Advanced Cell Biology. Lecture 10

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February 7th, 2011

Outline

Proteins

Proteins in general

Shape and structure of proteins

Outline

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Shape and structure of proteins

Previous final question: the answer

What is the difference between NADH and NADPH?

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What is the difference between NADH and NADPH?

- Letter P :-)
- Phosphate group
- Participation in catabolic vs. anabolic reactions, respectively

Proteins

- Unbranched polymers of L-amino acids, normally synthesized on ribosomes
- After synthesis, proteins normally undergo 2D folding, 3D shaping and (sometimes) chemical modification and hyper-polymerization

Functions (review)

- Enzymatic (pepsin, Rubisco)
- Structural (collagen, keratin)
- Transport (hemoglobin, serum albumin)
- Movement (myosin, dinein)
- Storage (ferritin, ovalbumin)
- Signal (insulin, EGF)
- Sensitivity (rhodopsin, acetylcholine receptor)
- Gene regulation (lactose repressor, homeodomain proteins)
- Other (antifreeze, fluorescent etc.)

Amino acid sequence

- Protein = polypeptide backbone + side chains
- Side chains could be negative, positive, uncharged polar and nonpolar

Classification of side chains

AMINO ACID			SIDE CHAIN
Aspartic acid	Asp	D	negative
Glutamic acid	Glu	E	negative
Arginine	Arg	R	positive
Lysine	Lys	K	positive
Histidine	His	H	positive
Asparagine	Asn	N	uncharged polar
Glutamine	Gln	Q	uncharged polar
Serine	Ser	S	uncharged polar
Threonine	Thr	T	uncharged polar
Tyrosine	Tyr	Y	uncharged polar

POLAR AMINO ACIDS
(hydrophilic)

AMINO ACID			SIDE CHAIN
Alanine	Ala	A	nonpolar
Glycine	Gly	G	nonpolar
Valine	Val	V	nonpolar
Leucine	Leu	L	nonpolar
Isoleucine	Ile	I	nonpolar
Proline	Pro	P	nonpolar
Phenylalanine	Phe	F	nonpolar
Methionine	Met	M	nonpolar
Tryptophan	Trp	W	nonpolar
Cysteine	Cys	C	nonpolar

NONPOLAR AMINO ACIDS
(hydrophobic)

