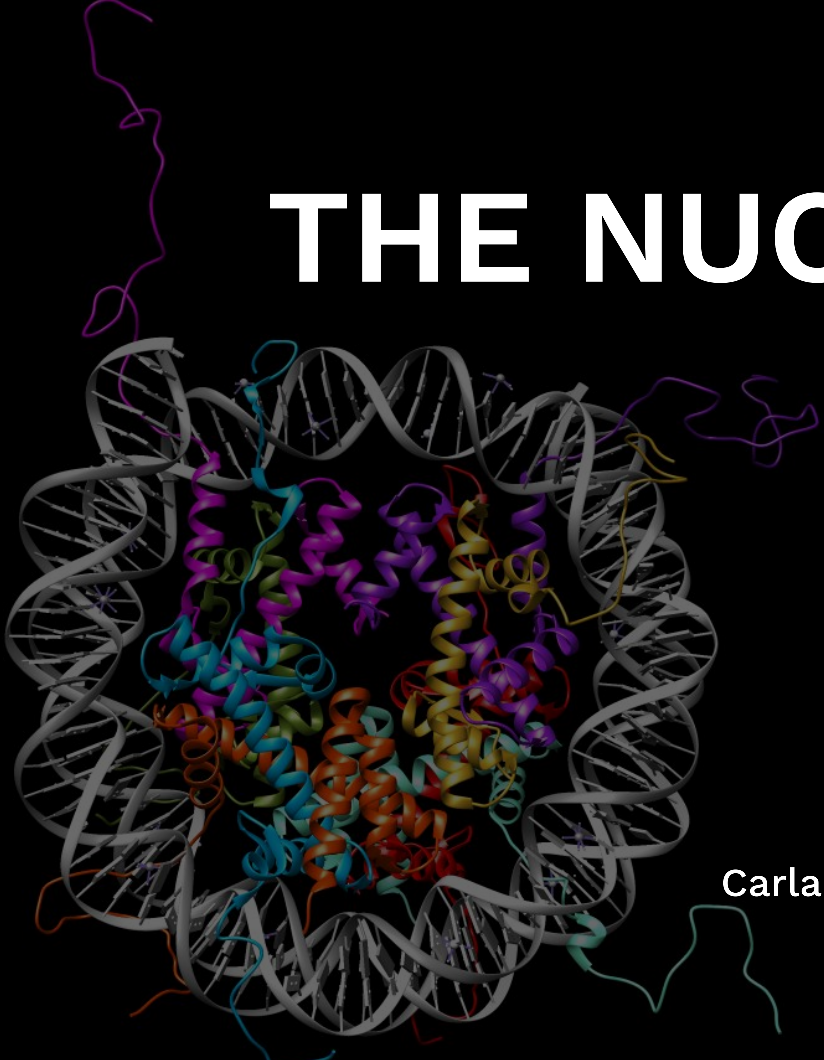
THE NUCLEOSOME

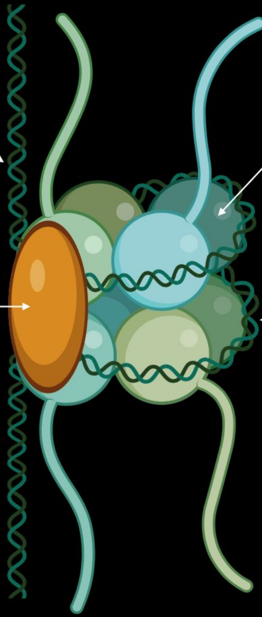


Carla Cifuentes, Ainhoa Larrañaga and Berta Sambola
Structural Biology - 2023/2024

INDEX

1. THE NUCLEOSOME
2. INTERACTIONS
3. POST-TRANSLATIONAL MODIFICATIONS
4. LINKER HISTONE: H1
5. EVOLUTION
6. CONCLUSIONS

THE NUCLEOSOME



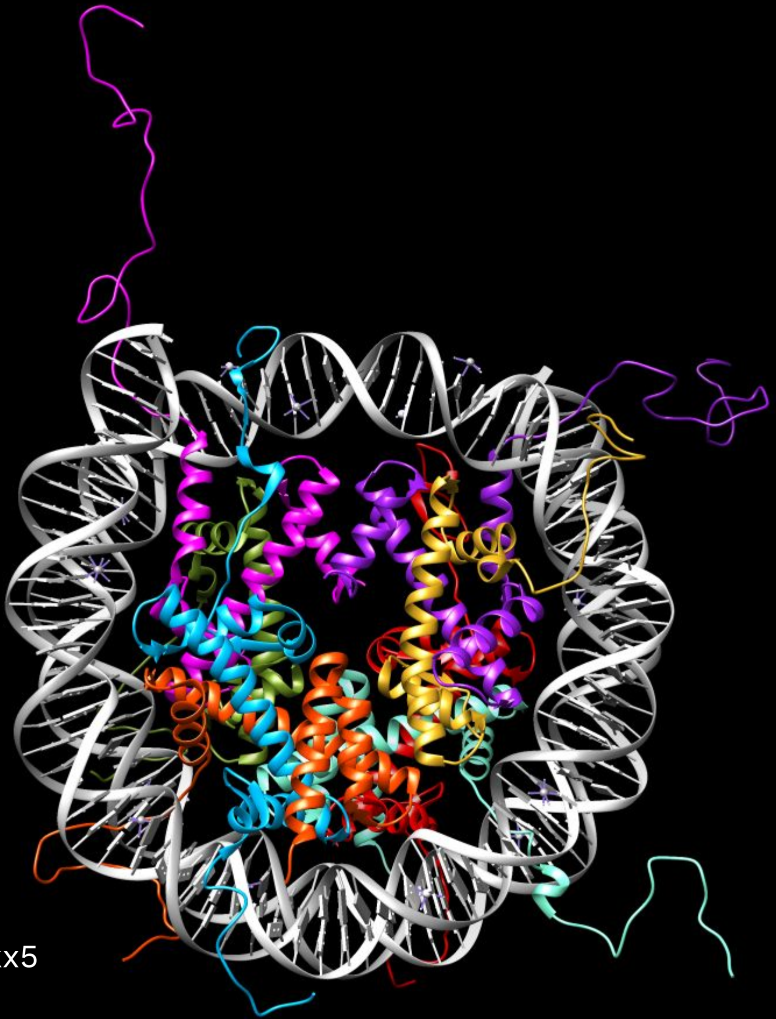
Linker DNA

Octamer of histones core:
H2A, H2B, H3, H4 (each one x2)

Histone H1

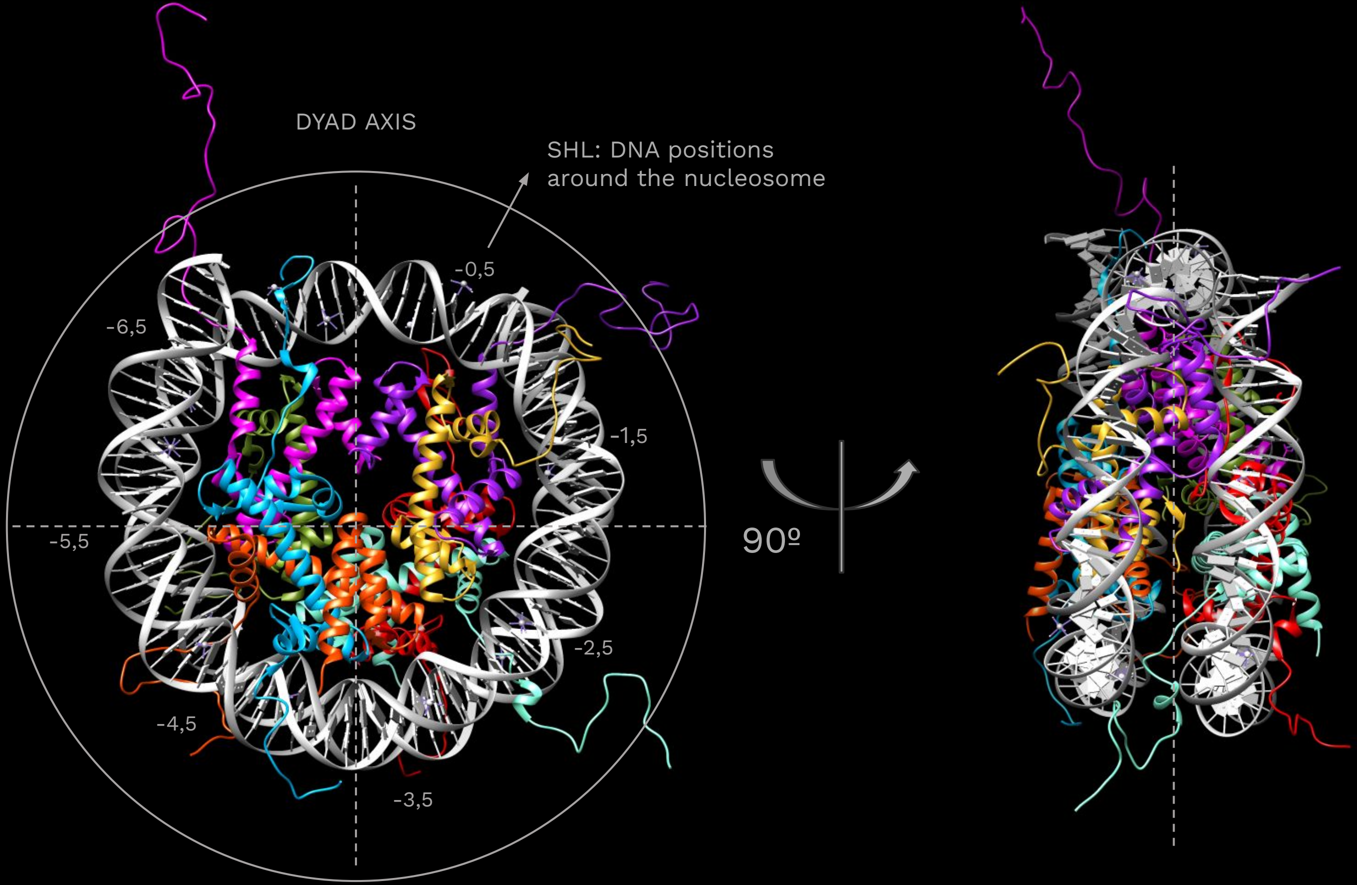
Core DNA

Involved in binding between nucleosomes to further compact the chromatin.



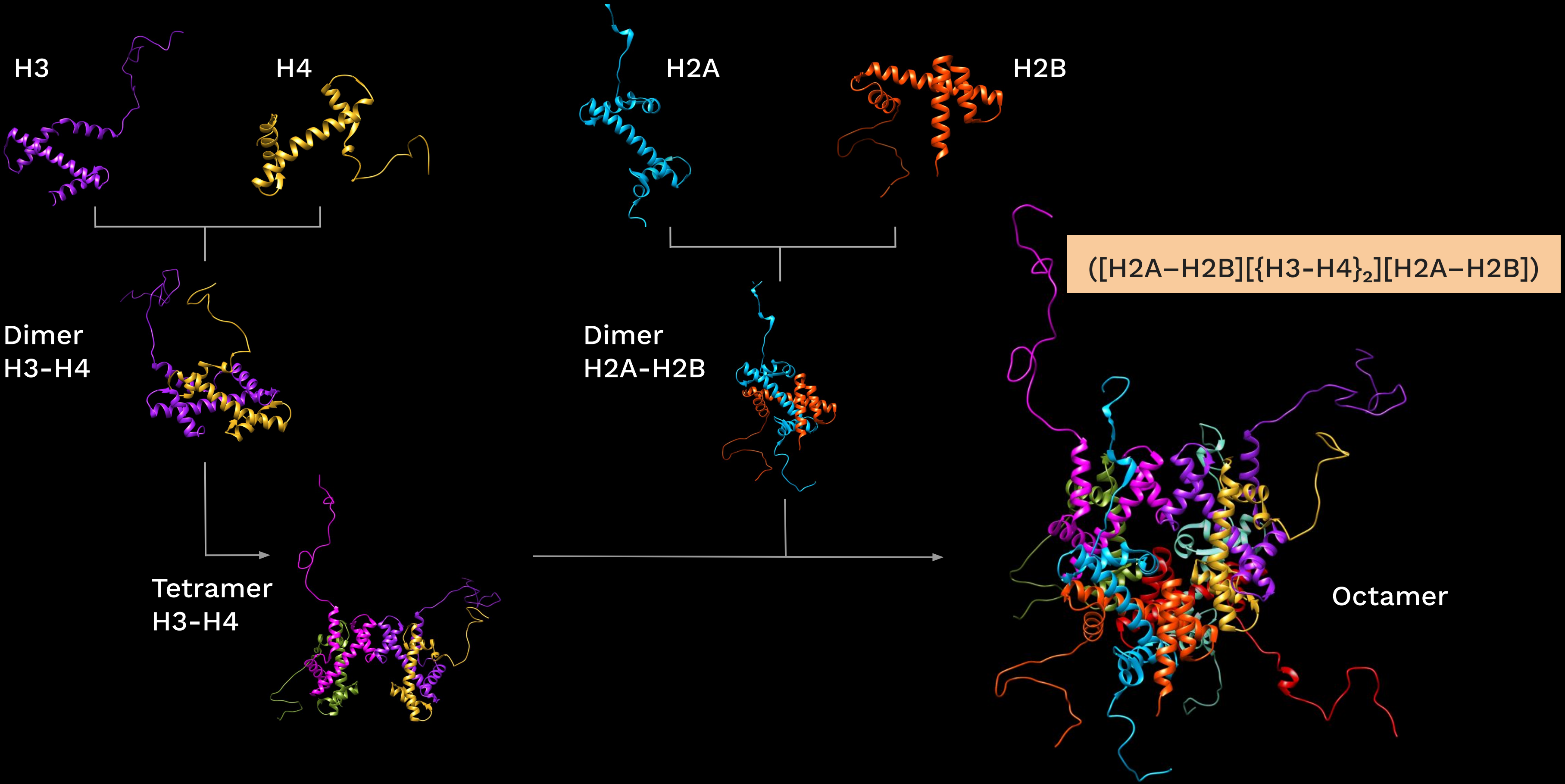
PDBid: 1kx5

Nucleosome axis



SHL: DNA positions around the nucleosome

Histone structure and nucleosome assembly



H3

H4

H2A

H2B

Dimer
H3-H4

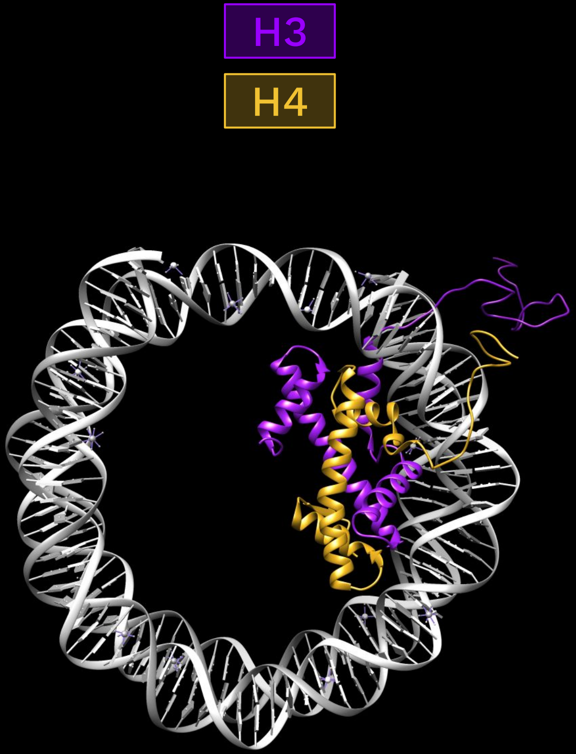
Dimer
H2A-H2B

$([\mathrm{H2A{-}H2B}][\{\mathrm{H3{-}H4}\}_2][\mathrm{H2A{-}H2B}])$

Tetramer
H3-H4

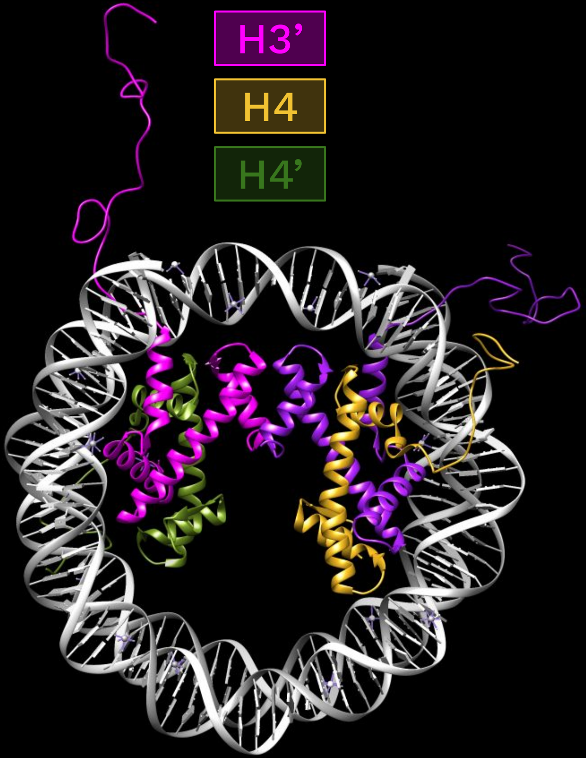
Octamer

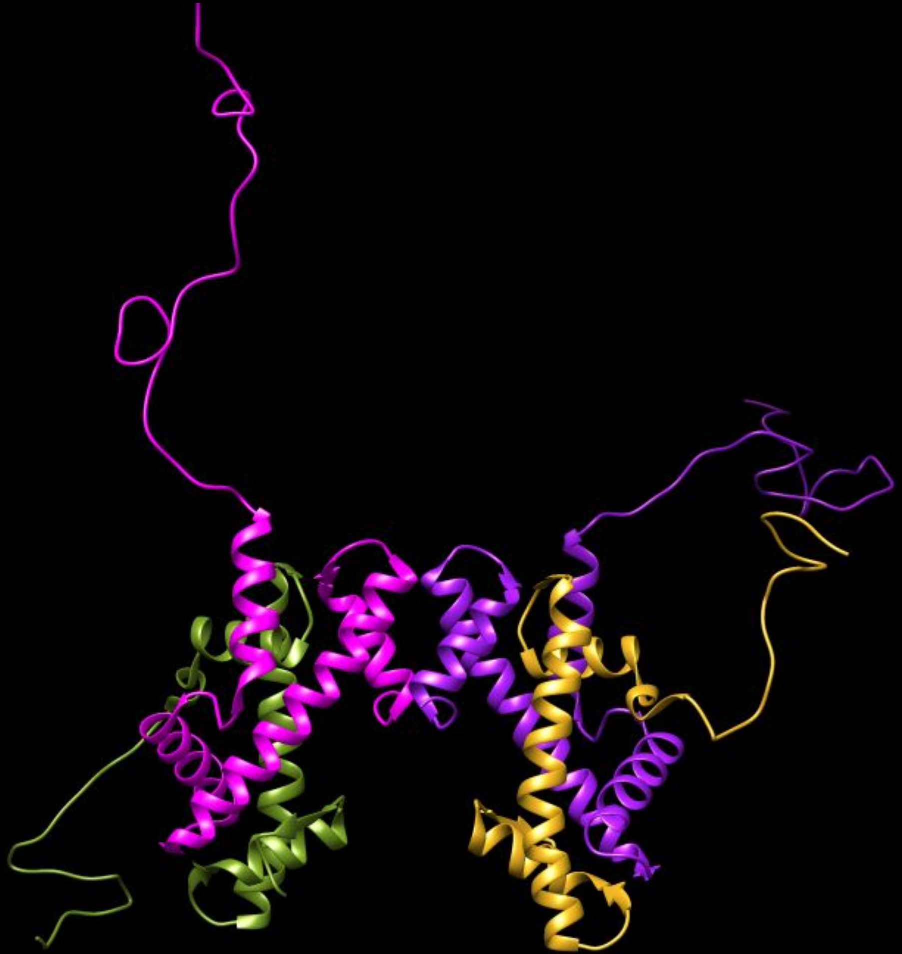
H3-H4 dimer



H3-H4 tetramer

H3
H3’
H4
H4’

