What are the requirements in basic molecular biology subjects (Genetics, Biochemistry, Cell Biology)?

Please study the next pages of this document. These have been assembled by a tutor after many international students failed the first Cell Biology exam at the end of the winter semester, so as to better prepare them for the lecture.

They summarize the study background of students of the Bachelor Biochemistry or Biology in Jena in the area of Cell biology and Biomedicine - for those students who have a different study background. They also activate the English vocabulary for students from Jena.

Have these topics been part of your bachelor education? Do you know most of what is presented here? Would you feel comfortable with attending a comprehensive lecture in Cell Biology that builds on this knowledge and therefore does not repeat it?

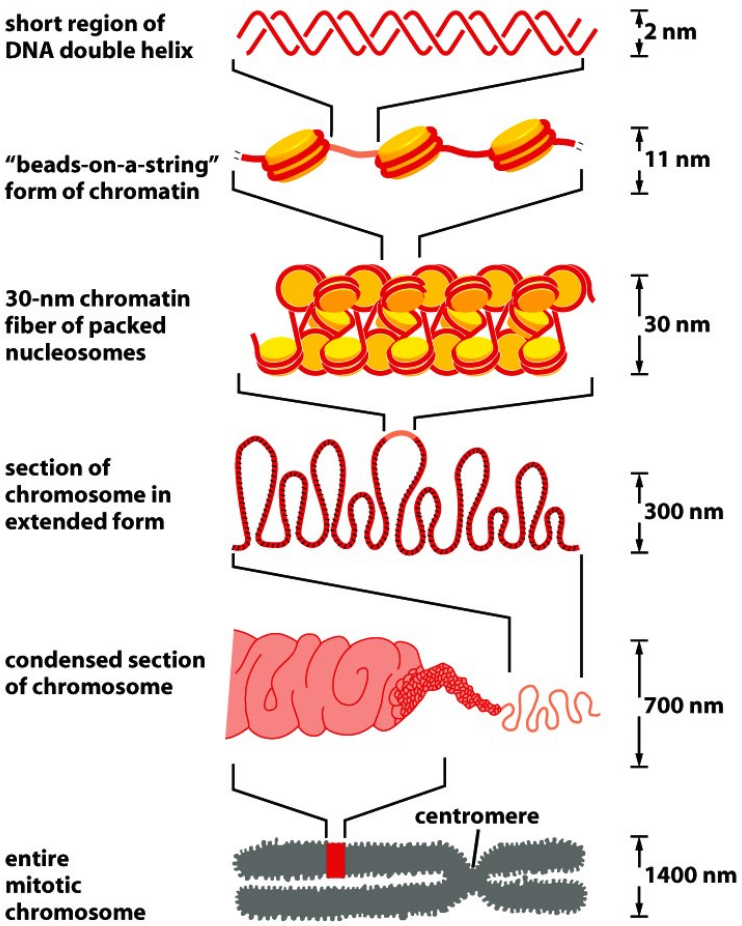
If the answer is „yes“, and your background in Genetics and Biochemistry is relatively similar, you are welcome in Jena to study the Master Biochemistry.

Lecture 1

Regulation of gene expression

Epigenetics and cellular plasticity

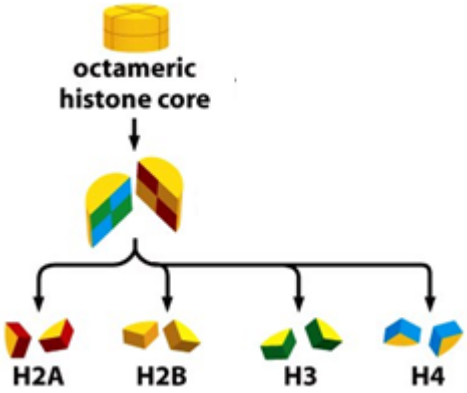
Packaging of DNA

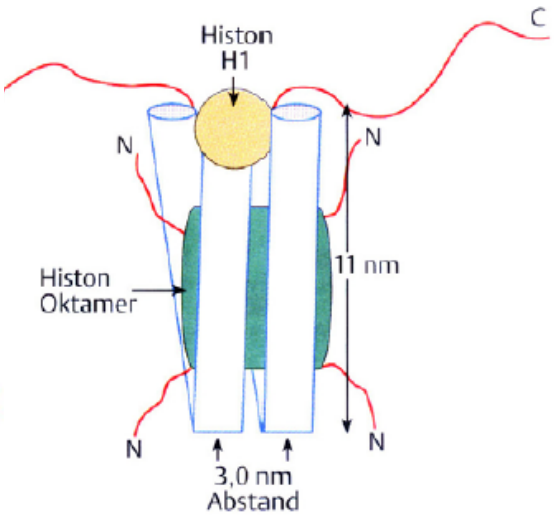


- DNA organized in protein complex = chromatin
- Smallest structural unit is a nucleosome

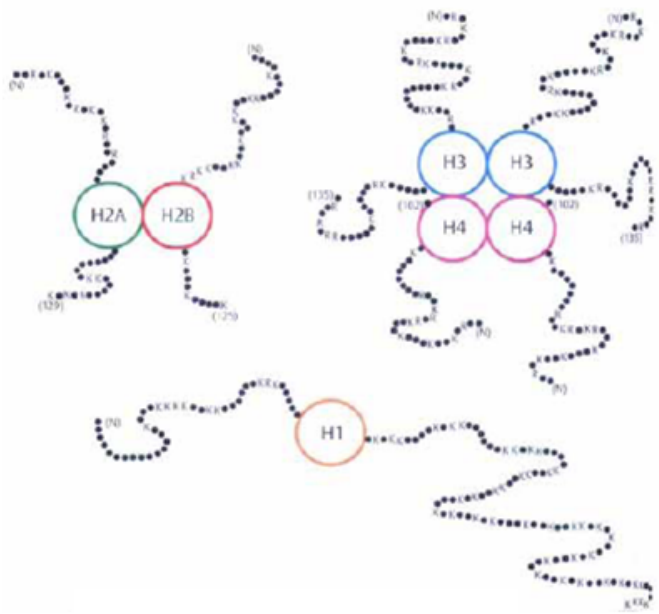
Nucleosome:

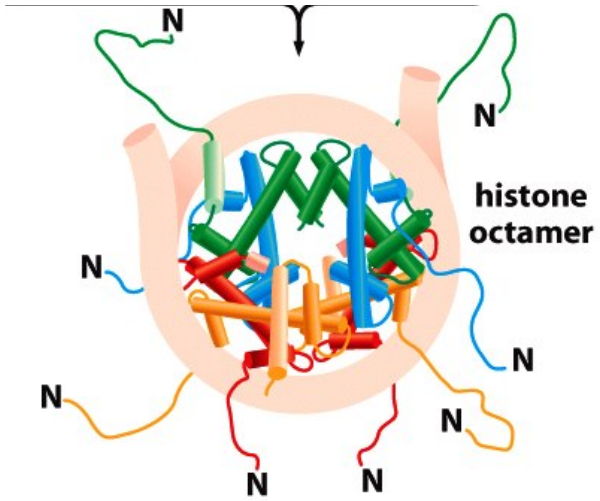
- Octamer of alkaline histone proteins encircled by ca. 150 bp DNA
- Each two of H2A, H2B, H3 and H4 build octamer
- H1 binds linker between 2 nucleosomes





Histone modifications



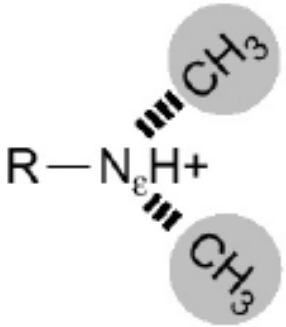


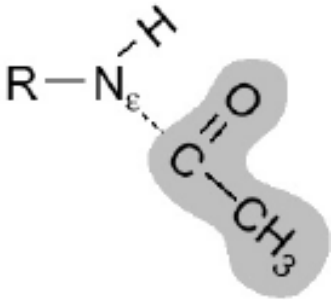
- Long, flexible, alkaline N-terminal ends of histones have posttranscriptionally modified AA
- Modification decides about accessibility of DNA

e.g. modification of lysine:

Heterochromatin (repressive chromatin):
- Positively charged lysine (methylated/not modified)
- Good binding to neighboring nucleosomes
- Dense packaging of chromatin structure

Euchromatin (active chromatin):
- Loss of the positive charge because of acetylation
- Lower affinity to neighboring nucleosomes
- Disaggregation of chromatin structure

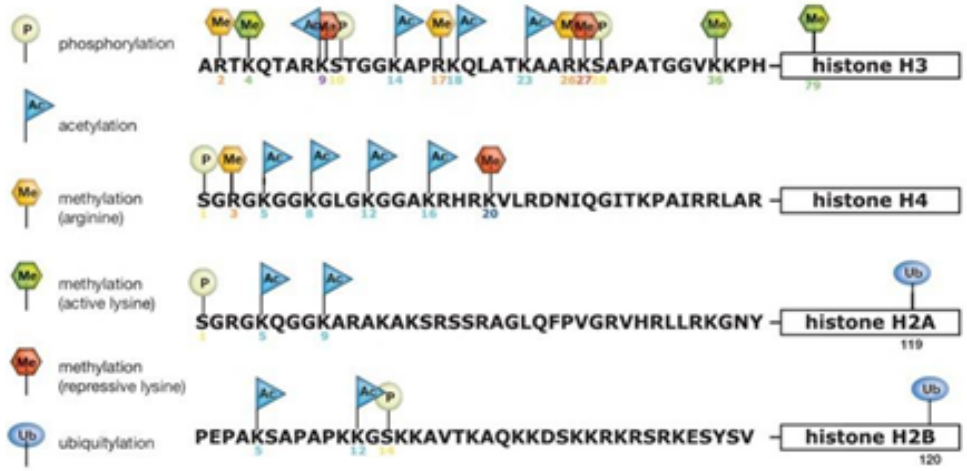




Histone code

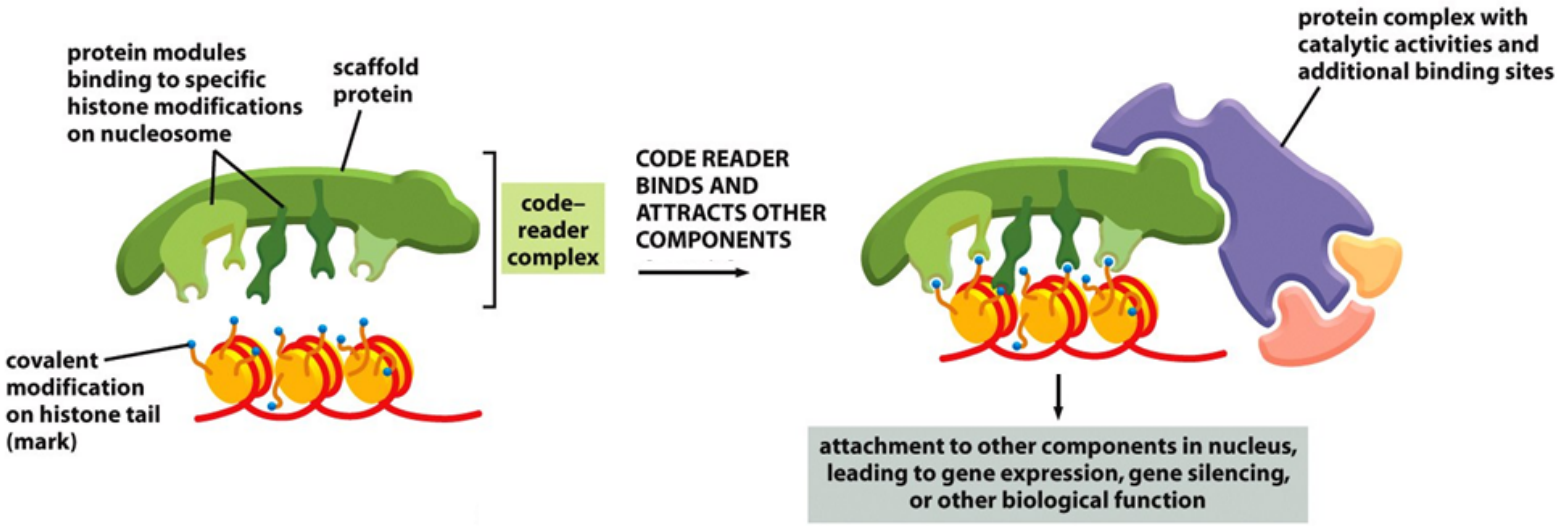
modification of histones:

- Acetylation of lysine
- Methylation of lysine and arginine
- Phosphorylation of serine
- Ubiquitination of lysine (globular domain)

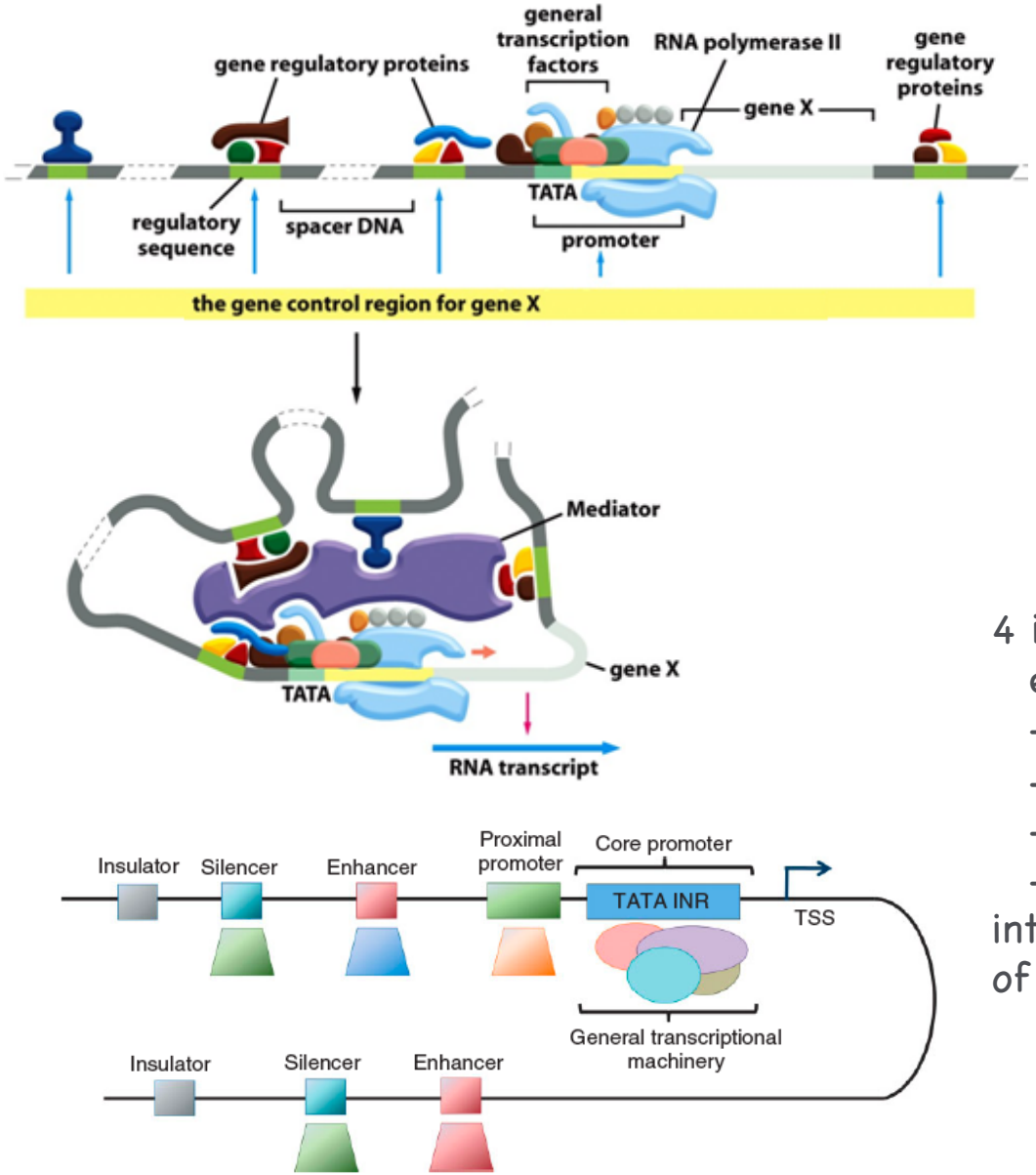


Histone code theory:

- Combinations of posttranscriptional modifications affect gene activity
- Causes changes in affinity of cofactors, remodeling factors, polymerases, …
- Code readers bind via modification to nucleosomes and recruit other proteins



Gene regulatory elements



Gene regulatory elements:

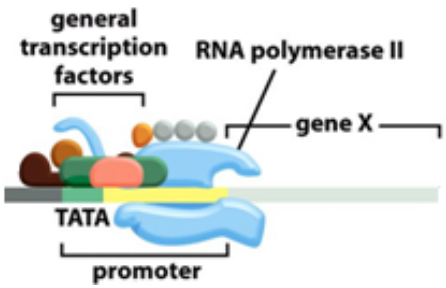
- All DNA sequences that are part of control or initiation of transcription
- Bound by transcription factors: every protein that takes part in regulation or initiation of transcription (transcription factors also bind polymerases)

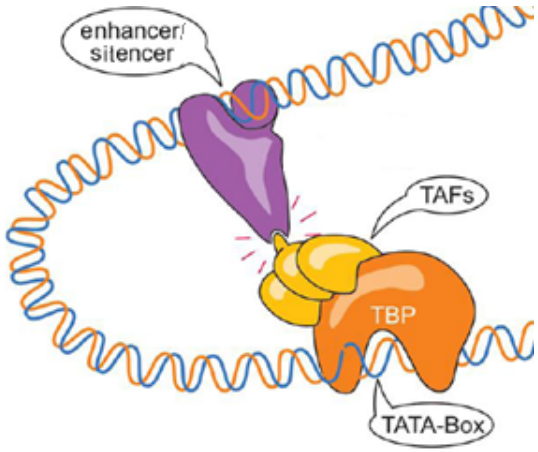
4 important classes of gene regulatory elements:

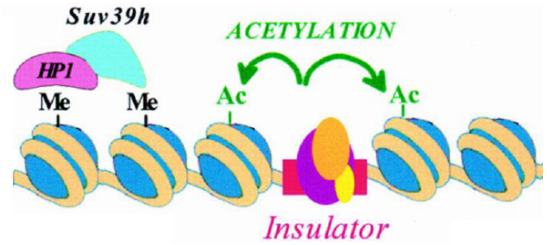
- Promoter
- Enhancer
- Silencer
- Insulator

interplay or competition determines activity of individual genes

Gene regulatory elements







All gene regulatory elements are DNA sequences.

