От организации хроматина к пониманию функционирования геномов эукариот

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МГУ имени М.В.Ломоносова

Лекция 3.
Хроматин: от ДНК до супрануклеосомной структуры.

Апрель 2023

http://intbio.org/2024_chromatin_sirius/

О строении и свойствах нуклеиновых кислот (ДНК/РНК)

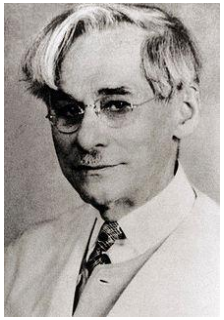
Развитие представлений о ДНК

1869

Friedrich Miescher

Albrecht Kossel

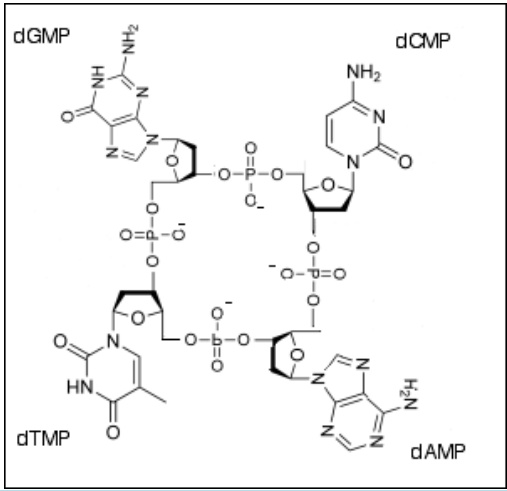
~1919



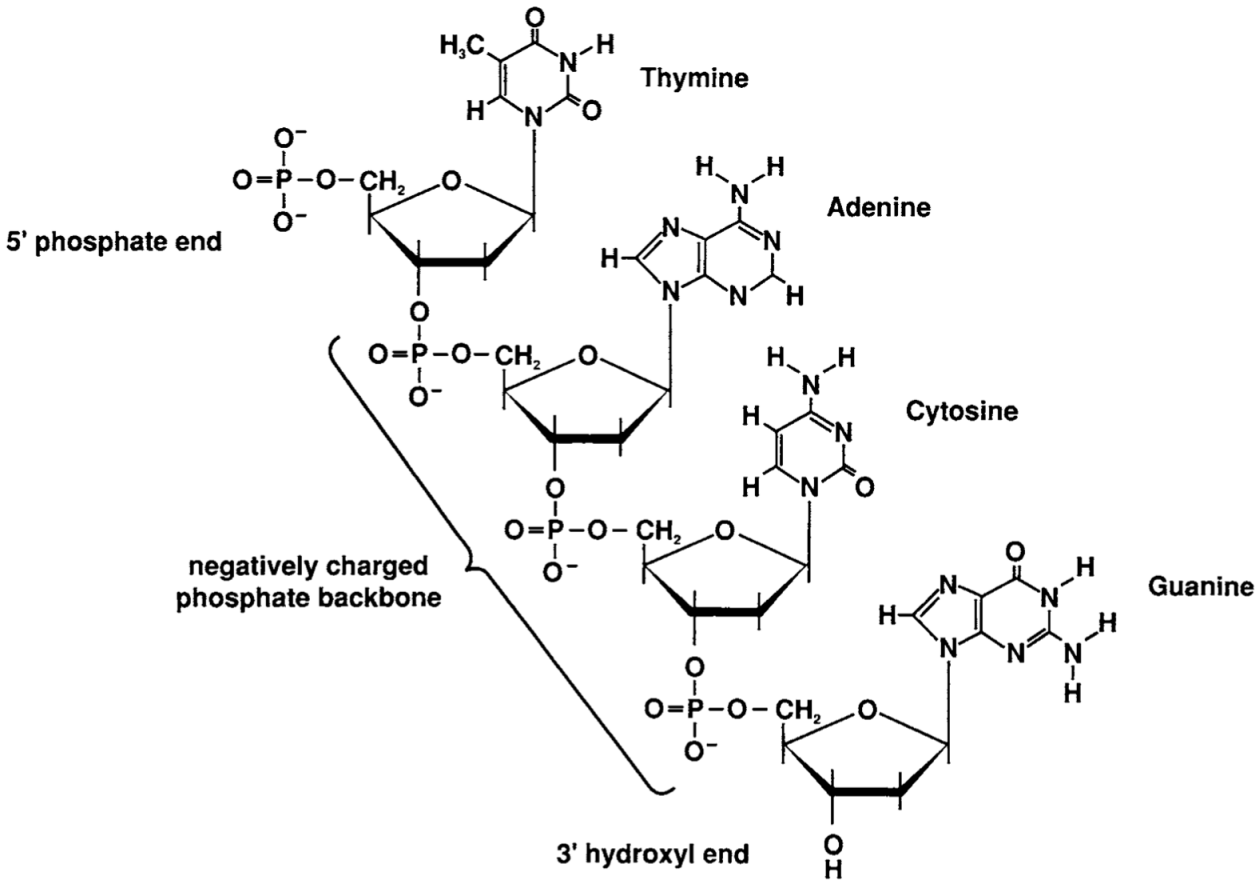
Phoebus Levene

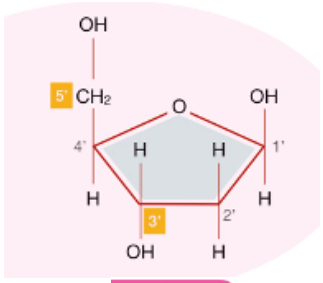
1896: изолировал нуклеиновые кислоты из нейтрофилов (нуклин)

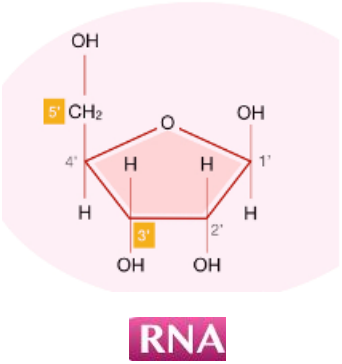
1885-1901:
выделил аденин, тимин, гуанин, урацил
Нобелевская премия 1910

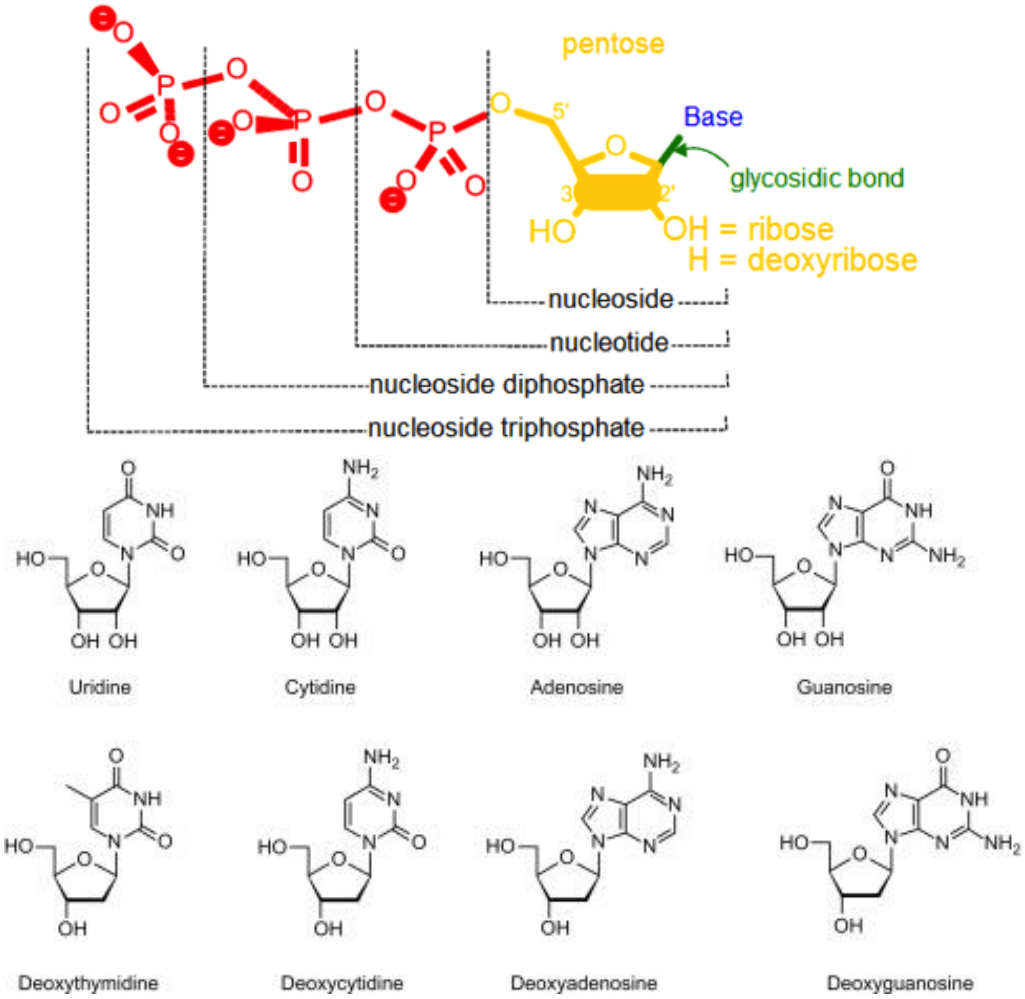


Структура ДНК/РНК

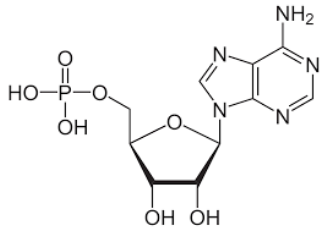




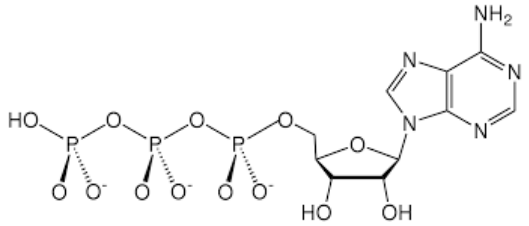




The name of the base is generally used as the name of the nucleotide, although this is technically incorrect.

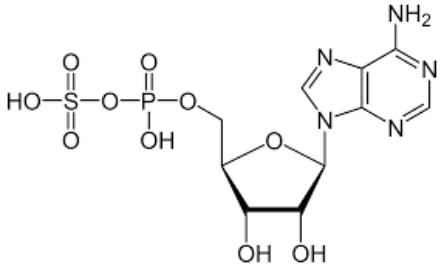


adenosine monophosphate (AMP)

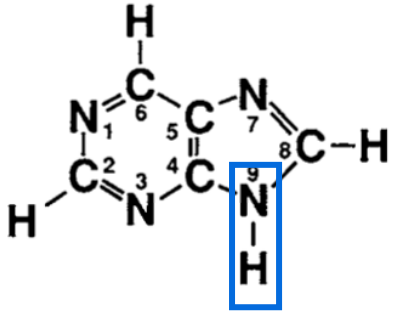


adenosine triphosphate (ATP)

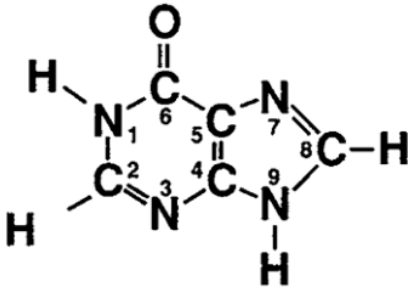
AMP derivateives => adenylyl



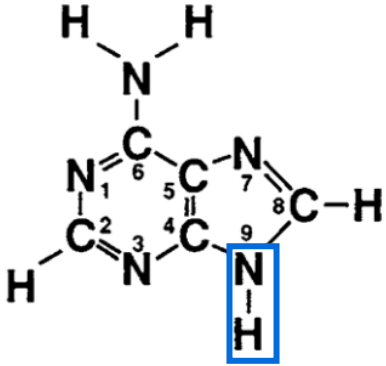
adenylyl sulfate



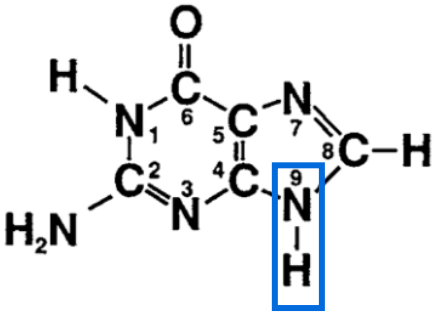
Purine (R)



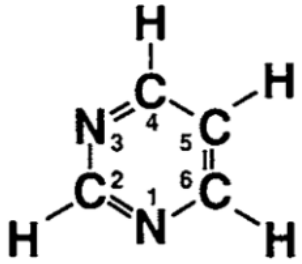
Hypoxanthine



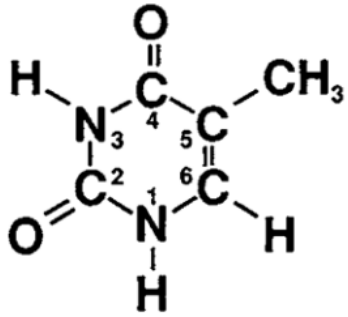
Adenine
(A)



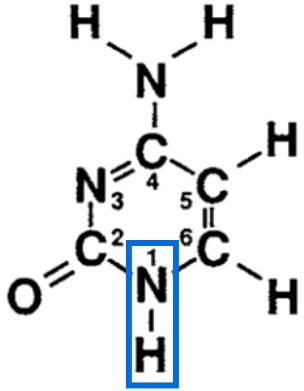
Guanine
(G)



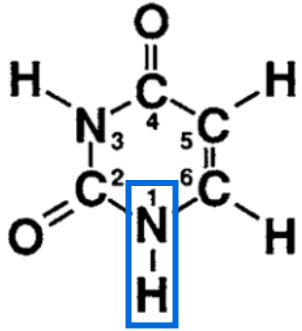
Pyrimidine (Y)



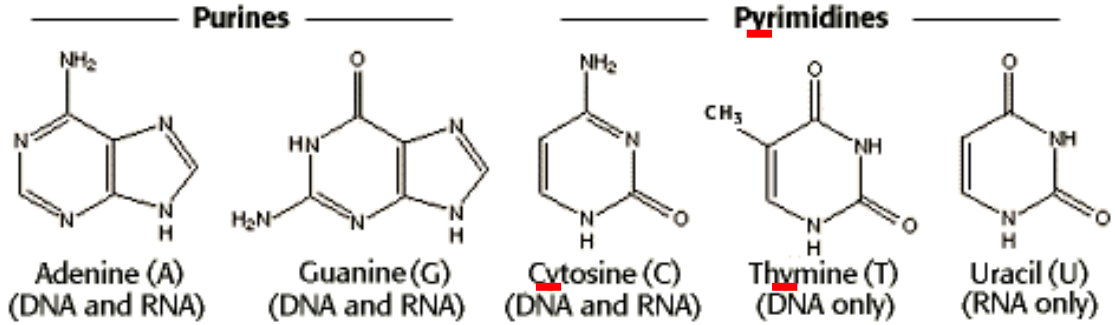
Thymine
(T)



Cytosine
(C)



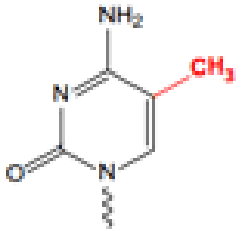
Uracil
(U)



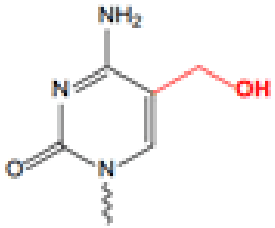
Однобуквенные обозначения классов оснований

	A	T	G	C
Weak/Strong	W	W	S	S
Purine/Pyrimidine	R	Y	R	Y

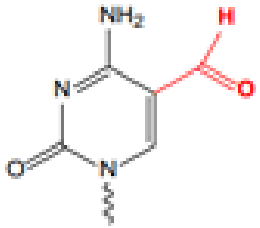
Некоторые модифицированные основания



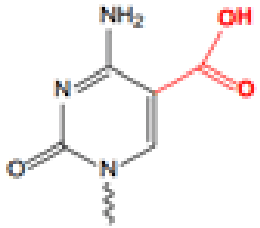
5-mC



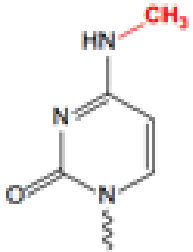
5-hmC



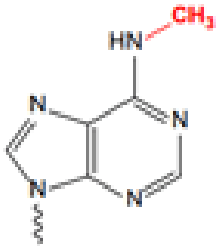
5-fC



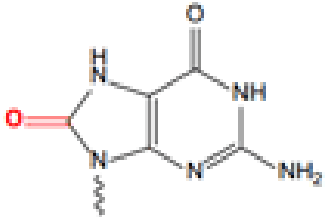
5-caC



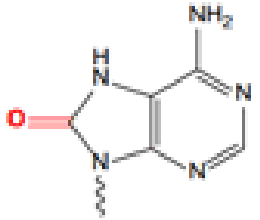
4-mC



6-mA

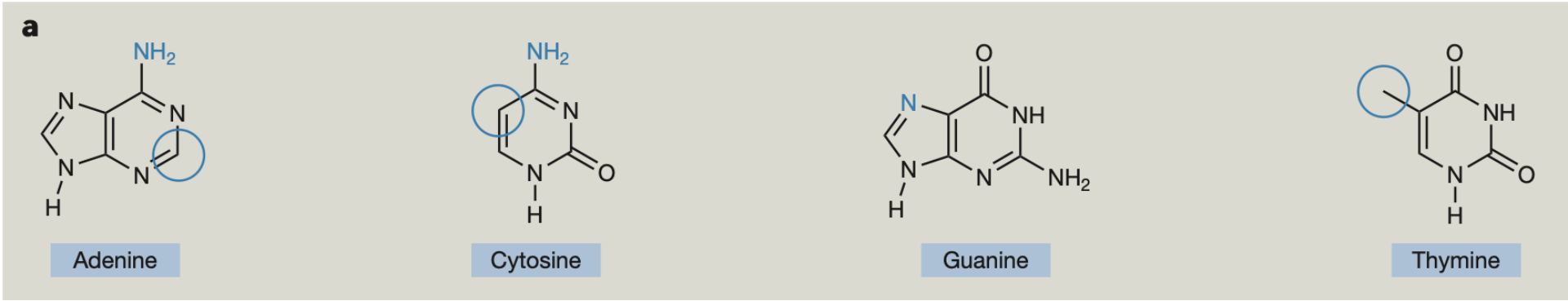


8-oxoG



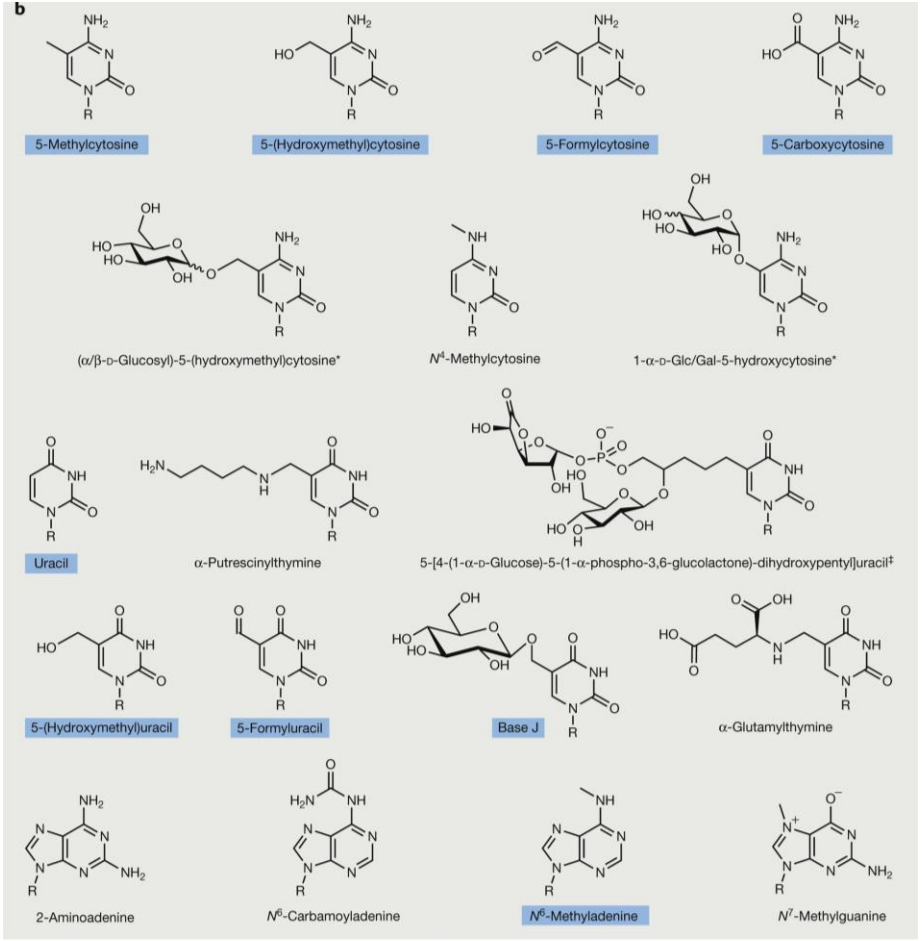
8-oxoA

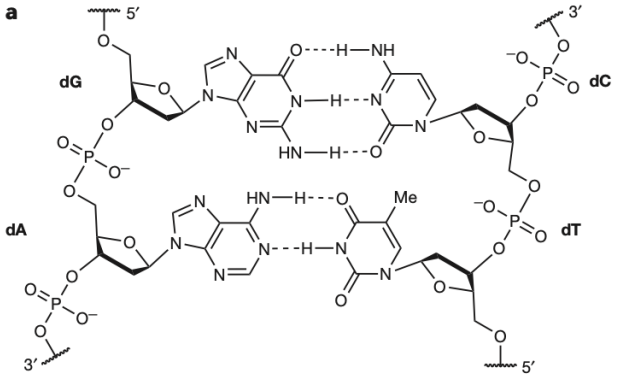
Разнообразие модификаций азотистых оснований ДНК

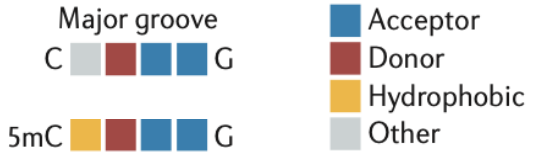


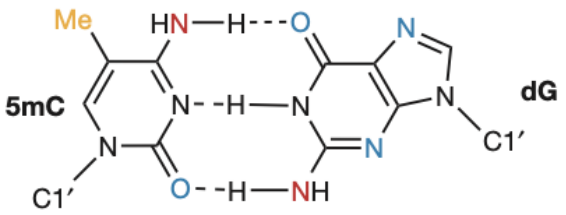
10.1038/s41570-017-0069

Разнообразие модификаций азотистых оснований ДНК









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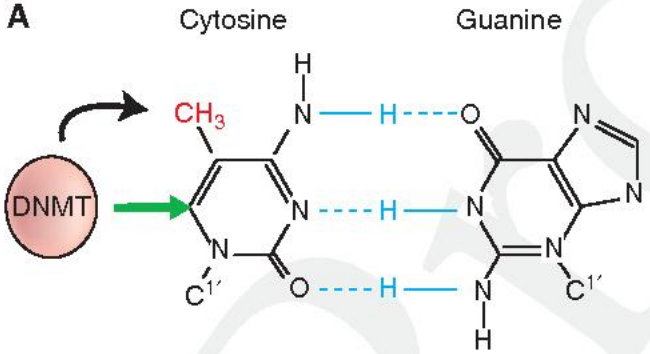
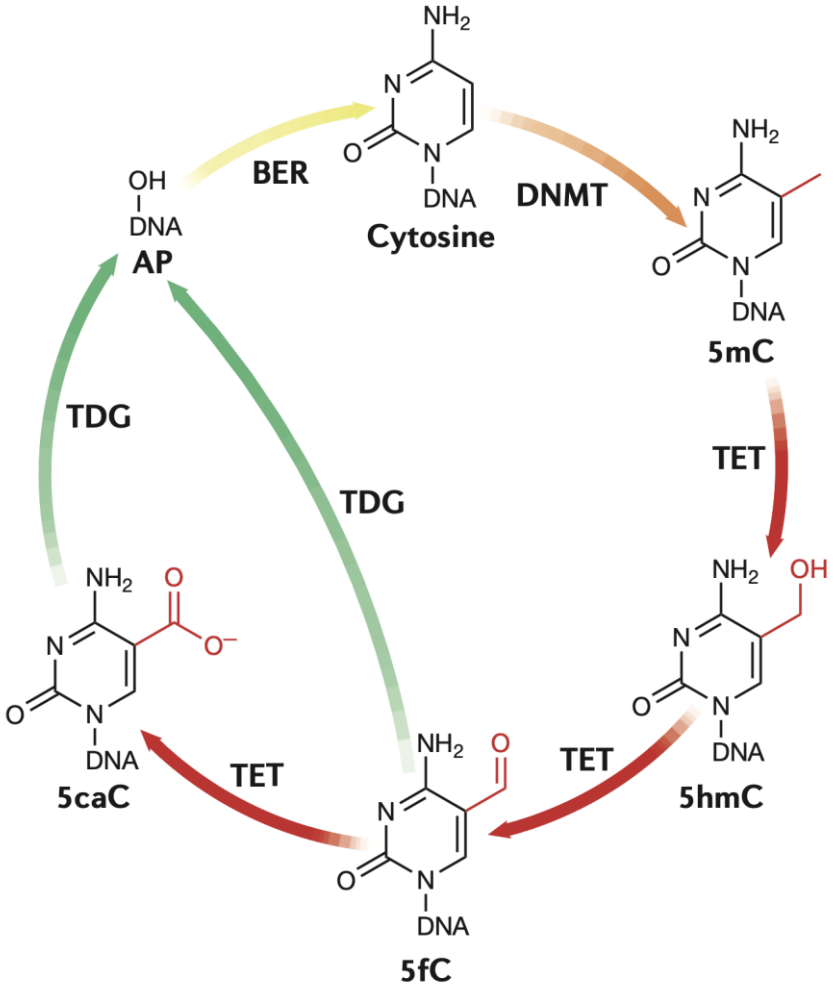
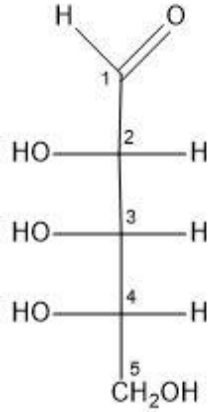
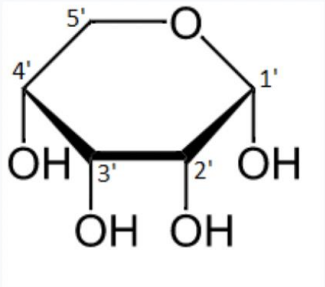

A
Cytosine
Guanine
DNMT
CH3
B


BER
DNMT
TET
TET
TET
TDG
TDG
Cytosine
5mC
5hmC
5fC
5caC
AP
DNA
OH
NH2
O
O−

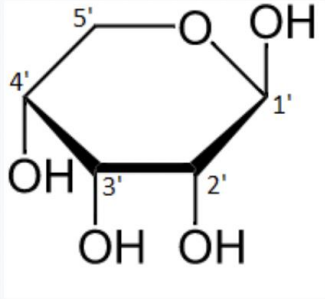
IUPAC nucleotide code	Base
A	Adenine
C	Cytosine
G	Guanine
T (or U)	Thymine (or Uracil)
R	A or G
Y	C or T
S	G or C
W	A or T
K	G or T
M	A or C
B	C or G or T
D	A or G or T
H	A or C or T
V	A or C or G
N	any base
. or -	gap

Ribose

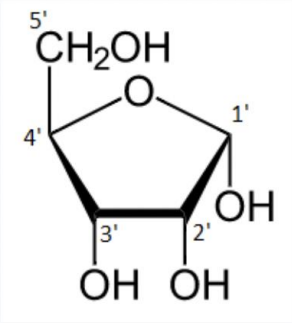




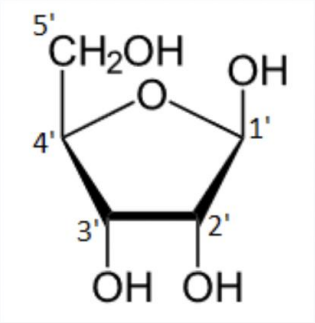
α-D-Ribopyranose



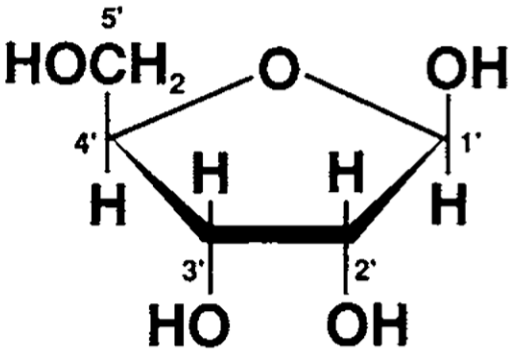
β-D-Ribopyranose



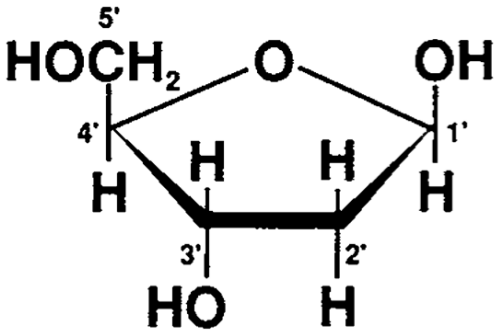
α-D-Ribofuranose



β-D-Ribofuranose



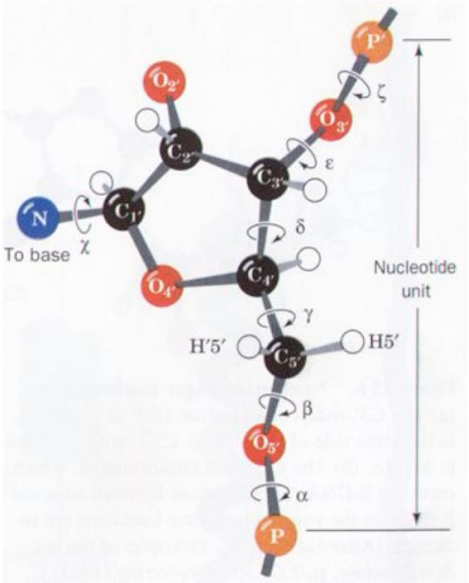
β-D-ribose

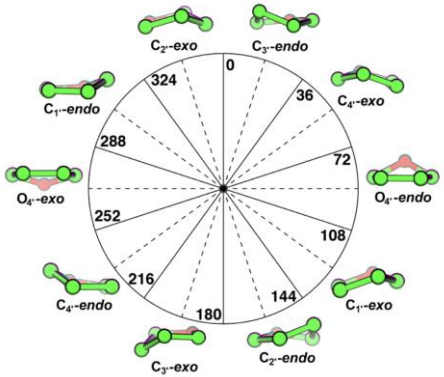


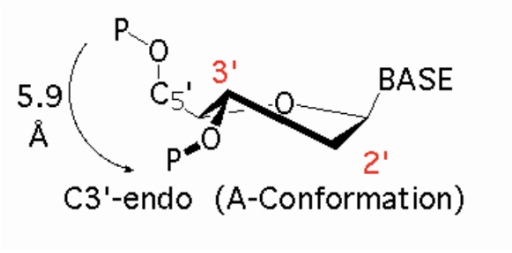
β-D-2-Deoxyribose

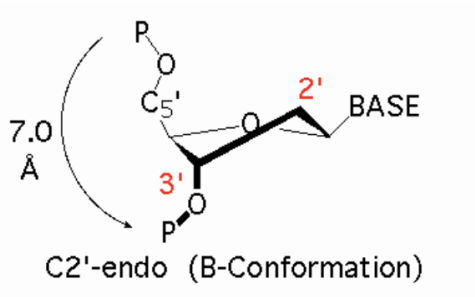
Пентозы (от др.-греч. πέμπτος — «пять» + фр. *-ose* — суффикс, обозначающий принадлежность к сахарам) — общее родовое химическое название класса пятиуглеродных моносахаридов, то есть сахаров, общей формулой которых является $C_5(H_2O)_5$, или $C_5H_{10}O_5$.[1]

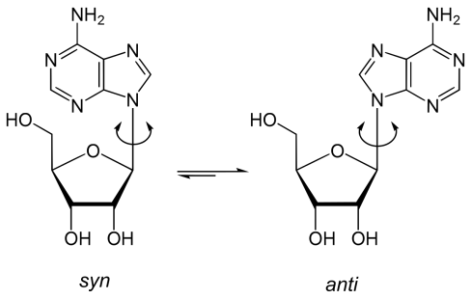
Конформации нуклеотидов





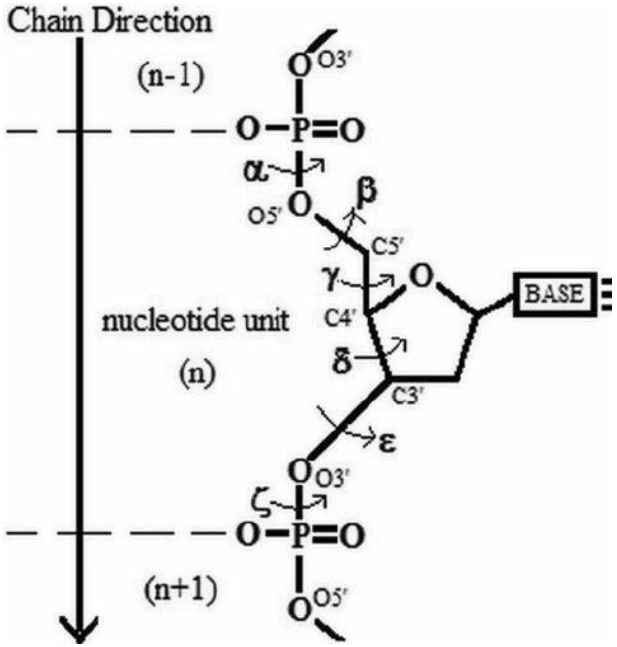




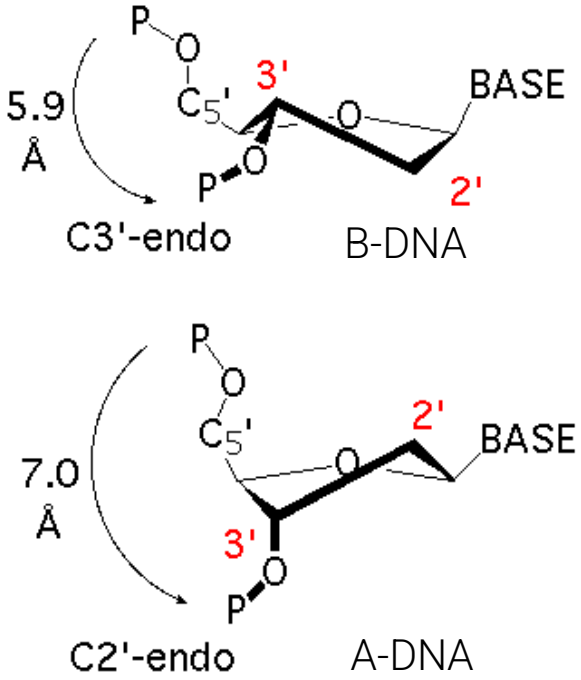


- Nucleotides are flexible and can be twisted about their C-O-P bonds
- There are 7 torsion angles in a nucleotide
- One torsion angle joins base to sugar
- The deoxyribose ring is “puckered” and not flat
- Puckering influences position of PO_4 on the 3’ and 5’ position of the ring

