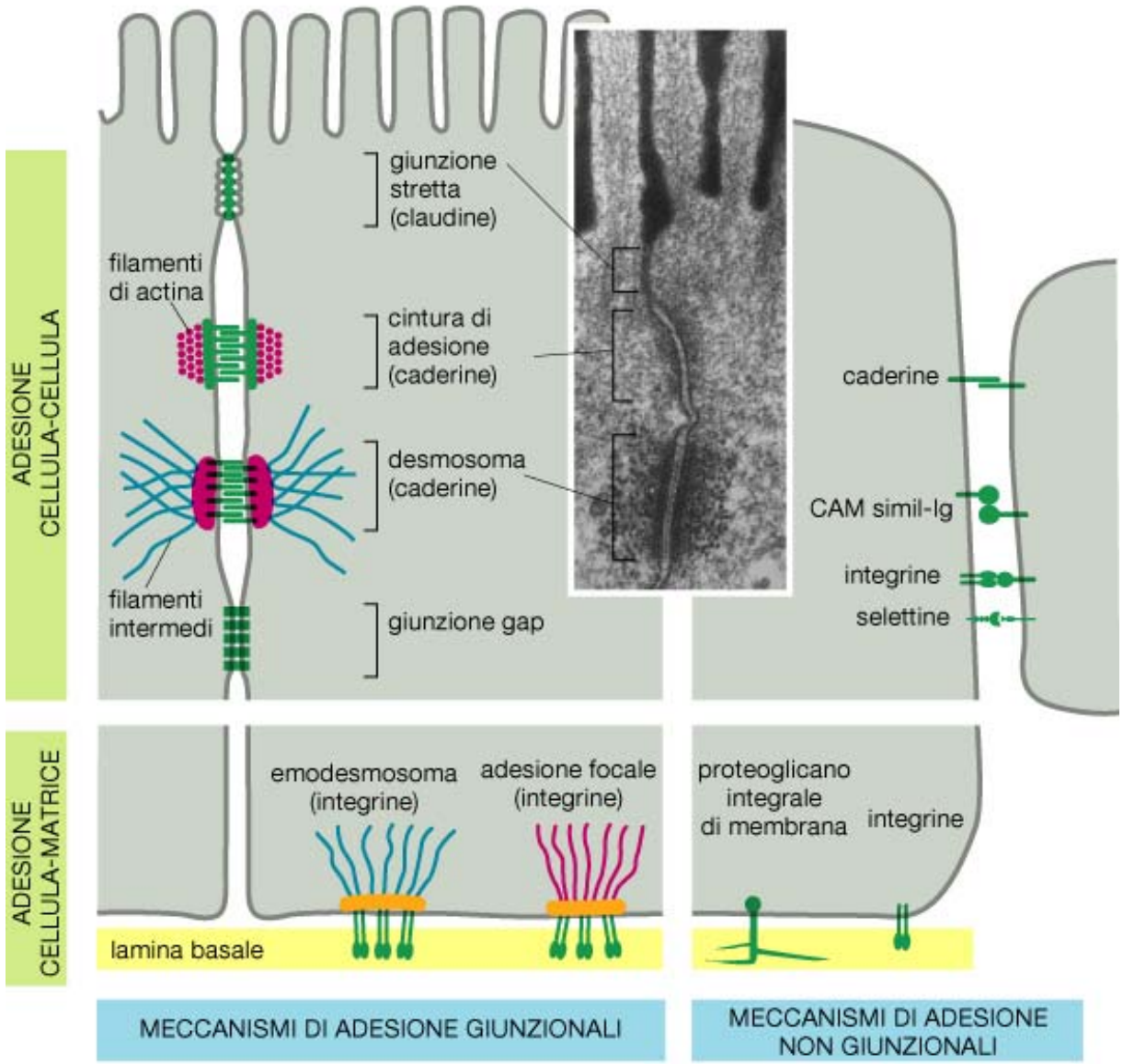
Specializzazione

Proteine trasportatrici

Domini di membrana con distribuzione selettiva di trasportatori



Schema riassuntivo sistemi di adesione cellulare



