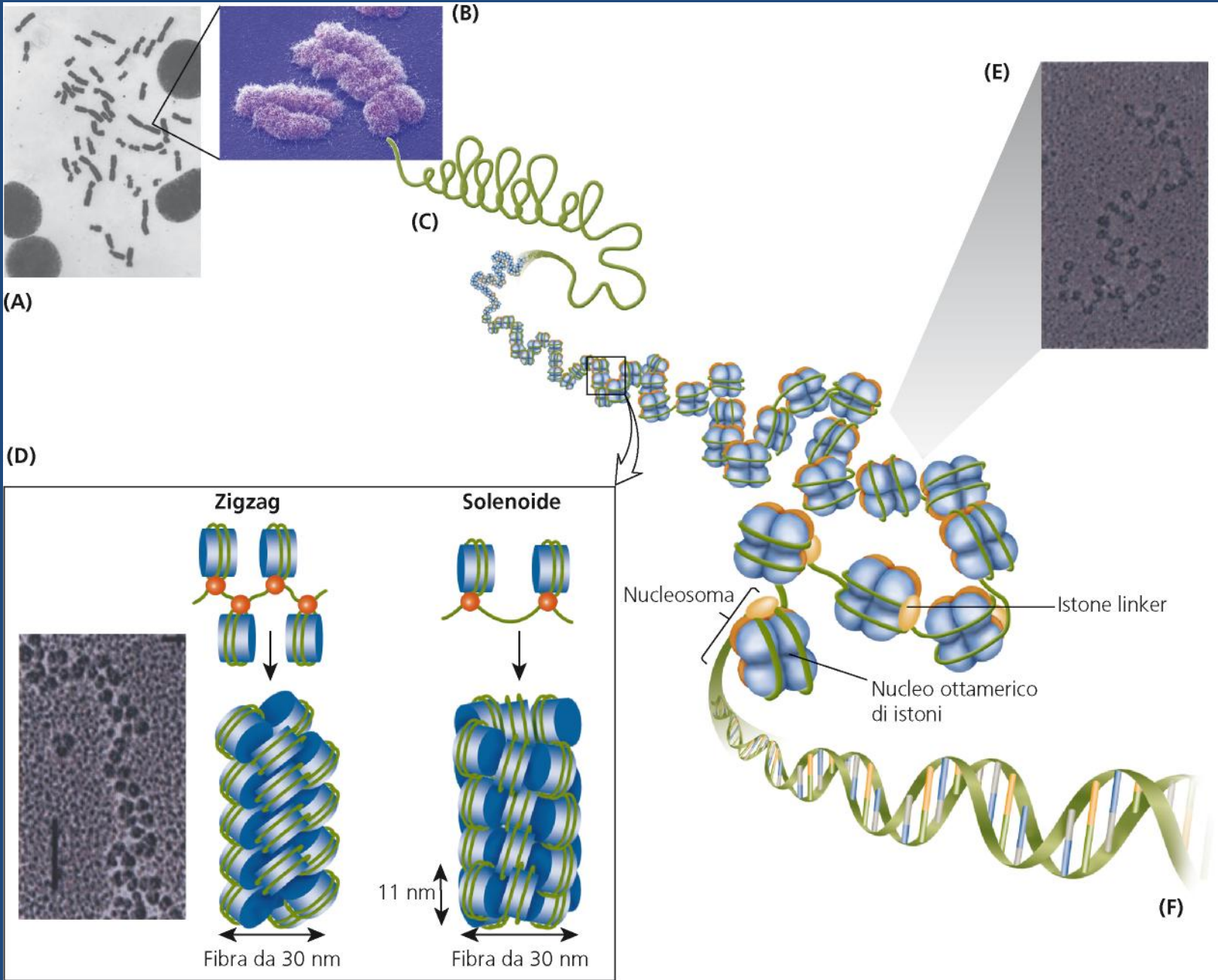


Organizzazione della cromatina



Organizzazione della cromatina

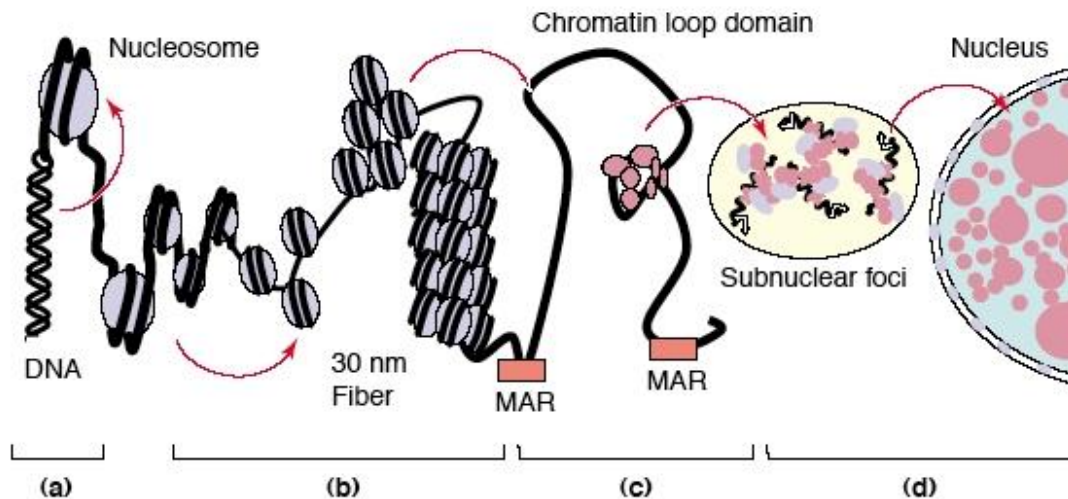


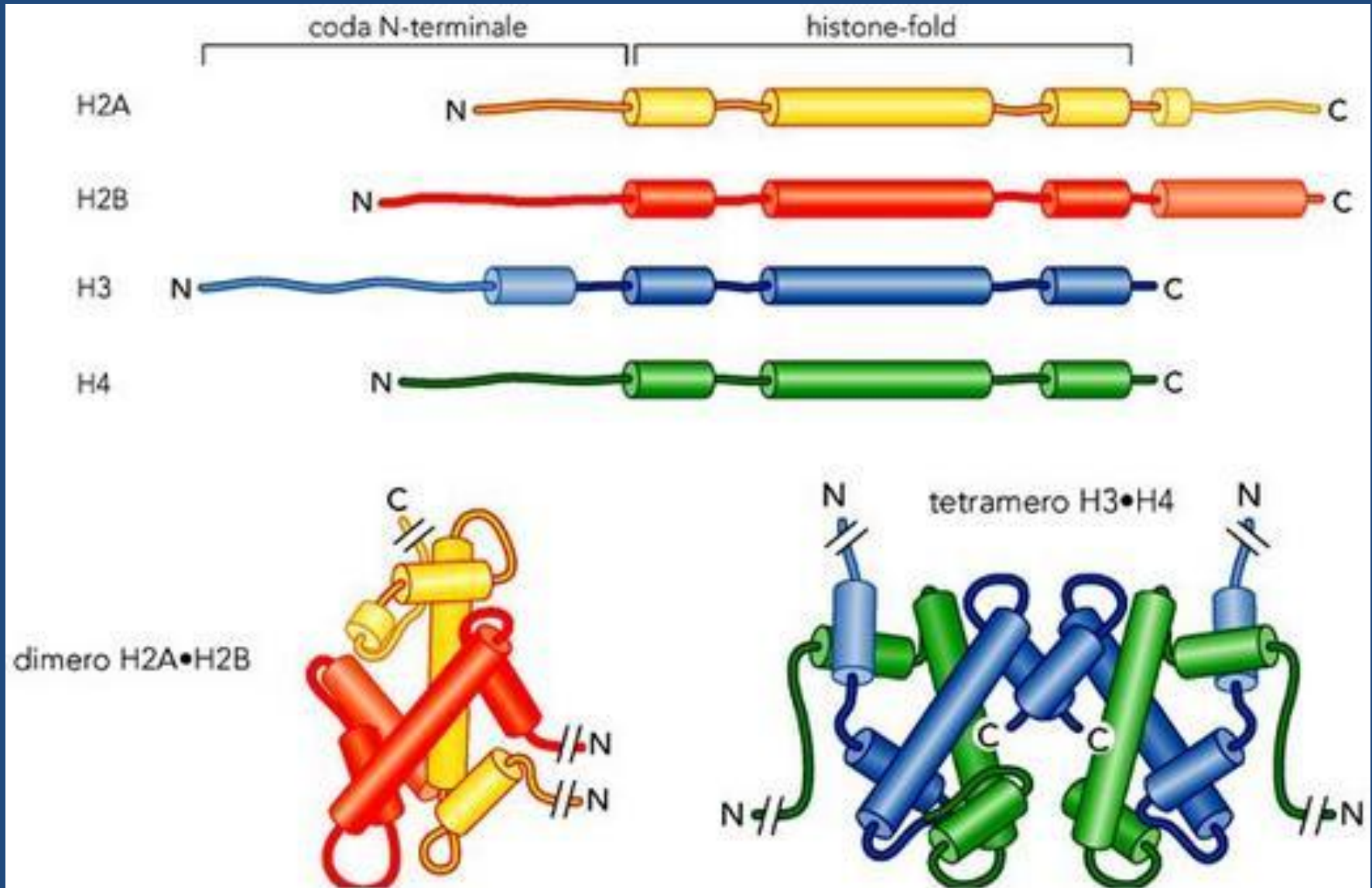
Figure 2. Multiple levels of nuclear organization regulate cellular processes. The primary level of nuclear organization, the ordering of genes, promoter elements and origins provide the genetic potential for physiological control (a). Chromatin structure and nucleosome organization reduce distances between regulatory sequences, facilitate crosstalk between DNA regulatory elements and render elements competent for interactions with positive and negative regulatory factors (b and c) [66]. The components of higher-order nuclear architecture, which include nuclear pores [67], the nuclear matrix