НУКЛЕИНОВИ КИСЕЛИНИ

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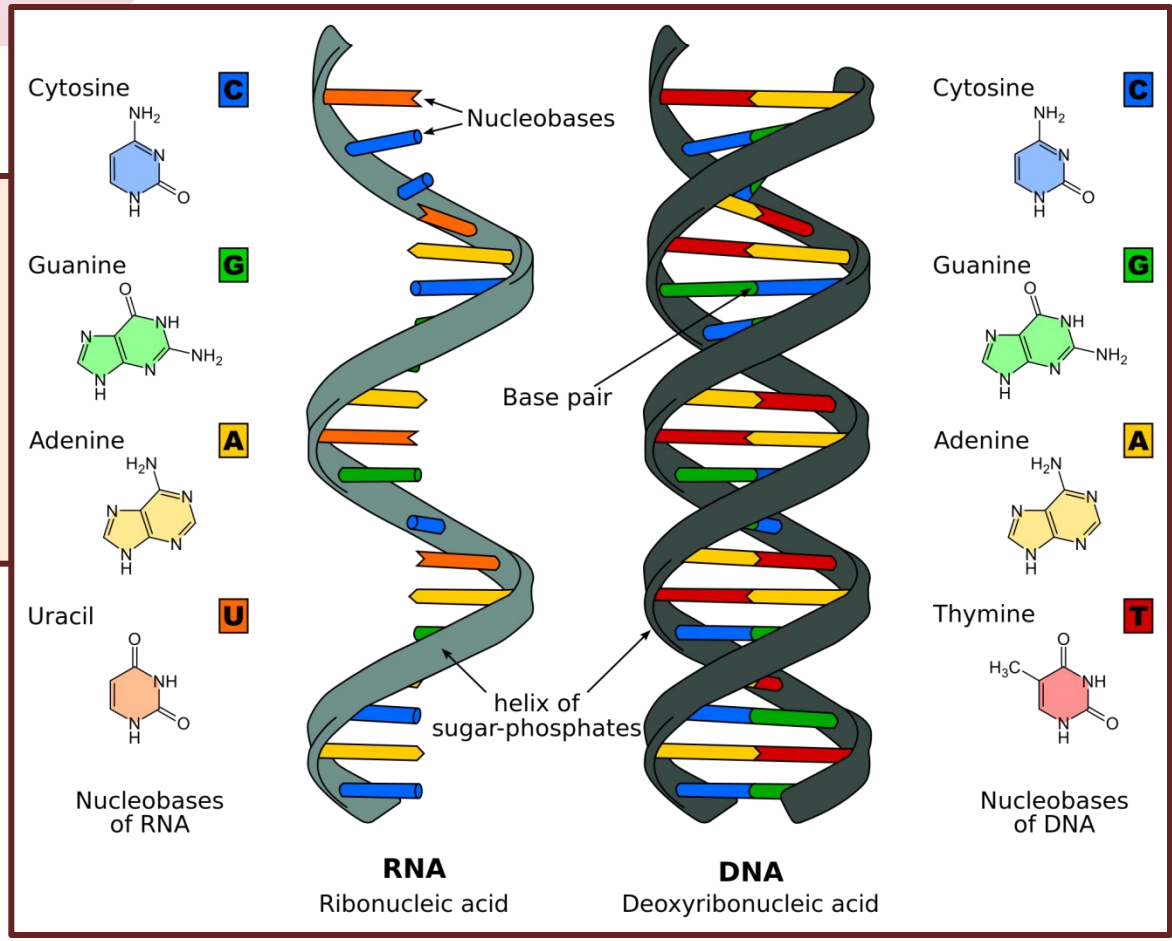
Нуклеинови киселини:

1. Определение:

- хетеробиополимери
- Изградени от **нуклеотиди**
- **фосфодиестерни връзки**



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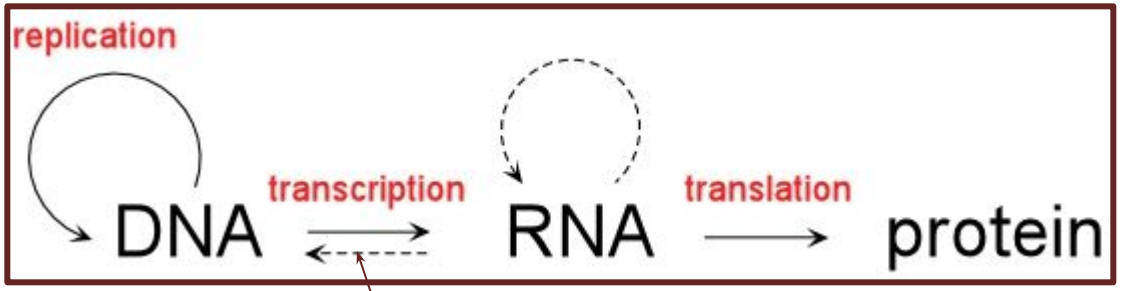
Нуклеинови киселини:

2. Биологична роля:

- Съхранение и предаване на генетичната информация
- Определят свойствата
- **Централна догма на молекулярната биология**



Обратна транскрипция (вируси – напр. HIV)

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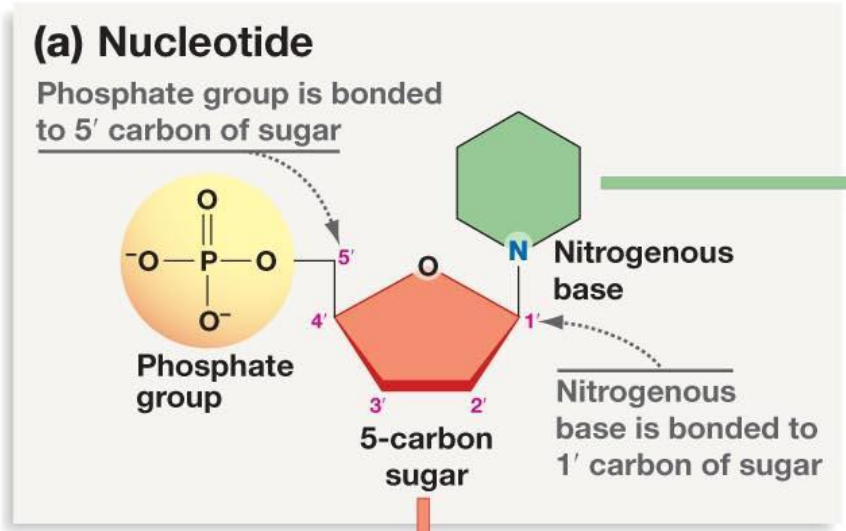
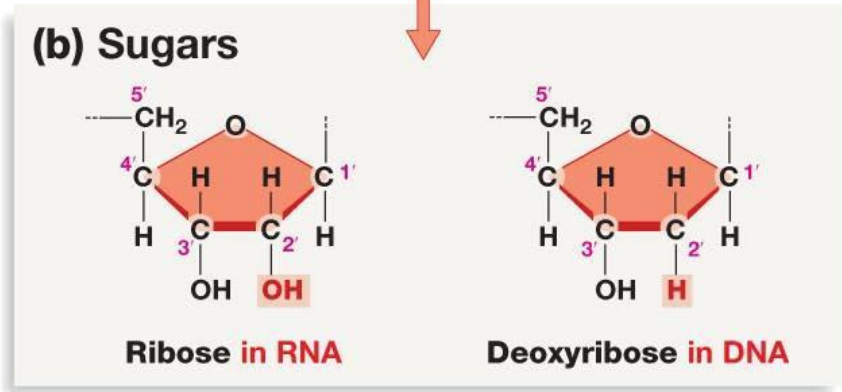
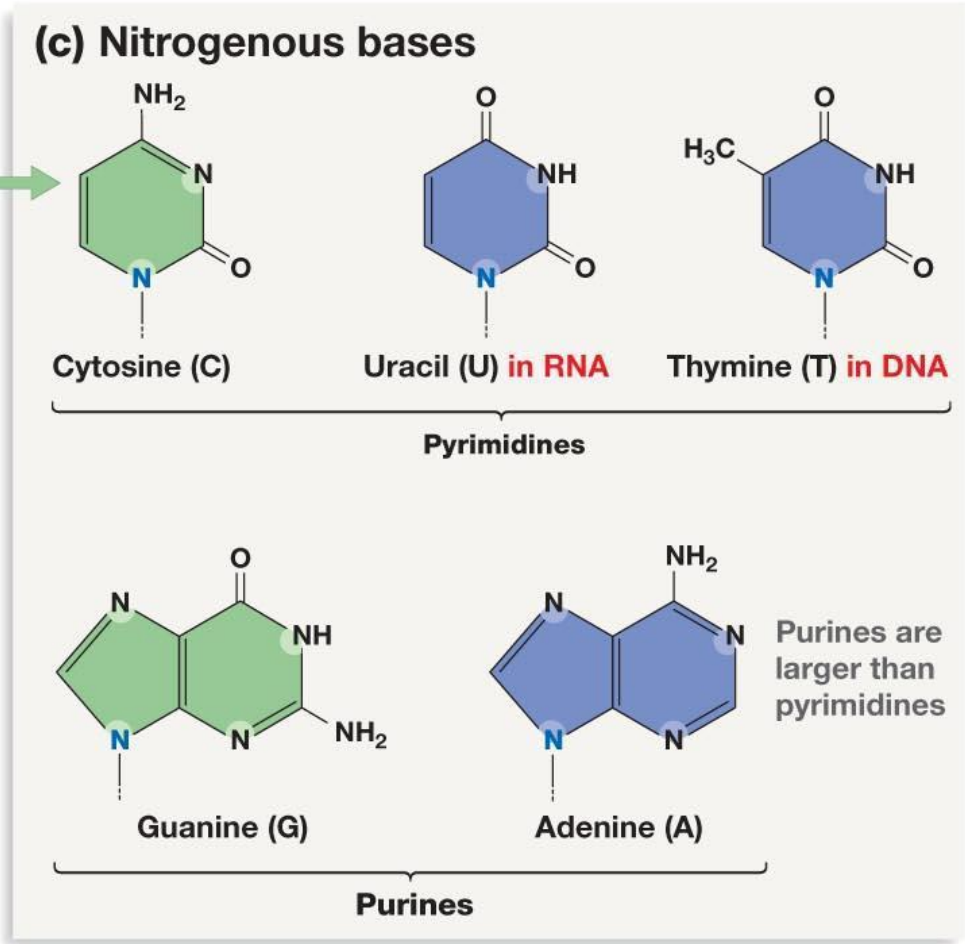
Състав на НК - нуклеотиди







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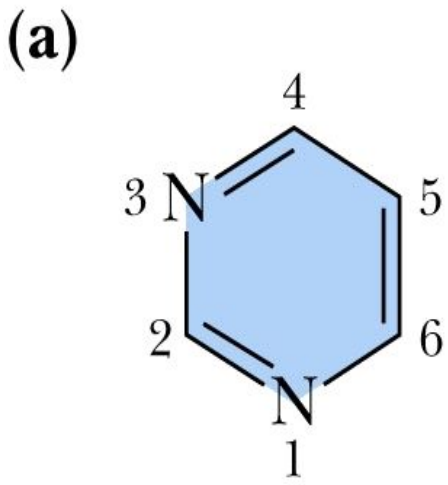
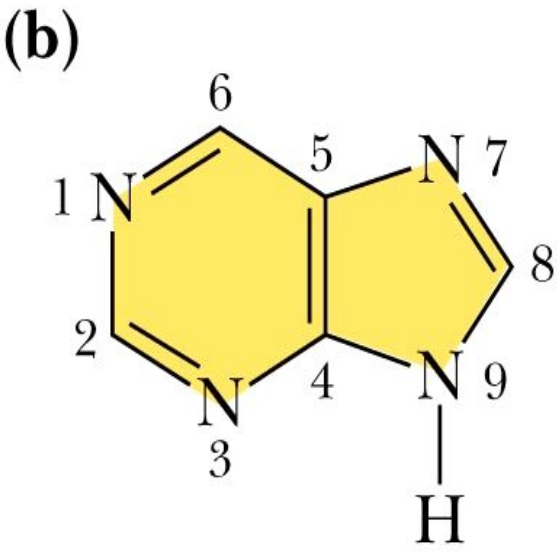
Структура на азотната база

Номерация!



Пиримидинов пръстен



Пуринов пръстен

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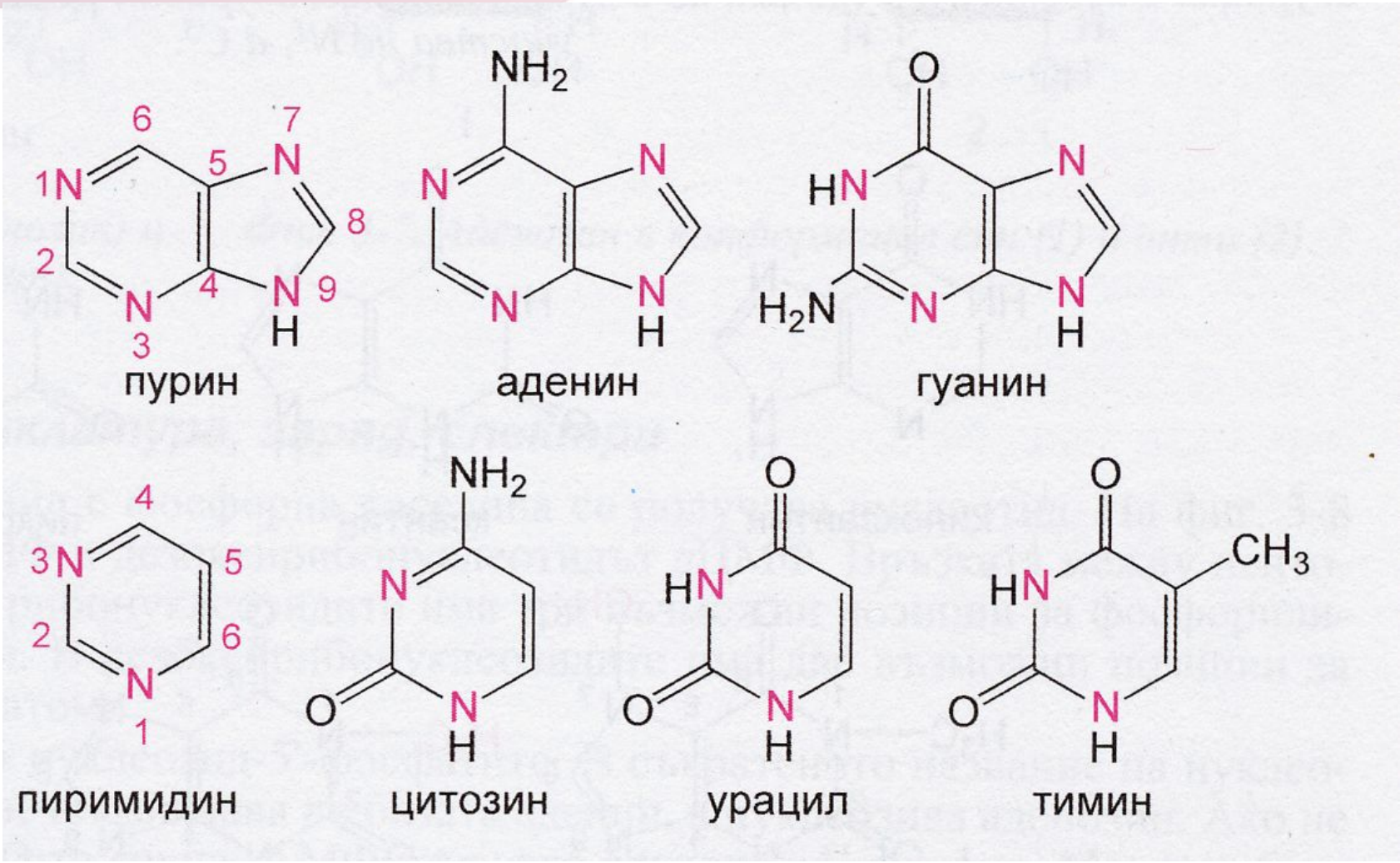
Пуринови и пиримидинови бази



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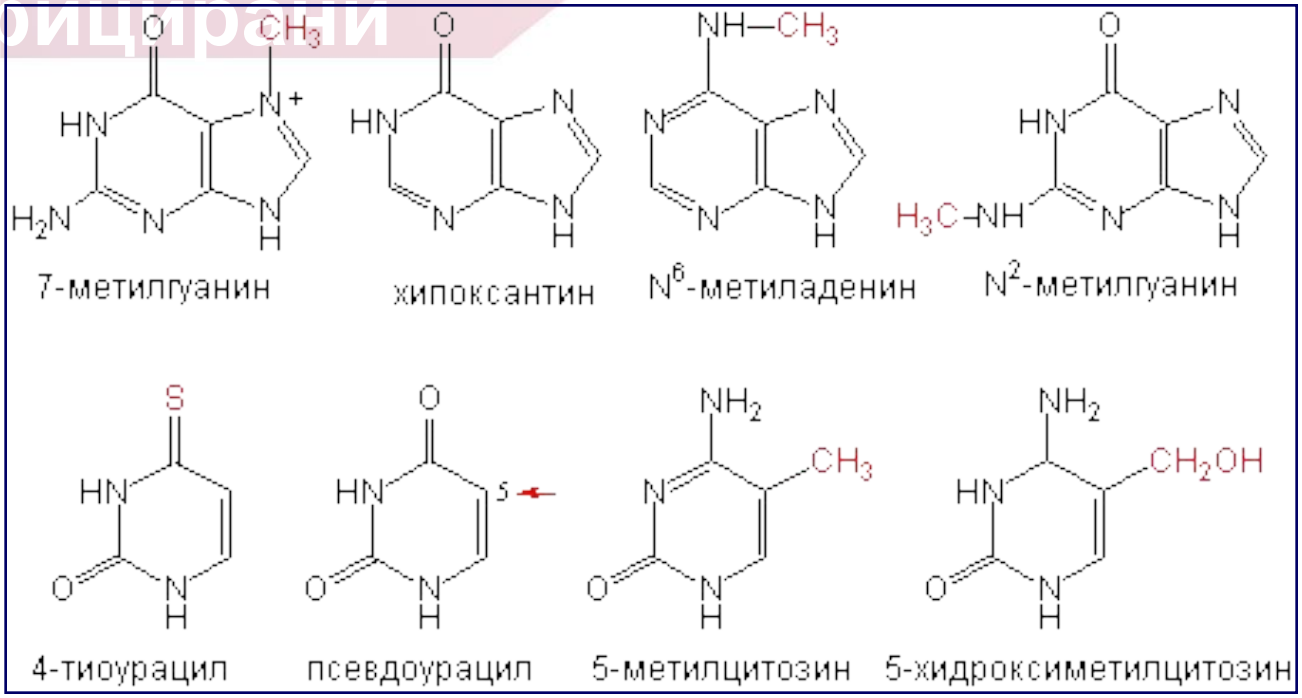
Минорни бази – химически модифицирани



Метилиране:

- Разпознаване свои-чужди
- Разпознаване стара-нова верига
- GC-“острови“

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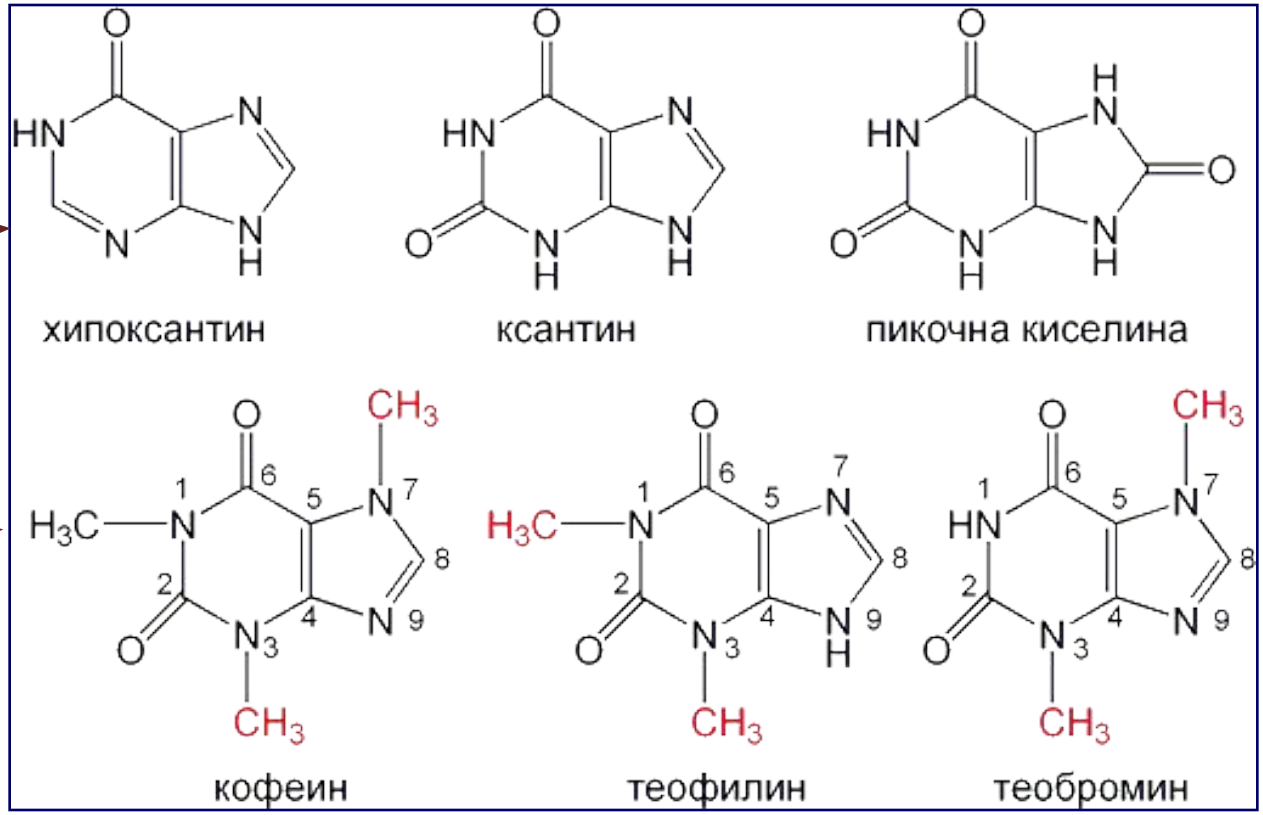
Бази, които не участват в състава на НК, но са с важно значение

При разграждане на нуклеотиди

В кафе и чай



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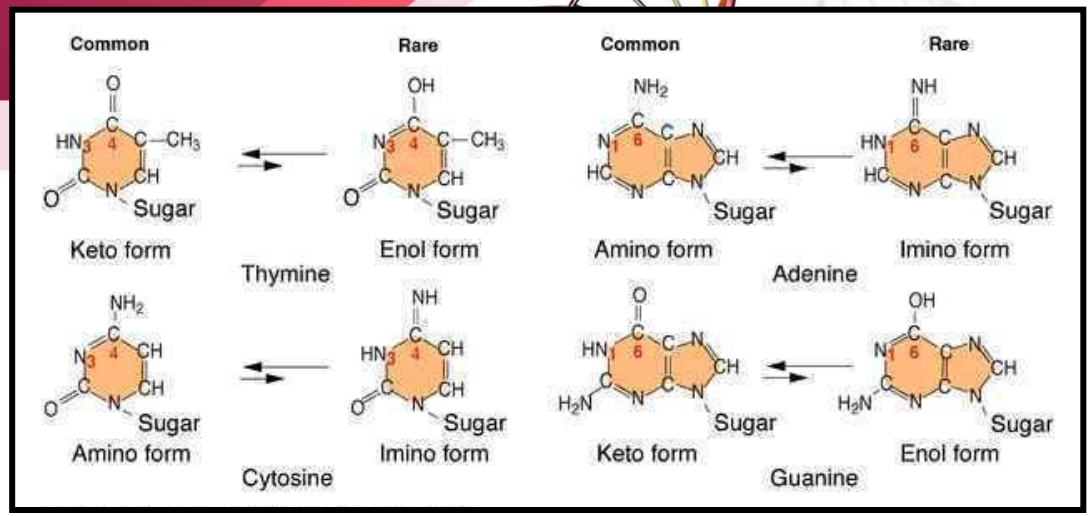
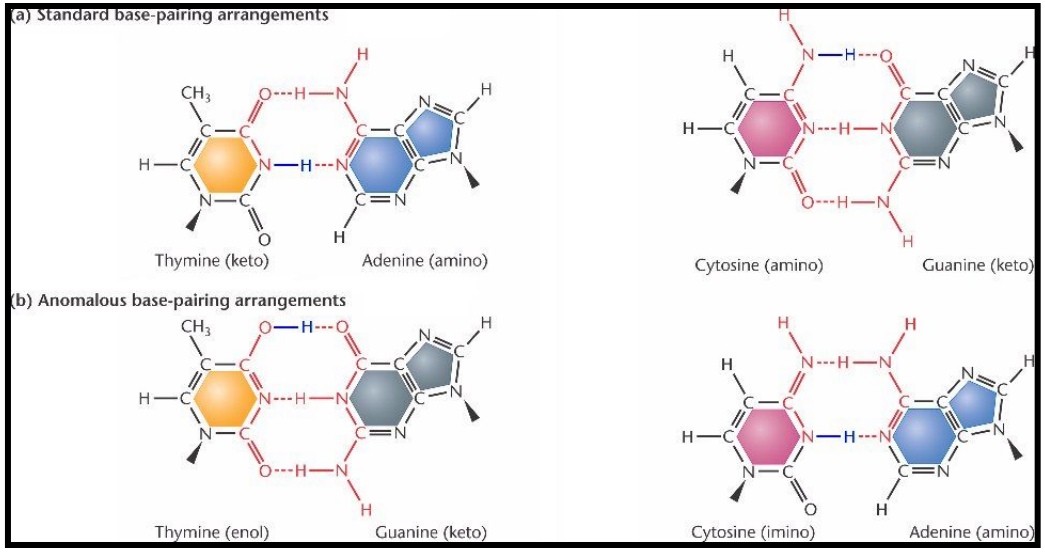
Тавтомерия на азотните бази

- Лактам-лактимна (кето-енолна)
- Амино-имино



Неправилно сдвояване -> мутагенно



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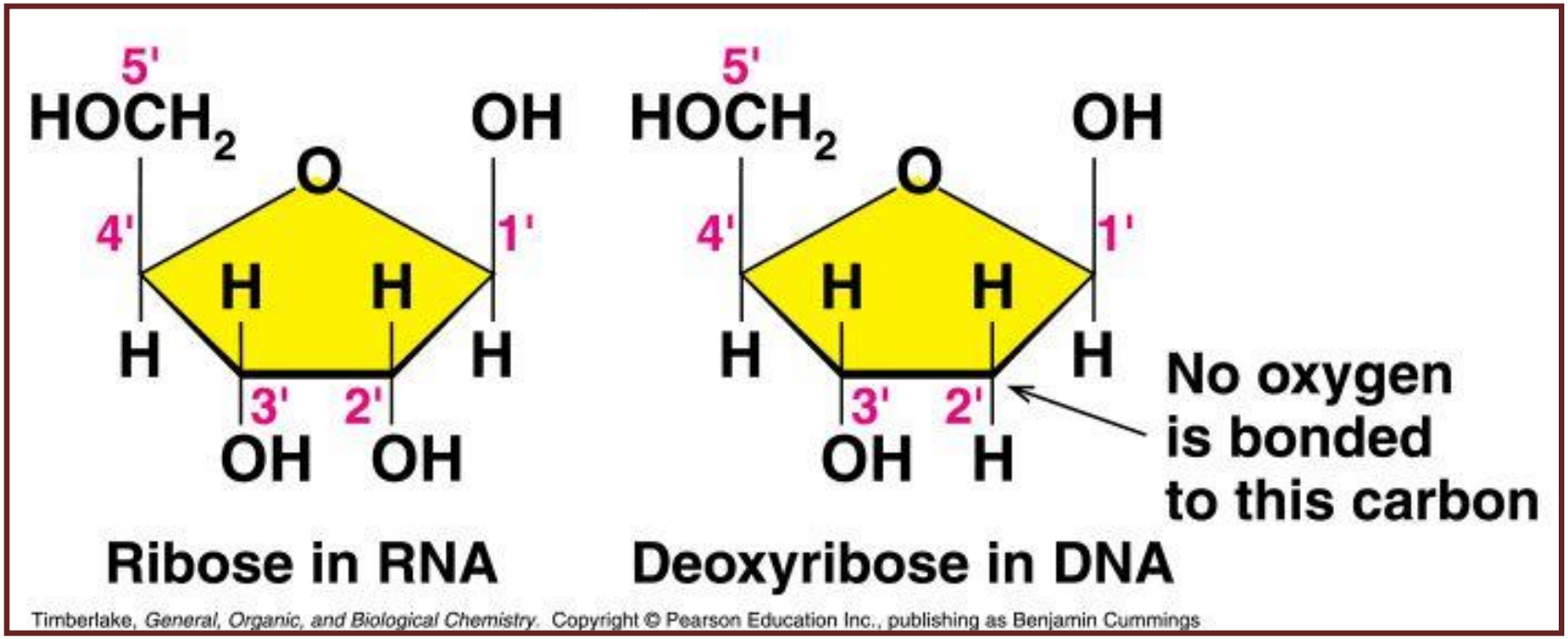
Пентоза

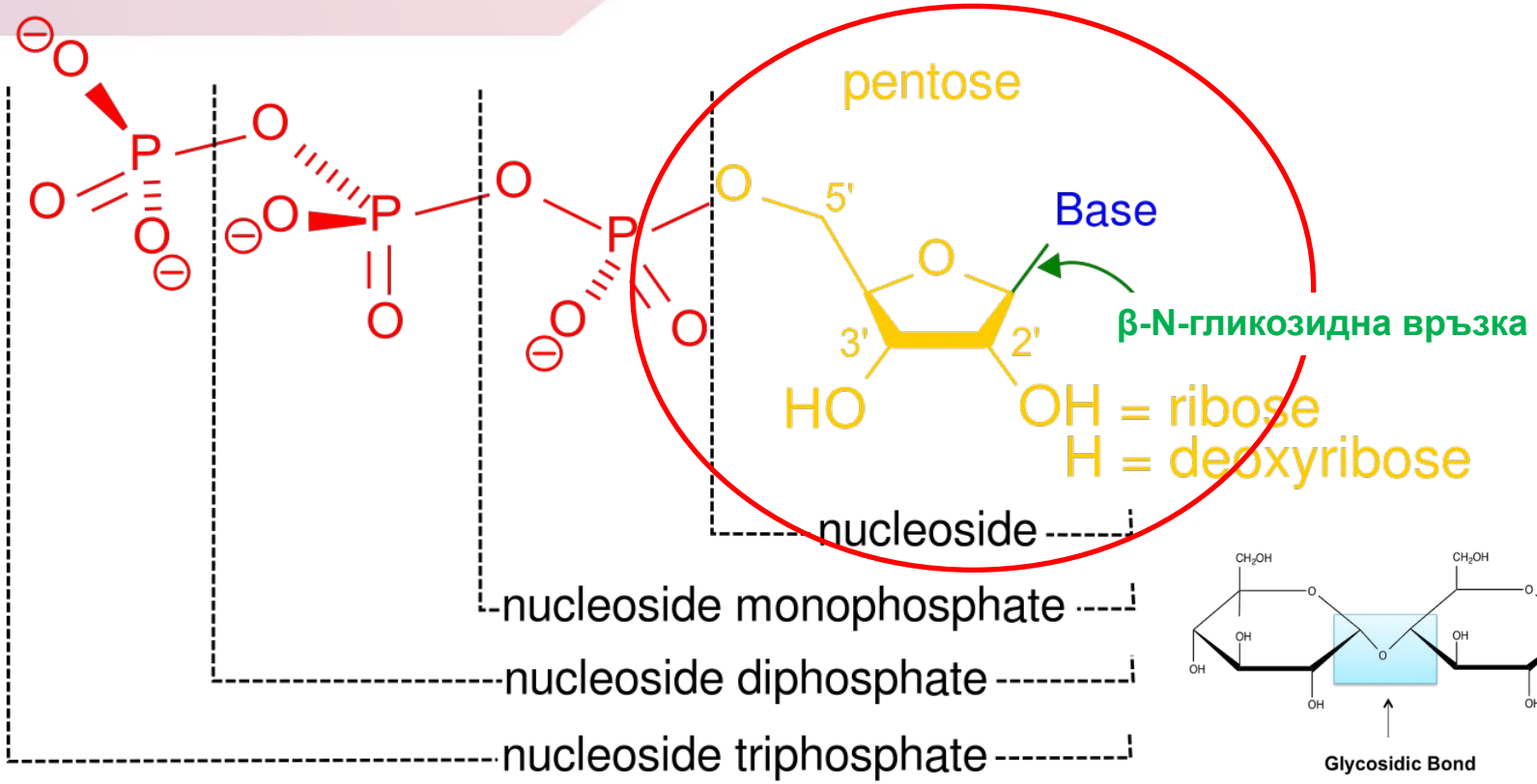


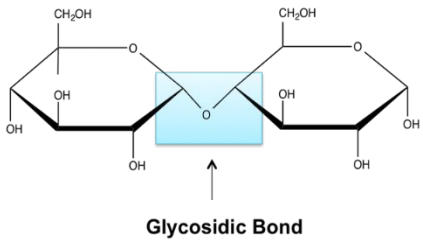
Два вида пентозни захари:

- РНК -> рибоза
- ДНК -> дезоксирибоза

Номериране на въглеродните атоми

Нуклеозиди





Наименования:

- Пуринови: -озин (аденозин, гуанозин)
- Пиримидинови: -идин (тимидин, цитидин, уридин)

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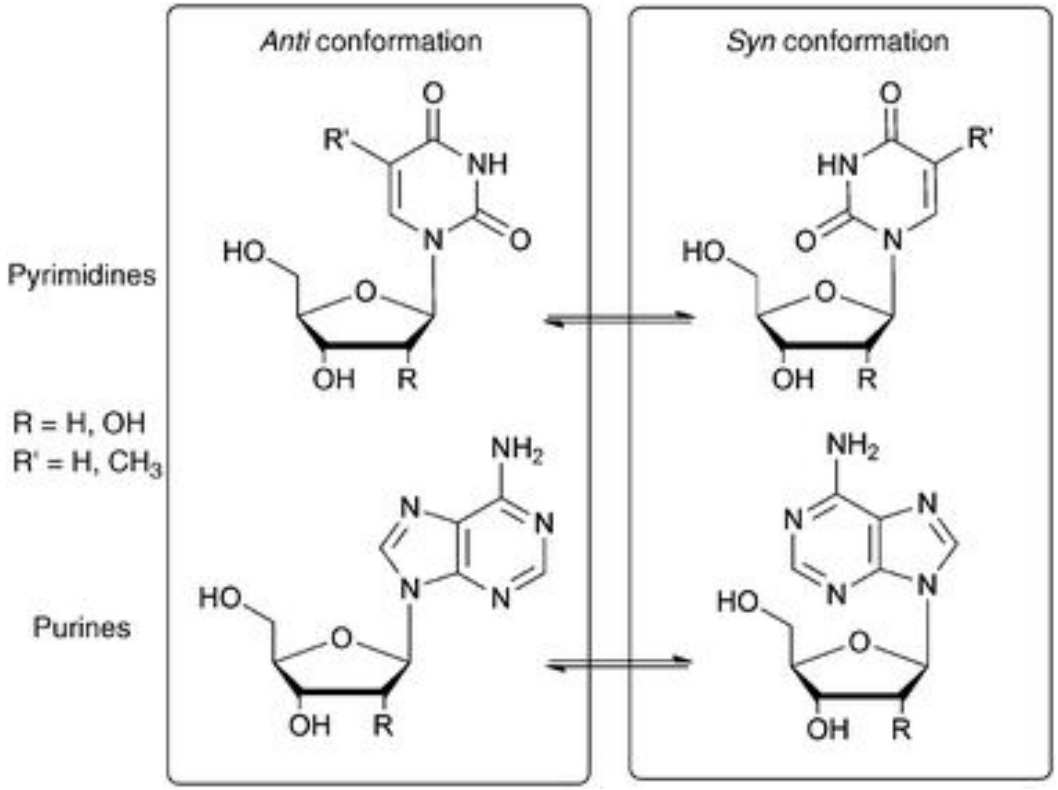
Нуклеозиди

2 конформационни форми:

- Син
- **Анти** – преобладаващо!



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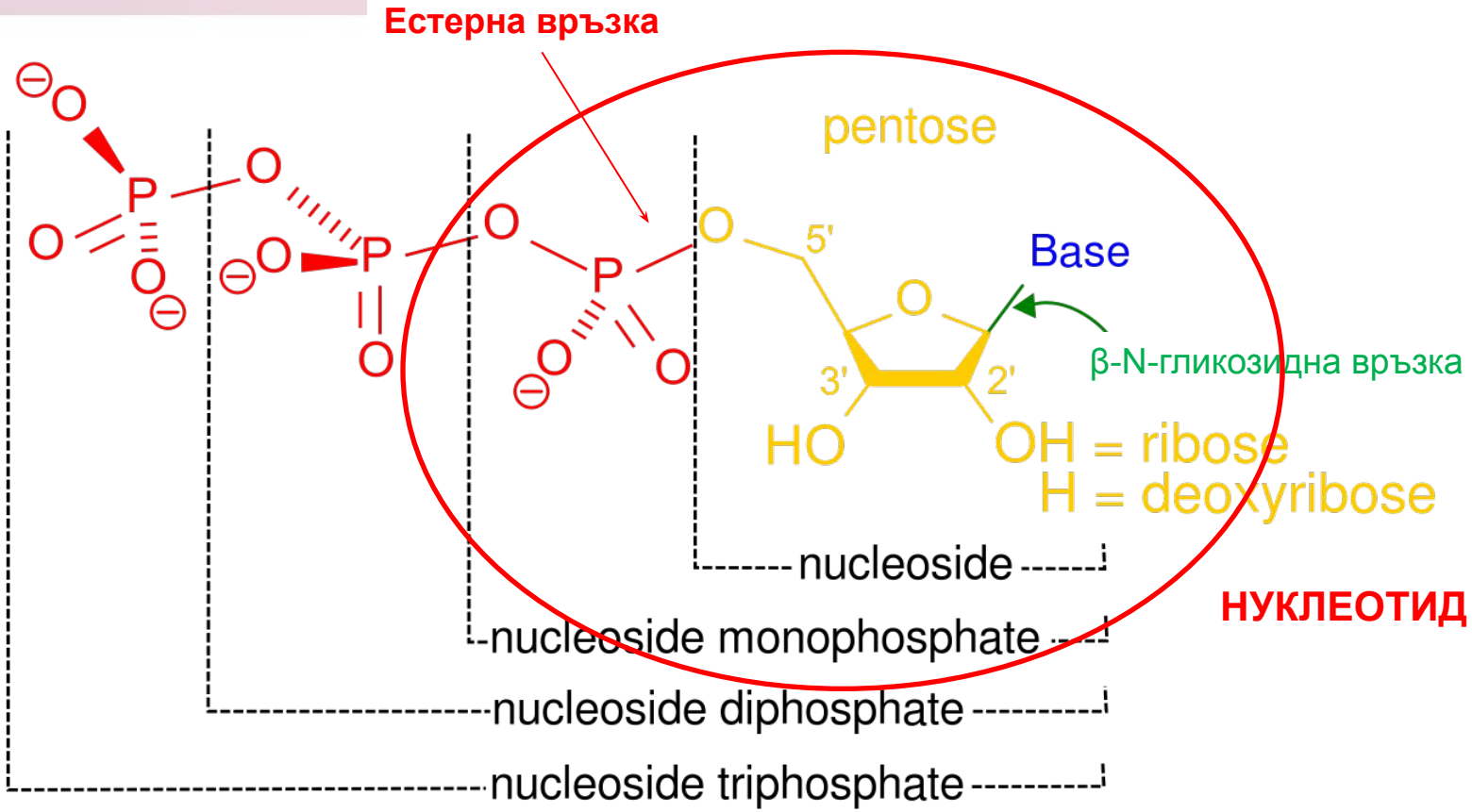
Нуклеозиди



