Nucleic acids: Structure, properties and signifikance. Nuclear DNA, histones

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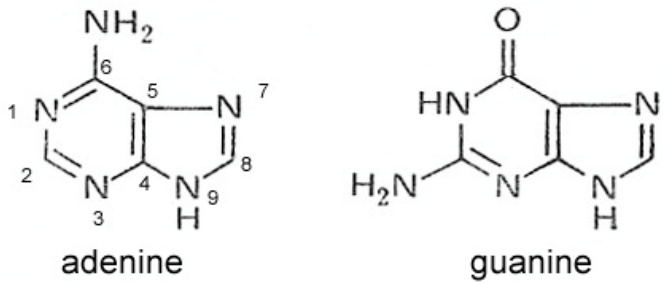
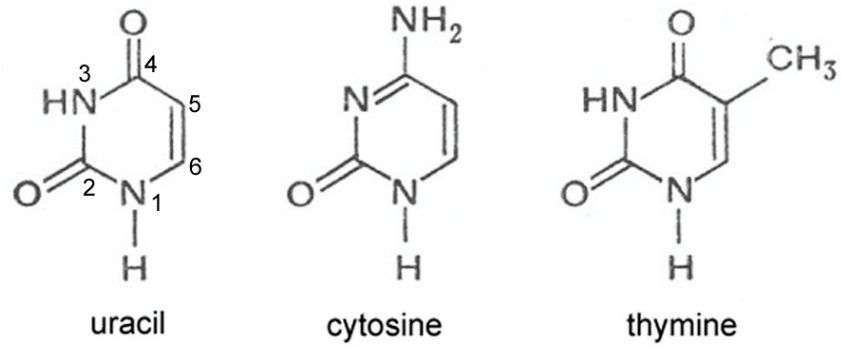
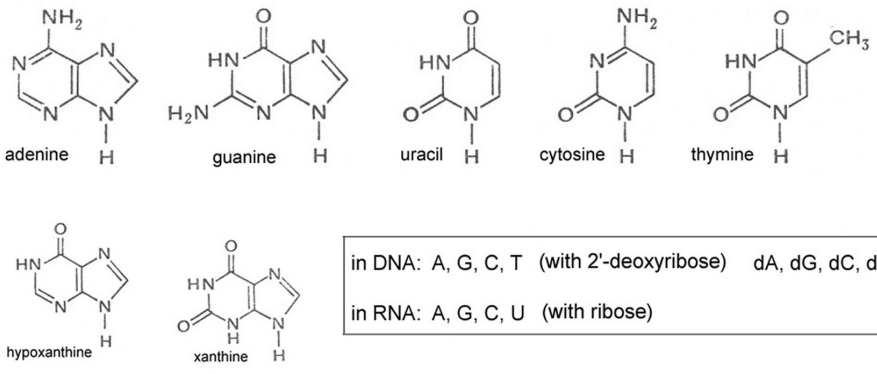


purine bases

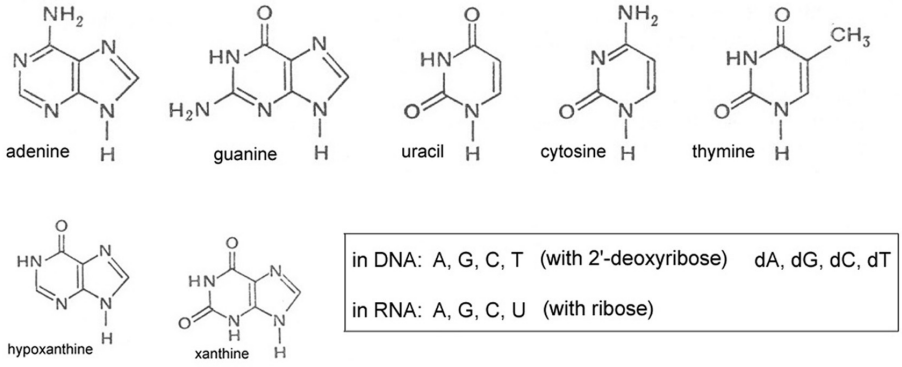


pyrimidine bases



in DNA: A, G, C, T (with 2'-deoxyribose) dA, dG, dC, dT

in RNA: A, G, C, U (with ribose)