DNA structure, properties and its description

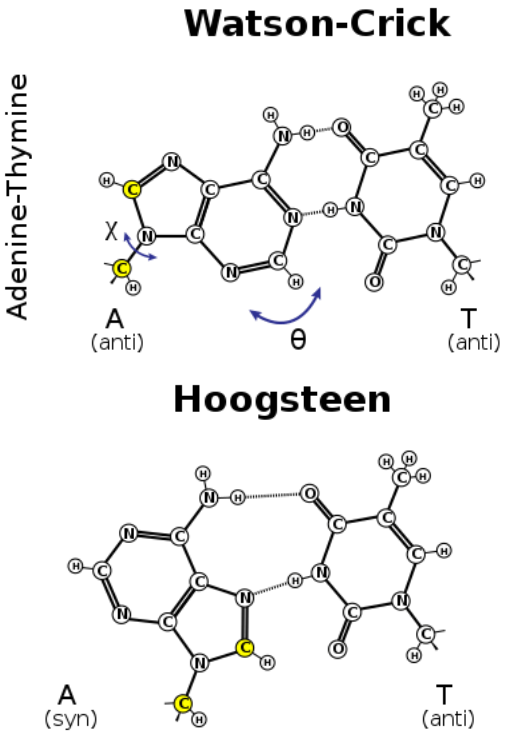


DNA backbone



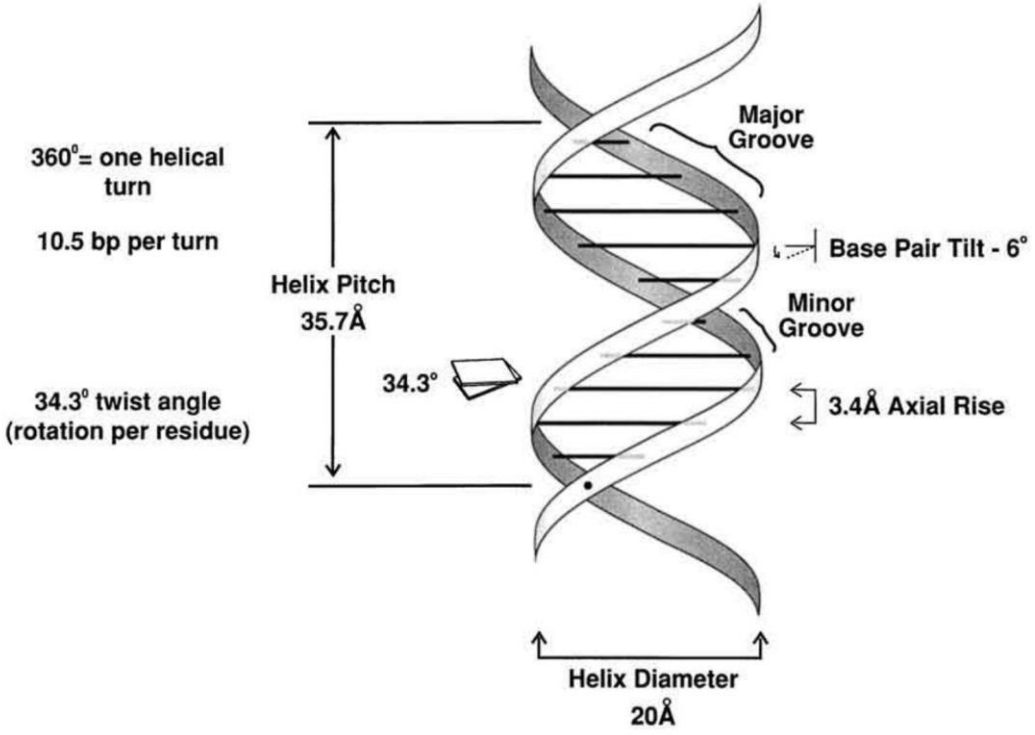
sugar puckering

20 possible states

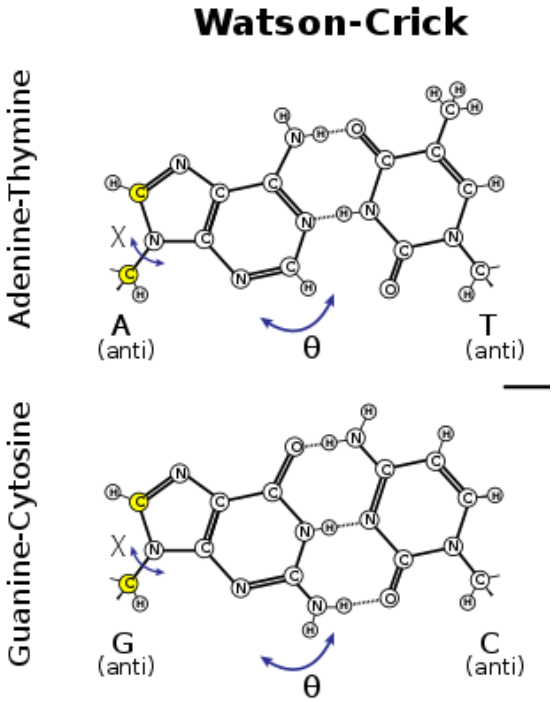


glycosidic bond angle

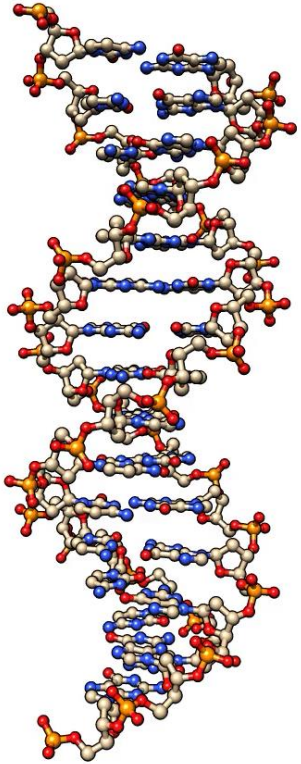
Двойные спирали ДНК/РНК



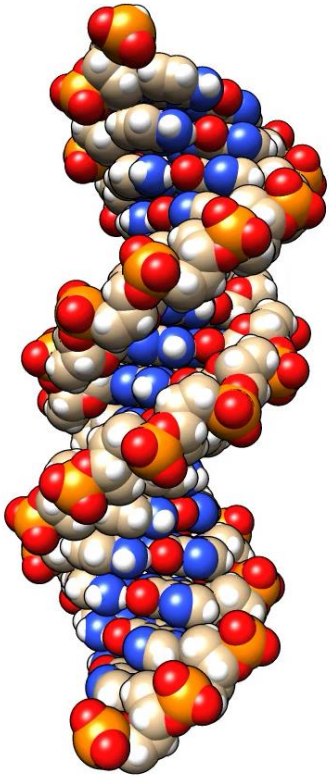
B-DNA



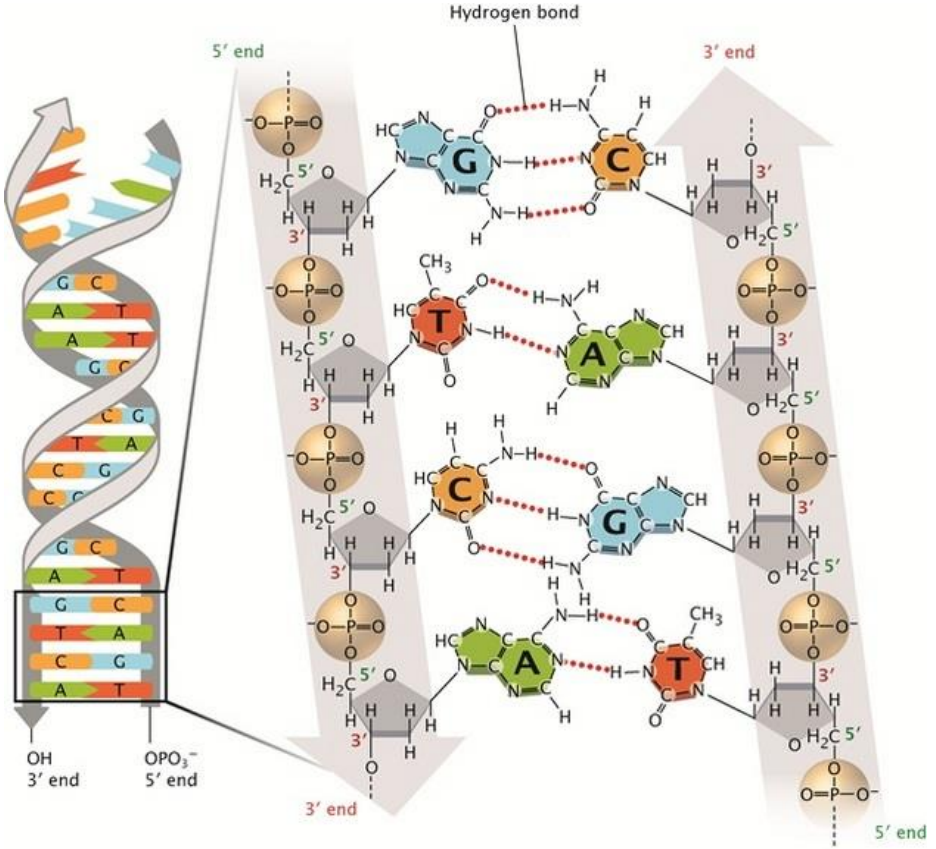
B-DNA



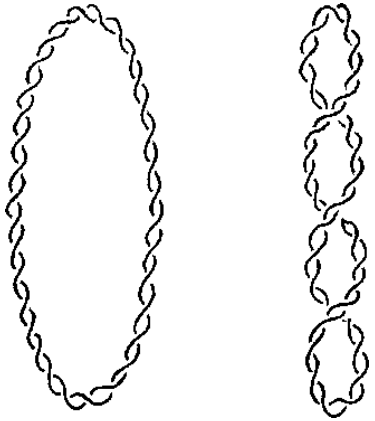
Ideal B-DNA

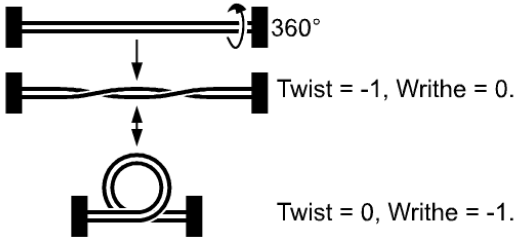


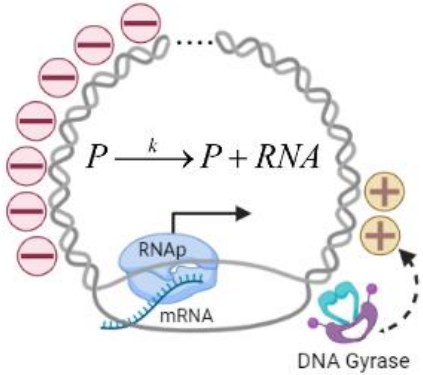
Ideal B-DNA



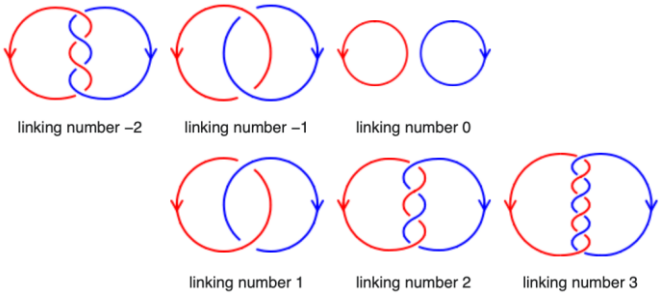
Supercoiling



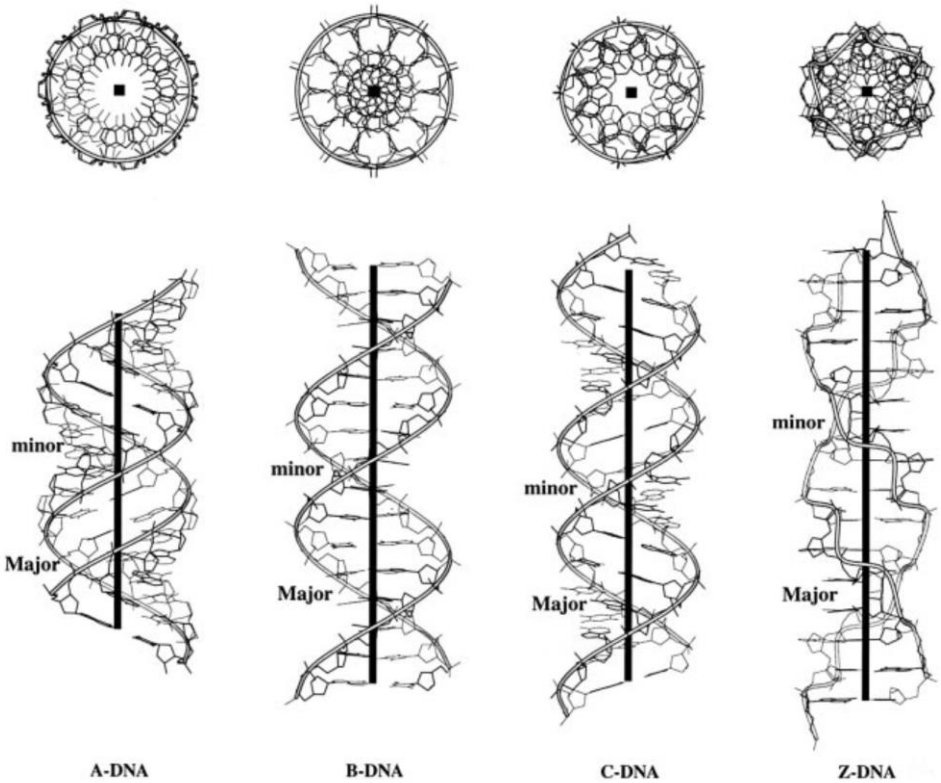




$$Lk = Tw + Wr$$



Двойные спирали ДНК/РНК



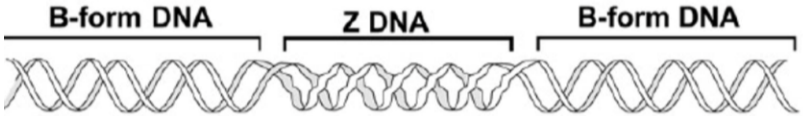
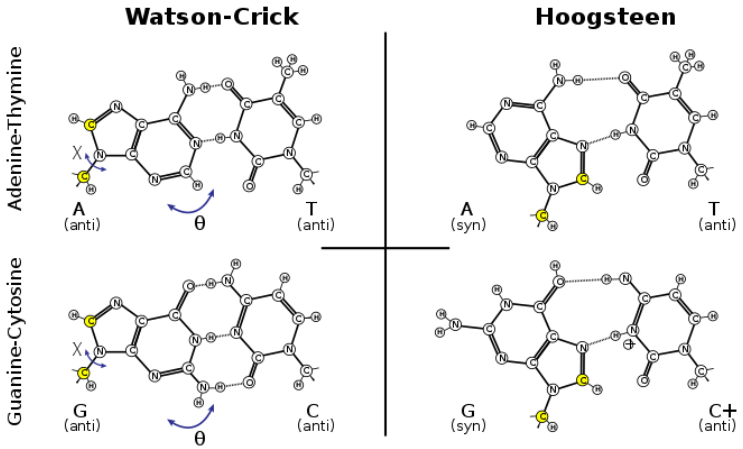
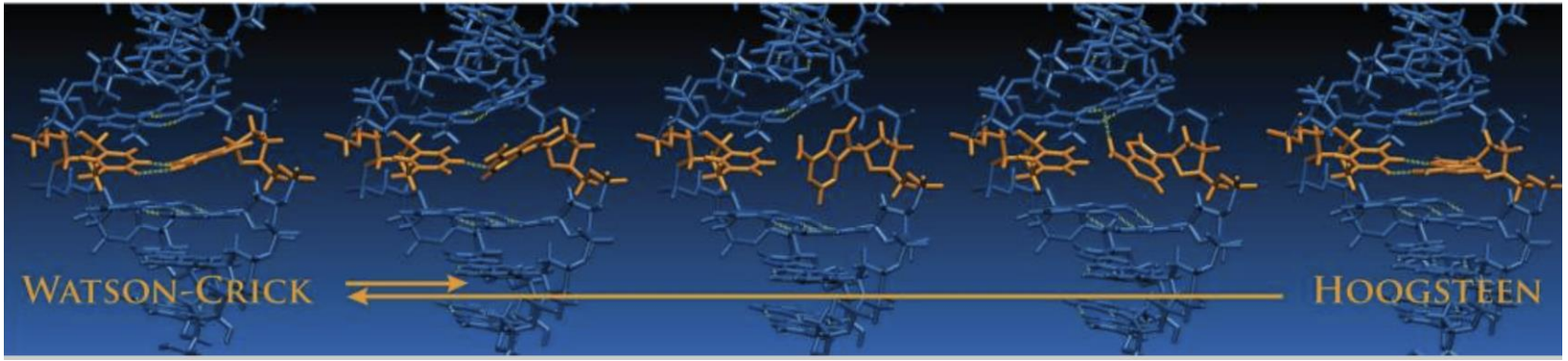


Table 1 Structural parameters of DNA helices

Structural Parameter	A-DNA	B-DNA	Z-DNA
Direction of helix rotation	Right handed	Right handed	Left handed
Residue per helical turn	11	10.5	12
Axial rise per residue	2.55 Å	3.4 Å	3.7 Å
Pitch (length) of the helix	2.82 Å	34 Å	44.4 Å
Base pair tilt	20°	-6°	7°
Rotation per residue	32.7°	34.3°	-30°
Diameter of helix	23 Å	20 Å	18 Å
Configuration dA, dT, dC	anti	anti	anti
of glycosidic bond dG	anti	anti	syn
Sugar Pucker dA, dT, dC	C3' endo	C2' endo	C2' endo
dG	C3' endo	C2' endo	C3' endo

Правая и левая спираль



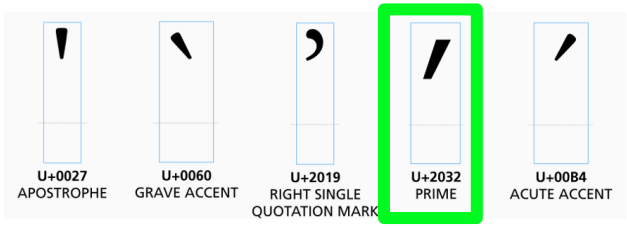


excited states in CA/TG steps of duplex DNA

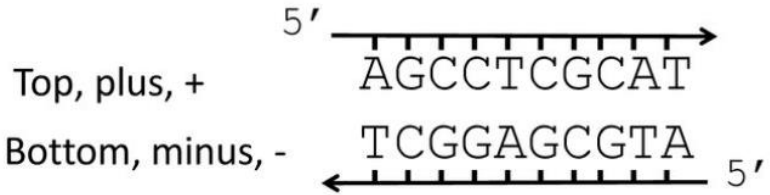
10.1038/nature09775 (2011)

Правила записи последовательностей

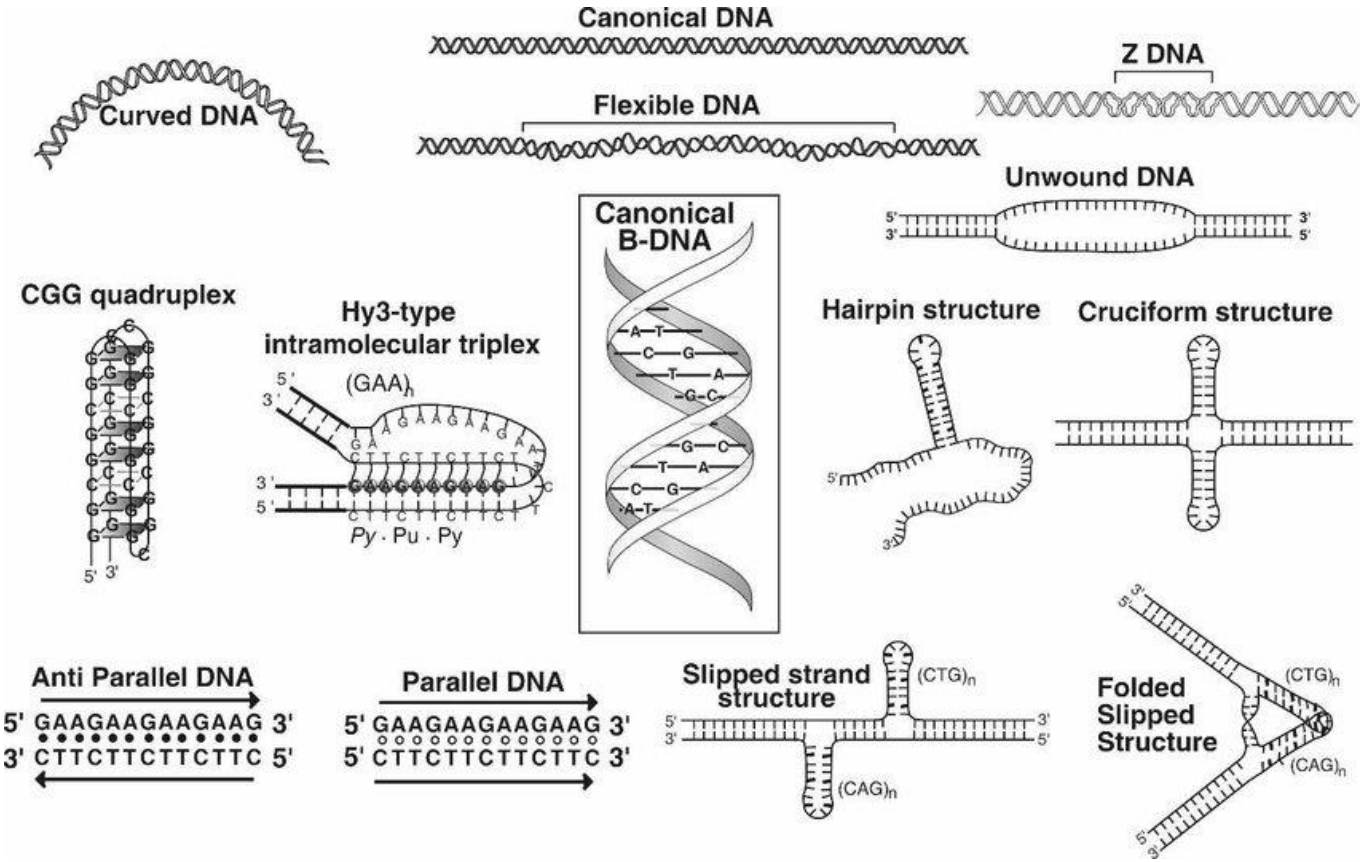
- ДНК от 5' (штрих) к 3' (штрих)
- Белок от N к С-концу



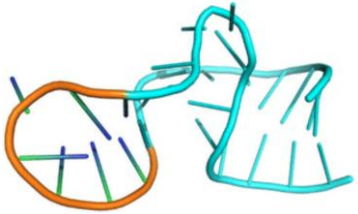
- Диаграмма двух комплЕментарных цепей ДНК делается так:
- Верхняя цепь 5' к 3' , нижняя 3' к 5'.
- При записи гена – верхняя кодирующая (смысловая), нижняя матричная.



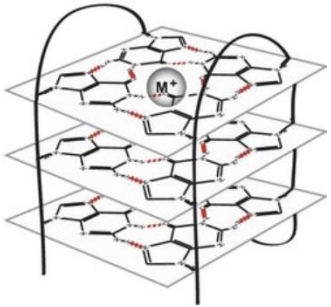
Неканонические структуры ДНК



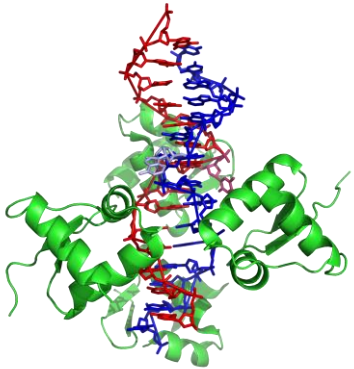
Неканонические структуры ДНК



DNA aptamer



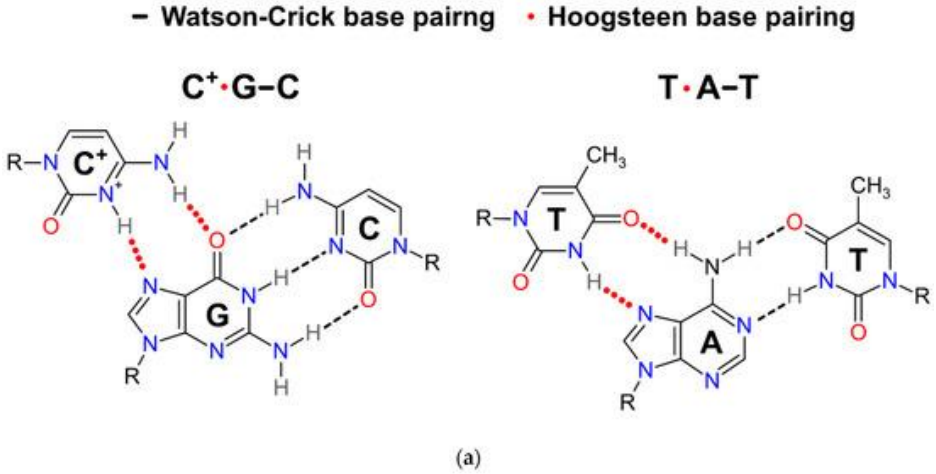
G-quadruplex



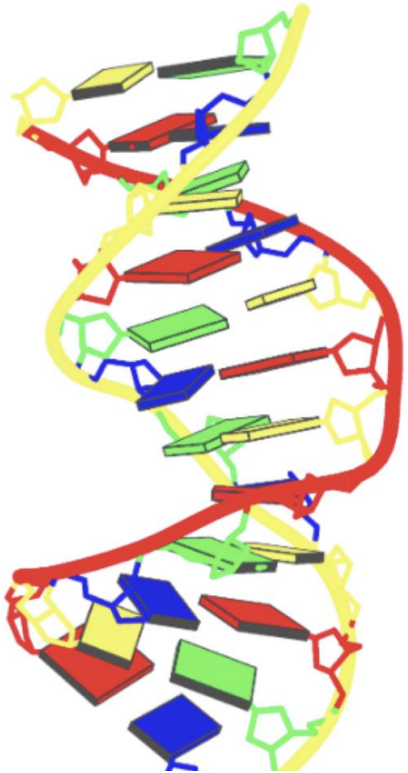
B-Z-junction

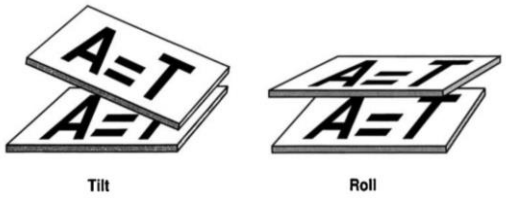
RNA-DNA triplex

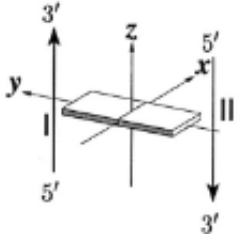
Неканонические структуры ДНК



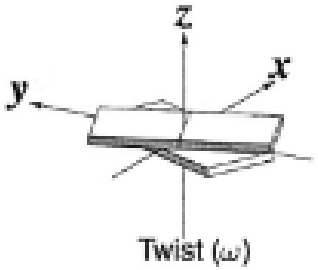
DNA structure, properties and its description



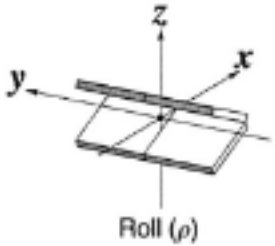




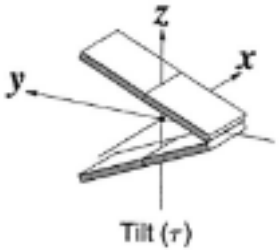
Coordinate frame



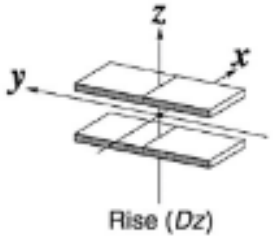
Twist (ω)



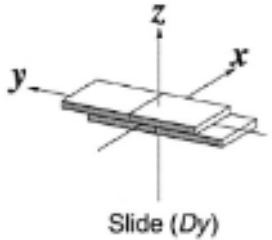
Roll (ρ)



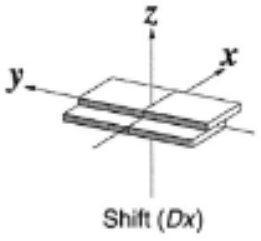
Tilt (τ)



Rise (Dz)



Slide (Dy)

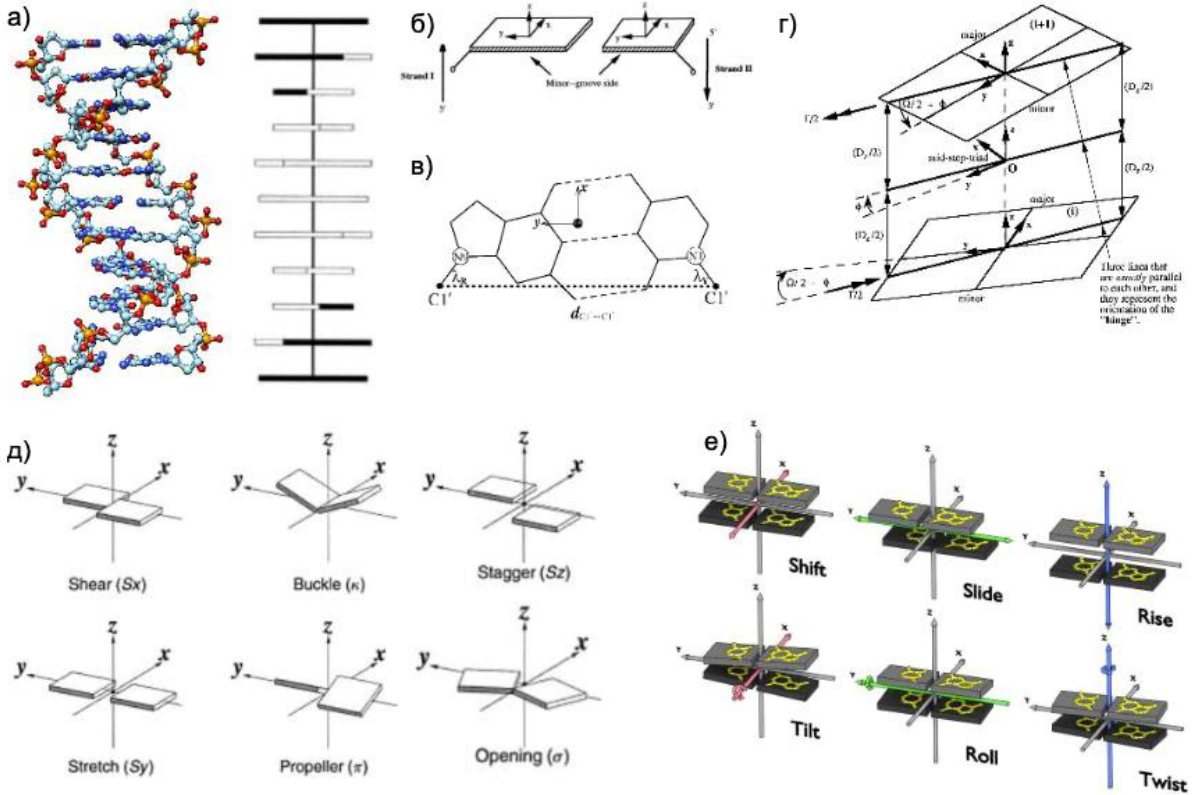


Shift (Dx)

dinuleotide steps

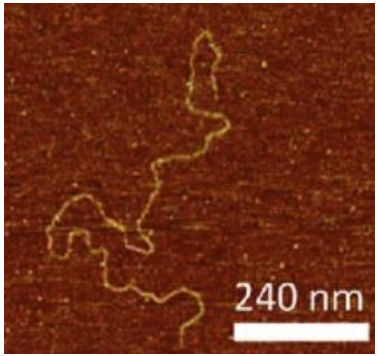
http://x3dna.org

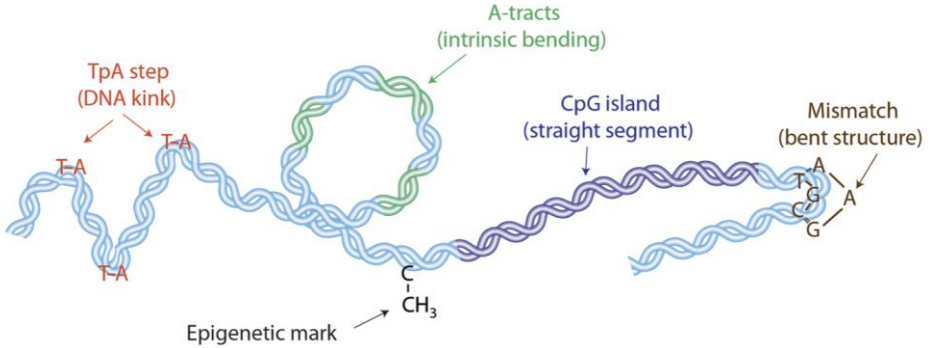
Динуклеотидные параметры



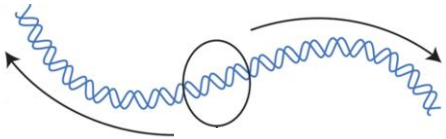
Гибкость ДНК

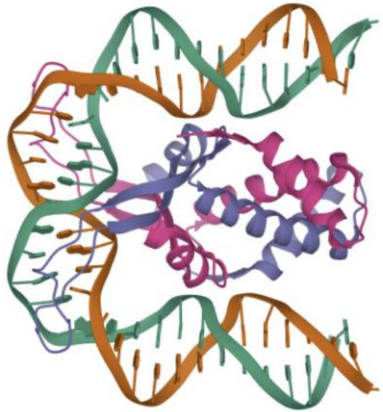
B-DNA persistence length: 50 nm (150 bp)





Worm-like chain model of flexibility

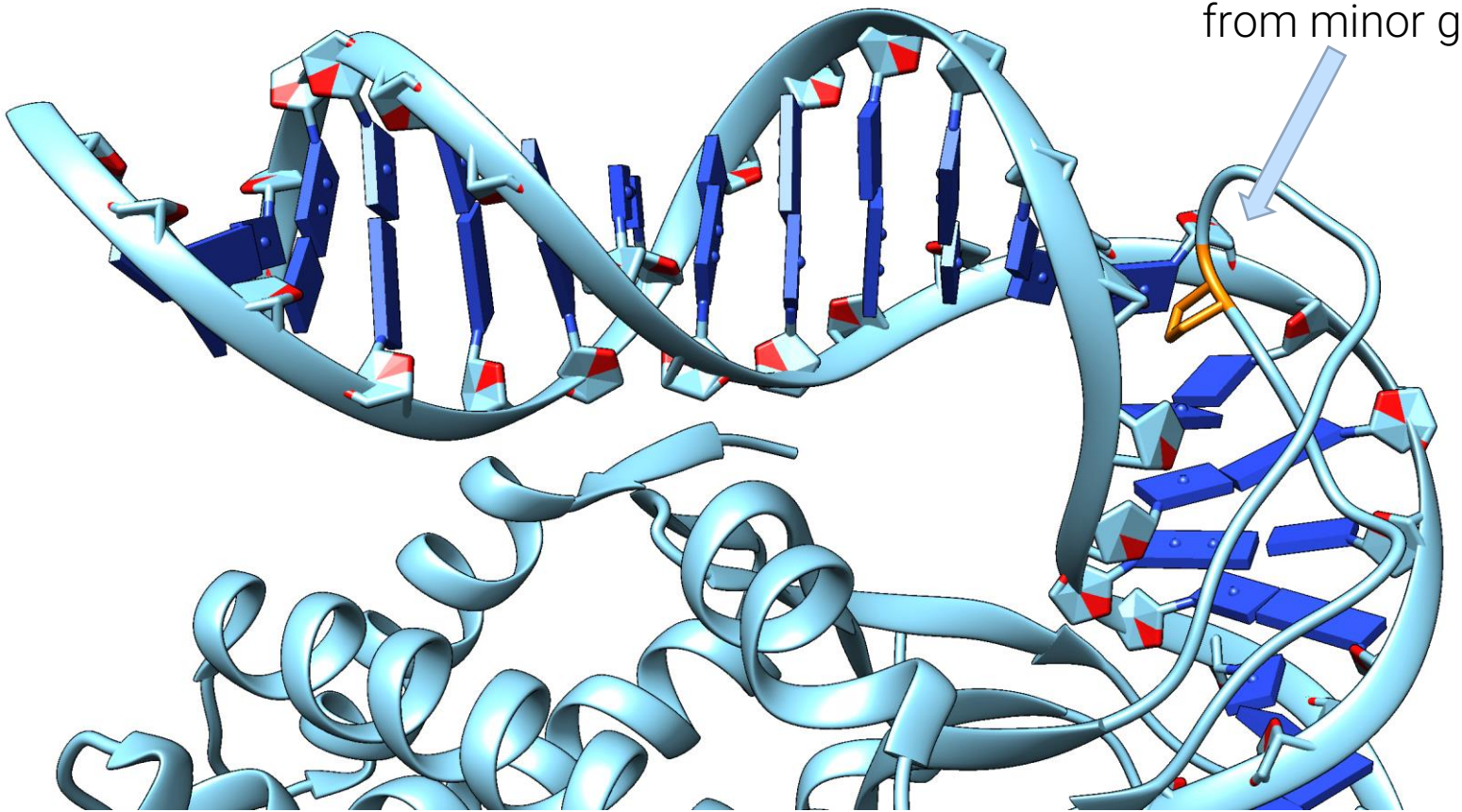




DNA-bending protein Hbb (Borrelia burgdorferi)

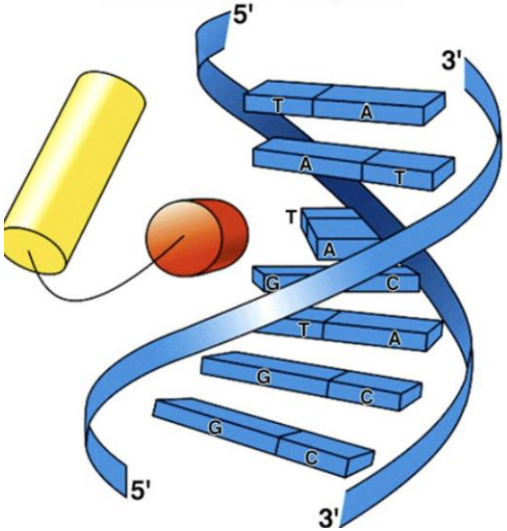
10.1039/C7NR04231K, 10.1017/S0033583521000068

Proline intercalates from minor groove



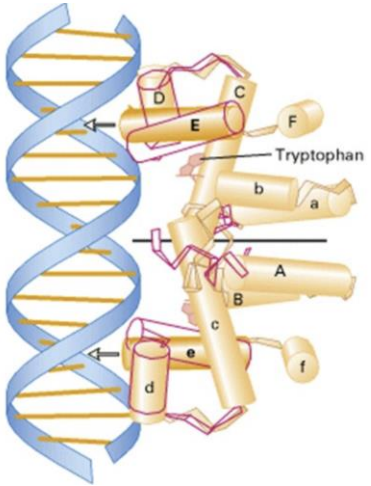
DNA-protein interactions

Direct readout



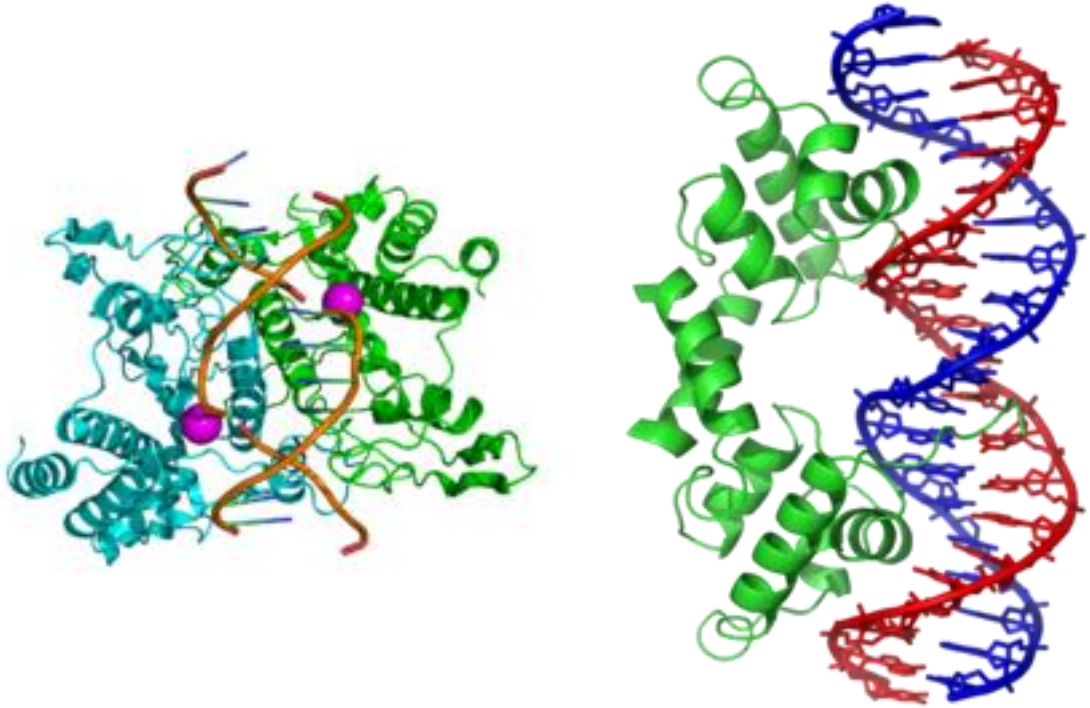
Direct H-bonds with bases

Indirect readout



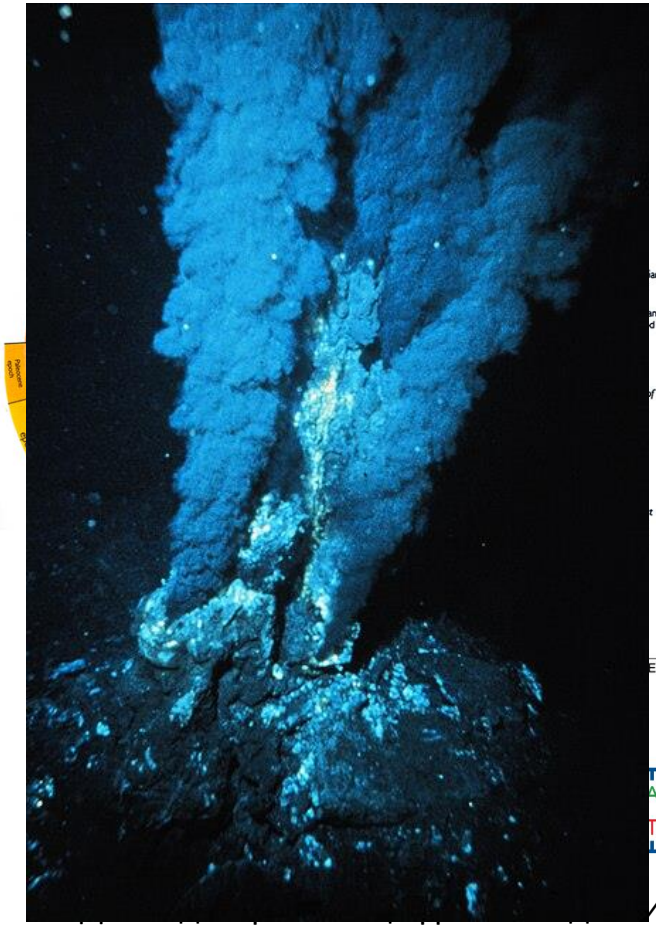
No direct H-bonds with bases
DNA shape and flexibility matters

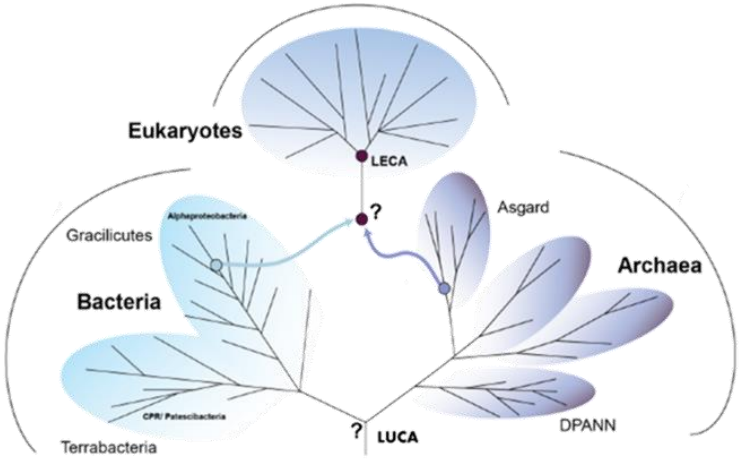
DNA-protein interactions – dimers and cooperativity



“Nothing in Biology Makes Sense Except in the Light of Evolution”

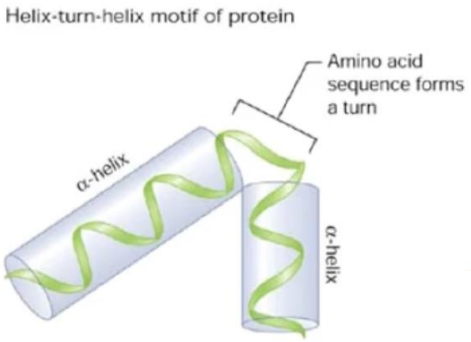
Феодосий Григорьевич Добржанский

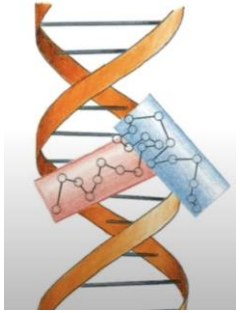


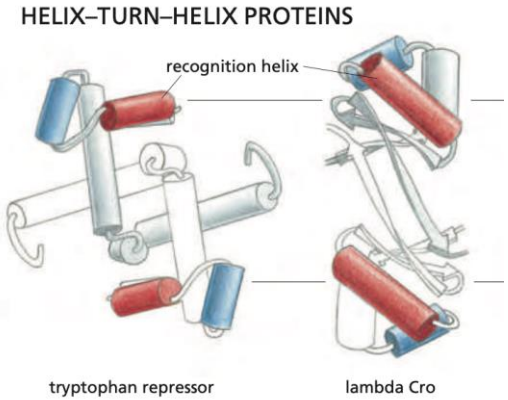


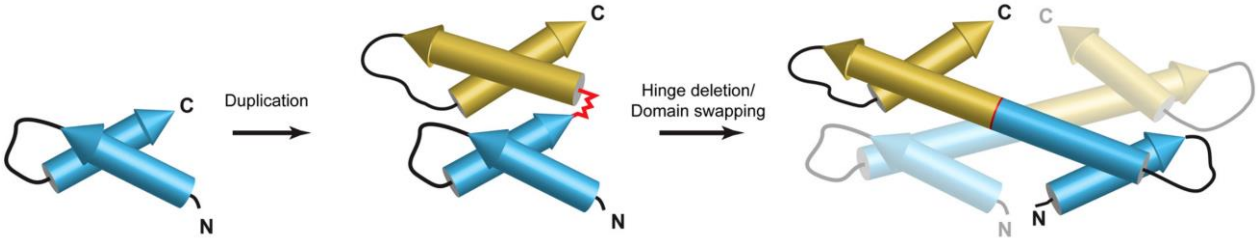
ивые системы – информационные системы

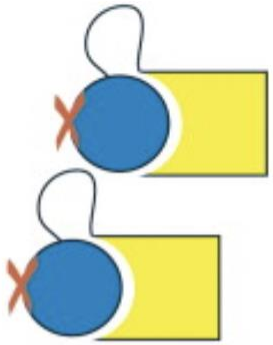
Возникновение гистонов (?)