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Folding bonds

- Electrostatic
- Hydrogen
- van der Waals

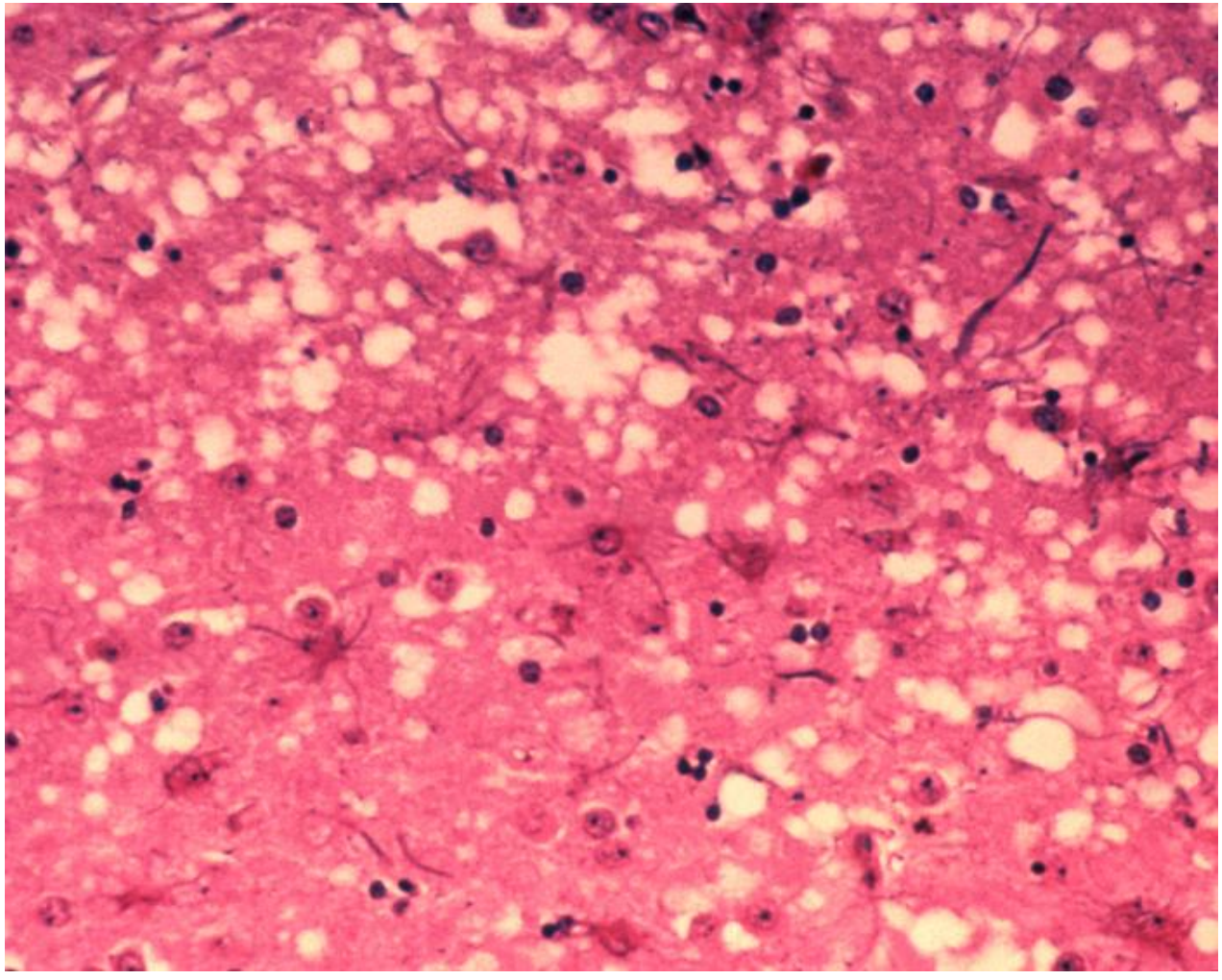
Conformation and denaturation

- Conformation: final 3D structure with minimal Gibbs energy
- At high temperatures, conformations breaks, this is denaturation
- Most proteins may return to previous conformation after renaturation

Prions

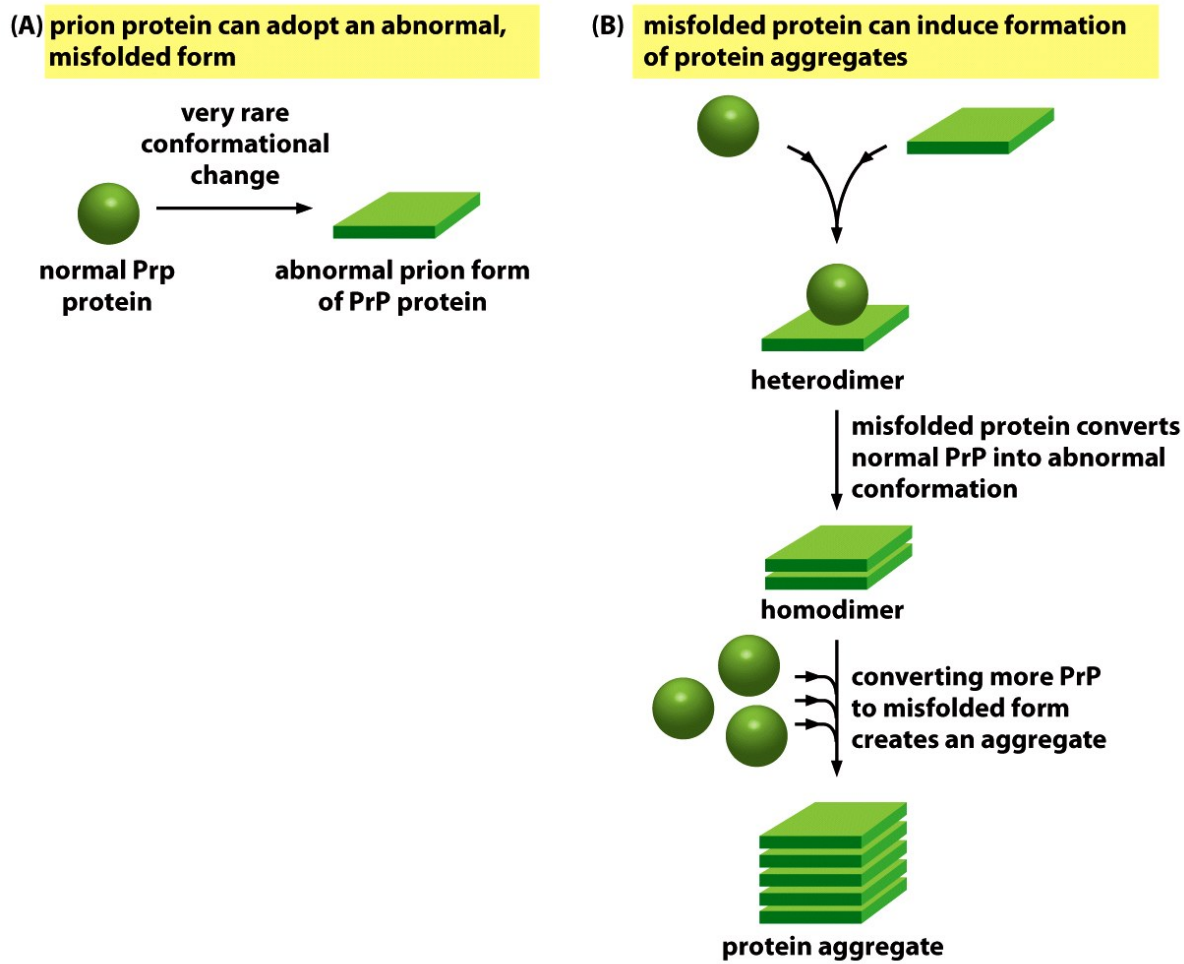
- Scrapie and Bovine Spongiform Encelopathy (BSE, “cow madness”) caused by proteins
- In humans: Creutzfeldt-Jakob disease (CJD) and Kuru
- These proteins, prions (PrP) induce convertion non-PrP to misfolded form which causes a disease
- Infectious and non-infectious forms have same amino acid sequence but different 3D structure

