Molecular base of DNA inheritance

Premedical - Biology

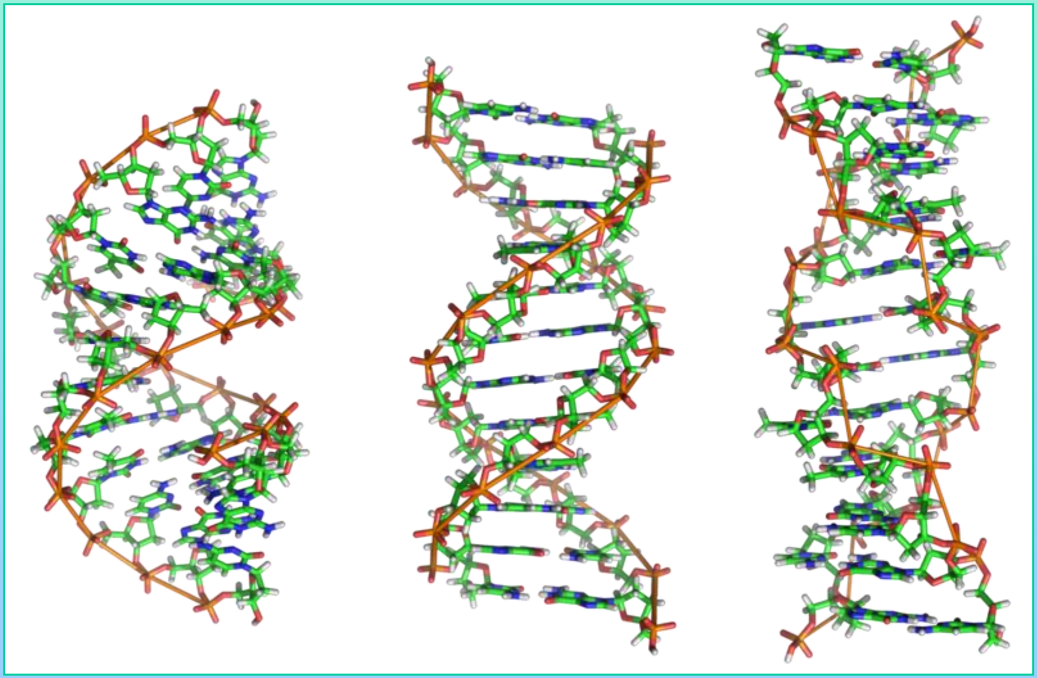
Alternate DNA structures

DNA exists in many possible conformations that include

A-DNA, B-DNA, and Z-DNA forms.

only B-DNA and Z-DNA have been directly observed in functional organisms.

The double helix of **B-DNA** is right-handed, there are approximately 10.5 base pairs per turn, and the diameter of the double helix is 2.37 nm.



From left to right, the structures of A, B and Z DNA

http://biotech.christopher-vidal.com/dnamolecule.htm

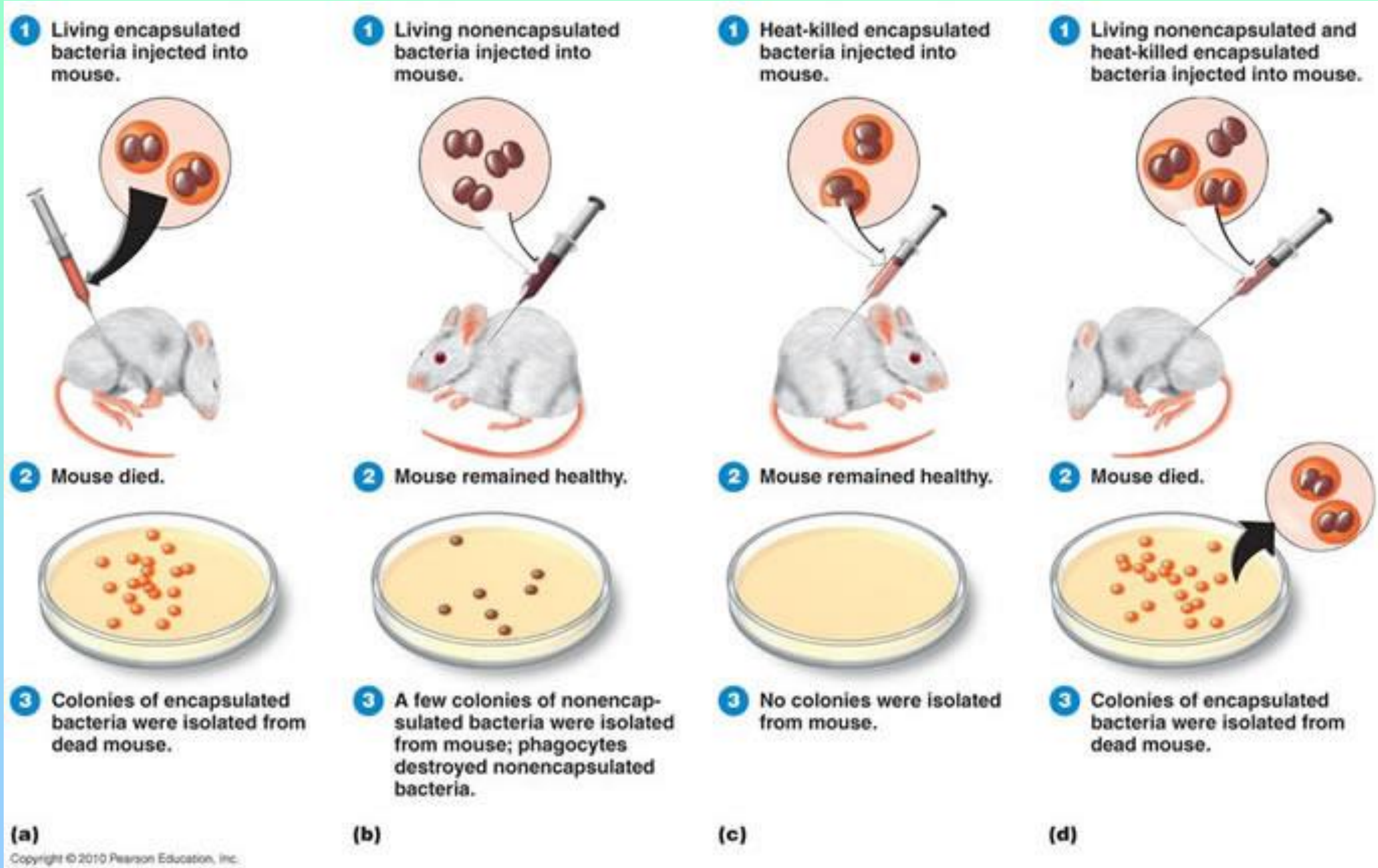
A proof that DNA is a carrier of **genetic information** - 1928

- Griffith‘s experiment of bacterial transformation is a proof, that DNA is carrier of genetic information.

  The main function of DNA is a storage of genetic information and it offers the way, how to have every information in two copies.

  Recombination of bacterial genetic material by transport and intake of naked DNA into recipient cells
- Avery, McLeod, McCarthy (1944) – the same effect with isolated DNA

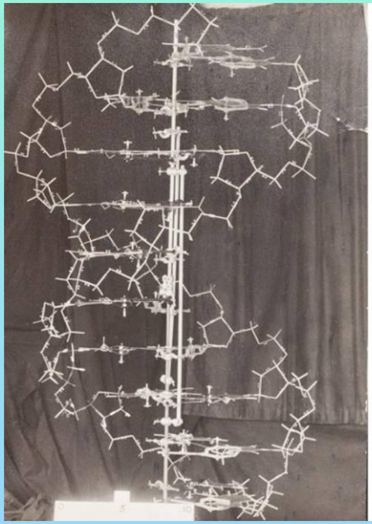
Bacterial transformation

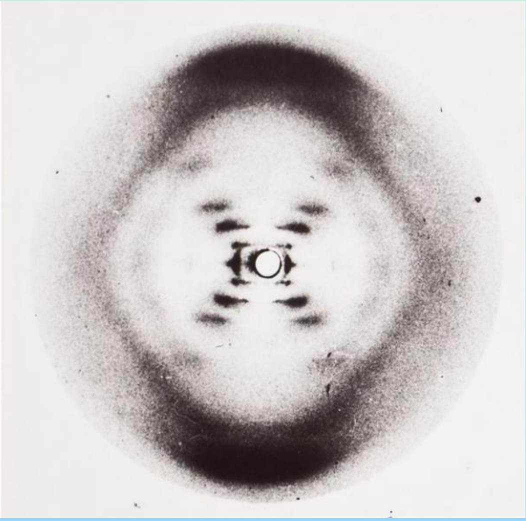


S-smooth with capsule, R-rough non-encapsulated *S. pneumonie*

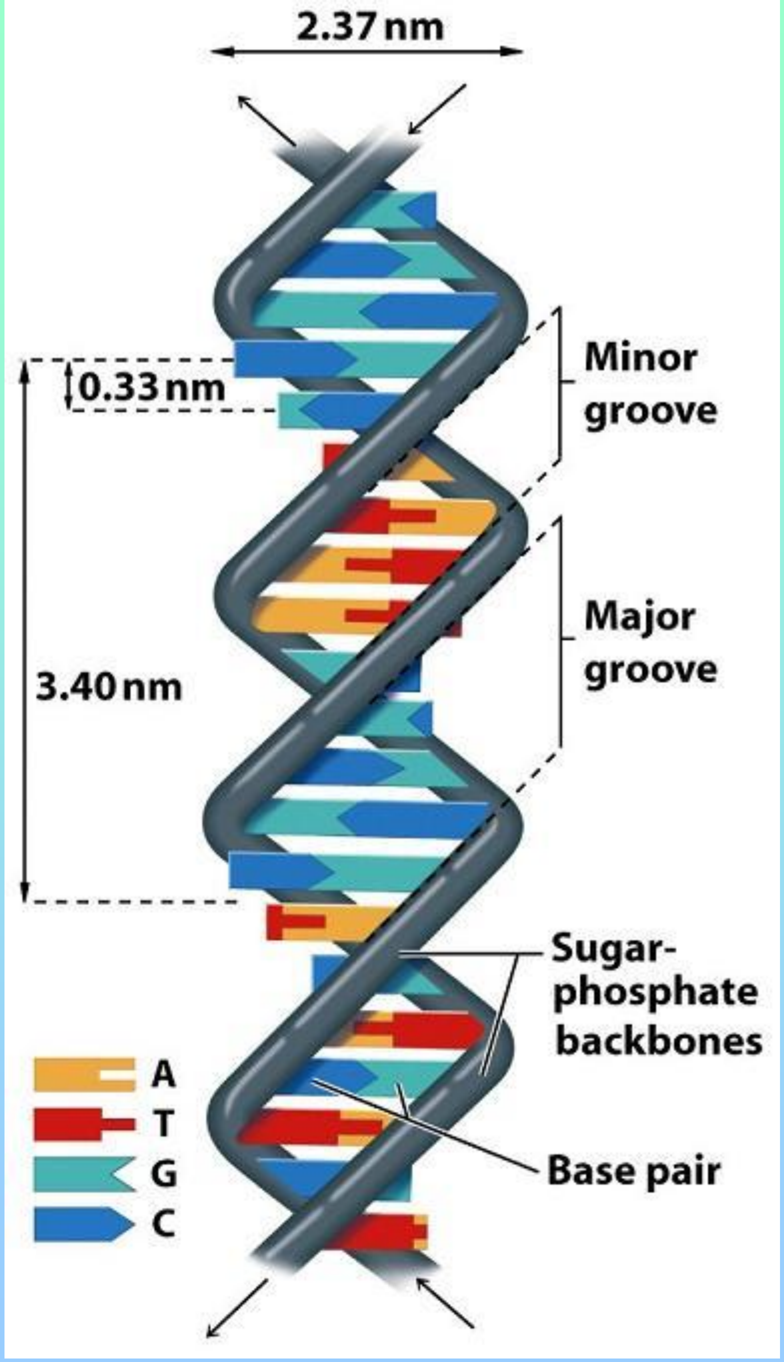
In 1953 **James D. Watson a Francis Crick** used data of **x-ray diffraction** collected by **Rosalind Franklin** and proposed that double helix is the three-dimensional structure of DNA.