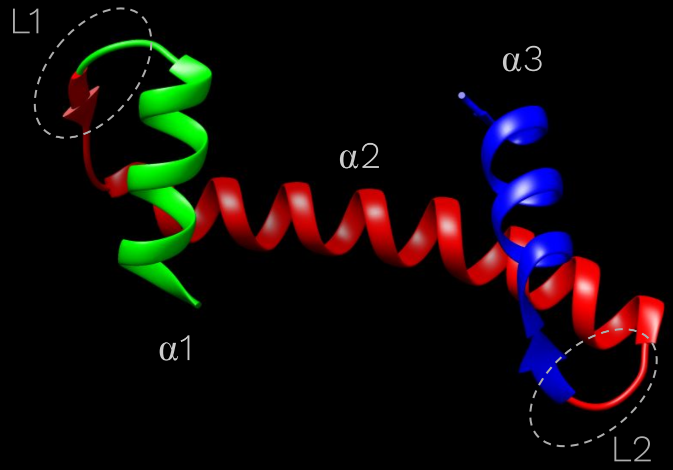




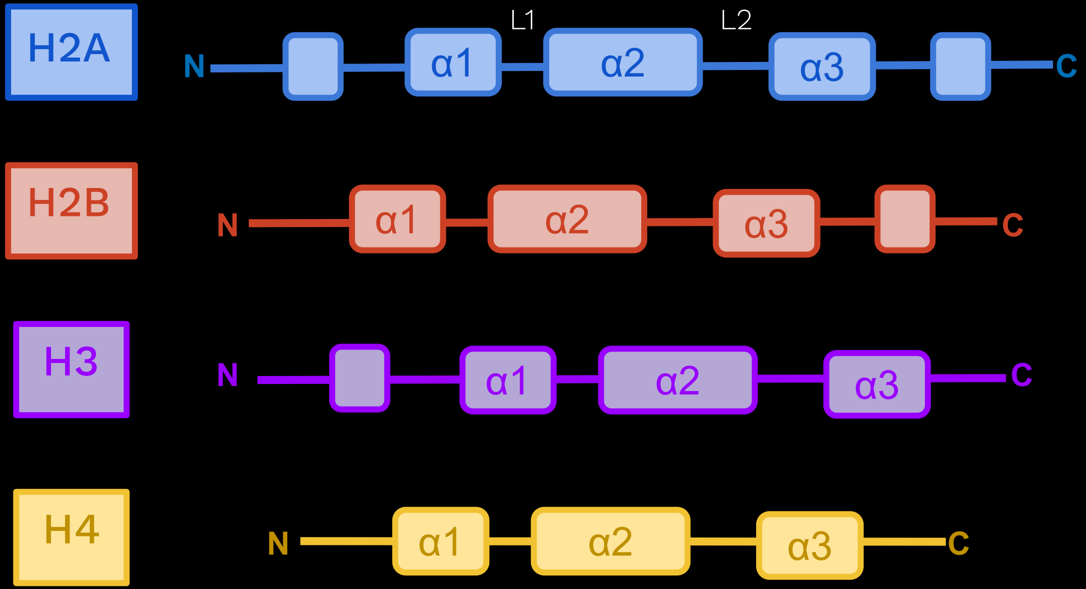
H2A-H2B dimer

SCOP Classification: Histone core proteins

Class	All alpha proteins
Fold	Histone fold
Superfamily	Histone fold superfamily
Family	Nucleosome core histones



Histone fold



H2A

N α1 L1 α2 L2 α3 C

H2B

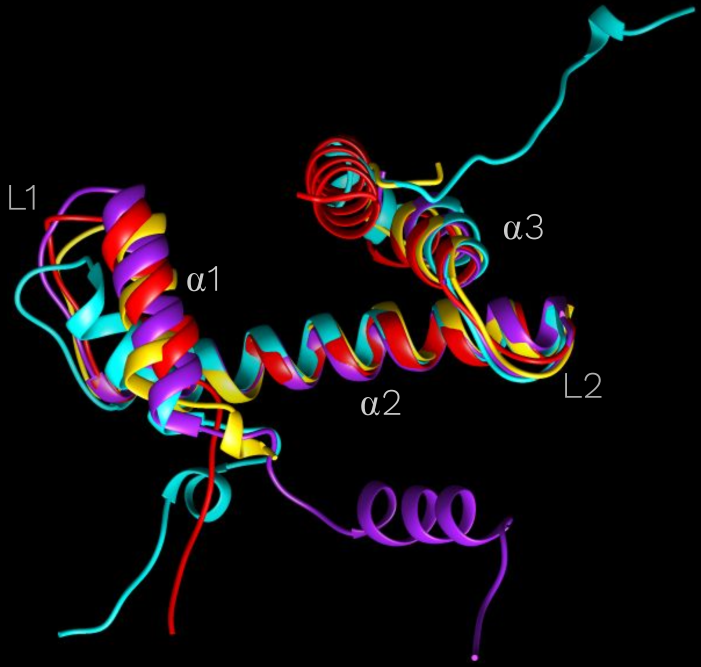
N α1 α2 α3 C

H3

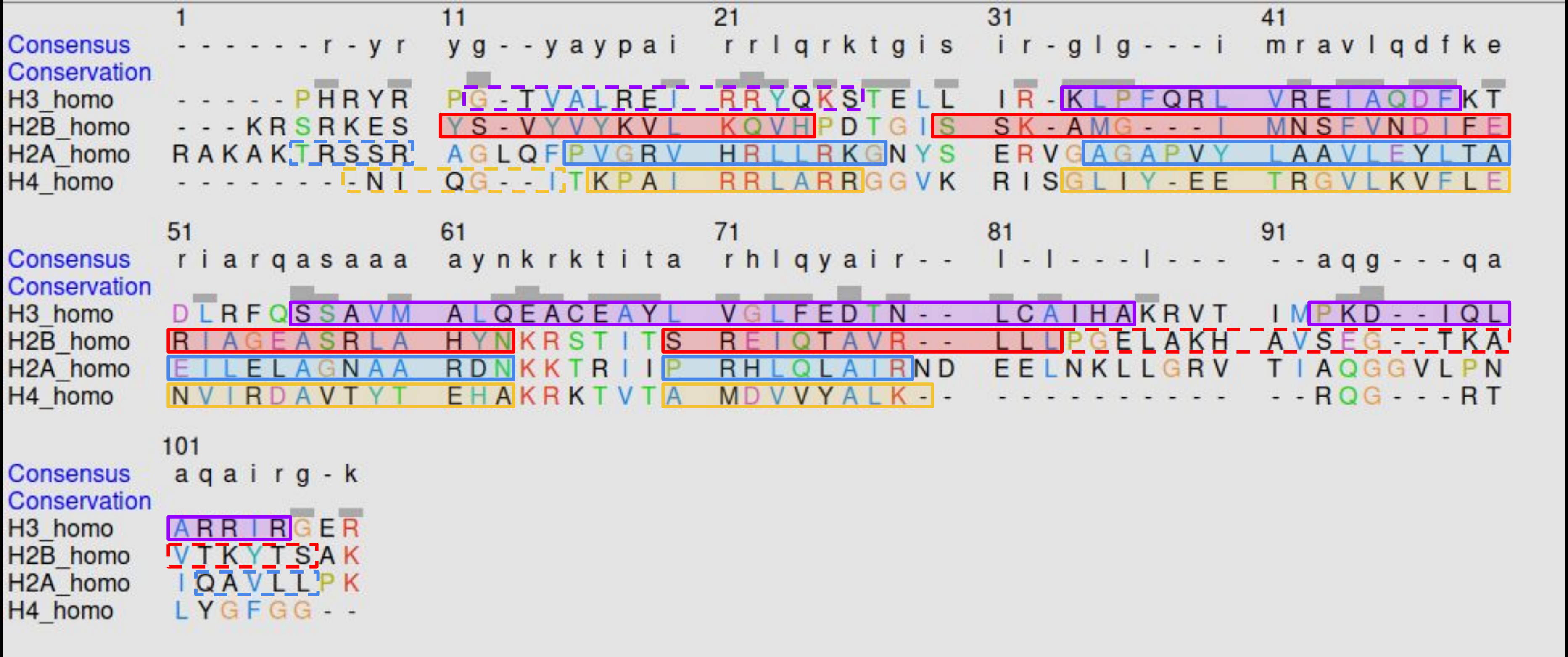
N α1 α2 α3 C

H4

N α1 α2 α3 C

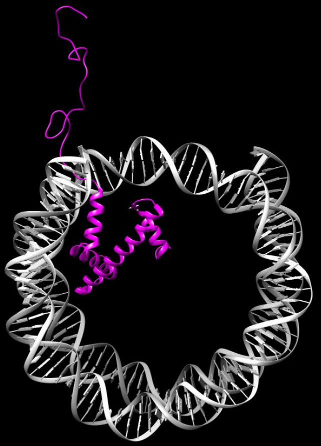


Histone alignment



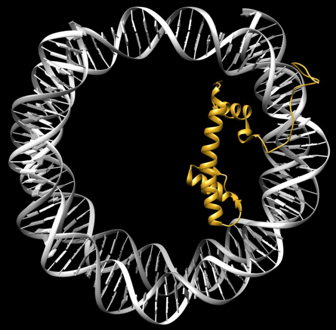
```
              1                     11                    21                    31                    41
Consensus     - - - - - - r - y r   y g - - y a y p a i   r r l q r k t g i s   i r - g l g - - - i   m r a v l q d f k e
Conservation
H3_homo       - - - - - P H R Y R   P G - T V A L R E I   R R Y Q K S T E L L   I R - K L P F Q R L   V R E I A Q D F K T
H2B_homo      - - - K R S R K E S   Y S - V Y V Y K V L   K Q V H P D T G I S   S K - A M G - - - I   M N S F V N D I F E
H2A_homo      R A K A K T R S S R   A G L Q F P V G R V   H R L L R K G N Y S   E R V G A G A P V Y   L A A V L E Y L T A
H4_homo       - - - - - - - - N I   Q G - - I T K P A I   R R L A R R G G V K   R I S G L I Y - E E   T R G V L K V F L E

              51                    61                    71                    81                    91
Consensus     r i a r q a s a a a   a y n k r k t i t a   r h l q y a i r - -   l - l - - - l - - -   - - a q g - - - q a
Conservation
H3_homo       D L R F Q S S A V M   A L Q E A C E A Y L   V G L F E D T N - -   L C A I H A K R V T   I M P K D - - I Q L
H2B_homo      R I A G E A S R L A   H Y N K R S T I T S   R E I Q T A V R - -   L L L P G E L A K H   A V S E G - - T K A
H2A_homo      E I L E L A G N A A   R D N K K T R I I P   R H L Q L A I R N D   E E L N K L L G R V   T I A Q G G V L P N
H4_homo       N V I R D A V T Y T   E H A K R K T V T A   M D V V Y A L K - -   - - - - - - - - - -   - - R Q G - - - R T

              101
Consensus     a q a i r g - k
Conservation
H3_homo       A R R I R G E R
H2B_homo      V T K Y T S A K
H2A_homo      I Q A V L L P K
H4_homo       L Y G F G G - -
```

Histone tails



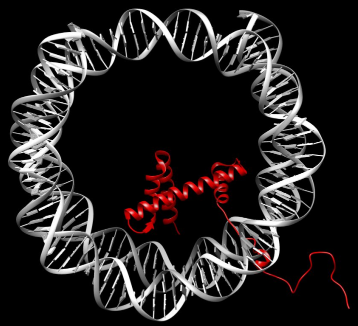
H3 N-terminal tail

DNA wrapping.



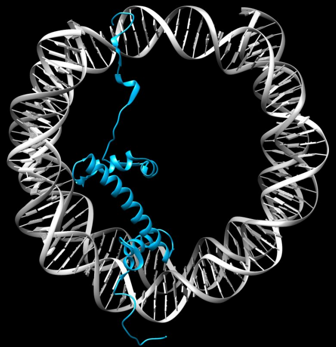
H4 N-terminal tail

Internucleosomal binding.



H2B N-terminal tail

Modulation of the nucleosome position.



H2A N-terminal tail

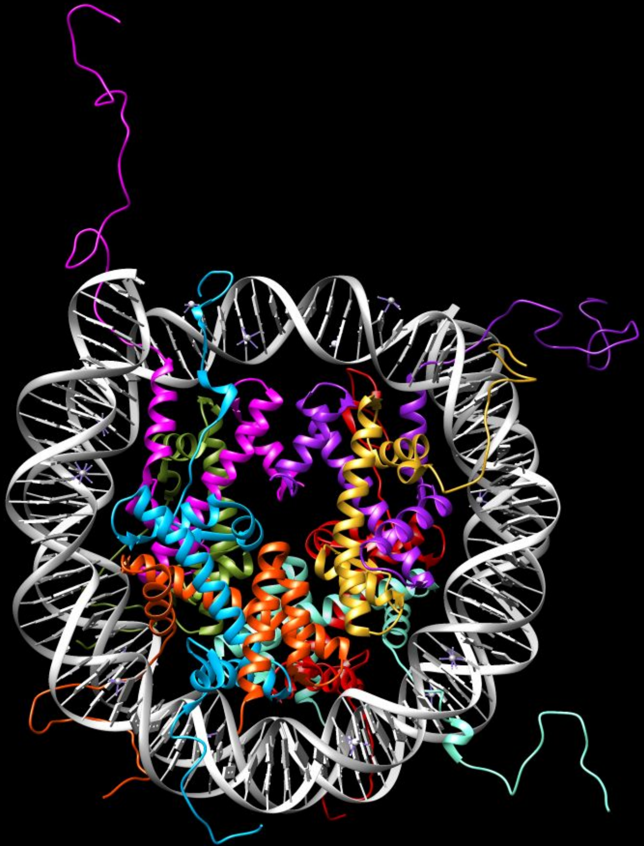
Internucleosomal binding.

H2A C-terminal tail

Binding to the linker DNA.

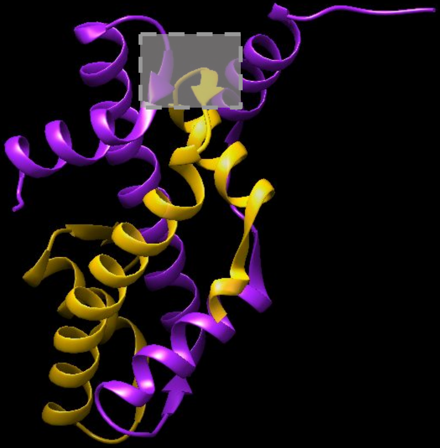
- Modulate nucleosome recognition and influence the condensed state of the chromatin fiber.