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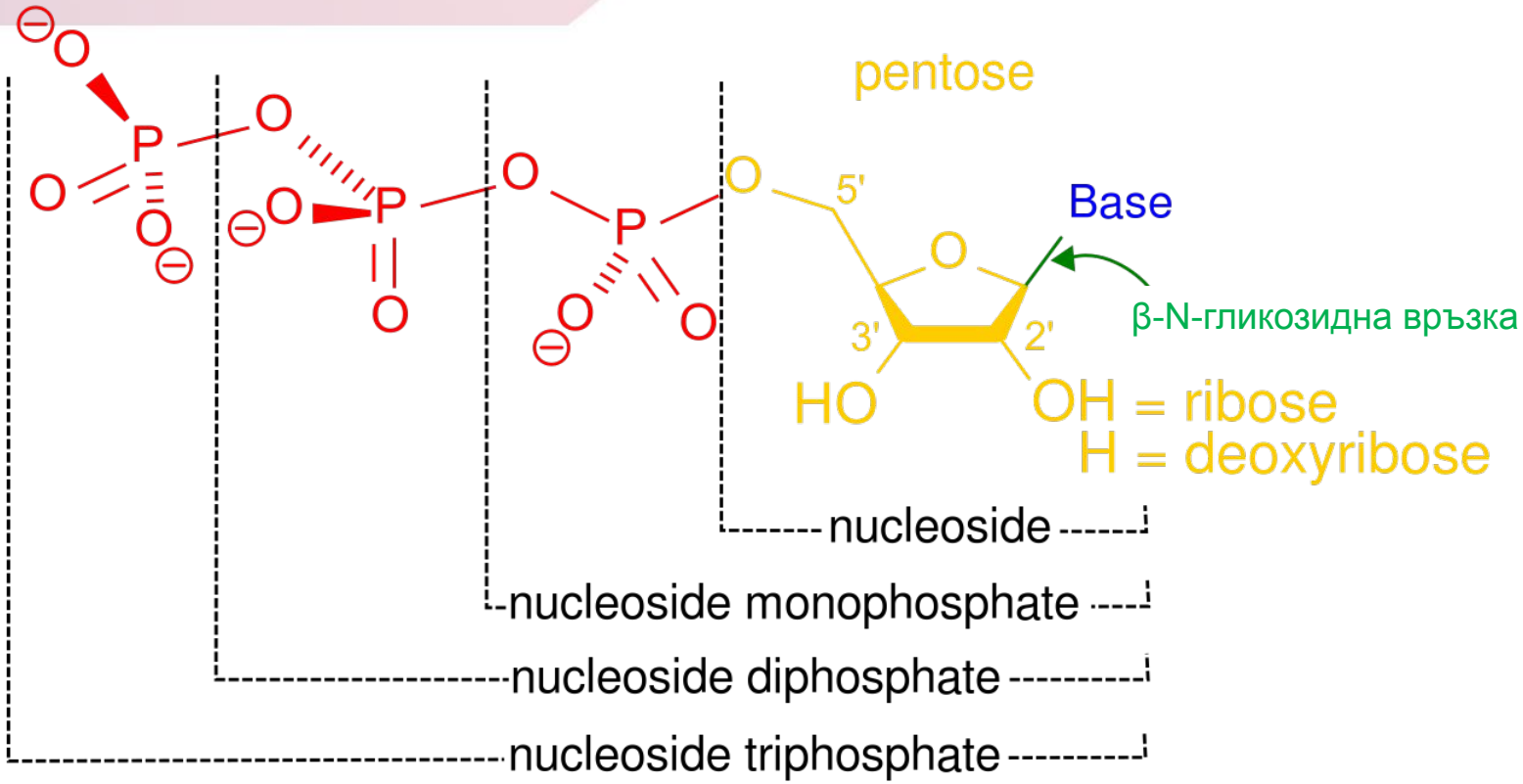
Нуклеозид-моно-, ди- и трифосфати



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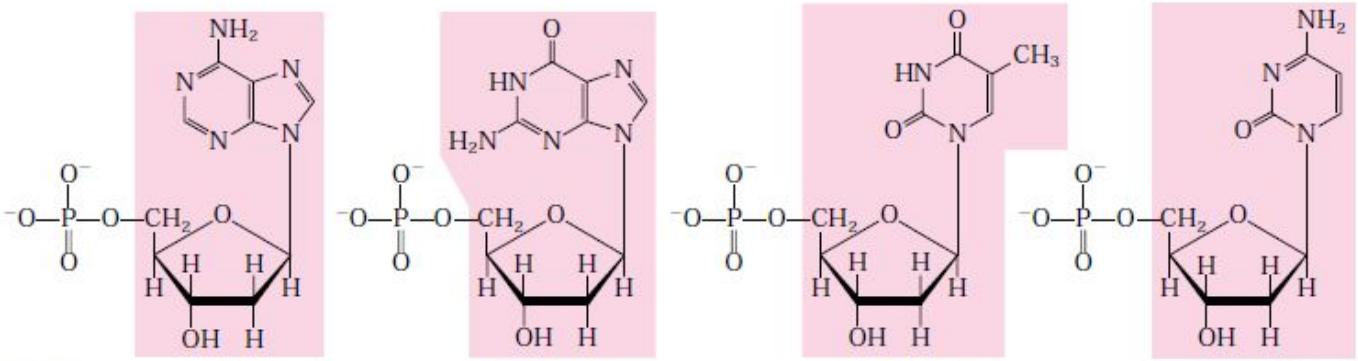
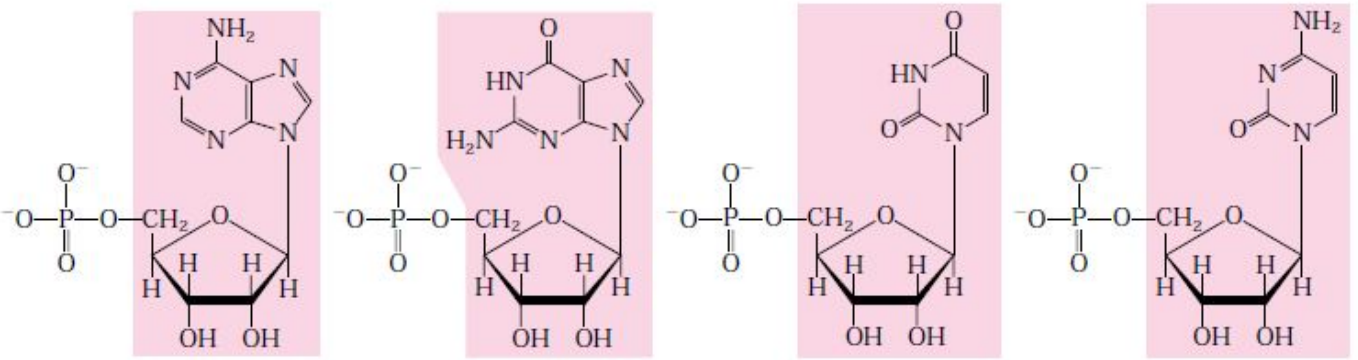
Нуклеотиди в състава на ДНК и



Nucleotide:	Deoxyadenylate (deoxyadenosine 5′-monophosphate)	Deoxyguanylate (deoxyguanosine 5′-monophosphate)	Deoxythymidylate (deoxythymidine 5′-monophosphate)	Deoxycytidylate (deoxycytidine 5′-monophosphate)
Symbols:	A, dA, dAMP	G, dG, dGMP	T, dT, dTMP	C, dC, dCMP
Nucleoside:	Deoxyadenosine	Deoxyguanosine	Deoxythymidine	Deoxycytidine

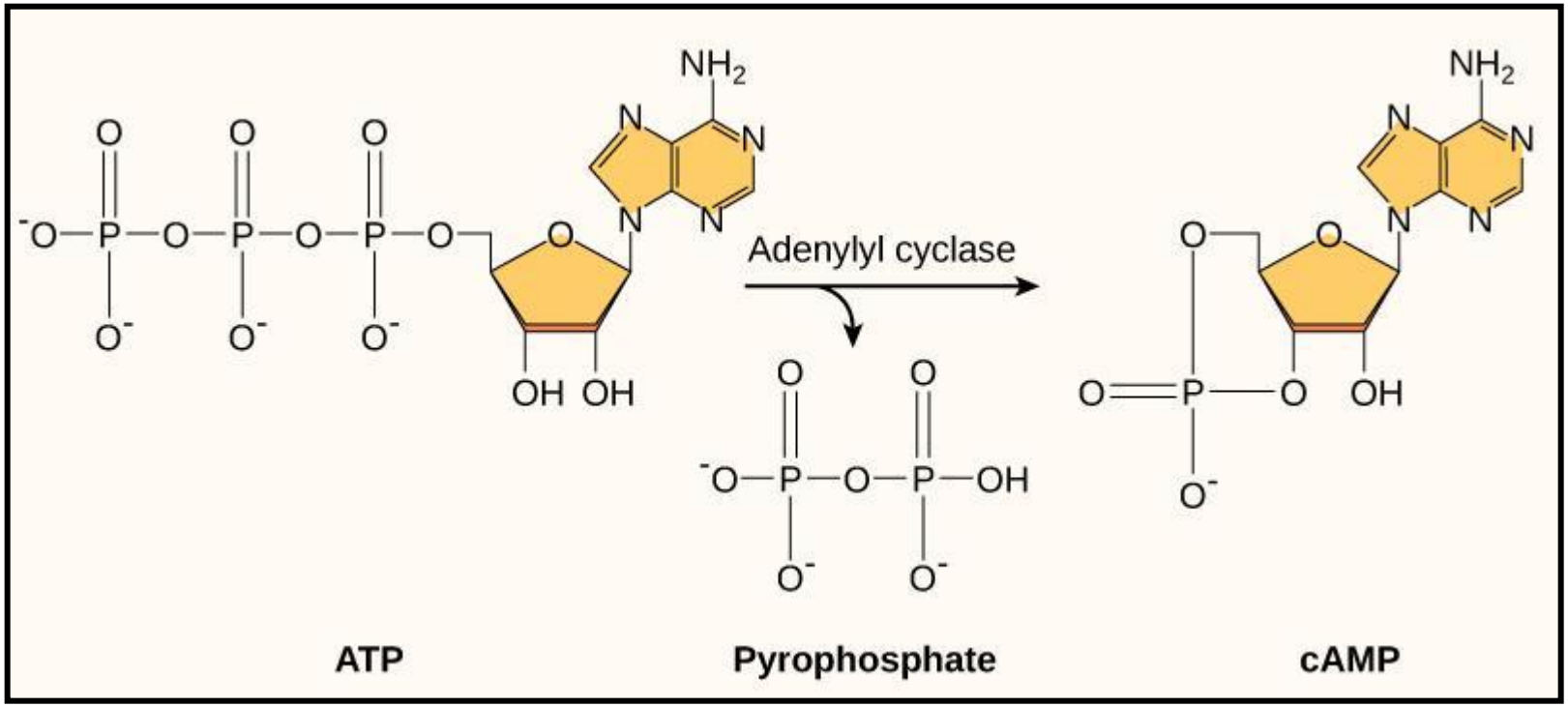
(a) Deoxyribonucleotides



Nucleotide:	Adenylate (adenosine 5′-monophosphate)	Guanylate (guanosine 5′-monophosphate)	Uridylate (uridine 5′-monophosphate)	Cytidylate (cytidine 5′-monophosphate)
Symbols:	A, AMP	G, GMP	U, UMP	C, CMP
Nucleoside:	Adenosine	Guanosine	Uridine	Cytidine

(b) Ribonucleotides

Цикличен нуклеотид



Роля - **Вторичен посредник**

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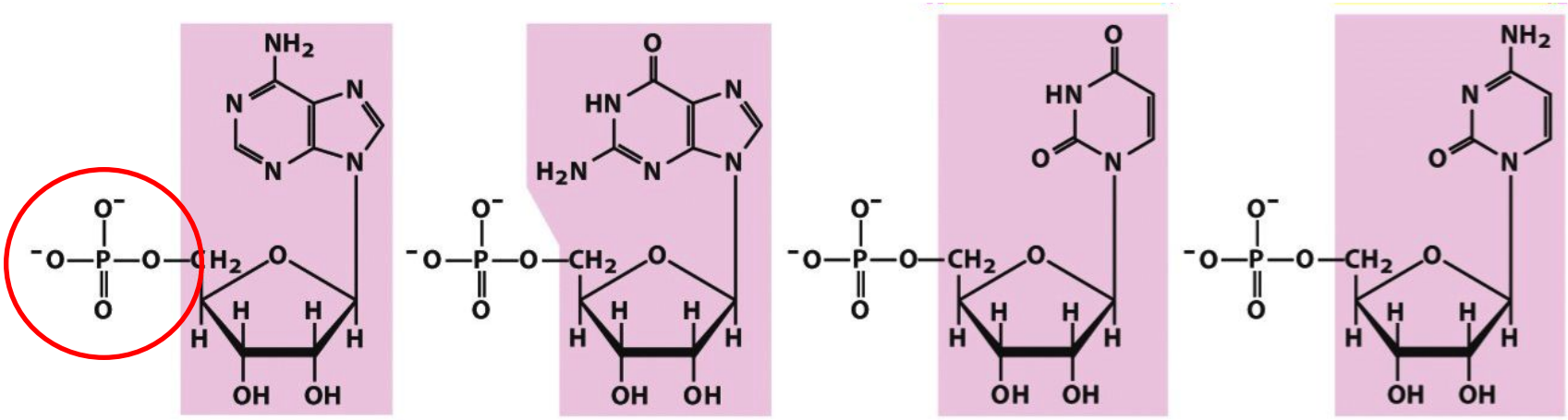
Заряд на нуклеотидите



Nucleotide:	Adenylate (adenosine 5′-monophosphate)	Guanylate (guanosine 5′-monophosphate)	Uridylate (uridine 5′-monophosphate)	Cytidylate (cytidine 5′-monophosphate)
Symbols:	A, AMP	G, GMP	U, UMP	C, CMP
Nucleoside:	Adenosine	Guanosine	Uridine	Cytidine

Ribonucleotides

Figure 8-4b
Lehninger Principles of Biochemistry, Fifth Edition
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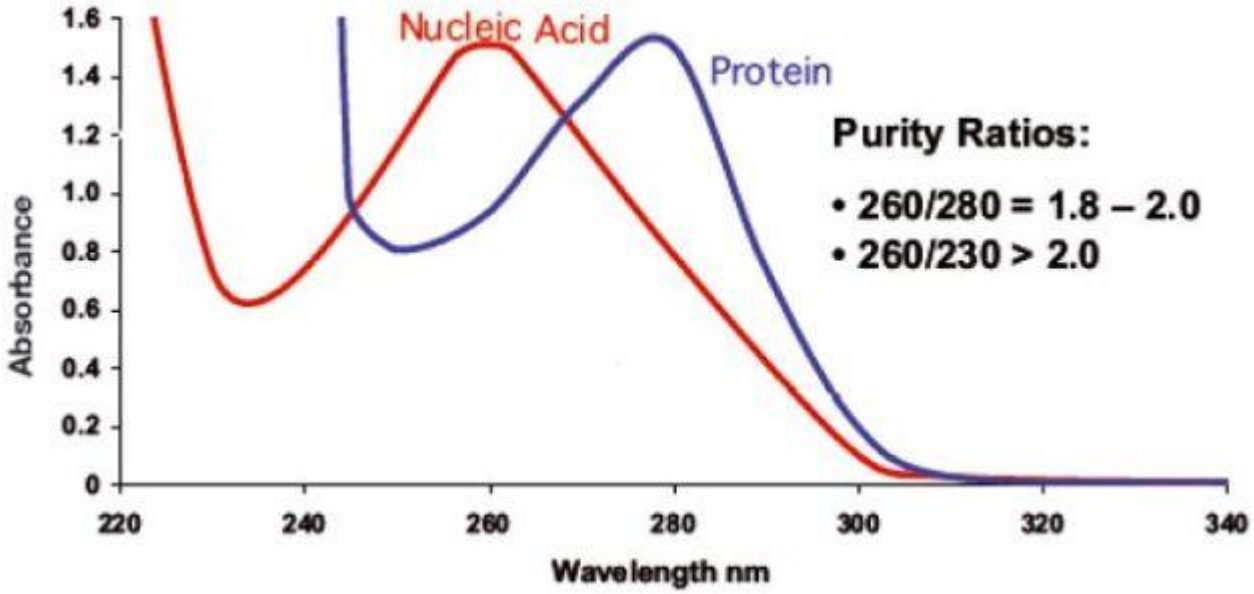
Спектър на поглъщане

- Максимум на поглъщане – **260 nm** (UV)
- Мутагенно действие на UV



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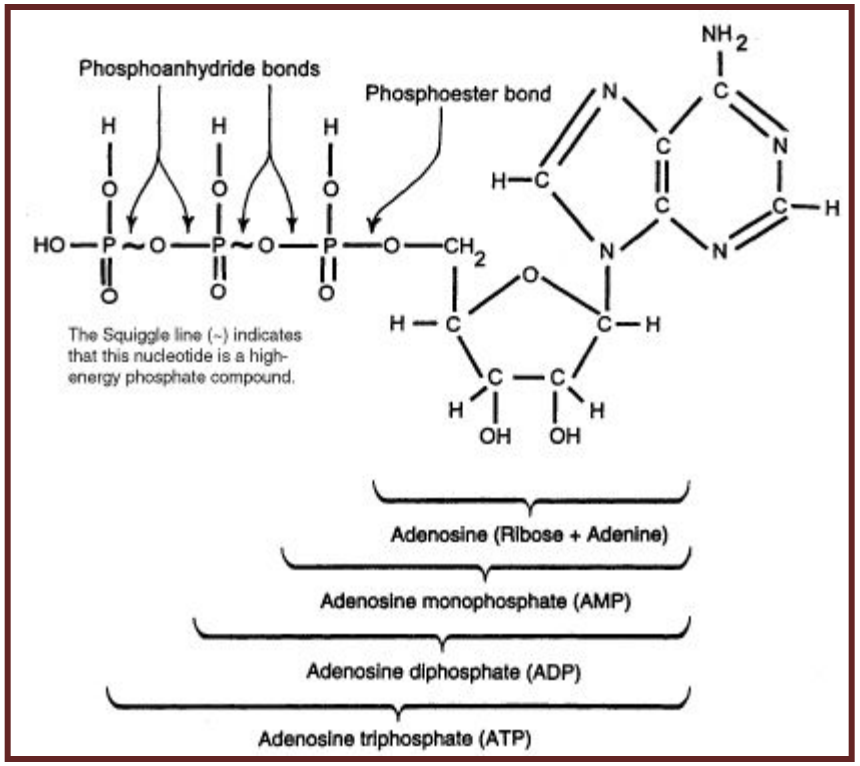
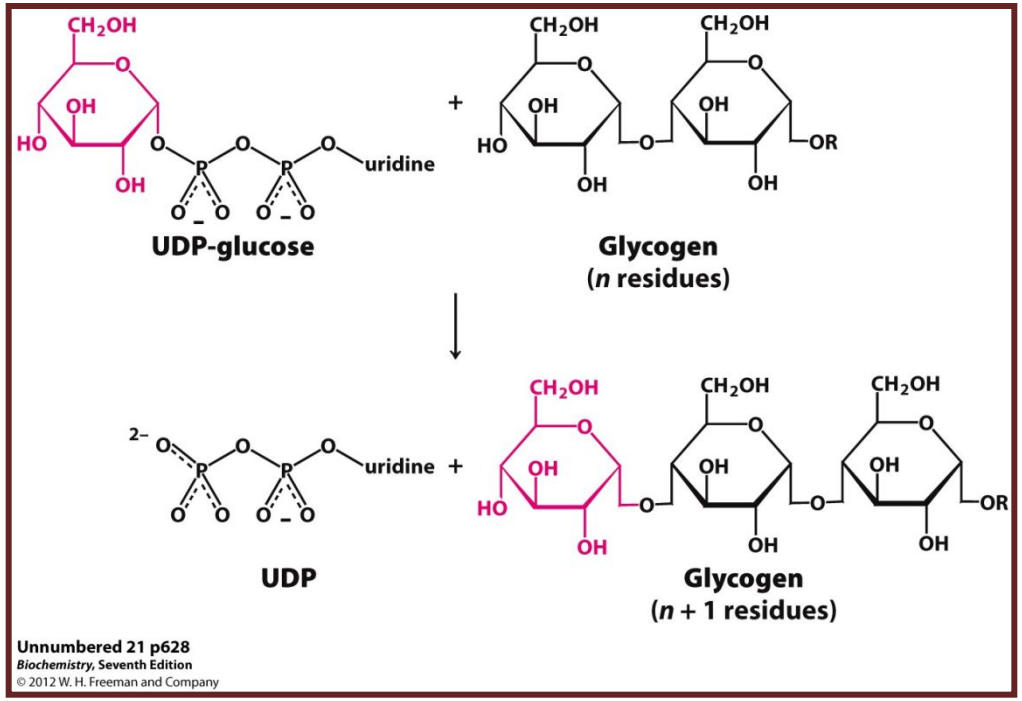
Роля на нуклеотидите