Promoter:

- Binding of polymerase and transcription factors
- Start of transcription

Enhancer:

- next to promoter or more than 1000 bp distant to promoter (may affect initiation complex through looping)
- Binding of activating transcription factors
- Enhancement of transcription rate

Silencer:

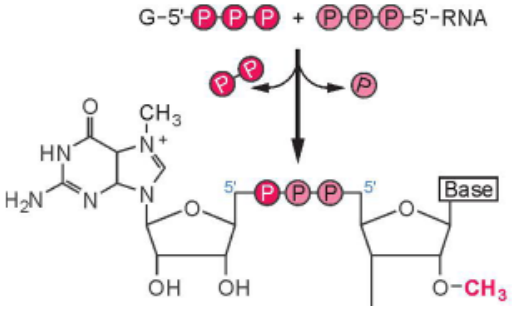
- next to promoter or more than 1000 bp distant to promoter
- Binding of repressive factors
- Binding affinity of polymerase and activating transcription factors is decreased
- Therefore: decrease of transcription rate

Insulator:

- Binding of regulatory factors
- Inhibiting impact of regulatory factors to neighboring genes

Stability of mRNA

Modification of mRNA:

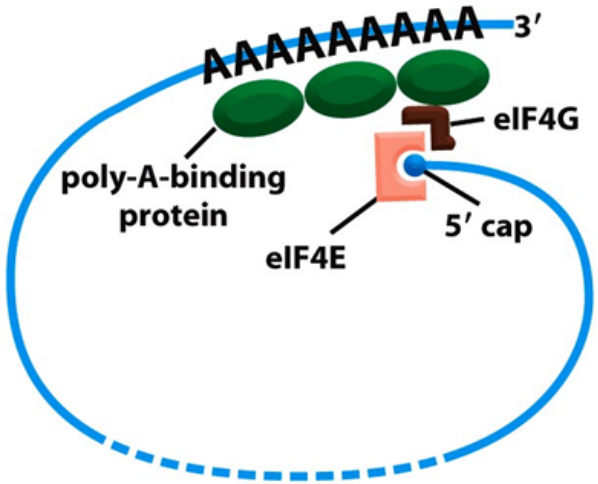


- mRNA modified at 5`- and 3`- end
- 5`capping: 7-methylguanosine bound to 5`end
- 3`polyadenylation: poly(A)-polymerase synthesizes poly(A)-tail

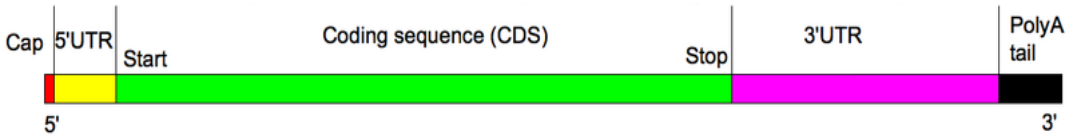
5` Cap and Poly(A) stabilize mRNA and enable recognition for storage or translation:

•No recognition by exosome (complex of ribonucleases)
•Enabling translation:
- Initiating transport of mRNA to cytosol
- Causing circular mRNA structure
  (eIF4E binds 5`cap; PABP (poly(A) tail binding protein) binds poly(A); eIF4G connects them)
- 5`cap allows 40S subunit binding to mRNA
- PABP enhances translation efficiency

•Enabling storage in storage particles



Stability of mRNA



5` UTR and 3` UTR can affect stability:

•5` UTR:

•Binding site of translation initiation factors

•binding site of regulatory proteins for ribosome function, elongation factors, mRNA stability

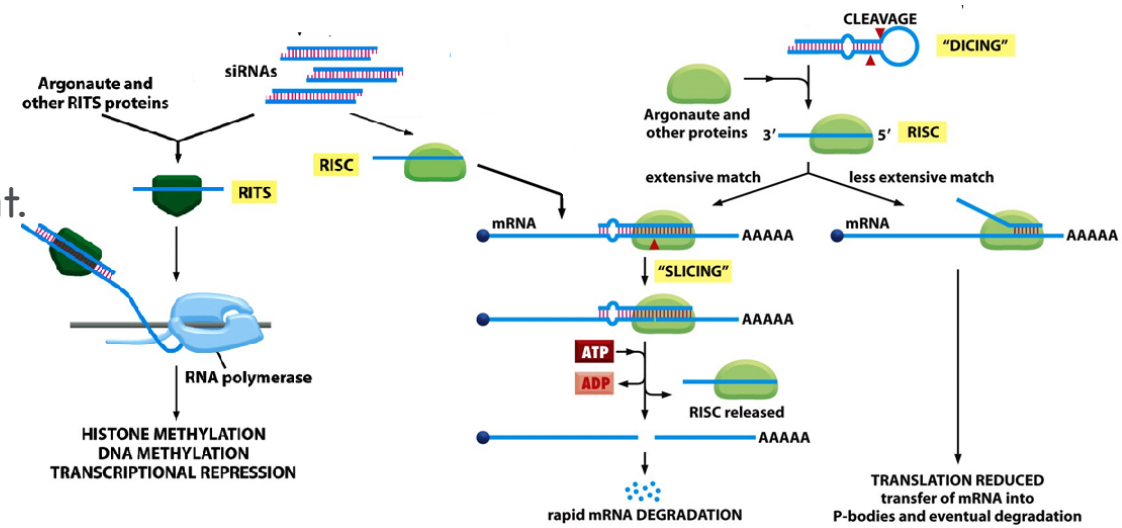
•3` UTR:

•Contains polyadenylation signal

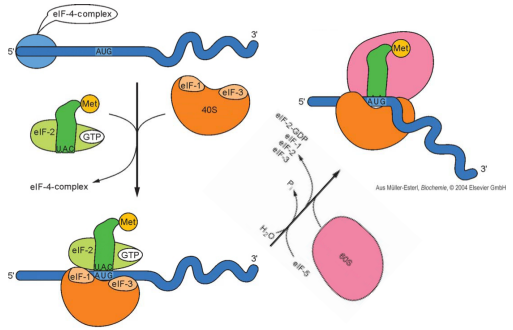
•Can be binding site of regulatory proteins, which regulate stability or translation of mRNA

Small regulatory RNAs influence degradation or translation of mRNA

- **miRNA:**
- Transcribed as hairpin structure and then cut to 19 – 23 nt.
- **siRNA:**
- Processed out of dsRNA to 20 – 25 nt.
- Dependent on complementarity , they lead to degradation of mRNA or inhibition of translation
- One regulatory RNA may regulate multiple cognate mRNAs

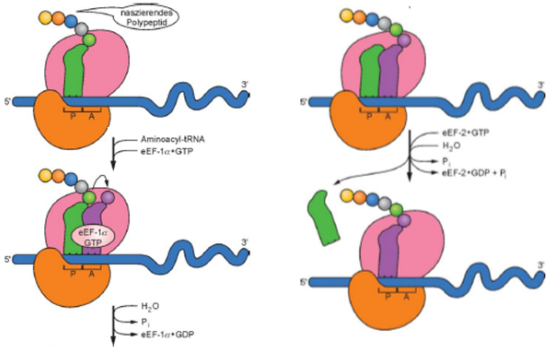


Translation



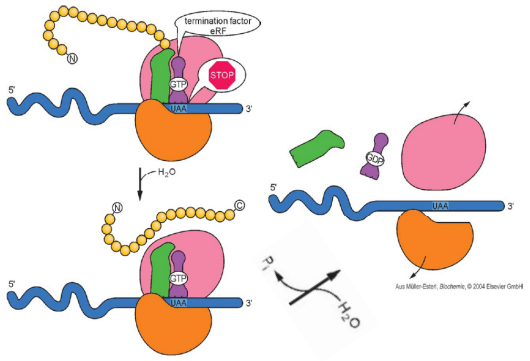
Initiation

- **eIF1** and **eIF3** bind to 40S subunit
- **eIF4** binds to mRNA
- Small subunit and **eIF2** scan mRNA for first AUG
- Loading of initiator $tRNA^{Met}$ by **eIF2**
- Association of 60S ribosome subunit



Elongation

- "New" tRNA binds A site
- After binding of **eEF-1 α,** formation of petide bond by peptidyl transferase
- Previous tRNA leaves complex
- "New" tRNA binds E site



Termination

- Binding of release factor **eRF** to first stop codon at A site
- Hydrolysis of peptide chain from last tRNA

Lecture 2

Regulation of protein function

Protein modification

Modification of AA side chains can affect:

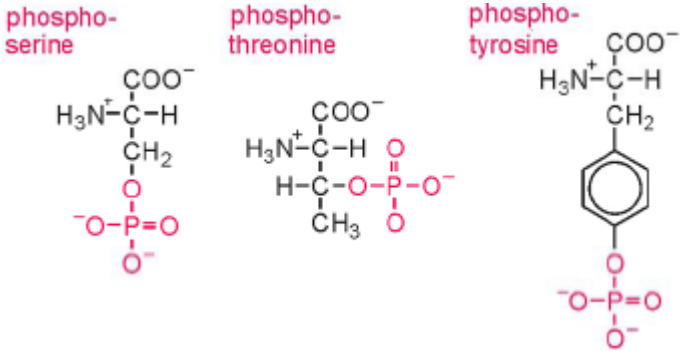
- Protein properties
- Interaction sites
- Activity and signaling function
- localization
- Stability
- Folding

Phosphorylation:

• of serine, threonine and tyrosine by kinases

• Changes charge and can affect folding, interaction sites, activity

• E.g. activation of Cdk by phosphorylation

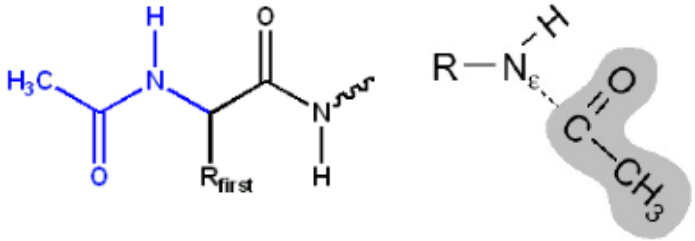


Acetylation:

• Lysine and N-terminus of proteins by acetyl transferases

• Can affect folding, interaction sites, activity, charge

• E.g. histone acetylation increases accessibility of DNA

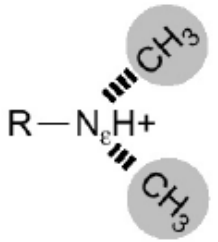


Methylation:

• Lysine and arginine by methyl transferases

• Can affect folding, interaction sites, activity, charge

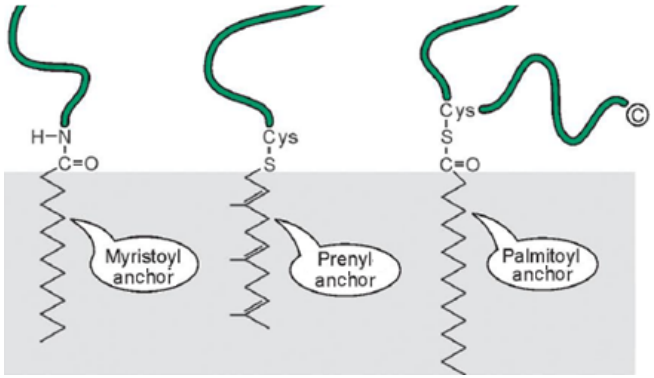
• E.g. histone methylation decreases accessibility of DNA



Protein modification

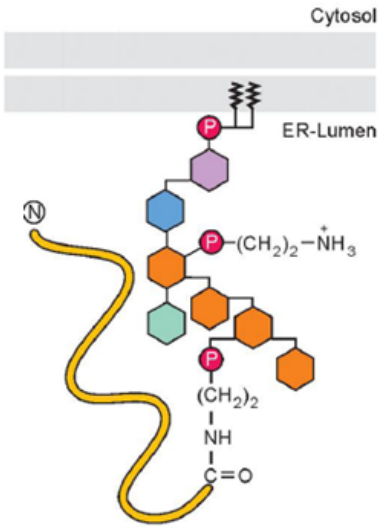
Attachment of lipids:

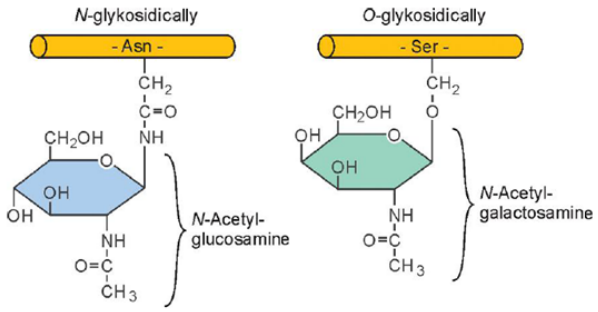
- Covalent attachment of fatty acid to N-terminus, serine and cysteine (lipid anchor)
- Allows protein to attach to membranes
- E.g. farnesylation of Ras



GPI anchor:

- Attachment of Glycosylphosphatidylinositol to C-terminus of protein via ethanolamine phosphate bridge
- Allows protein to attach to membranes
- E.g. acetylcholinesterase





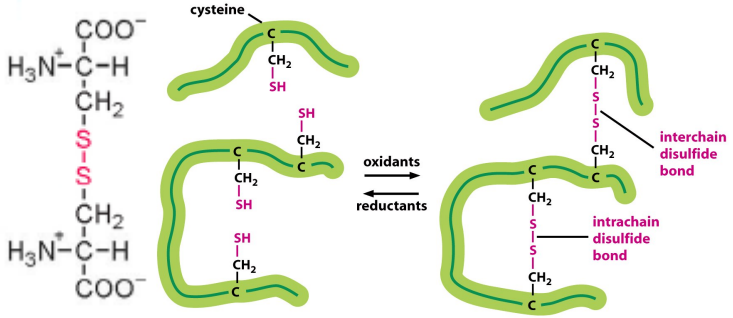
Glycosylation:

- N-glycosylation of asparagine (in ER)
- O-glycosylastion of serine and threonine (in Golgi)
- Modification by glycosyltransferase
- Can change folding, interaction sites, stability
- Extracellular proteins are often stabilized by glycosylation

Protein modification

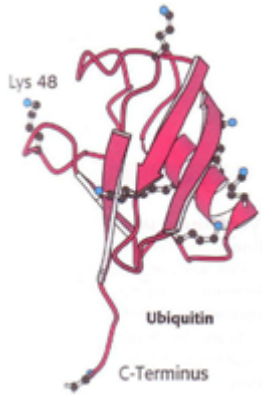
Disulfide bridges:

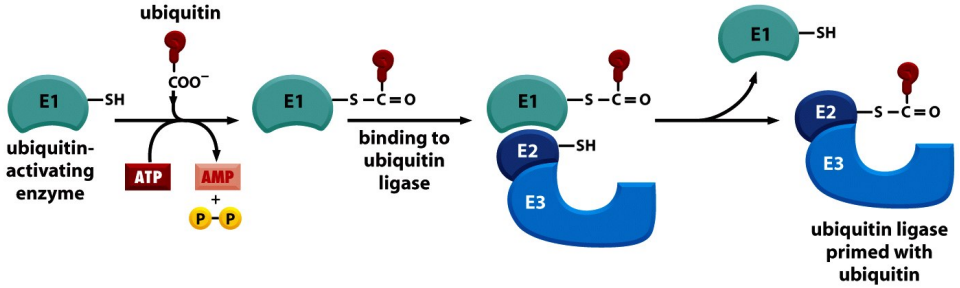
- Inter- or intramolecular covalent linkage of 2 cysteines
- Formed initially in ER
- Changes folding of protein
- E.g. insulin, antibodies

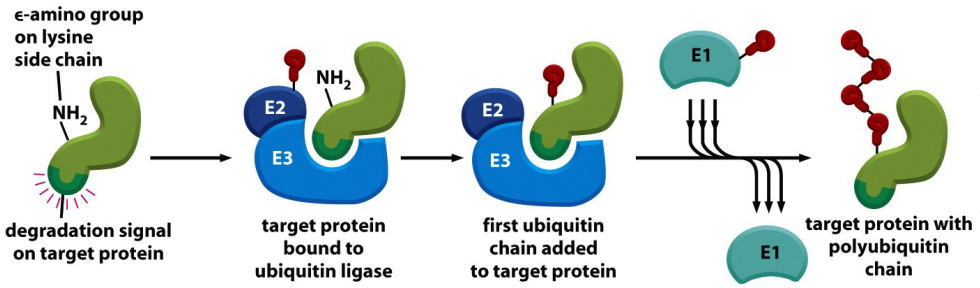


Attachment of proteins:

- Attachment of other (often small) proteins
- Changes properties or function or leads to degradation
- E.g. ubiquitination by ubiquitin ligase as signal for decay





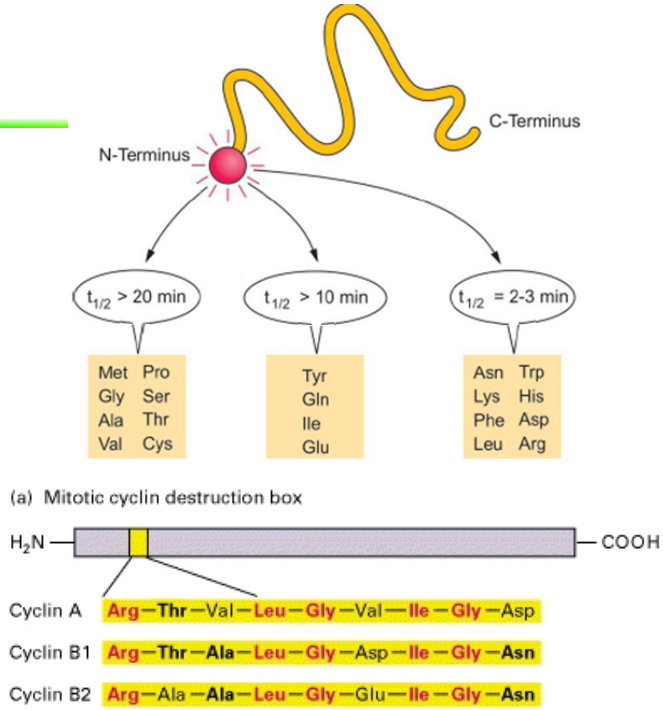


- C-terminus of Ub is bound to thiol group of **Ubiquitin acitivating enzyme E1**
- Transfer of Ub to a thiol group of **ubiquitin conjugating enzyme E2**
- Transfer of Ub to lysine side chain of target protein by **ubiquitin ligase E3**
- other Ub are loaded with their C-terminus to e.g. lysine 48 (isopeptide bonds)

