Демидюк
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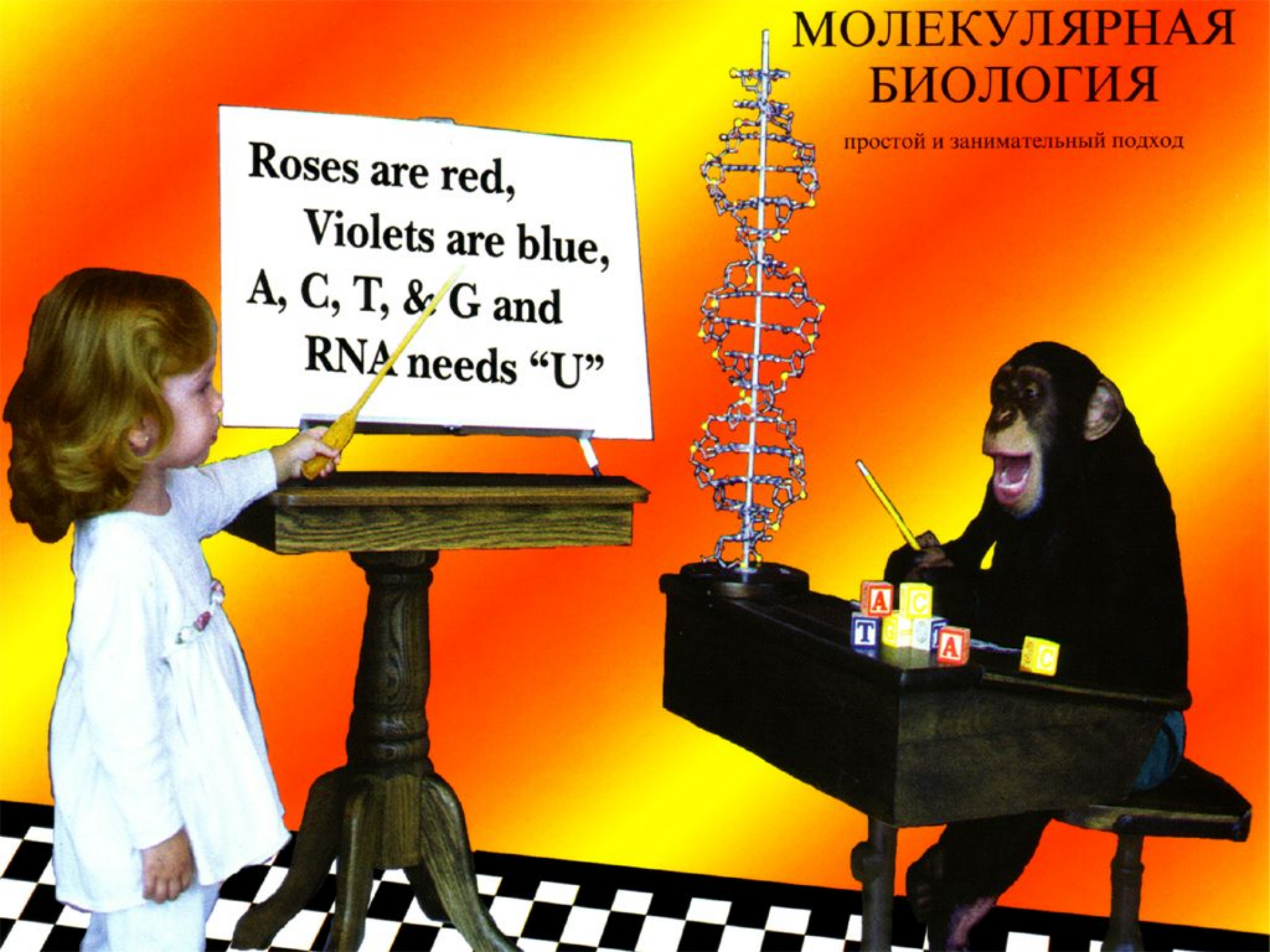
МОЛЕКУЛЯРНАЯ БИОЛОГИЯ

простой и занимательный подход



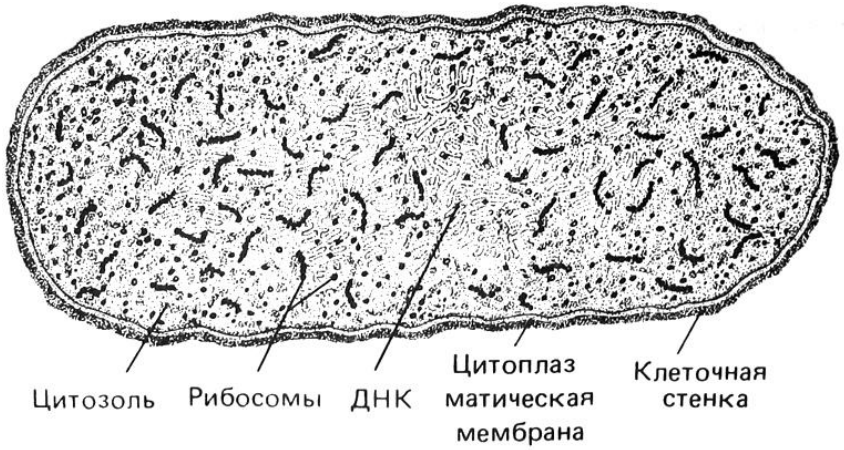

Я решила изучать китайский в этом семестре. В нем более 30.000 иероглифов! Давай изучать его вместе!
Не пойдет! Я выбрала молекулярную биологию. Там всего 5 основных знаков!
許許中
國多字
許多字
許國字
U T
A
C
G

СТРОЕНИЕ КЛЕТОК

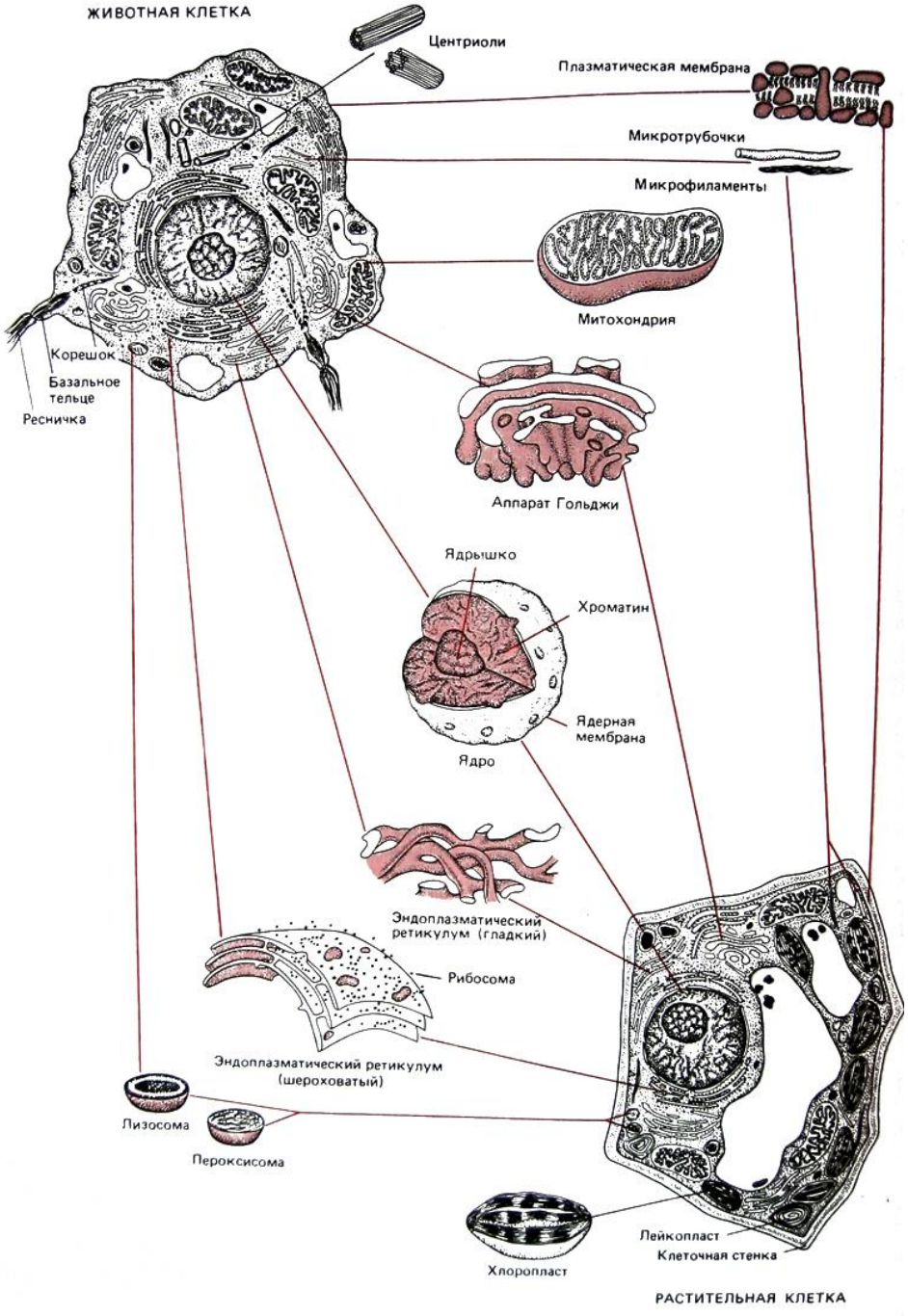
Эукариоты – организмы клетки, которых содержат ядро; внутри ядра заключены хромосомы. Многие эукариотические организмы – многоклеточные

Прокариоты – одноклеточные организмы, лишенные ядра, с хромосомами, находящимися в цитоплазме

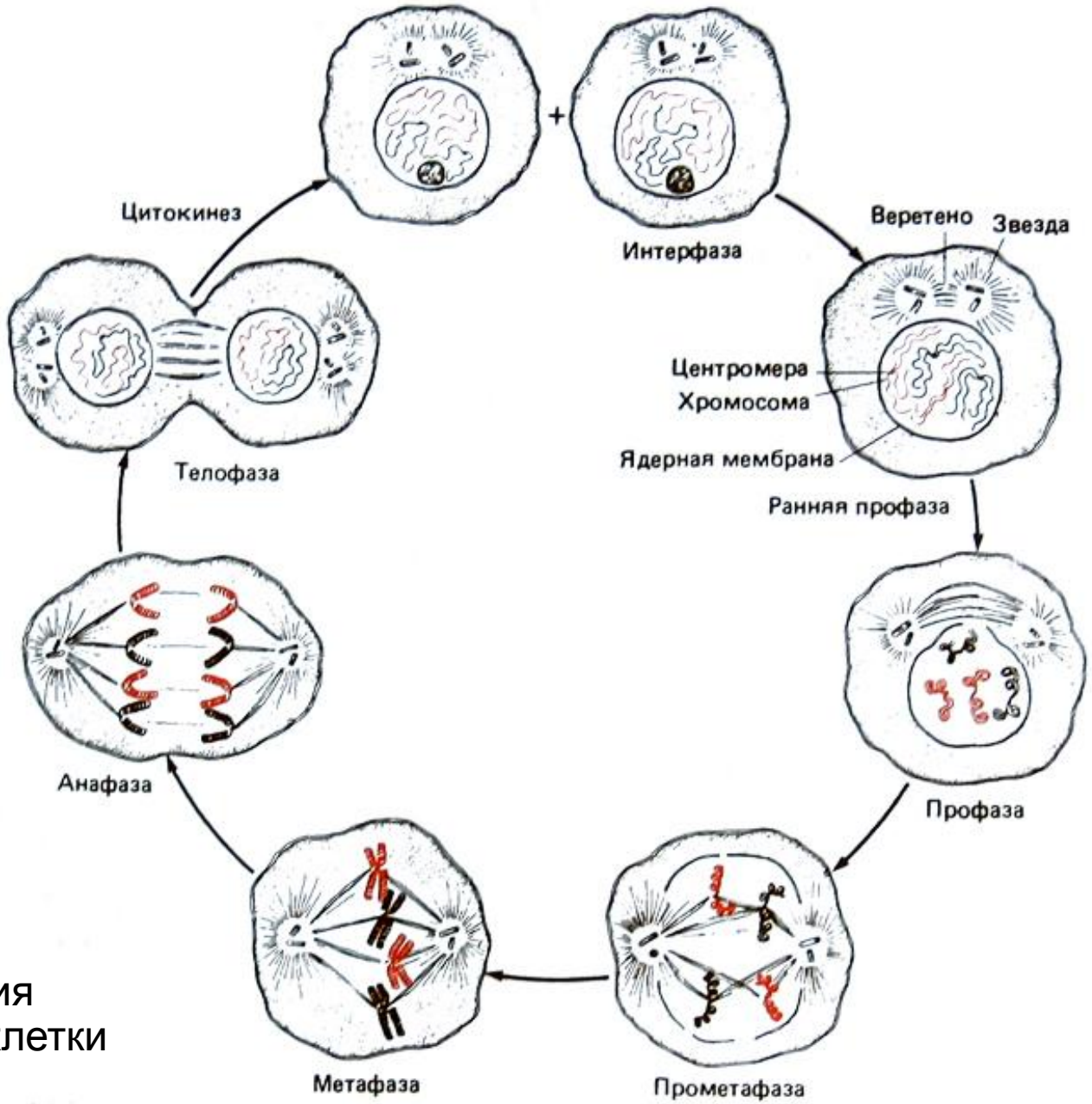
ПРОКАРИОТИЧЕСКАЯ КЛЕТКА



ЭУКАРИОТИЧЕСКИЕ КЛЕТКИ



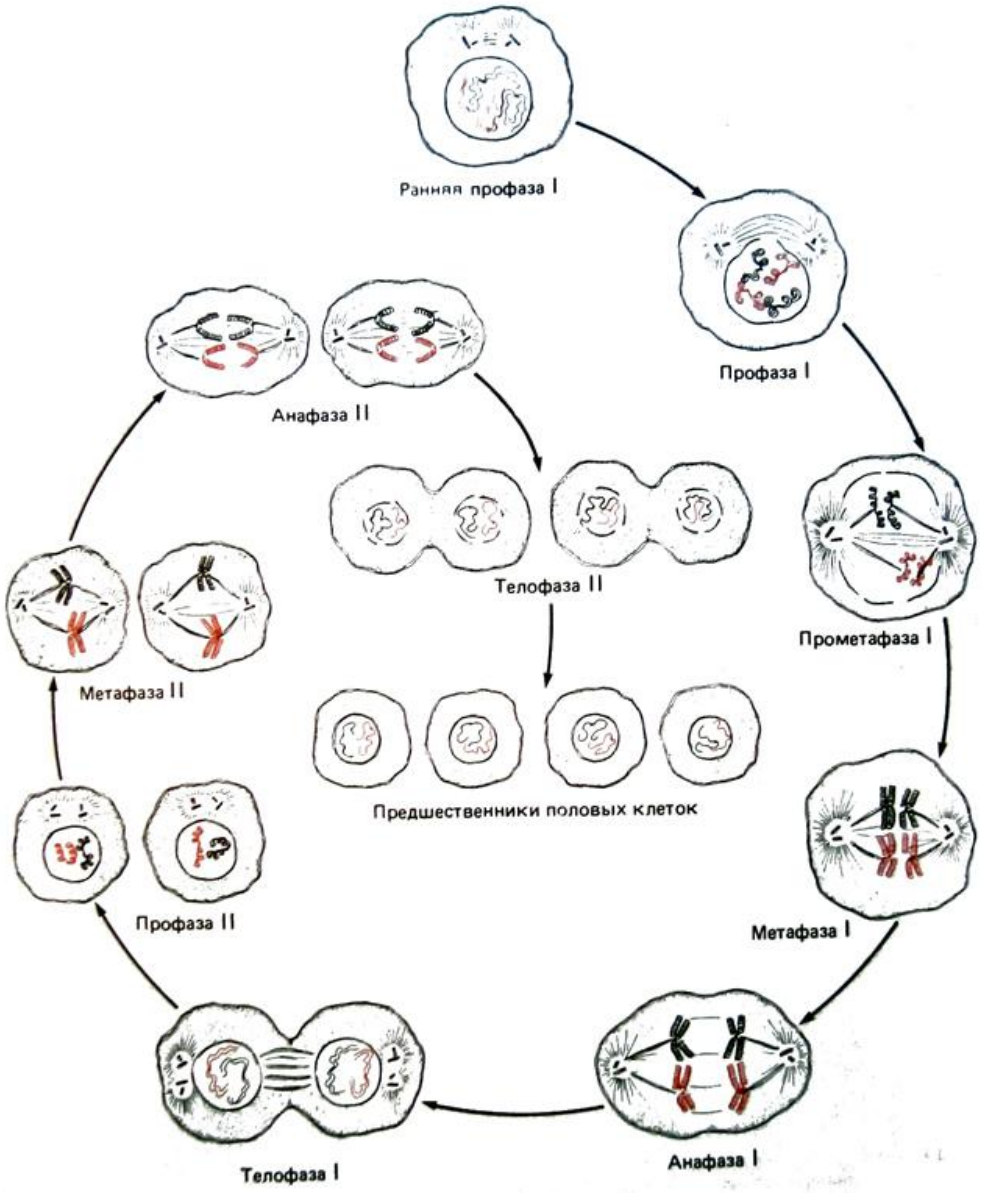
МИТОЗ



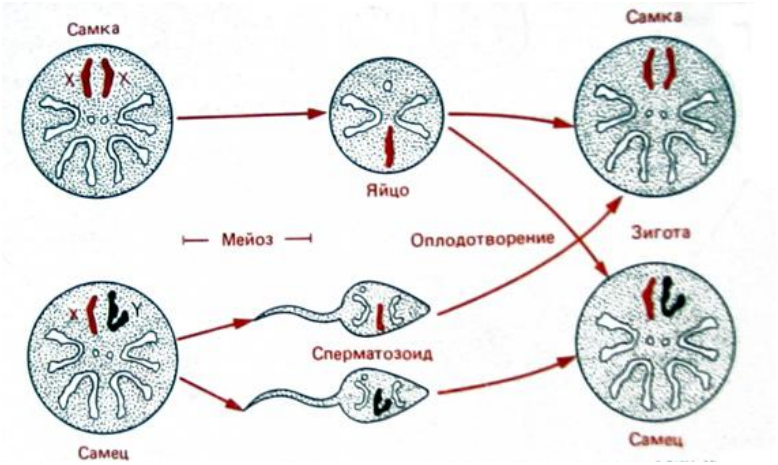
Этапы деления диплоидной клетки

МИТОЗ

МЕЙОЗ И ОБРАЗОВАНИЕ ГАМЕТ



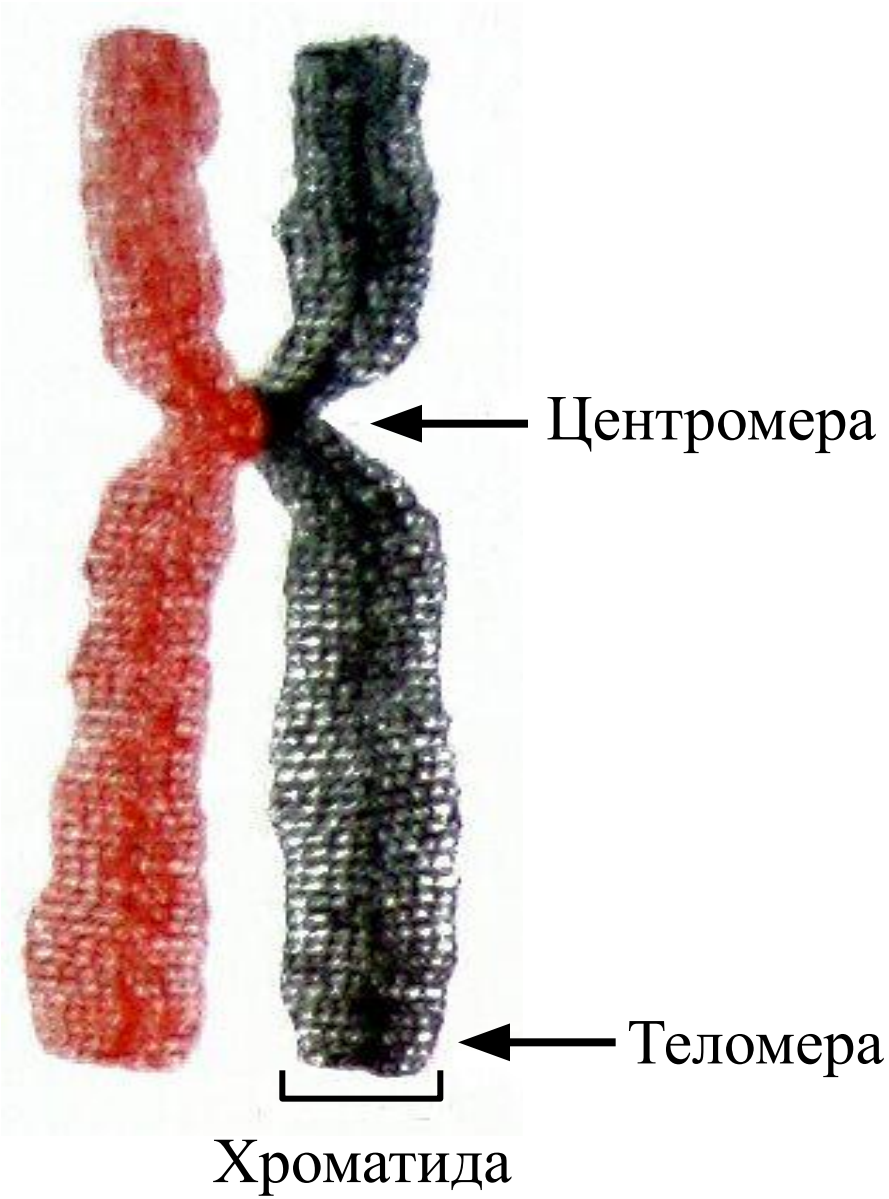
Мейоз: этапы деления диплоидной клетки на четыре гаплоидные дочерние клетки



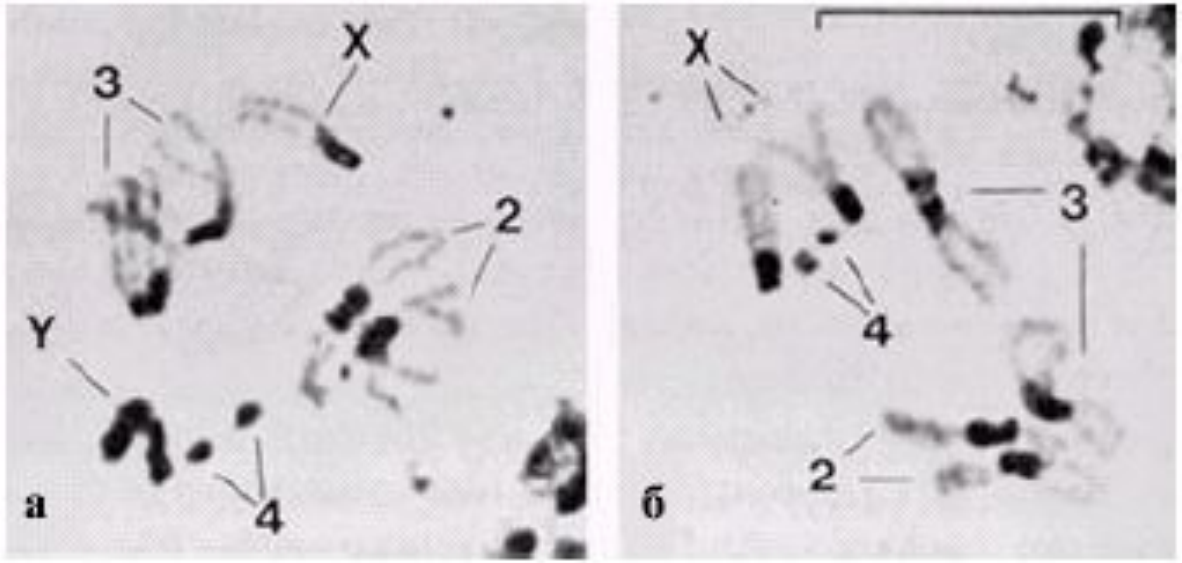
Образование гаплоидных гамет при мейозе и слияние двух гамет с образованием диплоидной клетки при оплодотворении.

