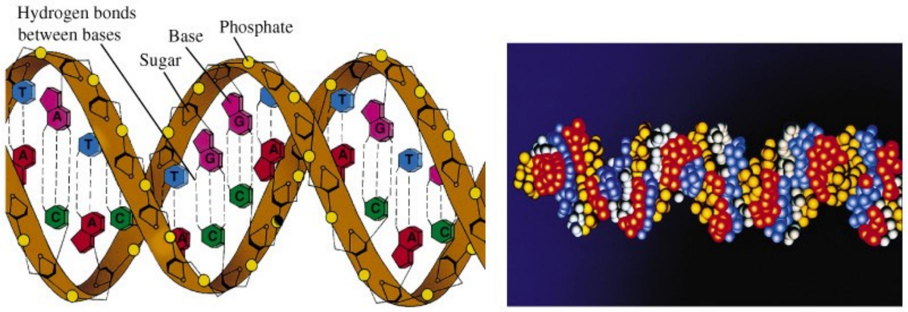
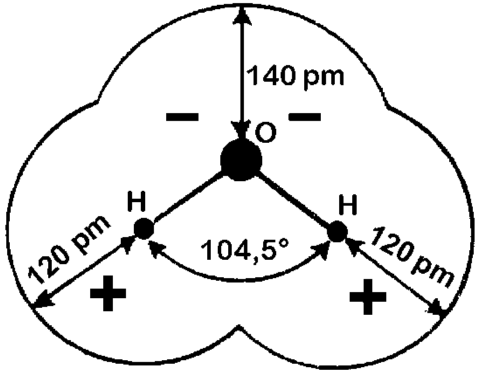


(a) (b)

Lectures on Medical Biophysics

Structure of living matter

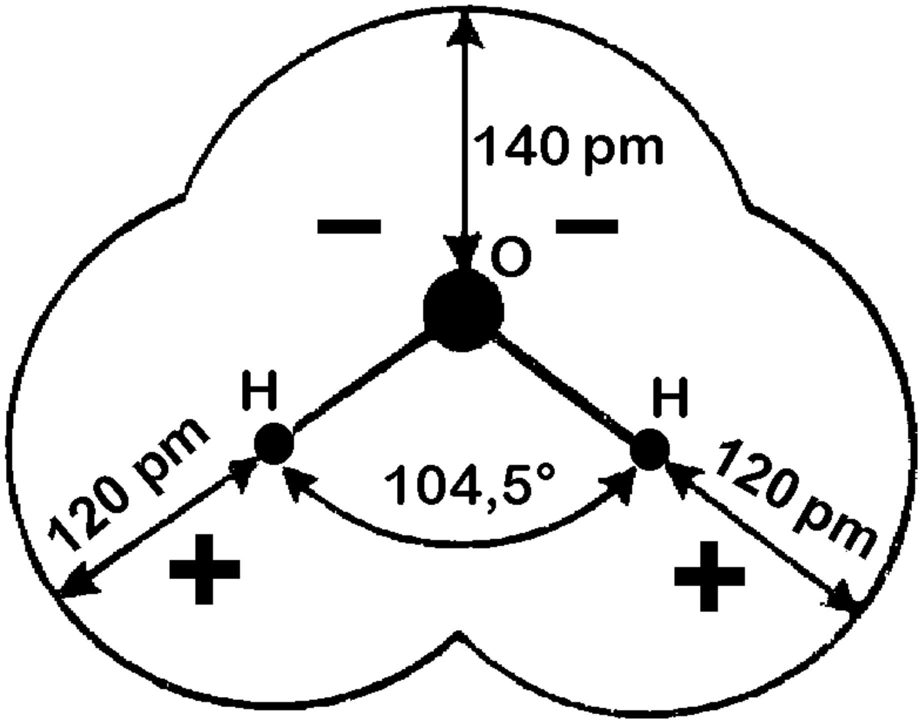


Lecture outline

Water
Properties of colloids
Structure of proteins
Structure of nucleic acids

This lecture deals only with selected components of living matter with distinct biophysical properties. Importance of some other components, e.g. electrolytes will be shown in the lecture on bioelectric phenomena. Check on further information in textbooks of biology and biochemistry.

Water



Molecules of water are strongly polar because of oxygen electronegativity. Moreover, between the oxygen and hydrogen atoms of neighbouring molecules, **hydrogen bonds** are formed. They join water molecules in aggregates – clusters.

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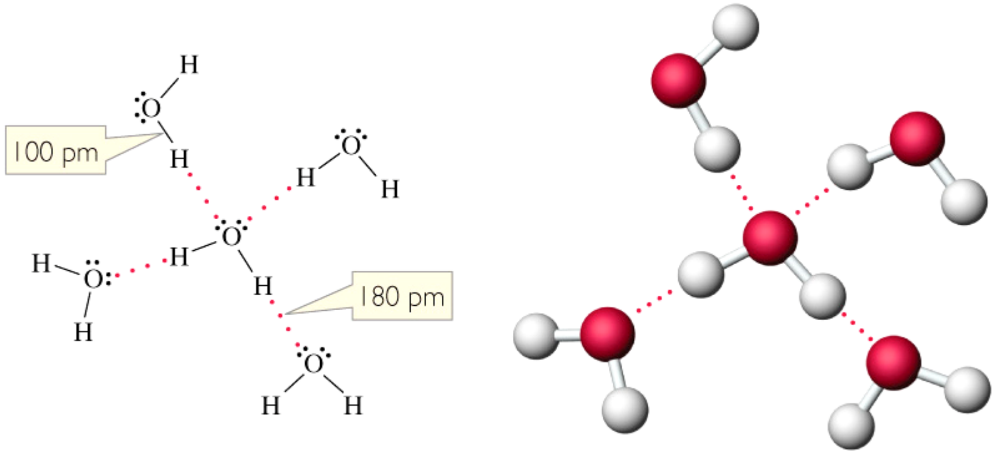
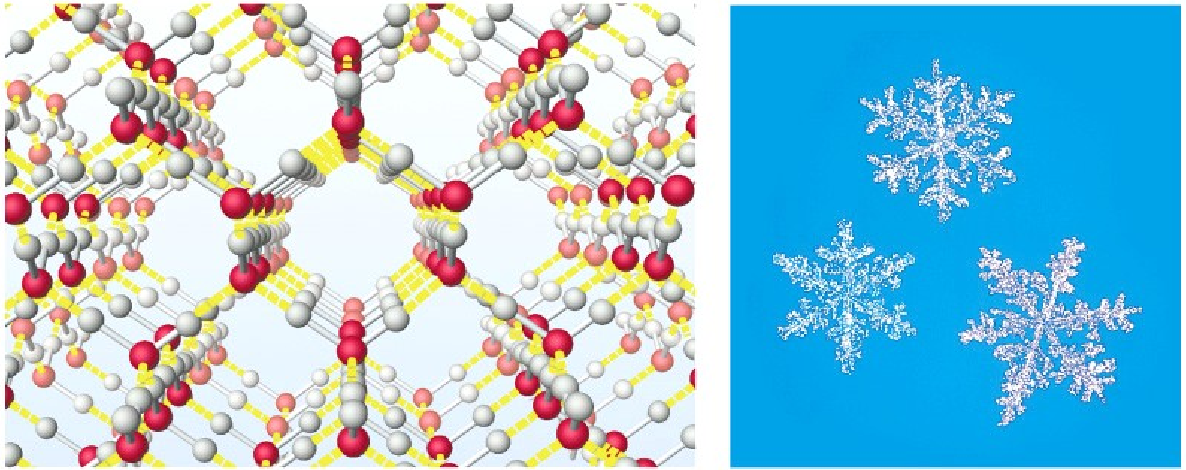
Hydrogen bonds between water molecules

Liquid water



(a) (b)

Ice



(a) (b)

Pictures: http://cwx.prenhall.com/bookbind/pubbooks/hillchem3/medialib/media_portfolio/11.html

