CENTRE NATIONAL DE LA RECHERCHE SCIENTIFIQUE

Inserm
Institut national de la santé et de la recherche médicale

Université Nice SOPHIA ANTIPOLIS

ipmc

MASTER MAPI, 2010

Les sciences de la vie: de la molécule aux applications sociétales

Dr Fabrice DUPRAT
Institut de Pharmacologie Moléculaire et Cellulaire

Pourquoi faire des sciences de la vie ?

Qu'est-ce qu'une protéine ?

Qu'est-ce qu'une bactérie ?

A quoi sert la thérapie génique ?

Comprendre les pôles de compétitivité en SDV

Quelques chiffres …

Côte d'Azur: CA >2 milliards €
> 250 sociétés
> 10000 emplois

CHU: 6500 employés (1er employeur du 06)

+300 chercheurs, 50 laboratoires
(INSERM, CNRS, INRA, CEA, UNSA)

1 des 5 cancéropoles à Nice

cancéropôle
Provence-Alpes-Côte d'Azur

1 des 3 génopoles à Sophia

réseau national genopole®

Industries et services des Alpes Maritimes

A-PHARMACONSULT
AMO France SAS
AGA MEDICAL
AGILENT TECHNOLOGIES
AIR LIQUIDE
ALFAMED
ALLERGAN France
AMITIS
ARKOPHARMA
ASEPTA LABORATOIRES
BAYER CROPSCIENCE
CLL PHARMA
CODAN France
COOPERVISION
CORADIN
CPCAD
DERMOTECHNIC
DKZ France Créations
DOW AGROSCIENCES
DOW AGROSCIENCES DISTRIBUTION
DOW AGROSCIENCES EXPORT
EA PHARMA
EUROPHTA
FMS – Future Medical Systems
GALDERMA R&D
GENACTIS
HORUS PHARMA
IMMUNOSEARCH
INTEGRA NEUROSCIENCES IMPLANTS
IRIS PHARMA
KAERYS
LA MESTA CHIMIE FINE - GROUPE AET
LABORATOIRE ELAIAPHARM
LABORATOIRE FERRIER
Laboratoire PHYTALLIANCE YD COSMETICS
LABORATOIRE VETERINAIRE DEPARTEMENTAL
LABORATOIRES ARION
LABORATOIRES BOIRON
LABORATOIRES GENEVRIER
LABORATOIRES PHAGOGENE & DEC AZUR
LABORATOIRES SOPHILENE
LIMA France
LPG SYSTEMS
LUXCLEAR PHARMA
MANE
MEDIAN TECHNOLOGIES
MEDICAPTEURS France
MXM
NEURELEC
NICOX
NIXE
NUSIL TECHNOLOGY EUROPE
NUTREVA
OCTALIA TECHNOLOGIES
OPHTALMIS
ORTHOMED SA
PARALLEL DESIGN
QUANTIFICARE
ROHM AND HAAS France
SKINETHIC
SKINPHARMA
SO.F.I.A COSMETIQUES
SOCIETE EUROPEENNE DE CARDIOLOGIE
STERLAB
STRYKER EMEA
SUPRALOG
SYNOPTIC
TELEMAQ
THERAMEX
TRAUMA CARE INSTITUTE - STRYKER TRAUMA & AIOD
TXCELL
VENOME TECH
VIBRANT MED-EL HEARING TECHNOLOGY
VINCIENCE – ISP
VIRBAC

Objectifs de ce cours

Acquérir un vocabulaire de base.

Comprendre les grands concepts.

Projets multidisciplinaires à forte valeur ajoutée.

Informatique
Electronique
Optique
Matériaux
Télécom
Etc …

Plan du cours

QU'EST-CE QU'UN ETRE VIVANT ?

EVOLUTION DES ESPECES
Origine de la vie

LE MONDE DE L'INFINIMENT PETIT
De la population à la cellule
Cellules animale, bactérienne, végétale

LES MOLECULES DU VIVANT
Eau, lipides, glucides, ions, protéine, acides nucléiques

ADN-ARN-PROTEINES
Gènes, génétique, biologie moléculaire, puces à ADN

BIOLOGIE CELLULAIRE
Division cellulaire, cultures cellulaires

APPLICATIONS
Environnement, toxicologie, pôles de compétitivité

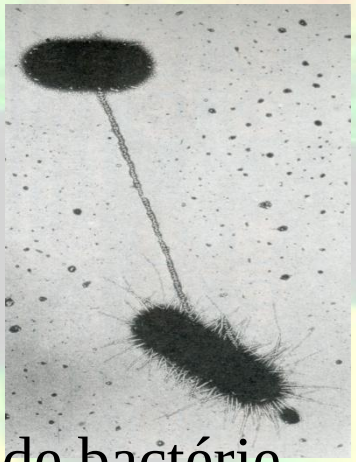
CONCLUSION

QU'EST-CE QU'UN ETRE VIVANT ?

Définitions

Larousse:
"Ensemble des phénomènes (nutrition, assimilation, croissance, reproduction...) communs aux êtres organisés et qui constituent leur mode d'activité propre, de la naissance à la mort."

"Un organisme est dit vivant lorsqu'il échange de la matière et de l'énergie avec son environnement en conservant son autonomie, lorsqu'il se reproduit et évolue par sélection naturelle".



Reproduction de bactérie

L'ensemble diffère de la somme des parties

Na

Sodium (métal)

+

Cl

Chlore gazeux

=

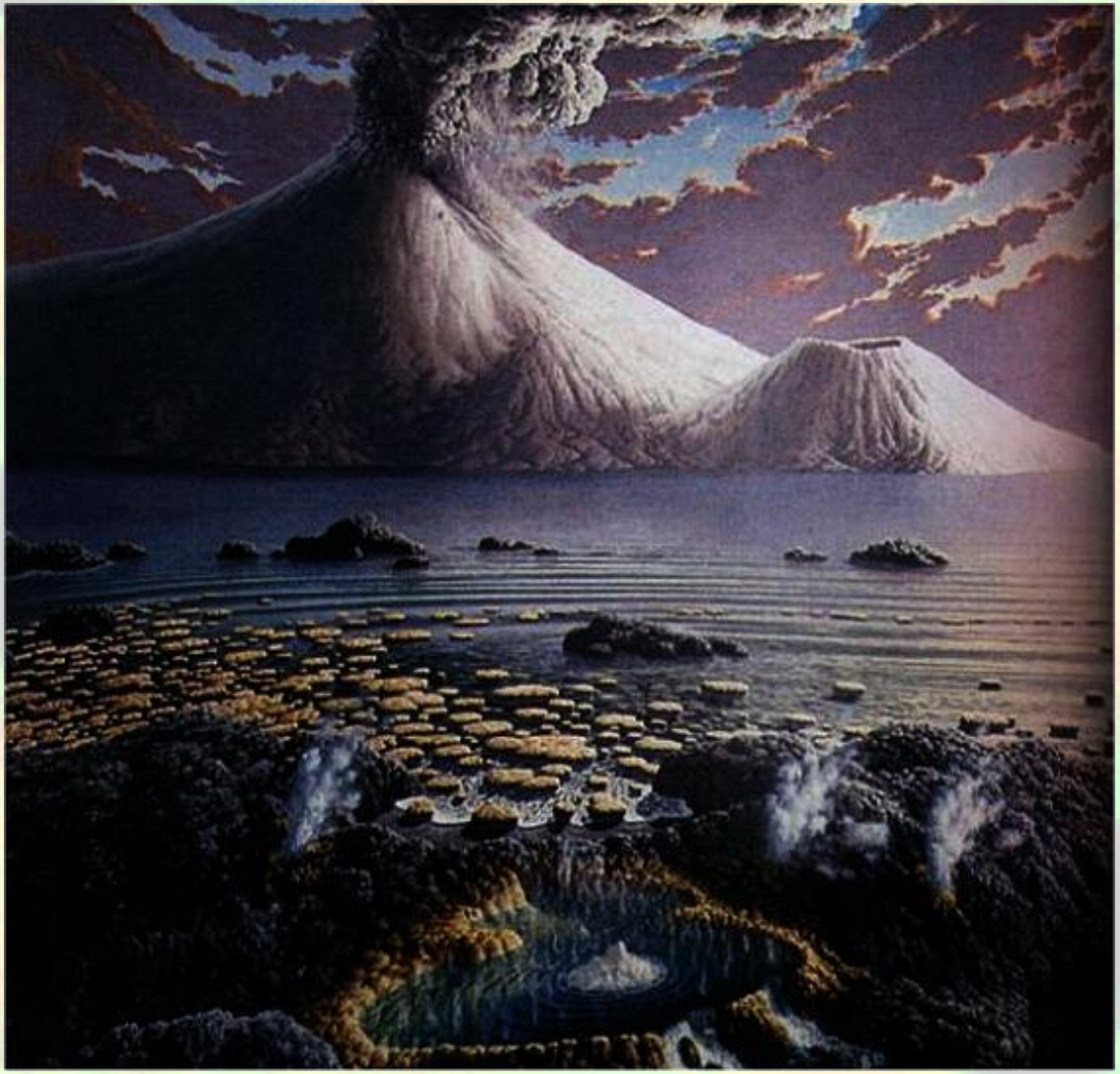
Chlorure de sodium

NaCl

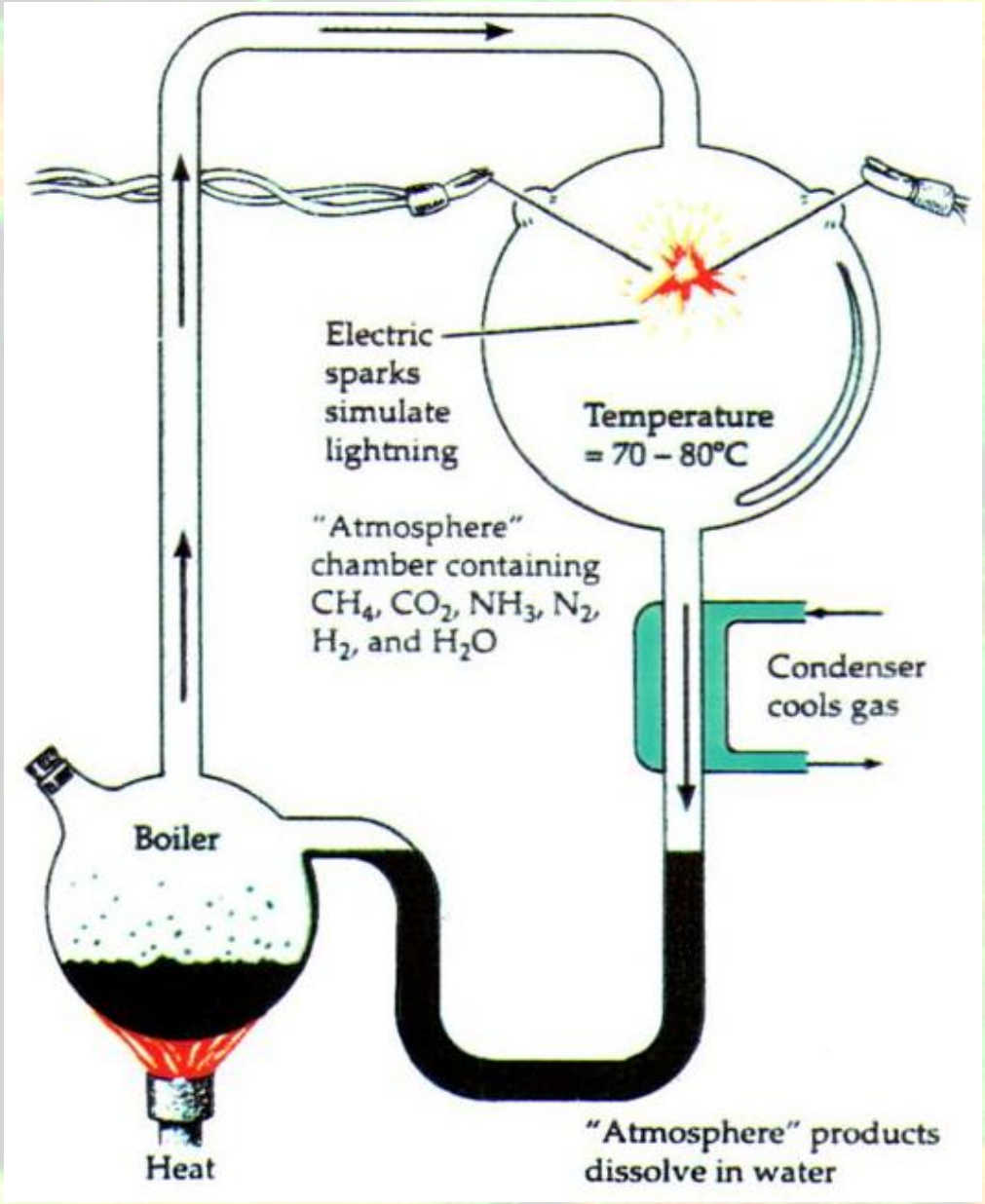
= Emergence

EVOLUTION DES ESPECES

L’origine de la vie



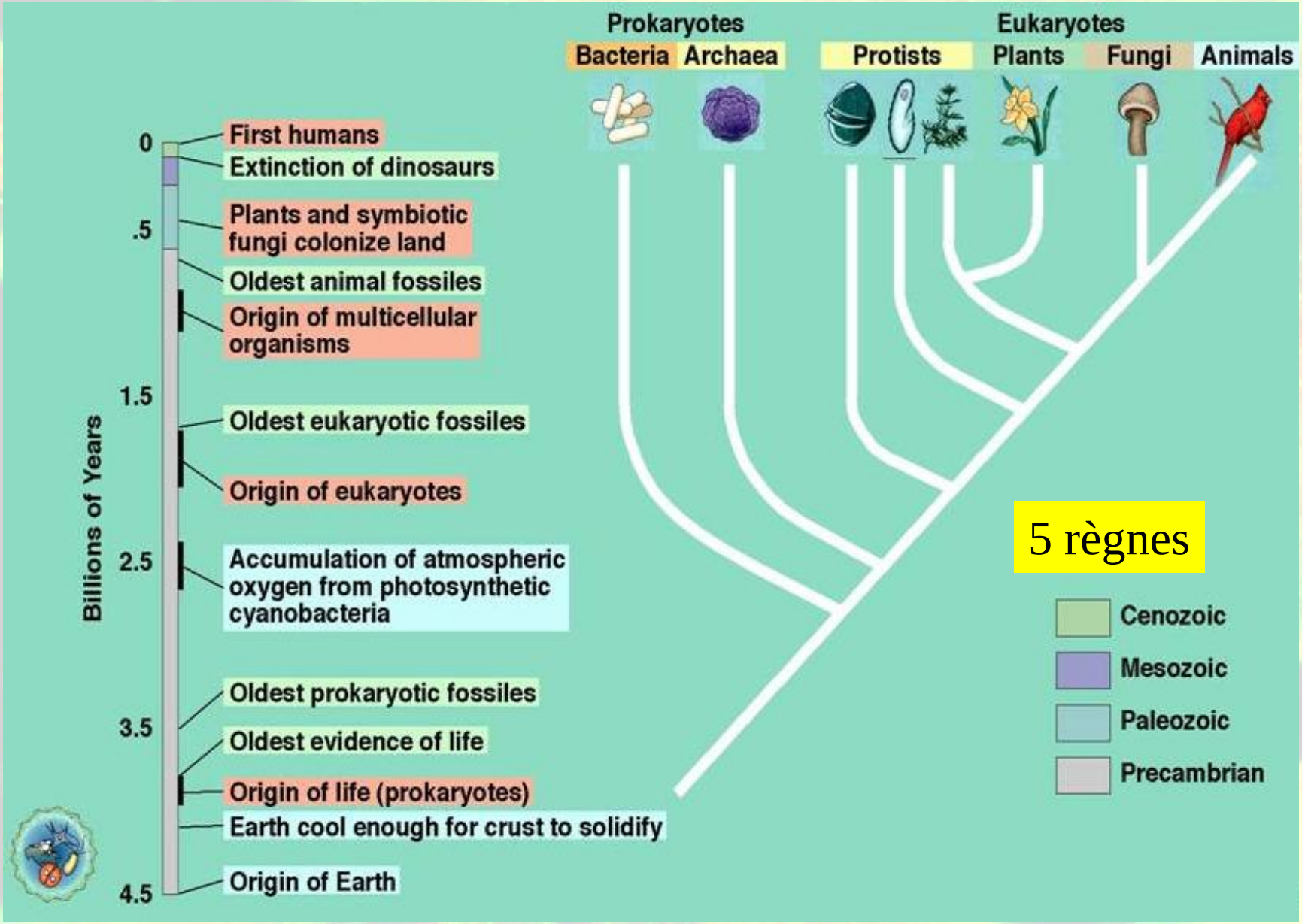
L'origine de la vie



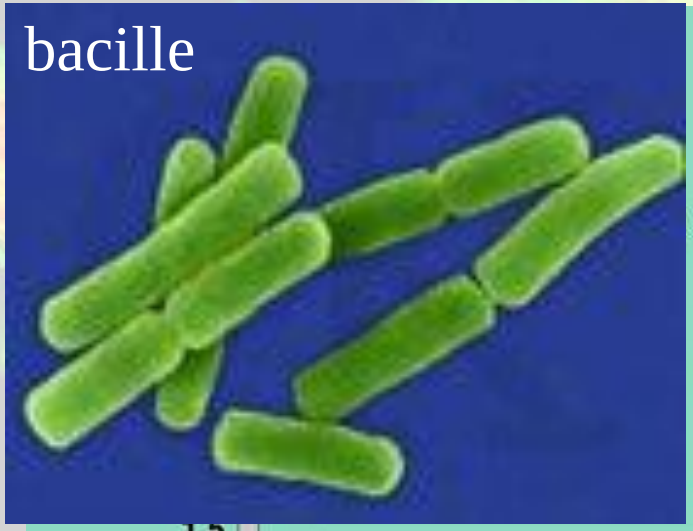
Méthane
Dioxyde de carbone
Ammoniaque
Azote
Hydrogène
Eau

Acides aminés

Evolution des espèces



Evolution des espèces



Evolution des espèces

Evolution des espèces

Prokaryotes
Bacteria
Archaea
Eukaryotes
Protists
Plants
Fungi
Animals

First humans
Extinction of dinosaurs
Plants and symbiotic fungi colonize land
Oldest animal fossiles
Origin of multicellular organisms
Oldest eukaryotic fossiles
Origin of eukaryotes
Accumulation of atmospheric oxygen from photosynthetic cyanobacteria
Oldest prokaryotic fossiles
Oldest evidence of life
Origin of life (prokaryotes)
Earth cool enough for crust to solidify
Origin of Earth