СТРОЕНИЕ ХРОМОСОМ

Фотография некоторых хромосом человека, полученная с помощью сканирующего электронного микроскопа

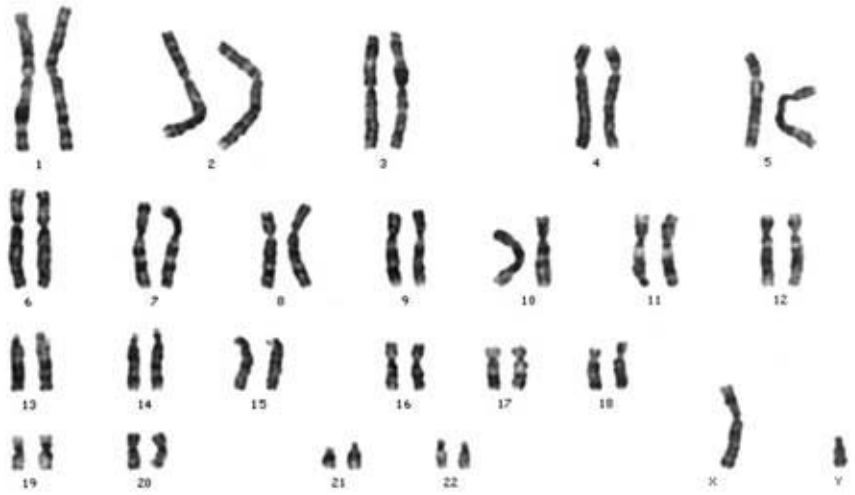


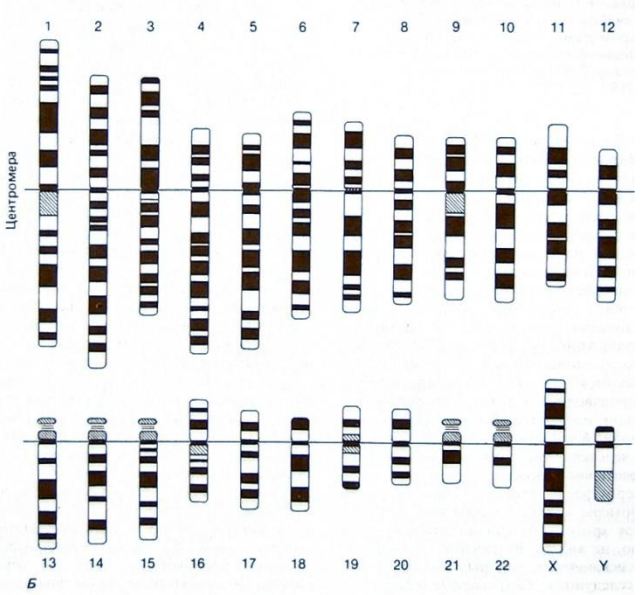
ЭУХРОМАТИН И ГЕТЕРОХРОМАТИН



Локализация эу-(светлые части хромосом) и гетерохроматина (интенсивно окрашенные участки) в кариотипе дрозофилы по результатам С-окрашивания. а - самец, б - самка. Цифры - номера хромосом. X и Y - половые хромосомы. Шкала 10 мкм.

КАРИОТИП И ИДИОГРАММА





Нормальный кариотип человека (мужчина) и идиограмма хромосом построенная на его основе

ГЕН - ХРОМОСОМА - ДНК

Грегор Мендель

Томас Морган

Фридрих Мишер

Ген - гипотетическая единица информации, регулирующая наследование индивидуальных признаков организма

Ген - участок ДНК, кодирующий одну полипептидную цепь или одну молекулу тРНК, рРНК или sРНК

Геном - суммарная ДНК одного набора хромосом и внехромосомных генетических элементов организма.

ХРОНОЛОГИЯ ОТКРЫТИЙ, ПОДГОТОВИВШИХ СОЗДАНИЕ УОТСОНОМ И КРИКОМ МОДЕЛИ ДВОЙНОЙ СПИРАЛИ ДНК

1868 г. Обнаружен нуклеин. Современное название - хроматин. Фридрих Мишер

1889 г. Нуклеин разделен на нуклеиновую кислоту и белок. Появился термин "нуклеиновая кислота". Рихард Альтман

1900 г. Все азотистые основания были описаны химиками.

1909 г. В нуклеиновых кислотах обнаружены фосфорная кислота и рибоза. Левин

1930 г. Найдена дезоксирибоза. Левин

1938 г. Рентгеноструктурный анализ показал, что расстояние между нуклеотидами в ДНК 3,4 Ангстрема. При этом азотистые основания уложены стопками. Уильям Астбюри, Флорин Белл

1947 г. С помощью прямого и обратного титрования установлено, что в ДНК есть водородные связи между группами N-H и C=O. Гулланд

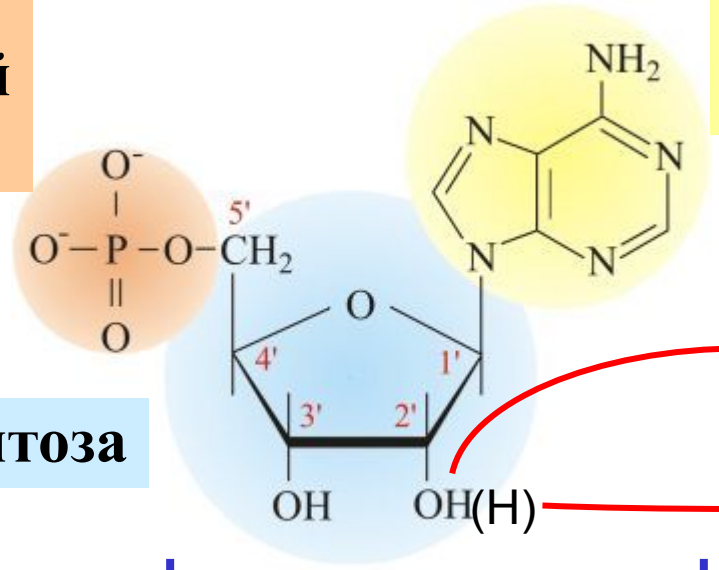
1953 г. С помощью кислотного гидролиза ДНК с последующей хроматографией и количественным анализом установлены закономерности: А/Т=1; Г/Ц=1; (Г+Ц)/(А+Т)=К - коэффициент специфичности, постоянен для каждого вида. Эрвин Чаргафф (Правила Чаргаффа)

СТРУКТУРА НУКЛЕИНОВЫХ КИСЛОТ

Нуклеиновые кислоты являются нерегулярными полимерами, мономеры которых – нуклеотиды

остаток фосфорной кислоты

азотистое основание



пентоза

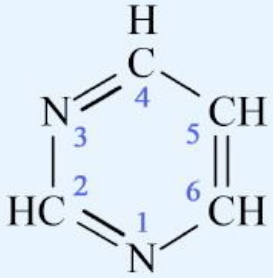
В РНК пентоза – *рибоза*, в ДНК – *дезоксирибоза*

НУКЛЕОЗИД

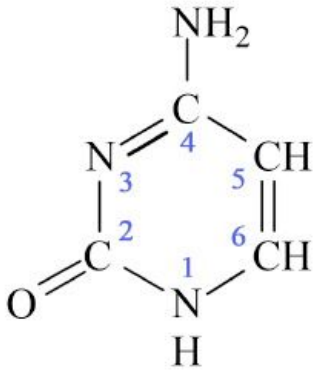
НУКЛЕОТИД

НУКЛЕОТИД = НУКЛЕОЗИД + ФОСФОРНАЯ КИСЛОТА =
= АЗОТИСТОЕ ОСНОВАНИЕ + ПЕНТОЗА + ФОСФОРНАЯ КИСЛОТА

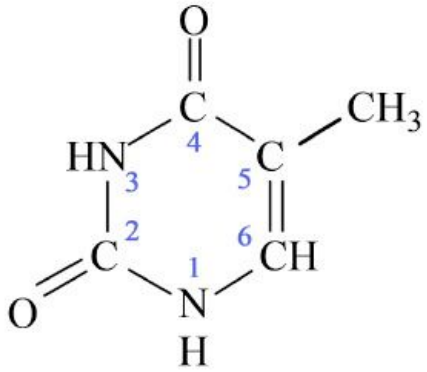
СТРУКТУРА НУКЛЕИНОВЫХ КИСЛОТ



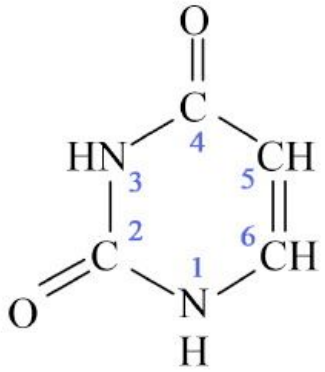
Pyrimidine



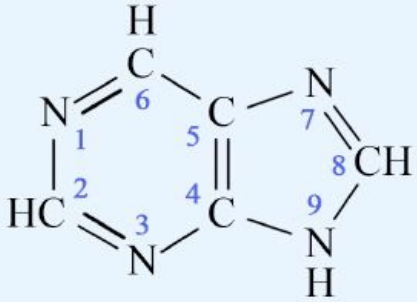
Cytosine
(in DNA & RNA)



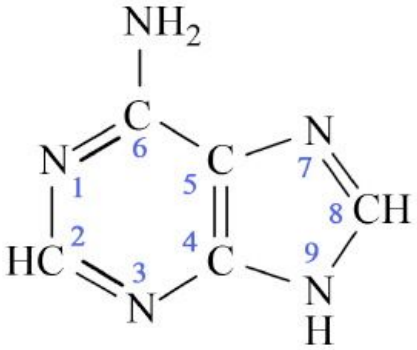
Thymine
(in DNA
& some RNA)



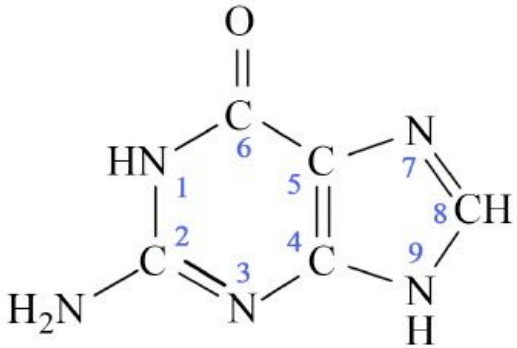
Uracil
(in RNA)



Purine



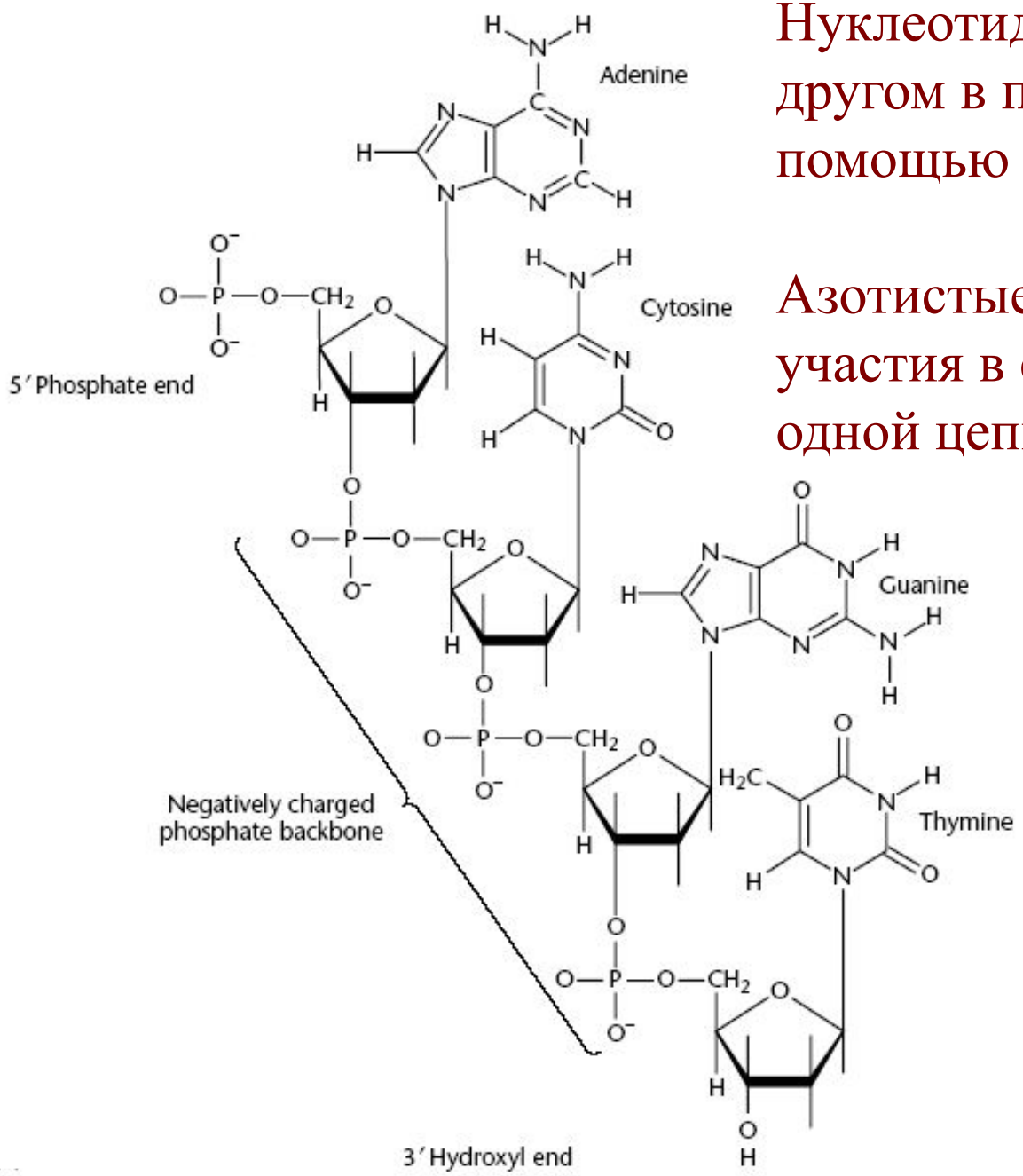
Adenine
(in DNA & RNA)



Guanine
(in DNA & RNA)

Существует два класса азотистых оснований.
Пурины **(два гетероцикла): аденин (A) и гуанин (G).**
Пиримидины **(один гетероцикл): тимин (T), цитозин (C) и урацил (U).**
T встречается в ДНК, U – в РНК

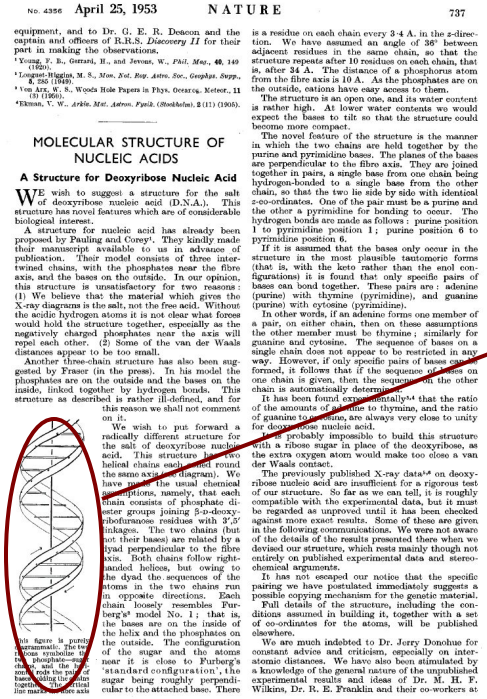
СТРУКТУРА НУКЛЕИНОВЫХ КИСЛОТ



Нуклеотиды соединяются друг с другом в полимерную цепочку с помощью фосфодиэфирных связей.

Азотистые основания не принимают участия в соединении нуклеотидов одной цепи.

СПИРАЛЬНАЯ СТРУКТУРА ДНК



No. 4356 April 25, 1953 NATURE 737

equipment, and to Dr. G. E. R. Deacon and the captain and officers of R.R.S. *Discovery II* for their part in making the observations.

¹ Young, F. B., Gerrard, H., and Jevons, W., *Phil. Mag.*, **40**, 149 (1920).
² Longuet-Higgins, M. S., *Mon. Not. Roy. Astro. Soc., Geophys. Supp.*, **5**, 285 (1949).
³ Von Arx, W. S., Woods Hole Papers in Phys. Oceanog., Meteor., **11** (3) (1950).
⁴ Ekman, V. W., *Arkiv. Mat. Astron. Fysik. (Stockholm)*, **2** (11) (1905).

MOLECULAR STRUCTURE OF NUCLEIC ACIDS

A Structure for Deoxyribose Nucleic Acid

We wish to suggest a structure for the salt of deoxyribose nucleic acid (D.N.A.). This structure has novel features which are of considerable biological interest.

A structure for nucleic acid has already been proposed by Pauling and Corey[1]. They kindly made their manuscript available to us in advance of publication. Their model consists of three inter-twined chains, with the phosphates near the fibre axis, and the bases on the outside. In our opinion, this structure is unsatisfactory for two reasons: (1) We believe that the material which gives the X-ray diagrams is the salt, not the free acid. Without the acidic hydrogen atoms it is not clear what forces would hold the structure together, especially as the negatively charged phosphates near the axis will repel each other. (2) Some of the van der Waals distances appear to be too small.

Another three-chain structure has also been suggested by Fraser (in the press). In his model the phosphates are on the outside and the bases on the inside, linked together by hydrogen bonds. This structure as described is rather ill-defined, and for this reason we shall not comment on it.

We wish to put forward a radically different structure for the salt of deoxyribose nucleic acid. This structure has two helical chains each coiled round the same axis (see diagram). We have made the usual chemical assumptions, namely, that each chain consists of phosphate di-ester groups joining β-D-deoxyribofuranose residues with 3′,5′ linkages. The two chains (but not their bases) are related by a dyad perpendicular to the fibre axis. Both chains follow right-handed helices, but owing to the dyad the sequences of the atoms in the two chains run in opposite directions. Each chain loosely resembles Furberg's[2] model No. 1; that is, the bases are on the inside of the helix and the phosphates on the outside. The configuration of the sugar and the atoms near it is close to Furberg's 'standard configuration', the sugar being roughly perpendicular to the attached base. There is a residue on each chain every 3·4 A. in the z-direction. We have assumed an angle of 36° between adjacent residues in the same chain, so that the structure repeats after 10 residues on each chain, that is, after 34 A. The distance of a phosphorus atom from the fibre axis is 10 A. As the phosphates are on the outside, cations have easy access to them.

The structure is an open one, and its water content is rather high. At lower water contents we would expect the bases to tilt so that the structure could become more compact.

The novel feature of the structure is the manner in which the two chains are held together by the purine and pyrimidine bases. The planes of the bases are perpendicular to the fibre axis. They are joined together in pairs, a single base from one chain being hydrogen-bonded to a single base from the other chain, so that the two lie side by side with identical z-co-ordinates. One of the pair must be a purine and the other a pyrimidine for bonding to occur. The hydrogen bonds are made as follows: purine position 1 to pyrimidine position 1; purine position 6 to pyrimidine position 6.

If it is assumed that the bases only occur in the structure in the most plausible tautomeric forms (that is, with the keto rather than the enol configurations) it is found that only specific pairs of bases can bond together. These pairs are: adenine (purine) with thymine (pyrimidine), and guanine (purine) with cytosine (pyrimidine).

In other words, if an adenine forms one member of a pair, on either chain, then on these assumptions the other member must be thymine; similarly for guanine and cytosine. The sequence of bases on a single chain does not appear to be restricted in any way. However, if only specific pairs of bases can be formed, it follows that if the sequence of bases on one chain is given, then the sequence on the other chain is automatically determined.

It has been found experimentally[3,4] that the ratio of the amounts of adenine to thymine, and the ratio of guanine to cytosine, are always very close to unity for deoxyribose nucleic acid.

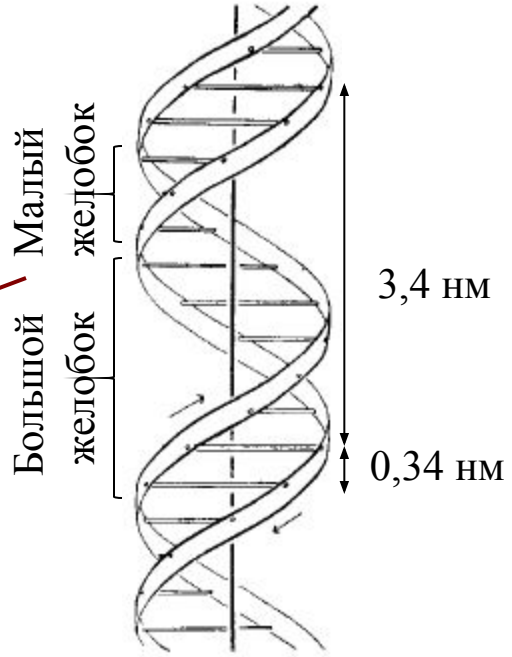
It is probably impossible to build this structure with a ribose sugar in place of the deoxyribose, as the extra oxygen atom would make too close a van der Waals contact.

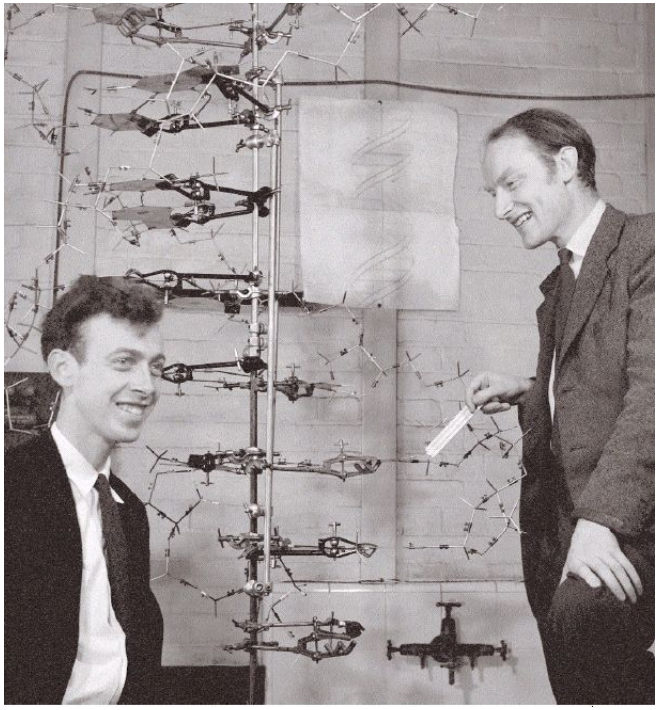
The previously published X-ray data[5,6] on deoxyribose nucleic acid are insufficient for a rigorous test of our structure. So far as we can tell, it is roughly compatible with the experimental data, but it must be regarded as unproved until it has been checked against more exact results. Some of these are given in the following communications. We were not aware of the details of the results presented there when we devised our structure, which rests mainly though not entirely on published experimental data and stereochemical arguments.

It has not escaped our notice that the specific pairing we have postulated immediately suggests a possible copying mechanism for the genetic material.

Full details of the structure, including the conditions assumed in building it, together with a set of co-ordinates for the atoms, will be published elsewhere.

We are much indebted to Dr. Jerry Donohue for constant advice and criticism, especially on interatomic distances. We have also been stimulated by a knowledge of the general nature of the unpublished experimental results and ideas of Dr. M. H. F. Wilkins, Dr. R. E. Franklin and their co-workers at

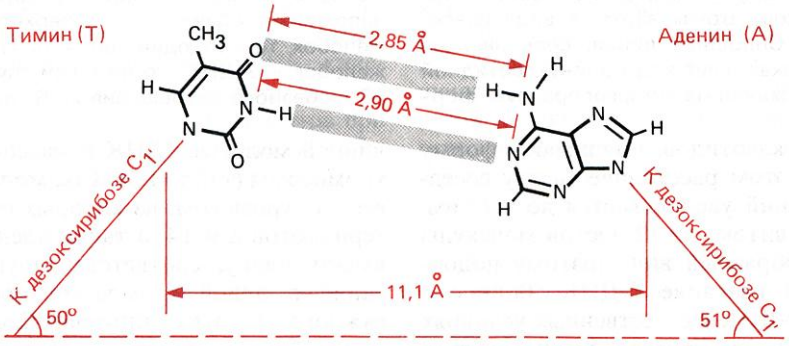


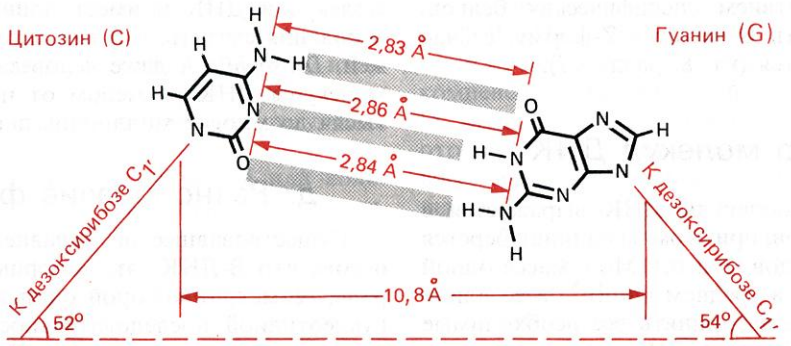


Д. Уотсон и Ф. Крик.1953 г.

PyMol

Уотсон-Криковские взаимодействия





The third Bond

When James Watson and Francis Crick unveiled their structure of DNA, one of the two kinds of base pair in the molecule was given two hydrogen bonds instead of three. Who spotted the third bond and when?