BSE



Kuru

How prions are working



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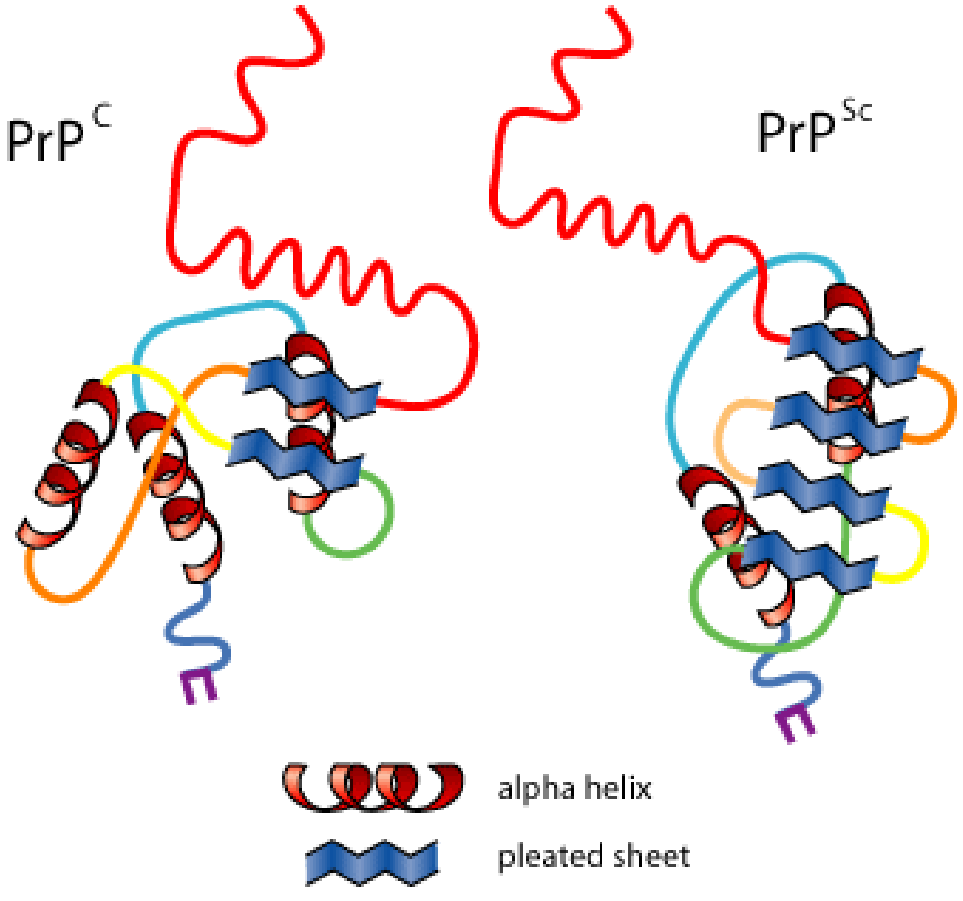
Non-infectious and infectious conformations of prions



