

Definizioni

- **Acidi nucleici:** molecole che codificano l'informazione genetica.
DNA, RNA
- **Genoma:** insieme delle sequenze di DNA di un organismo
- **Codice genetico:** è lo schema attraverso cui la cellula traduce una sequenza di basi (codoni o triplette di basi) in una sequenza di aminoacidi
- **Gene:** *segmento di DNA che codifica per una catena polipeptidica*

Acido nucleico

Scoperto nel 1869 da Miescher

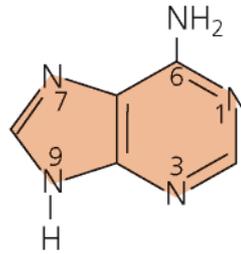
Trovato come un precipitato che si forma quando estratti nucleari sono stati trattati con acido.

Composto da C, N, O, e un alto contenuto di P

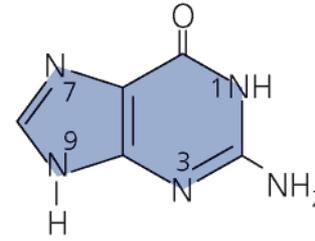
Comunemente presente nei nuclei cellulari da cui il nome acido nucleico

Basi

Purine

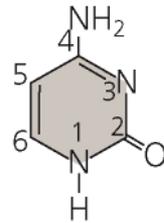


Adenina (A)

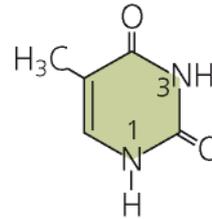


Guanina (G)

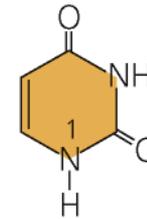
Pirimidine



Citosina (C)

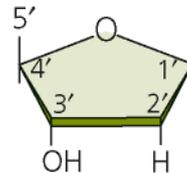


Timina (T)
(DNA)

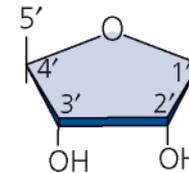


Uracile (U)
(RNA)

Zuccheri

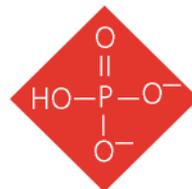


2'-deossiribosio
(DNA)



Ribosio
(RNA)

Fosfato



Anche rappresentato come

P

Il DNA e l'informazione genetica

1944 Avery, MacLeod e McCarty identificano il DNA come molecola trasportatrice dell'informazione genetica

1953 Watson e Crick propongono la struttura del DNA

1958 Crick propone il dogma centrale della biologia

1990 Inizia lo Human Genome Project (Celera Genomics)

- **Un principio “trasformante” converte il ceppo R in S**

Esperimento di Avery-MacLeod-McCarty 1944

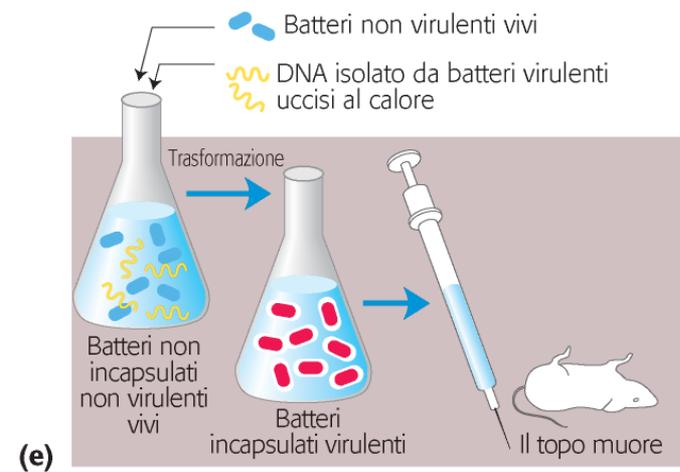
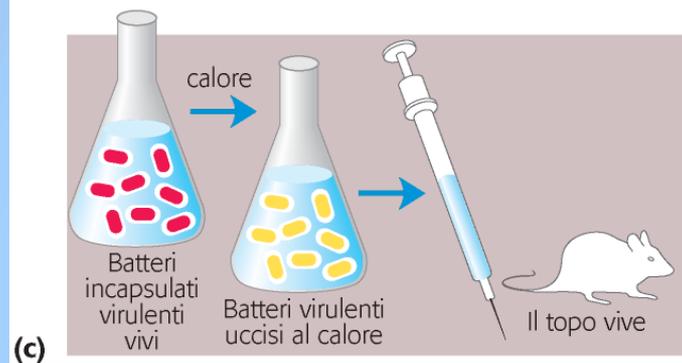
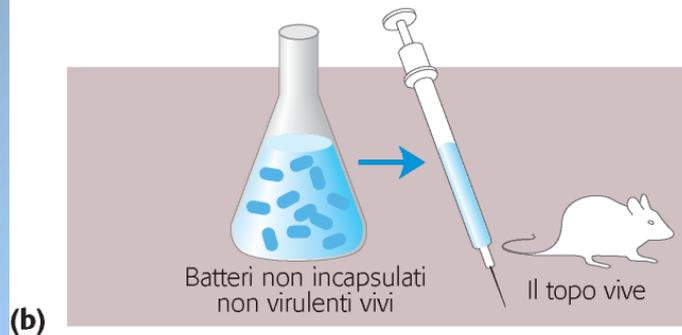
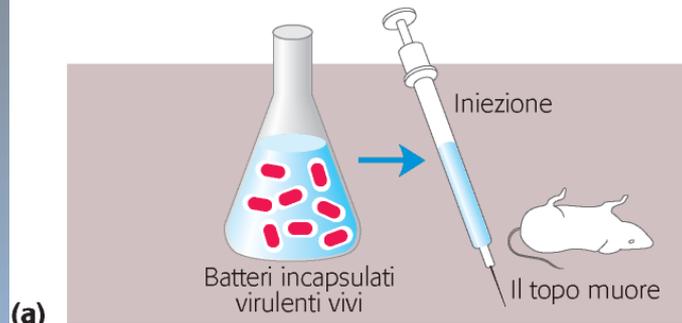
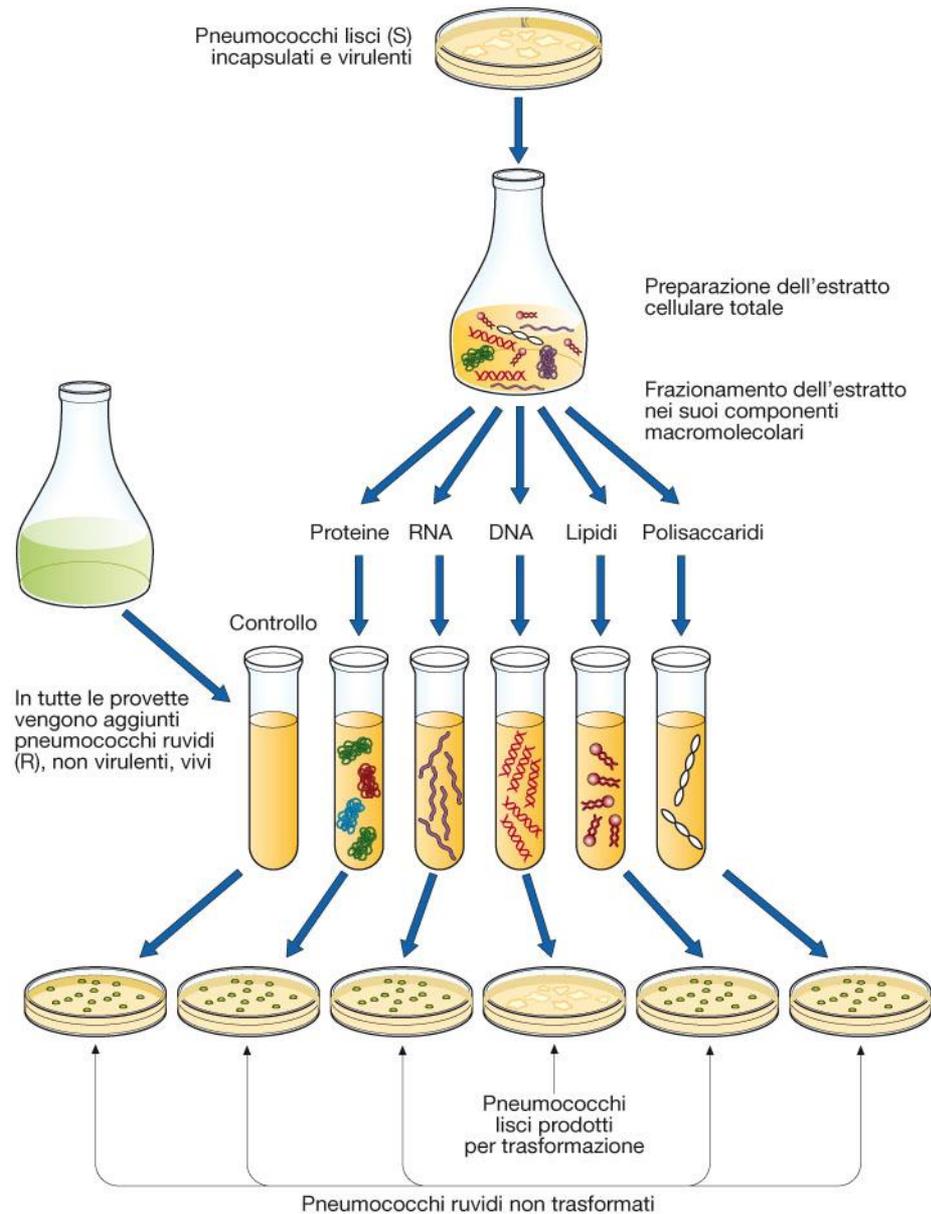
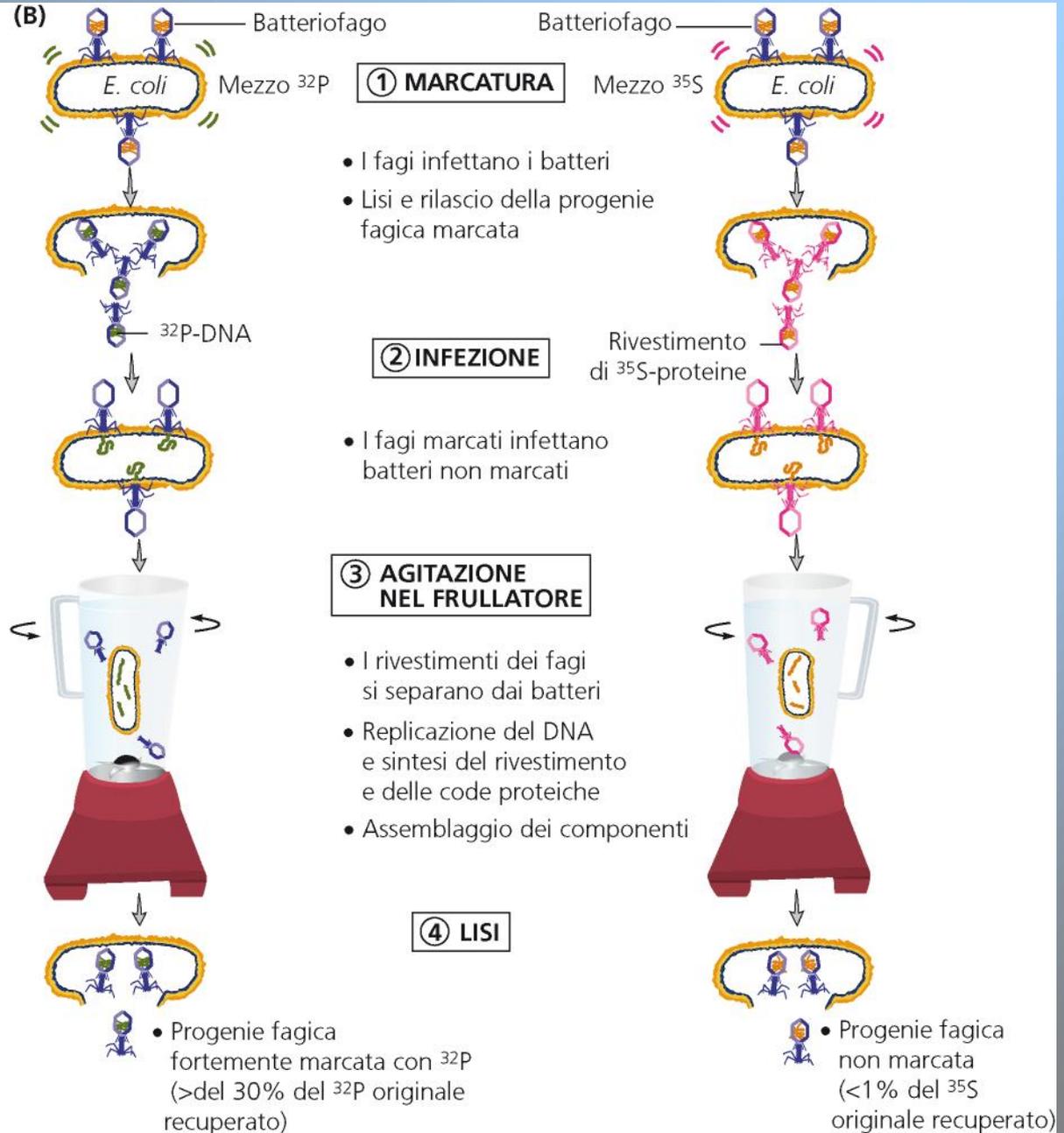
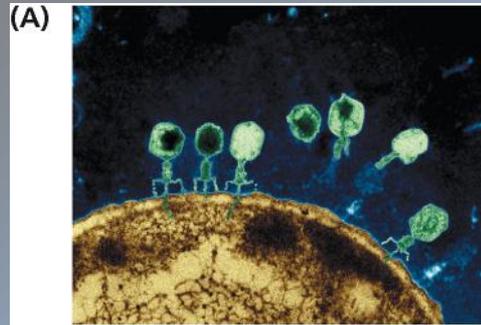


Figura 1.10 La "bomba di Avery":

Avery e colleghi, a partire dai Pneumococchi lisci e virulenti, fecero un estratto cellulare che era in grado di trasformare il ceppo ruvido. In seguito purificarono tutte le componenti dell'estratto, che divisero in tubi diversi. Solo il DNA era in grado di trasformare il ceppo di Pneumococco ruvido nel ceppo liscio e patogeno, dimostrando che solo il DNA era il principio trasformante.

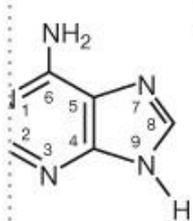


L'esperimento del "frullatore" - Hershey e Chase, 1952



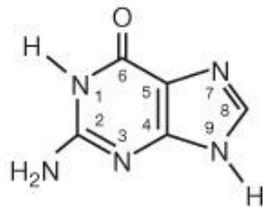
La struttura fisica del DNA

Componenti

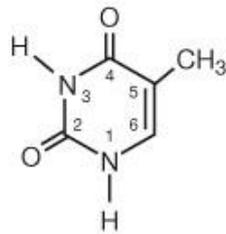


Purine

Adenina (A)

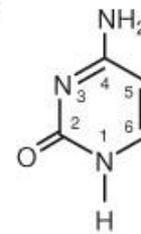


Guanina (G)



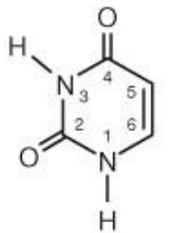
Pyrimidine

Timina (T)

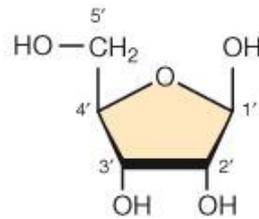


Citosina (A)

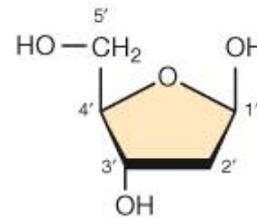
Figura 2.1A Strutture dei componenti chimici degli acidi nucleici.



Uracile (T)



Ribosio



Deossiribosio

Nucleosidi e Nucleotidi

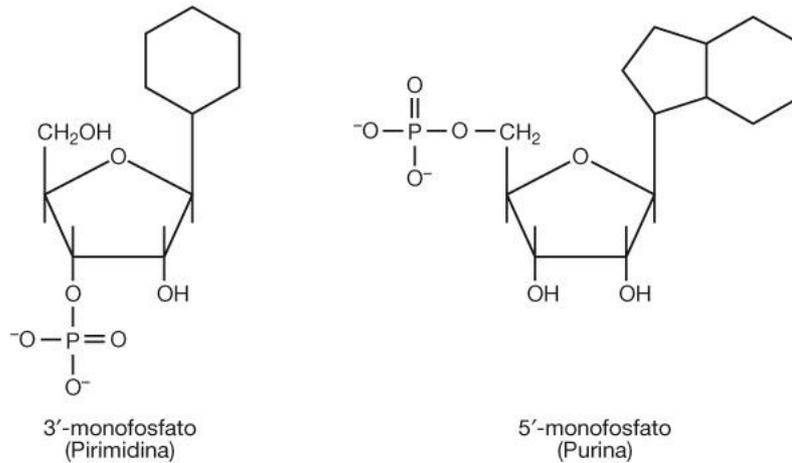


Figura 2.2 I nucleotidi possono portare il gruppo fosfato in posizione 5' o 3'.

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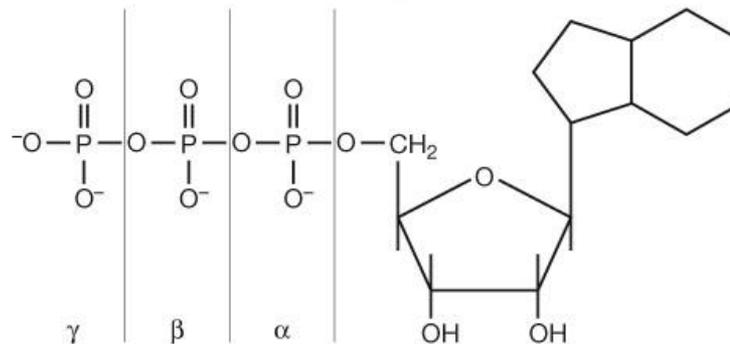


Figura 2.3 Nomenclatura dei fosfati in un nucleoside trifosfato. Il fosfato in posizione α è quello che forma lo scheletro degli acidi nucleici.

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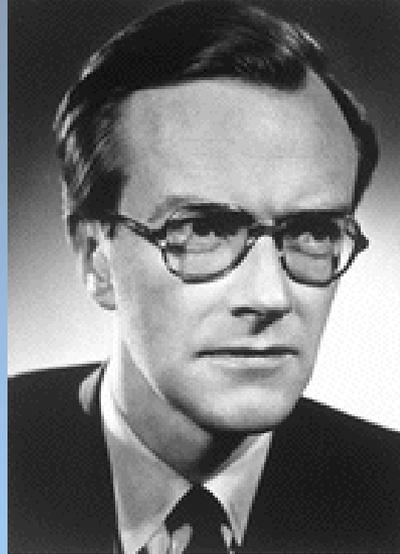
Regole di Chargaff

- 1 La composizione in basi del DNA varia da una specie all'altra
- 2 Le molecole di DNA isolate da tessuti diversi hanno la stessa composizione in basi
- 3 La composizione del DNA non si modifica con l'età e lo stato nutrizionale
- 4 In tutte le molecole di DNA la somma dei residui purinici è uguale alla somma dei residui pirimidinici ($A+G = T+C$)

Tabella 2.2 Composizione in basi del DNA di varie specie.

FONTE	A	G	C	T	A/T	G/C	G+C	Py/Pu
<i>Escherichia coli</i>	26,0	24,9	25,2	23,9	1,08	0,99	50,1	1,04
<i>Mycobacterium tuberculosis</i>	15,1	34,9	35,4	14,6	1,03	0,99	70,3	1,00
Lievito	31,7	18,3	17,4	32,6	0,97	1,05	35,7	1,00
Bue	29,0	21,2	21,2	28,7	1,01	1,00	42,4	1,01
Maiale	29,8	20,7	20,7	29,1	0,92	1,00	41,4	1,01
Uomo	30,4	19,9	19,9	30,1	1,01	1,00	39,8	1,01

Maurice Wilkins
(1916 - 2004)

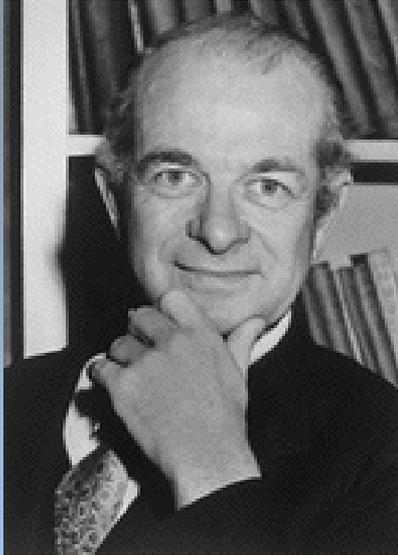


Francis Crick
(1916 - 2004)

James Watson
(1928 -)



Linus Pauling
(1901 - 1994)

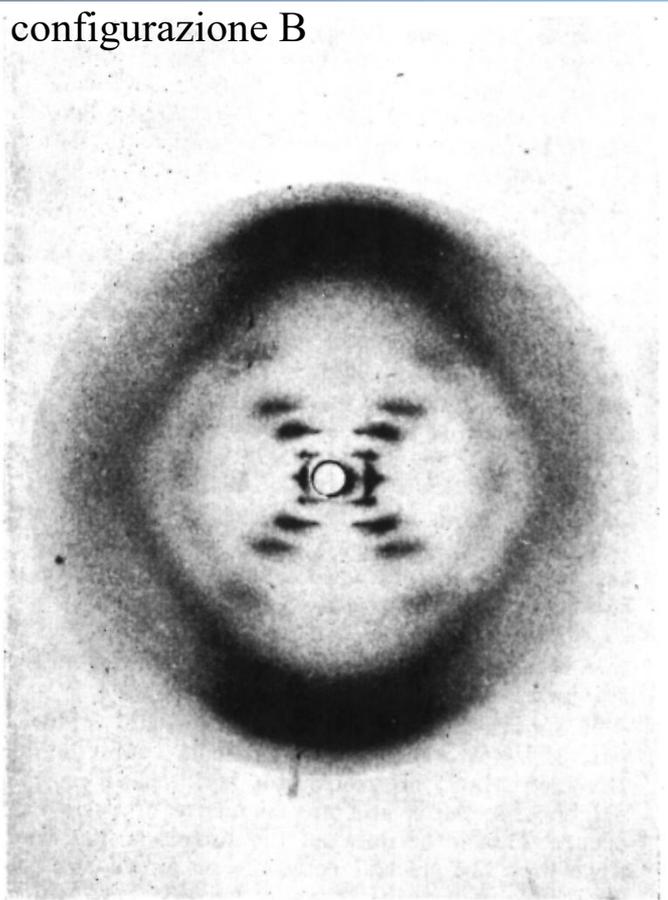


Rosalind Franklin
(1920 - 1958)