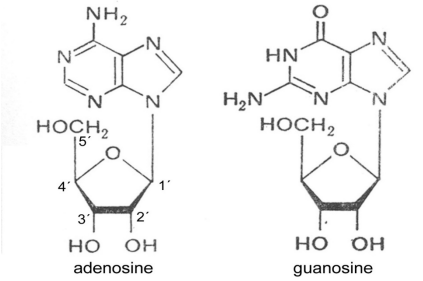
in DNA: A, G, C, T (with 2'-deoxyribose) dA, dG, dC, dT

in RNA: A, G, C, U (with ribose)

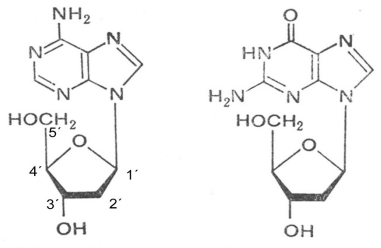
Nucleic bases – purines and pyrimidines

Ribonucleo**s**ides - base + ribose
Deoxyribonucleo**s**ides - base + 2´- deoxyribose

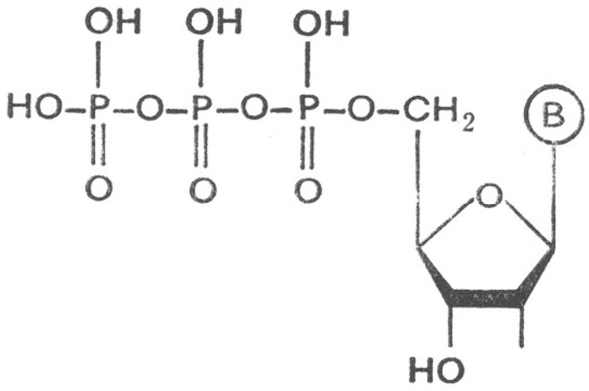
Nucleo**t**ides, deoxynucleo**t**ides - base + pentose + phosphate