The B form described by James Watson and Francis Crick is believed to predominate in cells.





DNA controls the development of biochemical, anatomical and physiological and behavioral traits of **all known living organisms.**



https://sandwalk.blogspot.com/2007/12/dna-denaturation-and-renaturation-and.html

Two families of nitrogenous bases: **pyrimidines, purines**

Pyrimidine has a six-membered ring of carbon and nitrogen;

Cytosine (C), Thymine (T) and Uracil (U)

Purines - the six-membered ring is fused to a five-membered ring;

Adenine (A), Guanine (G)

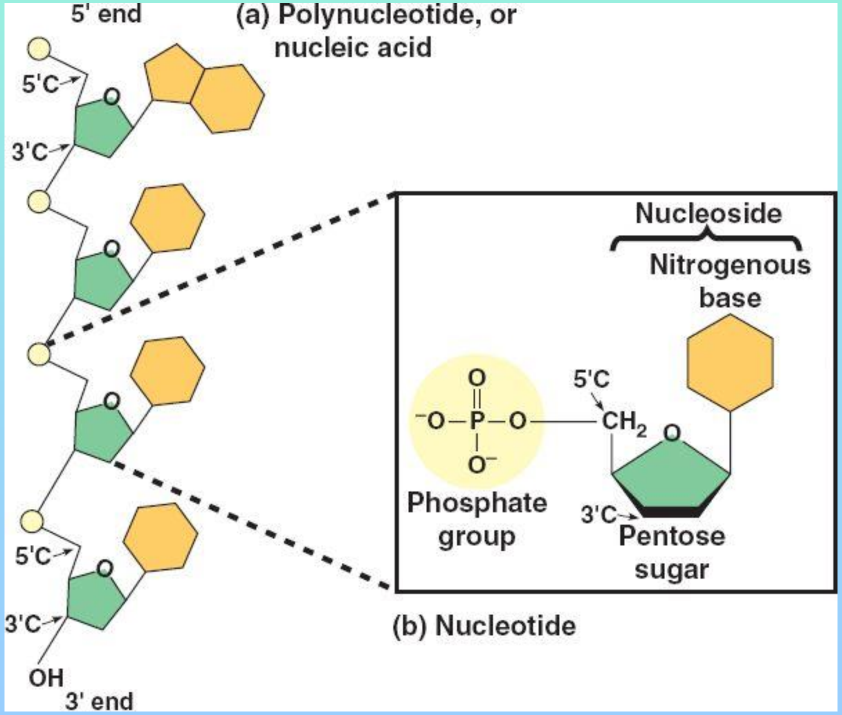
Monomers are nucleotides:

organic molecule called

a nitrogenous base, a pentose

(five-carbon sugar) and

phosphate group



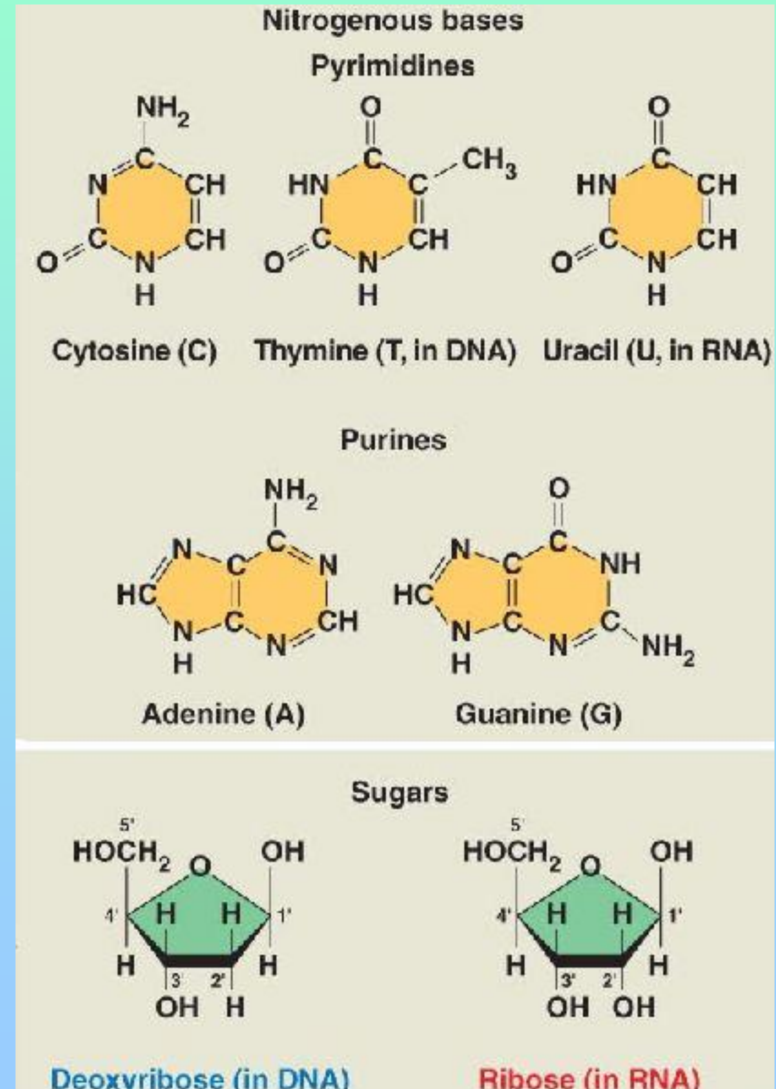
Nucleotide

Nucleoside - nitrogenous base bound to sugar

Bases:

Adenine, guanine and cytosine are found in both types of nucleic acid.

Thymine is found only in DNA and uracil only in RNA.



Sugars:

Ribose in RNA,

Deoxyribose in DNA

Two polynucleotides turn around imaginary axis to form **double helix.**

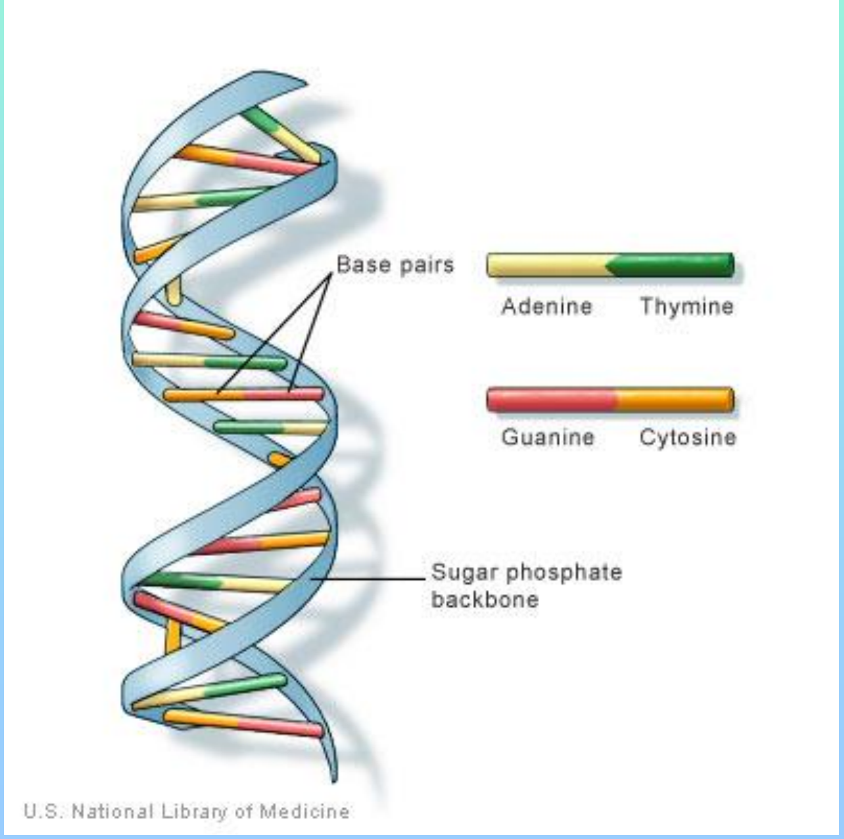
Nucleotides are bound by **covalent bonds** called **phosphodiester linkages** between phosphate of one and the sugar of the next.

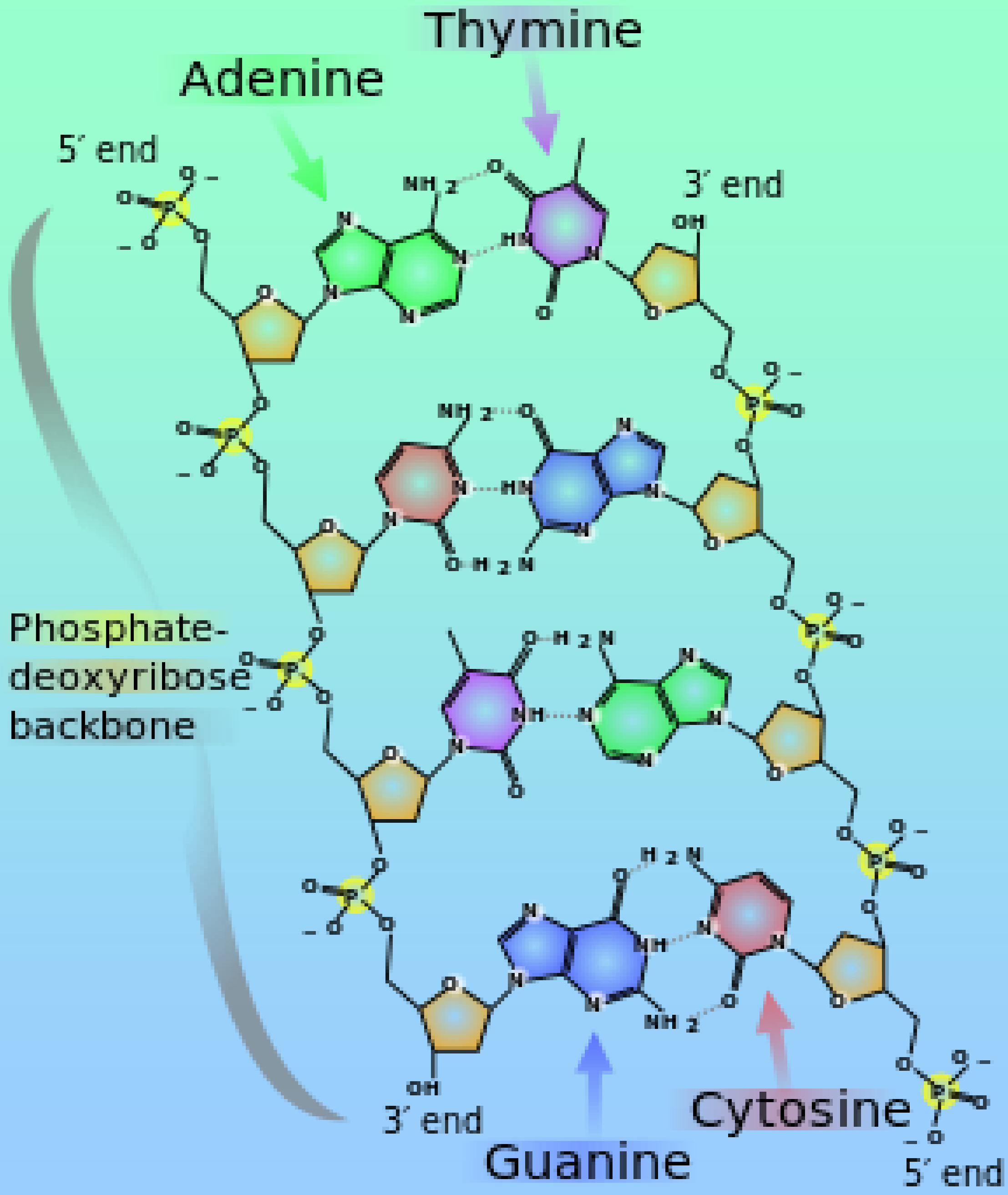
Two polynucleotides are held

by **hydrogen bonds** between

the paired bases and

by **van der Waals** attractions.