Colloids

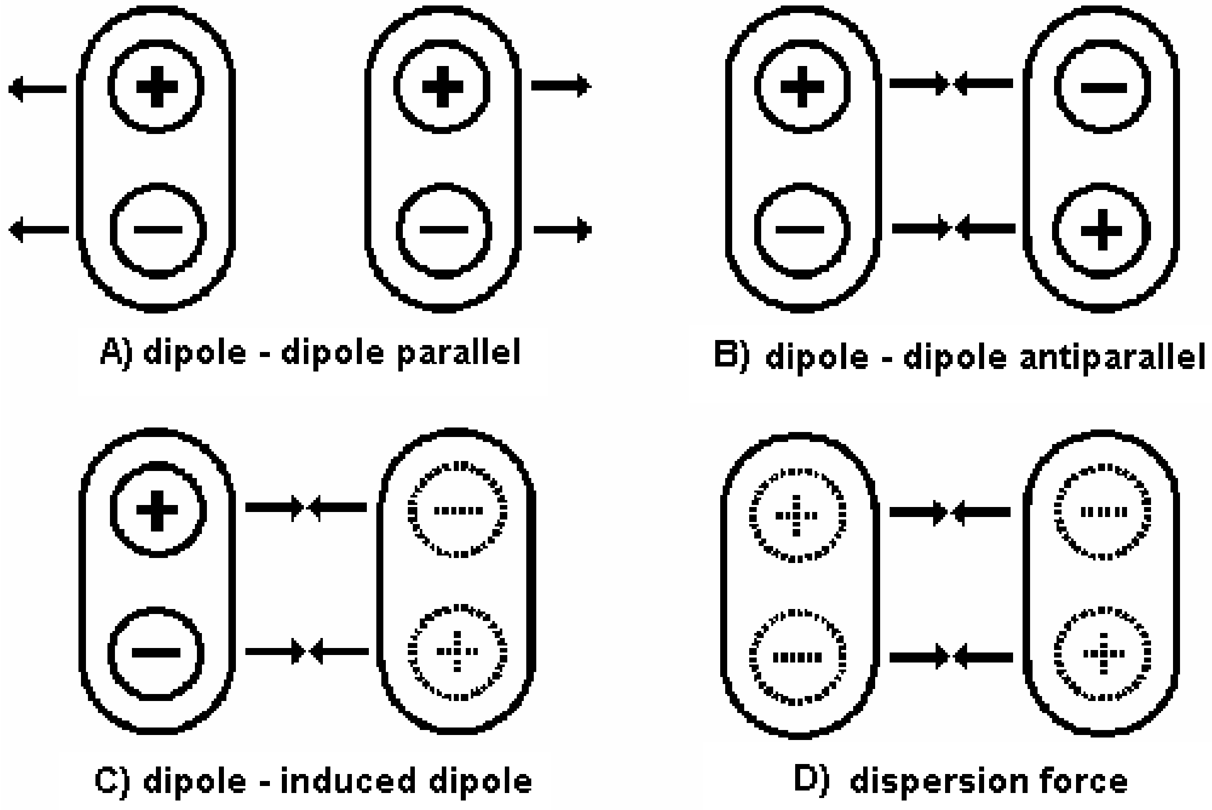
Colloids – also known as non-true solutions – the solution consists of solute particles of diameter about 10 – 1000 nm dispersed in the solvent.

We can distinguish two types of colloids according to the type of binding forces:

- Micellar colloids (also associative, small particles are bound together by *van der Waals bonds*)
- Molecular colloids (particles are macromolecules which subunits are bound together by *covalent bonds*)

Weak chemical bonds

Hydrogen bonds
Hydrophobic interaction
van der Waals bonds



Also London forces, sometimes not classified as van der Waals bonds

Properties of colloids

Mechanical: rigidity, elasticity, viscosity – caused by covalent and weak chemical bonds

These properties depend on the form of colloid:

sol (liquid) or gel (solid). Gel formation = gelatinisation

Optical:

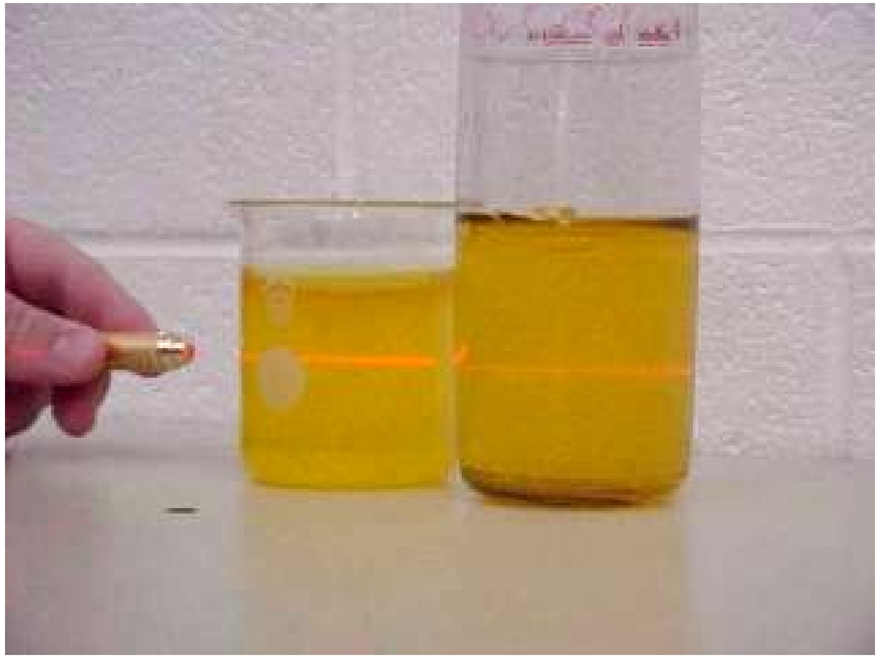
> **Light scatter**: Tyndall effect (opalescence). Light can be scattered off the colloid particles. Track of a light beam passing through a colloid is made visible by the light scattered by the colloidal particles.
>
> **Optical activity**: Colloidal particles can rotate the plane of polarization of plane-polarised light passing through the colloid

Electrical: see lecture on instrumental methods in molecular biophysics

Tyndall effect in micellar and molecular colloids

- In solution of colloidal gold

http://mrsec.wisc.edu/edetc/cineplex/gold/



- In solution of gelatin (a protein)

http://link.springer-ny.com/link/service/journals/00897/papers/0006002/620095mb.htm

Types of Colloids - Biopolymers

- According to the affinity of the biopolymer to solvent (water)
  - **Lyophilic (hydrophilic)** - form stable solutions
  - **Lyophobic (hydrophobic)** - form unstable solutions
- According to the shape of the biopolymer (the shape is also influenced by the solvent!)
  - **Linear** (fibrillar – DNA, myosin, synthetic polymers…..also scleroproteins, mostly insoluble in pure water)
  - **Spherical** (globular – haemoglobin, glycogen … also spheroproteins, mostly soluble in pure water)

Chemical composition of proteins

According to the products of hydrolysis:

- simple (only amino acids in hydrolysate)
- conjugated (not only amino acids in hydrolysate)
  - Nucleoproteins
  - Haemoproteins
  - Flavoproteins
  - Metalloproteins
  - Lipoproteins
  - …..

(see Biochemistry)

Structure of proteins

- Structural units of proteins are amino acids (AA), connected by peptide bond:

  -RCH-NH-CO-RCH-,

  which can hydrolyse:

  $$-RCH-NH-CO-RCH- + H_2O \longleftrightarrow -RCH-NH_2 + -RCH-COOH$$

- The carboxylic and amino groups can dissociate or protonise. E.g. the glutamic and asparagic acids have one free carboxylic group:

  $$-COOH \longleftrightarrow -COO^- + H^+$$

- AA lysine and arginine have one free amino group, which can protonise:

  $$-NH_2 + H^+ \longleftrightarrow -NH_3^+$$

- In proteins, 20 different AA can be found which can be divided into AA with polar and non-polar side chain.
- AA with aromatic ring or heterocycle (phenylalanine, tyrosine, tryptophan) strongly absorb UV light around 280 nm.
- AA cysteine contains sulphhydryl (thiol) group (-SH), which is oxidised by dehydrogenation and connected with dehydrogenated group of another cysteine residue by covalent disulphidic bridge (bond -S-S-).