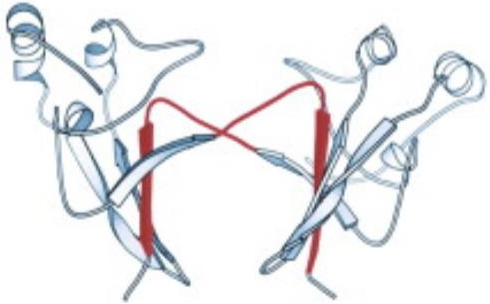


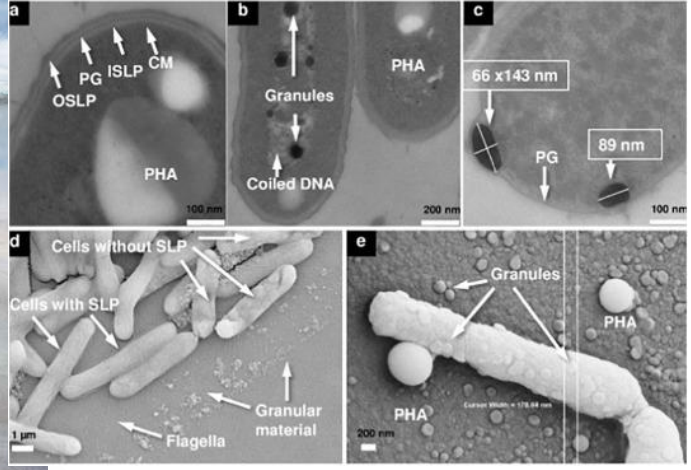




monomers

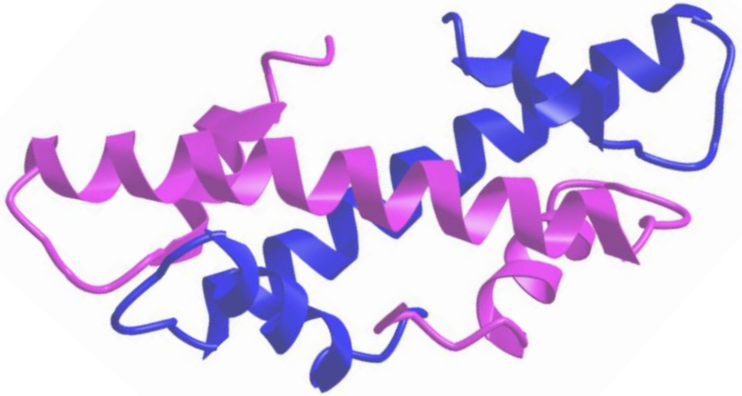
domain swapped dimers





[Methanothermus Fervidus](#)

Геном 1.2 Мб, 1311 белков

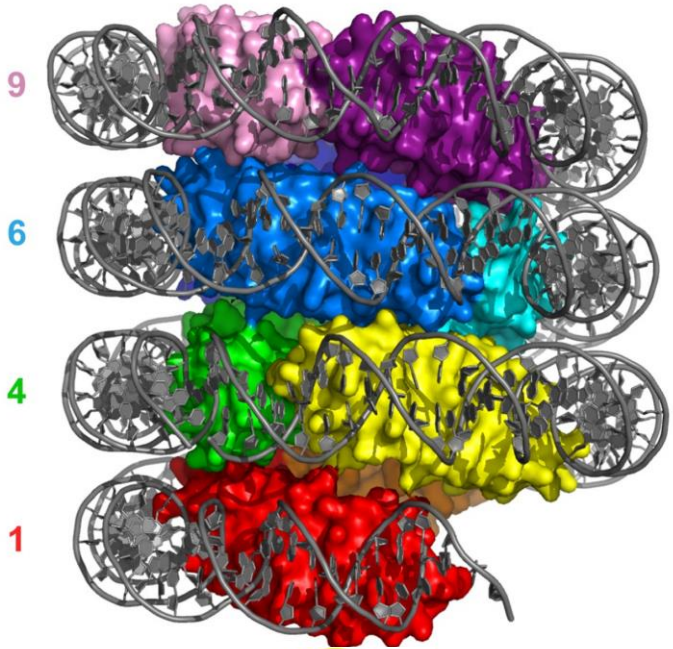


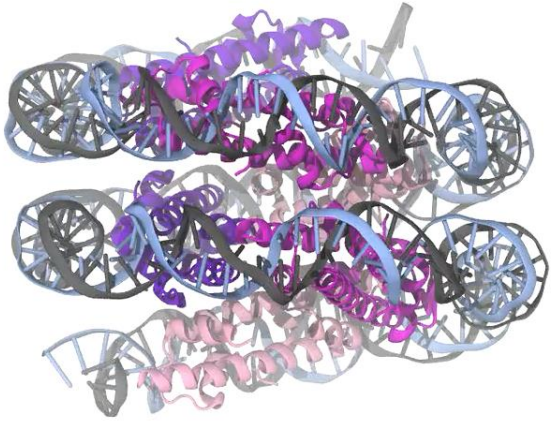
Димер белка HMfB

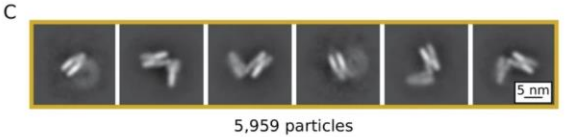
Histone Mf B

69 аминокислот

”Slinky” hypernucleosome







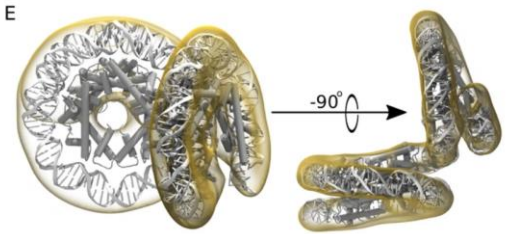
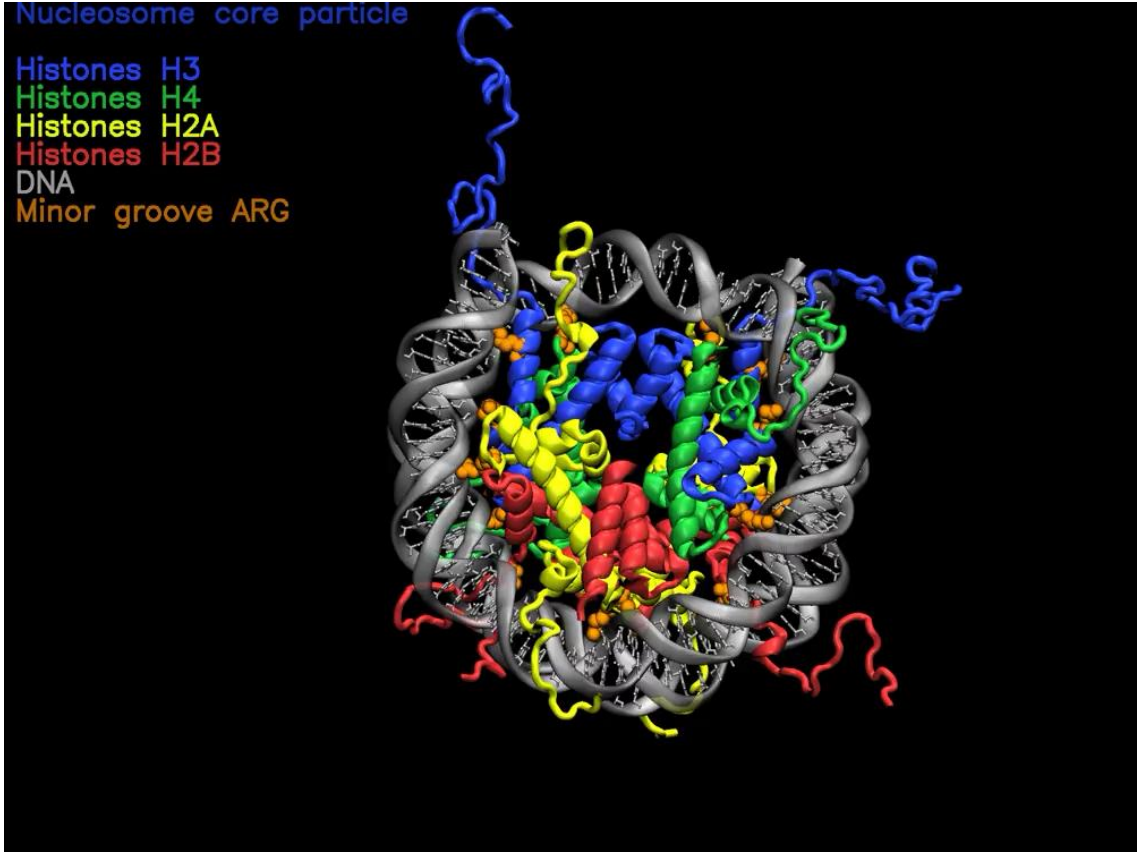


Table 1. Phylogenetic subdivision of the archaeal domain.

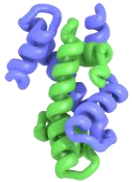
Superphylum	Phylum	Class	Histones
Asgard Archaea	Candidatus Heimdallarchaeota		Y
	Candidatus Lokiarchaeota		Y
	Candidatus Odinarchaeota		Y
	Candidatus Thorarchaeota		Y
DPANN	Candidatus Aenigmarchaeota		Y
	Candidatus Diapherotrites		Y
	Candidatus Huberarchaea		Y
	Candidatus Micrarchaeota		Y
	Nanoarchaeota		Y
	Candidatus Nanohaloarchaeota		Y
	Candidatus Pacearchaeota		Y
	Candidatus Parvarchaeota		N
	Candidatus Woesearchaeota		Y
TACK	Candidatus Bathyarchaeota		Y
	Crenarchaeota		Y*
	Candidatus Geothermarchaeota		N
	Candidatus Korarchaeota		Y
	Thaumarchaeota		Y
	Candidatus Verstraetearchaeota		N
-	**Euryarchaeota**	Archaeoglobi	Y
		Hadesarchaea	Y
		Halobacteria	Y
		Methanobacteria	Y
		Methanococci	Y
		Methanomicrobia	Y
		Methanonatronarchaeia	Y
		Methanopyri	Y
		Theionarchaea	Y
		Thermococci	Y
		Thermoplasmata	Y

Division of Archaea in superphyla and phyla, including the euryarchaeal classes. Presence (Y) or absence (N) of histone-coding genes on the genome of the members of the phyla and classes have been indicated. An asterisk indicates that histone-coding genes have been found in a minority of species belonging to the phylum.
Abbreviations: DPANN, Diapherotrites, Pacearchaeota, Aenigmarchaeota, Nanoarchaeota, Nanohaloarchaeota; TACK, Thaumarchaeota, Aigarchaeota, Crenarchaeota, Korarchaeota.

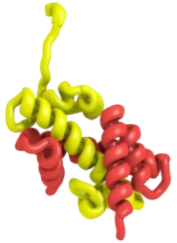
Ncleosome core structure



Histone H3-H4 dimer

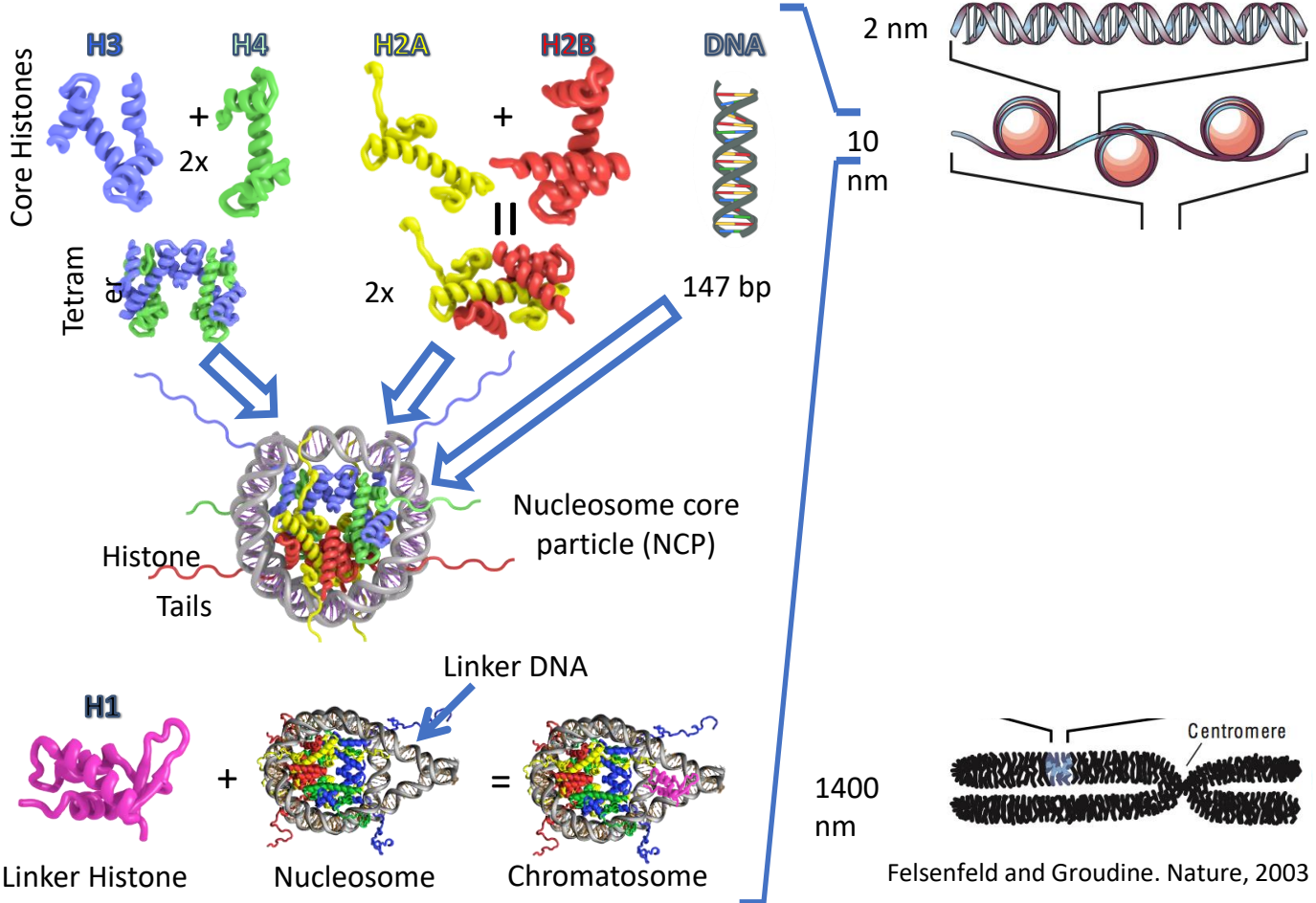


Histone H2A-H2B dimer



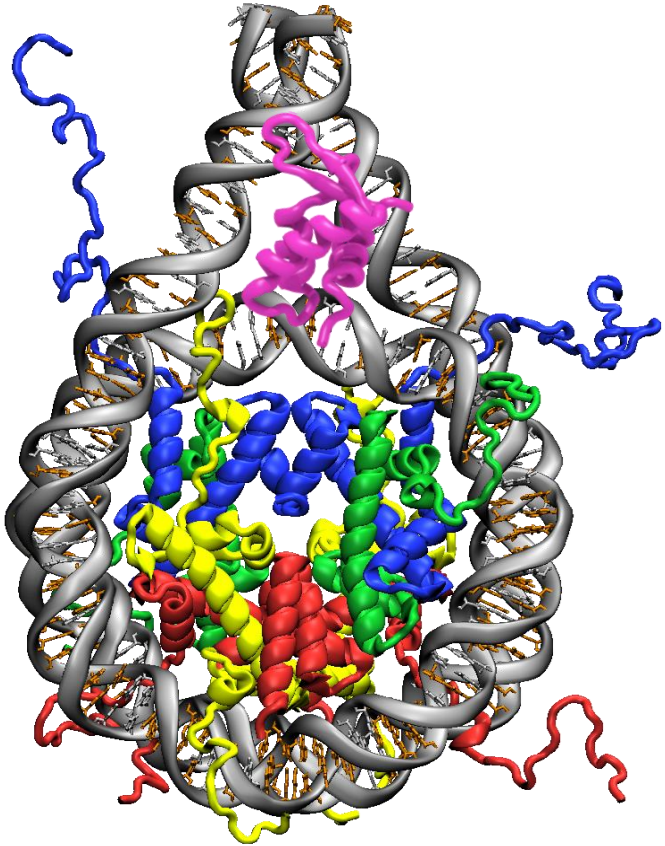
Luger, K.; Mäder, A. W.; Richmond, R. K.; Sargent, D. F.; Richmond, T. J. *Nature* **1997**, *389* (6648), 251–260.

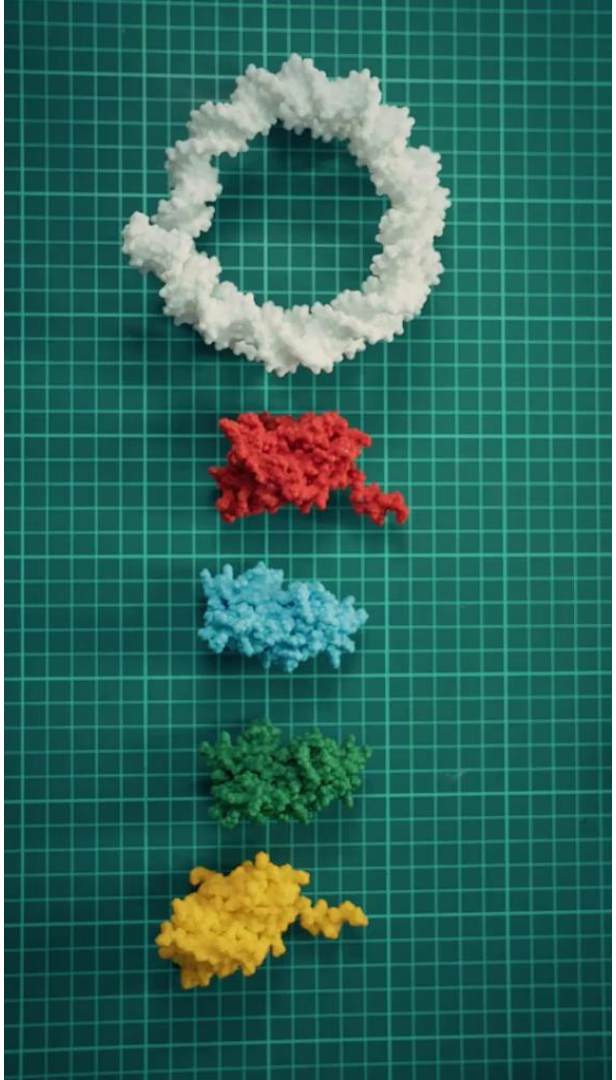
Nucleosome structure



Felsenfeld and Groudine. Nature, 2003

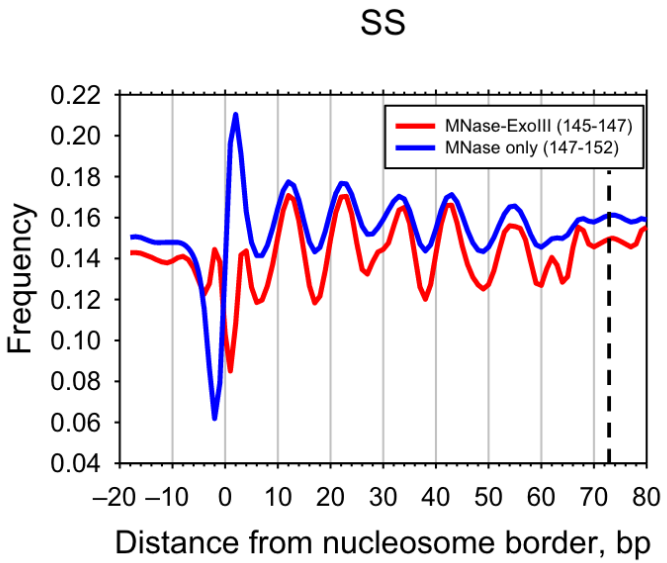
Хроматосома

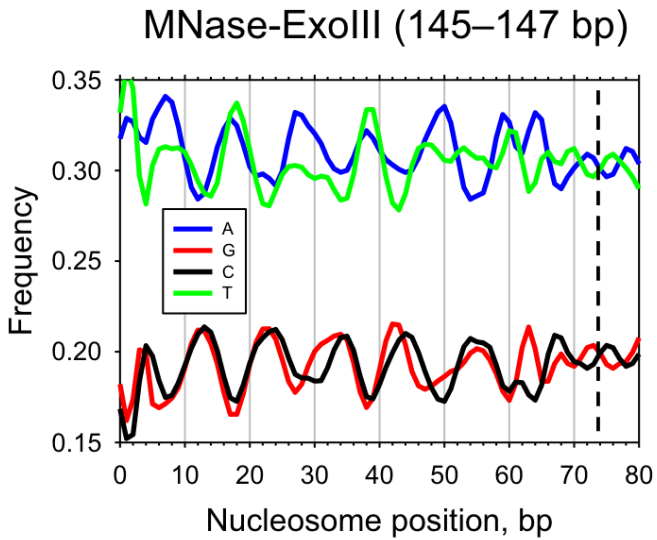




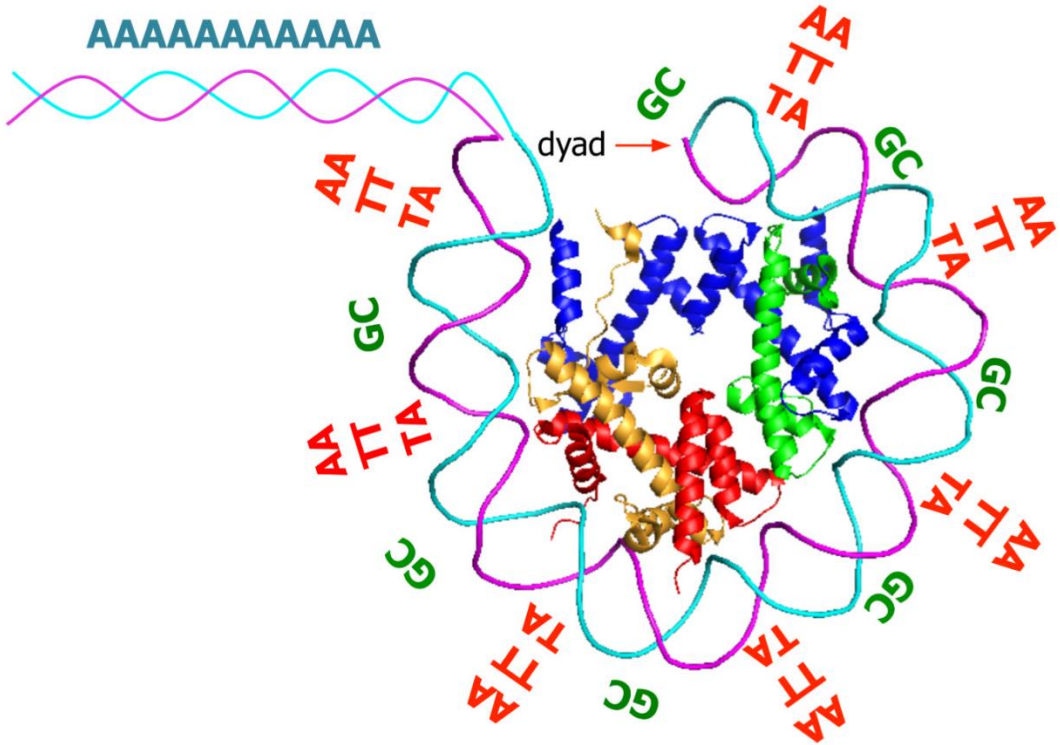
“Plastic” model of a nucleosome
https://github.com/molsim/nuclLEGO

Позиционирование, эффекты indirect readout





Cole, H. A.; Cui, F.; Ocampo, J.; Burke, T. L.; Nikitina, T.; Nagarajavel, V.; Kotomura, N.; Zhurkin, V. B.; Clark, D. J. Novel Nucleosomal Particles Containing Core Histones and Linker DNA but No Histone H1. *Nucleic Acids Res* **2016**, *44* (2), 573–581. https://doi.org/10.1093/nar/gkv943.

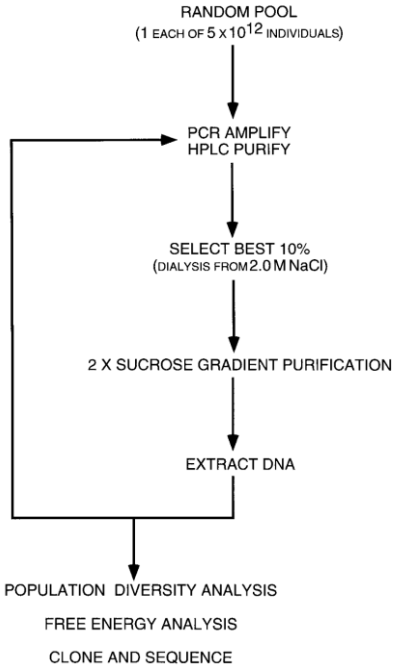


Struhl, K.; Segal, E. Determinants of Nucleosome Positioning. *Nat. Struct. Mol. Biol.* **2013**, *20* (3), 267–273. https://doi.org/10.1038/nsmb.2506.

601 Widom sequence – nucleosome positioning sequence

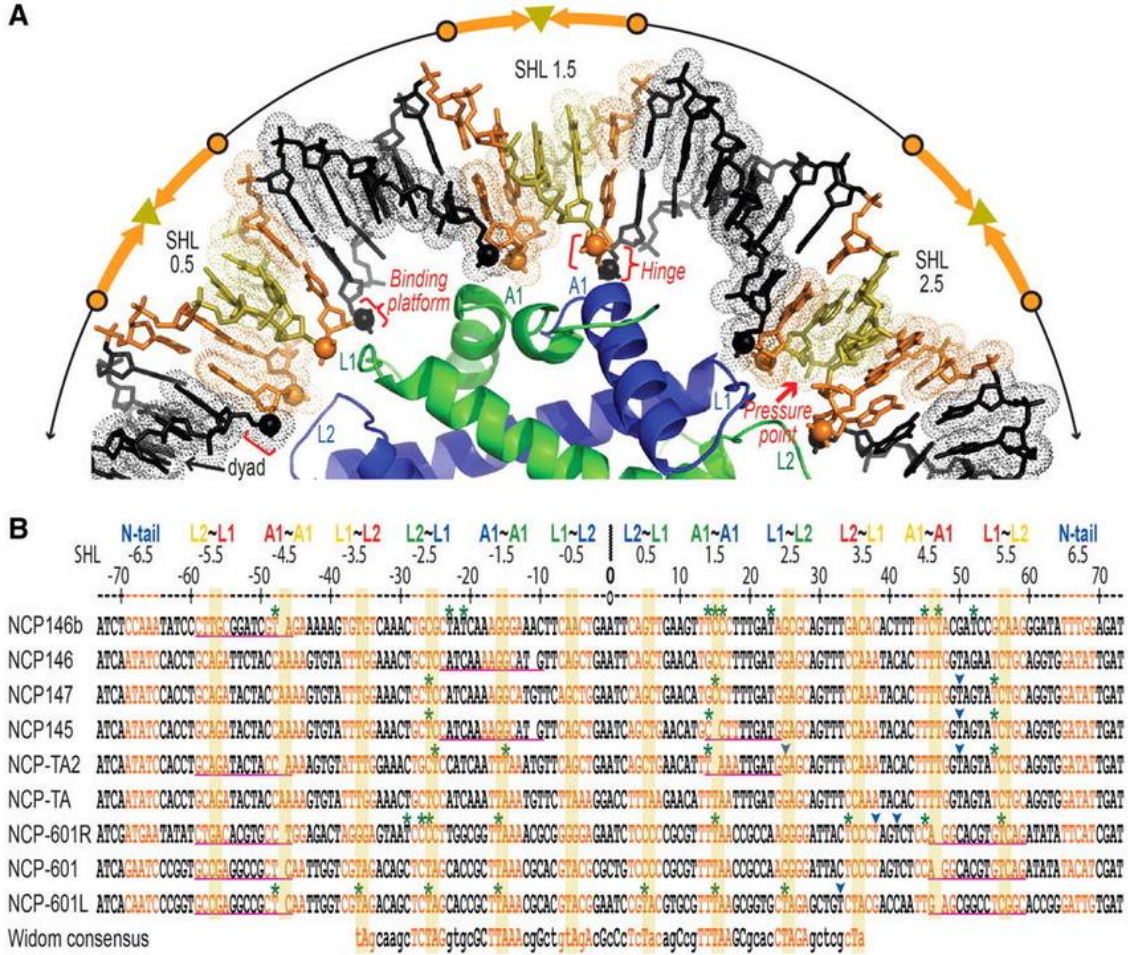
Table 2. Free energies of individual clones from round 15

Clone no.	$\Delta\Delta G^{a}$ (kcal mol^{-1}) relative to 5S molecule
601	-2.9 ± 0.33 ($n = 7$)
603	-2.7 ± 0.31 ($n = 6$)
607	-2.5 ± 0.32 ($n = 5$)
611	-2.5 ± 0.32 ($n = 5$)
612	-2.1 ± 0.48 ($n = 5$)
613	-2.3 ± 0.31 ($n = 5$)
618	-2.3 ± 0.31 ($n = 5$)
623	-2.6 ± 0.31 ($n = 6$)
626	-2.8 ± 0.31 ($n = 6$)



Lowary, P. T. & Widom, J. New DNA sequence rules for high affinity binding to histone octamer and sequence-directed nucleosome positioning. *J. Mol. Biol.* **276**, 19–42 (1998).

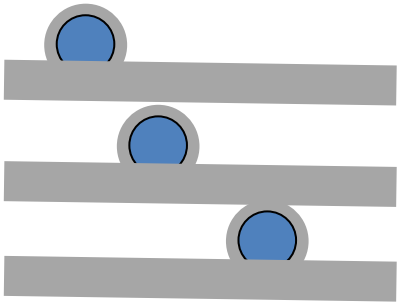
601 Widom sequence – nucleosome positioning sequence

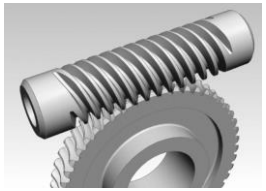


Nucleosome sliding and positioning

- Nucleosome positioning is important for:
  - Gene expression
  - Binding of TF (including pioneer factors)

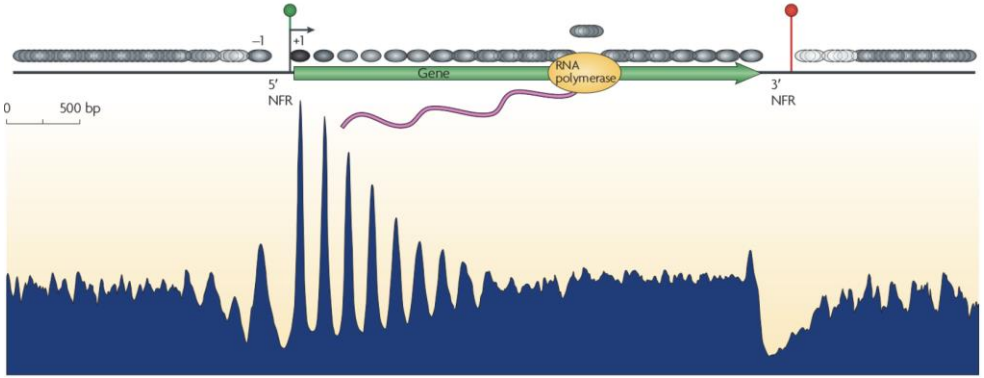
- Shifting DNA by 1 bp rotates DNA by 36 degrees



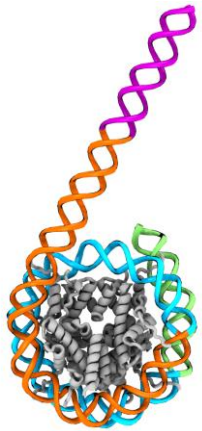


Translational positioning

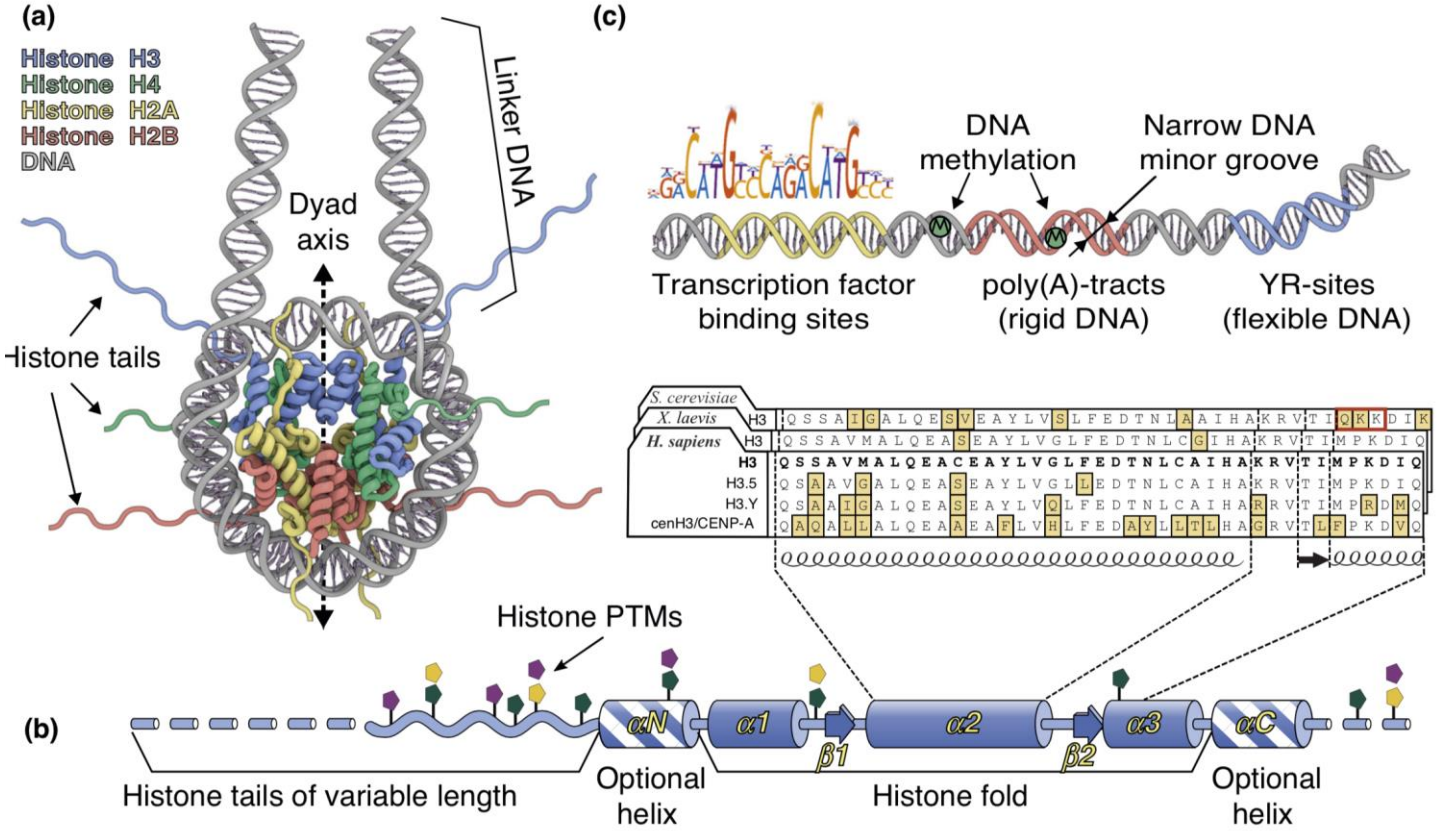
Rotational positioning



Cizhong Jiang and B. Franklin Pugh, Nature Reviews Genetics



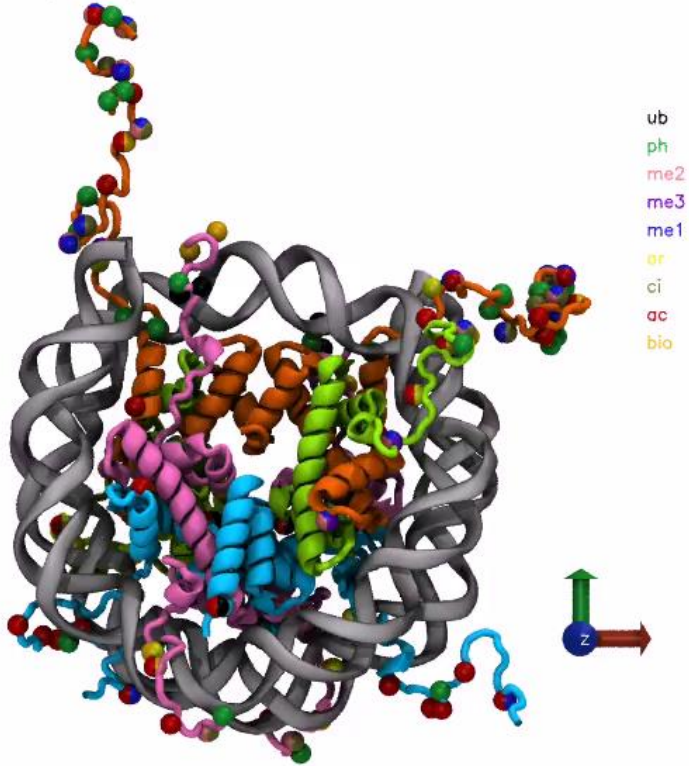
Nucleosome compositional variability



Armeev, G. A.; Gribkova, A. K.; Pospelova, I.; Komarova, G. A.; **Shaytan, A. K.** Linking Chromatin Composition and Structural Dynamics at the Nucleosome Level. *Current Opinion in Structural Biology* **2019**, *56*, 46–55.

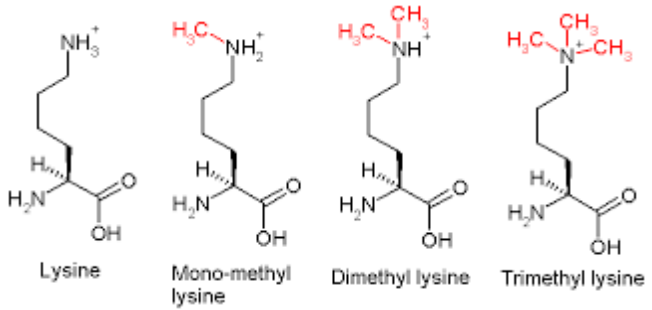
Histone post-translational modifications

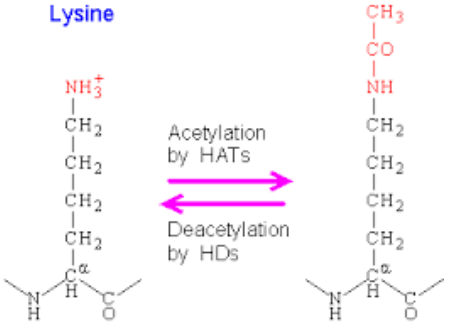
Nucleosome structure (1KX5)

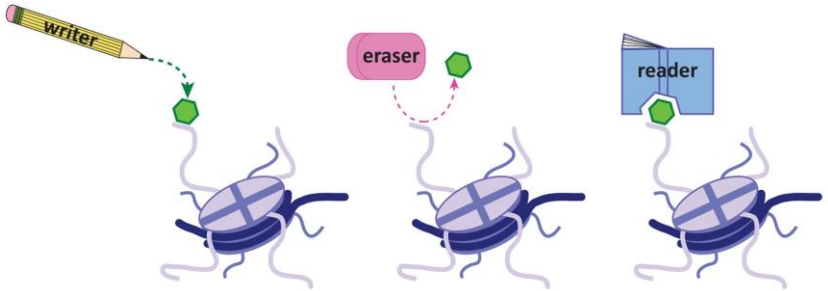


H2A	H2B	H3	H4
H2AS1ph	H2BK5ac	H3R2me1	H4S1ph
H2AR3me2	H2BK5me1	H3R2me2	H4R3me1
H2AR3ci	H2BK12ac	H3R2ci	H4R3me2
H2AK5ac	H2BS14ph	H3T3ph	H4R3ci
H2AK9ac	H2BK15ac	H3K4ac	H4K5ac
H2AK9bio	H2BK16ac	H3K4me1	H4K8ac
H2AK13bio	H2BK20ac	H3K4me2	H4K8bio
H2AK13ar	H2BK30ar	H3K4me3	H4K12ac
H2AK119ub	H2BK46ac	H3S6ph	H4K12bio
H2AT120ph	H2BK120ac	H3T6ph	H4K16ac
H2AK121ub	H2BK120ub	H3R8ci	H4K16ar
H2AK125bio		H3K9ac	H4K20me1
H2AK127bio		H3K9me1	H4K20me2
H2AK129bio		H3K9me2	H4K20me3
H2AS137ph		H3K9me3	H4K91ac
H2AS139ph		H3K9bio	H4K91ub
H2AY142ph		H3S10ph	
		H3T11ph	
		H3K14ac	
		H3R17me1	
		H3R17me2	
		H3R17ci	
		H3K18ac	
		H3K18bio	
		H3K23ac	
		H3R26me1	
		H3R26ci	
		H3K27ac	
		H3K27me1	
		H3K27me2	
		H3K27me3	
		H3K27ar	
		H3S28ph	
		H3S31ph	
		H3K36ac	
		H3K36me3	
		H3K36me1	
		H3K36me2	
		H3K37ar	
		H3Y41ph	
		H3T45ph	
		H3K56ac	
		H3K79me1	
		H3K79me2	

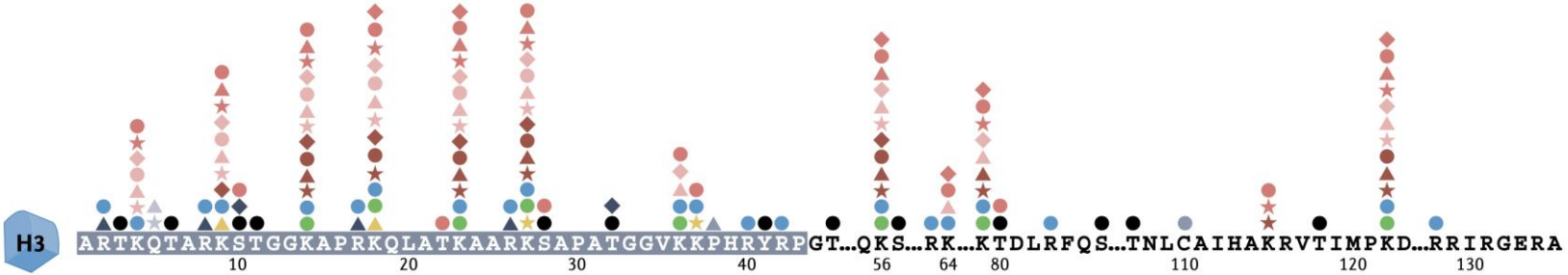
Histone post-translational modifications

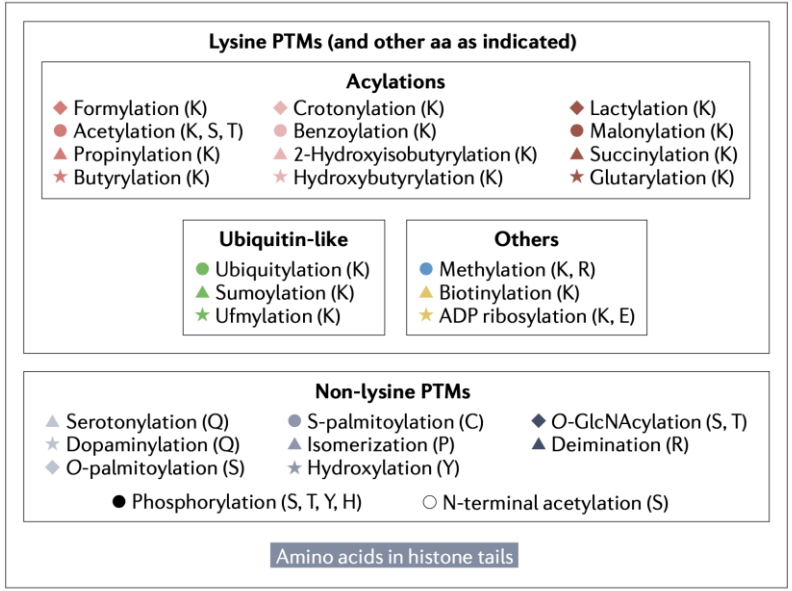






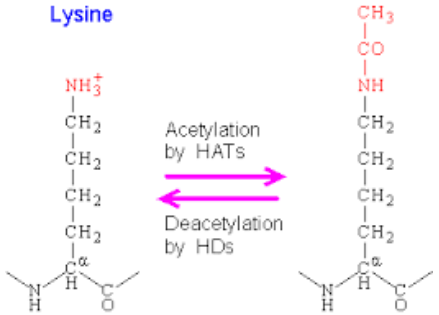
Jenuwein, T. (2001). Translating the Histone Code. Science, 293(5532), 1074–1080. doi:10.1126/science.1063127

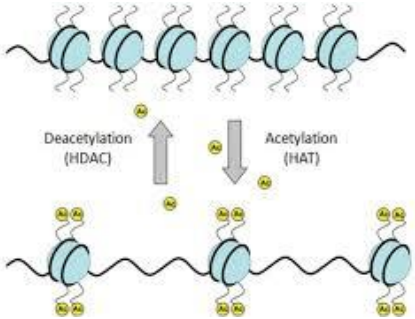




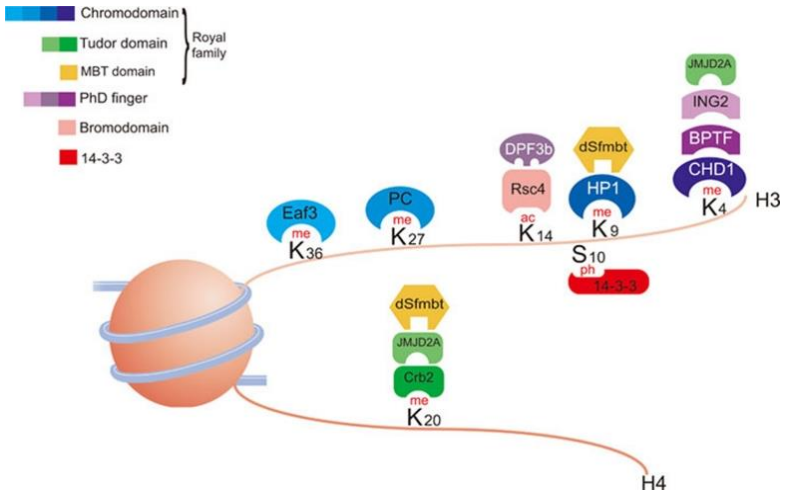
Millán-Zambrano,G., Burton,A., Bannister,A.J. and Schneider,R. (2022). *Nat Rev Genet*