Protein degradation

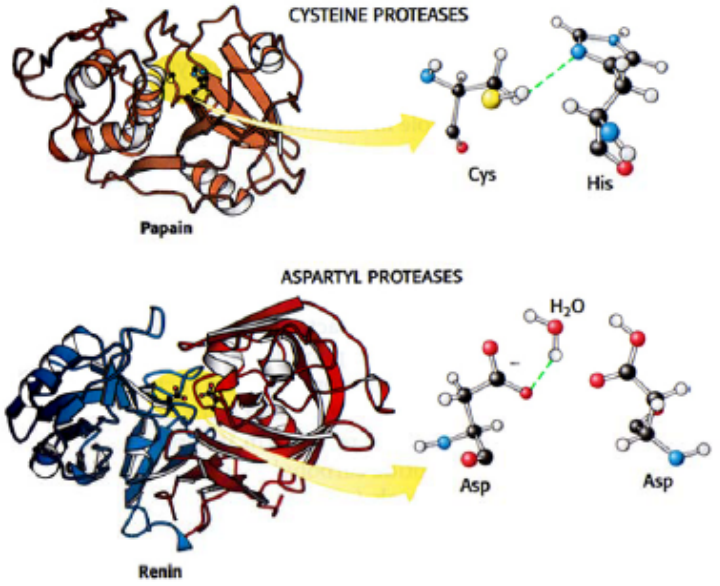
Determination of protein life time:

- Life time of eukaryotic proteins varies strongly between some seconds and many days
- Life time is determined by N-terminal AA (N-end rule) or presence of destruction boxes (like in cyclins)
- E.g. fast degradation: insulin
  slow degradation: hemoglobin



Proteolysis:

- Site-specific proteases (Cysteine-/Aspartyl-/Metallo-) may cleave proteins directly
- Causes their activation or inactivation
- E.g. caspase cleavage during apoptosis or cleavage of factor VIII by thrombin

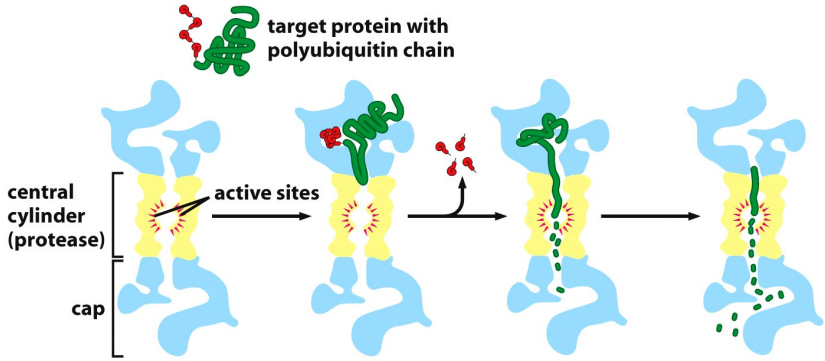


Protein degradation

Proteasomal degradation: main degradation pathway

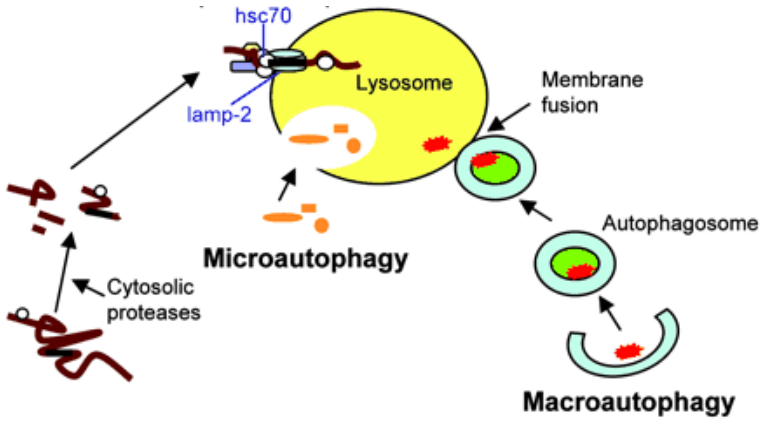
- Decay of proteins with K48 – linked polyubiquitination at lysine side chain or N-terminus
- Proteasome:

- ATP-dependent protease complex
- Barrel-like structure of 4 rings
- 19S subunit: recognition of ubiquitin chain and protein with ATPases
- 20S subunit: contains 3 different catalytic centers for decay of target proteins



Lysosomal degradation:

- Degradation of lipids, nucleic acids, sugar, proteins
- Protein uptake by micro- or macroautophagy or by LAMP2 (*lysosomal associated membrane protein*) after unfolding by HSP70
- Hydrolysis of proteins by cathepsins

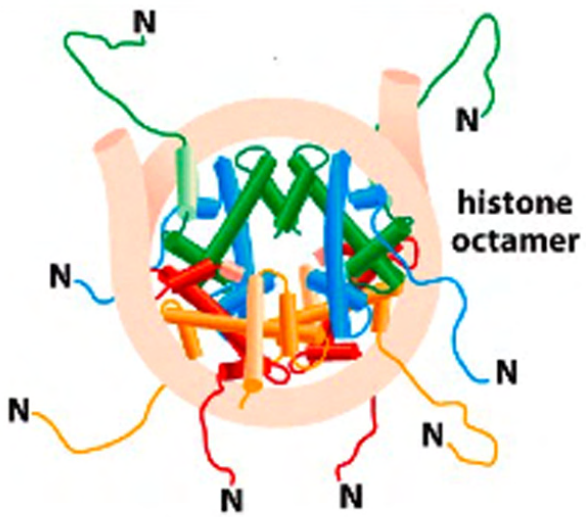


Prescript of the lecture "Molecular Cell Biology"

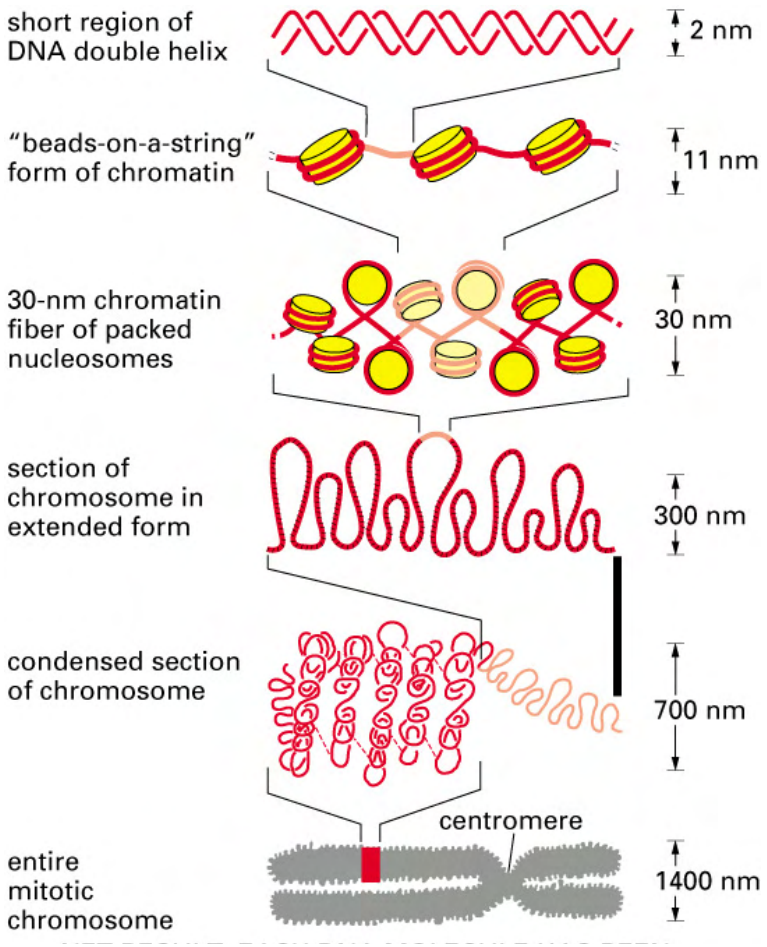
Lecture 3
The cell Nucleus

Structure and Function

Structure of Chromatin

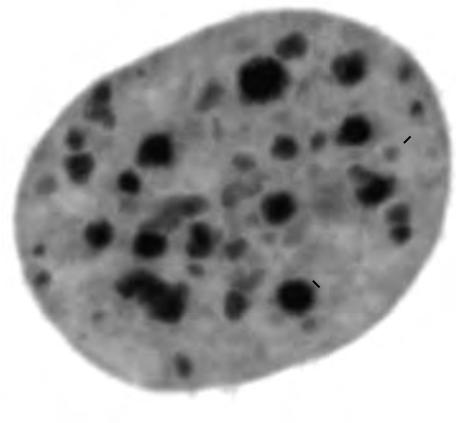


- Nucleosome structure:
  - Octamer core nucleosome + 146 bp of DNA double helix = 1 nucleosome
  - Octamer consists of two of the following core histones: H2A, H2B, H3 and H4
  - 146 bp of DNA double helix wrapped in 1.65 turns around nucleosome
  - N-terminal parts of core histones protrude from nucleosome
  - posttranslational modifications at N-termini: epigenetic marking of chromatin

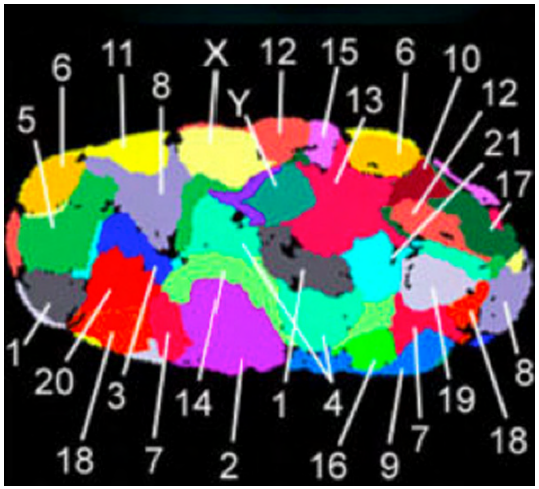


- Distinct condensation steps result in chromatin of different packaging density

Basic organization of chromatin within the cell nucleus

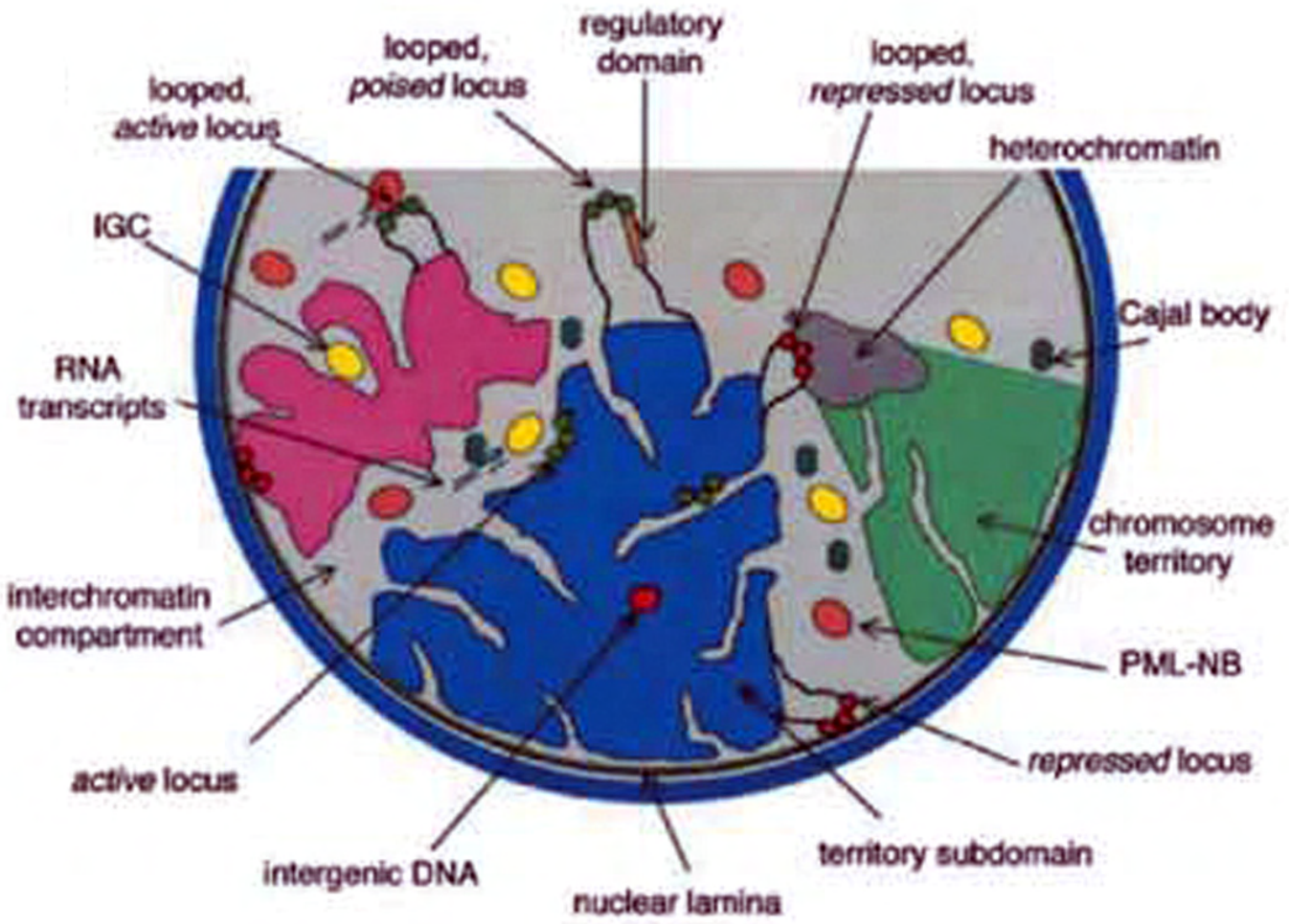


- Euchromatin: loosely packed, transcriptionally active)
- Heterochromatin: densely packed; transcriptionally (mostly) inactive



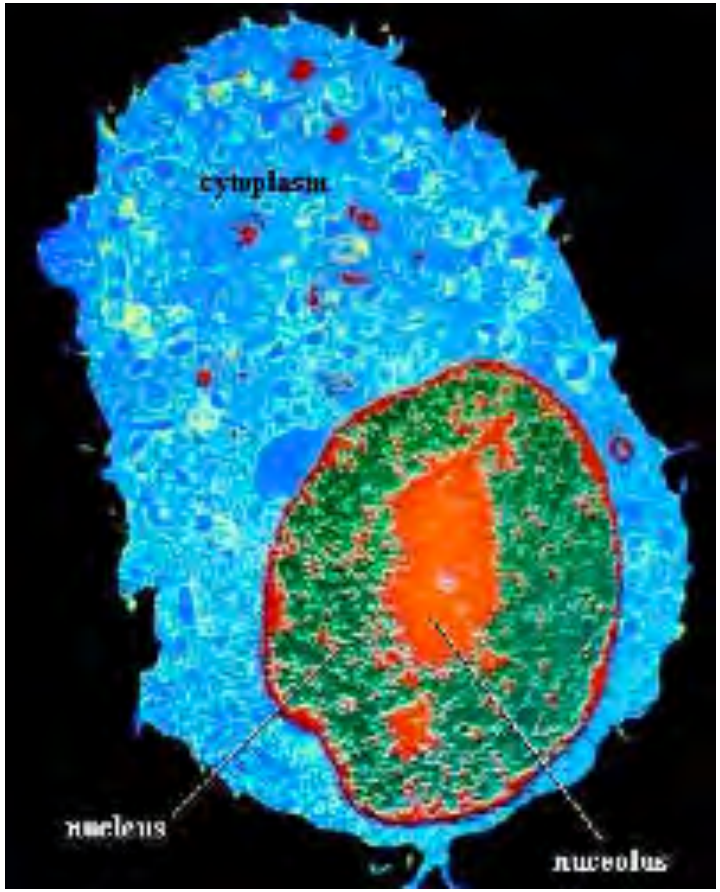
- Chromosome territories visualized by fluorescence *in situ* hybridization (FISH): each chromosome occupies a distinct volume in the nucleus

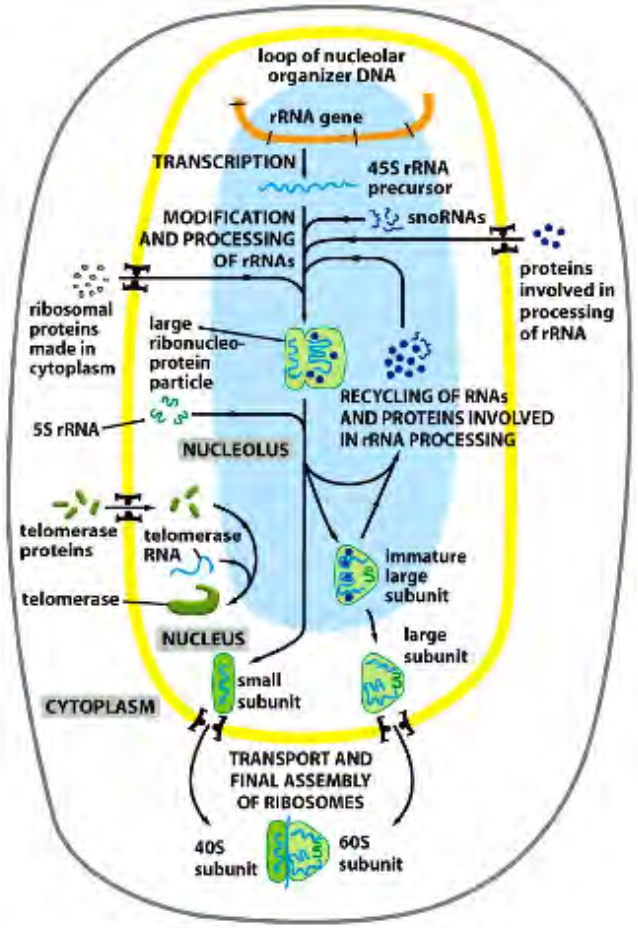
Main substructures in the Nucleus



- The nucleus is compartmentalized with respect to particular functions
- The most prominent substructures include chromosome territories, the interchromatin compartment, the nucleolus, nuclear bodies and the nuclear envelope

Nucleolus





- The nucleolus is the site of ribosome biogenesis (rRNA synthesis; assembly of ribosomal subunits
- The nucleolus assembles at clusters of genes encoding rRNAs