Ribonucleosides

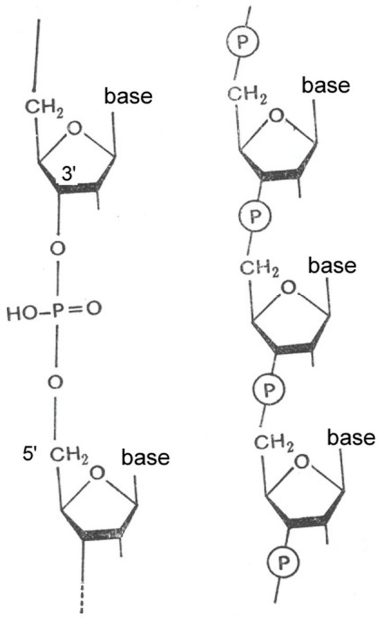


Deoxyribonucleosides

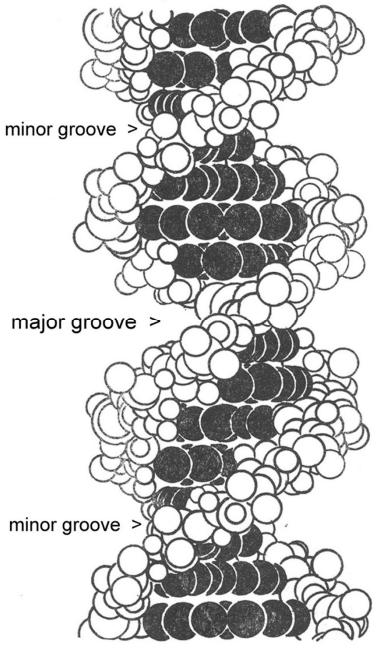


2'-deoxynucleoside 5'-triphosphate

DNA structure: phosphodiester bonds

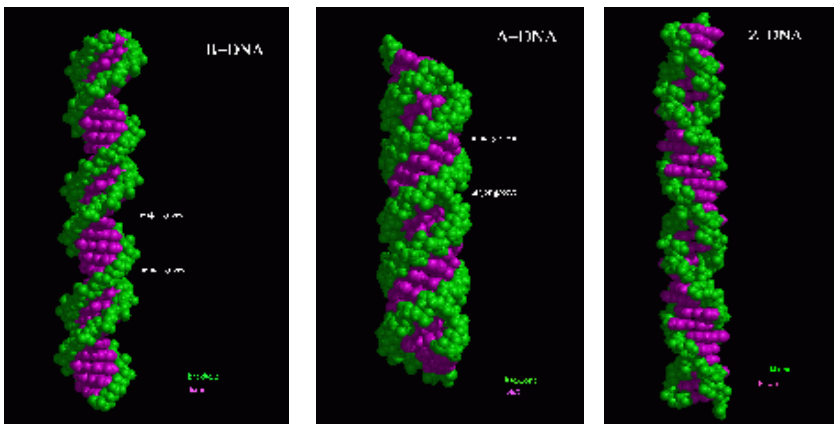


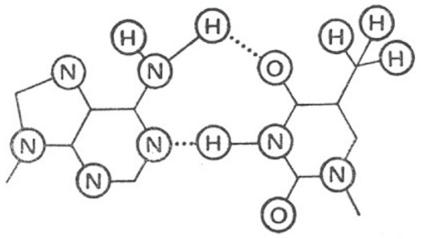
Double helix of DNA



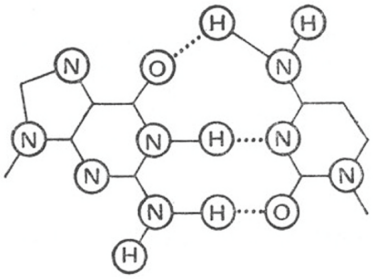
~ 10 base pairs
(3.4 nm)

B-DNA A-DNA Z-DNA

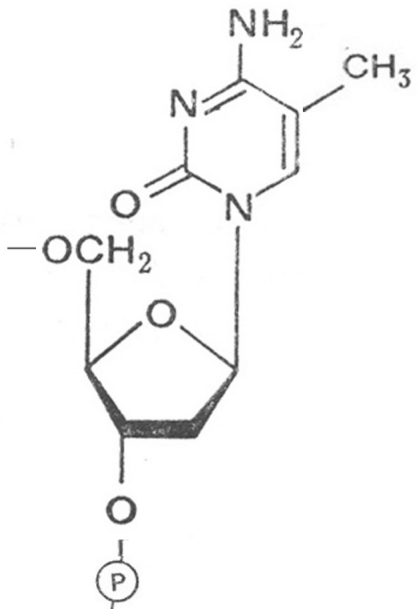




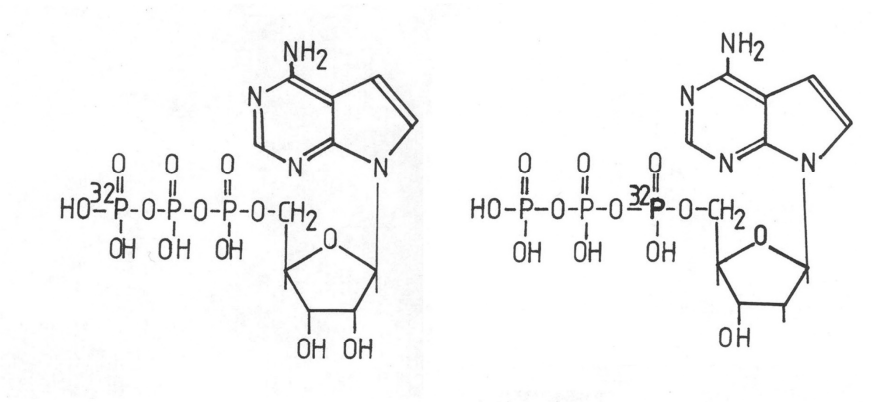
Base pairing: C with G, A with T (U)