Effects of histone PTMs





Influence through changes in physical interactions

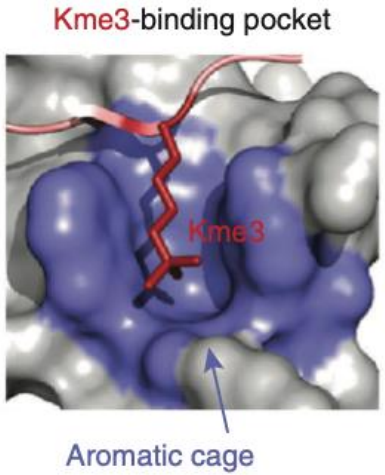


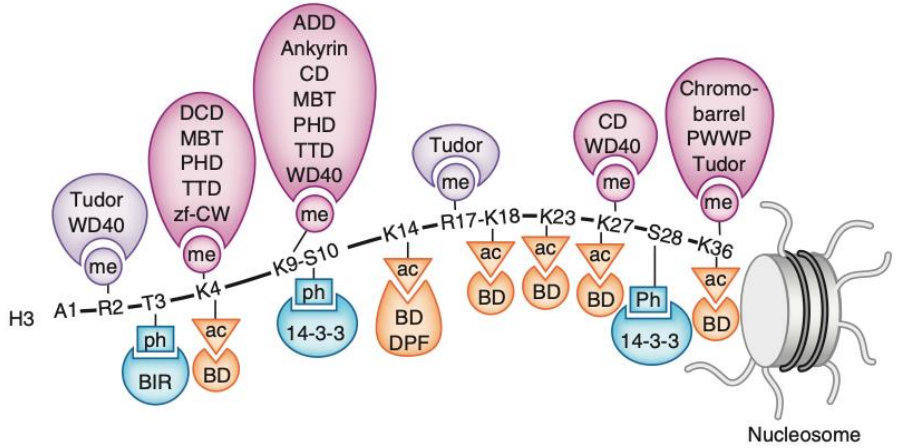
Influence through ”effector” domains and proteins

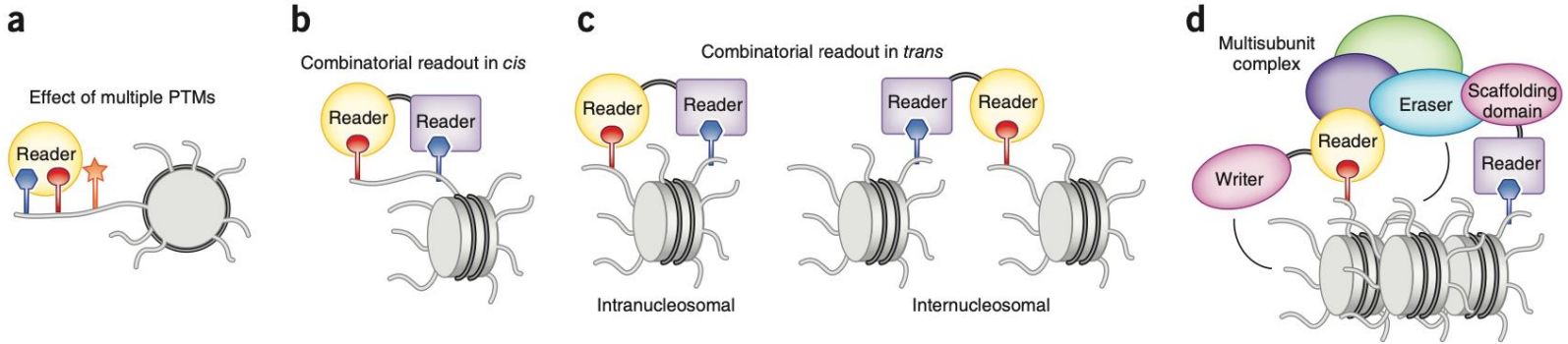
Table 1 Histone readers and their target PTMs

Recognition of	Reader	Histone PTM
Methyllysine	ADD	H3K9me3
	Ankyrin	H3K9me2, H3K9me1
	BAH	H4K20me2
	Chromo-barrel	H3K36me3, H3K36me2, H4K20me1, H3K4me1
	Chromodomain	H3K9me3, H3K9me2, H3K27me3, H3K27me2
	DCD	H3K4me3, H3K4me2, H3K4me1
	MBT	H3Kme1, H3Kme2, H4Kme1, H4Kme2
	PHD	H3K4me3, H3K4me2, H3K9me3
	PWWP	H3K36me3, H4K20me1, H4K20me3, H3K79me3
	TTD	H3K4me3, H3K9me3, H4K20me2
	Tudor	H3K36me3
	WD40	H3K27me3, H3K9me3
	zf-CW	H3K4me3
Methylarginine	ADD	H4R3me2s
	Tudor	H3Rme2, H4Rme2
	WD40	H3R2me2
Acetyllysine	Bromodomain	H3Kac, H4Kac, H2AKac, H2BKac
	DBD	H3KacKac, H4KacKac
	DPF	H3Kac
	Double PH	H3K56ac
Phosphoserine or phosphothreonine	14-3-3	H3S10ph, H3S28ph
	BIR	H3T3ph
	Tandem BRCT	H2AXS139ph
Unmodified histone	ADD	H3un
	PHD	H3un
	WD40	H3un

Chromatin readers

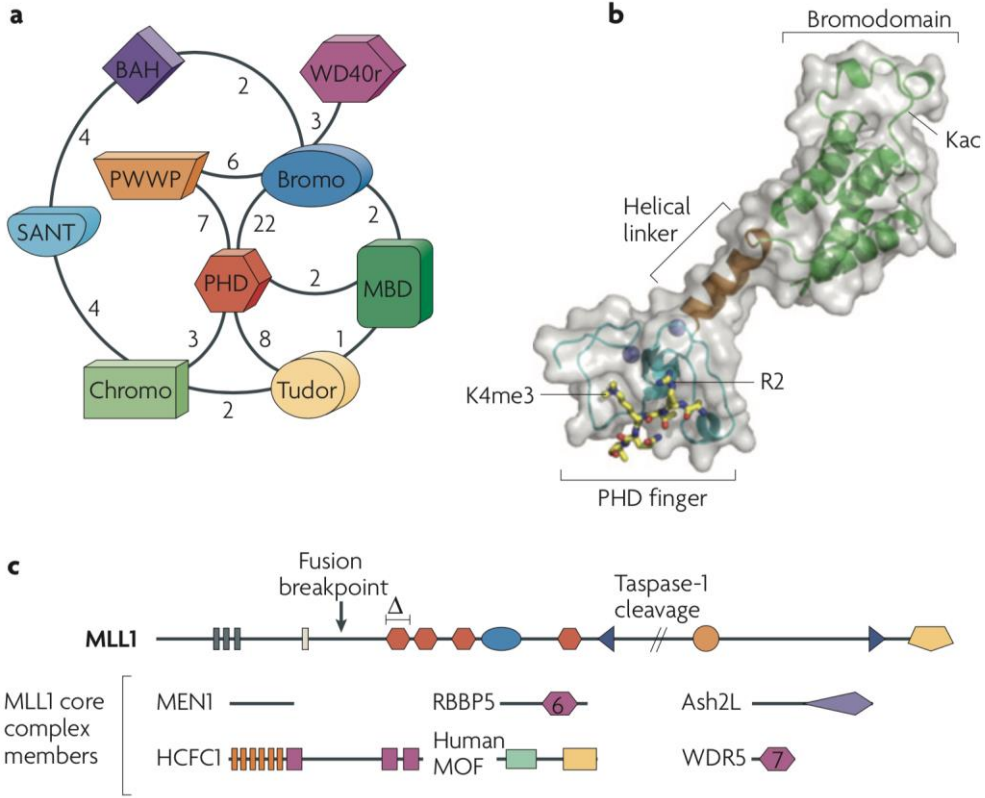






Musselman,C.A., Lalonde,M.-E., Côté,J. and Kutateladze,T.G. (2012. *Nat Struct Mol Biol*, **19**, 1218–1227.

Effector domains



Ruthenburg, A. J., et al. (2007). "Multivalent engagement of chromatin modifications by linked binding modules." Nat Rev Mol Cell Biol **8**(12): 983-994.

Human histones (~ 100 genes)

https://histdb.intbio.org/human/

Histone type	Histone variant	Canonical isoform	HGNC symbol	NCBI gene ID
H1	H1.0		H1-0	3005
H1	H1.1		H1-1	3024
H1	H1.2		H1-2	3006
H1	H1.3		H1-3	3007
H1	H1.4		H1-4	3008
H1	H1.5		H1-5	3009
H1	TS H1.6		H1-6	3010
H1	TS H1.7		H1-7	341567
H1	OO H1.8		H1-8	132243
H1	OO H1.8		H1-8	132243
H1	TS H1.9(?)		H1-9P	373861
H1	H1.10		H1-10	8971

H2A	TS H2A.1		H2AC1	221613
H2A	canonical H2A	isoform_2	H2AC4	8335
H2A	canonical H2A	isoform_7	H2AC6	8334
H2A	canonical H2A	isoform_9	H2AC7	3013
H2A	canonical H2A	isoform_2	H2AC8	3012
H2A	canonical H2A	isoform_1	H2AC11	8969
H2A	canonical H2A	isoform_10	H2AC12	85235
H2A	canonical H2A	isoform_1	H2AC13	8329
H2A	canonical H2A	isoform_8	H2AC14	8331
H2A	canonical H2A	isoform_1	H2AC15	8330
H2A	canonical H2A	isoform_1	H2AC16	8332
H2A	canonical H2A	isoform_1	H2AC17	8336
H2A	canonical H2A	isoform_3	H2AC18	8337
H2A	canonical H2A	isoform_3	H2AC19	723790
H2A	canonical H2A	isoform_6	H2AC20	8338
H2A	canonical H2A	isoform_4	H2AC21	317772
H2A	H2A.J(?)		H2AJ	55766
H2A	canonical H2A	isoform_5	H2AW	92815
H2A	H2A.X		H2AX	3014
H2A	H2A.Z.1		H2AZ1	3015
H2A	H2A.Z.1		H2AZ1	3015
H2A	H2A.Z.2		H2AZ2	94239
H2A	H2A.Z.2		H2AZ2	94239
H2A	H2A.Z.2		H2AZ2	94239
H2A	H2A.Z.2		H2AZ2	94239
H2A	H2A.Z.2		H2AZ2	94239
H2A	H2A.Z.2		H2AZ2	94239
H2A	H2A.Z.2		H2AZ2	94239
H2A	H2A.Z.2		H2AZ2	94239
H2A	H2A.Z.2		H2AZ2	94239
H2A	macroH2A.1		MACROH2A1	9555
H2A	macroH2A.1		MACROH2A1	9555
H2A	macroH2A.1		MACROH2A1	9555
H2A	macroH2A.1		MACROH2A1	9555
H2A	macroH2A.2		MACROH2A2	55506
H2A	macroH2A.2		MACROH2A2	55506
H2A	H2A.B.1		H2AB1	474382
H2A	H2A.B.2		H2AB2	474381
H2A	H2A.B.2		H2AB3	83740
H2A	H2A.P		H2AP	25763
H2B	TS H2B.1		H2BC1	255626

H2B	TS H2B.1		H2BC1	255626
H2B	canonical H2B	isoform_8	H2BC3	3018
H2B	canonical H2B	isoform_1	H2BC4	8347
H2B	canonical H2B	isoform_11	H2BC5	3017
H2B	canonical H2B	isoform_1	H2BC6	8344
H2B	canonical H2B	isoform_1	H2BC7	8343
H2B	canonical H2B	isoform_1	H2BC8	8339
H2B	canonical H2B	isoform_2	H2BC9	8345
H2B	canonical H2B	isoform_1	H2BC10	8346
H2B	canonical H2B	isoform_4	H2BC11	8970
H2B	canonical H2B	isoform_9	H2BC11	8970
H2B	canonical H2B	isoform_4	H2BC11	8970
H2B	canonical H2B	isoform_9	H2BC11	8970
H2B	canonical H2B	isoform_12	H2BC12	85236
H2B	canonical H2B	isoform_7	H2BC13	8340
H2B	canonical H2B	isoform_5	H2BC14	8342
H2B	canonical H2B	isoform_10	H2BC15	8341
H2B	canonical H2B	isoform_14	H2BC15	8341
H2B	canonical H2B	isoform_10	H2BC15	8341
H2B	canonical H2B	isoform_14	H2BC15	8341
H2B	canonical H2B	isoform_15	H2BC17	8348
H2B	canonical H2B	isoform_6	H2BC18	440689
H2B	canonical H2B	isoform_13	H2BC18	440689
H2B	canonical H2B	isoform_6	H2BC18	440689
H2B	canonical H2B	isoform_13	H2BC18	440689
H2B	canonical H2B(?)		H2BC21	8349
H2B	H2B.S(?)		H2BS1	54145
H2B	canonical H2B	isoform_3	H2BU1	128312
H2B	H2B.W		H2BW1	158983
H2B	?		H2BW2	286436
H2B	?		H2BW2	286436
H2B	?		H2BE1	114483833

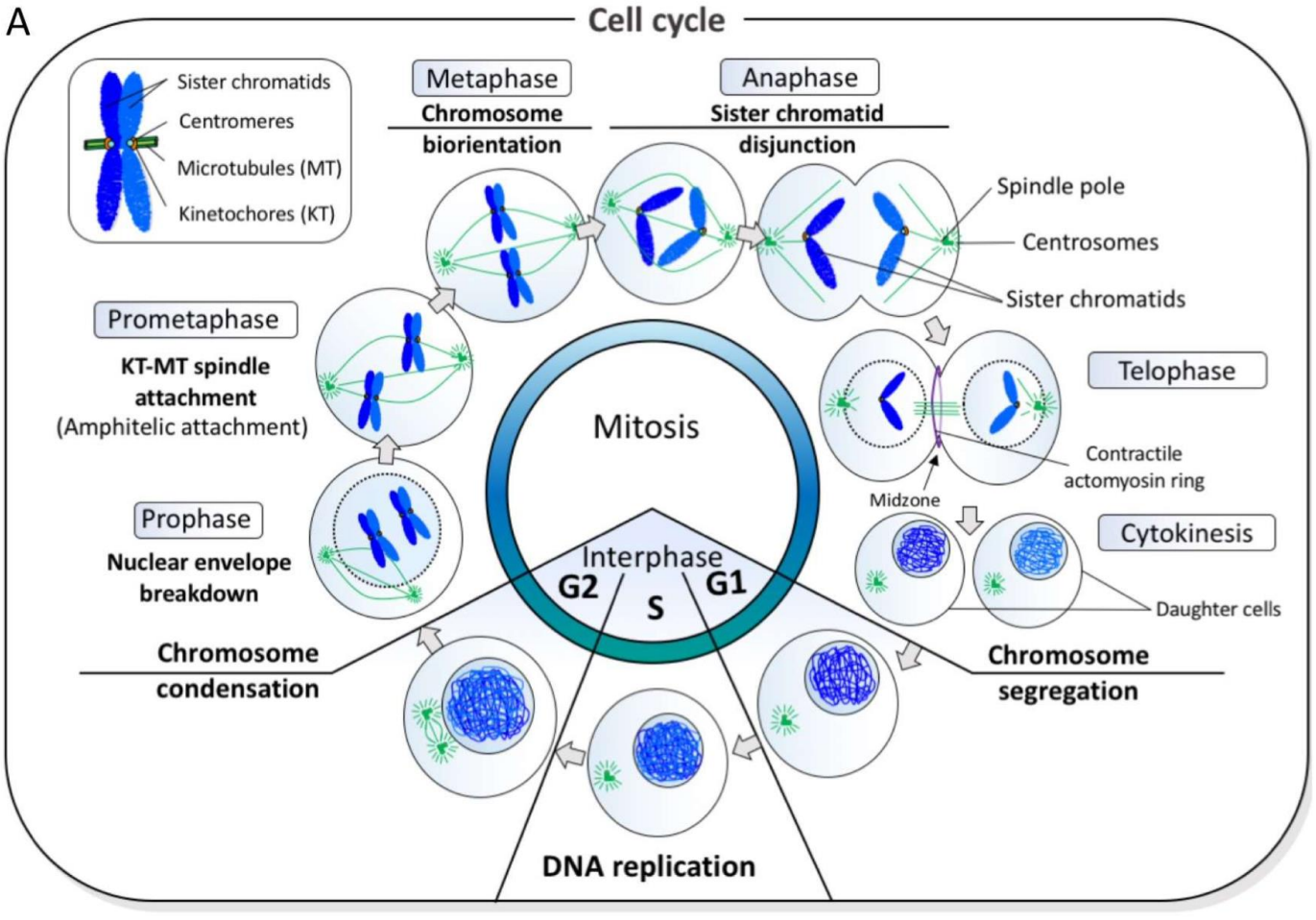
H3	canonical H3.1	isoform_1	H3C1	8350
H3	canonical H3.1	isoform_1	H3C2	8358
H3	canonical H3.1	isoform_1	H3C3	8352
H3	canonical H3.1	isoform_1	H3C4	8351
H3	canonical H3.1	isoform_1	H3C6	8353
H3	canonical H3.1	isoform_1	H3C7	8968
H3	canonical H3.1	isoform_1	H3C8	8355
H3	canonical H3.1	isoform_1	H3C10	8357
H3	canonical H3.1	isoform_1	H3C11	8354
H3	canonical H3.1	isoform_1	H3C12	8356
H3	canonical H3.2	isoform_1	H3C13	653604
H3	canonical H3.2	isoform_1	H3C14	126961
H3	canonical H3.2	isoform_1	H3C15	333932
H3	H3.Y.1		H3Y1	391769
H3	H3.Y.2		H3Y2	340096
H3	canonical H3(?)		H3-2	440686
H3	H3.3		H3-3A	3020
H3	H3.3		H3-3A	3020
H3	H3.3		H3-3A	3020
H3	H3.3		H3-3B	3021
H3	H3.3		H3-3B	3021
H3	H3.3		H3-3B	3021
H3	H3.3		H3-3B	3021
H3	H3.3		H3-3B	3021
H3	TS H3.4		H3-4	8290
H3	H3.5		H3-5	440093
H3	cenH3		CENPA	1058
H3	cenH3		CENPA	1058

H4	canonical H4	isoform_1	H4C1	8359
H4	canonical H4	isoform_1	H4C2	8366
H4	canonical H4	isoform_1	H4C3	8364
H4	canonical H4	isoform_1	H4C4	8360
H4	canonical H4	isoform_1	H4C5	8367
H4	canonical H4	isoform_1	H4C6	8361
H4	canonical H4	isoform_2	H4C7	8369
H4	canonical H4	isoform_1	H4C8	8365
H4	canonical H4	isoform_1	H4C9	8294
H4	canonical H4	isoform_1	H4C11	8363
H4	canonical H4	isoform_1	H4C12	8362
H4	canonical H4	isoform_1	H4C13	8368
H4	canonical H4	isoform_1	H4C14	8370
H4	canonical H4	isoform_1	H4C15	554313
H4	canonical H4	isoform_1	H4-16	121504

Epigenetics & Chromatin

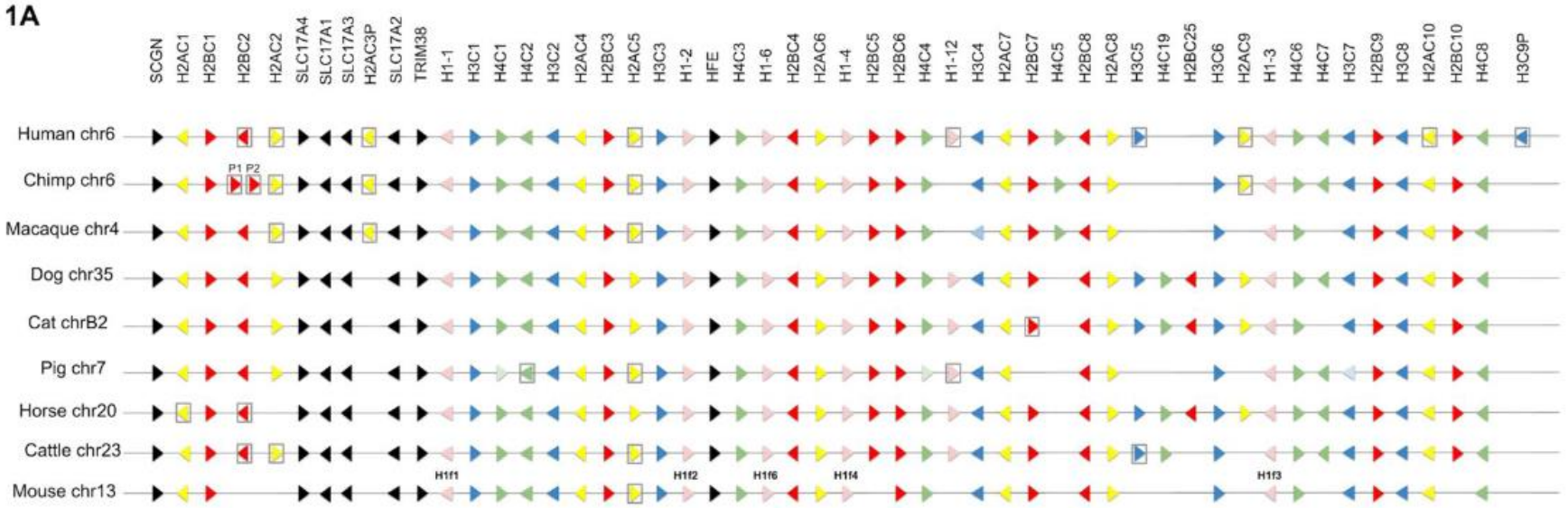
A standardized nomenclature for mammalian histone genes

Ruth L. Seal[1,2*], Paul Denny[1], Elspeth A. Bruford[1,2], Anna K. Gribkova[3], David Landsman[4], William F. Marzluff[5], Monica McAndrews[6], Anna R. Panchenko[7], Alexey K. Shaytan[3] and Paul B. Talbert[8]



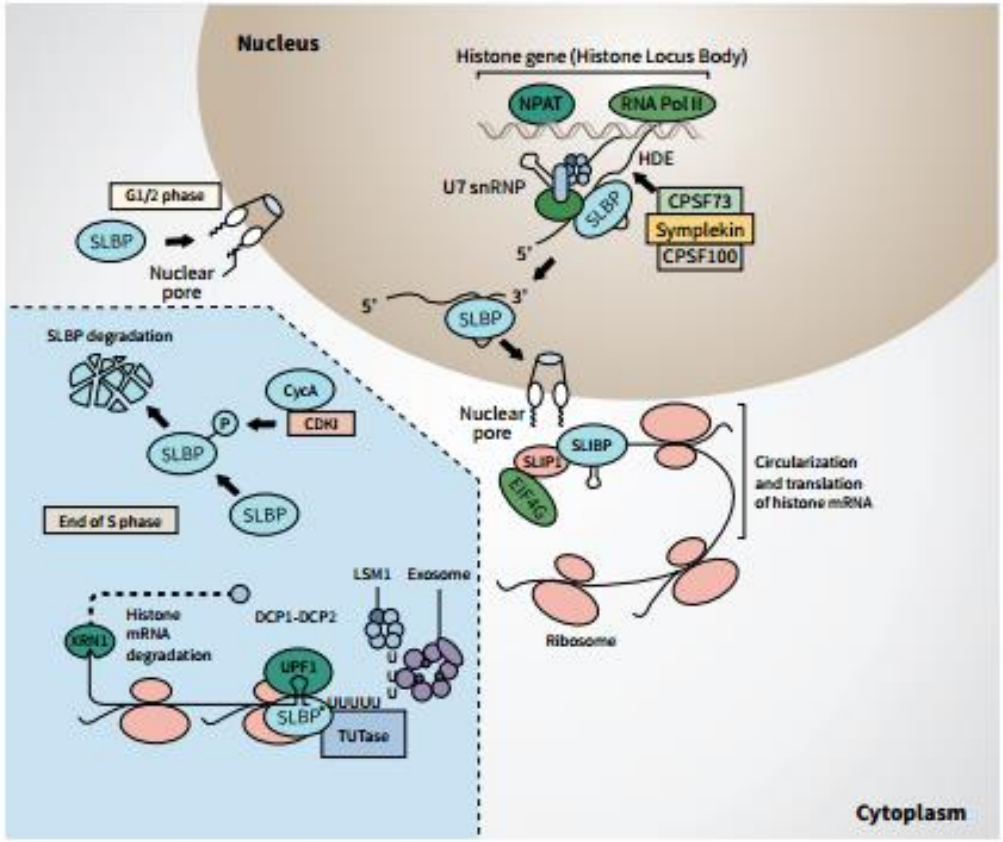
Genes **2018**, *9*, 623; doi:10.3390/genes9120623

Канонические гистоны (replication dependent)



Нарабатываются в S-фазу, не имеет polyA хвоста, регулитруются на пост-транскрипционном уровне.

Histone locus body



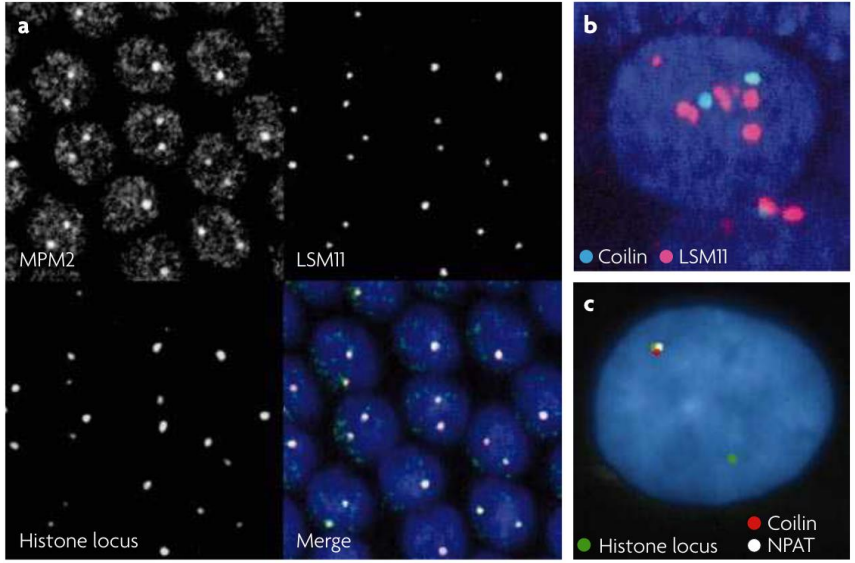


Figure 3 | **The Cajal body and the histone locus body (HLB). a** | HLB in *Drosophila*

Marzluff, W. F.; Wagner, E. J.; Duronio, R. J. Metabolism and Regulation of Canonical Histone MRNAs: Life without a Poly(A) Tail. *Nat Rev Genet* **2008**, *9* (11), 843–854. https://doi.org/10.1038/nrg2438.

Гистоновые варианты (replication independent)

- Находятся вне генных кластеров, Экспрессируются в течение всего клеточного цикла, Замещают канонические варианты.

Histone type: H3

canonical H3 28 / 3746
Alternate names: ca H3
Taxonomic span: Eukaryotes

cenH3 14 / 429
Alternate names: CENP-A, cid, CNA1, CNP1, Cse4, HCP-3, HTR12
Taxonomic span: Eukaryotes

H3.3 15 / 1180
Alternate names: hv2, soH3-1, soH3-2
Taxonomic span: Eukaryotes

H3.5 2 / 2419
Alternate names: *None*
Taxonomic span: Hominids

H3.Y 8 / 136
Alternate names: H3.X
Taxonomic span: Primates

TS H3.4 2 / 4014
Alternate names: H3.1t
Taxonomic span: Mammals

Histone type: H2A

canonical H2A 37 / 8482
Alternate names: ca H2A
Taxonomic span: Eukaryotes

H2A.1 2 / 1328
Alternate names: TH2A, TS H2A.1
Taxonomic span: Mammals

H2A.B 15 / 285
Alternate names: H2A.Bbd, H2A.Lap1(mouse)
Taxonomic span: Mammals

H2A.L 17 / 257
Alternate names: H2A.Lap2, H2A.Lap3, H2AL, H2AL1, H2AL2
Taxonomic span: Certain mammals

H2A.P 11 / 141
Alternate names: CXorf27, H2A.Lap4, HIP17, Huntingtin-interacting protein M, HYPM
Taxonomic span: Placentalia

H2A.W 9 / 2092
Alternate names: H2A with SPKK motifs
Taxonomic span: Plants

H2A.X 23 / 2487
Alternate names: member X
Taxonomic span: Eukaryotes except nematode

H2A.Z 26 / 5492
Alternate names: D2, H2A.V, H2A.Z, H2A.Z-1, H2A.Z-2, H2A.Zc, H2Av, H2AvD, Htz1p, hv1, member Z
Taxonomic span: Eukaryotes

macroH2A 10 / 2436
Alternate names: macroH2A1, macroH2A1.1, macroH2A1.2, macroH2A2, macroH2A2.1, macroH2A2.2, mH2A
Taxonomic span: Vertebrates(?)

Histone type: H4

canonical H4 14 / 15978
Alternate names: ca H4
Taxonomic span: Eukaryotes

Histone type: H2B

canonical H2B 29 / 13275
Alternate names: ca H2B
Taxonomic span: Eukaryotes

H2B.1 3 / 658
Alternate names: H2B.1, hTSH2B, TH2B, TS H2B.1
Taxonomic span: Mammals

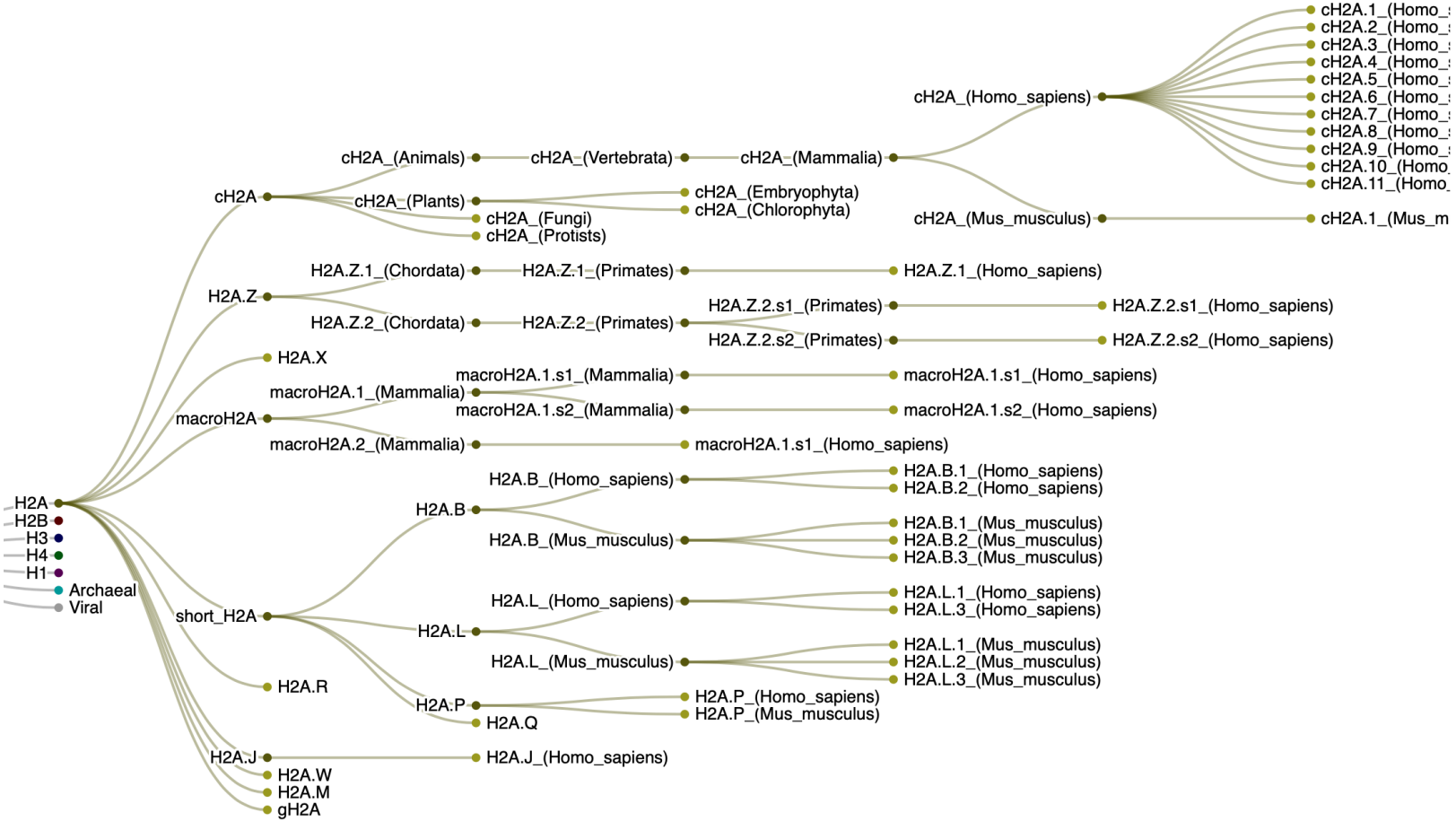
H2B.W 6 / 389
Alternate names: H2BFWT, member W, type W-T
Taxonomic span: Mammals

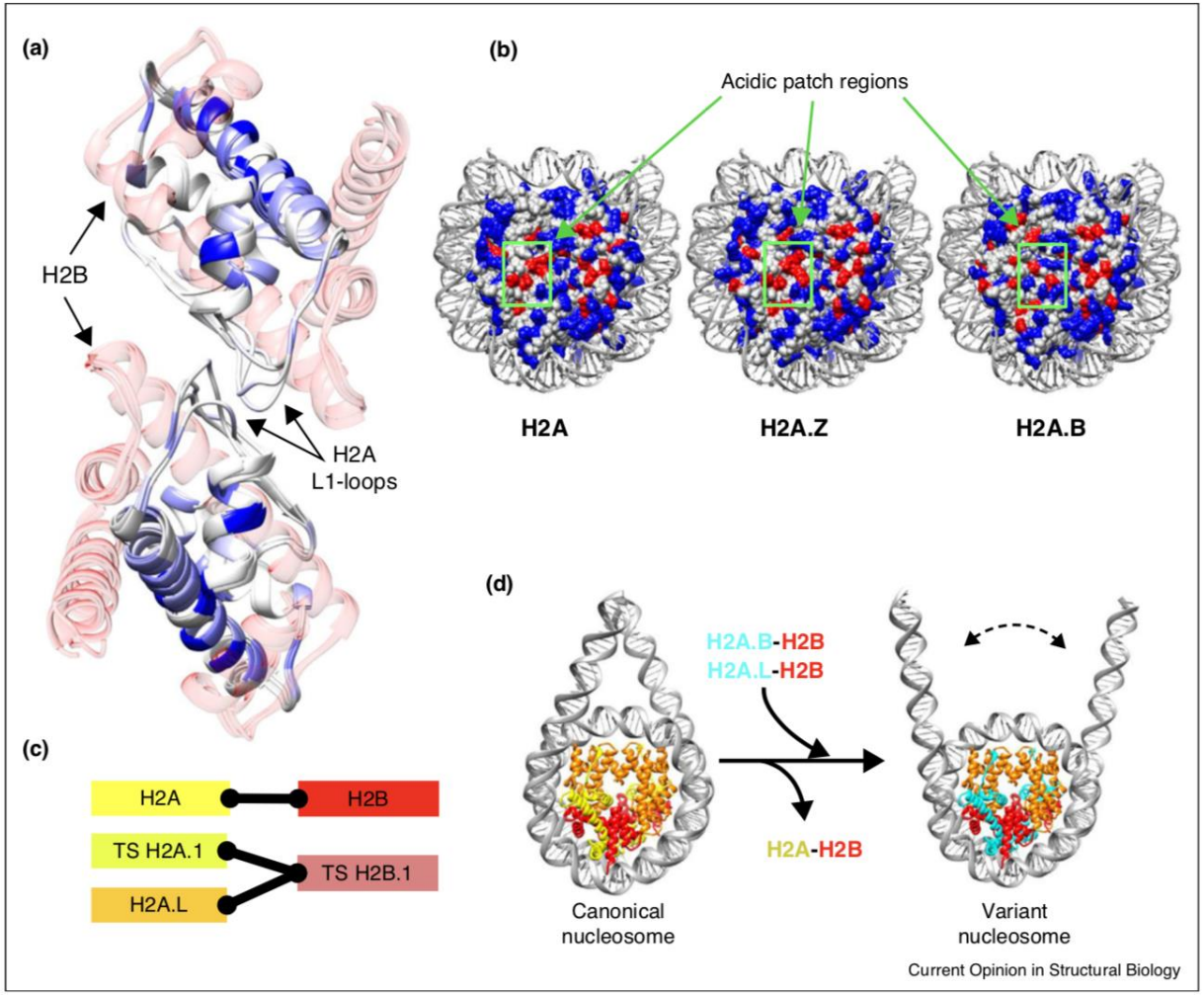
H2B.Z 2 / 371
Alternate names: H2Bv
Taxonomic span: Apicomplexa

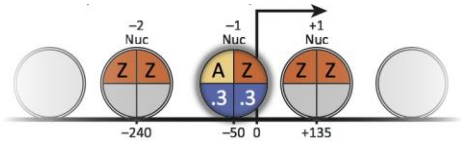
sperm H2B 5 / 80
Alternate names: cleavage H2B, early H2B
Taxonomic span: Echinoidea(?)

subH2B 11 / 122
Alternate names: H2BL1, subH2Bv
Taxonomic span: Primates, rodents, marsupials, and bovids

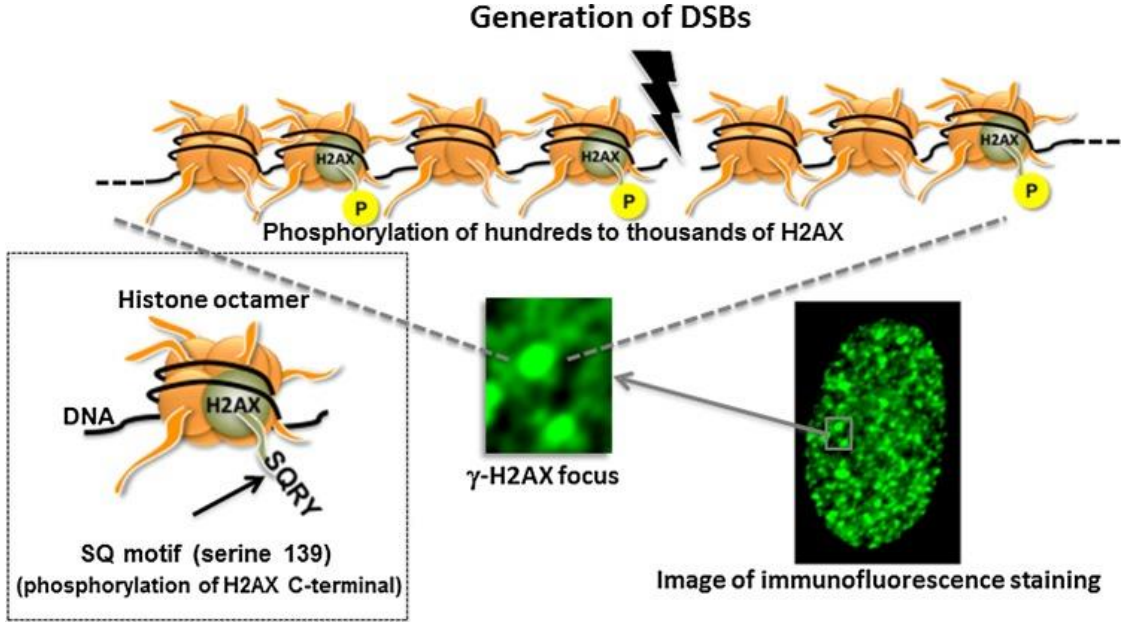
Гистоновые варианты H2A

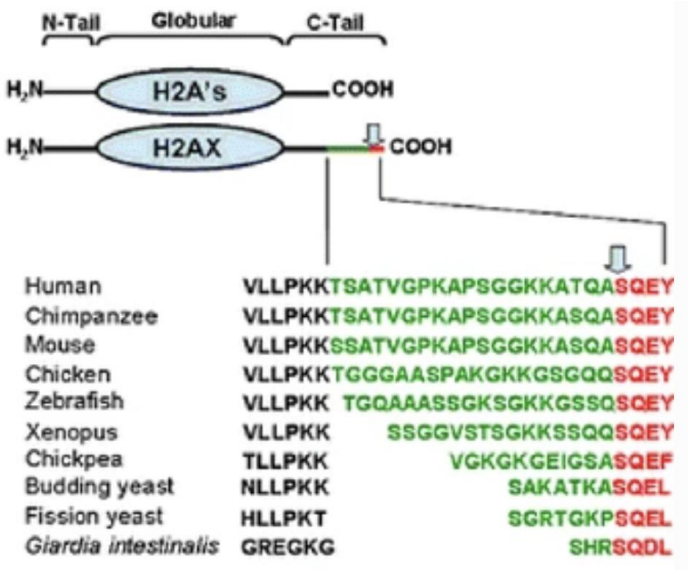



(a)
H2B
H2A
L1-loops
(b)
Acidic patch regions
H2A
H2A.Z
H2A.B
(c)
H2A
H2B
TS H2A.1
TS H2B.1
H2A.L
(d)
H2A.B-H2B
H2A.L-H2B
H2A-H2B
Canonical
nucleosome
Variant
nucleosome
Current Opinion in Structural Biology


−2
Nuc
−1
Nuc
+1
Nuc
Z
Z
A
Z
.3
.3
Z
Z
−240
−50
0
+135

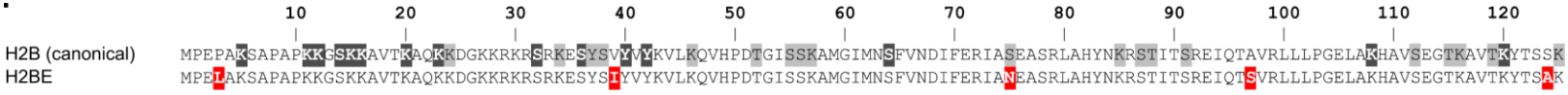
H2A.X – маркер повреждений ДНК

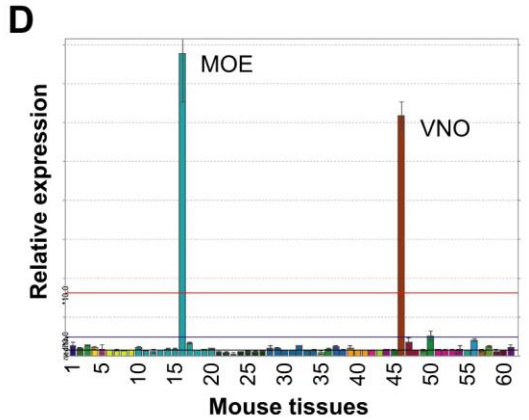




Разнообразие и функции вариантов у млекопитающих

- Варианты гистонов активно эволюционируют
- Есть варианты встречающиеся только у приматов (H3.Y), у гоминид (H3.5)
- Обладают специфической экспрессией (пример H2B.E у мышей)





1	brown fat	17	olfactory bulb	33	umbilical cord	49	pancreas
2	adipose tissue	18	spinal cord - lower	34	uterus	50	pituitary
3	adrenal gland	19	spinal cord - upper	35	oocyte	51	digits
4	bone	20	substantia nigra	36	heart	52	epidermis
5	bone marrow	21	blastocysts	37	large intestine	53	snout epidermis
6	amygdala	22	embryo day 10.5	38	small intestine	54	spleen
7	frontal cortex	23	embryo day 6.5	39	B220+ B-cells	55	stomach
8	preoptic	24	embryo day 7.5	40	CD4+ T-cells	56	thymus
9	trigeminal	25	embryo day 8.5	41	CD8+ T-cells	57	thyroid
10	cerebellum	26	embryo day 9.5	42	liver	58	trachea
11	cerebral cortex	27	fertilized egg	43	lung	59	bladder
12	dorsal root ganglia	28	mammary gland	44	lymphocyte	60	kidney
13	dorsal striatum	29	ovary	45	skeletal muscle	61	retina
14	hippocampus	30	placenta	46	VNO		
15	hypothalamus	31	prostate	47	salivary gland		
16	MOE	32	testis	48	tongue		

Santoro, S. W.; Dulac, C. The Activity-Dependent Histone Variant H2BE Modulates the Life Span of Olfactory Neurons. *Elife* **2012**, *1*, e00070. https://doi.org/10.7554/eLife.00070.