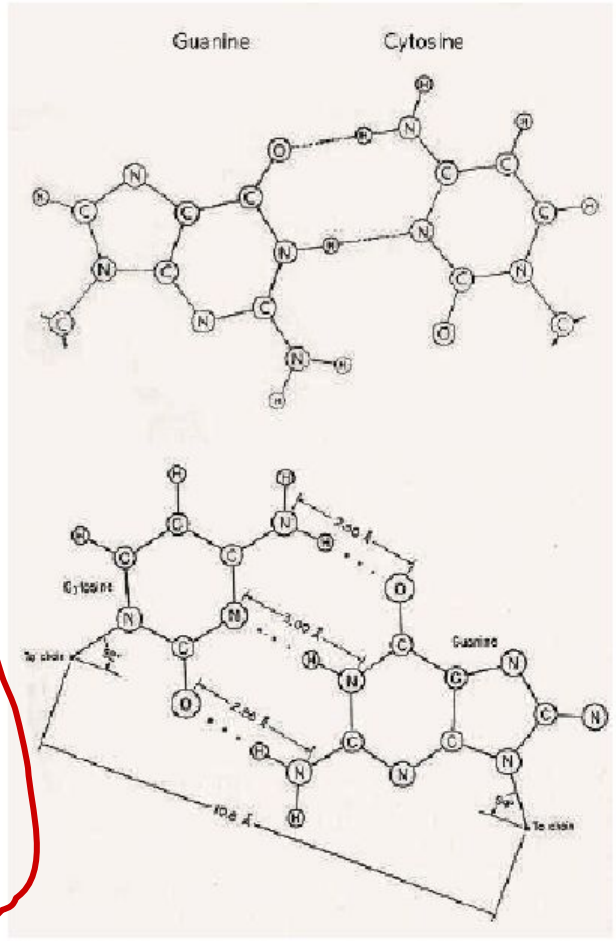
Simon Wain-Hobson

It is a truth universally acknowledged that a guanine–cytosine (GC) base pair has three hydrogen bonds whereas adenine–thymine (AT) has two. But James Watson and Francis Crick didn't see it that way back in 1953 when they published the structure of DNA. In their second DNA paper published in May of that year, the GC base pair is shown with only two hydrogen bonds (see top figure). So who spotted the third bond? When? And why was it initially passed over?

In his book *The Double Helix*, Watson notes that "The formation of a third hydrogen bond between guanine and cytosine was considered but rejected because a crystallographic study of guanine hinted that it would be very weak".

The third hydrogen bond in a GC pair makes its first published appearance in a paper by Linus Pauling and Robert Corey[1] in 1956 (see bottom figure). However, the first hint of the third bond in the scientific literature actually comes in a footnote to a paper published earlier that year by Jerry Donohue, a physical chemist and crystallographer.

In this paper[2], which describes the possible ways in which pyridines and purines



The third hydrogen bond in a guanine–cytosine base pair (bottom) was missed in the 1953 description of DNA (top).

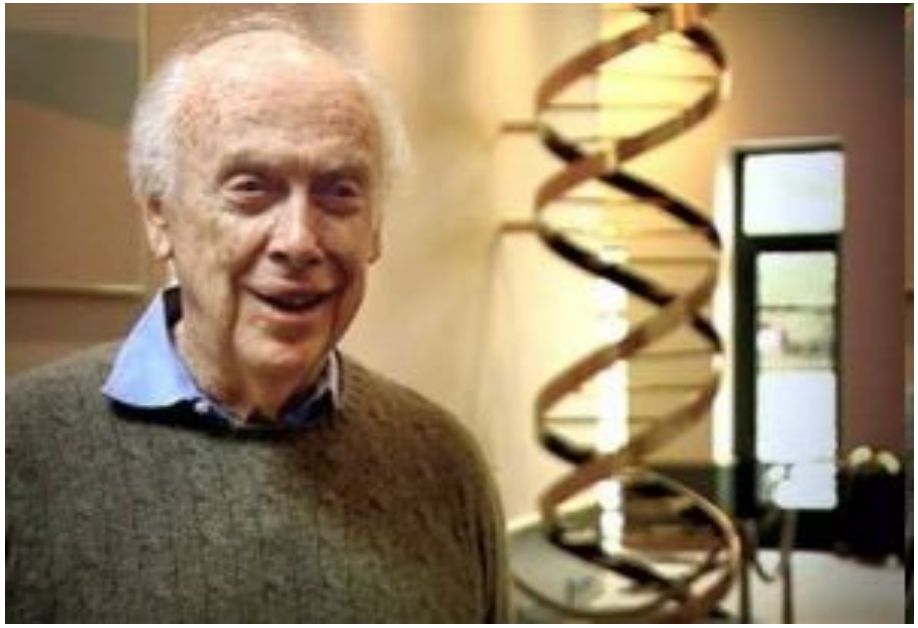
of about 15° was allowed".

Donohue shared the same office as Watson and Crick at the Cavendish Laboratory. It was he who advised Watson over which tautomeric forms of pyrimidines and purines to use in their DNA model.

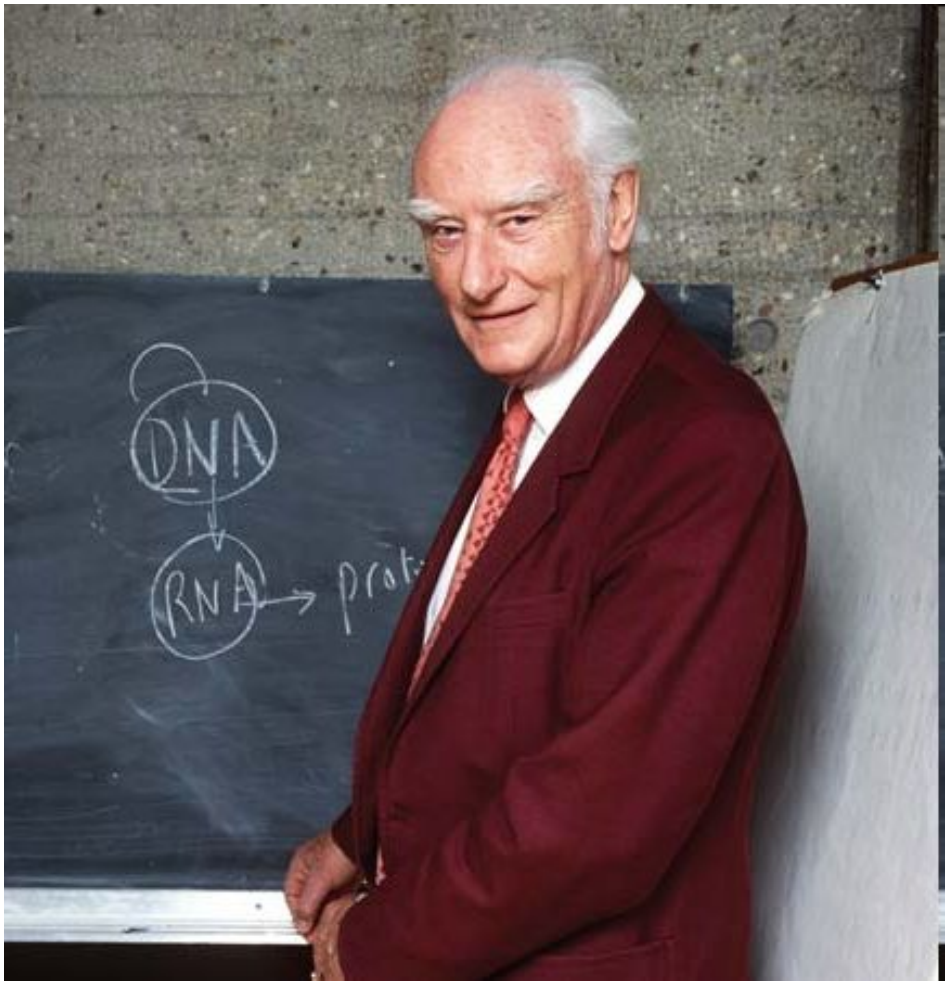
The acknowledgement, "We are much indebted to Dr. Jerry Donohue for constant advice and criticism, especially in inter-atomic distances," appears at the end of the first DNA paper — indeed before mention of Maurice Wilkins and Rosalind Franklin, both key players in the discovery of DNA's structure. So it may be presumed that Watson and Crick deferred to Donohue and cut the third bond.

Pauling and Corey, however, arrived at the right structure thanks to a strong dose of structural common sense. They note that the structure for guanine contains "a small error" in that angles of the bonds adjacent to the keto group are irregular.

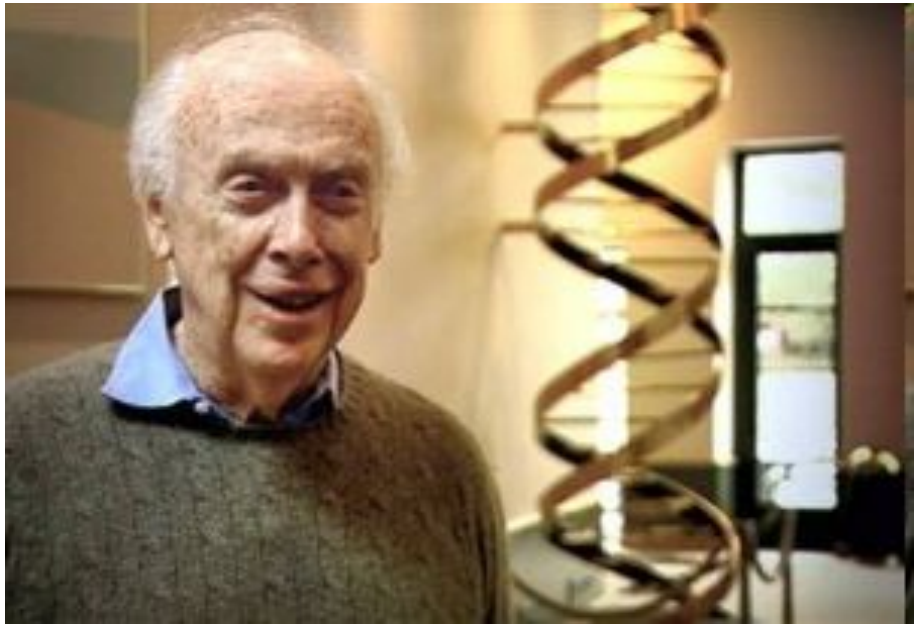
James Watson Francis Crick

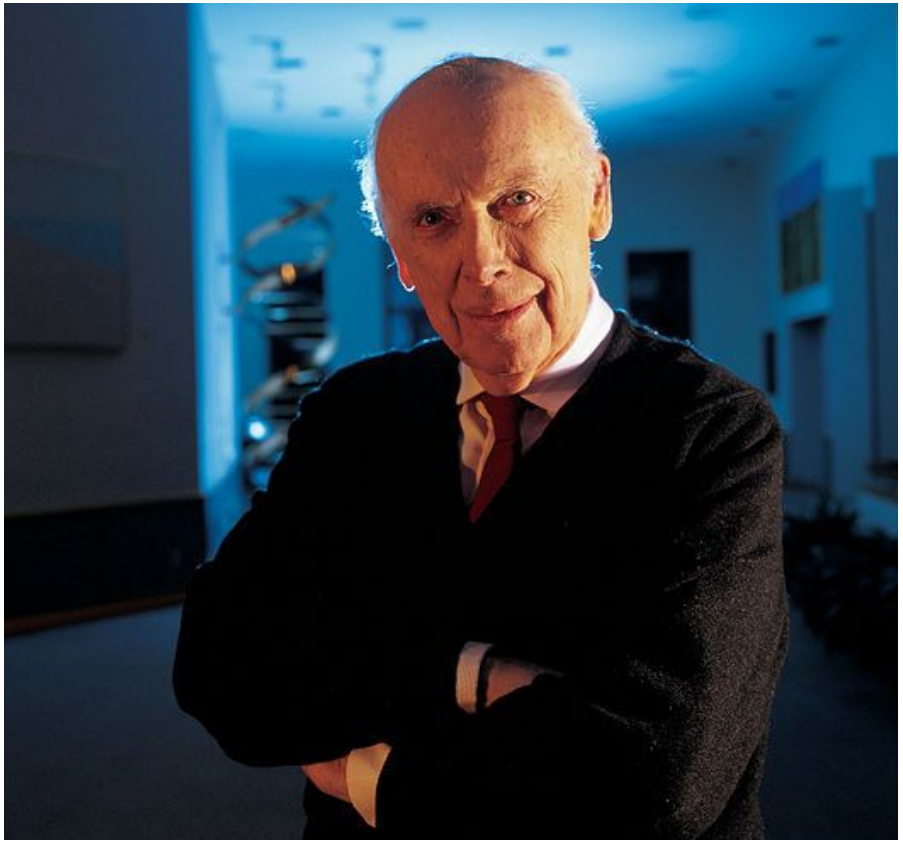


James Watson



Francis Crick

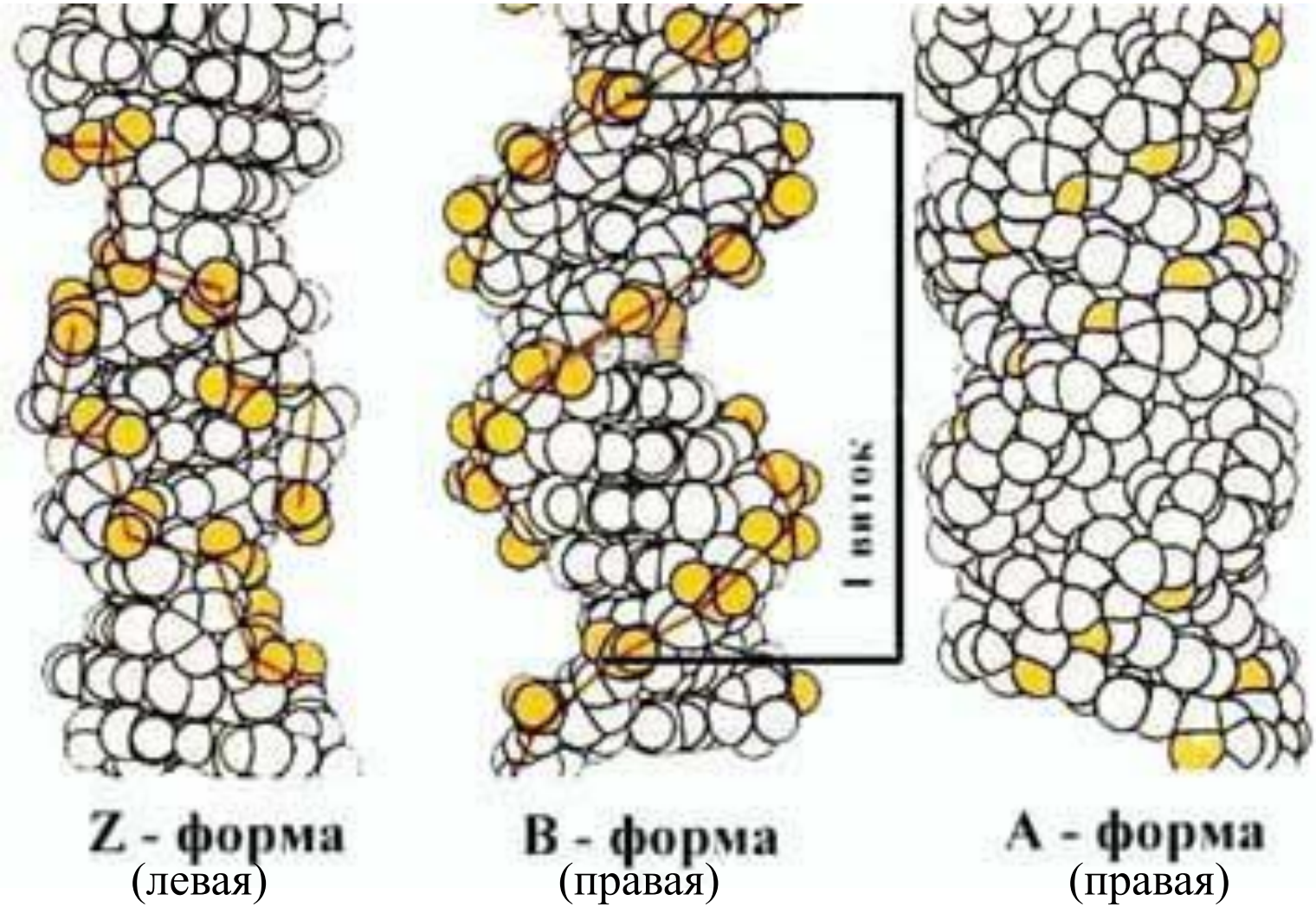




James Watson

Francis Crick

АЛЬТЕРНАТИВНЫЕ ФОРМЫ ДВОЙНОЙ СПИРАЛИ



Z - форма (левая)

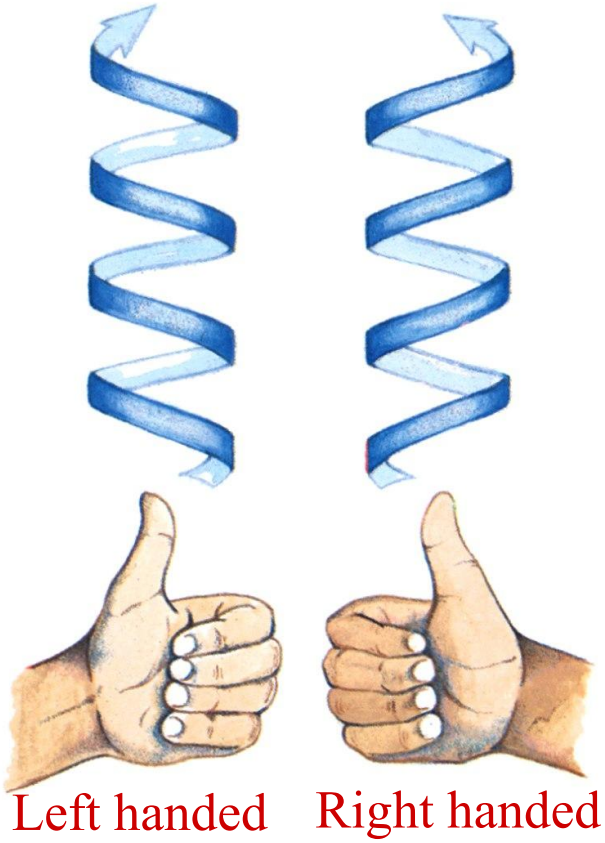
B - форма (правая)

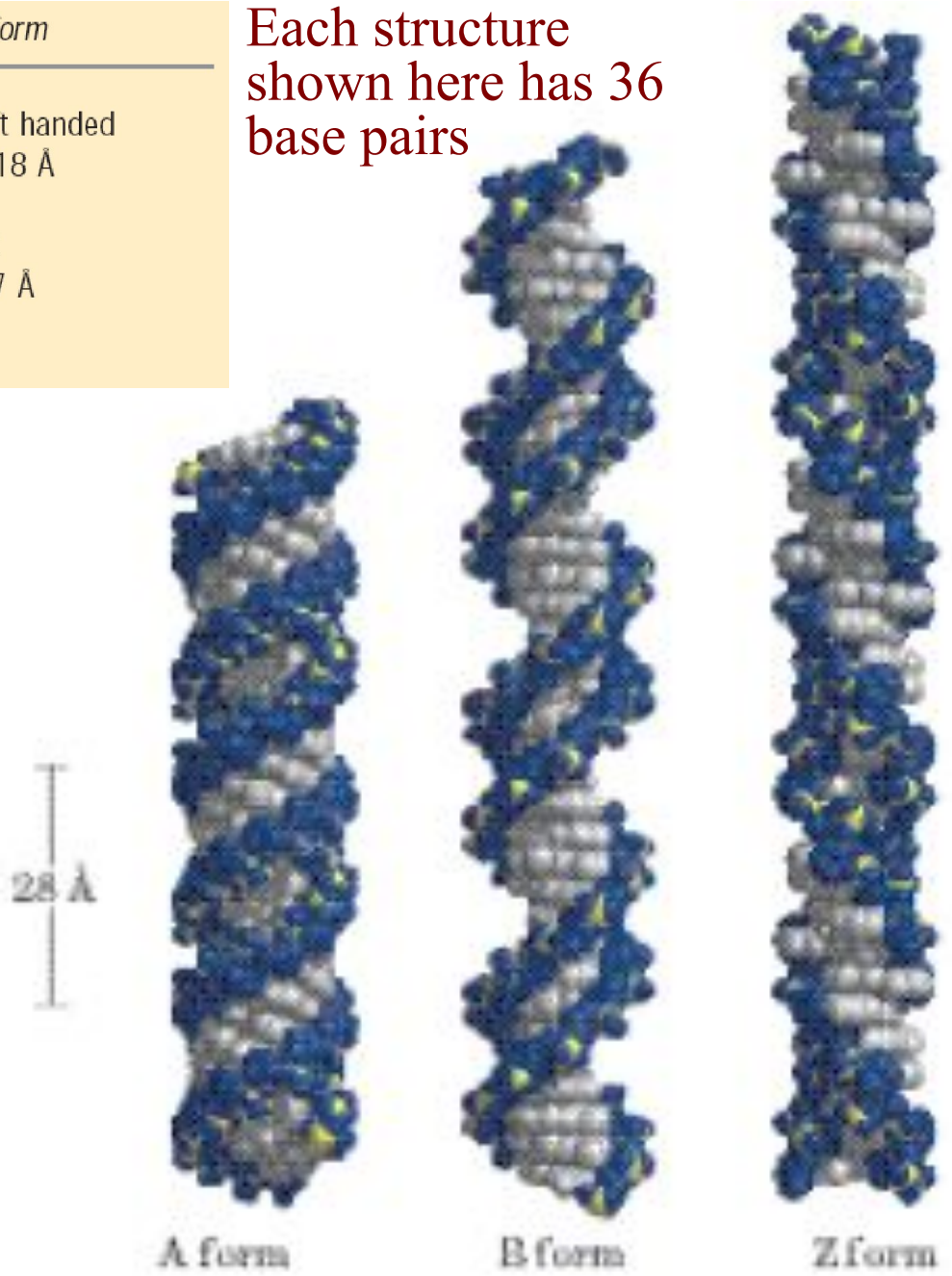
A - форма (правая)

12.3 АЛЬТЕРНАТИВНЫЕ ФОРМЫ ДВОЙНОЙ СПИРАЛИ

	A form	*B form*	*Z form*
Helical sense	Right handed	Right handed	Left handed
Diameter	~26 Å	~20 Å	~18 Å
Base pairs per helical turn	11	10.5	12
Helix rise per base pair	2.6 Å	3.4 Å	3.7 Å
Base tilt normal to the helix axis	20°	6°	7°

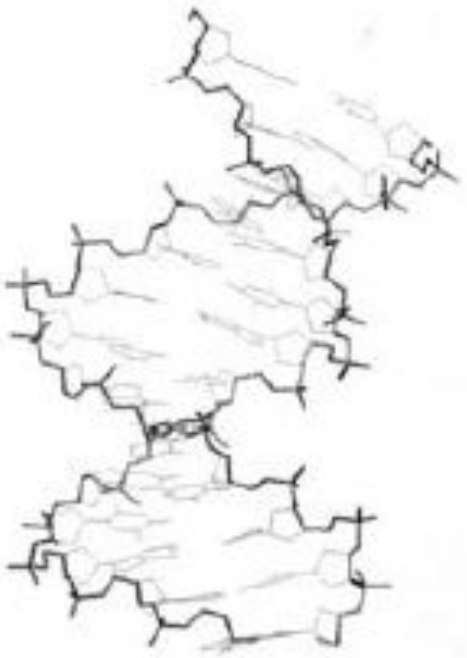
Each structure shown here has 36 base pairs



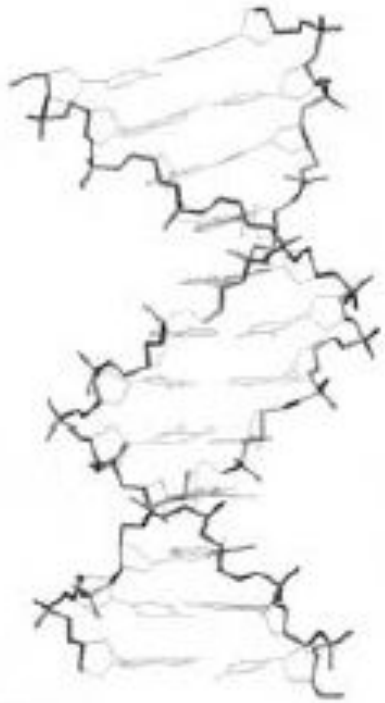


	A form	*B form*	*Z form*
Helical sense	Right handed	Right handed	Left handed
Diameter	26 Å	20 Å	18 Å
Base pairs per helical turn	11	10.5	12
Helix rise per base pair	2.6 Å	3.4 Å	3.7 Å
Base tilt normal to the helix axis	20°	6°	7°