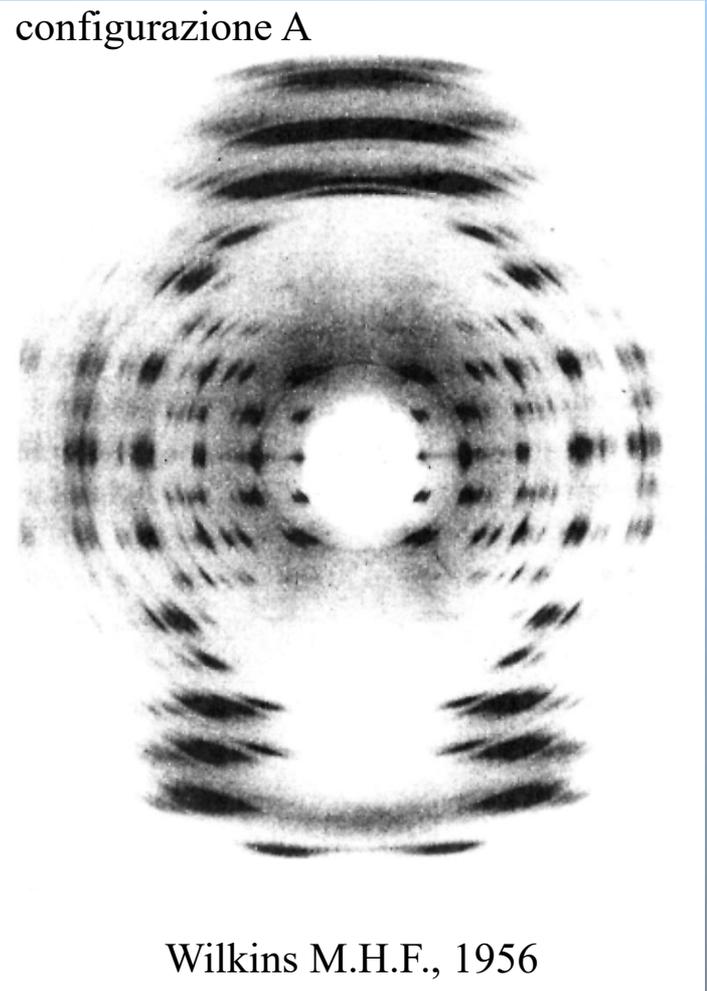
Diffrazione dei raggi X di fibre di DNA

configurazione B



Franklin R.E. & Gosling R., 1953

configurazione A



Wilkins M.H.F., 1956

La catena polinucleotidica

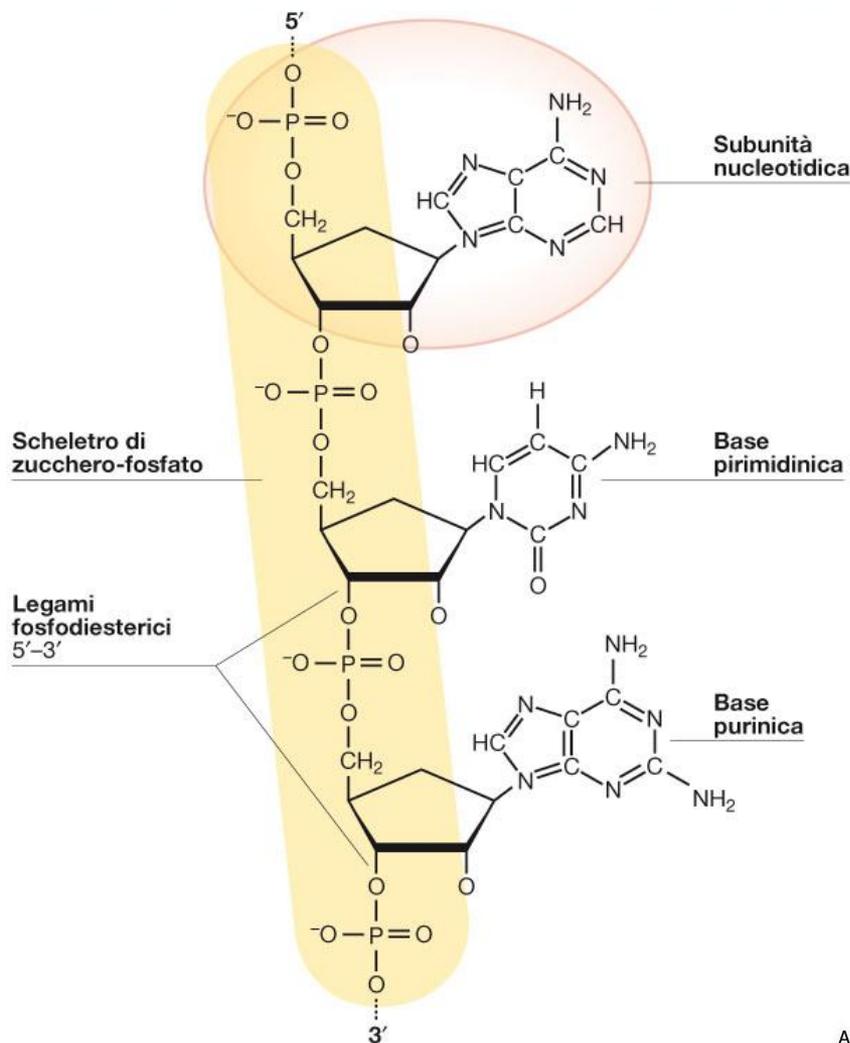
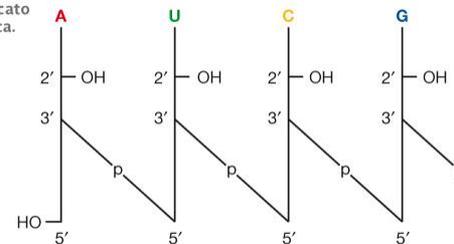
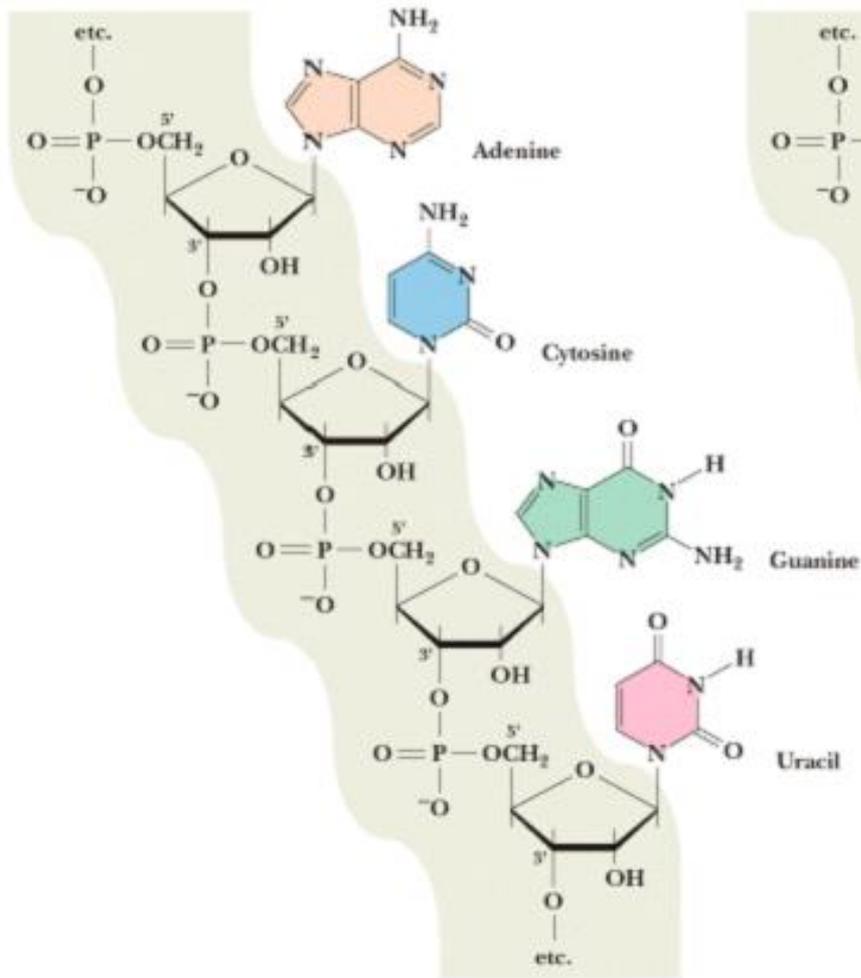


Figura 2.5 Una catena polinucleotidica ha una struttura ripetitiva. Essa consiste di una serie di legami 5'-3' zucchero-fosfato che formano un'impalcatura dalla quale protrudono le basi.

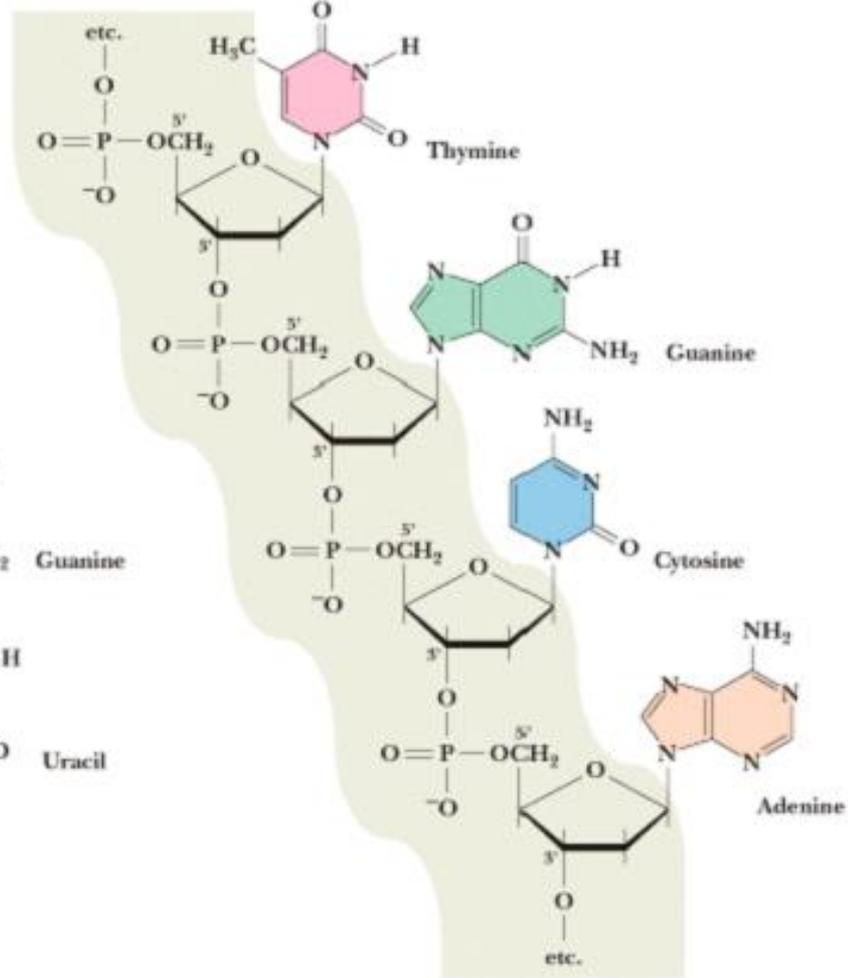
Figura 2.6 Schema semplificato di una catena polinucleotidica.

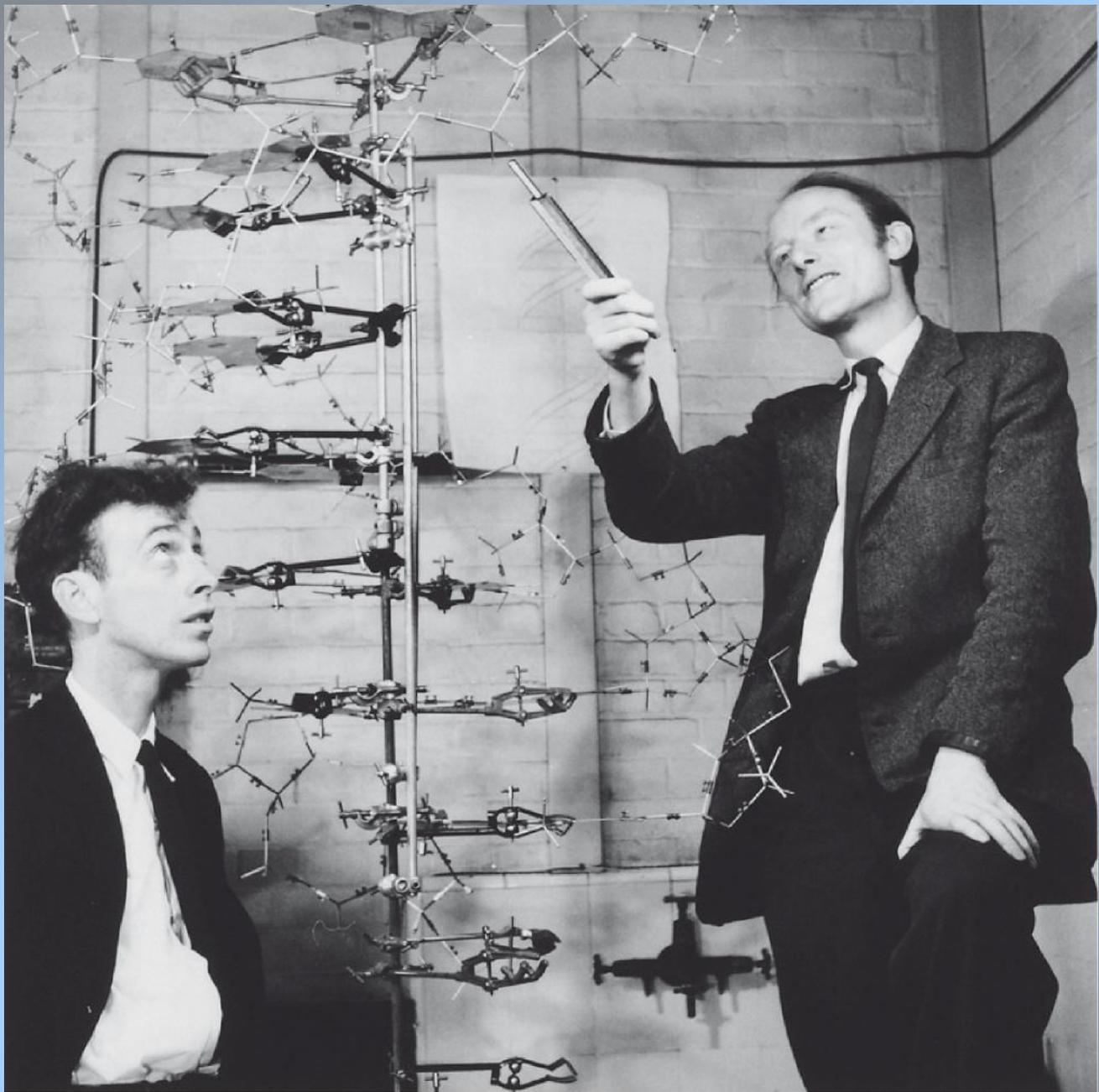


Ribonucleic acid
RNA



Deoxyribonucleic acid
DNA





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 intertwined 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 diester 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 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 every 3.4 Å. in the z-direction. We have assumed an angle of 36° between adjacent



This figure is purely diagrammatic. The two ribbons symbolize the two phosphate-sugar chains, and the horizontal rods the pairs of bases holding the chains together. The vertical line marks the fibre axis.

residues in the same chain, so that the structure repeats after 10 residues on each chain, that is, after 34 Å. The distance of a phosphorus atom from the fibre axis is 10 Å. 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 the other chain, so that the two lie side by side with identical z-coordinates. 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.

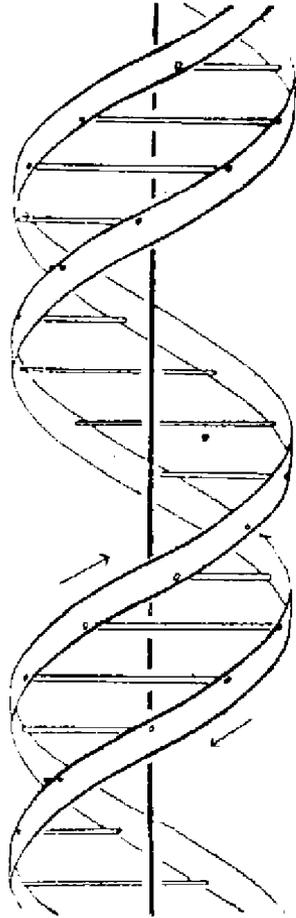
We are much indebted to Dr. Jerry Donohue for constant advice and criticism, especially on interatomic distances. We have also been stimulated by a knowledge of the general nature of the unpublished experimental results and ideas of Dr. M. H. F. Wilkins, Dr. R. E. Franklin and their co-workers at King's College, London. One of us (J. D. W.) has been aided by a fellowship from the National Foundation for Infantile Paralysis.

J. D. WATSON
F. H. C. CRICK

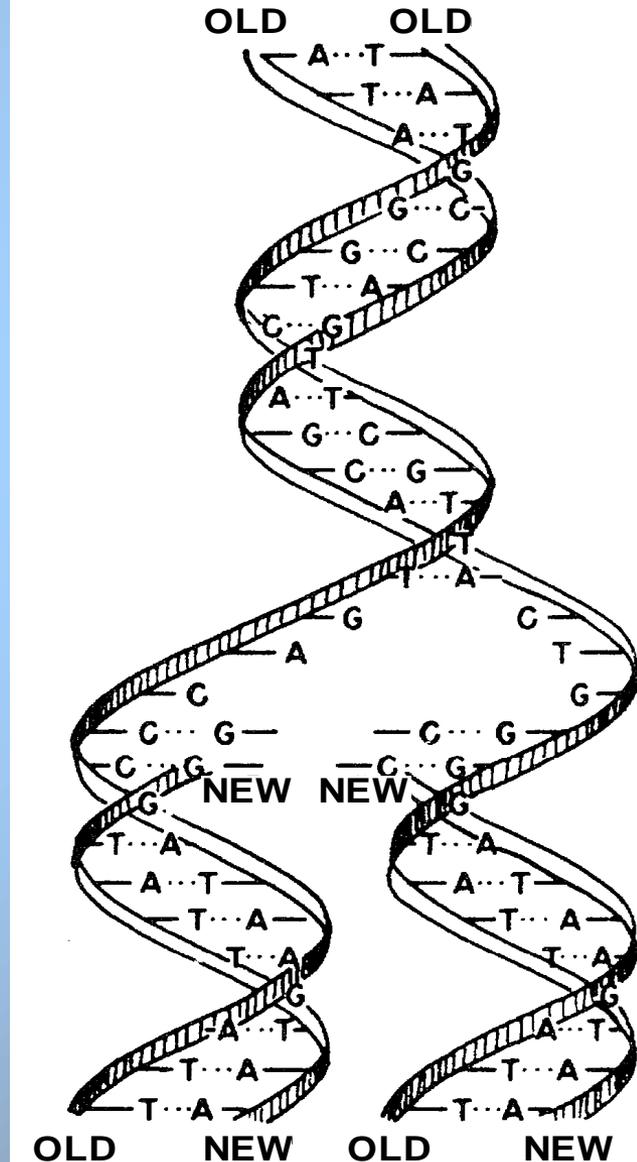
Medical Research Council Unit for the Study of Molecular Structure of Biological Systems, Cavendish Laboratory, Cambridge.

1. Pauling, L., and Corey, R. B., Nature, 171, 346 (1953); Proc. U.S. Nat. Acad. Sci., 39, 84 (1953).
2. Furberg, S., Acta Chem. Scand., 6, 634 (1952).
3. Chargaff, E., for references see Zamenhof, S., Brawerman, G., and Chargaff, E., Biochim. et Biophys. Acta, 9, 402 (1952).
4. Wyatt, G. R. J. Gen. Physiol., 36, 201 (1952).
5. Astbury, W. T., Symp. Soc. Exp. Biol. 1, Nucleic Acid, 66 (Camb. Univ. Press, 1947).
6. Wilkins, M. H. F., and Randall, J. T., Biochim. et Biophys. Acta, 10, 192 (1953).

Il modello a doppia elica di Crick e Watson suggerisce un meccanismo di replicazione

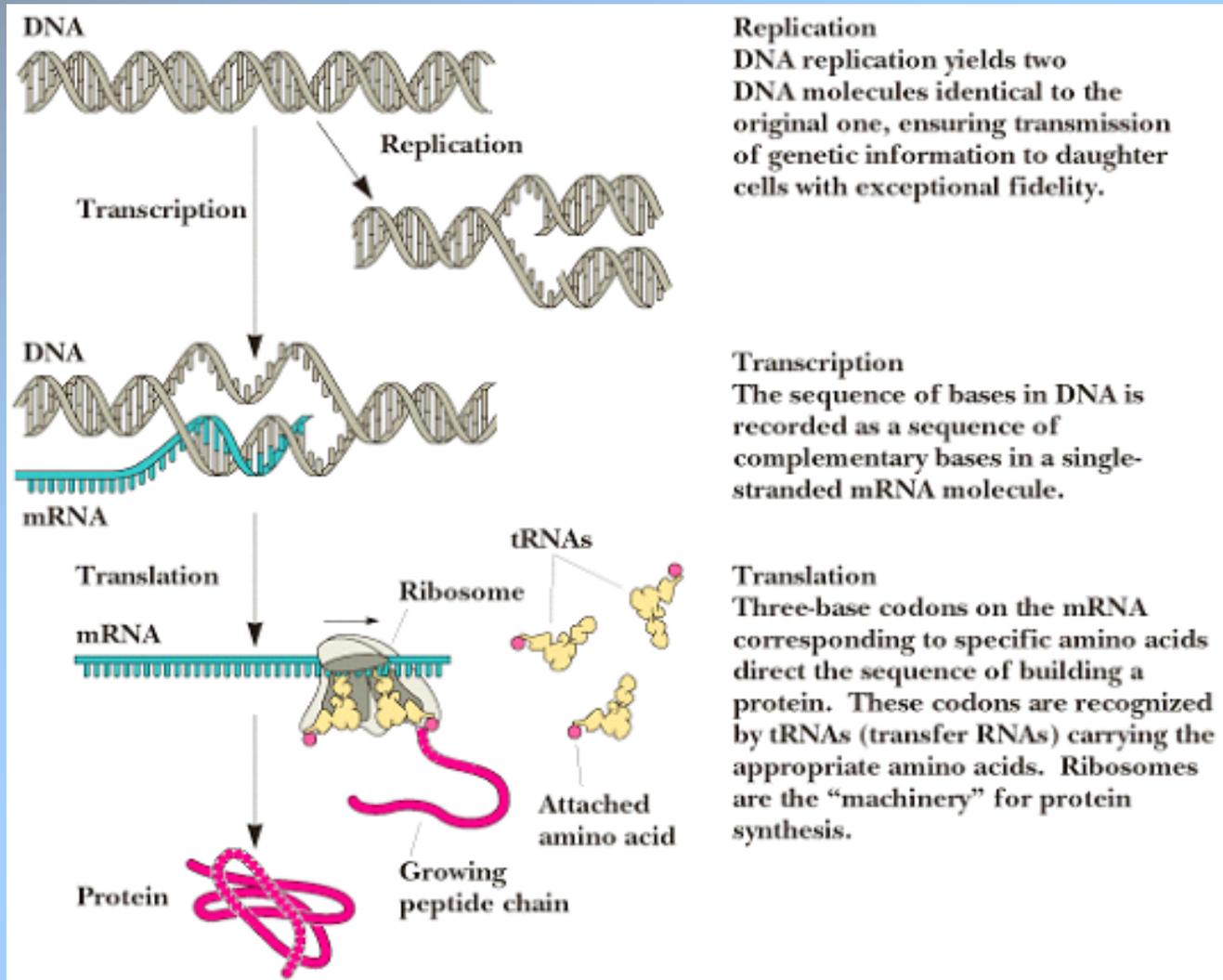


This figure is purely diagrammatic. The two ribbons symbolize the two phosphate-sugar chains, and the horizontal rods the pairs of bases holding the chains together. The vertical line marks the fibre axis



Dogma centrale della biologia

1956 Francis Crick



Replication

DNA replication yields two DNA molecules identical to the original one, ensuring transmission of genetic information to daughter cells with exceptional fidelity.

Transcription

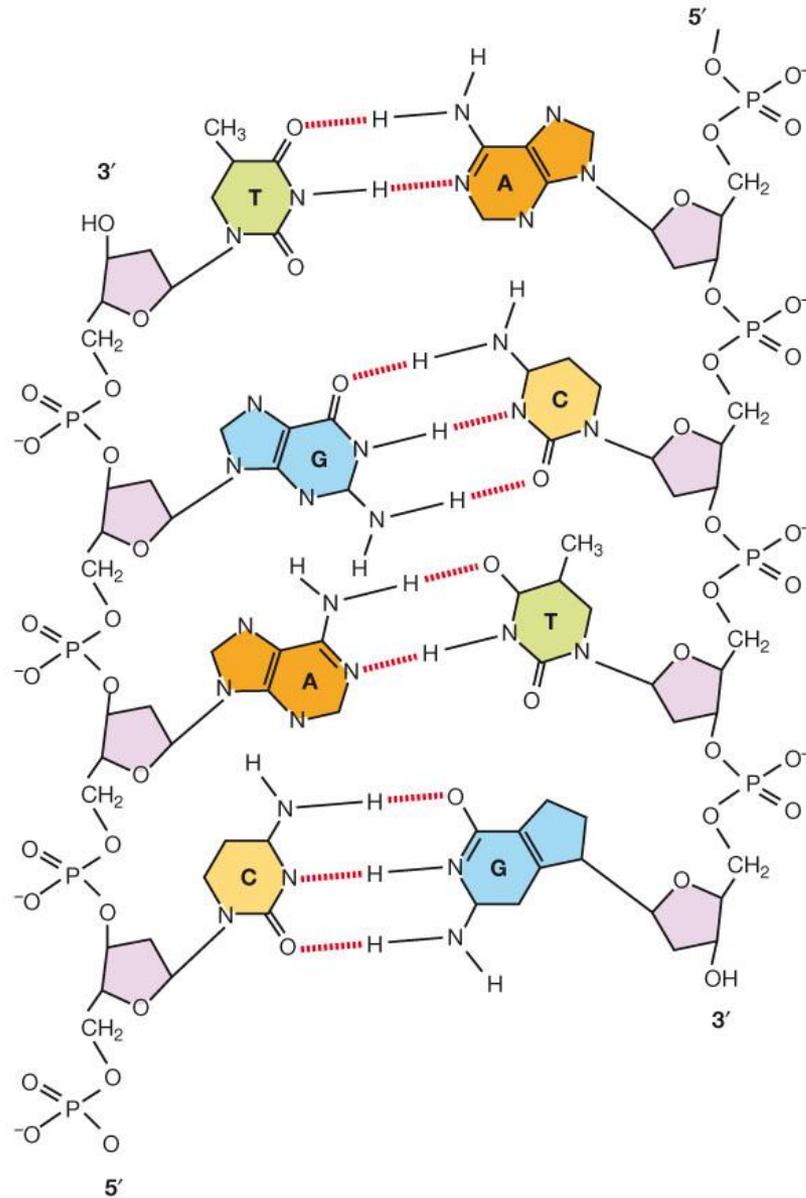
The sequence of bases in DNA is recorded as a sequence of complementary bases in a single-stranded mRNA molecule.

Translation

Three-base codons on the mRNA corresponding to specific amino acids direct the sequence of building a protein. These codons are recognized by tRNAs (transfer RNAs) carrying the appropriate amino acids. Ribosomes are the "machinery" for protein synthesis.