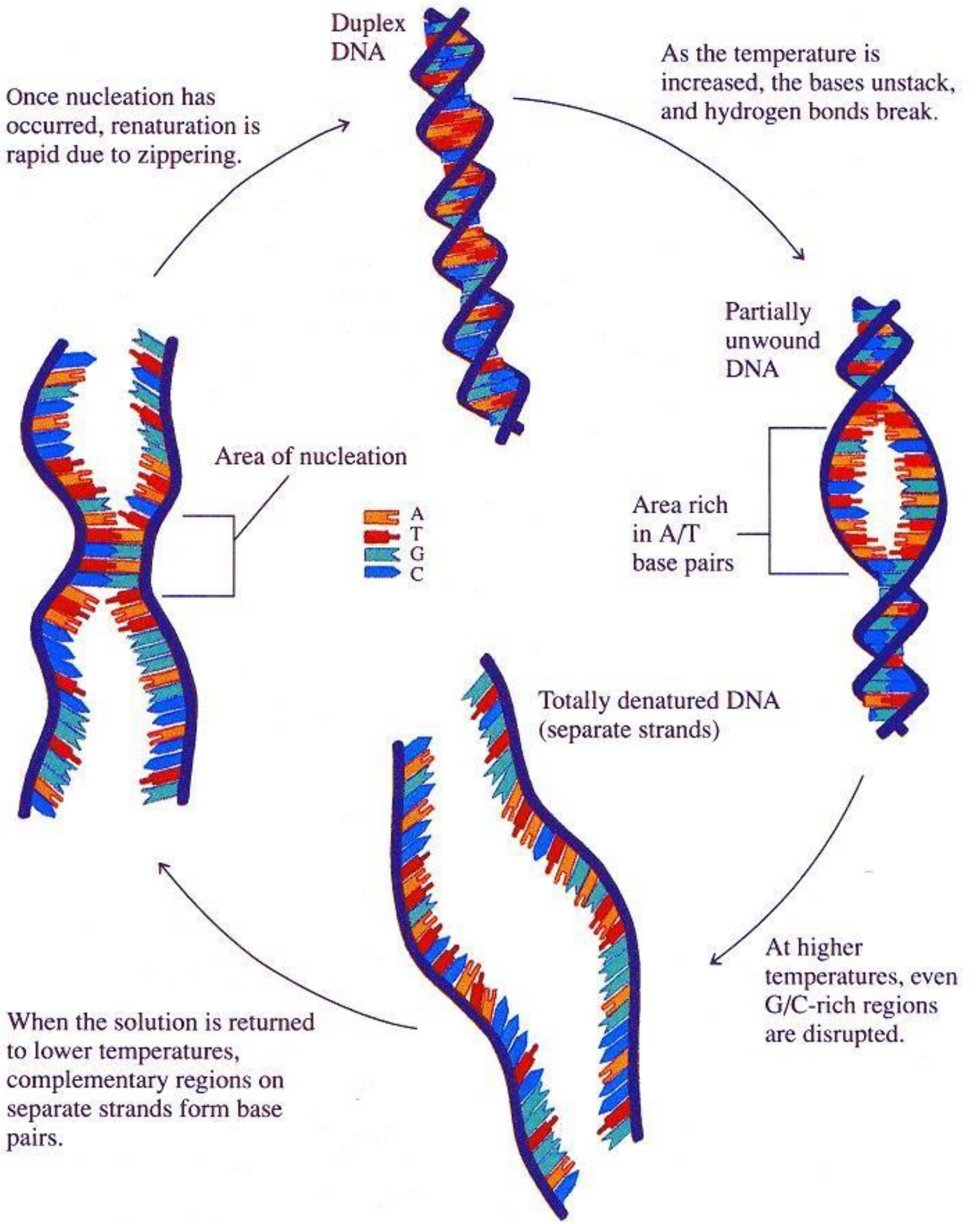




The greater the number of GC pairs, the tighter and more stable the DNA is.

Hybridization (ss + ss => ds) a formation of a complementary nucleic acid duplex by association of single strands, usually between DNA strands or previously unassociated DNA strands.

- **DNA denaturation** (ds=> ss + ss), also called **DNA melting**, is the process, by which double-stranded deoxyribonucleic acid unwinds and separates into 2 single-strands backbones.



Moran, L.A. et al. (1994) "Biochemistry" Neil Patterson Publishers/Prentice Hall p. 24-16

http://sandwalk.blogspot.cz/2007/12/dna-denaturation-and-renaturation-and.html

DNA molecules - thousands or millions of base pairs

Adenine always pairs with thymine,

Guanine always pairs with cytosine.

Replicaton

Two strands of double helix

are **complementary** and

are **antiparallel.**

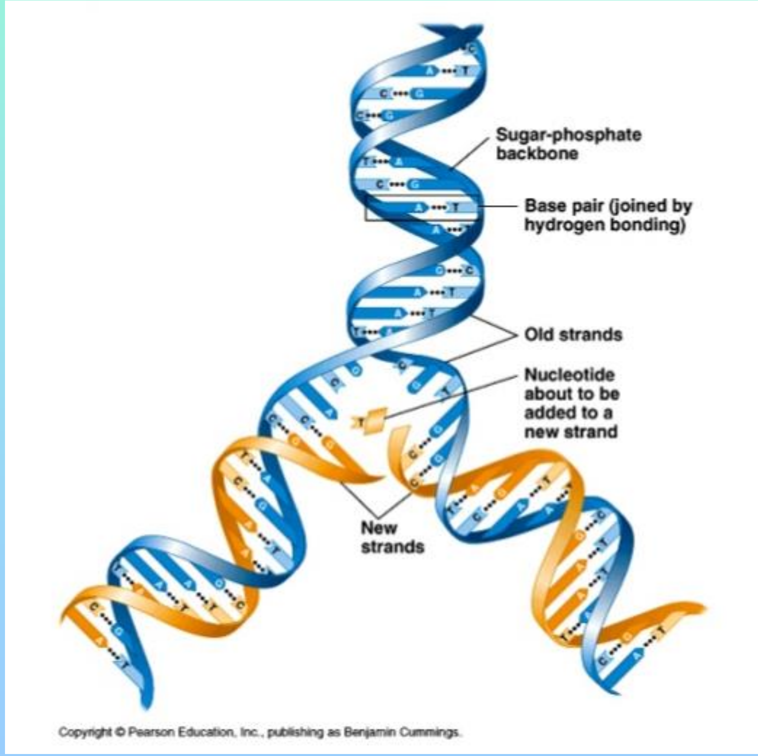
In preparation for cell division,

each strand serves

as a template to order nucleotides

into a new complementary strand

= **Semiconservative replication**



Replication

Circular bacterial chromosome has a **single starting point – origin = ORI** and replicates by the mechanism **of rolling circle.**

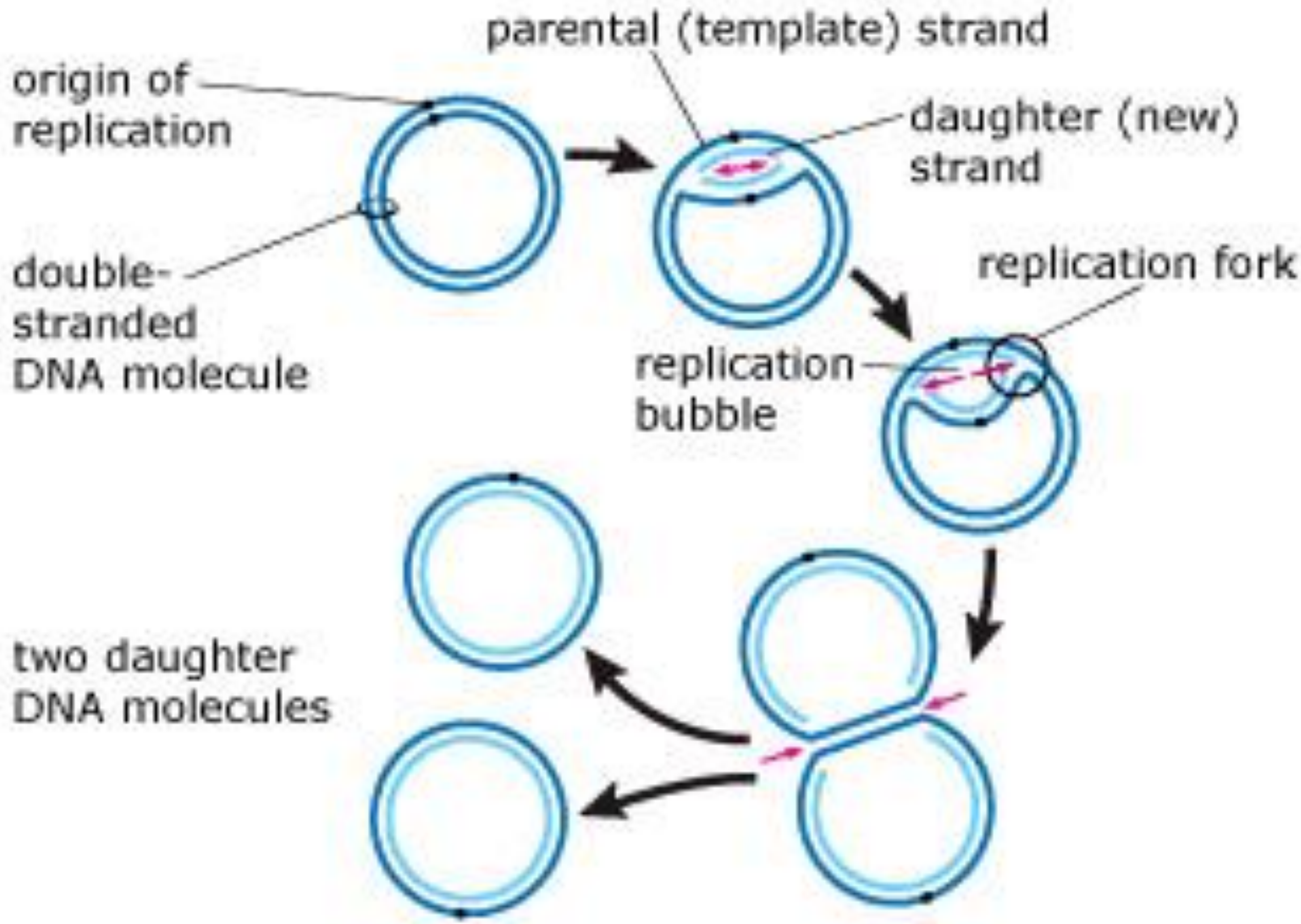
Replication of eukaryotic genome starts in **many starting points**, runs simultaneously and **asynchronously**

DNA replication proceeds in both directions, at the ends of replication bubble is a **replication fork.**

Enzymes of replication:

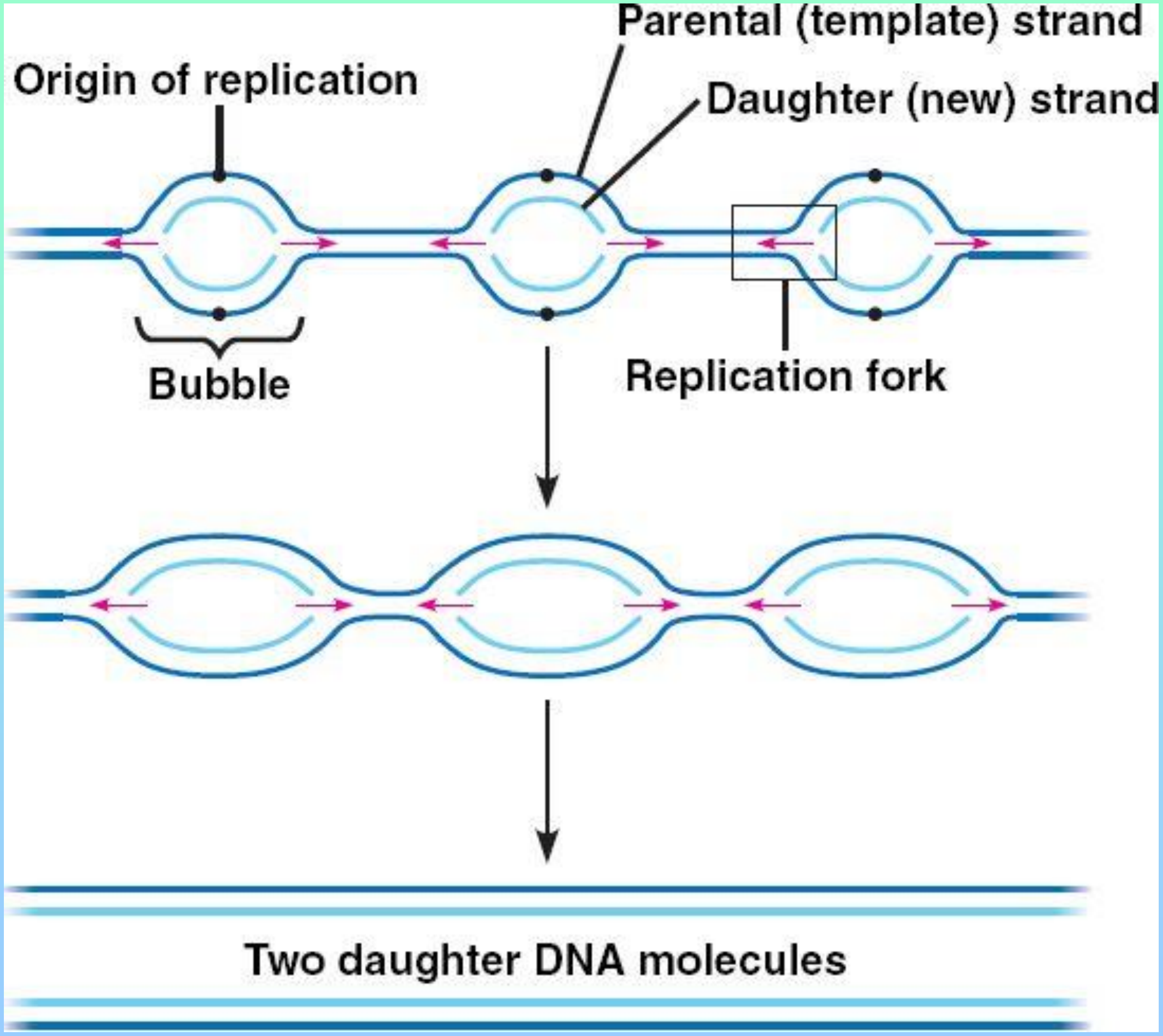
DNA polymerase – addition of nucleotides **only to the free 3‘ end**, new strand can elongate only in one direction (5´→ 3´), + and correction of mistakes

Origin of replication in *E. coli*



From *Biology* by Campbell and Reece

Origins of replication in *Eukaryotes*



Replication

Helicase – unwinding

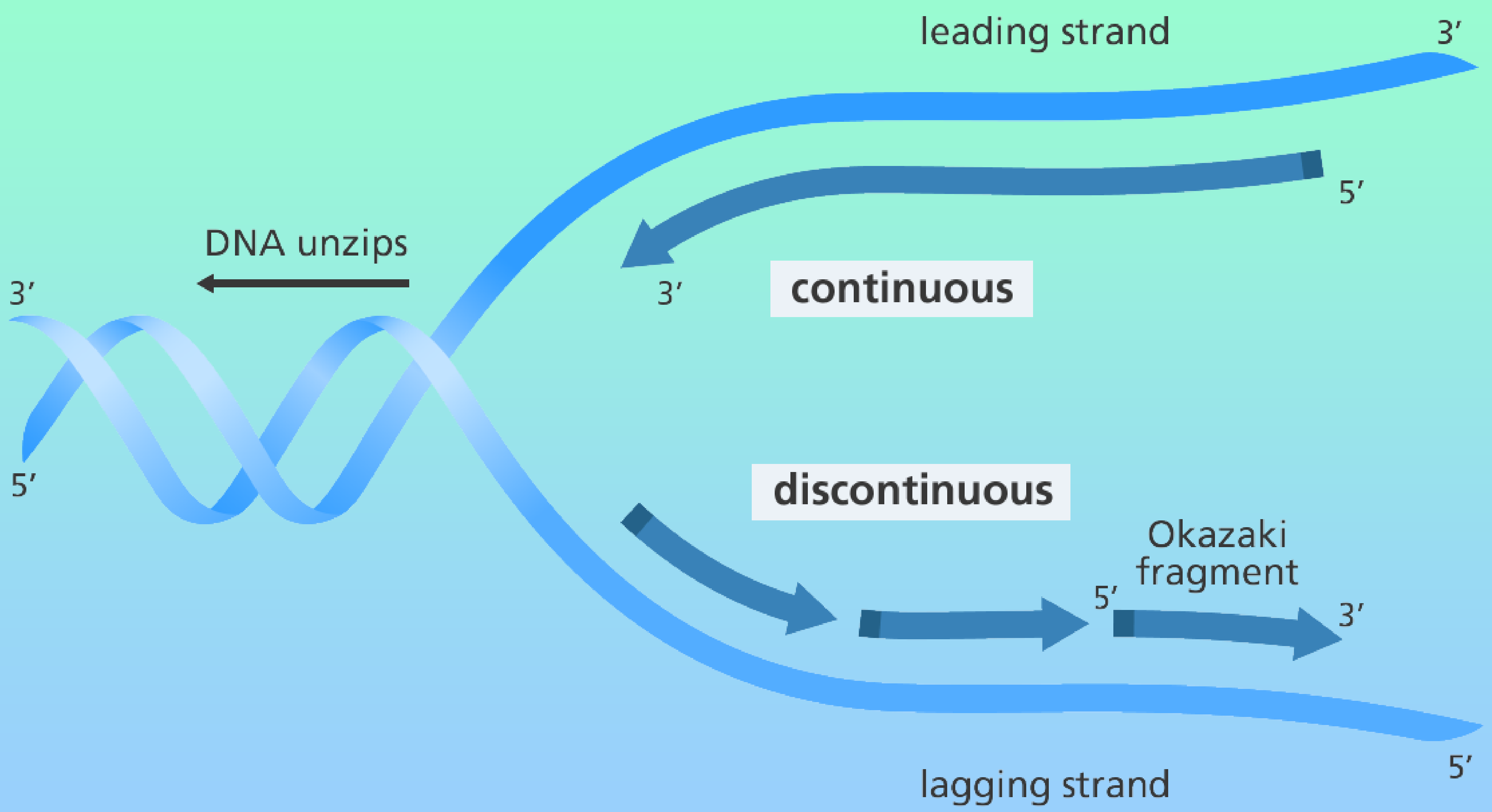
Primase - RNA primers

- **leading strand: a** new strand in the direction 5´→ 3´
- **lagging strand:** is synthetized discontinuously by series of segments = **Okazaki fragments** in the direction 5´→ 3´, but the direction of lagging strand is 3´→ 5´

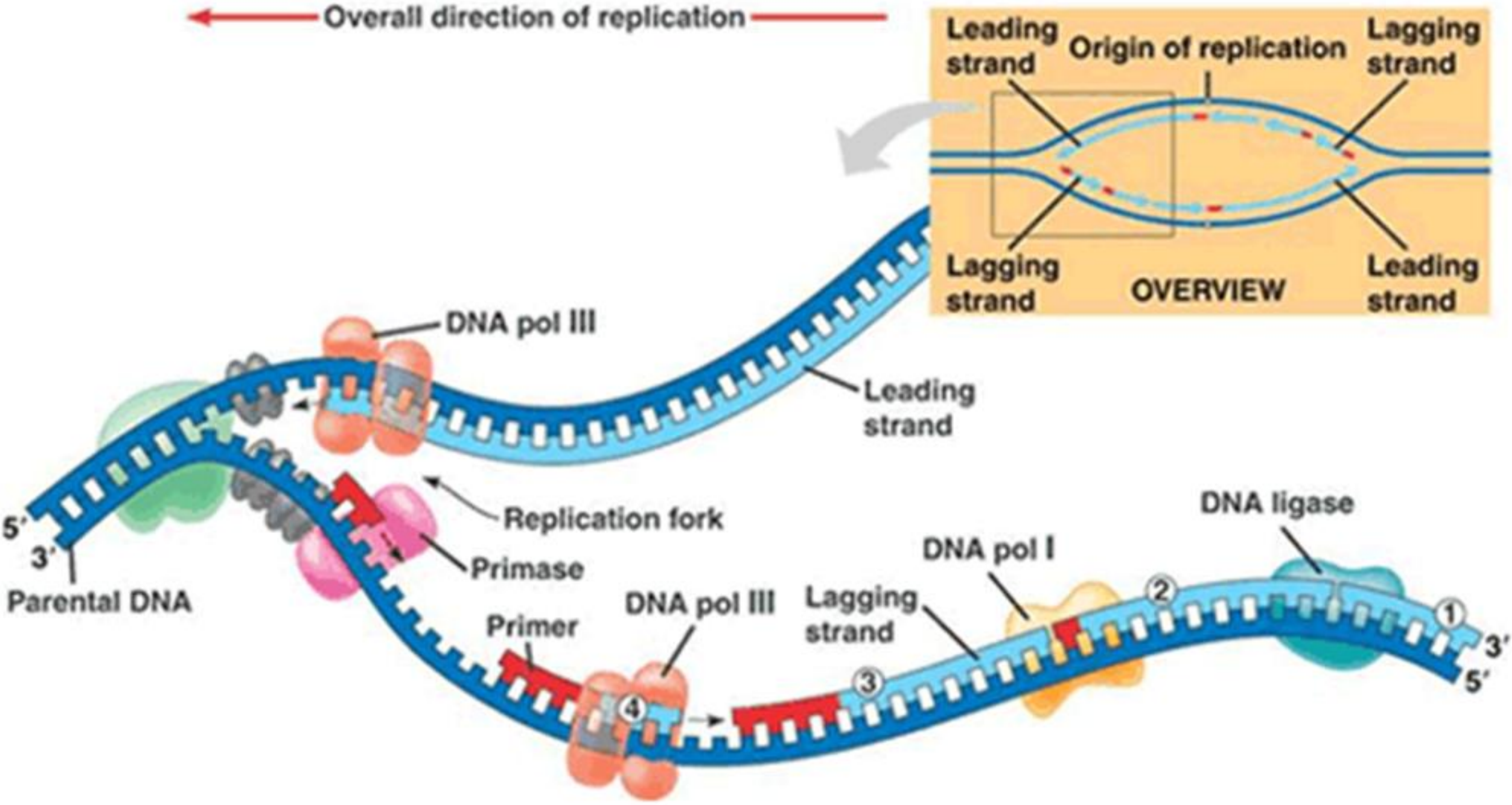
enzyme **DNA Ligase** connects these segments

Primers are short segments of RNA, 100 to 200 bases long. Okazaki fragments occur in replicating DNA in both prokaryotes and eukaryotes. They form up on the ‘lagging’ strand during replications and are joined by ligation. (Reiji Okazaki, Japanese geneticist.)