1. Висок потенциал за групов пренос – **макроергични връзки** (киселинно-ахидридни фосфатни връзки)
2. Участие в **метаболизма**





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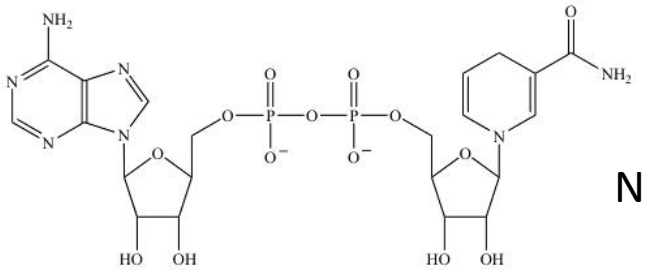
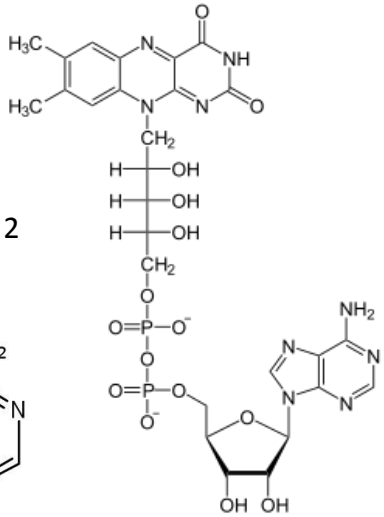
Роля на нуклеотидите

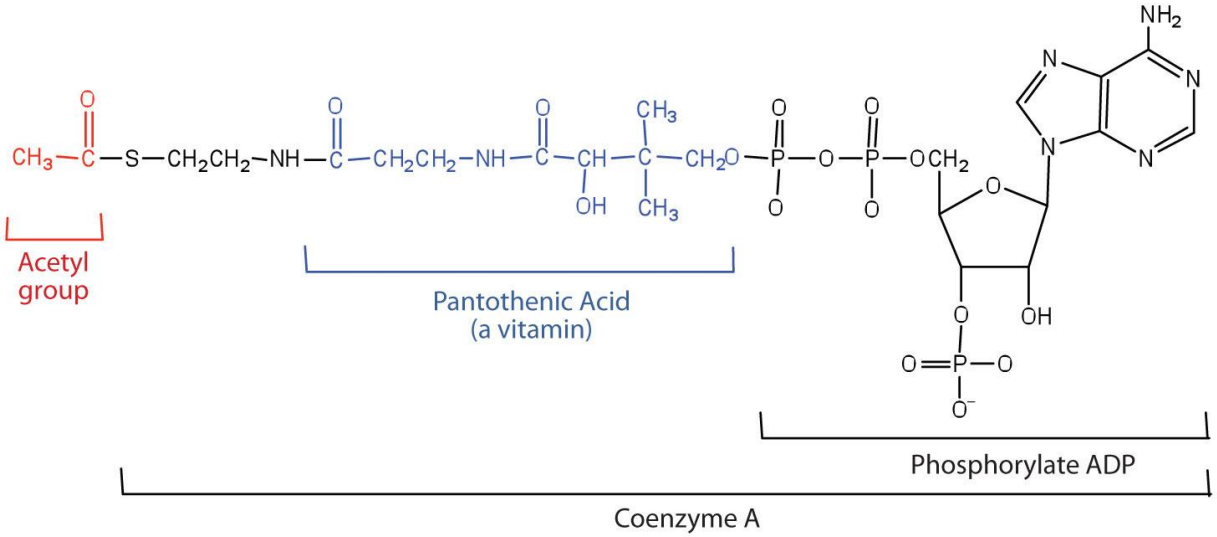
3. Участие в състава на по-сложни **коензими**



NADH

FADH$_2$





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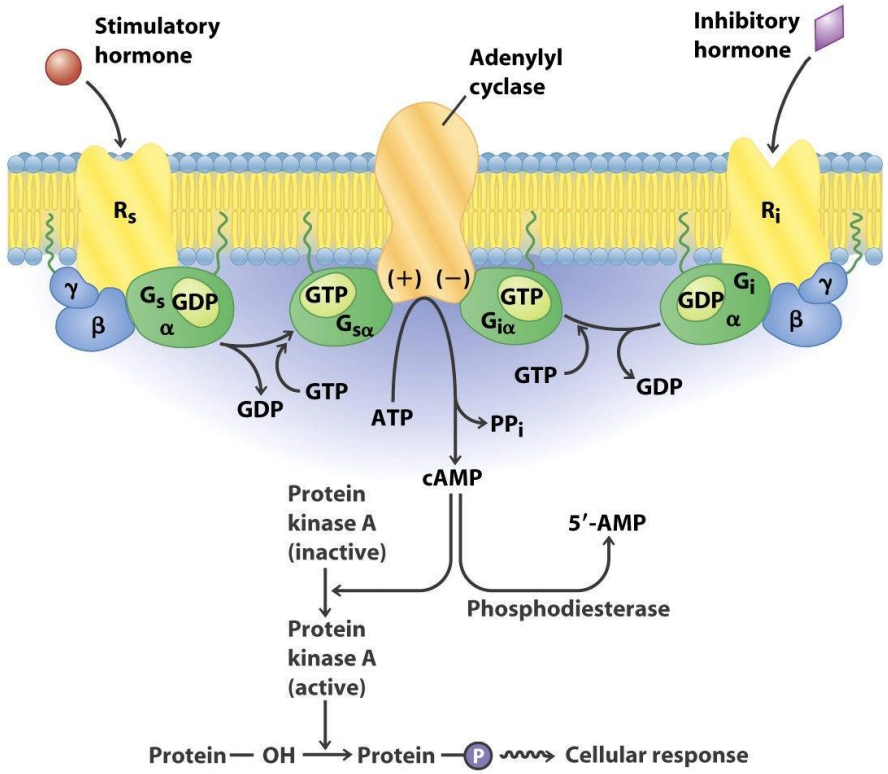
Роля на нуклеотидите

4. **Регулаторен** ефект – съотношение ADP/ATP
5. **Алостерични ефектори**
6. Циклични нулеотиди (cAMP, cGTP) – **сигнална трансдукция**



Principles of Biochemistry, 4/e
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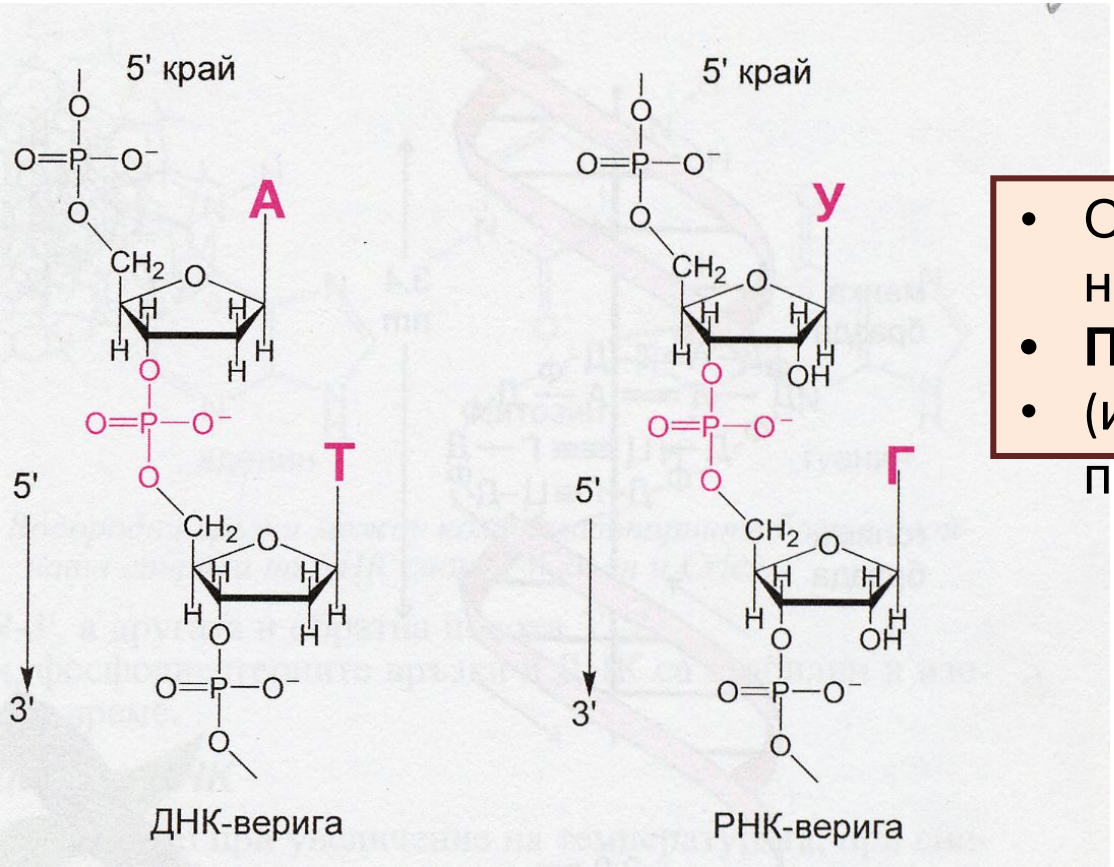
Първична структура

- **Последователността на нуклеотидите** в ПНВ
- Определя свойствата
- **Ковалентни 3‘-5‘-фосфодиестерни връзки**



- Отворени вериги, **линейни**, неразклонени
- **Полярни** - 2 различни края
- (изкл. Митохондрии, прокариоти)

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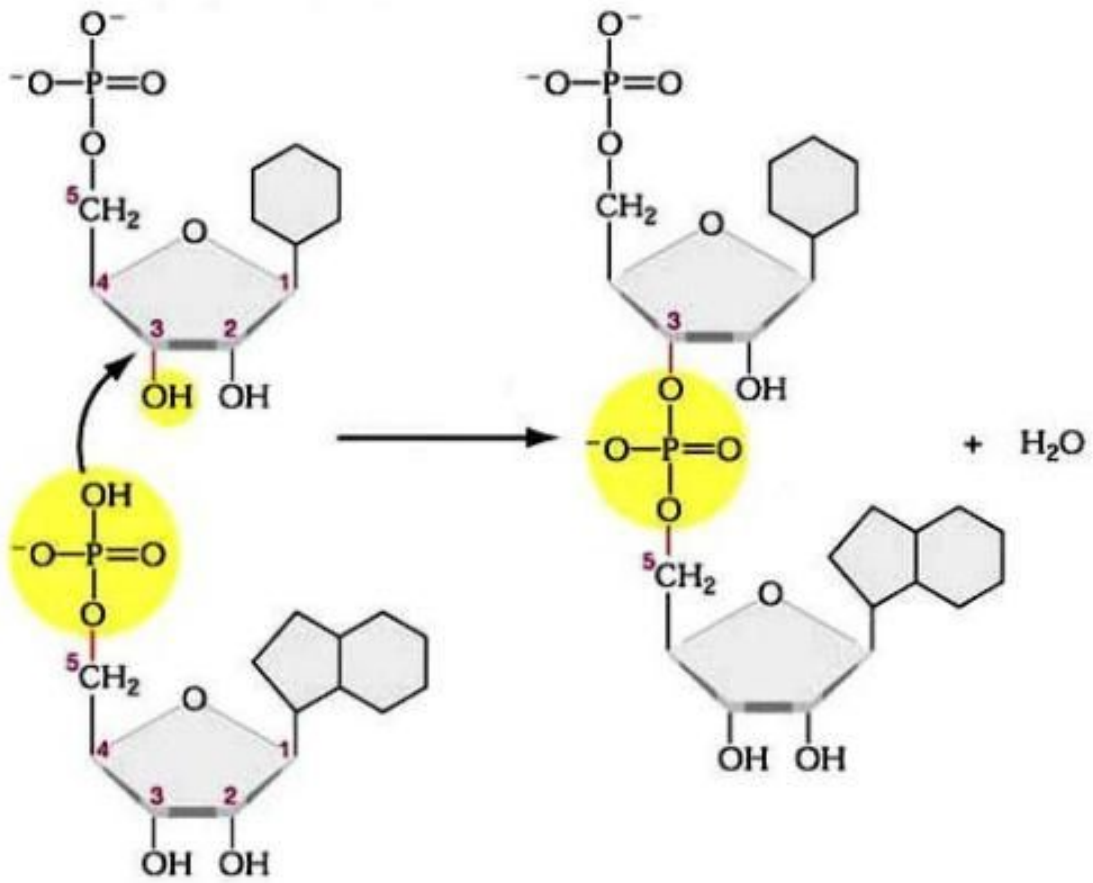
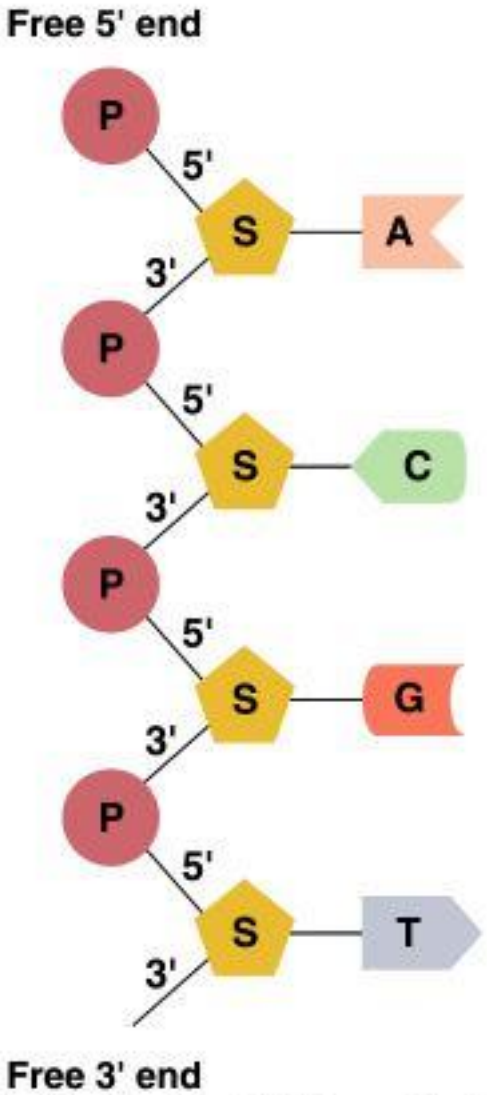
Фосфодиестерна връзка



Посока

- Нуклеиновите киселини имат **свободна 5‘-фосфатна група** в единия си край и **3‘-хидроксилна група** в другия край
- Нуклеотидната последователност се дава в посока **5‘→3‘**
- Например:

5’—A—C—G—T—3’



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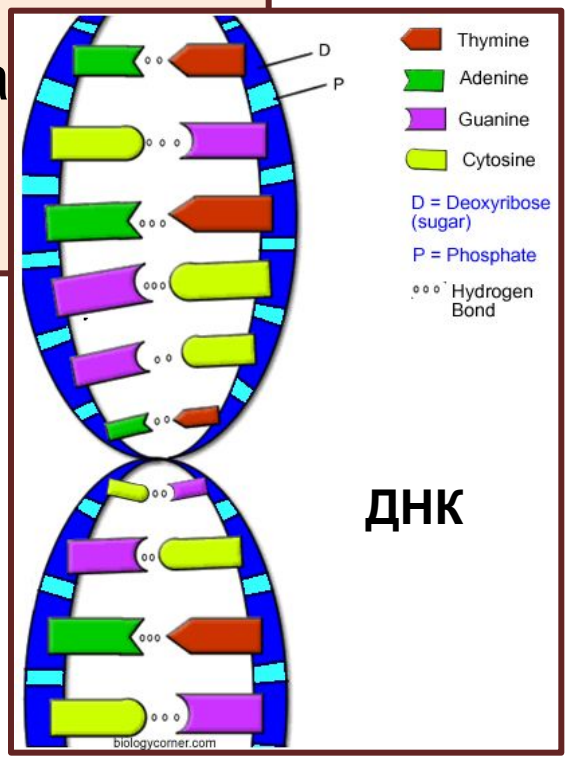
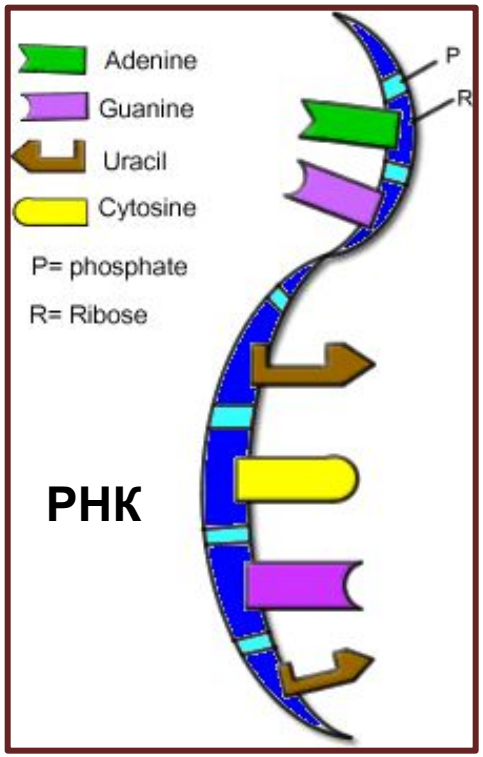
Разлика между ДНК и РНК

- Пентоза
- Пиримидиновите бази
- Молекулна маса
- Локализация в клетката
- функции





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ДНК

- **Размери**:
- E. coli $4x10^6$bp
- човек – хаплоиден геном с 23 хромозоми – $3x10^9$ bp

- **Локализация:**
- ~99% от ДНК при еукариоти – **в ядрото** -> хроматин
- ~1% - **в митохондриите**, 2-10 копия, кръгова молекула

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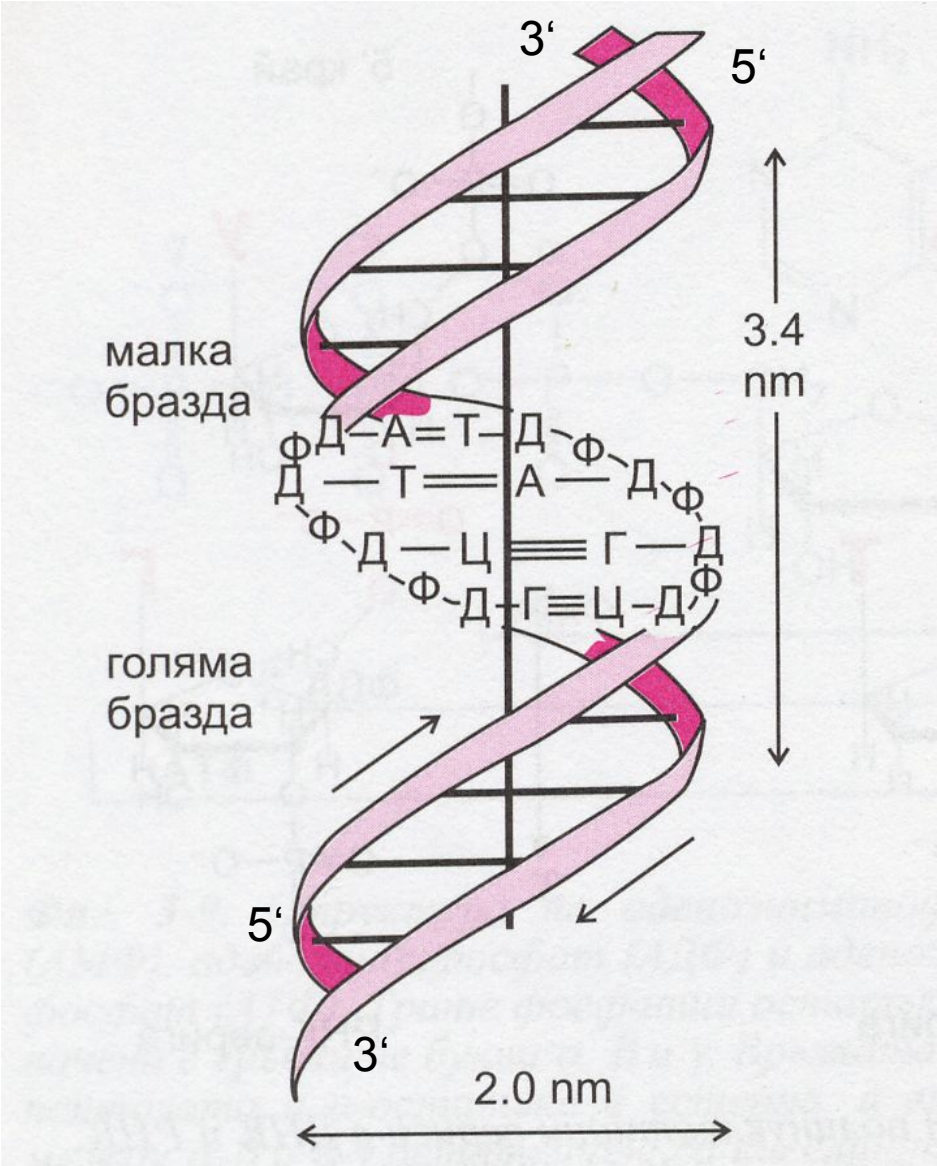
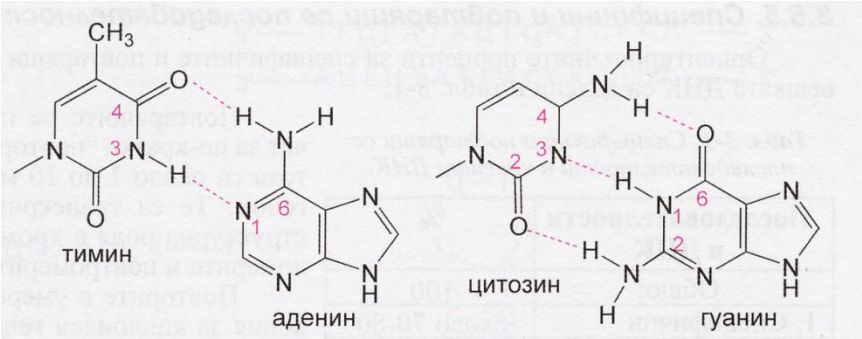
Модел на Watson и Crick за двойноспирална структура на ДНК