In DNA, cytosin can be methylated



Radioactive phosphates in NTP/dNTP



γ-^{32}P-ATP α-^{32}P-dATP

DNA	**RNAs**
STRUCTURE:	
2´-deoxyribose	**ribose**
- thymine	**- uracil**
- double helix, higher order structures in the nucleus	**- single strand with a secondary structure**
FUNCTION:	
- storage of genetic information	**- role in the expression of genetic information**
Basic processes in which they participate:	
- replication, transcription (ssDNA as template)	**- transcription, translation**
Localization in the cell:	
- nucleus, (mitochondria)	**- nucleus, cytoplasm, (mitochondria)**
Formation of hybrids:	
DNA x DNA	
DNA x RNA	
RNA x RNA	

cDNA=complementary DNA (complementary to mRNA) reverse transcriptase

DNA can be easily:
- isolated as a pure nucleic acid, free of proteins and RNA
- cleaved at specific sites with restriction enzymes and recombined
- sequenced

Types of DNA:
- genomic (nuclear): high molecular weight DNA (> 100 kb long)
- cDNA (copy of messenger RNA)

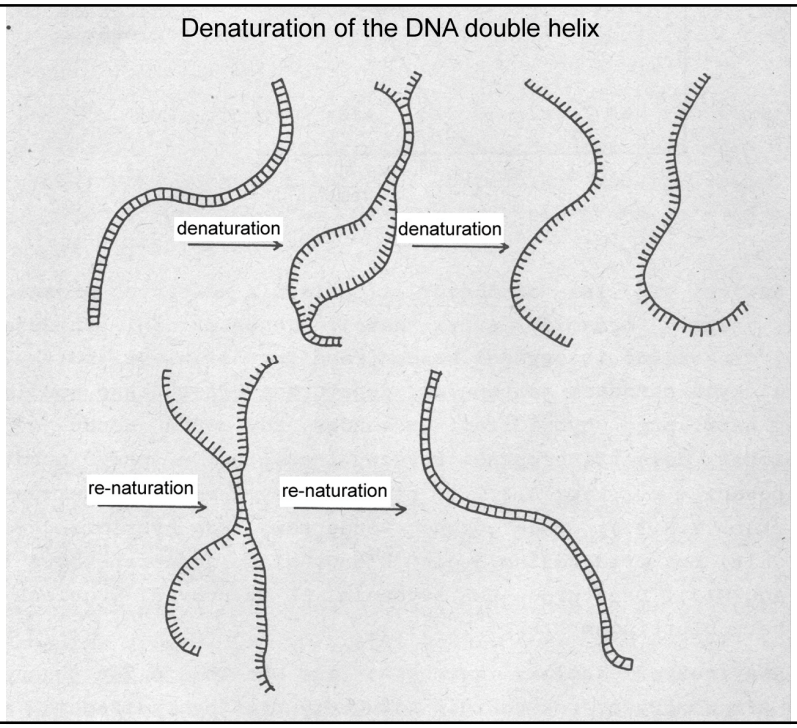
linear (genomic DNA, DNA of some DNA viruses, cleaved circular DNA) or circular (plasmids, *E.Coli* chromosome,…)

DNA double strand:
5´... T C G C G C T A A A C T C C C T ...3´ = upper strand, the same sequence as in mRNA
3´... A G C G C G A T T T G A G G G A ...5´

when these strands are separated, they have different nucleotide composition
and can be separated (e.g. by electrophoresis under non-denaturing conditions)

or
5´... T C G C G C T A A A C T C C C T ...3´
(the complementary strand is usually not shown)

in RNA: 5´... U C G C G C U A A A C U C C C U ...3´



Genomic DNA:

Genes,
Satelite DNA

Repetitive DNA – LINEs, SINEs, ...

HUMAN GENOMIC DNA (~ 3,3 x 10^9 nucleotides)

Genes:

- protein-coding regions of DNA *
  - solitary genes incl. introns) about 15%
  - duplicated genes, gene families about 15%
- tandem genes coding rRNA, tRNA, snRNA and histones (20-300 tandem repeats) 0,3 %

* Sequences coding protein sequences (exons) form only about 1,5% of total DNA!

Max. about 1/3 of DNA are transcription regions, the rest is "non-gene DNA" (=repetitive sequences and noncharacterized DNA).