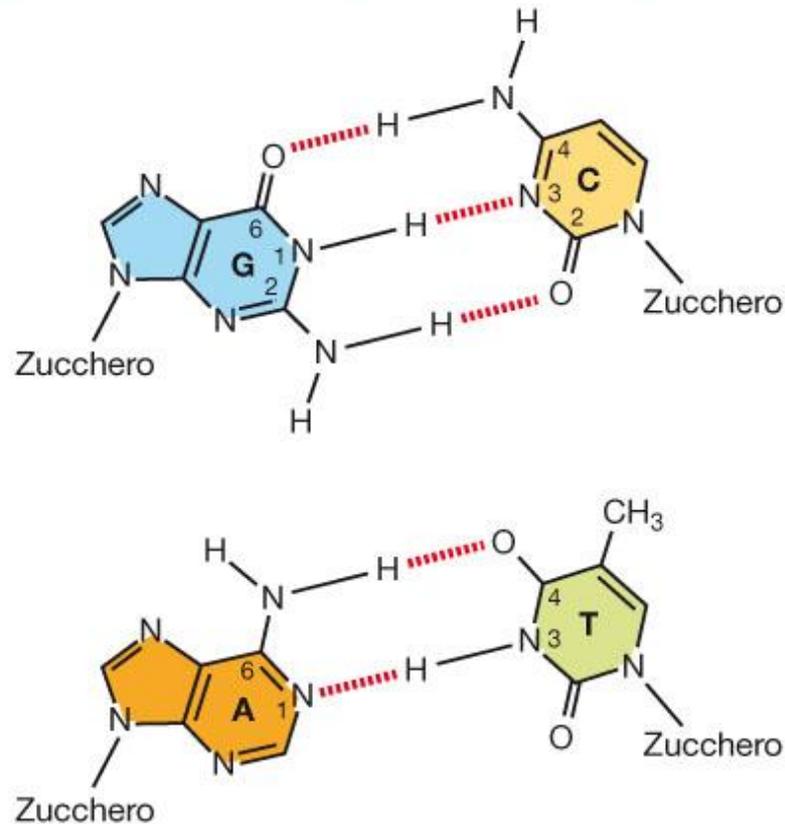
La struttura fisica del DNA

Figura 2.16 Struttura chimica della doppia elica del DNA.

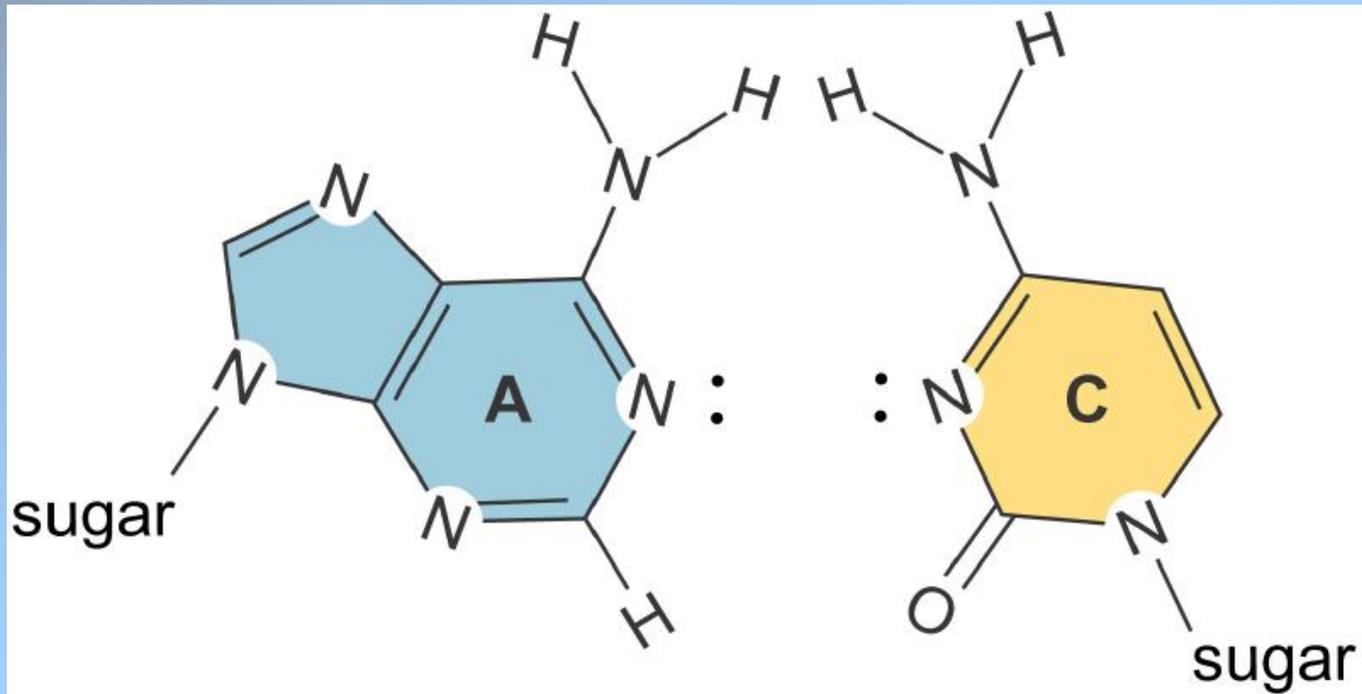


L'appaiamento delle basi implica la formazione di legami idrogeno

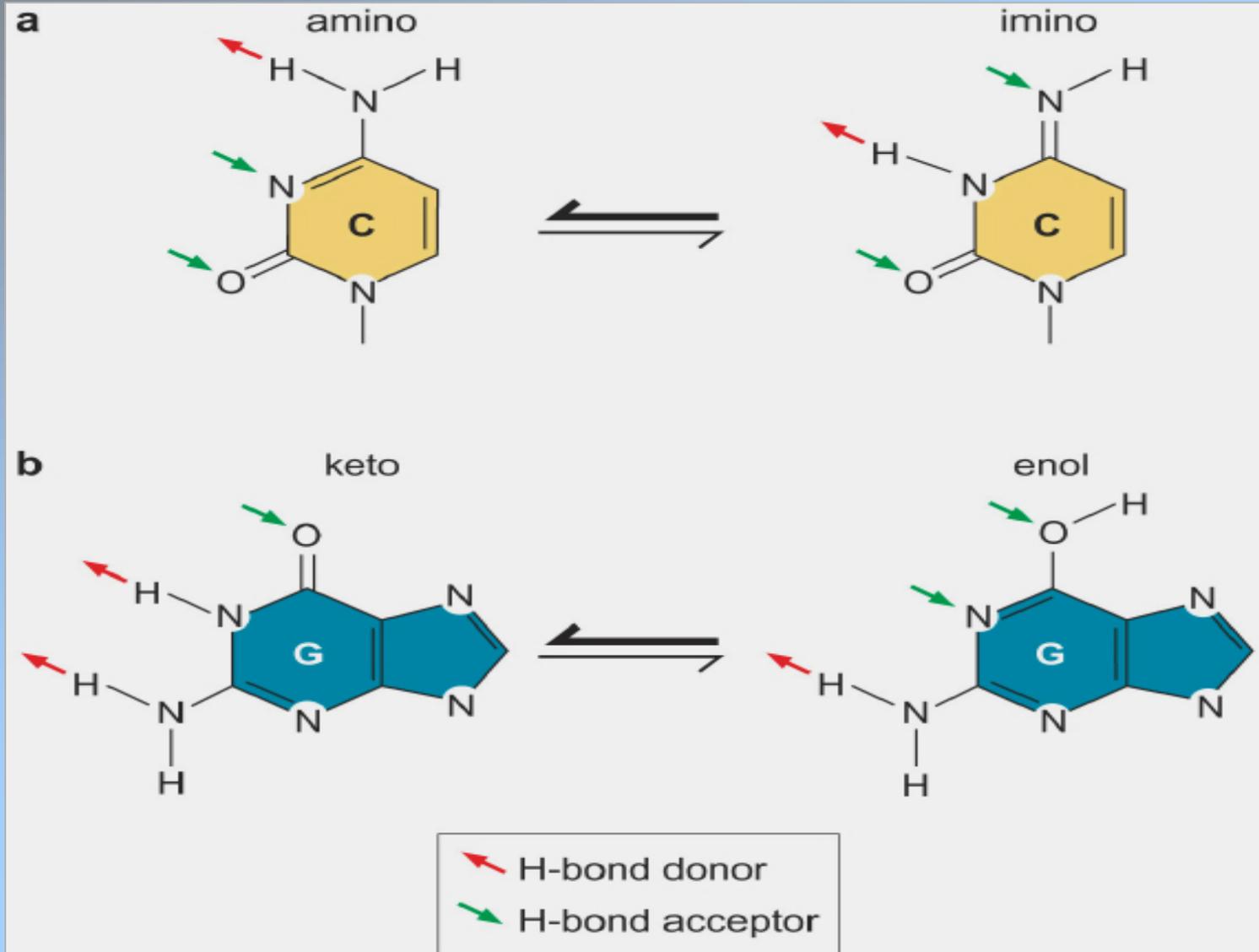
Figura 2.17 Posizione delle coppie di basi nella struttura del DNA.

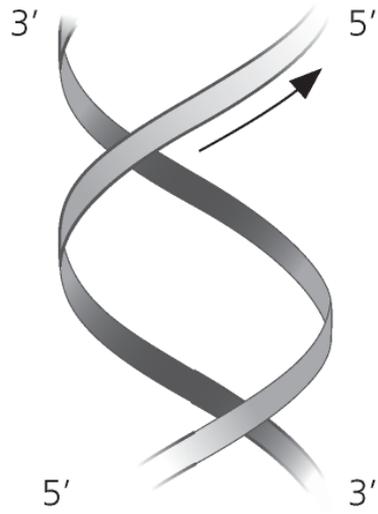


A:C incompatibility

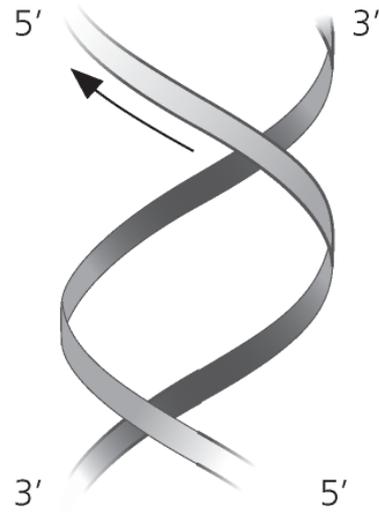


Forme tautomeriche

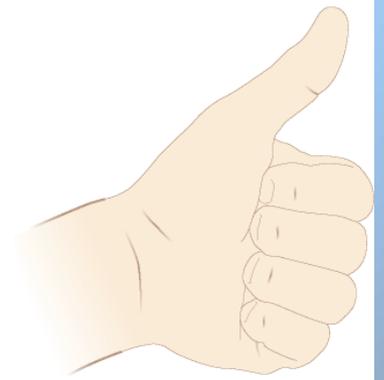




destrorsa



sinistrorsa



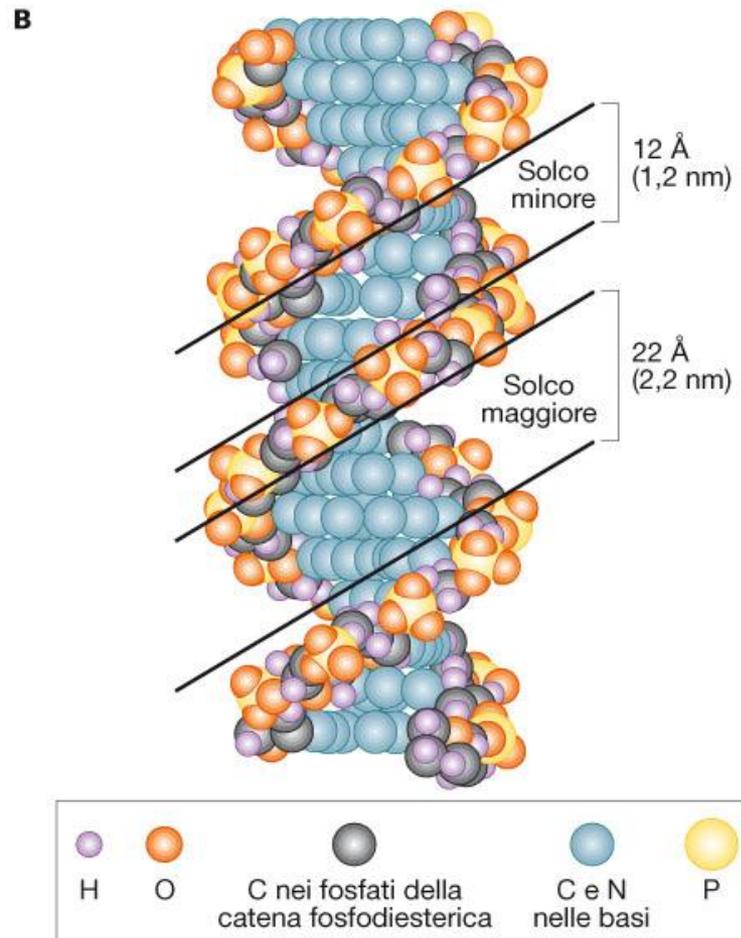
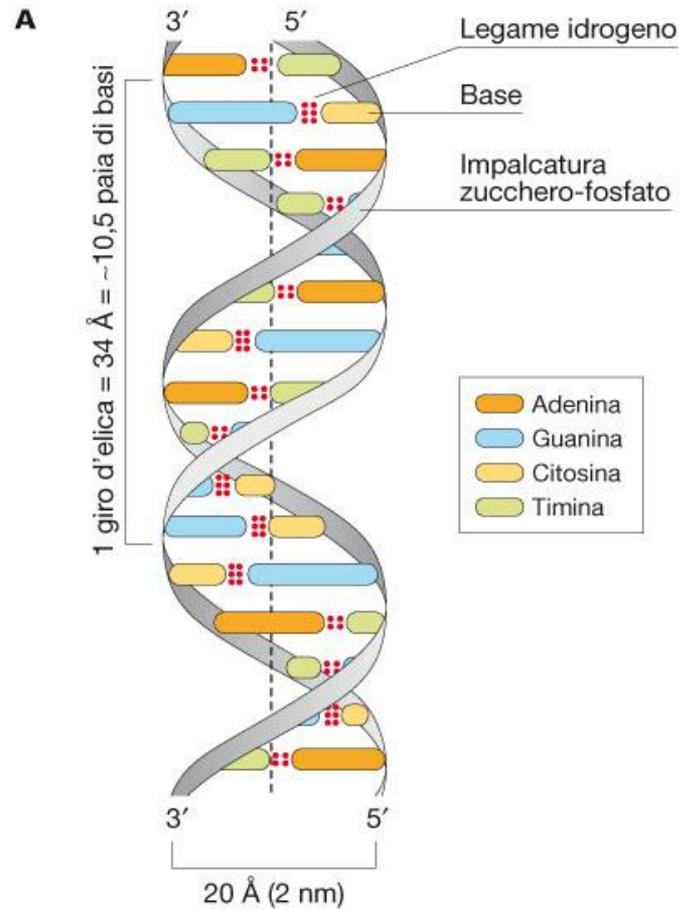


Figura 2.15 Struttura a doppia elica regolare del DNA.

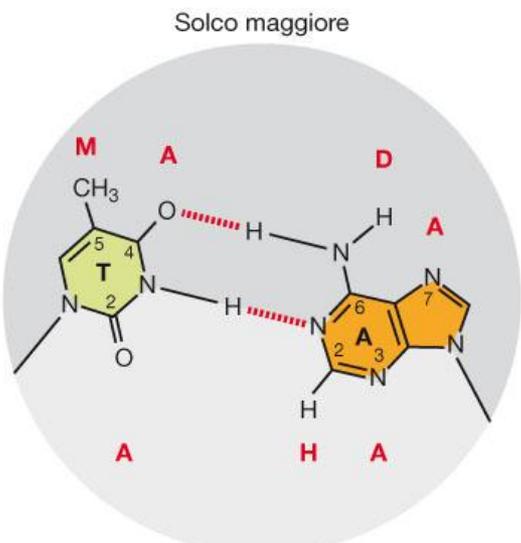
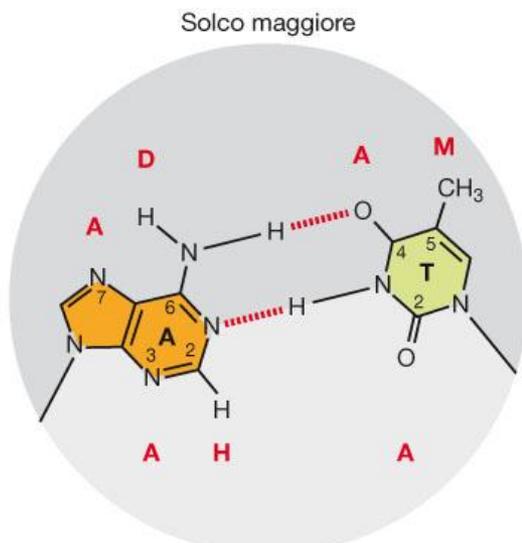
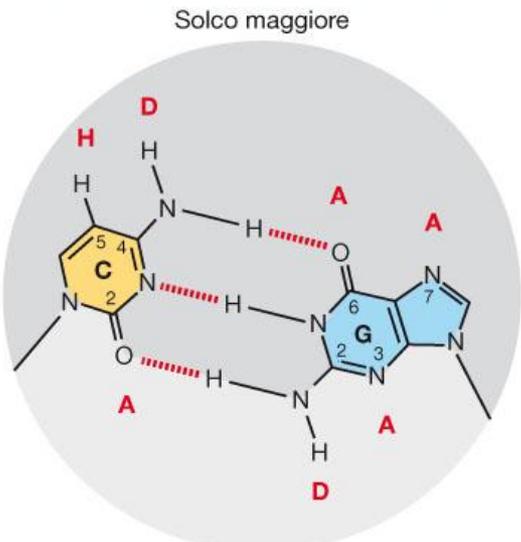
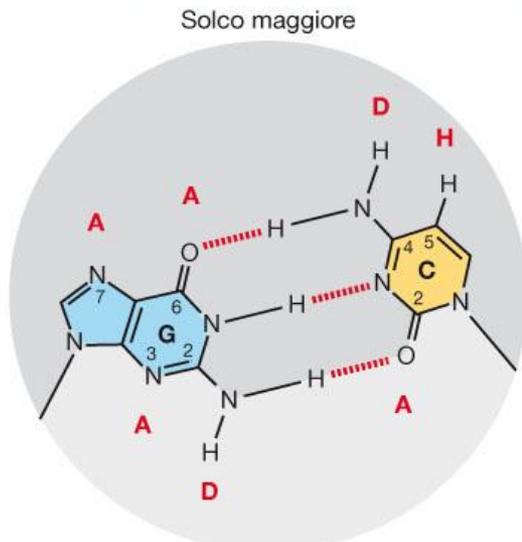


Figura 2.18 I due solchi della struttura del DNA.
 A: accettore di legami idrogeno; D: donatore di legami idrogeno; H: idrogeni non polari; M: gruppi metilici.
 Si noti la posizione di legame delle basi con gli zuccheri, spostata rispetto all'asse centrale delle basi appaiate. Questa posizione crea un'asimmetria nella molecola generando i due solchi di dimensioni diverse.

Tabella 2.3 Energie di impilamento delle coppie di basi.

Tipo di dinucleotide (5'–3')-(3'–5')	Energia di impilamento (kcal/mole/coppia impilata)
(GC)-(GC)	–14,59
(AC)-(GT)	–10,51
(TC)-(GA)	–9,81
(GG)-(CG)	–9,69
(GG)-(CC)	–8,26
(AT)-(AT)	–6,57
(TG)-(CA)	–6,57
(AG)-(CT)	–6,78
(AA)-(TT)	–5,37
(TA)-(TA)	–3,82

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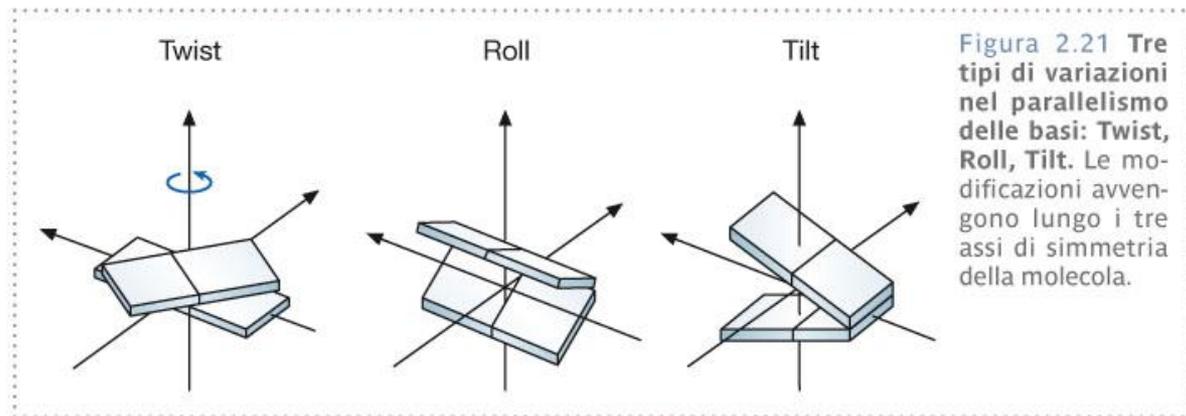
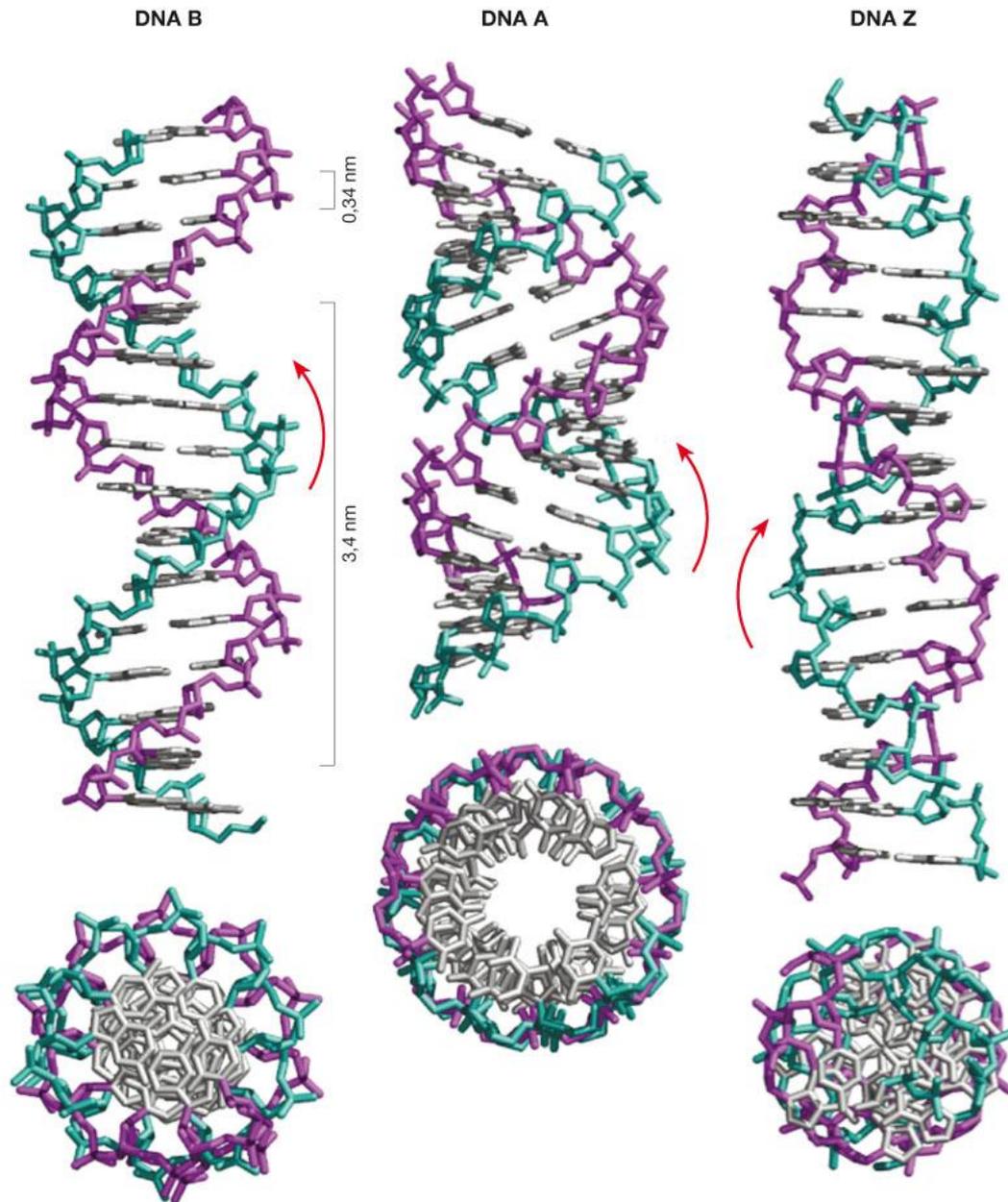


Figura 2.21 Tre tipi di variazioni nel parallelismo delle basi: Twist, Roll, Tilt. Le modificazioni avvengono lungo i tre assi di simmetria della molecola.