Molar absorption coefficient ε

Wavelength (nm)

Absorption spectrum of free phenylalanine, tyrosine and tryptophan in UV range

•According:http://www.fst.rdg.ac.uk/courses/fs460/lecture6/lecture6.htm

Structure of proteins

Disulphidic bridges (in yellow) stabilise the protein structure (bovine ribonuclease A)

•http://cwx.prenhall.com/horton/medialib/media_portfolio/text_images/FG04_28a-b.JPG

Structure of proteins

- **Primary** (sequence of covalently bound AA residues)
- **Secondary** (mutual spatial arrangement of neighbouring links of the polypeptide chain – given mainly by hydrogen bonds)
  - α-helix
  - β-structure (pleated sheet)
  - other
- **Tertiary** (spatial arrangement of the polypeptide chain as a whole – given by hydrophobic and hydrogen bonds, stabilised by -S-S- bridges)
- **Quaternary** (a way of non-covalent association of individual polypeptide chains (subunits) in whole of higher order)
  - Homogeneous – all subunits are identical
  - Heterogeneous – subunits of two or more kinds

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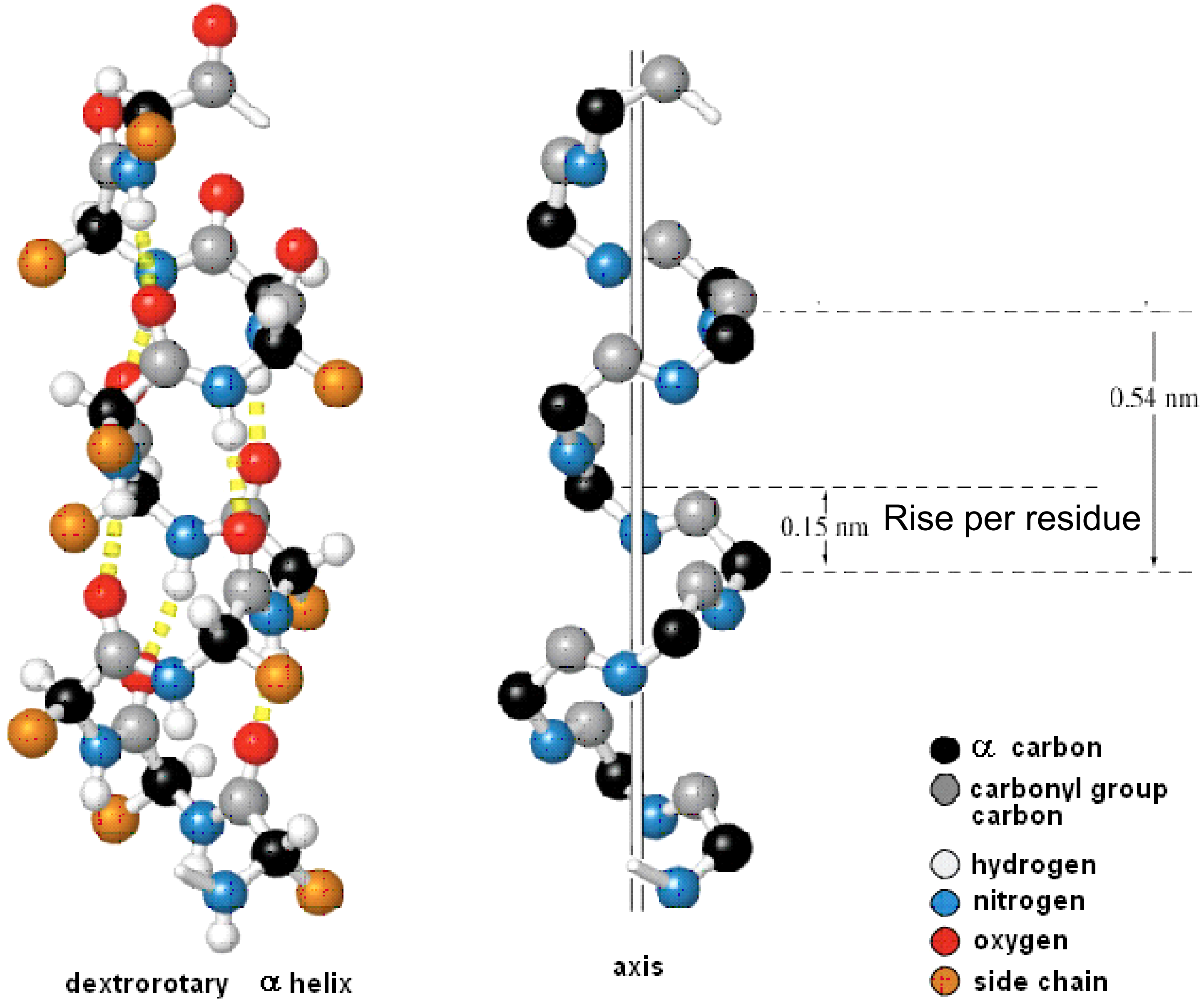
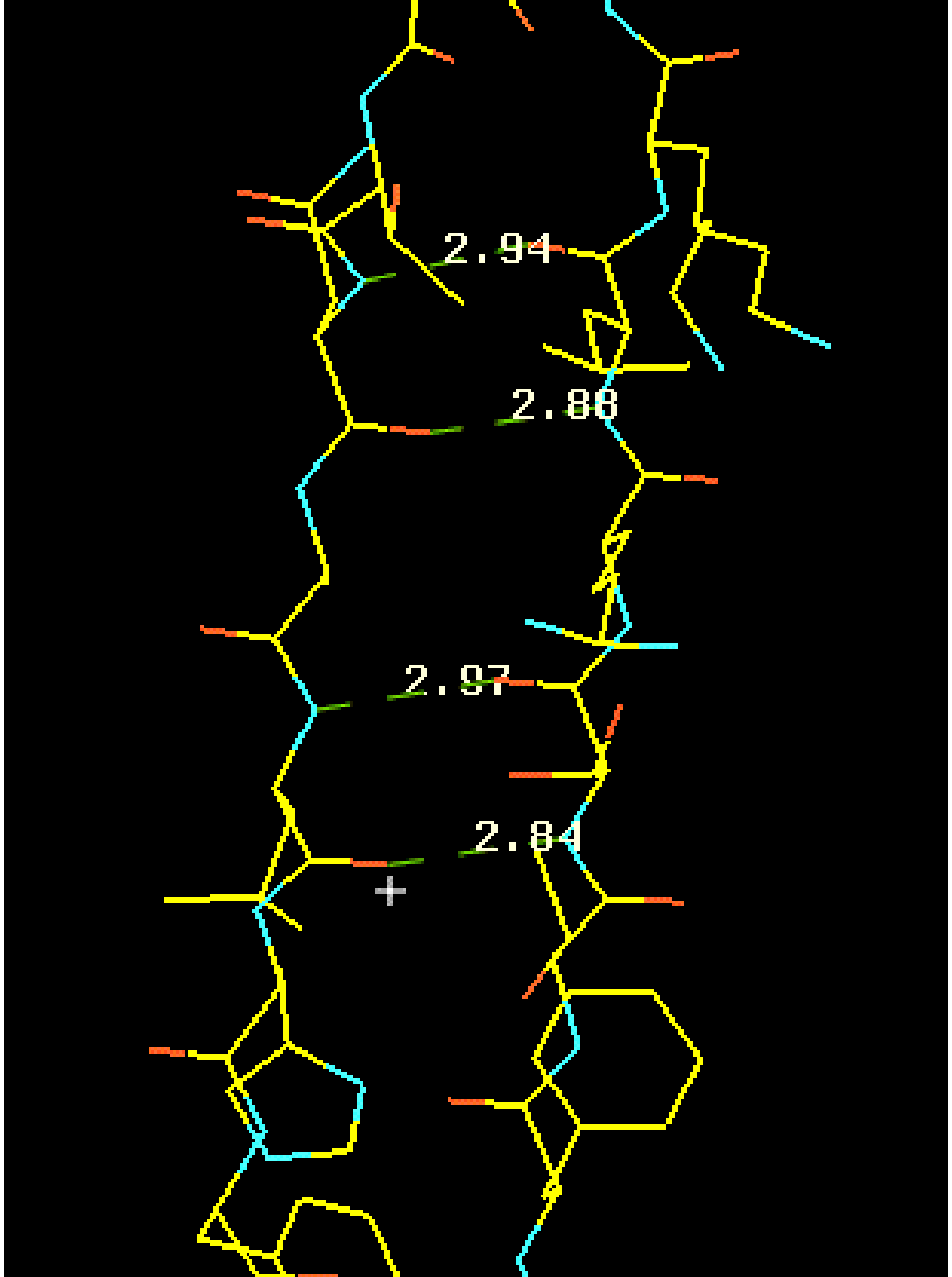