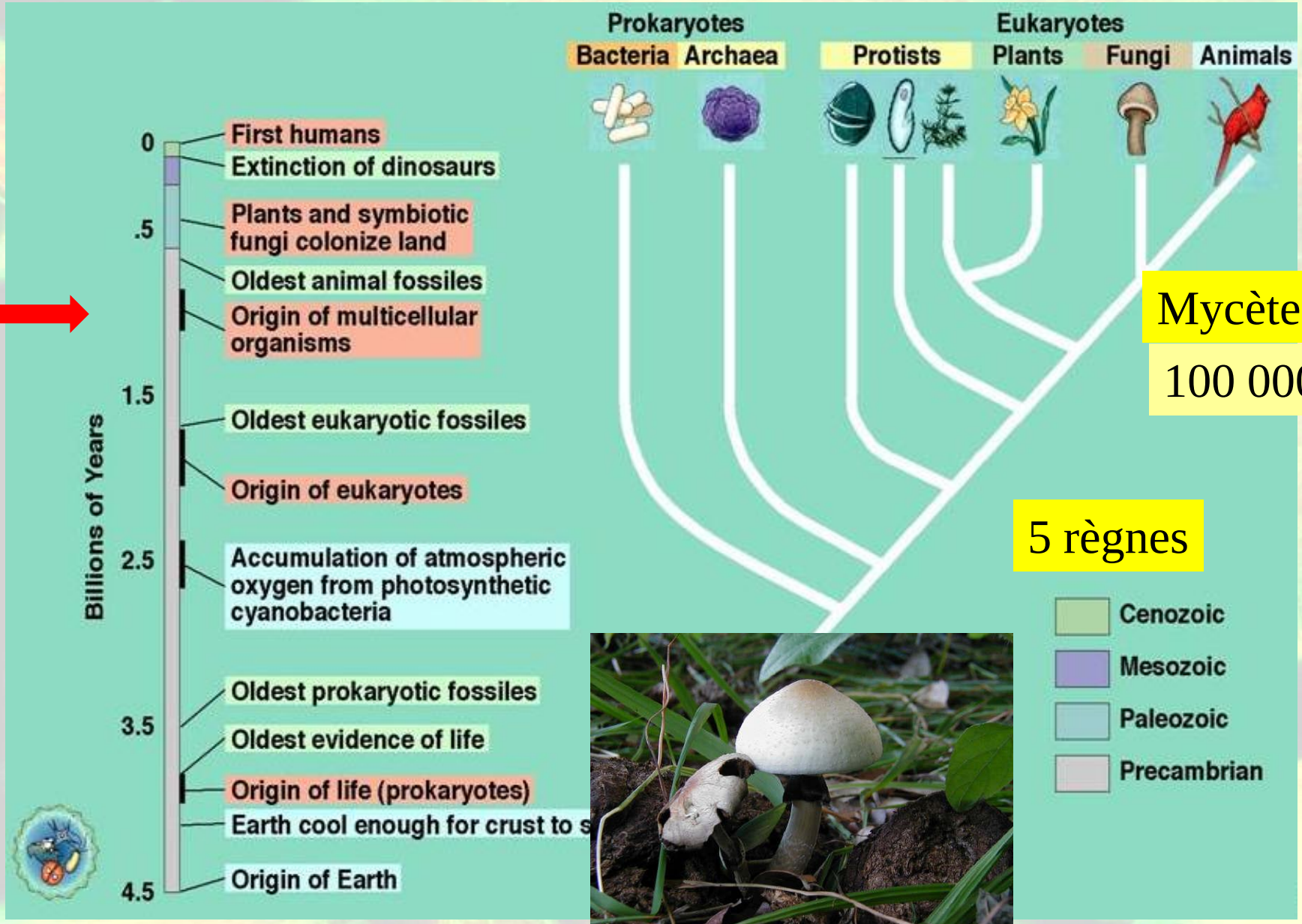
Billions of Years
.5
1.5
2.5
3.5
4.5

Végétaux
166 000

5 règnes

Cenozoic
Mesozoic
Paleozoic
Precambrian

Evolution des espèces

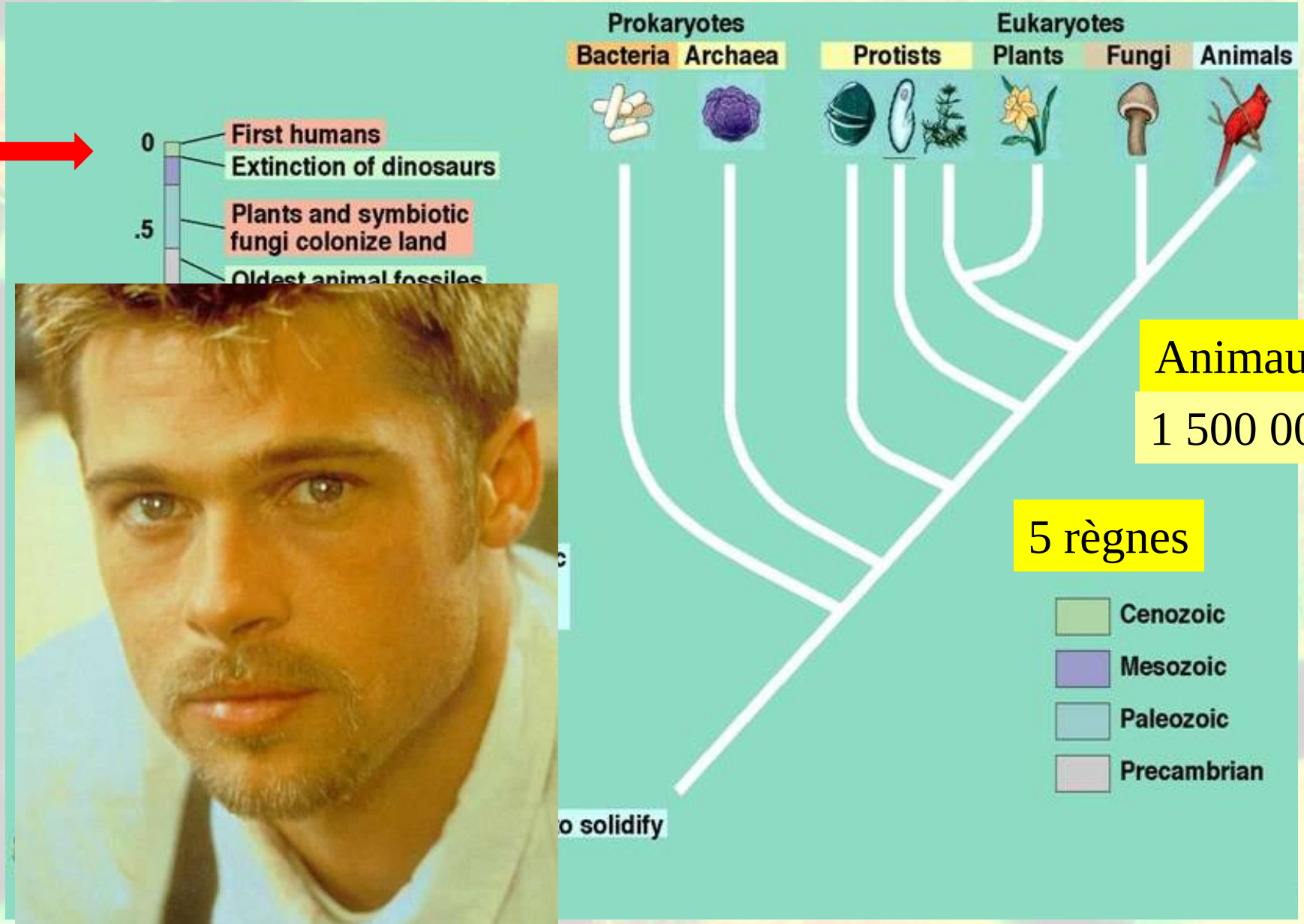


Mycètes

100 000

5 règnes

Evolution des espèces

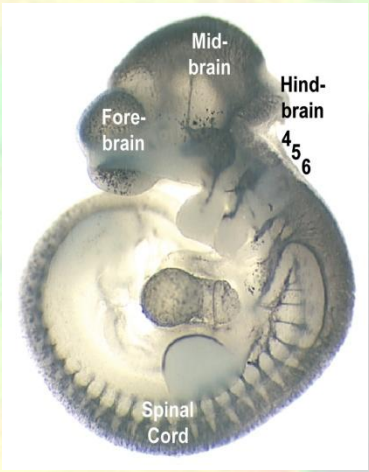


Animaux

1 500 000

5 règnes

Le jeux des fœtus et embryons animaux



Poulet

Humain

Xenope

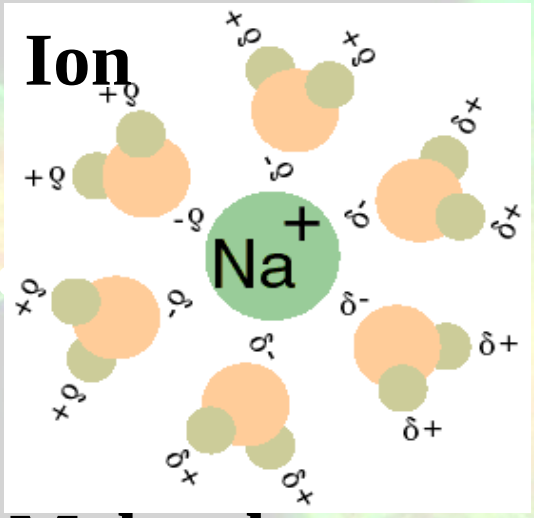
Chat

Souris

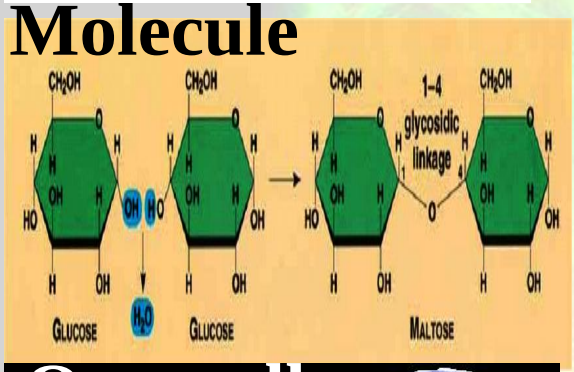
LE MONDE DE L'INFINIMENT PETIT

Des ions aux populations

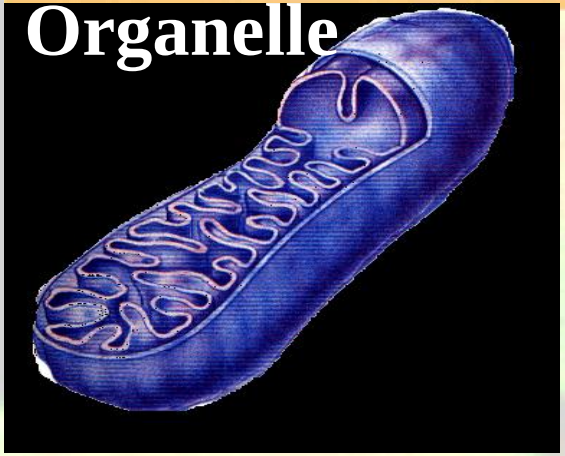
Ion



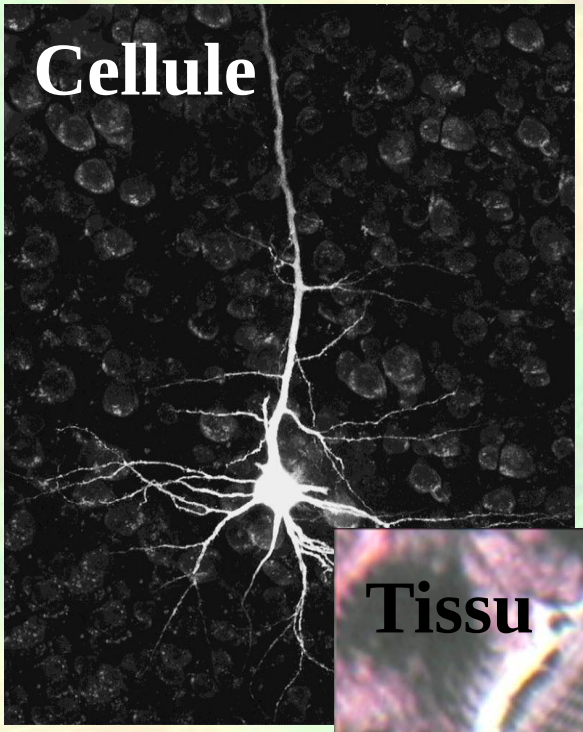
Molecule



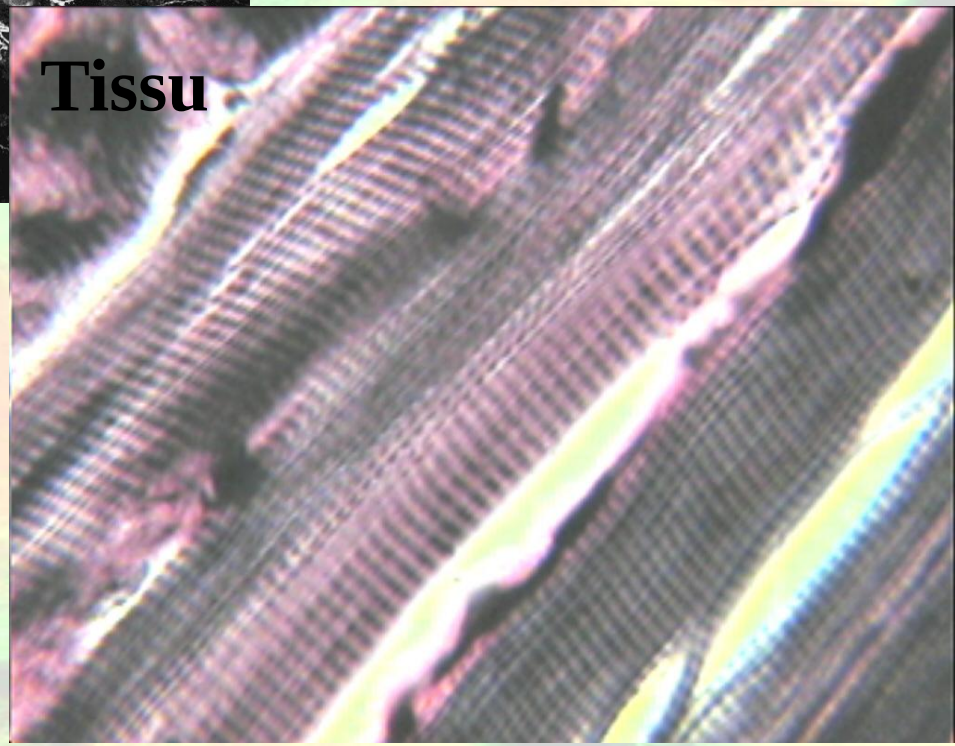
Organelle



Cellule

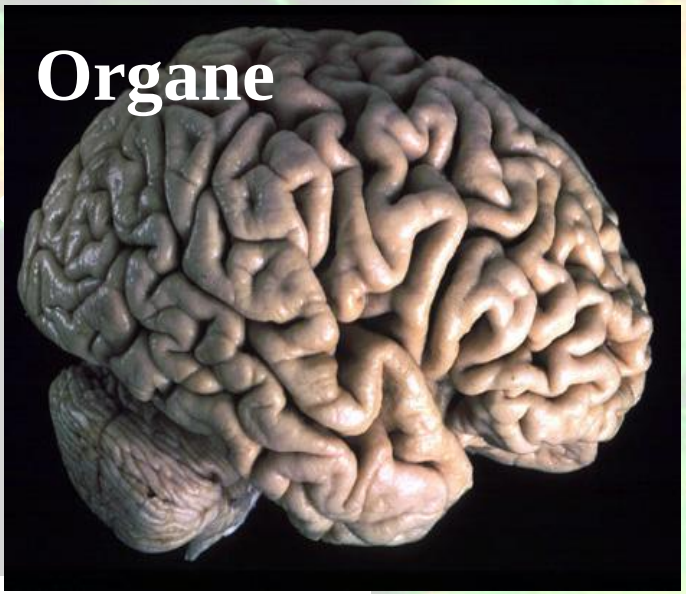


Tissu

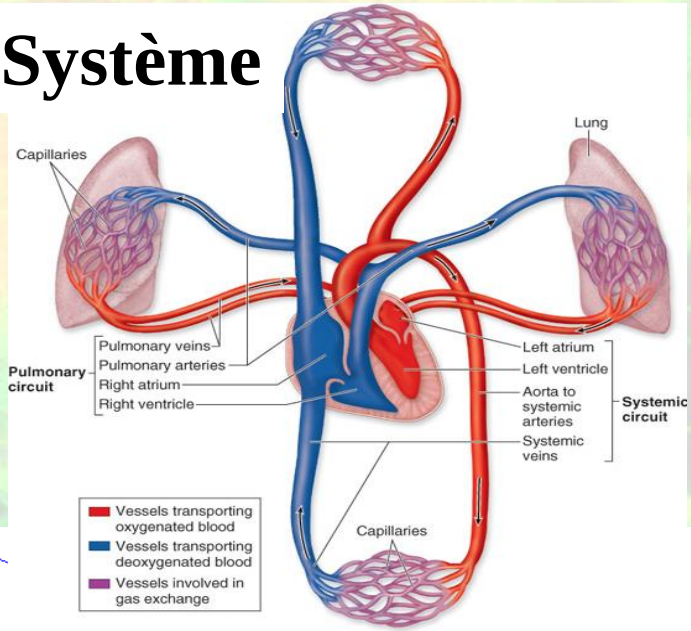


Des ions aux populations

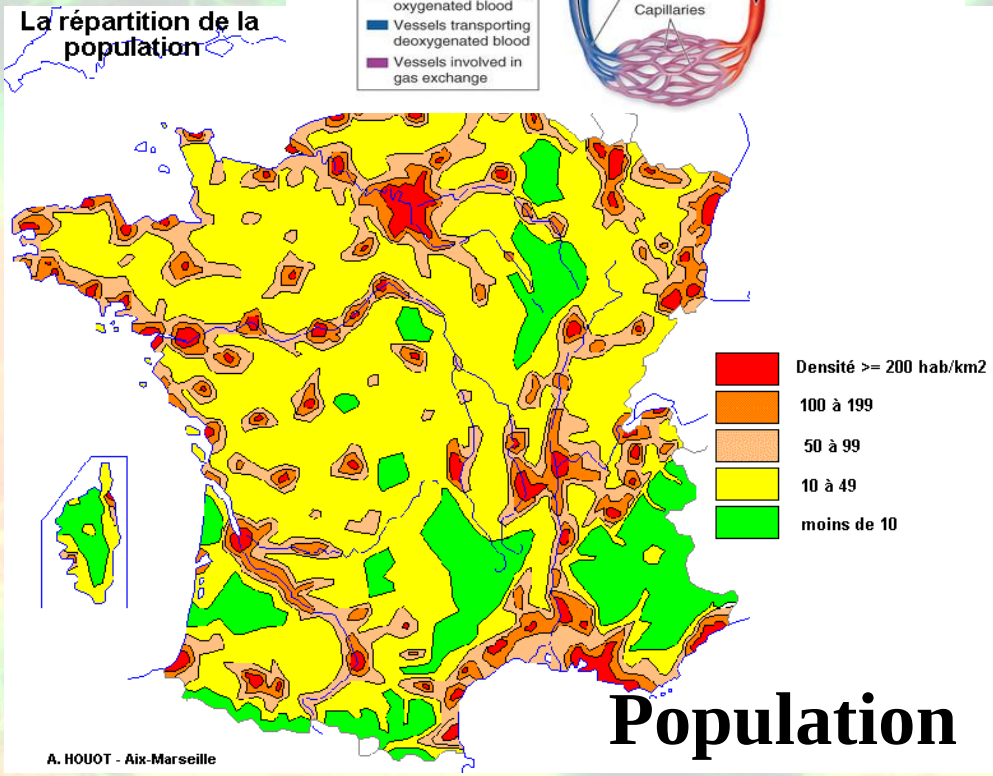
Organe



Système

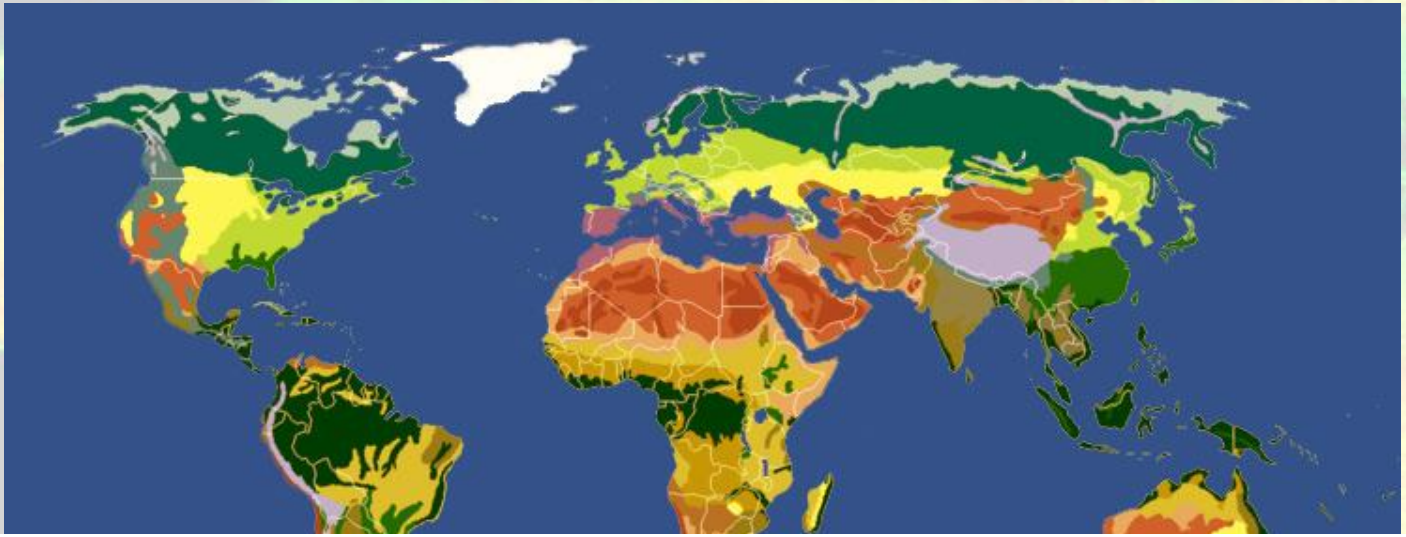


Organisme



Population

Biomes

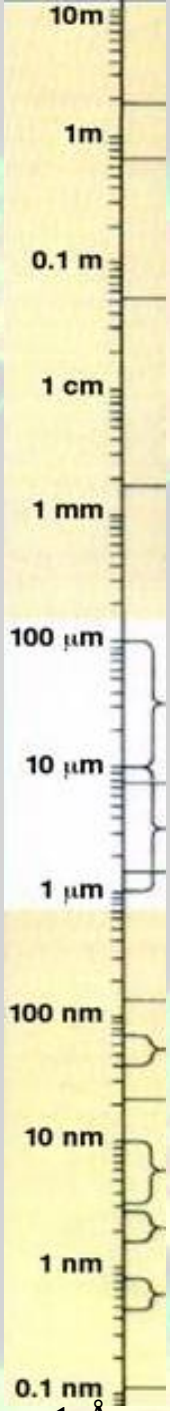


E**cosystème** = plusieurs organismes interdépendants (plantes, animaux , …) dans une zone géographique définie.

Biomes = zones avec un climat, un relief similaire + les mêmes populations d'animaux et de végétaux

http://www.windows.ucar.edu/tour/link=/earth/Life/biosphere.html

Dimensions en biologie



Hauteur d'un humain

Longueur de certains neurones

Insectes

Structures du cerveau

Cellule

Noyau

Bactérie

Mitochondrie

Virus

Ribosomes

Protéines

Lipides

Ions

= 1 Å

Oeil

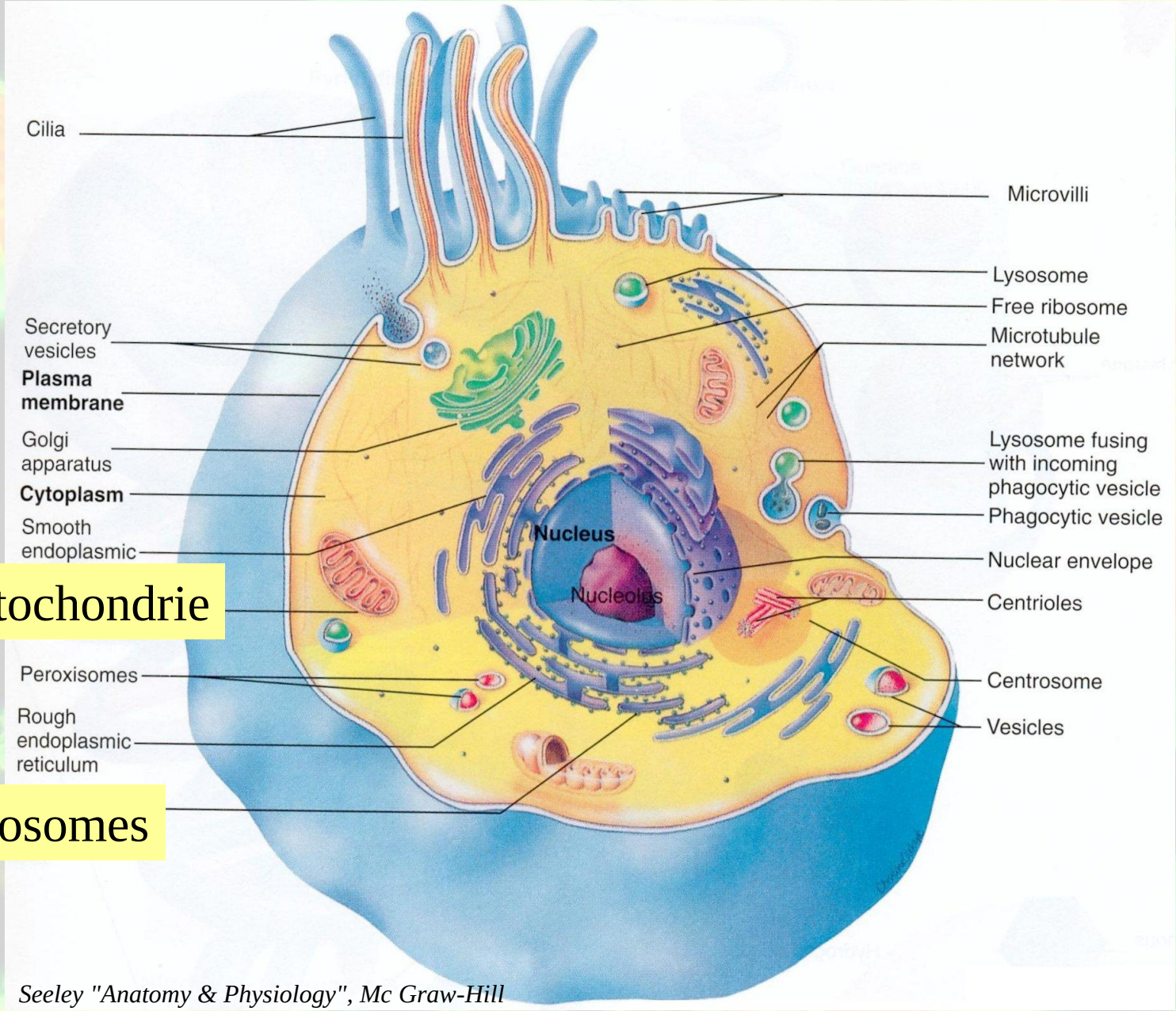
Loupe binoculaire
(x2 to x60)

Microscope photonique
(x20 to x1000)

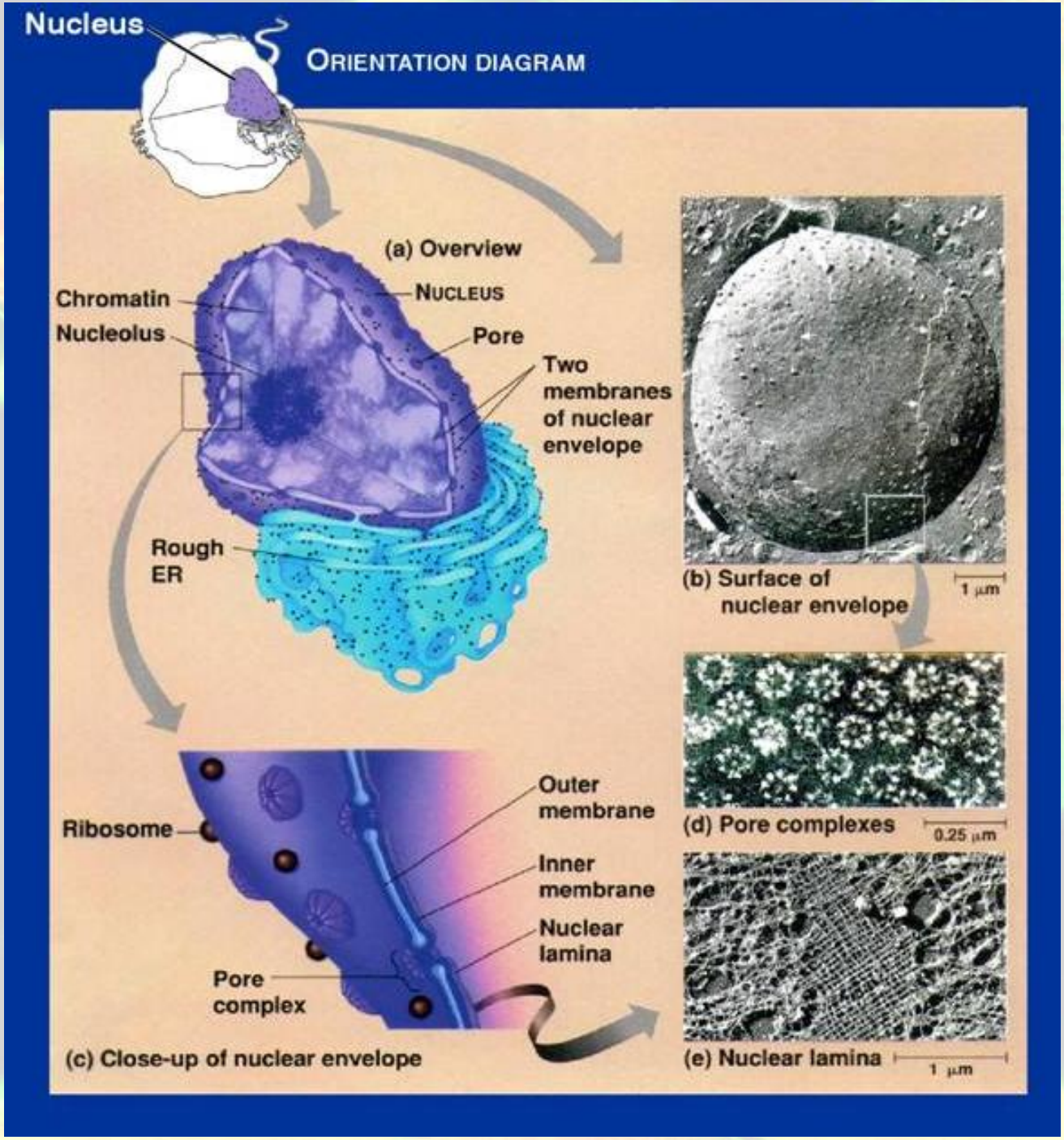
Microscope électronique

Microscope à Force atomique (AFM)

La cellule animale



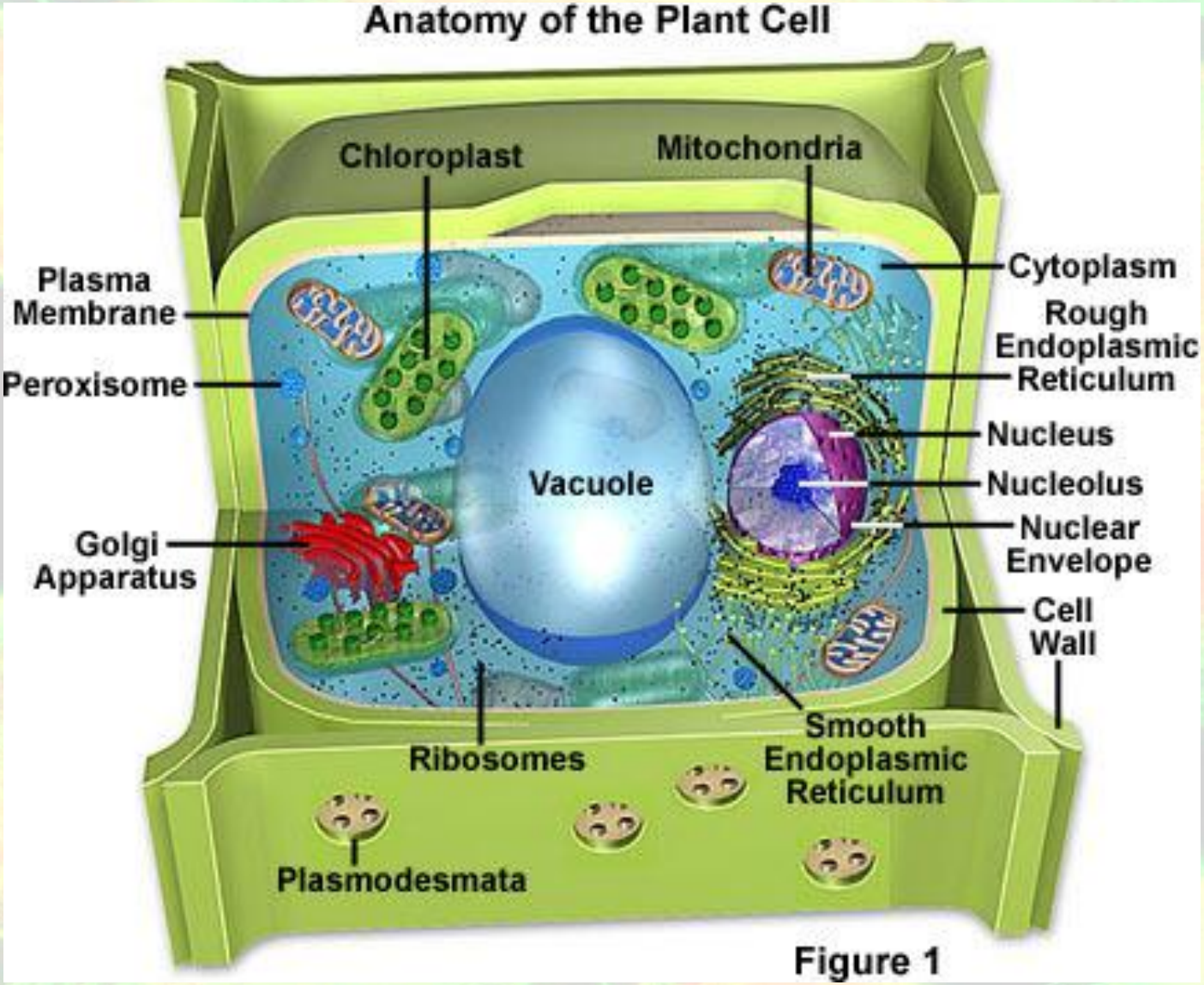
Seeley "Anatomy & Physiology", Mc Graw-Hill


Nucleus
ORIENTATION DIAGRAM
(a) Overview
Chromatin
Nucleolus
NUCLEUS
Pore
Two membranes of nuclear envelope
Rough ER
(b) Surface of nuclear envelope
1 μm
(d) Pore complexes
0.25 μm
Ribosome
Outer membrane
Inner membrane
Nuclear lamina
Pore complex
(c) Close-up of nuclear envelope
(e) Nuclear lamina
1 μm

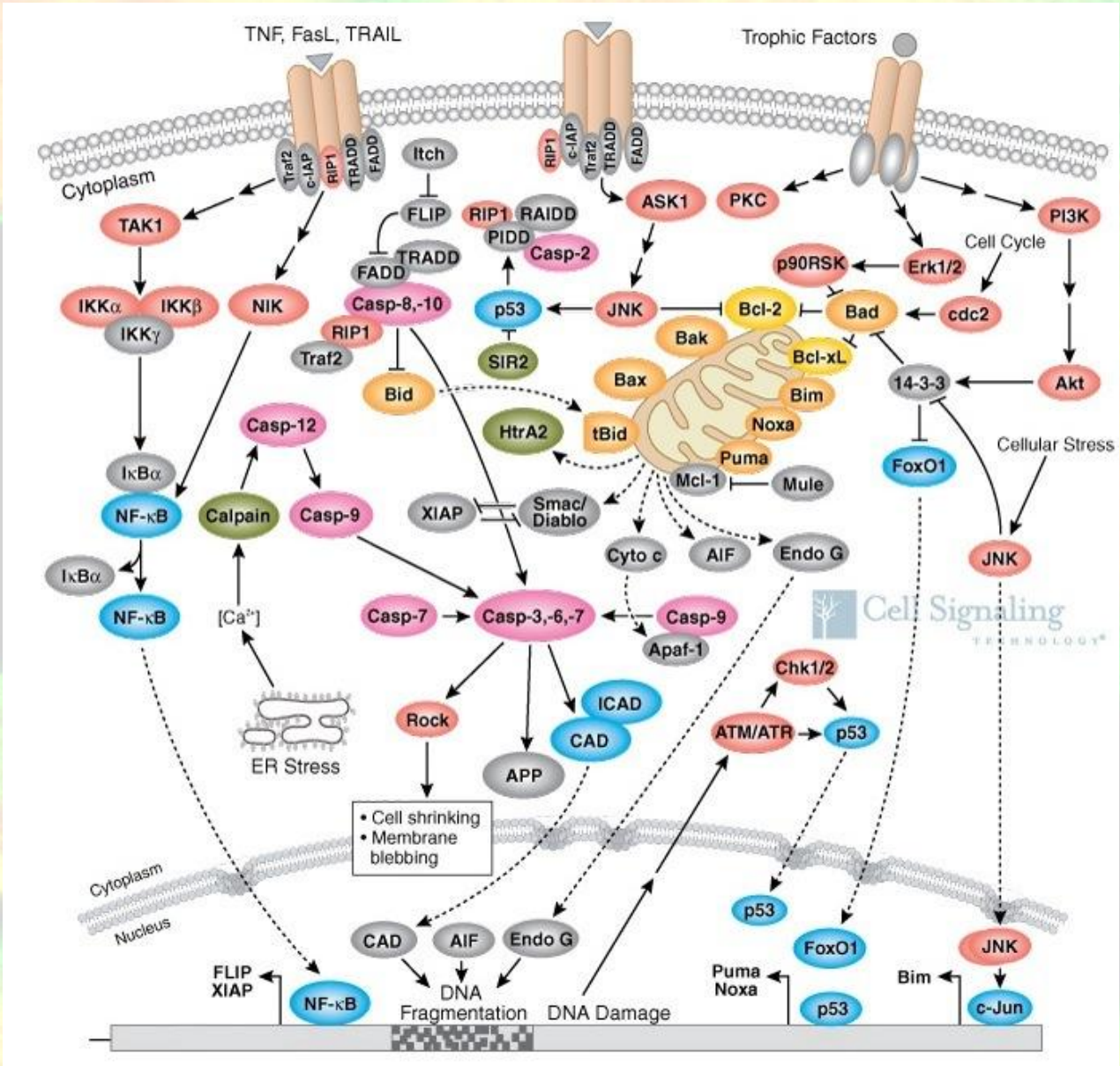
Le noyau

La cellule bactérienne

La cellule végétale

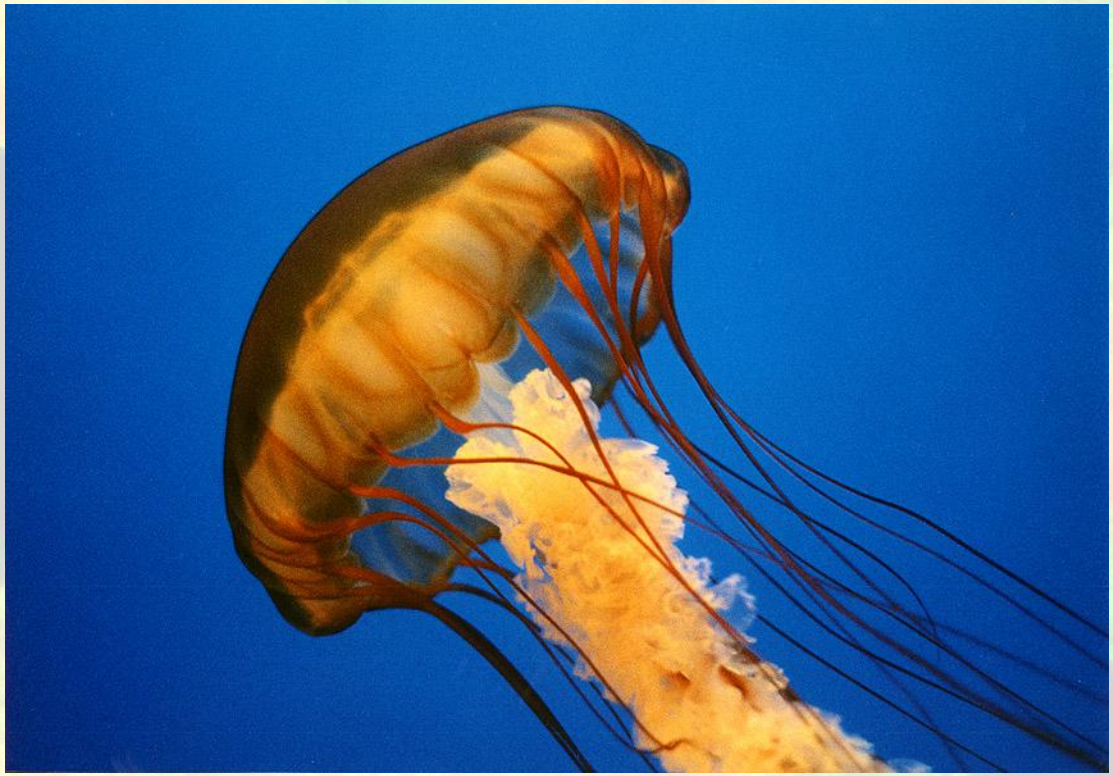


La biologie = interactions de quelques protéines



LES MOLECULES DU VIVANT

L'eau



= 99% H_2O

Propriétés étonnantes de l'eau

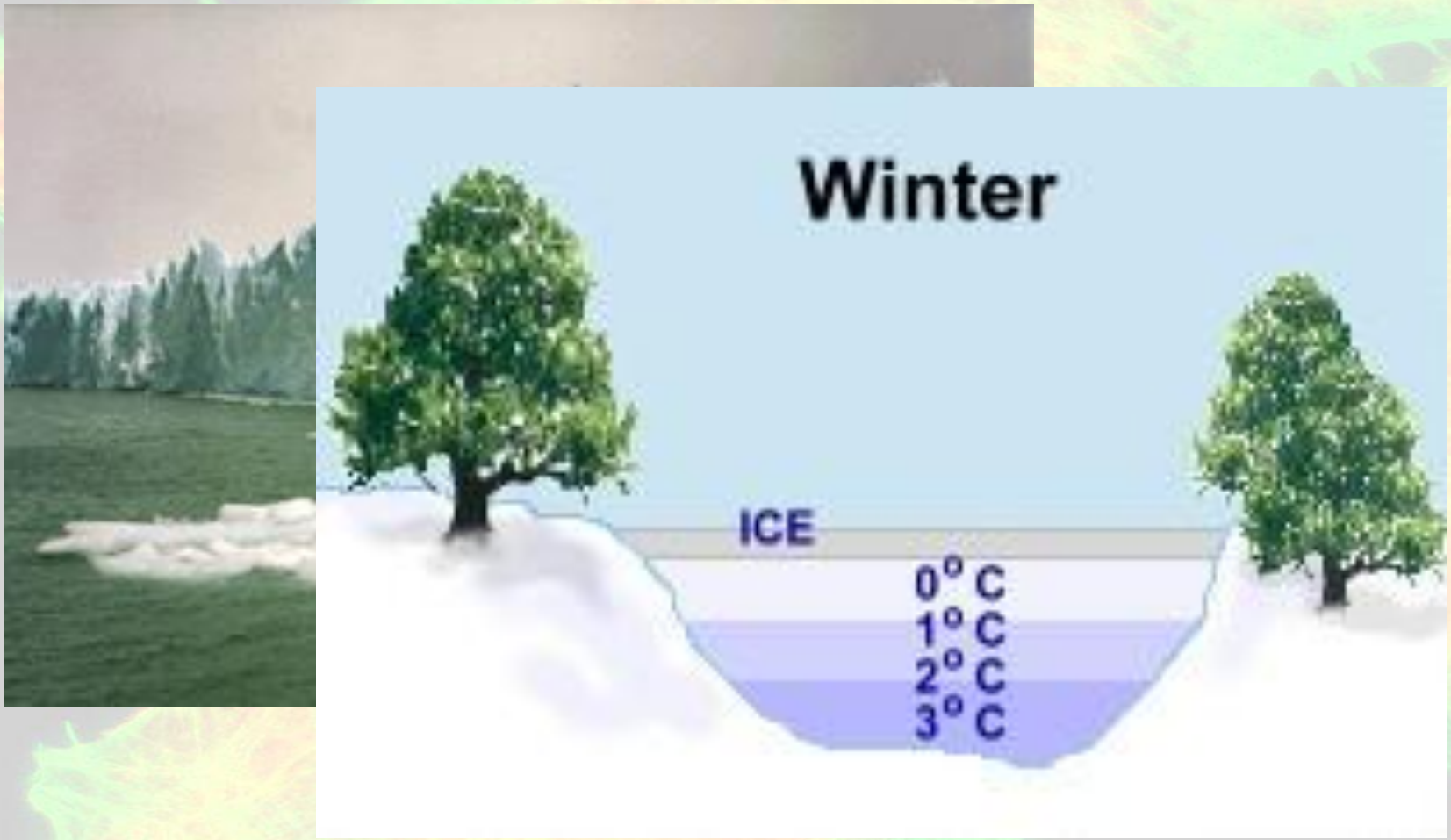
Excellent solvant

➡ L'hydratation permet de nombreuses réactions biochimiques

Forte tension de surface

➡ Permet à l'eau de circuler dans les racines

Propriétés étonnantes de l'eau

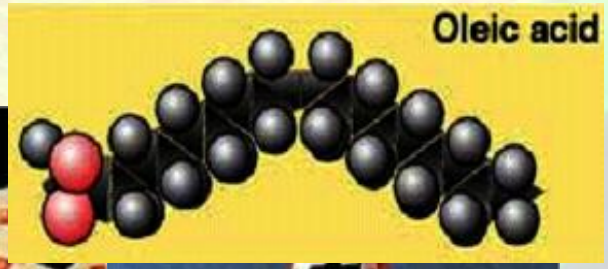


Expansion lors de la congélation

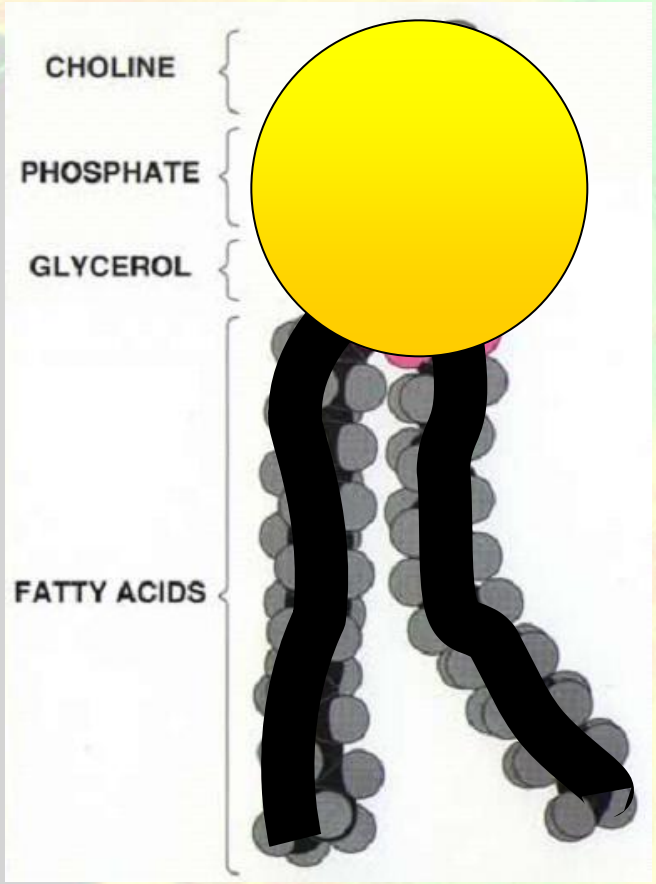
➡ Les plans d'eau ne gèlent pas entièrement