HISTONE INTERACTIONS

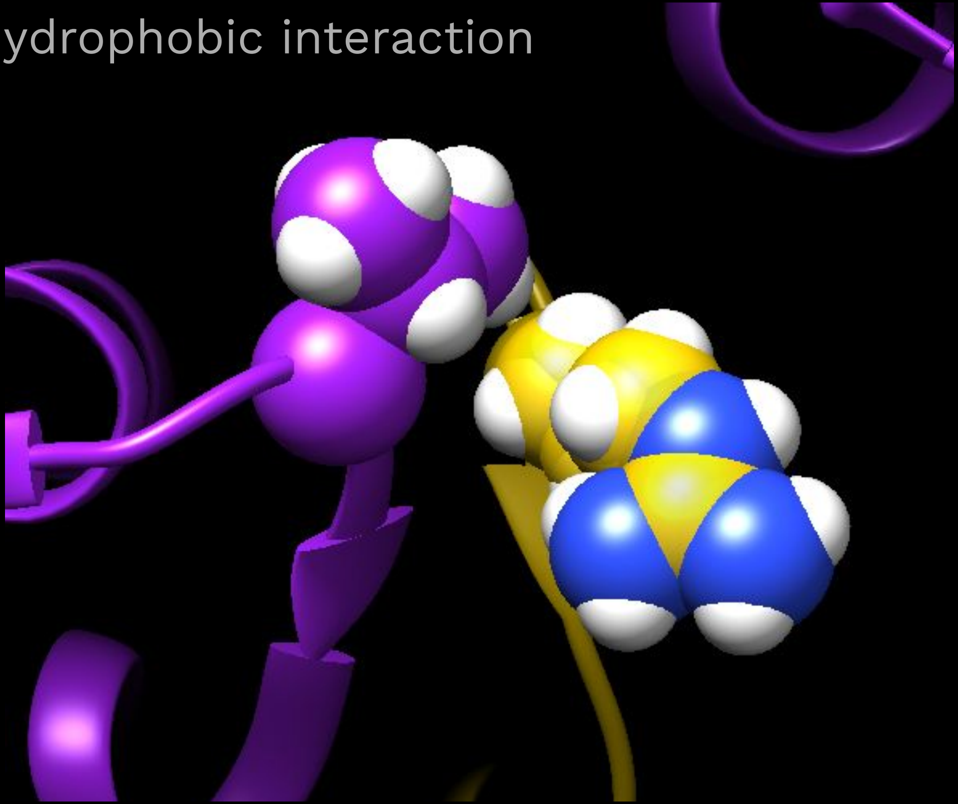


Dimer H3-H4

H3 - H4	
Val-117	Arg-45

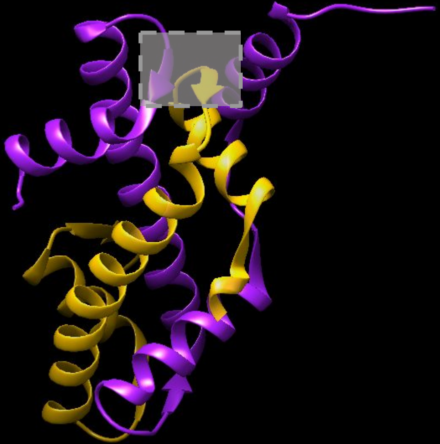


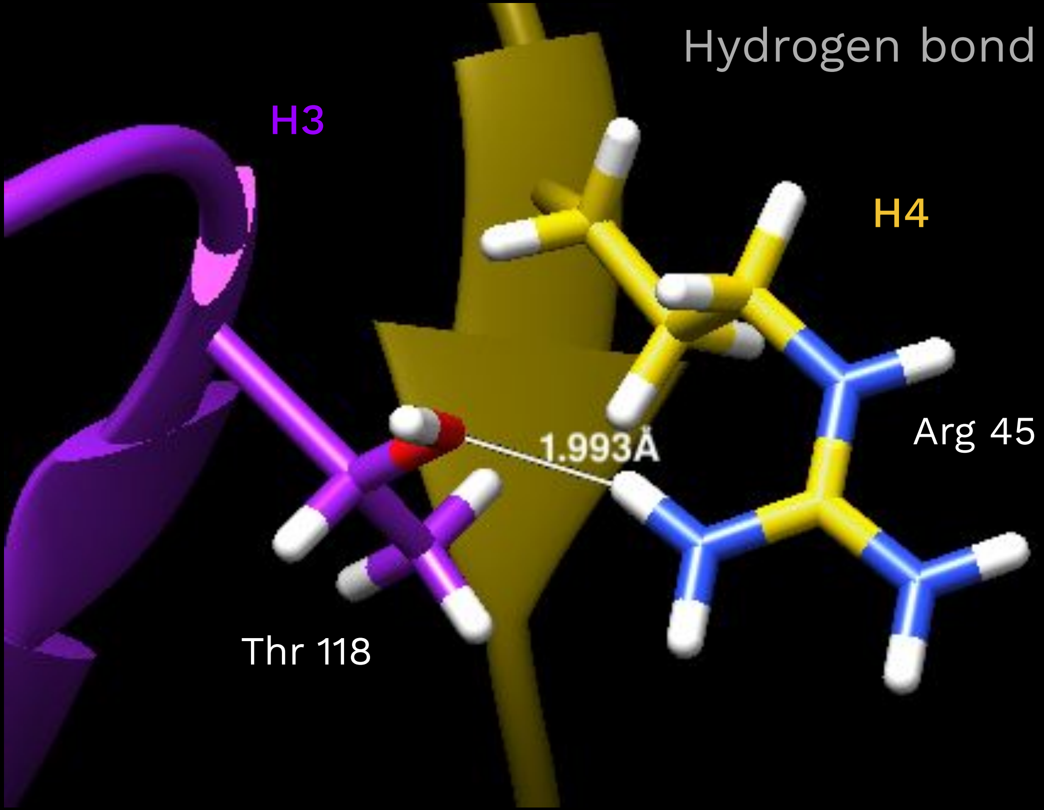
Hydrophobic interaction



Dimer H3-H4

H3 - H4	
Thr-118	Arg-45

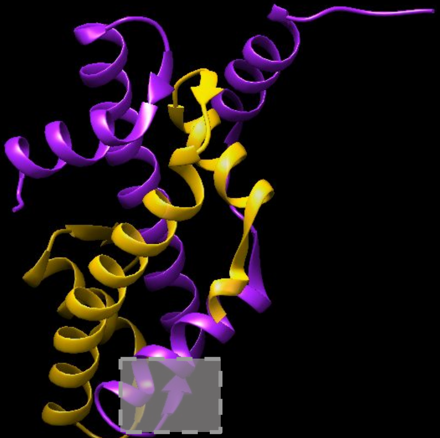


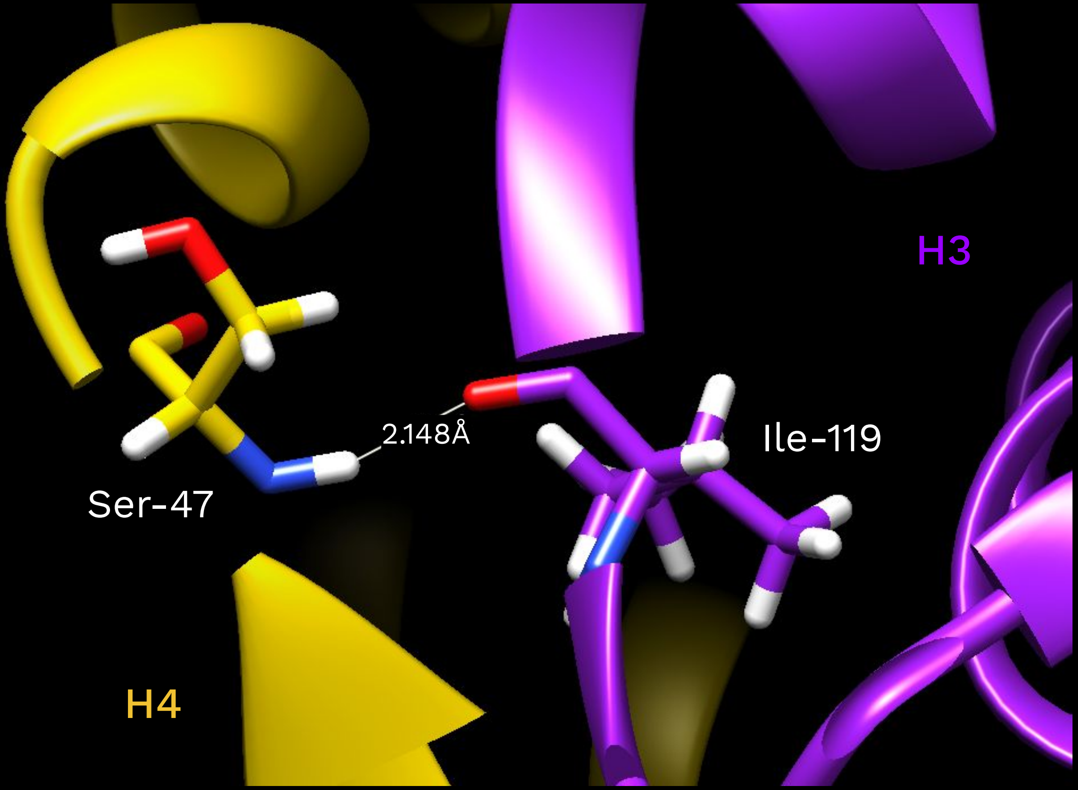


Dimer H3-H4

H3 - H4

Ile-119	Ser-47

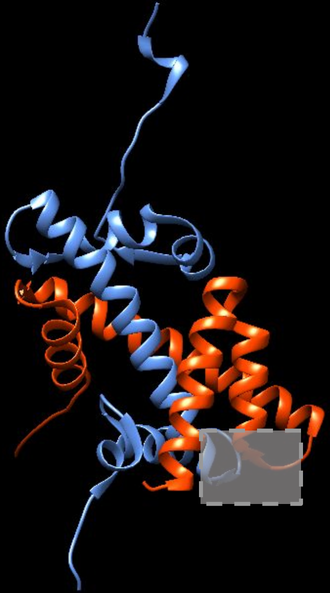


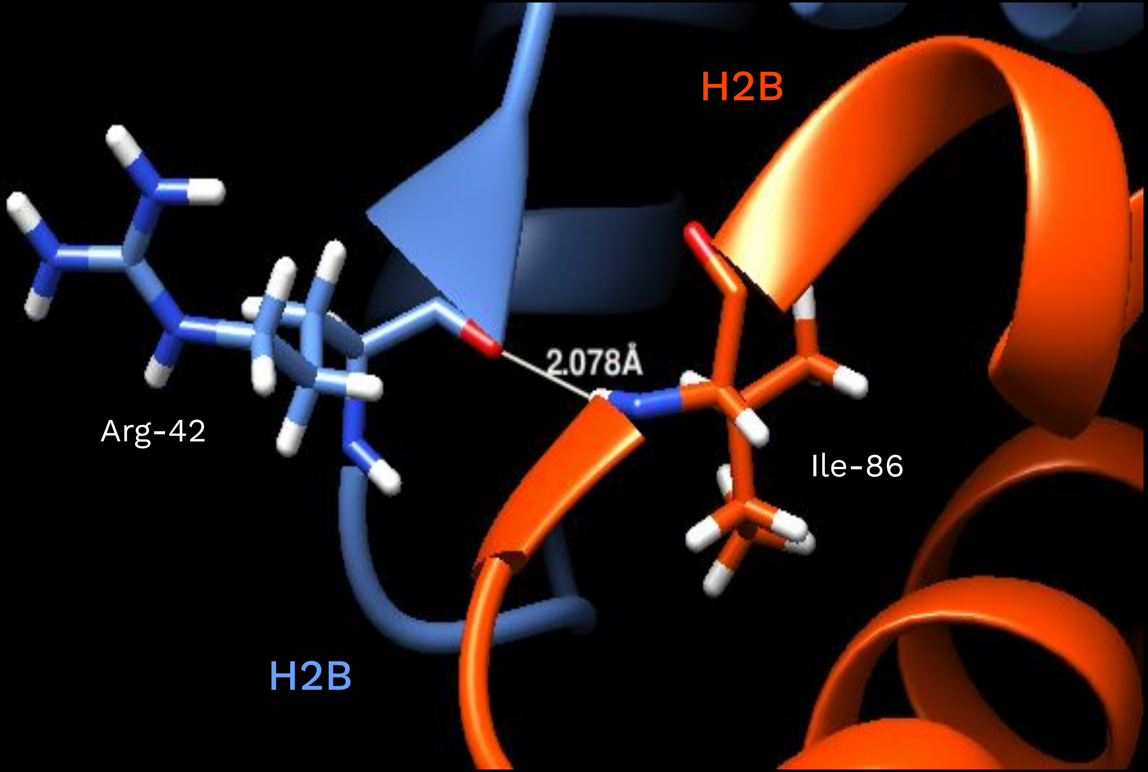


Hydrogen bond

Dimer H2A-H2B

H2A-H2B	
Arg-42	Ile-86



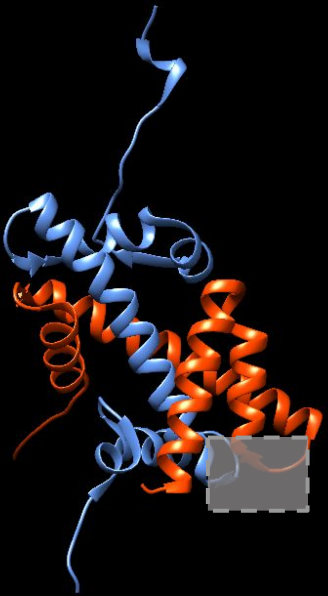


Hydrogen bond

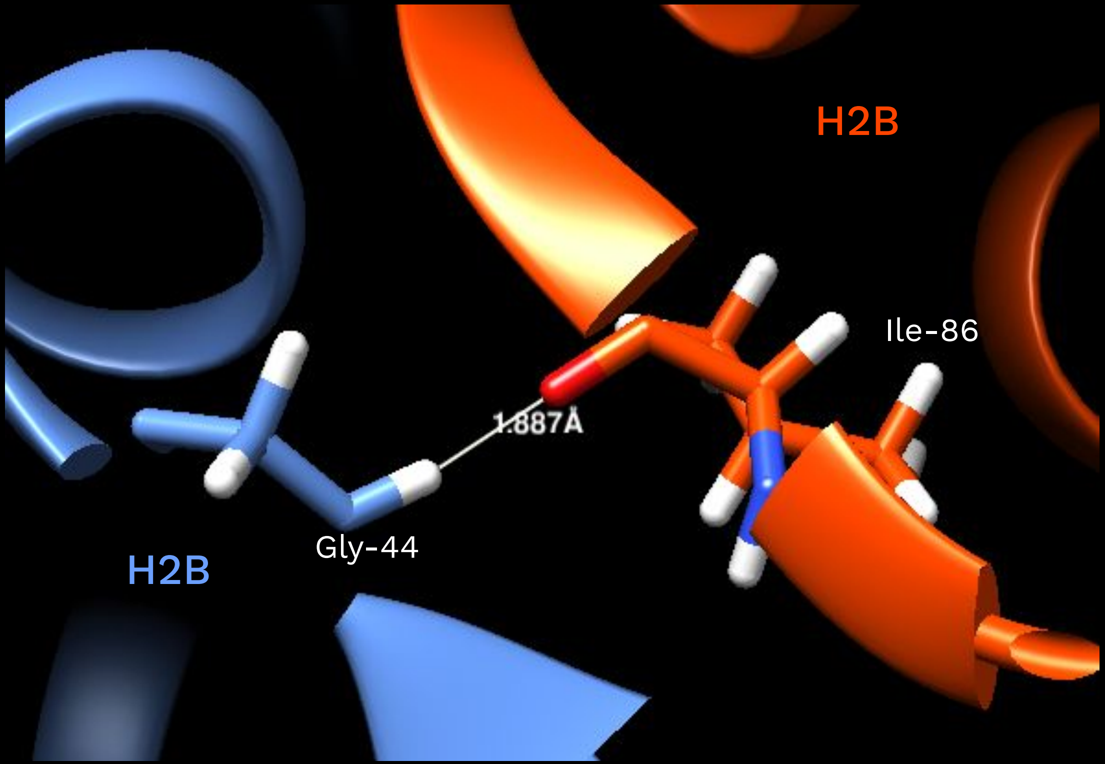
Dimer H2A-H2B

H2A-H2B

Gly-44	Ile-86



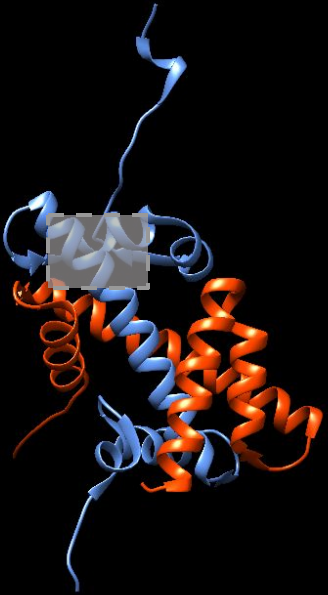
Hydrogen bond



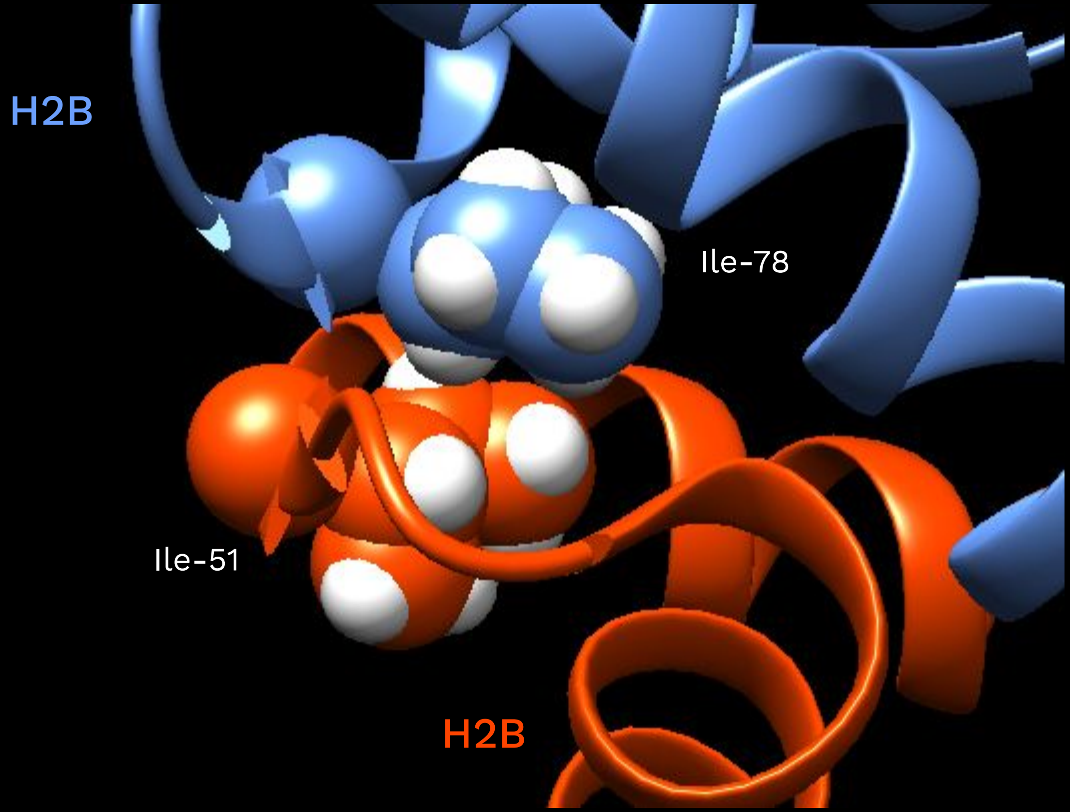
Dimer H2A-H2B

H2A-H2B

Ile-78	Ile-51



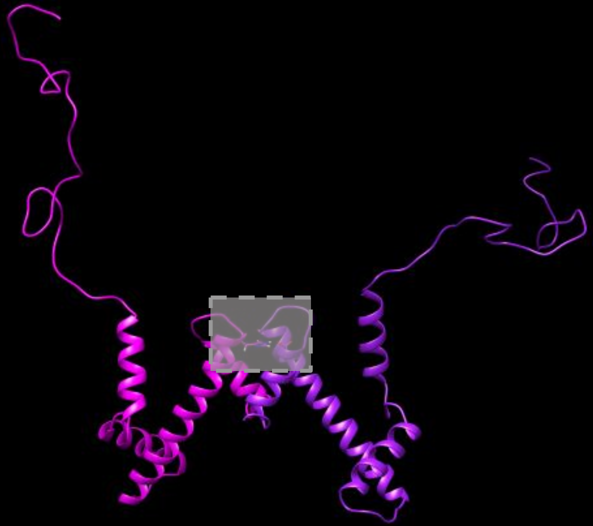
Hydrophobic interaction

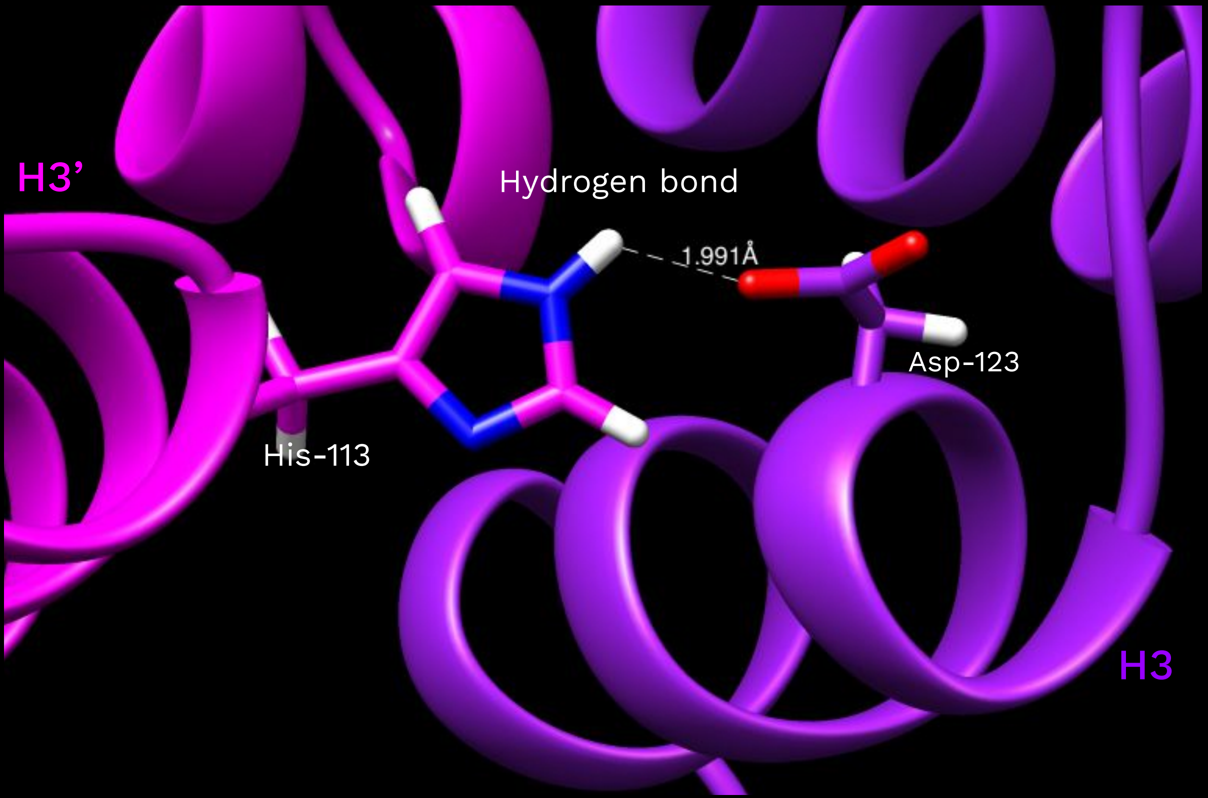


Tetramer H3-H4

H3 - H3’

Asp-123	His-113

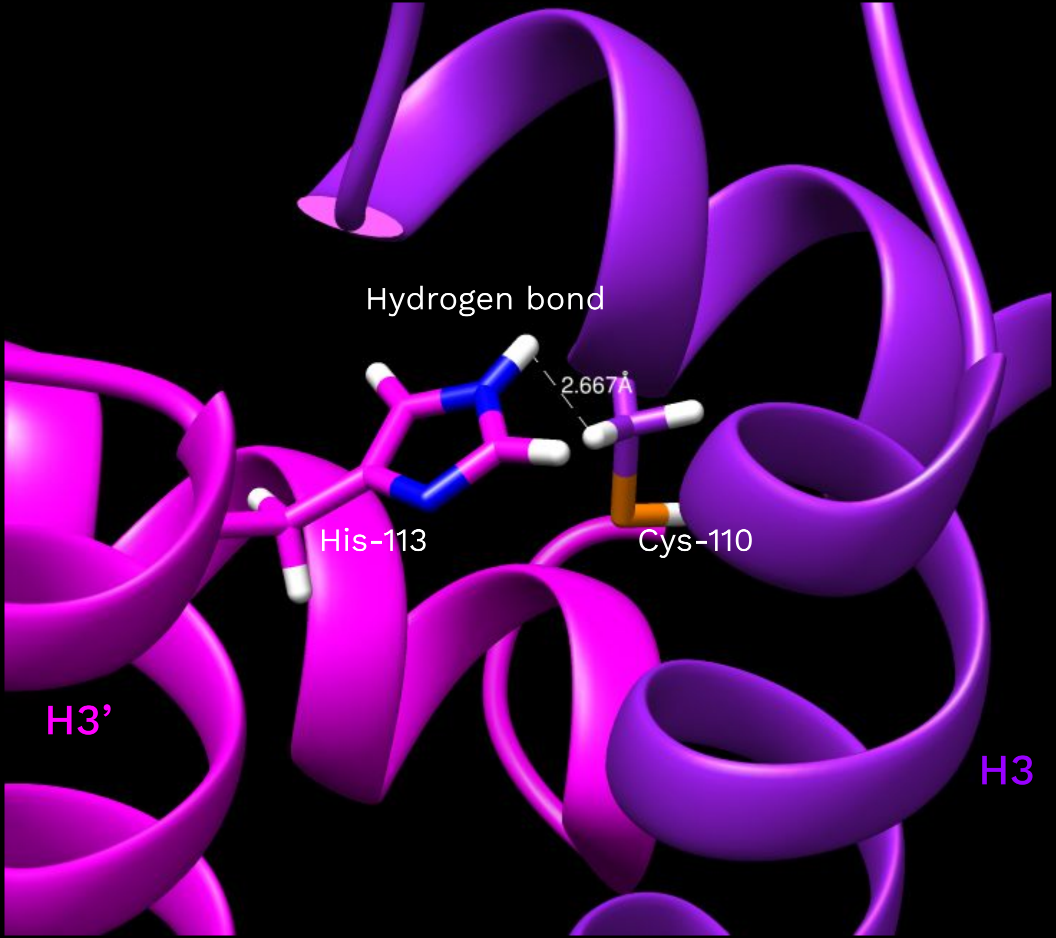




Tetramer H3-H4

H3 - H3’