and specialized intranuclear domains, contribute to the bidirectional exchange of regulatory information between the nucleus and cytoplasm [68], as well as to the subnuclear distribution and activities of genes and regulatory factors (d) (reviewed in Refs [1,6,12]).

La cromatina è suddivisa in regioni dove è altamente condensata, (eterocromatina), e in regioni meno condensate (eucromatina).

La cromatina è un complesso di DNA, proteine istoniche e non istoniche, la cui unità fondamentale viene definita nucleosoma.

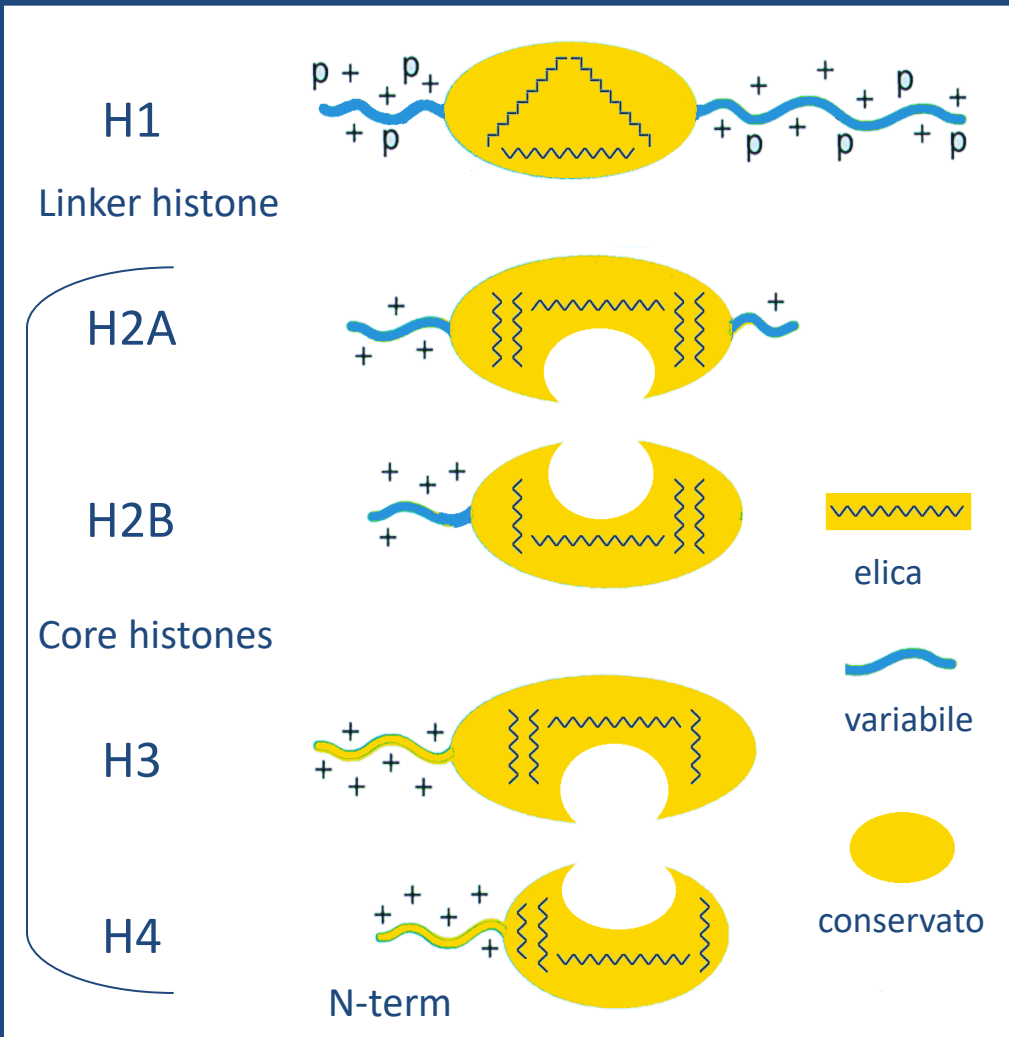
GLI ISTONI

Gli istoni



Gli Istoni

Piccole proteine basiche
altamente conservate



Histone acetylation

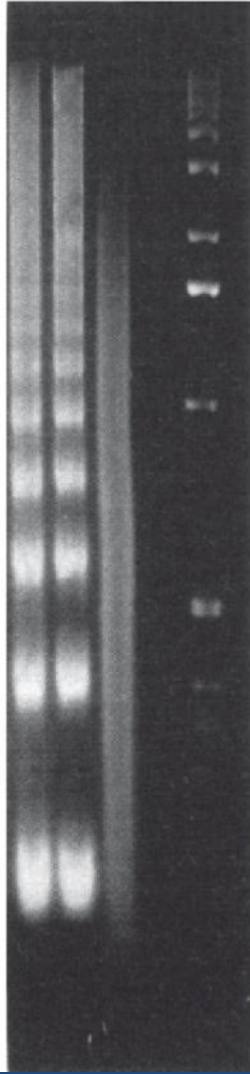
is a reversible modification of lysines in the N-termini of the core histones.