H2B.E – участвует в регуляции жизни обонятельных нейронов

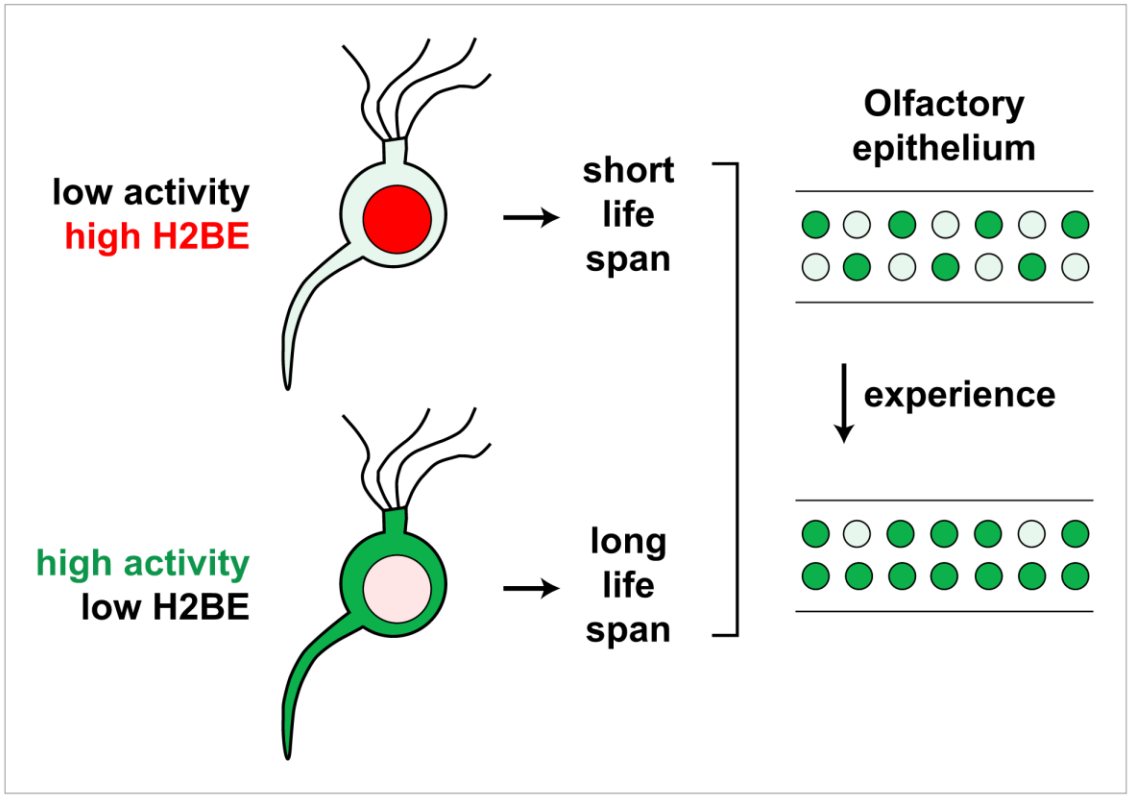
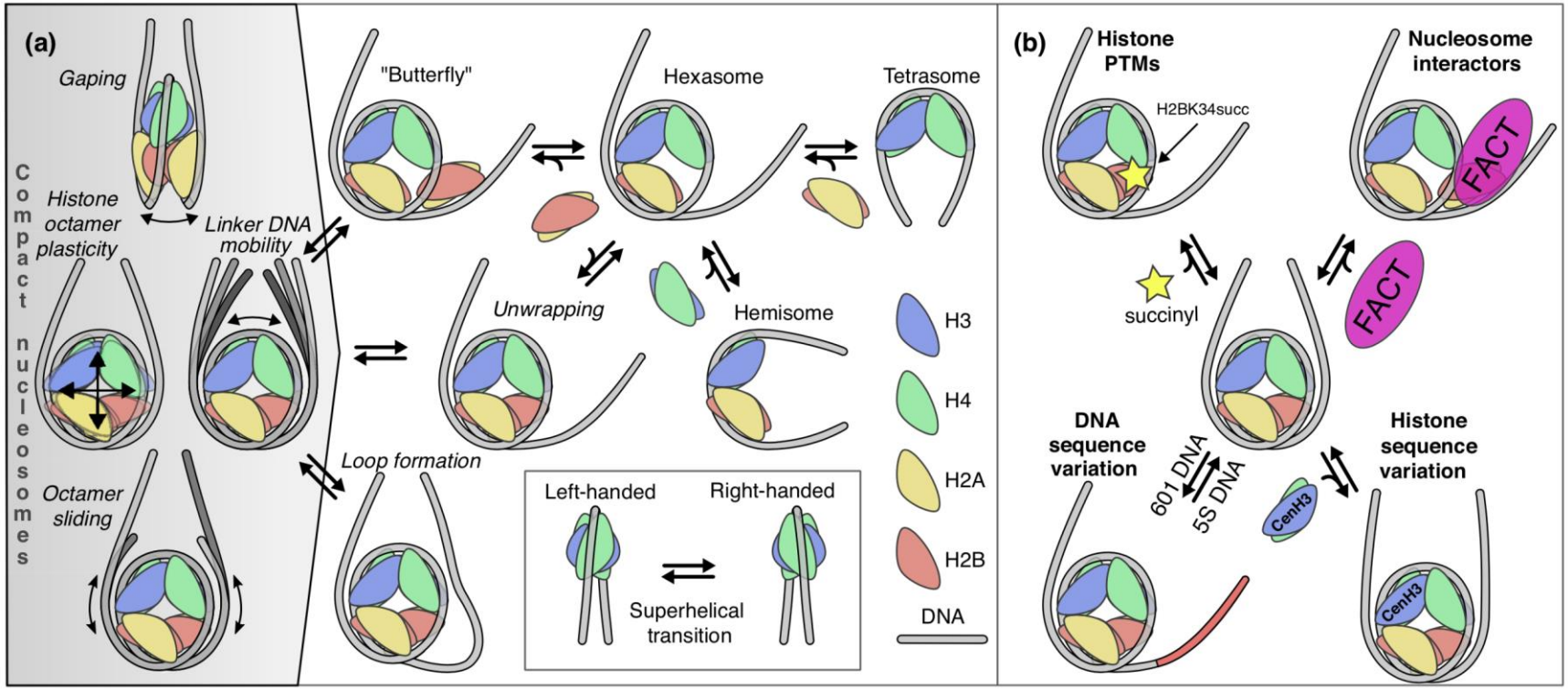


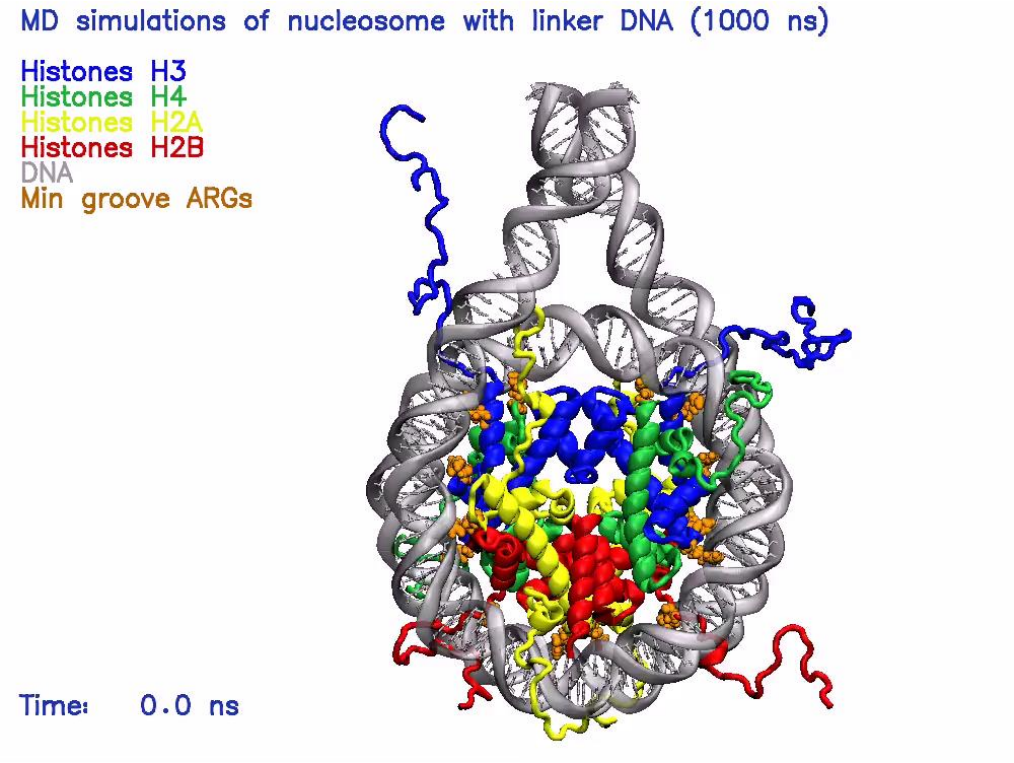
Figure 12. Model for the effects of neuronal activity on H2BE expression level, life span and resulting neuronal representation.

Nucleosome structural variability

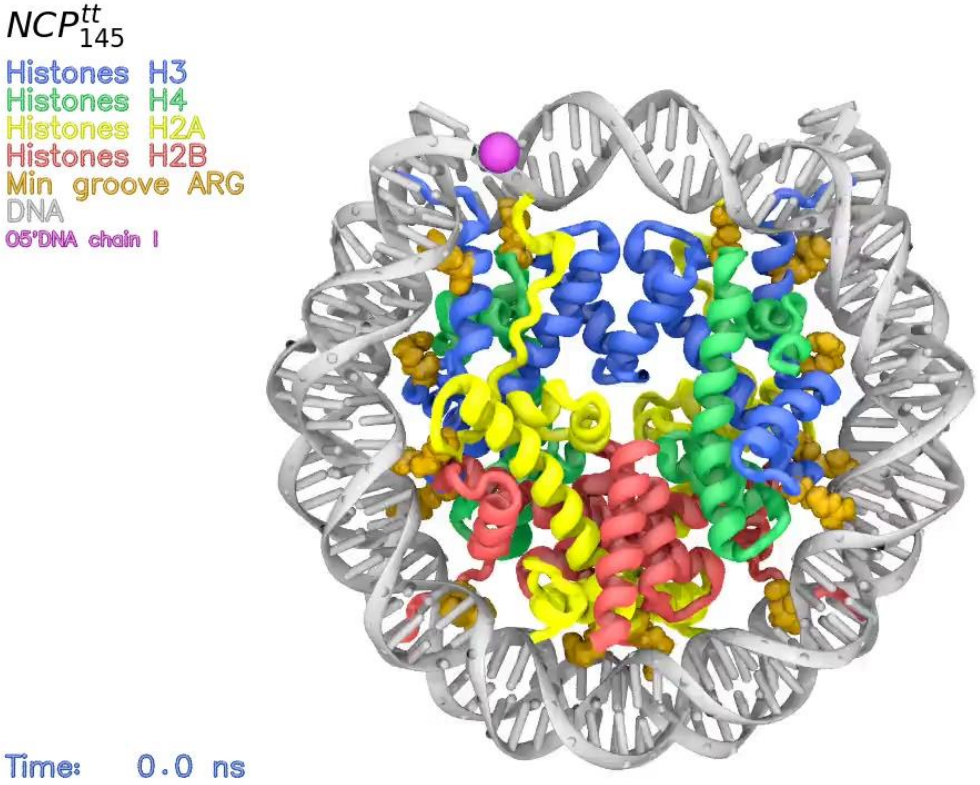


Armeev, G. A.; Gribkova, A. K.; Pospelova, I.; Komarova, G. A.; **Shaytan, A. K.** Linking Chromatin Composition and Structural Dynamics at the Nucleosome Level. *Current Opinion in Structural Biology* **2019**, *56*, 46–55.

Nucleosome dynamics

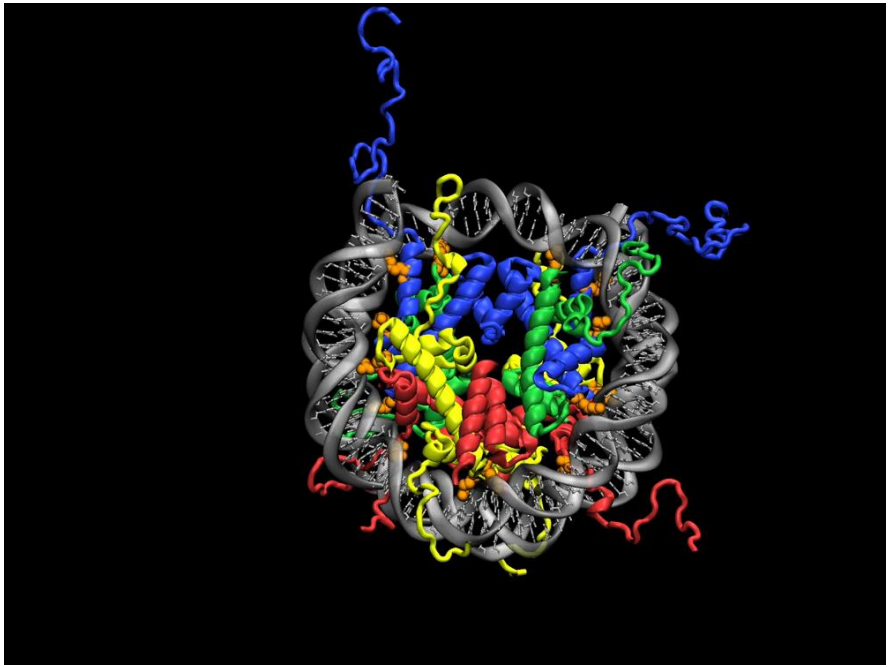


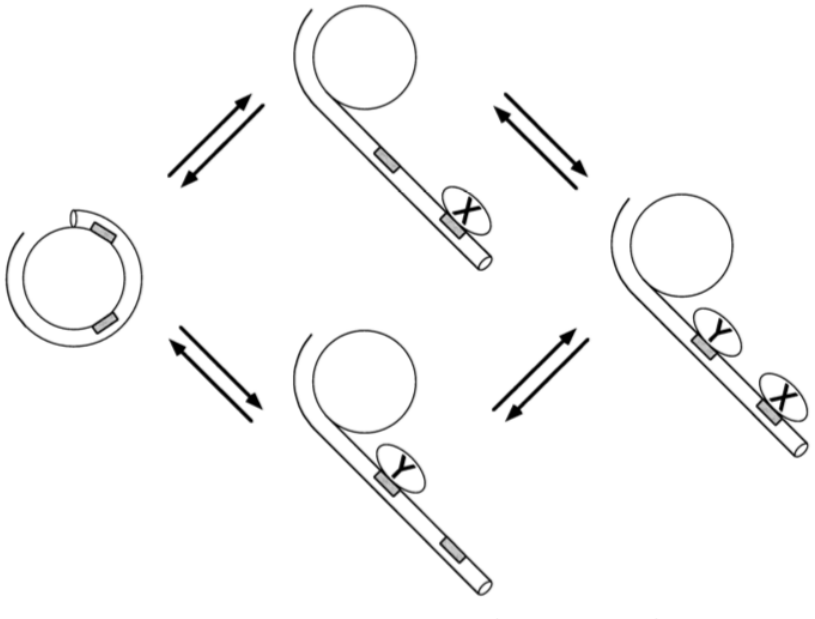
Shaytan, A. K.; Armeev, G. A.; Goncearenco, A.; Zhurkin, V. B.; Landsman, D.; Panchenko, A. R. Coupling between Histone Conformations and DNA Geometry in Nucleosomes on a Microsecond Timescale: Atomistic Insights into Nucleosome Functions. *Journal of Molecular Biology* 2016, *428* (1), 221–237. https://doi.org/10.1016/j.jmb.2015.12.004.



Armeev,G.A., Kniazeva,A.S., Komarova,G.A., Kirpichnikov,M.P. and Shaytan,A.K. (2021) Histone dynamics mediate DNA unwrapping and sliding in nucleosomes. *Nat Commun.*, 12.

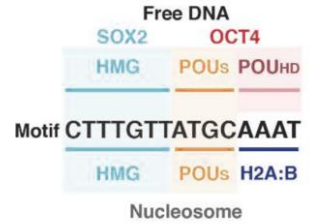
DNA unwrapping and transcription factor binding

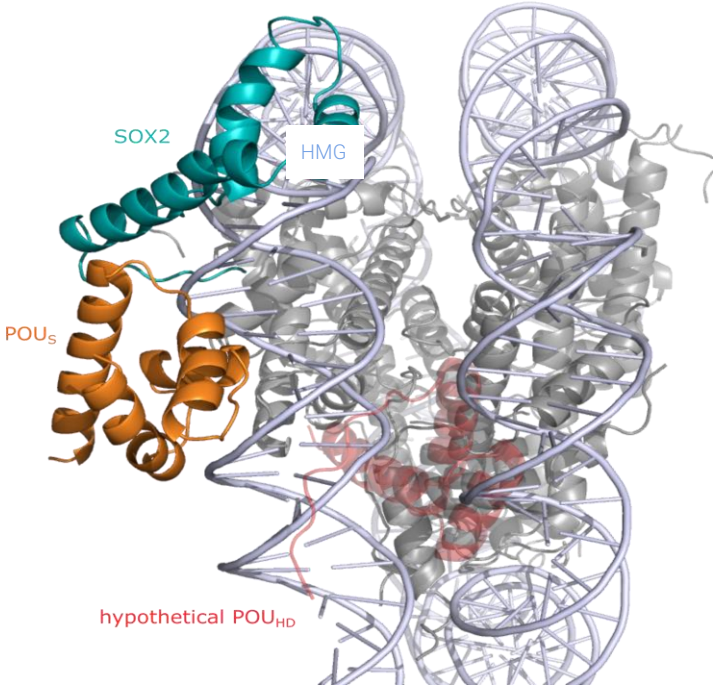


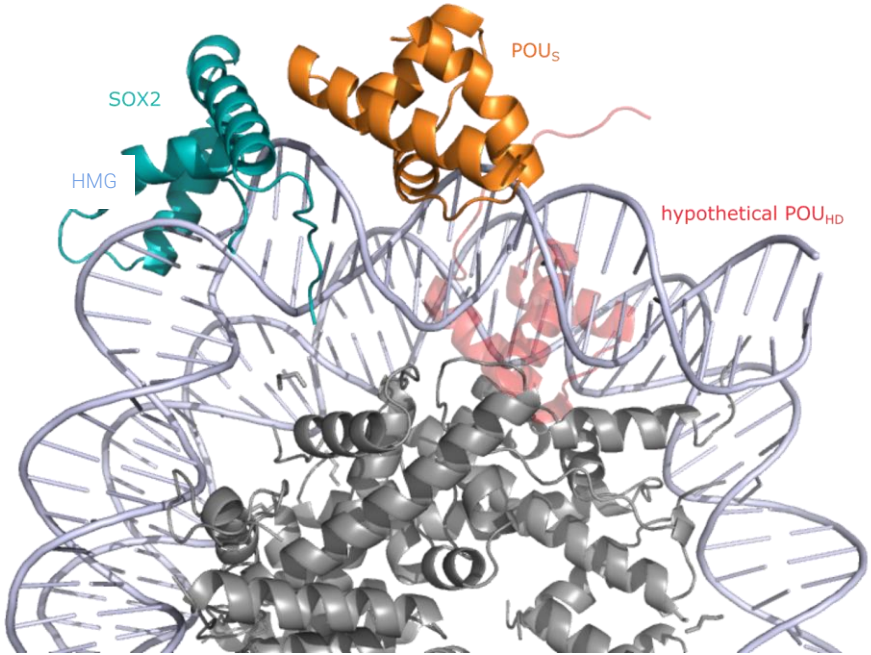


Polach, K. J. and J. Widom (1995). "Mechanism of protein access to specific DNA sequences in chromatin: a dynamic equilibrium model for gene regulation." J Mol Biol **254**(2): 130-149.

Пионерные факторы и нуклеосомы

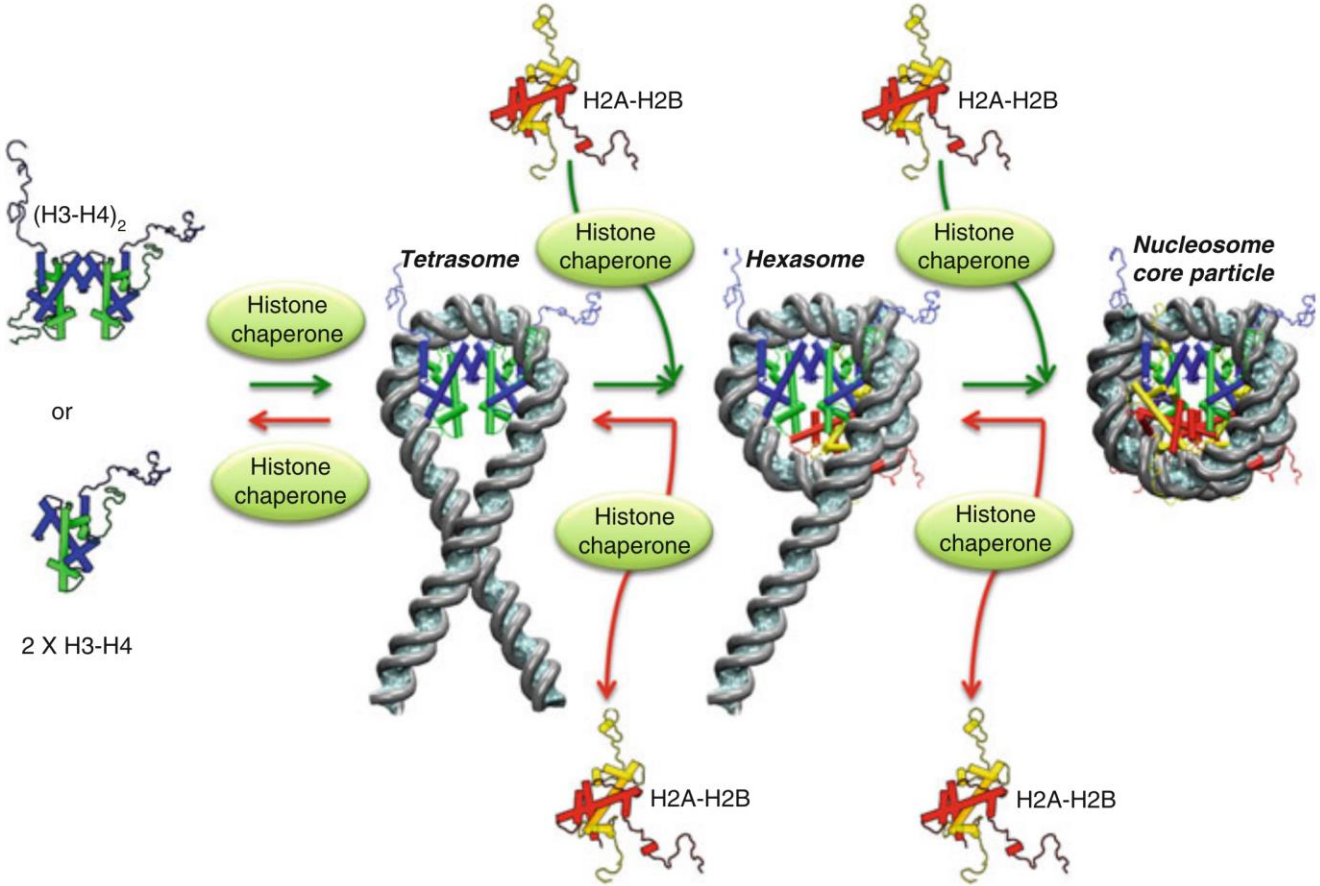




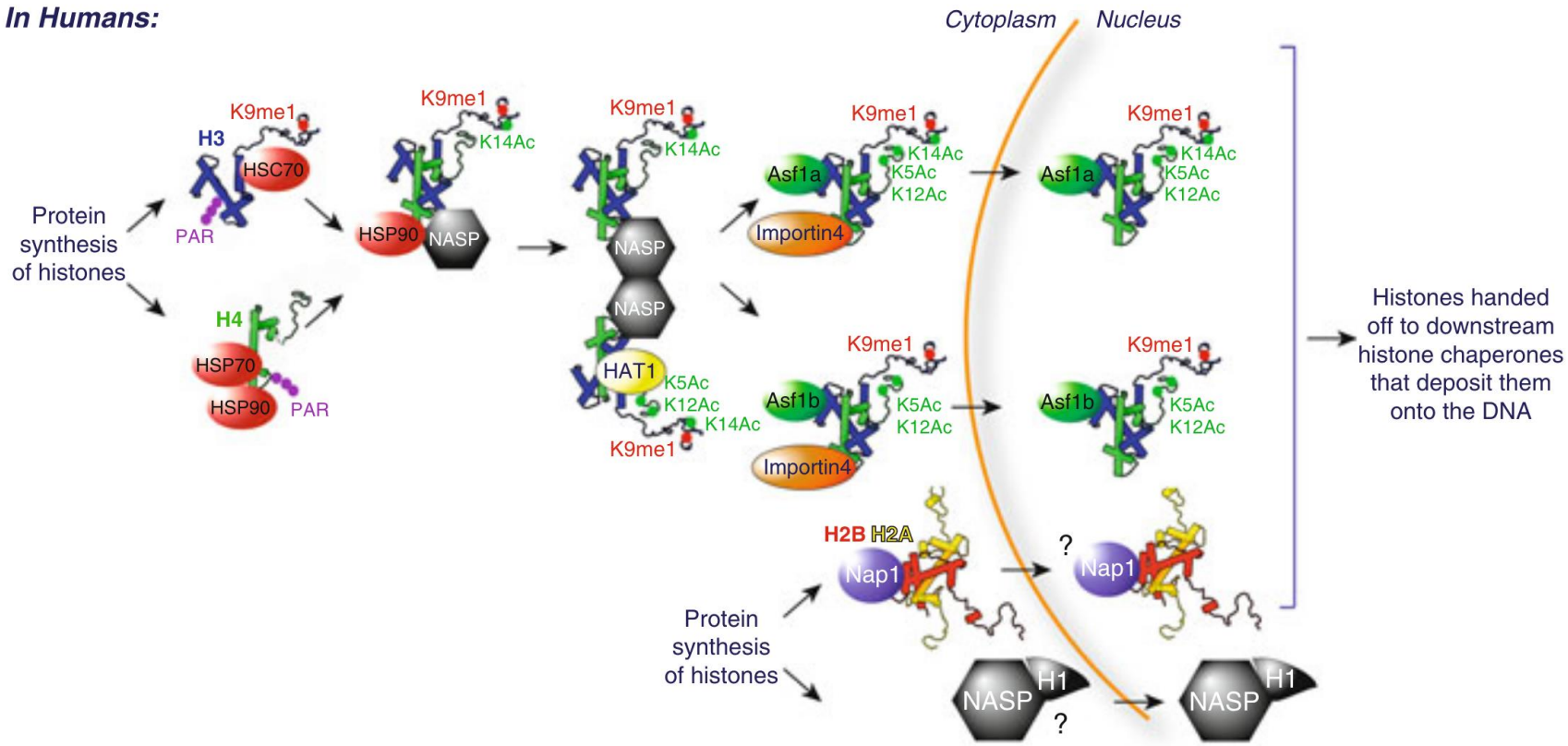


6yov + POU_{HD} из 1gt0,
выровнен по POU_S

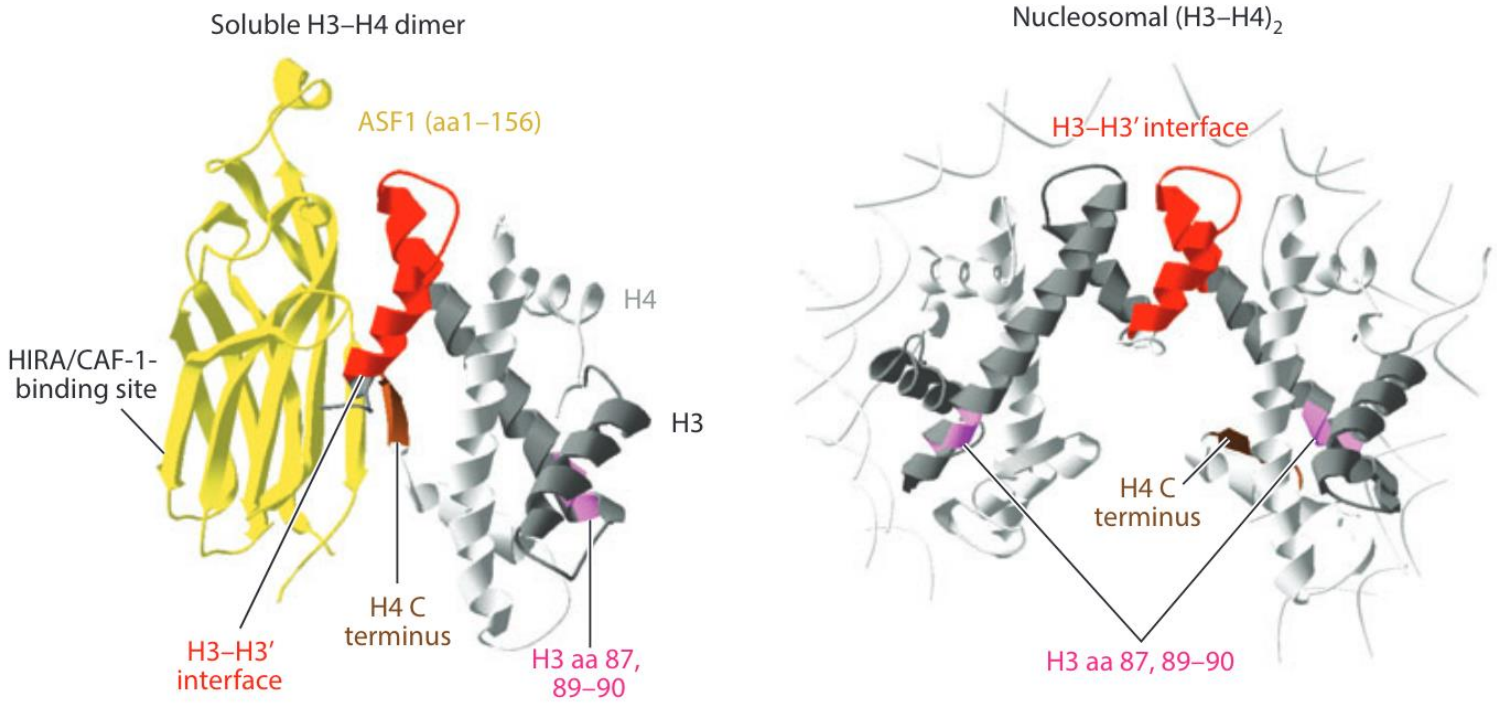
Сборка нуклеосом



Шапероны гистонов



a ASF1 binds a dimer of H3–H4



Gurard-Levin, Z. A., Quivy, J.-P. & Almouzni, G. Histone Chaperones: Assisting Histone Traffic and Nucleosome Dynamics. *Annual Review of Biochemistry* 83, 487–517 (2014).

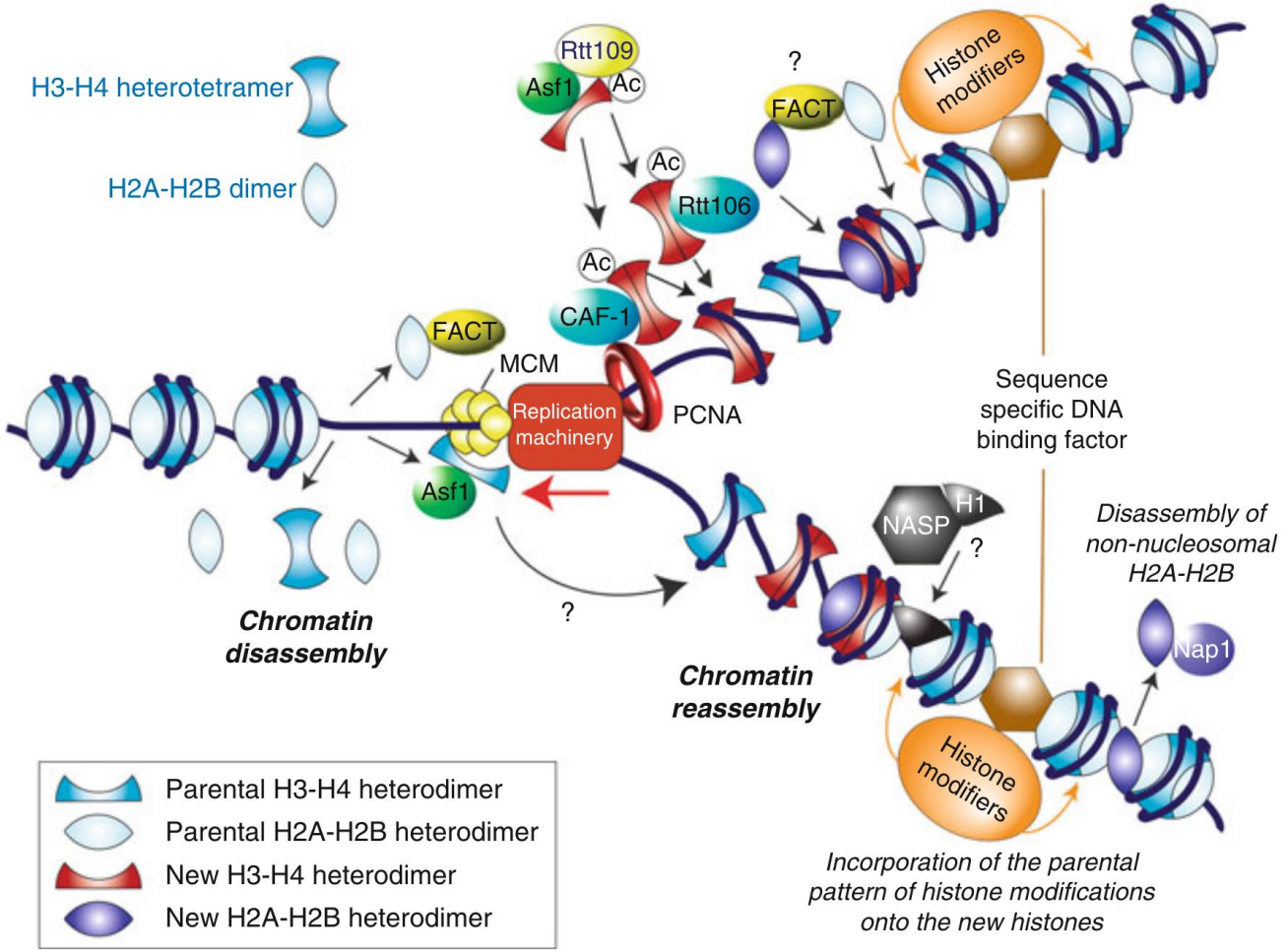


Fig. 2.3 Replication-dependent chromatin disassembly and assembly. Schematic showing chromatin disassembly ahead of the replication fork and stepwise chromatin reassembly behind

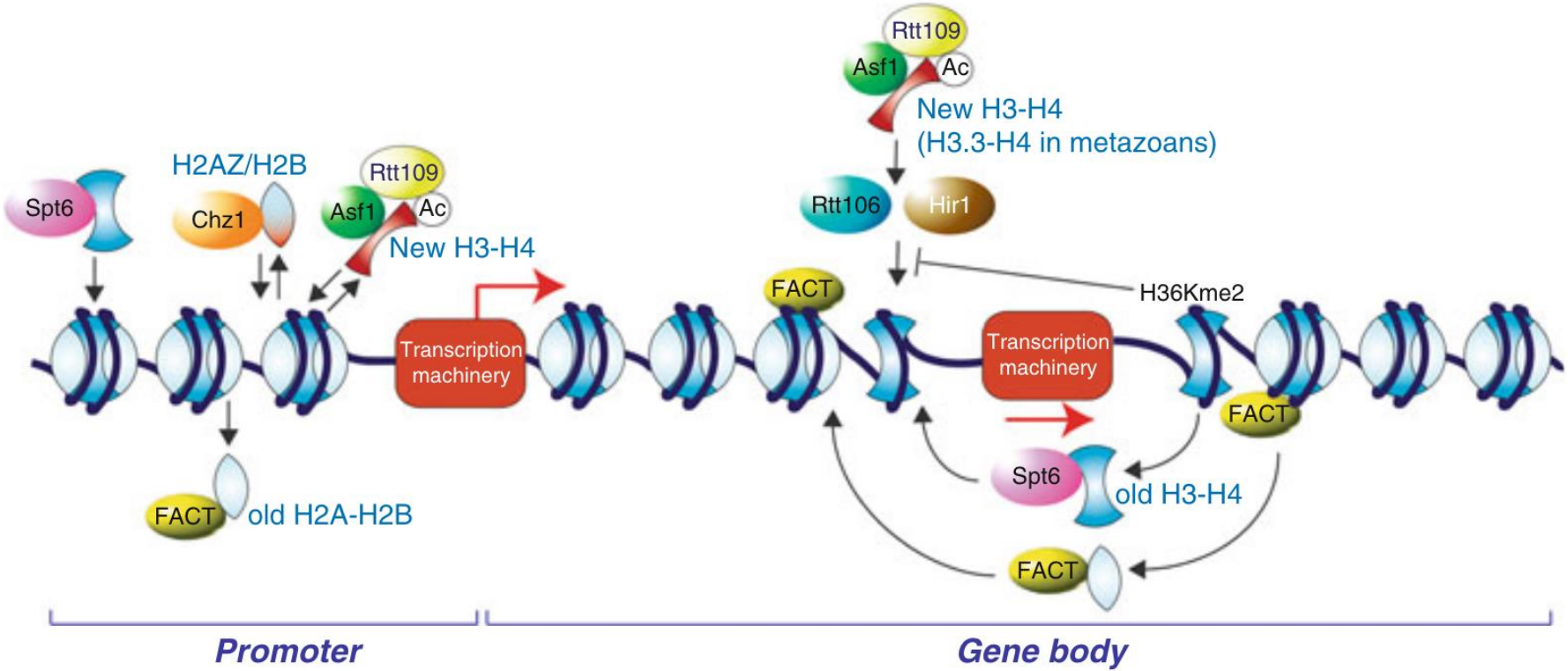
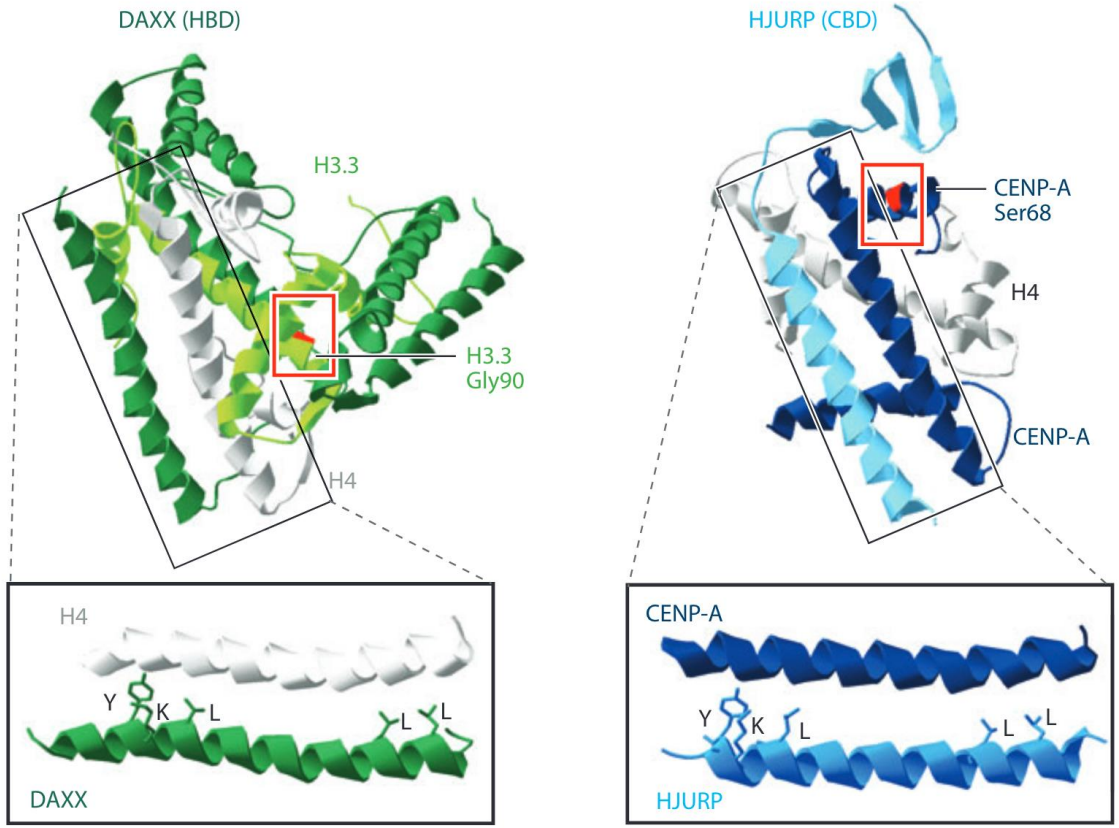


Fig. 2.5 Replication-independent chromatin disassembly and assembly. Some histone chaper-

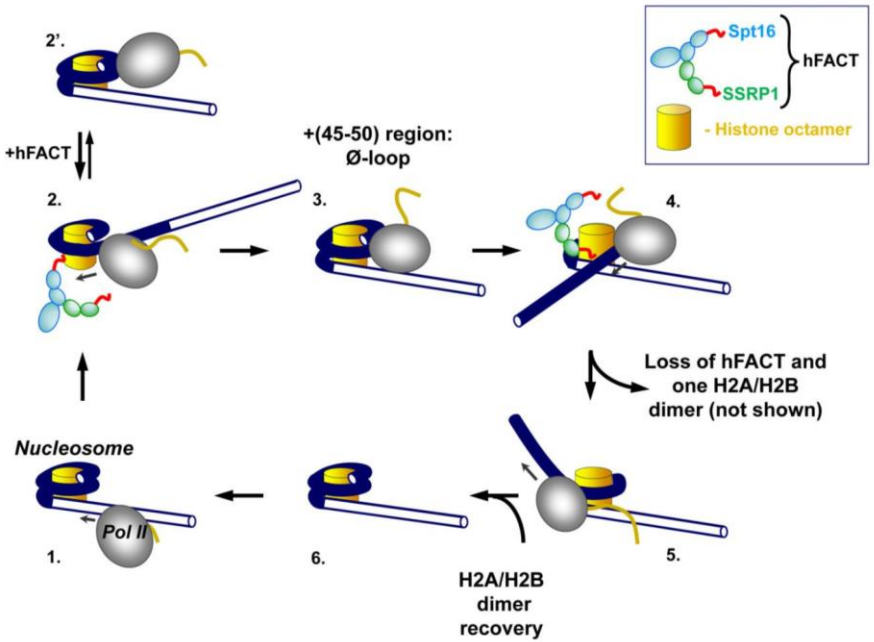
Fundamentals of Chromatin, Workman, J. L., Abmayr, S. M., Eds.; Springer New York: New York, NY, 2014. https://doi.org/10.1007/978-1-4614-8624-4.