12.5 АЛЬТЕРНАТИВНЫЕ ФОРМЫ ДВОЙНОЙ СПИРАЛИ

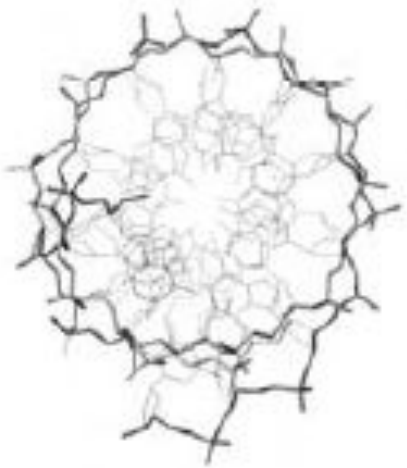


A-DNA
d(AGCTTGCCTTGAG)

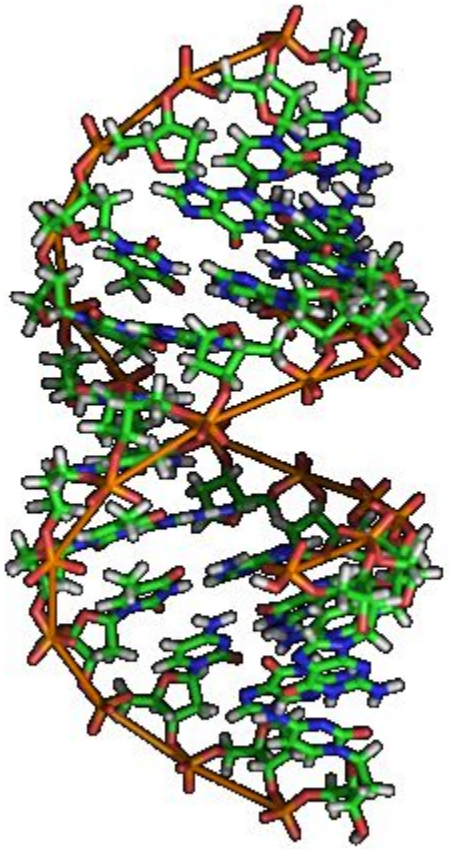


B-DNA
d(CGCGAATTCGCG)

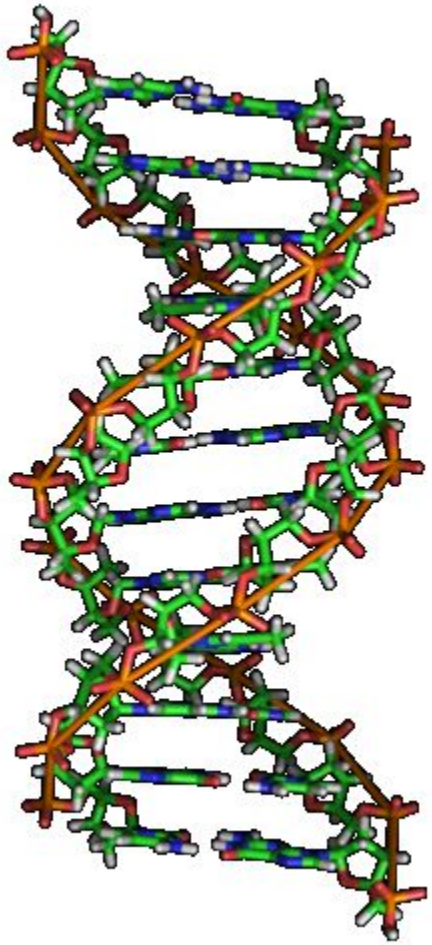
Z-DNA
d(CGCGCGTTTTCGCG)



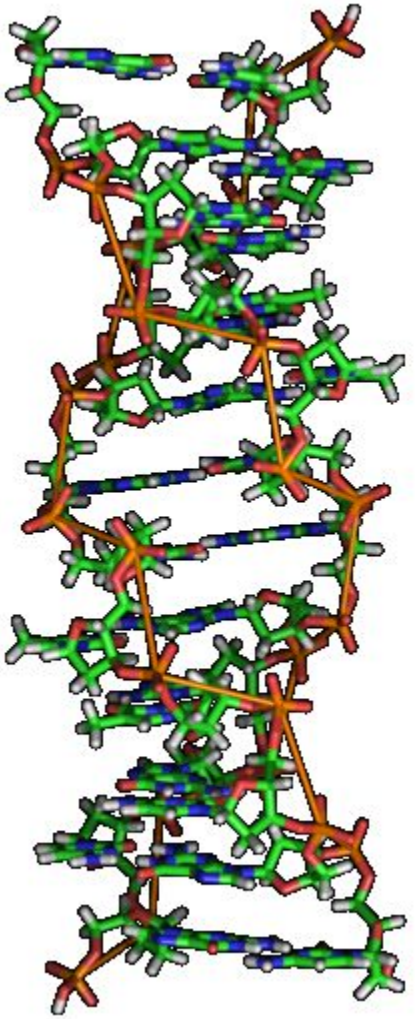
12.55 АЛЬТЕРНАТИВНЫЕ ФОРМЫ ДВОЙНОЙ СПИРАЛИ



A-form



B-form



Z-form

The A form is favored in many solutions that are relatively devoid of water

Оказалось, однако, что наряду с правыми существуют и *левые* спирали ДНК. Первоначально левая спираль, получившая название *Z-формы* (рис. 15), была обнаружена у полинуклеотида с чередующейся последовательностью $d(GC)_n$. Цепи поли(dG-dC) самокомплементарны и в растворе с низкой ионной силой образуют правые двойные спирали B-типа. При высокой концентрации солей или добавлении спирта эта двойная спираль переходит в левую Z-форму.

Whether A-DNA occurs in cells is uncertain, but there is evidence for some short stretches (tracts) of Z-DNA in both prokaryotes and eukaryotes. These Z-DNA tracts may play a role (as yet undefined) in regulating the expression of some genes or in genetic recombination.

Biological significance of Z-DNA

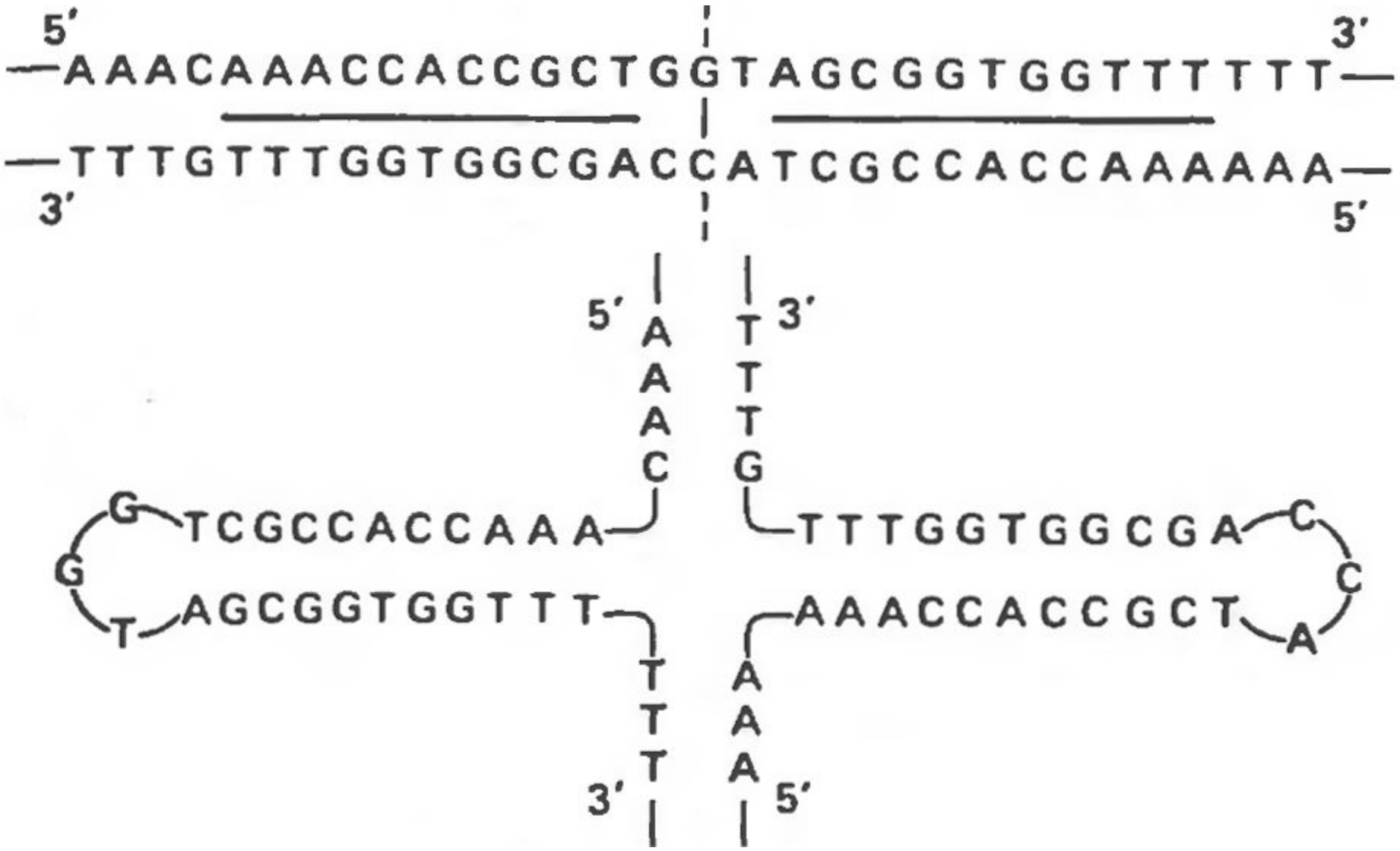
While no definitive biological significance of Z-DNA has been found, it is commonly believed to provide torsional strain relief (supercoiling) while DNA transcription occurs. The potential to form a Z-DNA structure also correlates with regions of active transcription. A comparison of regions with a high sequence-dependent, predicted propensity to form Z-DNA in human chromosome 22 with a selected set of known gene transcription sites suggests there is a correlation.

Z-DNA formed after transcription initiation in some cases may be bound by RNA modifying enzymes, such as ADAR1, which then alter the sequence of the newly-formed RNA.

In 2003, Biophysicist Alexander Rich of the Massachusetts Institute of Technology noticed that a poxvirus virulence factor, called E3L, mimicked a mammalian protein that binds Z-DNA. In 2005, Rich and his colleagues pinned down what E3L does for the poxvirus. When expressed in human cells, E3L increases by five- to 10-fold the production of several genes that block a cell's ability to self-destruct in response to infection.

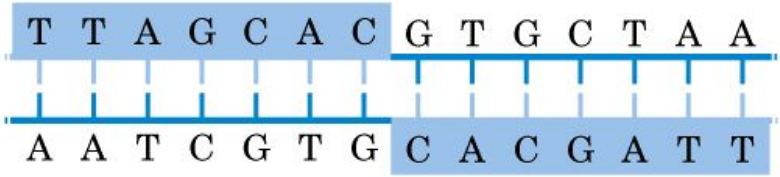
Rich speculates that the Z-DNA is necessary for transcription and that E3L stabilizes the Z-DNA, thus prolonging expression of the anti-apoptotic genes. He suggests that a small molecule that interferes with the E3L binding to Z-DNA could thwart the activation of these genes and help protect people from pox infections.

Крестообразные структуры ДНК



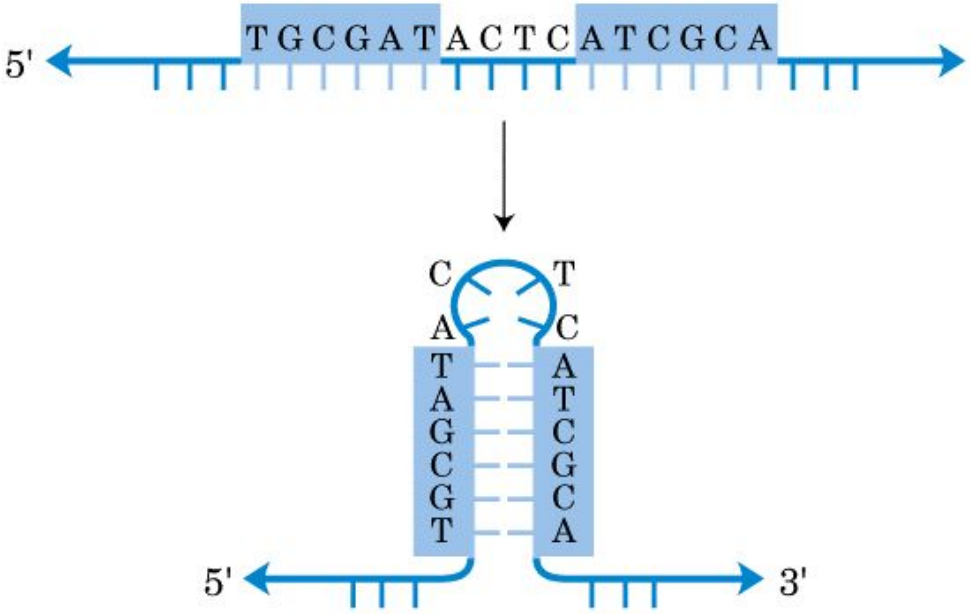
Шпильки и крестообразные структуры ДНК

Палиндром – слово или фраза, которая одинаково читается в обоих направлениях: ***ROTATOR***.
(SAIPPUAKIVIKAUPPIAS = продавец мыла – самое длинное в мире слово-палиндром.)

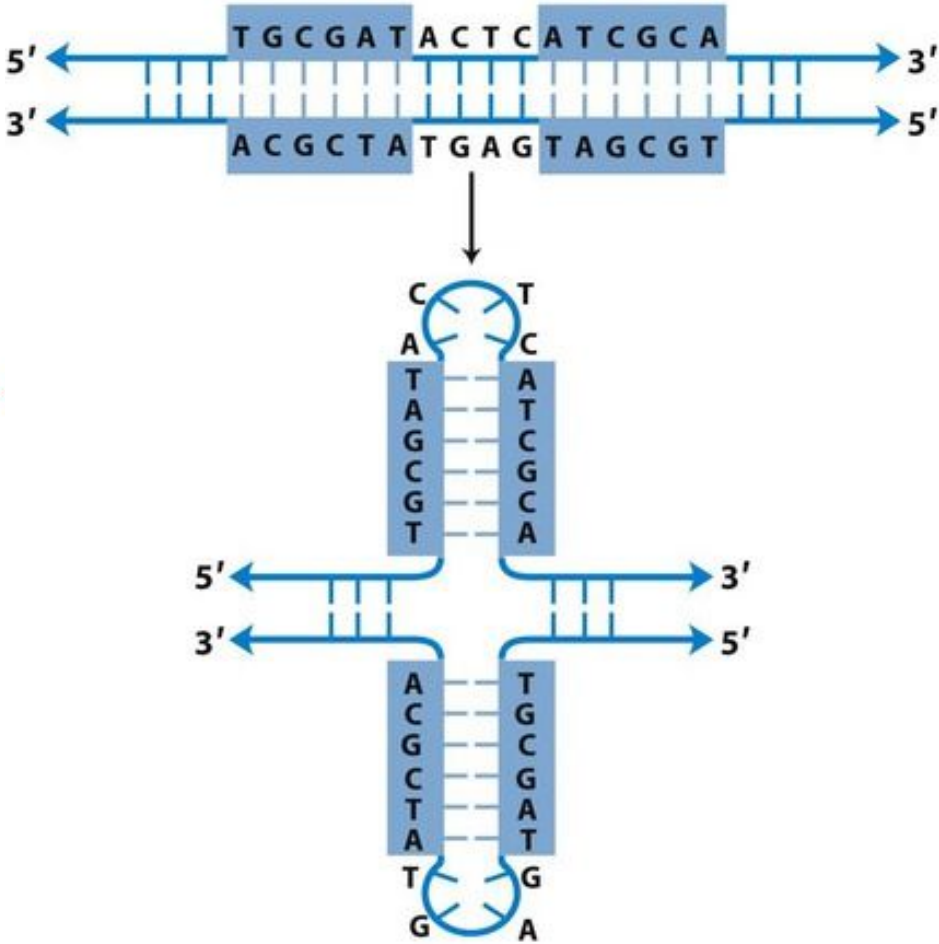


Палиндром

Этот термин используют для обозначения участков двухцепочечной ДНК с ивертированными повторами.

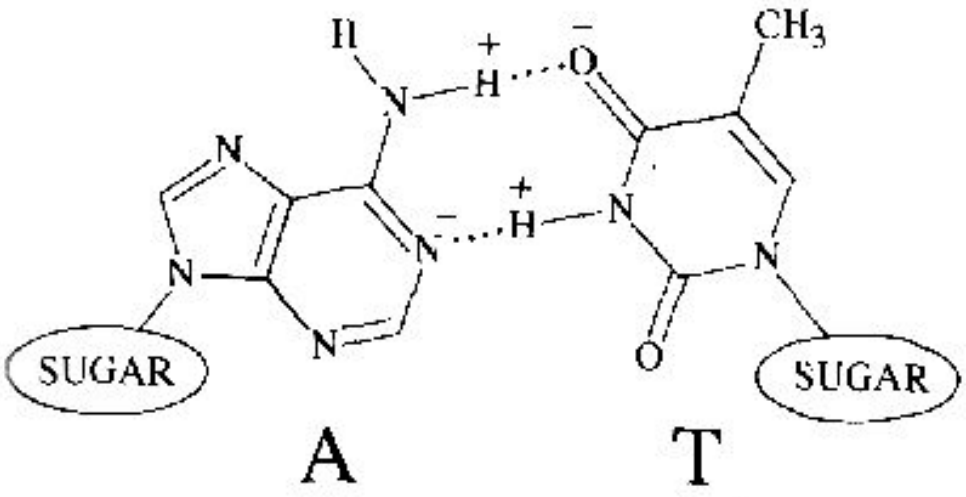


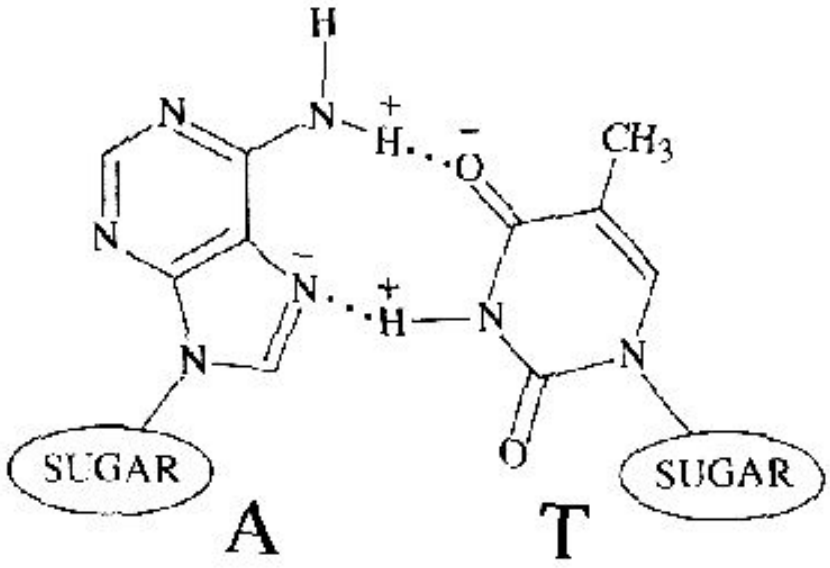
Шпилька



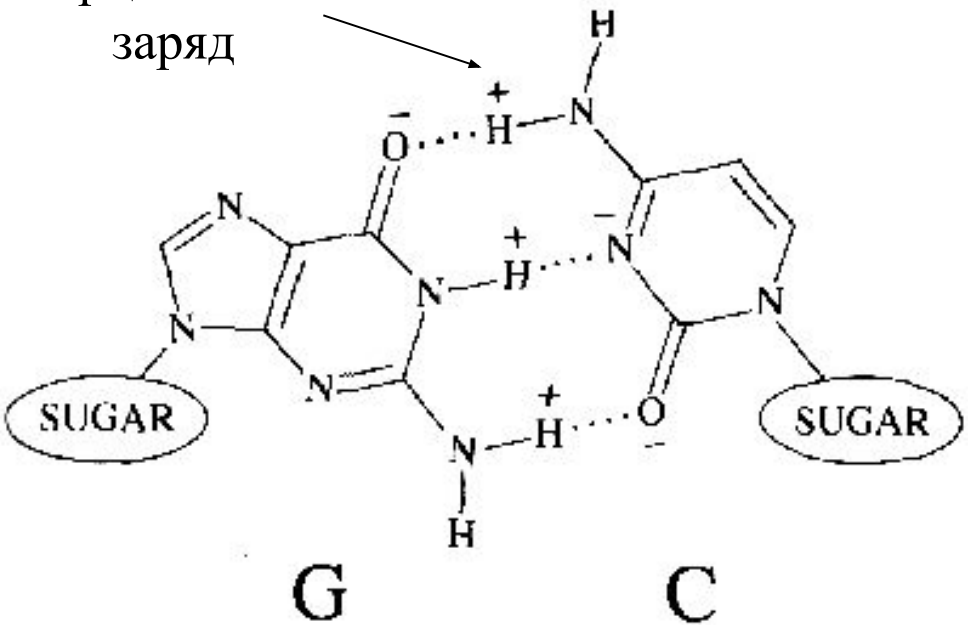
Крестообразная структура

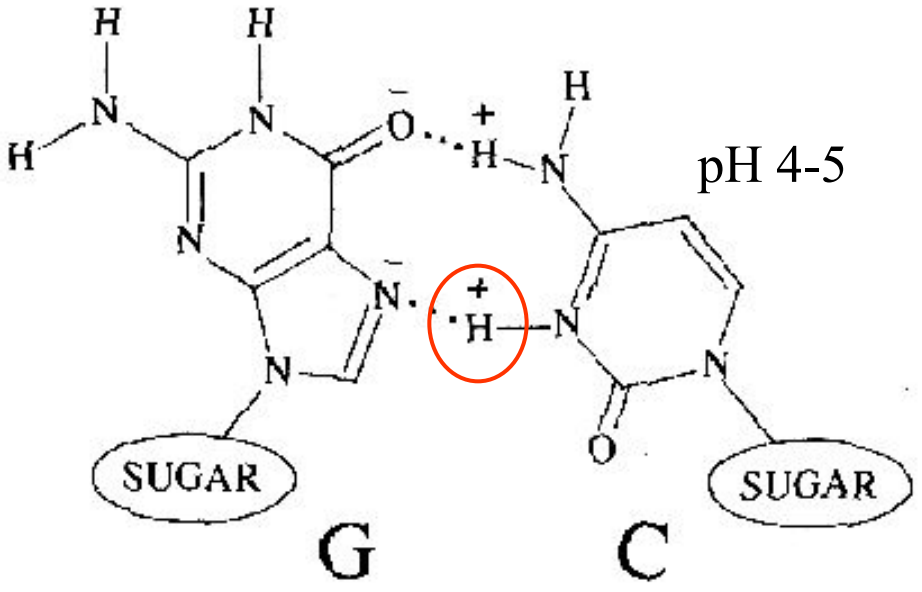
12.7 *Пары Хугстина (Hoogsteen base-pare)*