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Impilamento delle basi

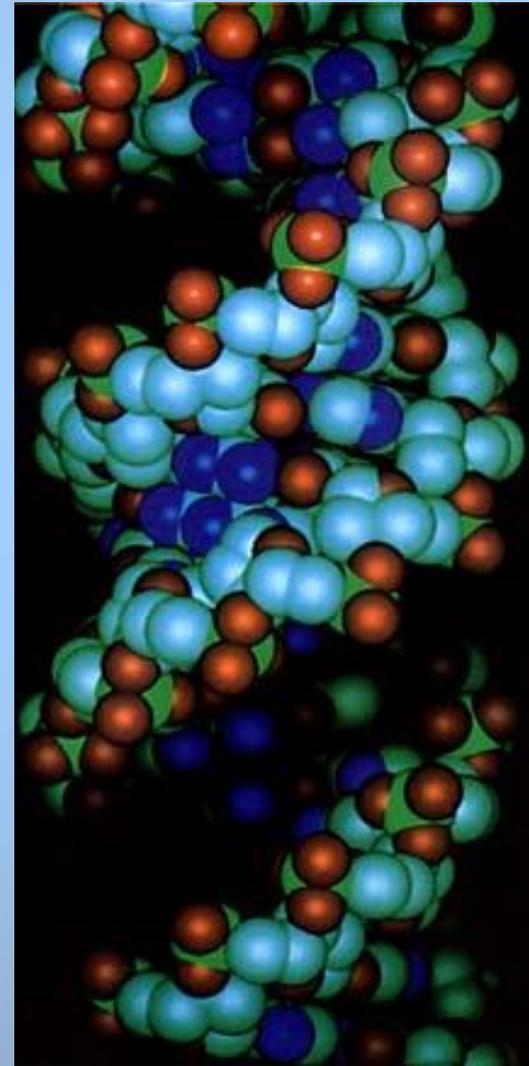
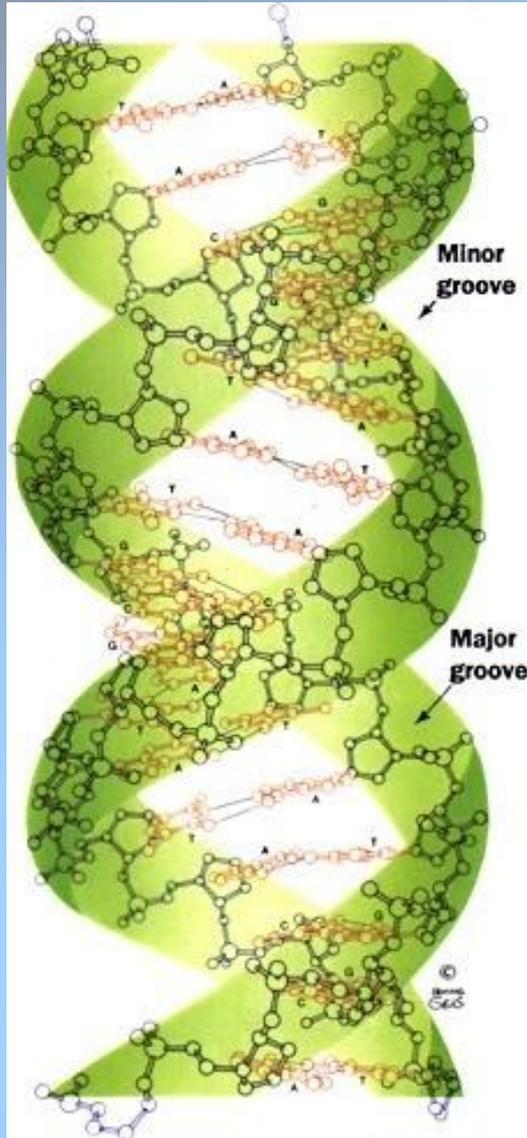
Figura 2.22 Tre diverse possibili strutture di DNA: B, A e Z.



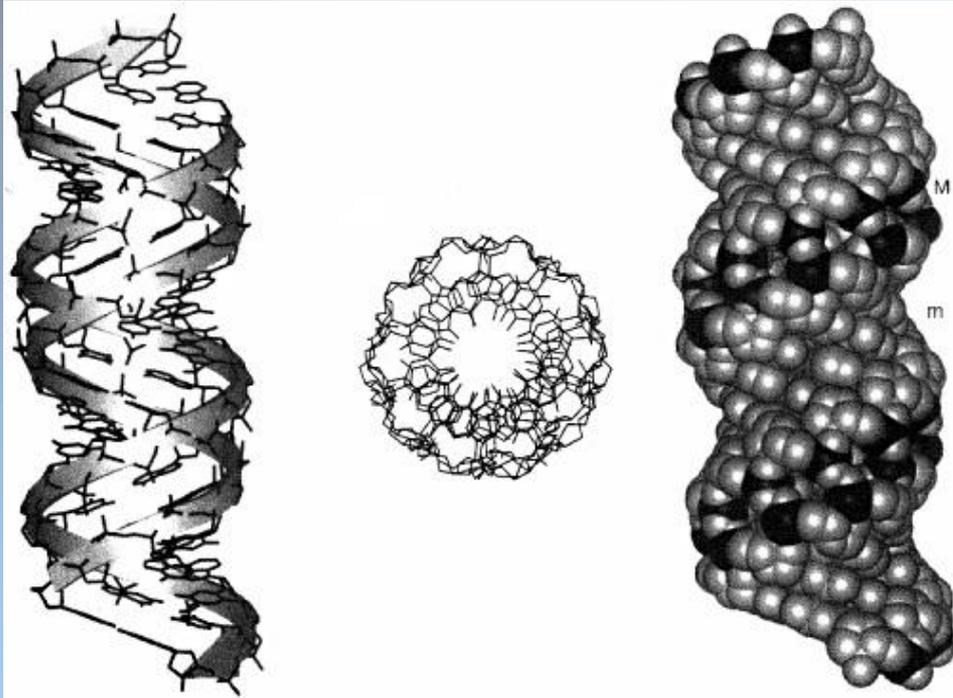
La struttura del DNA (B)

- Il DNA ha una forma ad elica regolare, diametro 20\AA , passo 34\AA
- Legami idrogeno tra le basi
- L'impilamento delle basi è determinato da interazioni idrofobiche
- Ogni coppia è ruotata di 36°
- Solchi maggiore (22\AA) e minore (12\AA)
- Avvolgimento in senso orario (elica destrorsa)

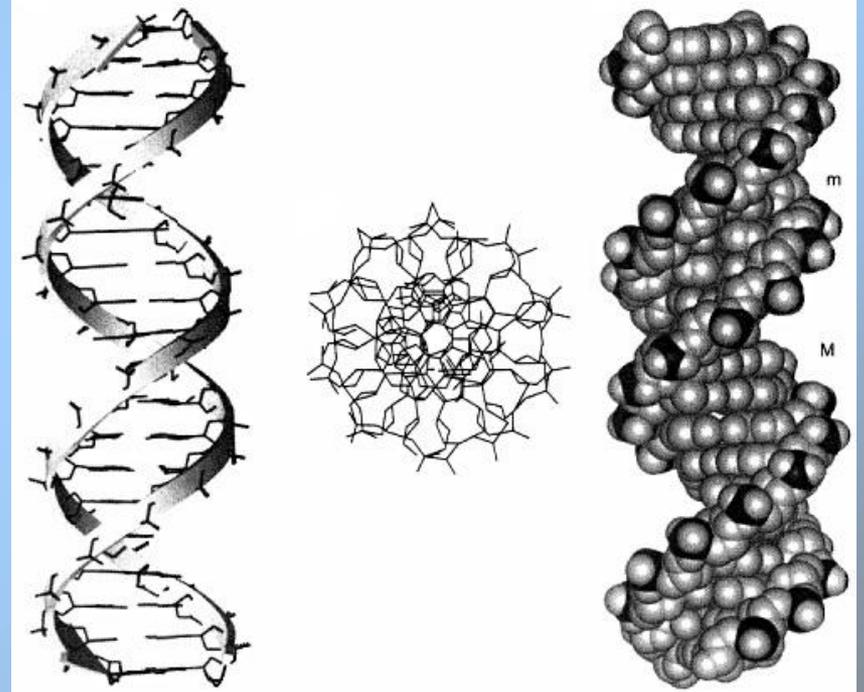
A DNA (bassa umidità)



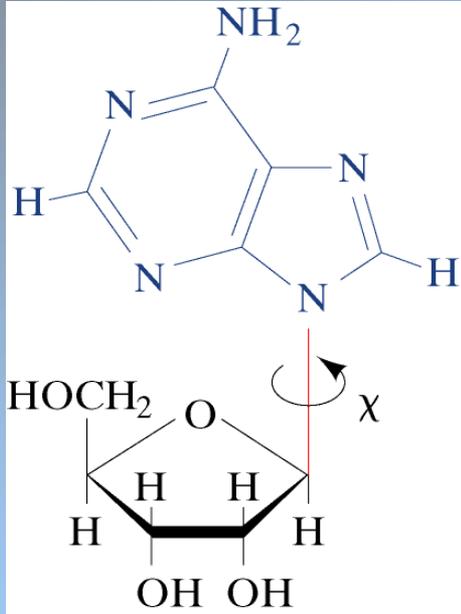
Canonical A DNA



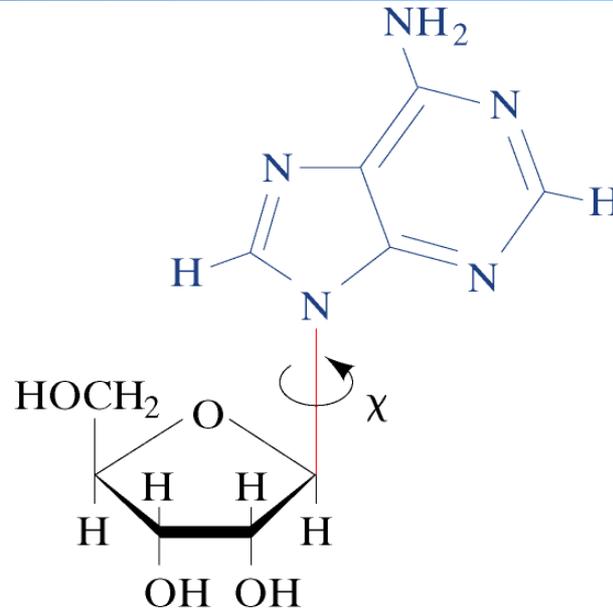
Canonical B DNA



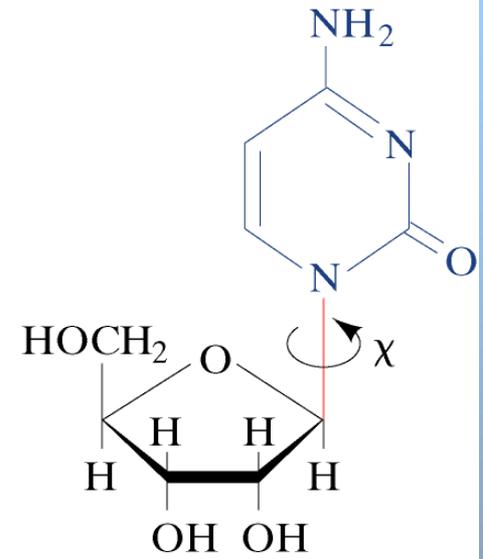
Z-DNA



***sin*-Adenosina**



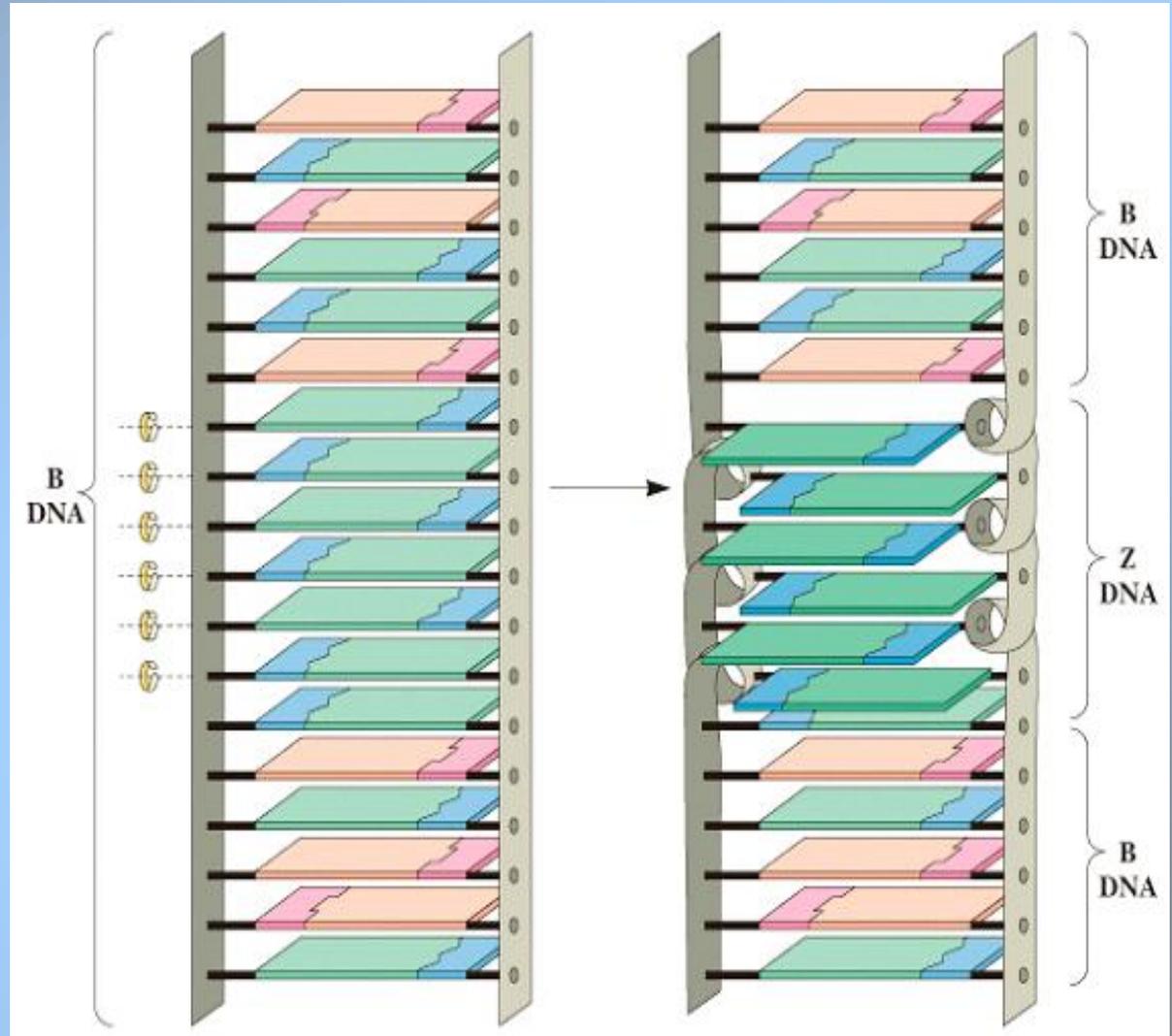
***anti*-Adenosina**



***anti*-Citidina**

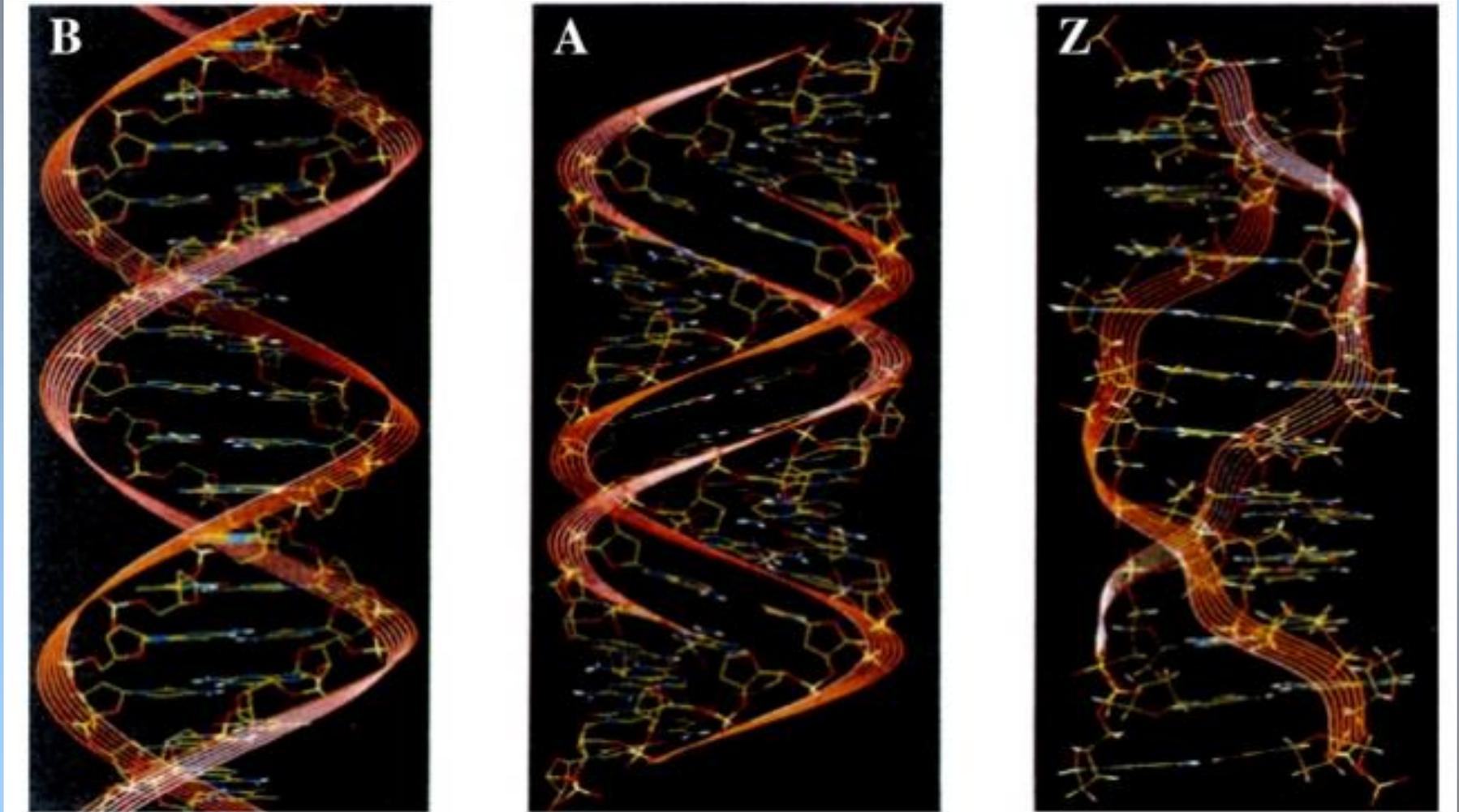
Struttura Z del DNA

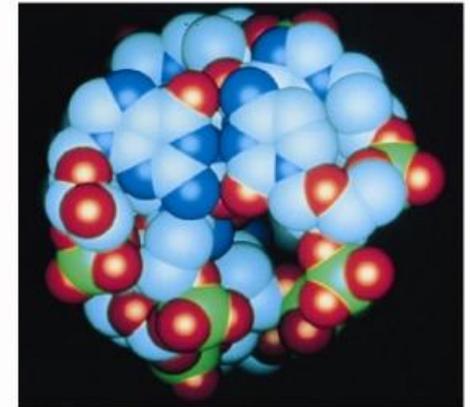
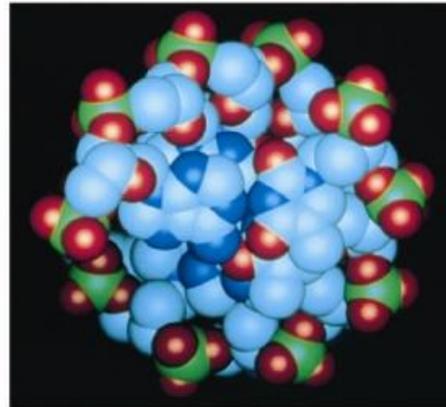
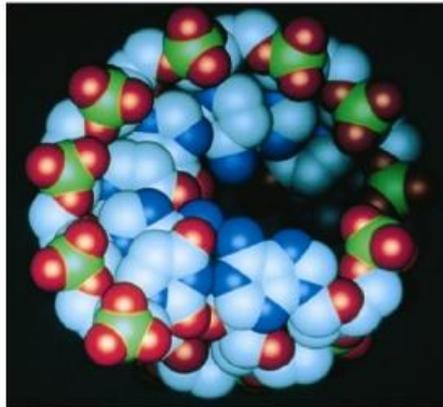
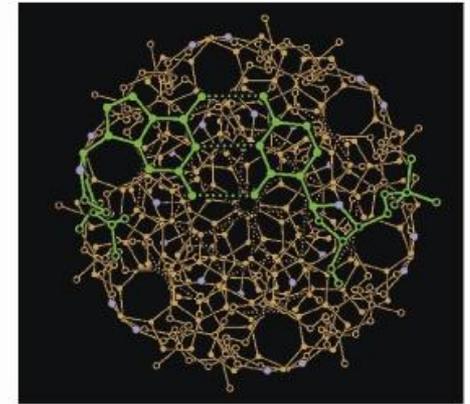
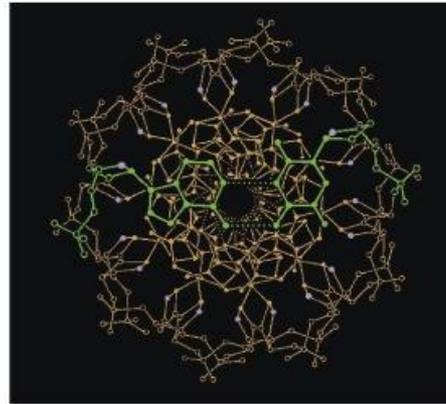
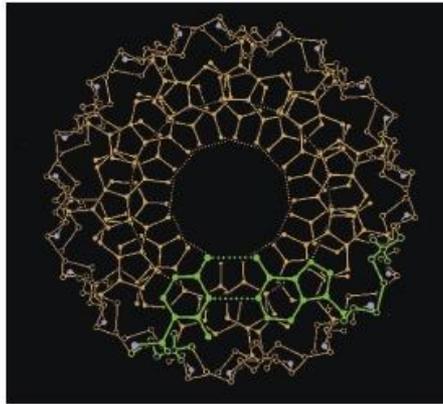
- Tipica in regioni di DNA ricche in G:C
- G in conformazione sin-
- C in conformazione anti- ma con il nucleotide ruotato di 180°



Proprietà	DNA A	DNA B	DNA Z
Senso di rotazione dell'elica	Destrorsa	Destrorsa	Sinistrorsa
Diametro dell'elica	22 Å	20 Å	18 Å
Paia di basi per giro d'elica	10,9	10 A	12
Distanza tra le coppie di basi	2,6 Å	3,4 Å	3,7 Å
Inclinazione delle basi rispetto all'asse	20°	6°	7°
Conformazione del legame glicosidico	Anti	Anti	Sin (purine) Anti (pirimidine)
Morfologia generale	Corto e largo	Più lungo e sottile	Allungato e sottile
Solco maggiore	Estremamente stretto e molto profondo	Largo e di profondità intermedia	Appiattito sulla superficie dell'elica
Solco minore	Molto largo e poco profondo	Stretto e di profondità media	Estremamente stretto e molto profondo
Posizione dell'asse dell'elica	Solco maggiore	Attraverso le coppie di basi	Solco minore

Confronto tra le forme B, A e Z del DNA





DNA A

DNA B

DNA Z

▲ **FIGURA 9.9-continua** (b) Vista dall'alto. Entrambe le parti includono modelli tridimensionali generati al computer (in basso). Le immagini in alto mostrano invece le corrispondenti rappresentazioni a sfera e bastoncino. Nella forma A, le coppie di basi hanno una pronunciata torsione rispetto all'asse dell'elica. Nella forma B, le coppie di basi giacciono in un piano che è quasi perpendicolare all'asse dell'elica. Il DNA-Z è un'elica sinistrorsa ed in questo differisce da DNA-A e DNA-B, entrambi destrorsi. (Robert Stadola, Fox Chase Cancer Research Center. Illustration, Irving Geis. Diritti di proprietà dell'Howard Hughes Medical Institute. Da non riprodurre senza permesso.)

Sequenze ripetute

Sequenza ripetuta in modo diretto:



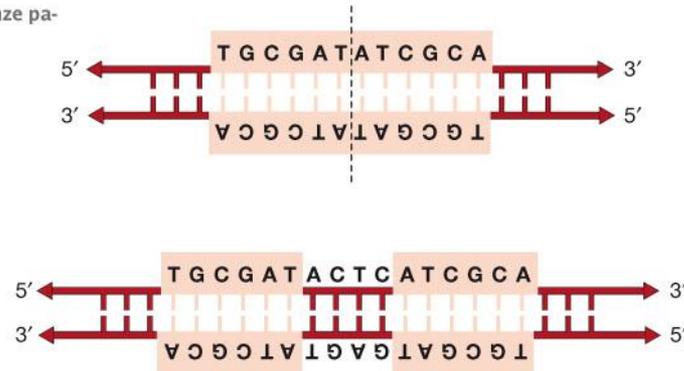
Sequenza ripetuta in modo speculare:



Sequenza "palindromica":



Figura 2.28 Sequenze palindromiche.