Rough classification of 3D forms

- Filaments (collagen)
- Sheets (silk)
- Rings (porin)
- Spheres (myoglobin)

Four ways to depict a 3D structure

- Backbone
- Ribbon
- Wire
- Space-filling

SH2 3D structure movie

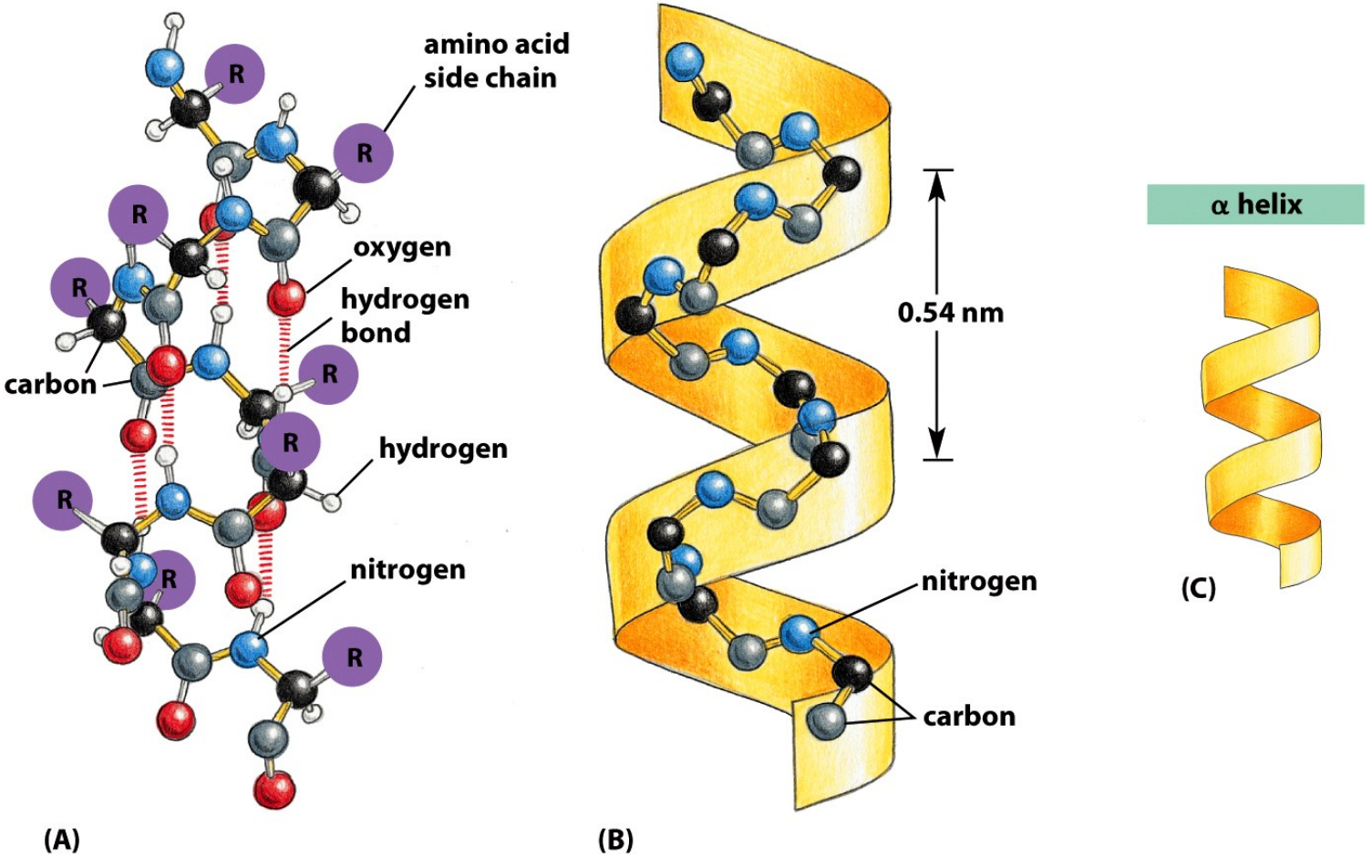
Folding patterns

- α helix: spiral pattern
- β sheet: linear pattern
- They may coexist in the same molecule

α helix

- Typically, hydrogen bonds connect every fourth amino acid
- Several α helices may coil around each other and form coiled coil, as in collagen and other structural proteins