Парциальный заряд

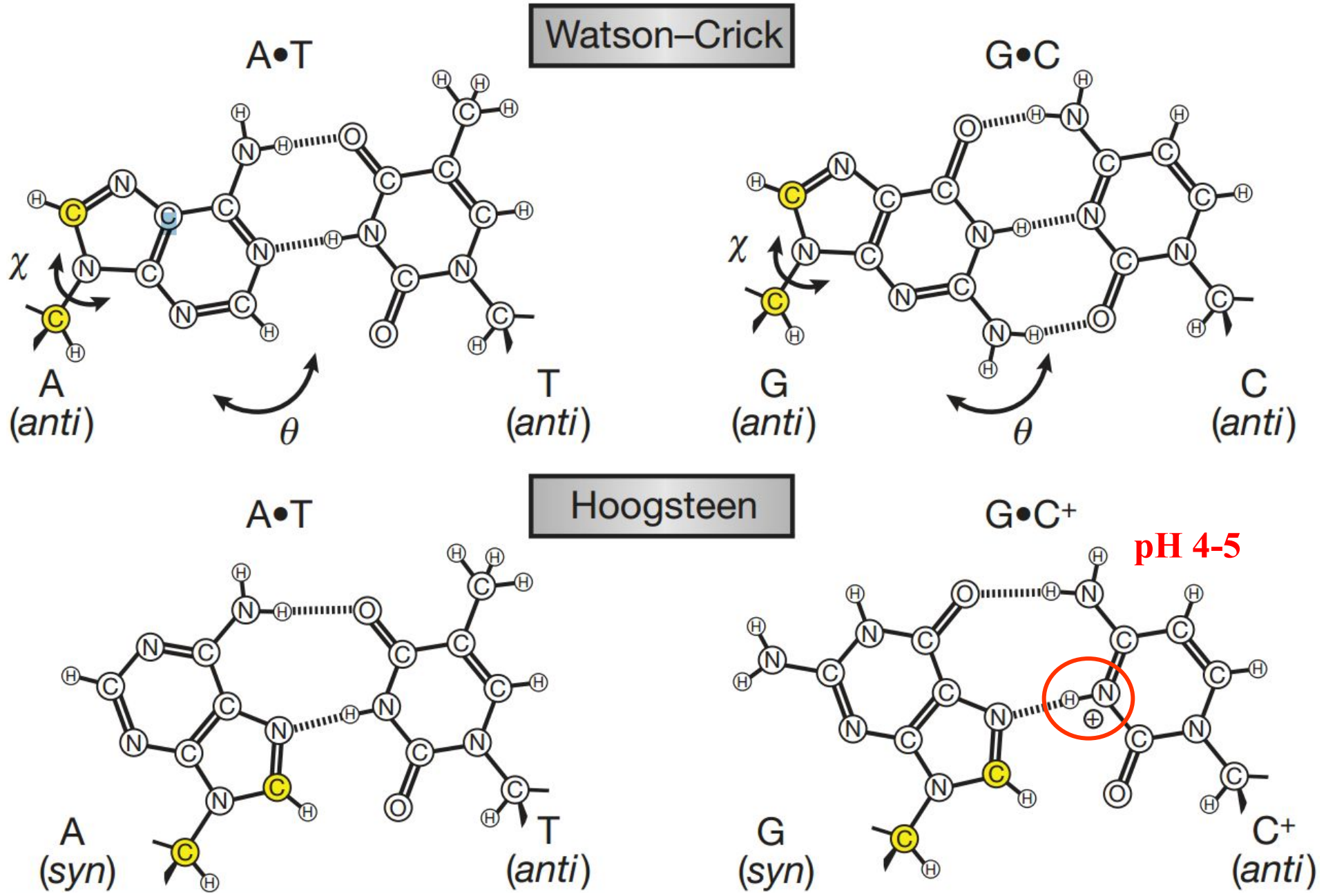




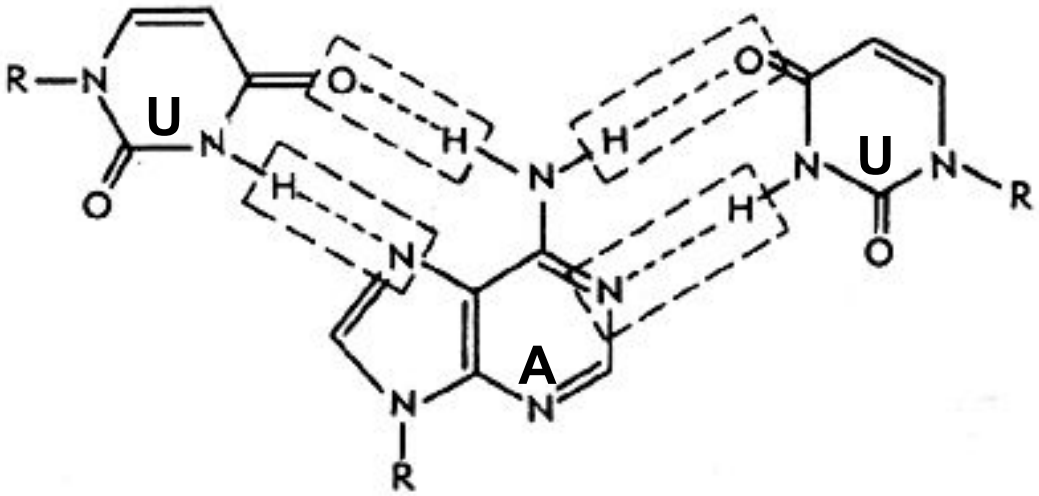
Уотсон-Криковские пары

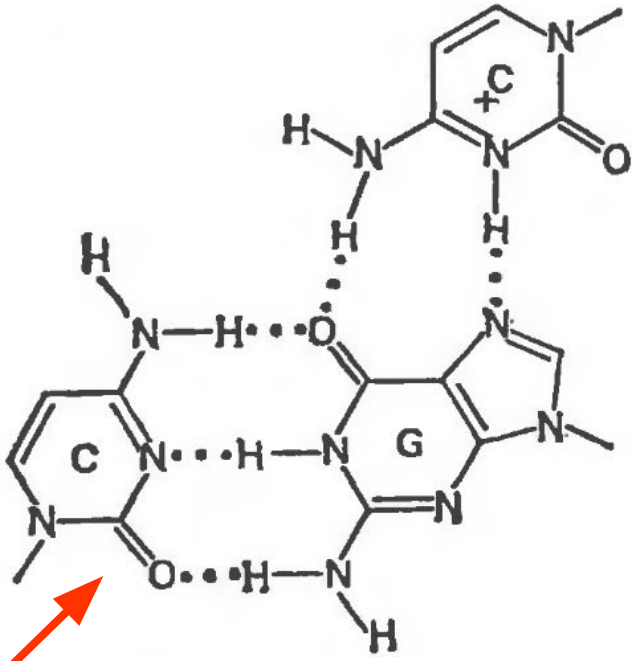
Хугстиновские пары

12.7 *Пары Хугстина (Hoogsteen base-pare)*



12.8 *Пары Хугстина в альтернативных структурах ДНК*





Взаимное расположение гетероциклов в тройном комплексе полиадениловой кислоты с двумя цепями полиуридиловой

Взаимное расположение гетероциклов в тройной спирали Н-ДНК

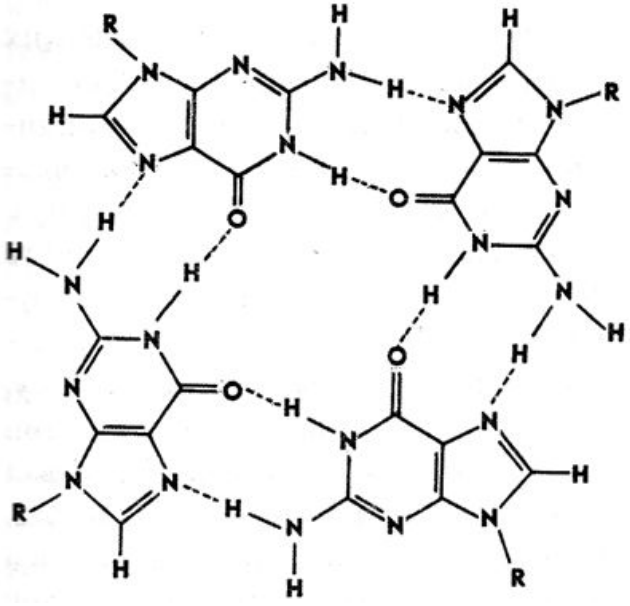
H-форма ДНК (H-ДНК)

Если ДНК содержит гомопиримидин - гомопуриновые последовательности, то под влиянием отрицательной сверхспирализации она может переходить в форму H-ДНК.

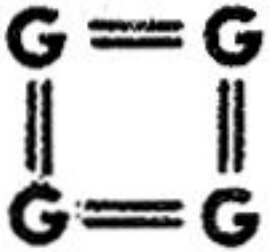
Возможная структура H-ДНК. Полипиримидиновая цепь (серая) лежит в большой бороздке двойно спирали. Полипуриновая цепь (оригинальный партнер) остается неспаренной.

Наличием H-формы объясняют существование в природных ДНК областей, сверхчувствительных к нуклеазам, специфичным к однотяжевым полинуклеотидам (нуклеаза S1).

Альтернативные структуры НК



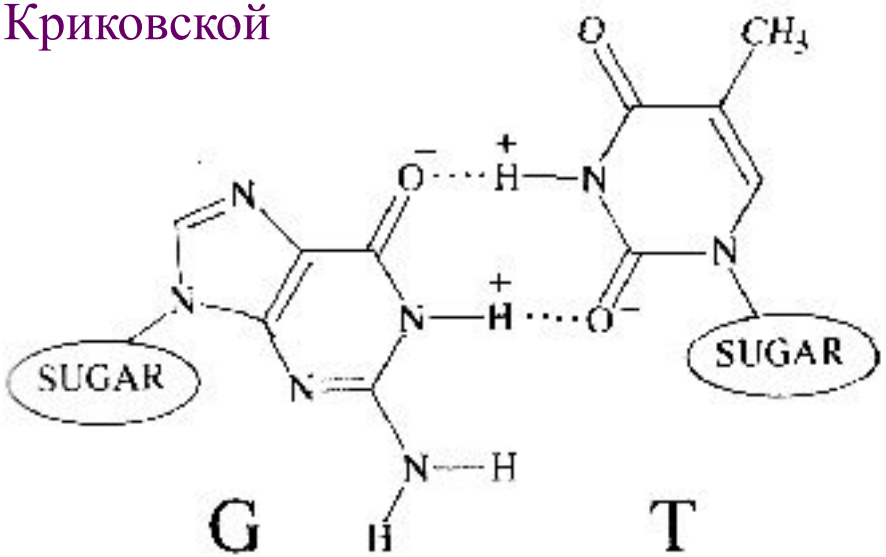
G-квартет



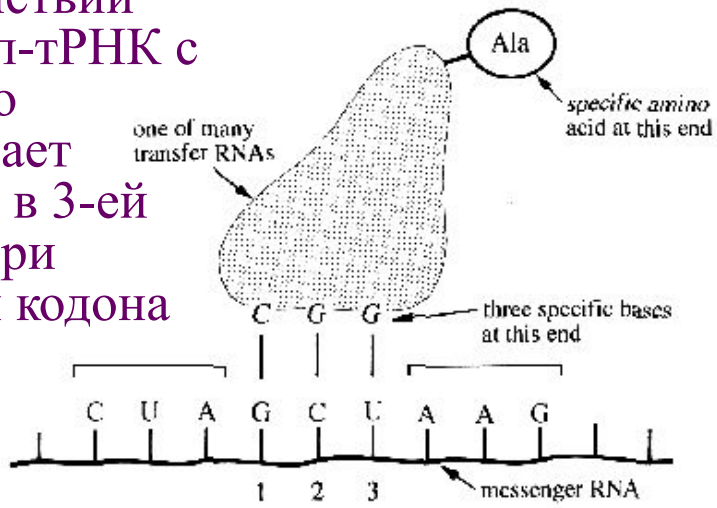
Пространственная структура ДНК-аптамера к тромбину

Пара G-T

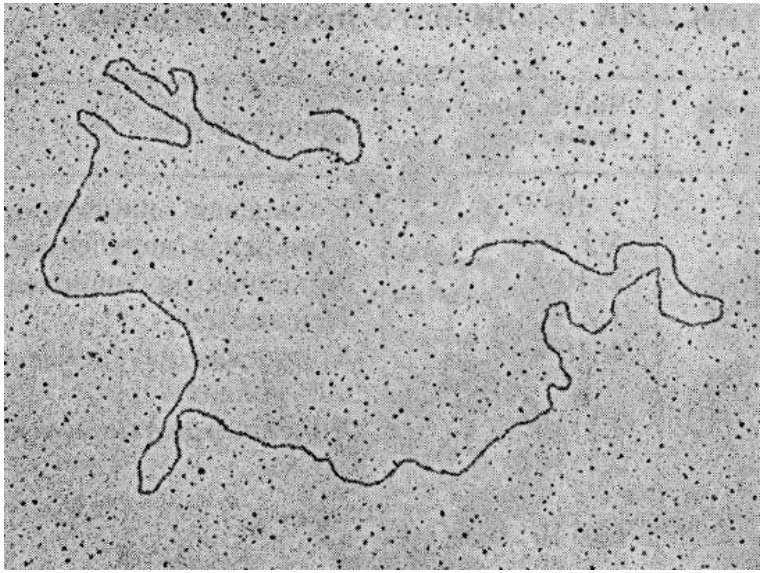
При спаривании G и T образуются две хорошие водородные связи. Кроме того геометрия этой пары близка к Уотсон-Криковской

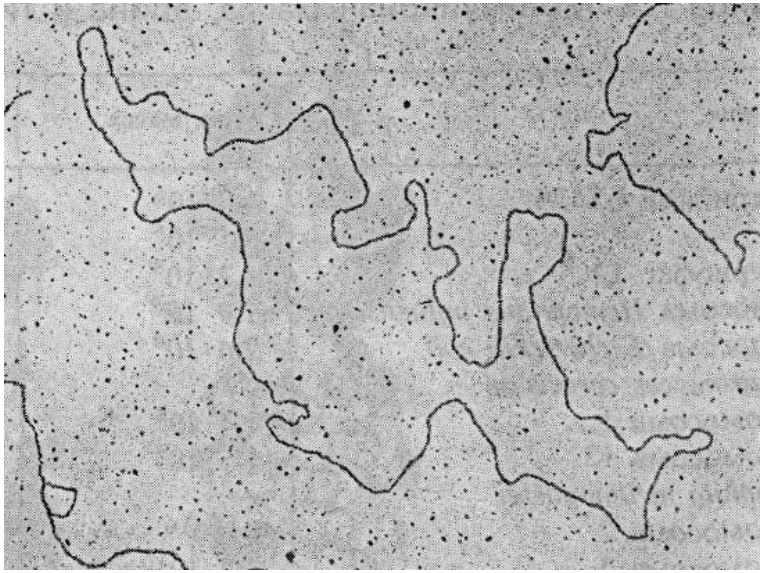


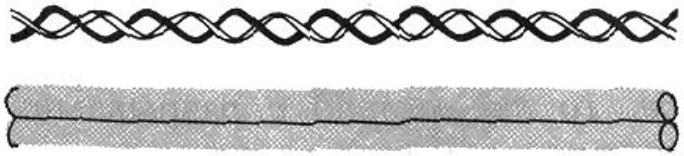
Очень близкая пара G-U является обычной при взаимодействии аминоацил-тРНК с мРНК. Это обеспечивает «качание» в 3-ей позиции при узнавании кодона

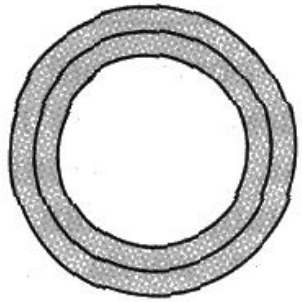


ЛИНЕЙНАЯ И КОЛЬЦЕВАЯ ДНК



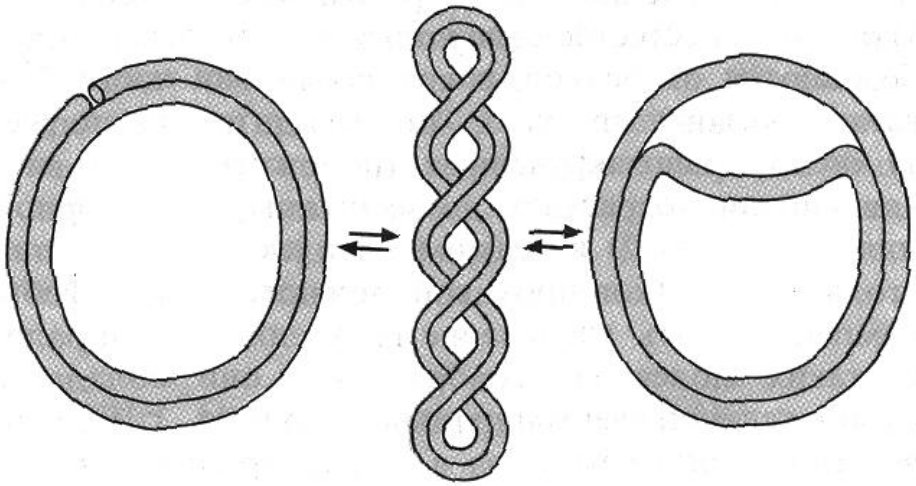


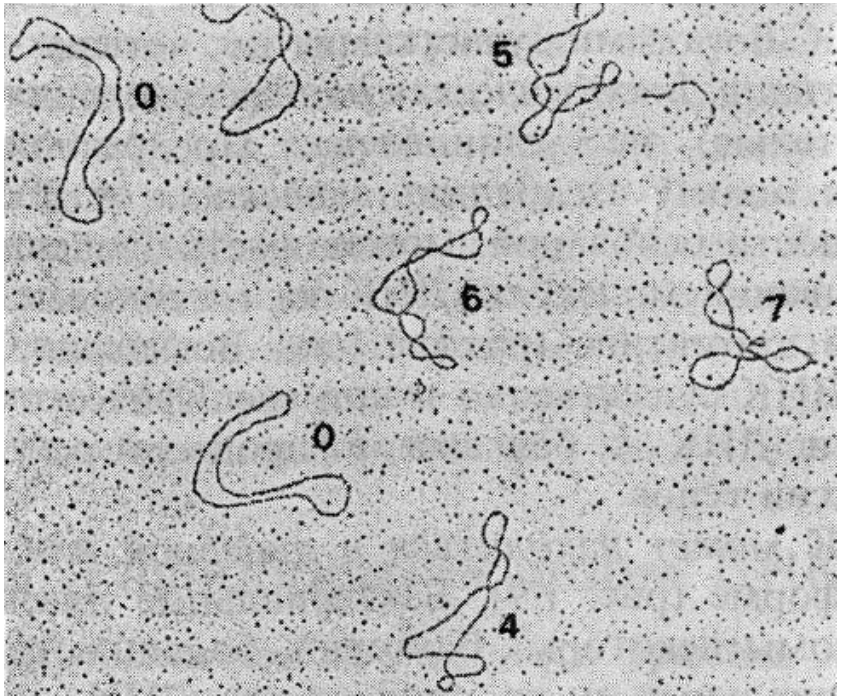




Электронные микрофотографии и схематическое представление линейной и кольцевой формы ДНК фага λ

СУПЕРСПИРАЛИЗАЦИЯ ДНК





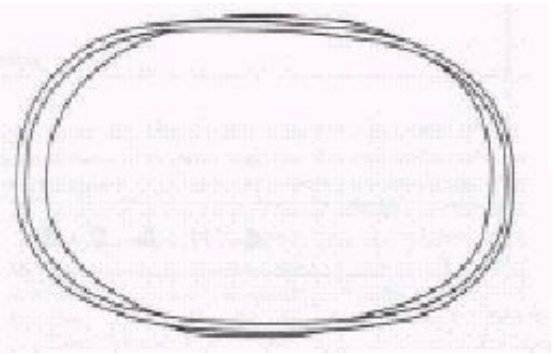
Двухцепочечная кольцевая ДНК фага M13 с разной степенью сверхспиральности. Цифрами обозначено число сверхвитков в каждой молекуле.

Сверхспирализация ДНК

Tw – twist number – число витков спирали ДНК

Wr – writhe number – число супервитков ДНК

Lk – linking number – число пересечений (зацеплений) одной полинуклеотидной цепи с другой



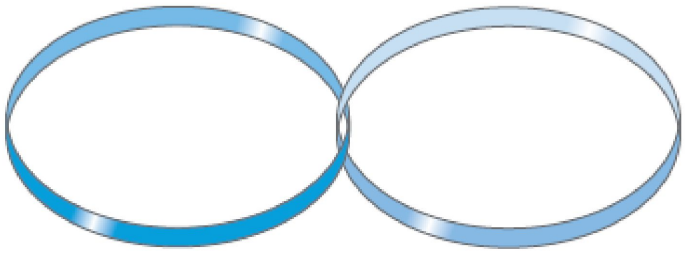
Twist - витки

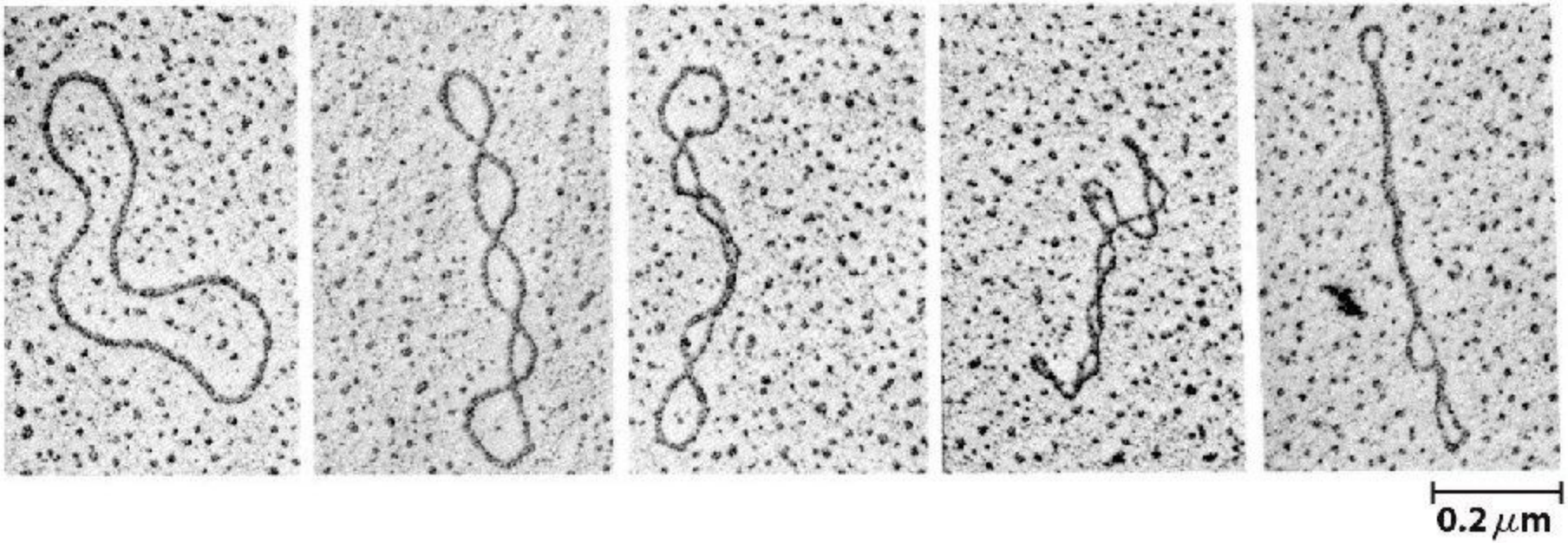
Writhe - супервитки

$$Lk = Wr + Tw$$

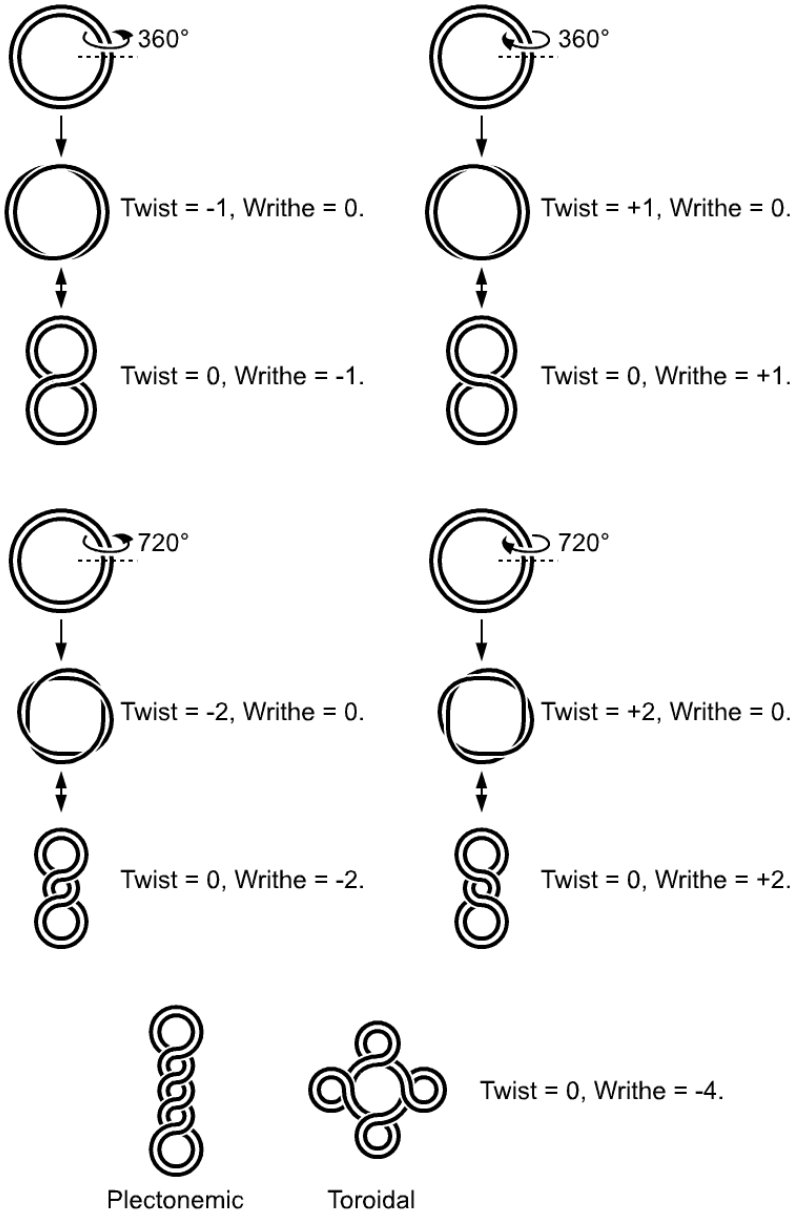
Lk - величина постоянная (инвариантная) для данной ковалентно замкнутой кольцевой ДНК

Плотность сверхвитков $\sigma = Wr/Tw$, для многих природных сверхспирализованных ДНК σ равно примерно −0,05.