Cys-110	His-113



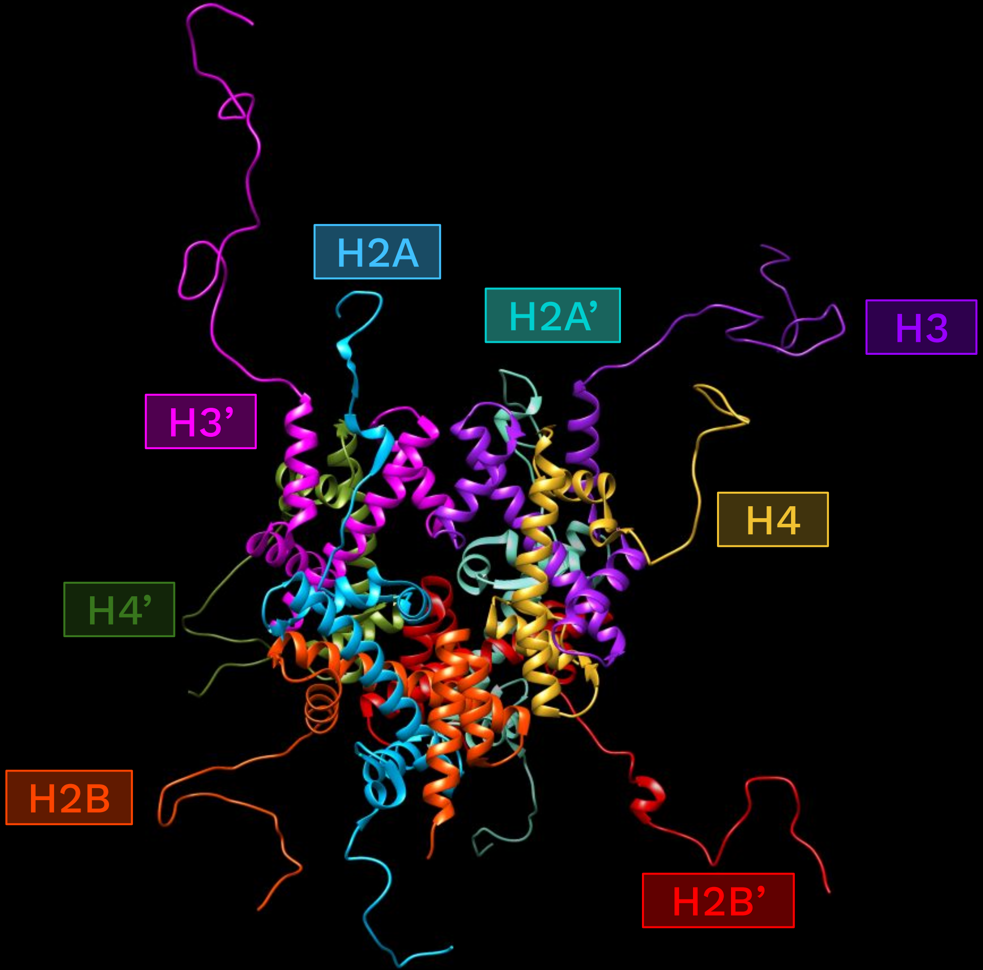
OCTAMER

H3 - H4
H2A - H2B } 4 histone fold dimers

H3 - H4 → 4 helix bundle → tetramer

+ H2A - H2B

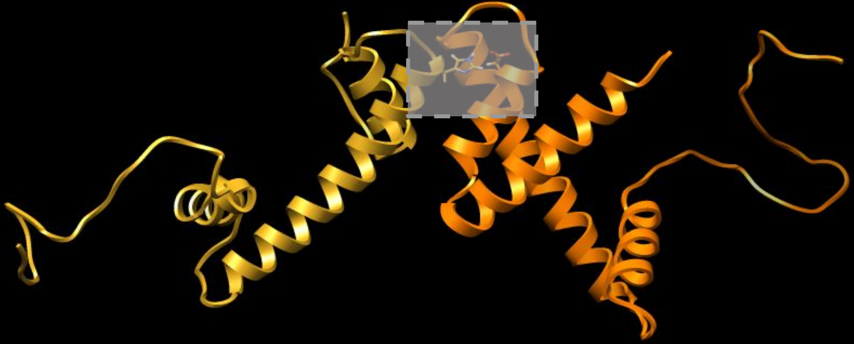
2nd 4 helix bundle → octamer

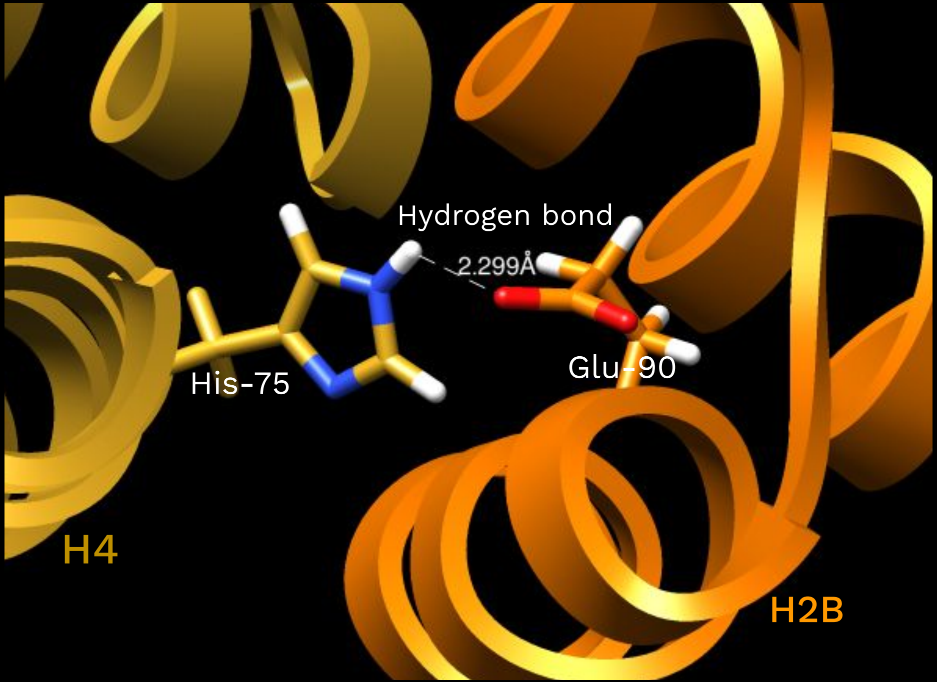


Octamer interactions

Histone 4 - Histone 2B

His 75	Glu 60
Arg 92	Glu 73

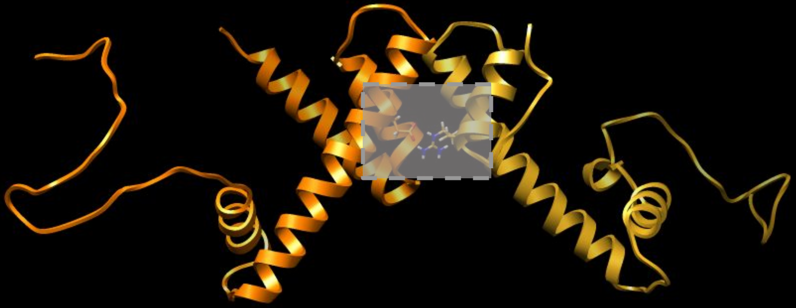


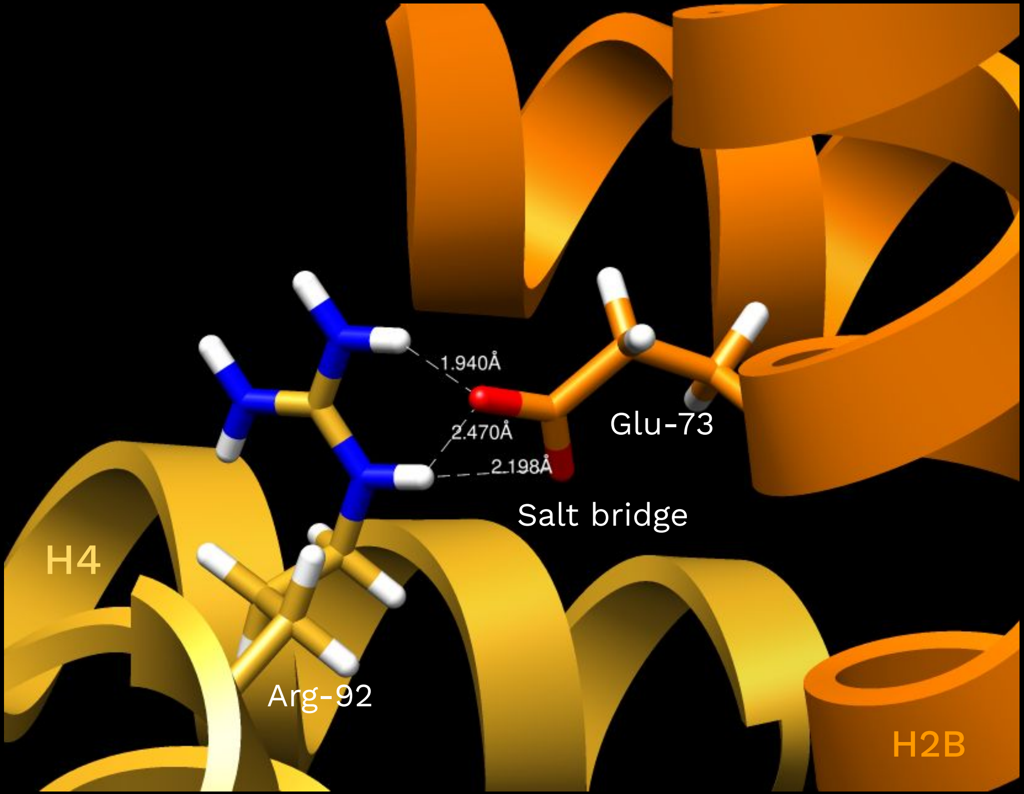


Octamer interactions

Histone 4 - Histone 2B

His 75	Glu 60
Arg 92	Glu 73

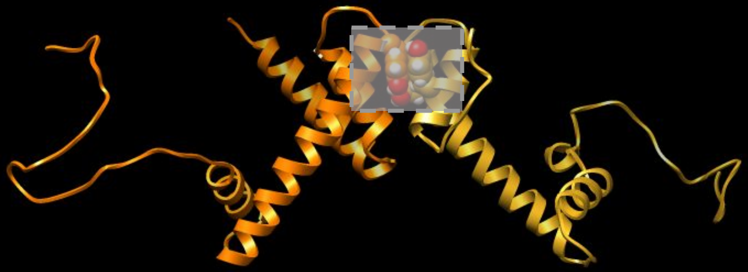


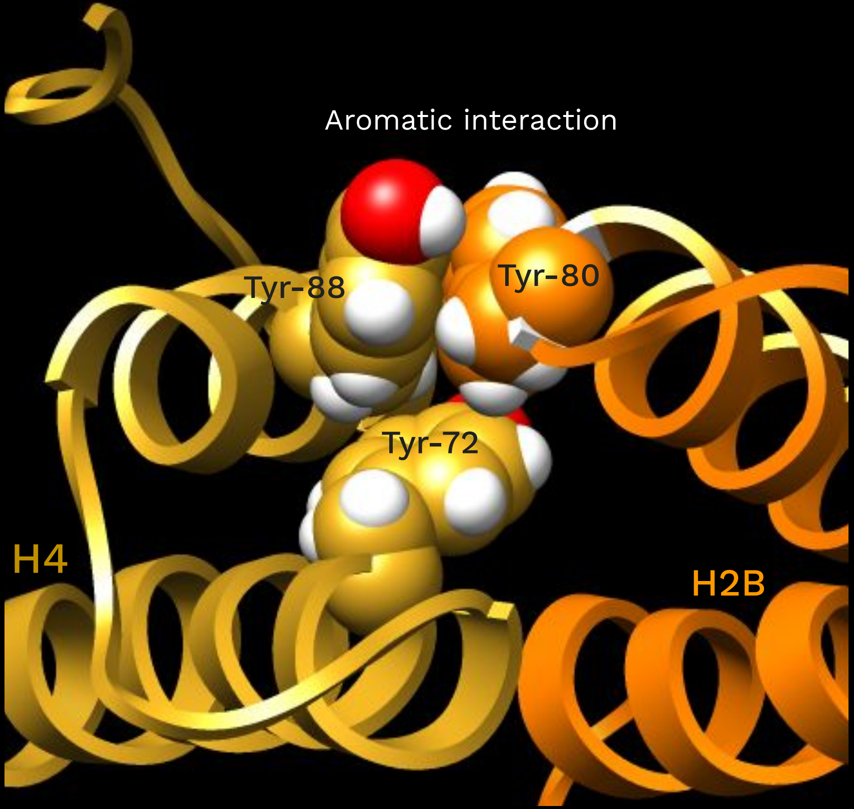


Octamer interactions

Octamer Hydrophobic Cluster

H4 Tyr-88	H4 Tyr-72	H2B Tyr-80

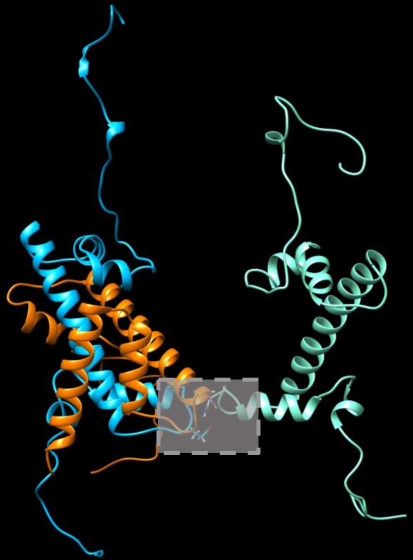


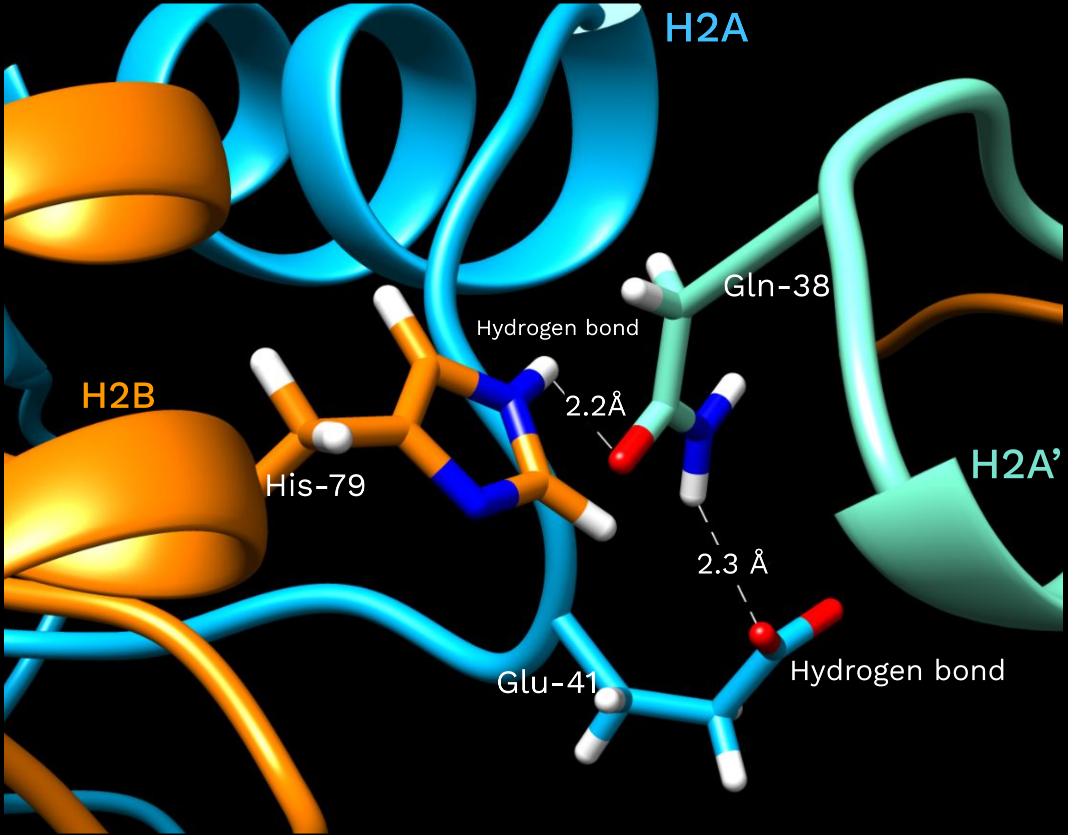


Octamer interactions

H2A - H2B - H2A’

Glu-41	His-79	Gln38

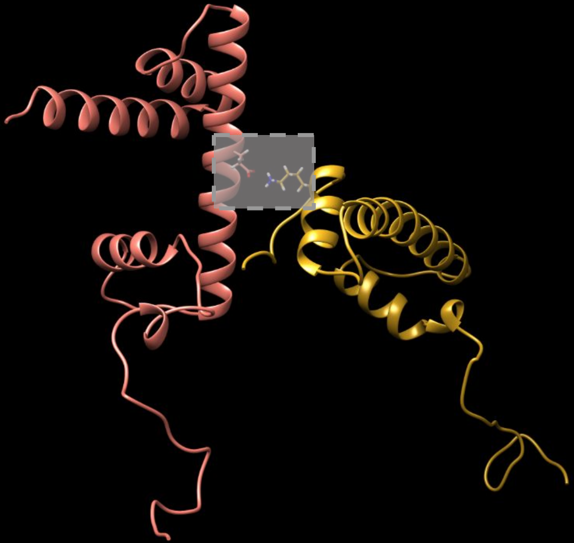


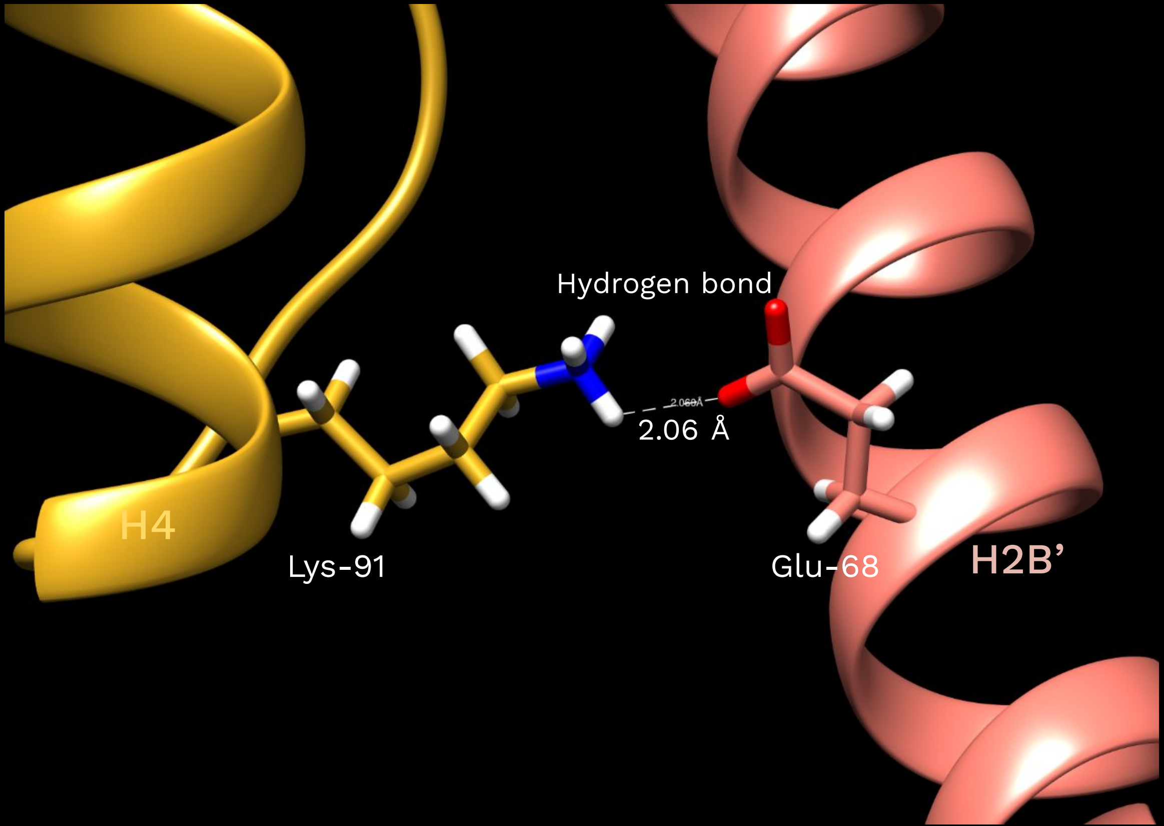


Octamer interactions

H4 - H2B’