α helix



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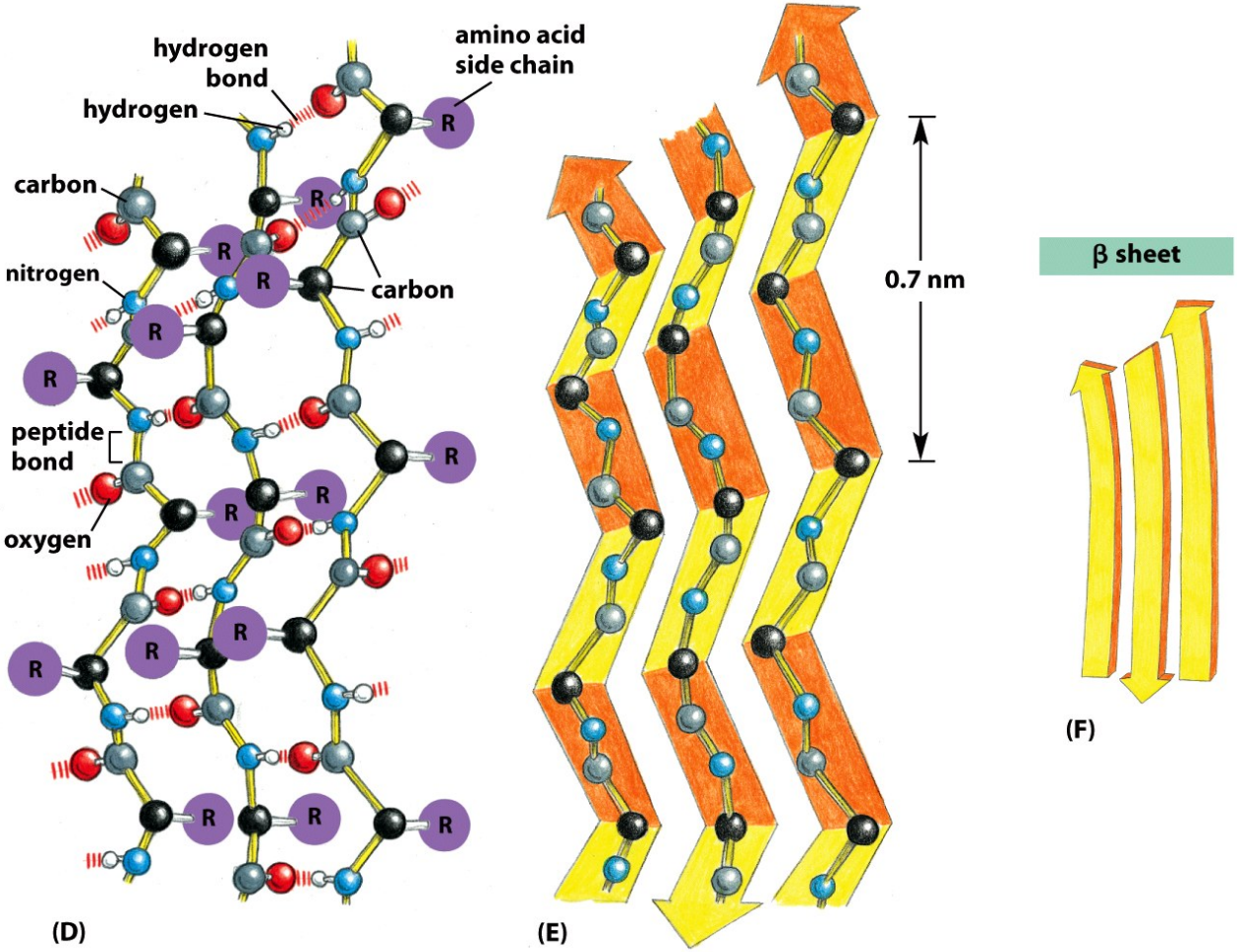
α helix movie

β sheets

- Hydrogen bonds connect different sub-chains
- Parallel: amino acid chain keeps the direction (from N to C) and forms loops
- Antiparallel: amino acid chain changes direction and forms completely flat structure