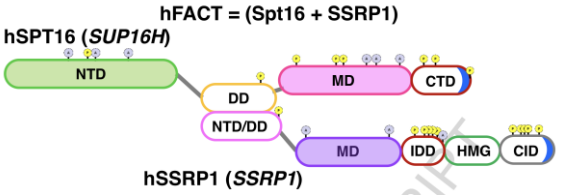
b Similar binding motifs: DAXX with H3.3–H4 and HJURP with CENP-A–H4



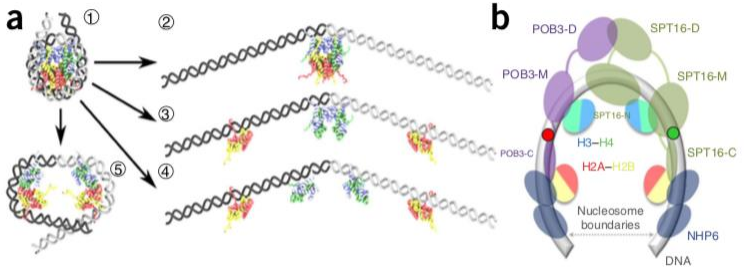
Gurard-Levin, Z. A., Quivy, J.-P. & Almouzni, G. Histone Chaperones: Assisting Histone Traffic and Nucleosome Dynamics. *Annual Review of Biochemistry* 83, 487–517 (2014).

Транскрипция через нуклеосомы





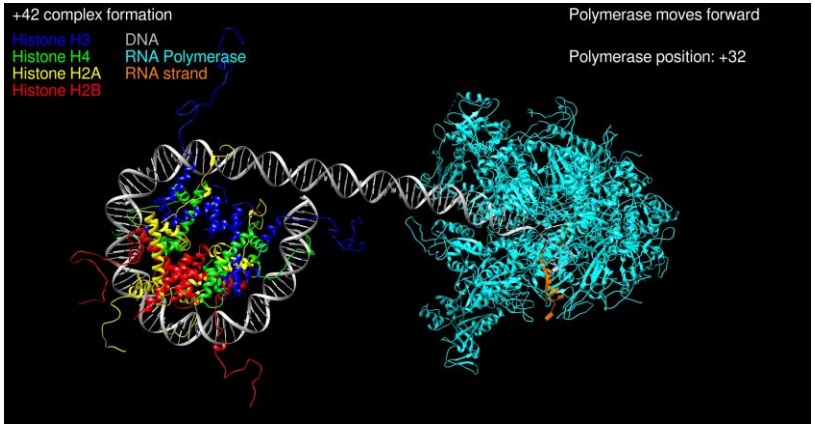
FACT chaperone

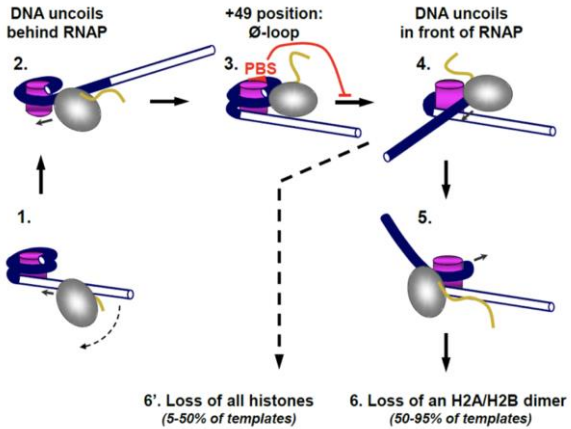


Valieva, M. E.; Armeev, G. A.; Kudryashova, K. S.; Gerasimova, N. S.; Shaytan, A. K.; Kulaeva, O. I.; McCullough, L. L.; Formosa, T.; Georgiev, P. G.; Kirpichnikov, M. P.; et al. Large-Scale ATP-Independent Nucleosome Unfolding by a Histone Chaperone. *Nature Structural & Molecular Biology* **2016**, *23* (12), 1111–1116. https://doi.org/10.1038/nsmb.3321.

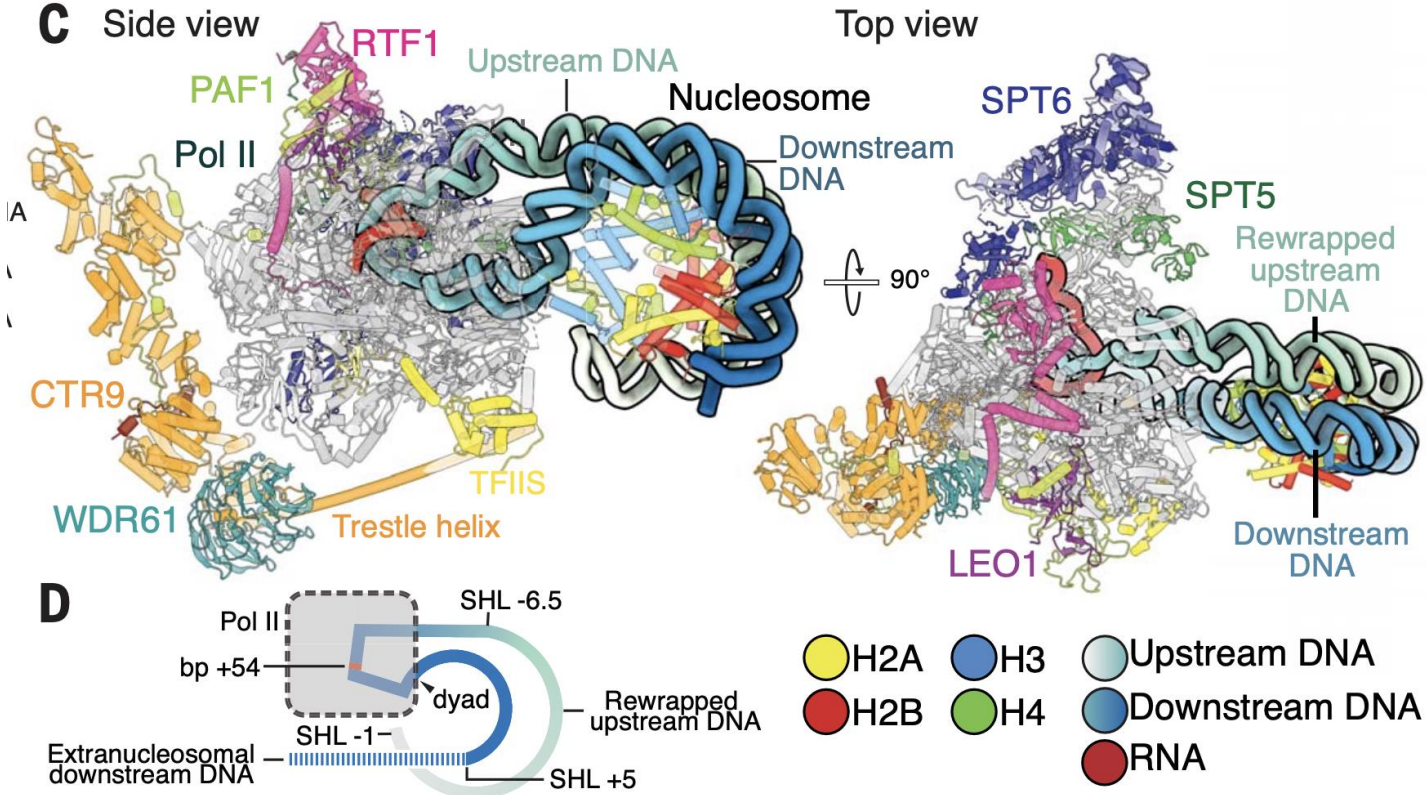
Gurova, K., Chang, H.-W., Valieva, M. E., Sandlesh, P., & Studitsky, V. M. (2018). *Structure and function of the histone chaperone FACT – Resolving FACTual issues. Biochimica et Biophysica Acta (BBA) - Gene Regulatory Mechanisms*.doi:10.1016/j.bbagrm.2018.07.008

Transcription through nucleosomes





Biochim Biophys Acta. 2013 January ; 1829(1): 76–83. doi:10.1016/j.bbagrm.2012.08.015.
Mechanism of Transcription through a Nucleosome by RNA polymerase II
Olga I. Kulaeva[1,2], Fu-Kai Hsieh[1], Han-Wen Chang[1], Donal S. Luse[3], and Vasily M. Studitsky[1,2,4]

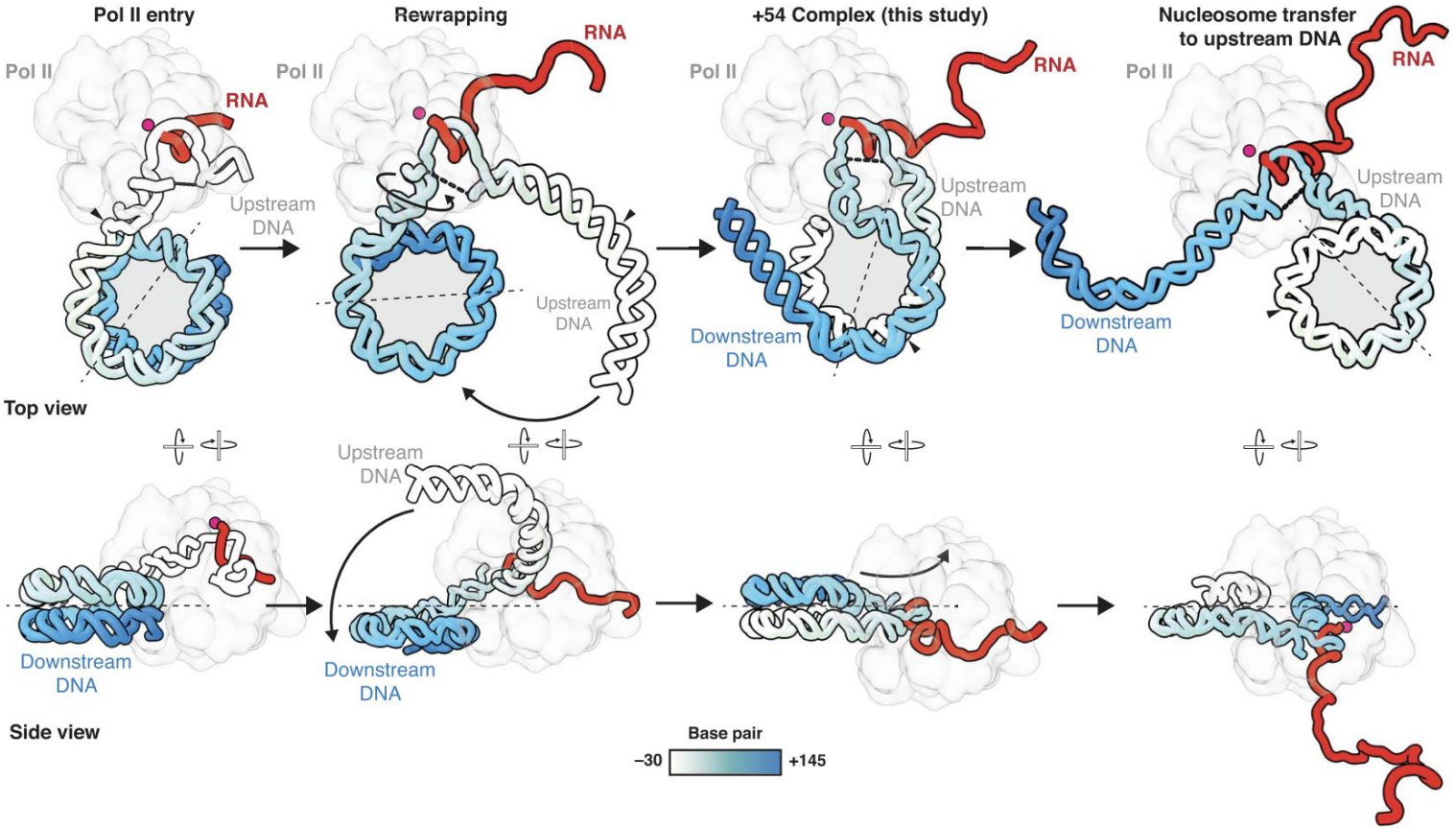


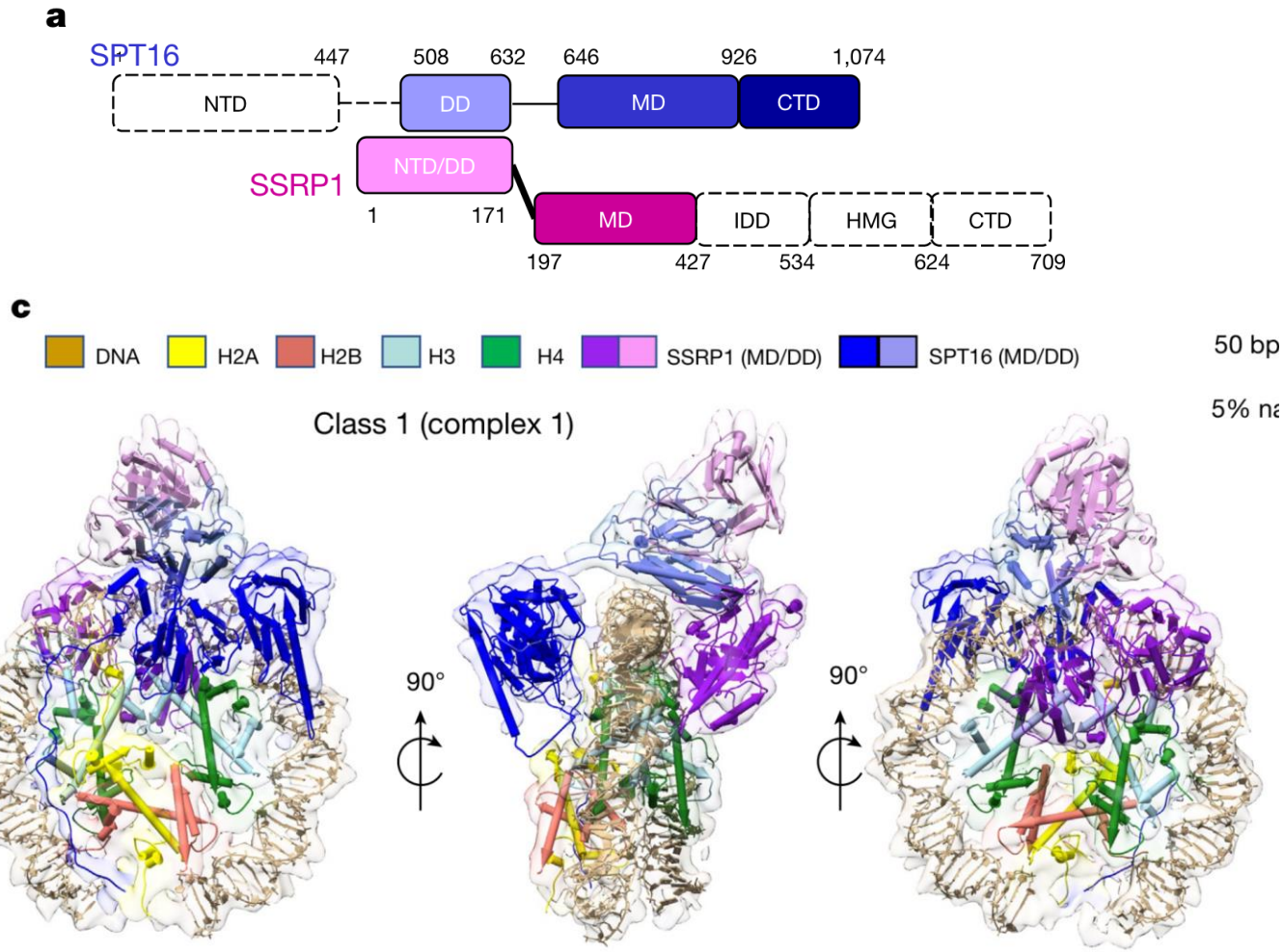
TRANSCRIPTION

Structural basis of nucleosome retention during transcription elongation

Martin Filipovski[1], Jelly H. M. Soffers[1], Seychelle M. Vos[2], Lucas Farnung[1]*

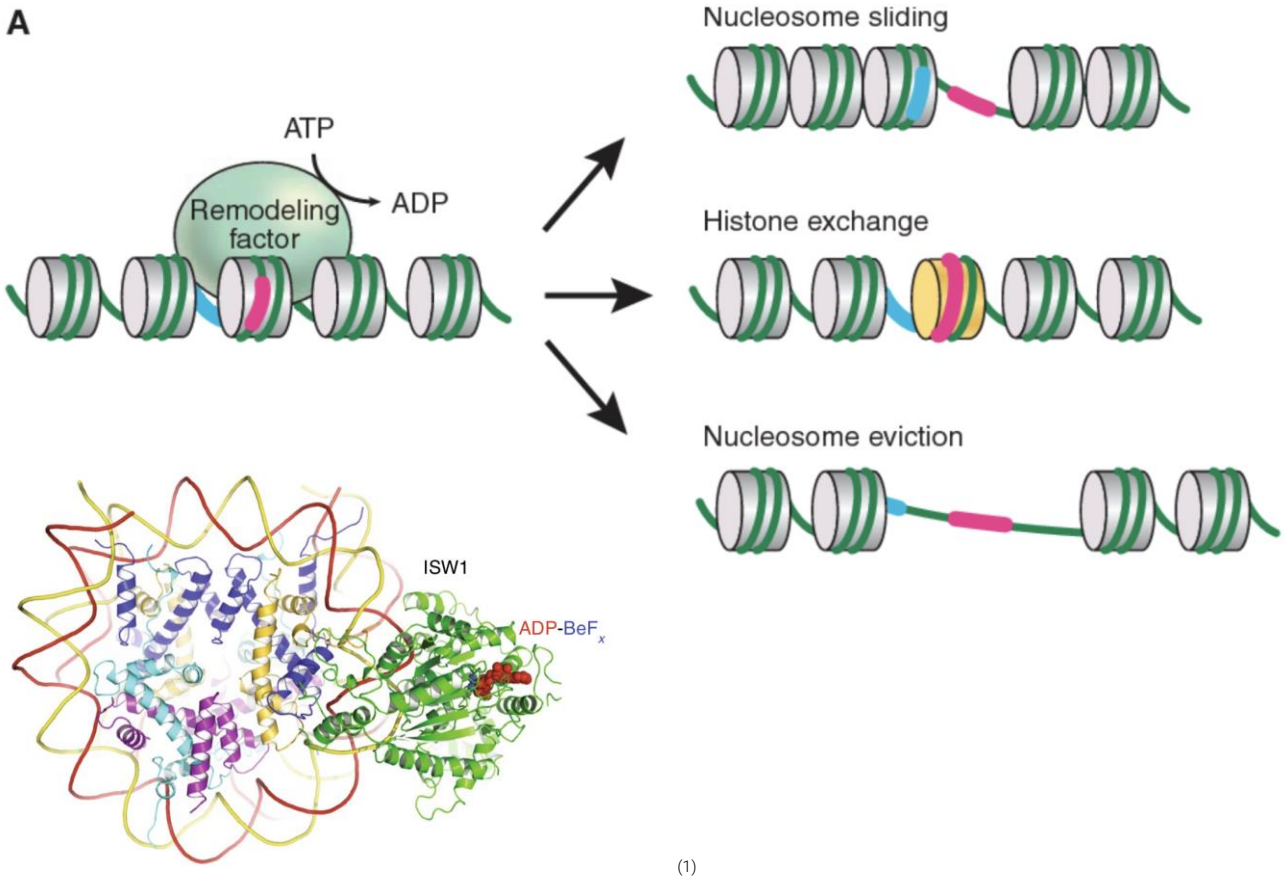
Filipovski *et al.*, *Science* **376**, 1313–1316 (2022)


Pol II entry
Rewrapping
+54 Complex (this study)
Nucleosome transfer to upstream DNA
Pol II
RNA
Upstream DNA
Downstream DNA
Top view
Side view
Base pair
–30
+145



Liu, Y. *et al.* FACT caught in the act of manipulating the nucleosome. *Nature* **577**, 426–431 (2020).

ATP-dependent nucleosome remodeling



(1) Yan, L.; Wu, H.; Li, X.; Gao, N.; Chen, Z. Structures of the ISWI–Nucleosome Complex Reveal a Conserved Mechanism of Chromatin Remodeling. *Nature Structural & Molecular Biology* **2019**, *26* (4), 258. https://doi.org/10.1038/s41594-019-0199-9.

Nucleosome remodeling and epigenetics. Peter B. Becker, Jerry L. Workman Published in Cold Spring Harbor perspectives in biology 2013 DOI:10.1101/cshperspect.a017905

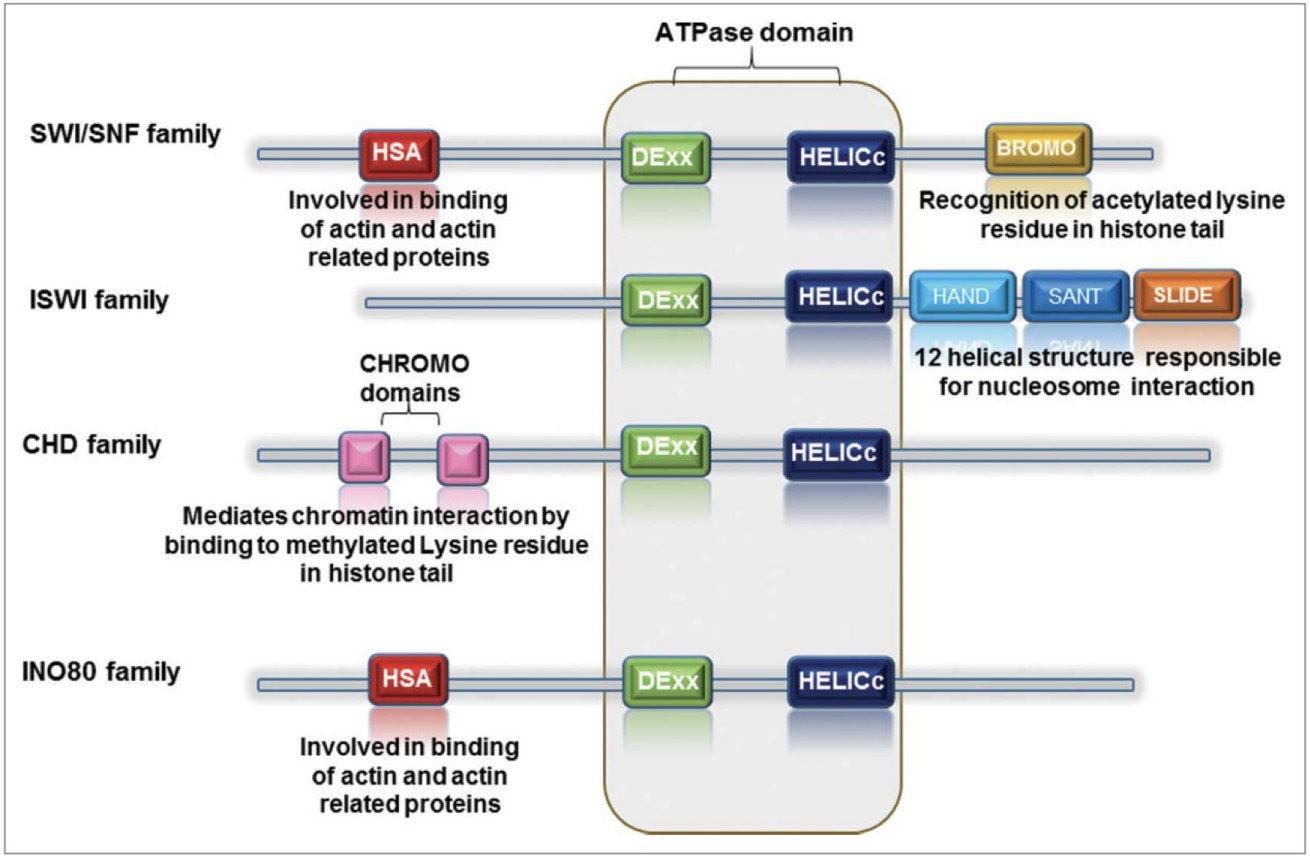
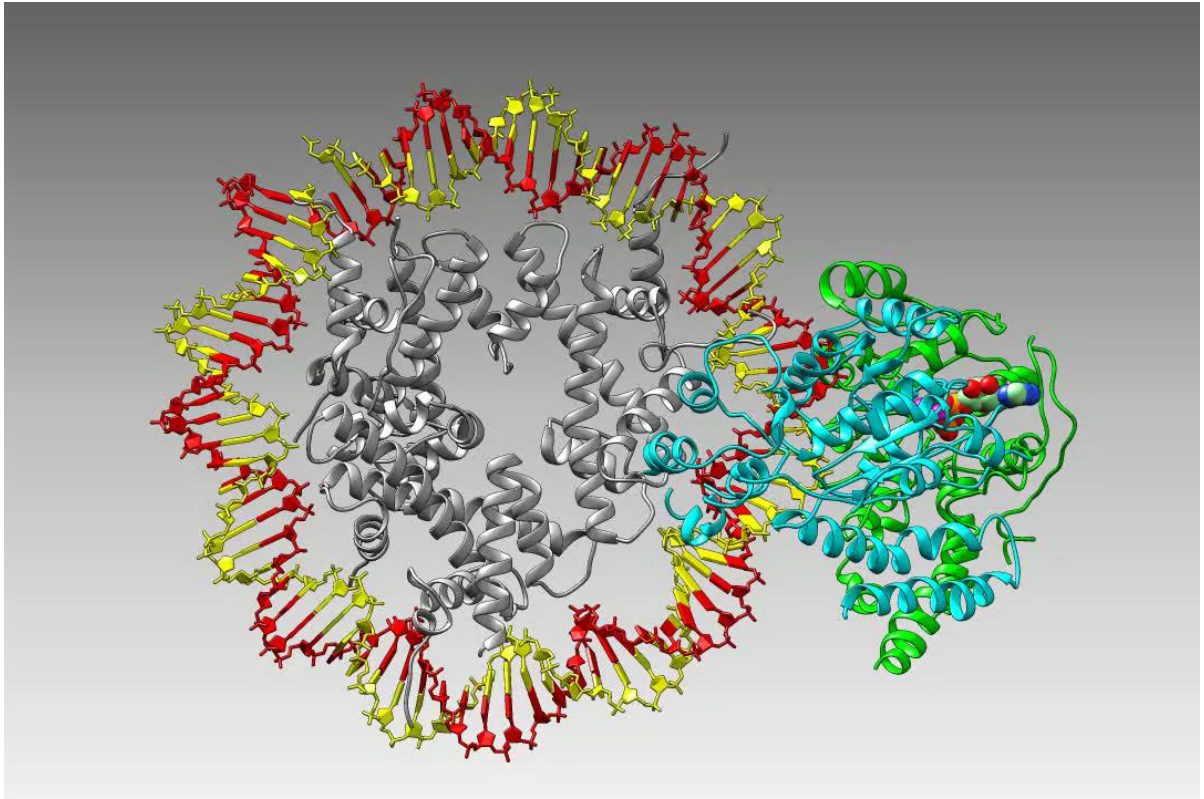


Figure 1. Diagrammatic representation of chromatin remodeler family highlighting the conserved domain with each family member. The DEX and HELICc domains are conserved throughout the family. However, HAND, SANT and SLIDE domains are specific to ISWI family, whereas BROMO domain distinguishes the SWI/SNF family. The presence of CHROMO domains is characteristic of CHD family.

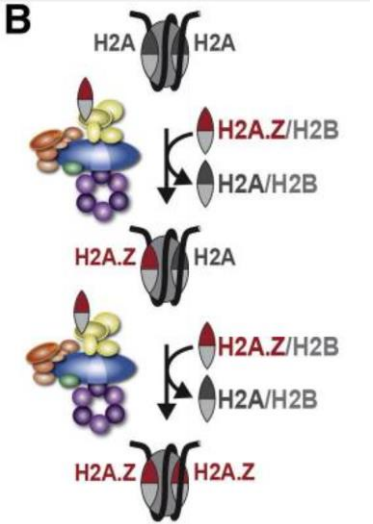
ATP-dependent nucleosome remodeling

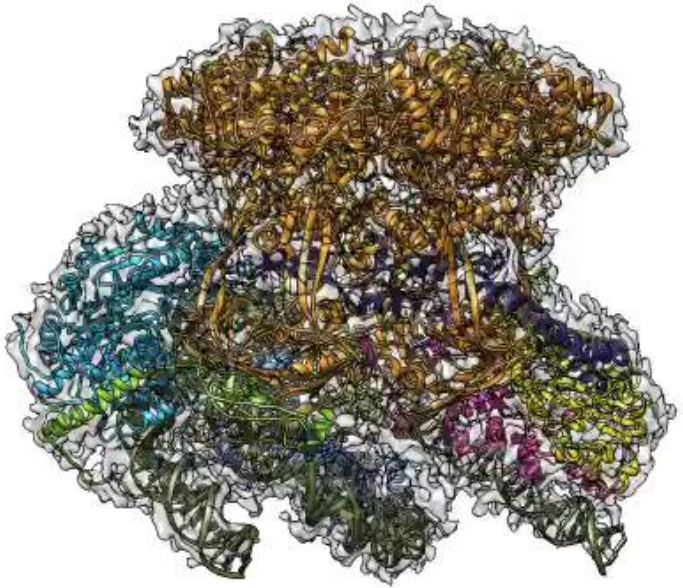


(1)
Li, M.; Xia, X.; Tian, Y.; Jia, Q.; Liu, X.; Lu, Y.; Li, M.; Li, X.; Chen, Z. Mechanism of DNA Translocation Underlying Chromatin Remodelling by Snf2. *Nature* **2019**, *567* (7748), 409–413. https://doi.org/10.1038/s41586-019-1029-2.

ATP-dependent nucleosome remodeling

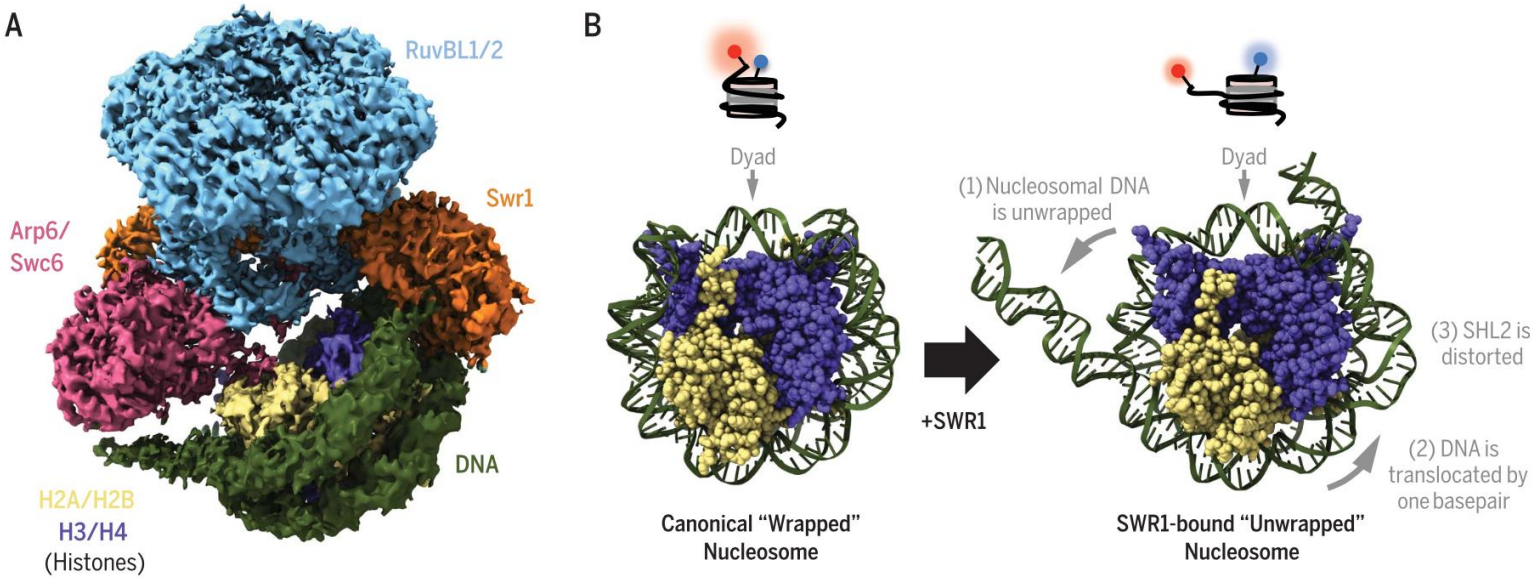
SWR1 remodeler replaces H2A with H2A.Z



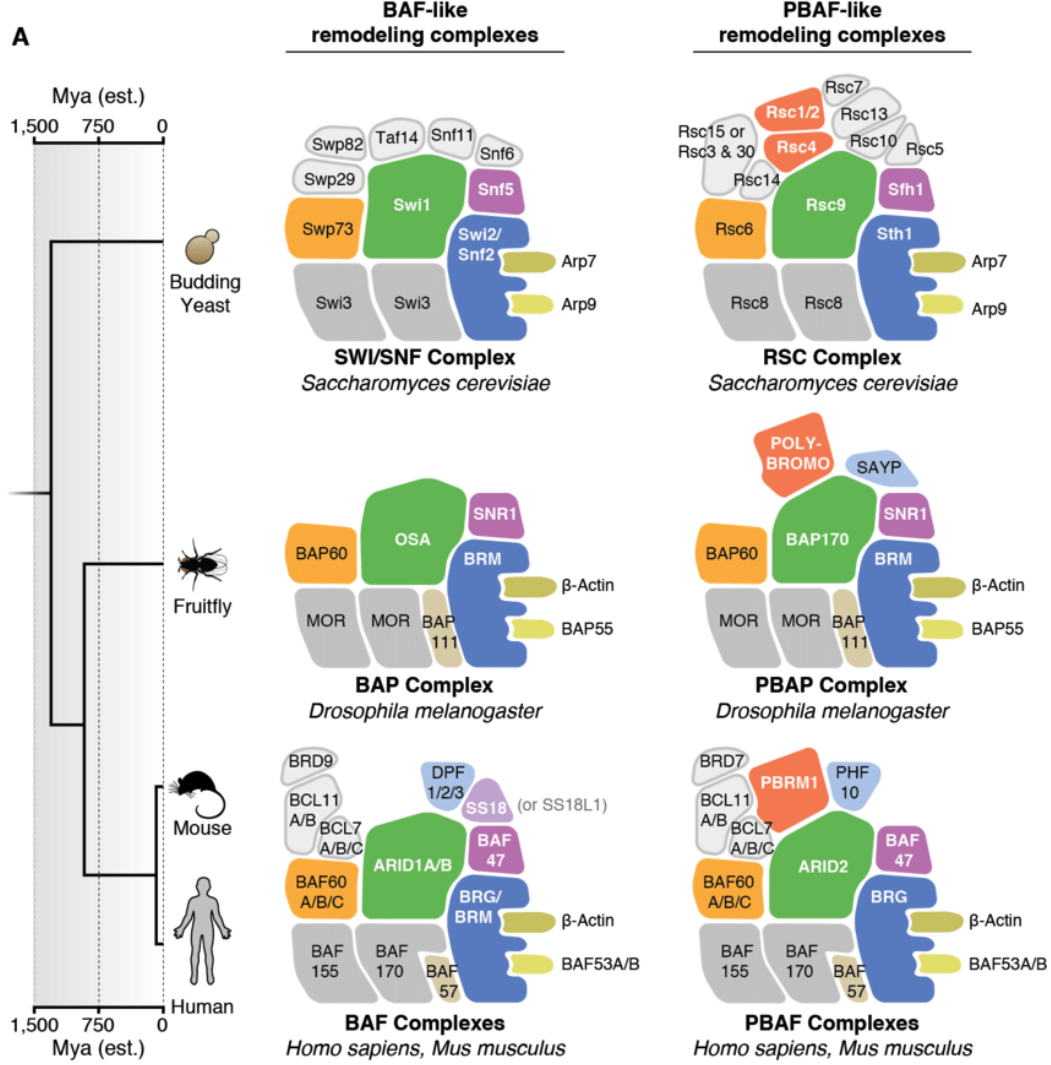


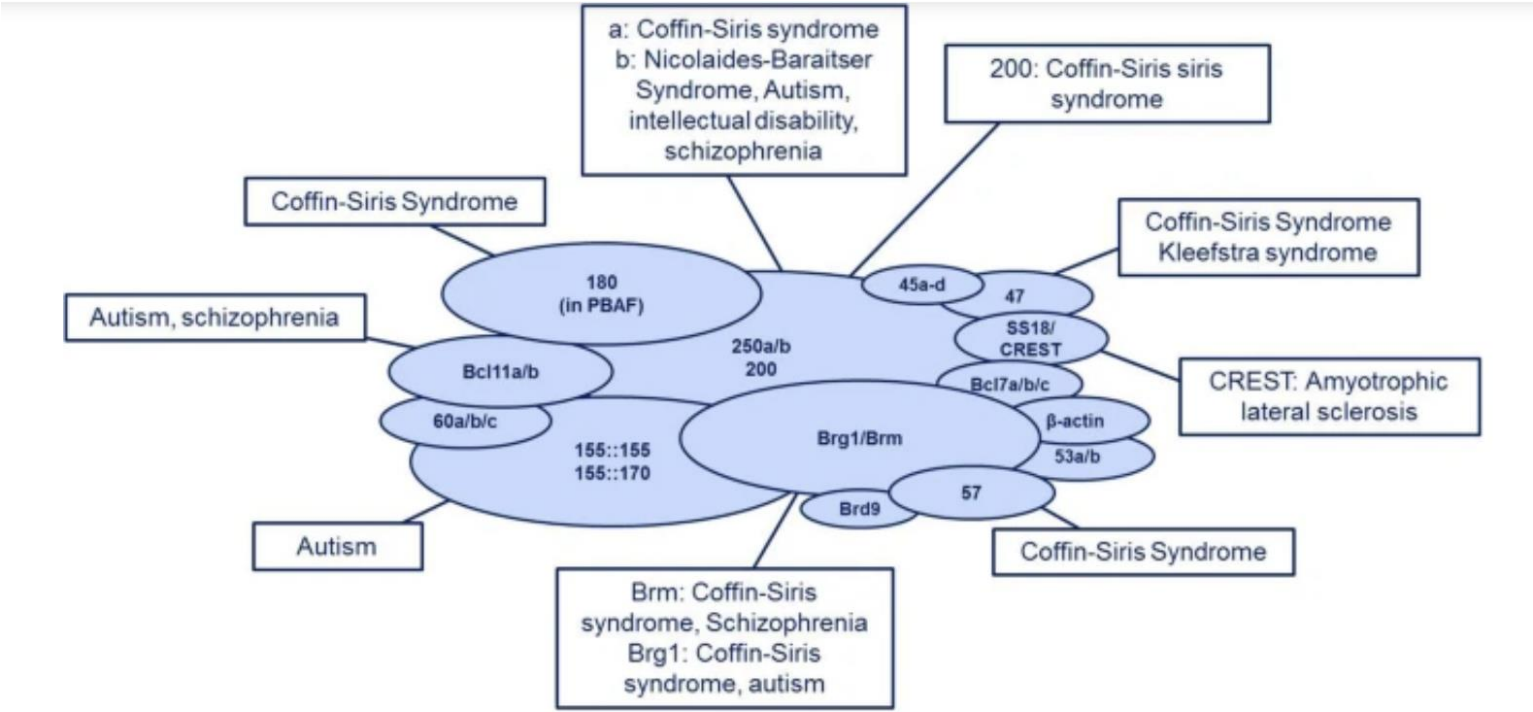
Willhoft, O.; Ghoneim, M.; Lin, C.-L.; Chua, E. Y. D.; Wilkinson, M.; Chaba
Complex. *Science* **2018**, *362* (6411), eaat7716. https://doi.org/10.1126/science.aat7716.

Ranjan, A., et al., *H2A histone-fold and DNA elements in nucleosome activate SWR1-mediated H2A.Z replacement in budding yeast*. Elife. 2015. **4**. & Nguyen et al., Cell 2013



Willhoft O, Ghoneim M, Lin CL, Chua EYD, Wilkinson M, Chaban Y, Ayala R, McCormack EA, Ocloo L, Rueda DS, Wigley DB. Structure and dynamics of the yeast SWR1-nucleosome complex. Science. 2018 Oct 12;362(6411):eaat7716.