Lys-91	Glu-68

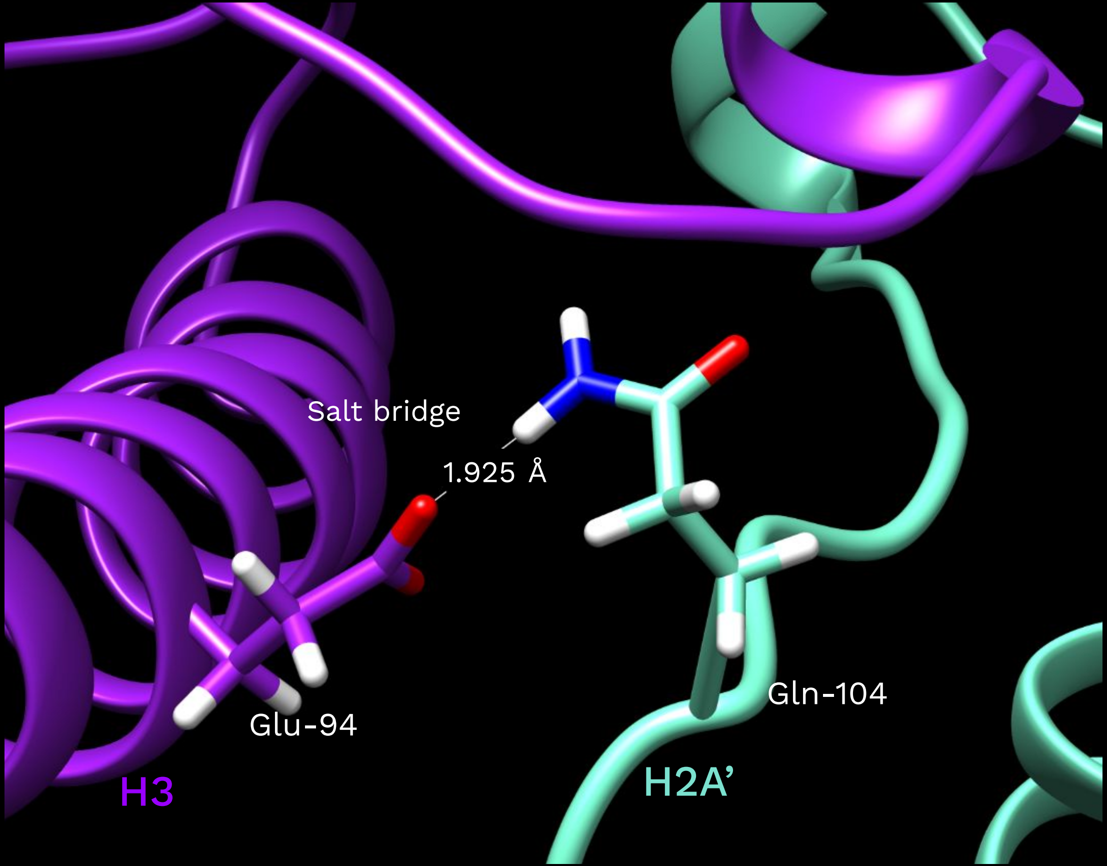




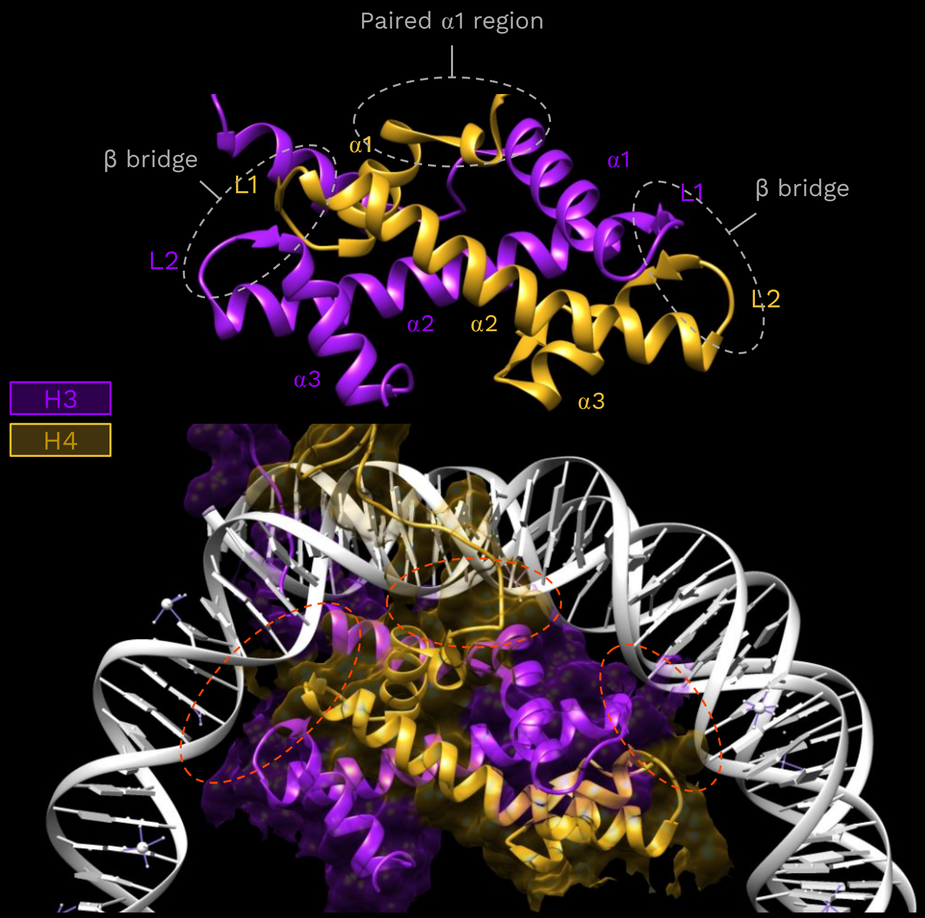
Octamer interactions

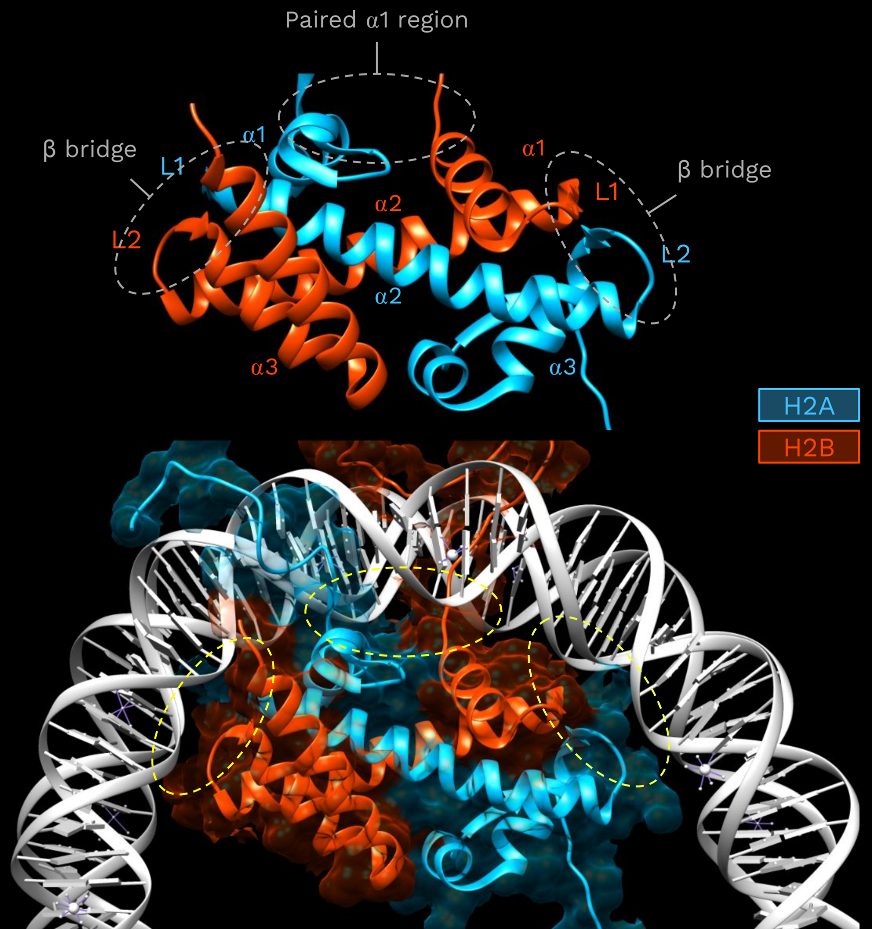
H3 - H2A’

Glu-94	Gln-104



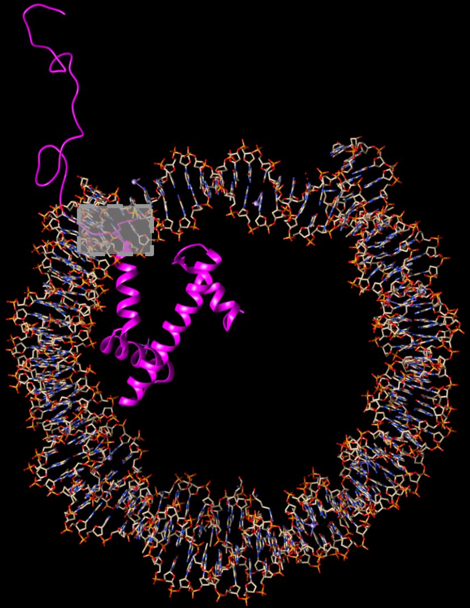
Contact sites for the DNA

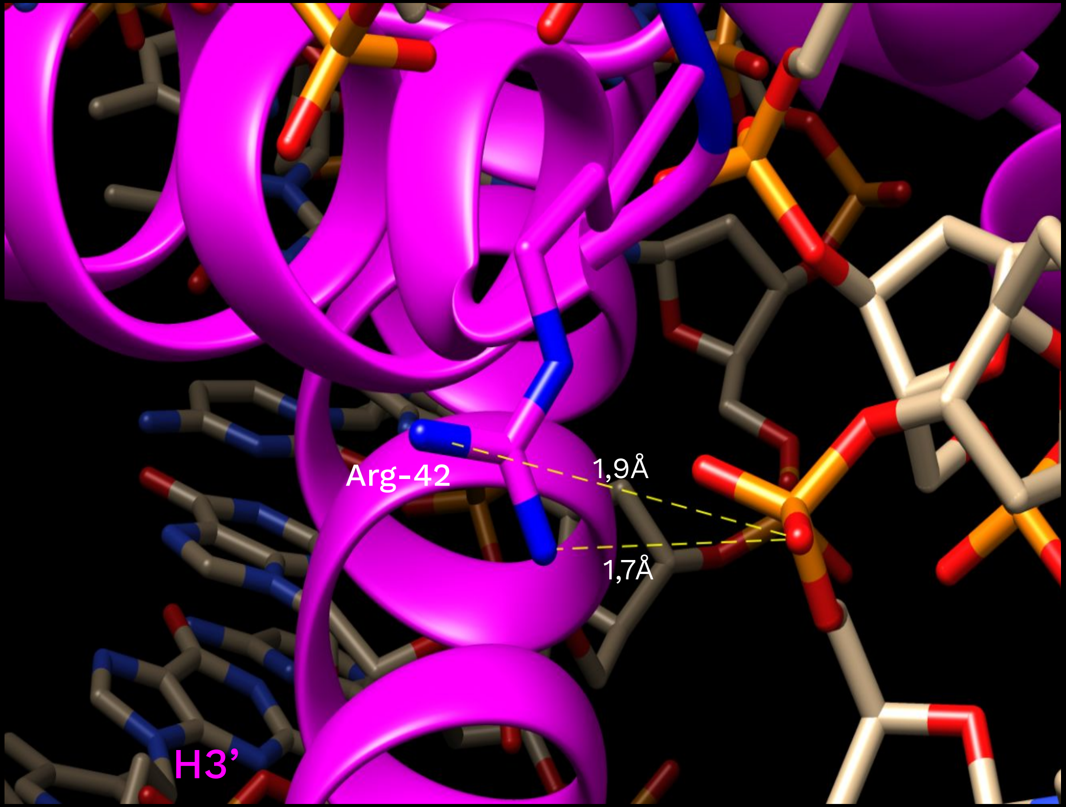




Salt bridge

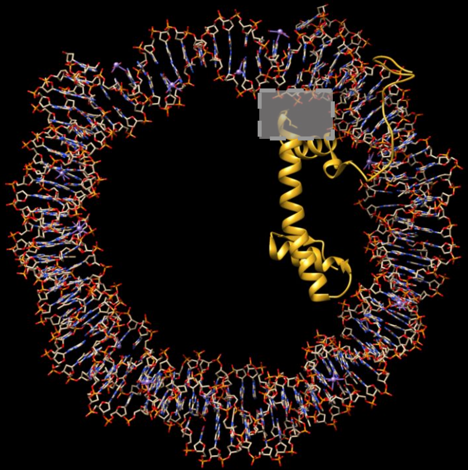
Most common mechanism.
Electrostatic attraction between the charged molecular entities of the guanidinium nitrogens to the phosphate group oxygens.

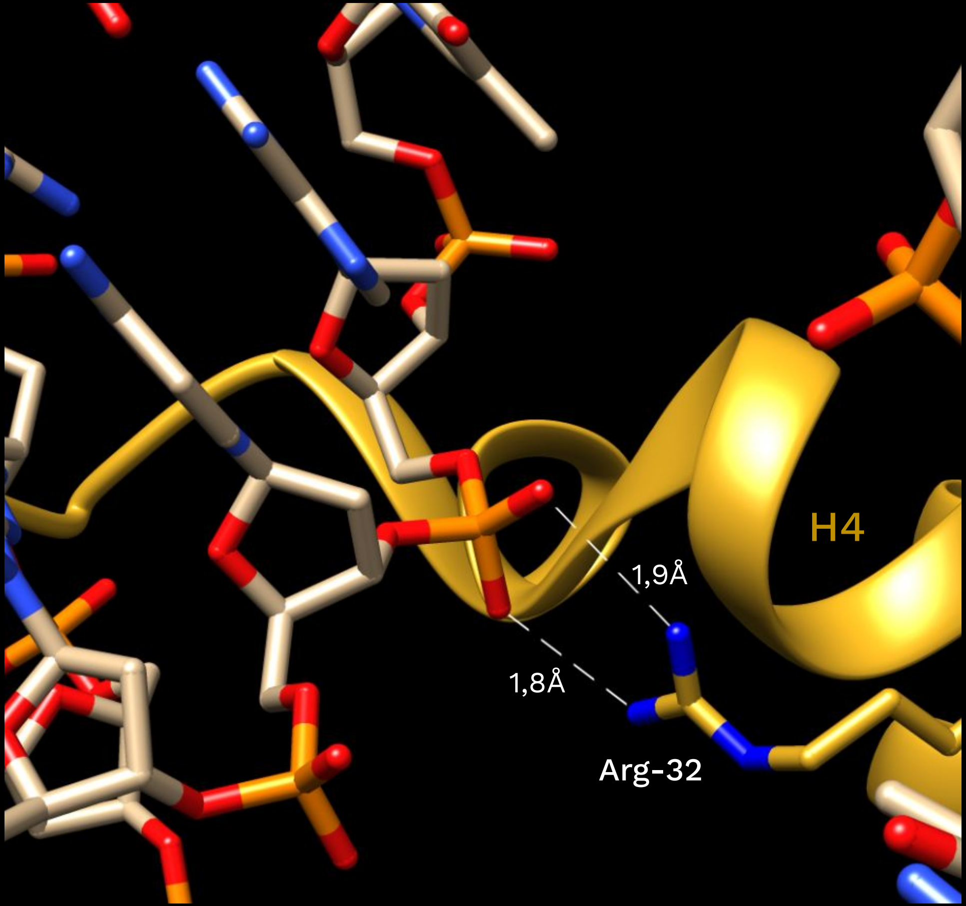




Hydrogen bond

Made from main-chain amide nitrogen atoms of amino acid.



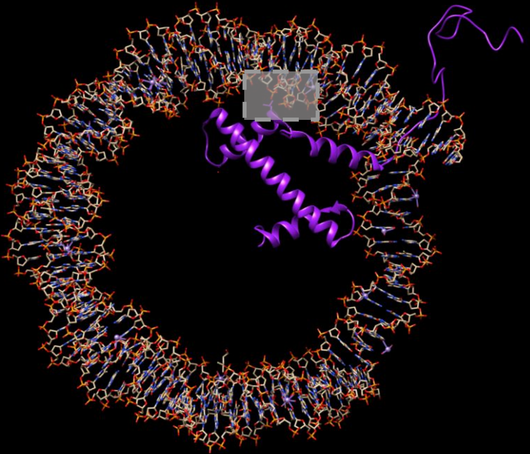


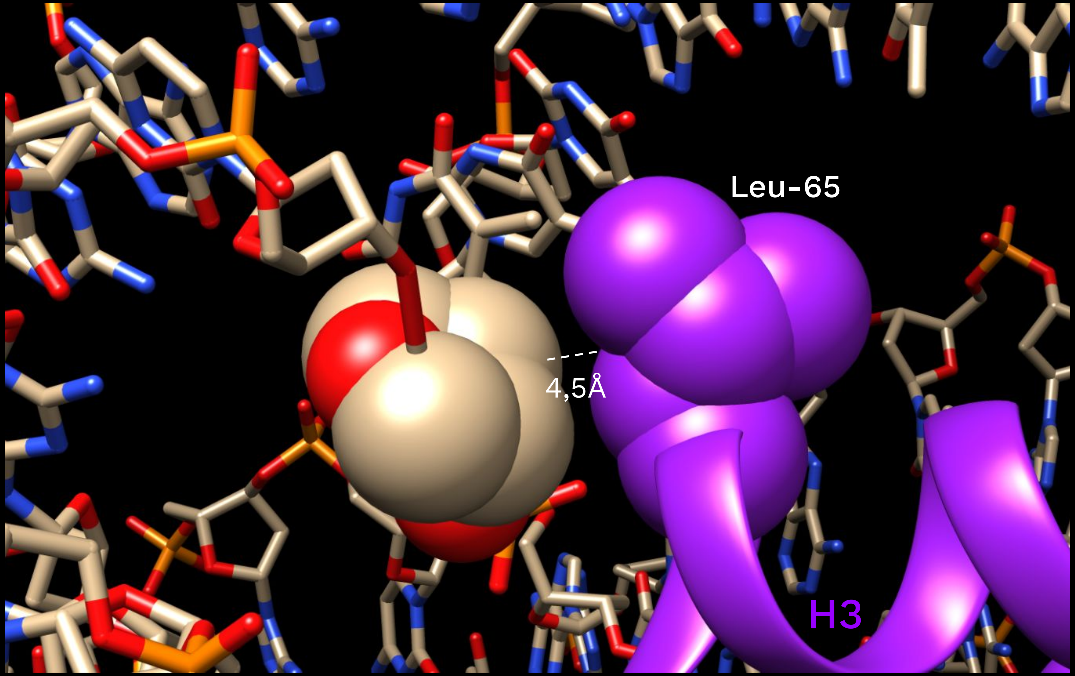
Non-polar interactions

Results when electrons are equally shared between atoms.

This contacts are made with deoxyribose groups.

(Leu-65) - (5-methyl group of thymidine)





POST-TRANSLATIONAL MODIFICATIONS

Acetylation

Addition of acetyl groups to lysine residues on the N-terminal tails.

Phosphorylation

Addition of phosphate groups to serine, threonine, or tyrosine residues of histone proteins.

Methylation

Addition of methyl groups to specific Lys, His or Arg residues on histone proteins.

Citrullination

Conversion of arginine residues to citrulline.

Acetylation

Lys acetylation neutralizes positive charge → Stabilization of histone-DNA and inter-nucleosomal electrostatic interactions → Reduced DNA compaction (euchromatin-like)

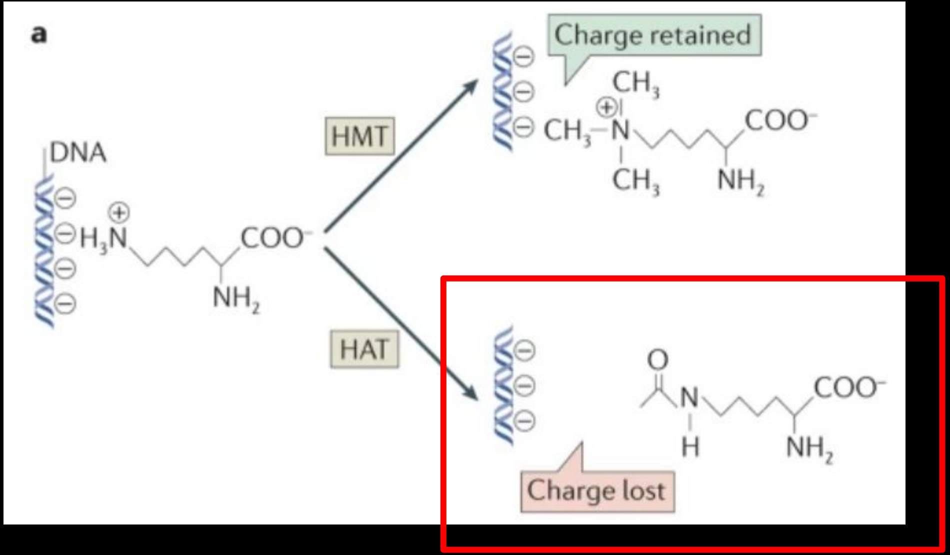


Figure: Tessarz P, Kouzarides T. Histone core modifications regulating nucleosome structure and dynamics. Nature Reviews Molecular Cell Biology. 2014;15(11):703-708. https://doi.org/10.1038/nrm3890

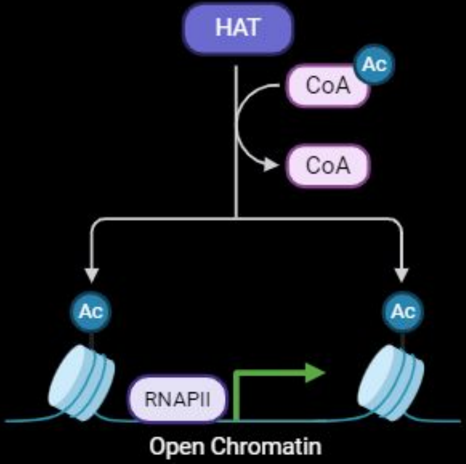
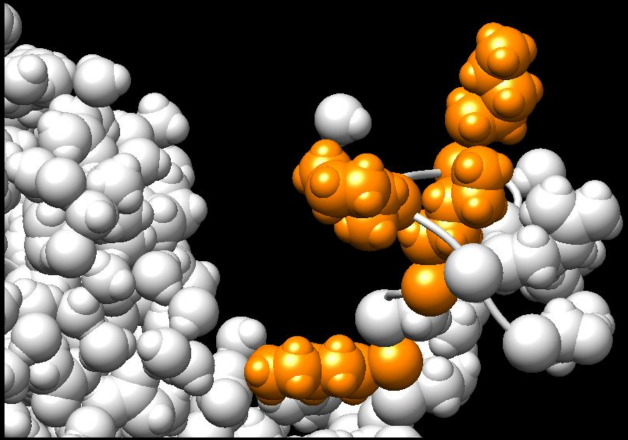


Figure: created with bio render

Acetylation

- Attract transcription factors and chaperones to **promote transcription**.
- N-terminal H4 acetylations (H4K5, H4K8, H4K12, H4K16): transcriptional activators.
- Influence in **histone crosstalk**.
- Acetylation patterns can contribute to the establishment and maintenance of **epigenetic memory**.