β sheet



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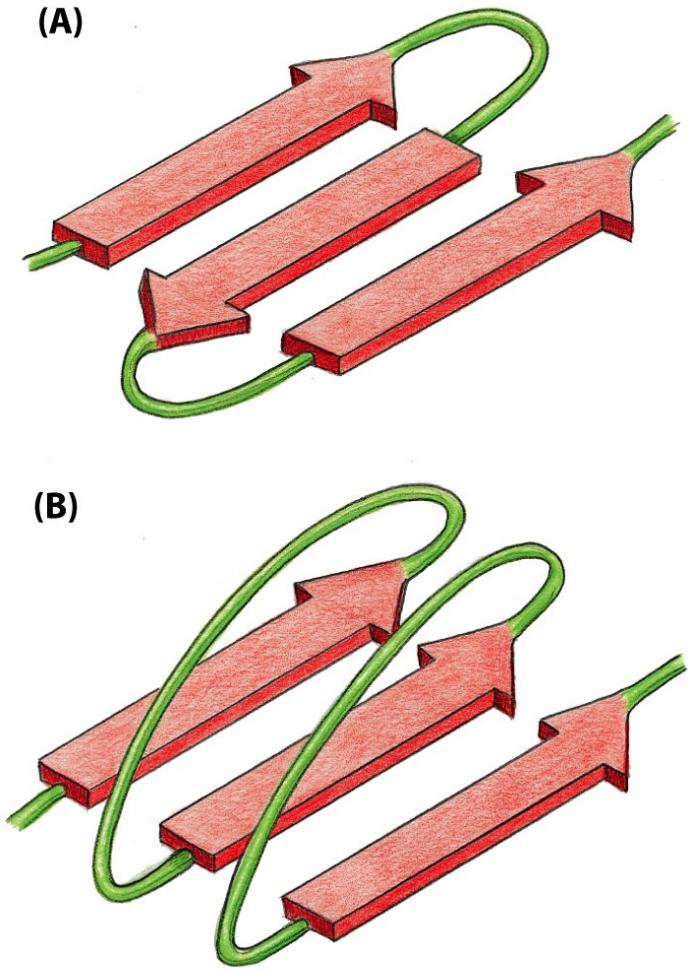
Antiparallel and parallel β sheets



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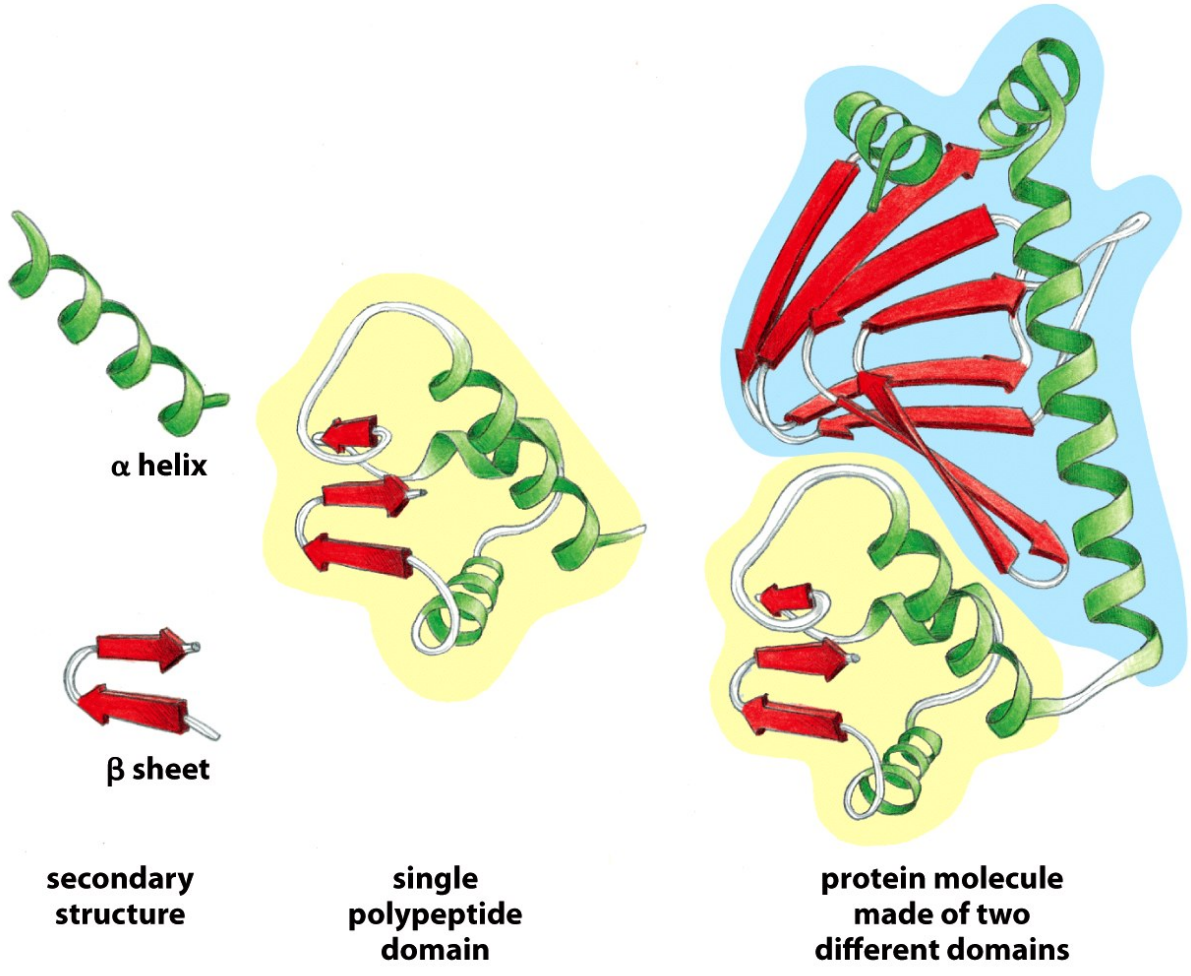
β sheets movie