HUMAN GENOMIC DNA (~ 3,3 x 10^9 nucleotides)

Repetitive sequences

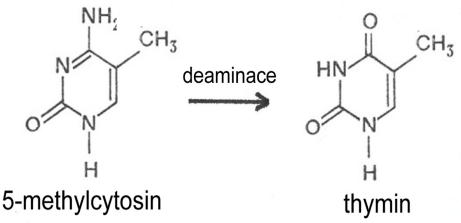
- **Satelite DNA** 3% of the genome
  - a) repeats of 14-500 nt., about 20-100 kb long (frequent in centromeric regions)
    - minisatelites (15-100 nt. repeats, 1-5 kd long), the differences are used for forensic identification of DNA samples (DNA fingerprinting).
  - b) microsatelites (1-13 nt., often only 1-4 nt, about 150 nt long)
    - telomeric DNA (cca 15 kb) – repeated sequence GGGTTA

- **Mobile DNA** (= transposons, „interspersed DNA, selfish DNA“) total about 45%
  - DNA transposons 3%
  - Retrotransposons 8%
    - LTR-retrotransposons
    - non-LTR-retrotransposons
      - LINEs (long interspersed nucl. elements) **L1**, L2, L3 21%
      - SINEs (short interspersed nucl. elements) (Alu sequences) 13 %

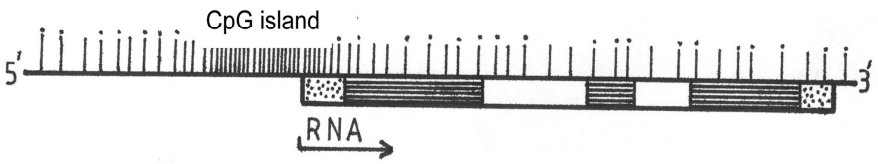
Noncharacterized DNA cca 25%

CpG islands

genomová DNA je často methylována na cytosinu



5-methylcytosin thymin



Types of RNA molecules

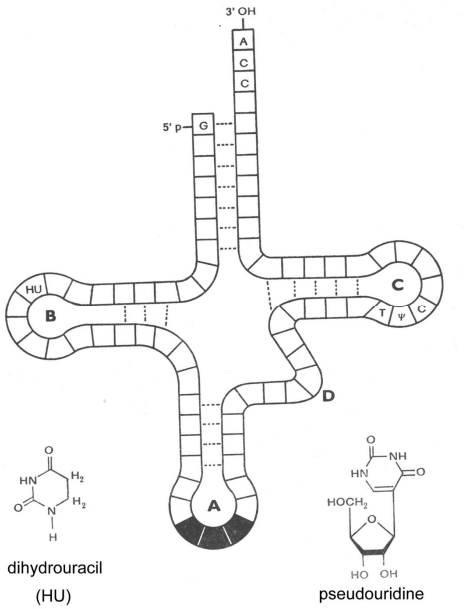
rRNA - ribosomal RNA (28S, 18S, 5,6S, 5S)

mRNA - messenger RNA

tRNA - transfer RNA

sn RNAs – small nuclear RNAs – they participate in splicing of mRNA, modifications of rRNA in the nucleolus, ...

Transfer RNA has a typical secondary structure



dihydrouracil
(HU)

pseudouridine

Organization of DNA in chromatin:

Nucleosome – chromatin fibre - condensed chromosome.

Chromatin is a dynamic structure and has an active role in transcription.

Euchromatin, heterochromatin.

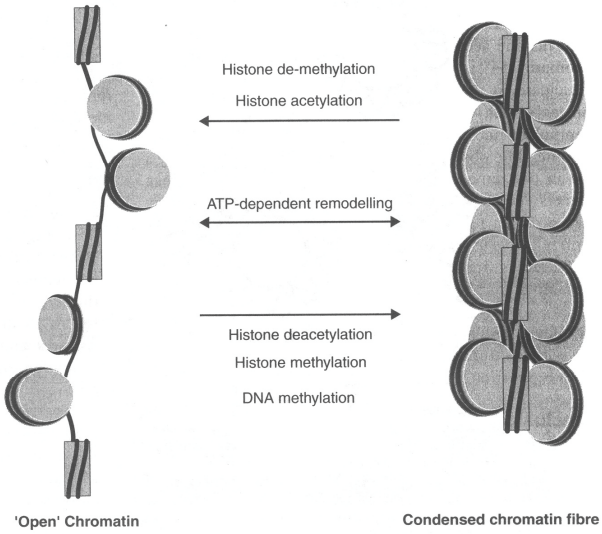
Nucleosomes

Histones 2A, 2B, 3 a 4 (total 8 molecules of histones in one nucleosome)