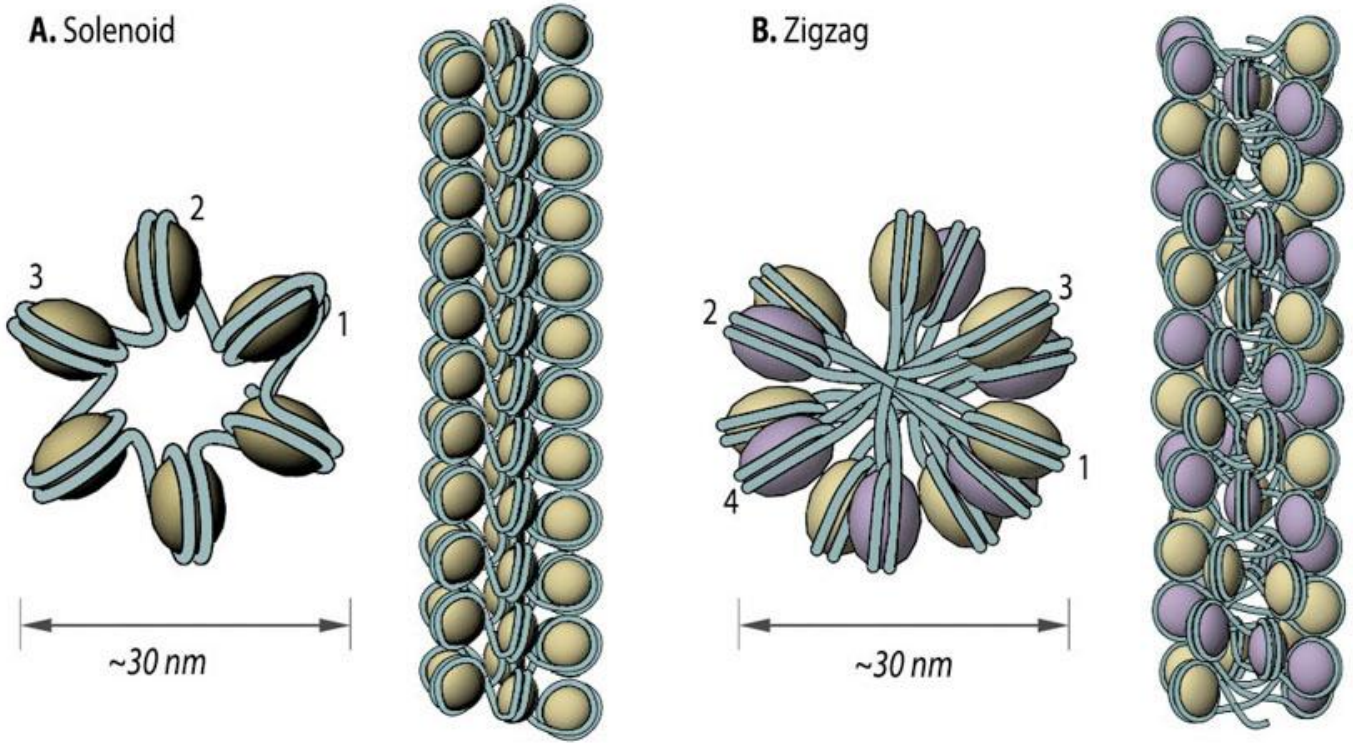

A
BAF-like remodeling complexes
PBAF-like remodeling complexes
Mya (est.)
1,500 750 0
Budding Yeast
Fruitfly
Mouse
Human
1,500 750 0
Mya (est.)
Swp82
Taf14
Snf11
Snf6
Swp29
Swi1
Snf5
Swp73
Swi2/ Snf2
Arp7
Arp9
Swi3
Swi3
SWI/SNF Complex
Saccharomyces cerevisiae
Rsc7
Rsc1/2
Rsc13
Rsc15 or Rsc3 & 30
Rsc4
Rsc10
Rsc5
Rsc14
Rsc9
Sfh1
Rsc6
Sth1
Arp7
Arp9
Rsc8
Rsc8
RSC Complex
Saccharomyces cerevisiae
OSA
SNR1
BAP60
BRM
β-Actin
MOR
MOR
BAP 111
BAP55
BAP Complex
Drosophila melanogaster
POLY-BROMO
SAYP
BAP170
SNR1
BAP60
BRM
β-Actin
MOR
MOR
BAP 111
BAP55
PBAP Complex
Drosophila melanogaster
BRD9
DPF 1/2/3
SS18
(or SS18L1)
BCL11 A/B
BCL7 A/B/C
ARID1A/B
BAF 47
BAF60 A/B/C
BRG/ BRM
β-Actin
BAF 155
BAF 170
BAF 57
BAF53A/B
BAF Complexes
Homo sapiens, Mus musculus
BRD7
PBRM1
PHF 10
BCL11 A/B
BCL7 A/B/C
ARID2
BAF 47
BAF60 A/B/C
BRG
β-Actin
BAF 155
BAF 170
BAF 57
BAF53A/B
PBAF Complexes
Homo sapiens, Mus musculus



The role of subunit mutations in developmental disorders. BAF subunit mutations have a high implication in human developmental disorders. The most frequent mutations and associations with human disease are summarised in this figure. Subunits being involved most frequently include the ATPase subunit BRM as well as the subunit BAF250b

Alfert, A., Moreno, N. & Kerl, K. The BAF complex in development and disease. *Epigenetics & Chromatin* **12**, 19 (2019).

Супрануклеосомная структура хроматина

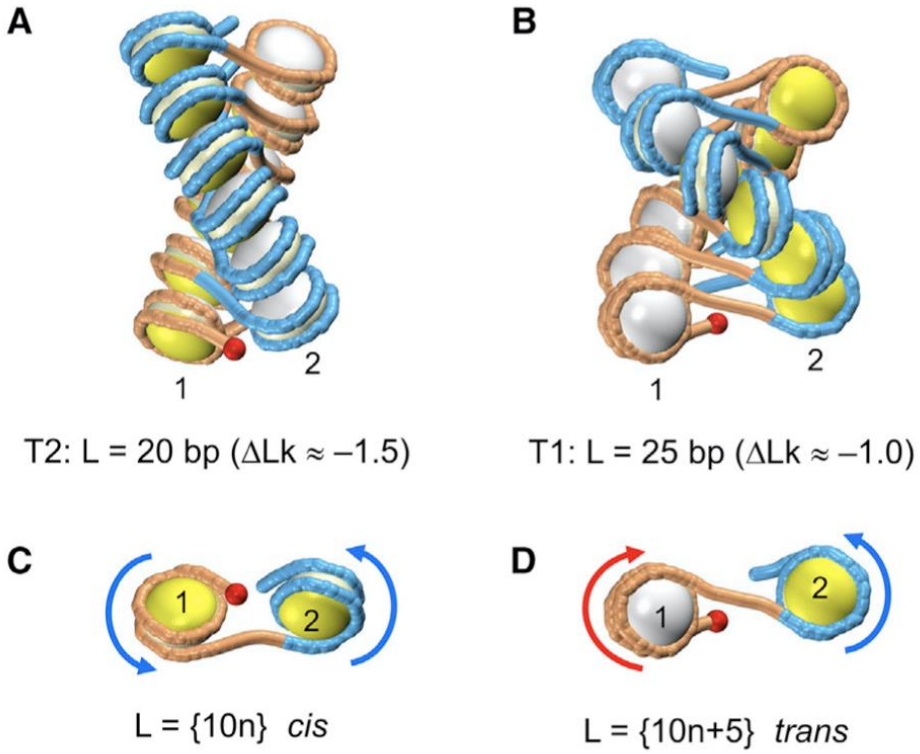


https://www.mechanobio.info/genome-regulation/what-are-nucleosomes/

Edward N. Trifonov (2015): Nucleosome repeat lengths and columnar chromatin structure., Journal of Biomolecular Structure and Dynamics, DOI: 10.1080/07391102.2015.1075158

Супрануклеосомная структура хроматина

Low expressed genes

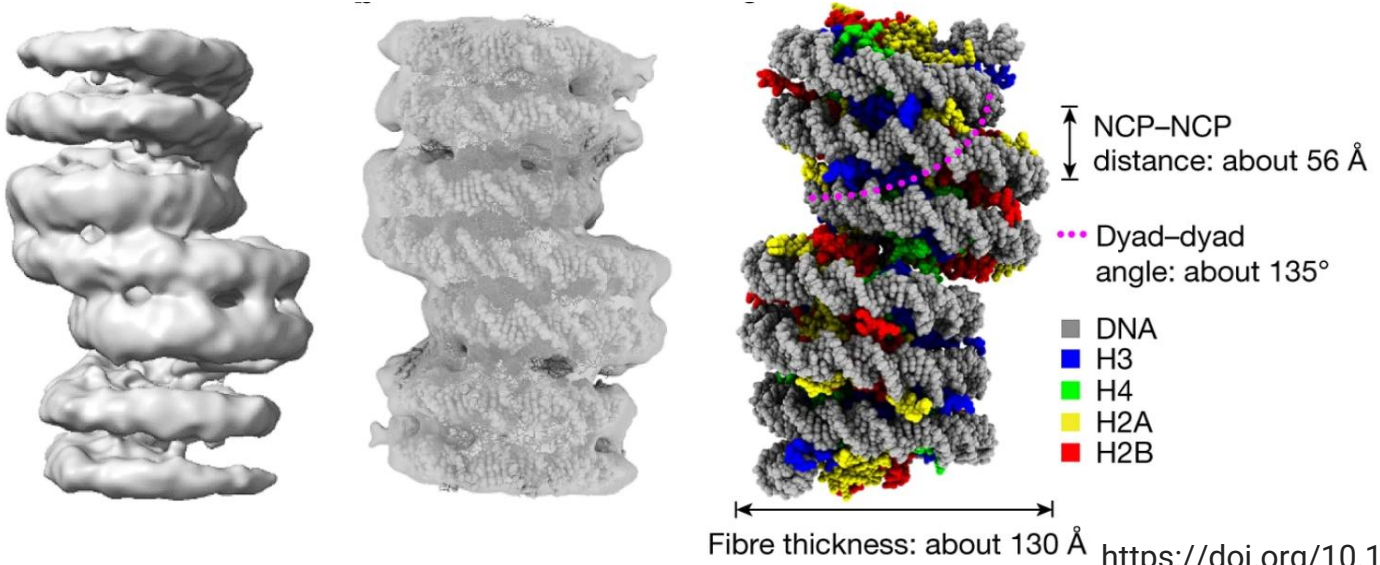


Highly expressed genes

Zhurkin, V. B.; Norouzi, D. Topological Polymorphism of Nucleosome Fibers and Folding of Chromatin. *Biophysical Journal* 2021, *120* (4), 577–585. https://doi.org/10.1016/j.bpj.2021.01.008.

Теломеры

- Mammalian telomeres consist of the conserved and tandemly arranged DNA sequence repeat TTAGGG
- the telomeric NCP was less stable and markedly more dynamic than NCPs that contained DNA-positioning sequences. The explanation for this difference is based on the physical properties of the G-rich telomeric TTAGGG 6-bp repeat, which disfavours nucleosome positioning and renders telomeric nucleosomes more mobile



https://doi.org/10.1038/s41586-022-05236-5

Супрануклеосомная структура хроматина

Регулярного расположения нуклеосом и 30-нм фибриллы не существует.
Могут быть нуклеосомные кластеры, клатчи, определенной струкутры.

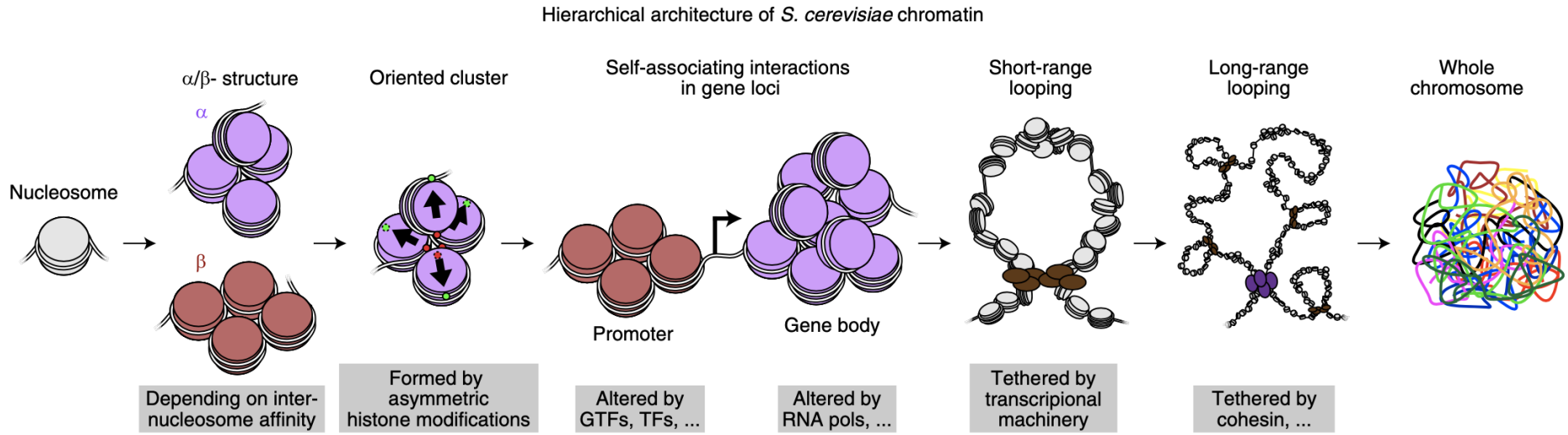
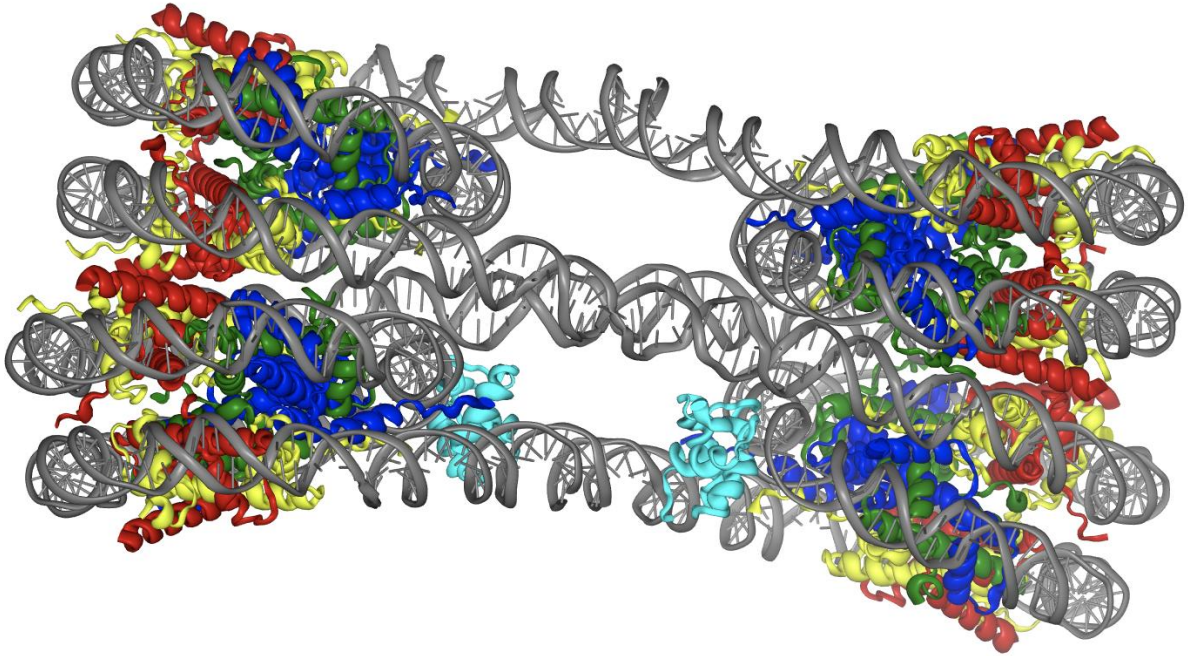


Figure 7. Model of Hierarchical Architecture of *S. cerevisiae* Chromatin from the Nucleosome Level to Whole Chromosomes

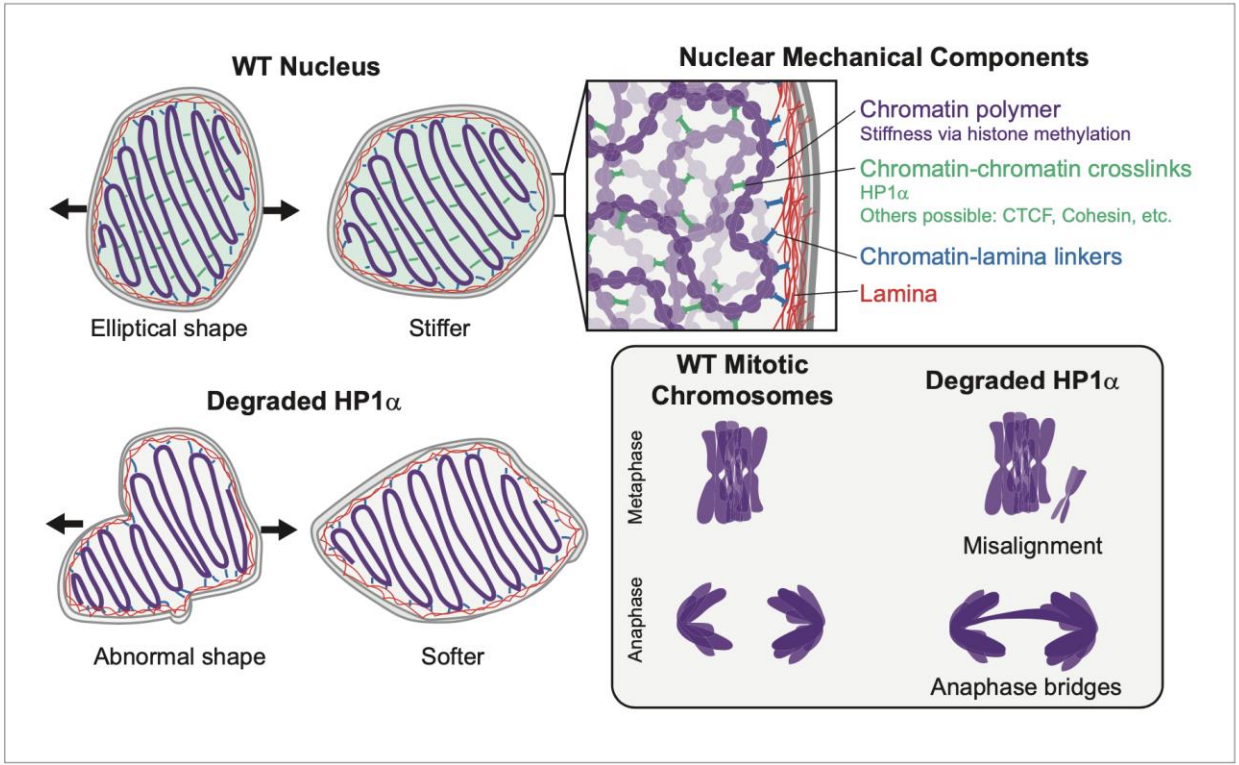
Ohno, M.; Ando, T.; Priest, D. G.; Kumar, V.; Yoshida, Y.; Taniguchi, Y. Sub-Nucleosomal Genome Structure Reveals Distinct Nucleosome Folding Motifs. *Cell* **2019**, *176* (3), 520-534.e25.

Супрануклеосомная структура хроматина

https://nucldb.intbio.org



Супрануклеосомная структура хроматина



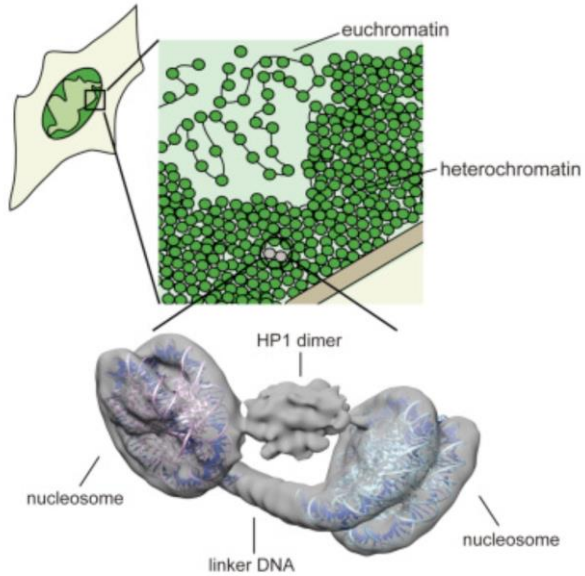
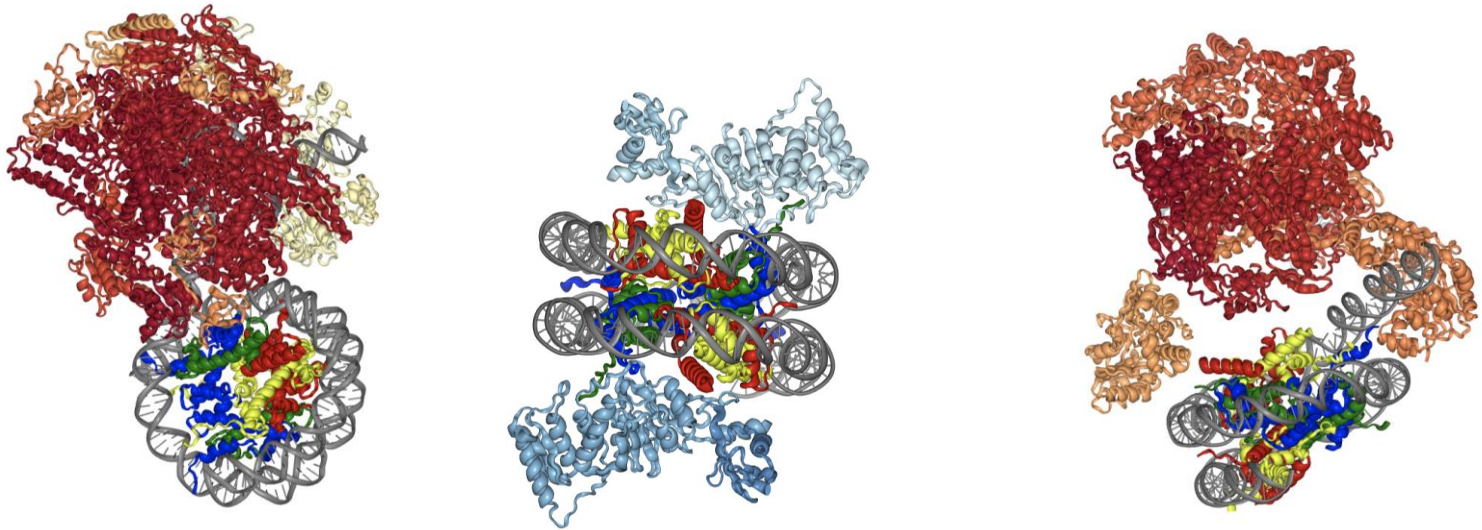


Figure 6. HP1α is a mechanical element of interphase nuclei and mitotic chromosomes. In wild-type (WT) nuclei, HP1α acts as a chromatin-chromatin

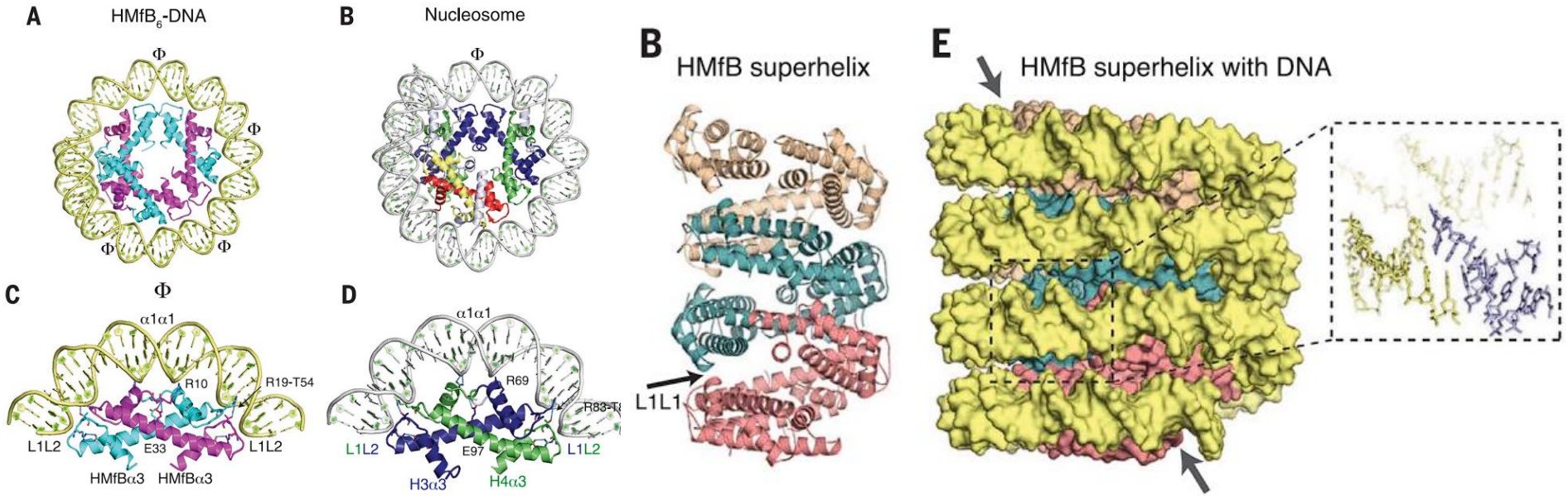
Strom, A. R.; Biggs, R. J.; Banigan, E. J.; Wang, X.; Chiu, K.; Herman, C.; Collado, J.; Yue, F.; Ritland Politz, J. C.; Tait, L. J.; Scalzo, D.; Telling, A.; Groudine, M.; Brangwynne, C. P.; Marko, J. F.; Stephens, A. D. HP1α Is a Chromatin Crosslinker That Controls Nuclear and Mitotic Chromosome Mechanics. *eLife* **2021**, *10*, e63972. https://doi.org/10.7554/eLife.63972.

Супрануклеосомная структура хроматина

https://nucldb.intbio.org

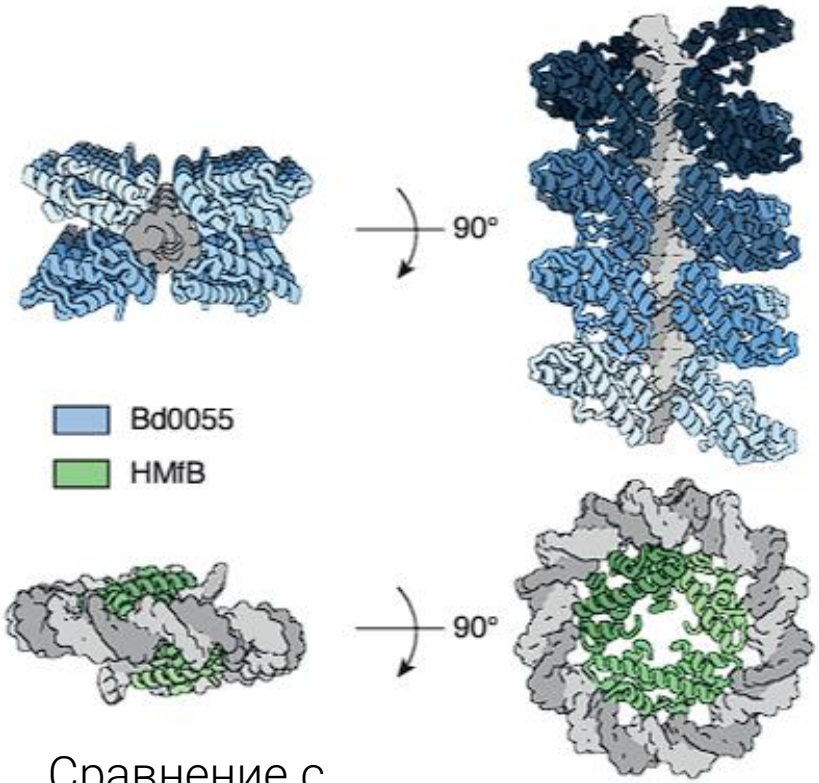


Гистоны архей

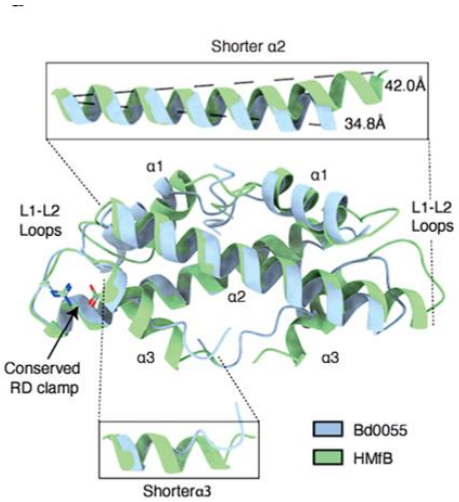


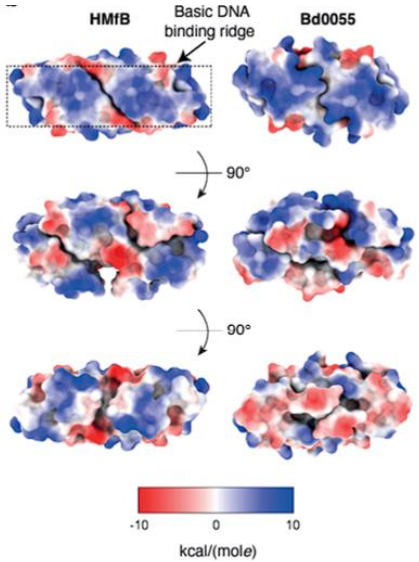
https://doi.org/10.1126/science.aaj1849

Бактериальные гистоны



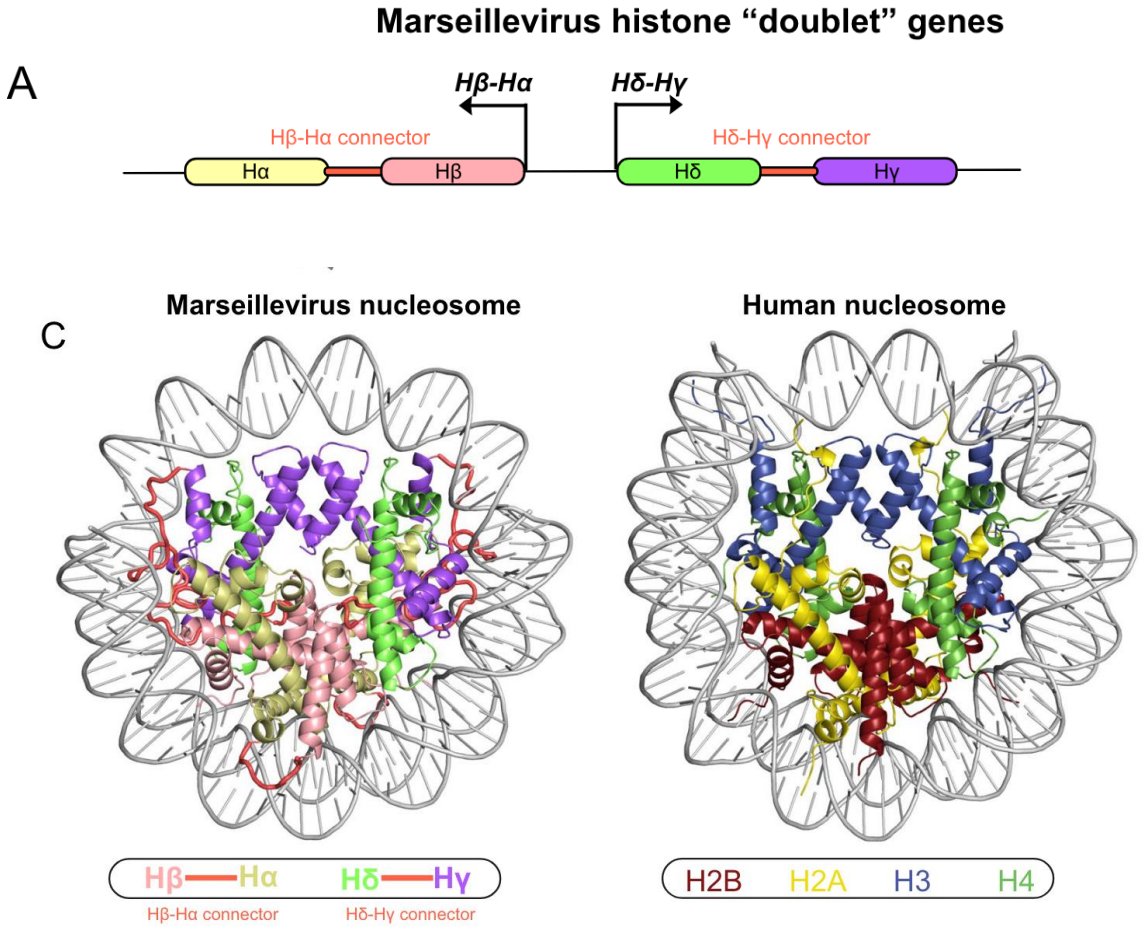
Сравнение с архейными

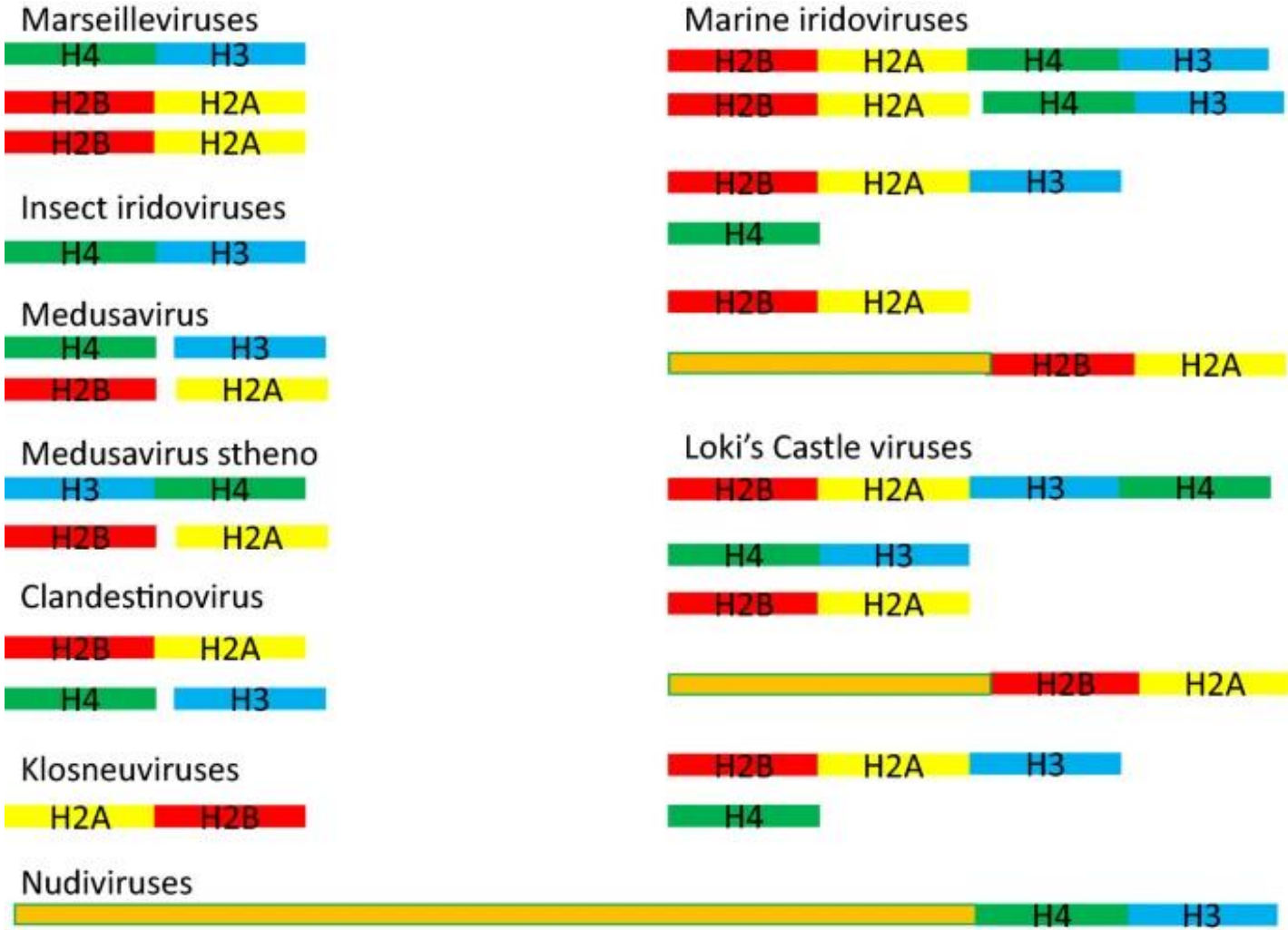




https://doi.org/10.1101/2023.01.26.525422

Вирусные гистоны




Marseilleviruses
H4
H3
H2B
H2A
H2B
H2A
Insect iridoviruses
H4
H3
Medusavirus
H4
H3
H2B
H2A
Medusavirus stheno
H3
H4
H2B
H2A
Clandestinovirus
H2B
H2A
H4
H3
Klosneuviruses
H2A
H2B
Nudiviruses
H4
H3
Marine iridoviruses
H2B
H2A
H4
H3
H2B
H2A
H4
H3
H2B
H2A
H3
H4
H2B
H2A
H2B
H2A
Loki's Castle viruses
H2B
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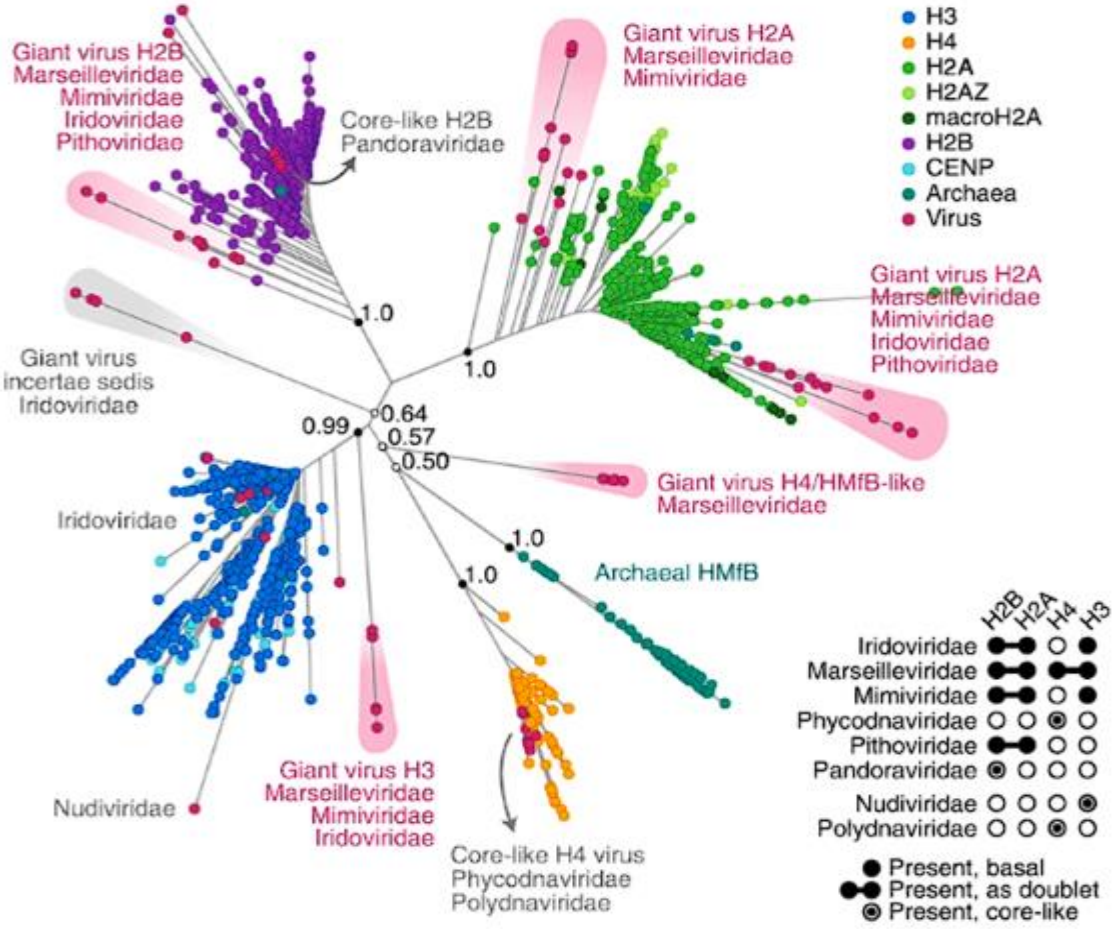
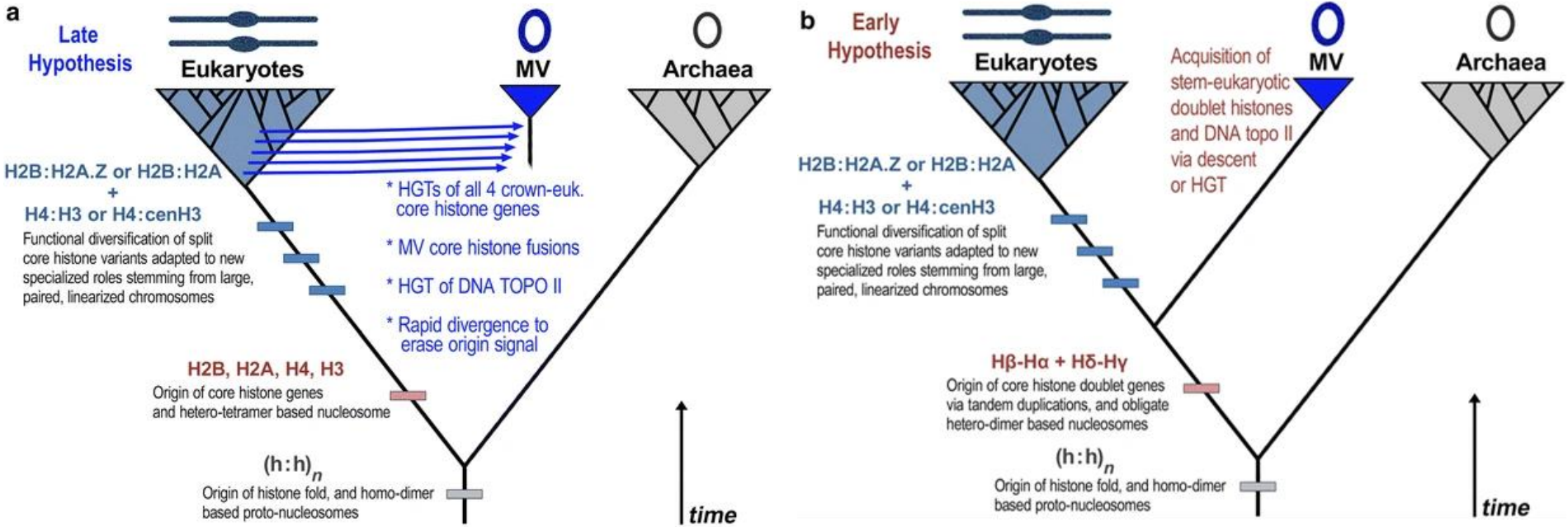
H2B
H2A
H2B
H2A
H3
H4



Phylogenetic analysis of histone domains, with a focus on viral homologues. Statistical supports (approximate Bayes posterior probabilities) are shown for the deepest node of each canonical eukaryotic or archaeal histone clade. The inset table summarizes the presence of doublet histone genes per lineage

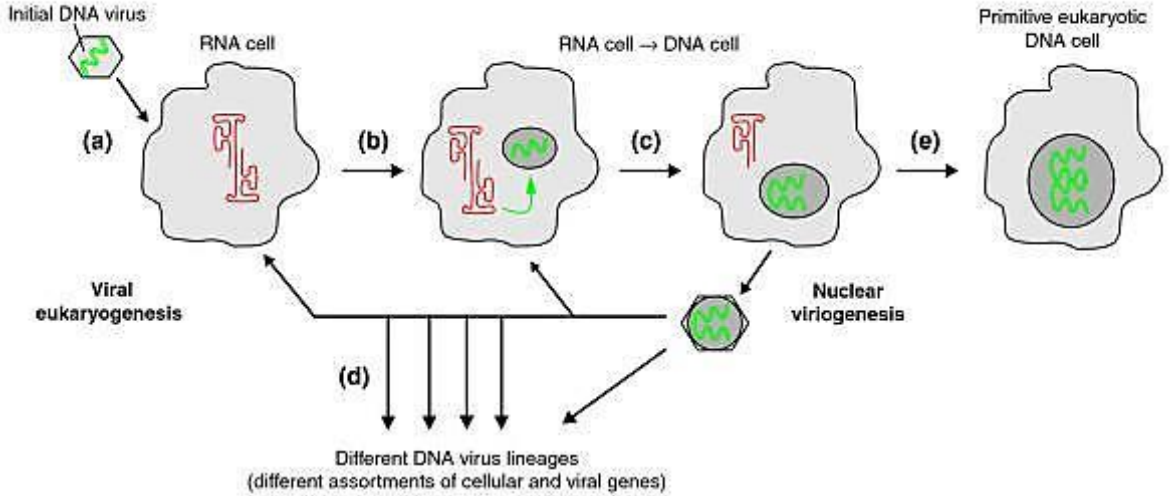
https://doi.org/10.1038/s41559-022-01771-6

Эволюция гистонов вирусов

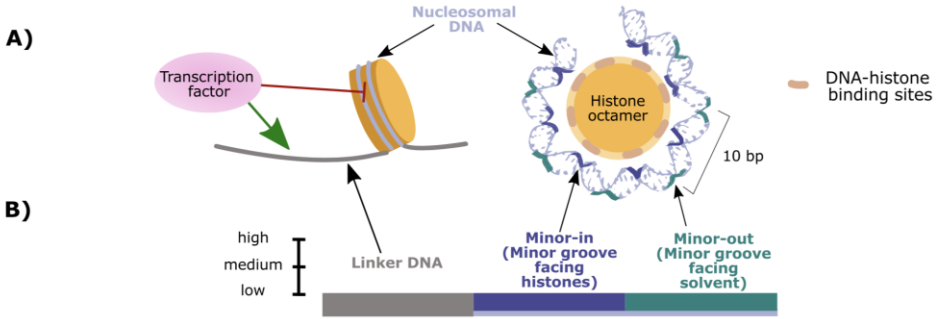


https://doi.org/10.1186/s13072-017-0162-0

viral karyogenesis (?)