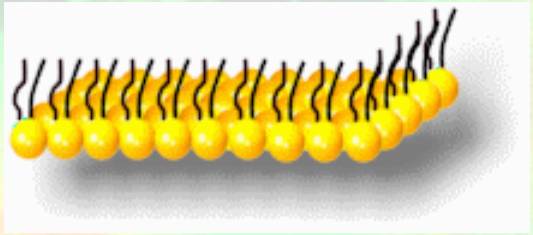
Les lipides (graisses)

Alimentation: produits laitiers, graines, huiles

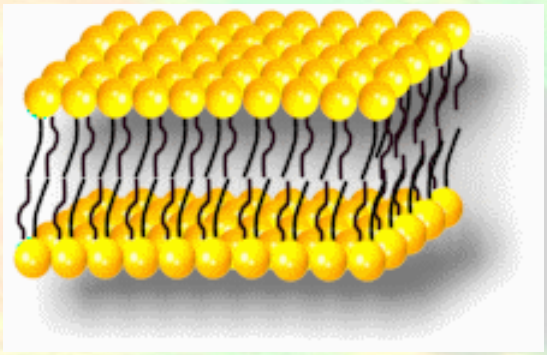


Structures:





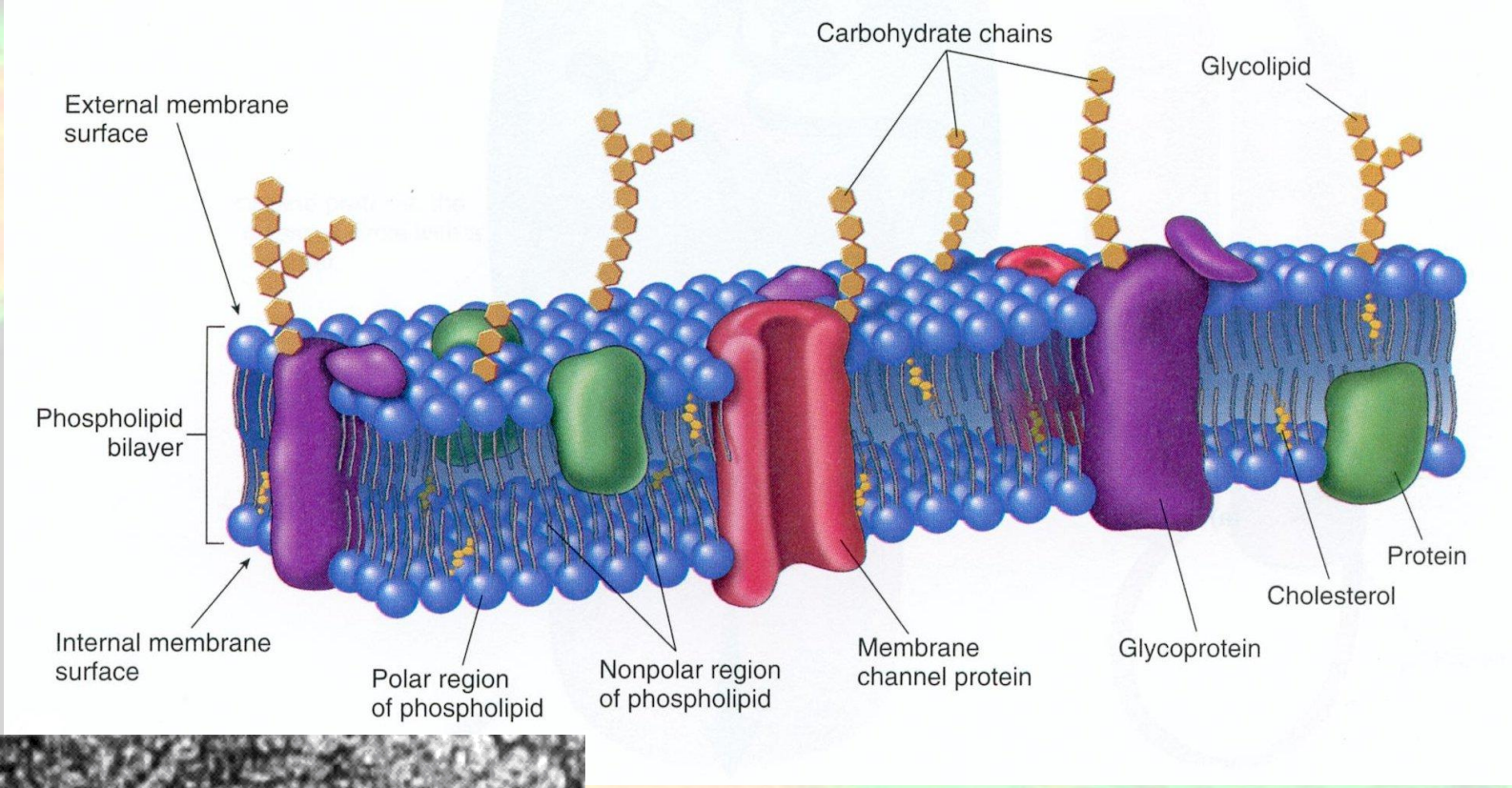
Liposomes

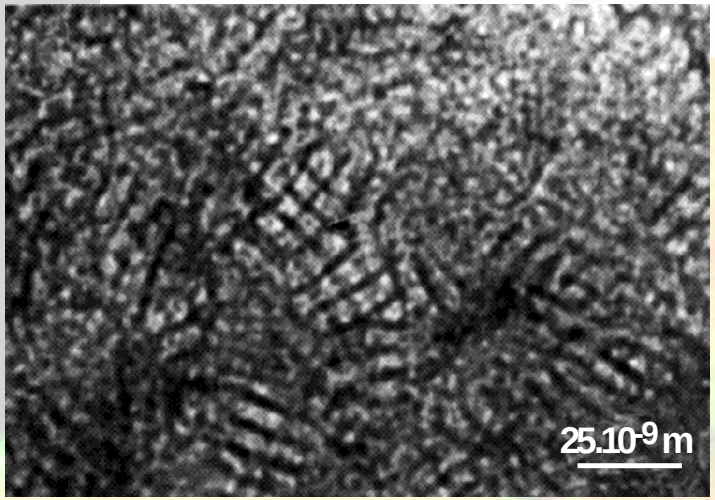


Bicouches

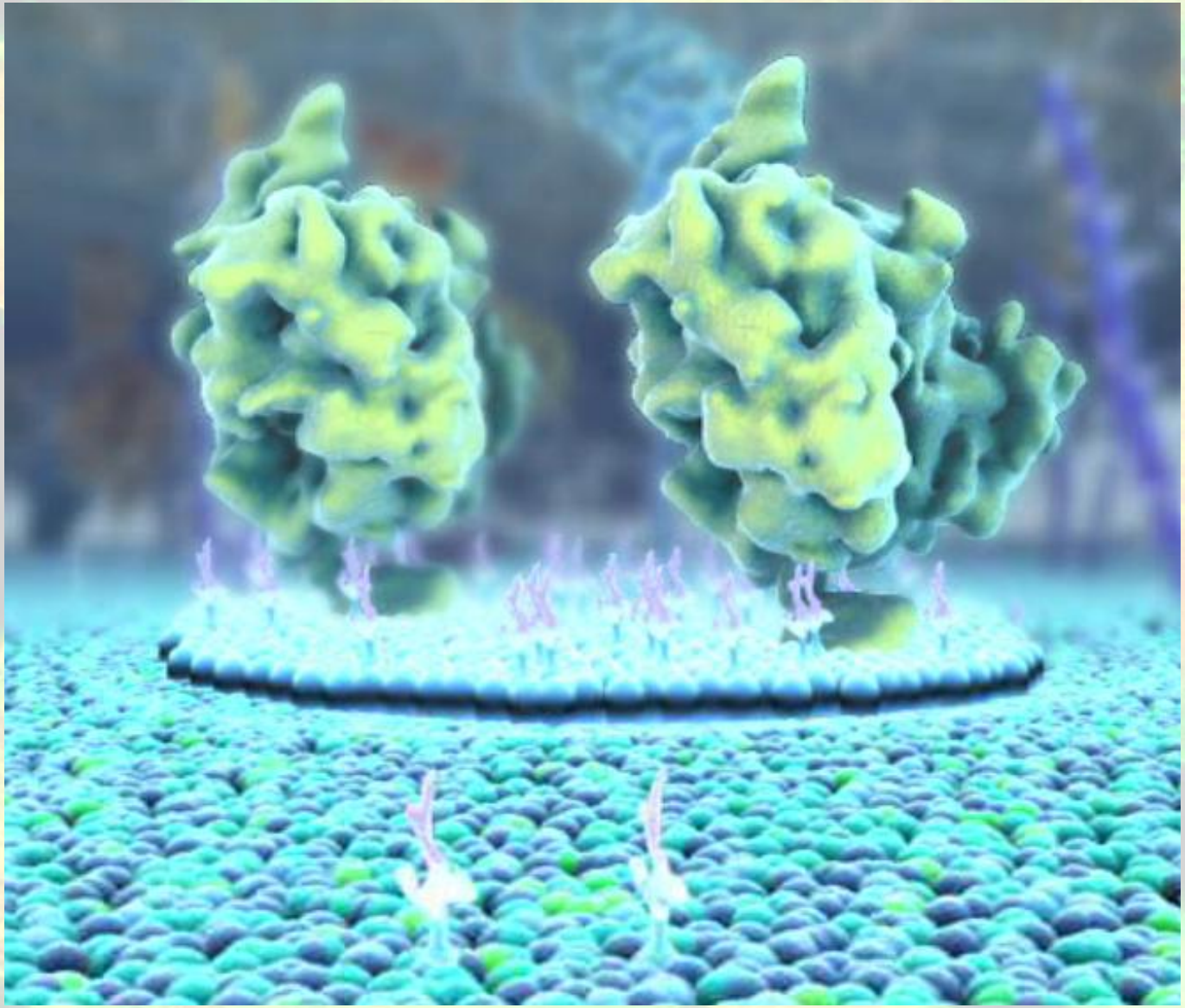
Rôles: Membranes, Signalisation, …

La membrane plasmique





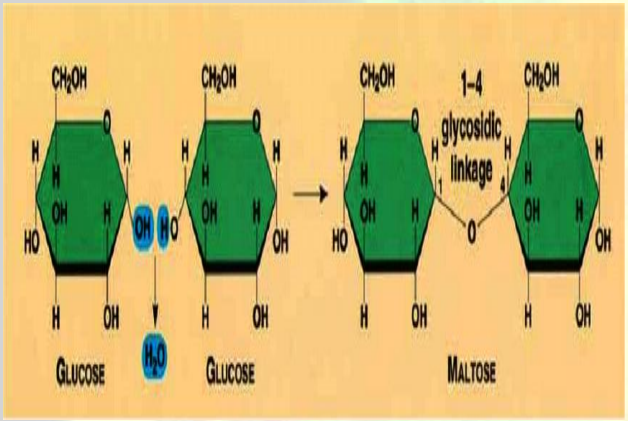
Radeaux lipidiques

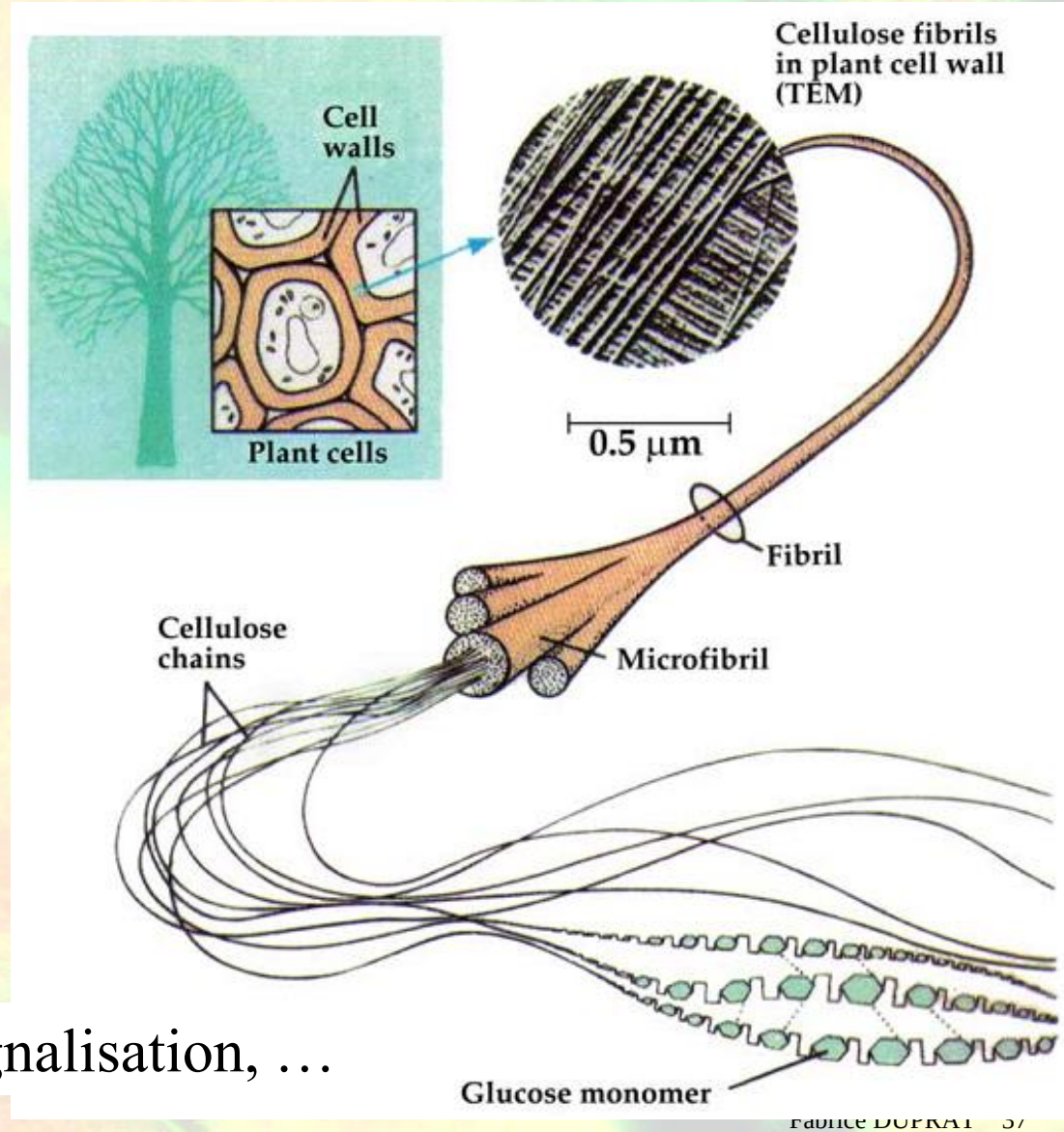


Les glucides (sucres)

Alimentation: fruits, légumes, pain, …

Structures:





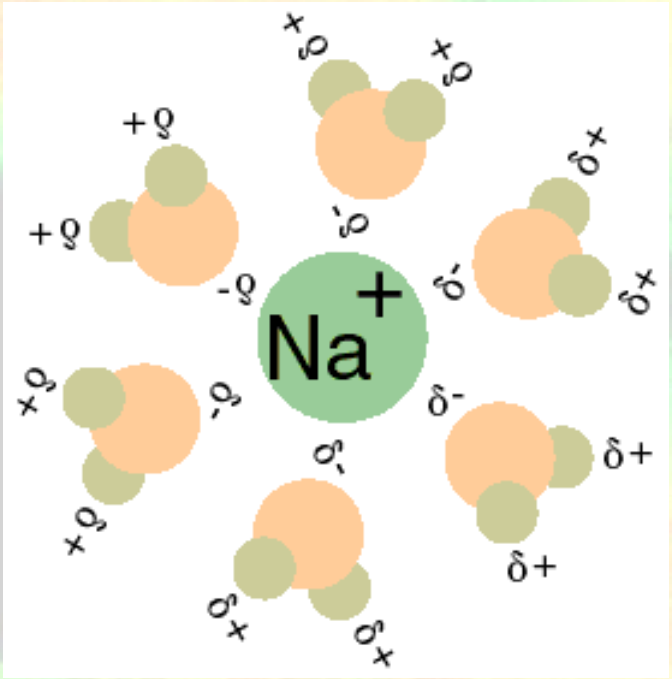
Rôles: Structure, énergie, signalisation, …

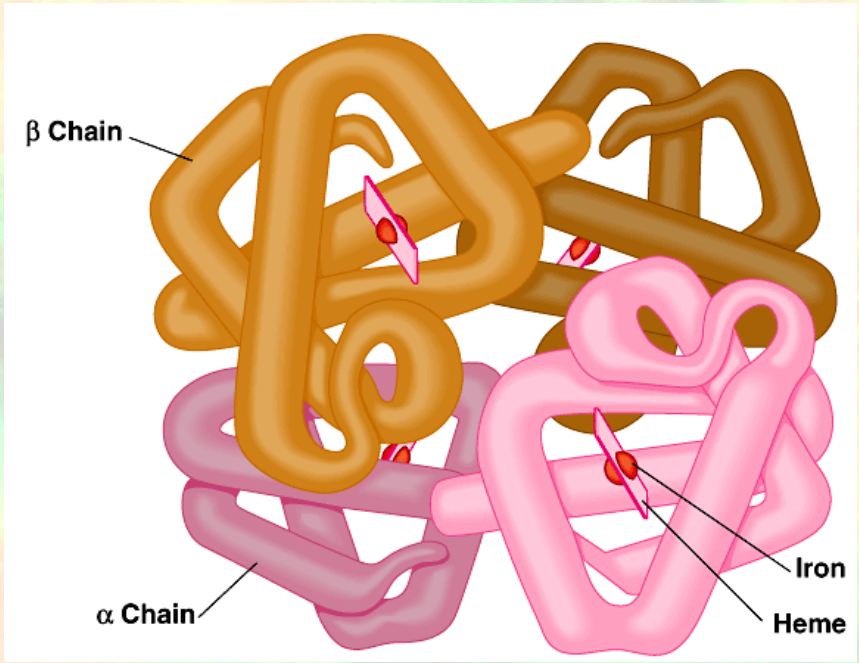
La chitine, glucide de structure

Bernard l'hermite

Les ions

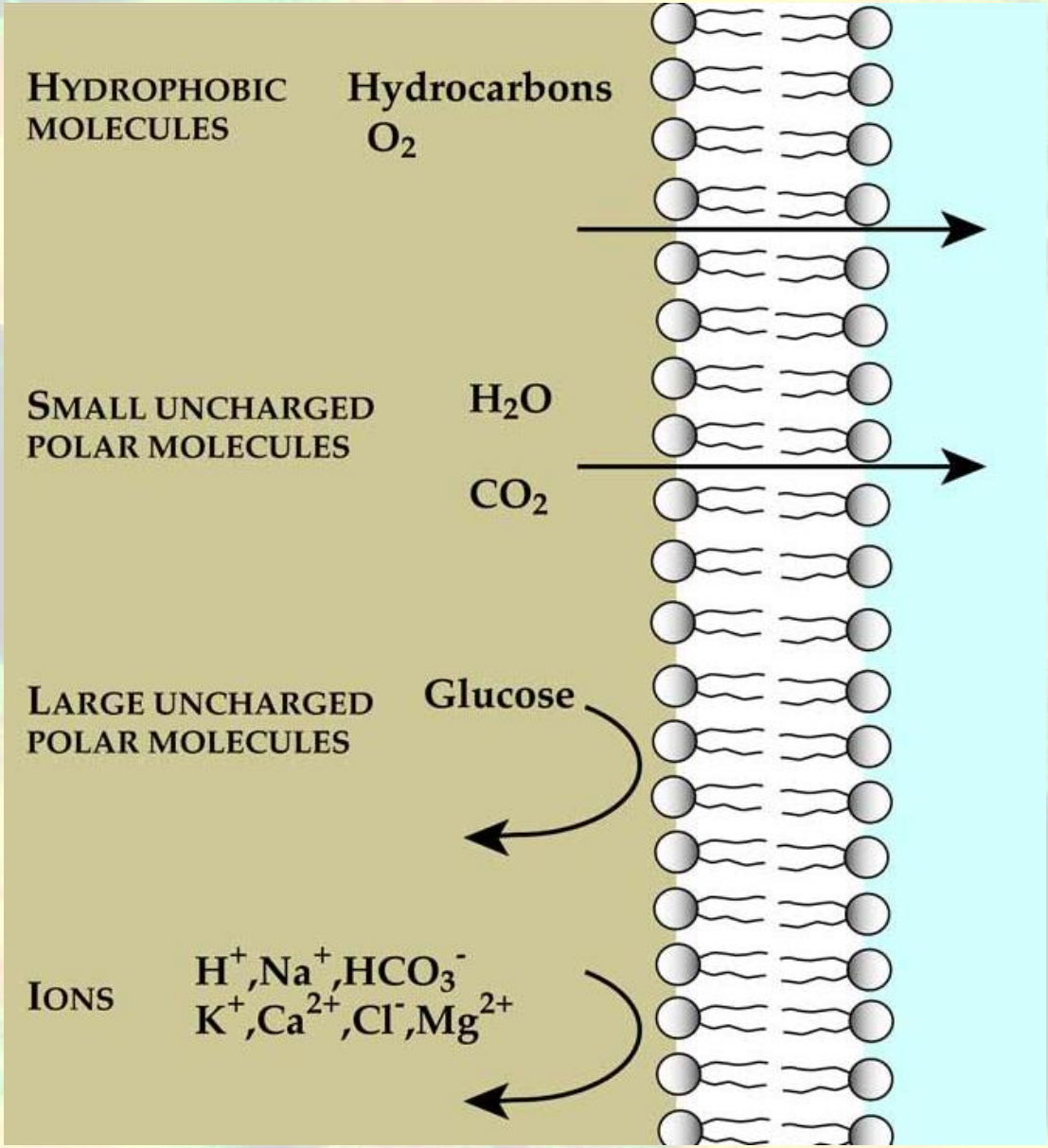
Alimentation: eau minérale, légumes





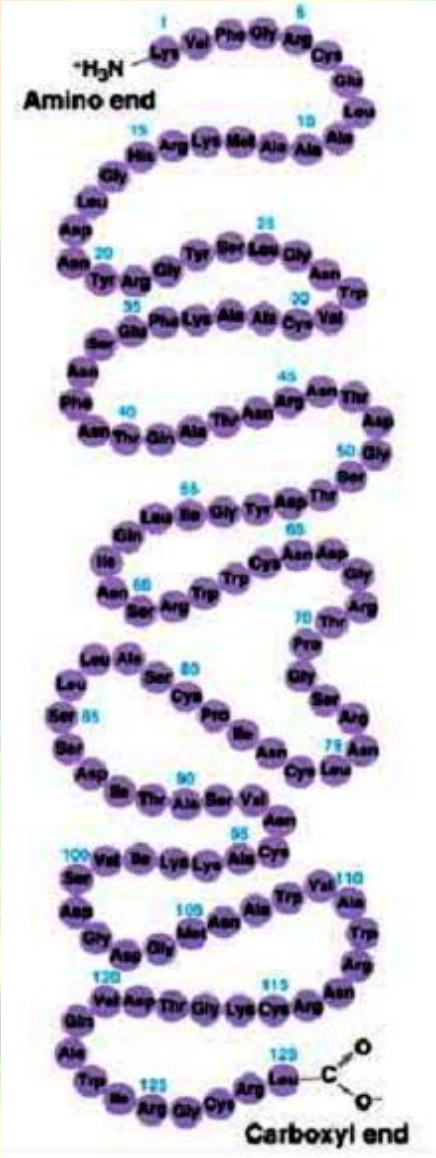
Rôle: signalisation, catalyse, …

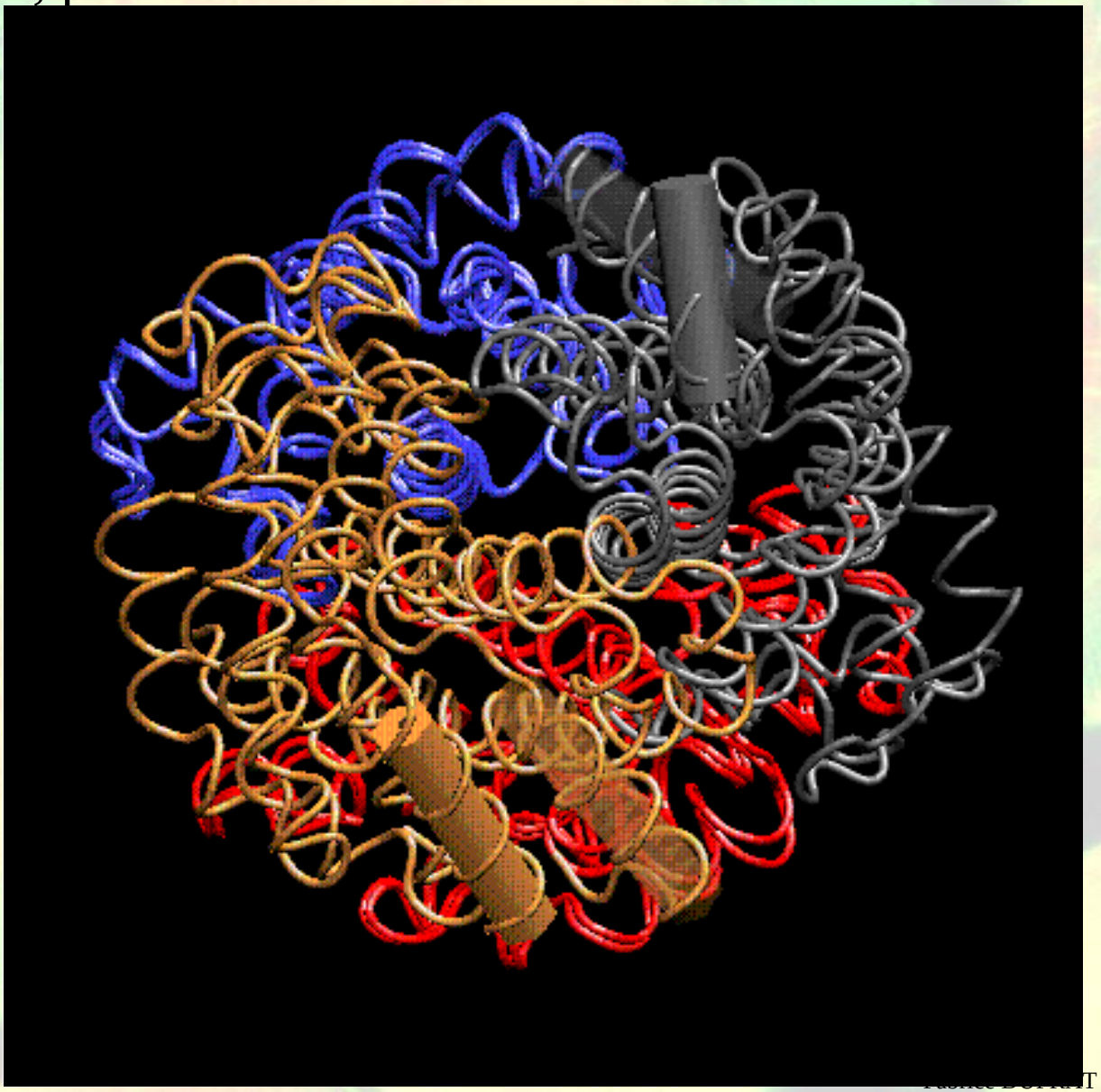
Perméabilité de la membrane plasmique



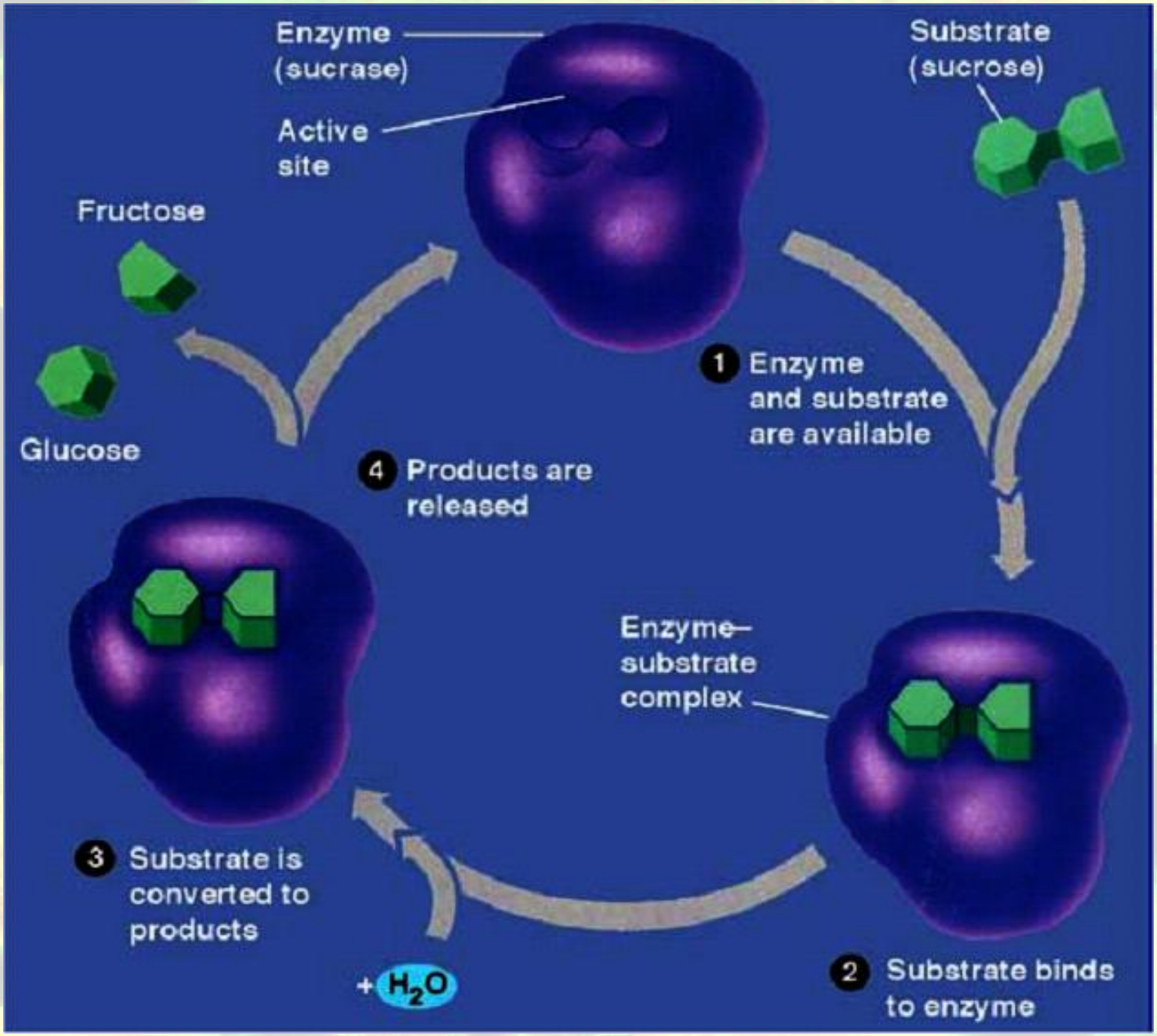
Les protéines (protides)