Protein levels of organization

- Primary
- Secondary and tertiary
- OR domain organization, when different part of one molecule fold independently
- Quaternary: subunits which are assembling through binding sites

Domain structure of protein



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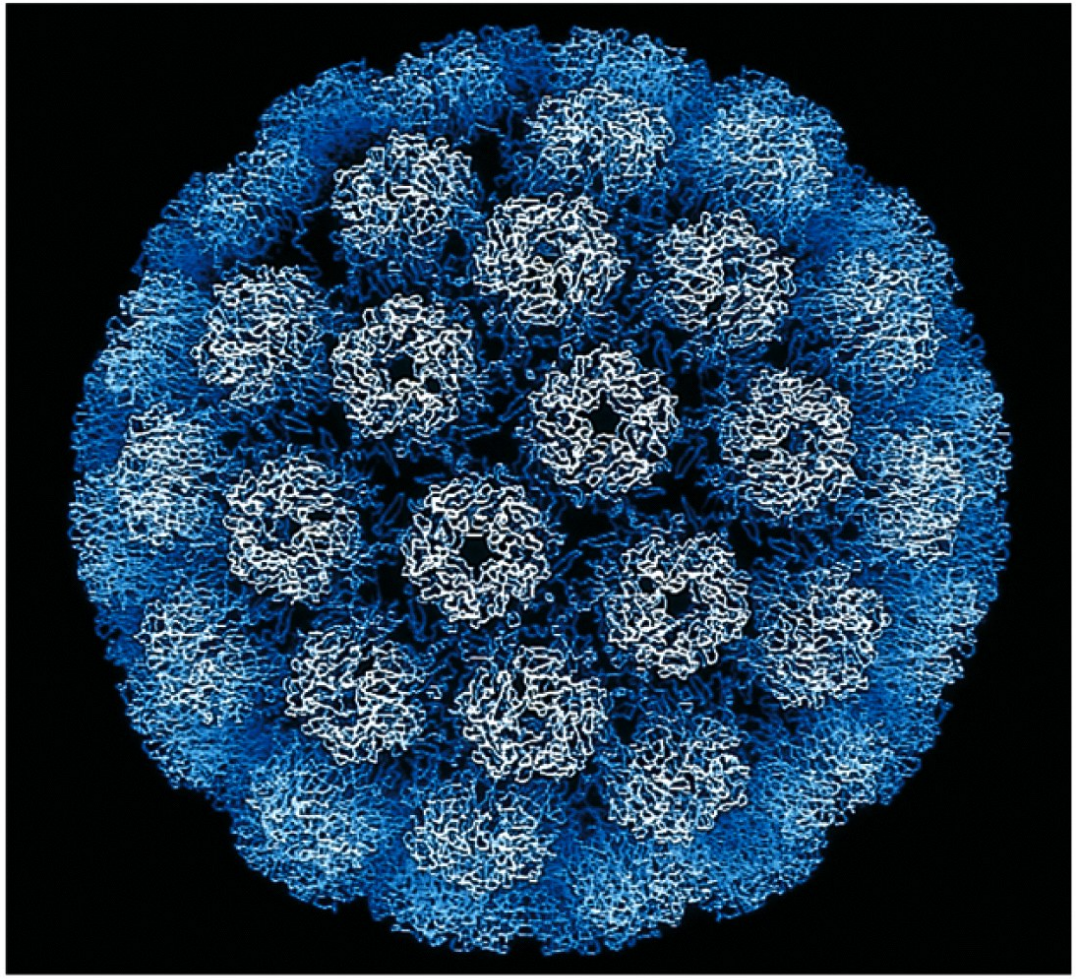
SV40 virus capsid made from multiple protein monomers