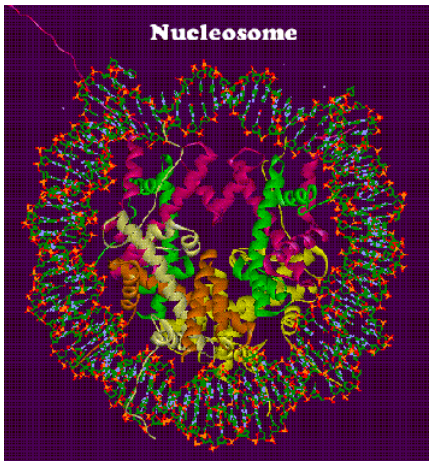
DNA: 146 bp., about two turns 0f DNA around the histone core +about 40-50 bp. spacer

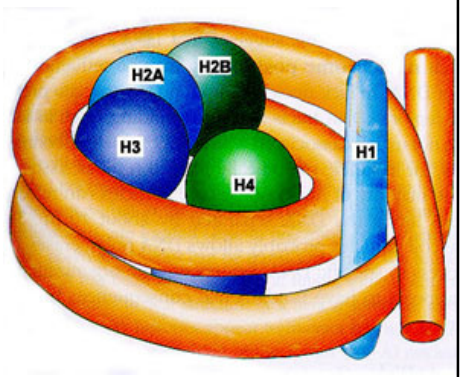
changes in histones: acetylation/deacetylation, "remodeling" – essential for transcription

DNA in the nucleus is organized into nucleosomes and higher order structures (nucleosome arrays and chromatin fibres)