H4 N-terminal hyperacetylation

Hyperacetylation → active genes

Hypoacetylation → silent regions (telomeres)

Acetylation

H3K56 acetylation → DNA replication, repair and transcription activation

- Keep nucleosome-free chromatin regions accessible
- Reduces the interaction with DNA
- Lowers H3-H4 binding affinity to DNA
- Enhance transcription factor binding

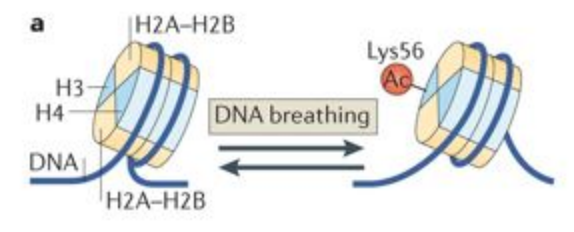
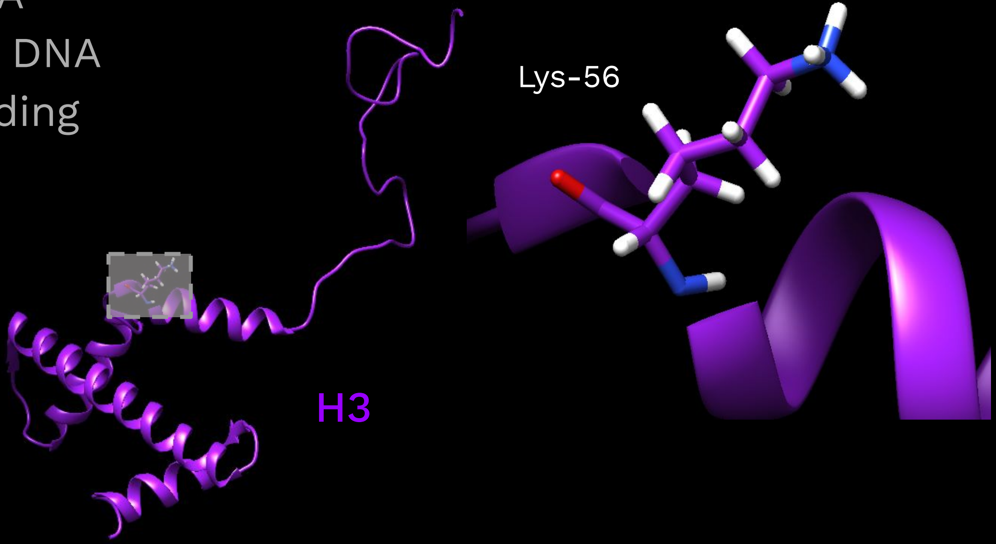


Figure: Tessarz P, Kouzarides T. Histone core modifications regulating nucleosome structure and dynamics. Nature Reviews Molecular Cell Biology. 2014;15(11):703-708. https://doi.org/10.1038/nrm3890



Methylation

- Occurs on all basic residues: arginine, lysines and histidines.
- Maintain positive charge → **electrostatic interaction with DNA.**
- Promotes **the compaction of the chromatin** (heterochromatin-like).

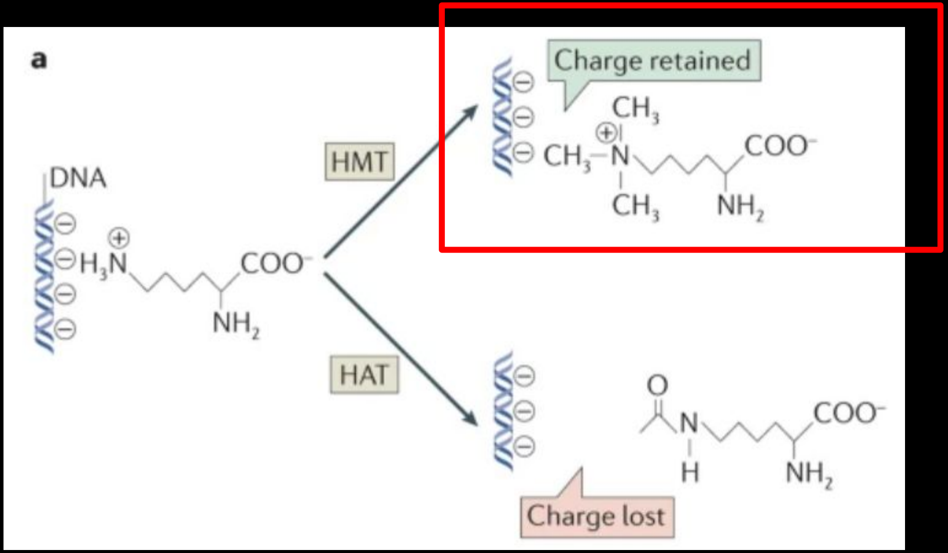


Figure: Tessarz P, Kouzarides T. Histone core modifications regulating nucleosome structure and dynamics. Nature Reviews Molecular Cell Biology. 2014;15(11):703-708. https://doi.org/10.1038/nrm3890

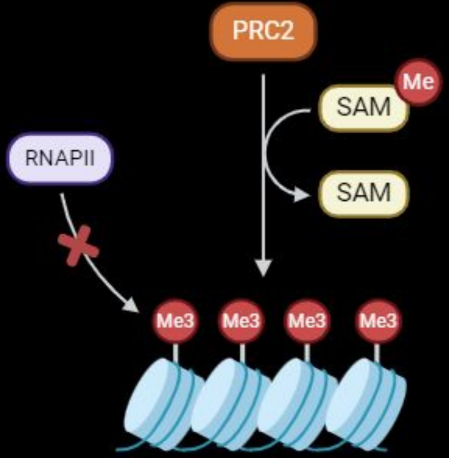
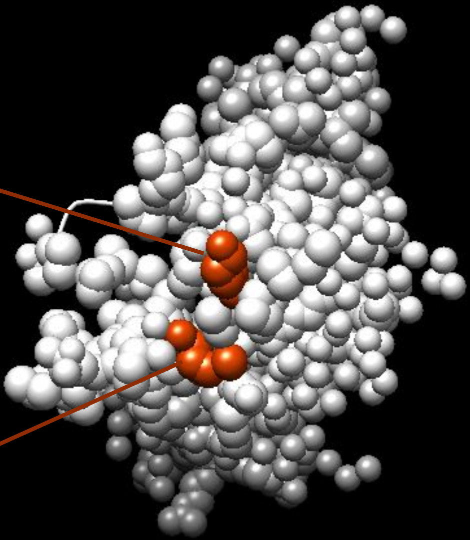


Figure: created with bio render

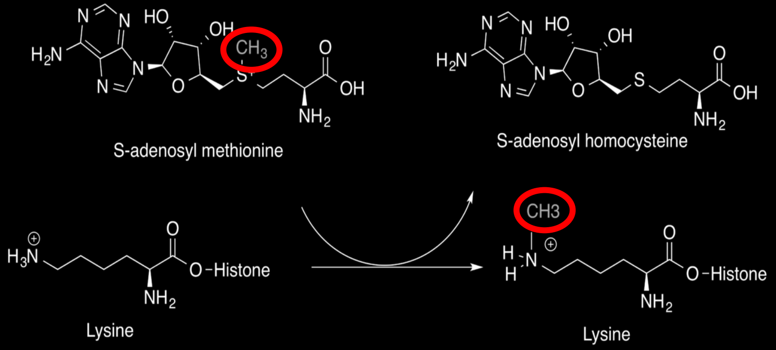
Methylation

Effects of histone methylation can be **context-dependent** and vary based on the specific residue modified and the degree of methylation.

H3K4 trimethylation:
transcription activation
+
activation pluripotency genes

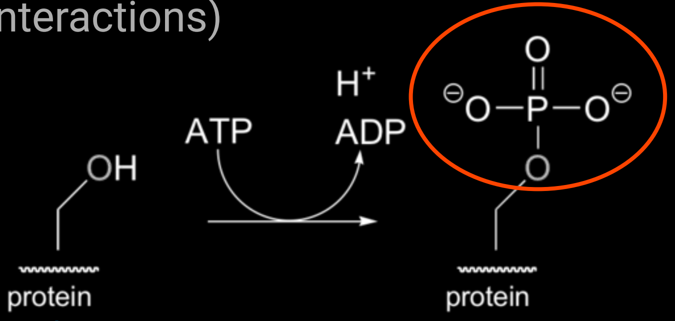


H3K9 methylation:
transcription repressor

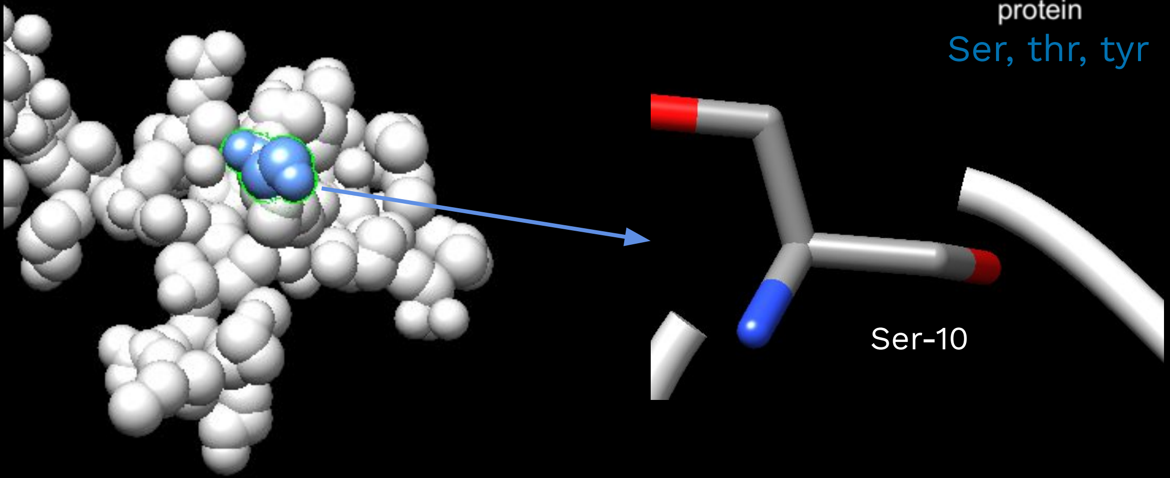


Phosphorylation

- Introduction of negative charges (affect DNA interactions)
- Nucleosome more accessible: transcriptional activation
- Response to DNA damage



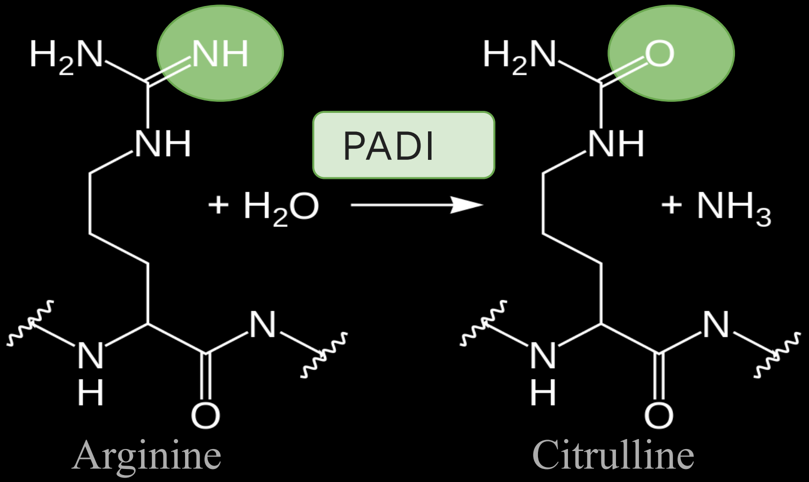
Ser, thr, tyr



H3S10 phosphorylation: involved in transcription and cell division, and promotes chromosome condensation

Citrullination

- Catalysed by the Ca2+-dependent peptidylarginine deiminase (PADI) enzymes
- Reduction in hydrogen-bonding ability
- Loss of positive charge: loss chromatin structure



H1R54 citrullination in the nucleosomal DNA binding region: extensive chromatin decondensation ⇒ loss of structure

LINKER HISTONE: H1

Formation of higher order chromatin structure

- Regulate specific gene transcription.
- Stabilize DNA wrapping around nucleosome.
- Suppress transcription of repetitive transposable DNA elements.

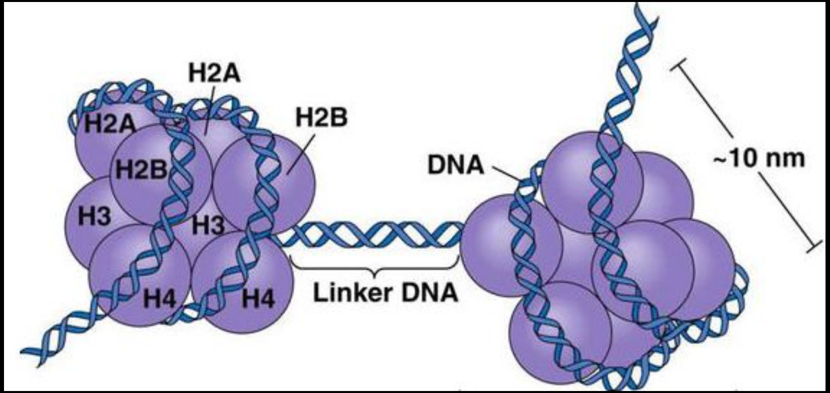


Figure from: http://www.info-farmacia.com/bioquimica/nucleosomas

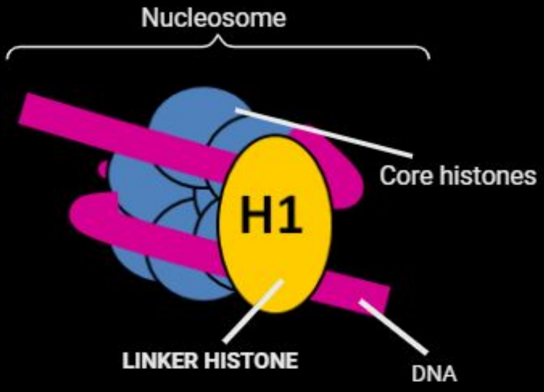
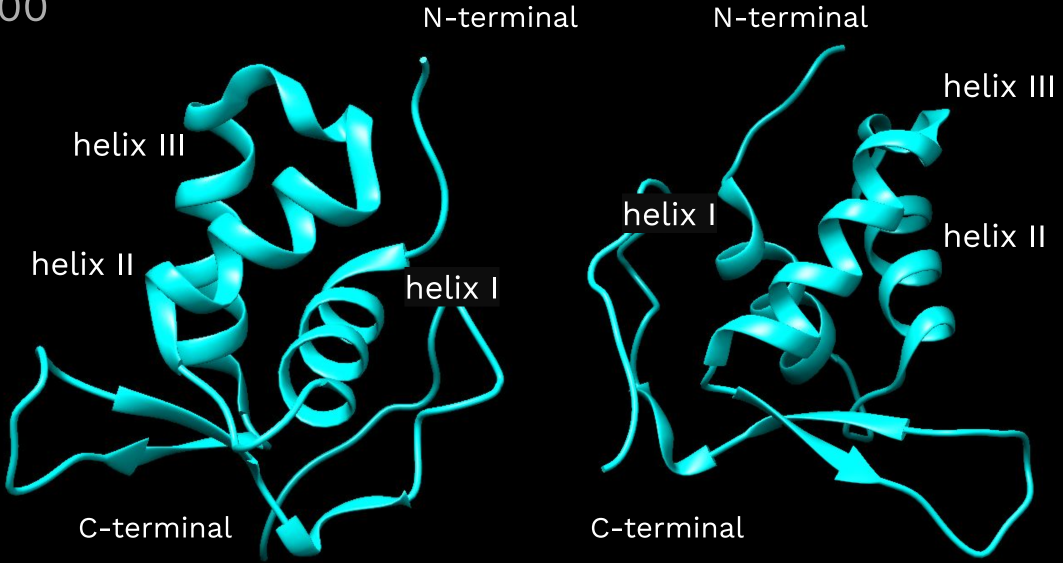


Figure: created with bio render

LINKER HISTONE H1 - STRUCTURE

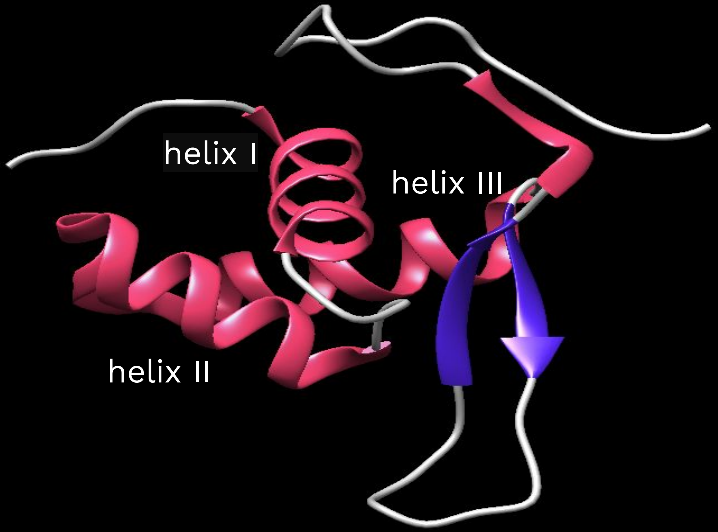
1. **Globular** domain: ~ 75 residues
2. **N-terminal** tail: 20-35 residues
3. Basic **C-terminal** domain: ~100 residues

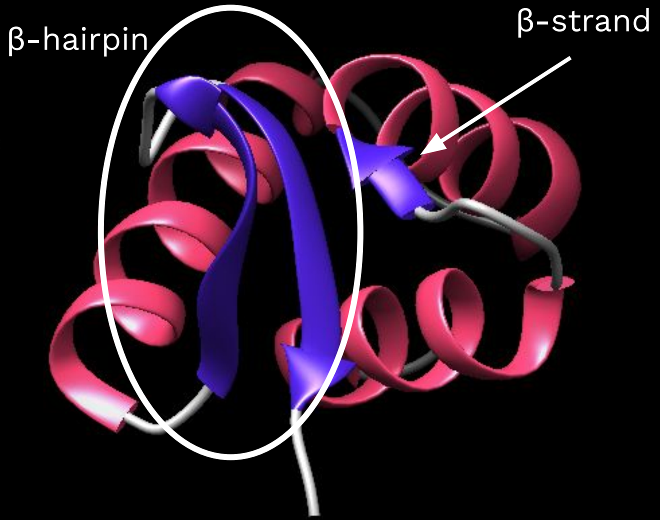


LINKER HISTONE H1 - STRUCTURE

1. Conserved **Globular** domain: ~ 75 residues

Helix-turn-Helix (HTH) → **Winged-helix fold**

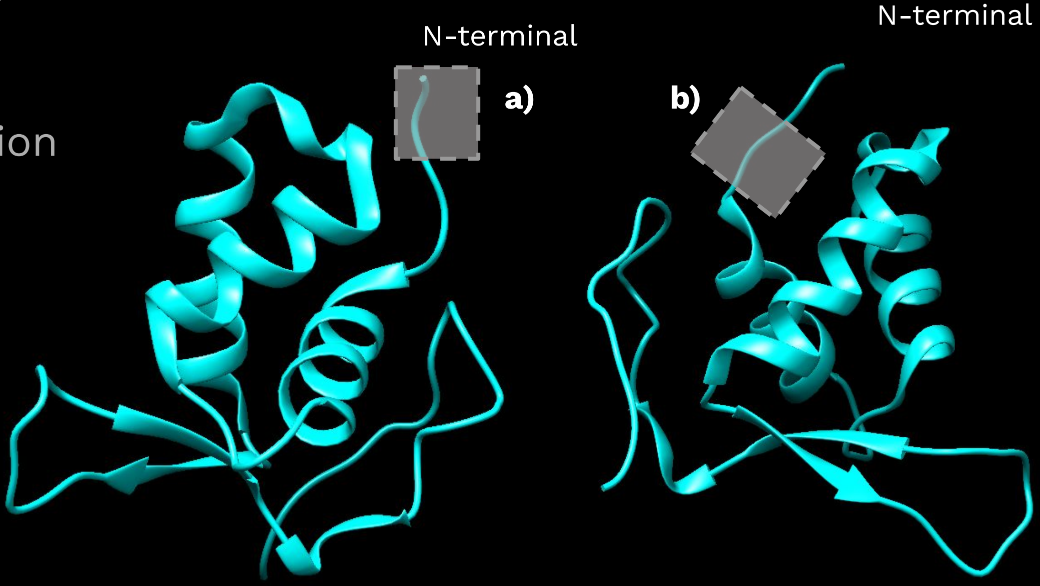




LINKER HISTONE H1 - STRUCTURE

1. Globular domain: ~ 75 residues
2. **N-terminal tail:** 20-35 residues
   a. Distal part: hydrophobic residues
   b. Proximal part: basic region