Nuclear envelope

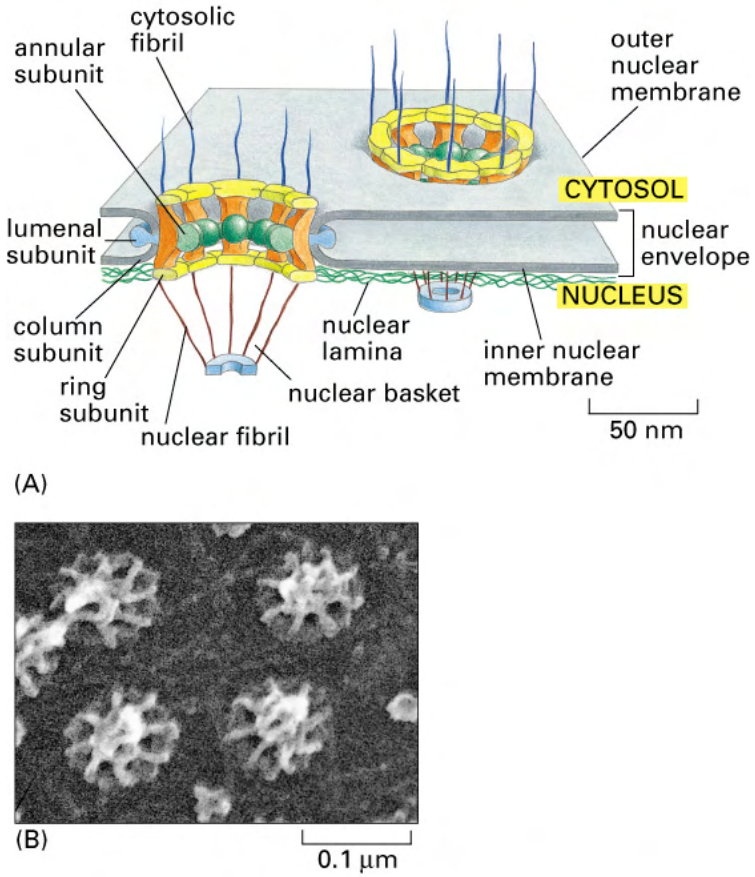
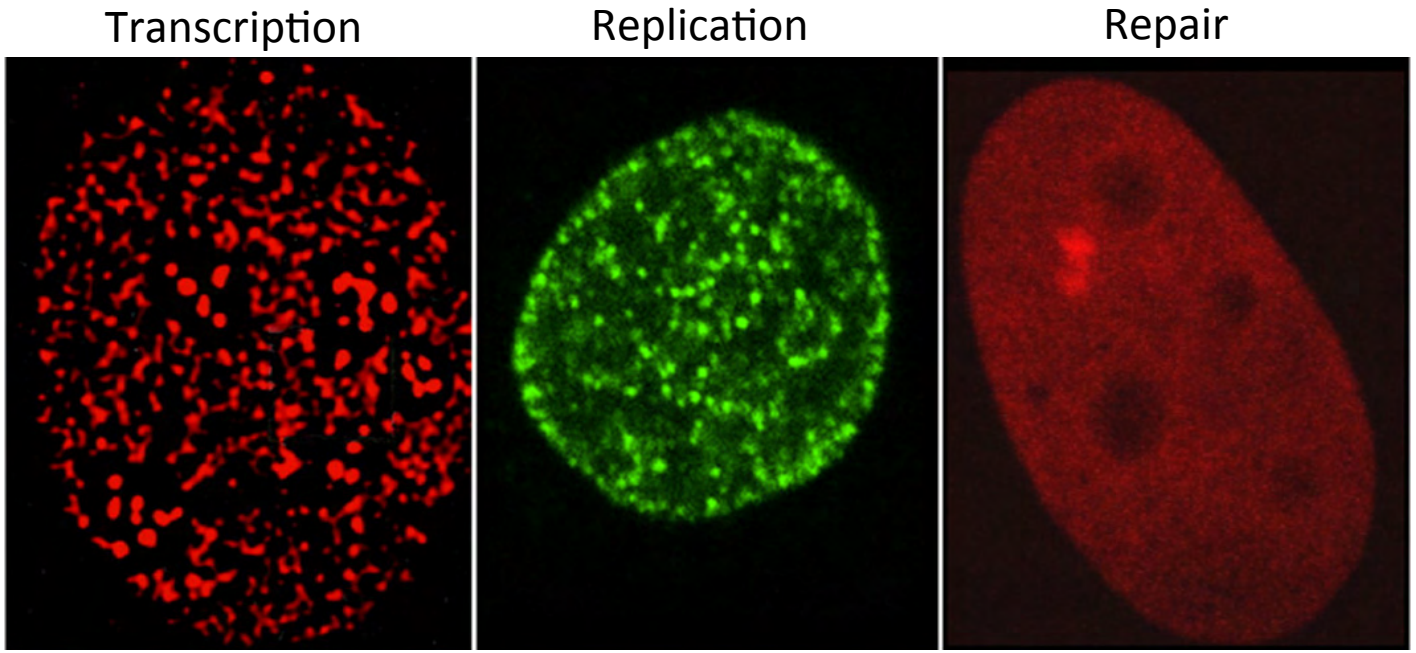


Figure 12–10 part 1 of 2. Molecular Biology of the Cell, 4th Edition.

- The nuclear envelope is a double-membrane layer containing nuclear pores
- Nuclear pores regulate the traffic of biomolecules between the nucleus and the cytoplasm
- The nuclear lamina consists of a stable protein network which supports the nuclear membrane structure

Organization of nuclear function

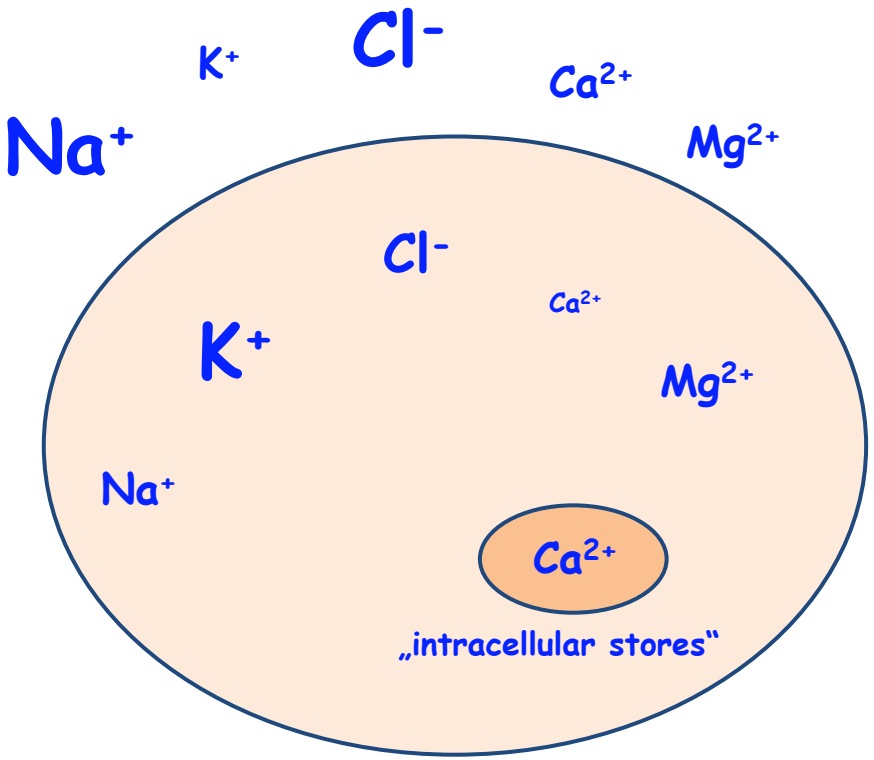


- RNA transcription, DNA replication and DNA repair occur in distinct small foci
- Active foci („factories“) contain all factors required for efficient transcription, replication or repair, respectively
- Most mRNA maturation steps (capping, splicing, polyadenylation, etc.) occur co-transcriptionally)

Lecture 4

Cellular Ca^{2+} homeostasis

Distribution of important ions



All major **ions are unevenly distributed** between cytosol and extracellular space

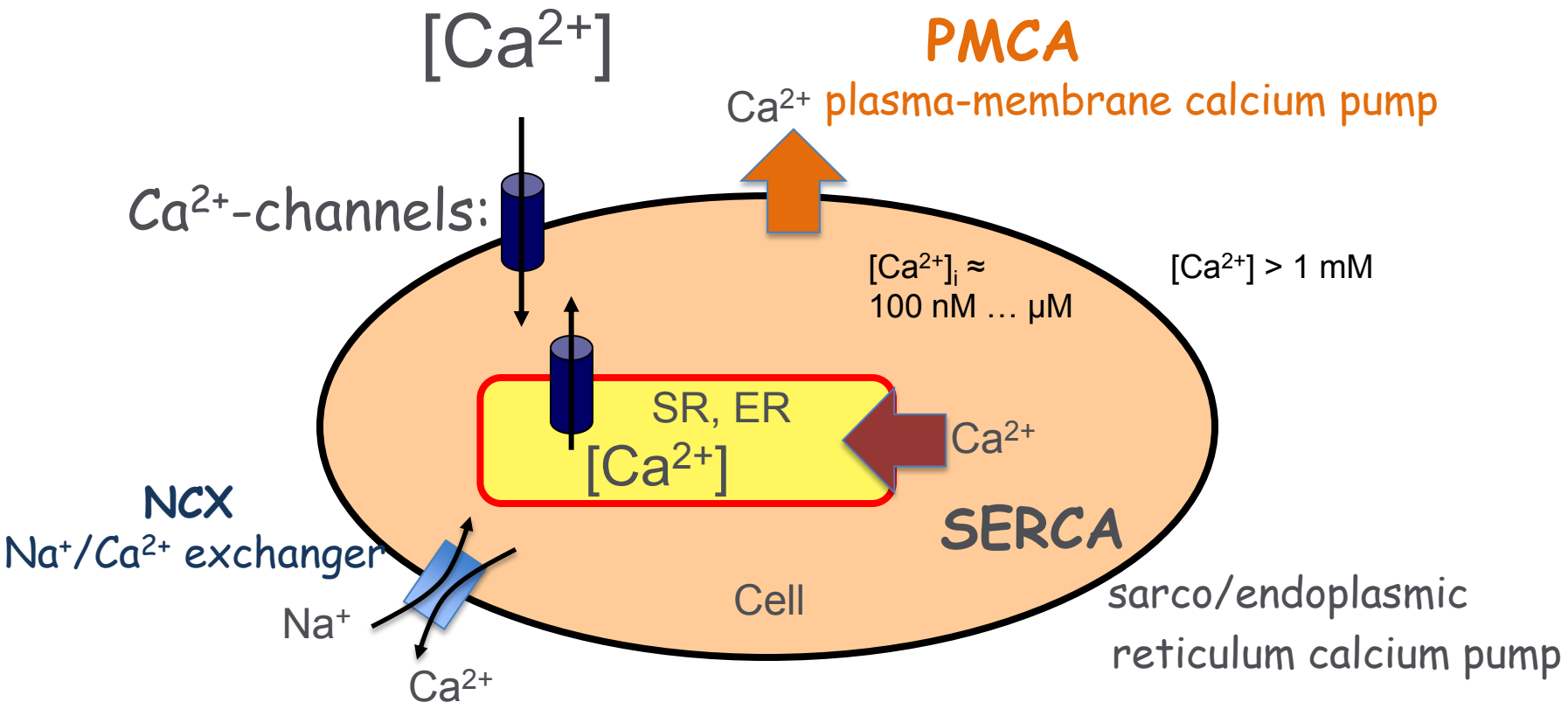
The concentrations of free ions differ between cell types, the "generic cell" has these approximate concentrations:

Ion	intracellular	extracellular
Na^+	15 mM	145 mM
K^+	120 mM	4.5 mM
Ca^{2+}	**100 nM**	1.5 mM
Mg^{2+}	0.5 mM	1.5 mM
Cl^-	20 mM	116 mM

All living cells spend ATP to generate and maintain the concentration gradients

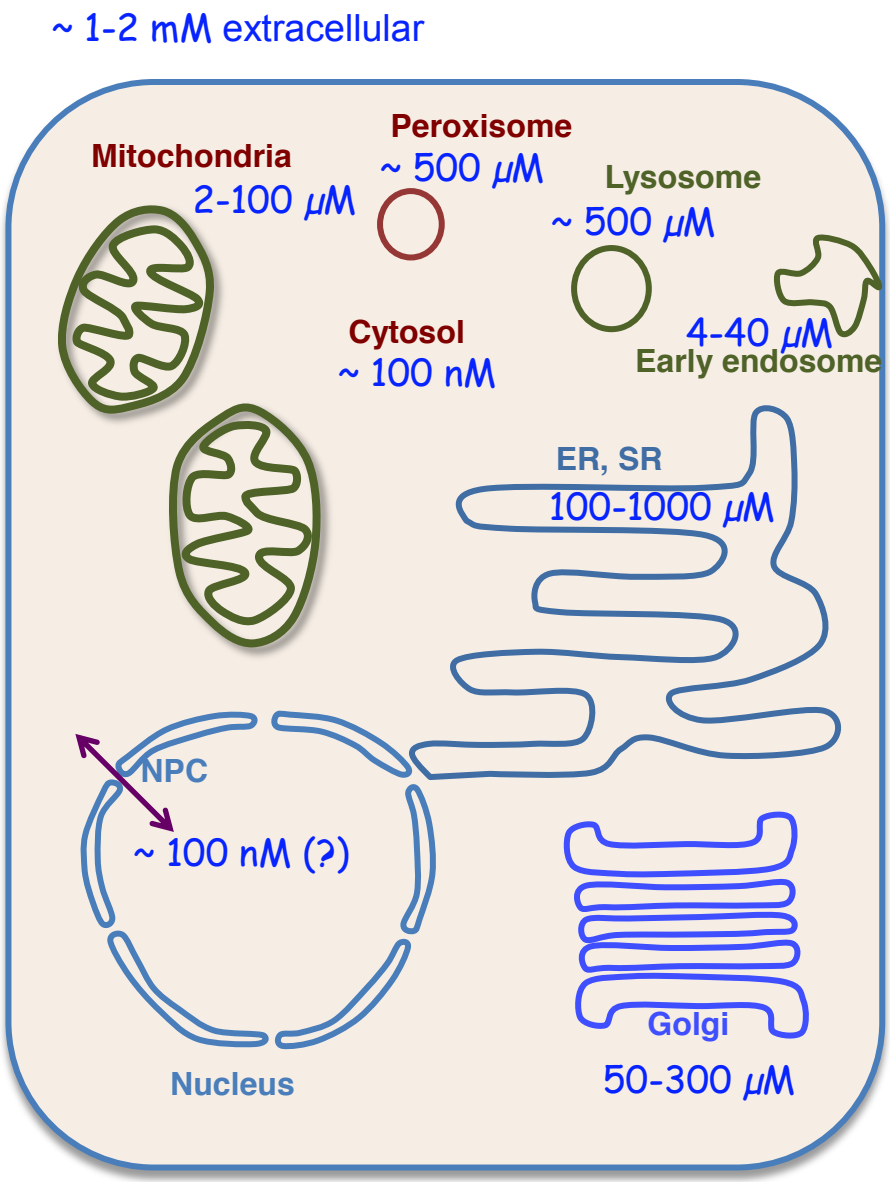
Ion transport proteins can be nonselective or highly selective for specific ions

Cellular Ca^{2+} homeostasis: pumps, exchangers, channels



- **ATP-driven pumps** in the plasma membrane and in the ER membrane are responsible for a low resting calcium concentration (100 nM) in most cells.
- **Na^+/Ca^{2+} exchangers** in the plasma membrane confer mass extrusion of Ca^{2+}, but have lower affinity than the pumps
- **Calcium channels** in plasma membrane and ER membrane can cause rapid increases of intracellular Ca^{2+} (1 – 10 μM).

Ca^{2+} concentrations in the cell



Internal stores

Most organelles have higher [Ca^{2+}] than the cytosol

But: all concentrations should be taken with care. Technical difficulties:

- free Ca^{2+} versus complexed Ca^{2+}
- sensors can affect the amplitude
- rapid changes occur in living cells
- "microdomains" versus whole lumen

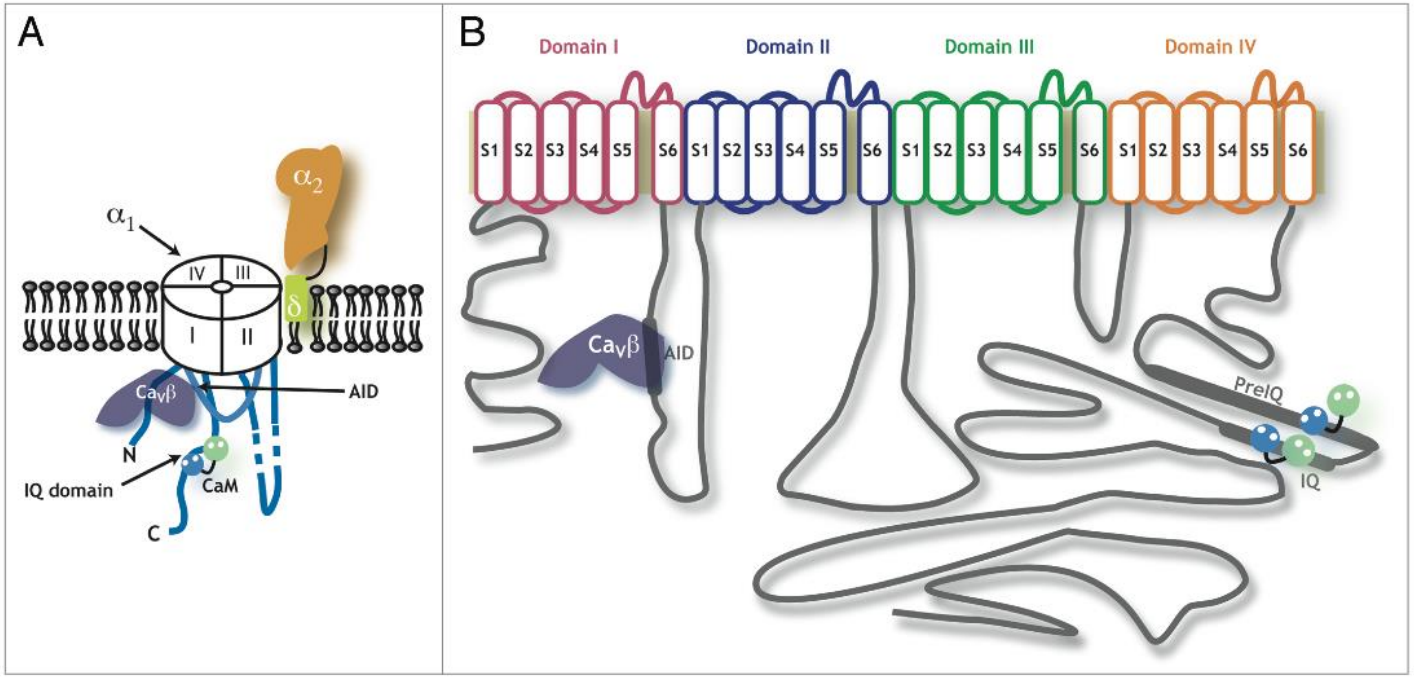
Endoplasmic reticulum:

the most important Ca^{2+} store with the highest concentrations

Nucleus:

connected to cytosol via nuclear pore complexes. Temporal elevation of nuclear [Ca^{2+}] possible

Voltage-gated calcium channels (Ca_v)



Voltage-gated cation channels can have specificities for K^+, Na^+ or Ca^{2+}.