Result:

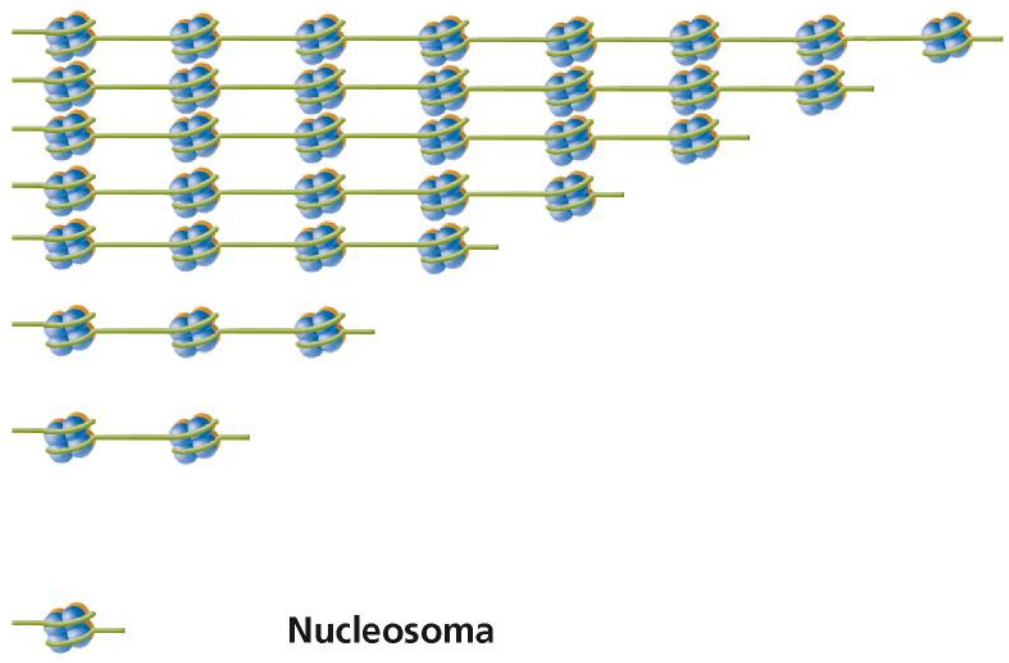
- reduced binding to DNA
- destabilization of chromatin

Histone Type	Molecular Weight	Number of Amino Acids	Approx. Content of Basic Amino Acids
H1	17,000–28,000	200–265	27% lysine, 2% arginine
H2A	13,900	129–155	11% lysine, 9% arginine
H2B	13,800	121–148	16% lysine, 6% arginine
H3	15,300	135	10% lysine, 15% arginine
H4	11,300	102	11% lysine, 4% arginine