DNA replication fork



Replication



Human chromosomes:

22 pairs of **autosomes**

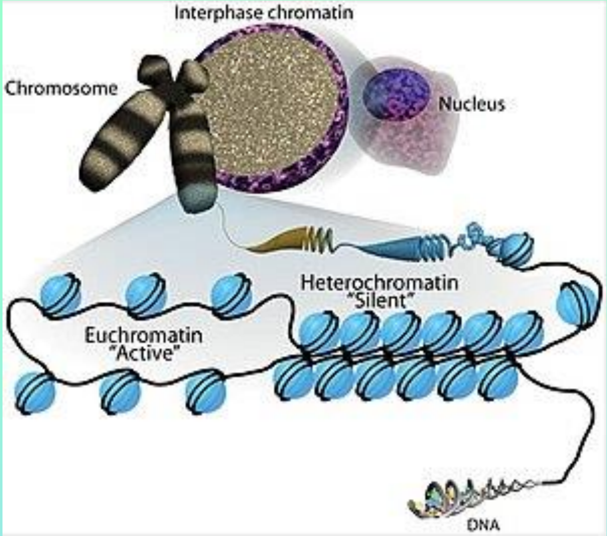
1 pair **of gonosomes (heterochromosomes)**

Karyotype: men **46, XY,**

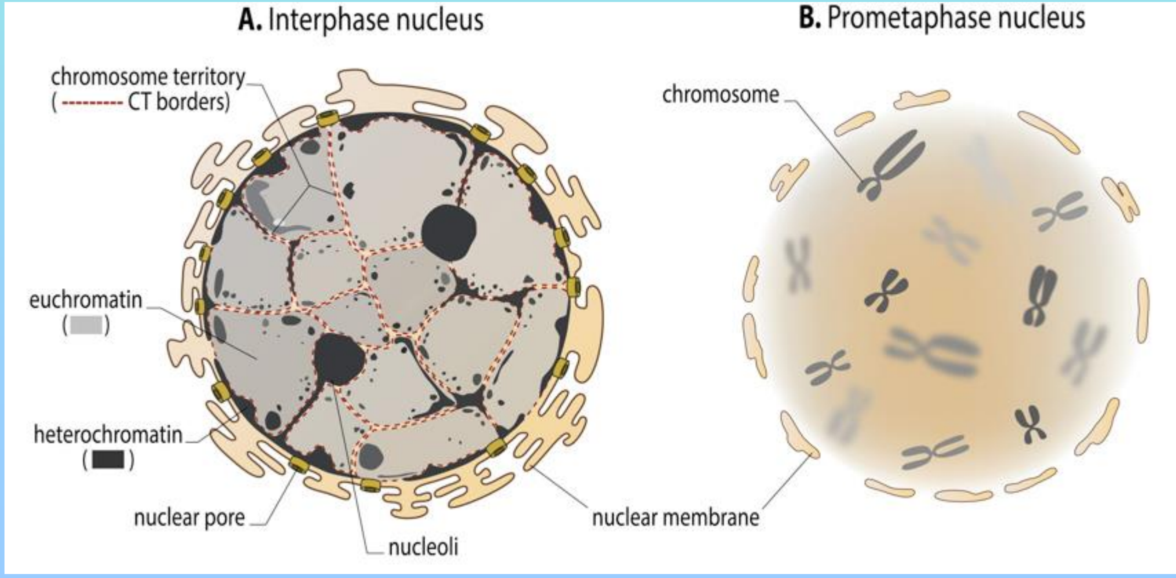
women **46, XX**

Euchromatin is

- despiralized in interphase
- spiralized in mitosis
- contains structural genes

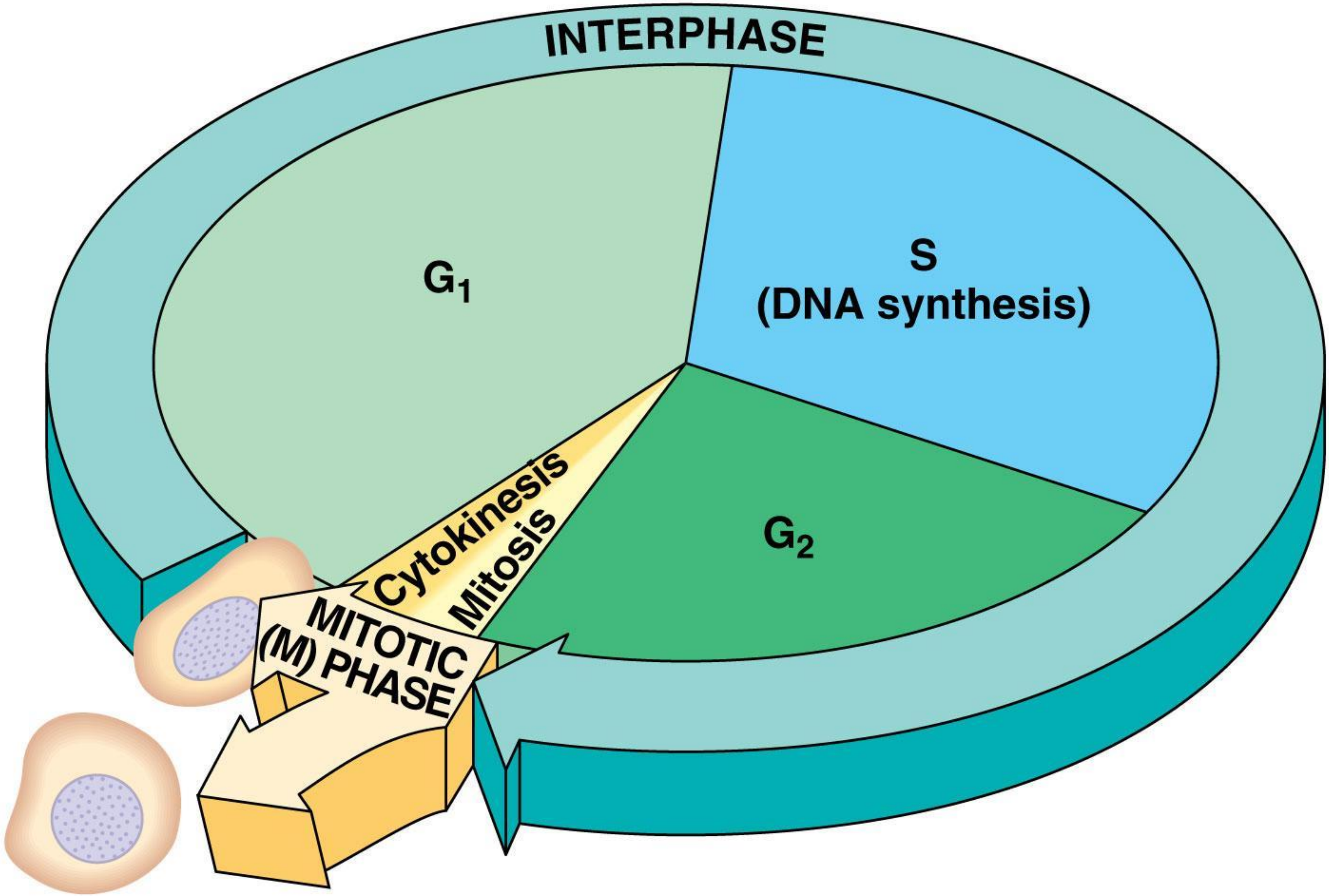


File:Sha-Boyer-Fig1-CCBy3.0.jpg



https://www.mbi.nus.edu.sg/mbinfo/what-are-chromatin-heterochromatin-and-euchromatin

Cell cycle



INTERPHASE
G_1
S
(DNA synthesis)
G_2
Cytokinesis
Mitosis
MITOTIC
(M) PHASE

Heterochromatin

– mostly repetitive sequences

Constitutive – centromeres of all chromosomes

Facultative - structurally euchromatin, but behaves as heterochromatin - **one of two X chromosomes in women = genetically inactive X = sex chromatin = Barr body**

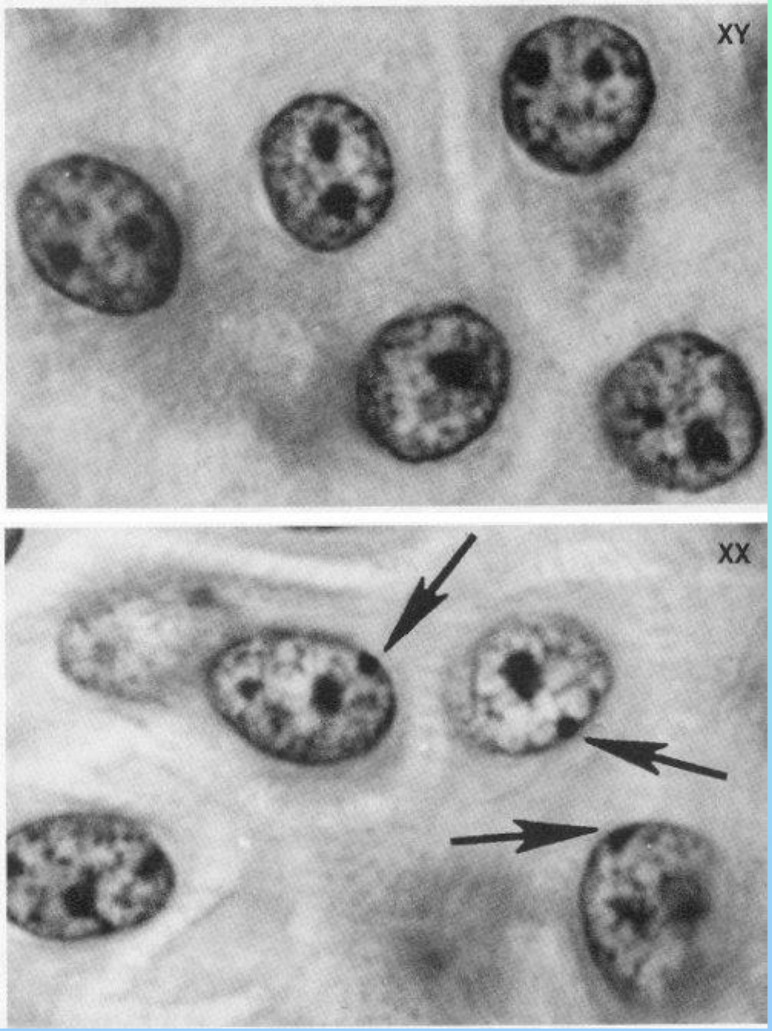


Figure after M. Barr (1963) by SM Carr

Ultrastructure of chromatin, chromosomes

- **DNA**
- **Histones – basic proteins**

H1, H2A, H2B, H3, H4

- **Non-histone proteins**

The whole length of DNA in diploid state is cca 2 m. Human genome contains cca 30 000 structural genes.