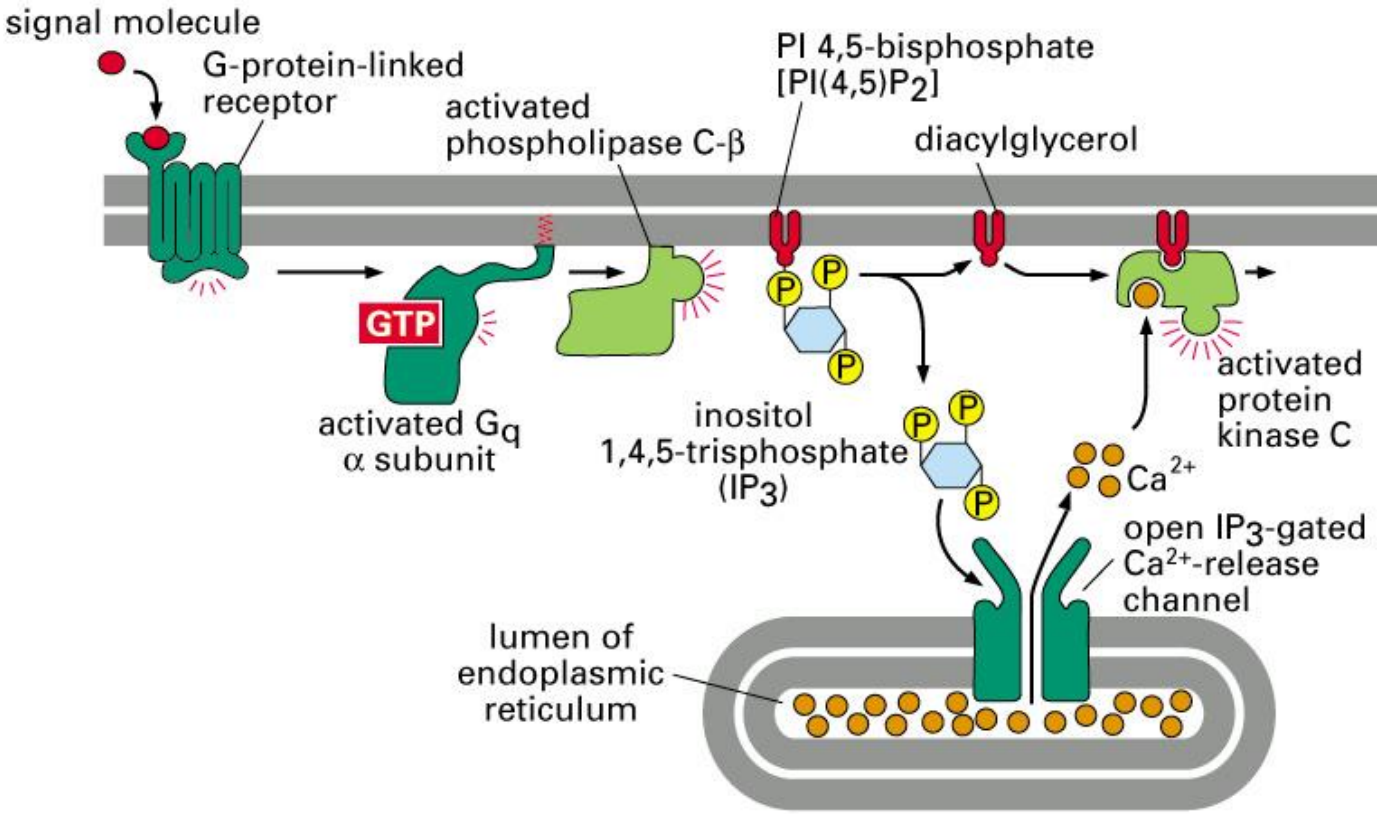
All channels of this type share **tetrameric symmetry** around a central pore.

In K^+ channels, four subunits assemble to form the functional channel unit.

In Na^+ and Ca^{2+}channels, the four "subunits" are **four domains** of one large protein.

Ca_V channels open upon membrane depolarization. The positively-charged S4 segments in each domain act as **voltage sensors.**

Ca^{2+} as classic second messenger



Two branches of the inositol phospholipid pathway

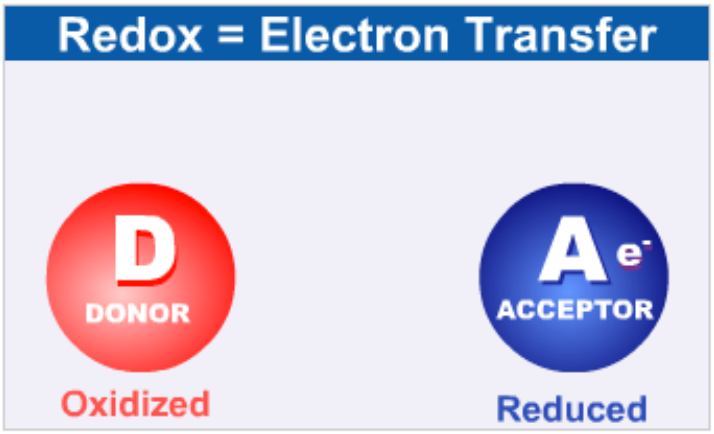
GPCR-triggered activation of phospholipase C results in two second messengers: **IP_3** (soluble) and **DAG** (membrane-delimited)

IP_3 causes Ca^{2+} release from the ER. Some downstream effectors can bind Ca^{2+} directly, others use Ca^{2+} sensor proteins like **calmodulin (CaM)**.

Lecture 5

Cellular redox homeostasis

Basics: redox reactions



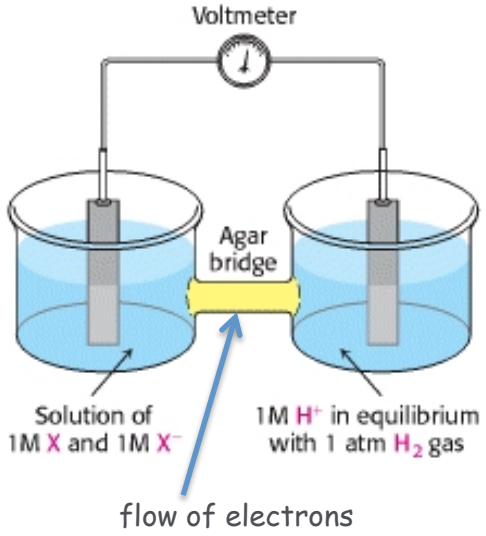
Electron transfer reactions have central importance in biology.

Loss of electrons by one chemical (**oxidation**) is coupled to the gain of electrons by another (**reduction**). The **reduction (redox) potential** describes the tendency to acquire electrons and thereby to be reduced.

Measured reduction potentials are normalized to H_2. A negative reduction potential means the oxidized form of a species has a lower affinity for e^- than H_2.

Strong **oxidants** (O_2) have positive potentials, strong **reductants** (NADH) have negative potentials.

Measurement of the redox potential



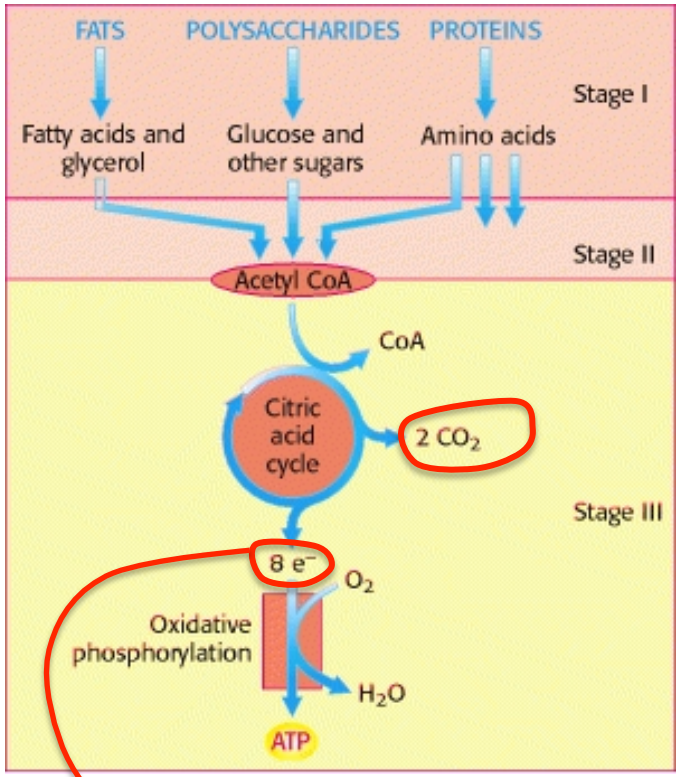
Basics: redox reactions

Oxidant	Reductant	*n*	E'_0 (V)
Succinate + CO_2	α-Ketoglutarate	2	- 0.67
Acetate	Acetaldehyde	2	- 0.60
Ferredoxin (oxidized)	Ferredoxin (reduced)	1	- 0.43
2 H^+	H_2	2	- 0.42
NAD^+	NADH + H^+	2	- 0.32
$NADP^+$	NADPH + H^+	2	- 0.32
Lipoate (oxidized)	Lipoate (reduced)	2	- 0.29
Glutathione (oxidized)	Glutathione (reduced)	2	- 0.23
FAD	$FADH_2$	2	- 0.22
Acetaldehyde	Ethanol	2	- 0.20
Pyruvate	Lactate	2	- 0.19
Fumarate	Succinate	2	0.03
Cytochrome *b* (+3)	Cytochrome *b* (+2)	1	0.07
Dehydroascorbate	Ascorbate	2	0.08
Ubiquinone (oxidized)	Ubiquinone (reduced)	2	0.10
Cytochrome *c* (+3)	Cytochrome *c* (+2)	1	0.22
Fe (+3)	Fe (+2)	1	0.77
½ O_2 + 2 H^+	H_2O	2	0.82

Important standard reduction potentials

E'_0 is the standard reduction potential at pH 7, 25°C; n is the number of transferred electrons.

Basics: Key aspects of human metabolism



In the human body, energy is generated from the **oxidation of food** with CO_2 as end product.

Under aerobic conditions, the final stage of oxidation is the **citric acid cycle**, regardless of the type of food.
Each molecule of acetyl CoA yields 4 pairs of electrons, 3 packed on NAD^+, 1 on FAD.

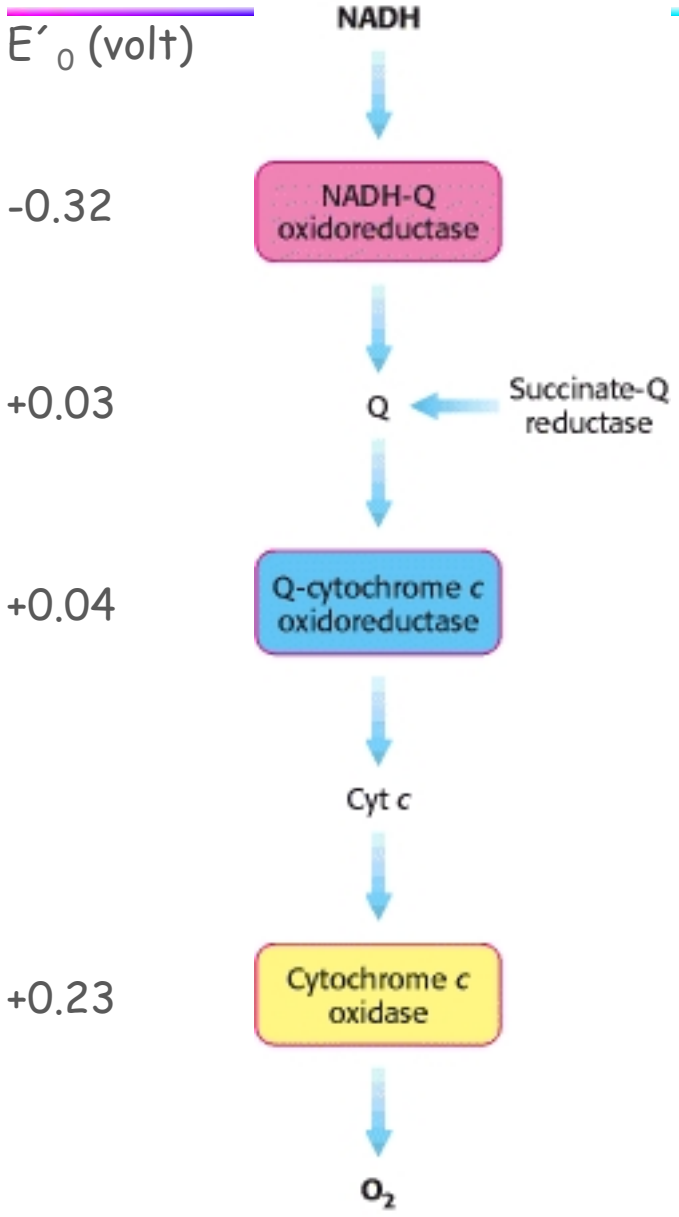
The electrons can be used for **ATP production** (oxidative phosphorylation) or for **anabolic pathways** (reductive biosynthesis).

➔ **The cytosol is a reducing environment**

FAD ➔ $FADH_2$
NAD^+ ➔ NADH + H^+

$NADP^+$ ➔ NADPH + H^+ ➔ biosynthesis

Basics: Electron transfer in the respiratory chain



In the **mitochondrial respiratory chain** electrons are transferred from NADH to oxygen.

The chain consists of four complexes. Electron transfer in NADH-Q reductase, Q-cytochrome c reductase and Cytochrome c oxidase is linked to the **pumping of protons** across the inner mitochondrial membrane (IMM).

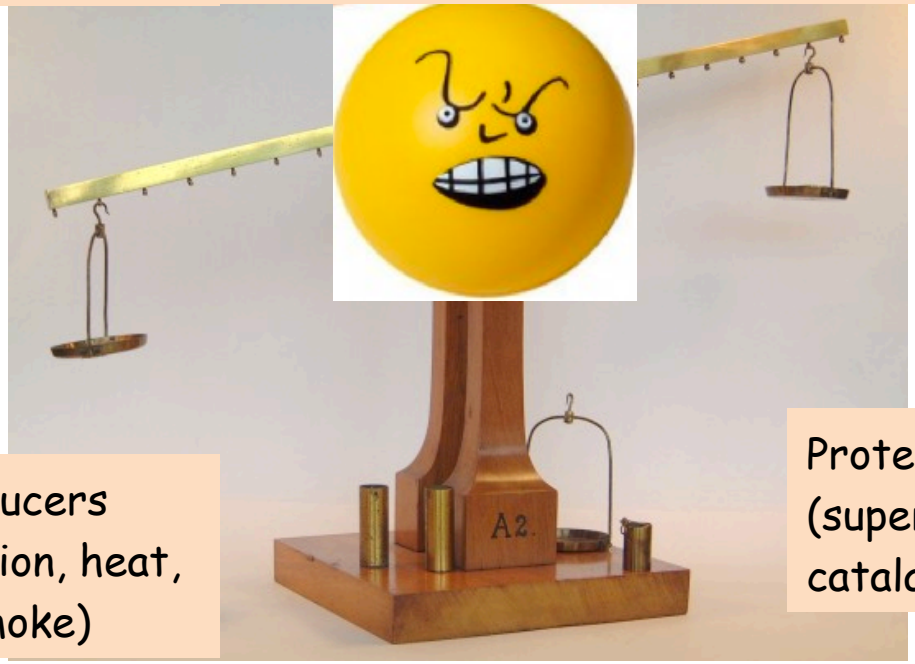
The normal function of the chain always generates a small percentage of partial oxidation product: **$^{\cdot}O_2^-$ the superoxide anion** (estimates: 0.1% - 5 % side product). Superoxide is a **reactive oxygen species (ROS).**

Basics: Oxidative stress

Oxidative stress is the imbalance between ROS production and the ability to detoxify the reactive intermediates and end products.

Endogenous ROS production

Buffer systems (glutathione, thioredoxin)



Exogenous ROS inducers (UV, ionizing radiation, heat, ozone, cigarette smoke)

Protective enzymes (superoxide dismutase, catalase)

Lecture 6

Cellular Shape

Movement of and within cells

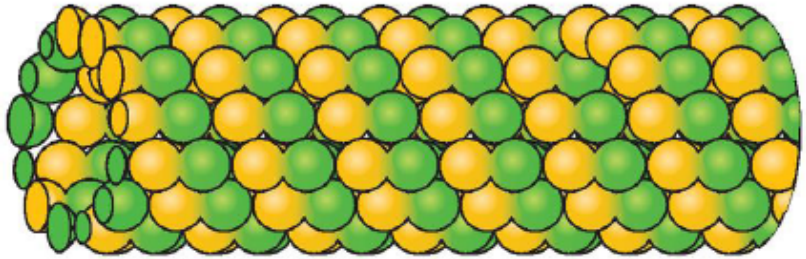
The cytoskeleton: 3 types of filaments

All mechanical and dynamic properties, as well as three-dimensional organization of cells based on a filamentous system = cytoskeleton.
It is build of 3 different filament types: actin, microtubules and intermediate filaments.

Actin forms static and mobile structures in the cell that determine cell shape.

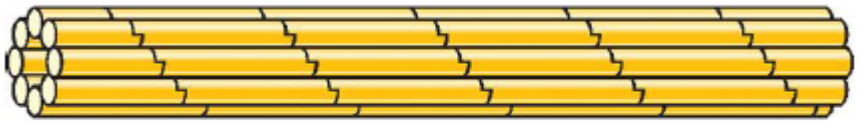
Actin filament Ø ~ 7 nm

Tubulin forms major „highways" within the cell along which organelles / chromosomes may move.