Alimentation: viande, poisson





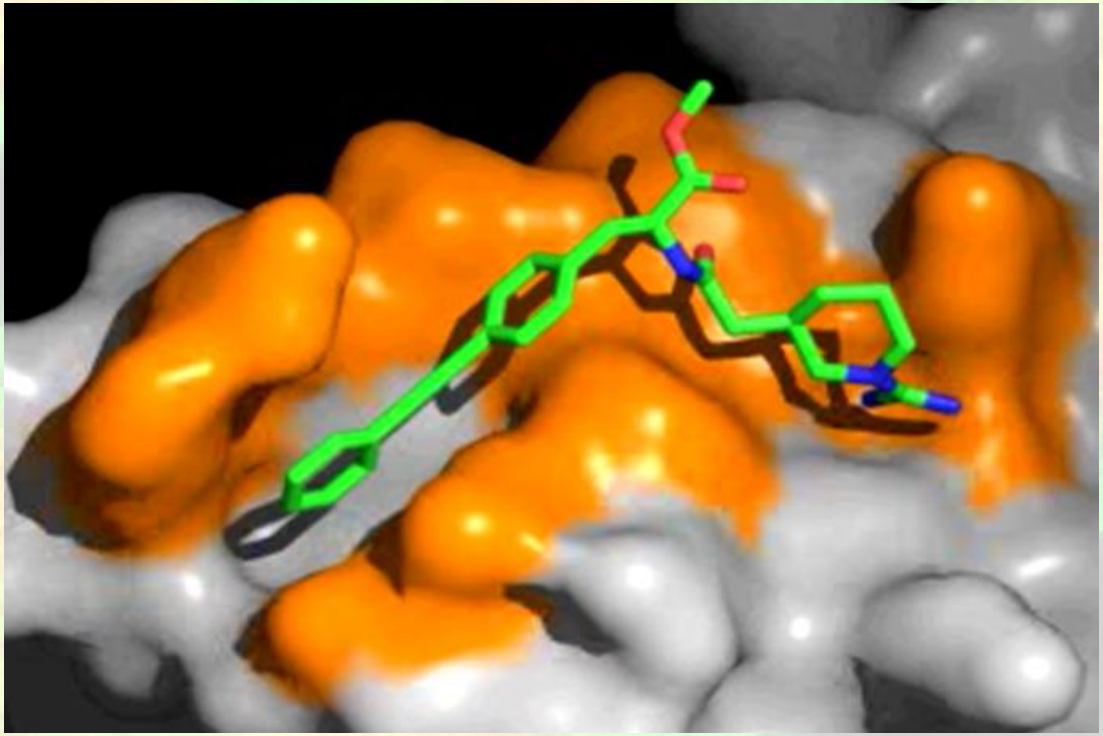
Enzymes, des protéines pour la catalyse



Protéines de structure: toile d'araignée

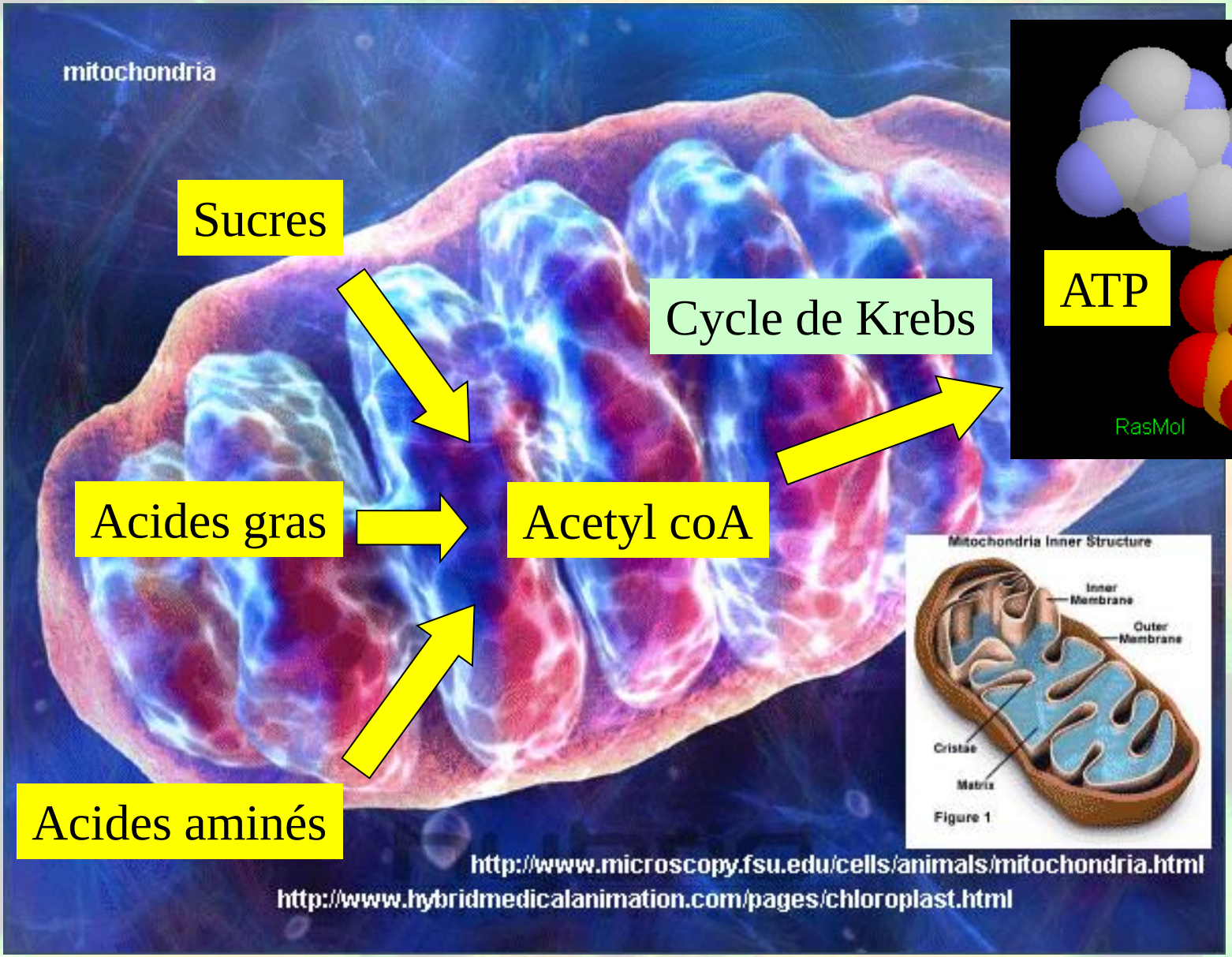
Réaction agoniste-récepteur

= la base du mode d'action des médicaments



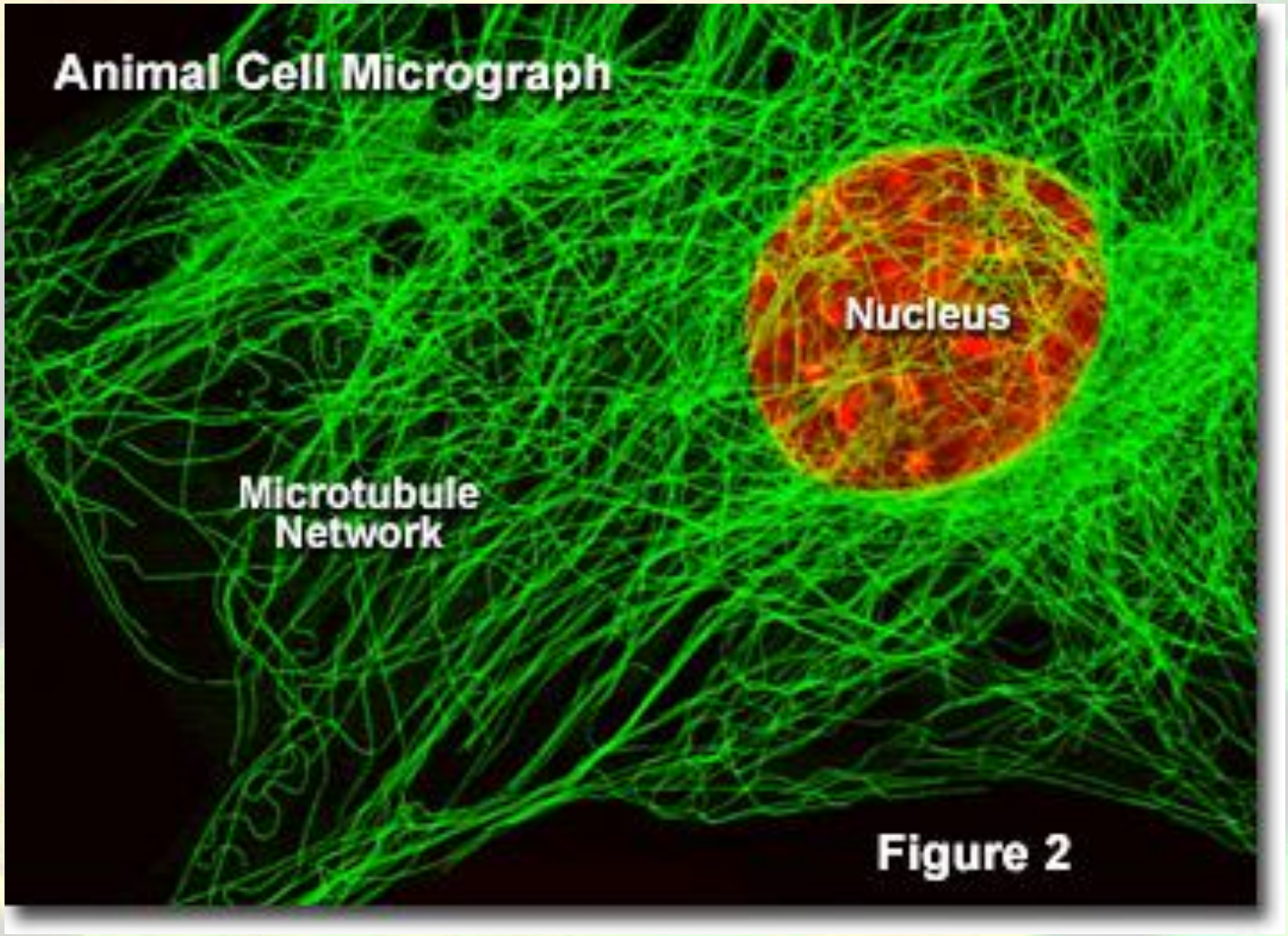
Arkin et al. (2003) PNAS

ATP (Adenosine Tri Phosphate)



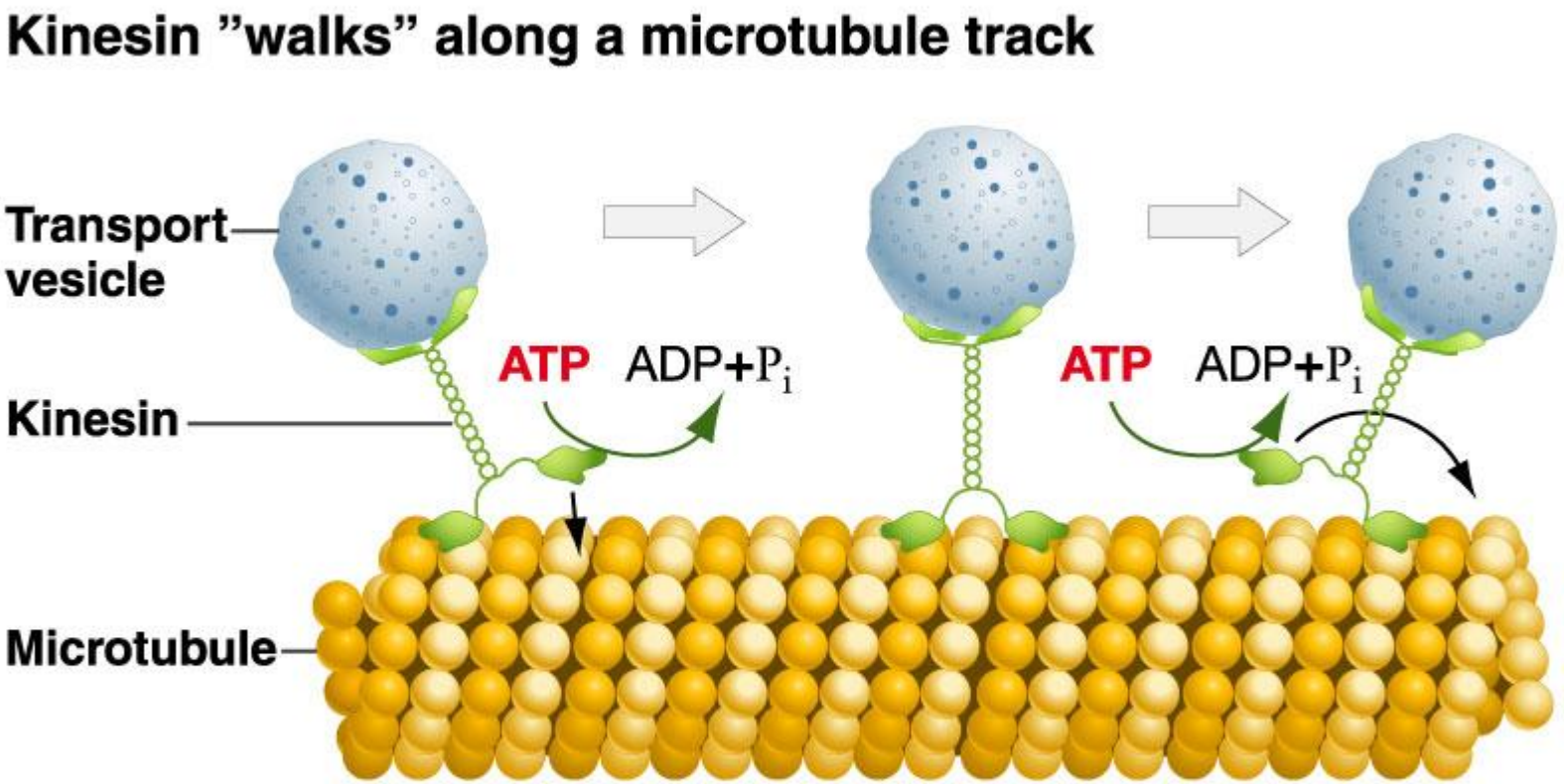
Cytosquelette: réseau d'actine

Protéine de structure: microtubules



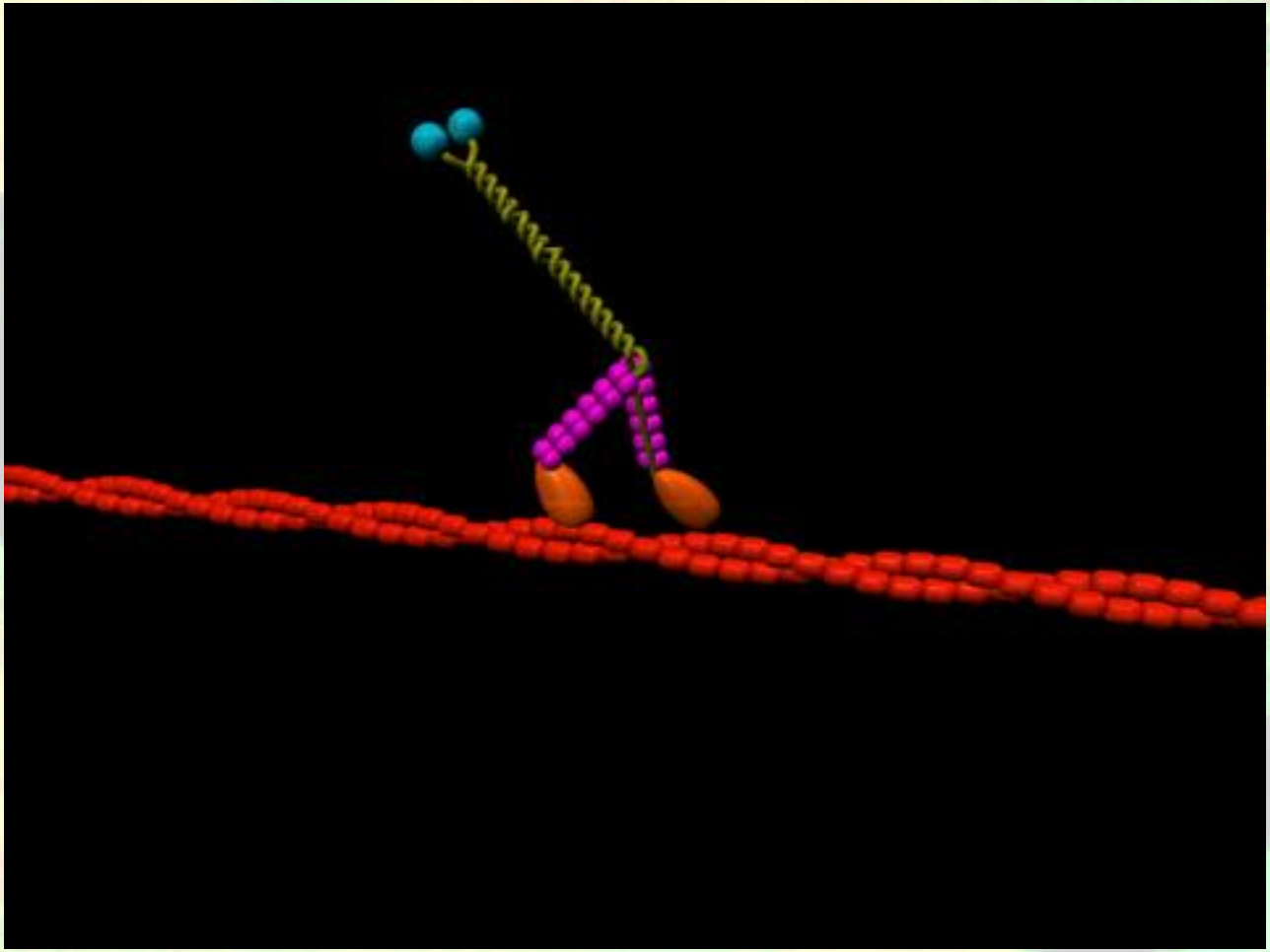
Réseau de microtubules

Microtubules et actine

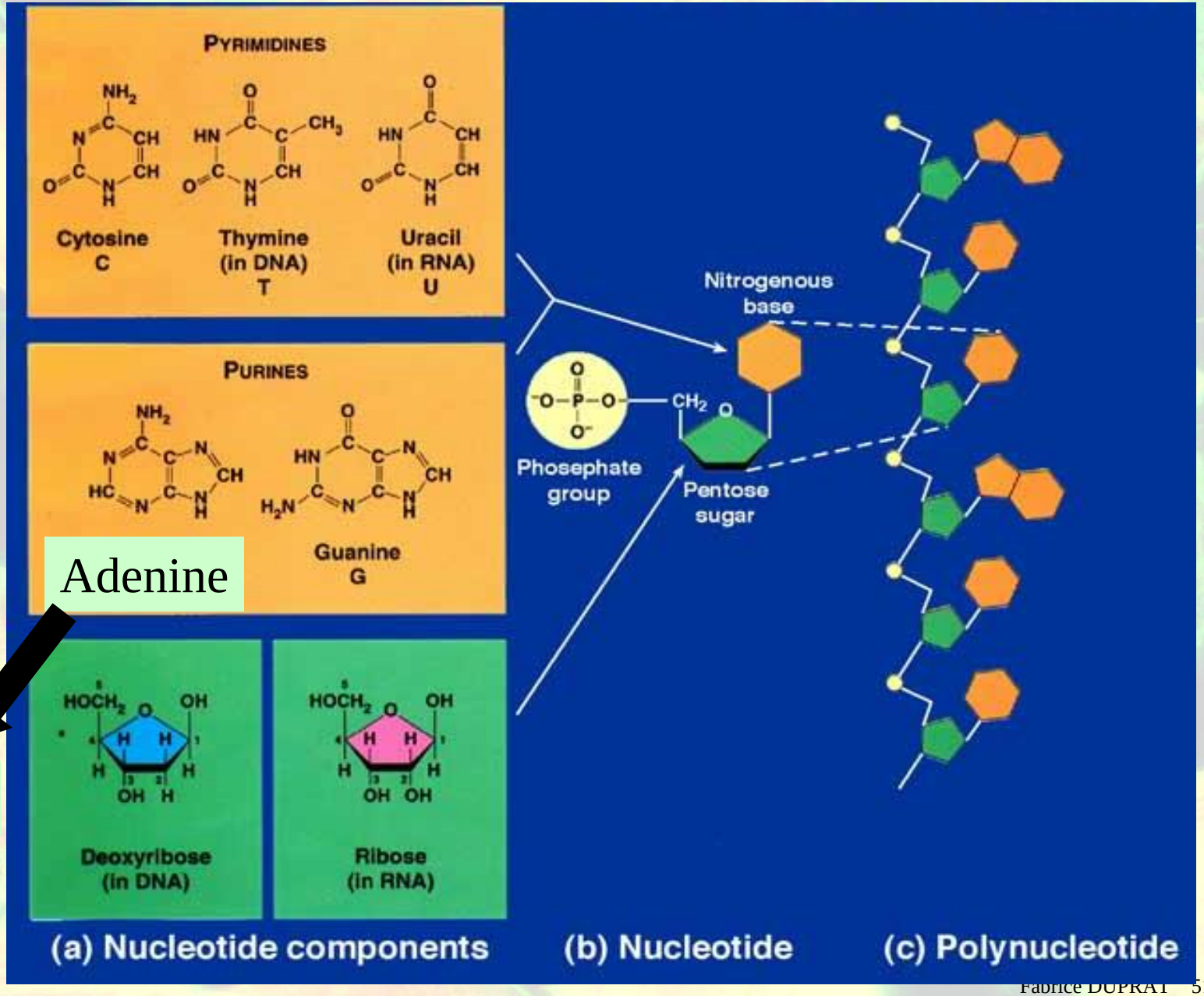


Nanobiotechnologies

Nanomachine

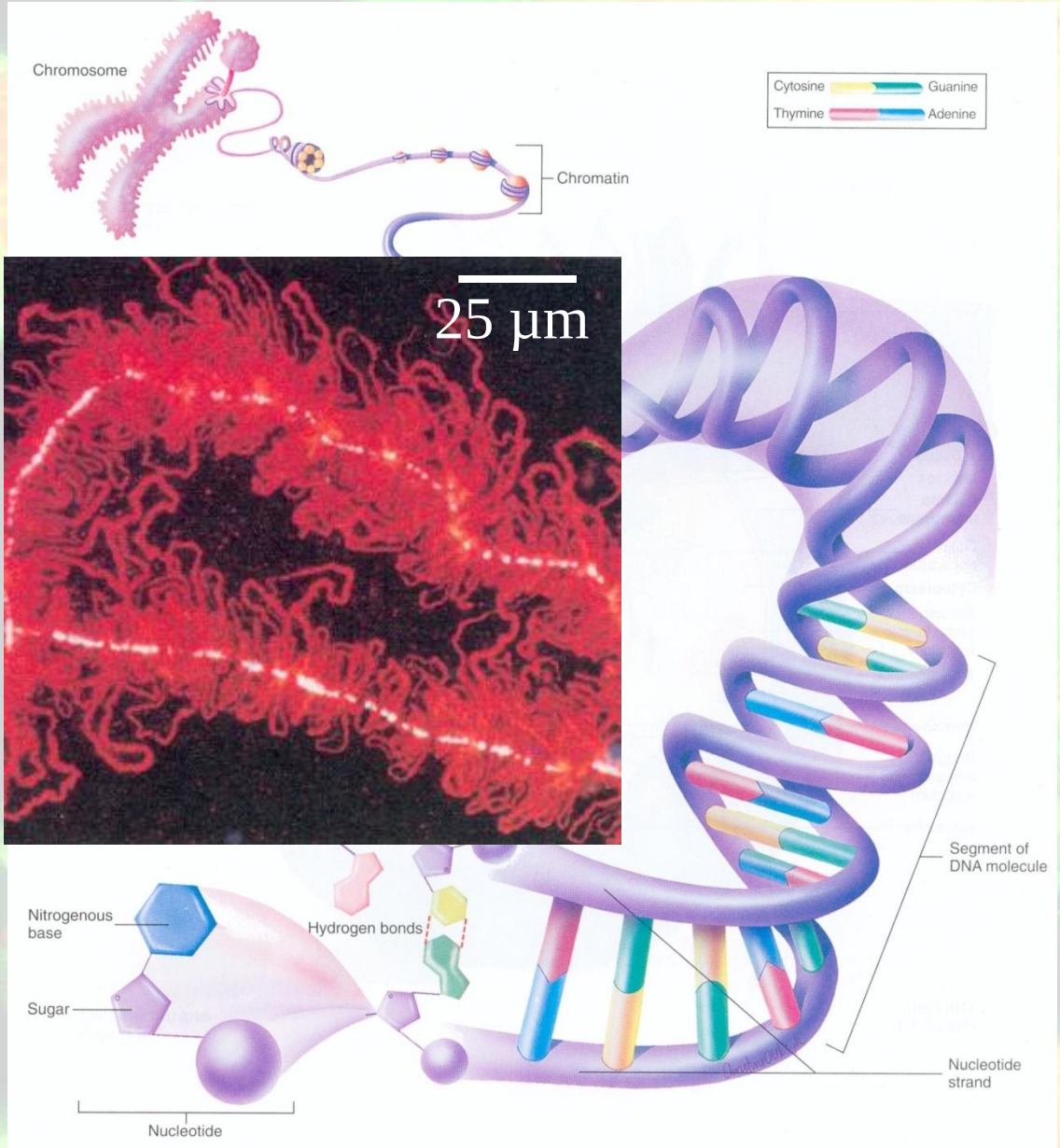


Acides nucléiques



L'AXE ADN-ARN-PROTEINE

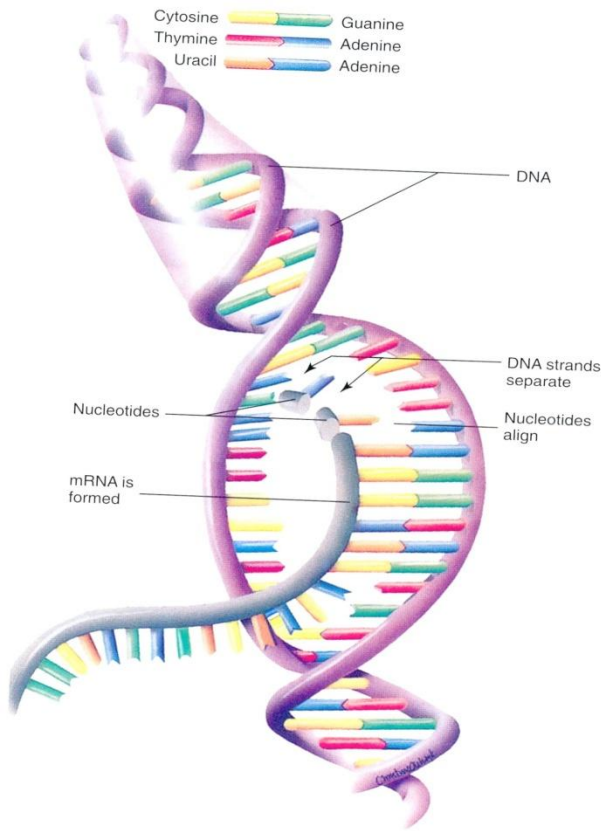
L'axe ADN-ARN-Protéines

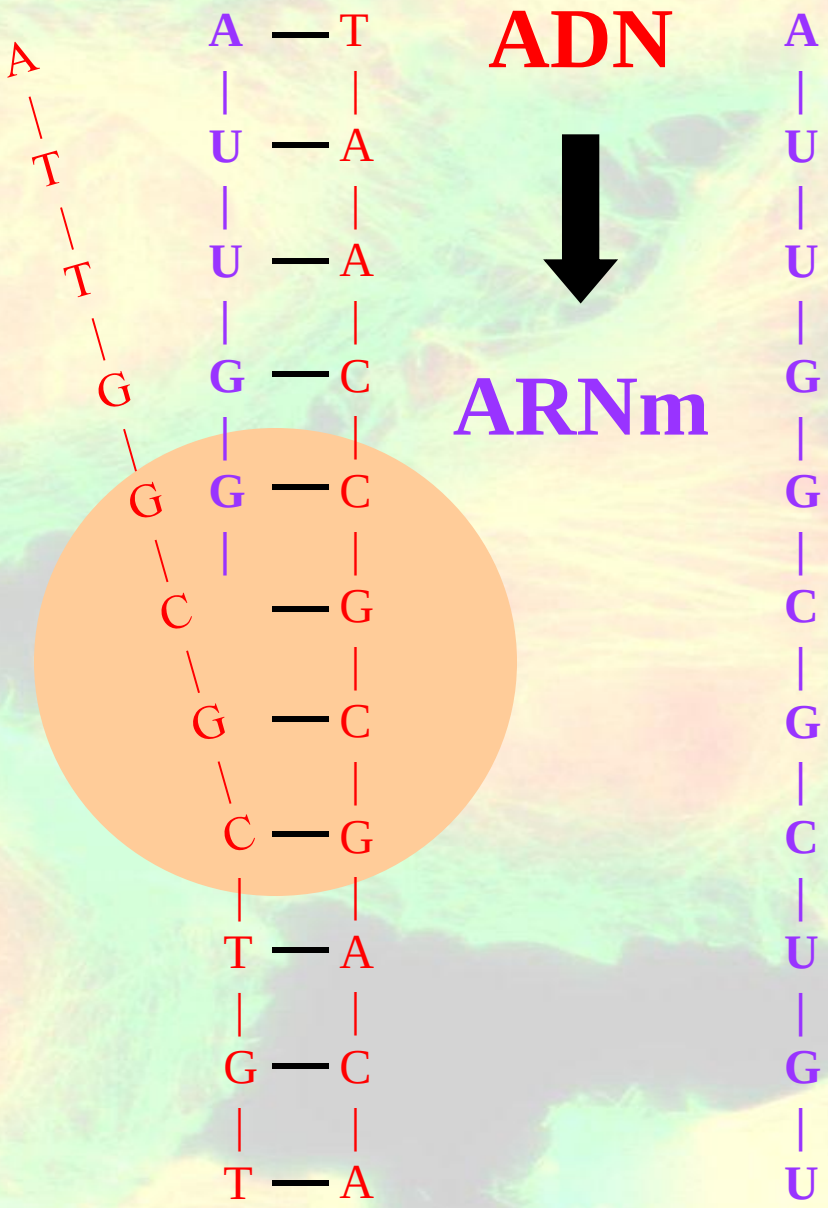


ADN

A — T
T — A
T — A
G — C
G — C
C — G
G — C
C — G
T — A
G — C
T — A

L'axe ADN-ARN-Protéines





L'axe ADN ARN Proteines

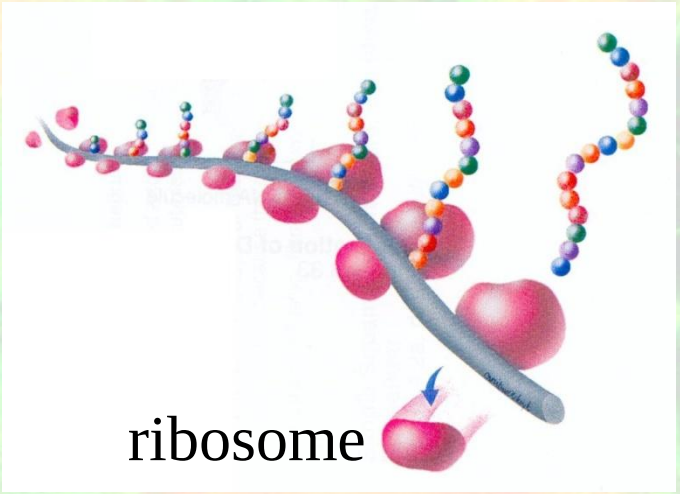
ARNm

A | U | U | G | G | G | C | G | C | U | G | U |

Acides aminés

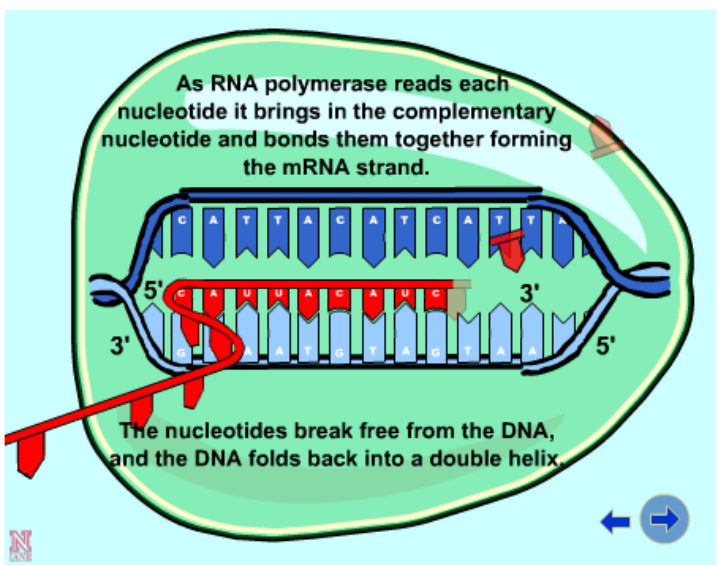
- Isoleucine
- Cystéine
- Tryptophane
- Tyrosine

Protéine



Seeley "Anatomy & Physiology", Mc Graw-Hill

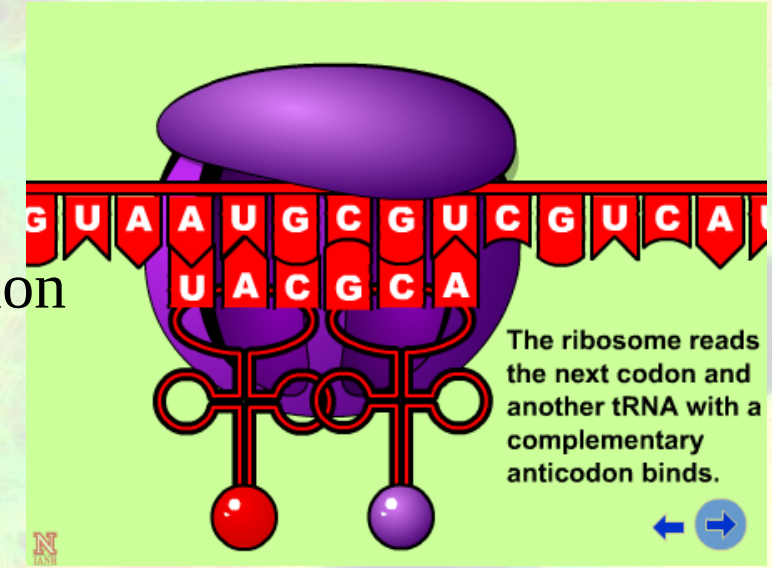
Transcription et traduction en animations