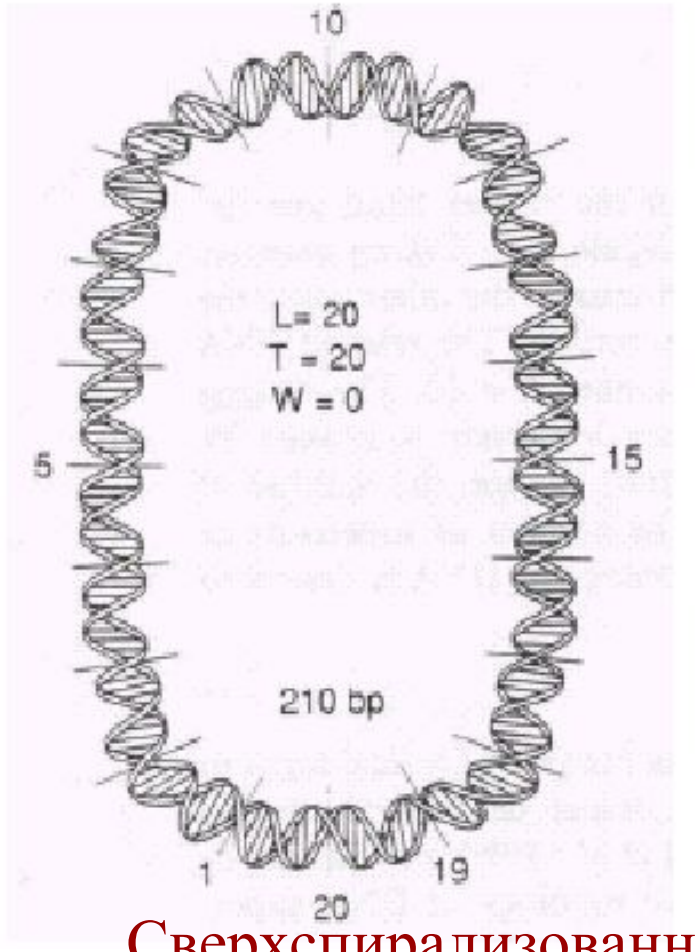


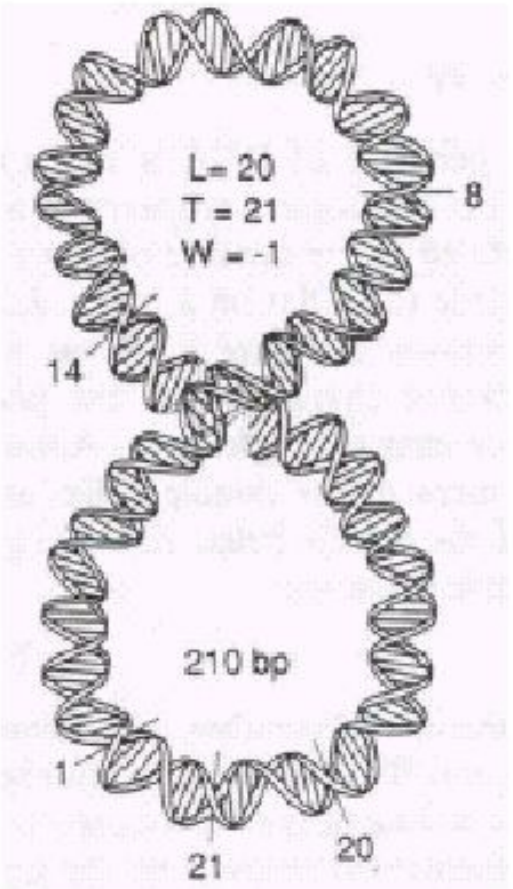
DNA double helix (coil)

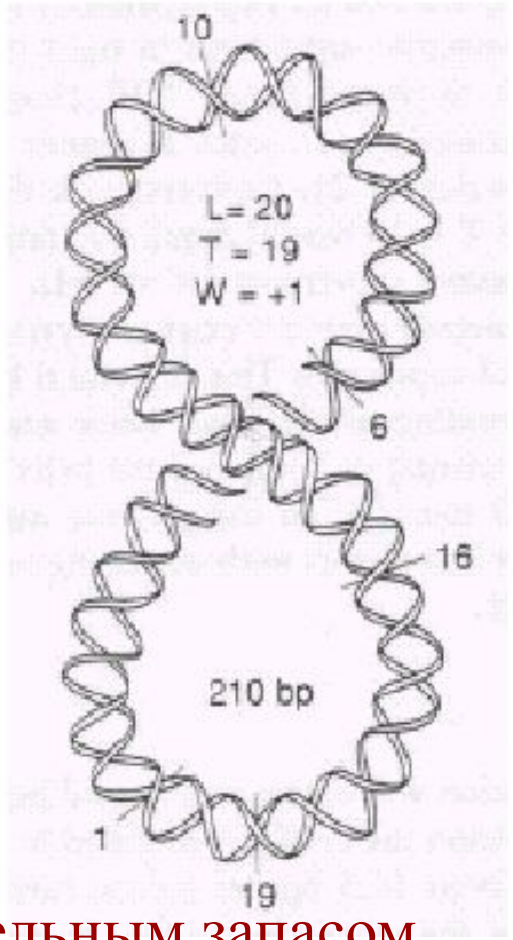


Сверхспирализация ДНК

Lk (число зацеплений) – постоянная величина для данной ковалентно замкнутой молекулы ДНК



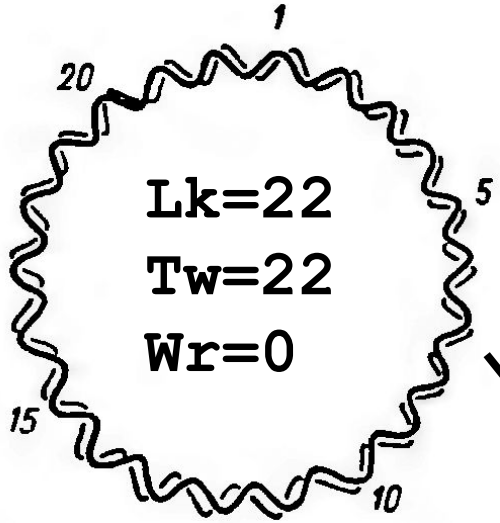




Сверхспирализованная ДНК обладает значительным запасом энергии по сравнению с ее релаксированной формой

$$\Delta G = K(Tw - Lk_0)^2$$

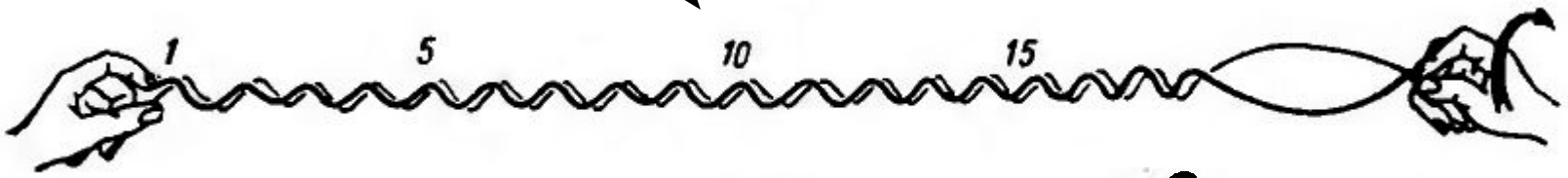
Сверхспирализация ДНК



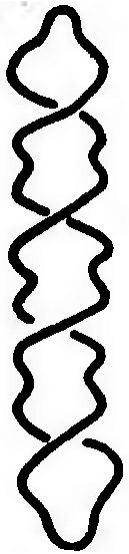
Релаксированная форма

Раскручивание на 4 витка

ΔLk=-4



Замыкание в ковалентно-непрерывное кольцо



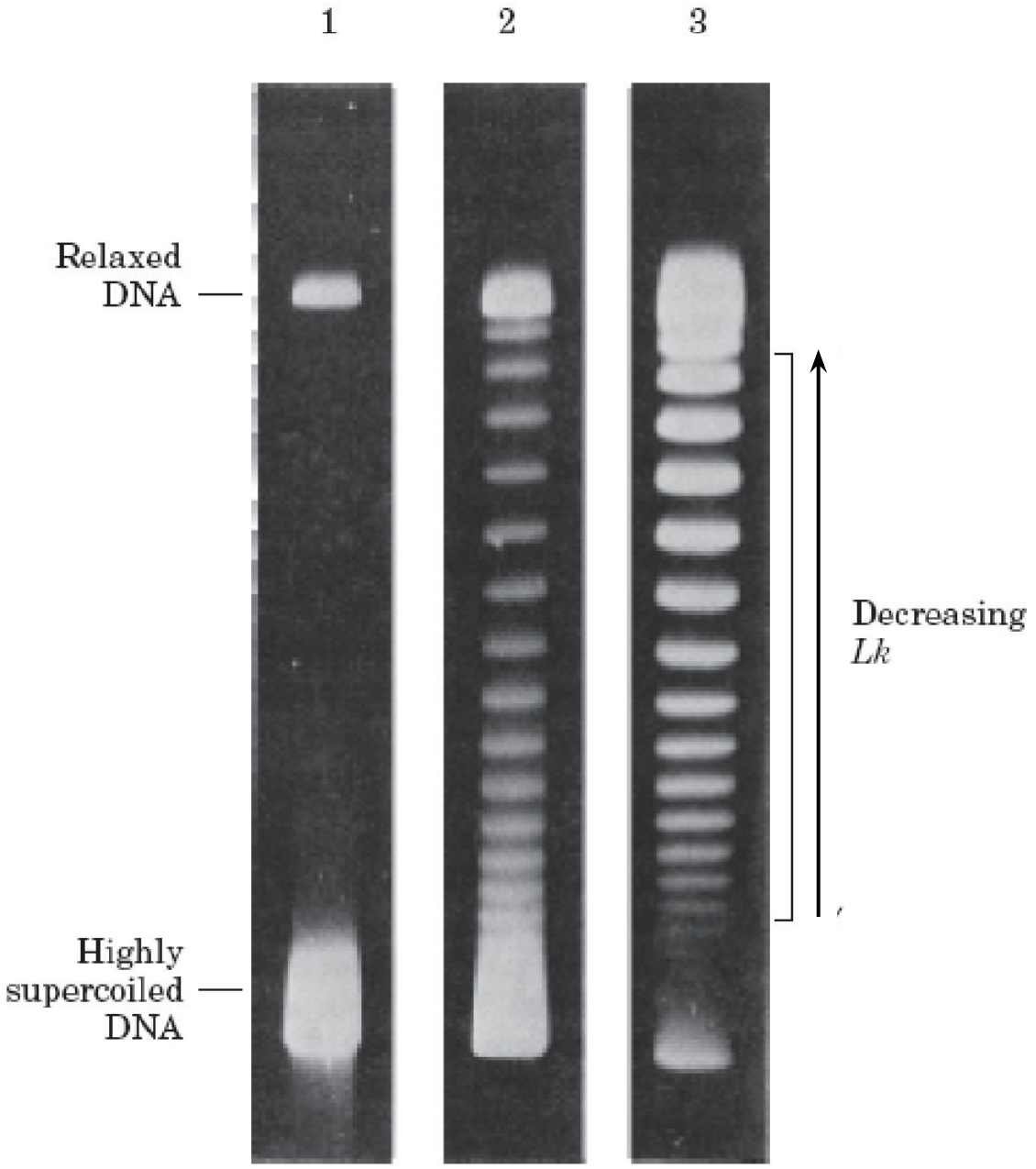
Сверхспираль

Lk=18

Tw=22

Wr=-4

Сверхспирализация ДНК

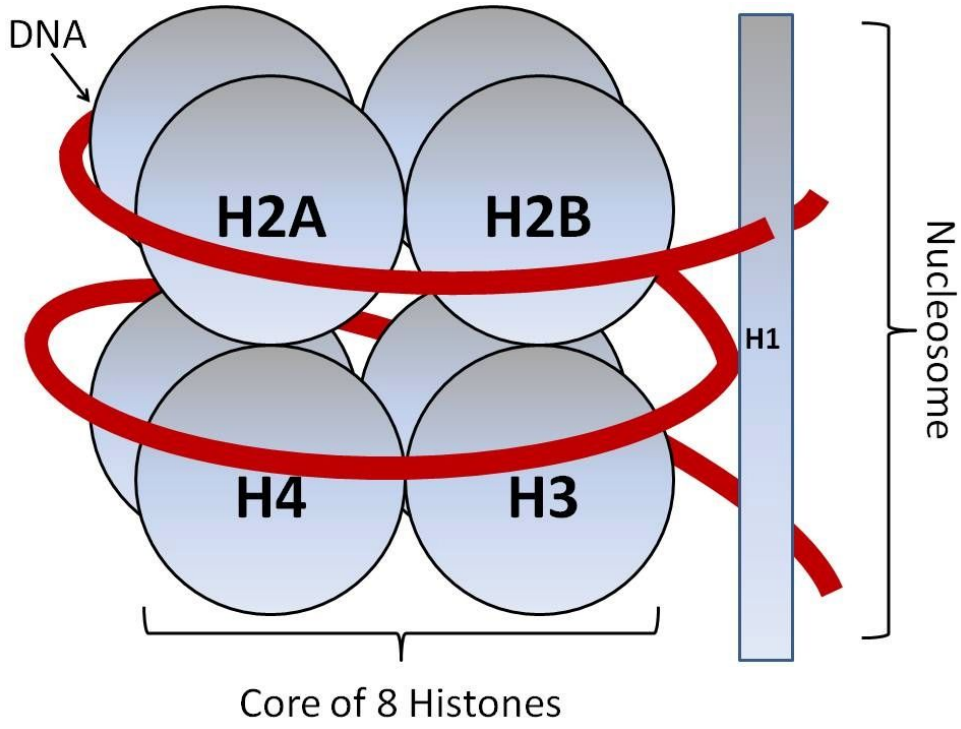


Visualization of topoisomers.
In this experiment, all DNA molecules have the same number of base pairs but exhibit some range in the degree of supercoiling. Because supercoiled DNA molecules are more compact than relaxed molecules, they migrate more rapidly during gel electrophoresis. The gels shown here separate topoisomers (moving from top to bottom) over a limited range of superhelical density.
In lane 1, highly supercoiled DNA migrates in a single band, even though different topoisomers are probably present.
Lanes2 and 3 illustrate the effect of treating the supercoiled DNA with a type I topoisomerase; the DNA in lane 3 was treated for a longer time than that in lane 2. As the superhelical density of the DNA is reduced to the point where it corresponds to the range in which the gel can resolve individual topoisomers, distinct bands appear. Individual bands in the region indicated by the bracket next to lane 3 each contain DNA circles with the same linking number; the linking number changes by 1 from one band to the next.

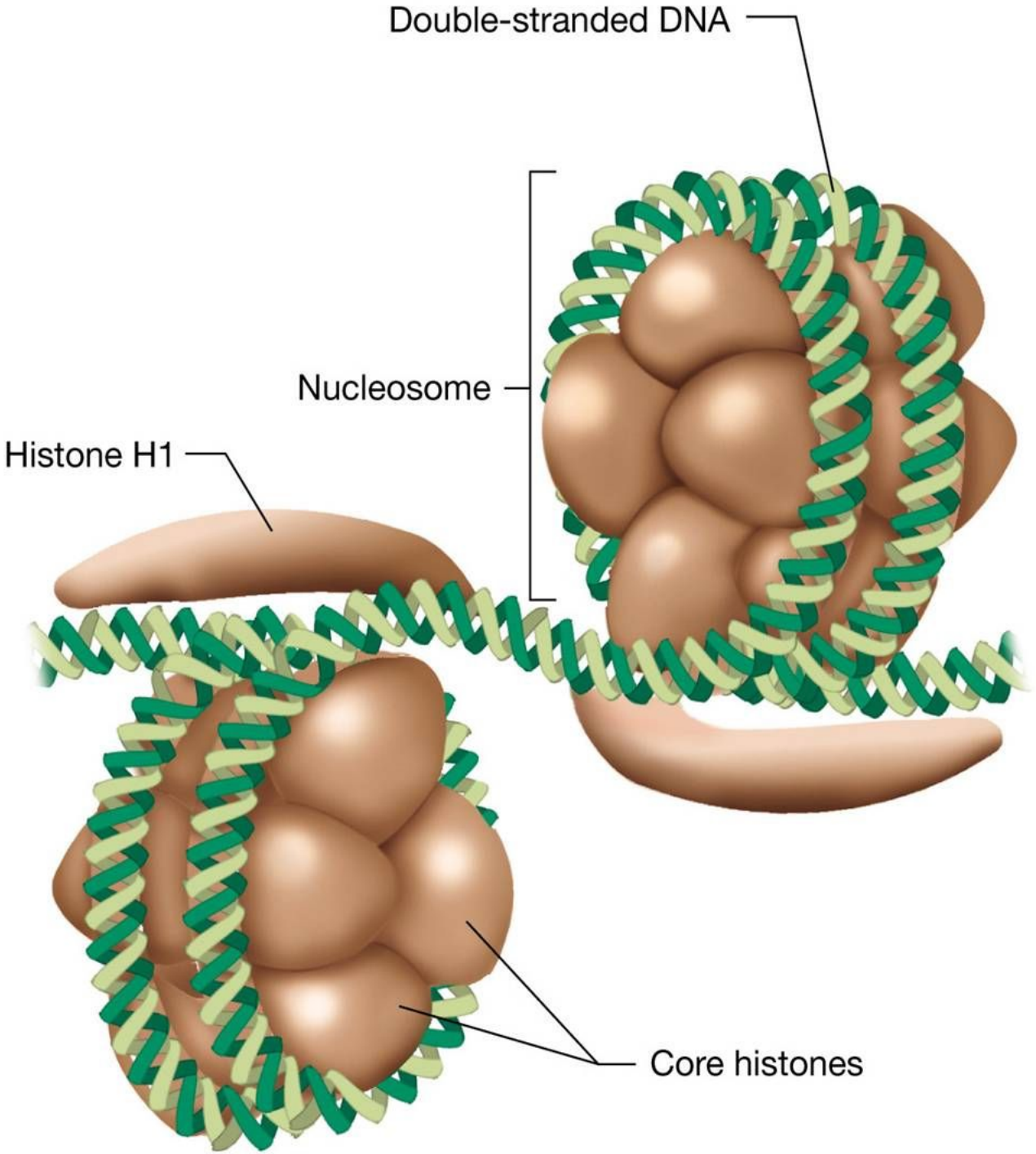
УПАКОВКА ДНК В ХРОМОСОМАХ. ГИСТОНЫ

Типичные характеристики гистонов млекопитающих

ТИП	Число АК	Мм, кДа	Число основных АК	Lys/Arg	Число кислых АК
H1 (кролик)	213	23,0	65	21	12
H2A(корова)	129	14,0	26	1,2	20
H2B(корова)	125	13,8	28	2,5	16
H3 (корова)	135	15,3	32	0,7	18
H4 (корова)	102	11,3	26	0,8	10



В такой структуре, ***нуклеосоме,*** с одним гистоновым октамером, ***нуклеосомным кором***, и молекулой гистона H1 ассоциированы 168 пар оснований спиральной ДНК


Double-stranded DNA
Nucleosome
Histone H1
Core histones

УПАКОВКА ДНК В ХРОМОСОМАХ. ГИСТОНЫ

Типичные характеристики гистонов млекопитающих

ТИП	Число АК	Мм, кДа	Число основных АК	Lys/Arg	Число кислых АК
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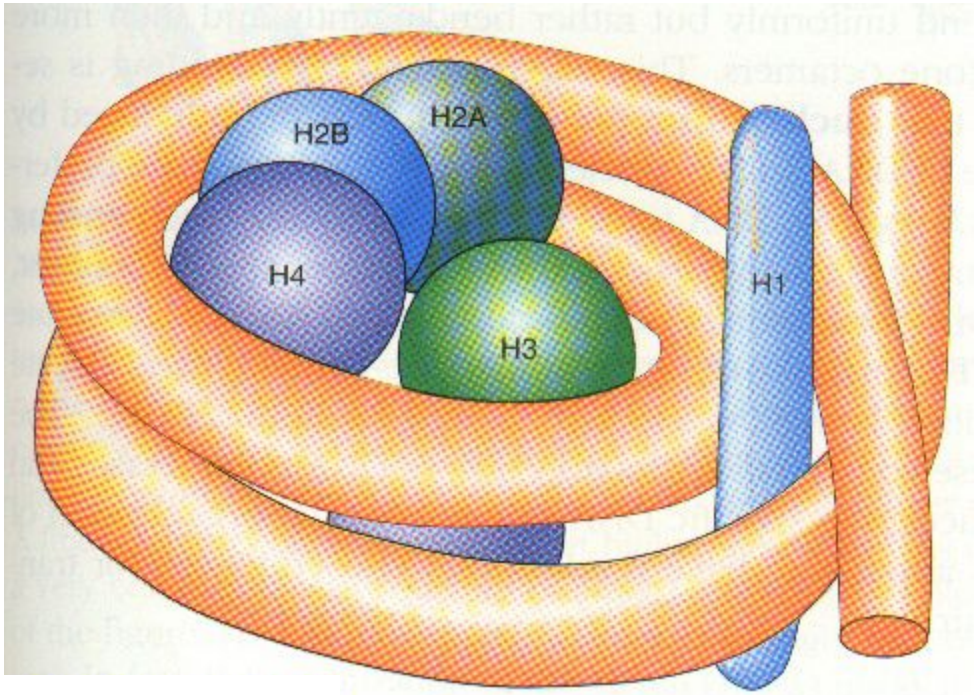
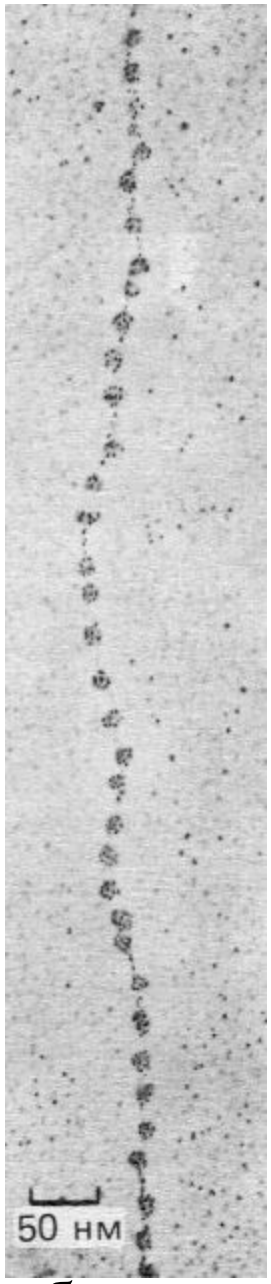


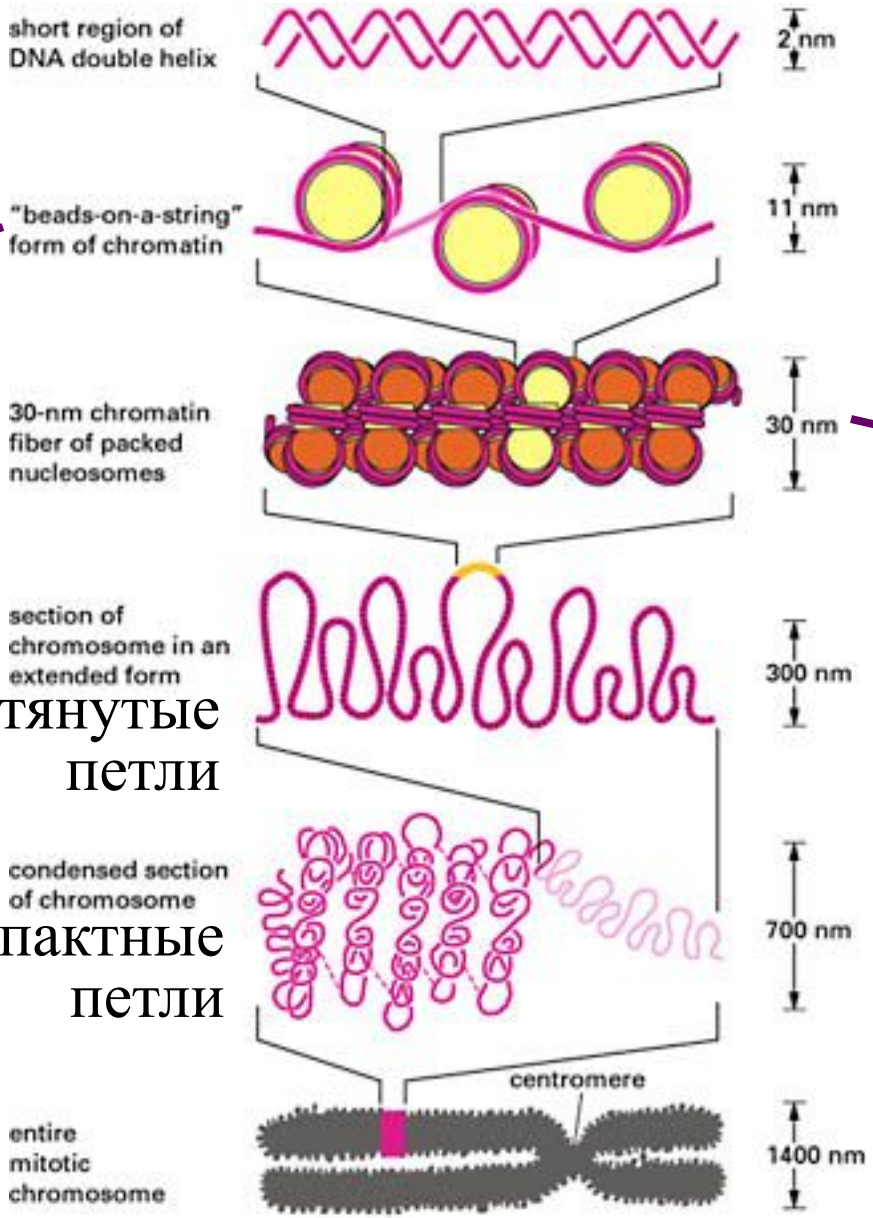
нуклеосома

В такой структуре с одним гистоновым октамером и молекулой гистона H1 ассоциированы 168 пар оснований спиральной ДНК