•Podle: http://cwx.prenhall.com/horton/medialib/media_portfolio/text_images/FG04_10.JPG



β-structure (pleated sheet – antiparallel model)

http://www-structure.llnl.gov/Xray/tutorial/protein_structure.htm

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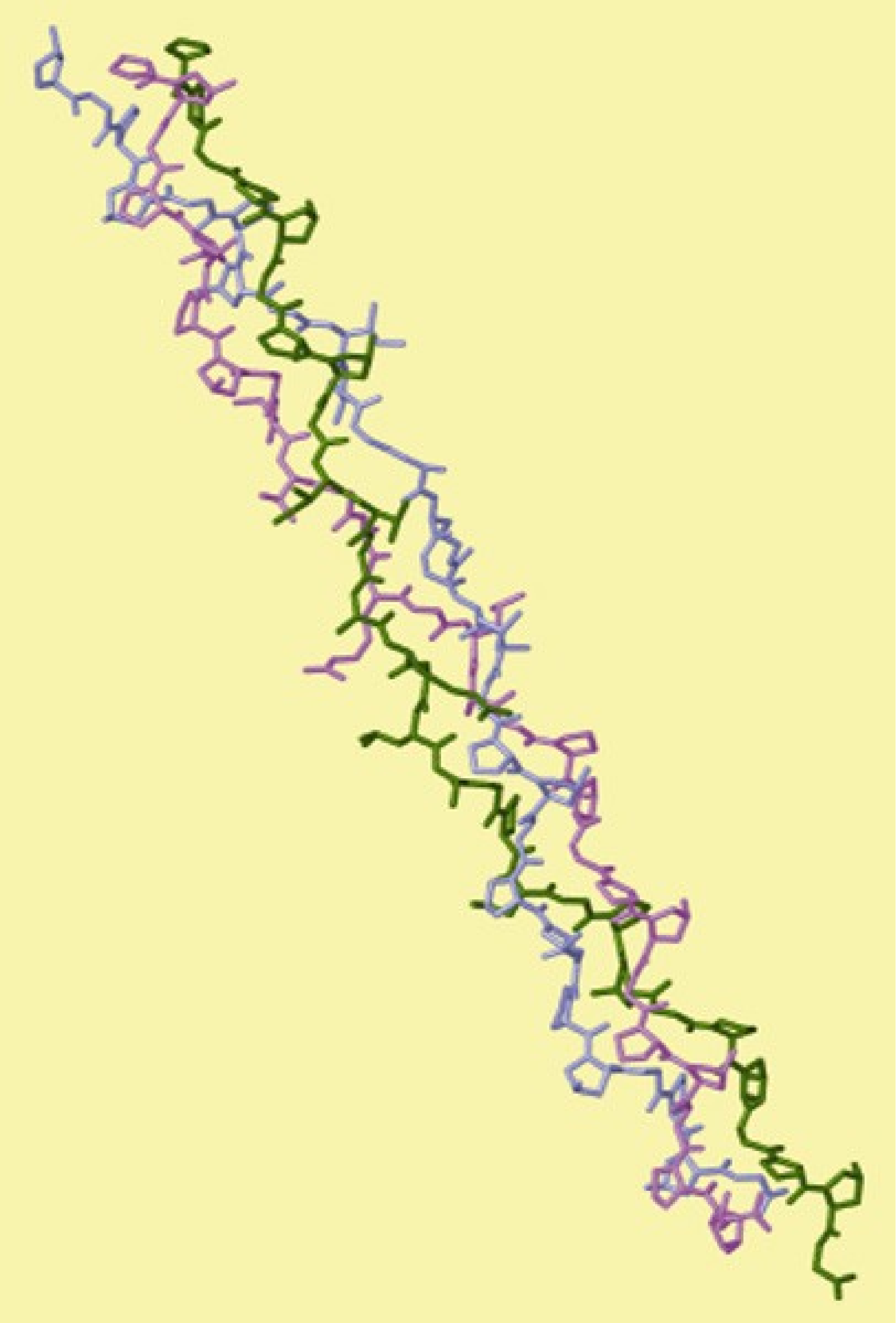

Triple helix of collagen

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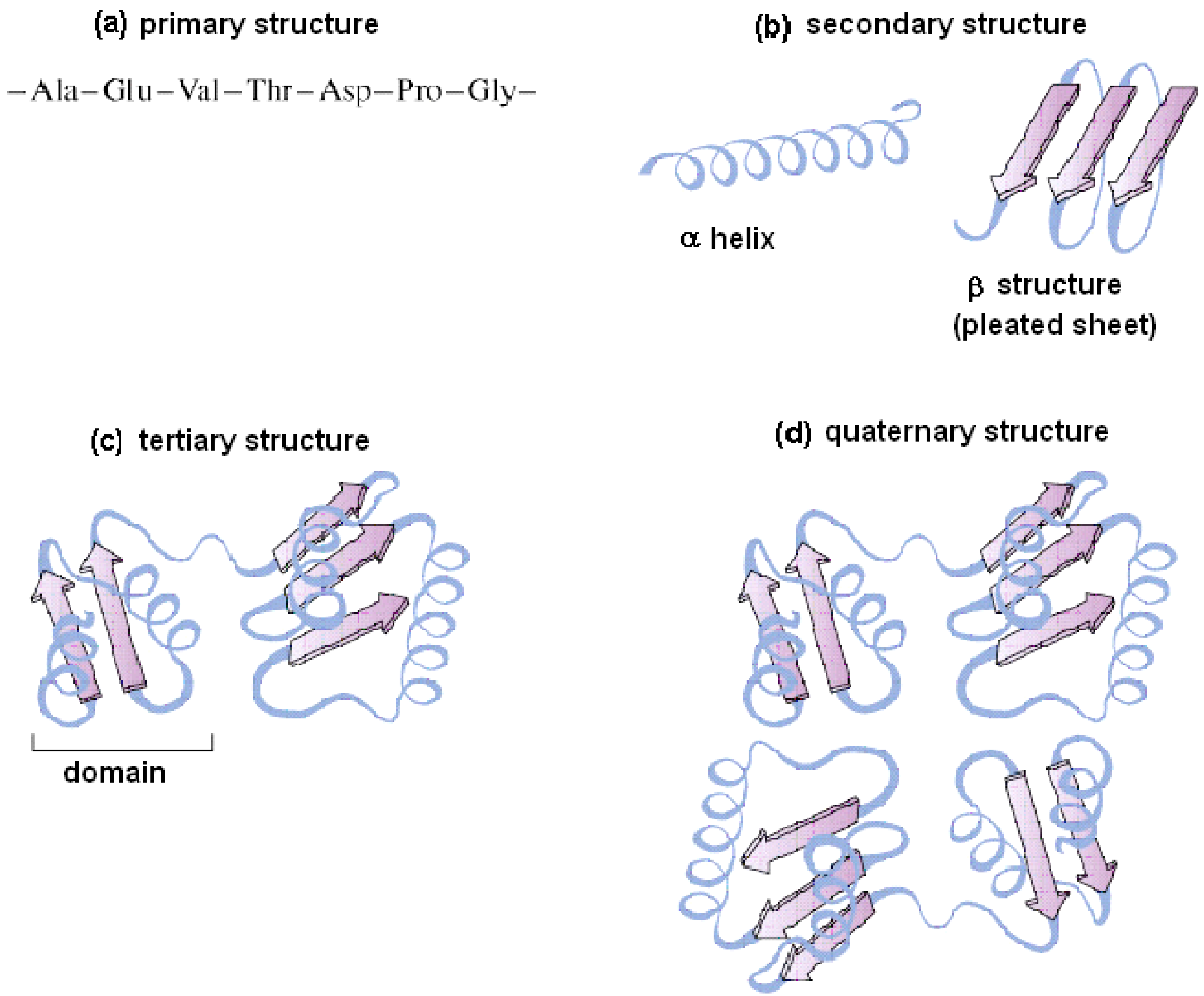

•Podle: http://cwx.prenhall.com/horton/medialib/media_portfolio/text_images/FG04_01.JPG

Structure of nucleic acids (NA)

- Mononucleotide (the structural subunit of NA) is formed by:
  - Pyrimidine (C, U, T) or purine (A, G) nitrogen base
  - Sugar (ribose or deoxyribose)
  - Phosphoric acid residue

- DNA: up to hundreds thousands of subunits. M.w. 10^7 – 10^{12}. Two chains (strands) form antiparallel double helix.
- RNA:
  - m-RNA (mediator, messenger)
  - t-RNA (transfer)
  - r-RNA (ribosomal)
  - (viral RNA, microRNA …… ?)