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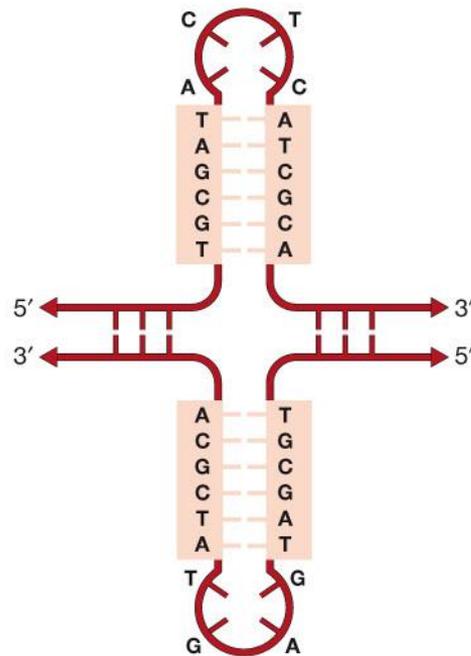
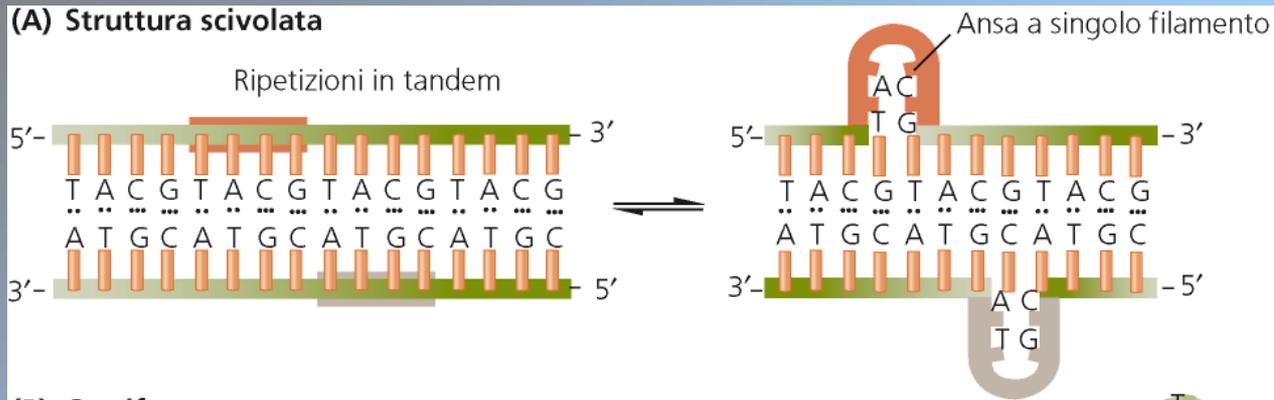


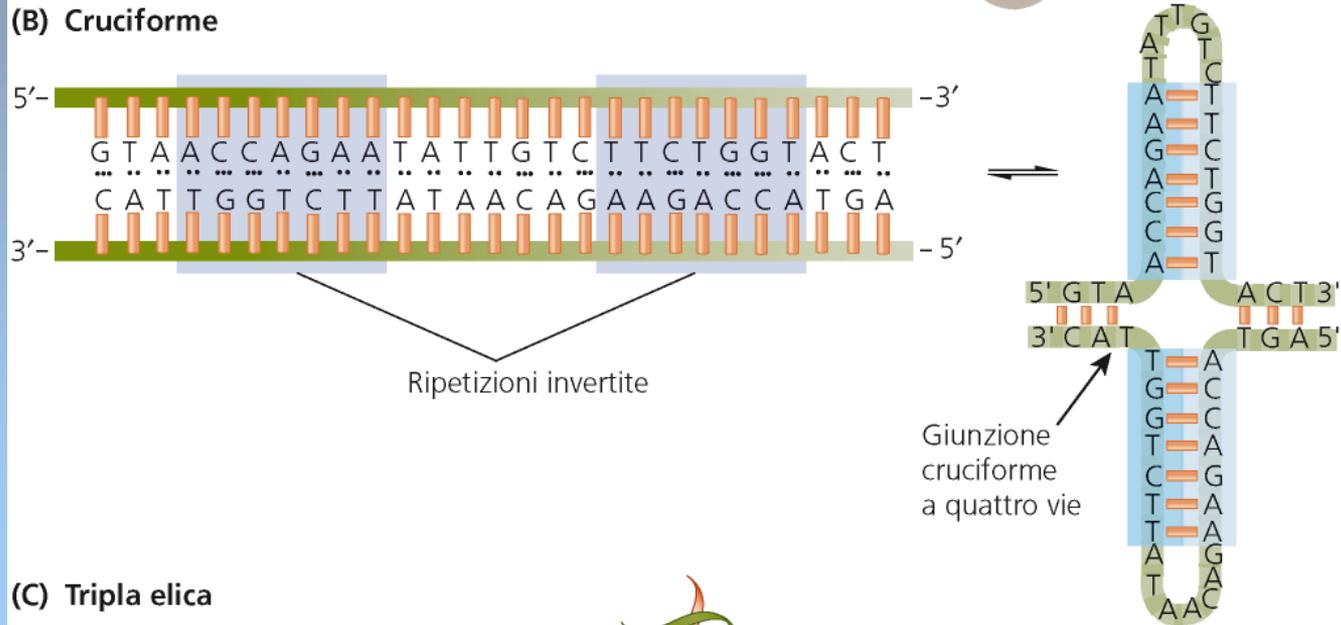
Figura 2.29 Una doppia elica contenente una sequenza palindromica può dare origine a una struttura "cruciforme".

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(A) Struttura scivolata



(B) Cruciforme



(C) Tripla elica

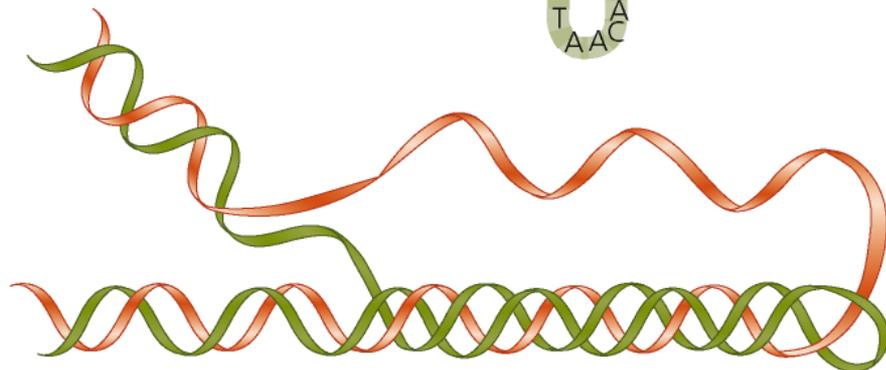
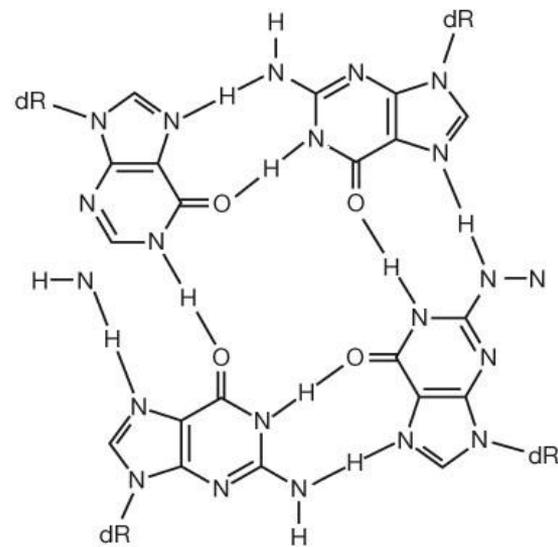


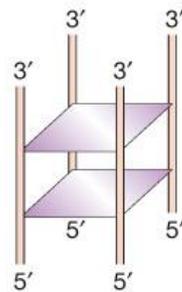
Figura 2.27 **Strutture a quattro eliche che si formano in presenza di quartetti G.**

(A) Struttura chimica del quartetto G. (B) Varie strutture che si possono formare con le combinazioni di tratti di DNA che contengono G ripetute.

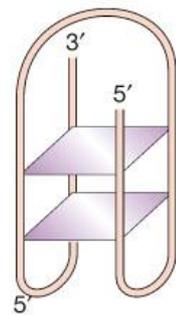
A



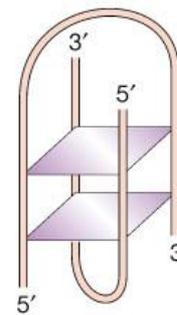
B



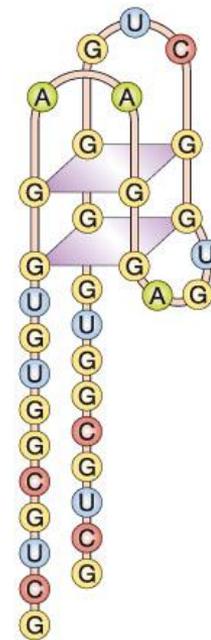
G4-DNA
intermolecolare



"Basket" tipo
G4 DNA
intramolecolare

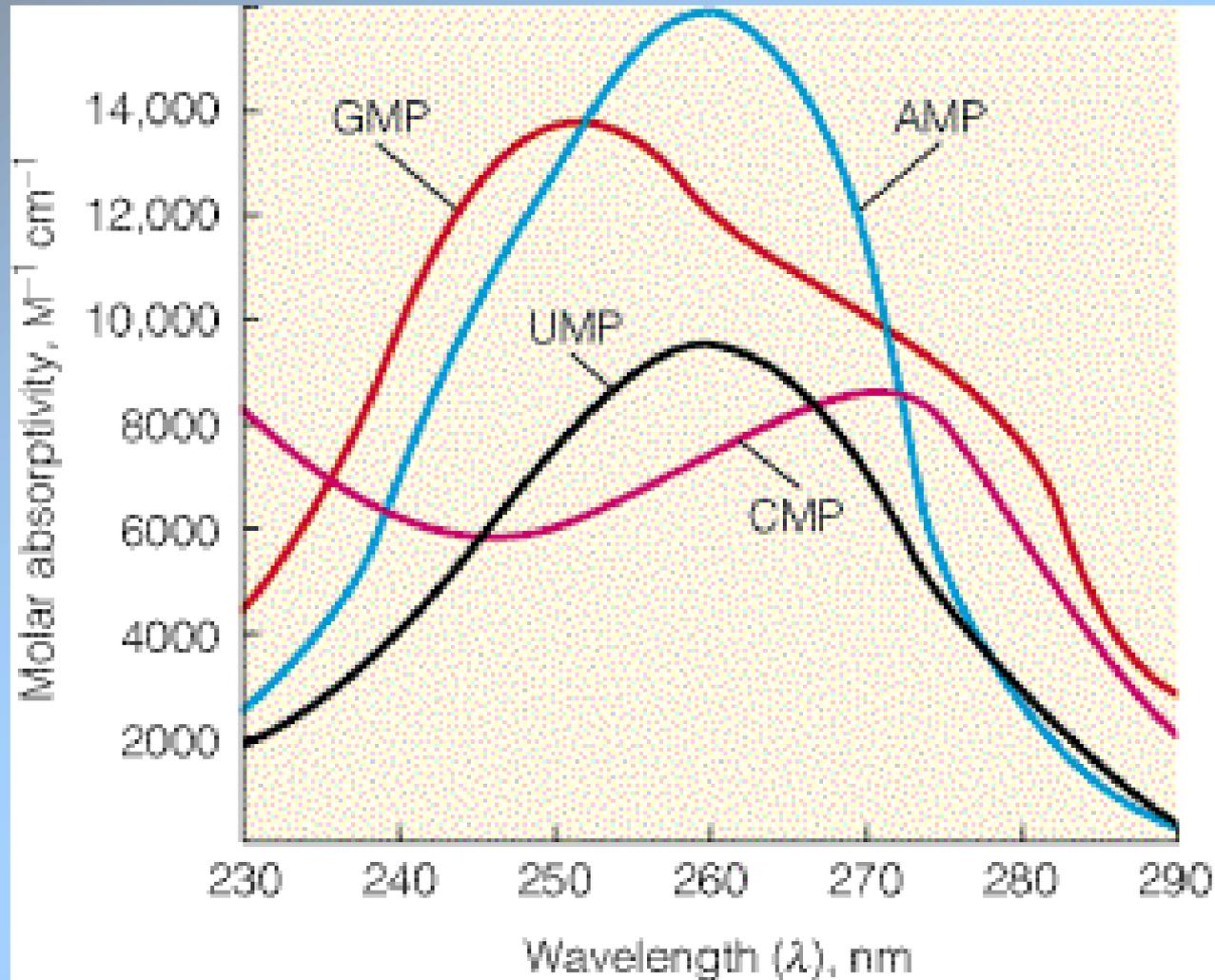


"Basket" tipo
G4 DNA
intermolecolare

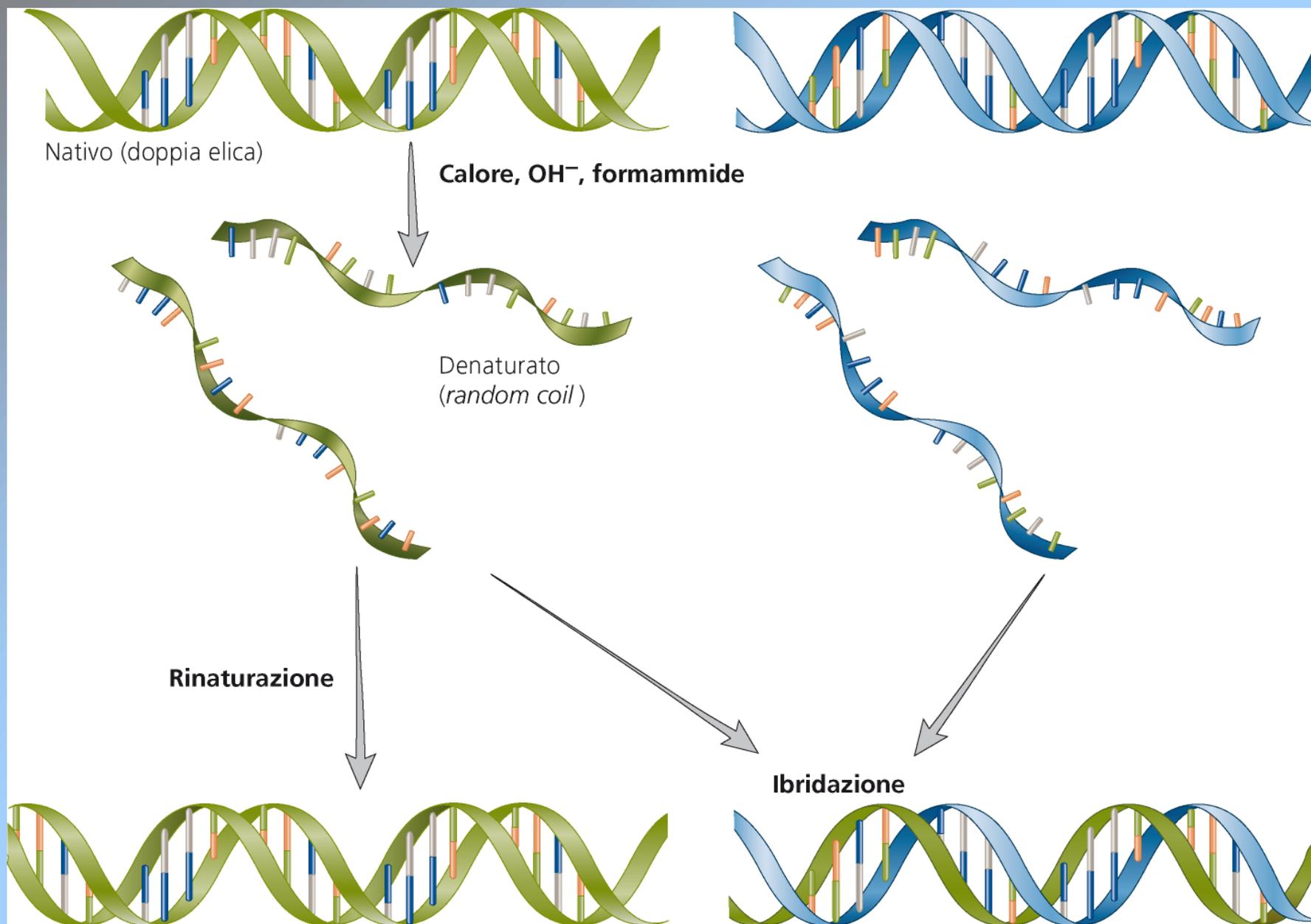


PROPRIETA' DEGLI ACIDI NUCLEICI

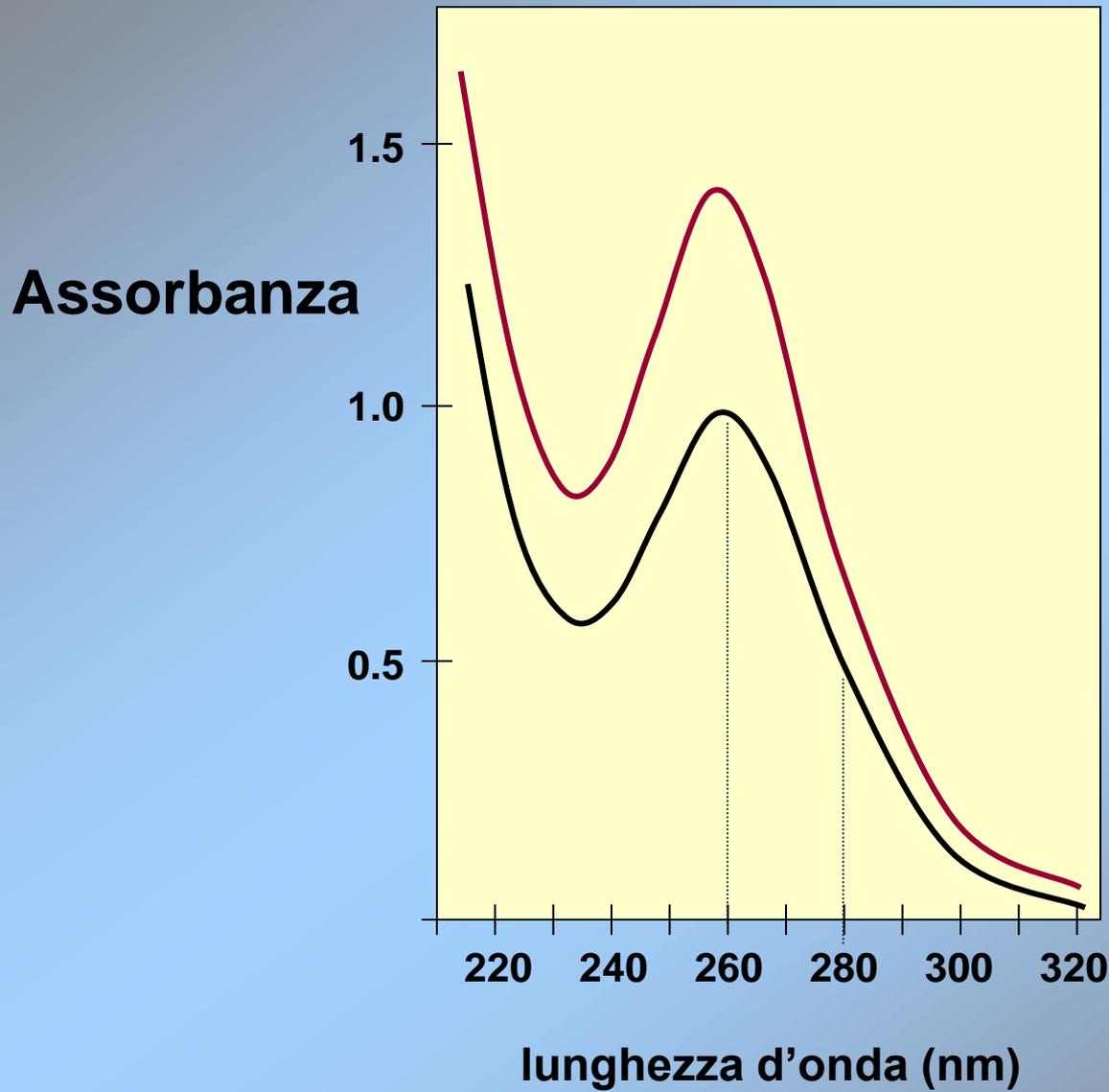
ASSORBIMENTO UV



DENATURAZIONE DEL DNA



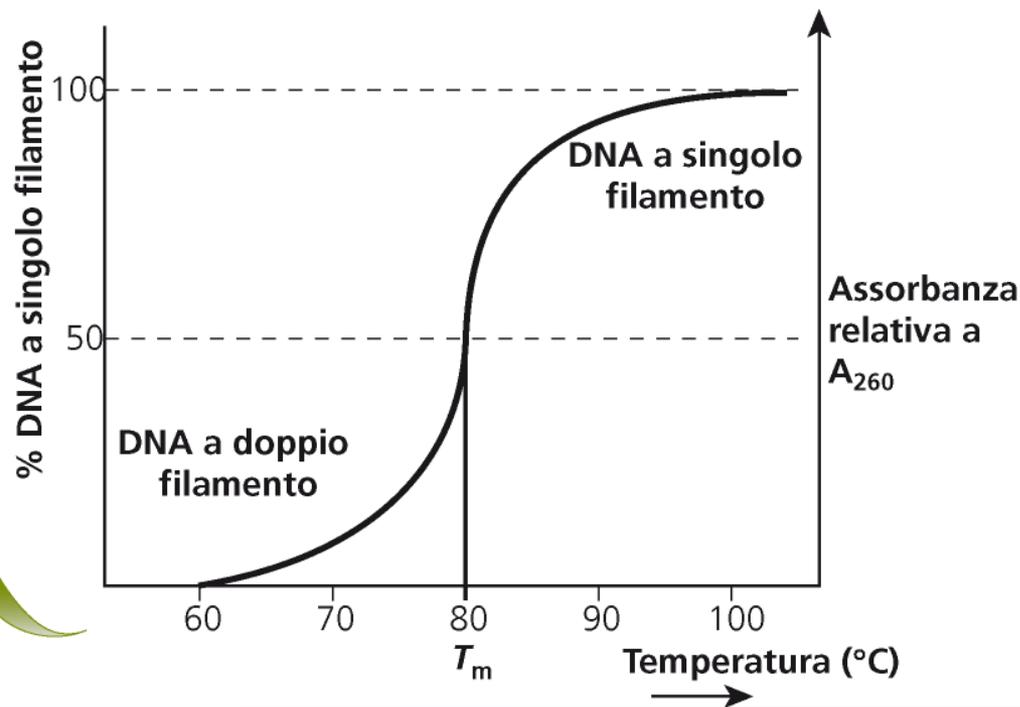
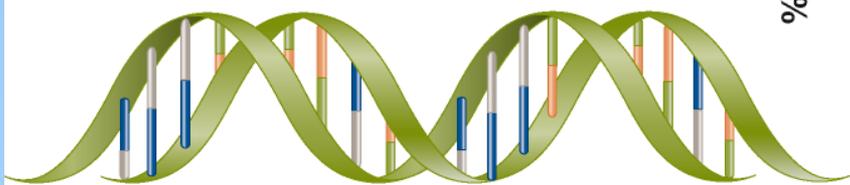
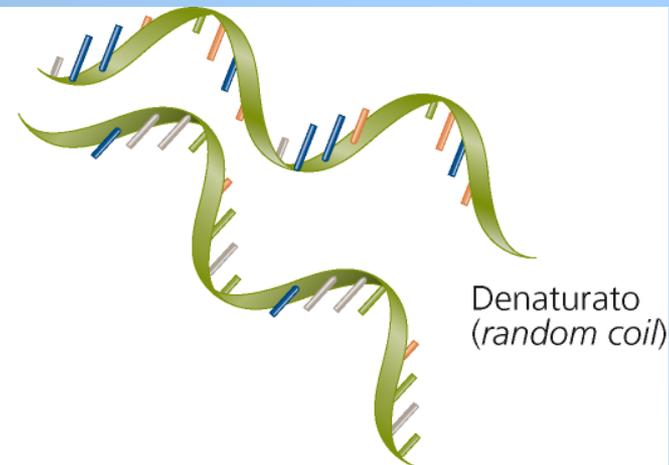
Spettro di assorbimento del DNA



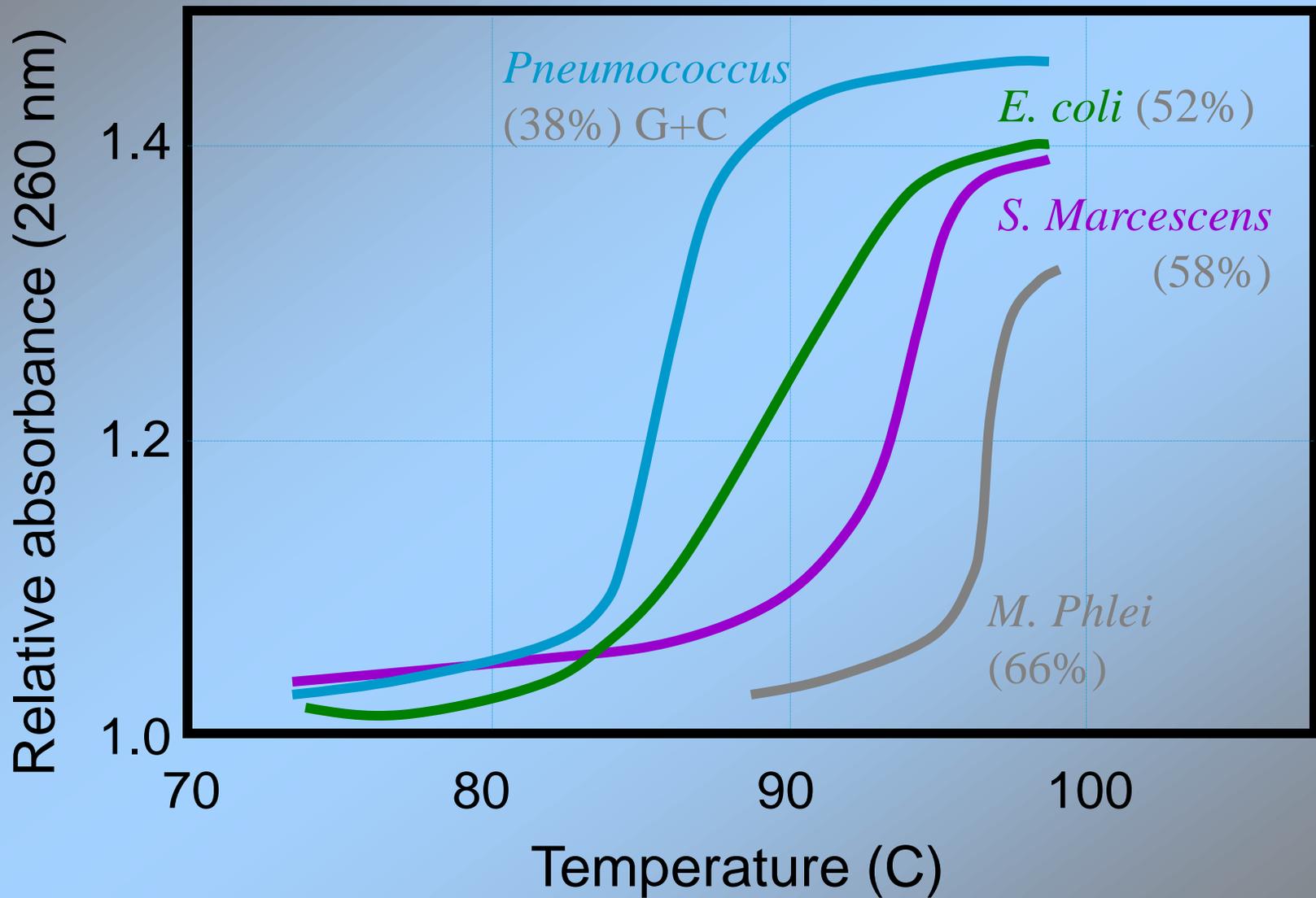
**effetto
ipercromico**

DENATURAZIONE DEL DNA

Temperatura di melting (T_m)



G+C Content Is Proportional to Tm



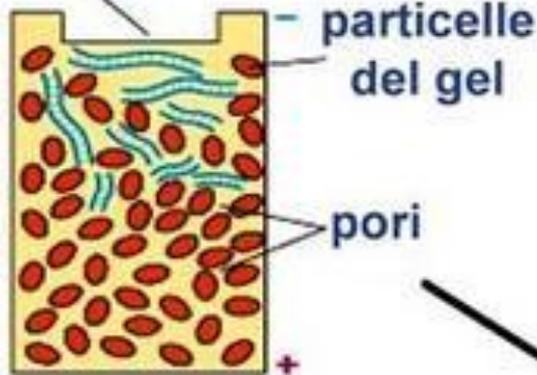
Separazione elettroforetica di frammenti di DNA

frammenti di DNA

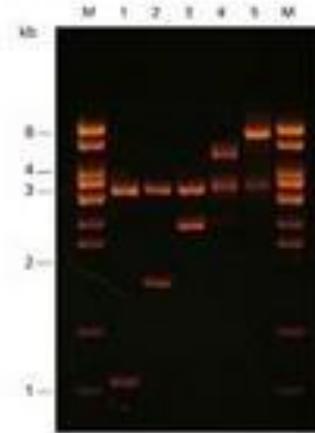


Caricare la miscela nel "pozzetto" di un gel di agarosio o poliacrilamide.