Mikrotubule Ø ~ 25 nm

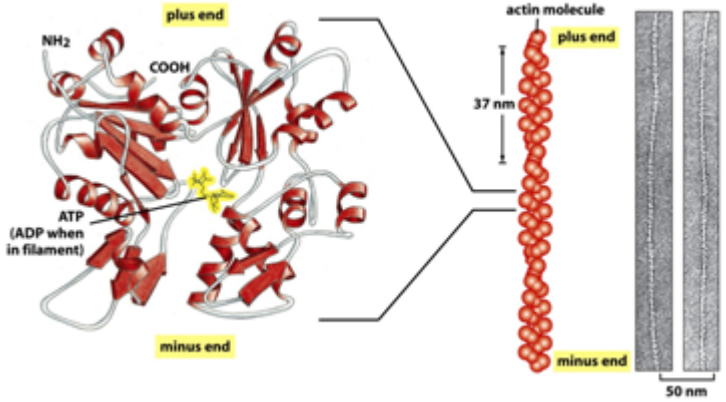
Intermediate filaments stabilize large cellular structures such as nuclei (lamin, in all cells) or cell-specifically as e.g. neurofilaments in axons.

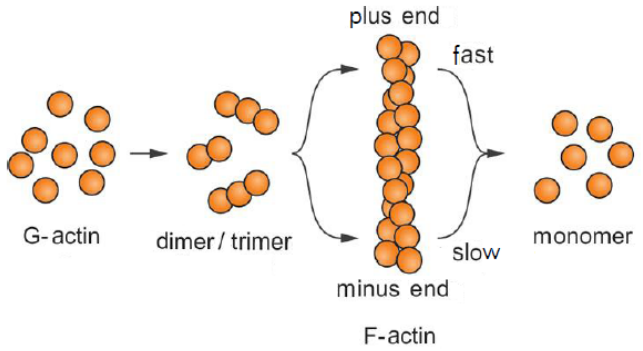


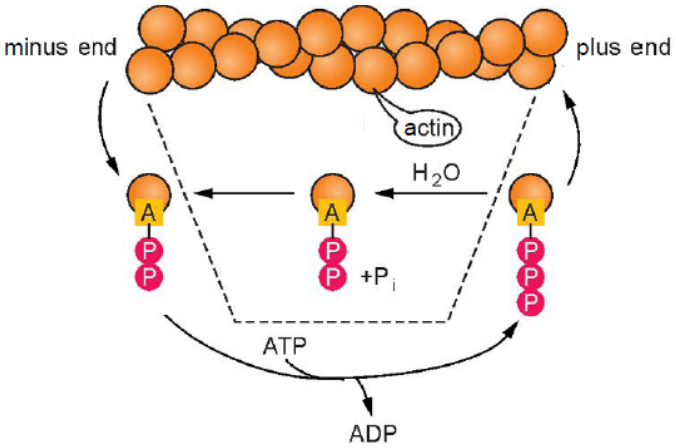
Intermediate filament Ø ~ 10 nm

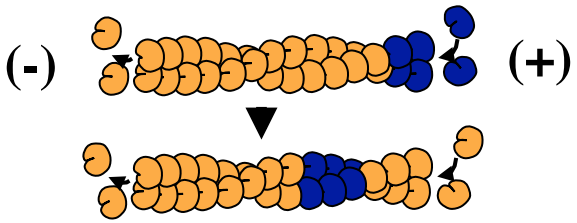
Actin structure and dynamics

- Globular monomers = G-actin
- ATP/ADP binding site
- ATP/ADP bound monomer can polymerize and build spontaneously and reversibly dimers and trimers
  →formation of filamentous F-actin
- Arrangement of monomers in a way that it looks like two twisted chains









<u>Treadmilling</u>**:**

- Dynamic organization of actin filaments because of different association and dissociation velocity at plus and minus end
- Plus end: fast association and slow dissociation of ATP-bound form = assembly
- Filament: hydrolysis of ATP to ADP
- Minus end: fast dissociation and slow association of ADP-bound form = disassembly

Actin regulators

Monomer binding proteins:

- promote or prohibit filament association
- E.g. profilin accelerates elongation
- E.g. thymosin bound monomers cannot incorporate

Filament binding proteins:

- Cofillin: promotes depolymerization
- Gelsolin, Serverin: severing actin filaments and leading to breakage
- CapZ, Villin: binding of filament ends and prevention of further polymerization and disassembly

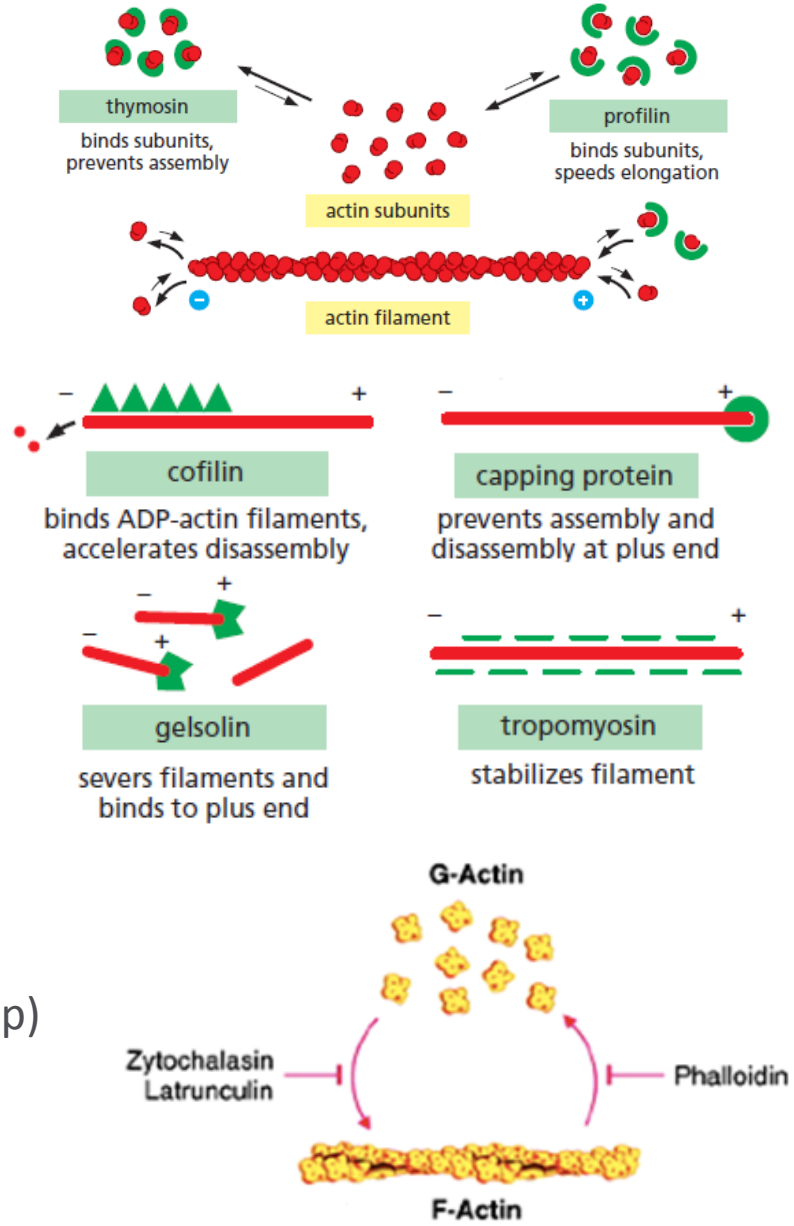
Fungal metabolites:

- Cytochalasin: Cell permeable mycotoxin

- Blocks actin filament formation by binding plus end
- Inhibition of cell division and movement

- Phalloidin: Toxin from *Amanita phalloides* (death cap)

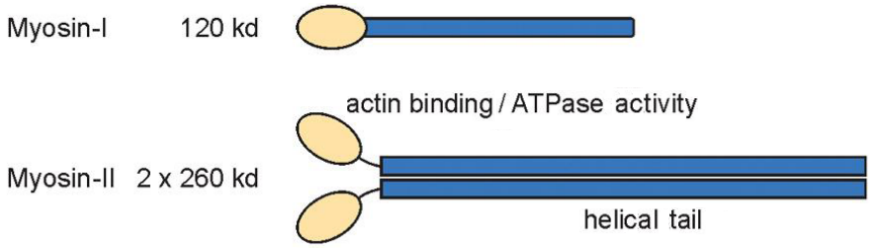
- Binds and stabilizes actin filament
- Blocks filament disassembly
- Inhibition of cell division and movement

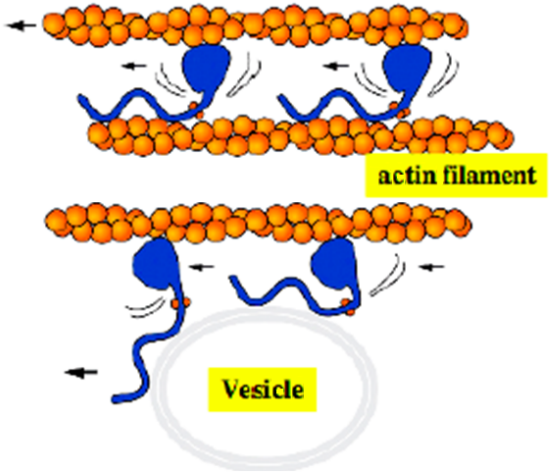


Myosin: Actin binding motor protein

Structure:

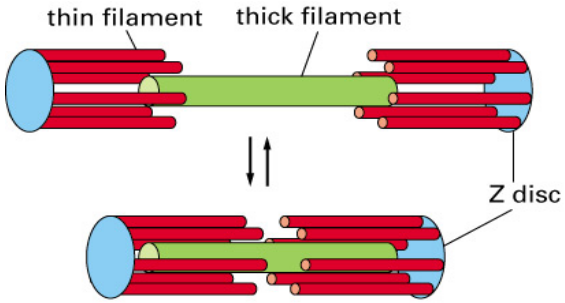
- Myosin I: head and tail domain
- Myosin II: - each two head and tail domains,
  - helical tails as coiled-coil structure
- Head domain binds actin and has ATPase activity
- Moves cargo on actin filaments towards plus end
- Moves actin filaments against each other during muscle contraction

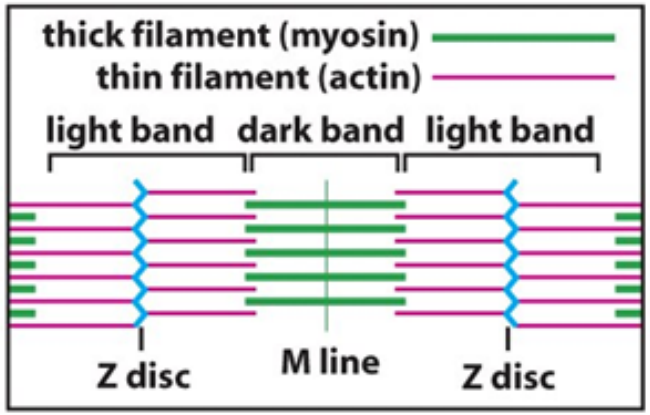


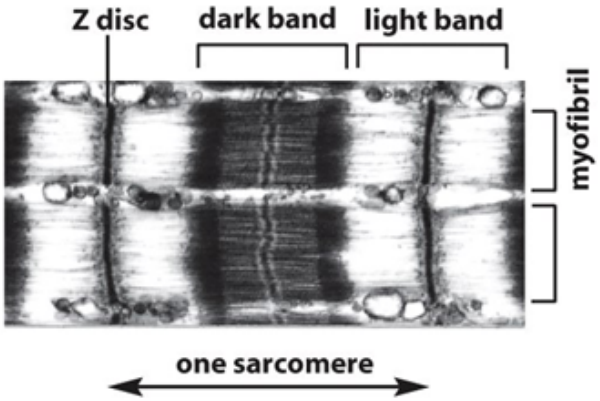


Sarcomere:

- Skeletal muscle fibers consist of sarcomeres
  = segment of muscle fiber between two neighboring Z lines
- Contains myosin (=thick filament) and actin (=thin filament)
- During skeletal muscle contraction sarcomere becomes shorter







Tubulin structure and dynamics

- Microtubules consist of tubulin heterodimers
- Both tubulin subunits have GTP/GDP binding site
- α-tubulin always bound to GTP (no exchange)
- β-tubulin can be bound to GTP or GDP
- Heterodimers form protofilaments by head-to-tail alignment
- 13 protofilaments build microtubule

Dynamic instability:

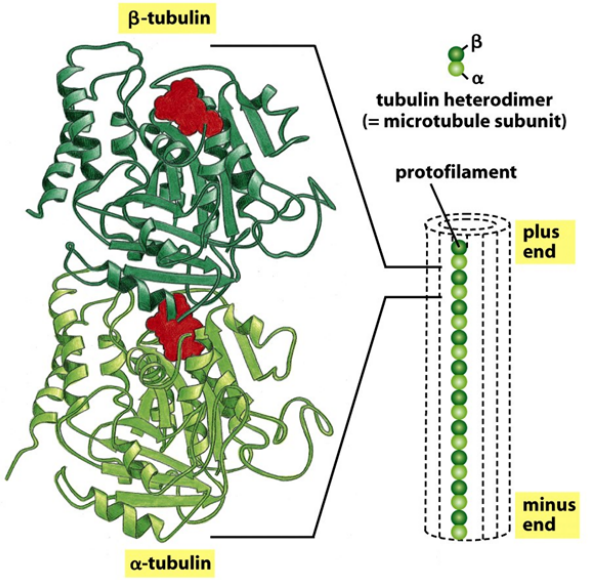
- Minus end:

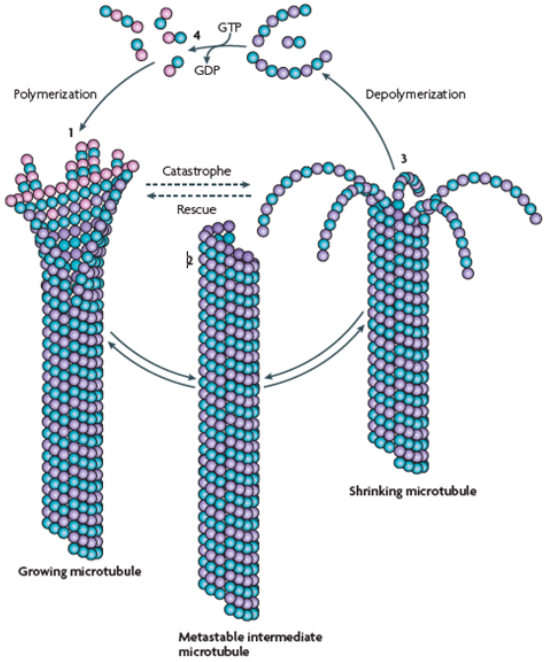
- α-tubulin
- No polymerization or dissociation
- Attached to MTOC (*microtubule organization center*)

- Plus end:

- β-tubulin
- Growing or shrinking
- Directed towards periphery

- GTP bound tubules have high affinity to each other
  → polymerization
- GTP hydrolyses leads to decrease of affinity
  → depolymerization

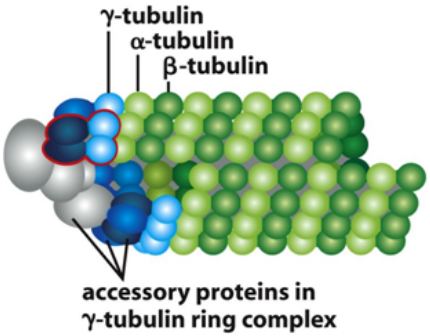


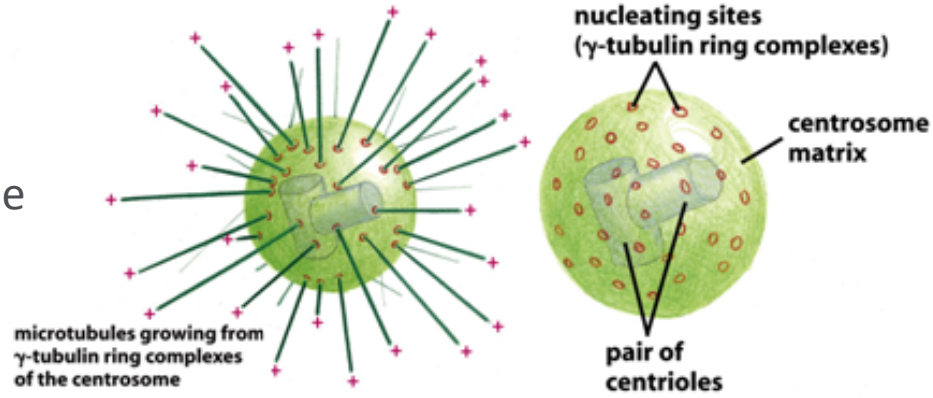


Organization and function of microtubules

Microtubule organization center (MTOC)
= centrosome

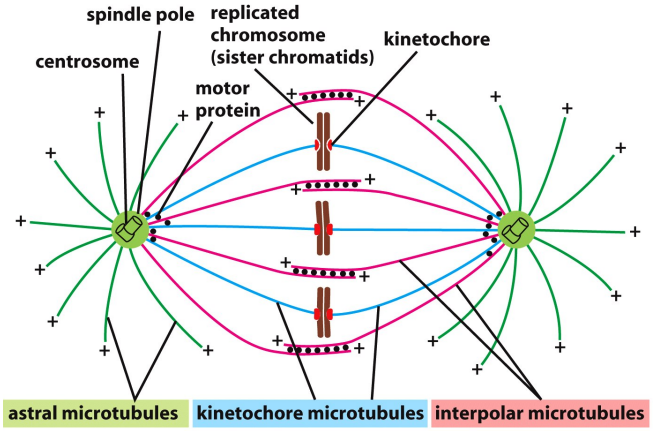
- In animal cells microtubule de novo association induced near nucleus in centrosomes
- Centrosomes contain more than 50 copies of γTuRC (*γ-tubulin ring complex*)
- γTuRC = nucleator of microtubules
- Minus ends bound via γ-tubulin to MTOC
- Plus ends grow astrally towards cell membrane
- Microtubules detect boundaries of the cell
- Centrosome self-arranges in center of cell by pushing of microtubules towards the membrane





Function:

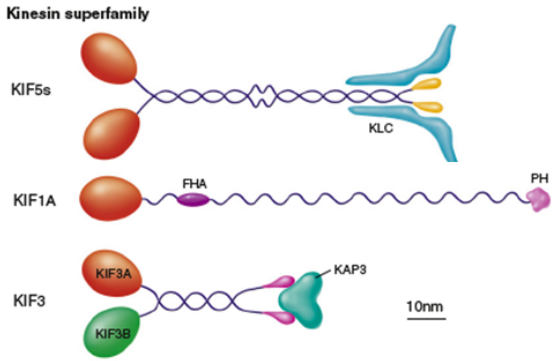
- Positioning of organelles
- Intracellular transport as platform for motor proteins
- Segregation of chromosomes during mitosis