Transcription

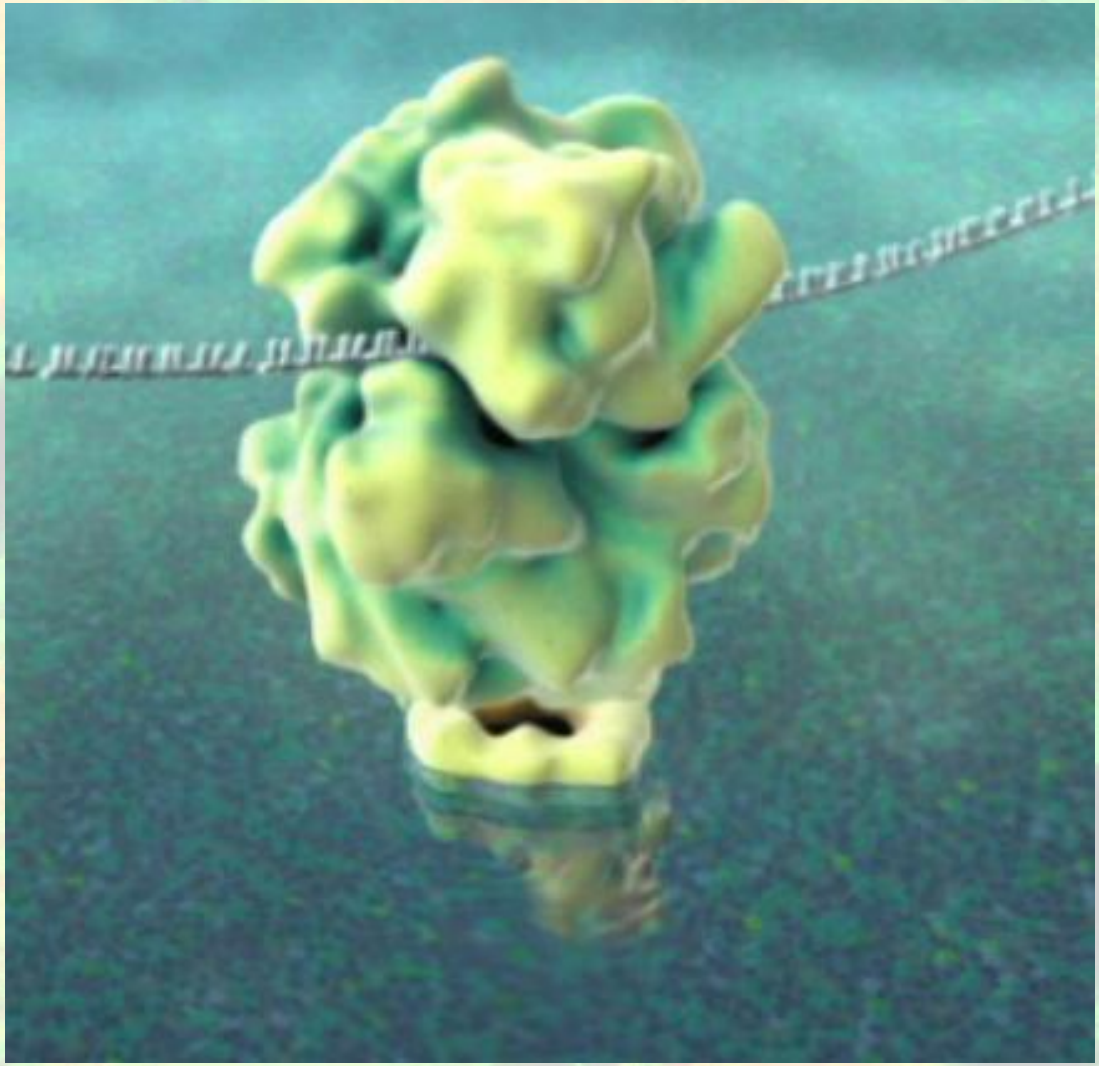
http://www-class.unl.edu/biochem/gp2/m_biology/animation/gene/gene_a2.html

1. Traduction

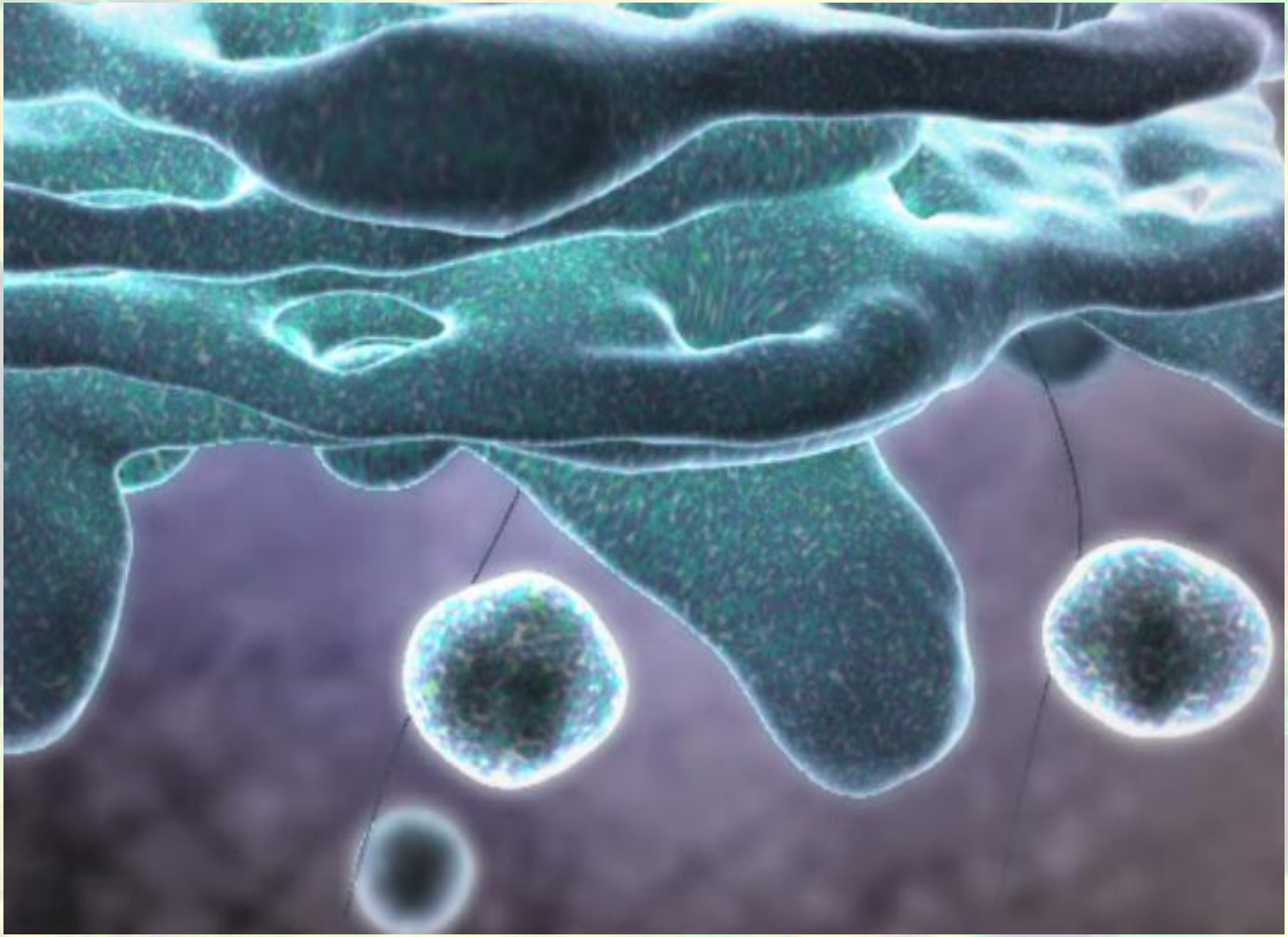


1. http://www-class.unl.edu/biochem/gp2/m_biology/animation/gene/gene_a3.html

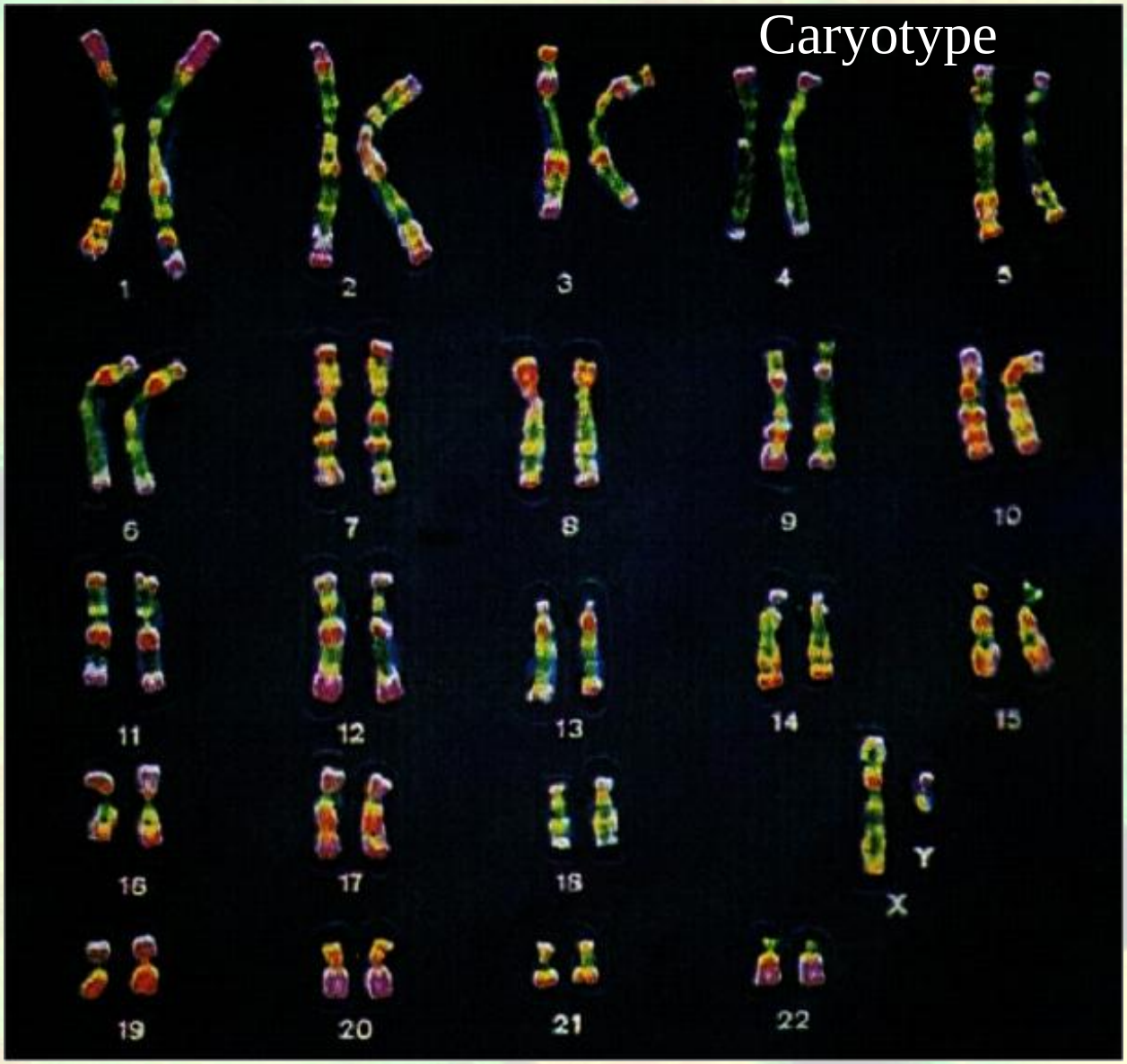
Synthèse protéique et réticulum endoplasmique



Appareil de Golgi

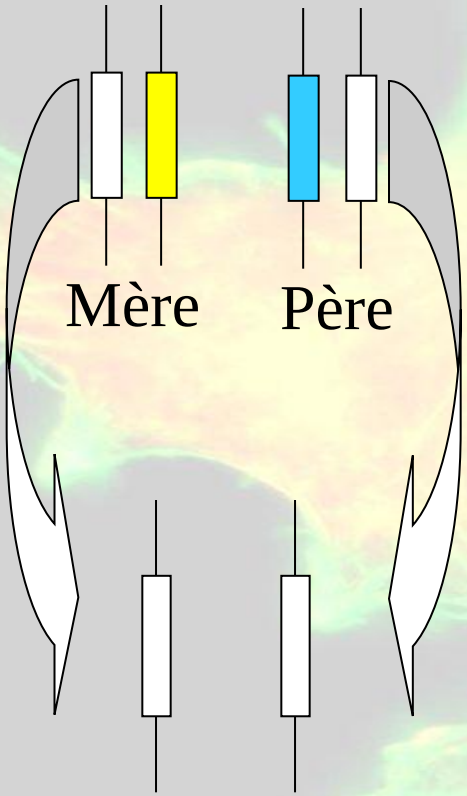


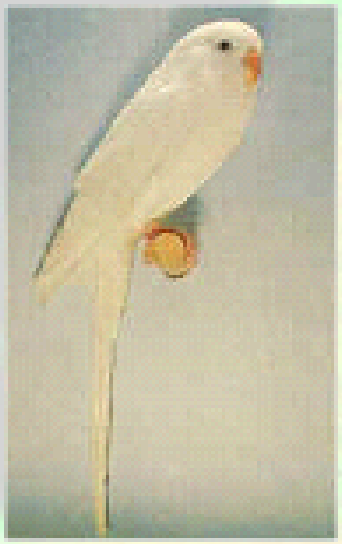
Génétique selon Mendel

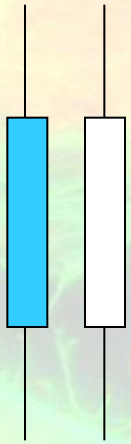


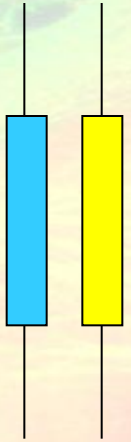
Grégor Mendel (1822-1884)

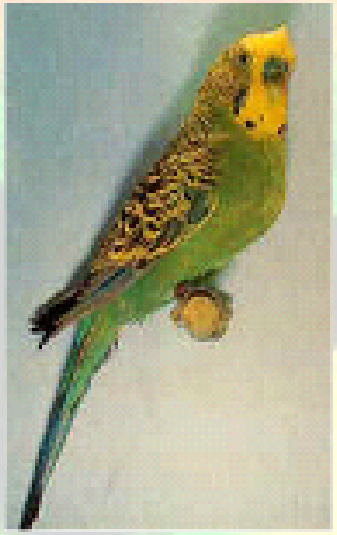
Couleur des plumes



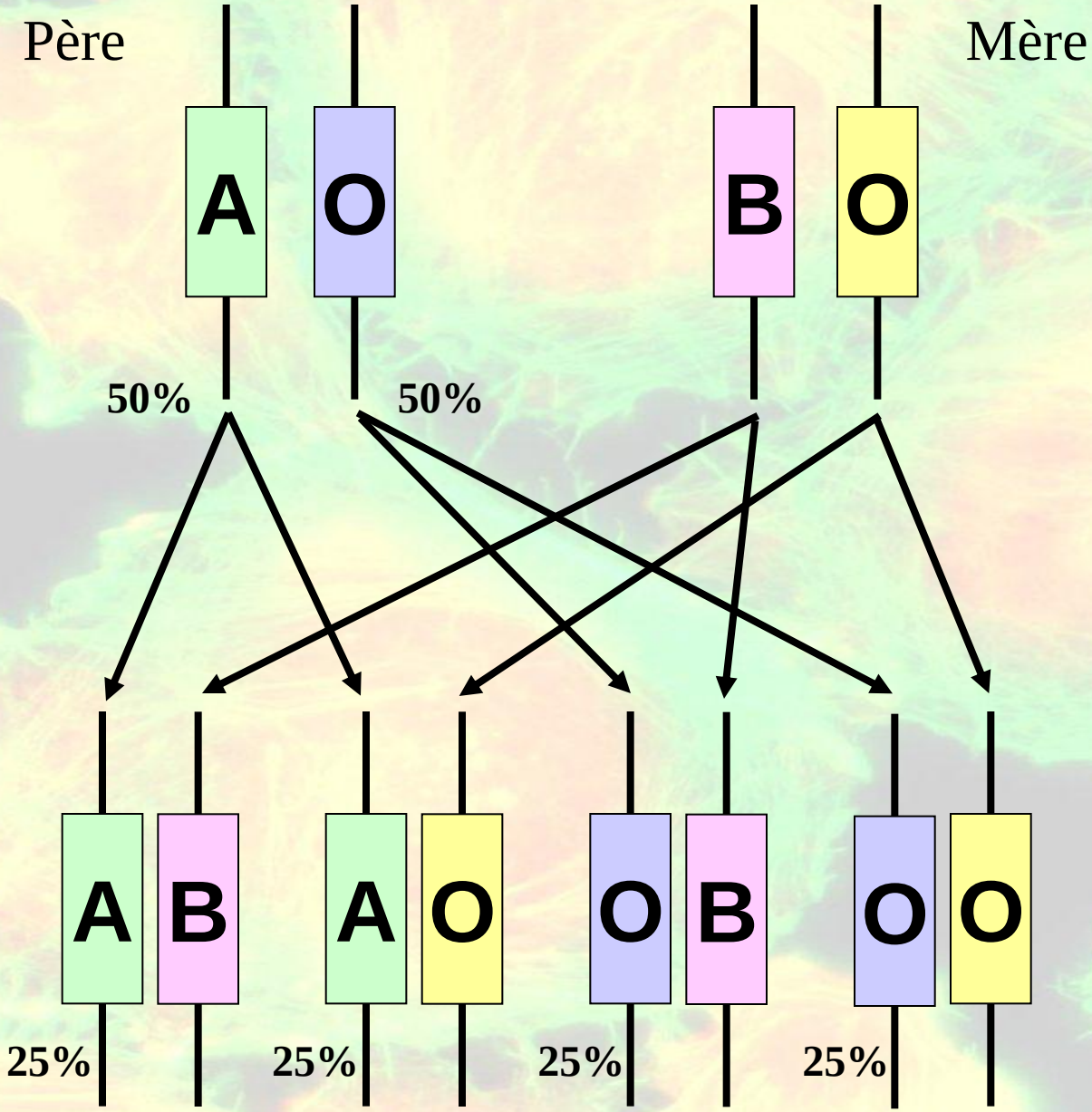


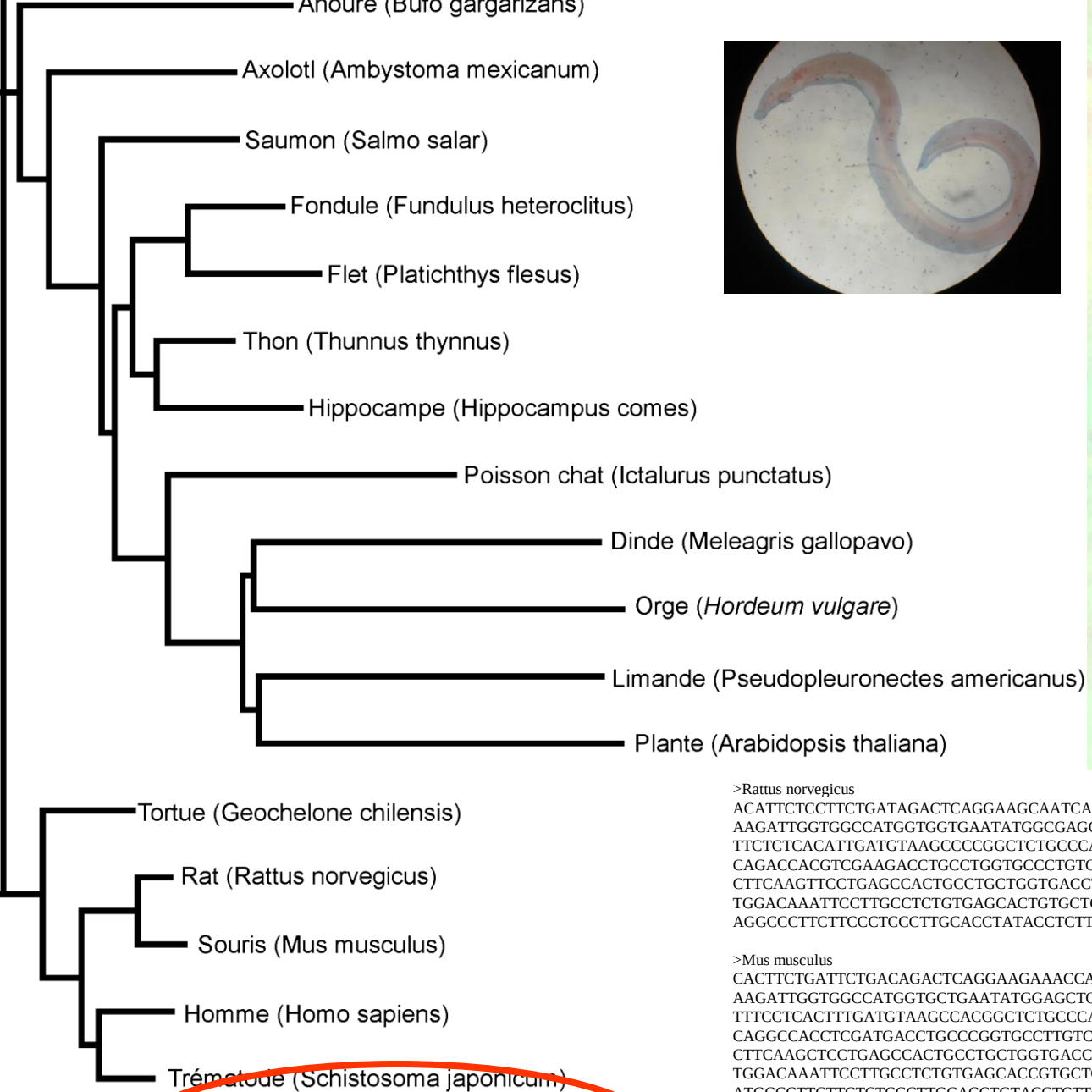






Groupes sanguins





Biochimie et évolution

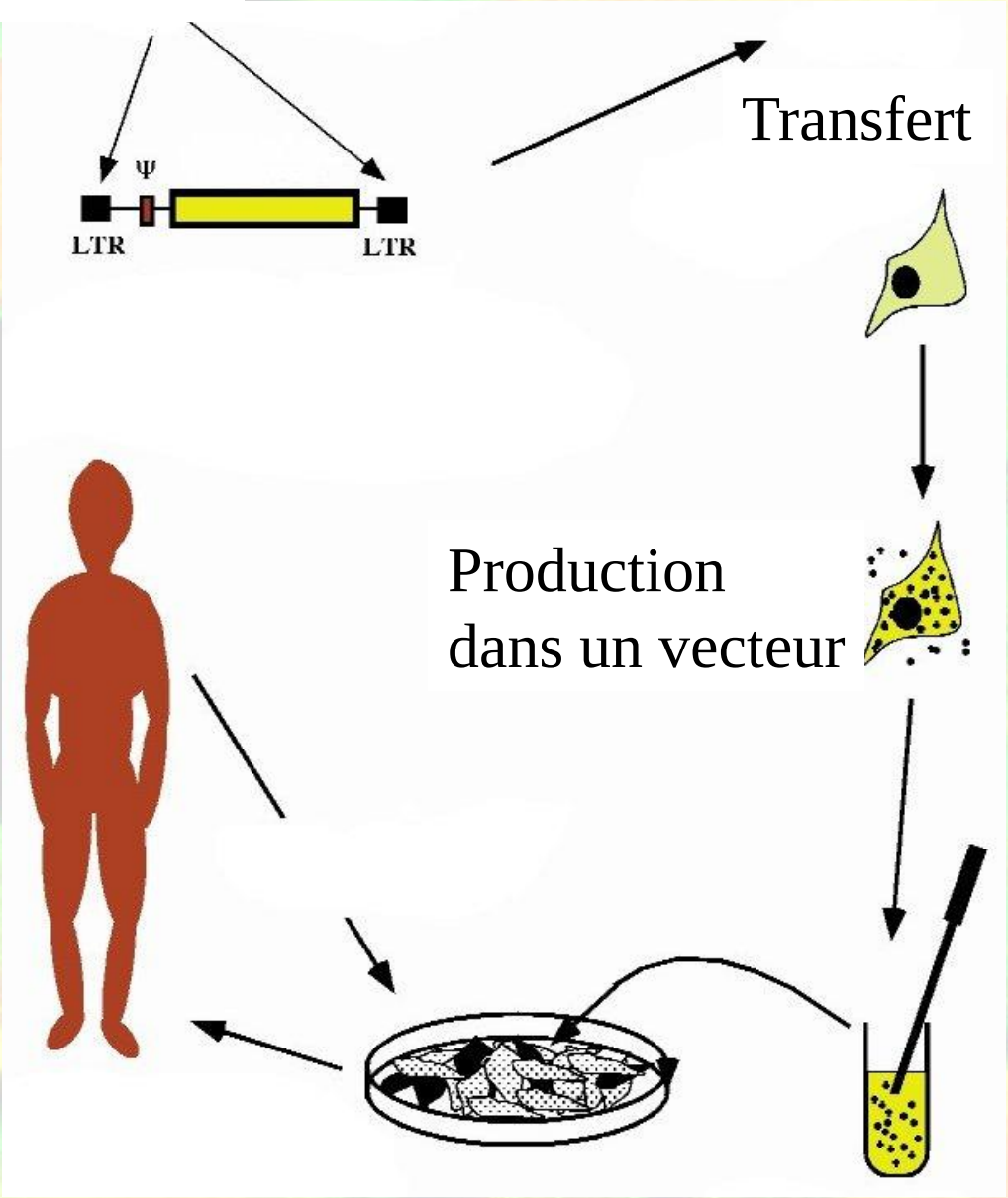
L'hémoglogine

>Rattus norvegicus
ACATTCTCCTTCTGATAGACTCAGGAAGCAATCATGGTGCTCTCTGCAGATGACAAAACCAACATCAAGAACTGCTGGGGG
AAGATTGGTGGCCATGGTGGTGAATATGGCGAGGAGGCCCTACAGAGGATGTTCGCTGCCTTCCCCACCACCAAGACCTAC
TTCTCTCACATTGATGTAAGCCCCGGCTCTGCCCAGGTCAAGGCTCACGGCAAGAAGGTTGCTGATGCCTTGGCCAAAGCTG
CAGACCACGTCGAAGACCTGCCTGGTGCCCTGTCCACTCTGAGCGACCTGCATGCCCACAAACTGCGTGTGGATCCTGTCAA
CTTCAAGTTCCTGAGCCACTGCCTGCTGGTGACCTTGGCTTGCCACCACCCTGGAGATTTCACACCCGCCATGCACGCCTCTC
TGGACAAATTCCTTGCCTCTGTGAGCACTGTGCTGACCTCCAAGTACCGTTAAGCCGCCTCCTGCCGGGCTTGCCTTCTGACC
AGGCCCTTCTTCCCTCCCTTGCACCTATACCTCTTGGTCTTTGAATAAAGCCTGAGTAGGAAGC*

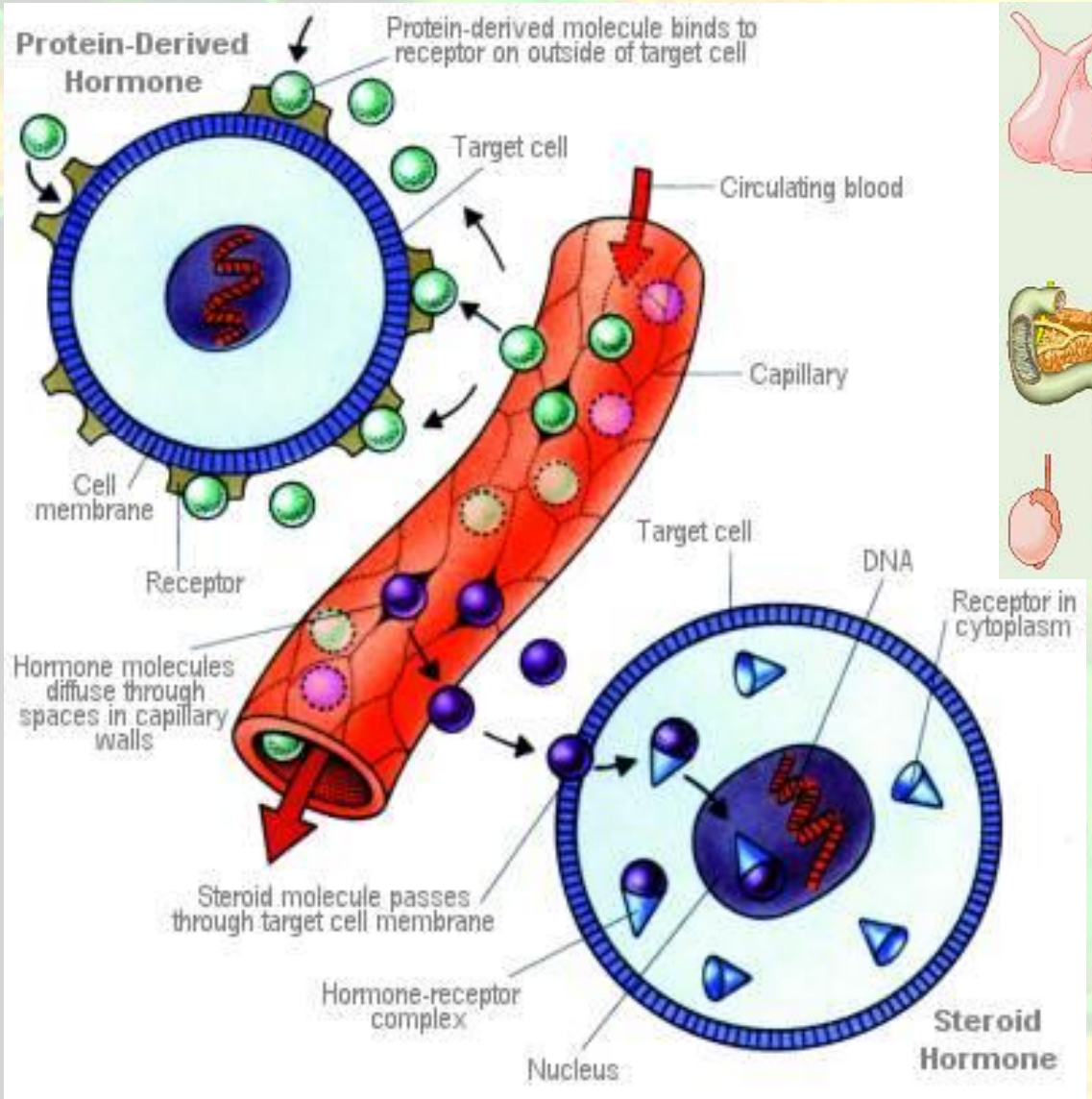
>Mus musculus
CACTTCTGATTCTGACAGACTCAGGAAGAAACCATGGTGCTCTCTGGGGAAGACAAAAGCAACATCAAGGCTGCCTGGGGG
AAGATTGGTGGCCATGGTGCTGAATATGGAGCTGAAGCCCTGGAAAGGATGTTTGCTAGCTTCCCCACCACCAAGACCTAC
TTTCCTCACTTTGATGTAAGCCACGGCTCTGCCCAGGTCAAGGGTCACGGCAAGAAGGTCGCCGATGCGCTGGCCAGTGCTG
CAGGCCACCTCGATGACCTGCCCGGTGCCTTGTCTGCTCTGAGCGACCTGCATGCCCACAAGCTGCGTGTGGATCCCGTCAA
CTTCAAGCTCCTGAGCCACTGCCTGCTGGTGACCTTGGCTAGCCACCACCCTGCCGATTTCACCCCCGCGGTACATGCCTCTC
TGGACAAATTCCTTGCCTCTGTGAGCACCGTGCTGACCTCCAAGTACCGTTAAGCTGCCTTCTGCGGGGCTTGCCTTCTGGCC
ATGCCCTTCTTCTCTCCCTTGCACCTGTACCTCTTGGTCTTTGAATAAAGCCTGAGTAGGAAGAAGCCTGCA*