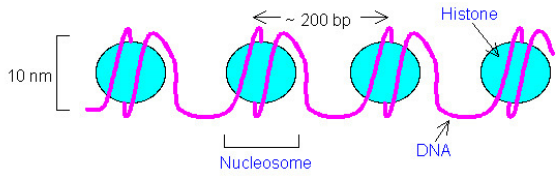


Nucleosome

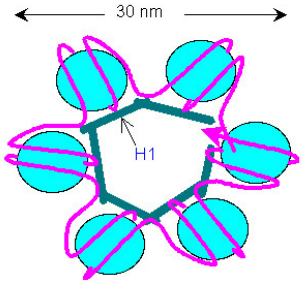




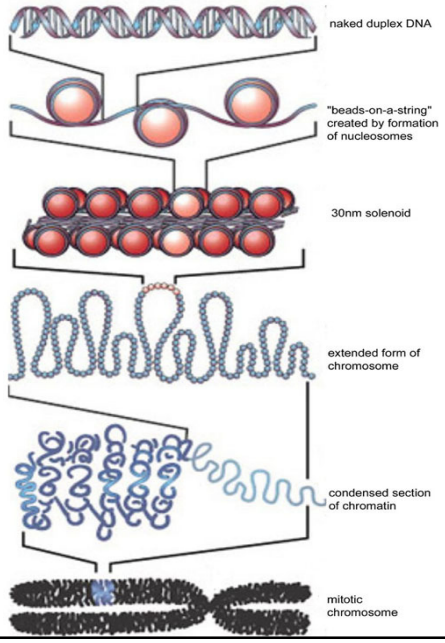
(a) Beads-on-a-String Conformation



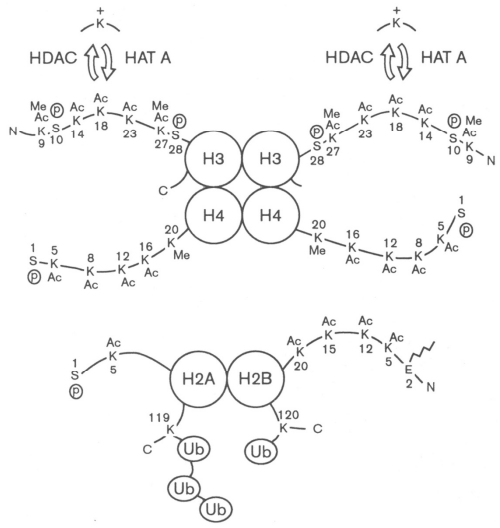
(b) One Turn of Solenoid



Organization of DNA in the nucleus

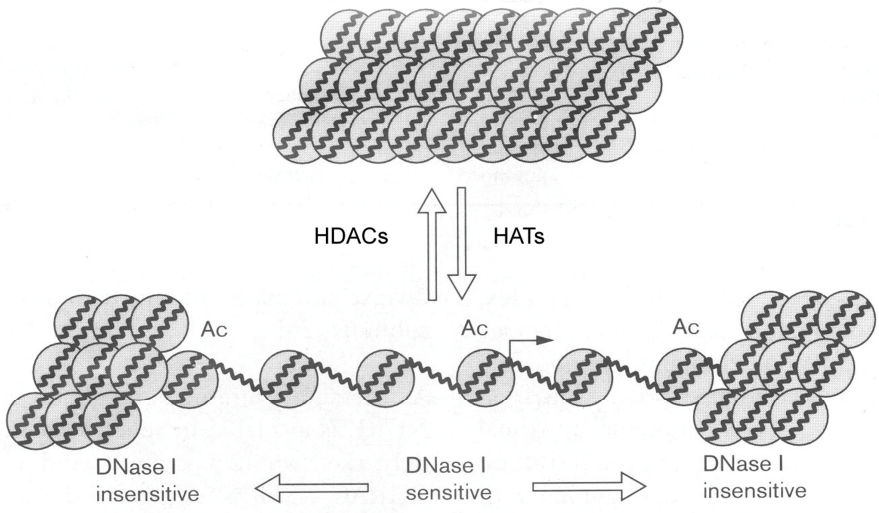


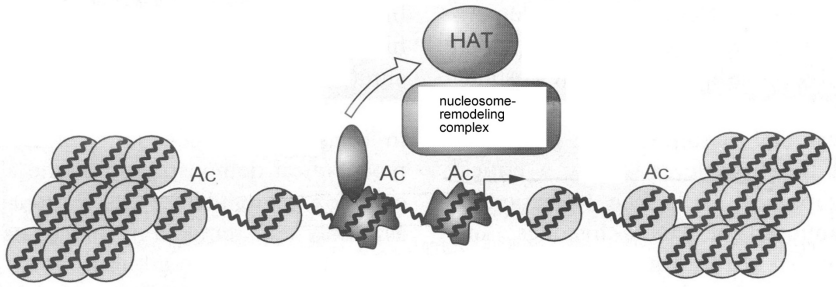
ACETYLATION AND DEACETYLATION OF HISTONES



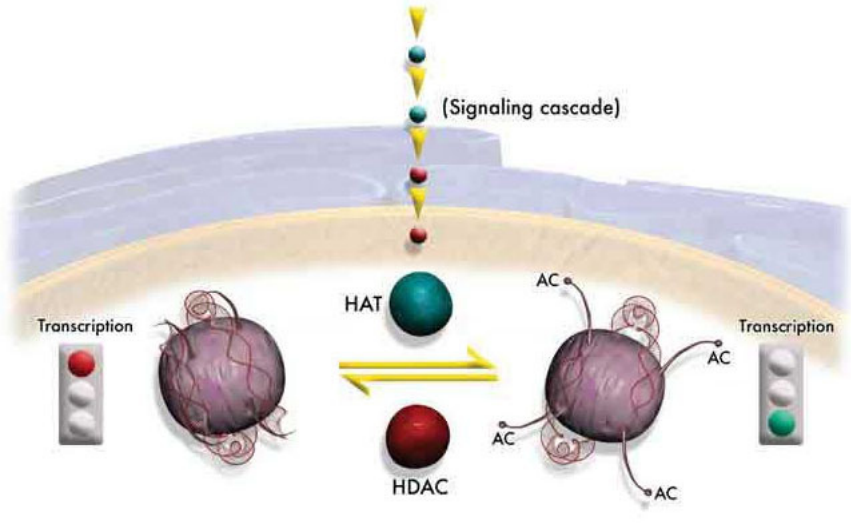
HAT = histone acetyltransferase HDAC = histone deacetylase

Acetylation (and deacetylation) of histones in nucleosomes affects the structure of chromatin