Organization of euchromatin in interphase

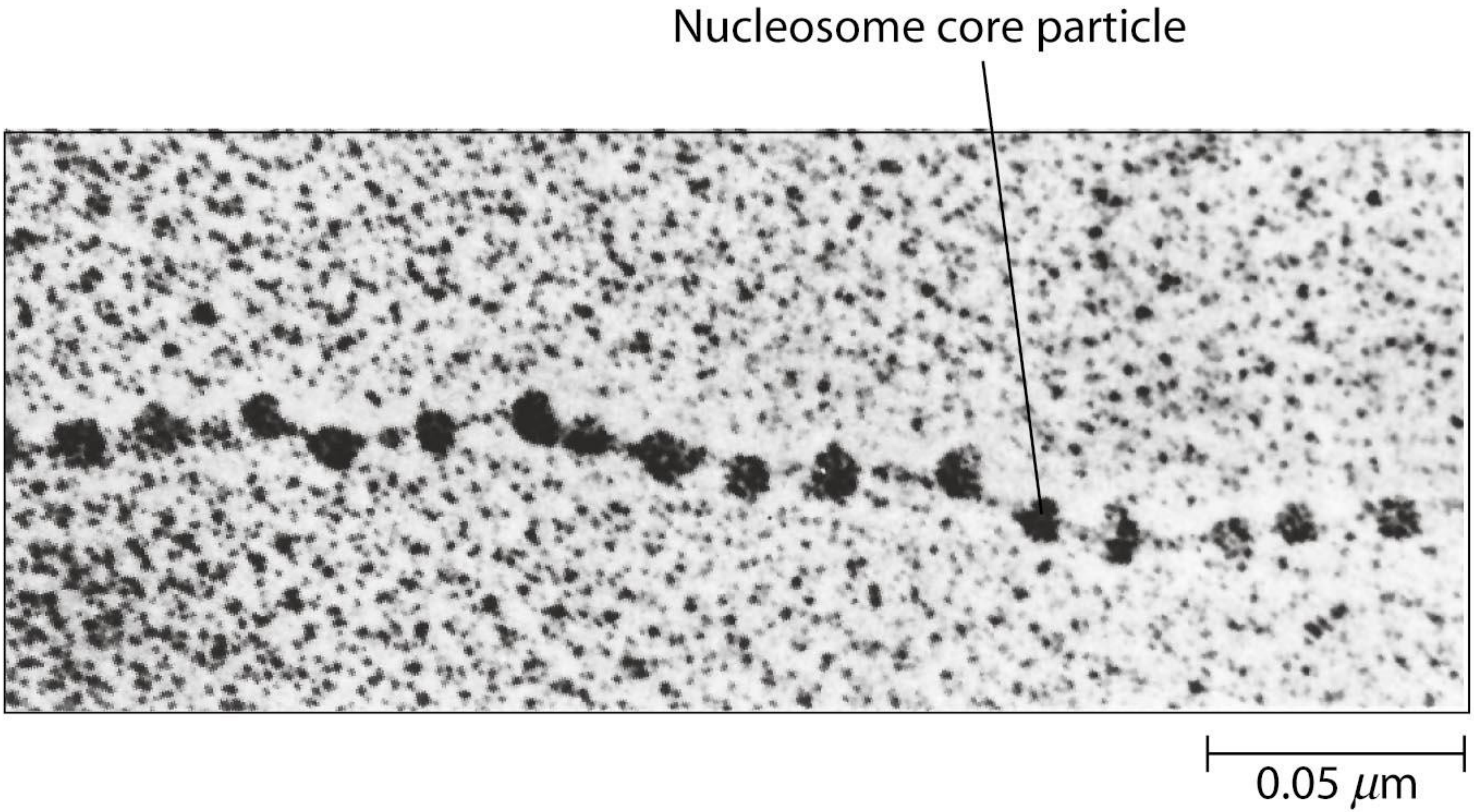
Nucleosome: **„bead on the string“**

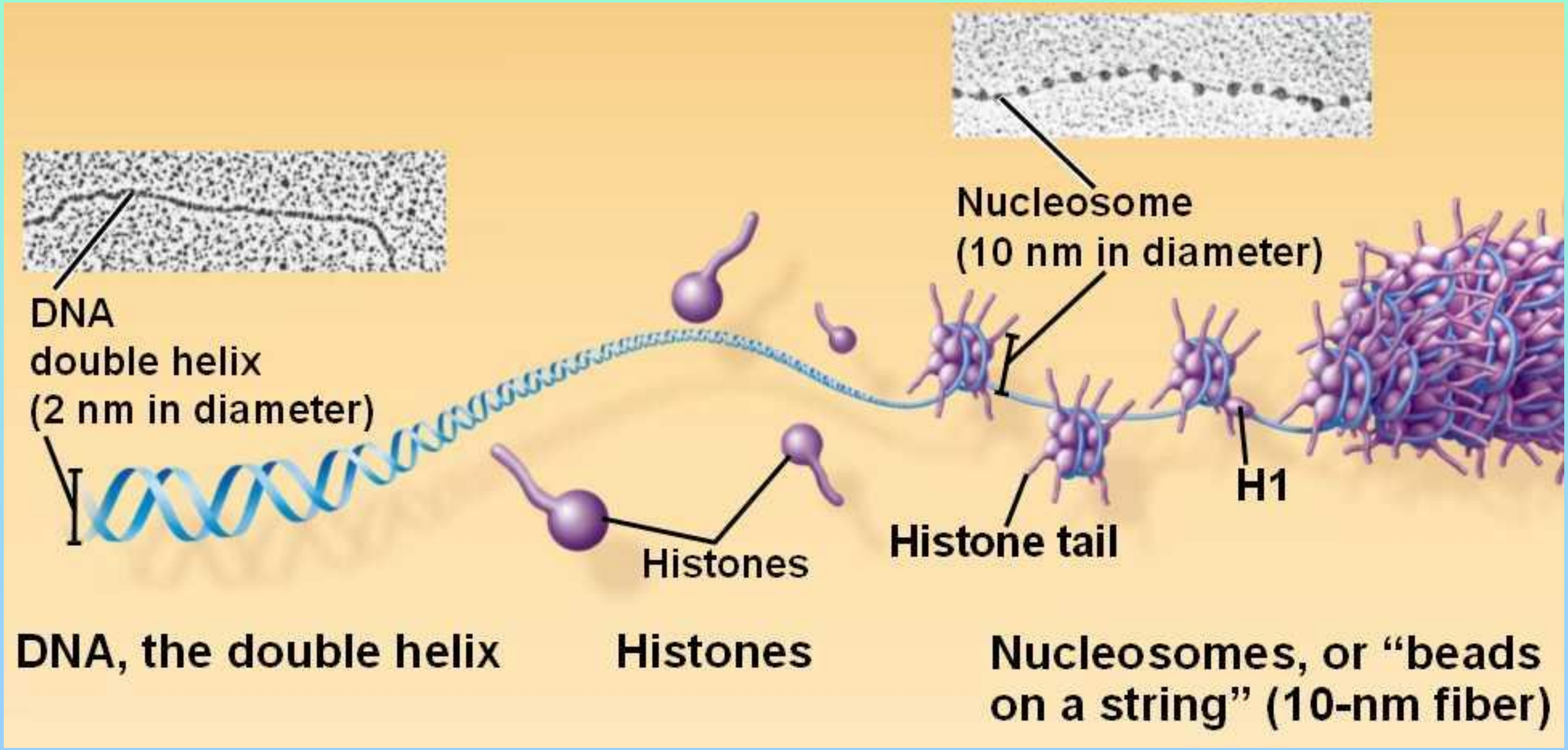
DNA double helix + histone core

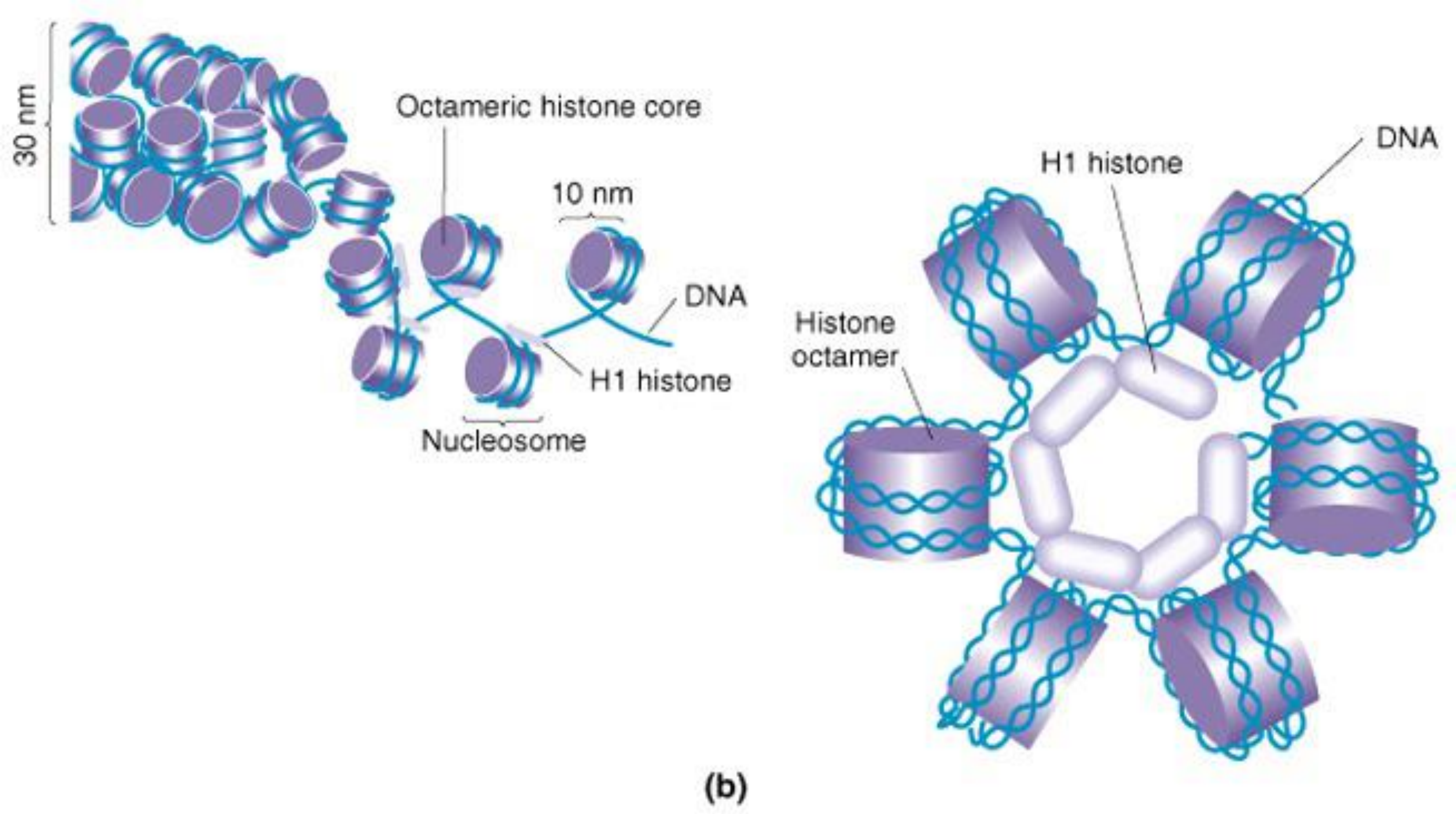
- Histone core = octamer of two copies of H2A,

  H2B, H3, H4 histons

- DNA double helix is turned around the core
- spacer segment between two nucleosomes is free or associated with H1 histone (appearance of beads on a string)


Nucleosome core particle
0.05 μm


Nucleosome
(10 nm in diameter)
DNA
double helix
(2 nm in diameter)
Histones
Histone tail
H1
DNA, the double helix
Histones
Nucleosomes, or "beads on a string" (10-nm fiber)