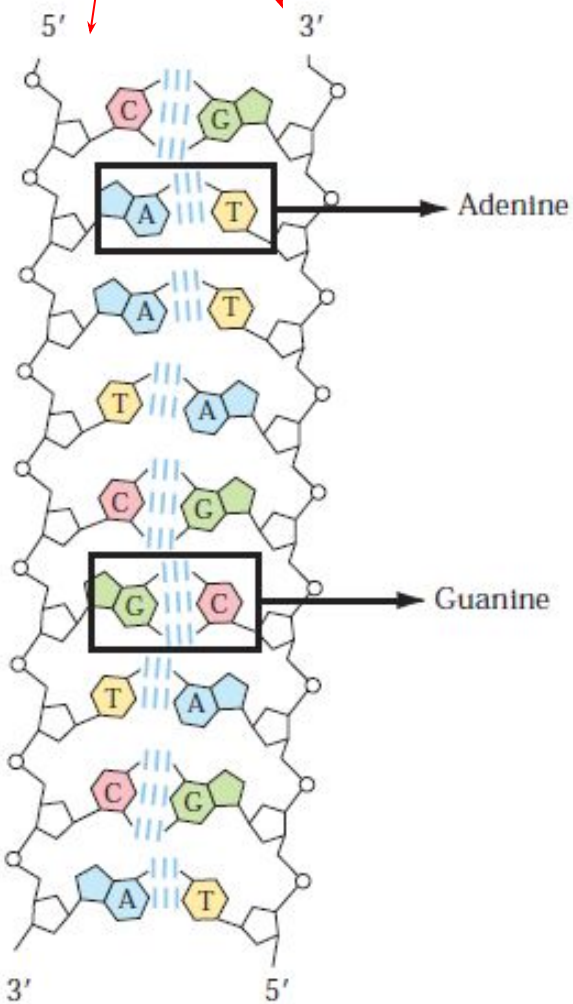
- 2 вериги
- Антипаралелни
- комплементарни
- 2 бразди

Водородни връзки



Модел на Watson и Crick за двойноспирална структура на ДНК

Дезоксирибофосфатни скелети



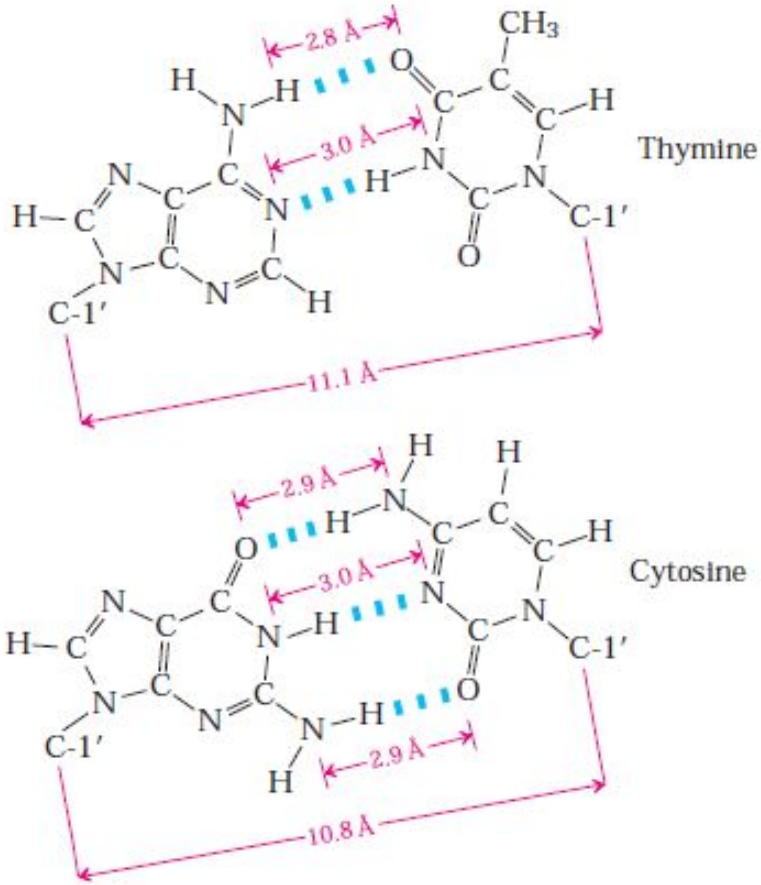
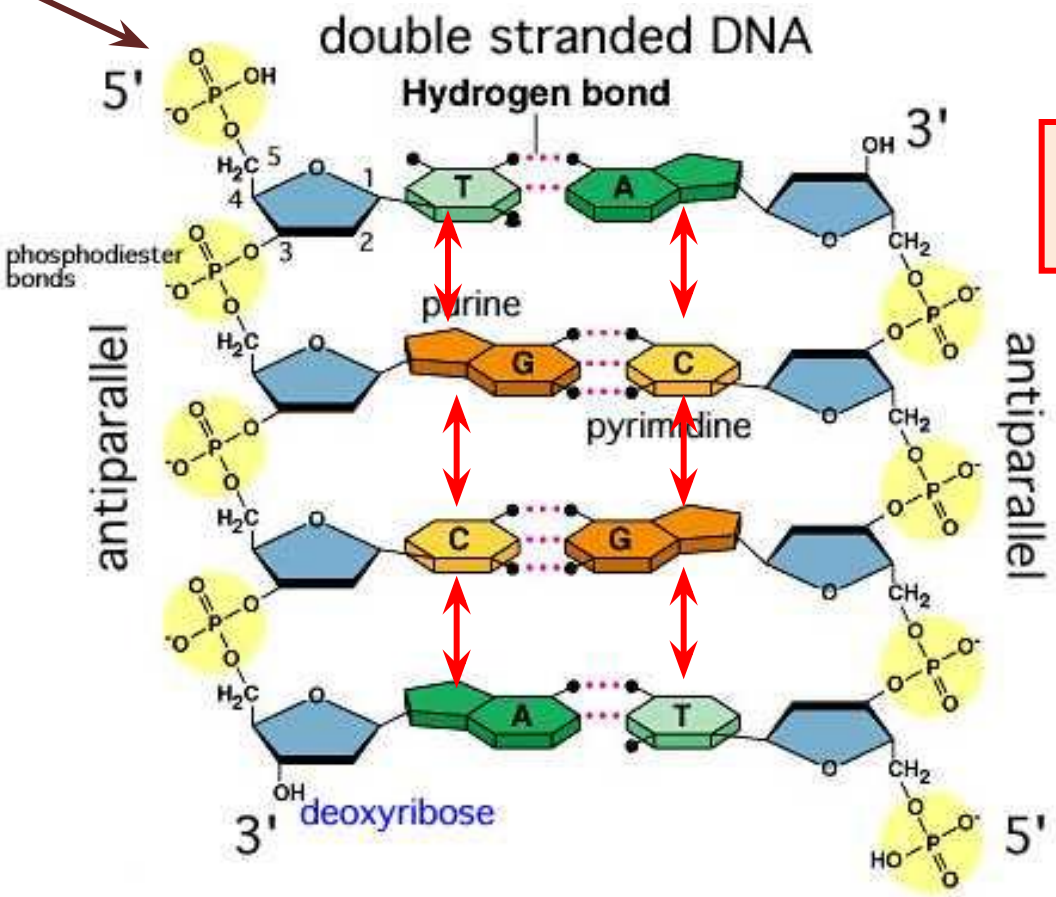


FIGURE 8–11 Hydrogen-bonding patterns in the base pairs defined by Watson and Crick. Here as elsewhere, hydrogen bonds are represented by three blue lines.

Модел на Watson и Crick за двойноспирална структура на ДНК

Отрицателен заряд по повърхността

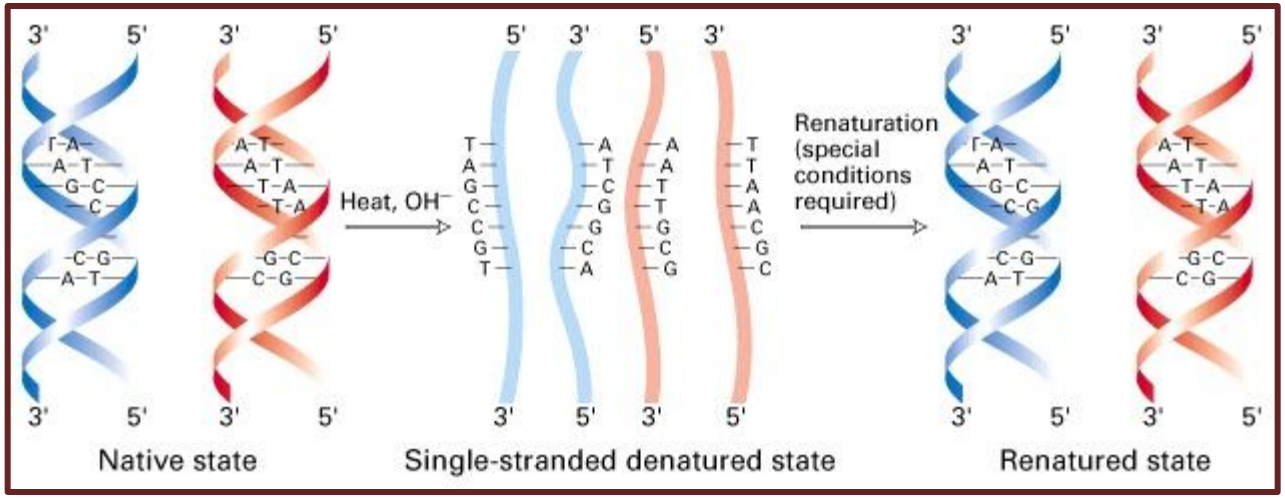


Стекинг взаимодействия

(π- взаимодействия)

Денатурация на ДНК

- Висока температура, ниска солева концентрация, алкална среда
- **Разделяне на двете вериги**, запазват се само фосфодиестерните връзки
- **Обратима** (ренатурация) – бавен процес

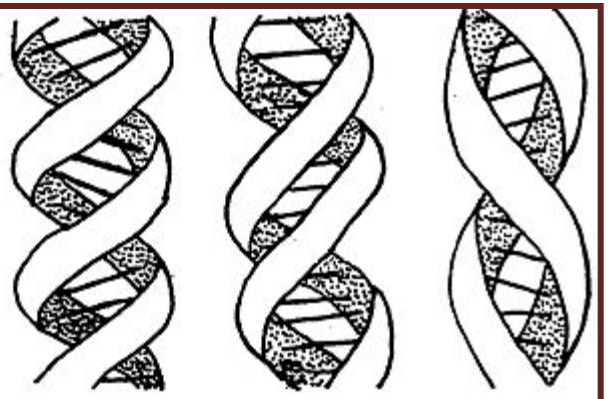


- **Хибридизация** – специфична асоциация на комплементарни вериги от различен произход

Конформационни форми на ДНК в следствие вариации в конформацията на нуклеотидите

3 форми: **B**, A и Z:

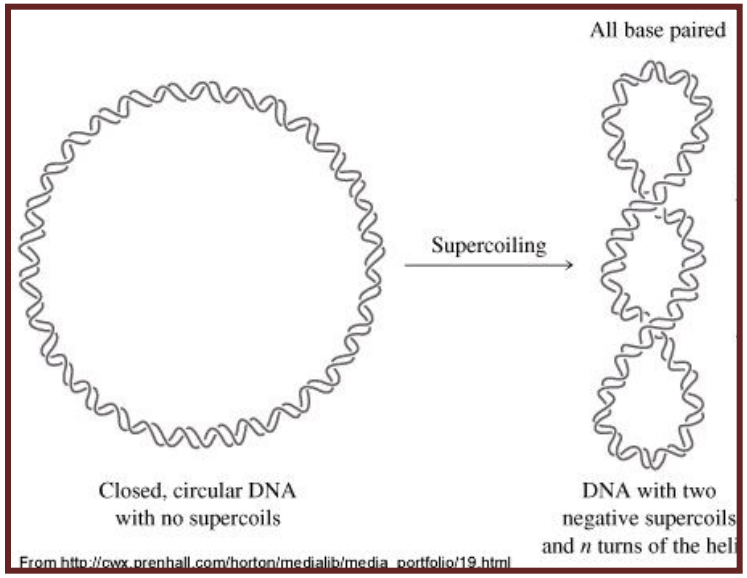
- **B** – най-стабилна, модел на Уотсън и Крик, преобладава във физиологични условия, дясновъртяща
- A – при дехидратация на B, по-компактна
- Z – по-разтегната, лявовъртяща, зигзагообразна

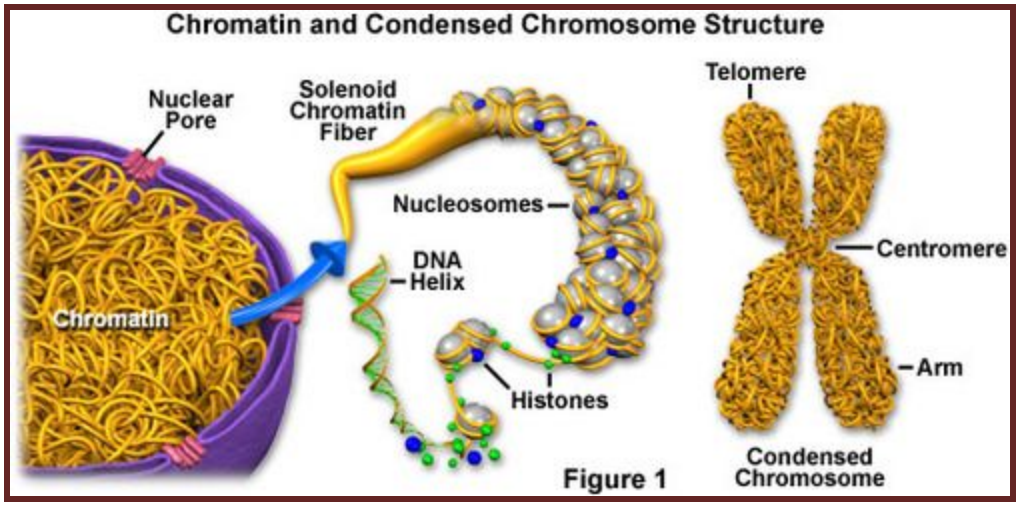


Form	A	B	Z
helical twist	right	right	left
base pairs per turn	11	10	12
occurrence	RNA, DNA	DNA	DNA

Суперспирализиране

- При огъване или извиване на оста на двойната спирала
- При про- и еукариоти
- Напрегната структура





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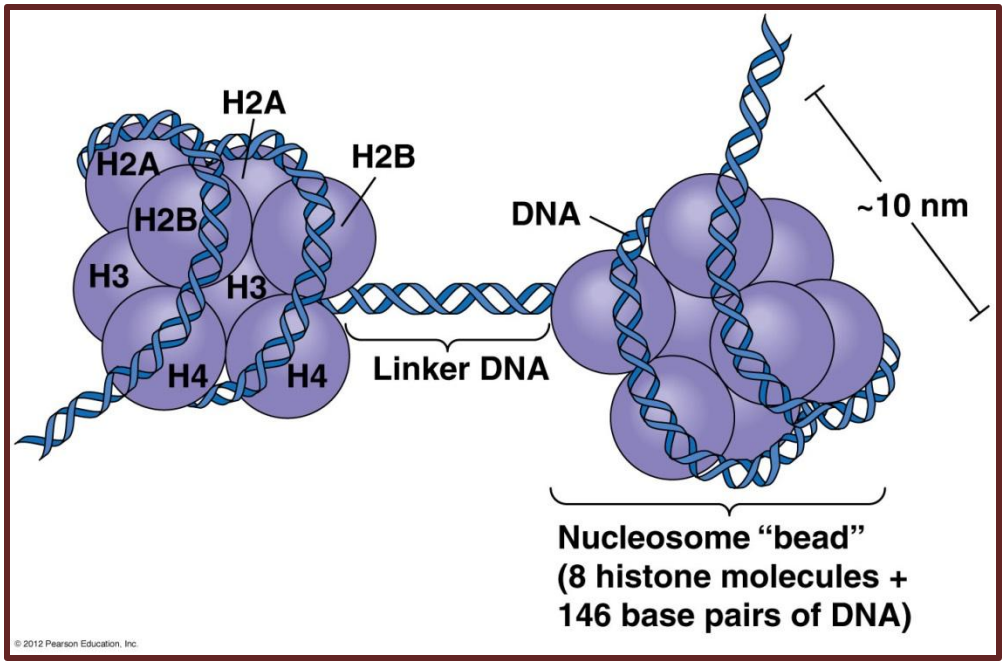
Хистонови белтъци

- **Консервативни**
- 5 вида: **H1, H2, H3A, H3B, H4**
- **Нуклеозоми**
- Богати на лизин и аргинин – **положително заредени**



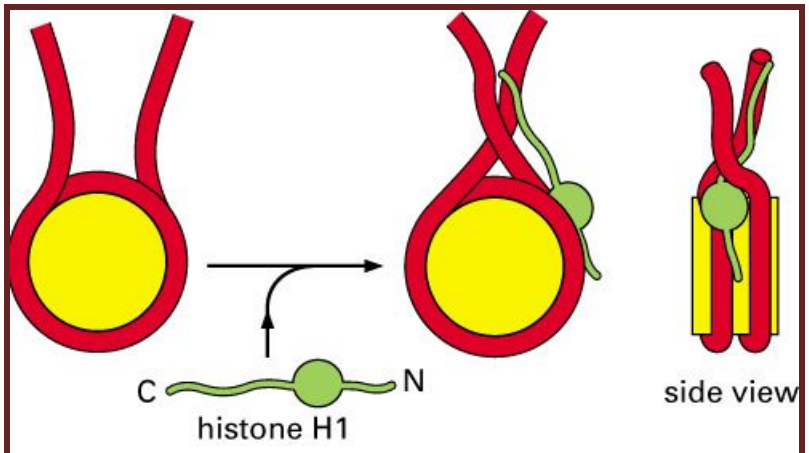


Figure 4–31. Molecular Biology of the Cell, 4th Edition.