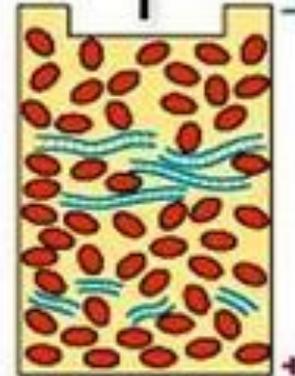
Applicare il campo elettrico.

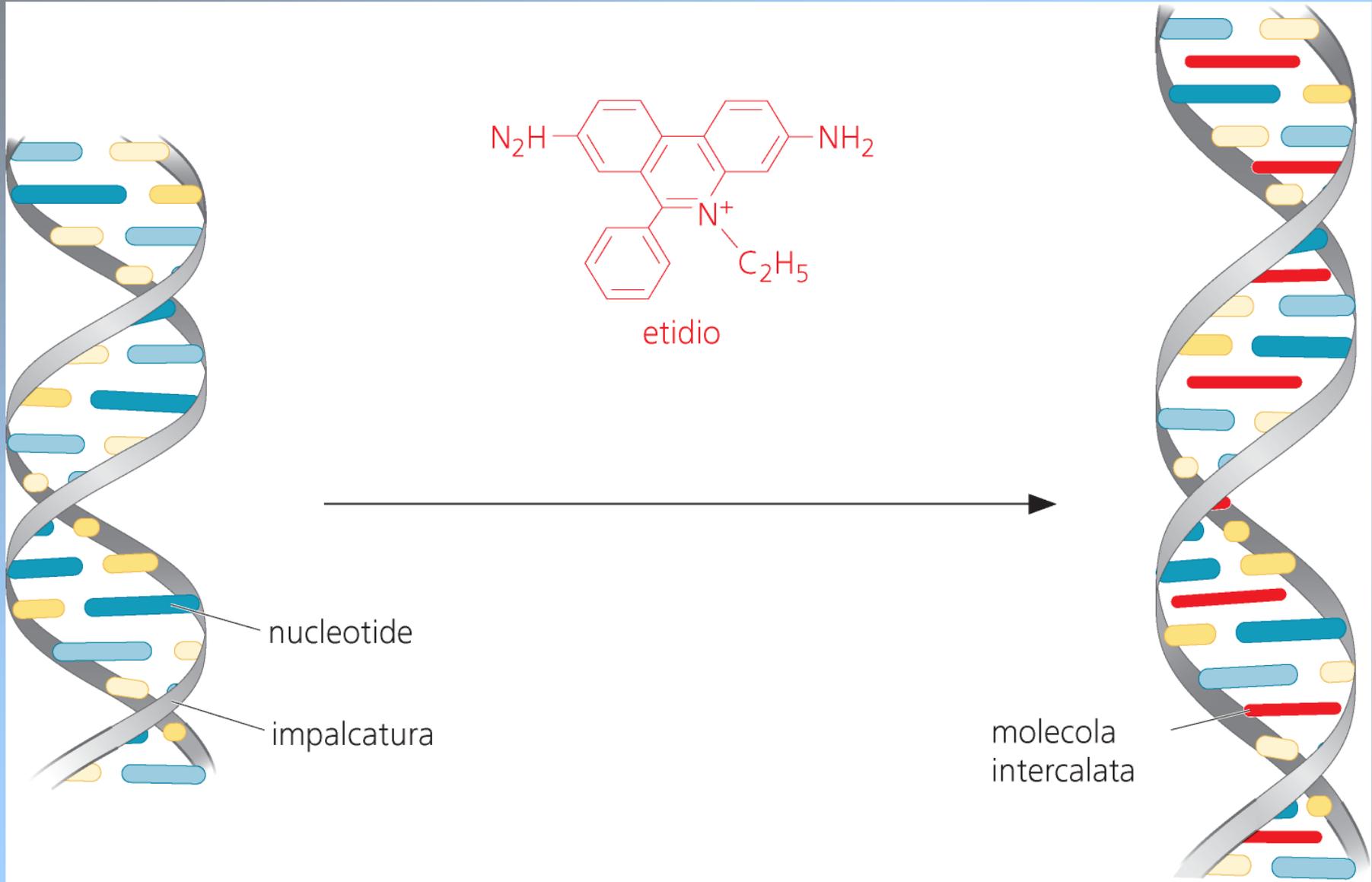


I frammenti di DNA migrano nel gel ad una velocità inversamente proporzionale alla loro lunghezza.



Frammenti di DNA di uguale dimensione formeranno "bande" discrete, evidenziate in luce UV per la presenza nel gel di un colorante fluorescente che s'intercala nella doppia elica del DNA (EtBr).

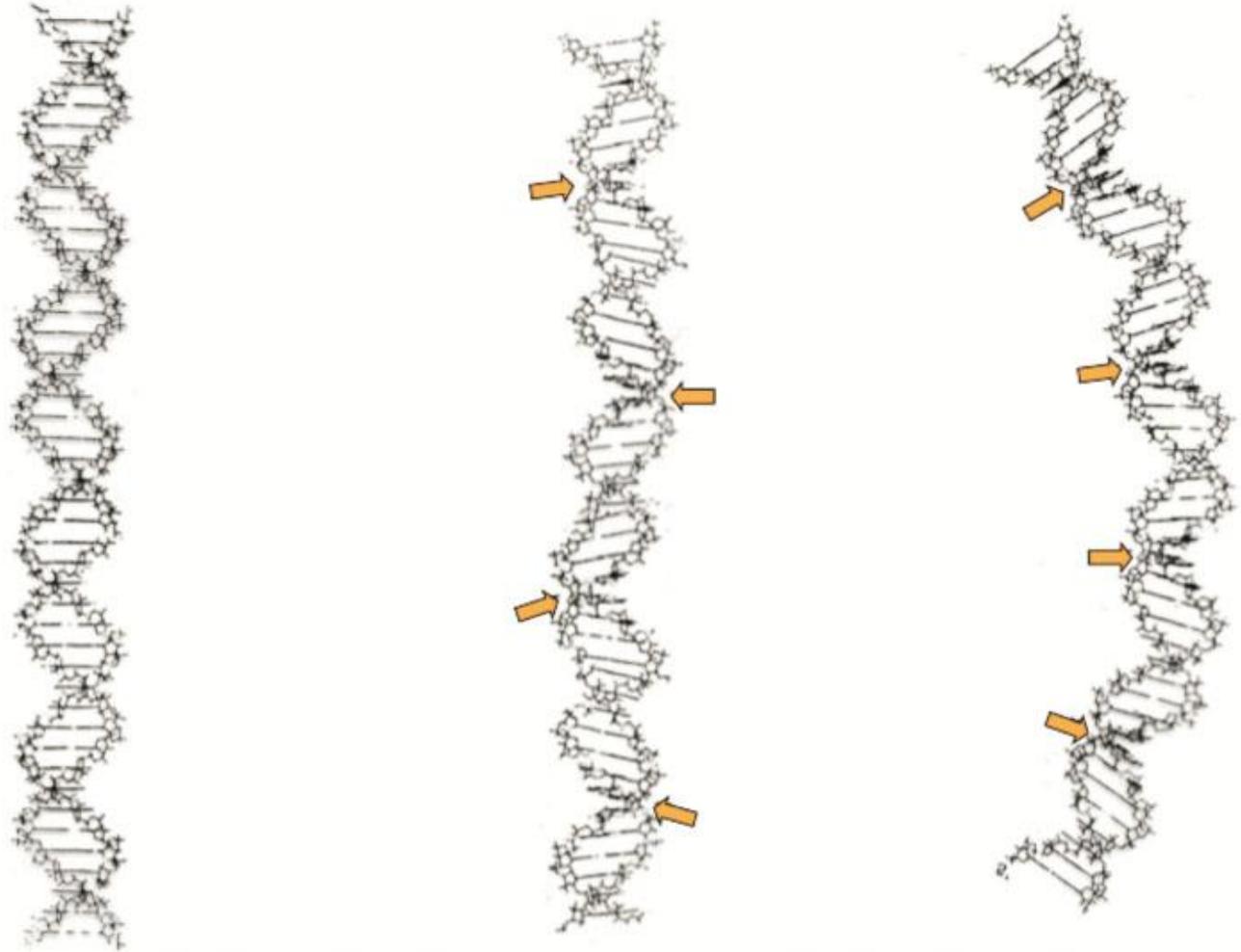




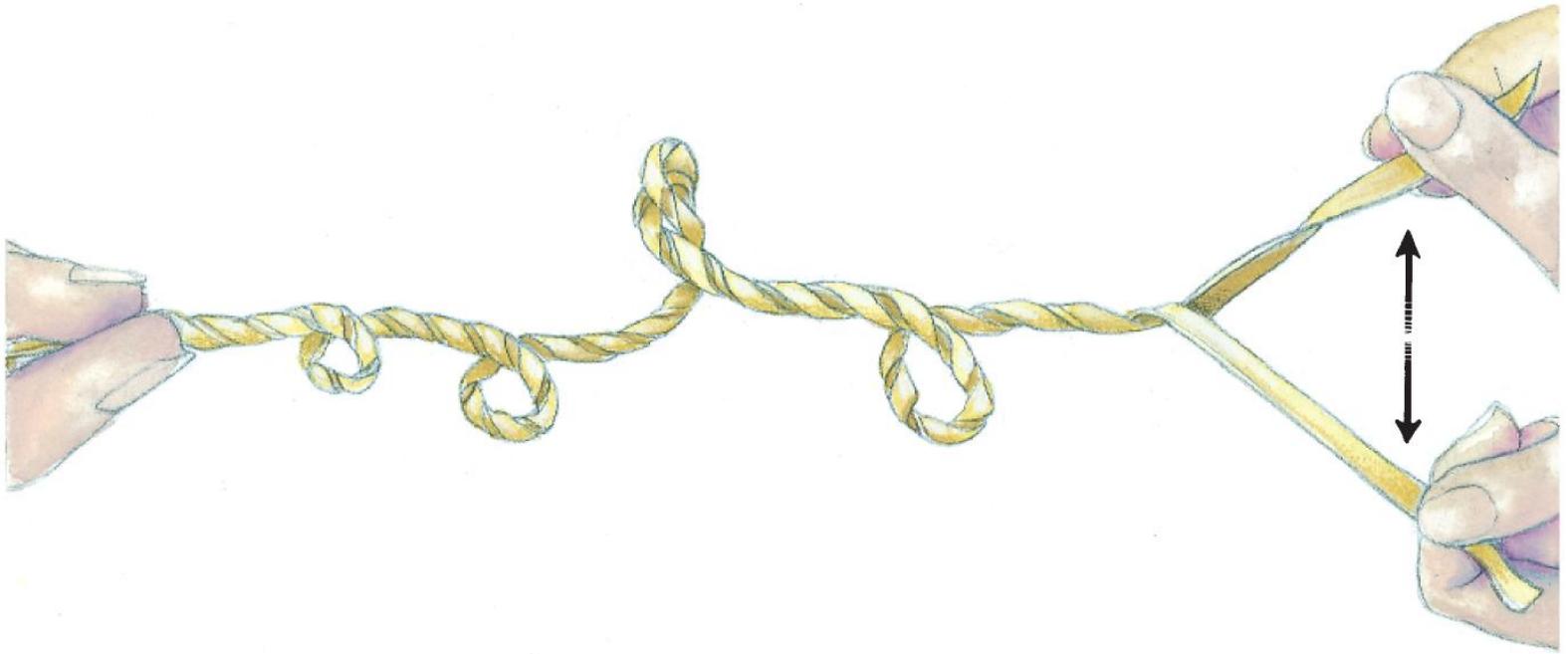
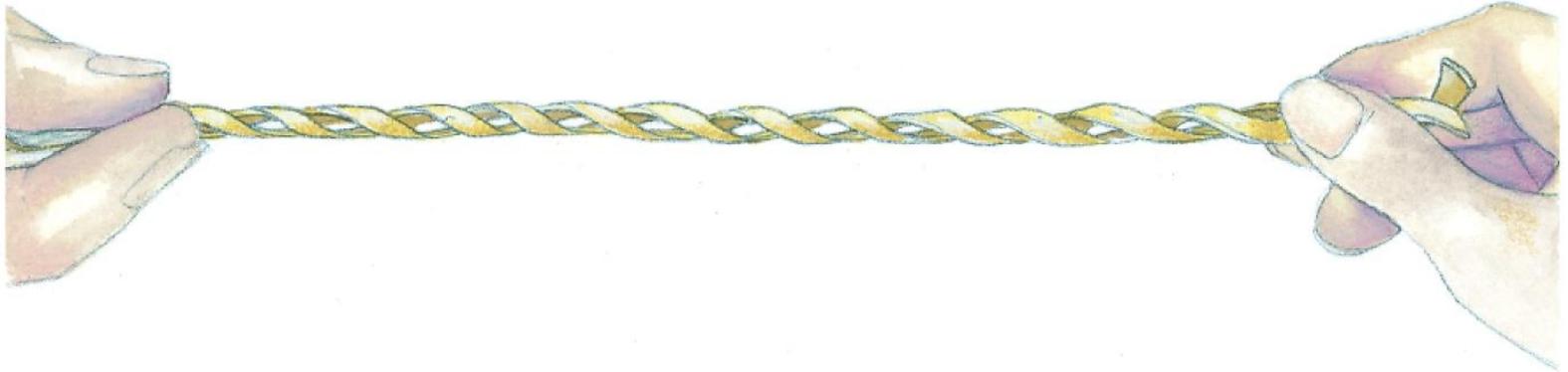
TOPOLOGIA DEL DNA

Figura 2.32 Il DNA può essere intrinsecamente curvo.

Le perturbazioni dovute ad A-T e G-C, se sono disposte in maniera casuale, tendono a elidersi. Se invece ci sono delle ripetizioni dello stesso tipo, posizionate sempre nella stessa direzione, si ottiene DNA curvo. Le frecce indicano i punti di flesso.







TOPOLOGIA DEL DNA

$$Lk = T + W$$

Il “linking number” (numero di legame topologico), Lk , uguale alla somma del numero di avvolgimenti (T) e del numero di superavvolgimenti (W).

Il numero di legame topologico linking number (Lk)

Ha due componenti:

Tw (twist)= numero di volte che un filamento incrocia l'altro (N di giri dell'elica: N bp/ N di bp per passo dell'elica). Ha segno + se elica è destrorsa.

Wr (writhe)= N di volte in cui l'asse della doppia elica incrocia se stesso nello spazio (superavvolgimenti). Se sinistrorso -, destrorso +.

$$Lk = Tw + Wr$$

Lk può cambiare solo se si rompono legami covalenti

Il numero di legame di una molecola rilassata è detto $Lk0$.

Una molecola rilassata:

$$Wr = 0 \quad \text{quindi} \quad Lk0 = Tw$$

Il linking number è un numero intero

Topoisomeri: stessa sequenza ma topologia diversa

TOPOLOGIA DEL DNA

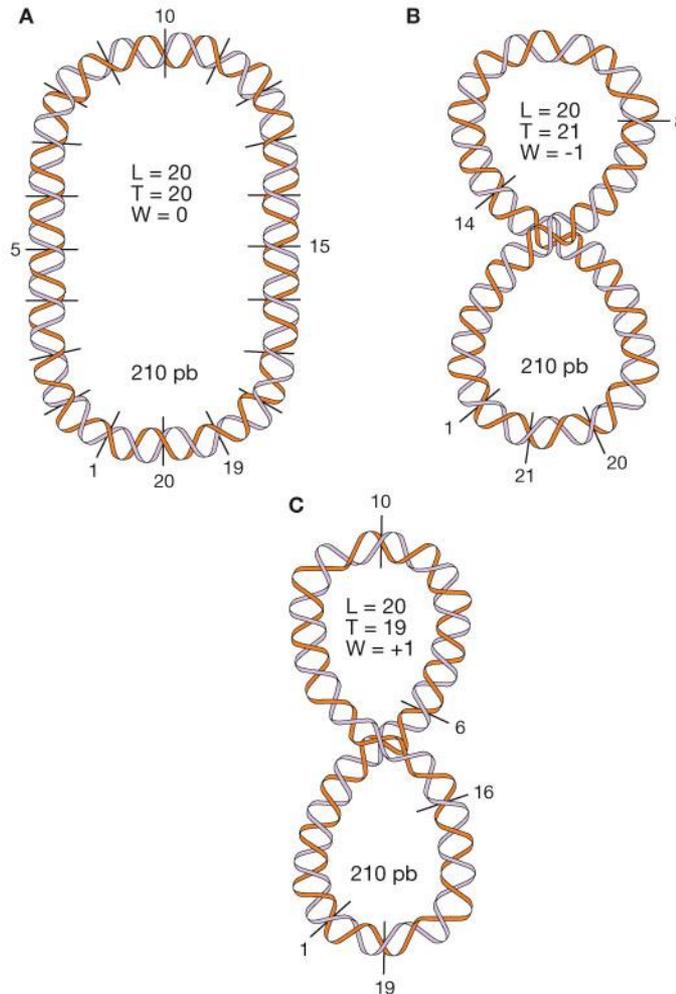


Figura 2.36

Relazione tra numero di legame e il twist e il writhe di una molecola di DNA circolare, covalentemente chiusa.

(A) Se si forza il DNA circolare a cambiare il suo writhe, senza tagliare la doppia elica, per compenso cambierà il twist, ma il numero di legame sarà lo stesso. (B) Il writhe è negativo e quindi il twist è positivo. (C) Il writhe è positivo e quindi il twist sarà negativo.

$$L = T + W$$

L = numero di legame

T = twist

W = writhe

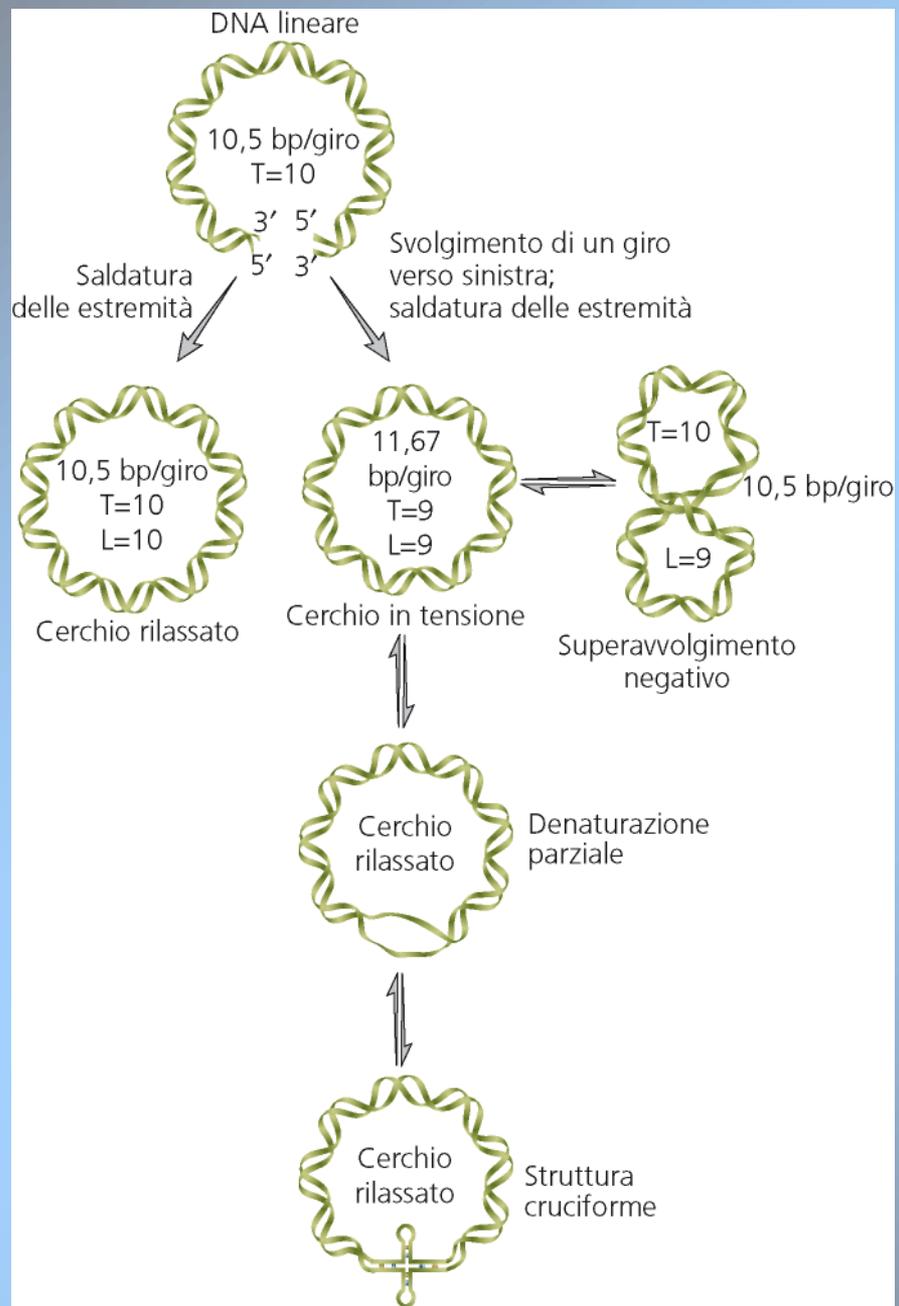
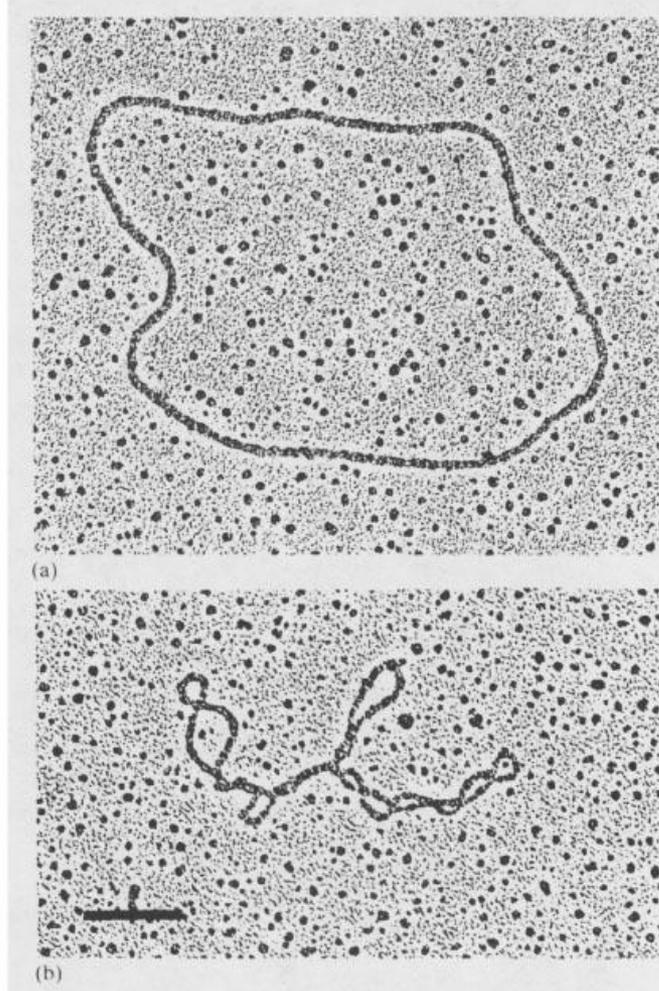


Figura 2.35 DNA circolare rilassato e superavvolto.