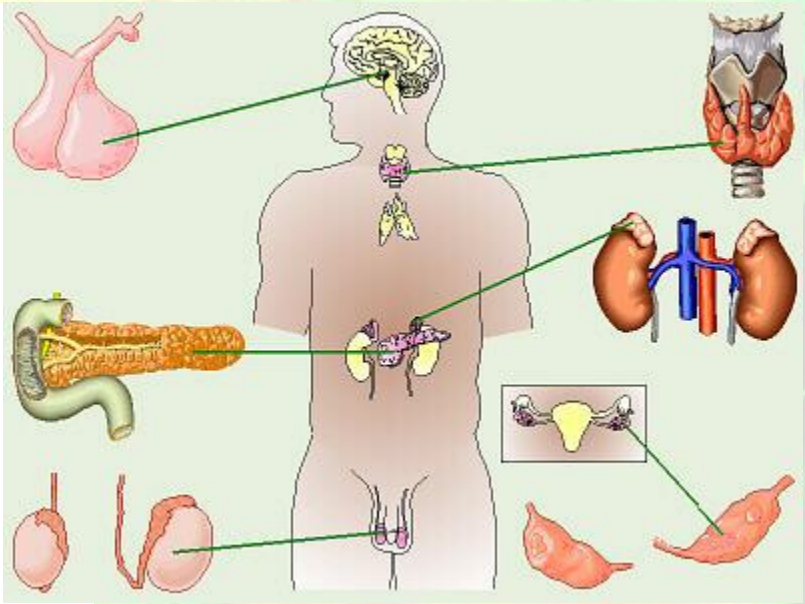
Application: Thérapie génique

Gène d'intérêt



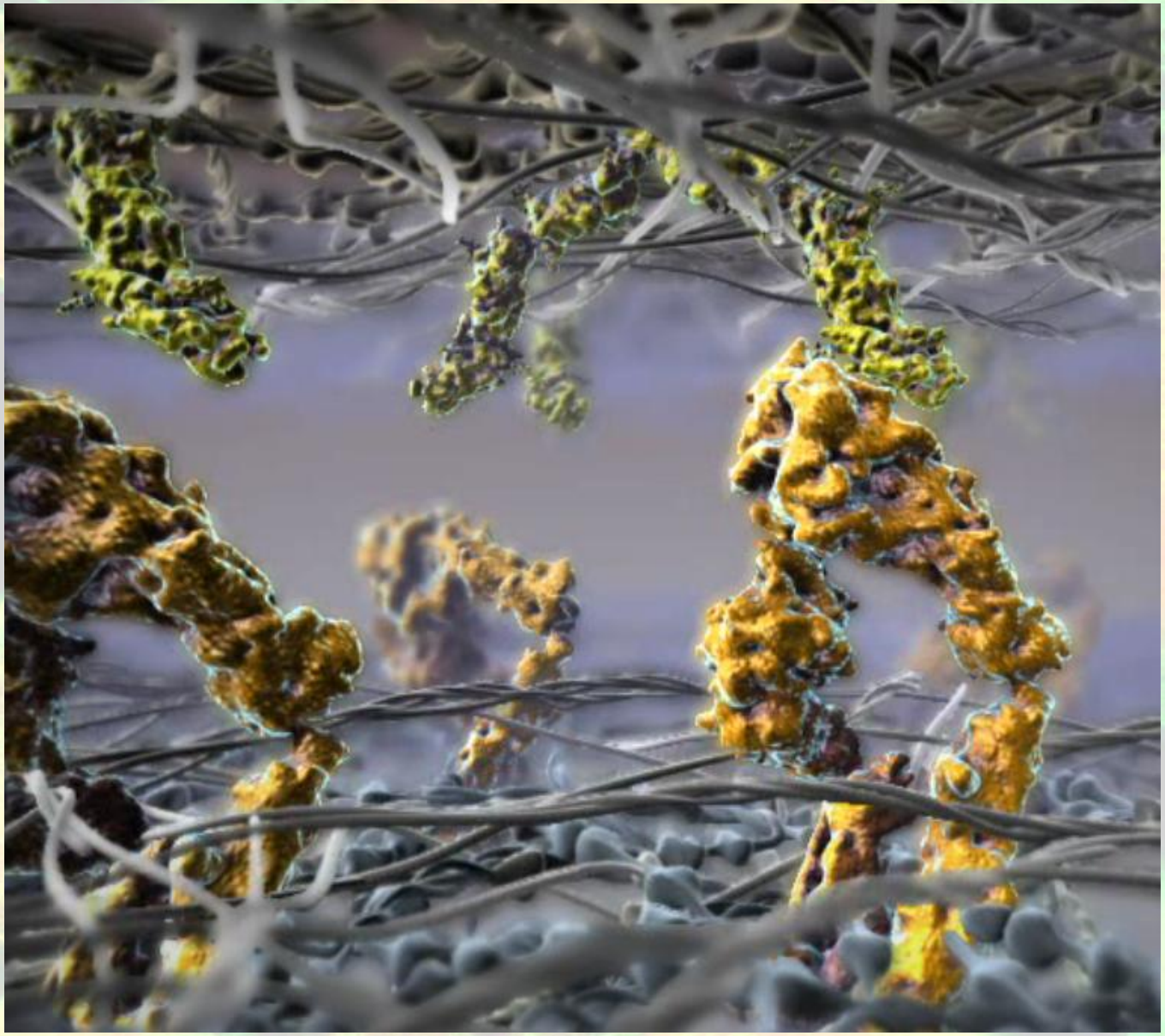
Hormones


Protein-Derived Hormone
Protein-derived molecule binds to receptor on outside of target cell
Target cell
Circulating blood
Capillary
Cell membrane
Receptor
Hormone molecules diffuse through spaces in capillary walls
Target cell
DNA
Receptor in cytoplasm
Steroid molecule passes through target cell membrane
Hormone-receptor complex
Nucleus
Steroid Hormone

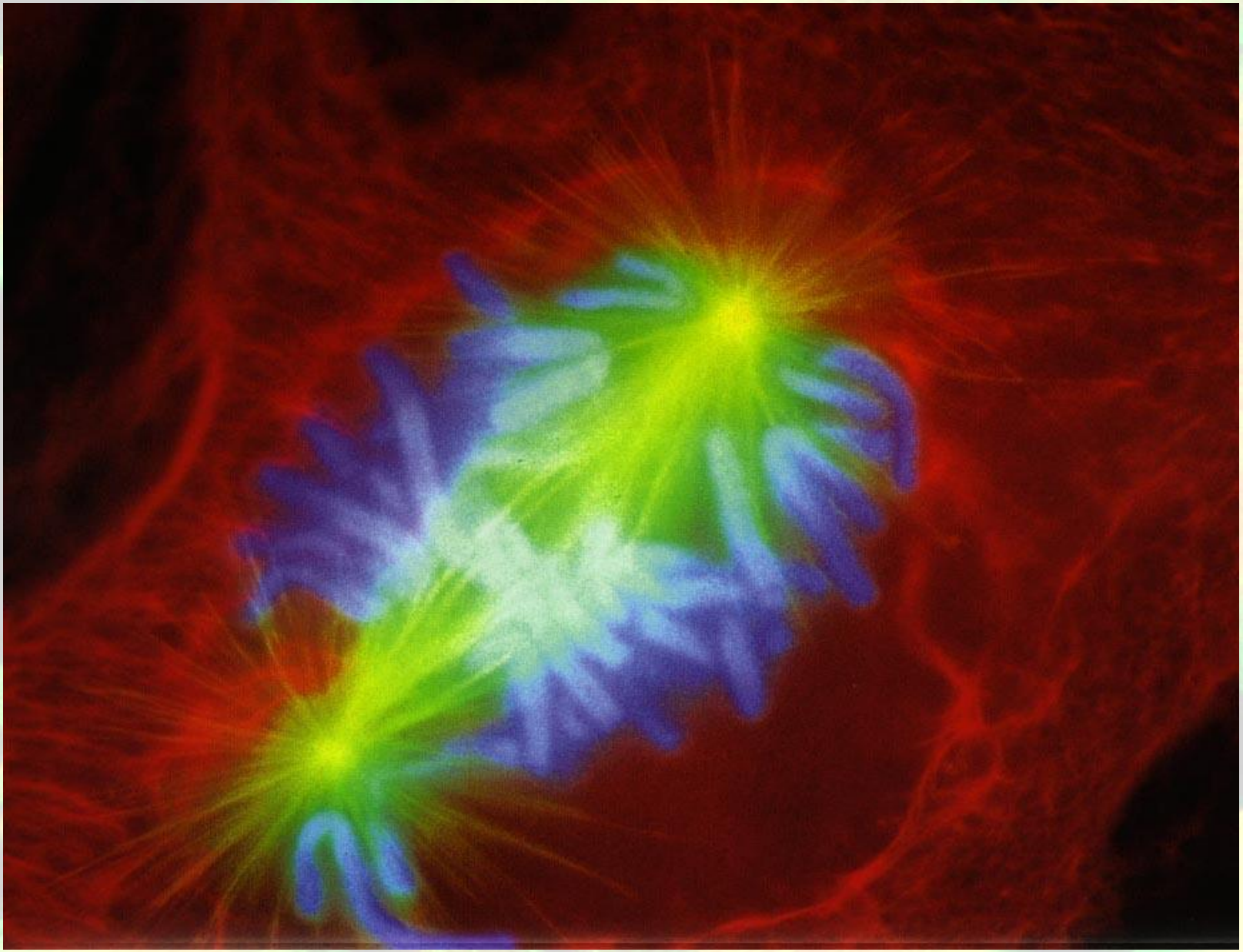


BIOLOGIE CELLULAIRE

Matrice extracellulaire



Division cellulaire

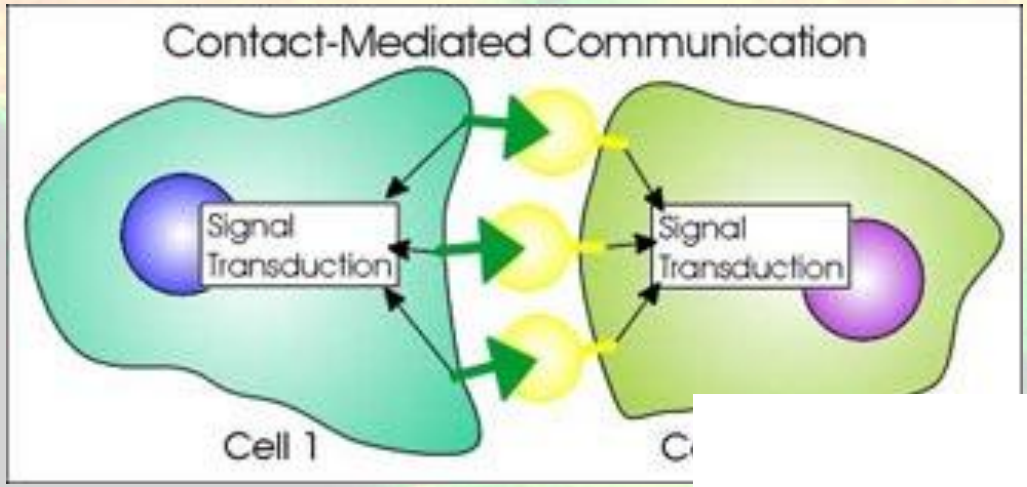


Division cellulaire

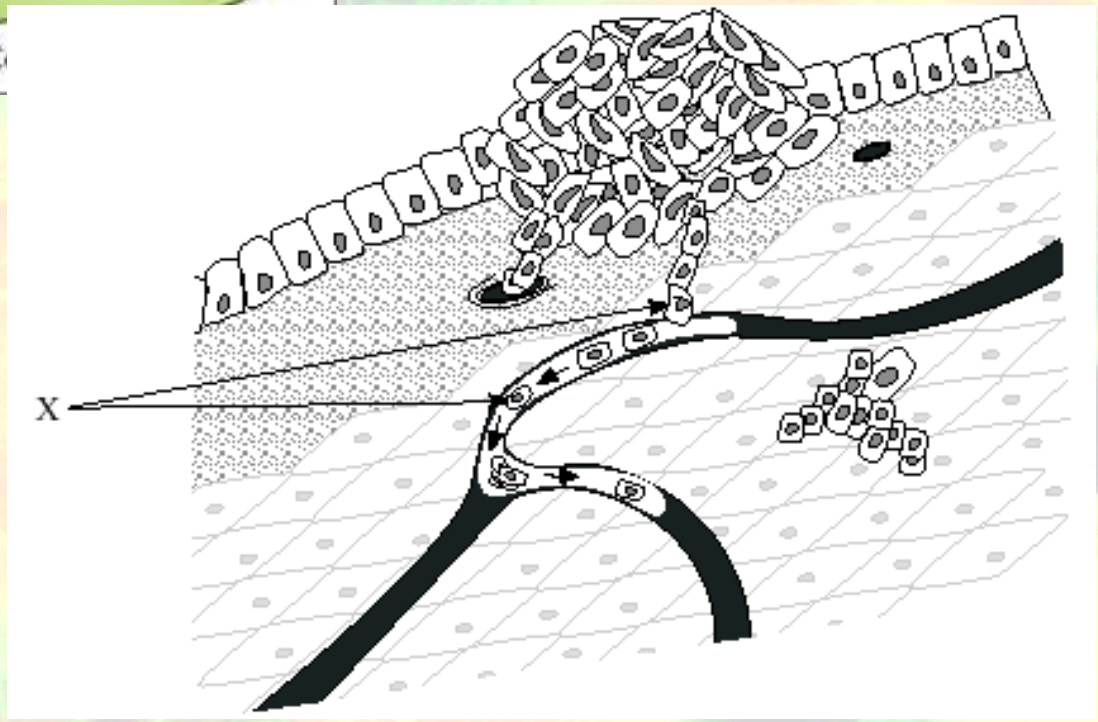
Telophase

H

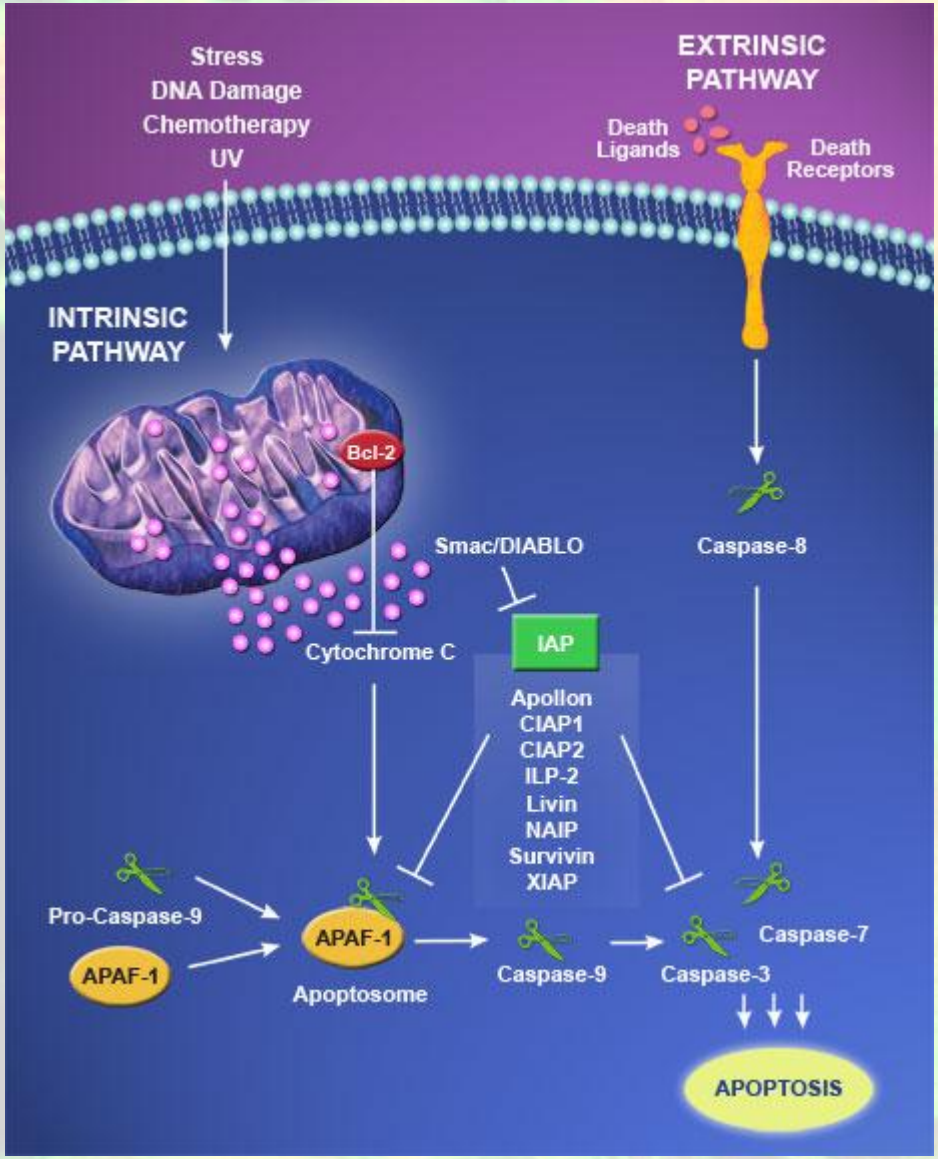
Inhibition de contact

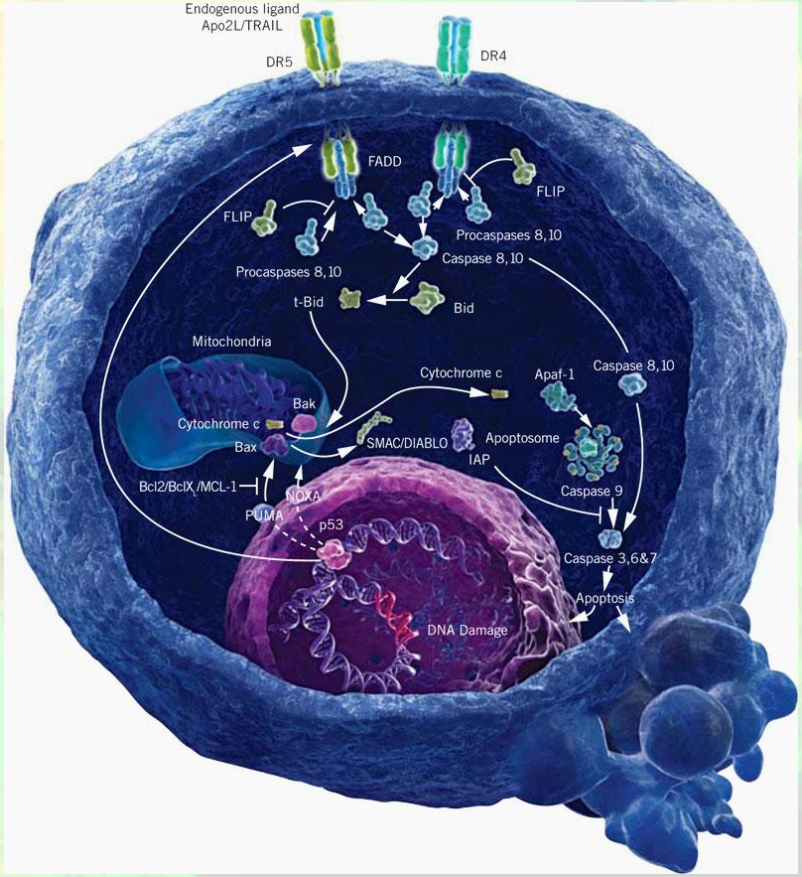


Cancer



Apoptose ou Mort programmée de la cellule





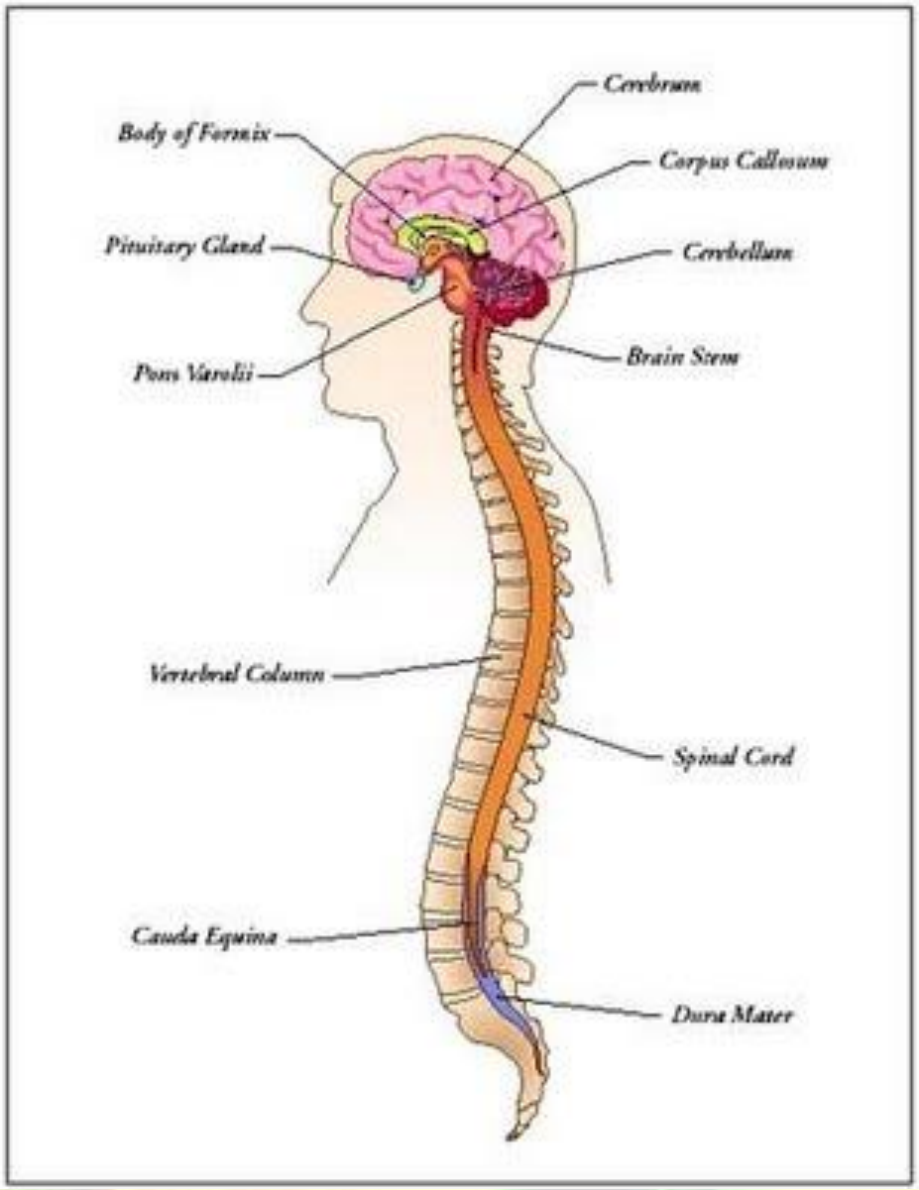
http://www.biooncology.com/bioonc/research/apoptosis/index.m