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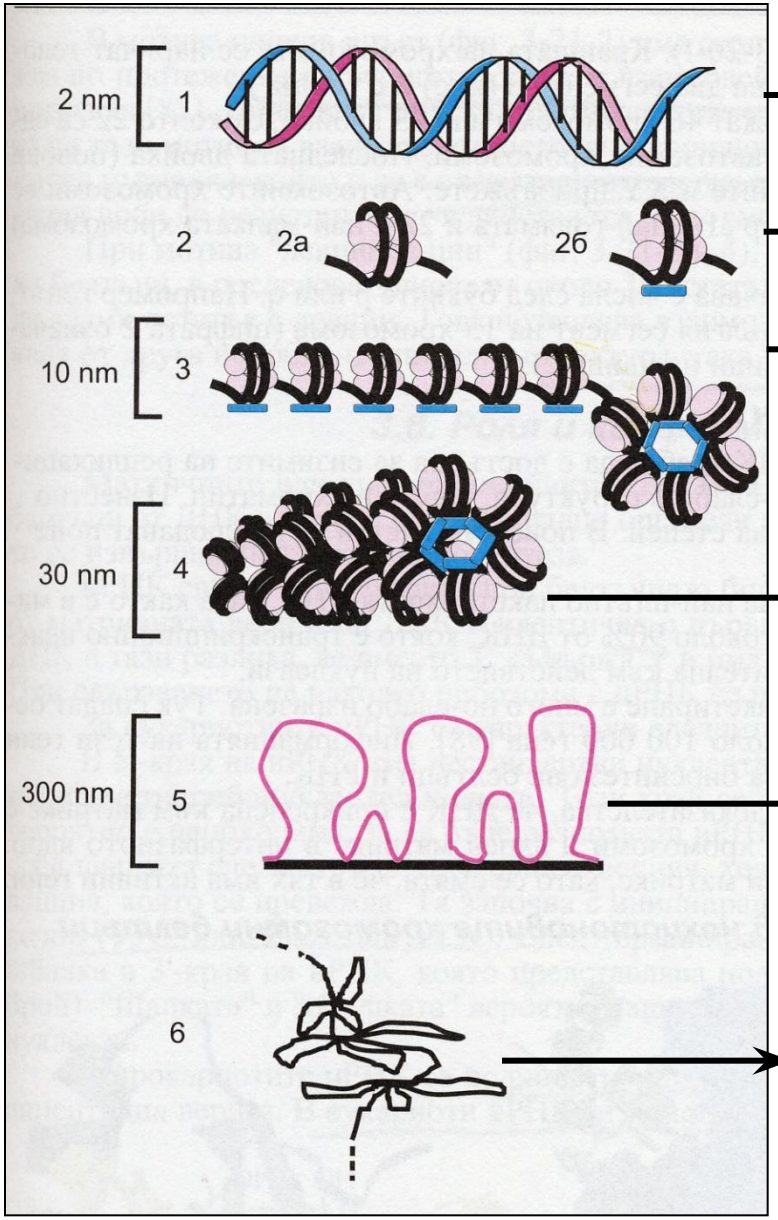
Суперспирализация и пакетиране на ДНК



ДНК

Нуклеозома – октамер от хистони (по два H2A, H2B, H3, H4)

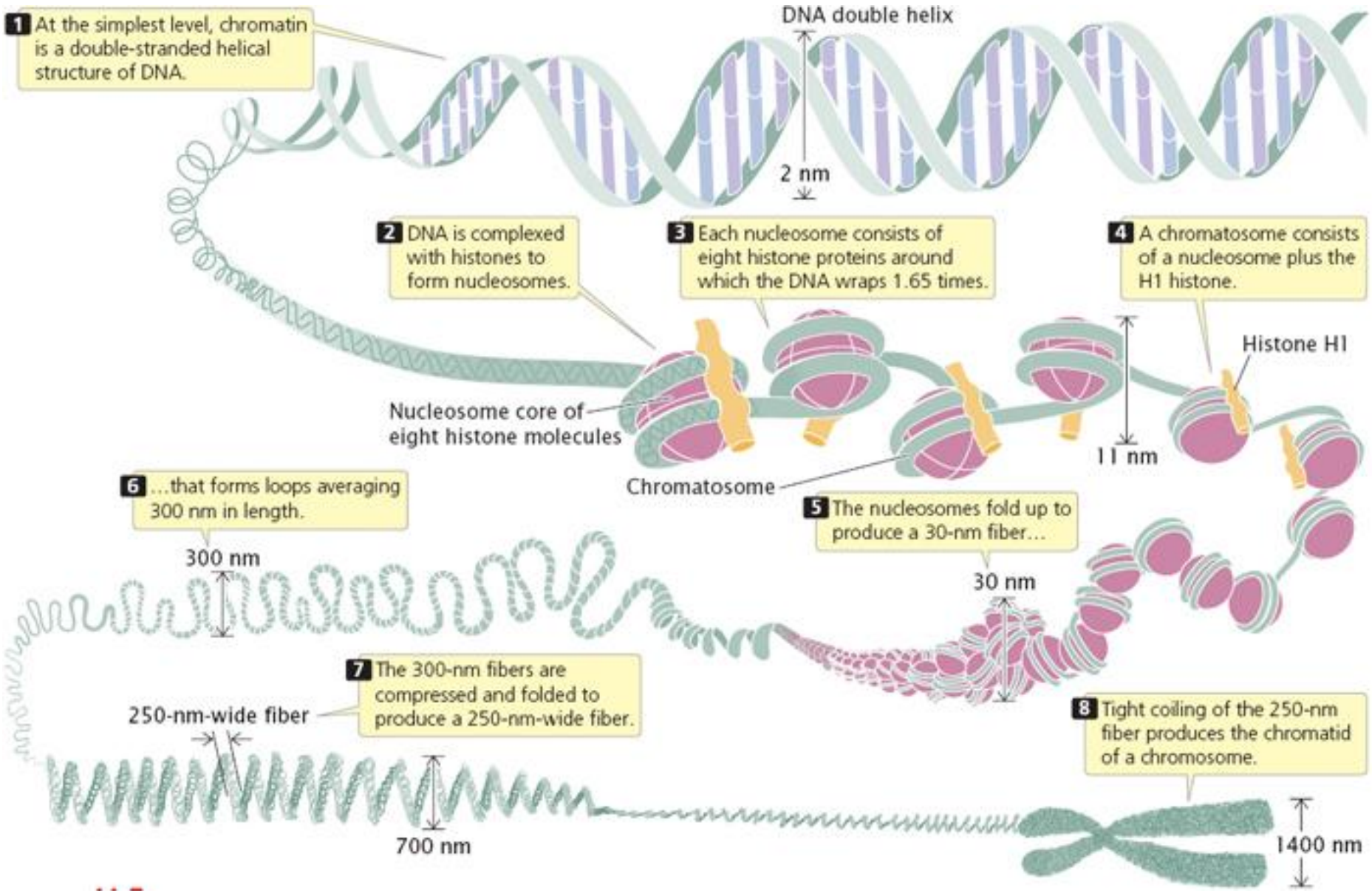
Хроматозома – H1

Нишка от нуклеозоми (10 nm)

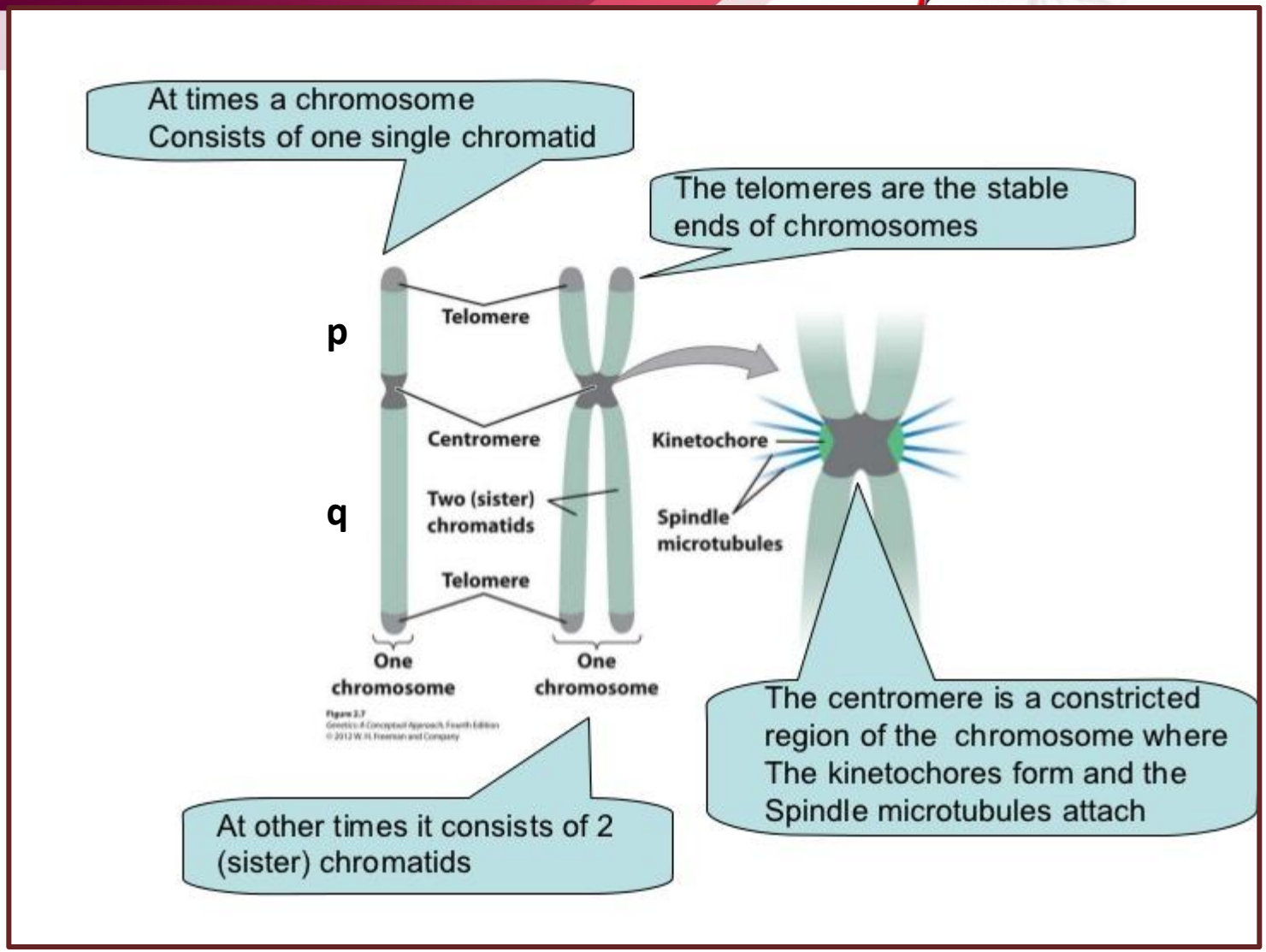
нишка с диаметър 30 nm (соленоид)

Структура с диаметър 300 nm (бримки)

Част от интерфазна хромозома (700 nm)


1 At the simplest level, chromatin is a double-stranded helical structure of DNA.
DNA double helix
2 nm
2 DNA is complexed with histones to form nucleosomes.
3 Each nucleosome consists of eight histone proteins around which the DNA wraps 1.65 times.
4 A chromatosome consists of a nucleosome plus the H1 histone.
Histone H1
Nucleosome core of eight histone molecules
11 nm
Chromatosome
5 The nucleosomes fold up to produce a 30-nm fiber…
30 nm
6 …that forms loops averaging 300 nm in length.
300 nm
7 The 300-nm fibers are compressed and folded to produce a 250-nm-wide fiber.
250-nm-wide fiber
700 nm
8 Tight coiling of the 250-nm fiber produces the chromatid of a chromosome.
1400 nm

Митотични хромозоми



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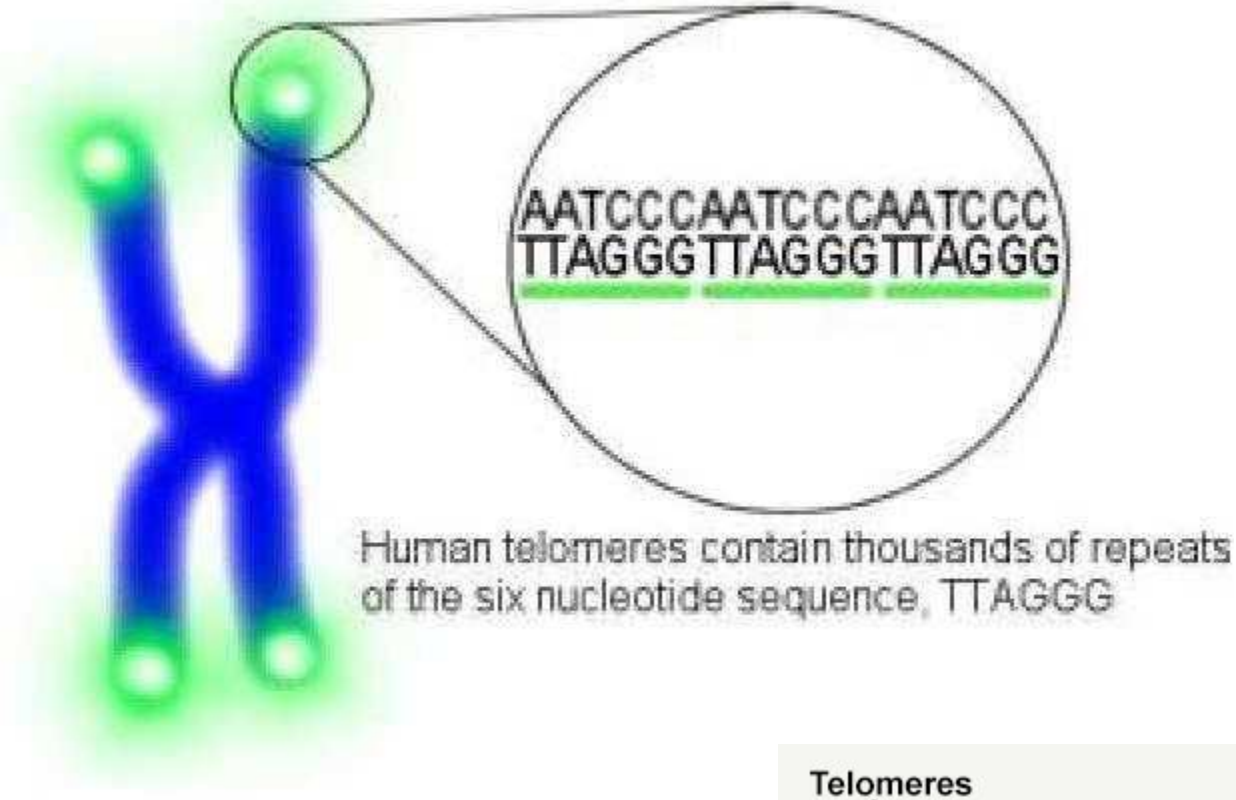
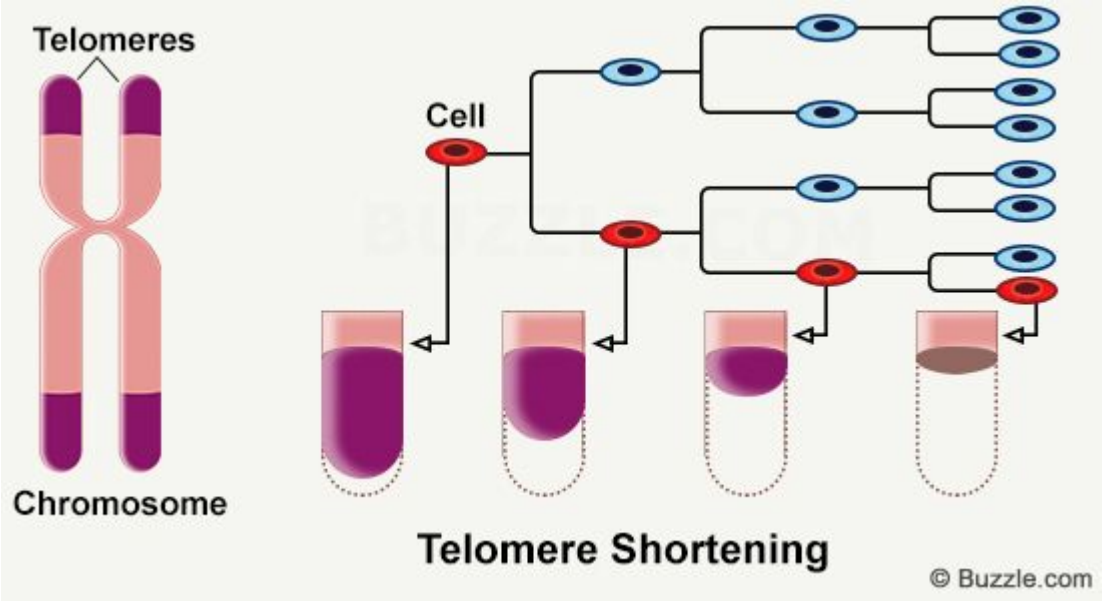
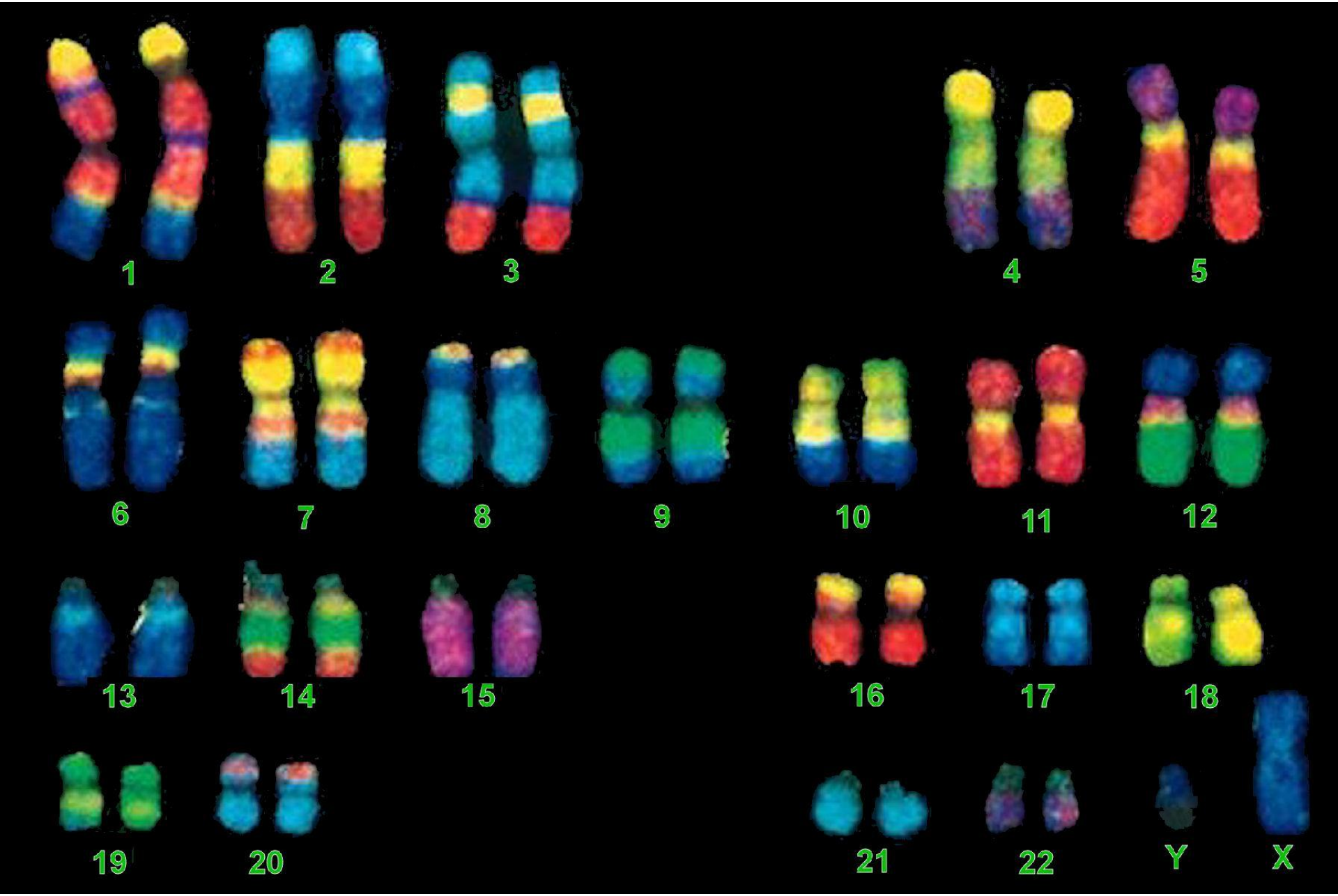
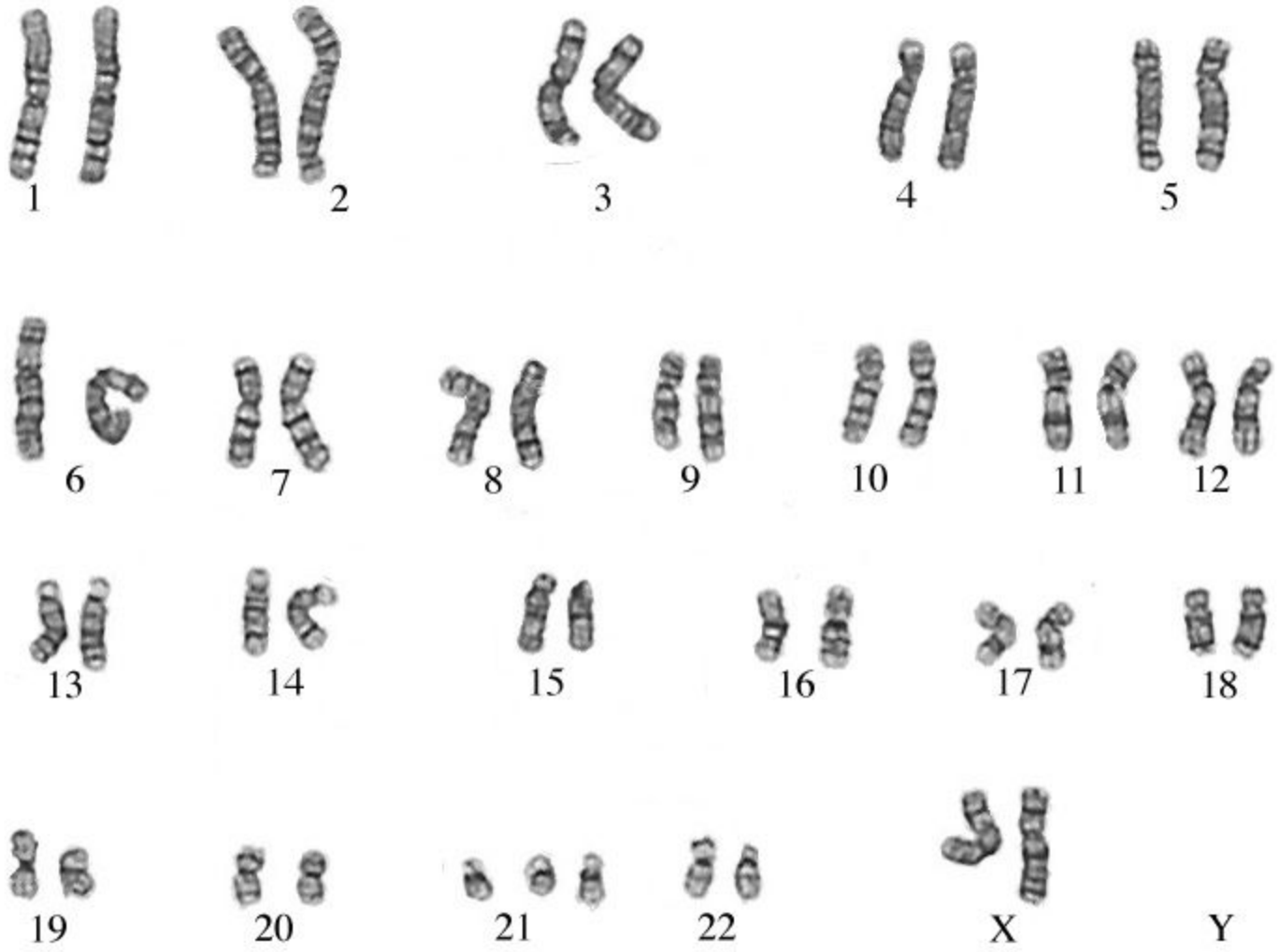