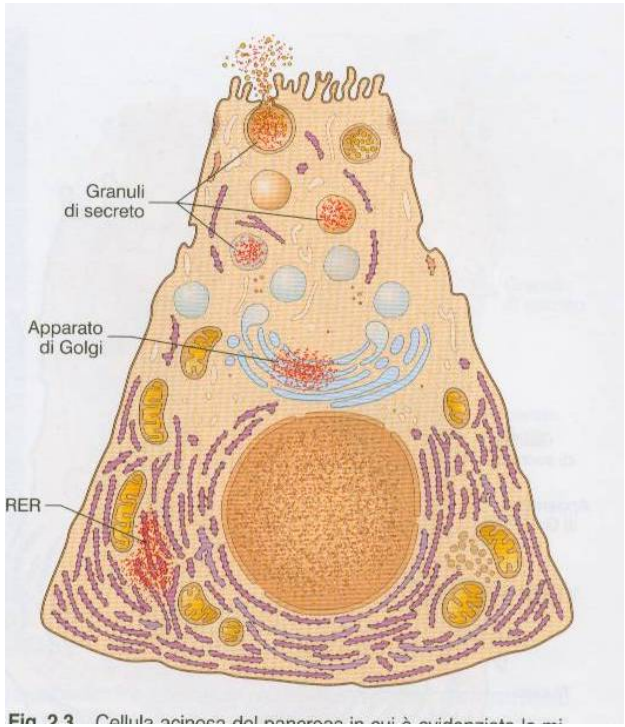
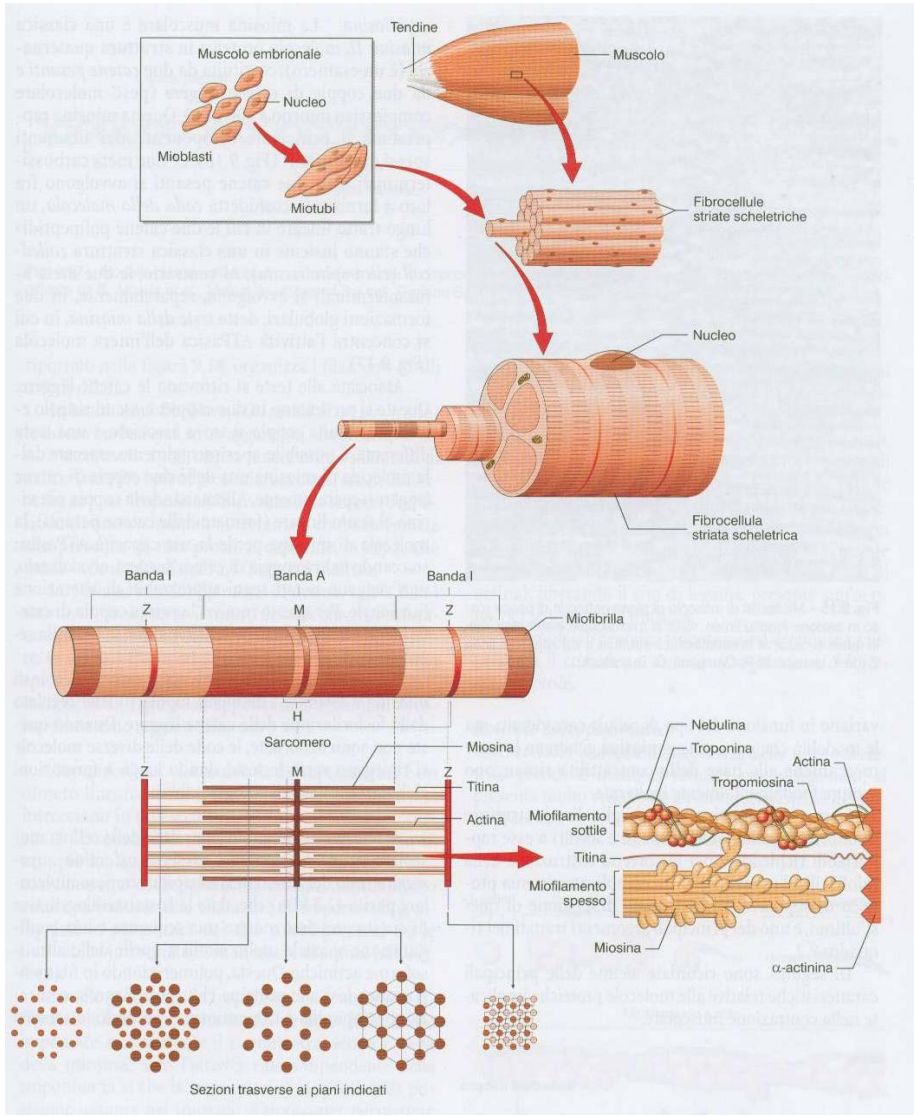


Fig. 2.3 Cellula acinosa del pancreas in cui è evidenziato lo mi



Excitable cells rely on ion channels