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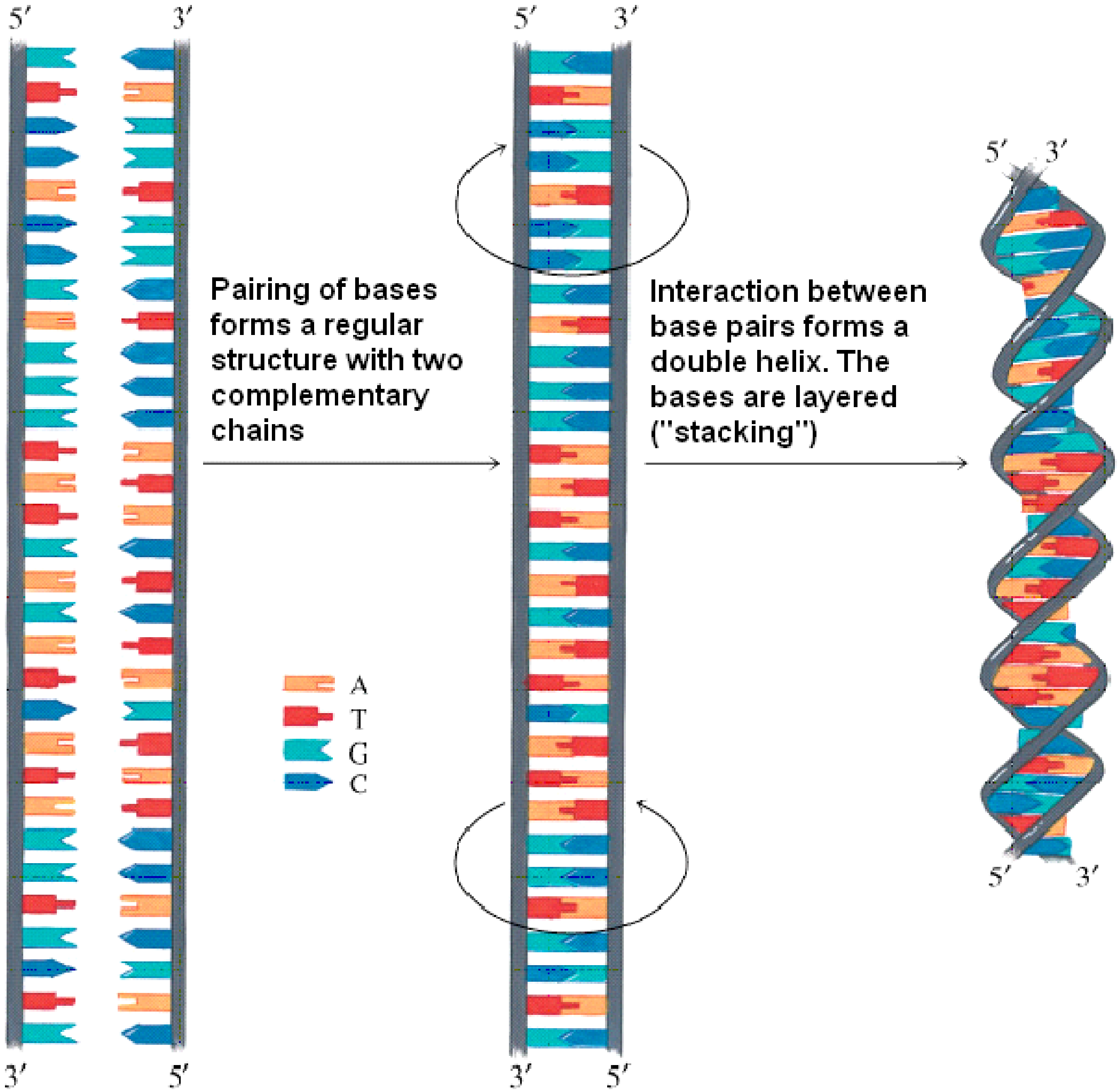

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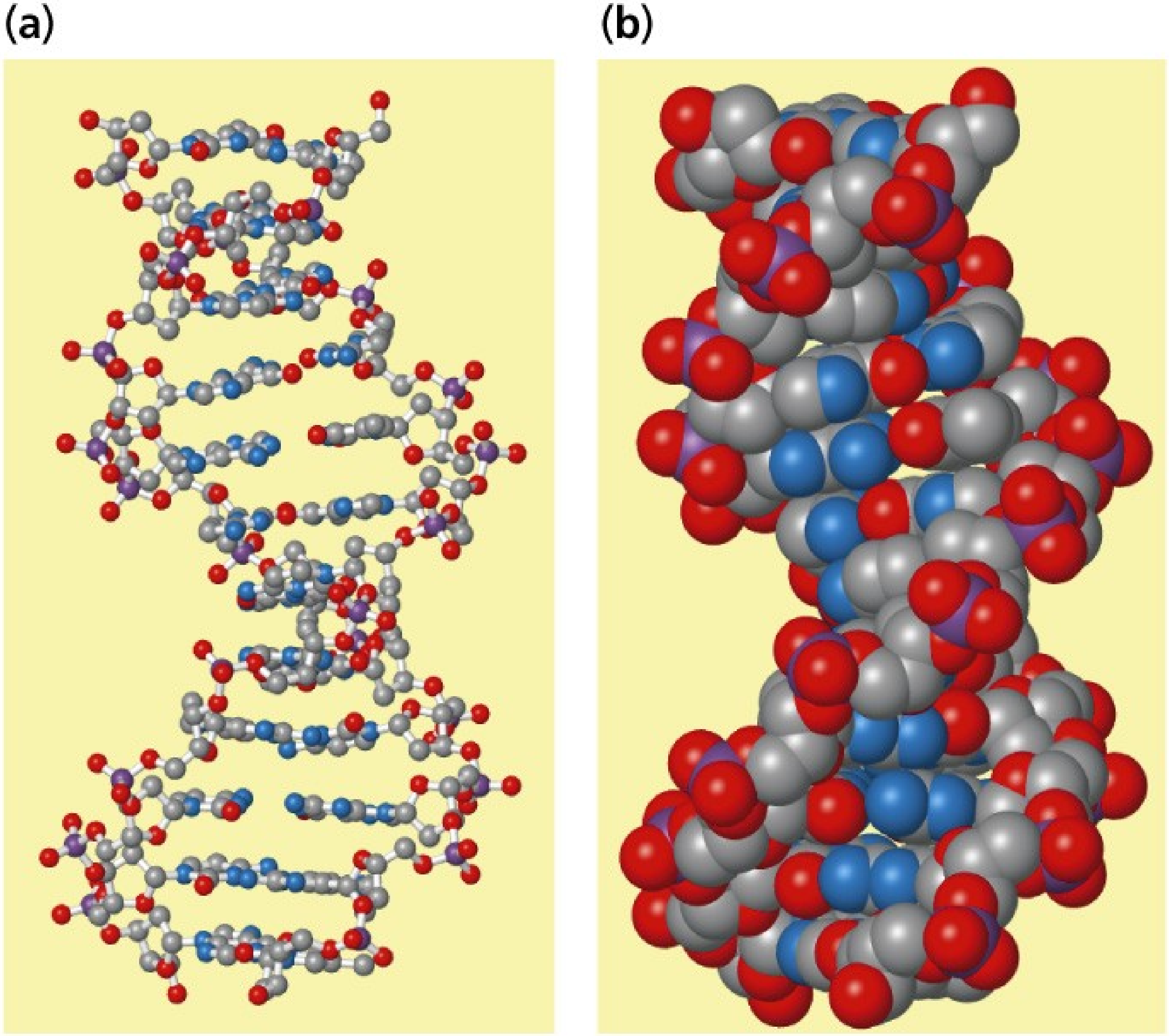
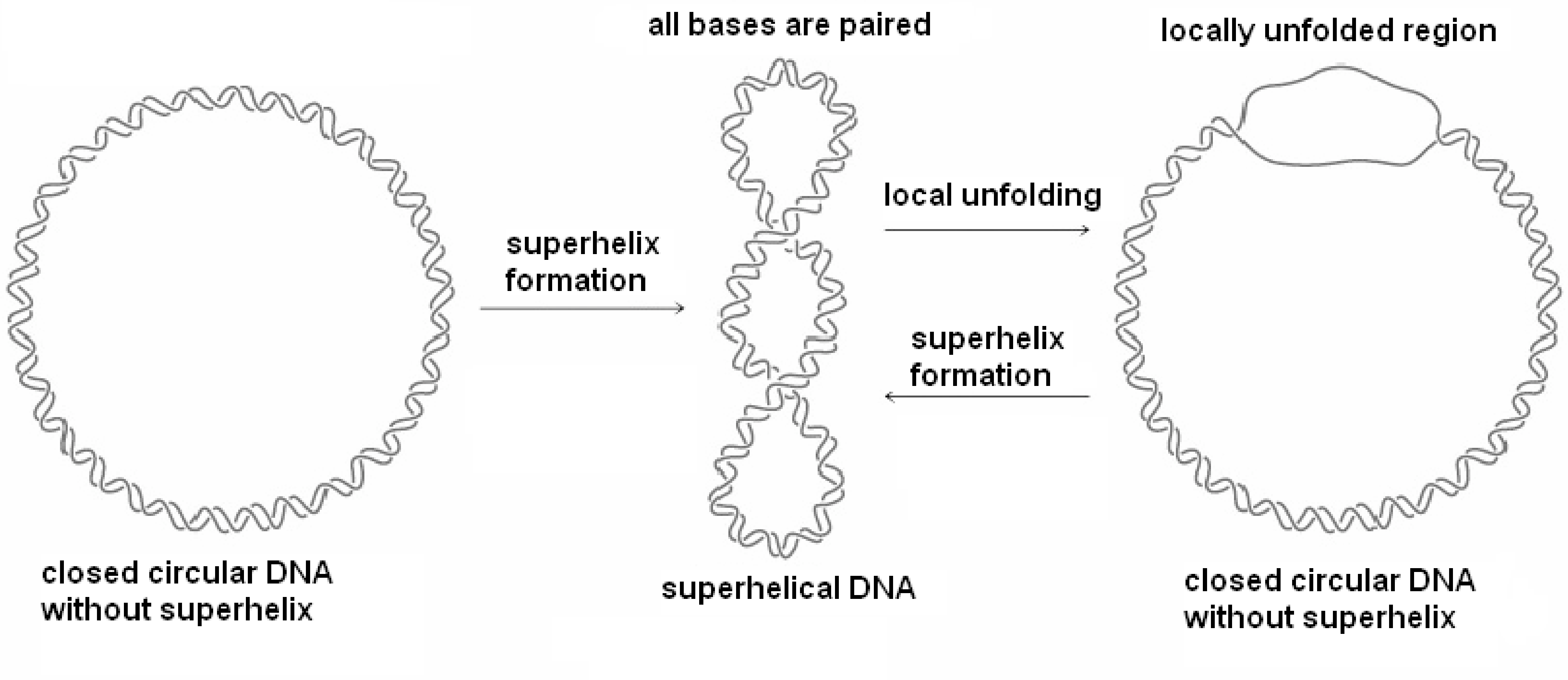