Système nerveux central

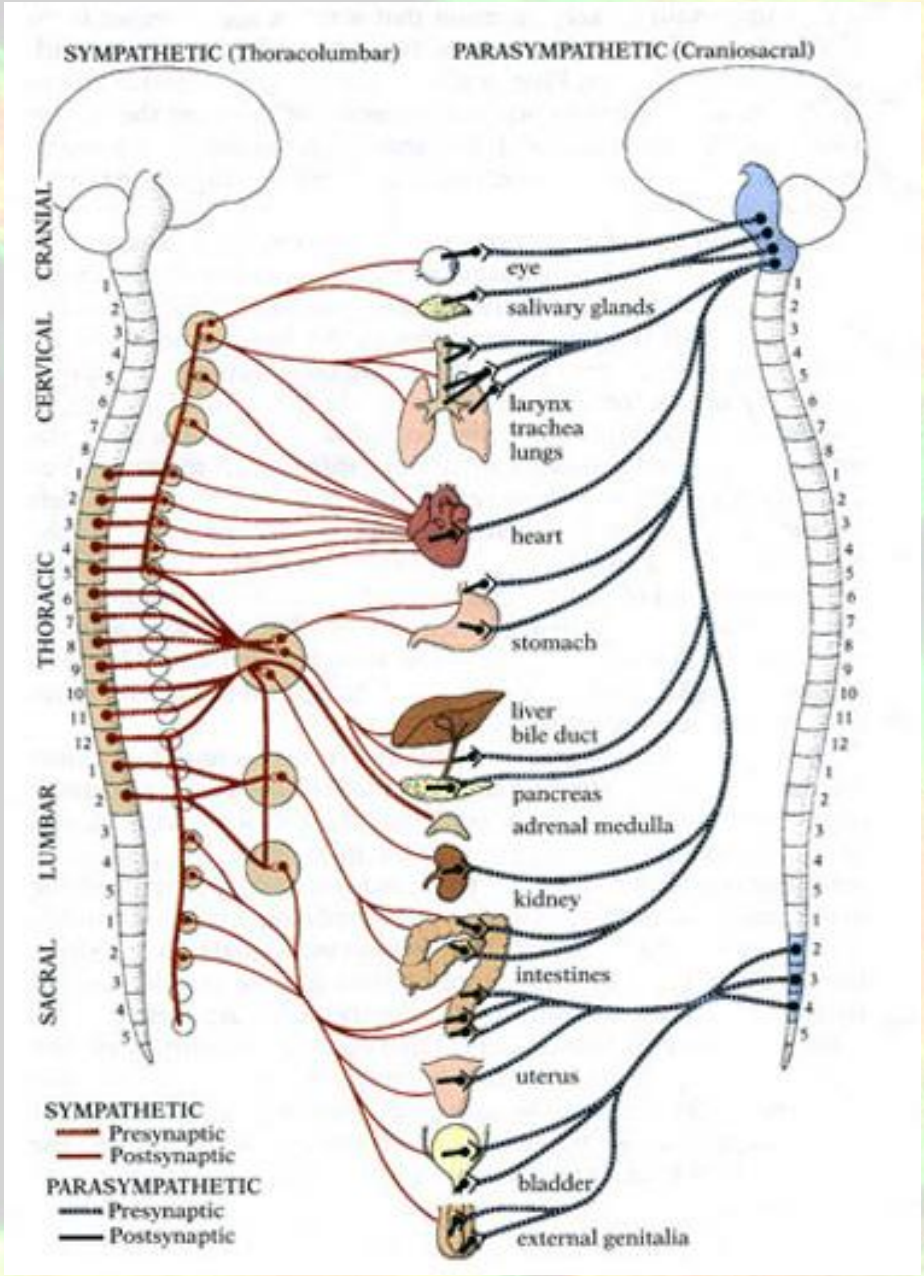
Cerveau

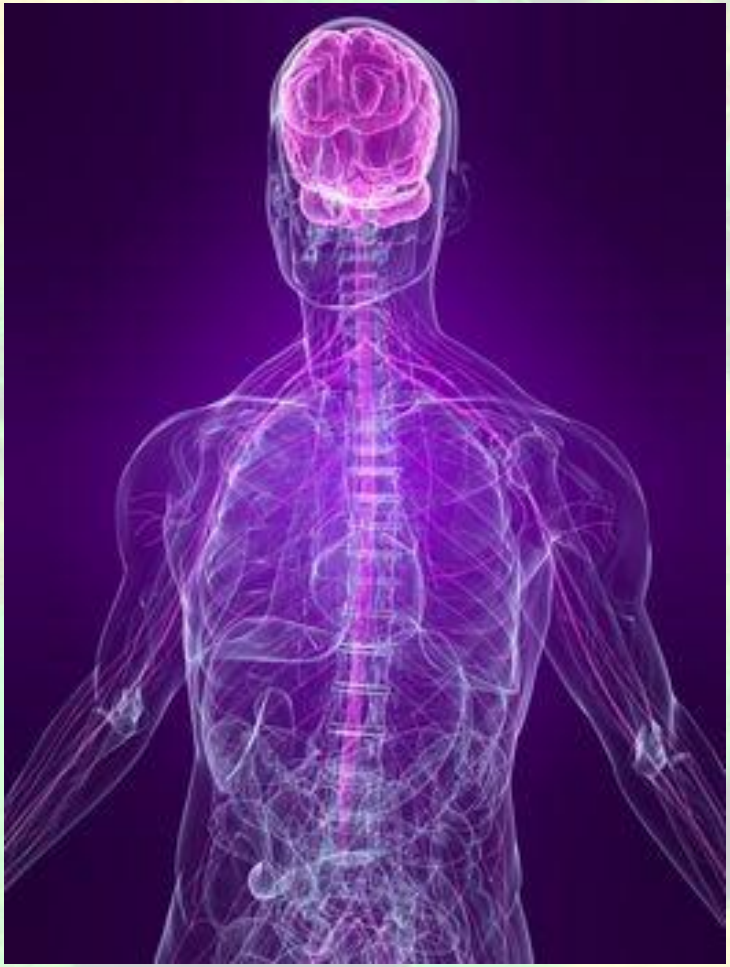
+

Moelle épinière

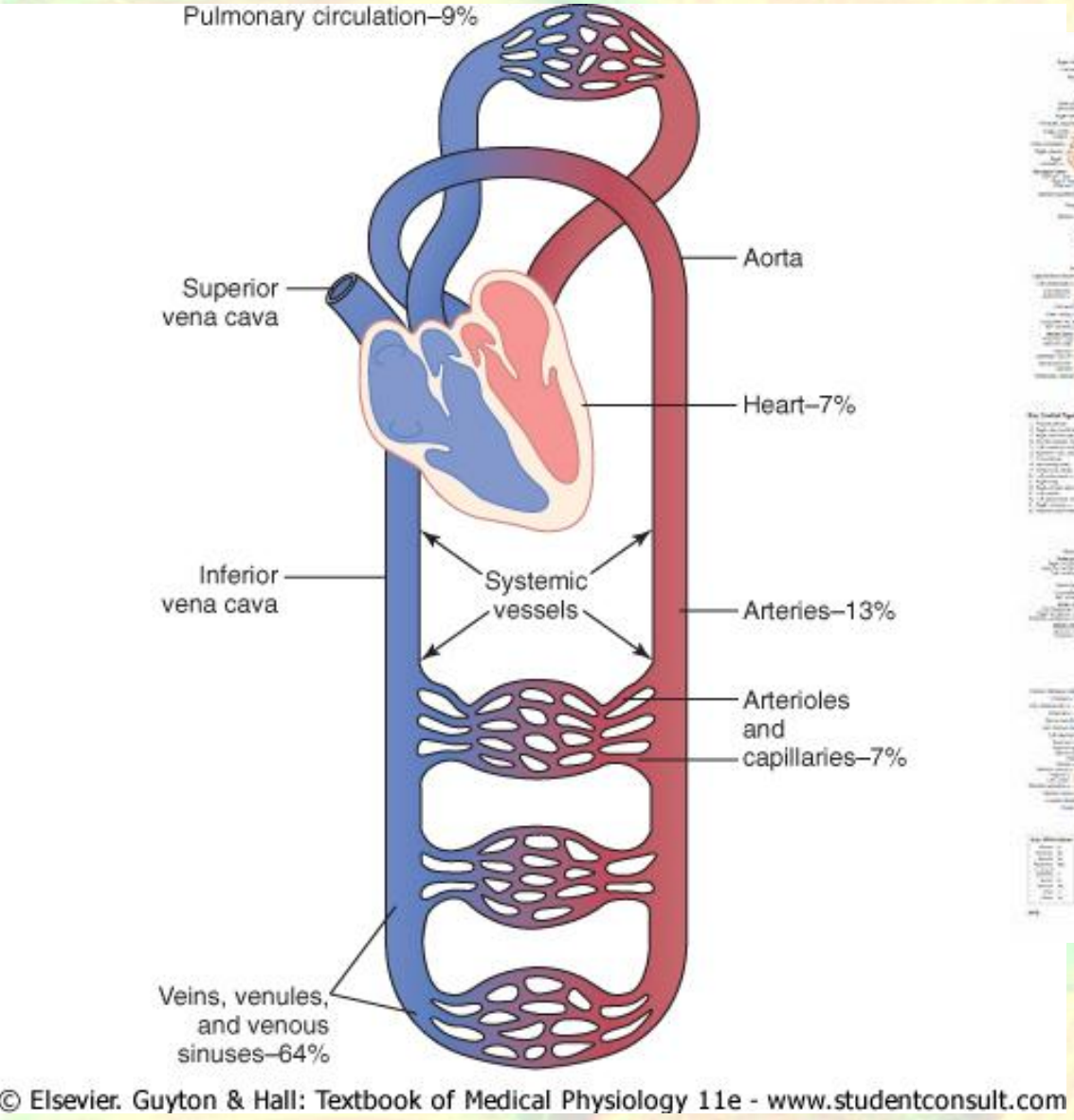


Système nerveux périphérique

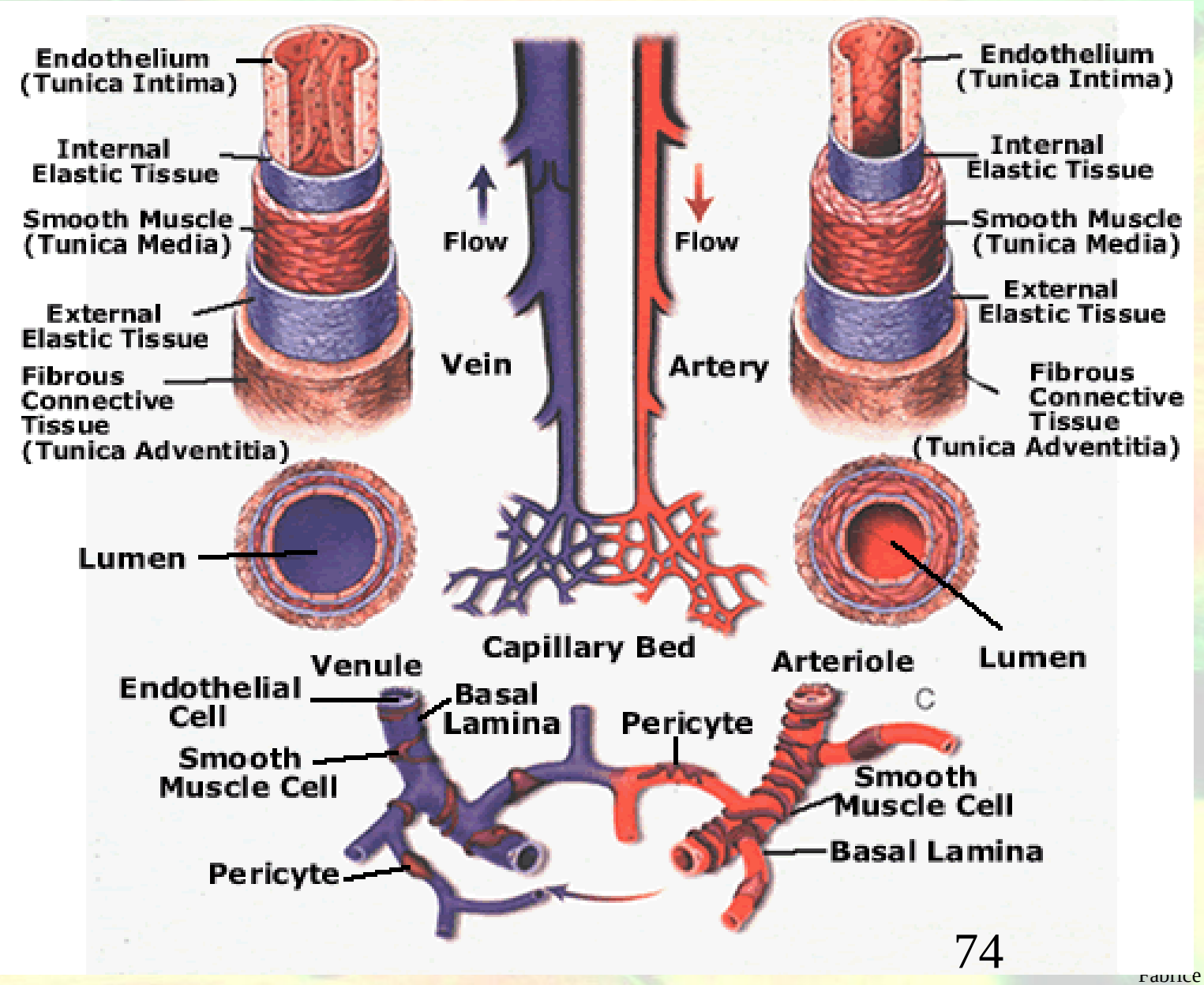




Système cardio-vasculaire

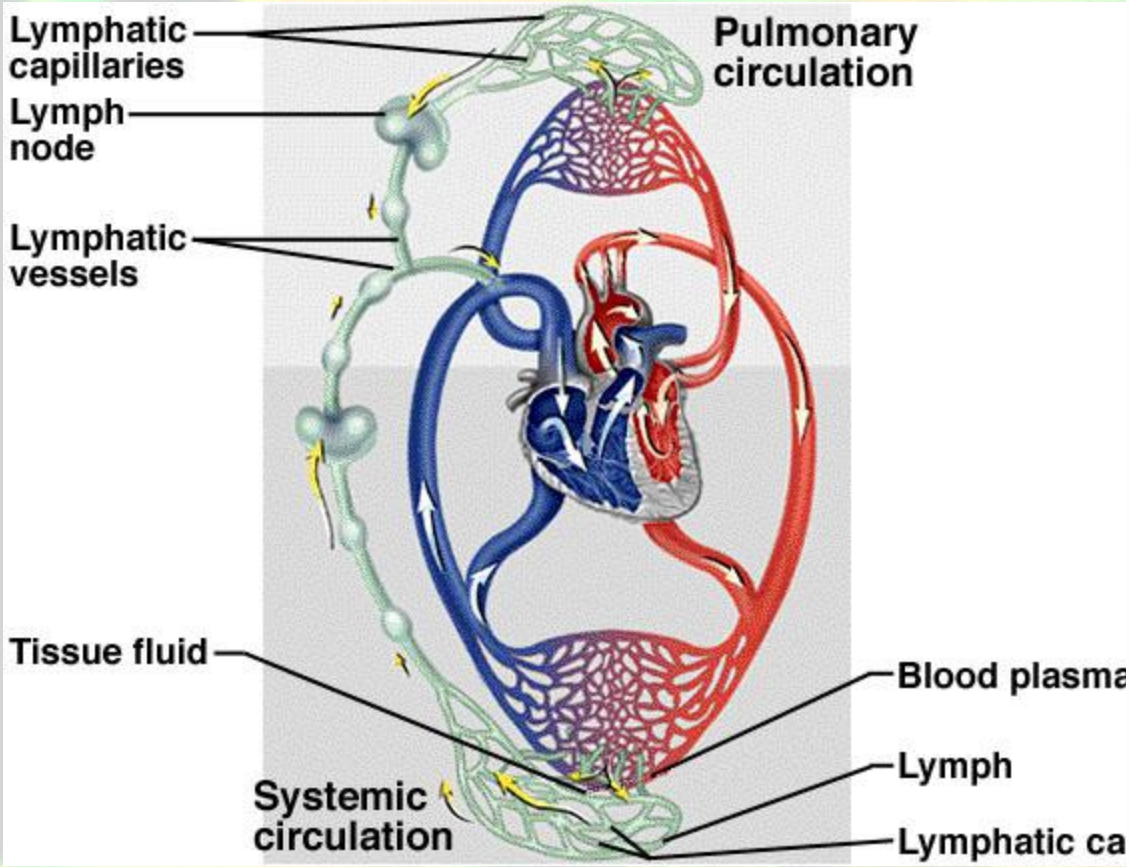


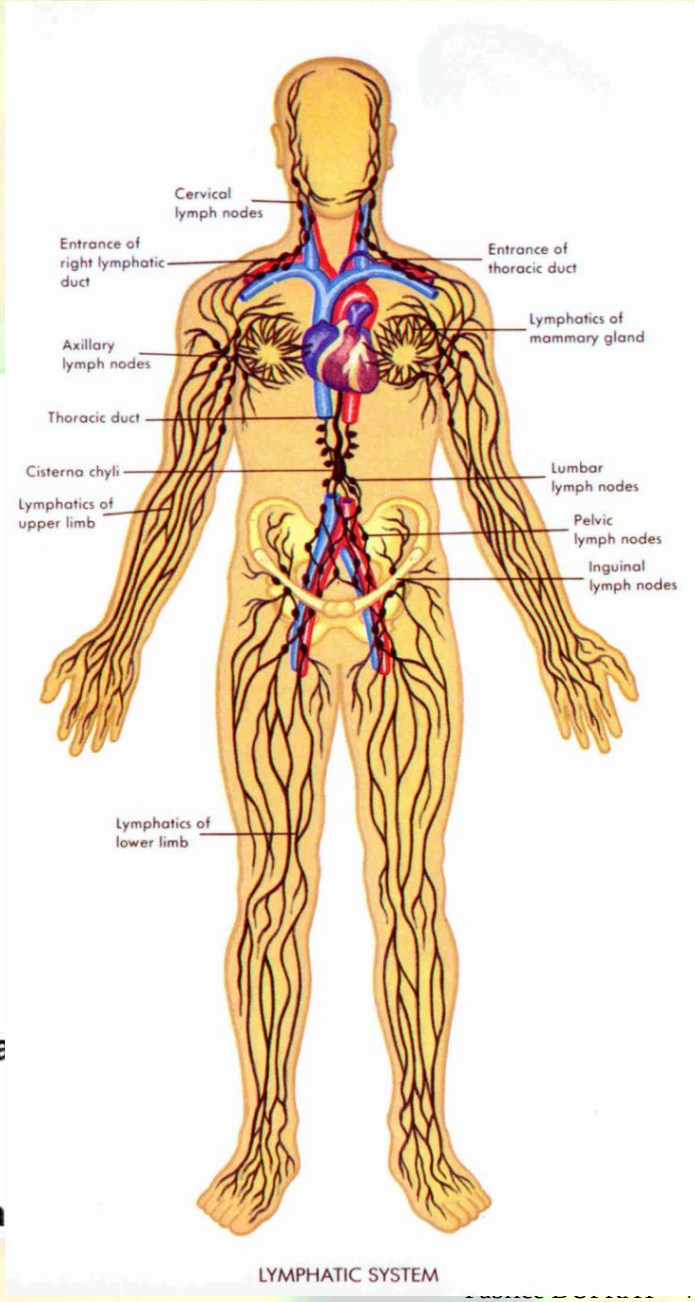
Vaisseaux sanguins



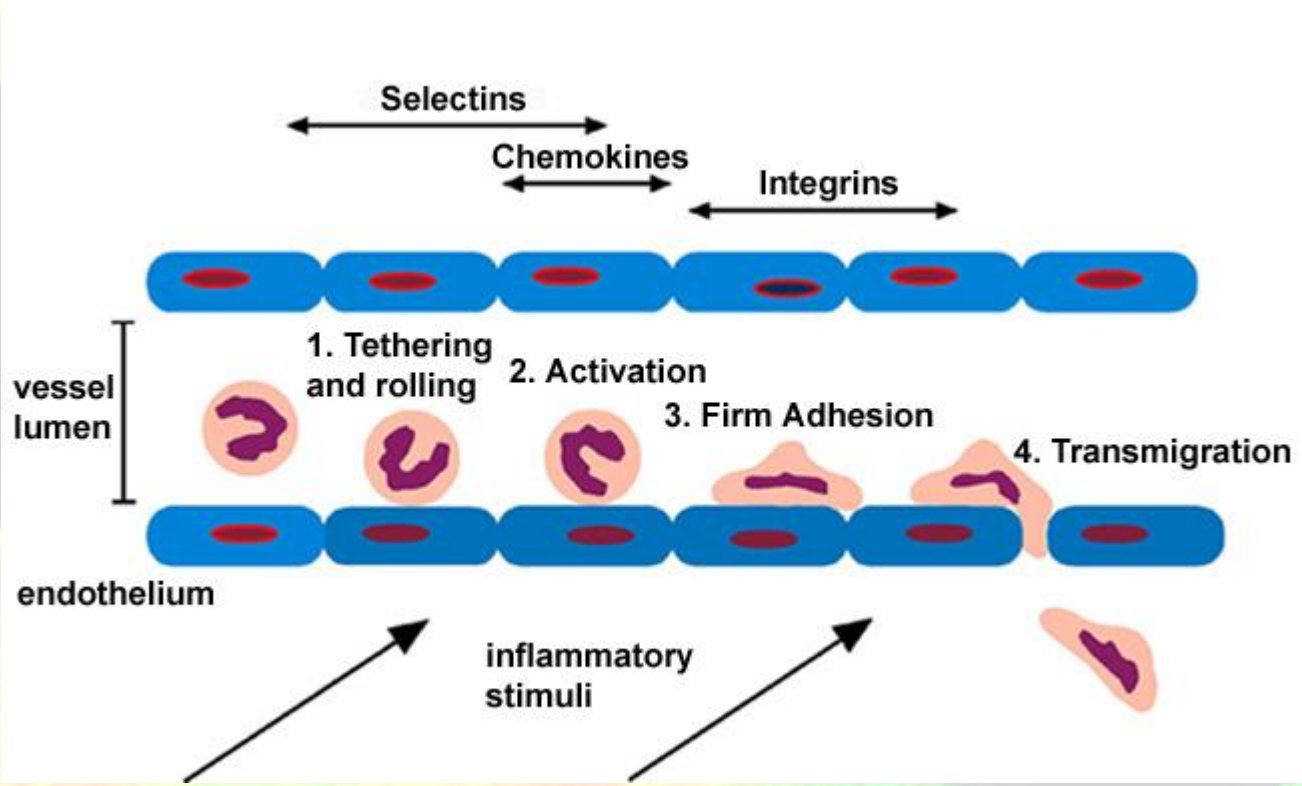
Système lymphatique

Retour dans les veines :
- jugulaire
- sous-claviaire gauche



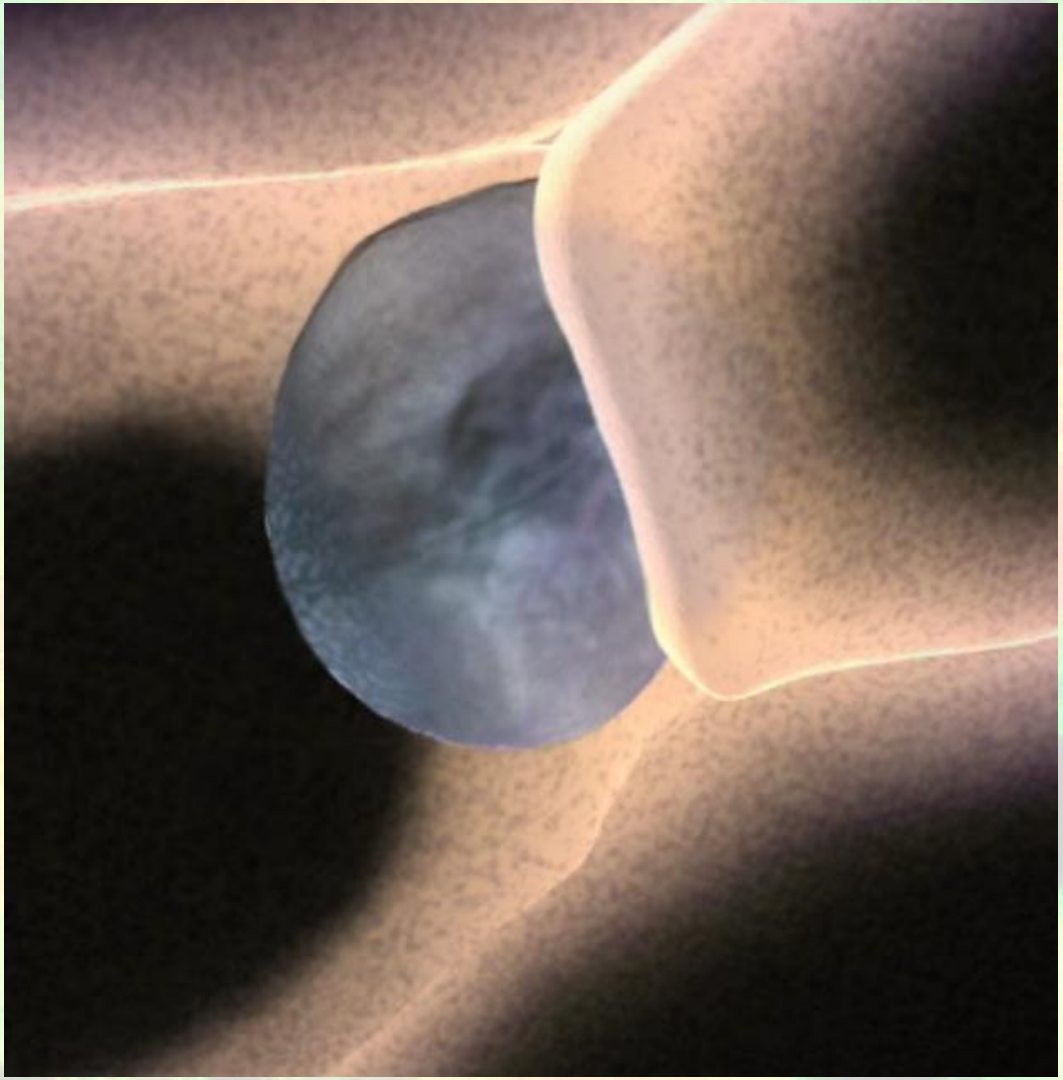


Migration des lymphocytes



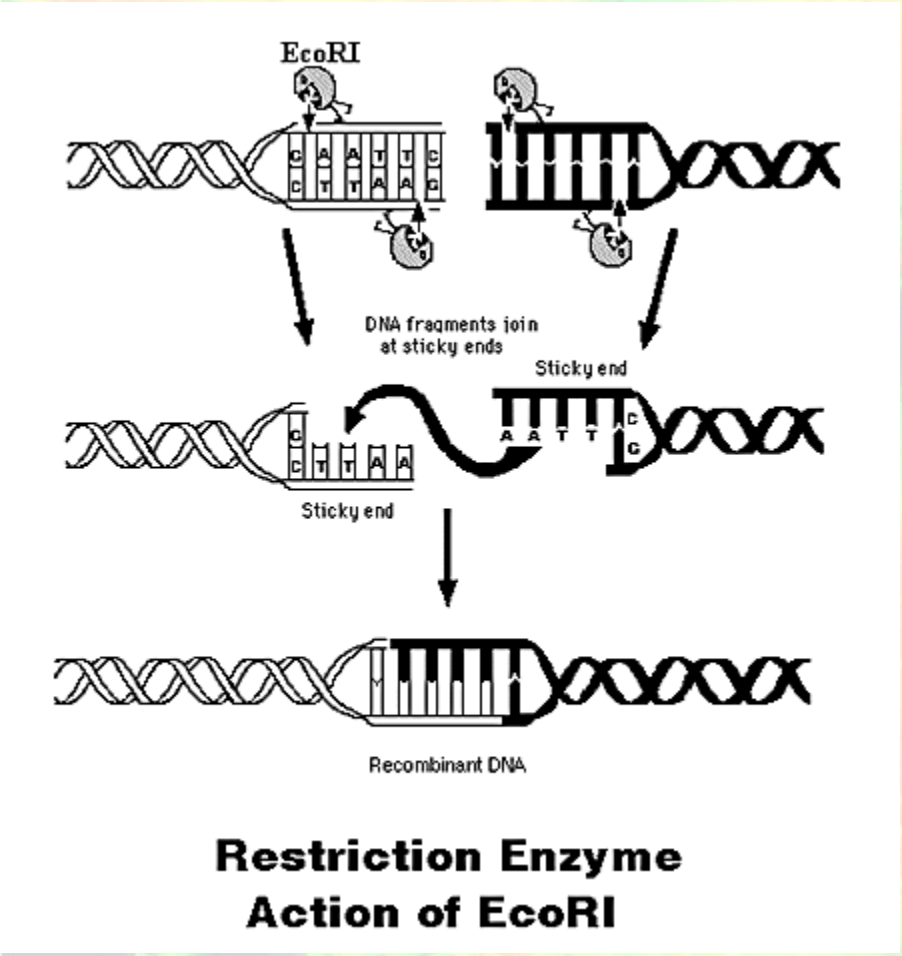
Greenwood *Vasc Pharm* 2002

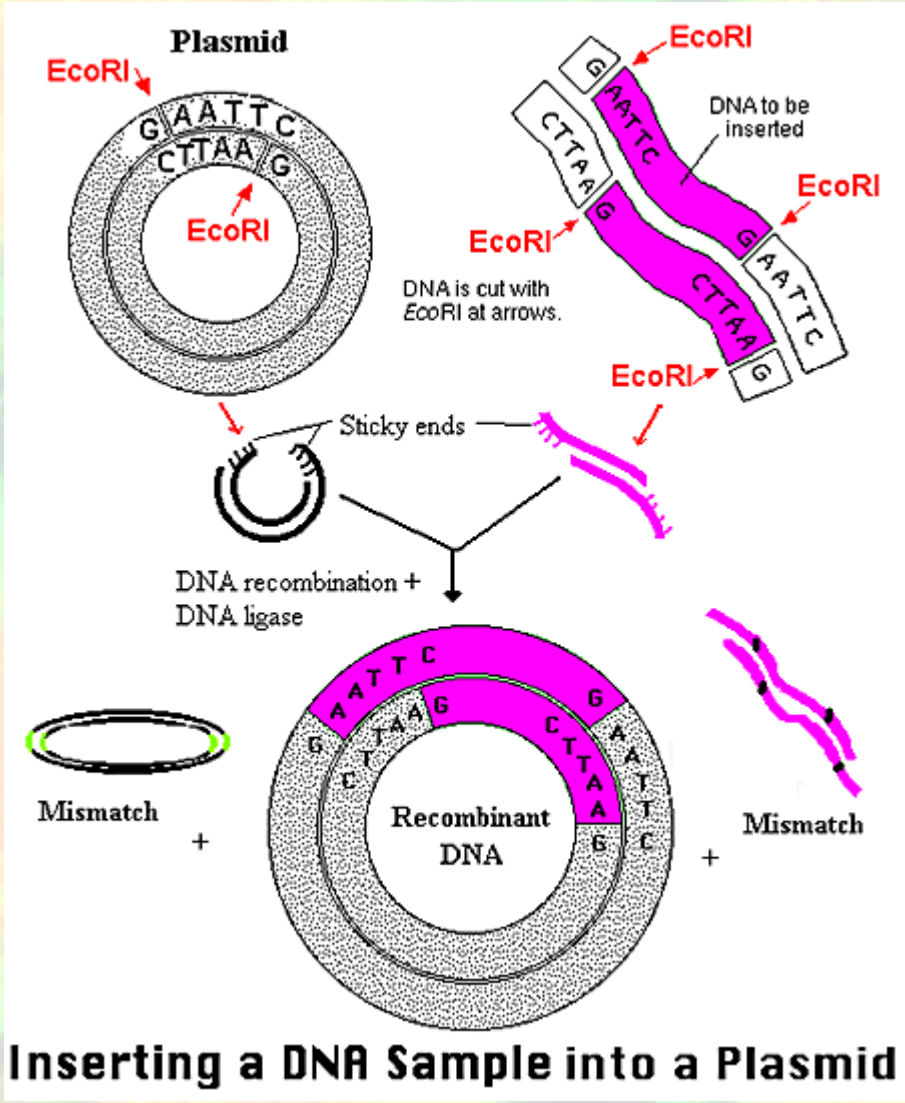
Transmigration des leucocytes



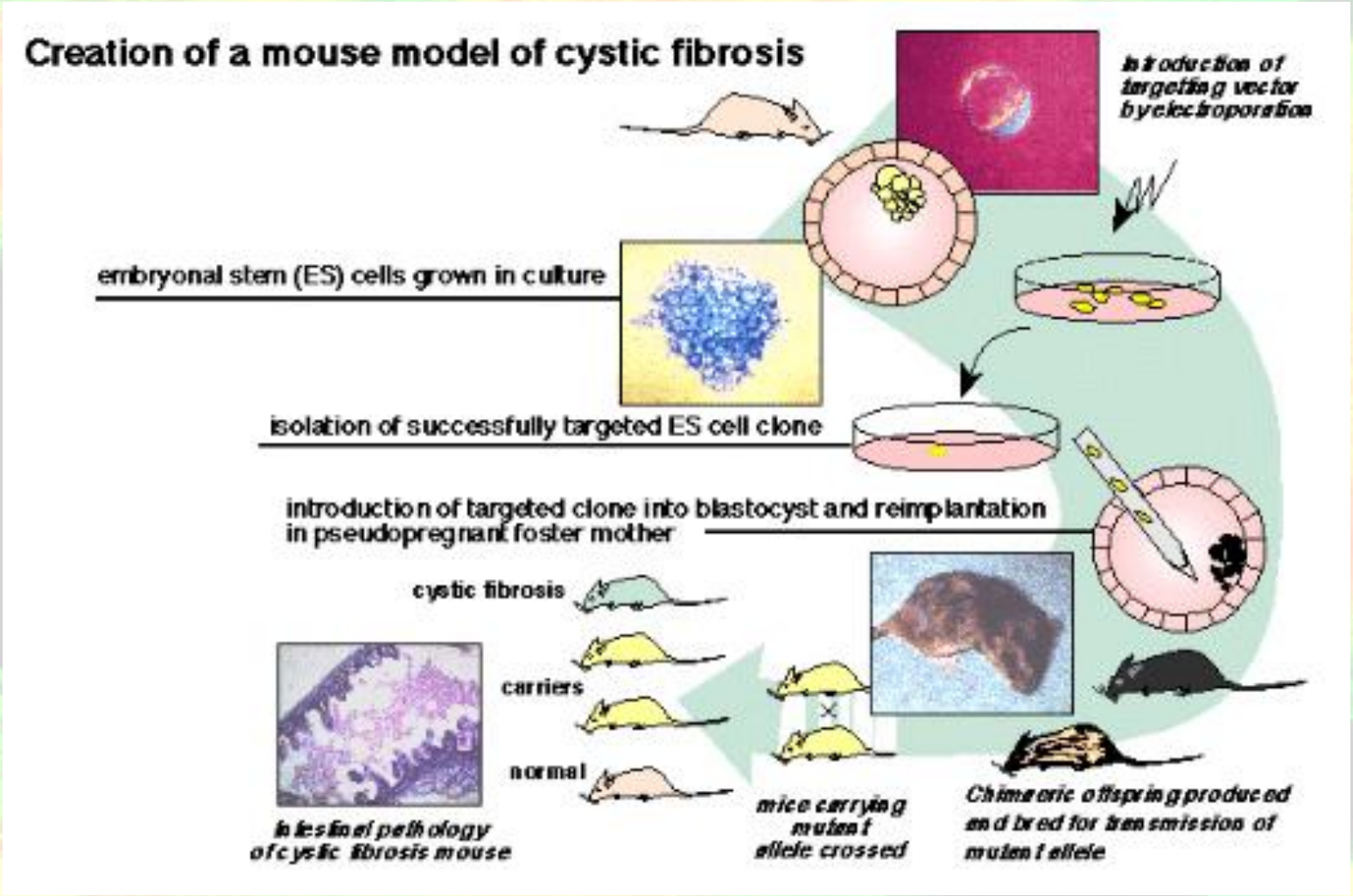
OUTILS DE LABORATOIRE

Enzymes de restriction



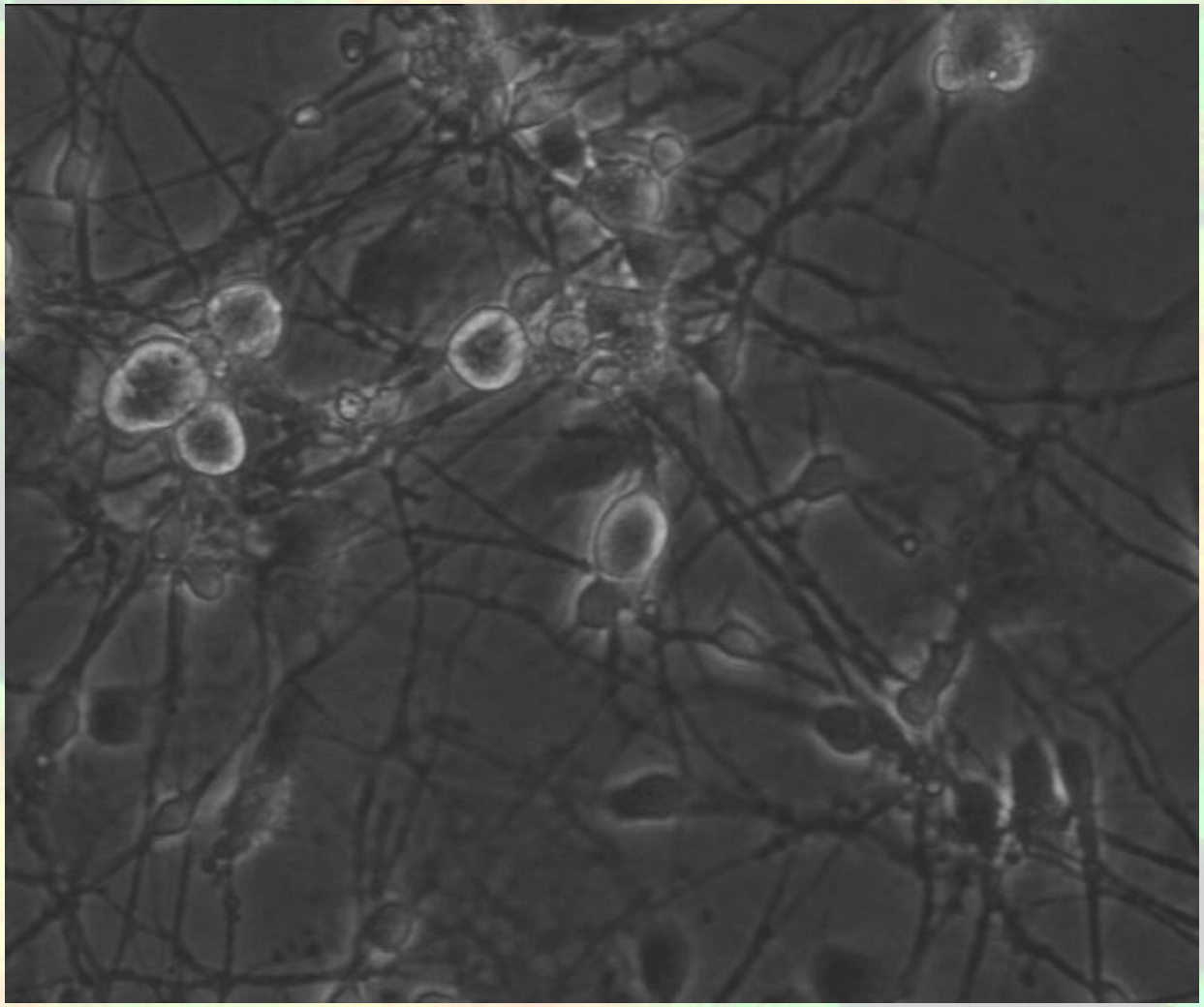


Mutagenese et modèle de souris



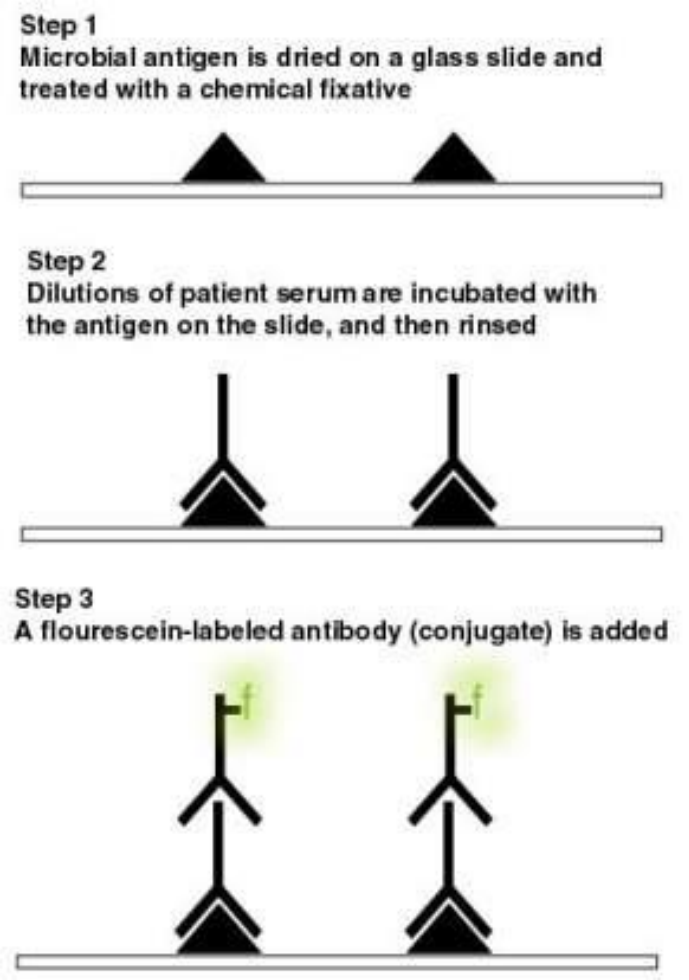
http://wwwold.hgu.mrc.ac.uk/Research/Devgen/Cysfib/julia.htm