Non-essential for the formation of higher-order chromatin structures

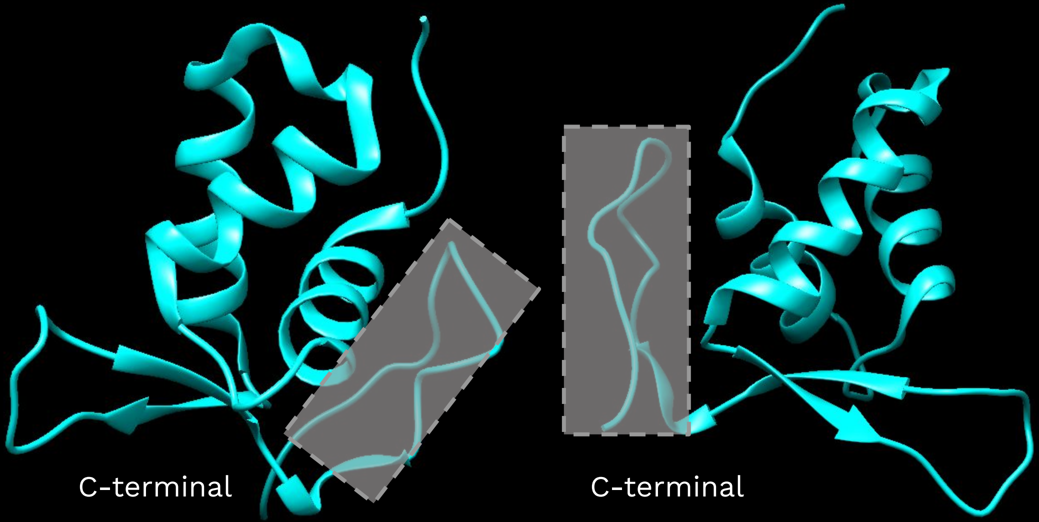


LINKER HISTONE H1 - STRUCTURE

1. Globular domain: ~75 residues
2. N-terminal tail: 20-35 residues
3. Basic **C-terminal domain**: ~100 residues
   ↳ 30-50 net positive charges

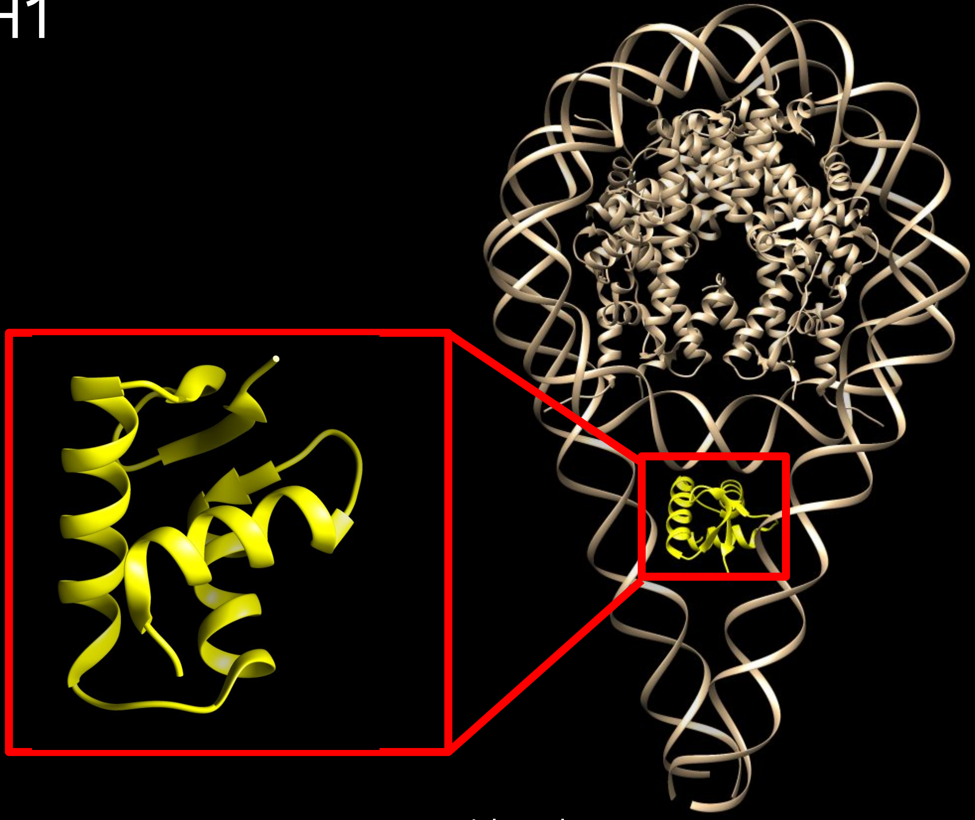
→ stabilize chromatin folding

- α-helix (24%)
- β-structure (25%)
- open loops (17%)
- turns (33%)



SCOP CLASSIFICATION: H1

Class	All alpha proteins
Fold	DNA/RNA-binding 3-helical bundle
Superfamily	Winged helix DNA-binding domain
Family	Linker histone H1/H5 globular domain-like
Protein	Histone H1/H5

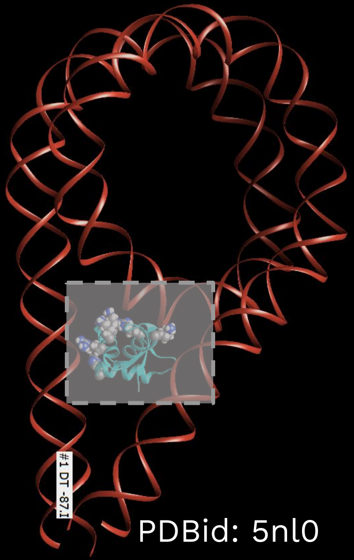


PDBid: 5nl0

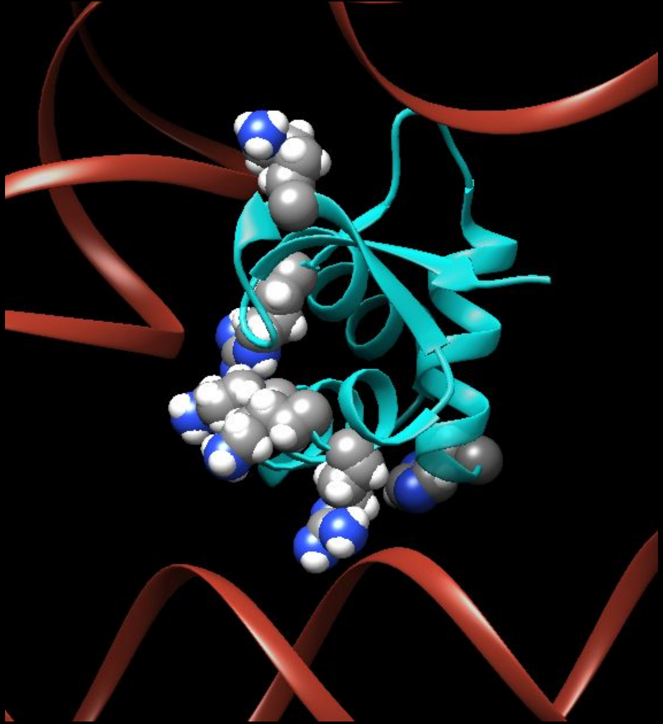
LINKER HISTONE H1 - DNA INTERACTIONS

Site 1 → minor groove

- His-25
- Arg-47
- Lys-69
- Lys-73
- Arg-74
- Lys-85



PDBid: 5nl0



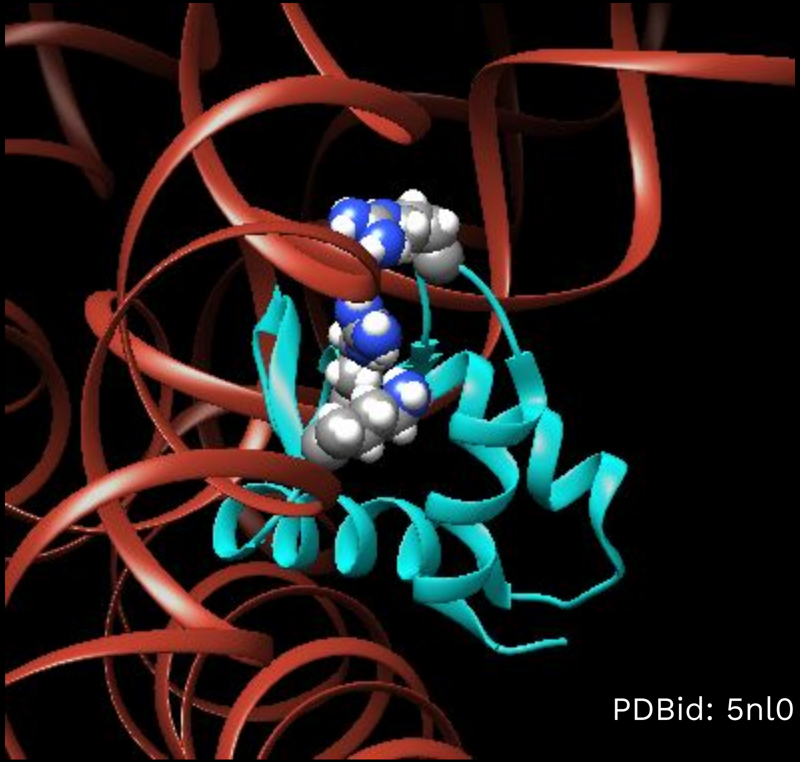
LINKER HISTONE H1 - DNA INTERACTIONS

Site 2 → major groove

Arg-42

Arg-94

Lys-97



PDBid: 5nl0

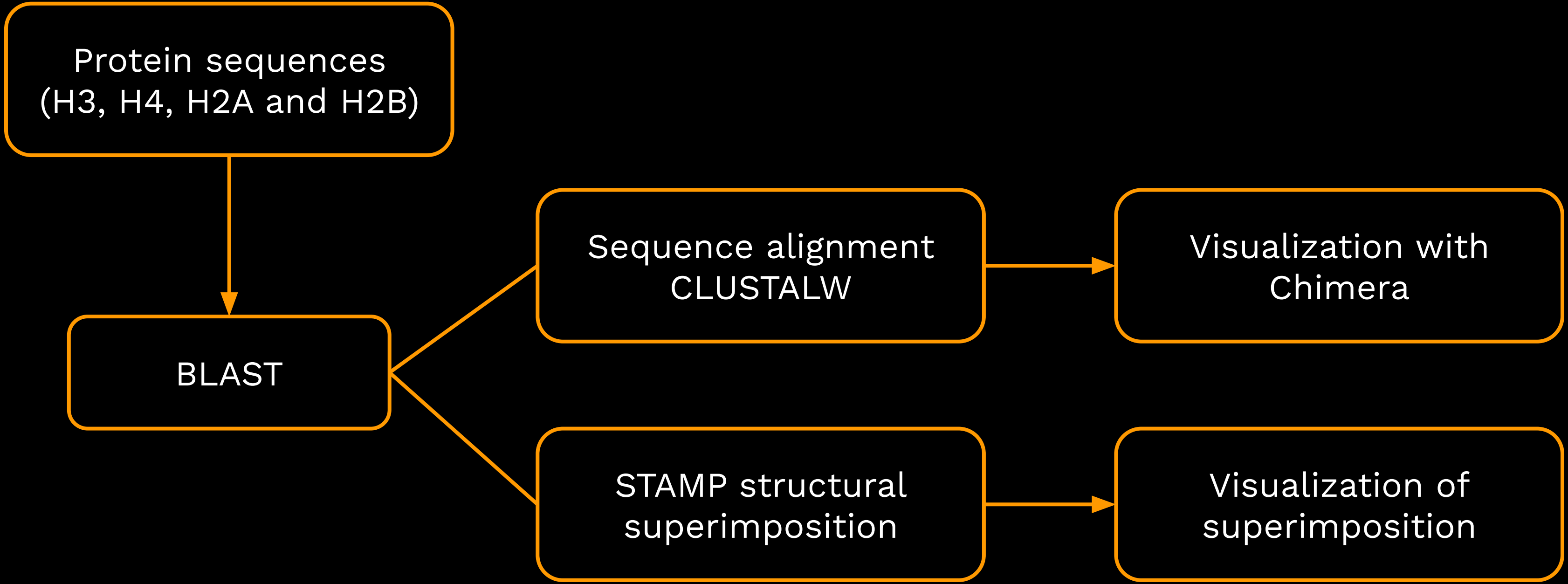
H1

	1	11	21	31	41
Consensus	---sasspsY	kElItkaiqa	lkerKGsSra	alkKyikd-f	y-vrkna---
Conservation					
Xenopus_laevis	SRRSASHPTY	SEMIAAAIRA	EKSRGGSSRQ	SIQKYIKS-H	YKVGHNA---
Homo_sapiens	--HAKPPYSY	ISLITMAIQQ	APG-KMLTLS	EIYQWIMDLF	PYYRENQQRW
Gallus_gallus	-----MAGPSV	TELITKAVSA	SKERKGLSLA	ALKKALAAGG	YDVEKN----
Drosophila_melanogaster	KASSPSSLTY	KEMILKSMPQ	LNDGKGSSRI	VLKKYVKDTF	SSKLKTSSNF
Saccharomyces_cerevisiae	---EASSKSY	RELIIEGLTA	LKERKGSSRP	ALKKFIKENY	P-IVGSASNF

	51	61	71	81	91
Consensus	dlqiklaikk	-lveaGvlvQ	pK--GasGsf	kLaKs-----	----------
Conservation					
Xenopus_laevis	DLQIKLSIRR	-LLAAGVLKQ	TKGVGASGSF	RLAKSDKAKR	SPGKK-----
Homo_sapiens	QNSIRHSLSF	NDCFVKVARS	PDKPGKGSYW	ALHPSSGNMF	ENGCYLRRQK
Gallus_gallus	NSRIKLGLKS	-LVSKGTLVQ	TKGTGASGSF	RLSK------	----------
Drosophila_melanogaster	DYLFNSAIKK	-CVENGELVQ	PK--GPSGII	KLNKKK---V	KLST------
Saccharomyces_cerevisiae	DLYFNNAIKK	-GVEAGDFEQ	PK--GPAGAV	KLAKK-----	----------

	101
Consensus	-----
Conservation	
Xenopus_laevis	-----
Homo_sapiens	RFKLA
Gallus_gallus	-----
Drosophila_melanogaster	-----
Saccharomyces_cerevisiae	-----

EVOLUTION



Protein sequences
(H3, H4, H2A and H2B)

BLAST

Sequence alignment
CLUSTALW

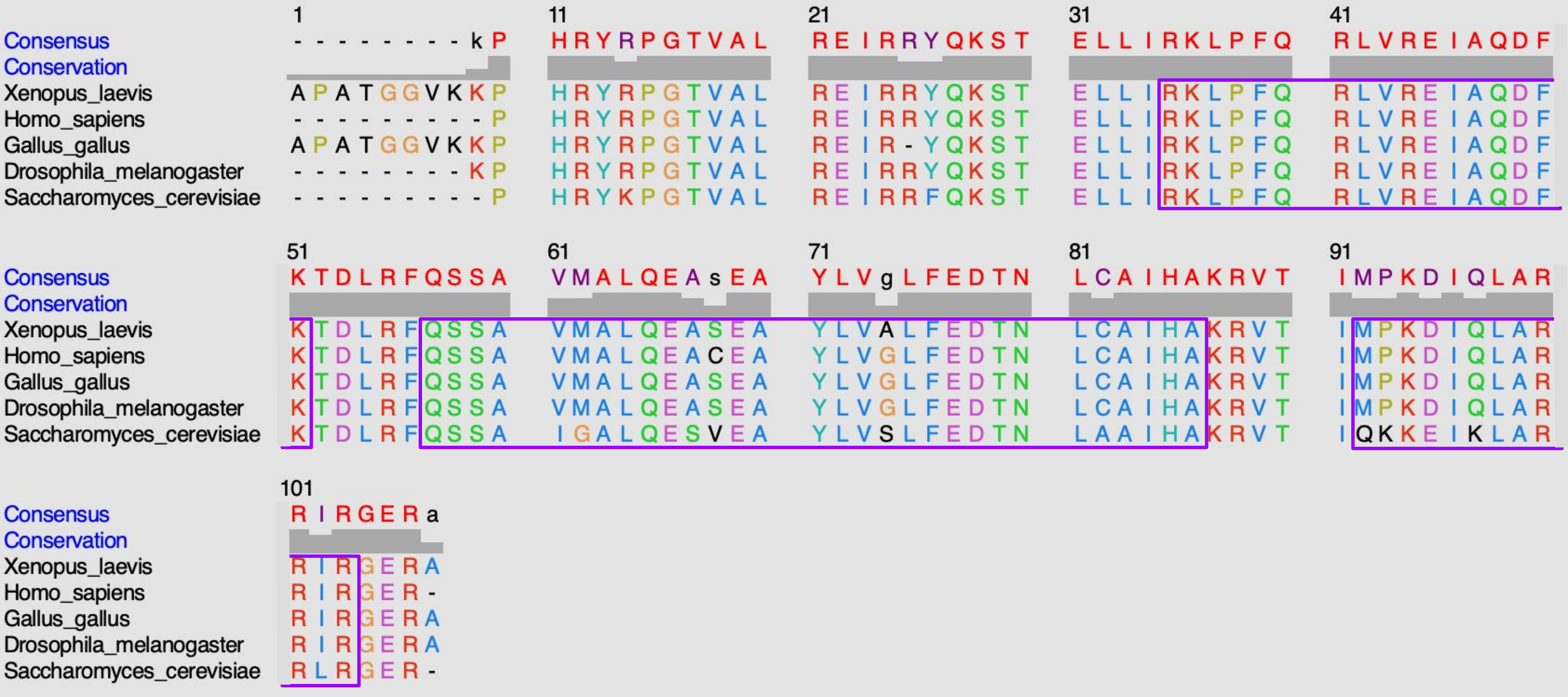
Visualization with
Chimera

STAMP structural
superimposition

Visualization of
superimposition

EVOLUTION

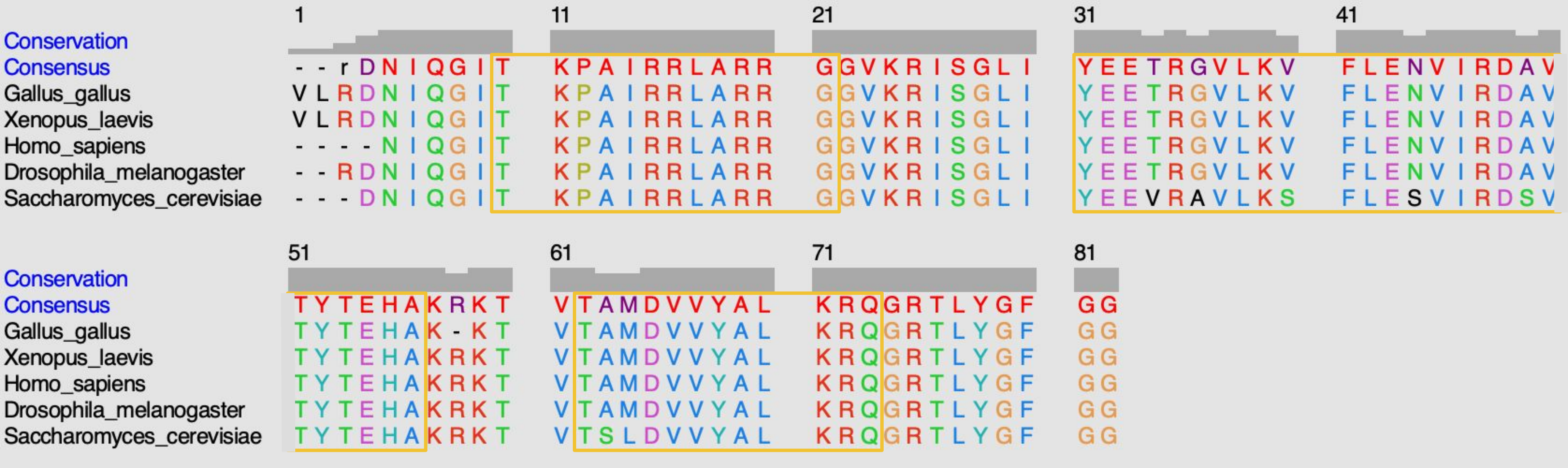
H3



```
                           1          11         21         31         41
Consensus                  --------kP HRYRPGTVAL REIRRYQKST ELLIRKLPFQ RLVREIAQDF
Conservation
Xenopus_laevis             APATGGVKKP HRYRPGTVAL REIRRYQKST ELLIRKLPFQ RLVREIAQDF
Homo_sapiens               ---------P HRYRPGTVAL REIRRYQKST ELLIRKLPFQ RLVREIAQDF
Gallus_gallus              APATGGVKKP HRYRPGTVAL REIR-YQKST ELLIRKLPFQ RLVREIAQDF
Drosophila_melanogaster    --------KP HRYRPGTVAL REIRRYQKST ELLIRKLPFQ RLVREIAQDF
Saccharomyces_cerevisiae   ---------P HRYKPGTVAL REIRRFQKST ELLIRKLPFQ RLVREIAQDF

                           51         61         71         81         91
Consensus                  KTDLRFQSSA VMALQEAsEA YLVgLFEDTN LCAIHAKRVT IMPKDIQLAR
Conservation
Xenopus_laevis             KTDLRFQSSA VMALQEASEA YLVALFEDTN LCAIHAKRVT IMPKDIQLAR
Homo_sapiens               KTDLRFQSSA VMALQEACEA YLVGLFEDTN LCAIHAKRVT IMPKDIQLAR
Gallus_gallus              KTDLRFQSSA VMALQEASEA YLVGLFEDTN LCAIHAKRVT IMPKDIQLAR
Drosophila_melanogaster    KTDLRFQSSA VMALQEASEA YLVGLFEDTN LCAIHAKRVT IMPKDIQLAR
Saccharomyces_cerevisiae   KTDLRFQSSA IGALQESVEA YLVSLFEDTN LAAIHAKRVT IQKKEIKLAR

                           101
Consensus                  RIRGERa
Conservation
Xenopus_laevis             RIRGERA
Homo_sapiens               RIRGER-
Gallus_gallus              RIRGERA
Drosophila_melanogaster    RIRGERA
Saccharomyces_cerevisiae   RLRGER-
```