Cromatina
DNA
Marcatori



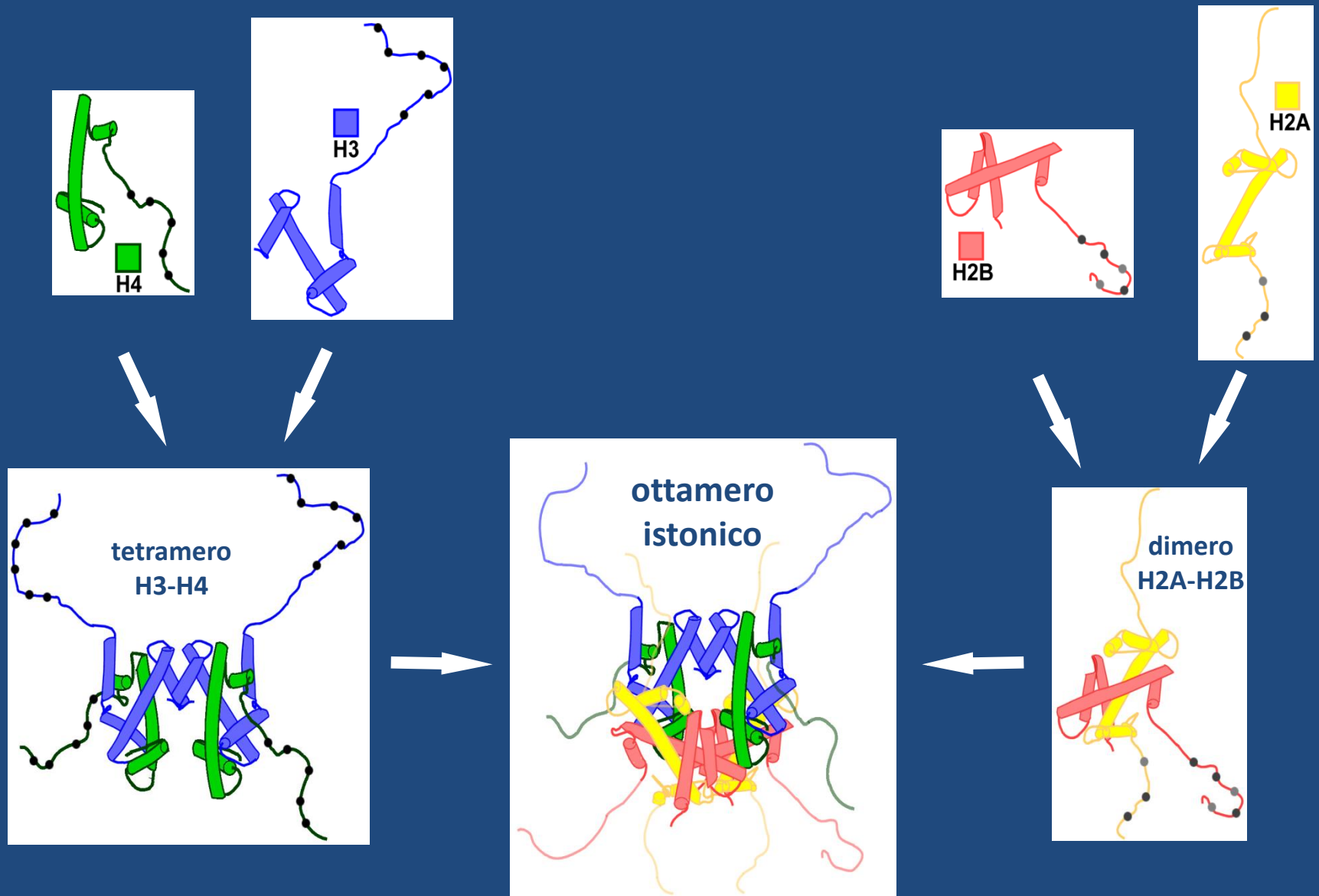
Lunghezza
ripetitiva
del nucleosoma



Nucleosoma

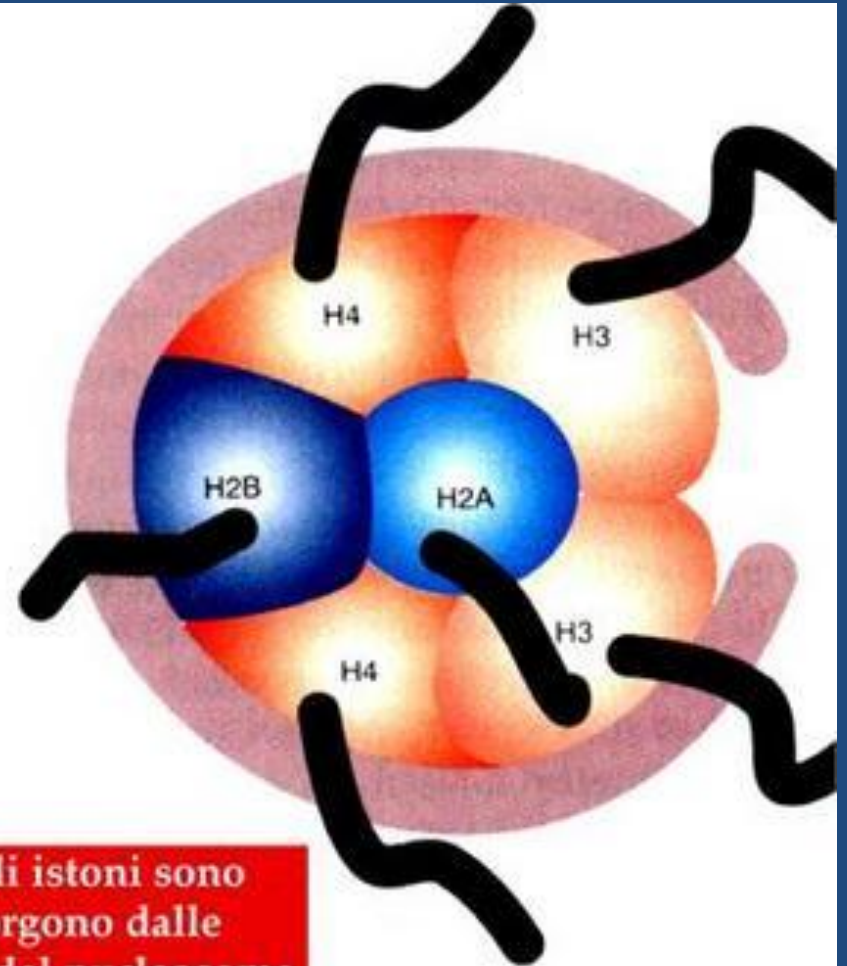
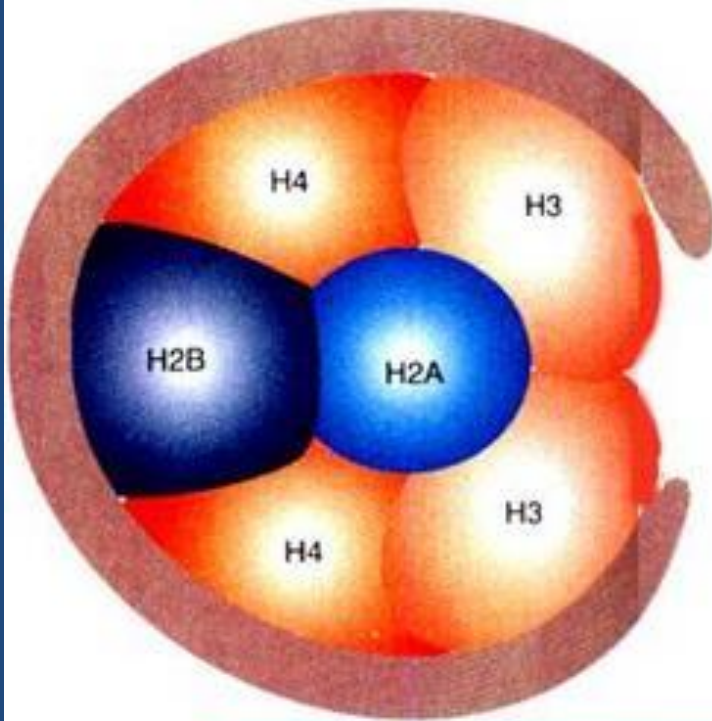
IL NUCLEOSOMA