AATCCCAATCCCAATCCC
TTAGGGTTAGGGTTAGGG
Human telomeres contain thousands of repeats
of the six nucleotide sequence, TTAGGG

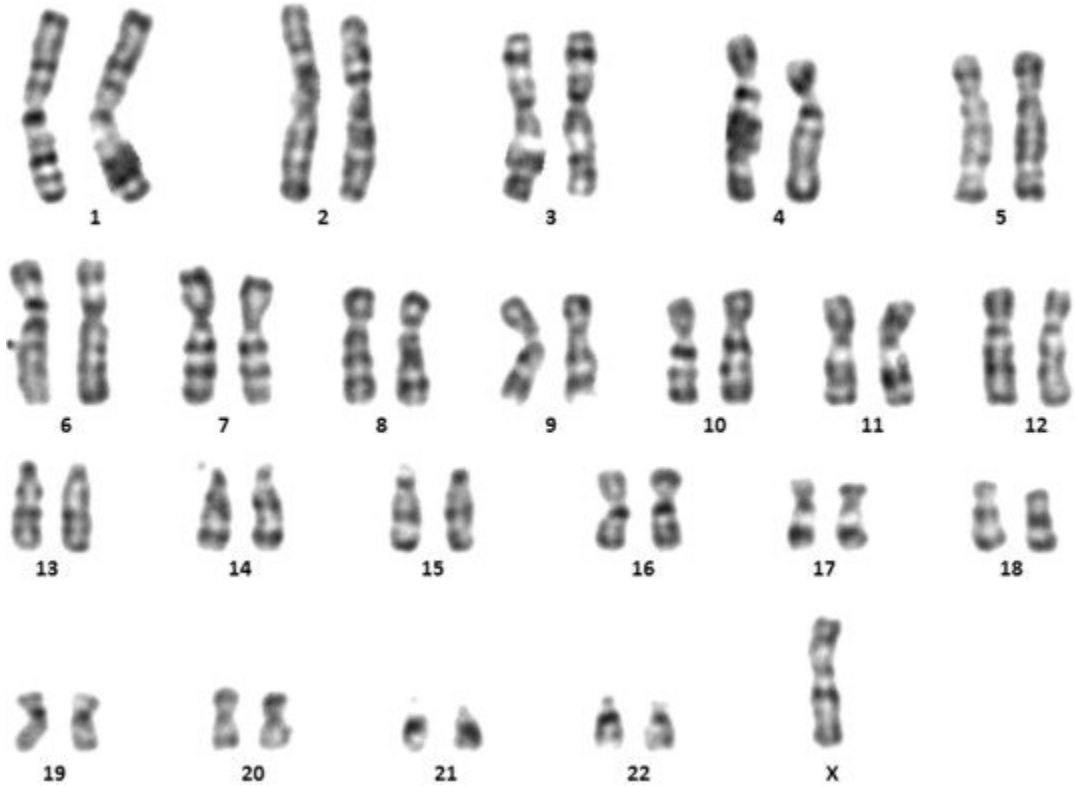

Telomeres
Chromosome
Cell
Telomere Shortening
© Buzzle.com

Хромозомен набор при човека



ZWK99012 KEY




1
2
3
4
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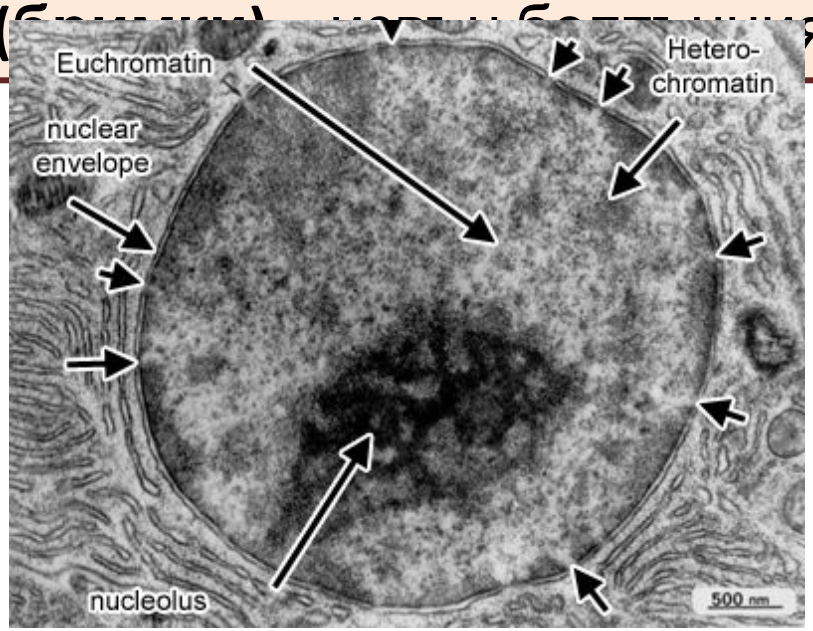
20
21
22
X

Интерфазен хроматин

- **По-слабо пакетирана** ДНК, достъпна за репликация и транскрипция
- Поне 3 форми на пакетиране:
  1. **Хетерохроматин** - ~90%, транскрипционно неактивна
  2. **Еухроматин** - ~10%, активна
  3. **Домени с извивки (**[illegible]**я** ядрен матрикс



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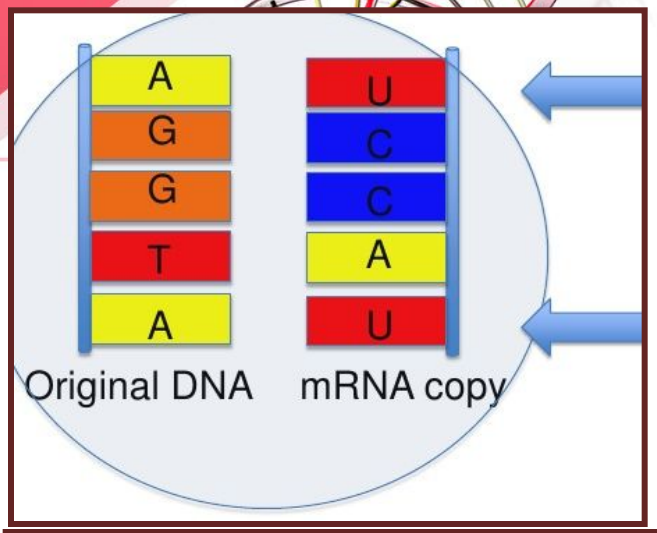
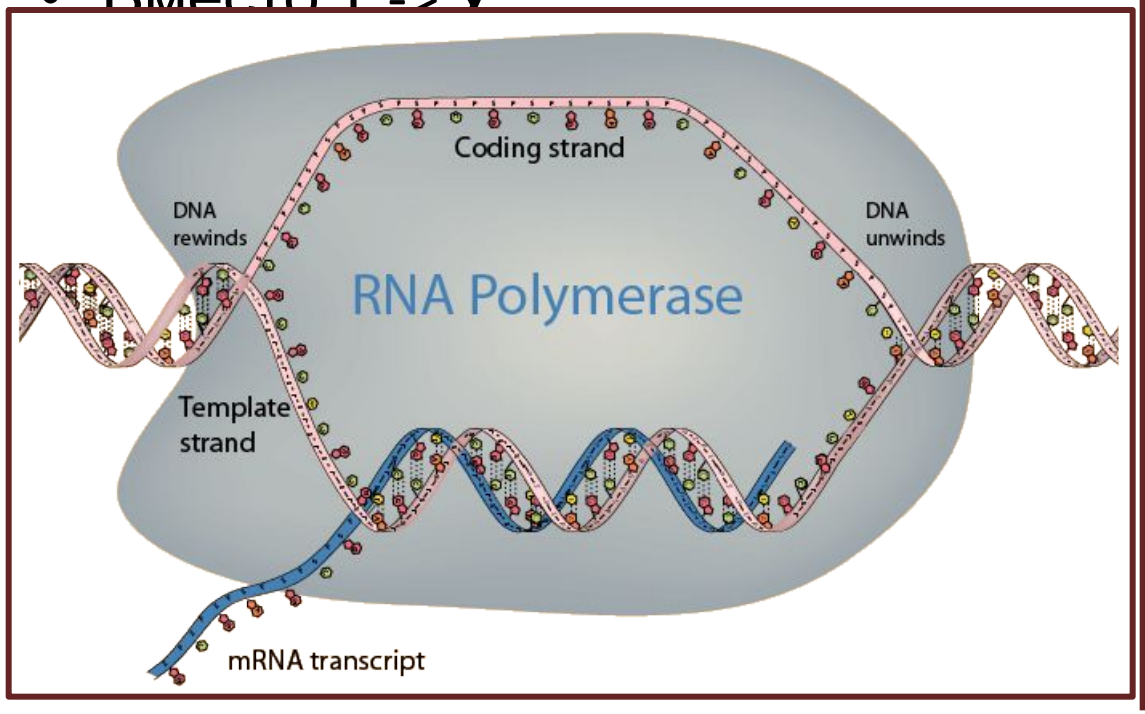
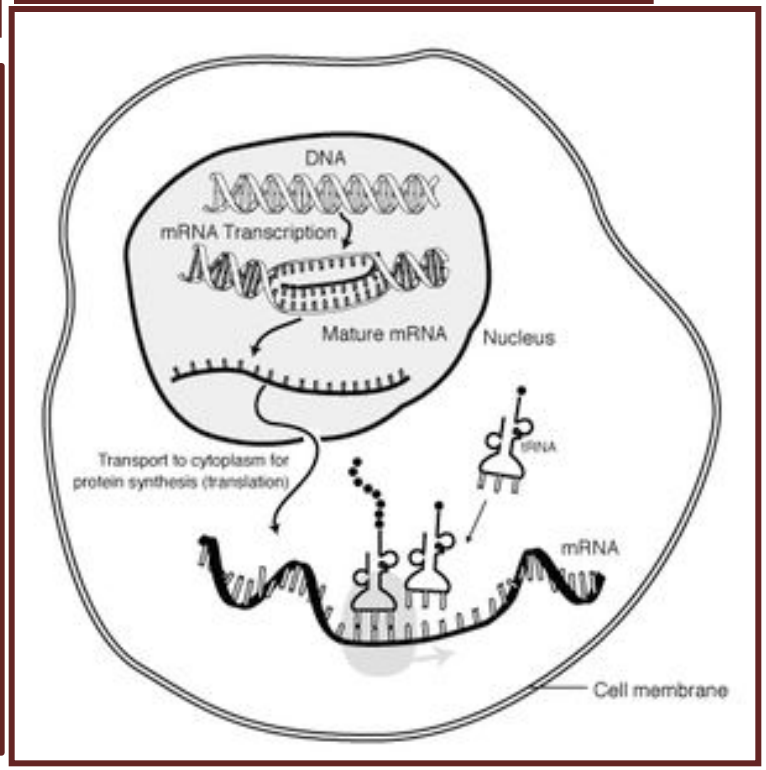
иРНК

- **Матрица за белтъчен синтез**
- Комплементарна на некодиращата ДНК-верига
- Вместо Т -> **У**







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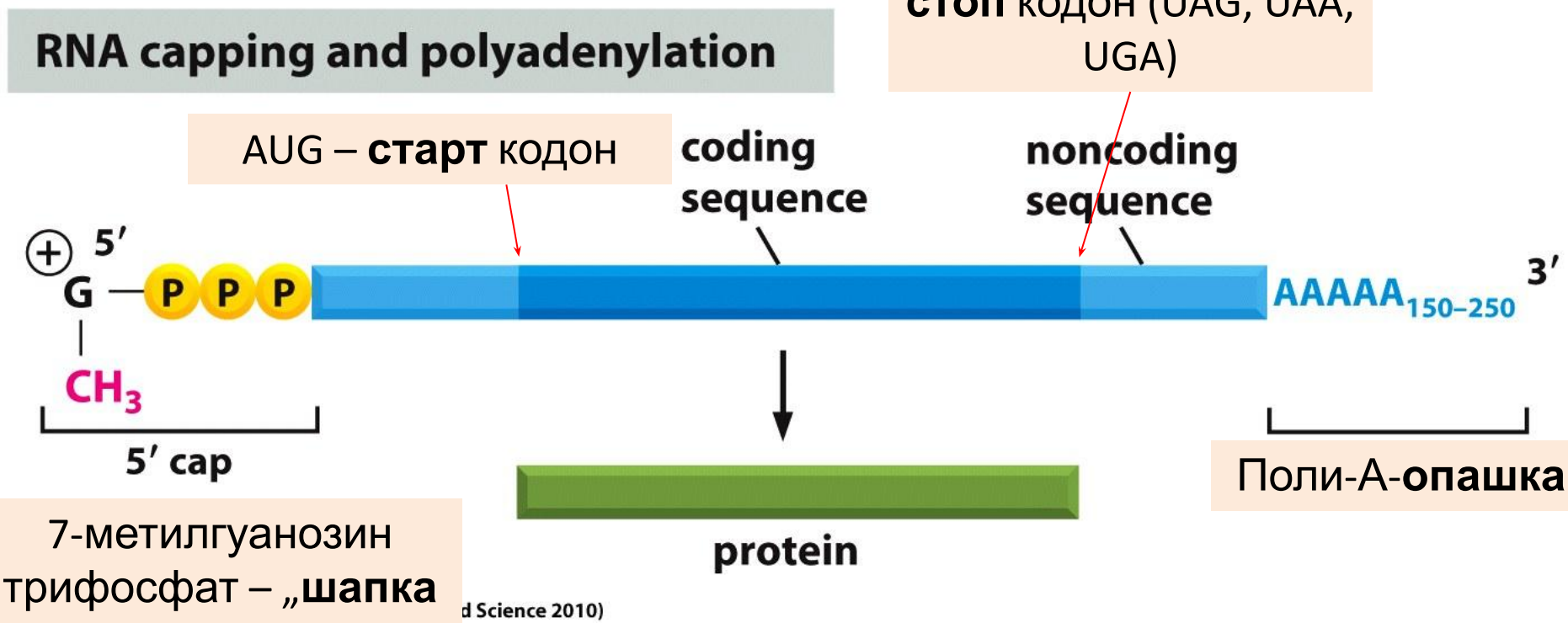
иРНК - еукариоти



Зреене!