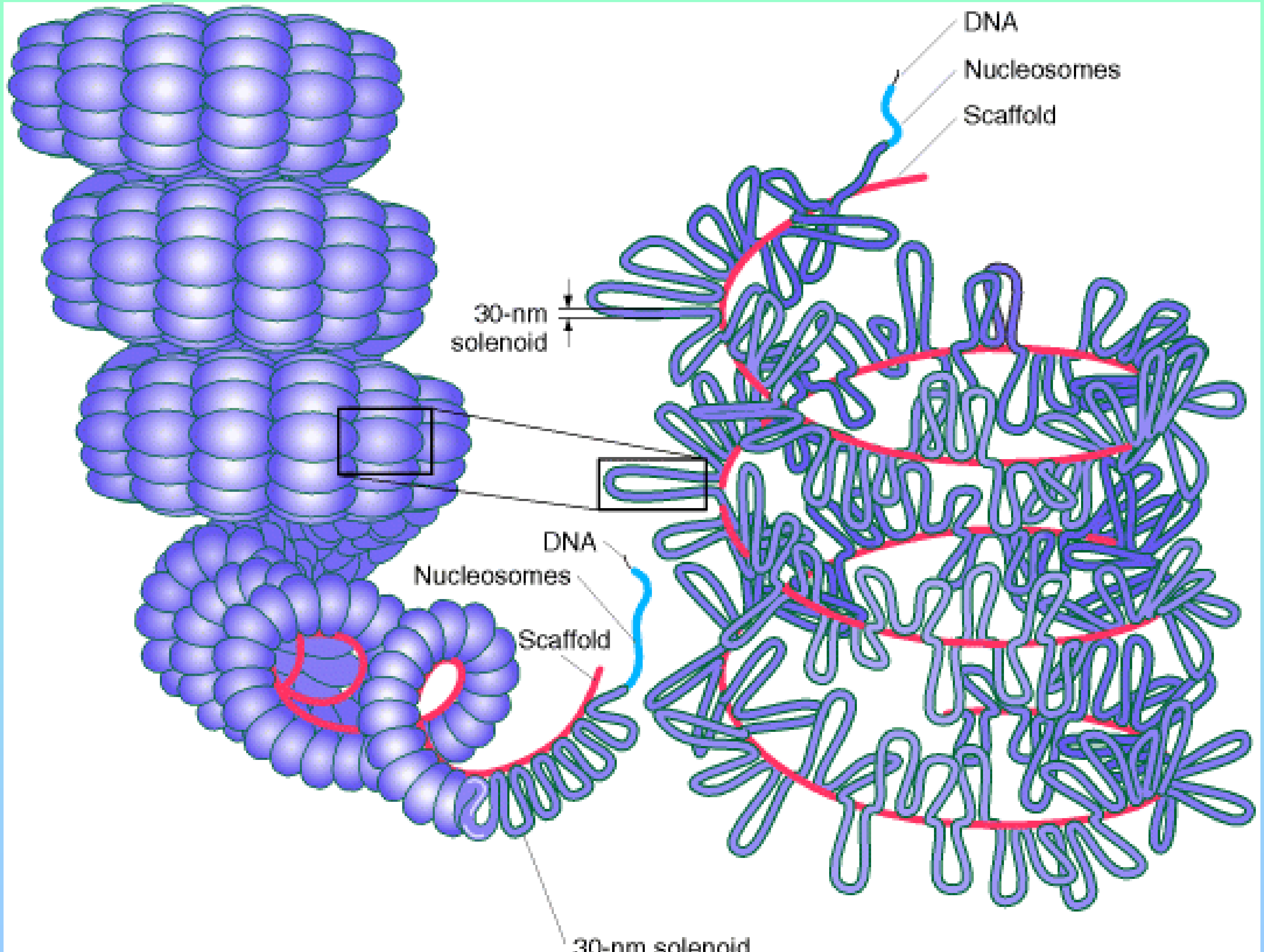
http://www.mun.ca/biology/desmid/brian/BIOL2250/Week_Two/1GeneW2b.html

Condensation of chromatin into chromosomes

- String of nucleosomes is coiled into **solenoid** (6 nucleosomes in each turn)

- Solenoid is packed into loops attached to n**onhistone protein scaffold** (Laemli loops)

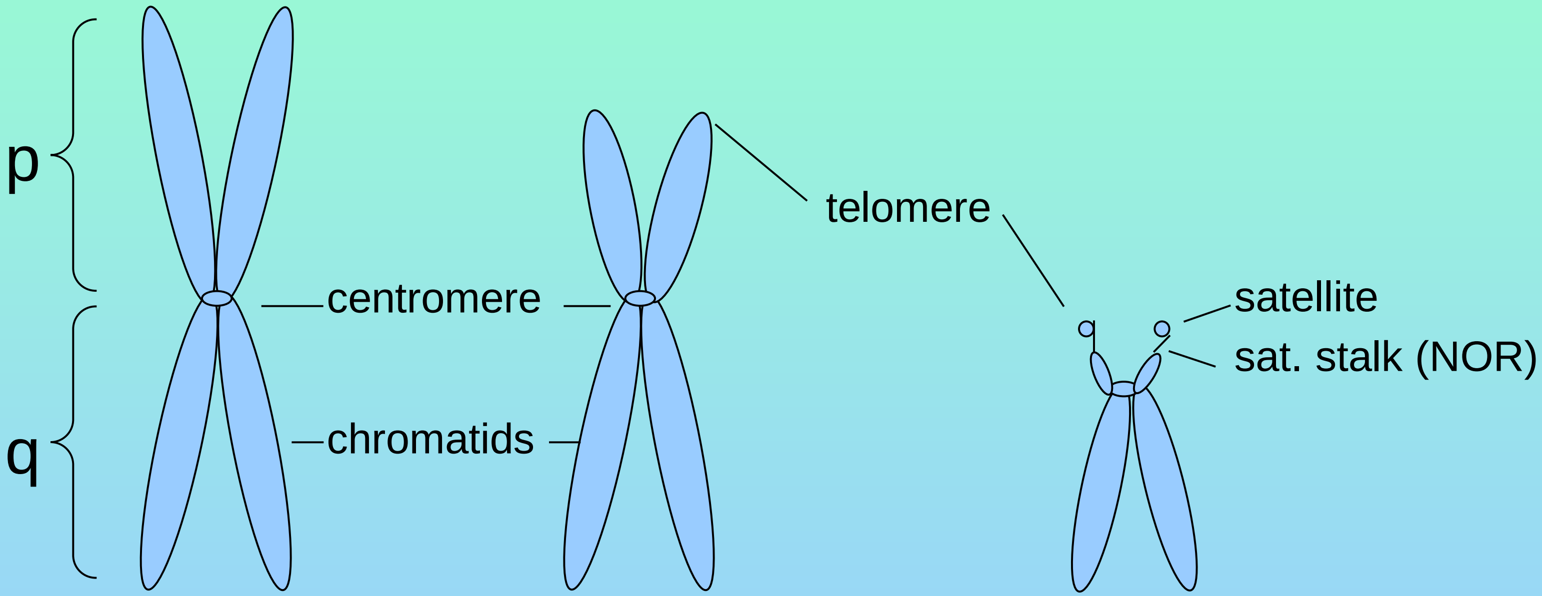
- nonhistone protein scaffold with loops is coiled into spiral structure of **chromatides**