УПАКОВКА ДНК В ХРОМОСОМАХ

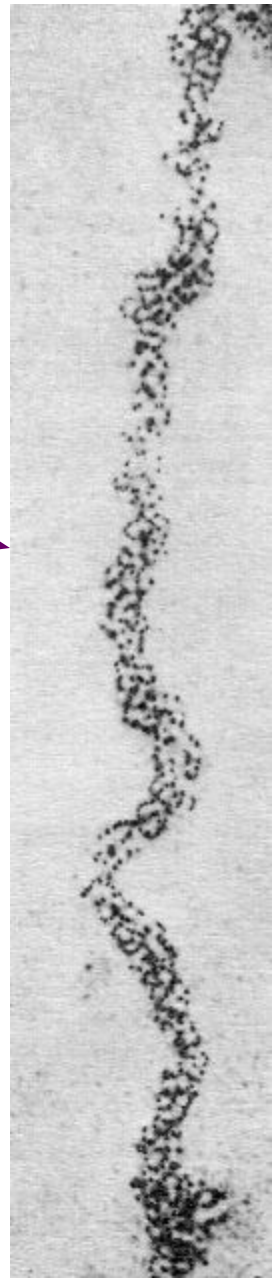


«бусы на нитке»



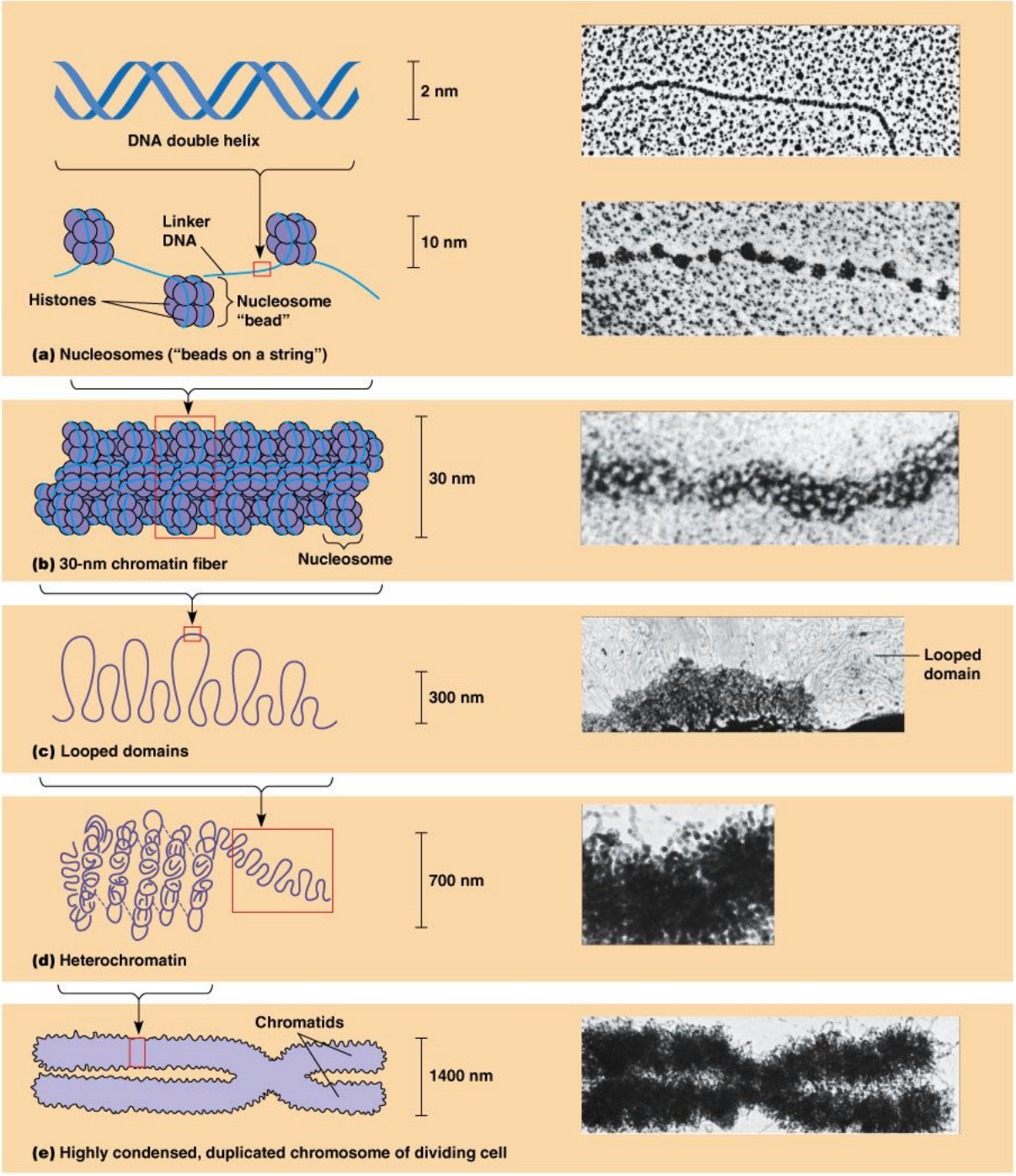
вытянутые петли

компактные петли



хроматиновые фибриллы

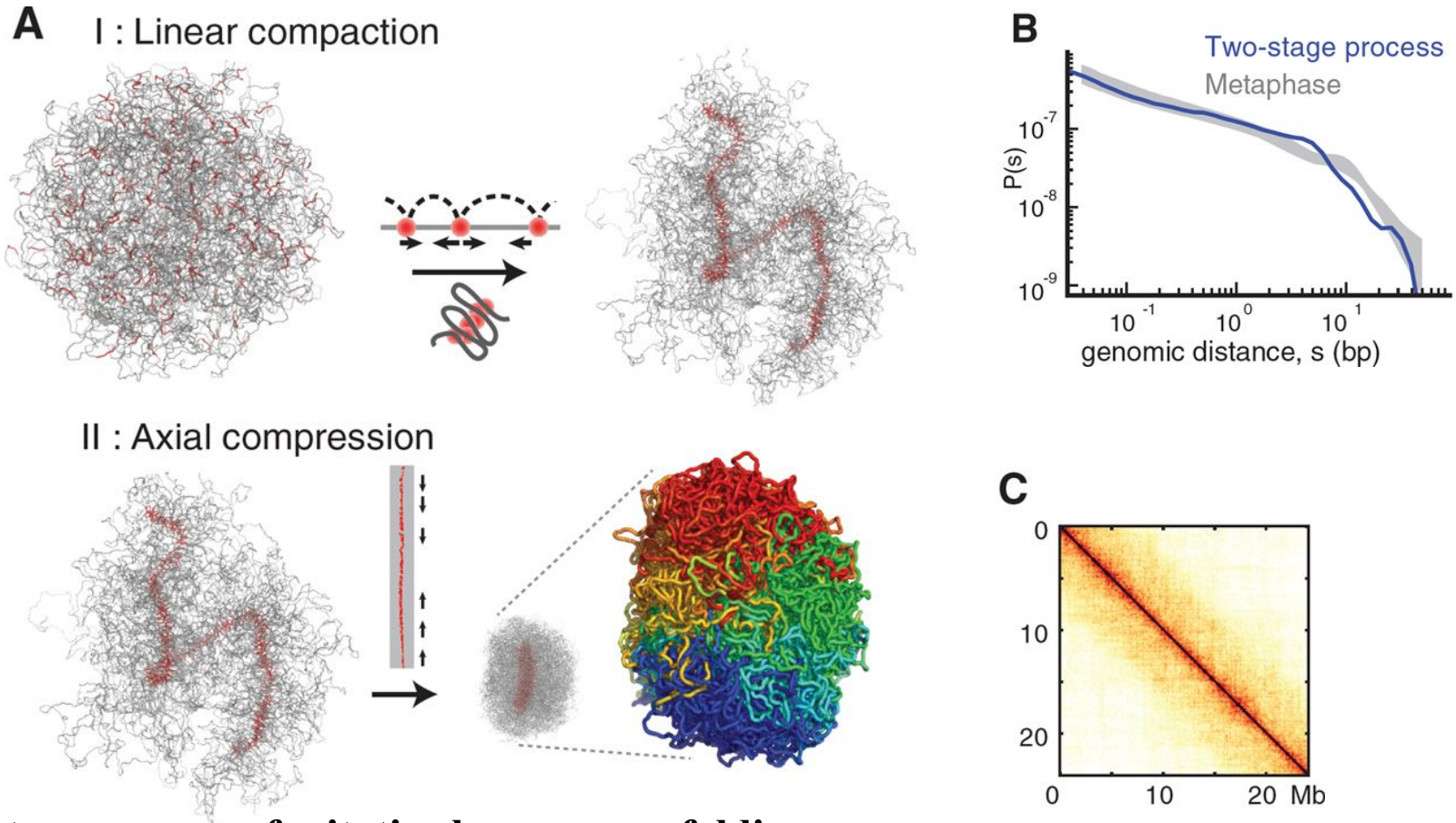
NET RESULT: EACH DNA MOLECULE HAS BEEN PACKAGED INTO A MITOTIC CHROMOSOME THAT IS 50,000x SHORTER THAN ITS EXTENDED LENGTH



Science. Nov 22, 2013; 342(6161): 948–953.

Organization of the mitotic chromosome

N. Naumova, M. Imakaev, G. Fudenberg, Y. Zhan, B.R. Lajoie, L.A. Mirny, J. Dekker



A two-stage process of mitotic chromosome folding

(A). Stage I: linear compaction by formation of consecutive chromosomal loops leads to the formation of a fiber of loop bases. Stage II: homogeneous axial compression of the fiber's backbone leads to formation of a dense chromosome. This two-stage process produces a chromosome with the appropriate cylindrical geometry and linear organization (genomic position is indicated by the coloring from blue to red). (B) Contact probability P(s) for the two-stage process compared with observed P(s) (grey shaded). (C). Average contact map for chromosomes folded by two-stage process.

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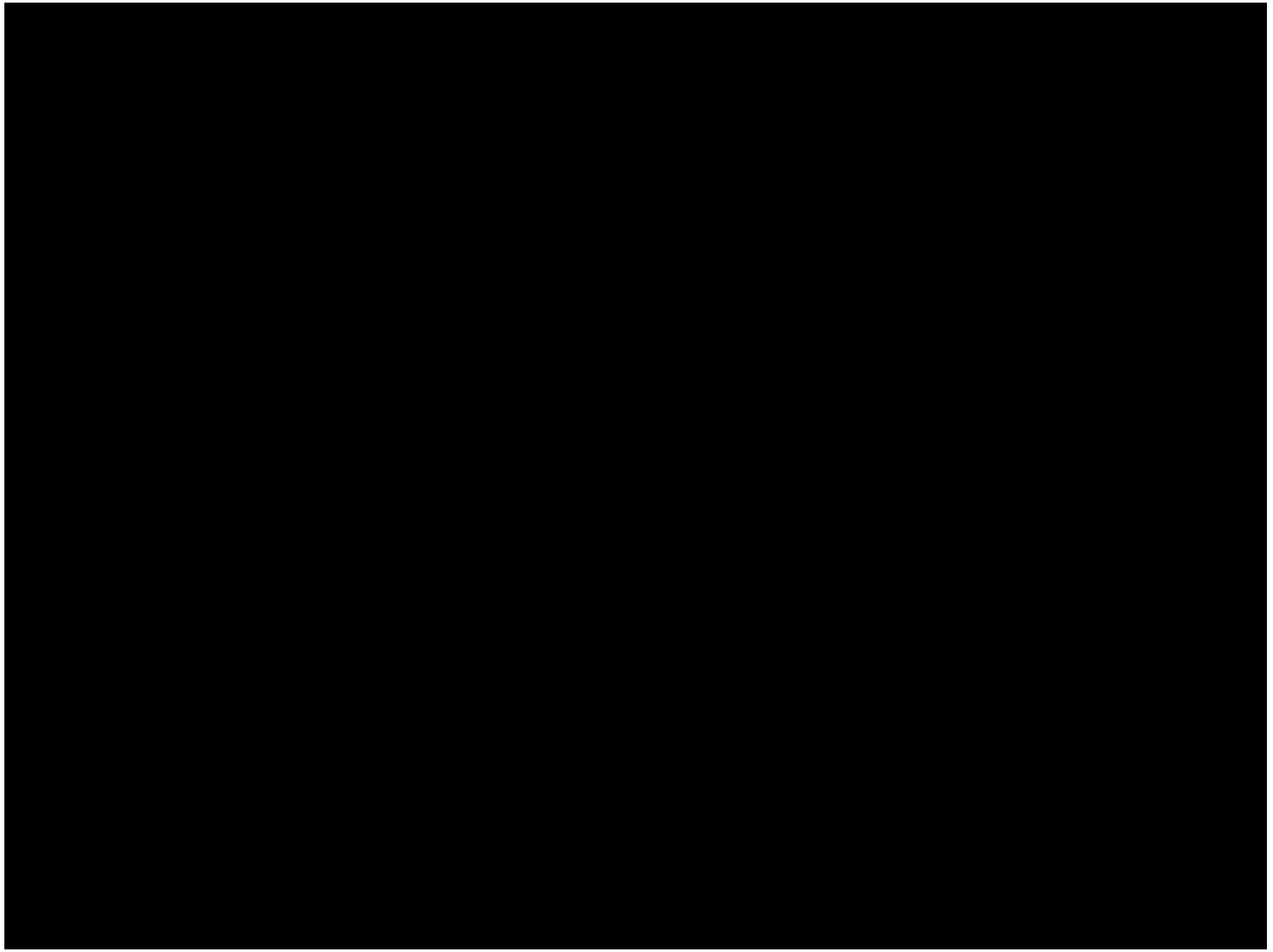


Movie M6. Two-step process of mitotic chromosome folding with highlighted loops.
14 loops, each separated by 20 intervening loops, are highlighted.

Science. Nov 22, 2013; 342(6161): 948–953.

Organization of the mitotic chromosome

N. Naumova, M. Imakaev, G. Fudenberg, Y. Zhan, B.R. Lajoie, L.A. Mirny, J. Dekker

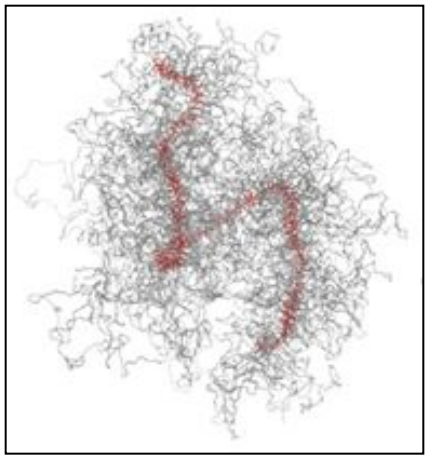
Movie M5. Two-step process of mitotic chromosome folding. Four monomers at the base of each loop (i.e. two monomers on each side) are shown in brown. Note, that the process of loop extrusion by SMC complexes was not explicitly modeled.

Movie M6. Two-step process of mitotic chromosome folding with highlighted loops. 14 loops, each separated by 20 intervening loops, are highlighted.

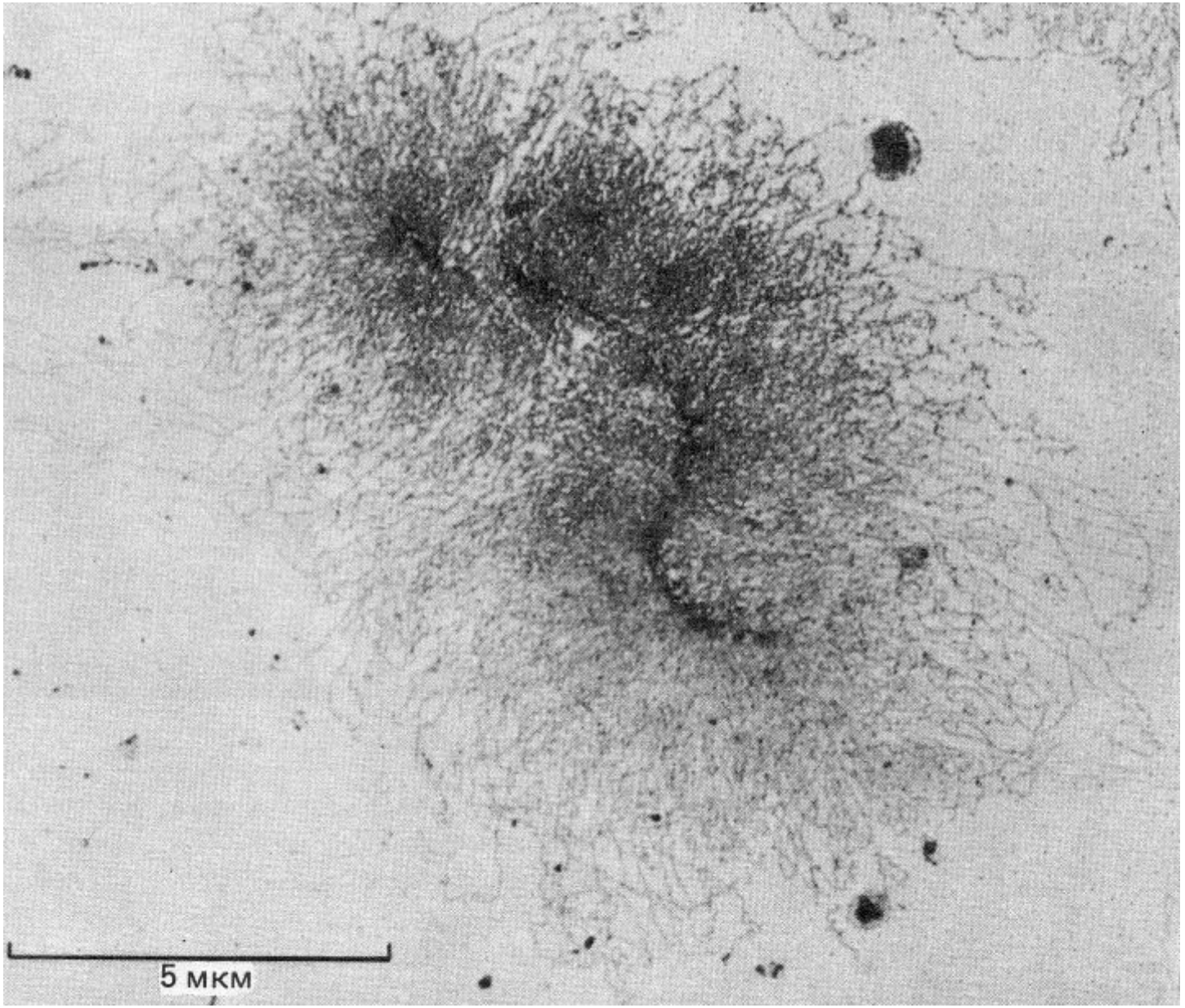
16.1

УПАКОВКА ДНК В ХРОМОСОМАХ

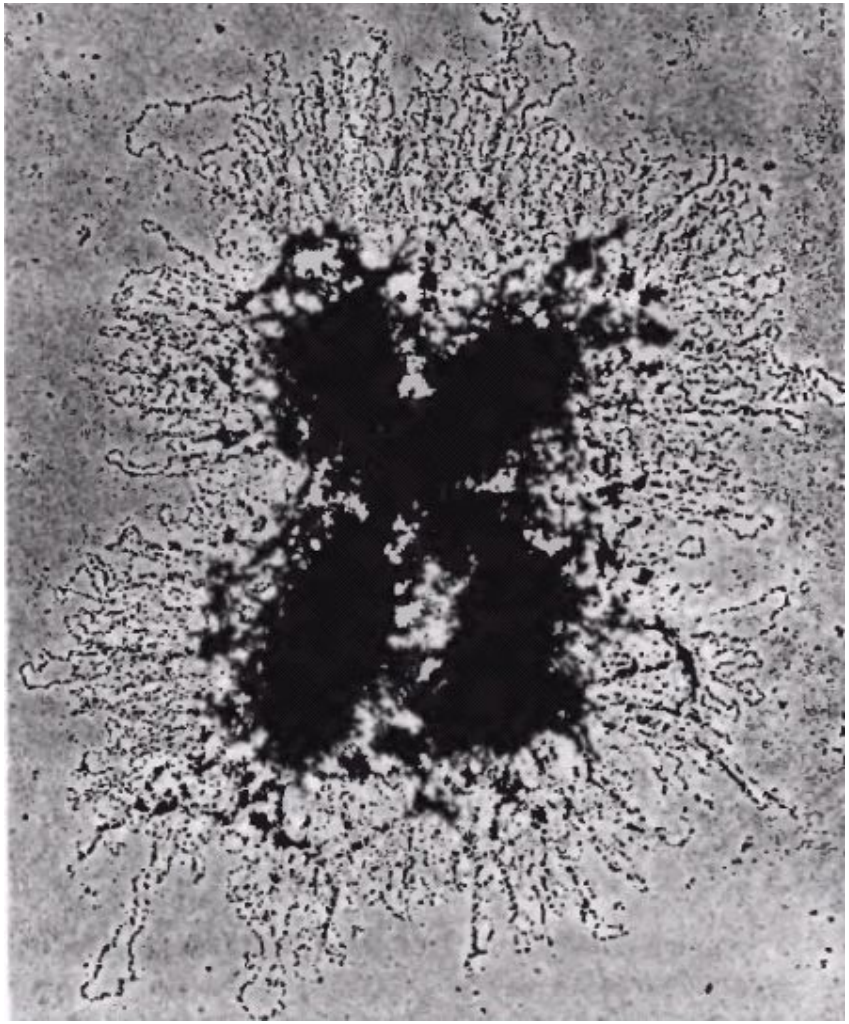
Петлевые участки (домены)

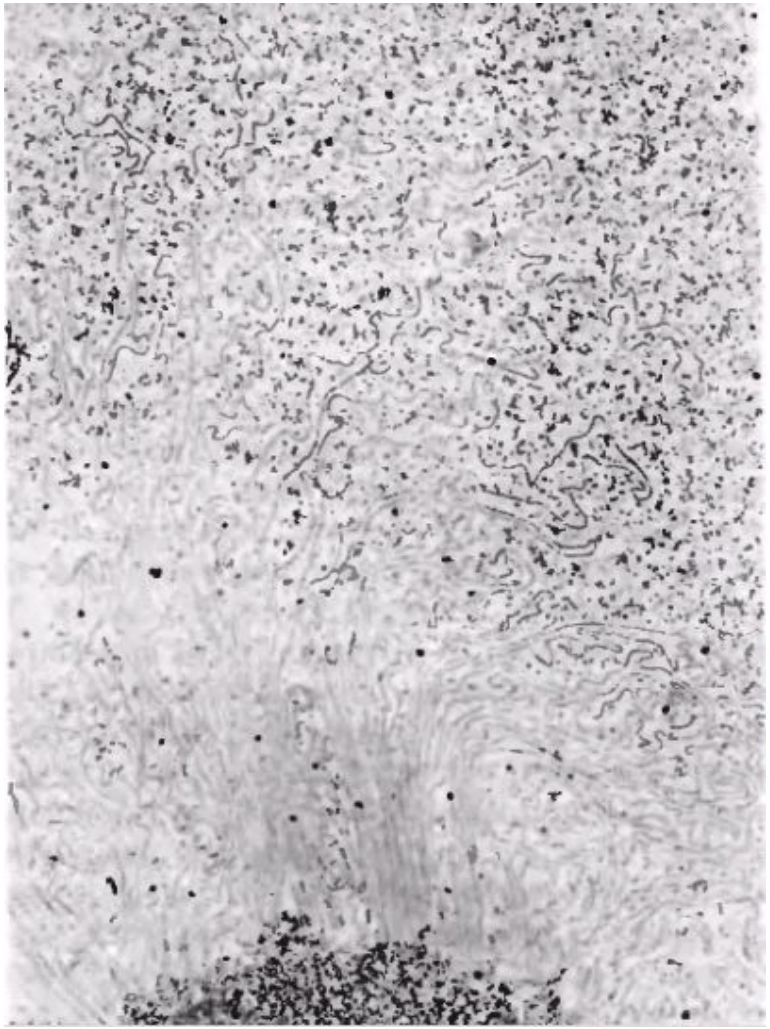


Электронная микрофотография одиночной хроматиды митотической хромосомы насекомого. Специальная обработка позволяет визуализировать петли хроматина, отходящие от центра хроматиды.