B-DNA

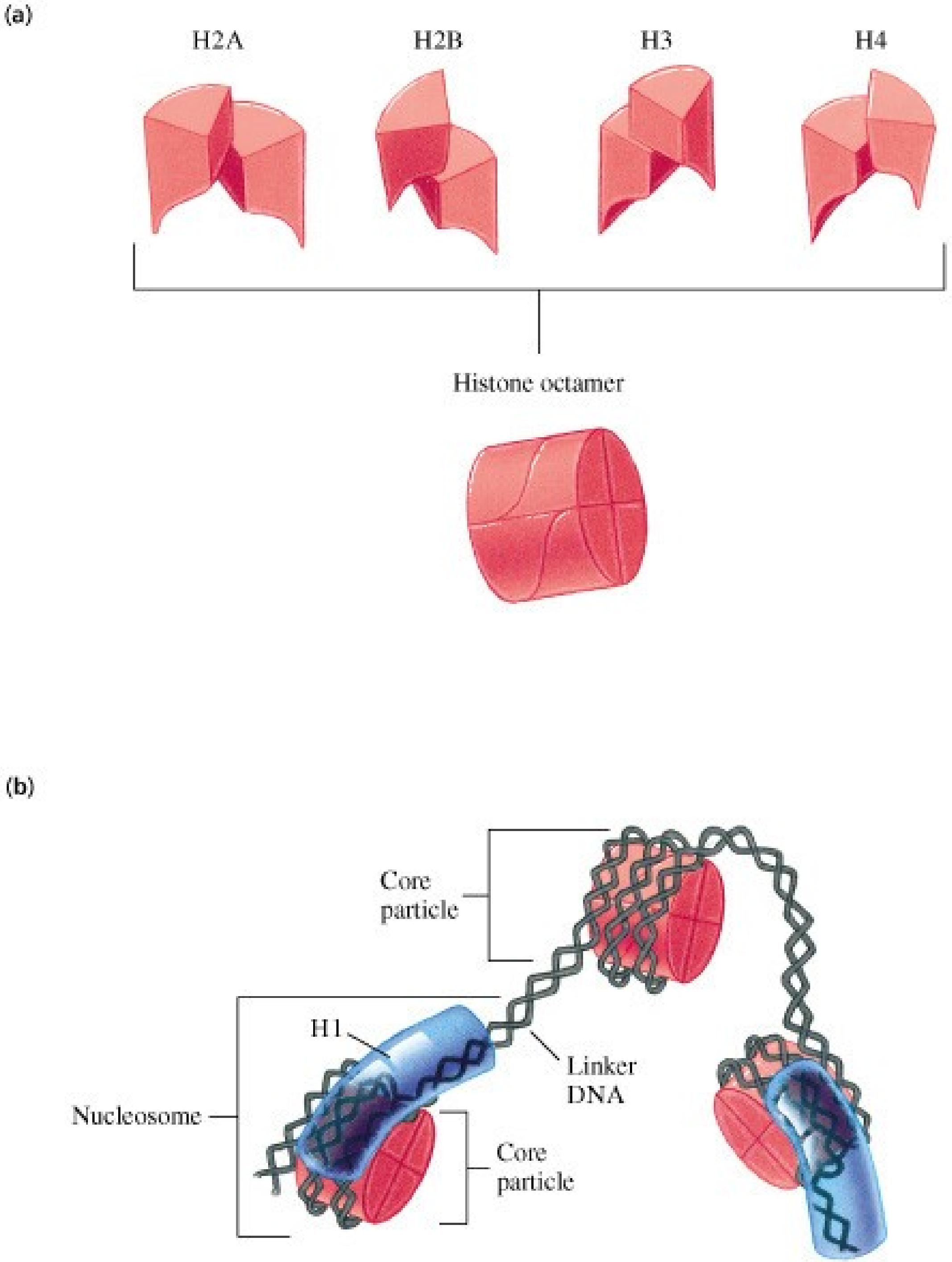
http://cwx.prenhall.com/horton/medialib/media_portfolio/text_images/FG19_15aC.JPG

A-DNA – dehydrated, B-DNA – commonly present under physiological conditions, Z-DNA – in sequences rich on CG pairs

Superhelical structure of circular DNA

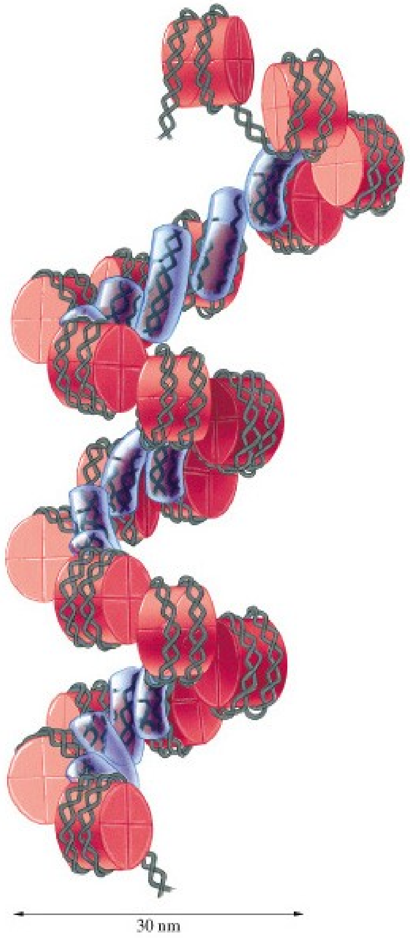


•Podle http://cwx.prenhall.com/horton/medialib/media_portfolio/text_images/FG19_191C.JPG