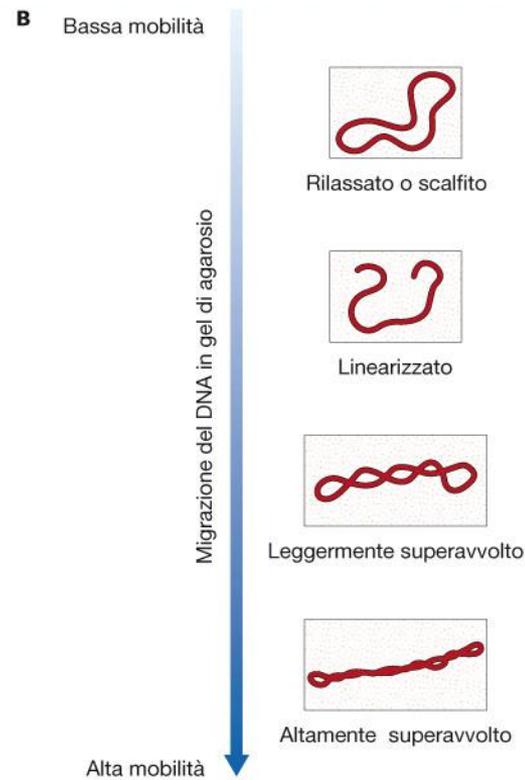
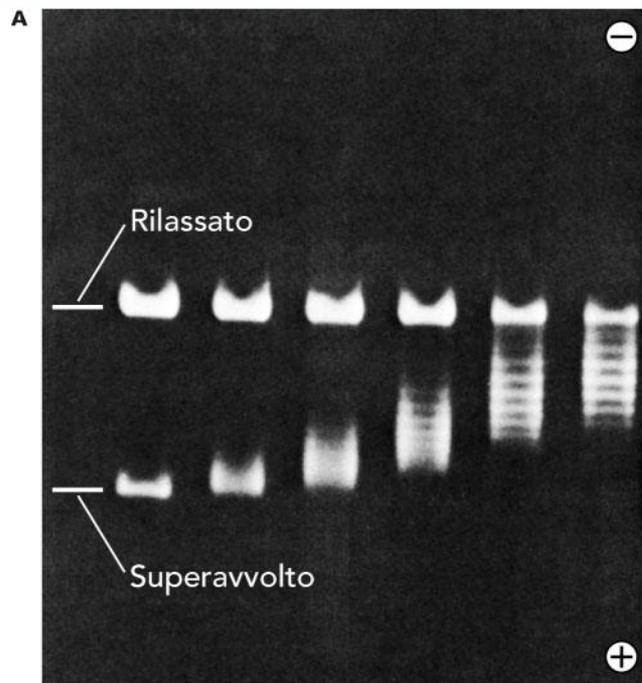


Figura 2.38 (A) Il DNA rilassato e superavvolto può essere separato mediante elettroforesi su gel. (B) Strutture corrispondenti alle posizioni delle varie bande del gel. (Per gentile concessione di James C. Wang, Harvard University).

Per modificare la topologia del DNA (il linking number) devono intervenire enzimi detti **TOPOISOMERASI** (o **nicking-closing enzymes**)

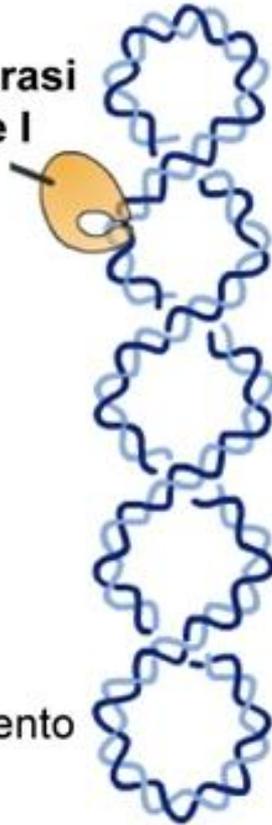
Esistono due tipi di TOPOISOMERASI:

Tipo I (producono rottura transitoria di un filamento)

Tipo II (rottura transitoria del doppio filamento)

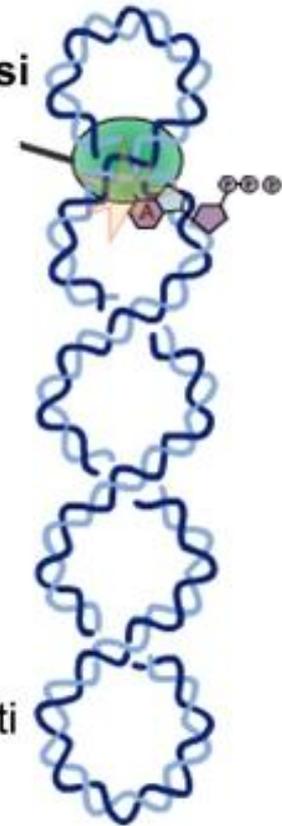
Topoisomerasi

topoisomerasi
di classe I



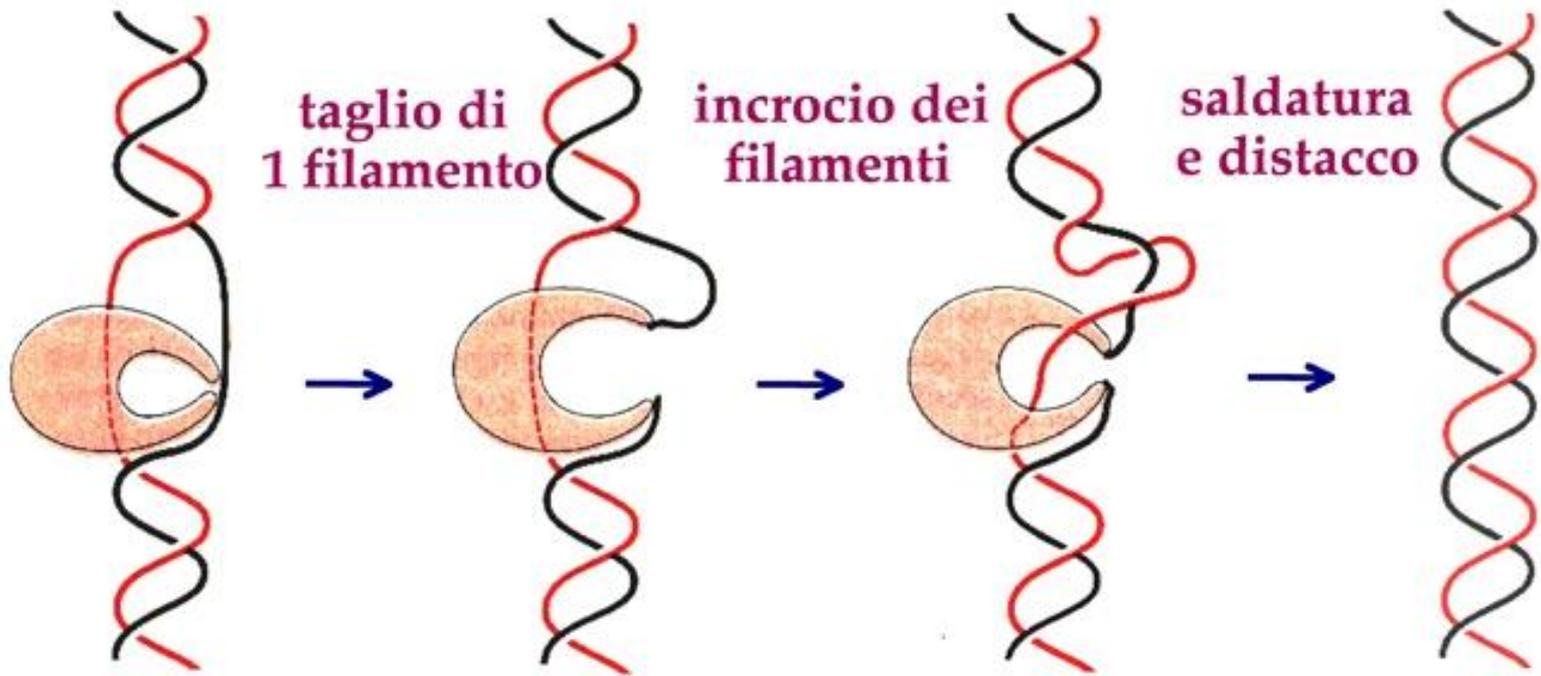
- incrementa Lk di 1
- taglia un solo filamento
- non richiede ATP

topoisomerasi
di classe II



- incrementa Lk di 2
- taglia entrambi i filamenti
- richiede ATP

Topoisomerasi I



Sfruttano l'energia torsionale del DNA

Topoisomerasi I

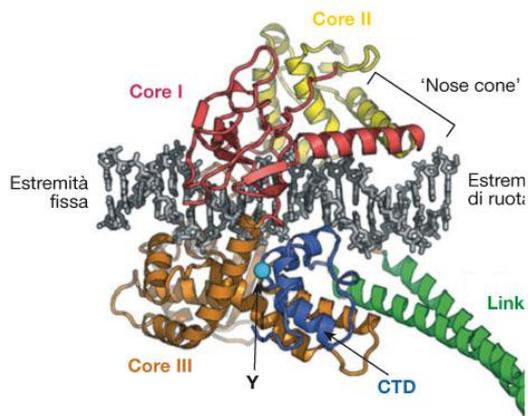
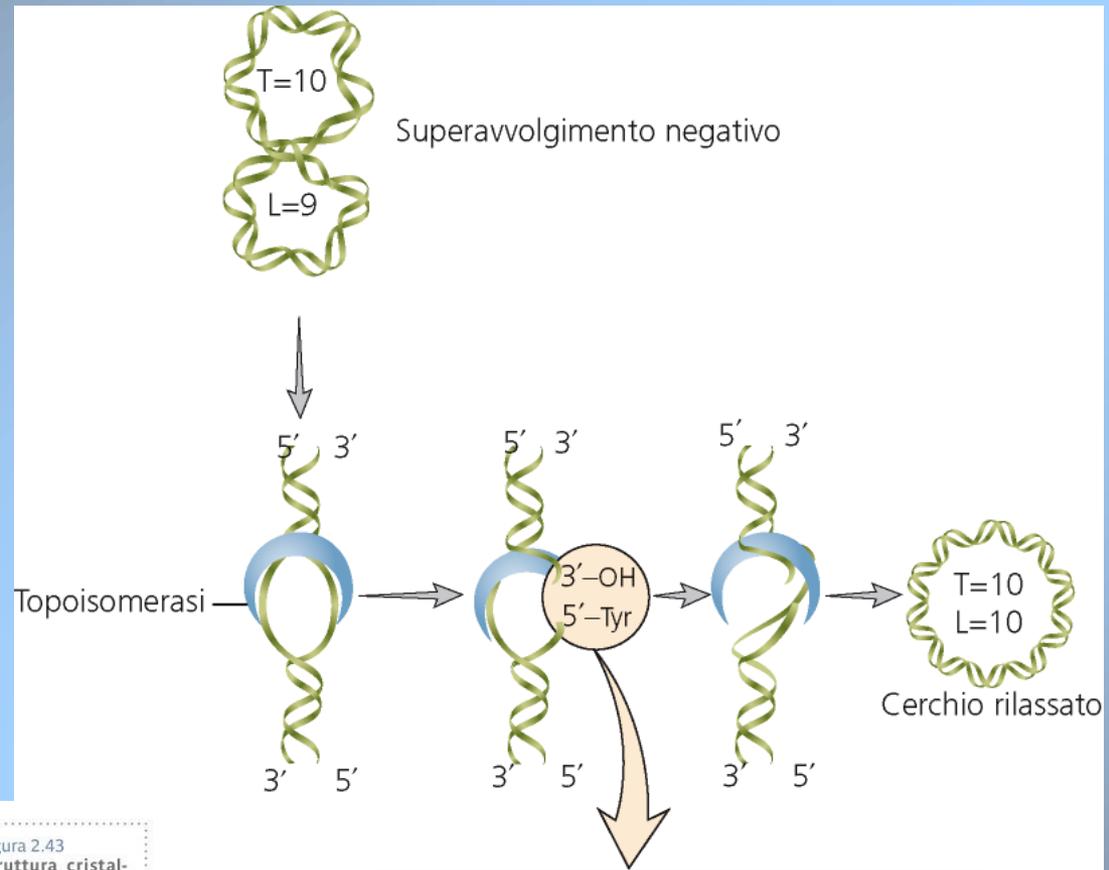
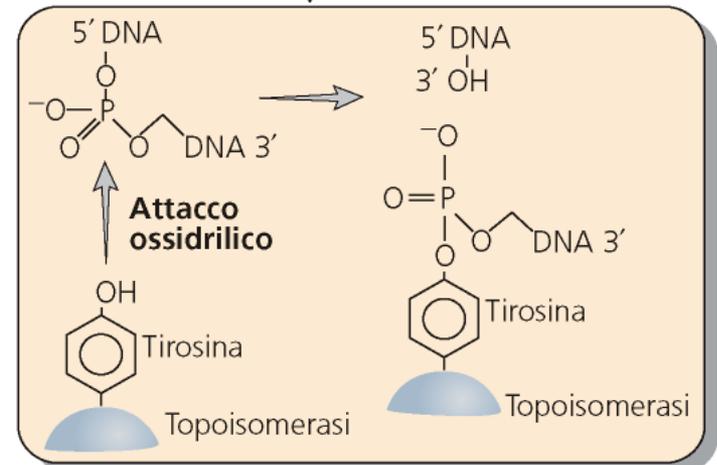


Figura 2.43
Struttura cristallografica della topoisomerasi IB. È possibile distinguere i vari domini e la posizione del DNA libero di ruotare.



Topoisomerasi II

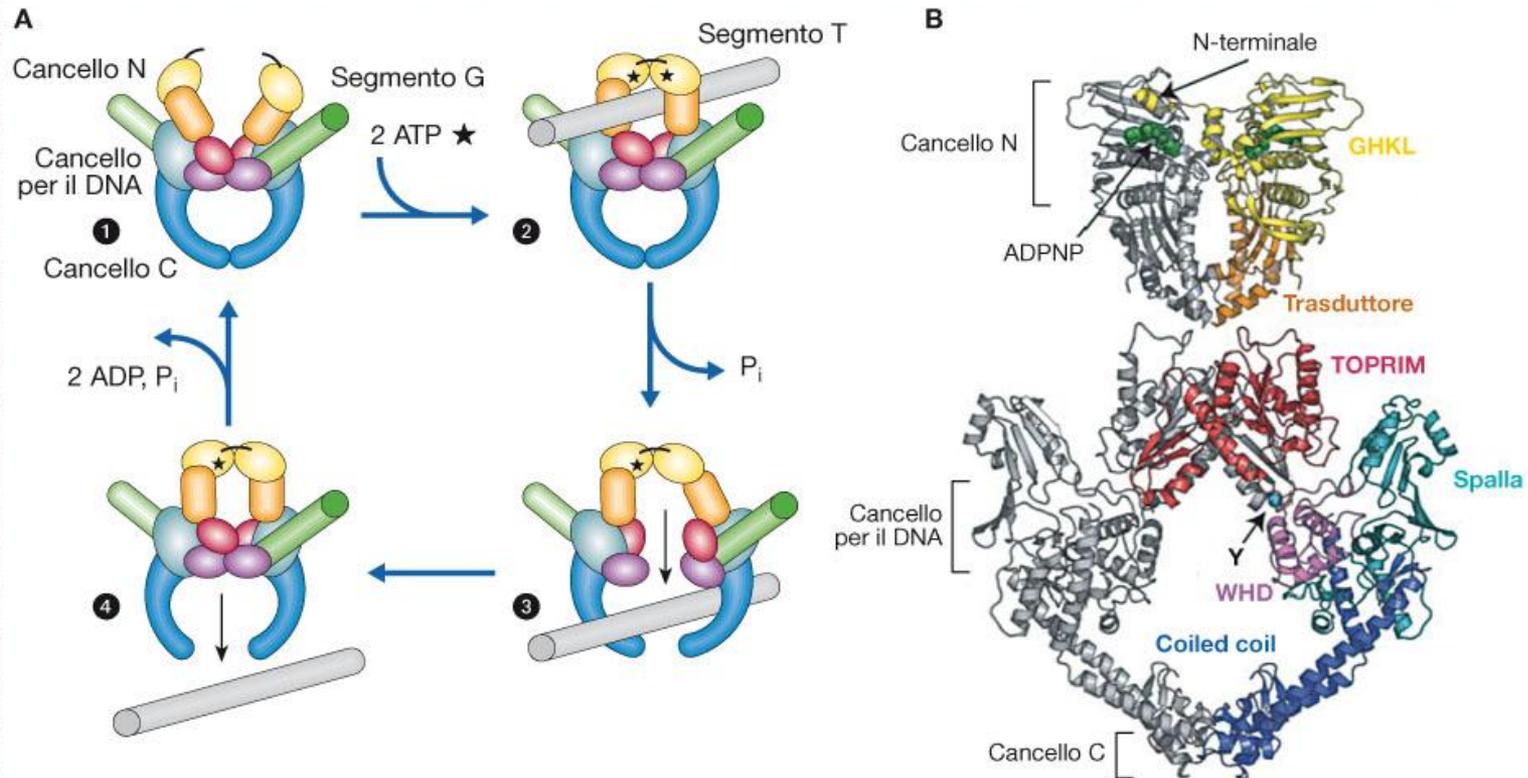


Figura 2.45 Struttura e meccanismo d'azione delle topoisomerasi di tipo II.

(A) Modello del "doppio cancello". (1) L'enzima ha una conformazione aperta pronta ad accettare al suo interno il segmento T (trasporto), mentre ha già al suo interno il segmento di DNA G (cancello). (2) Il legame con ATP genera un cambio di conformazione e il cancello N si chiude; successivamente l'idrolisi dell'ATP ge-

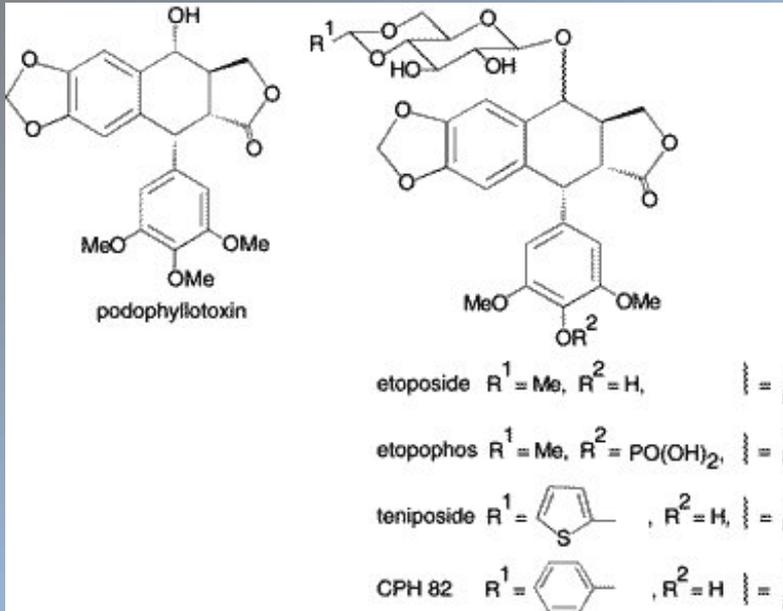
nera un nuovo cambio di conformazione (3), il DNA G viene aperto e il DNA T passa attraverso (4), provocando l'apertura del secondo cancello, e viene espulso dall'enzima.

(B) Struttura tridimensionale dell'enzima con il cancello N e in basso il cancello del DNA. Sono visibili anche i domini di legame dell'ATP (ADPNP).

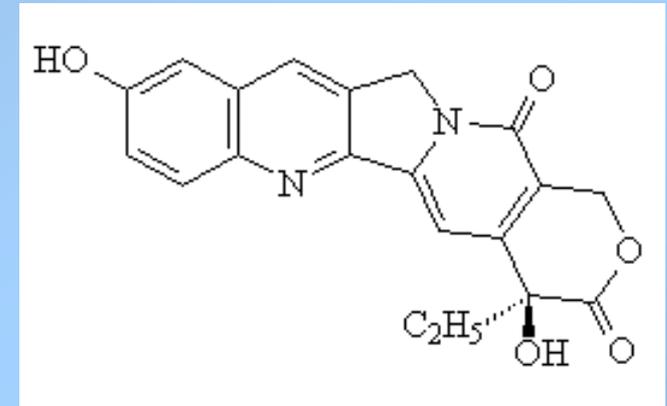
(Per gentile concessione di James Berger, Università di Berkeley).

Inibitori delle Topoisomerasi

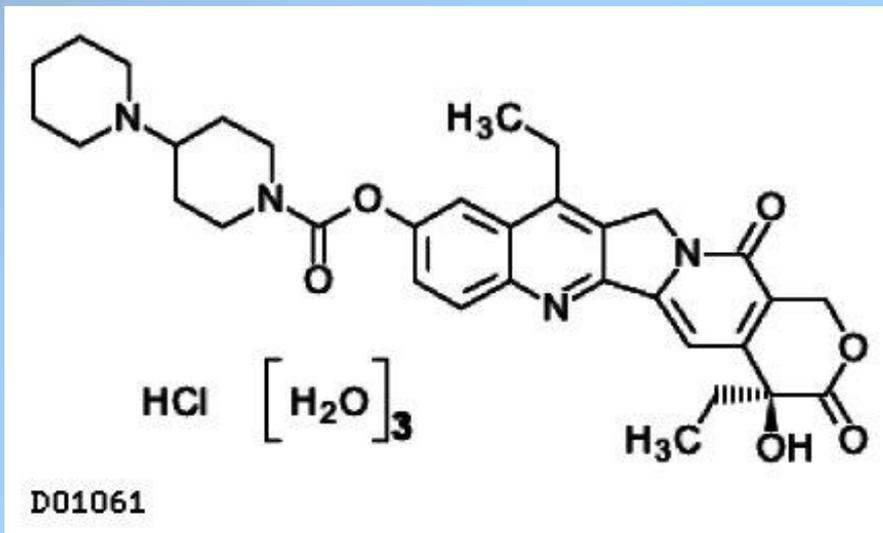
INIBITORI TOPOISOMERASI



Etoposide
Inibitore
topo II

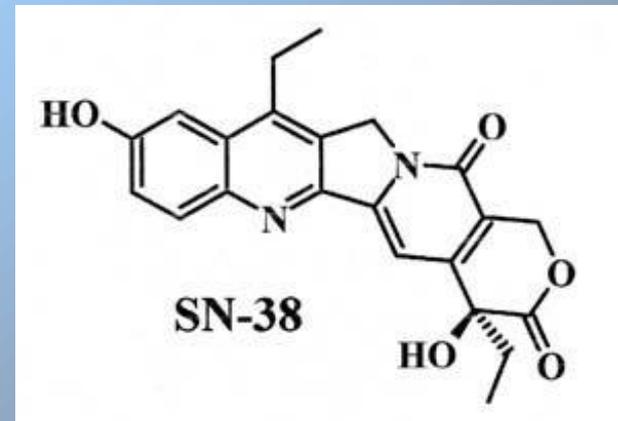


Camptothecin
Inibitore topo I



Irinotecan

Irinotecan $\xrightarrow{\text{carboxylesterase}}$ SN38



IL CODICE GENETICO

IL DOGMA CENTRALE

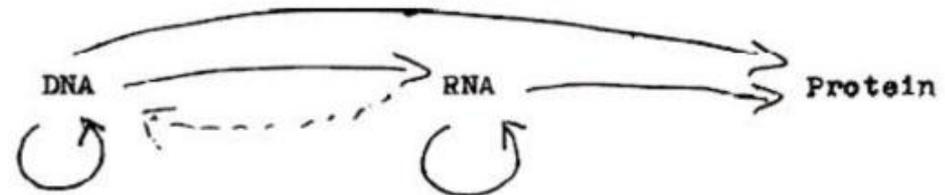
Figura 3.1 Schema originale di F. Crick che descrive per la prima volta il "dogma centrale".

Ideas on Protein Synthesis (Oct. 1956)

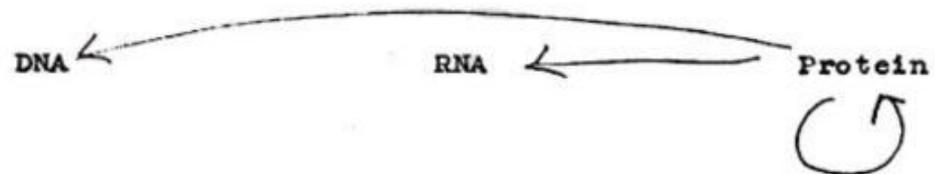
The Doctrine of the Triad.

The Central Dogma: "Once information has got into a protein it can't get out again". Information here means the sequence of the amino acid residues, or other sequences related to it.

That is, we may be able to have



but never



where the arrows show the transfer of information.