Microtubule binding motor proteins

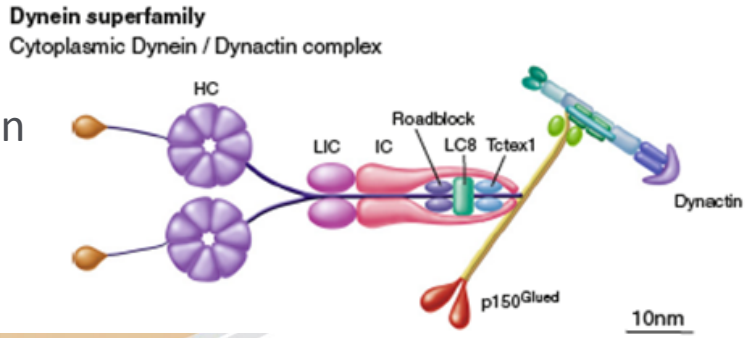
Kinesin:

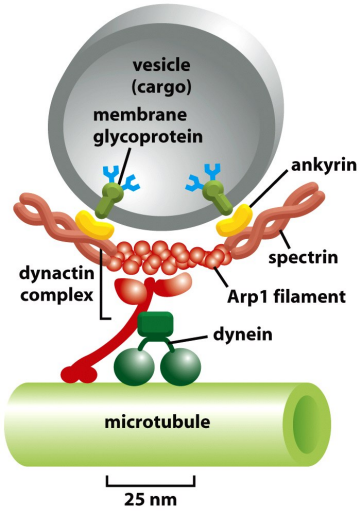
- Large protein family
- Mostly dimers with head, stalk and cargo binding domain
- Head domain = motor domain, binds ATP
- Moves on microtubules towards plus end
- Transport of organelles or vesicles

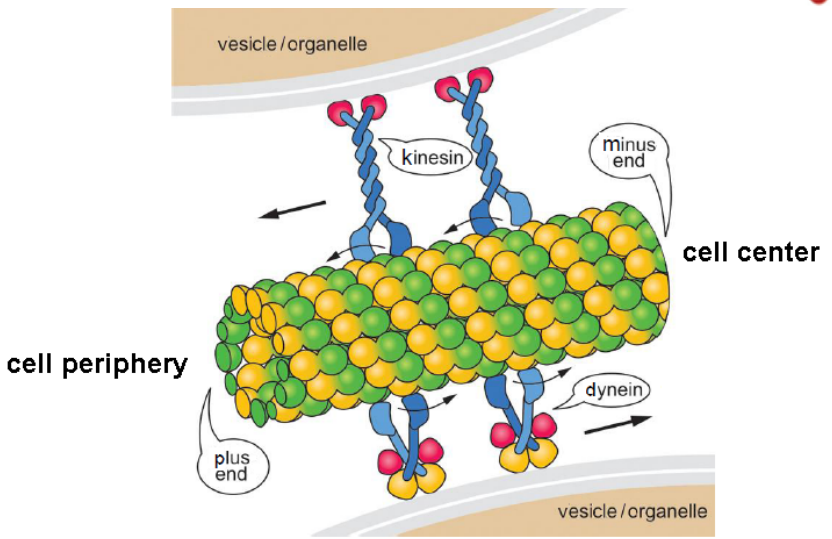


Dynein:

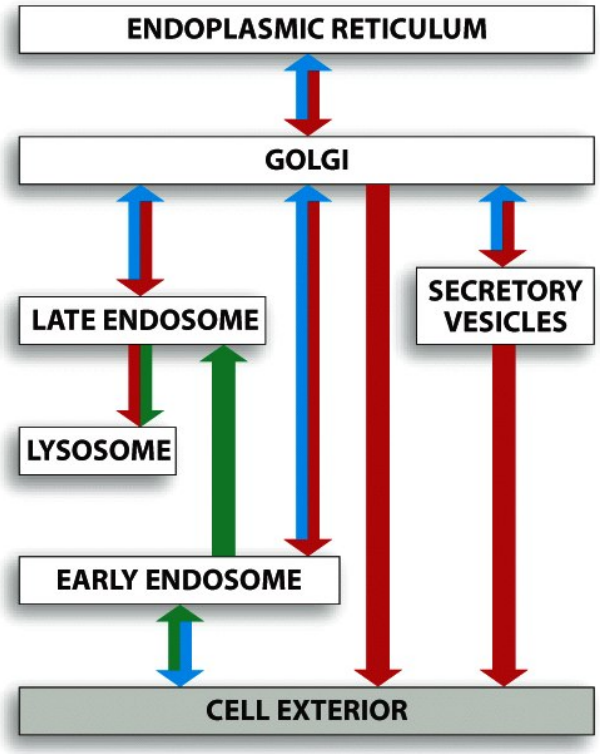
- Function as complex of many proteins including dynactin
- Moves on microtubules towards minus end
- Also binding of ATP
- Also transport of organelles or vesicles







The secretory pathway



Endoplasmic reticulum (ER)

- Cotranslational protein transport (rough ER)
- Vesicle budding for transport to Golgi

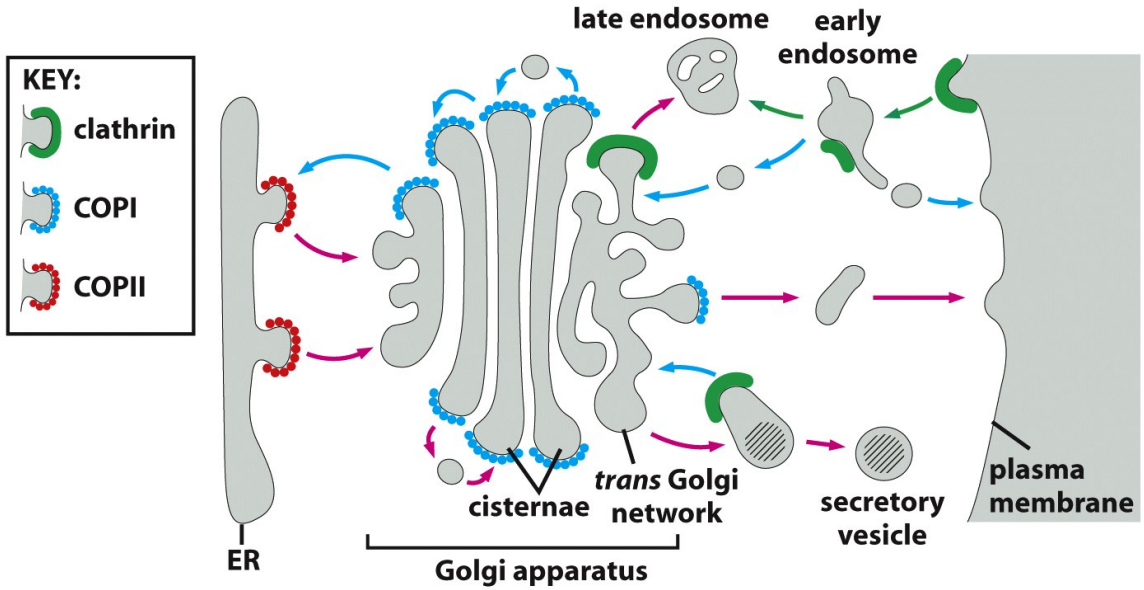
Golgi apparatus:

- Major sorting station for proteins / vesicles in cell
- Cis and trans side
- Glycosylation of proteins

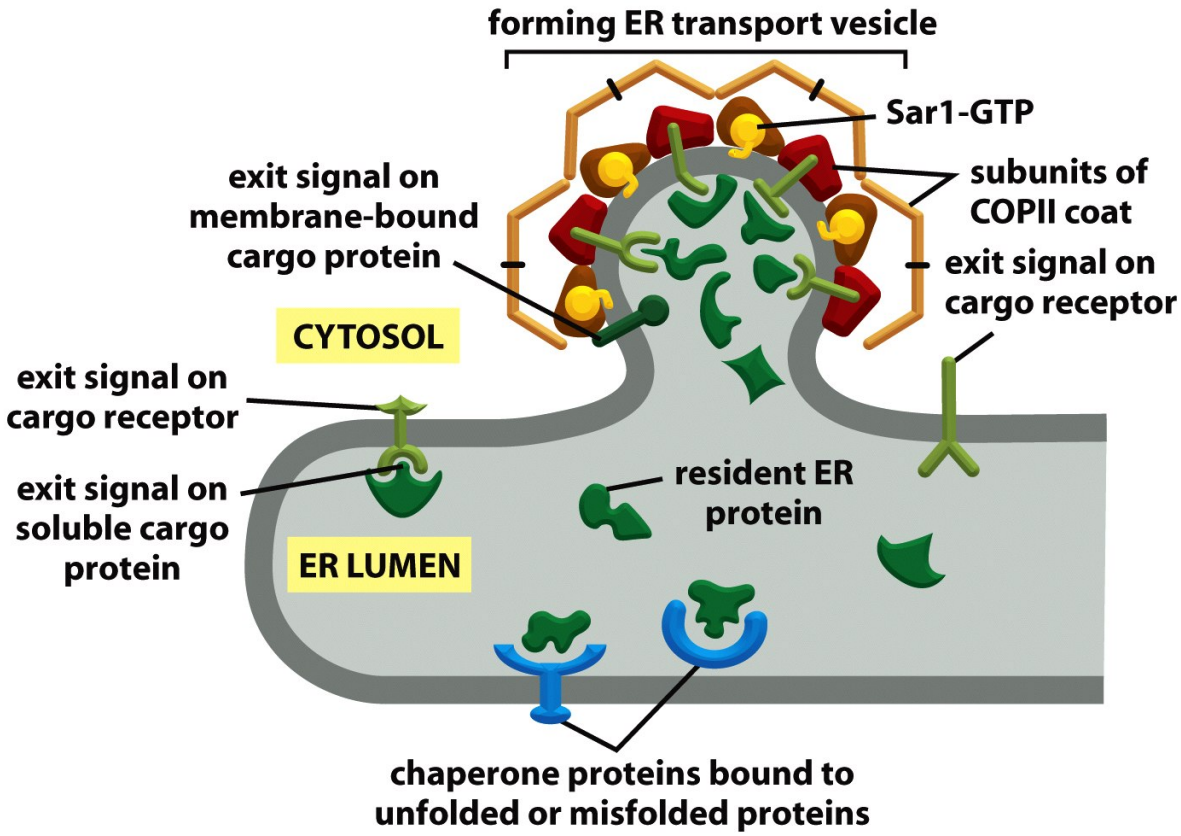
Vesicles:

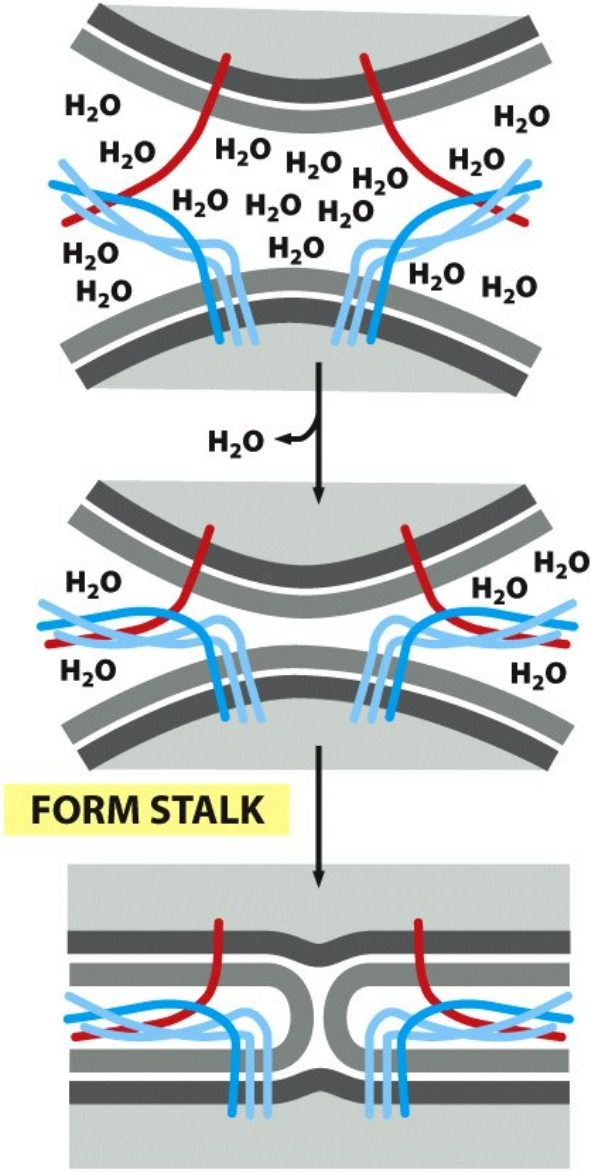
- Move from ER to Golgi, Golgi to plasma membrane and back
- May contain different coat structures / proteins

COP1:
from Golgi to ER/plasma membrane
COP2:
From ER to Golgi
Clathrin:
From Plasma membrane or golgi to endosome / lysosome



Vesicle formation and vesicle fusion





Vesicle formation:

Small GTPase (Sar1 or Arf1) leads to assembly of coat proteins to form vesicle, cargo proteins are enriched by receptors

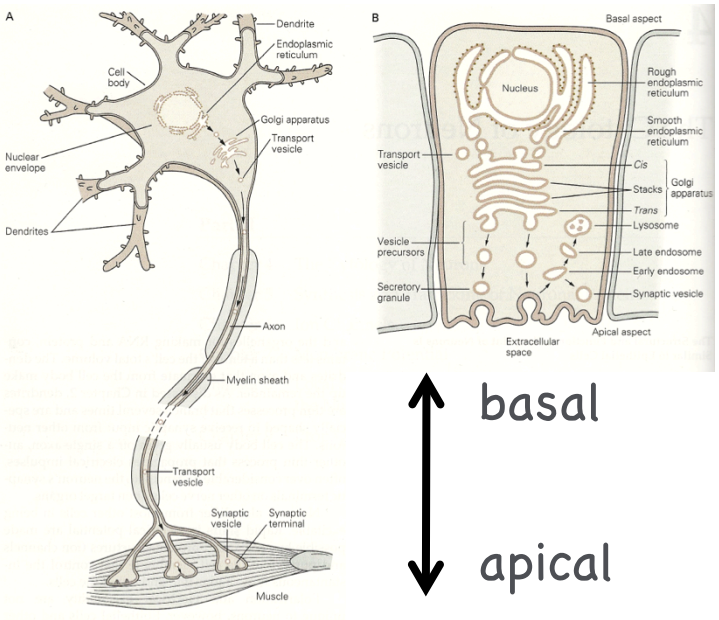
Vesicle fusions:

SNARE proteins on vesicle (v-SNARE) and target membrane (t-SNARE) form coiled coil to pull vesicle together for fusion

Lecture 7
Cell shape II

Cell polarity and attachment

Cell Polarity



basal

apical

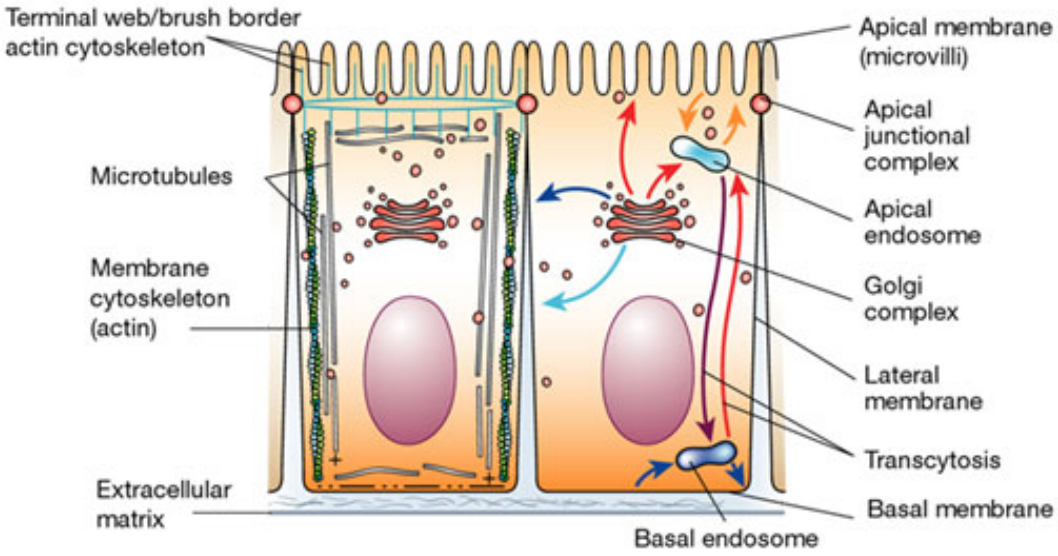
Neurons and epithelial cells (both of ectodermal origin) are polar, i.e. one can clearly differentiate two functionally distinct sides of the cells:

Neurons: Dendrites / Axon

Epithel: basal / apical side

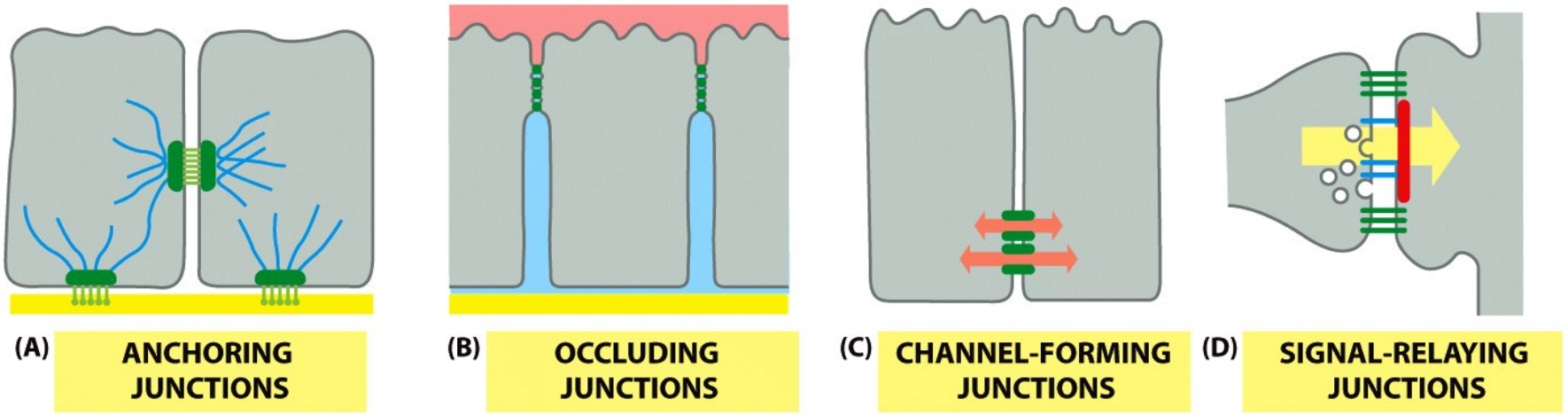
Note that neurobiologists put basal on top and apical on bottom, Cell biologists do it vice versa ☺

Intracellularly, cell polarity requires differential **protein sorting**, involving polar functions of the **cytoskeleton** and **vesicle transport**. Extracellularly, (tight) junctions and specific formations of the **extracellular matrix** (basal membrane) are involved in polarization.