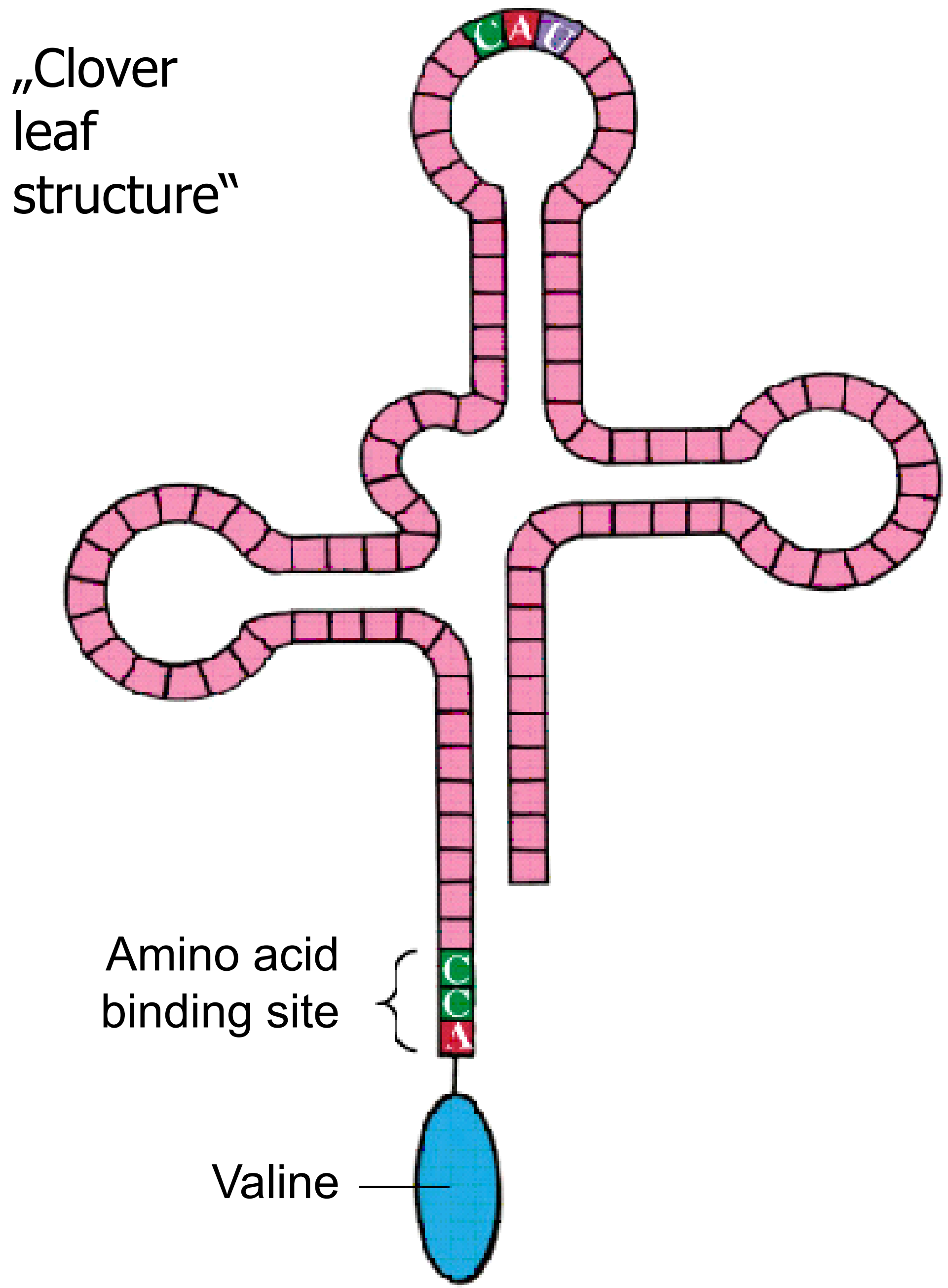
Structure of chromatin

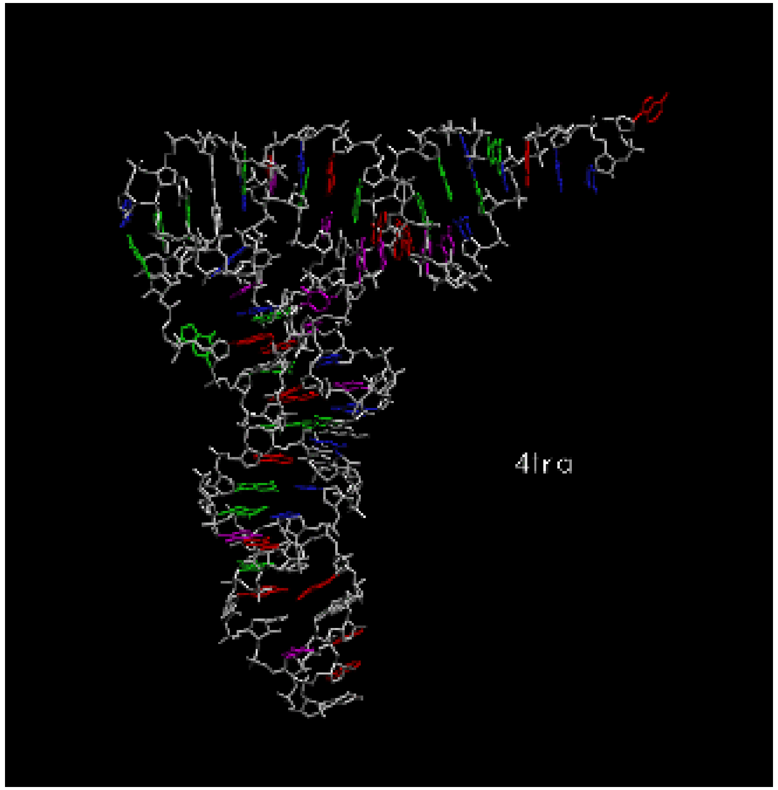
http://cwx.prenhall.com/horton/medialib/media_portfolio/text_images/FG19_23_00742.JPG, http://cwx.prenhall.com/horton/medialib/media_portfolio/text_images/FG19_25_00744.JPG



Transfer RNA for valine – schematic t-RNA from yeasts ↓

http://cwx.prenhall.com/bookbind/pubbooks/hillchem3/medialib/media_portfolio/text_images/CH23/FG23_14.JPG, http://www.imb-jena.de/cgi-bin/ImgLib.pl?CODE=4tra