EVOLUTION

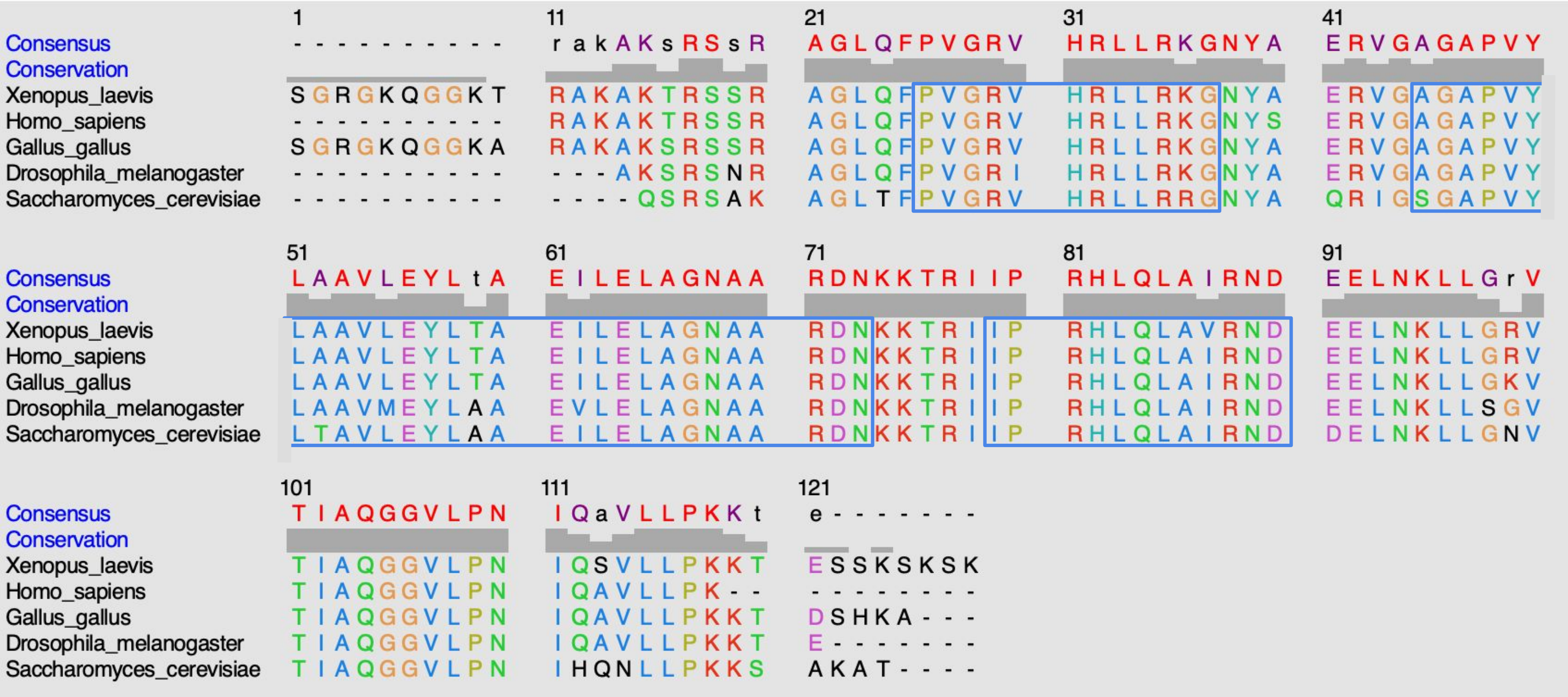
H4



	1	11	21	31	41	51	61	71	81
Conservation									
Consensus	- - r D N I Q G I T	K P A I R R L A R R	G G V K R I S G L I	Y E E T R G V L K V	F L E N V I R D A V	T Y T E H A K R K T	V T A M D V V Y A L	K R Q G R T L Y G F	G G
Gallus_gallus	V L R D N I Q G I T	K P A I R R L A R R	G G V K R I S G L I	Y E E T R G V L K V	F L E N V I R D A V	T Y T E H A K - K T	V T A M D V V Y A L	K R Q G R T L Y G F	G G
Xenopus_laevis	V L R D N I Q G I T	K P A I R R L A R R	G G V K R I S G L I	Y E E T R G V L K V	F L E N V I R D A V	T Y T E H A K R K T	V T A M D V V Y A L	K R Q G R T L Y G F	G G
Homo_sapiens	- - - - N I Q G I T	K P A I R R L A R R	G G V K R I S G L I	Y E E T R G V L K V	F L E N V I R D A V	T Y T E H A K R K T	V T A M D V V Y A L	K R Q G R T L Y G F	G G
Drosophila_melanogaster	- - R D N I Q G I T	K P A I R R L A R R	G G V K R I S G L I	Y E E T R G V L K V	F L E N V I R D A V	T Y T E H A K R K T	V T A M D V V Y A L	K R Q G R T L Y G F	G G
Saccharomyces_cerevisiae	- - - D N I Q G I T	K P A I R R L A R R	G G V K R I S G L I	Y E E V R A V L K S	F L E S V I R D S V	T Y T E H A K R K T	V T S L D V V Y A L	K R Q G R T L Y G F	G G

EVOLUTION

H2A



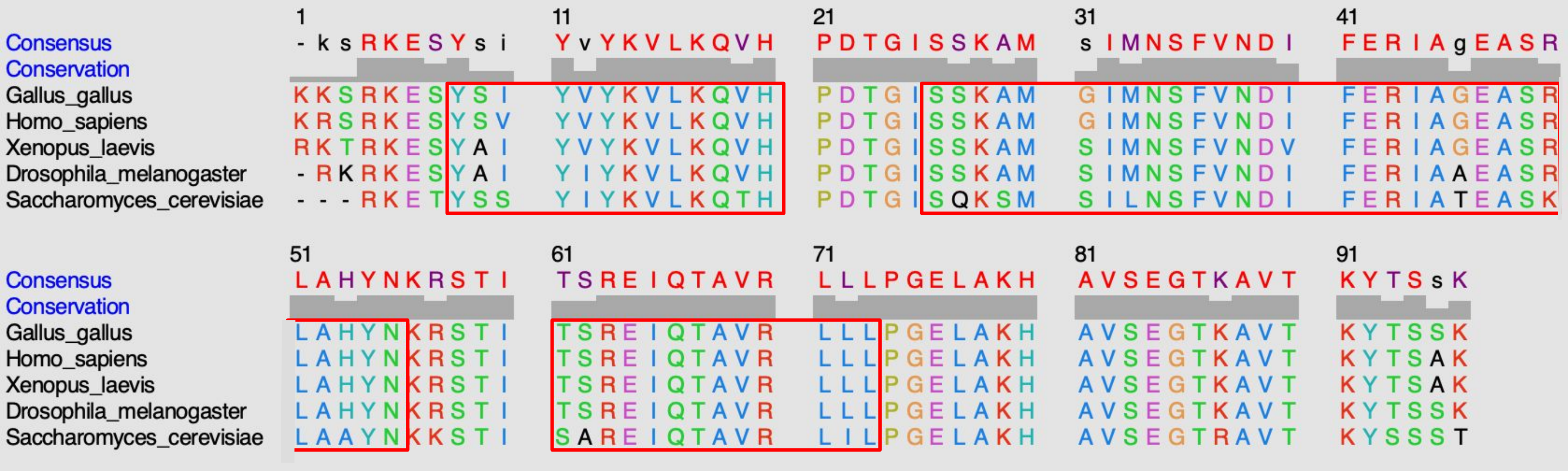
	1	11	21	31	41
Consensus	----------	rakAKsRSsR	AGLQFPVGRV	HRLLRKGNYA	ERVGAGAPVY
Conservation					
Xenopus_laevis	SGRGKQGGKT	RAKAKTRSSR	AGLQFPVGRV	HRLLRKGNYA	ERVGAGAPVY
Homo_sapiens	----------	RAKAKTRSSR	AGLQFPVGRV	HRLLRKGNYS	ERVGAGAPVY
Gallus_gallus	SGRGKQGGKA	RAKAKSRSSR	AGLQFPVGRV	HRLLRKGNYA	ERVGAGAPVY
Drosophila_melanogaster	----------	---AKSRSNR	AGLQFPVGRI	HRLLRKGNYA	ERVGAGAPVY
Saccharomyces_cerevisiae	----------	----QSRSAK	AGLTFPVGRV	HRLLRRGNYA	QRIGSGAPVY

	51	61	71	81	91
Consensus	LAAVLEYLtA	EILELAGNAA	RDNKKTRIIP	RHLQLAIRND	EELNKLLGrV
Conservation					
Xenopus_laevis	LAAVLEYLTA	EILELAGNAA	RDNKKTRIIP	RHLQLAVRND	EELNKLLGRV
Homo_sapiens	LAAVLEYLTA	EILELAGNAA	RDNKKTRIIP	RHLQLAIRND	EELNKLLGRV
Gallus_gallus	LAAVLEYLTA	EILELAGNAA	RDNKKTRIIP	RHLQLAIRND	EELNKLLGKV
Drosophila_melanogaster	LAAVMEYLAA	EVLELAGNAA	RDNKKTRIIP	RHLQLAIRND	EELNKLLSGV
Saccharomyces_cerevisiae	LTAVLEYLAA	EILELAGNAA	RDNKKTRIIP	RHLQLAIRND	DELNKLLGNV

	101	111	121
Consensus	TIAQGGVLPN	IQaVLLPKKt	e-------
Conservation			
Xenopus_laevis	TIAQGGVLPN	IQSVLLPKKT	ESSKSKSK
Homo_sapiens	TIAQGGVLPN	IQAVLLPK--	--------
Gallus_gallus	TIAQGGVLPN	IQAVLLPKKT	DSHKA---
Drosophila_melanogaster	TIAQGGVLPN	IQAVLLPKKT	E-------
Saccharomyces_cerevisiae	TIAQGGVLPN	IHQNLLPKKS	AKAT----

EVOLUTION

H2B



	1	11	21	31	41
Consensus	-ksRKESYsi	YvYKVLKQVH	PDTGISSKAM	sIMNSFVNDI	FERIAgEASR
Conservation					
Gallus_gallus	KKSRKESYSI	YVYKVLKQVH	PDTGISSKAM	GIMNSFVNDI	FERIAGEASR
Homo_sapiens	KRSRKESYSV	YVYKVLKQVH	PDTGISSKAM	GIMNSFVNDI	FERIAGEASR
Xenopus_laevis	RKTRKESYAI	YVYKVLKQVH	PDTGISSKAM	SIMNSFVNDV	FERIAGEASR
Drosophila_melanogaster	-RKRKESYAI	YIYKVLKQVH	PDTGISSKAM	SIMNSFVNDI	FERIAAEASR
Saccharomyces_cerevisiae	---RKETYSS	YIYKVLKQTH	PDTGISQKSM	SILNSFVNDI	FERIATEASK

	51	61	71	81	91
Consensus	LAHYNKRSTI	TSREIQTAVR	LLLPGELAKH	AVSEGTKAVT	KYTSsK
Conservation					
Gallus_gallus	LAHYNKRSTI	TSREIQTAVR	LLLPGELAKH	AVSEGTKAVT	KYTSSK
Homo_sapiens	LAHYNKRSTI	TSREIQTAVR	LLLPGELAKH	AVSEGTKAVT	KYTSAK
Xenopus_laevis	LAHYNKRSTI	TSREIQTAVR	LLLPGELAKH	AVSEGTKAVT	KYTSAK
Drosophila_melanogaster	LAHYNKRSTI	TSREIQTAVR	LLLPGELAKH	AVSEGTKAVT	KYTSSK
Saccharomyces_cerevisiae	LAAYNKKSTI	SAREIQTAVR	LILPGELAKH	AVSEGTRAVT	KYSSST

EVOLUTION

H3

Sc 9.13
0.27

H4

Sc 9.01
0.22

H2A

Sc 8.77
0.29

H2B

Sc 8.92
0.31

CONCLUSIONS

- Histone tails → important role in genetic regulation and in mediating intra and inter nucleosomal interactions.
- Stable interactions among histones but interactions with DNA are dynamic and subject to fluctuation.
- Post-translational modifications → modify histone affinity for chromatin and the binding of transcriptional cofactors.
- Histone 1 → indispensable role in the organization of chromatin.
- Histones have an extremely high degree of conservation between species.

BIBLIOGRAPHY

1. Cavalieri V. (2021). The Expanding Constellation of Histone Post-Translational Modifications in the Epigenetic Landscape. *Genes*, *12*(10), 1596. https://doi.org/10.3390/genes12101596
2. Cutter, A. R., & Hayes, J. J. (2015). A brief review of nucleosome structure. *FEBS letters*, *589*(20 Pt A), 2914–2922. https://doi.org/10.1016/j.febslet.2015.05.016
3. Greer, E., Shi, Y. (2012). Histone methylation: a dynamic mark in health, disease and inheritance. *Nat Rev Genet* 13, 343–357. https://doi.org/10.1038/nrg3173
4. Harp, J. M., Hanson, B. L., Timm, D. E., & Bunick, G. J. (2000). Asymmetries in the nucleosome core particle at 2.5 A resolution. *Acta crystallographica. Section D, Biological crystallography*, *56*(Pt 12), 1513–1534. https://doi.org/10.1107/s0907444900011847
5. Koyama, M., Kurumizaka, H. (2018). Structural diversity of the nucleosome. *The Journal of Biochemistry*, 163(2), 85–95. https://doi.org/10.1093/jb/mvx081
6. Kurumizaka, H., Kujirai, T., & Takizawa, Y. (2021). Contributions of Histone Variants in Nucleosome Structure and Function. *Journal of molecular biology*, *433*(6), 166678. https://doi.org/10.1016/j.jmb.2020.10.012
7. Luger, K., Mäder, A., Richmond, R. *et al.* (1997). Crystal structure of the nucleosome core particle at 2.8 Å resolution. *Nature* 389, 251–260. https://doi.org/10.1038/38444

BIBLIOGRAPHY

6. Kurumizaka, H., Kujirai, T., & Takizawa, Y. (2021). Contributions of Histone Variants in Nucleosome Structure and Function. *Journal of molecular biology*, *433*(6), 166678. https://doi.org/10.1016/j.jmb.2020.10.012
7. Luger, K., Mäder, A., Richmond, R. *et al.* (1997). Crystal structure of the nucleosome core particle at 2.8 Å resolution. *Nature* 389, 251–260. https://doi.org/10.1038/38444
8. Onufriev, A. & V. Schiessel, H. (2019). The nucleosome: from structure to function through physics. *Structural Biology*, 56, 119-130. https://doi.org/10.1016/j.sbi.2018.11.003
9. Roque, A., Ponte, I., & Suau, P. (2016). Interplay between histone H1 structure and function. *Biochimica et biophysica acta*, *1859*(3), 444–454. https://doi.org/10.1016/j.bbagrm.2015.09.009
10. Simon, M., North, J. A., Shimko, J. C., Forties, R. A., Ferdinand, M. B., Manohar, M., Zhang, M., Fishel, R., Ottesen, J. J., & Poirier, M. G. (2011). Histone fold modifications control nucleosome unwrapping and disassembly. *Proceedings of the National Academy of Sciences of the United States of America*, *108*(31), 12711–12716. https://doi.org/10.1073/pnas.1106264108
11. Tessarz, P., Kouzarides, T. (2014). Histone core modifications regulating nucleosome structure and dynamics. *Nature Reviews Molecular Cell Biology,* 15, 703–708. https://doi.org/10.1038/nrm3890

PEM QUESTIONS

1. Which statement describes the role of H1?
   a. H1 plays a significant role in connecting the nucleosome to the DNA linker.
   b. H1 has only one binding site.
   c. Both A and B are correct.
   d. H1 is a core histone protein.
   e. All of the above statements are correct.

2. Related to the histone's evolution:
   a. H1 is really conserved through evolution.
   b. Histone core proteins are really conserved through evolution.
   c. Histone 2A doesn't have any variants between different species.
   d. Only H4 and H3, that form the tetramer, are conserved through evolution.
   e. None of the above are correct.

3. What interactions make the histones' H3-H4 tetramer?
   a. Interactions between the H2B and H4 chains.
   b. Interactions between the H4 and H4' chains, creating a 4 helix bundle.
   c. Interactions between the H3 and H3' chains, creating a 4 helix bundle.
   d. Interactions between the H4 and H4' chains, creating two different 4 helix bundles.
   e. Interactions between the H3 and H3' chains, creating two different 4 helix bundle.

4. The octamer is comprised by:
   a. The H3-H4 tetramer and the H2A-H2B tetramer.
   b. The H3-H4 tetramer and two H2A-H2B dimers.
   c. The H3-H4 tetramer and two H2A-H2B dimers and H1.
   d. One H3-H4 dimer and the H2A-H2B tetramer.
   e. None of the above are correct.

5. Which of the following Histones present a N-terminal tail?
    a. Histone H3
    b. Histone H4
    c. Histone H2A
    d. Histone H2B
    e. All of the above.

6. Which of the following statements is incorrect?
    a. Histones basic structure is composed of 3 alpha helices and two loops.
    b. H2A has both a N-terminal and C-terminal tails.
    c. The loops are made of alpha proteins.
    d. H2A-H2B dimers can’t tetramerize.
    e. The core histones’ alignment presents many differences in the amino-acid residues.

7. About the histone core DNA-binding interactions:
    a. The interactions only happen within the β bridges and the DNA.
    b. Interactions happen in the β bridges and the paired $\alpha 1$ region of the histones.
    c. There are only salt-bridges and hydrogen bonds.
    d. The minor groove of the DNA backbone is not responsible for the interactions.
    e. The DNA backbone can create interactions because of it’s electropositivity.

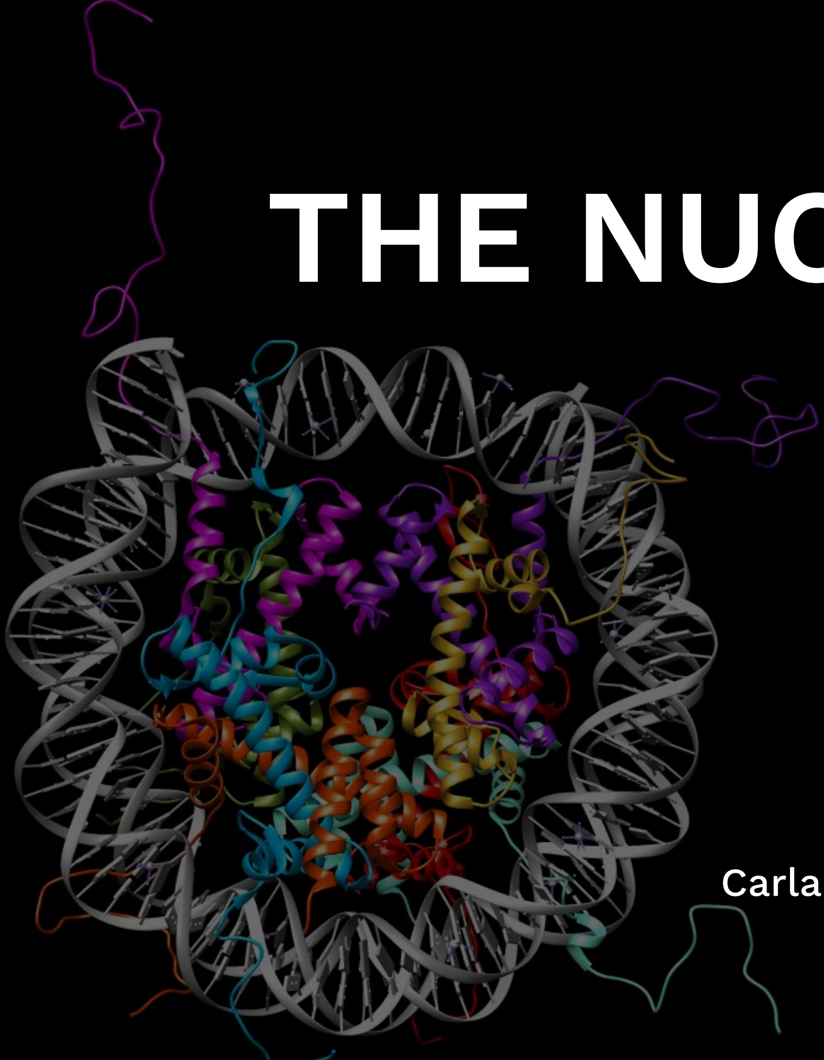
6.
7.

8. Which of the following statements is correct about the post-translational modifications?
    a. Phosphorylation decreases the chromatin accessibility
    b. Methylation occurs in acid residues
    c. Both A and B are correct
    d. The effect of methylation is context dependent
    e. All of the above statements are correct

9. Related to the post-translational modifications:
    a. Acetylation neutralizes the positive charge of lysine residues
    b. Citrullination consists on the conversion of histidine to citrulline
    c. Phosphorylation is not involved in DNA damage repair
    d. Methylations neutralized the positive charge of the basic residues
    e. Phosphorylation takes place in all aromatic residues

10. Which of the following statements is incorrect about the histone H1?
    a. The histone H1 has a winged-helix fold
    b. The N-terminal tail is a non-essential domain
    c. The “wings” or loops are small beta-sheets
    d. It contains a beta-hairpin
    e. It is categorized in the all alpha class, it does not have any beta structure

THE NUCLEOSOME



Carla Cifuentes, Ainhoa Larrañaga and Berta Sambola
Structural Biology - 2023/2024