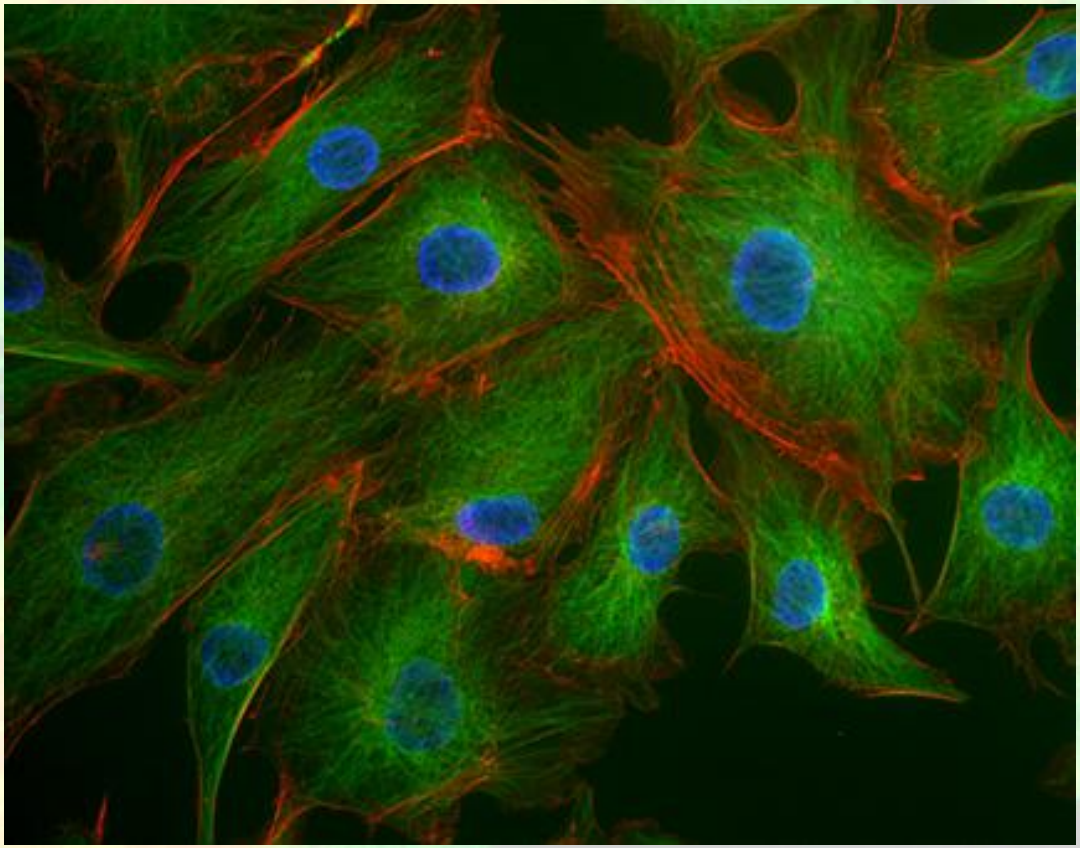
Cultures primaires



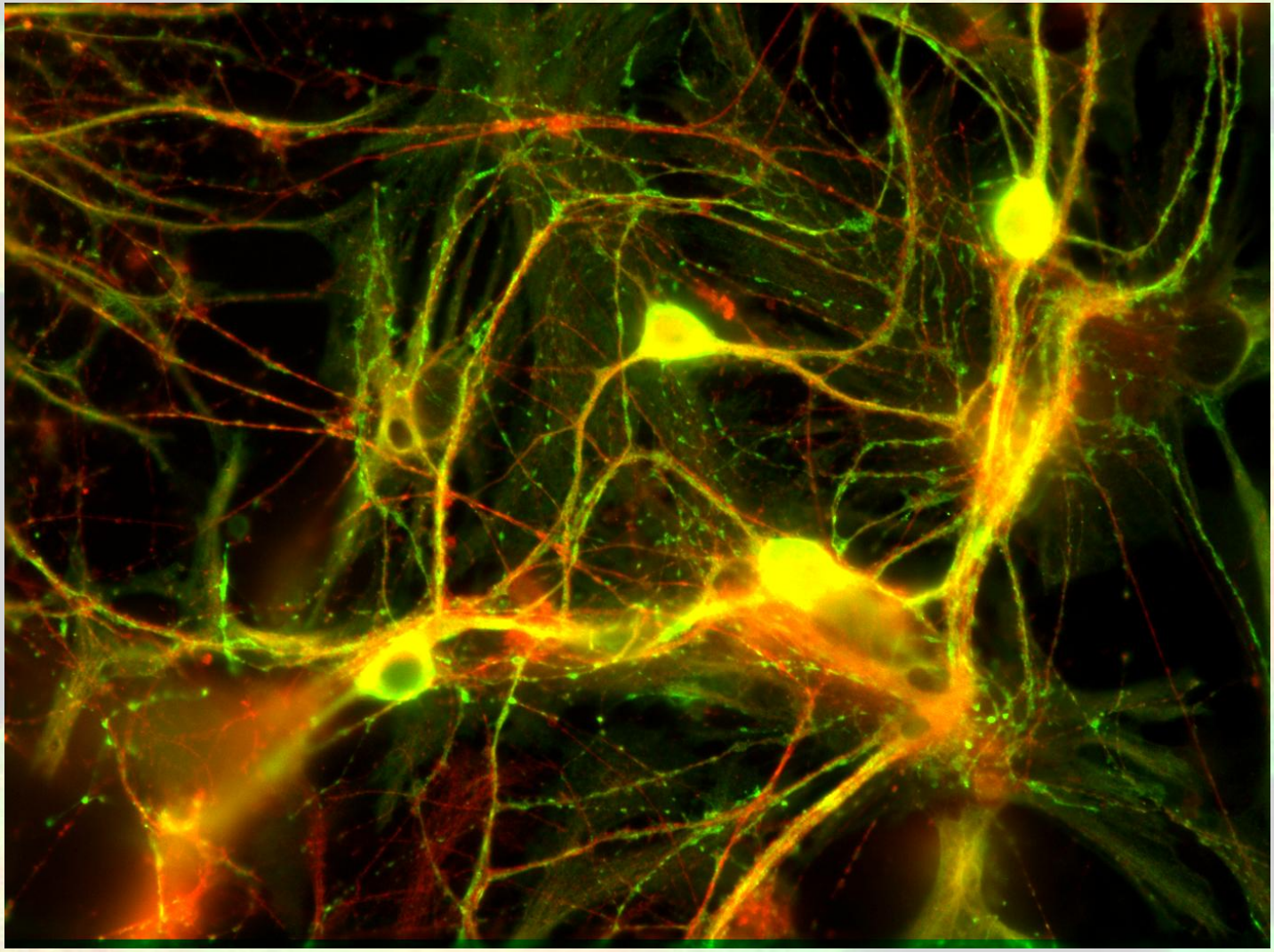
Neurones de ganglion de la racine dorsale de souris

Anticorps et imagerie



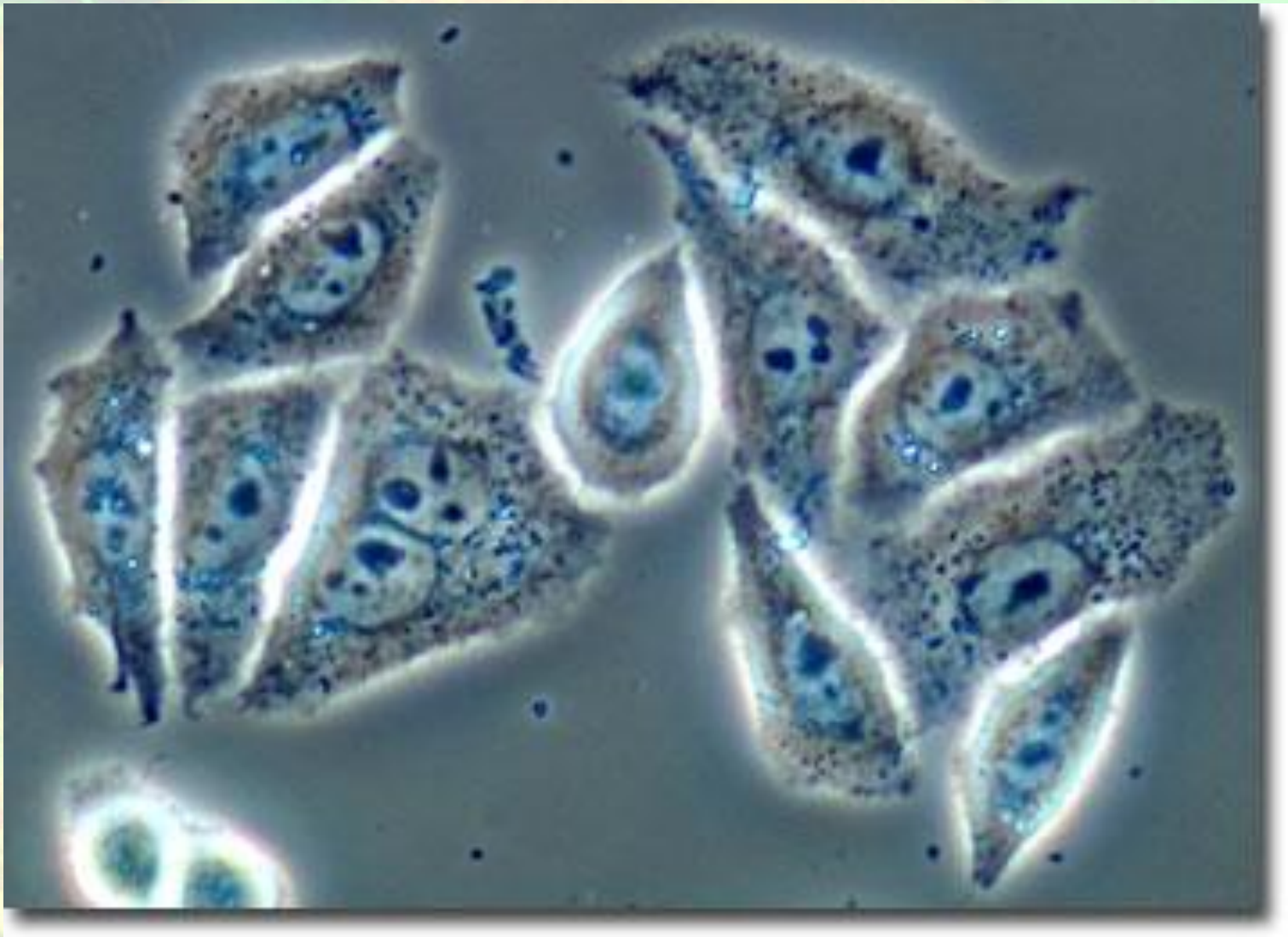


Cultures primaires



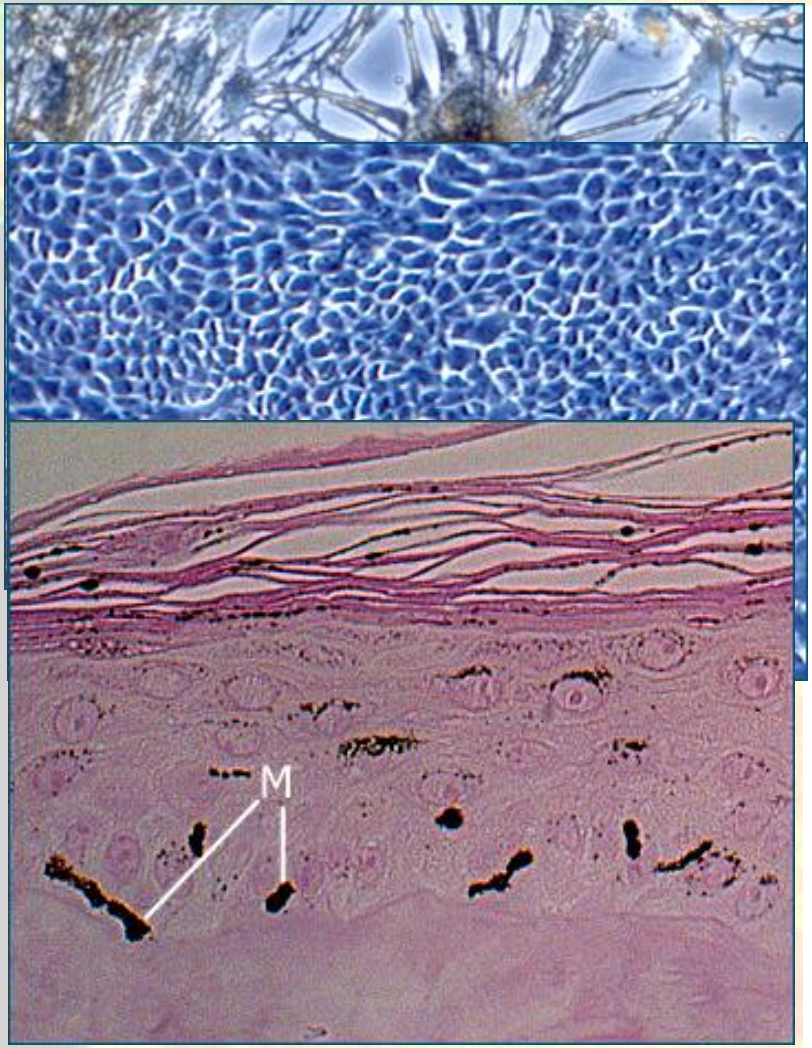
Anticorps fluorescents sur striatum de souris

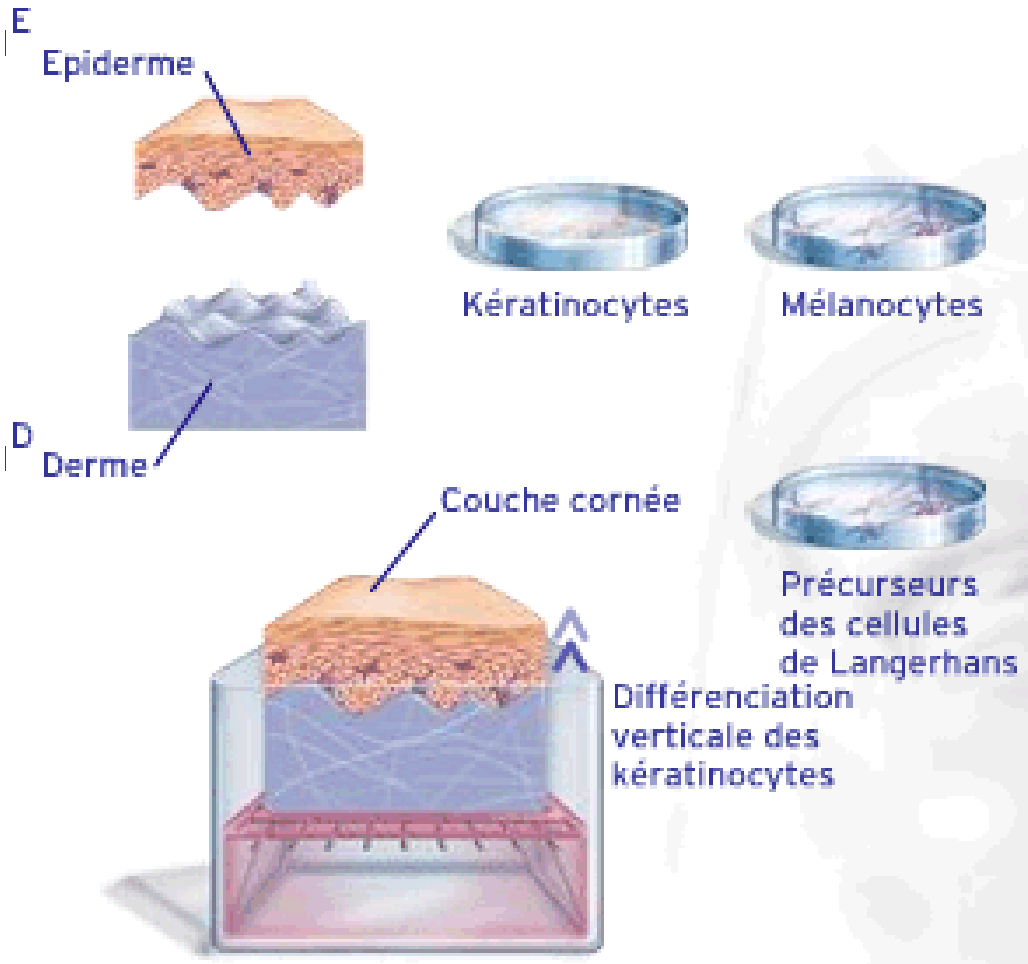
Lignée immortalisée (HELA)



APPLICATIONS

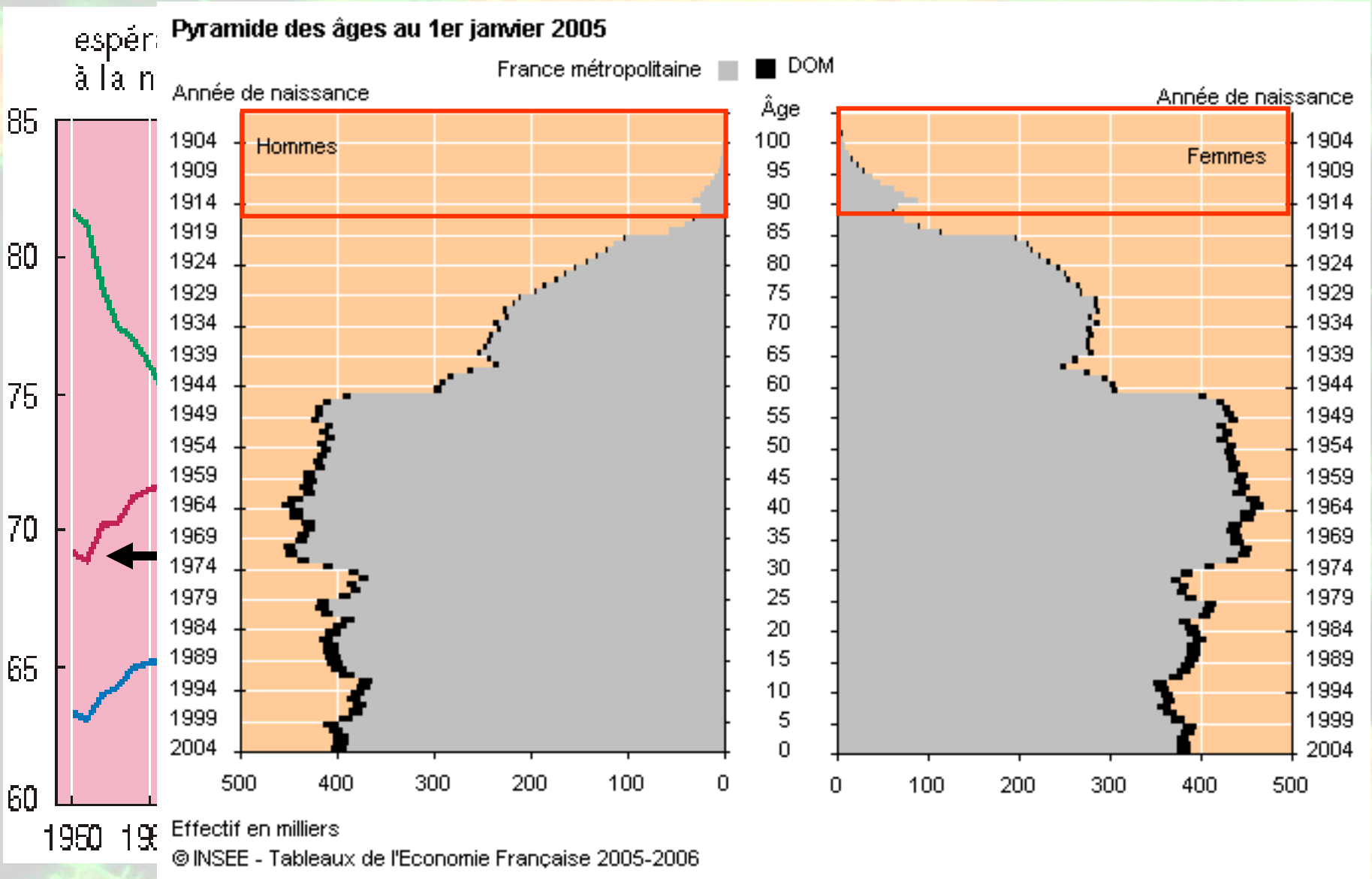
Substitut d'organe: Peau humaine artificielle





http://www.invitroskin.com

Espérance de vie en France



http://www.insee.fr/

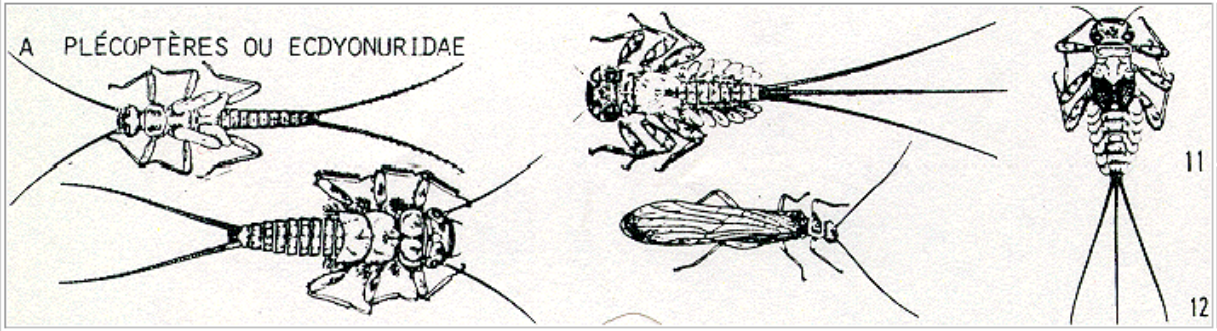
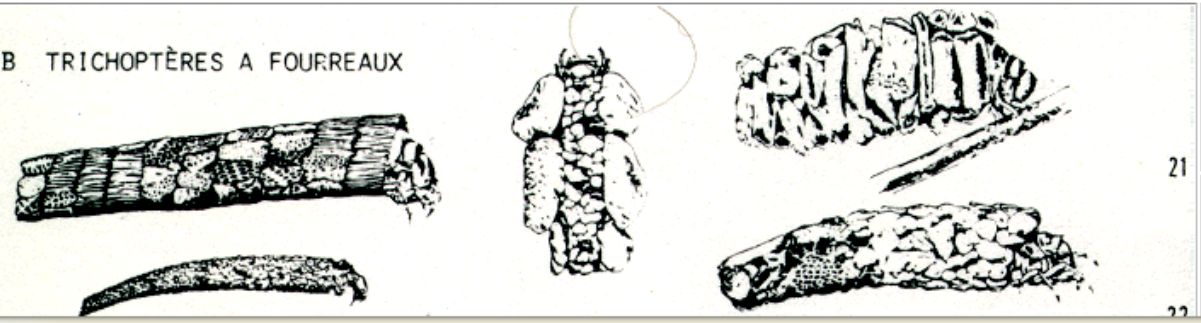
Environnement

Dénitrification de l'eau (bactéries)

Indices biologiques normalisés

Détermination normalisée de la faune et de la flore des milieux aquatiques

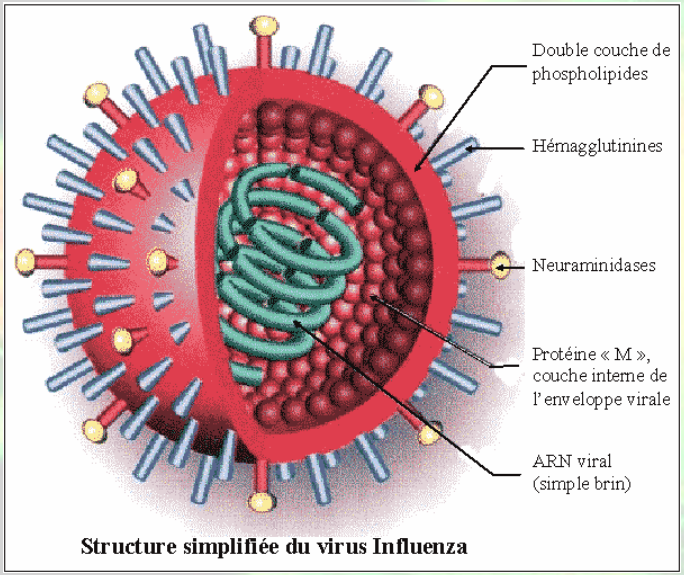
Grille de détermination d'un indice biotique

NATURE DES GROUPES FAUNISTIQUES classés par ordre de sensibilité décroissante à la pollution	NOMBRE D'UNITES SYSTEMATIQUES DANS L'ECHANTILLON						Classe dequalité
	Pour le groupe le plus sensible	NOMBRE TOTAL					
		1	2-5	6-10	11-15	16 et plus	
		VALEUR DE L'INDICE					
A PLÉCOPTÈRES OU ECDYONURIDAE  11	1		7	8	9	10	1A
12	1	5	6	7	8	9	
B TRICHOPTÈRES A FOURREAUX  21	1		6	7	8	9	
22	1	5	5	6	7	8	

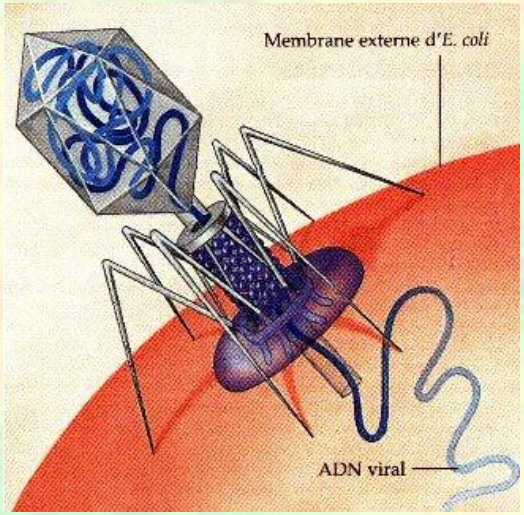
Industrie alimentaire

Clarification des jus de fruit, hydrolyse des pectines (polysaccharides)

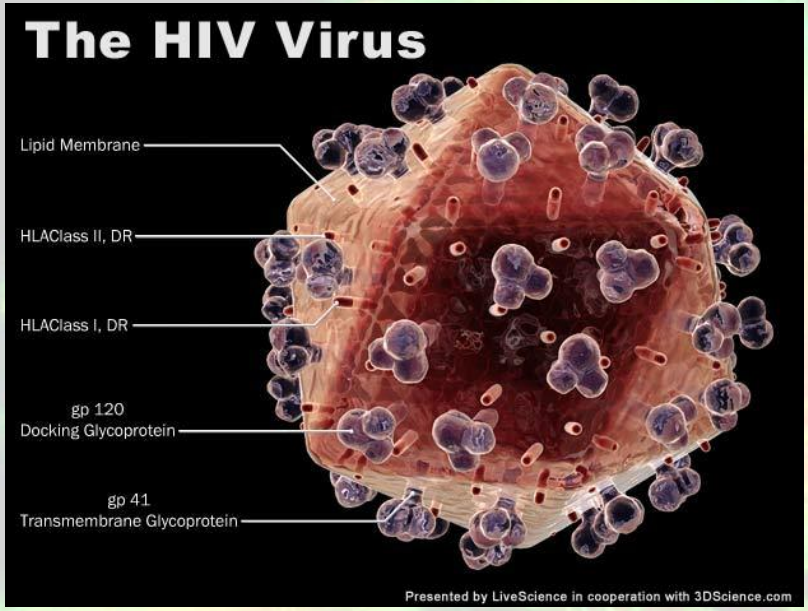
Fermentations (alcools, panification, biscuiterie, choucroute)



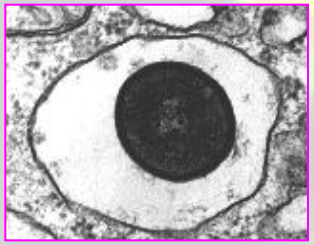
Structure simplifiée du virus Influenza

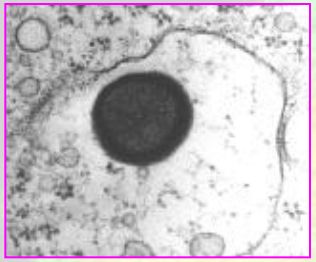


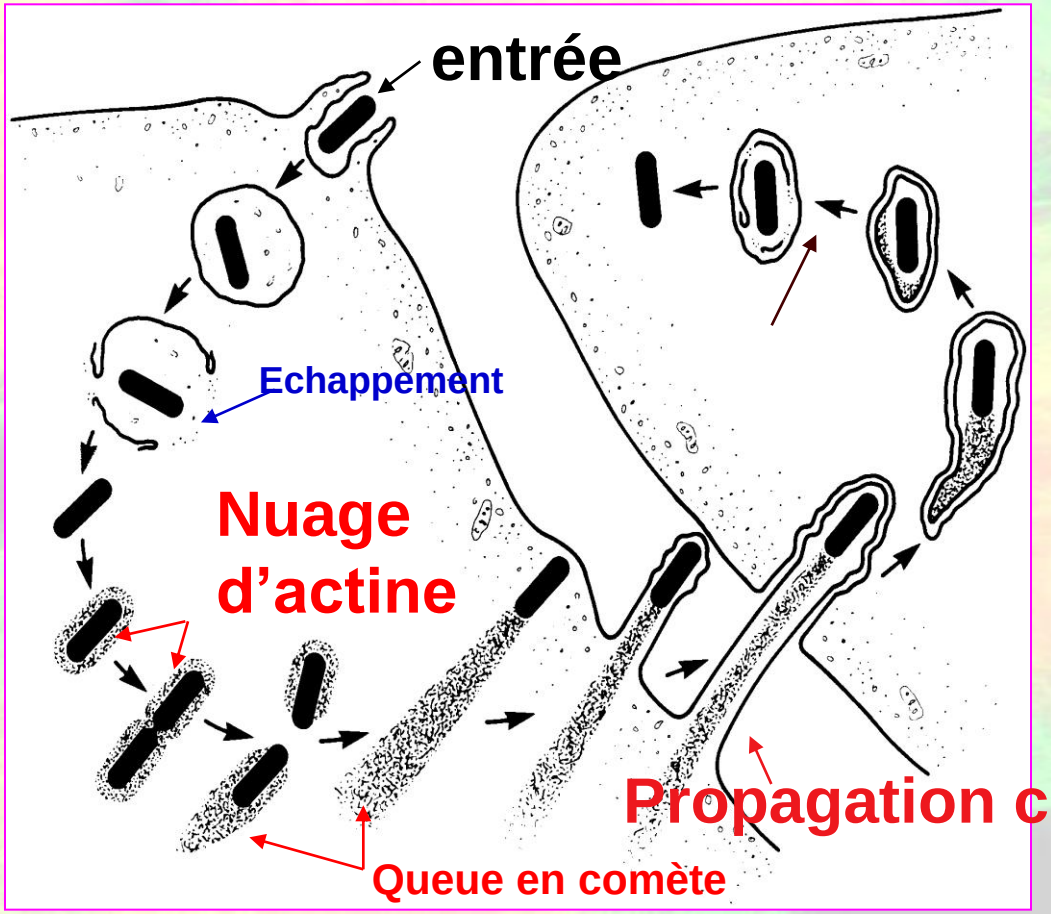
VIRUS A BACTERIES: LES PHAGES

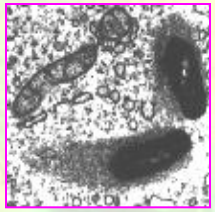


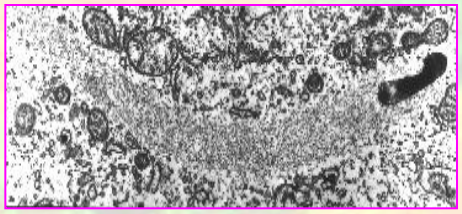
Cycle intracellulaire de Listeria monocytogenes











Portnoy D A et al. J Cell Biol 2002;158:409-414

CONCLUSION

SCIENCES DE LA VIE

Secteur économique d'avenir

Haute valeur ajoutée, très technologique

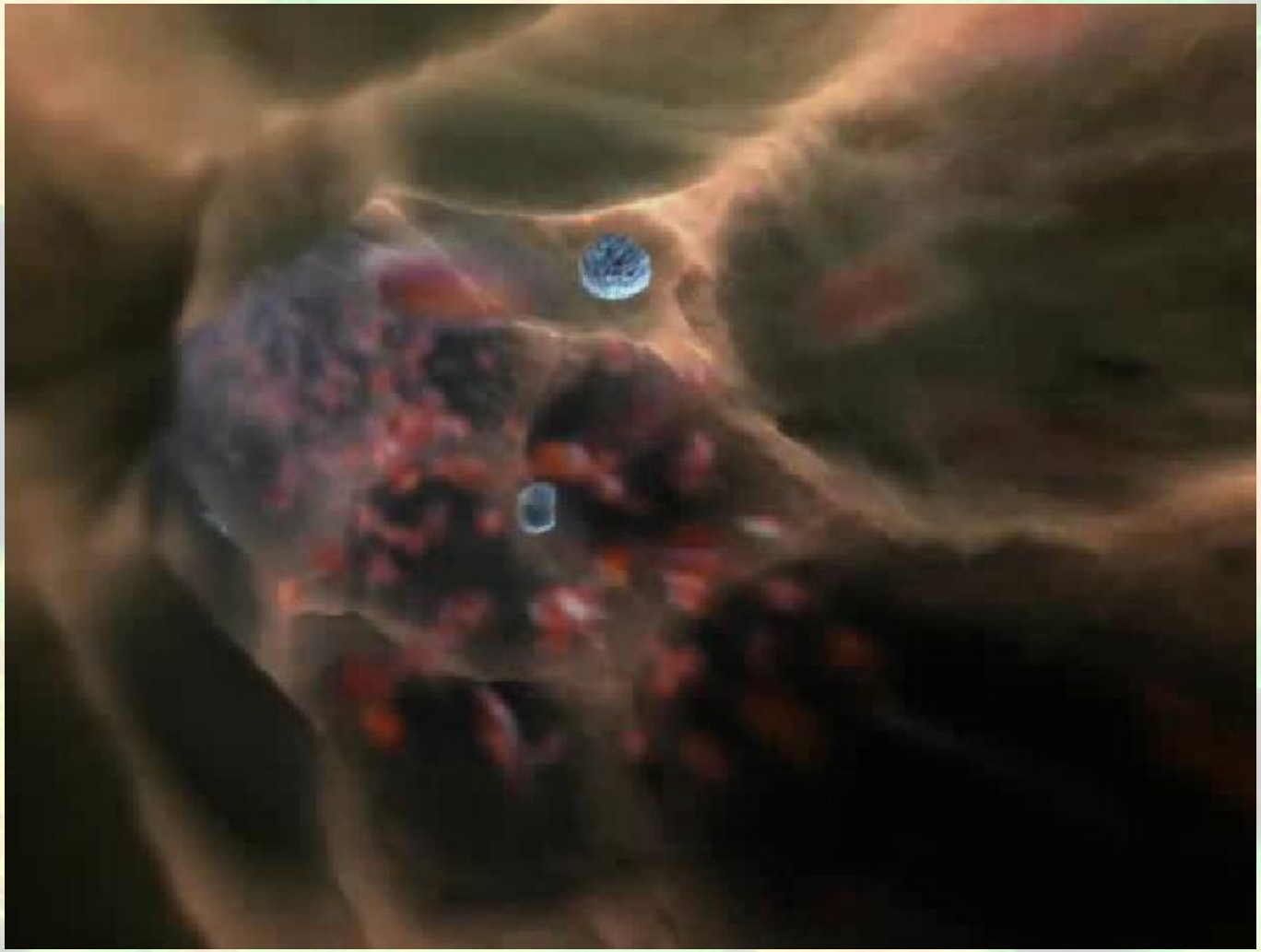
Nécessite de gros moyens financiers et humain

Il y a un besoin de savoir-faire très multidisciplinaire

http://cellimagelibrary.org/home

The inner life of the cell

http://aimediaserver.com/studiodaily/harvard/harvard.swf



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