Cell contacts

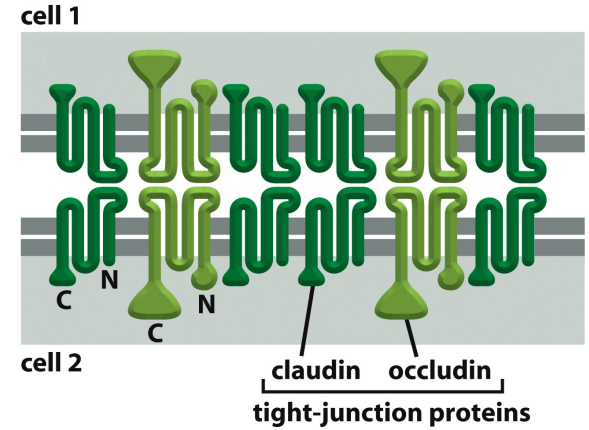
In epithelia, cell contacts may **anchor** the cells to each other or the matrix, or contribute to **tight junctions** between cells to form a barrier. In neurons or excitable cells, **gap junctions** or chemical **synapses** may be formed for communication.

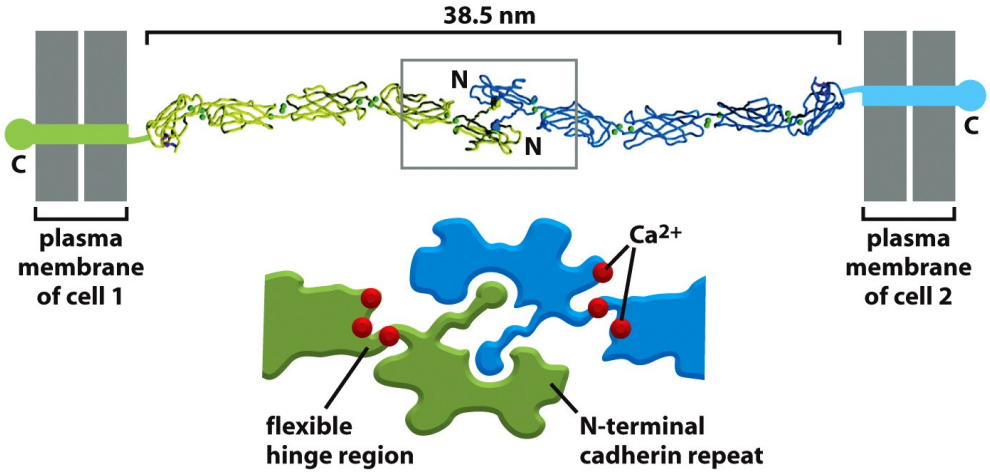


Anchoring junction	Tight junction	Gap junctions	Synapse
Cadherins Adherens junctions, desmosomes **Integrins** Focal adhesions, hemidesmosomes	**Claudin** **Occludin**	6 **Connexins** form Connexon	Vesicle fusion leads to **transmitter** release, which opens **membrane channels**

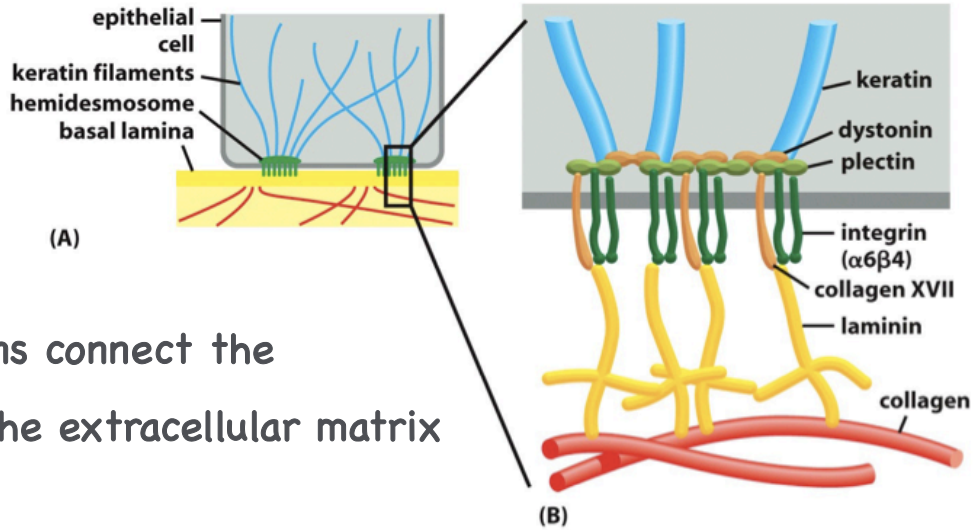
Contact proteins

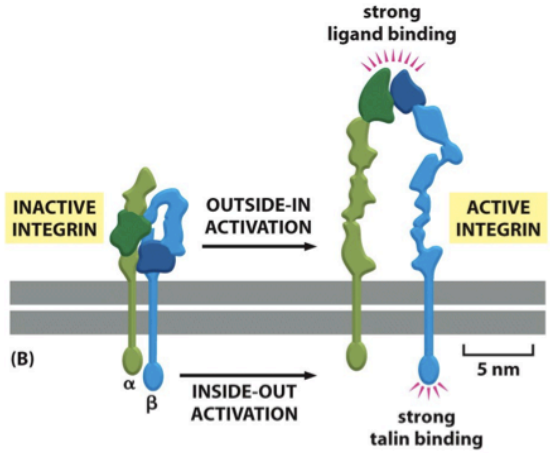
Claudin and occludin connect cells to form an impenetrable tight junction





Cadherins connect cells between each other in a **Calcium** – dependent manner





Activated integrins connect the cytoskeleton to the extracellular matrix

Contact combinations

4 types of anchoring junctions, 1 type with barrier function

Anchor proteins:
- claudin/occludin form tight junctions
- cadherins bind cadherins (other cells)
- integrins bind the extracellular matrix

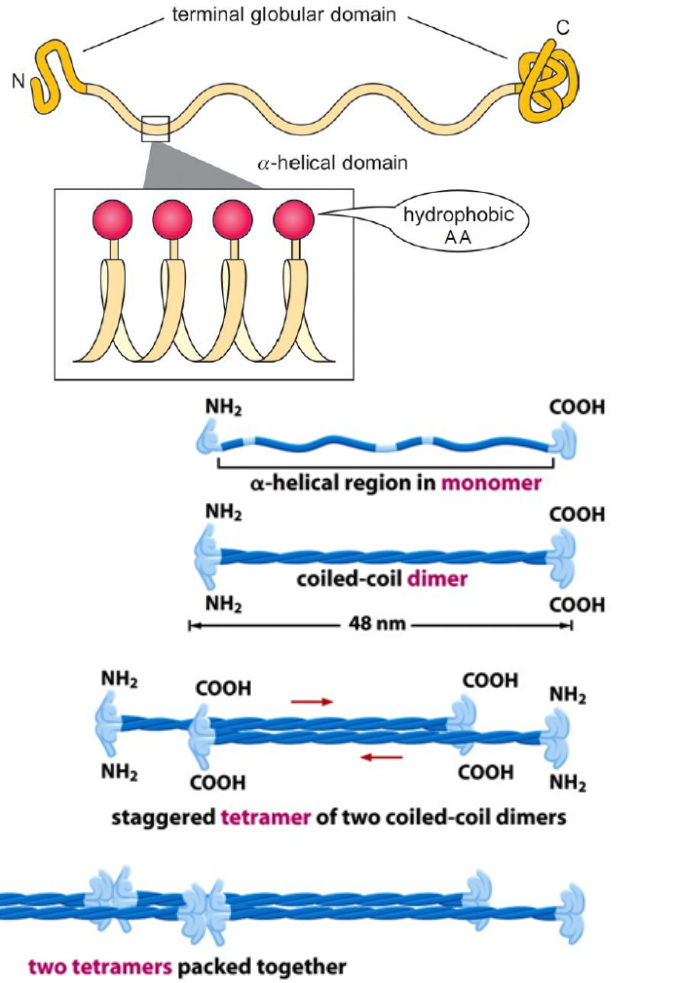
Type of connection	Name	Achor protein	Cytoskeletal protein for intracellular anchoring
between cells	**Tight junctions**	Claudin Occludin	
	Adherens junctions	Cadherins	Actin filaments
	Desmosomes	Cadherins	Intermediate filaments
From cell to matrix	**Focal adhesions**	Integrins	Actin filaments
	Hemidesmosomes	Integrins	Intermediate filaments

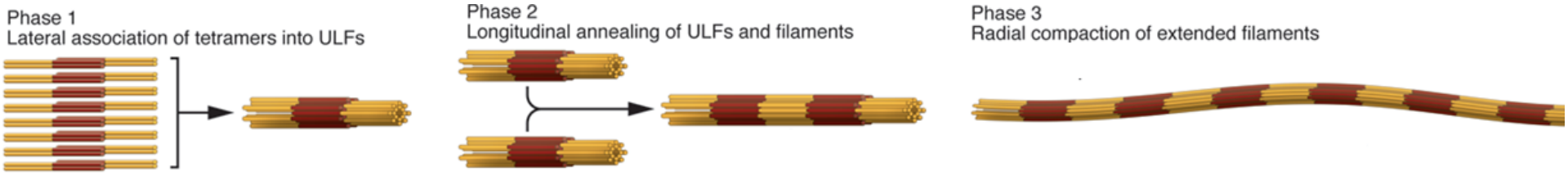
Intermediate filaments

- Ropelike fibers with diameter of around 10 nm
- Large and heterogeneous protein family

Structure:

- Monomer: linear molecules with central α-helical domain and terminal globular domains
- In α-helix each fourth AA has hydrophobic side chain
- Two monomers build coiled-coil dimer by hydrophobic interaction
- Dimers associate antiparallel staggered to tetramers
- Tetramers associate into ULFs (*unit length filaments*)
- Longitudinally annealing at first to short and then to long filaments
- Radial compaction into mature extended filaments

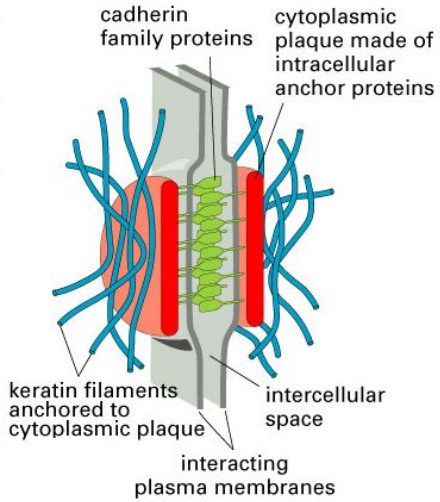




Anchoring of intermediate filaments

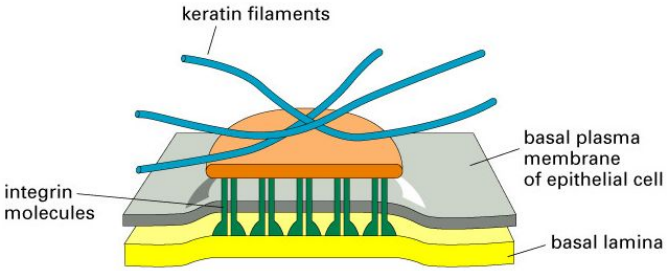
Desmosome:

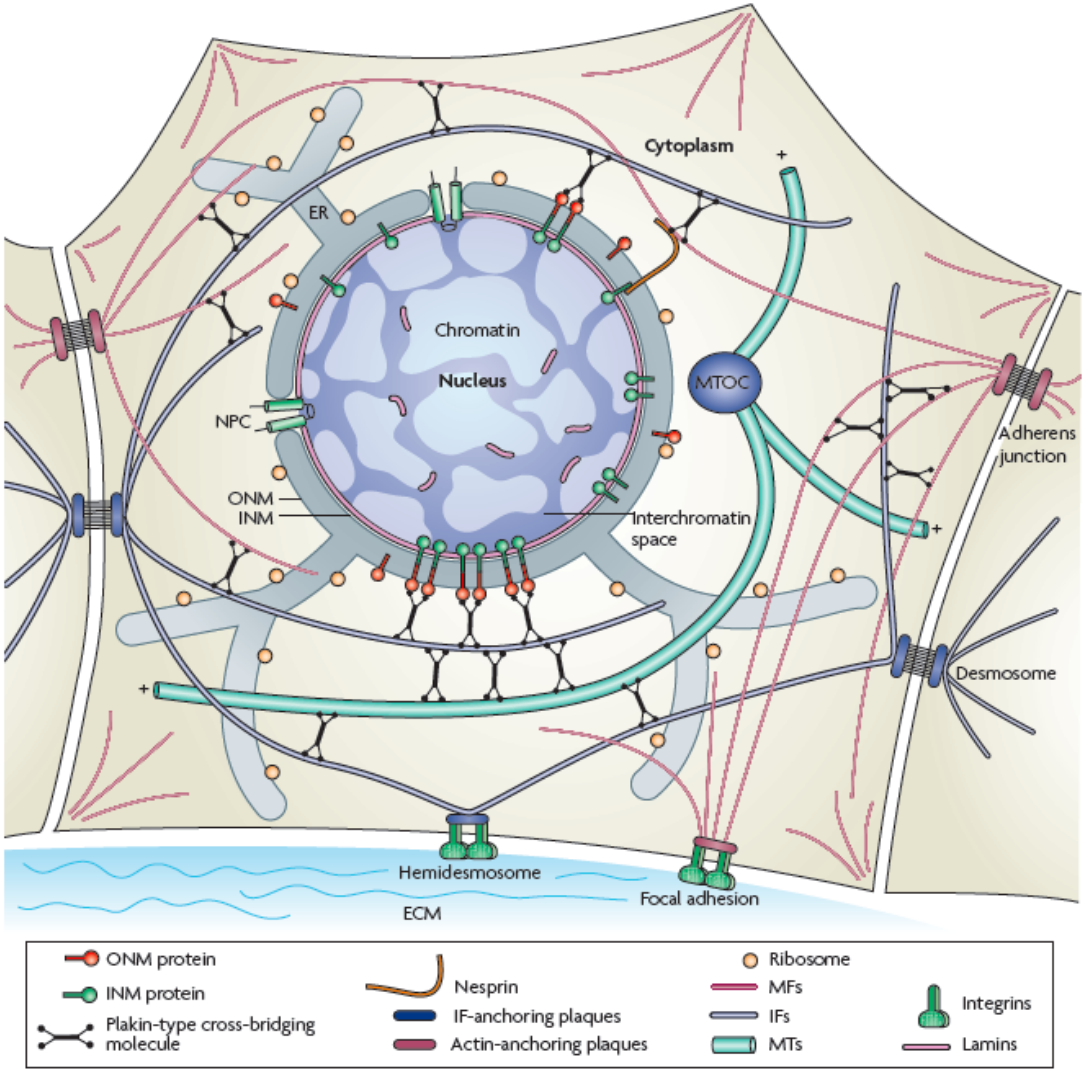
- Cell – cell junction
- Keratin or desmin is bound to cadherin in the membrane



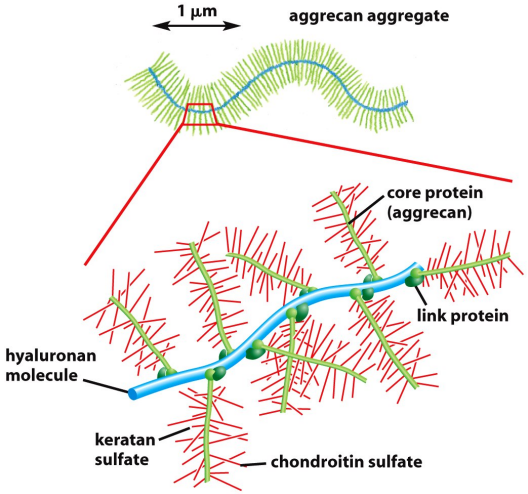
Hemidesmosome:

- Cell – matrix junction
- Keratin is bound to integrin



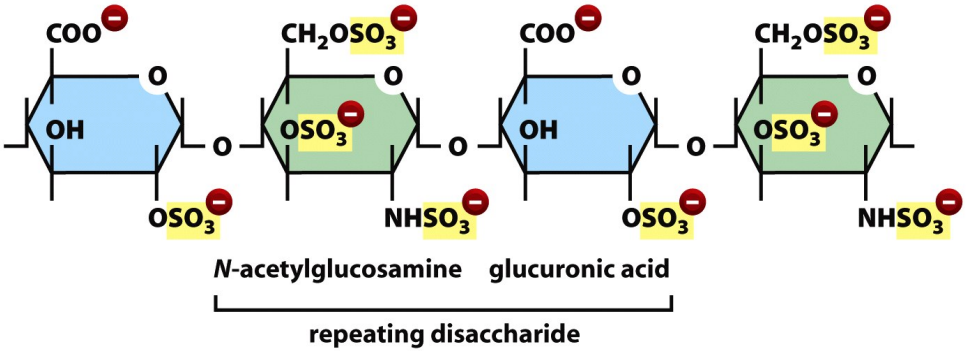


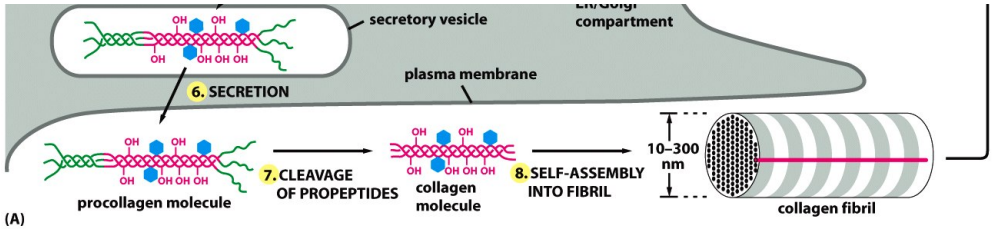
Extracellular Matrix

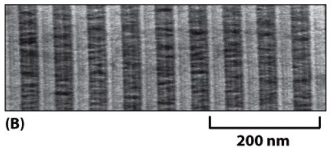


Complex aggregates of **polysaccharides** and **fibrillar proteins** form the extracellular matrix; negatively charged sugar residues attract cations surrounded by water molecules, leading to a gel-like structure

Glucosaminoglycanes are the basic structure in many polysaccharides







Fibrillar proteins include laminin, fibronectin and **collagens**; the latter form stable fibrils of triple helices including covalent crosslinks and **hydroxylysine / proline**