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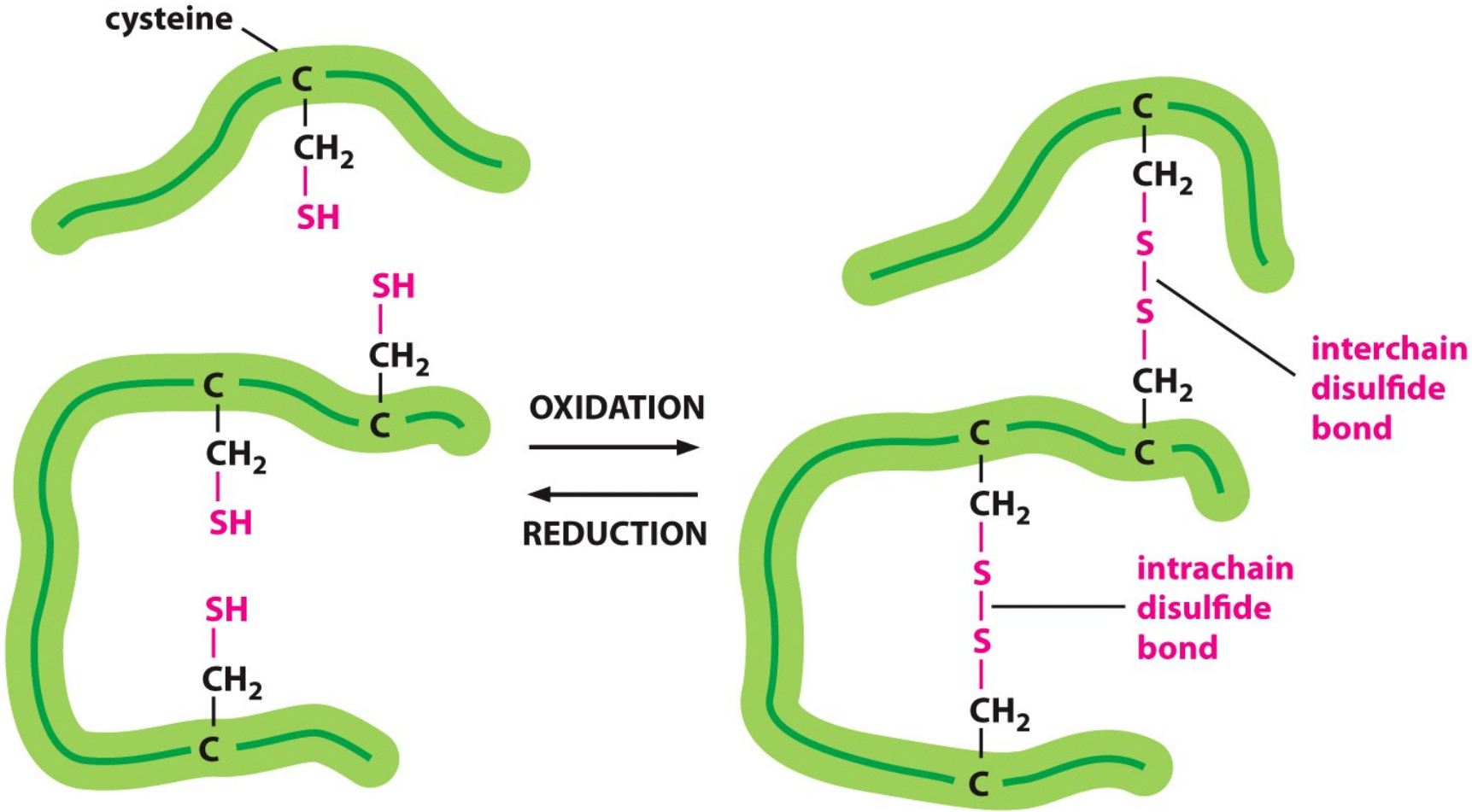
Quaternary structure movie

Stabilization of structure

- Disulfide bonds between cysteins
- Two variants: interchain or intrachain

Inter- and intramolecular disulfide bridges



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Final question (1 point)

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Which secondary structure is more appropriate for collagen:
α helix or β sheet?

Summary

- Most important protein secondary structures are α helices and β sheets

For Further Reading

A. Shipunov.
Advanced Cell Biology [Electronic resource].
2011—onwards.
Mode of access: `http://ashipunov.info/shipunov/school/biol_250`

B. Alberts et al.
Essential Cell Biology. 3rd edition.
Garland Science, 2009.
Chapter 4: pages 119–140.