Assemblaggio dell'ottamero istonico



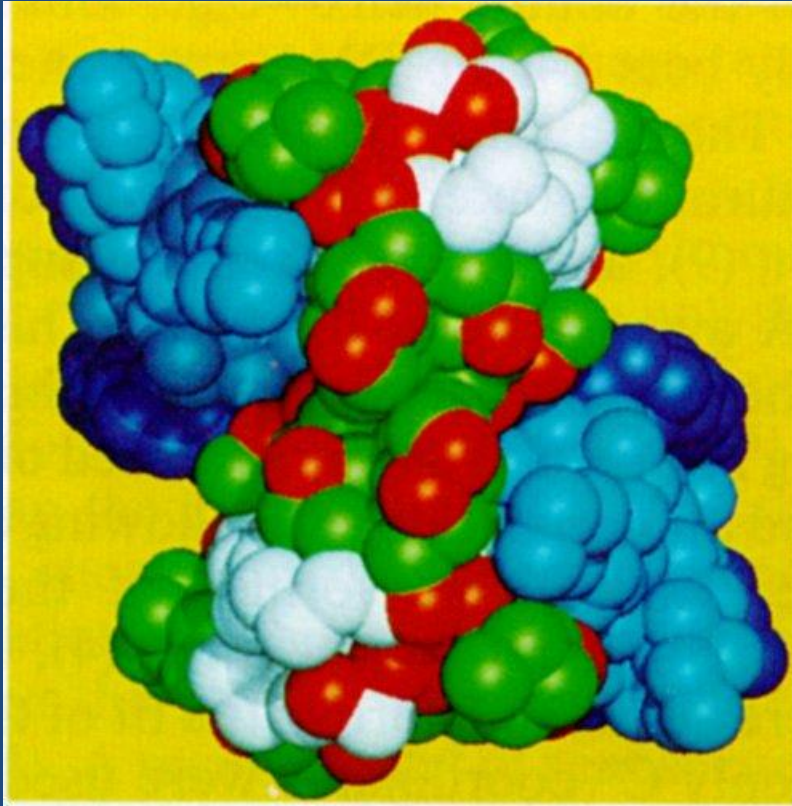
Ottamero istonico

Ci sono due coppie H2A-H2B

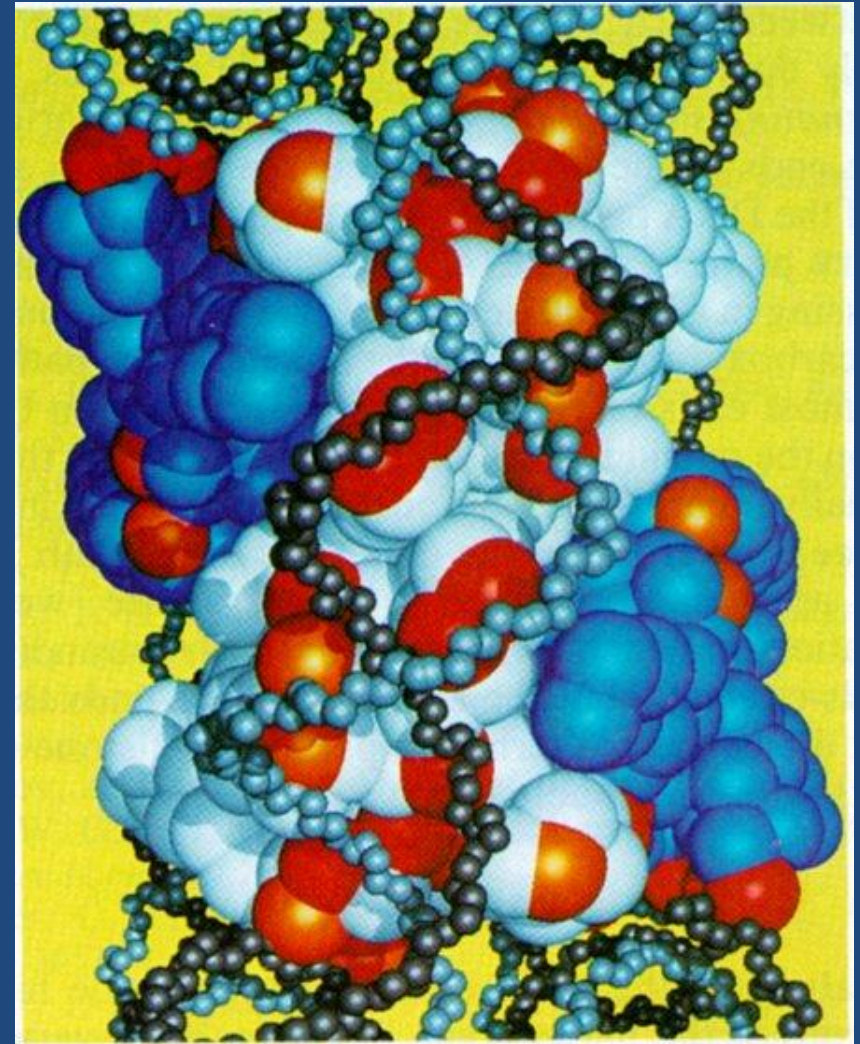


Le estremità N-terminali degli istoni sono ricche di residui basici e sporgono dalle superfici superiore ed inferiore del nucleosoma

Ottamero istonico



H4	white
H3	green
H2A	light blue
H2B	dark blue



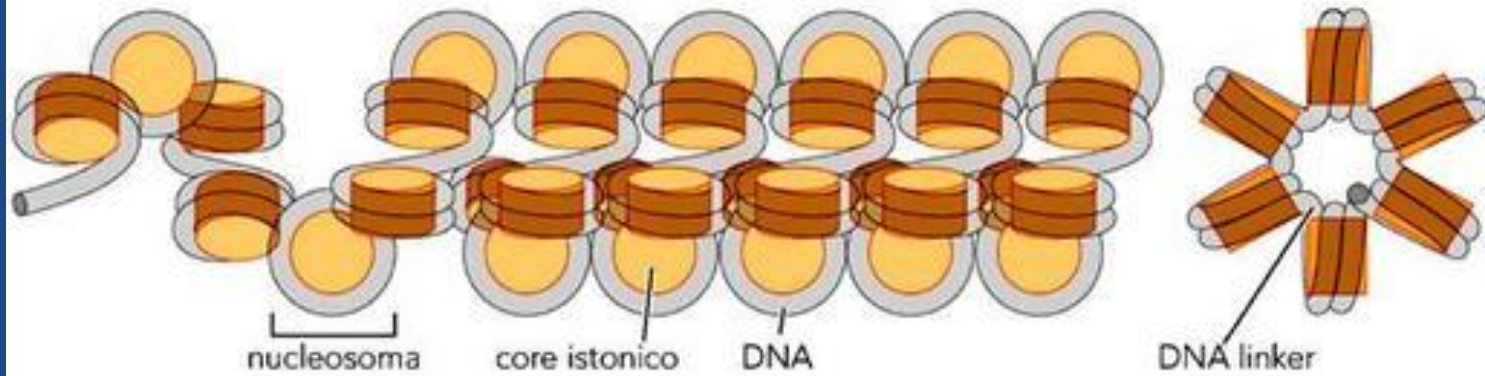
red: + (arg, lys)

orange: -OH (ser, thr)