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Разлики между про- и еукариоти

- **Прокариоти** – полицистронни
- **Еукариоти** – моноцистронни, интрони и

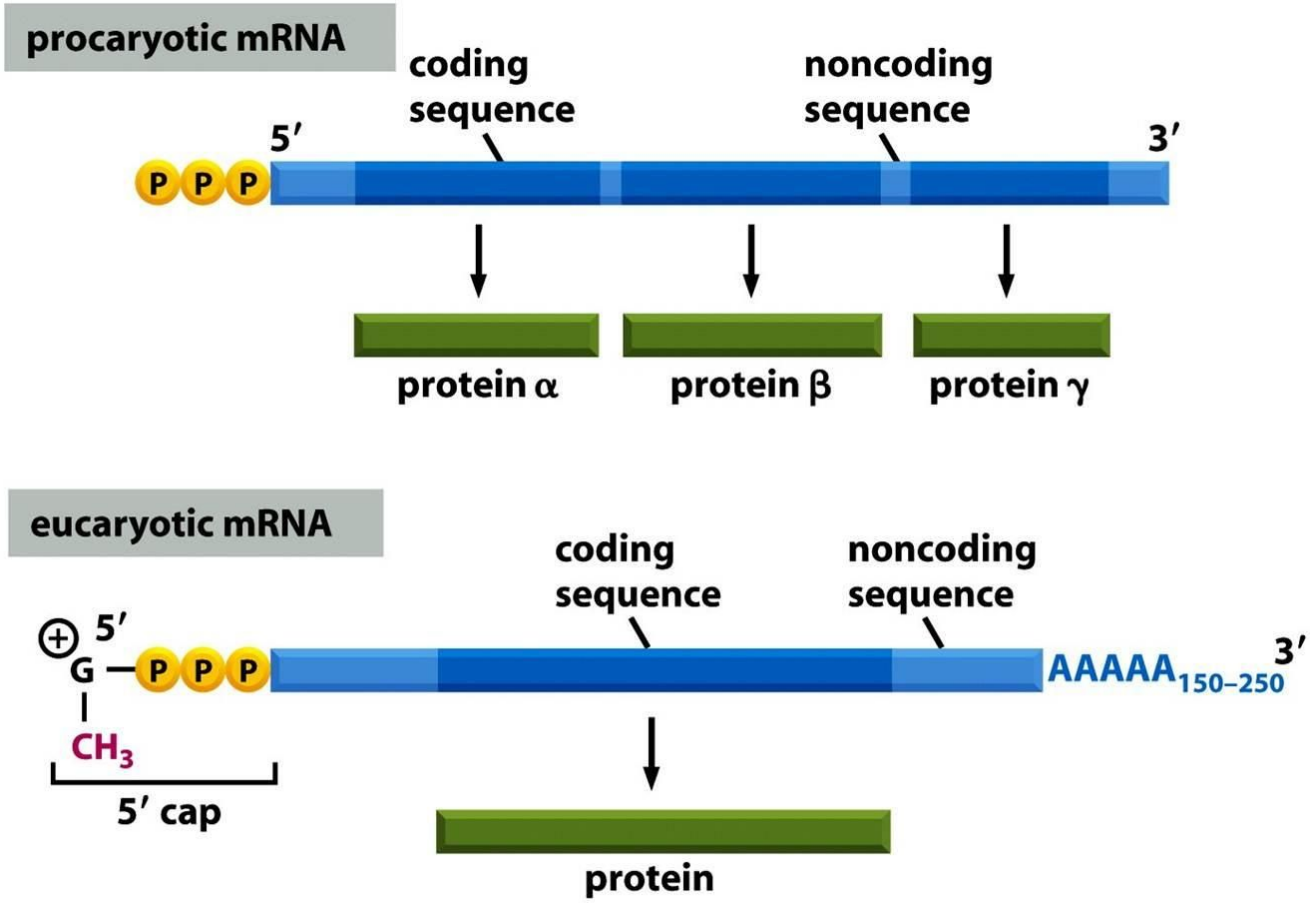

Figure 6-22a Molecular Biology of the Cell 5/e (© Garland Science 2008)

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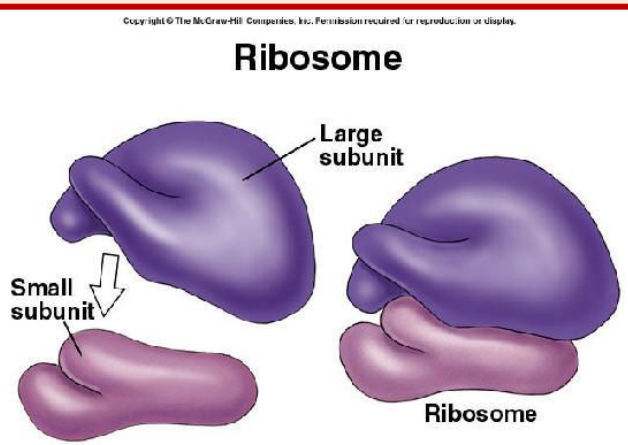
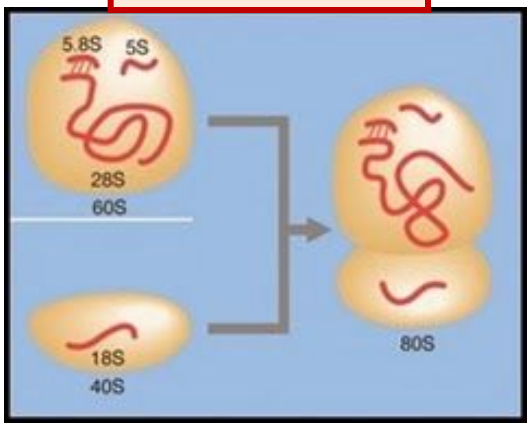
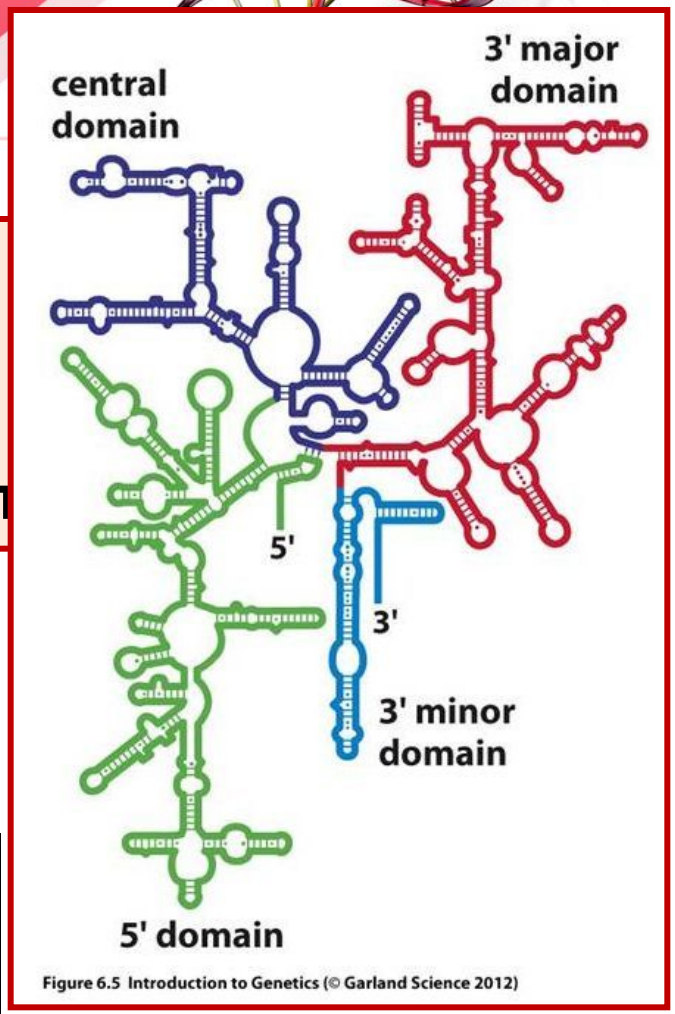
рРНК и рибозоми

- рРНК + белтъци -> рибозоми
- в преобладаващо количество
- **метилирани** във висока степен
- **двойноспирални и фуркетни участ**



еукариоти





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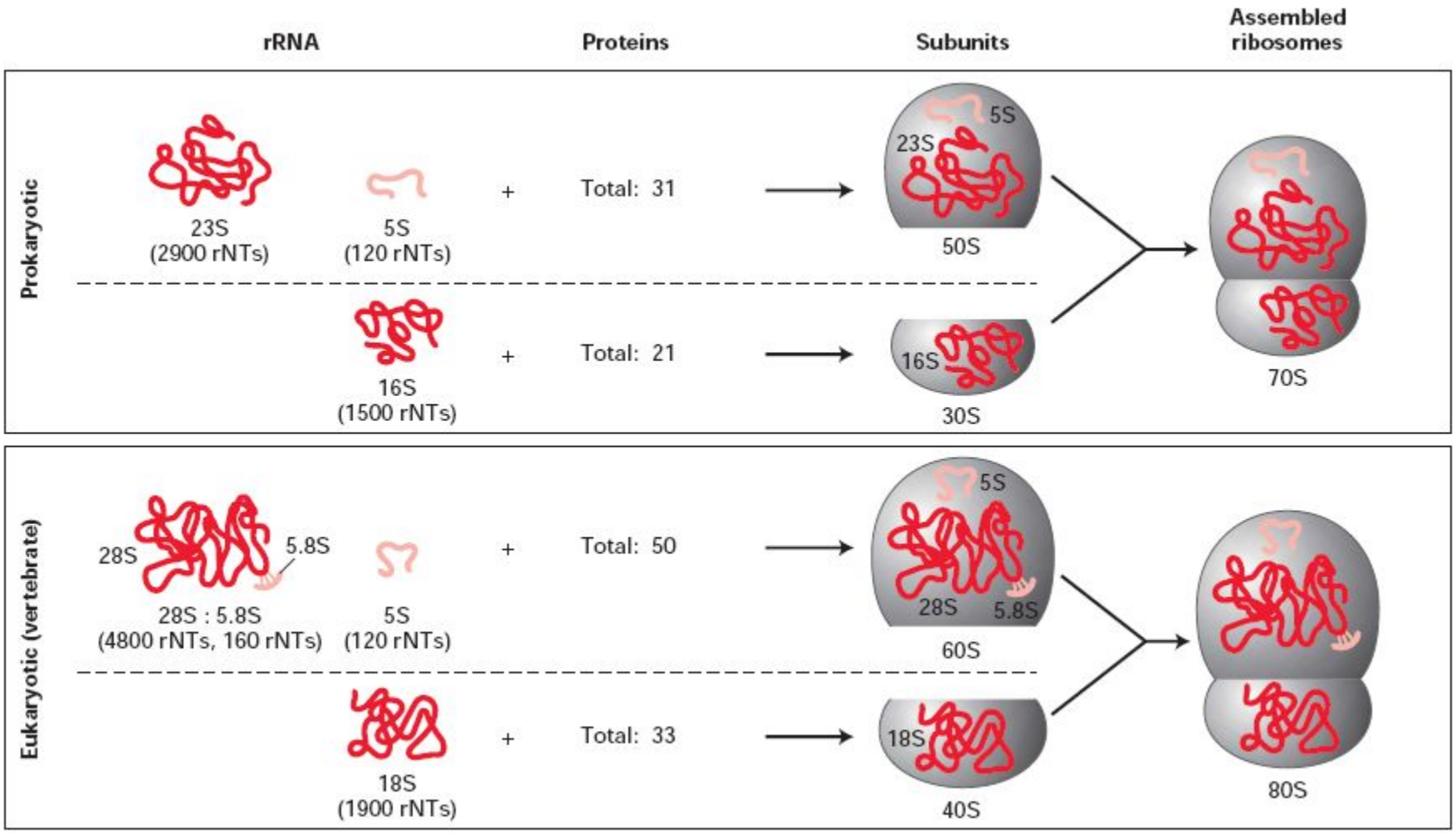
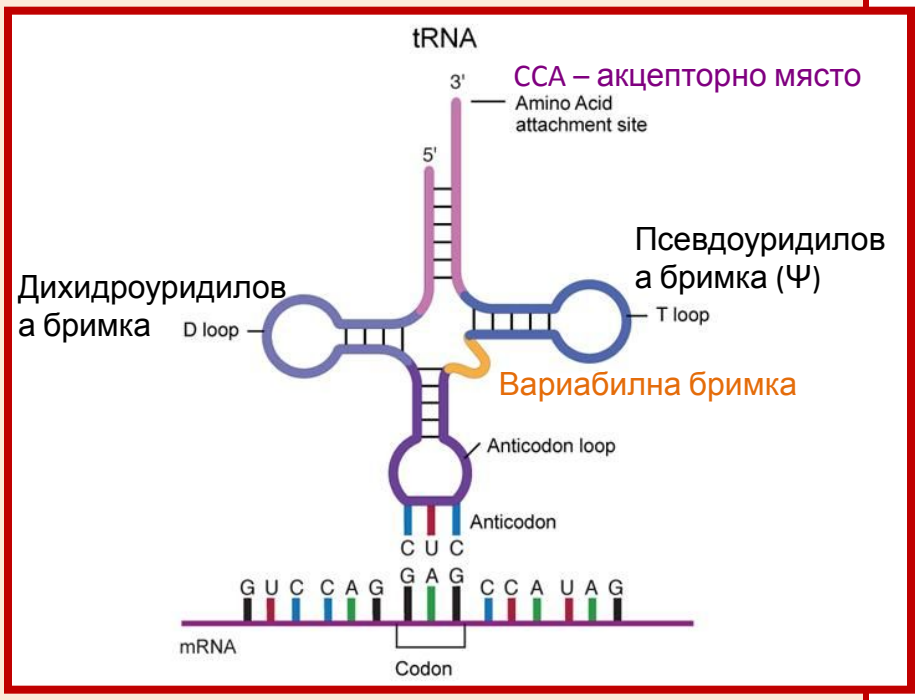

rRNA
Proteins
Subunits
Assembled ribosomes
Prokaryotic
23S
(2900 rNTs)
5S
(120 rNTs)
+
Total: 31
5S
23S
50S
16S
(1500 rNTs)
+
Total: 21
16S
30S
70S
Eukaryotic (vertebrate)
28S
5.8S
28S : 5.8S
(4800 rNTs, 160 rNTs)
5S
(120 rNTs)
+
Total: 50
5S
28S
5.8S
60S
18S
(1900 rNTs)
+
Total: 33
18S
40S
80S

тРНК

- ~15%
- най-малките, нискомолекулни
- **Поне по 1 специфична тРНК за всяка от 20те АК**
- **Минорни бази**
- „детелинов лист“

- **Адапторна молекула:**

1. акцепторен участък
2. псевдоуридилова бримка
3. Антикодонна бримка
4. Дихидроуридилова бримка
5. Вариабилна бримка



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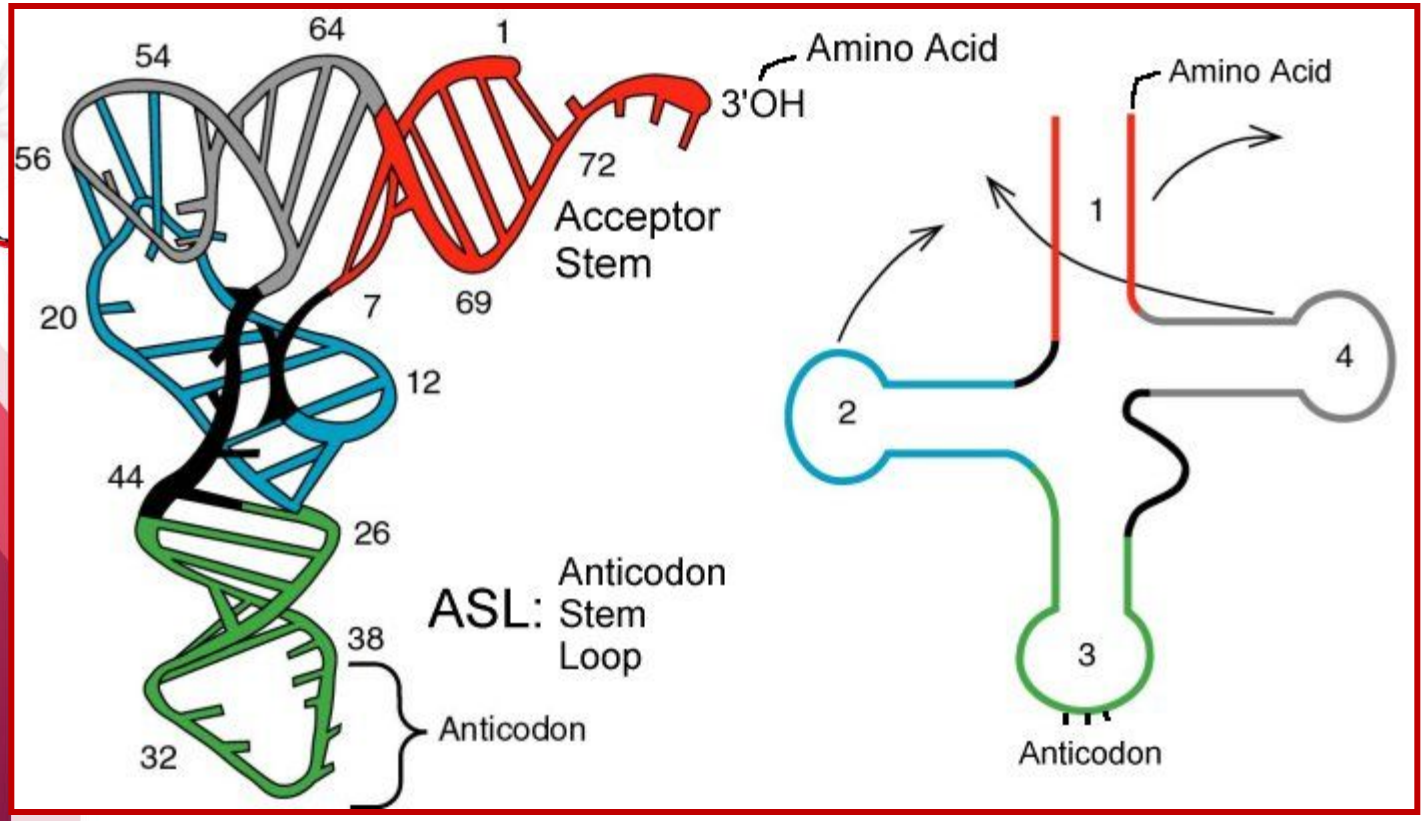
Третична структура на тРНК



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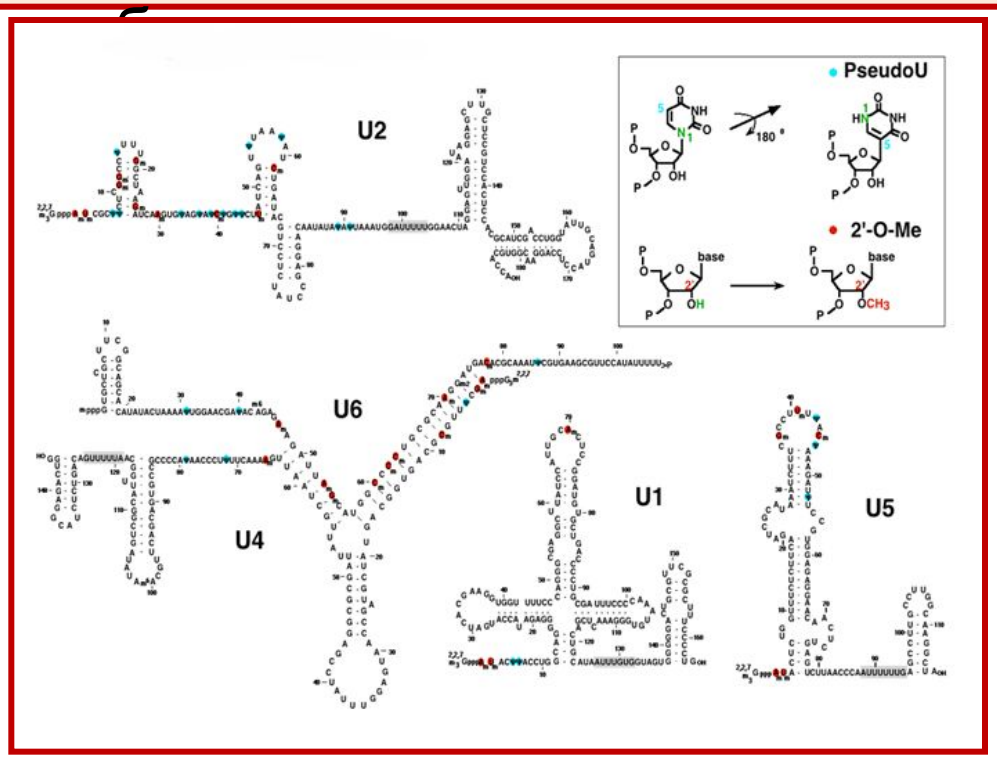
Малки ядрени РНК

- Малки, стабилни
- Под формата на **рибонуклеопротеини – snurps (small nuclear ribonucleoproteins)**
- Означават се с U1, U2 и т.н.
- Участват в процеса на **зреене на иРНК**, т.е. са



Хипотеза за „РНК свят“

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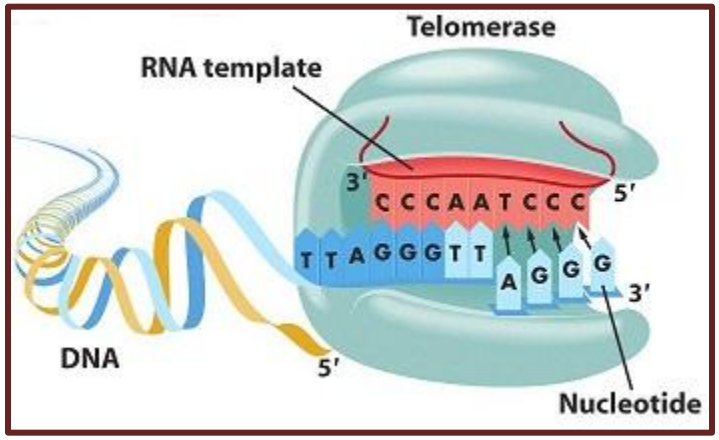
Рибозими

- **Каталитична функция**

- Примери:

- **snurps**
- 28S **рРНК** в еукариоти и 23S в прокариоти – белтъчен синтез (пептидил трансферазна активност)
- **Теломераза** – не е рибозим, а рибонуклеопротеин



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