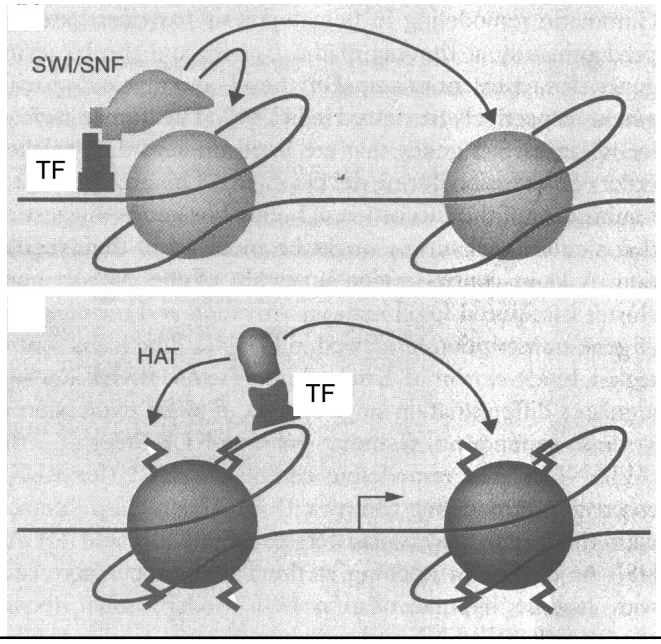


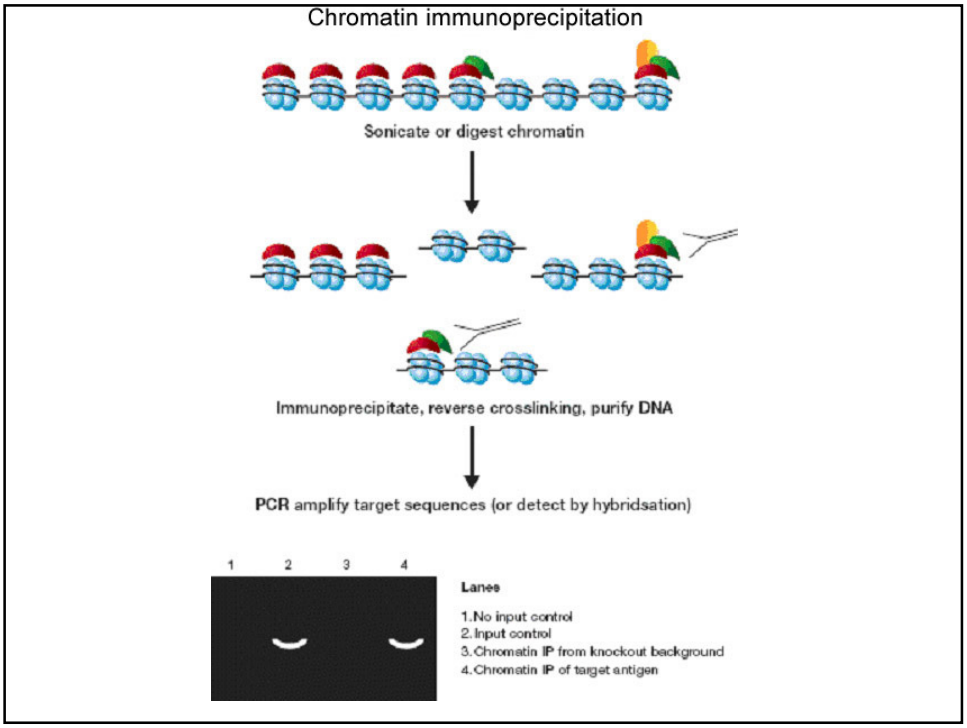
TRANSCRIPTION



Signaling to Chromatin

Transcription factor "recruits" nucleosome/remodeling complex (SWI/SNF) and histon acetyltransferase





We love DNA
Made of nucleotides.
Sugar, phosphate and a base
Bonded down one side.

Adenine and thymine
Make a lovely pair.
Cytosine without guanine
Would feel very bare.

Oh-h-h, de-oxy-ri-i-bo
Nu-u-cleic acid
RNA is ri-i-bo
Nu-u-cleic acid