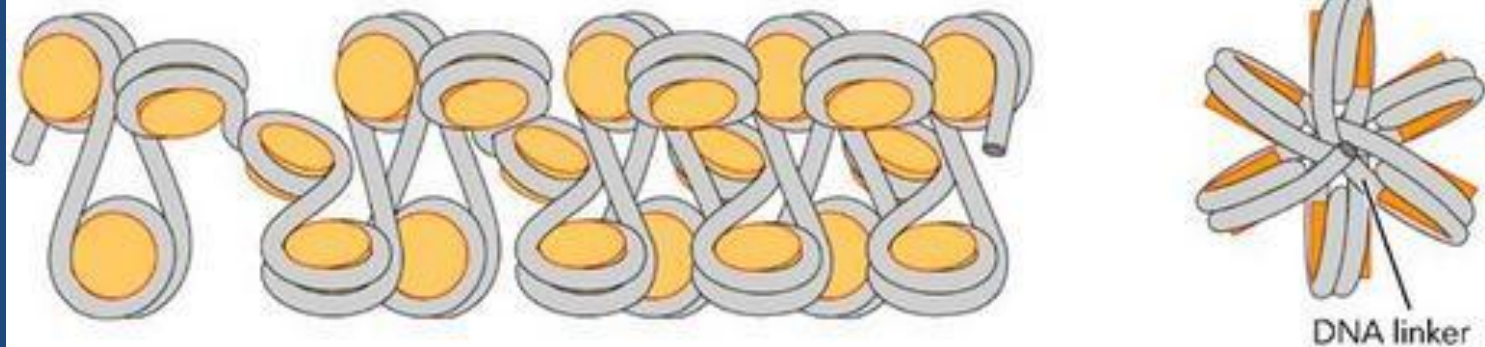
FIBRA CROMATINICA

La fibra cromatinica

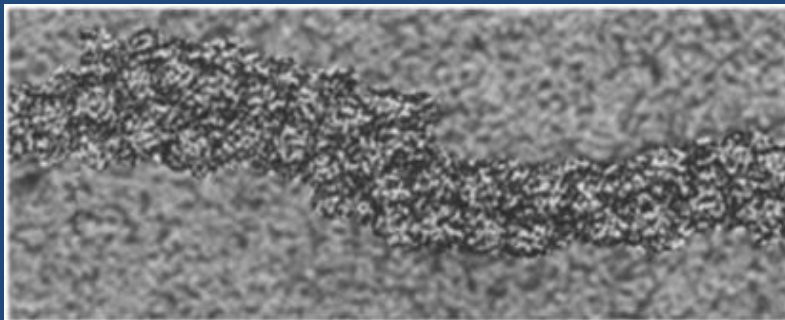
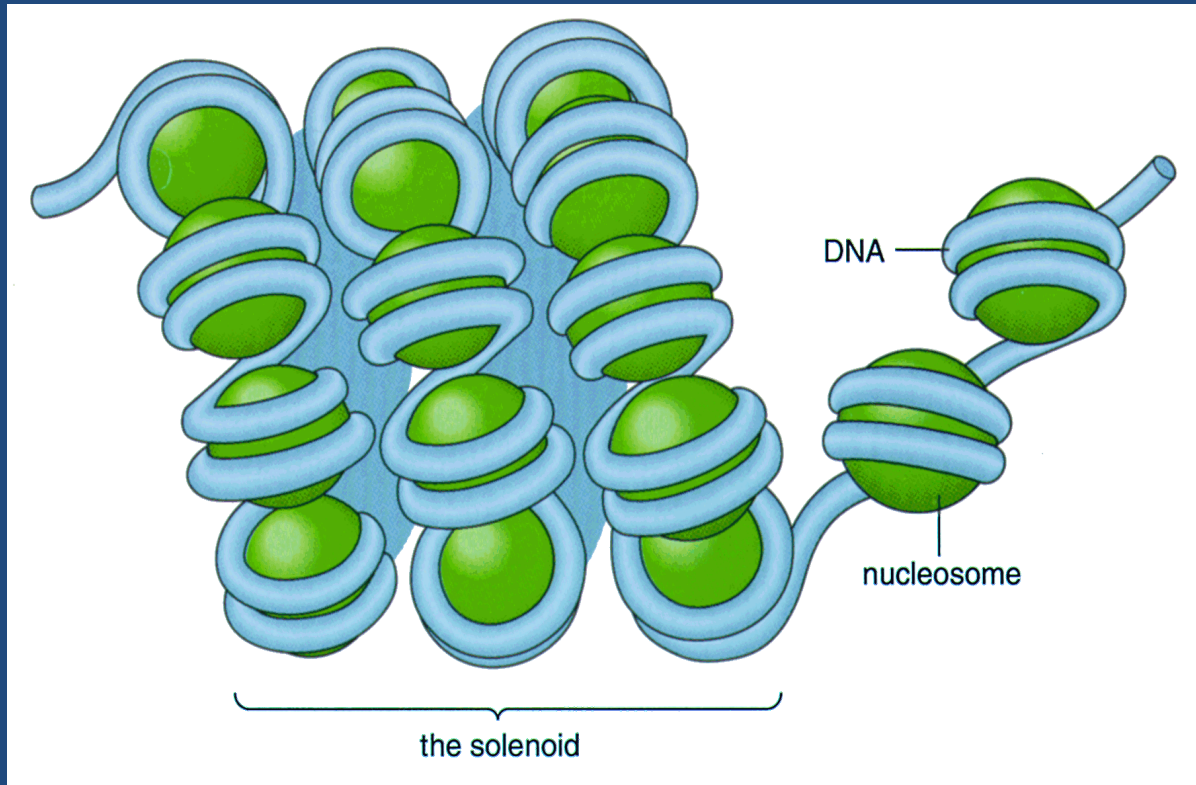
a solenoide