УПАКОВКА ДНК

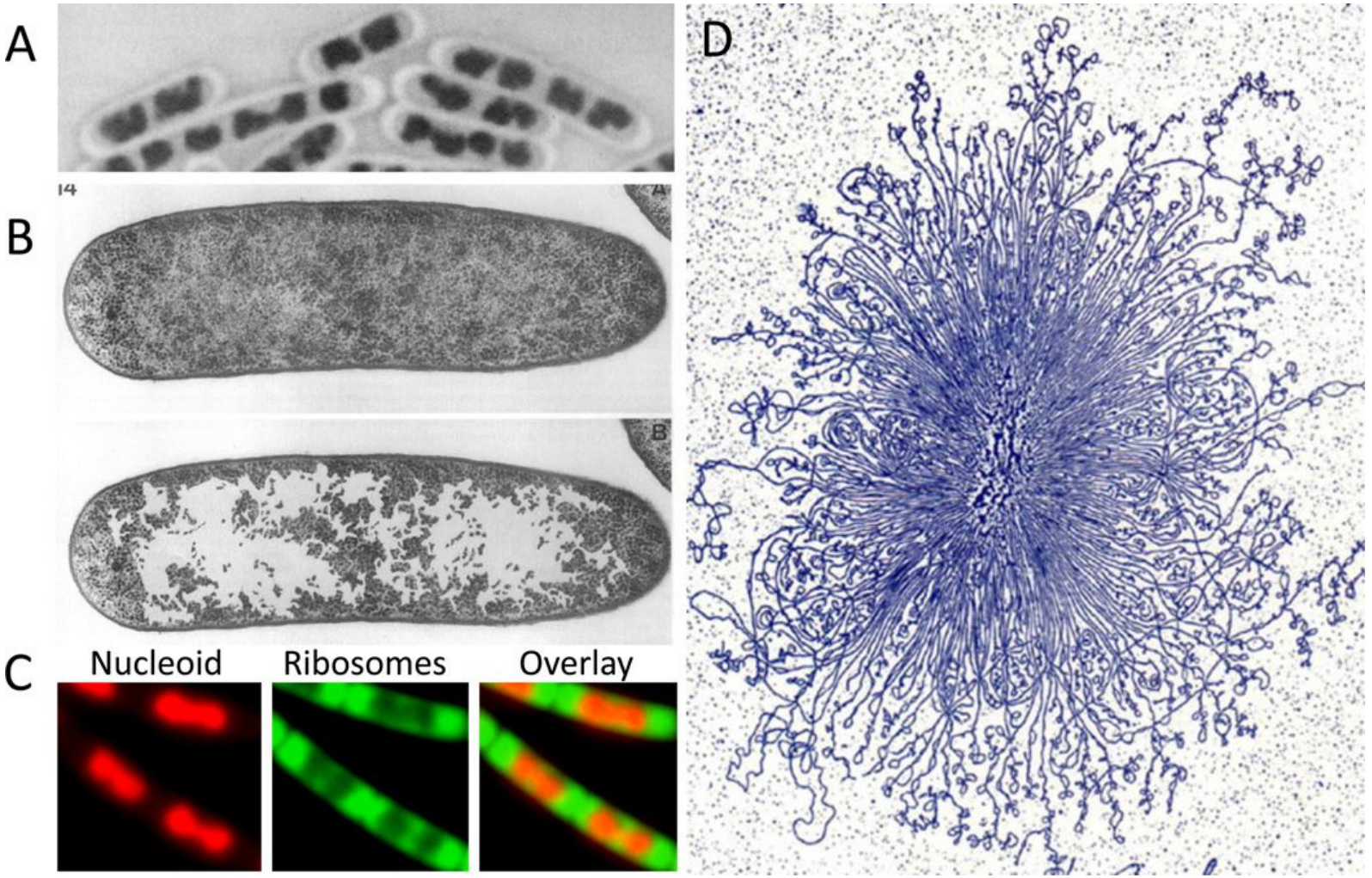




Хроматин зукариот состоит из петель разной длины, концы которых прикреплены к белковому матриксу. На микрофотографии слева представлена метафазная хромосома, из которой выходят нити хроматина. Видны петли, которые образуют эти нити, но места их присоединения к хромосоме не различаются. [W. C. Earnshaw, U. K. Laemmli, J. Cell Biol. **96** (1983), p. 84.] На электронной микрофотографии справа показаны хромосомы, обработанные декстрансульфатом и гепарином, очищенные и расправленные на подложке при помощи цитохрома. Обратите внимание, что концы петли, по-видимому, выходят из соседних точек белкового матрикса (внизу) [J. R. Paulson, U. K. Laemmli, Cell **12** (1977), p. 817. Оба снимка любезно предоставлены U. K. Laemmli.]

16.3

The bacterial nucleoid



(A) B. subtilis nucleoid stained with Giemsa using acid-treated cells. (B) The nucleoid of growing E. coli in thin section after cryo-fixation followed by freeze-substitution. The upper and lower panels show the same section; in the lower panel, the ribosome-free spaces were enhanced by coloring by hand. (A) and (B) are adapted from Robinow and Kellenberger 4. (C) Nucleoid (stained with DAPI, colored red) and ribosomes (RplA-GFP, colored green) in live B. subtilis cells growing in rich media. Despite this commonly depicted cloud-like appearance of the bacterial chromosome, the morphology of the nucleoid varies among bacteria, and is influenced by growth rate and environmental conditions. For example, the nucleoid in C. crescentus, and in slow-growing E. coli and B. subtilis, appears more diffuse and occupies a greater proportion of the cell cytoplasm (not shown). (D) A gently isolated E. coli nucleoid bound by cytochrome C, spread on an EM grid, stained with uranyl acetate and visualized by transmission electron microscopy. Adapted from Physics in the twentieth century. **Nature Reviews Genetics 14, 191-203 (2013)**

16.4 Topological organization of the bacterial chromosome

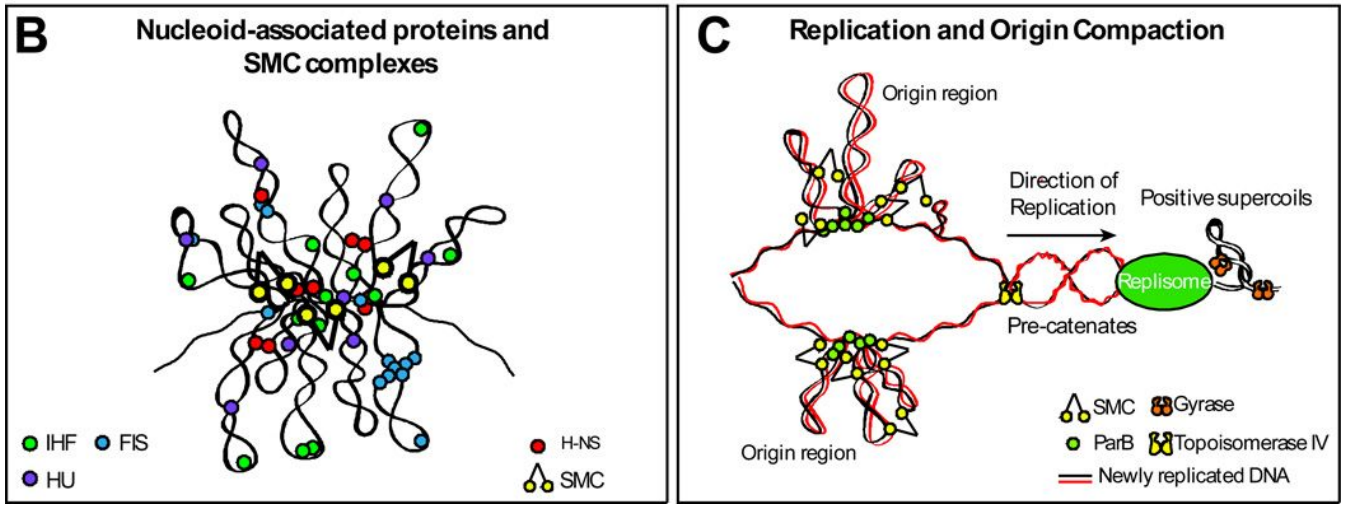
A

bottlebrush model

mov

HU, **H-NS**, **FIS** и **IHF** – гистоноподобные белки – участвуют в организации бактериальной хромосомы, а также влияют на экспрессию генов, репликацию и рекомбинацию ДНК.

Белки из семейства **SMC** (structural maintenance of chromosomes) играют роль «конденсинов» – суперспирализуют бактериальную ДНК, а также участвуют в ее репарации, рекомбинации, сегрегации дочерних хромосом и других процессах.

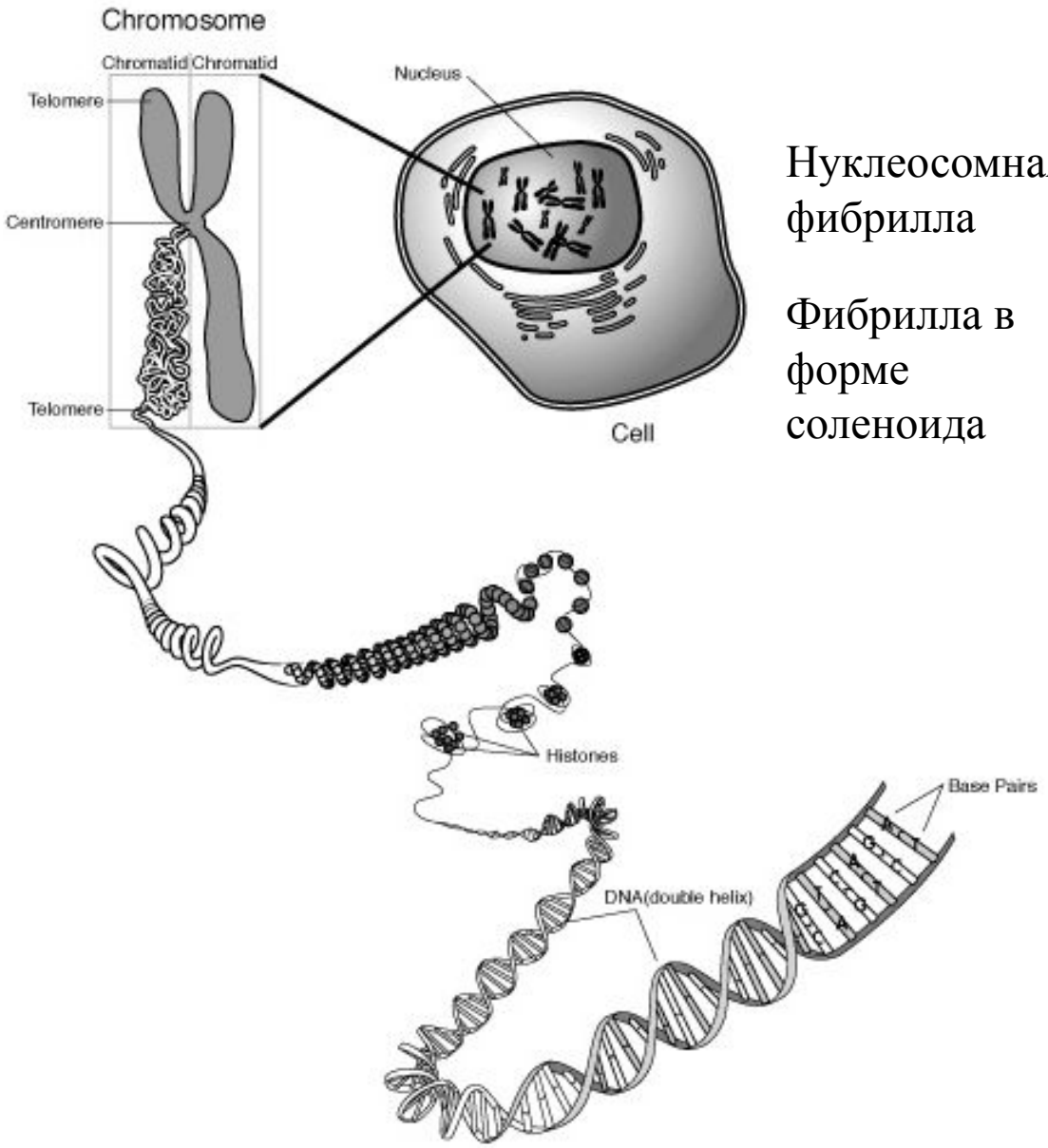


(A) Schematic representation of the bottlebrush model of the nucleoid. This diagram depicts the interwound supercoiled loops emanating from a dense core. The topologically isolated domains (microdomains) are on average 10 kb and therefore likely encompass several branched plectonemic loops. (B) Schematic representation of the small nucleoid-associated proteins and SMC. These proteins introduce DNA bends and also function in bridging chromosomal loci. (C) The diagram depicts replication fork progression and compaction of the origin region. Replication generates positive supercoils ahead of the fork, which can diffuse behind the replisome producing pre-catenanes. Positive supercoils are removed by DNA gyrase and pre-catenanes are unlinked by Topo IV. Newly replicated origin regions thought to be compacted by the SMC complexes that are recruited to the origin and by the action of small nucleoid-associated proteins (not shown).

Nature Reviews Genetics 14, 191-203 (2013)

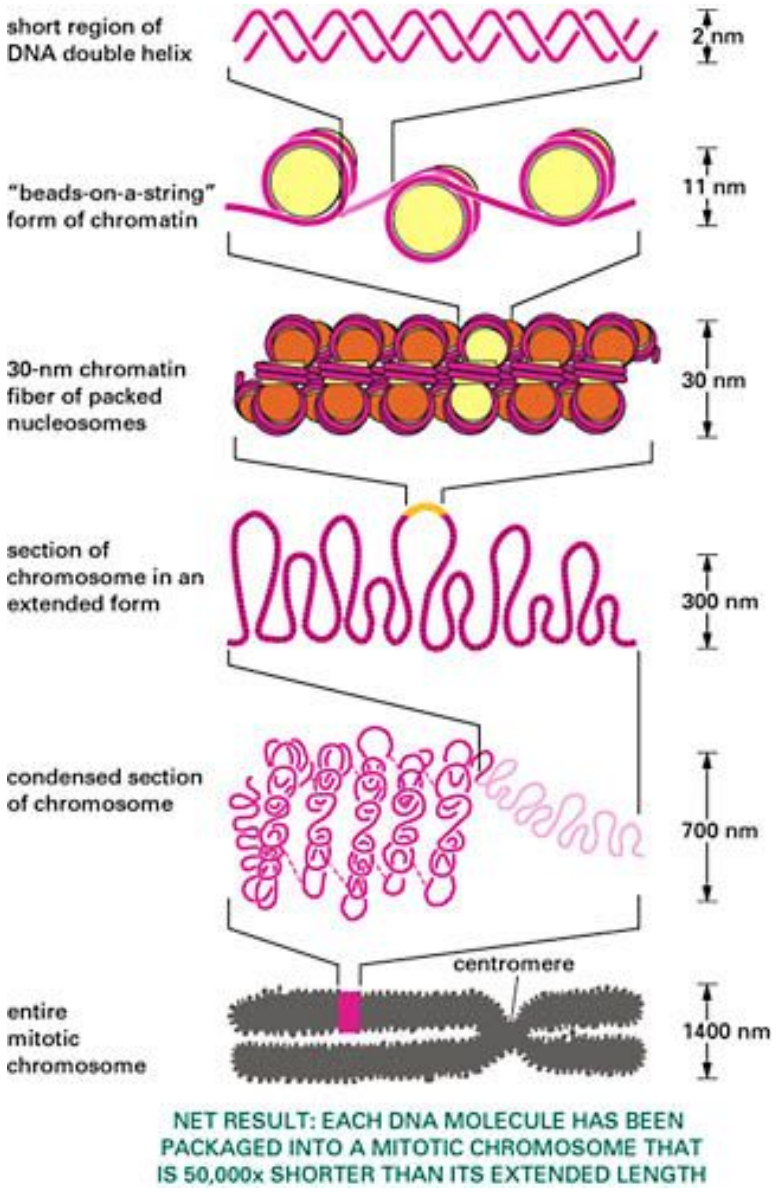
УПАКОВКА ДНК В ХРОМОСОМАХ

Метафазные хромосомы



Нуклеосомная фибрилла

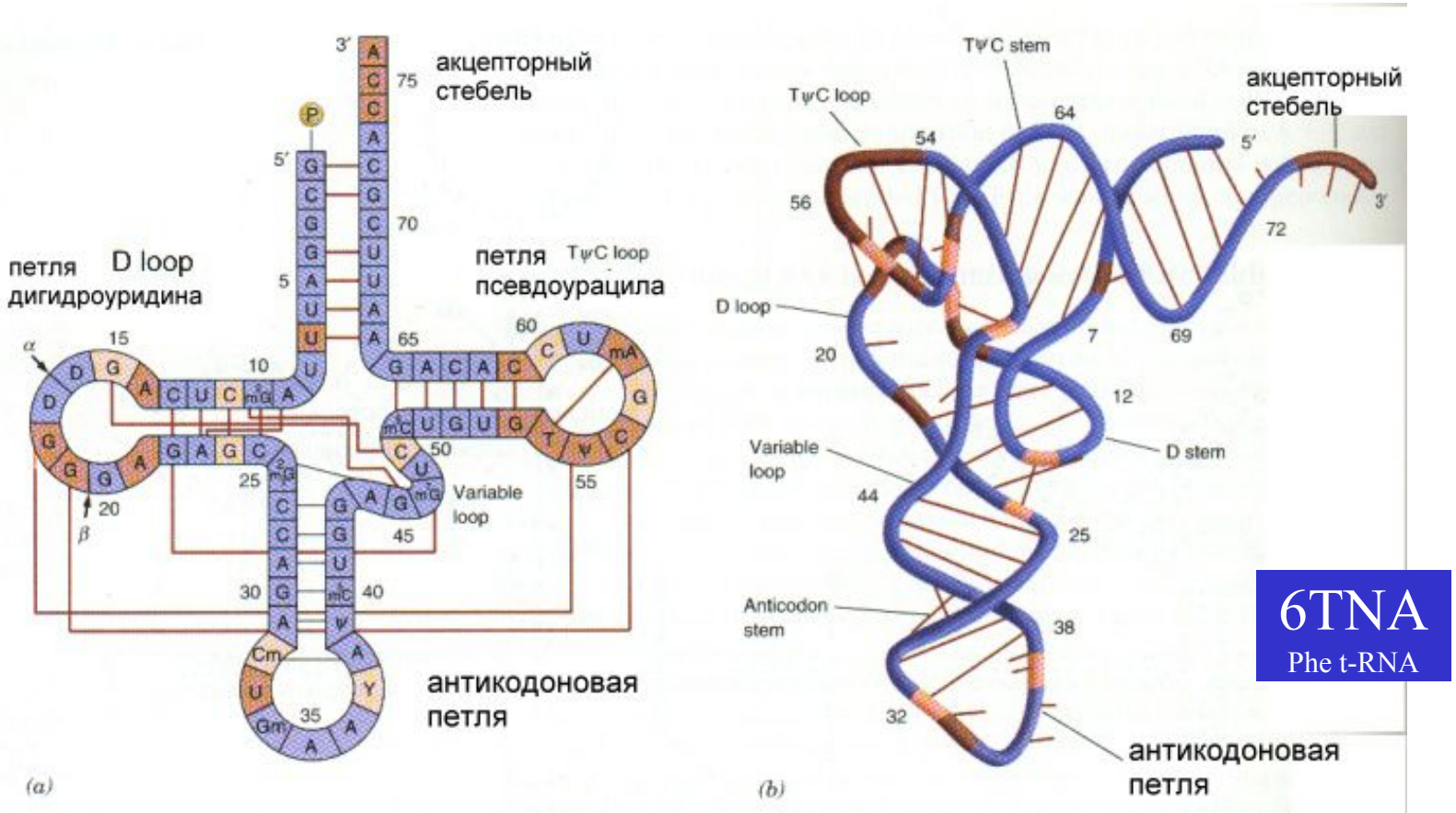
Фибрилла в форме соленоида



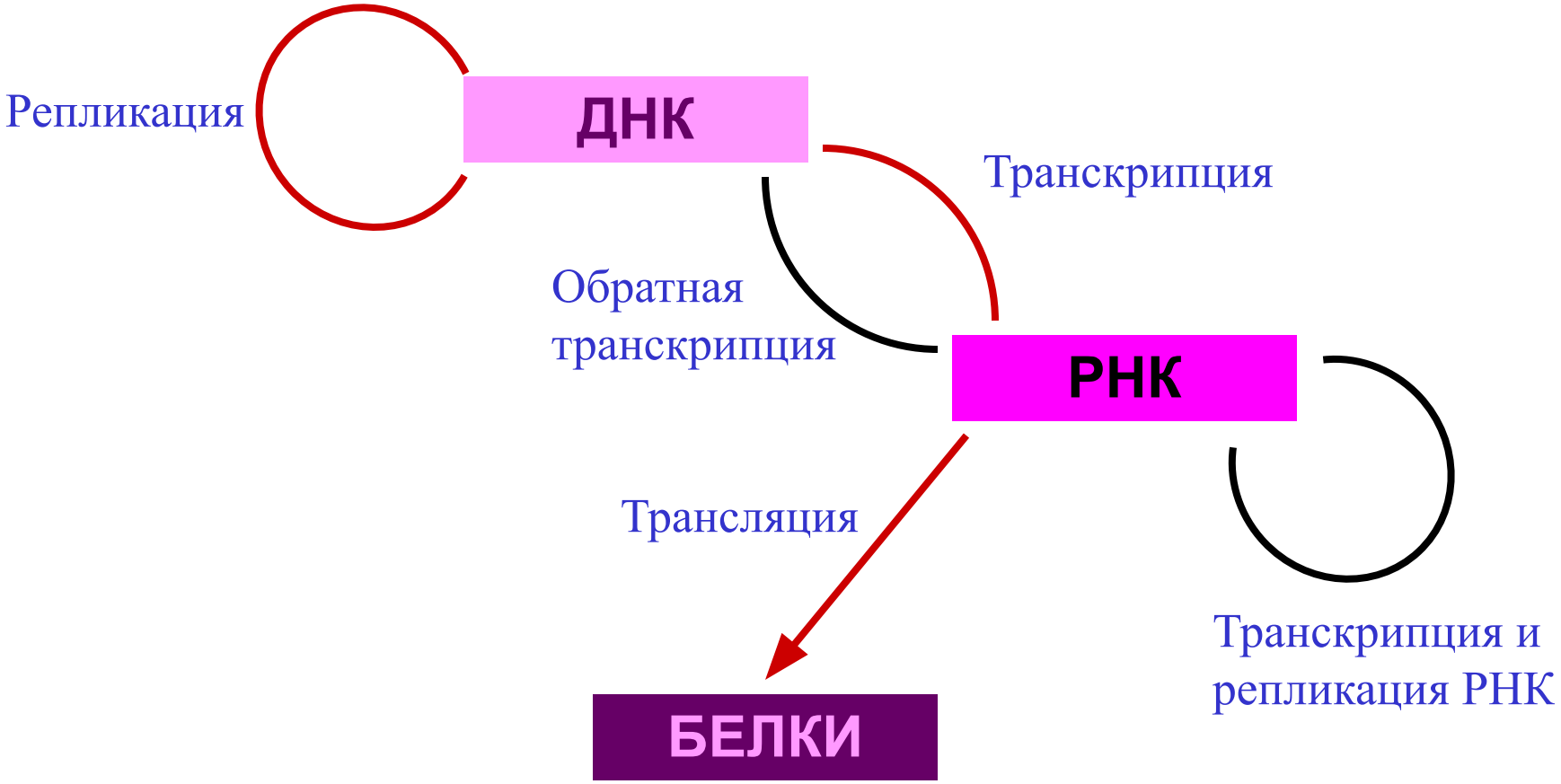
Типы РНК и их распространенность

rRNA, рРНК	рибосомальная	~80%
tRNA, тРНК	транспортная	~15%
mRNA, мРНК, иРНК	матричная или информационная	<5%
sRNA, мяРНК, мцРНК	малая (ядерная, цитоплазматическая)	<2%

СТРУКТУРА РНК



ИНФОРМАЦИОННАЯ СВЯЗЬ МЕЖДУ ДНК, РНК И БЕЛКАМИ



(центральная догма молекулярной биологии)