http://www.mun.ca/biology/desmid/brian/BIOL2250/Week_Two/1GeneW2b.html

Chromosome / in metaphase

metacentric **submetacentric** **acrocentric**

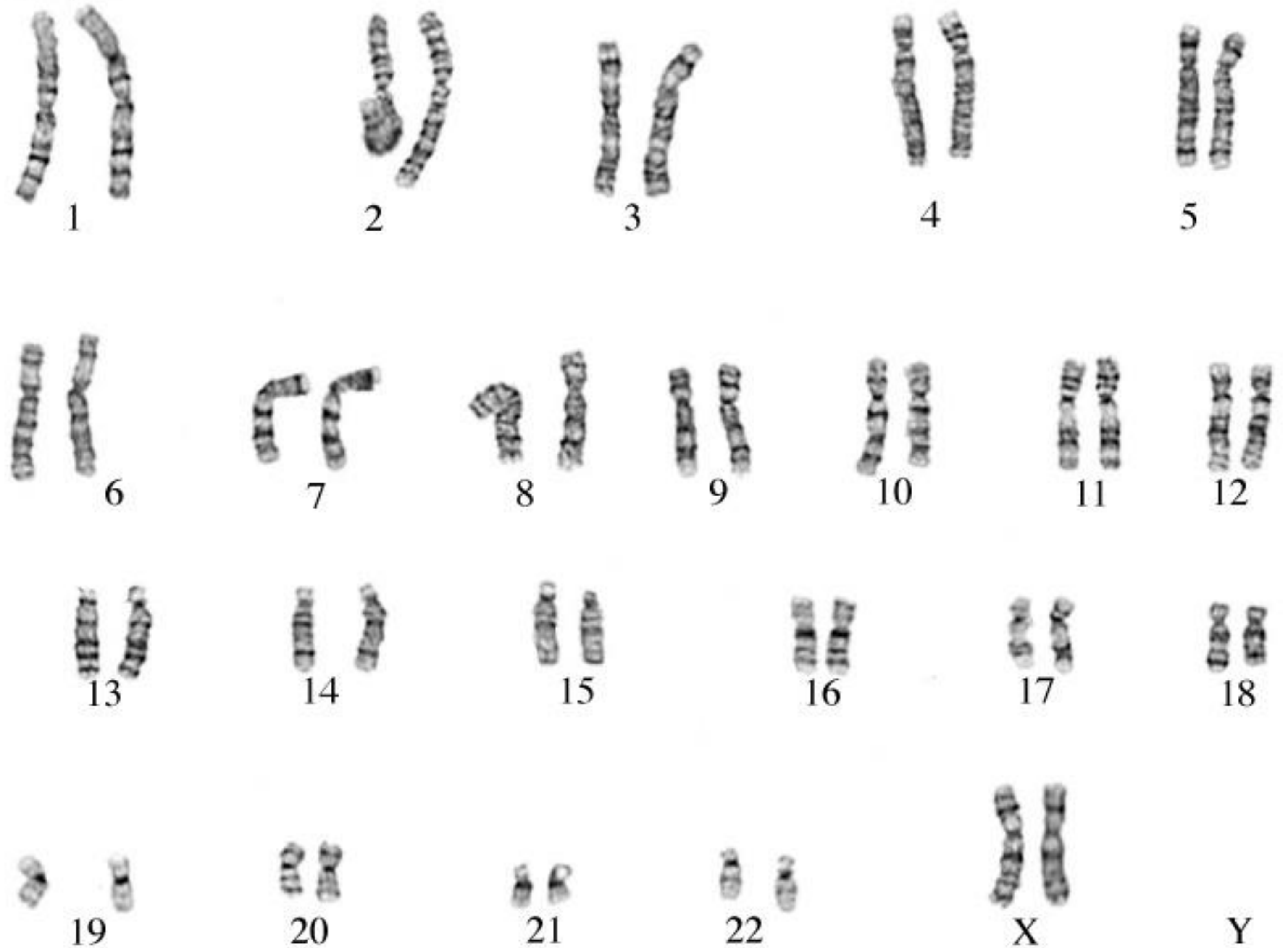


p = short arm

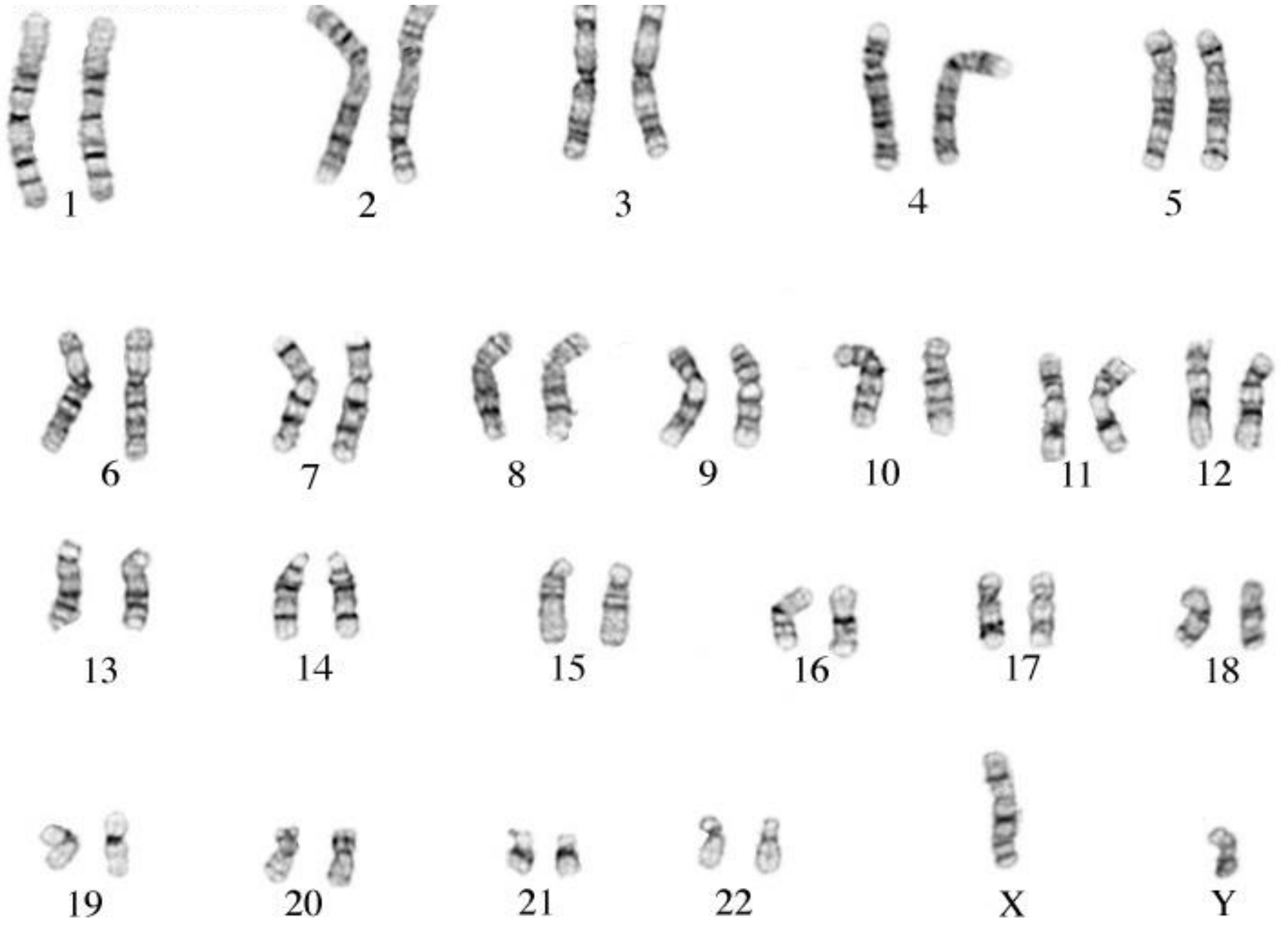
q = long arm

NOR = nucleolus organizer region (rRNA genes)

Karyotype of woman 46,XX – G banding

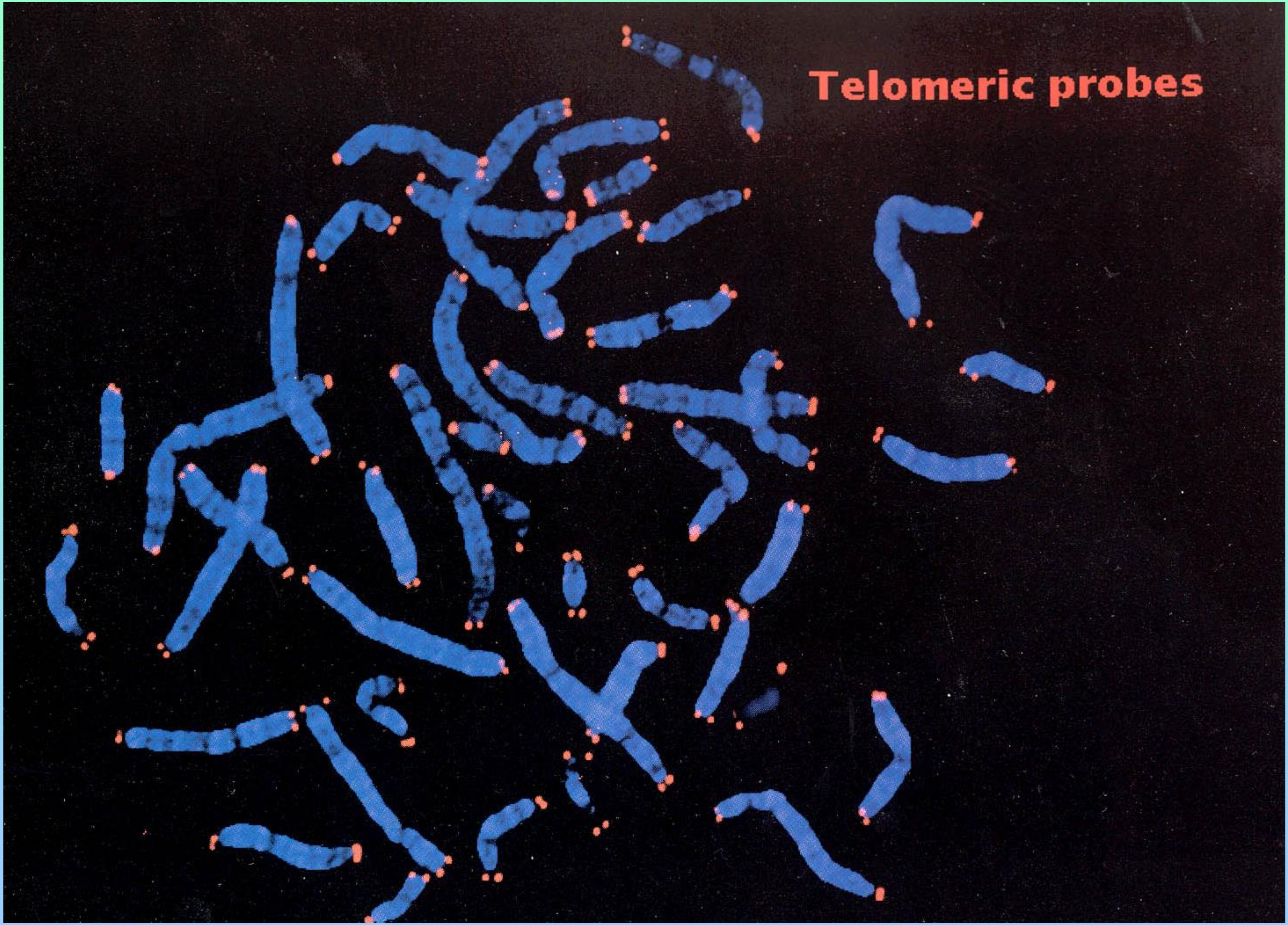


Karyotype of man - 46,XY – G bands



Telomeres

- multiple repetitions of one short nucleotide sequence TTAGGG [human]
- telomeric DNA protects genes from being eroded, protects from fusions
- **telomerase is** special enzyme
- reduction of number of telomeres after each replication
- abnormal activity of telomerase in tumor cells


Telomeric probes

Nucleotides

- are **structural units of RNA and DNA**
- serve as **sources of chemical energy: ATP, GTP**
- participate **in cellular signaling: cAMP, cGMP**
- are incorporated into **cofactors** of enzymatic reactions: **CoA, FAD, FMN, and NADP**

ATP powers cellular work

• multifunctional nucleotide used in cells as a **coenzyme**

"MOLECULAR UNIT OF CURRENCY" of intracellular energy transfer

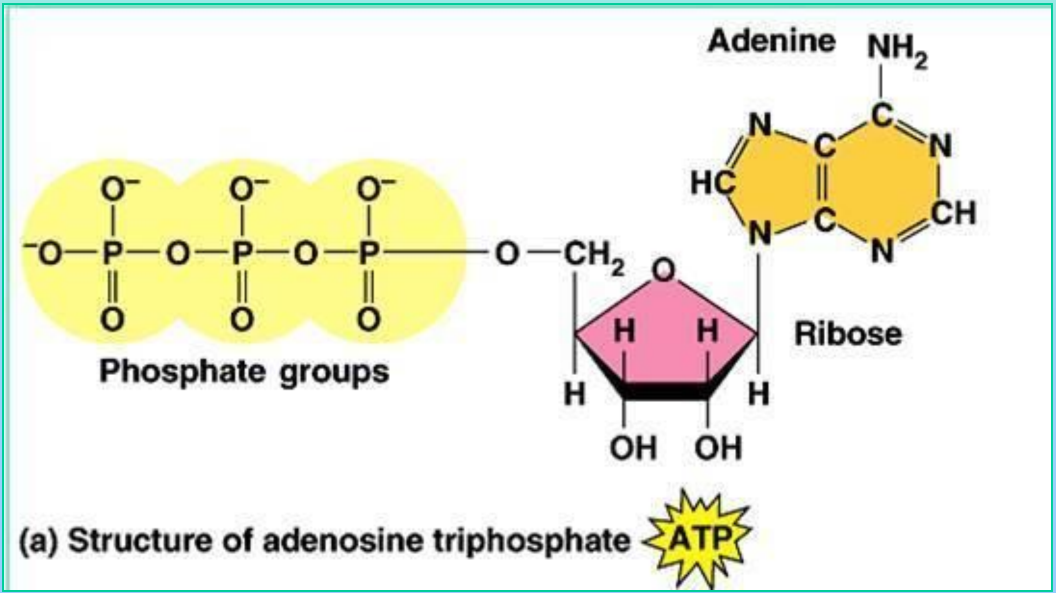
• produced in **photophosphorylation and cellular respiration**

• used in many cellular processes, including biosynthetic reactions, motility, and cell division.

ATP - closely related to one type of nucleotide found in nucleic acid [base **adenine** bonded to **ribose]**

• in RNA one phosphate group is attached to ribose

• chain **of three phosphate** groups attached to ribose



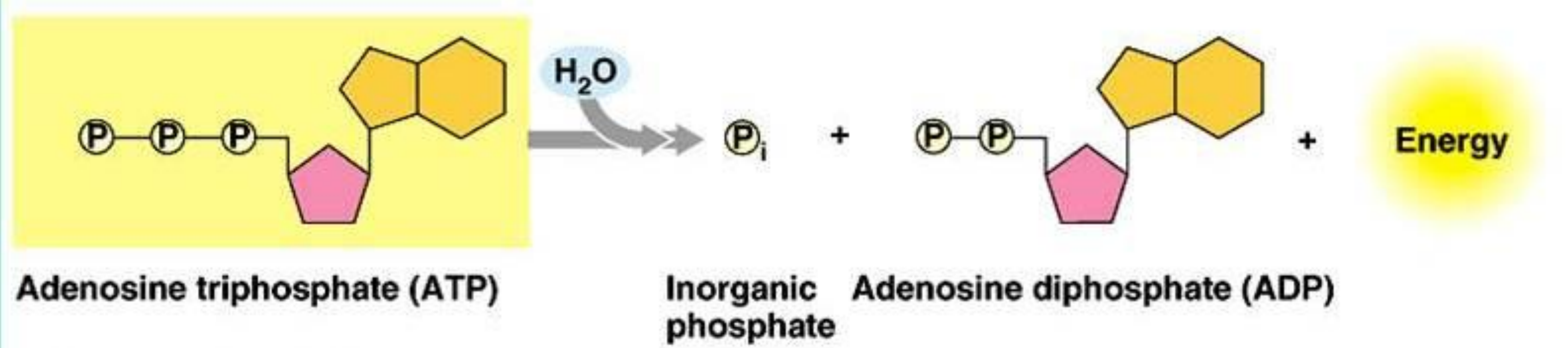
(a) Structure of adenosine triphosphate

Hydrolysis - inorganic phosphate leaves ATP

became adenosine diphosphate - ADP

The reaction is exergonic

High-energy phosphate bonds



(b) Hydrolysis of ATP

Campbell, Neil A., Reece, Jane B., Cain Michael L., Jackson, Robert B., Minorsky, Peter V.**, Biology**, Benjamin-Cummings Publishing Company, 1996 –2010.