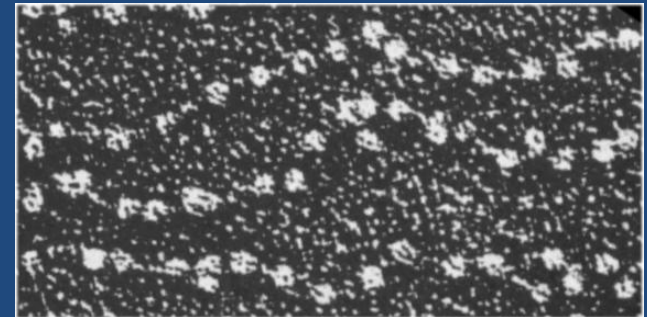
b zig-zag



La fibra cromatinica

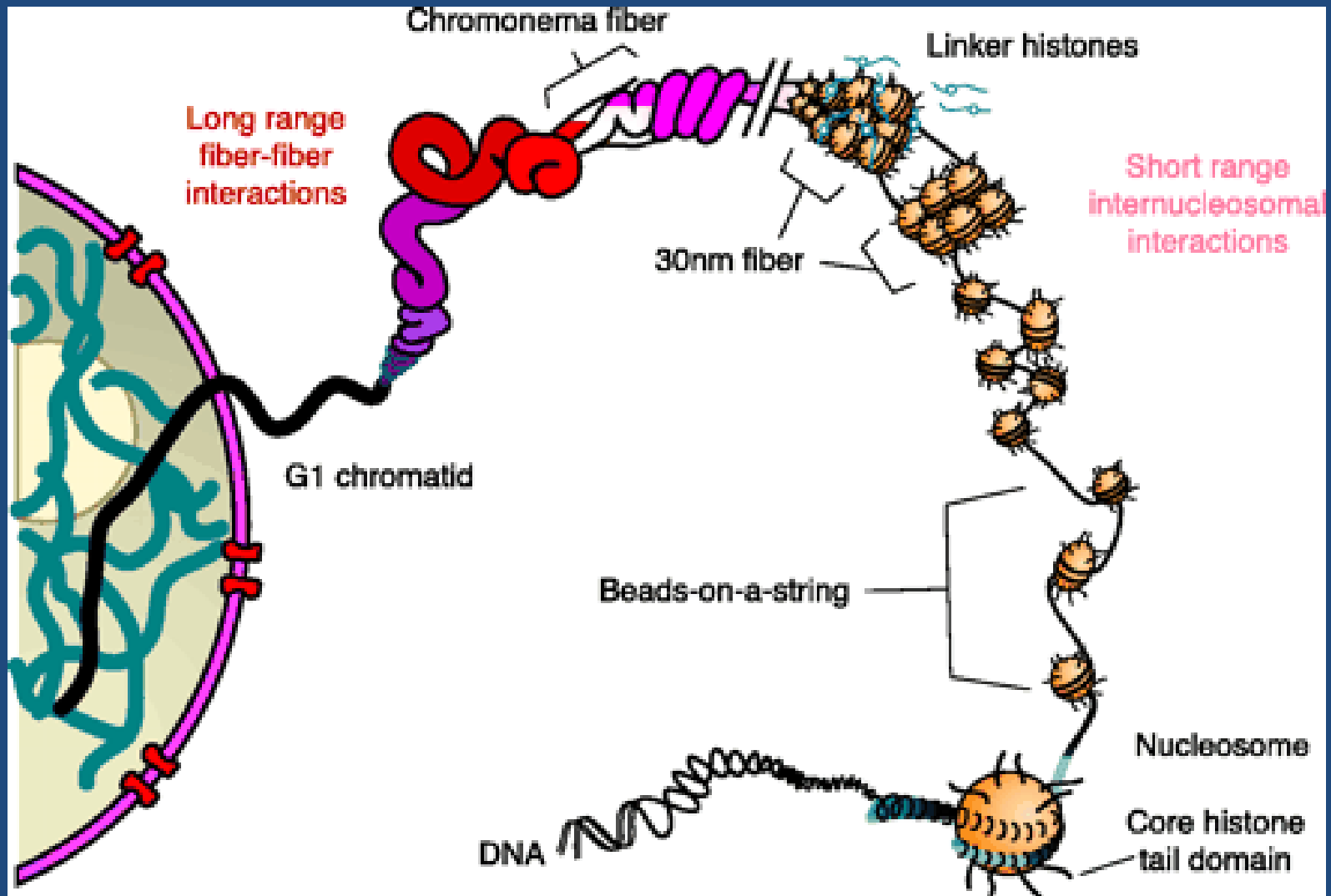


Fibra cromatinica di 30 nm

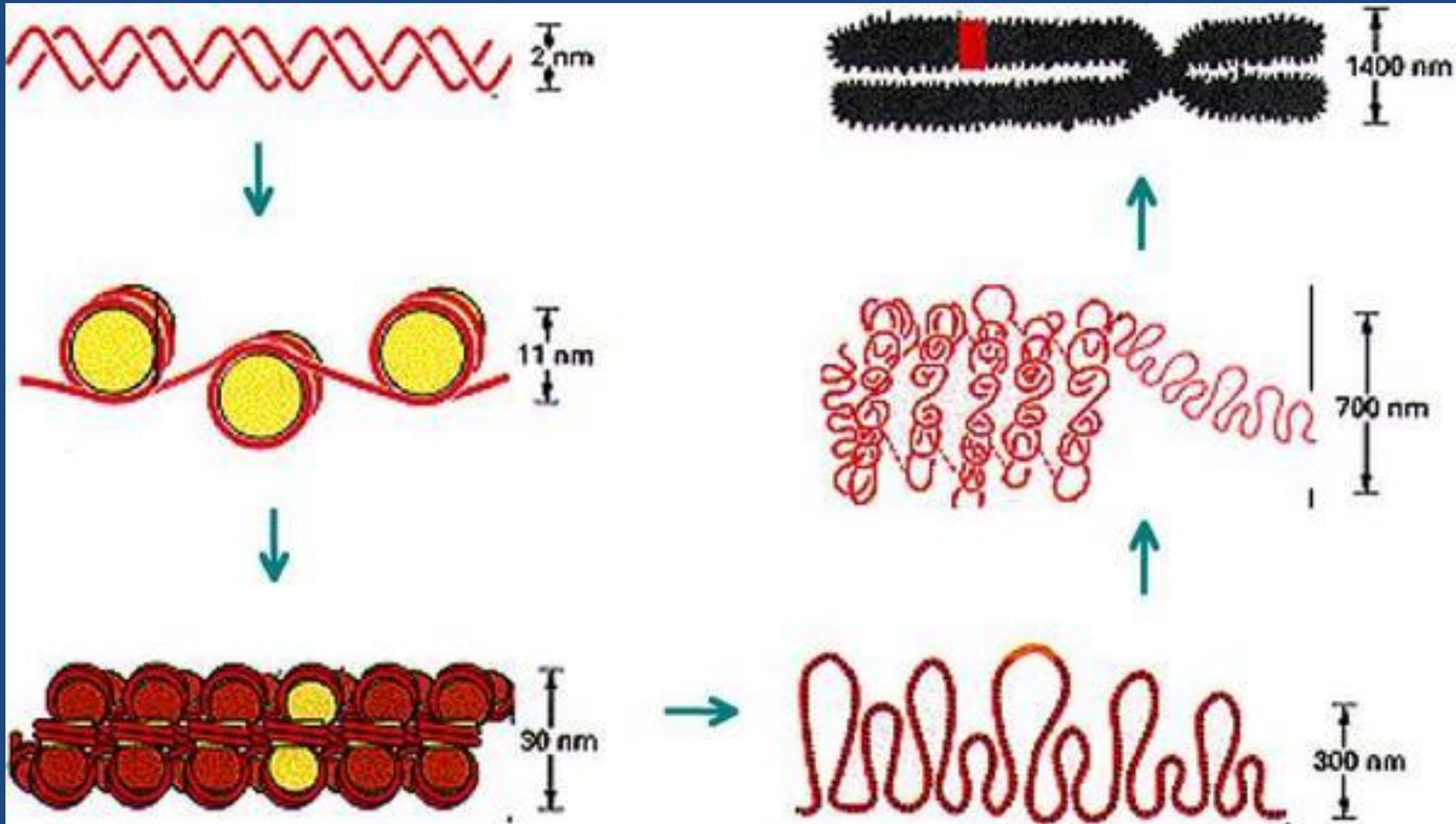


Nucleosomi distesi (11 nm beads)

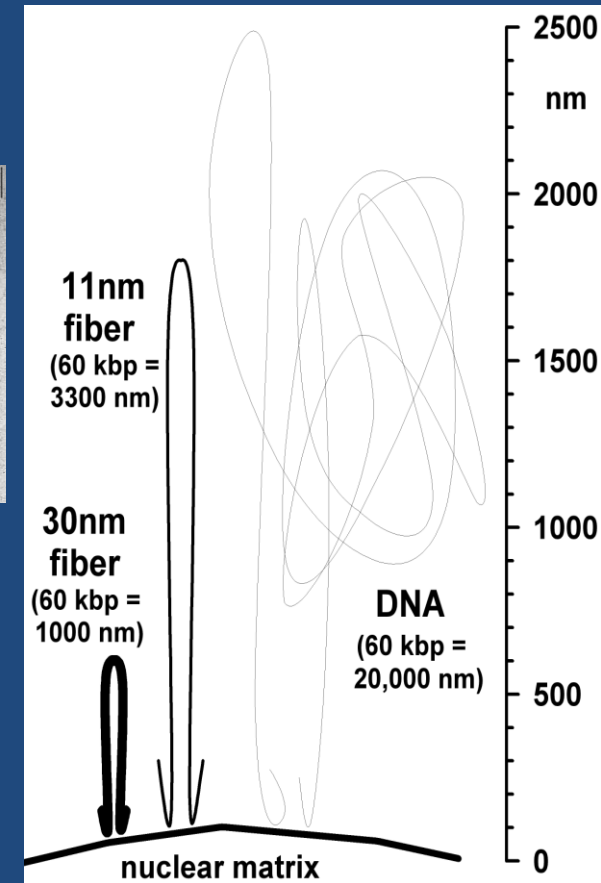
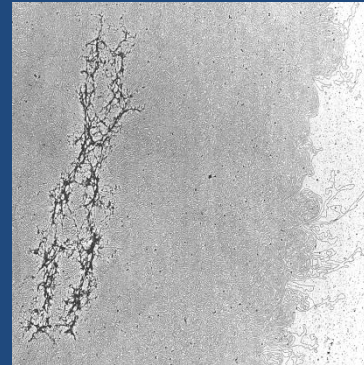
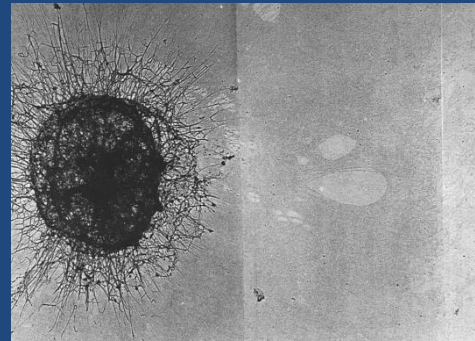
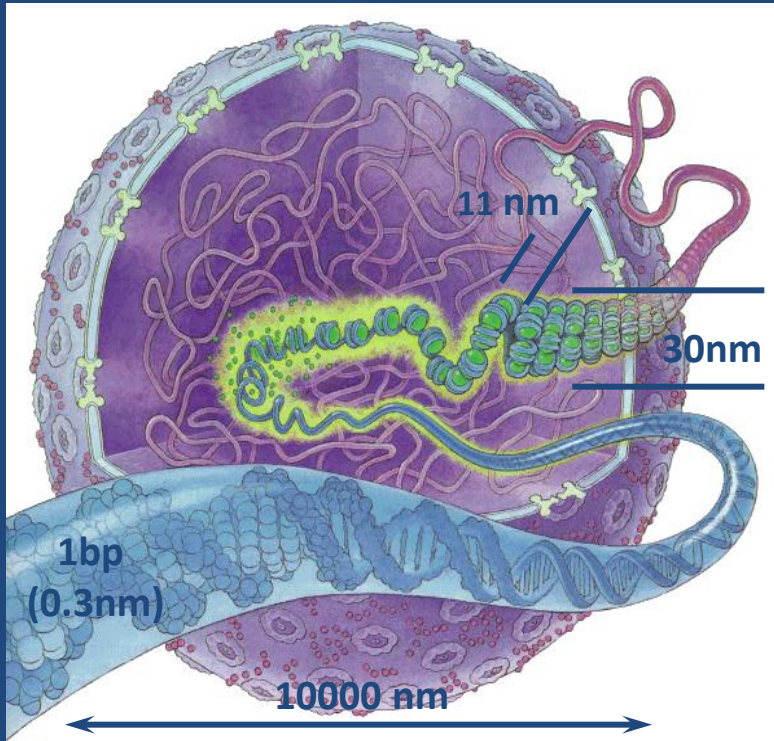
High order structures