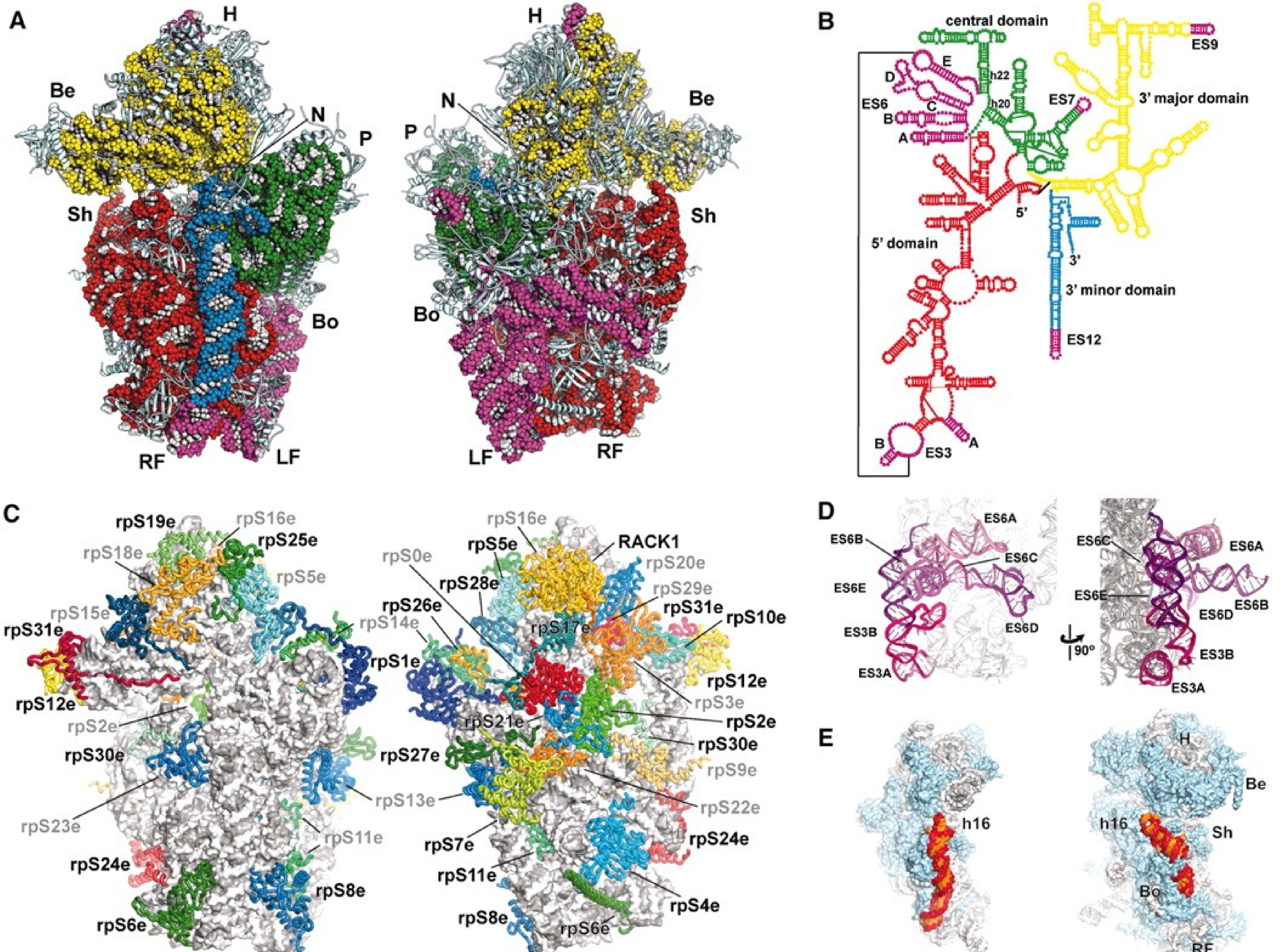


Ribosomal RNA

Next picture was published in: Science 11 February 2011: Vol. 331 no. 6018 pp. 730-736 in the article: **Crystal Structure of the Eukaryotic 40*S* Ribosomal Subunit in Complex with Initiation Factor 1 (**Julius Rabl, Marc Leibundgut, Sandro F. Ataide, Andrea Haag, Nenad Ban)

Description (for those interested in it):

Architecture of the 40*S*. (**A**) Front and back views of the tertiary structure of the 40*S* showing the 18*S* rRNA as spheres and colored according to each domain (5′ domain, red; central domain, green; 3′ major domain, yellow; 3′ minor domain, blue; ESs, magenta), and the proteins as gray cartoons (abbreviations: H, head; Be, beak; N, neck; P, platform; Sh, shoulder; Bo, body; RF, right foot; LF, left foot). (**B**) Secondary structure diagram of the *Tetrahymena thermophila* (a protist)18*S* RNA …showing the rRNA domains and the locations of the ESs. (**C**) Ribosomal proteins of the 40*S* are shown as cartoons in individual colors; rRNA is shown as gray surface. The 40*S* is shown as in (A). (**D**) View of the quaternary interactions between ES6 and ES3 at the back of the 40*S*. The RNA is displayed as a cartoon with the proteins omitted for clarity. ES6 helices are colored in a gradient from light to dark magenta and labeled from A to E... ES3 is highlighted in pink, and the rest of the 18*S* rRNA is colored in gray. (**E**) The position of helix h16 in bacterial 30*S* [left…] and in 40*S*.


A
H
Be
N
P
Sh
Bo
RF
LF
B
central domain
ES9
E
D
h22
ES6
C
h20
ES7
3' major domain
B
A
5'
5' domain
3'
3' minor domain
ES12
B
ES3
A
C
rpS19e
rpS16e
rpS25e
rpS18e
rpS5e
rpS15e
rpS31e
rpS14e
rpS1e
rpS12e
rpS2e
rpS30e
rpS27e
rpS13e
rpS23e
rpS11e
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rpS6e
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RACK1
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rpS10e
rpS17e
rpS12e
rpS3e
rpS21e
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rpS9e
rpS22e
rpS24e
rpS7e
rpS11e
rpS4e
rpS8e
rpS6e
D
ES6A
ES6B
ES6C
ES6E
ES3B
ES6D
ES3A
ES6C
ES6A
ES6E
ES6D
ES6B
90°
ES3B
ES3A
E
h16
H
Be
h16
Sh
Bo
RF

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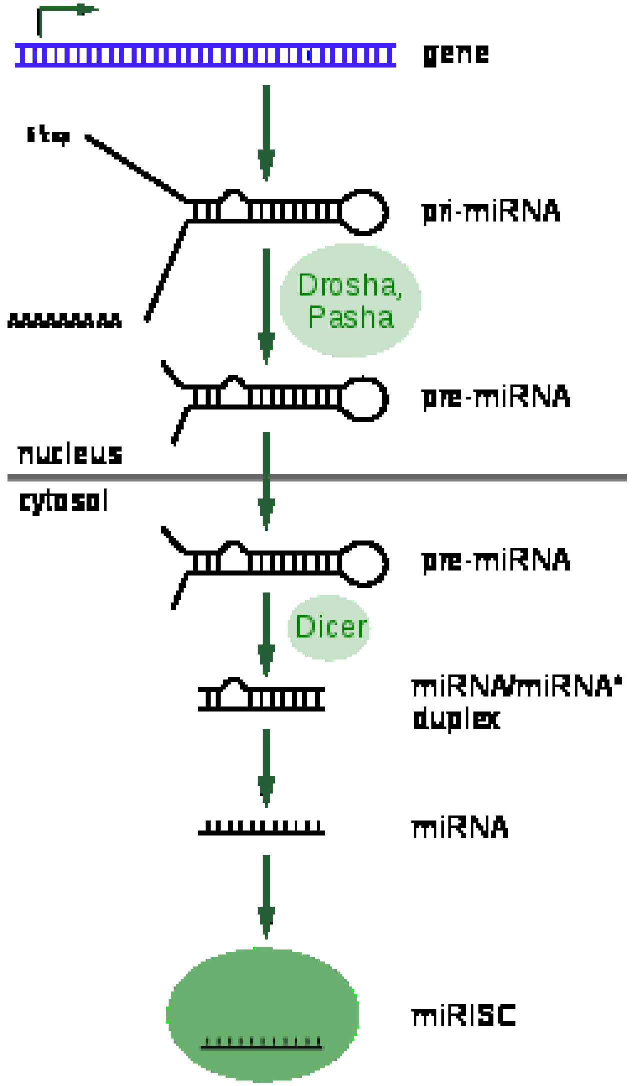
MicroRNA (source: Wikipedia)

MicroRNA or **miRNA** are single strand non-coding RNAs with a typical length of 21-23 nucleotides which take a part in regulation of gene expression. miRNAs are produced by transcription from DNA genes, but they are not translated into proteins.



- After modification by nucleases called „Drosha“ and „Pasha“ the pre-miRNA enters the cytoplasm where can interact with the endonuclease called „Dicer“ forming miRNA. It is bound into the RISC complex (RISC = RNA-induced silencing complex). Just the RISC is able to silence the gene expression, which is known as RNA interference.

Conformation changes and denaturation of biopolymers

- Changes in secondary, tertiary and quaternary structure of biopolymers are denoted as **conformation changes**.
- They can be both reversible and irreversible.
- **‘native’** state of a biopolymer: its **functional** state. Otherwise the biopolymer has been **‘denatured**’.

Denaturation factors

- **Physical:**
  - Increased temperature
  - Ionising radiation
  - Ultrasound
  - .....
- **Chemical:**
  - Changes of pH
  - Changes in electrolyte concentration
  - Heavy metals
  - Denaturation agents destroying hydrogen bonds – urea
  - .....
- Combination of above factors: ionising radiation or ultrasound act directly and/or indirectly (chemically via free radicals)

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