Nucleosomes and DNA mutations

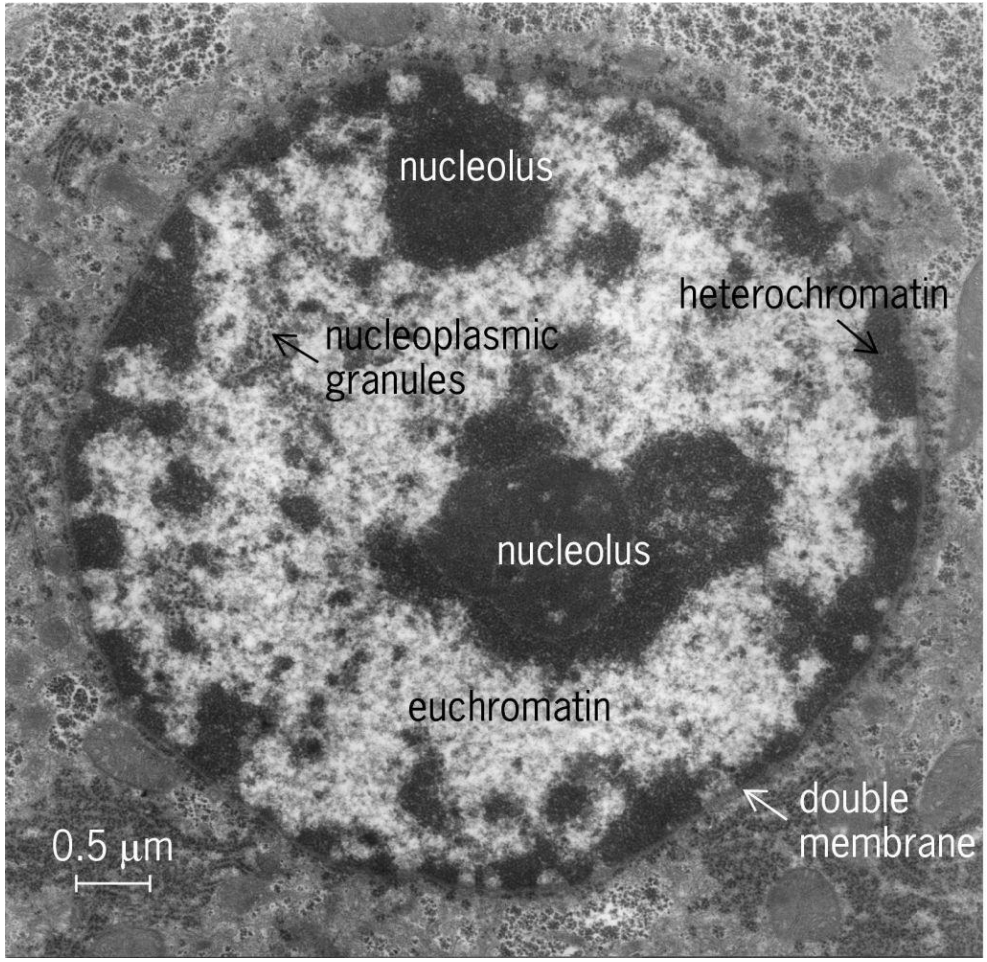


	UV-light (CPD, 6-4PP)	Smoking (BPDE-dG)	ROS (8-oxo-G)	Spontaneous deamination 5meC
Mutation type	C>T	C>A	T>C|G	C>T
DNA damage rate			?	
DNA repair rate	NER	NER	BER	MMR ? ?
Mutation rate			?	

Espiritu,D., Gribkova,A.K., Gupta,S., Shaytan,A.K. and Panchenko,A.R. (2021) Molecular Mechanisms of Oncogenesis through the Lens of Nucleosomes and Histones. *J. Phys. Chem. B*, 10.1021/acs.jpcb.1c00694.

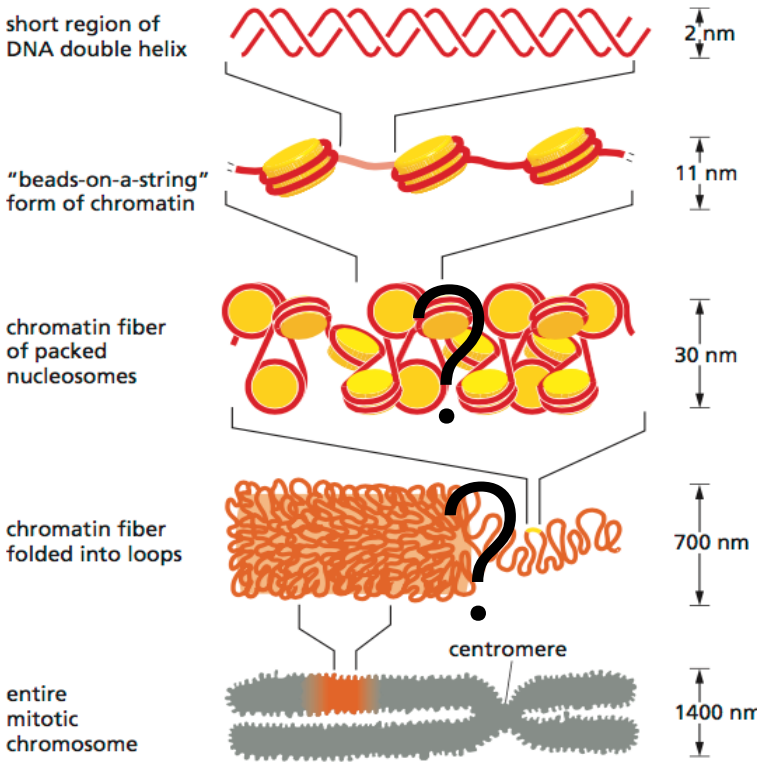
Спасибо за внимание!

Далее поговорим про устройство интерфазного хроматина на более больших масштабах



Представления о структуре хроматина

Устаревшее иерархическое представление

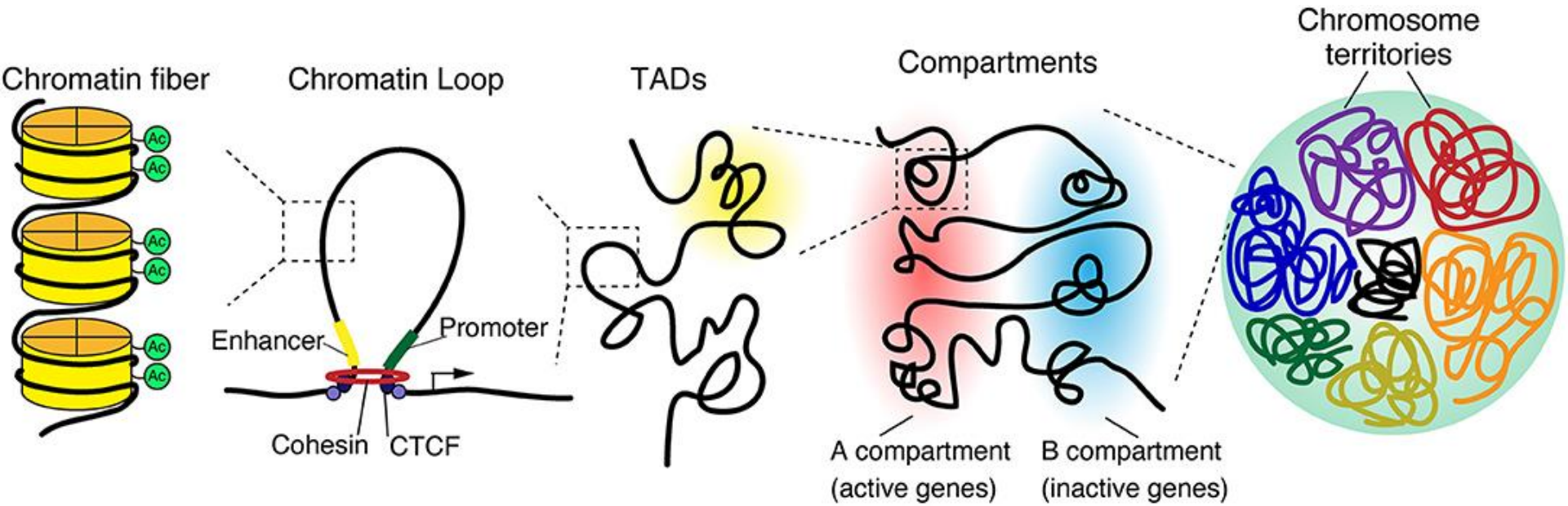


В естественных условиях не существует

Mol Biol of the CELL, Alberts et al, 2014

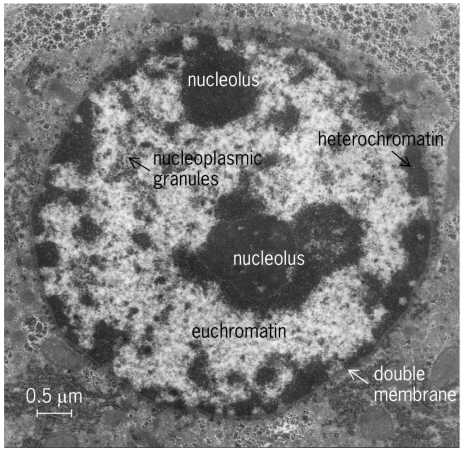
Представления о структуре хроматина

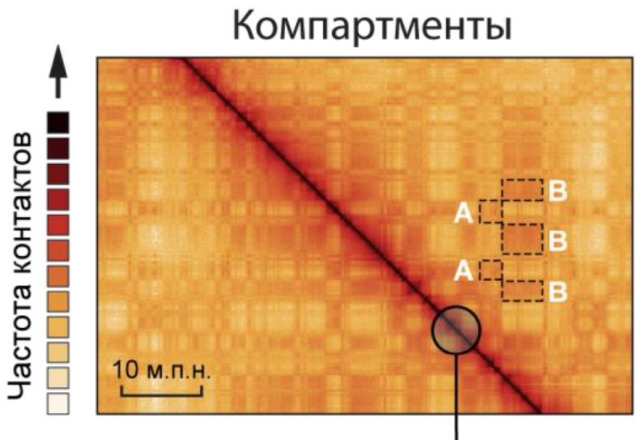
Более современное представление

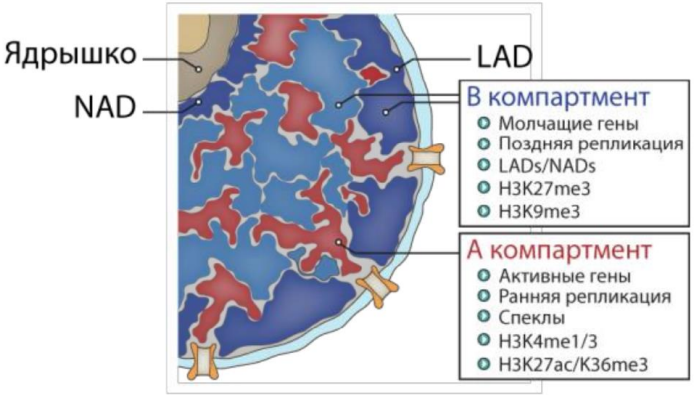


https://www.frontiersin.org/articles/10.3389/fcell.2020.626541/full

Концепция 1: Эу/гетерохроматин, А/В – компартменты

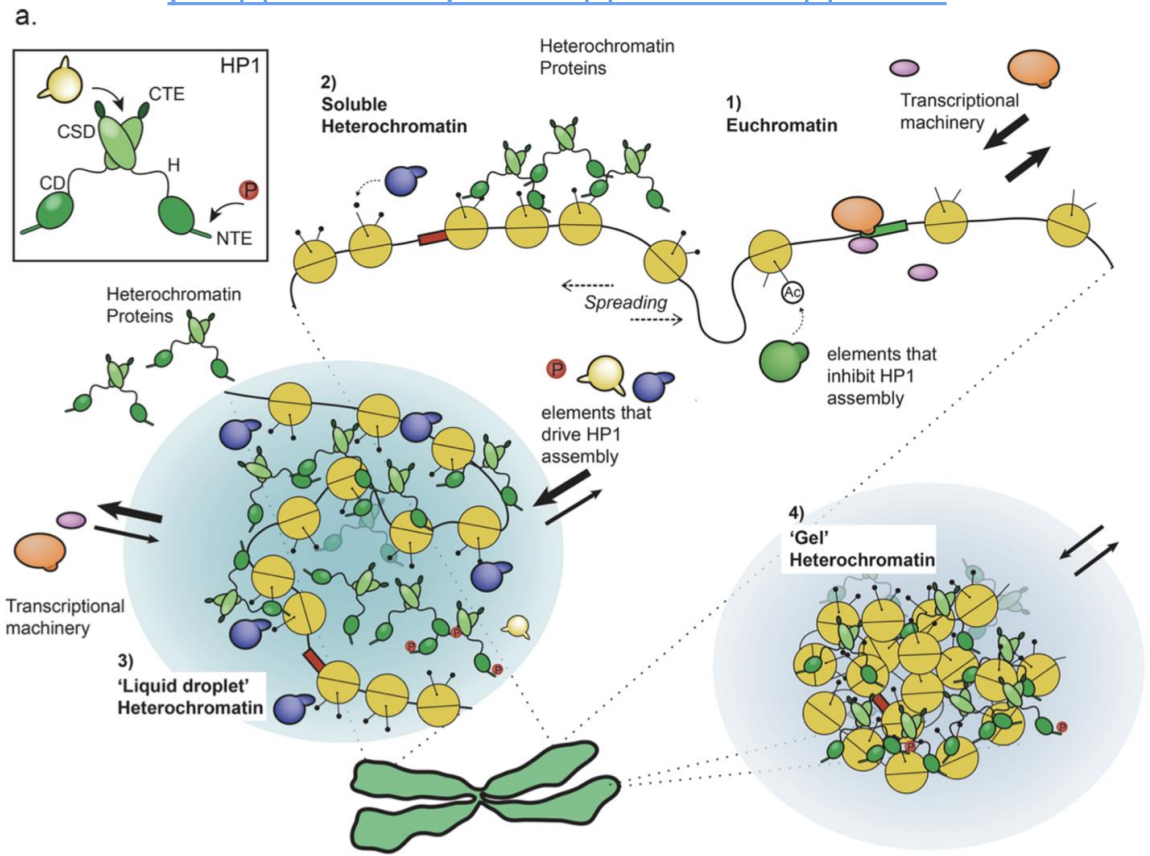






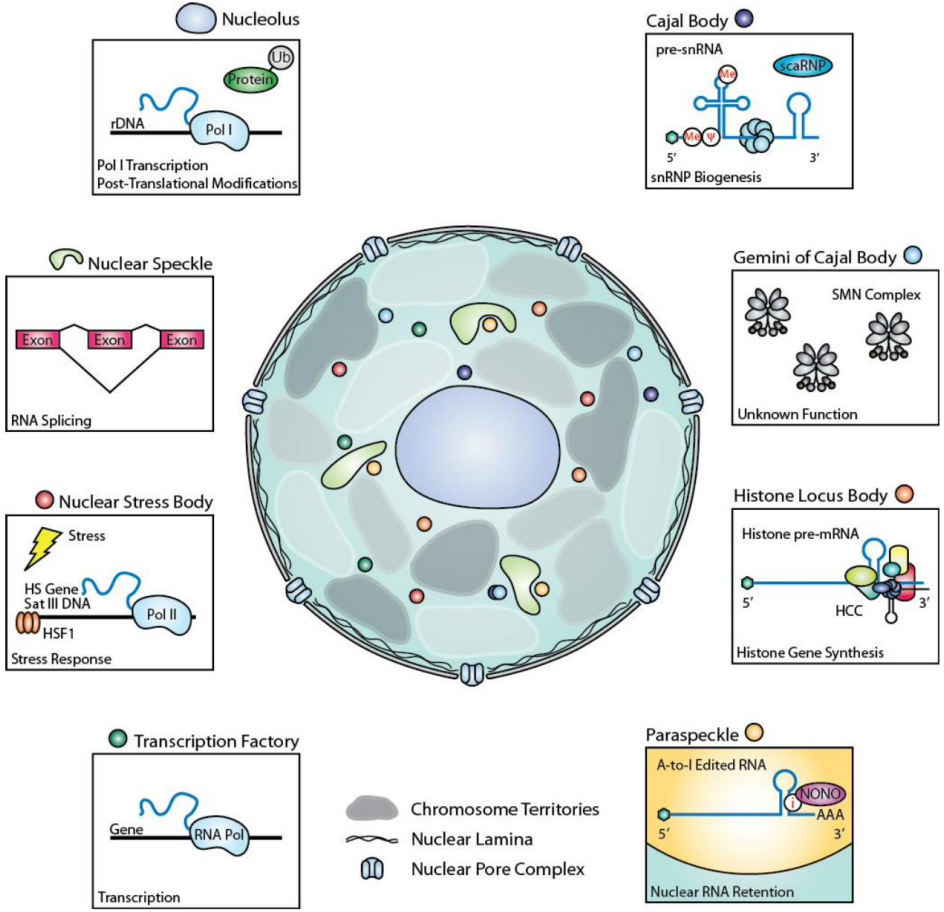
С.В. Ульянов – докторская диссертация 2023 г.

Концепция 2: ”Жидкие капли” разделение фаз жидкость-жидкость



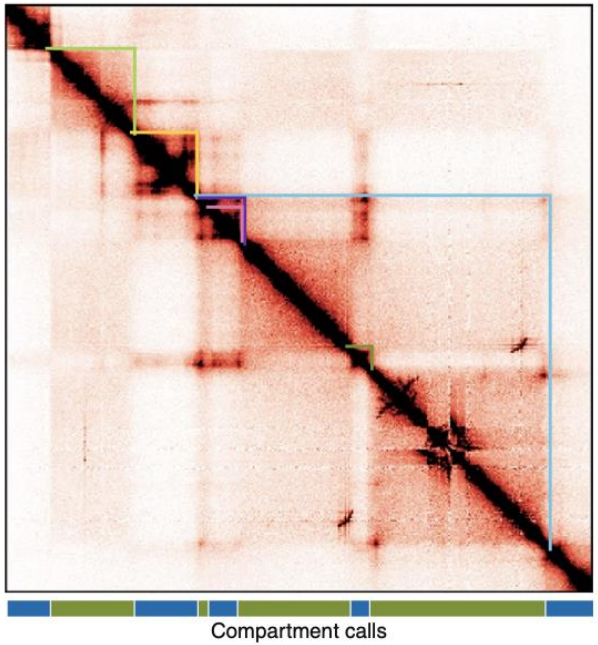
Larson AG, Narlikar GJ. 2018. Biochemistry 57: 2540–2548.

В формировании немембранных органелл важную роль играют статистические физические взаимодействия (разделение фаз)

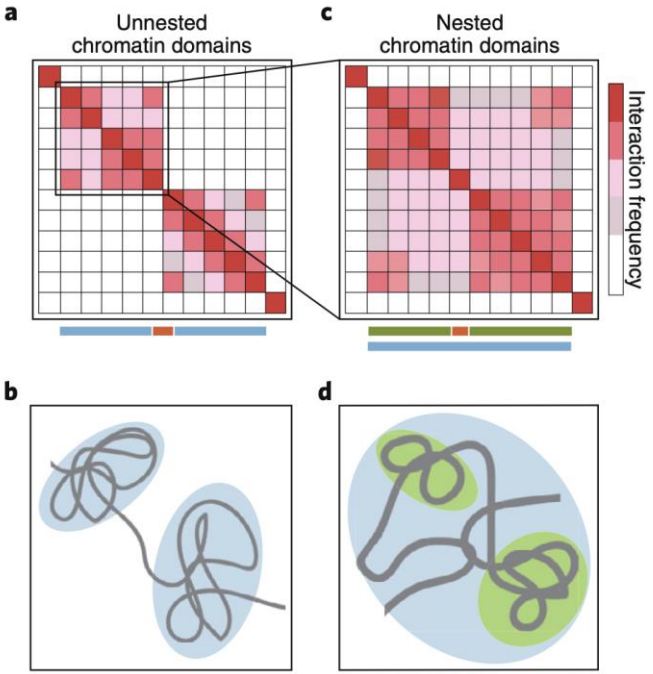


https://www.mdpi.com/2079-7737/2/3/976

Концепция 3: ТАДы – топологически ассоциирующие домены

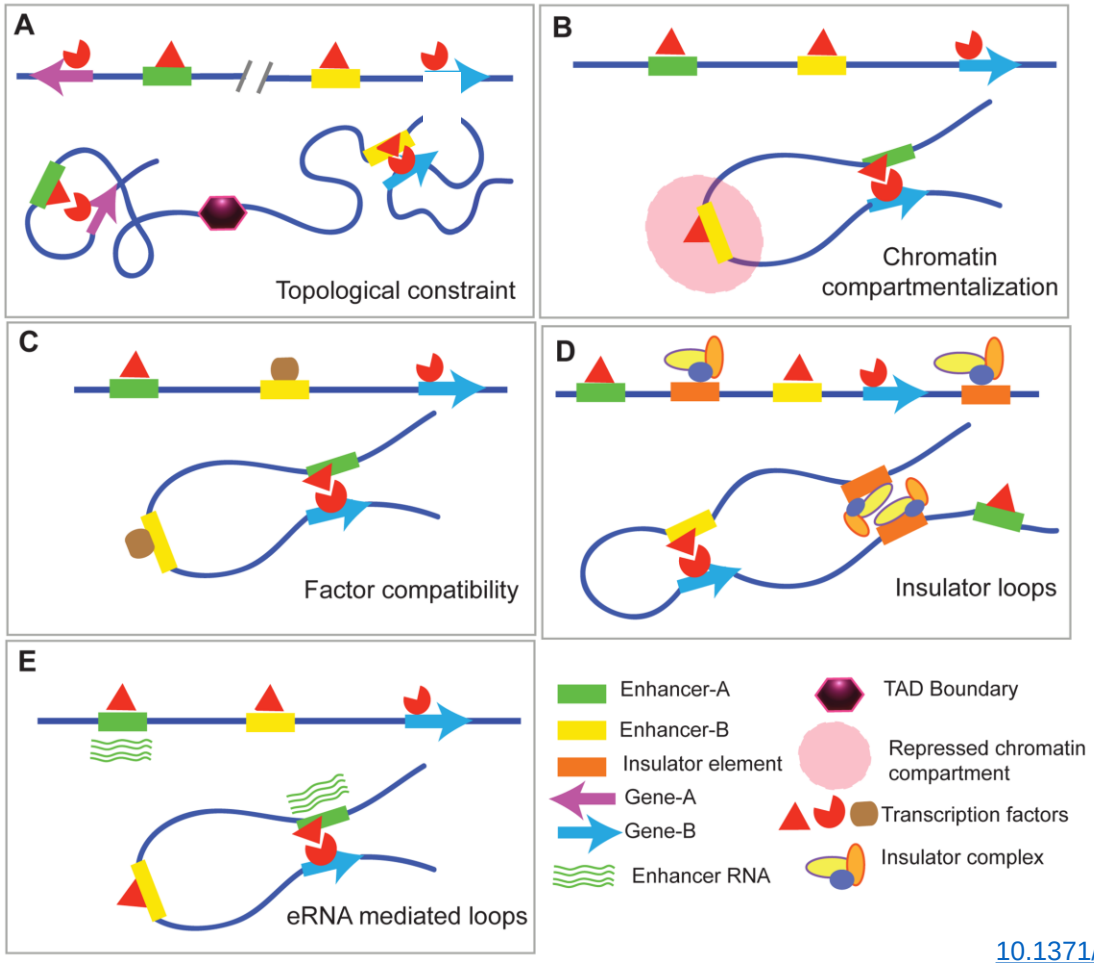


Карта контактов вдоль генома (метод Hi-C)



10.1038/s41588-019-0561-1

Концепция 4: ”Петли”, топология и взаимодействия элементов вдоль ДНК



10.1371/journal.pgen.1005640.g002

Концепция 5: Loop extrusion – экструзия петель

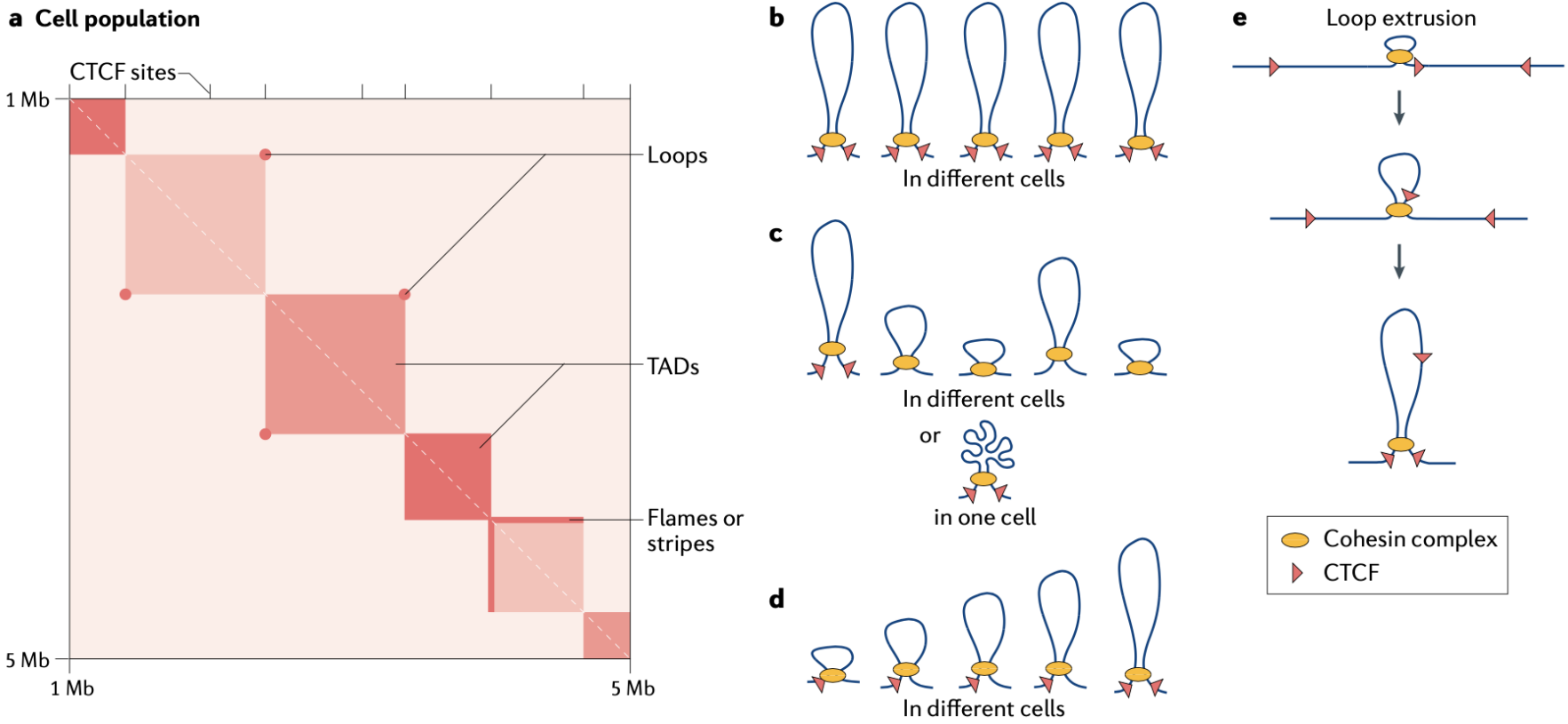
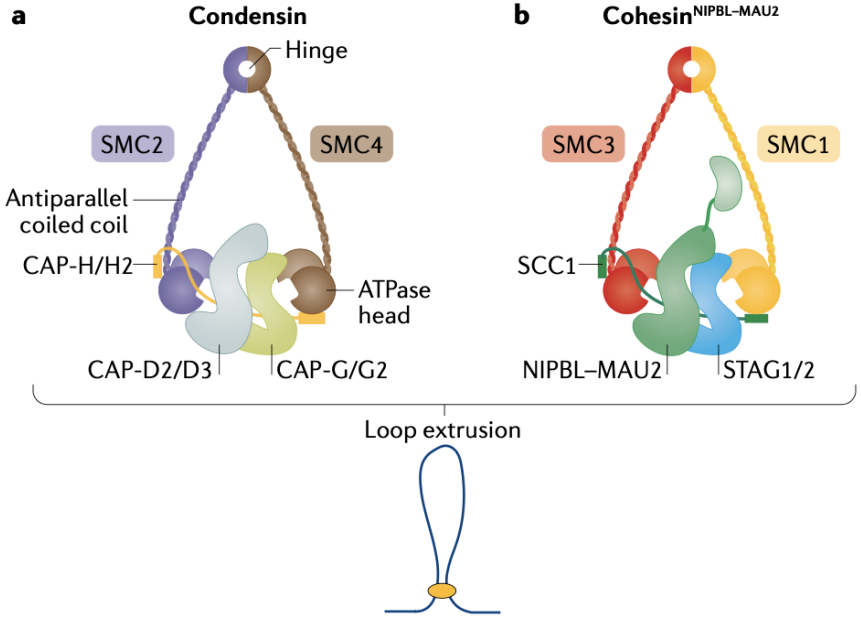


Fig. 1 | **Interphase genome organization. a** | Schematic representation of a Hi-C map depicting the organization, across

Концепция 5: Loop extrusion – экструзия петель



10.1126/science.aar7831

Концепция 6: Хромосомные территории

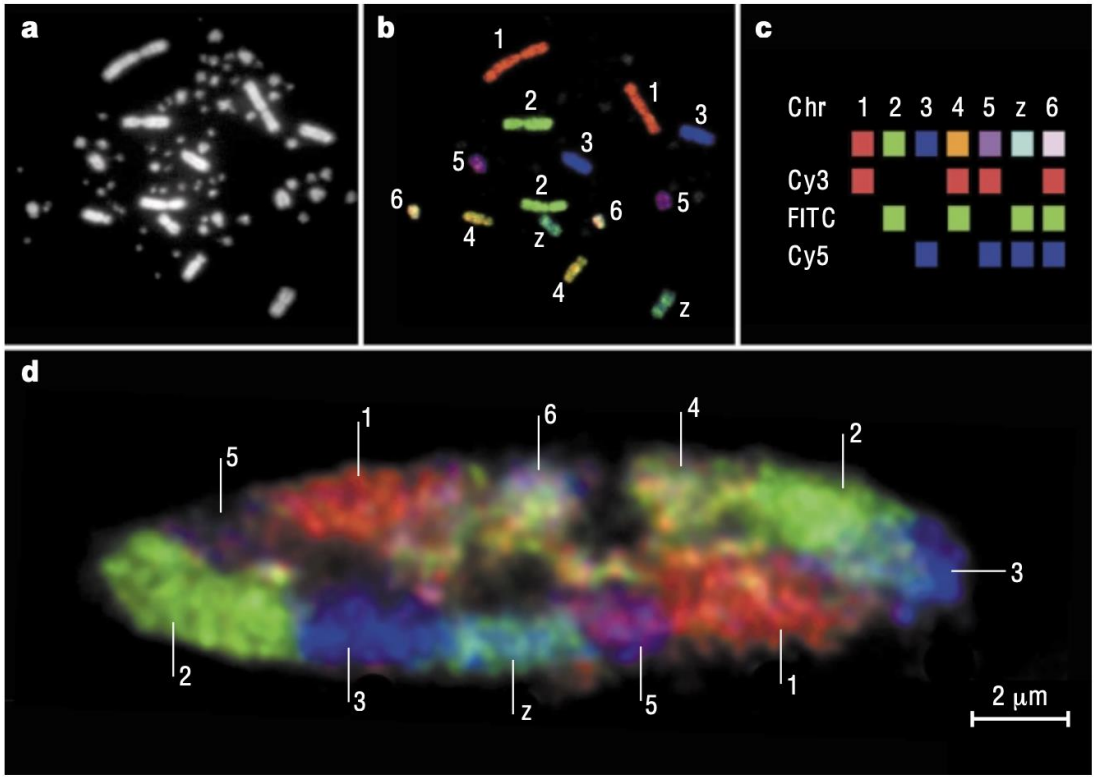
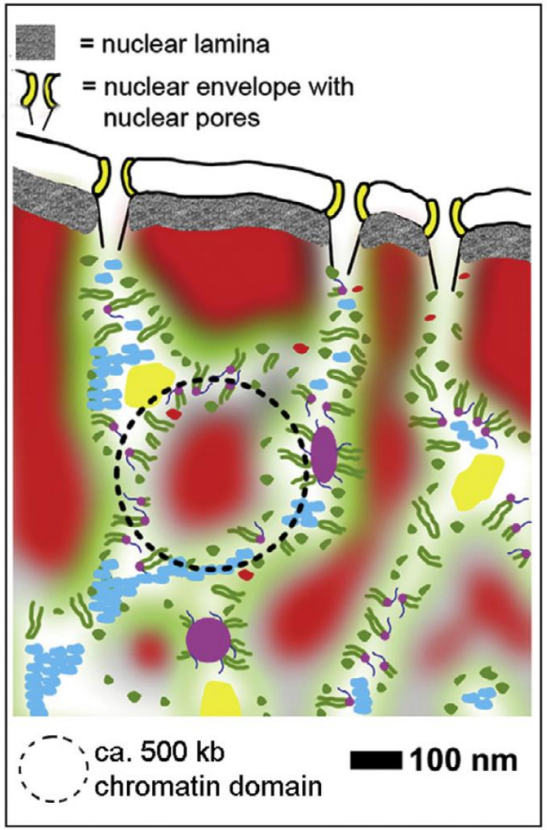


Figure 2 | **Chromosome territories in the chicken. a** | 4,6-diamidino-2-phenylindole (DAPI)-stained, diploid, chicken metaphase spread with macro- and microchromosomes. **b** | The same metaphase spread after multicolour fluorescence *in situ* hybridization with pseudocoloured chromosomes. Chicken chromosome paint probes (image courtesy of Johannes Wienberg) were labelled by a combinatorial scheme with oestradiol (1, 4, 5, 6),

Cremer, T.; Cremer, C. (2001). . Nature Reviews Genetics, 2(4), 292–301. doi:10.1038/35066075

Концепция 7:
active compartment/inactive compartment/interchromatin compartment

A



active nuclear compartment

ANC

Transcriptionally competent decondensed chromatin marked by „active“ histone marks

transcriptionally competent chromatin loops,

transcriptionally active chromatin loops

Interchromatin compartment, harboring

Transcription factories,

splicing speckles,

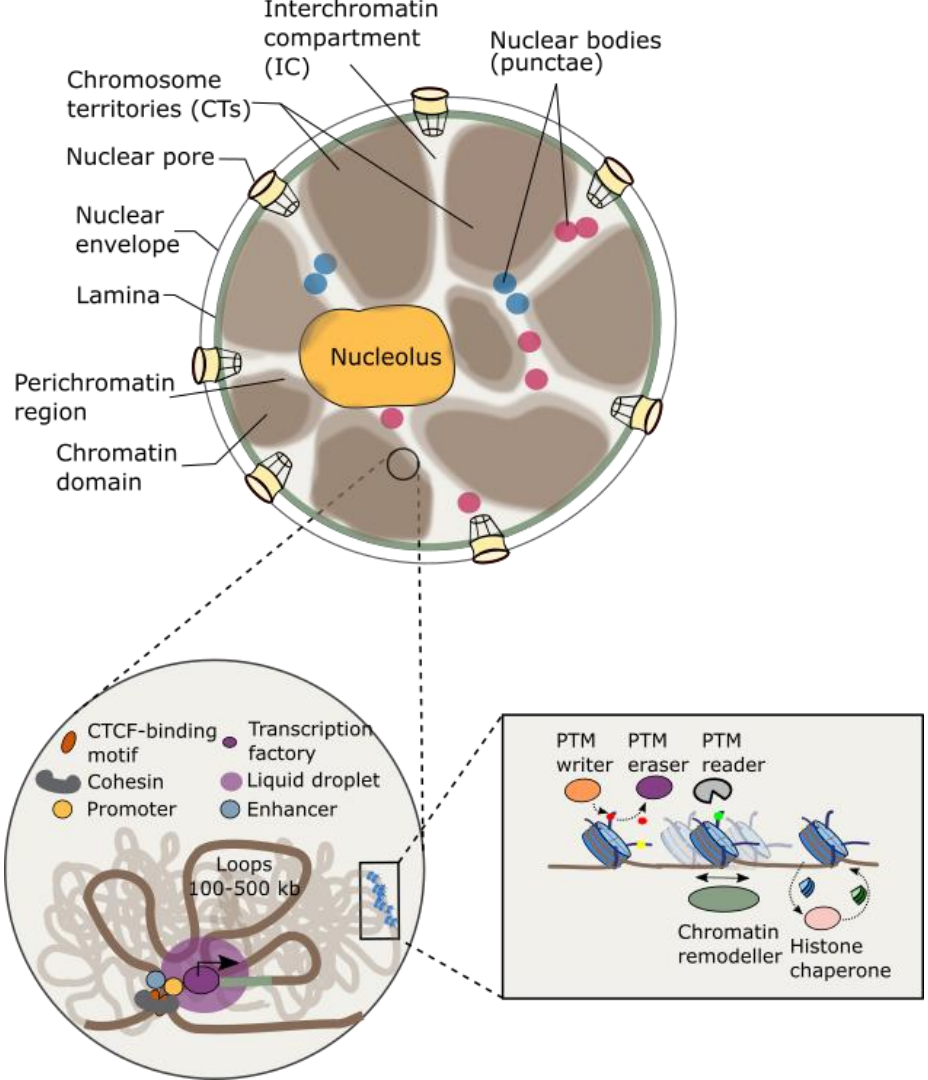
architectural proteins, e.g. CTCF, SAF-A, Matrin

inactive nuclear compartment

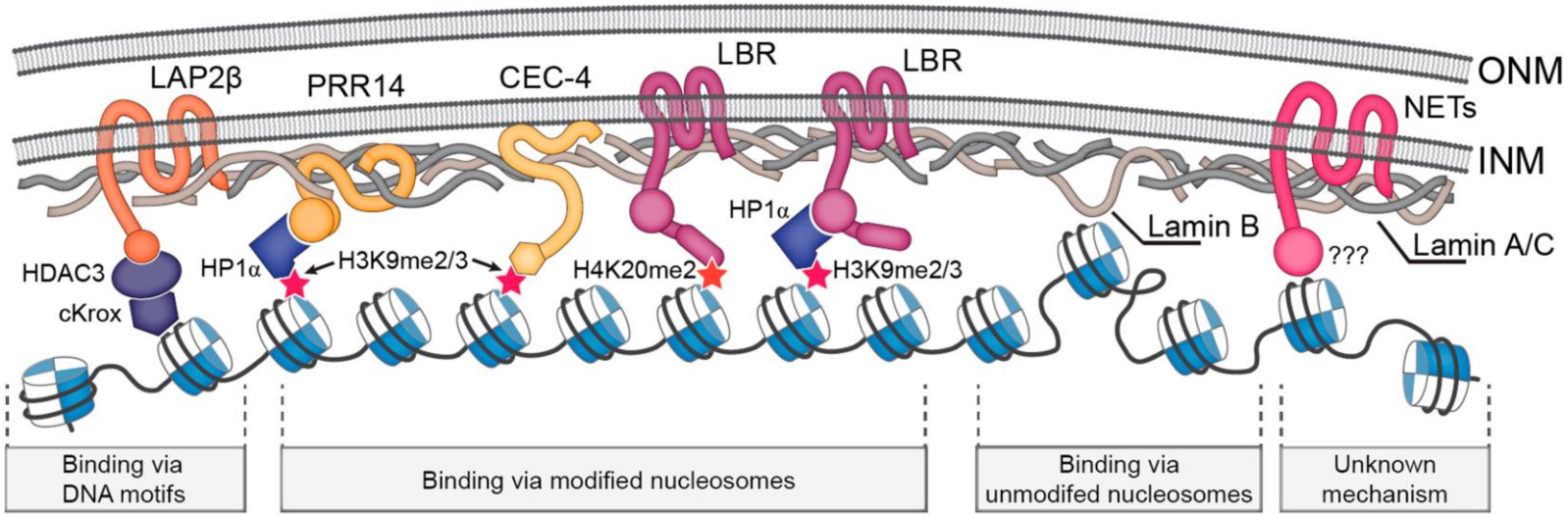
INC

Compacted part of chromatin domain clusters (CDCs) marked by repressive histone marks

B


Interchromatin compartment (IC)
Nuclear bodies (punctae)
Chromosome territories (CTs)
Nuclear pore
Nuclear envelope
Lamina
Nucleolus
Perichromatin region
Chromatin domain
CTCF-binding motif
Transcription factory
Cohesin
Liquid droplet
Promoter
Enhancer
Loops 100-500 kb
PTM writer
PTM eraser
PTM reader
Chromatin remodeller
Histone chaperone

Концепция 8:
ядерная ламина и lamina-associated domains



The Nuclear Lamina as an Organizer of Chromosome Architecture

by Yuri Y. Shevelyov [1,*] and Sergey V. Ulianov [2]