Compattamento del DNA nel cromosoma



Compattazione del DNA



			compact size	DNA	length	compaction
nucleus (human)	2 x 23 = 46 chromosomes	92 DNA molecules	10 μ m ball	12,000 Mbp	4 m DNA	400,000 x
mitotic chromosome	2 chromatids, 1 μ m thick	2 DNA molecules	10 μ m long X	2x 130 Mbp	2x 43 mm DNA	10,000 x
DNA domain	anchored DNA loop	1 replicon ?	60 nm x 0.5 μ m	60 kbp	20 μ m DNA	35 x
chromatin fiber	approx. 6 nucleosomes per 'turn' of 11 nm		30 nm diameter	1200 bp	400 nm DNA	35 x
nucleosome	disk 1 3/4 turn of DNA (146 bp) + linker DNA		6 x 11 nm	200 bp	66 nm DNA	6 - 11 x
base pair			0.33 x 1.1 nm	1 bp	0.33 nm DNA	1 x

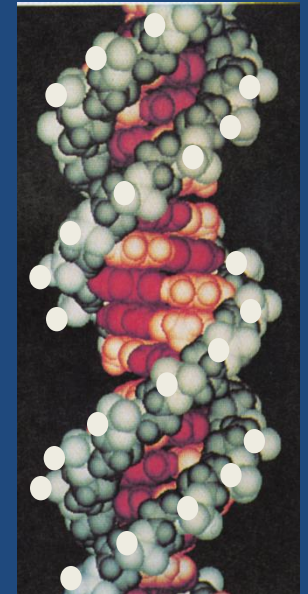
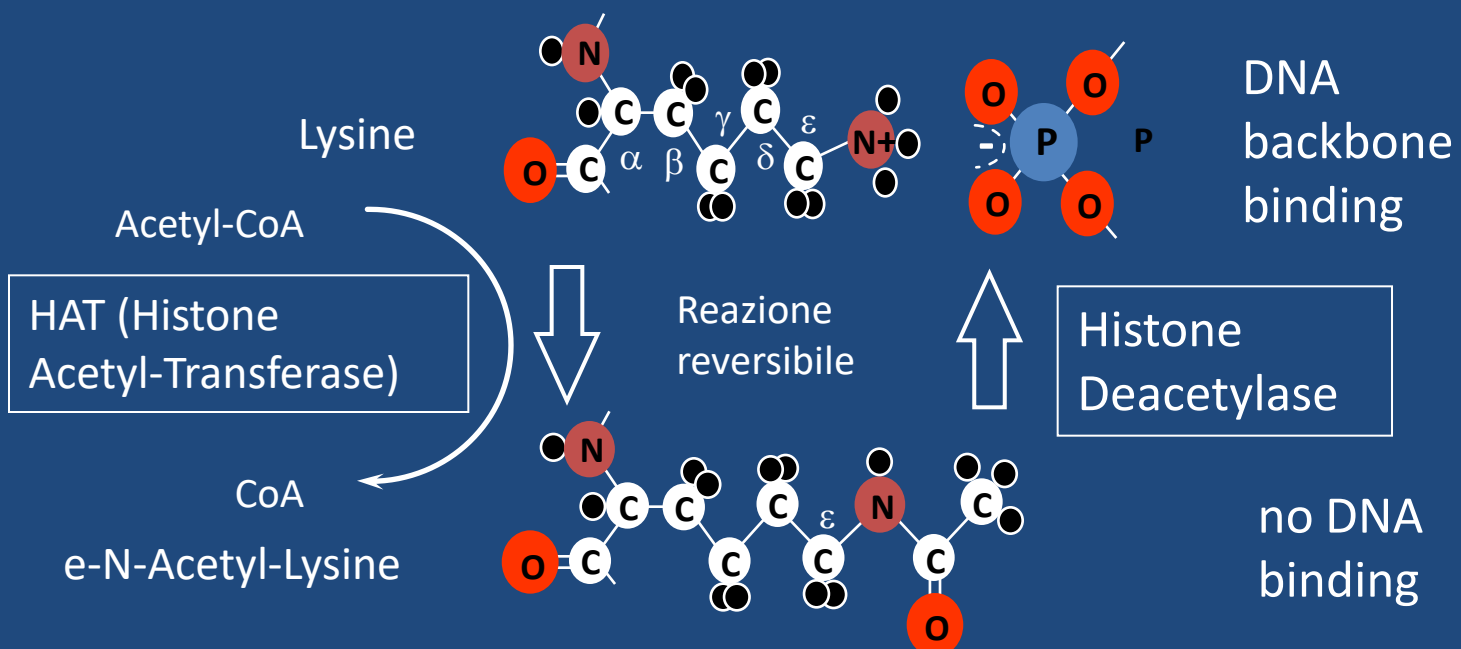
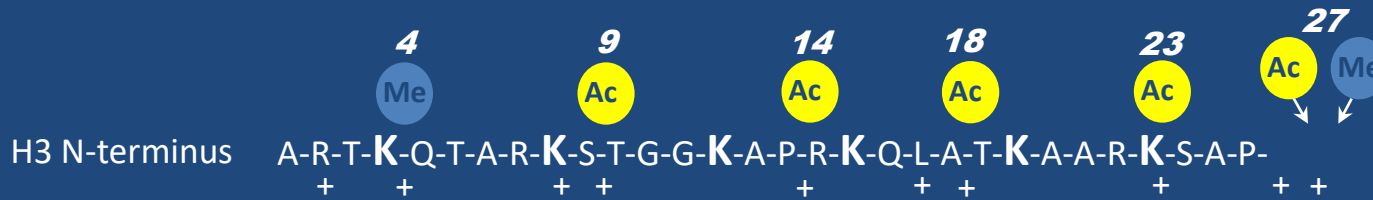
Compaction of DNA by histones

Compaction by chromosome scaffold / nuclear matrix

MODIFICHE ISTONICHE

Acetilazione delle lisine conservate

Le code N-terminali degli istoni H4 e H3 ed il loro pattern di acetilazione sono altamente conservati



Modifiche covalenti degli istoni

Modifiche apportate da specifici fattori proteici (writers) e rimosse da altri specifici fattori proteici (erasers)

Le modifiche vengono lette da appositi fattori (readers)

Acetilazione e metilazione delle lisine delle code istoniche (H3 e H4) sono coinvolte nel controllo e la regolazione della trascrizione

H4K16ac -> favorisce la trascrizione

H3K4me3 -> attivazione trascrizionale

H3K27me3 -> inattivazione trascrizionale

H3K9me-> inattivazione trascrizionale

La fosforilazione degli istoni è coinvolta in altri processi nucleari

H2A.X (S139) -> riparo del DNA

H3 (S10) -> stabilità cromosomi e divisione cellulare

H2B (S14) -> apoptosi