Figura 1

Replicazione



Trascrizione



RNA

Traduzione

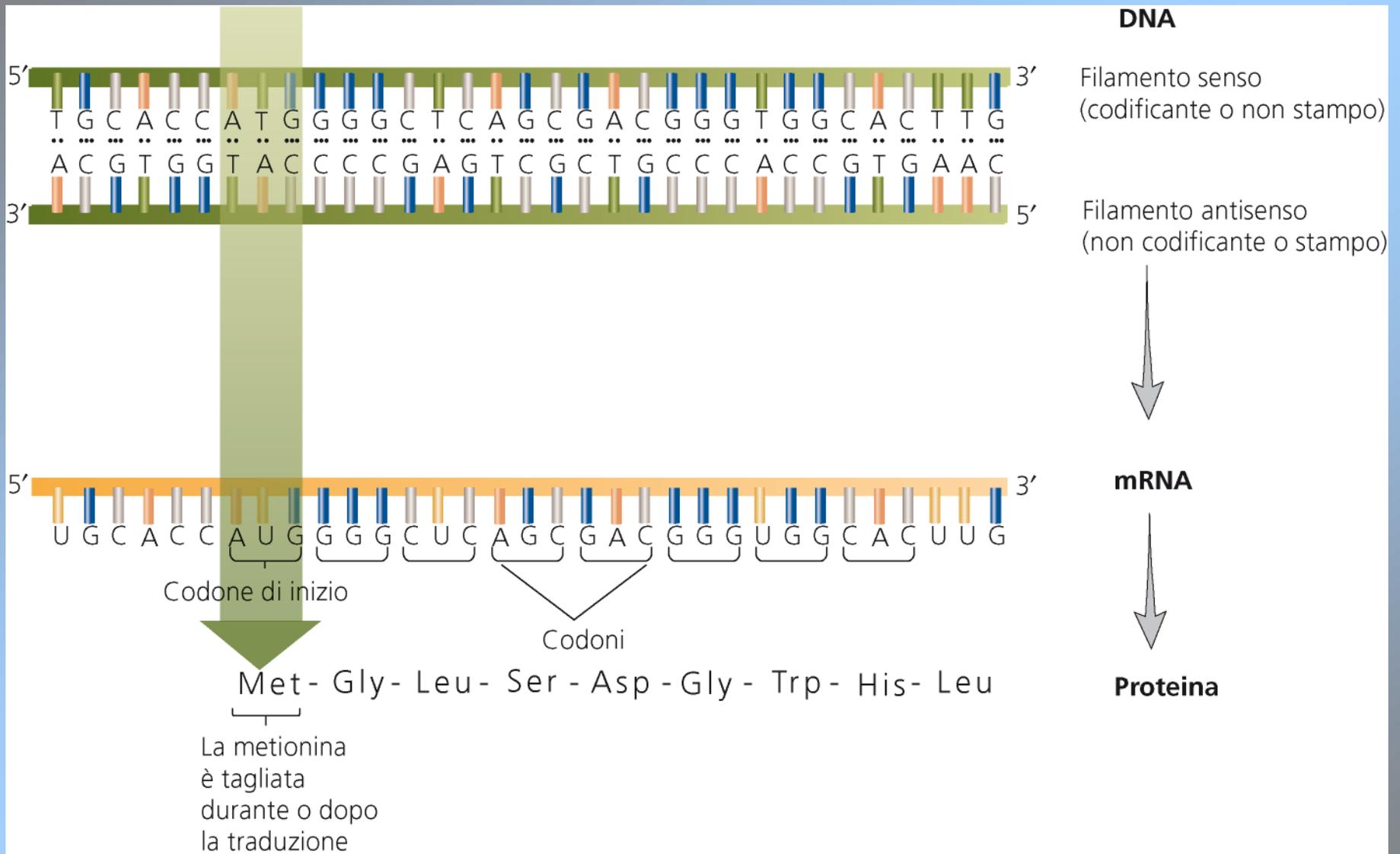


PROTEINA

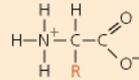


Trascrizione inversa



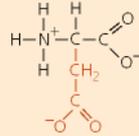


Aminoacido generale

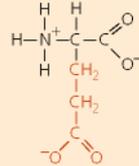


Acidi

Acido L-aspartico (Asp) (D)

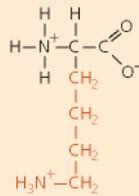


Acido L-glutammico (Glu) (E)

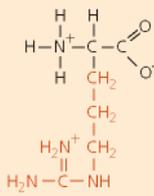


Basici

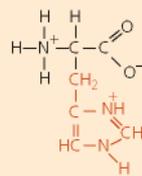
L-Lisina (Lys) (K)



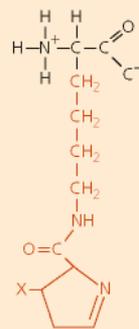
L-Arginina (ARG) (R)



L-Istidina (His) (H)



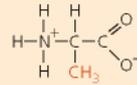
L-Pirrolisina (Pyr)



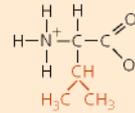
X=CH₃, NH₂ o OH

Non polari

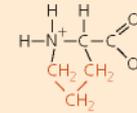
L-Alanina (Ala) (A)



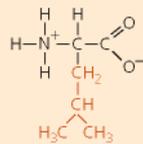
L-Valina (Val) (V)



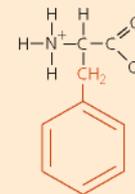
L-Prolina (Pro) (P)



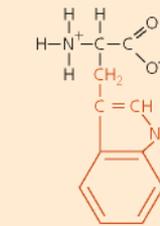
L-Leucina (Leu) (L)



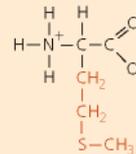
L-Fenilalanina (Phe) (F)



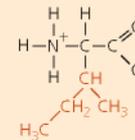
L-Triptofano (Trp) (W)



L-Metionina (Met) (M)

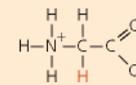


L-Isoleucina (Ile) (I)

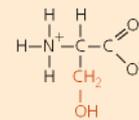


Polari (privi di carica)

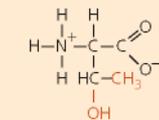
L-Glicina (Gly) (G)



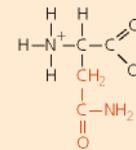
L-Serina (Ser) (S)



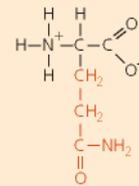
L-Treonina (Thr) (T)



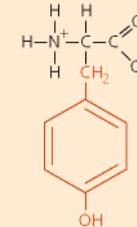
L-Asparagina (Asn) (N)



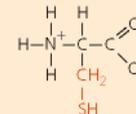
L-Glutammina (Gln) (Q)



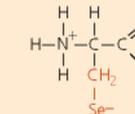
L-Tirosina (Tyr) (Y)



L-Cisteina (Cys) (C)



L-Selenocisteina (Sel)



I CODONI

Sequenza originale

ATG CTG CTC TGT GCC GCC ...
Met Leu Leu Cys Ala Ala ...

1 Nucleotide rimosso

ATG CTCTCT GTG CCG CC ...
Met Leu Ser Val Pro Pro ...

2 Nucleotidi rimossi

ATG CTTCTG TGC CGC C...
Met Pro Leu Cys Arg ...

3 Nucleotidi rimossi

ATG CTC TGT GCC GCC ...
Met Leu Cys Ala Ala ...

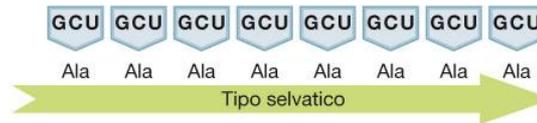
Risultano in proteine non funzionali (mutazione "frame shift")

Risulta solo nella delezione di un amminacido (ma la proteina può essere ancora funzionale)

Figura 3.2 Le mutazioni *frame-shift* (alterata fase di lettura) dimostrano che il codice è letto a triplette da un punto di inizio prestabilito. Inserzioni o delezioni che alterano la fase di lettura hanno come conseguenza una proteina completamente alterata, mentre doppi o tripli mutanti che ripristinano a valle la fase di lettura generano proteine con una regione mutata, ma con la maggior parte della proteina WT.

Figura 3.3 Crick e Brenner (1961) hanno studiato l'effetto di successive delezioni di nucleotidi nel DNA del fago T4. Introducendo delezioni di una, due o tre basi, hanno dimostrato che il codice genetico è letto a triplette, partendo da un punto di inizio fisso e senza "punteggiatura".

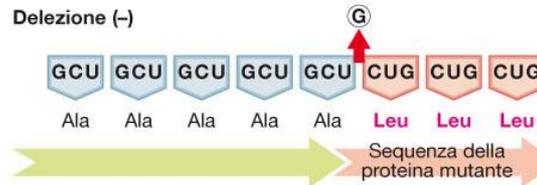
Tipo selvatico



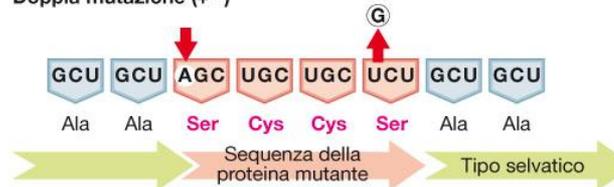
Inserzione (+)



Delezione (-)



Doppia mutazione (+ -)



Tripla mutazione (+++)



IL CODICE GENETICO

		Seconda posizione				
		U	C	A	G	
Prima posizione (estremità 5')	U	UUU Phe UUC UUA Leu UUG	UCU UCC Ser UCA UCG	UAU Tyr UAC UAA* Stop UAG* Stop	UUU Cys UUC UGA* Stop UUG Trp	U C A G
	C	CUU Leu CUC CUA CUG	CCU Pro CCC CCA CCG	CAU His CUC CUA Gln CUG	CUU Arg CUC CUA CUG	U C A G
	A	AUU Ile AUC AUA AUG° Met	ACU Thr ACC ACA ACG	AAU Asn AAC AAA Lys AAG	AGU Ser AGC AGA Arg AGG	U C A G
	G	GUU Val GUC GUA GUG	GCU Ala GCC GCA GCG	GAU Asp GAC GAA Glu GAG	GGU Gly GGC GAA GGG	U C A G

Figura 3.9 Rappresentazione del codice genetico universale usato dalla maggior parte degli organismi viventi. È evidente la degenerazione per cui un amminoacido è codificato da più di un codone.

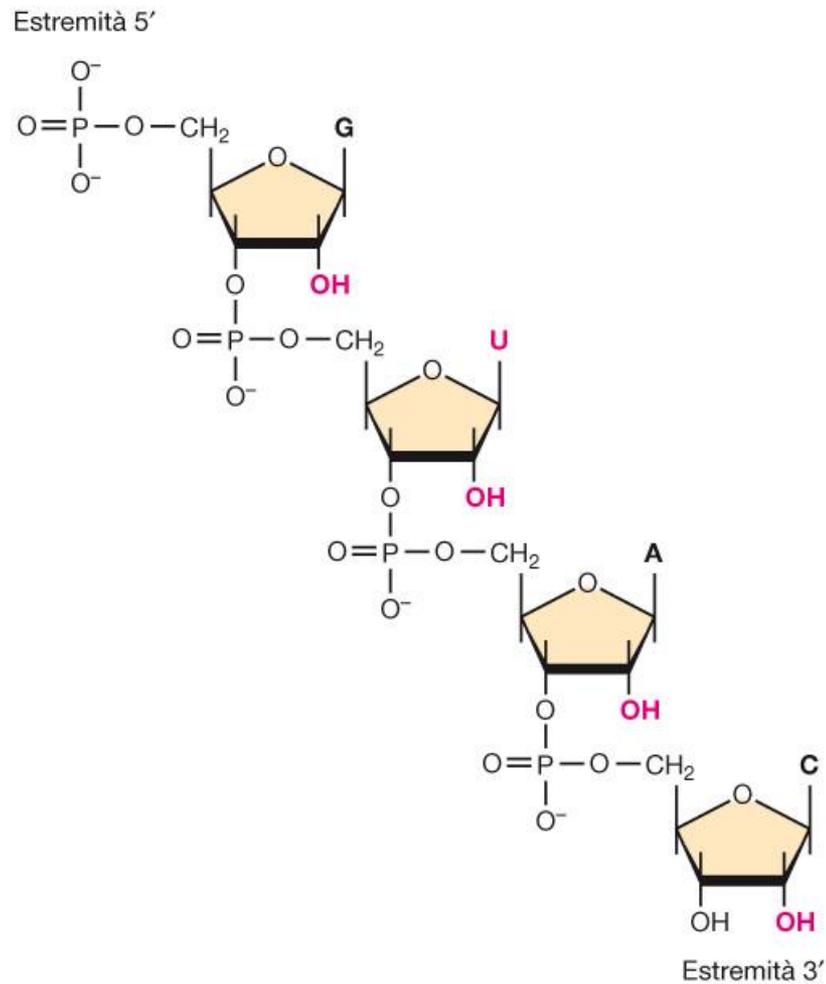
Evoluzione del codice genetico

Figura 3.13 **Evoluzione del codice genetico.** Il codice genetico si è evoluto per rendere massima l'efficienza della traduzione e per minimizzare gli effetti delle mutazioni: le transizioni (più frequenti) in tutte e tre le posizioni del codone producono cambiamenti meno drastici delle trasversioni (meno frequenti).

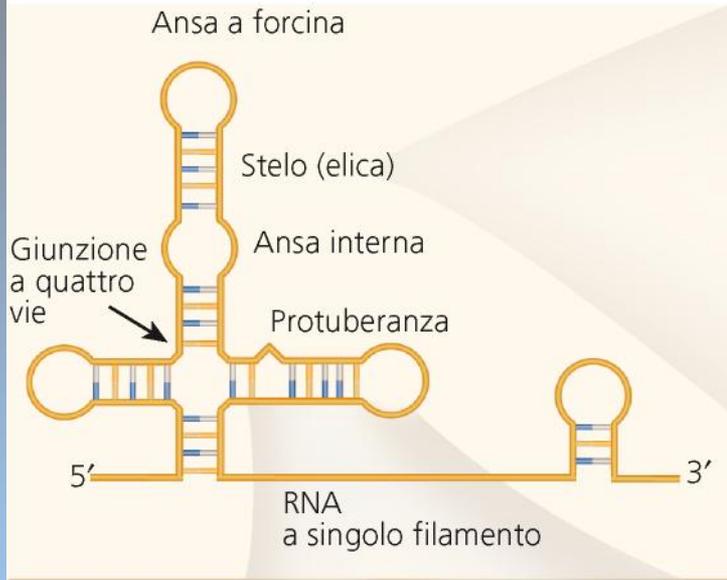


STRUTTURA DELL'RNA

Figura 2.47 **Struttura chimica dell'RNA.** Come si vede, sono presenti i gruppi OH nella posizione 2' dello zucchero e l'uracile al posto della timina.



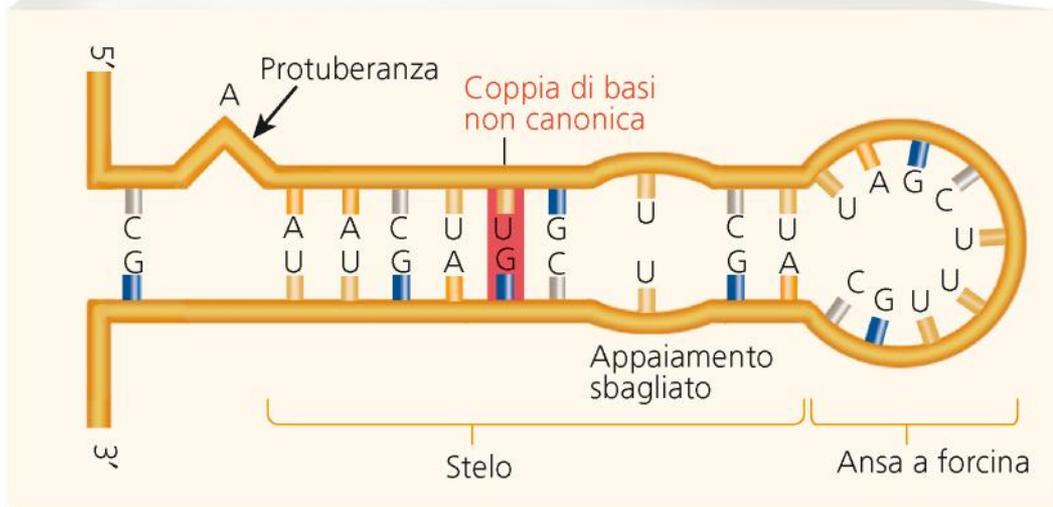
Strutture secondarie nell'RNA



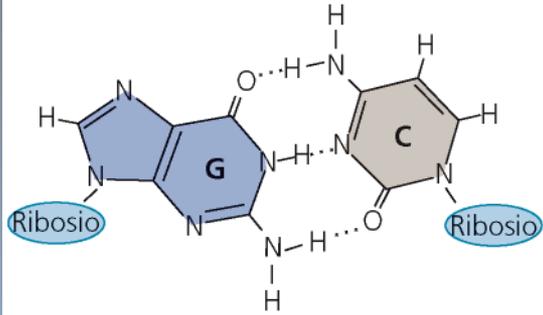
Scanalatura secondaria

Scanalatura principale

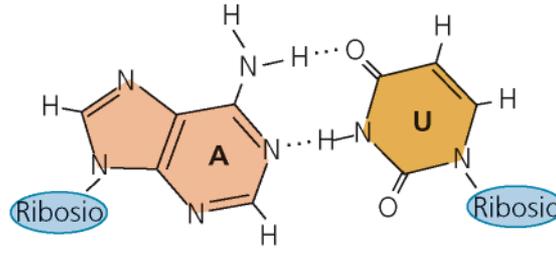
Una doppia elica di RNA



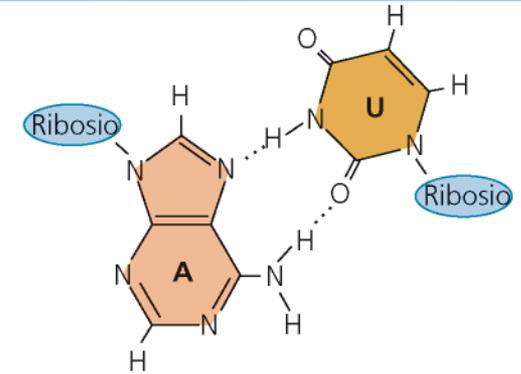
Appaiamenti di basi canonici



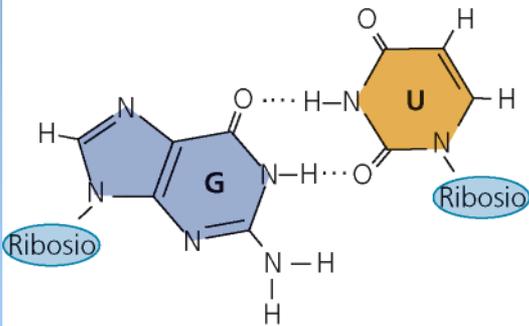
CG Watson-Crick



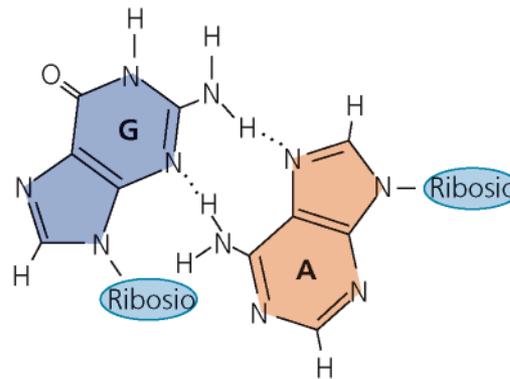
AU Watson-Crick



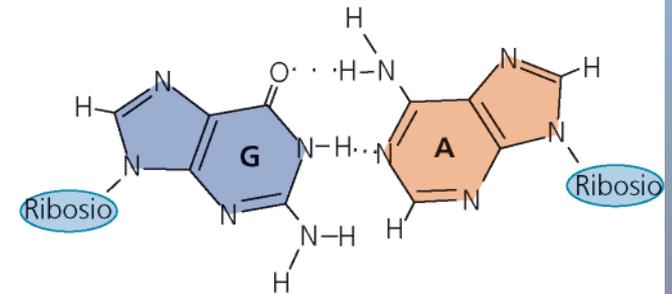
AU Hoogsteen inversa



GU tentennante

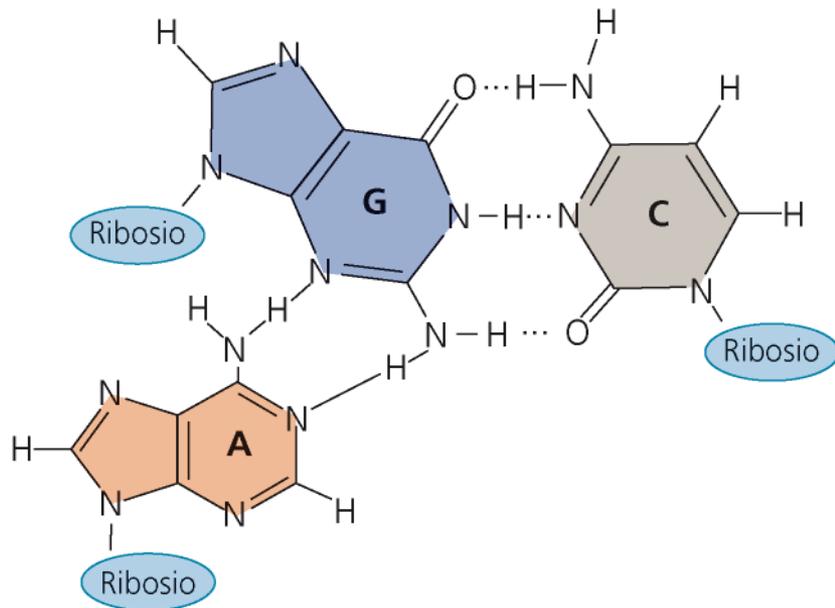


GA troncata

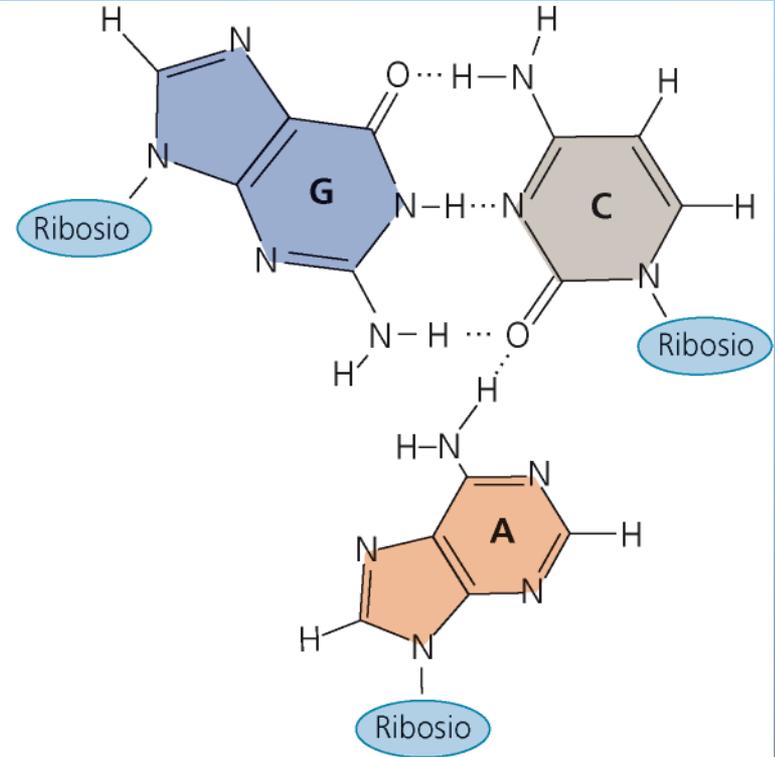


GA immino

Appaiamenti di basi non canonici

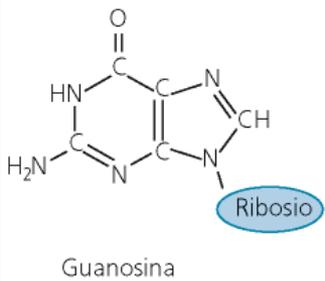
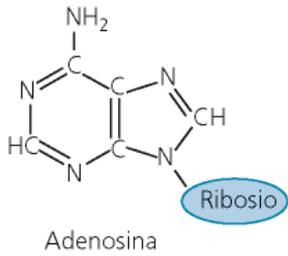


AGC ammino N3, N1-ammino;
Watson-Crick

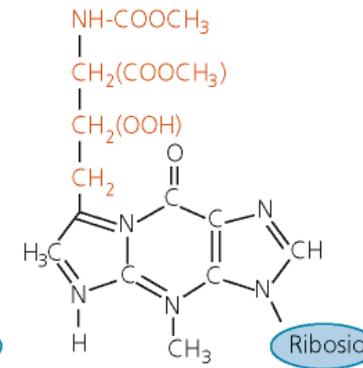
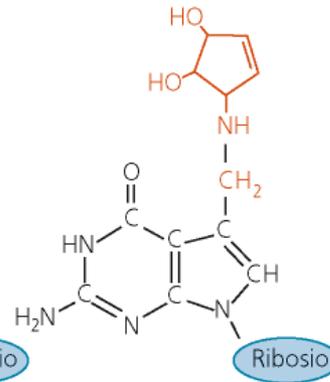
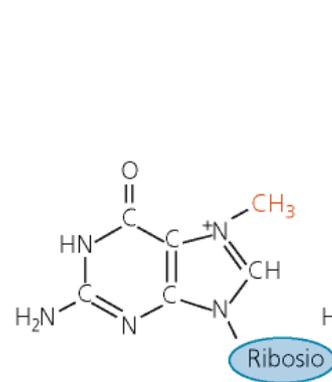
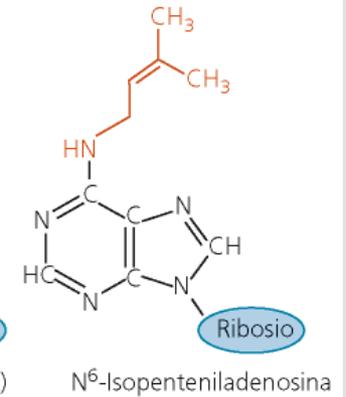
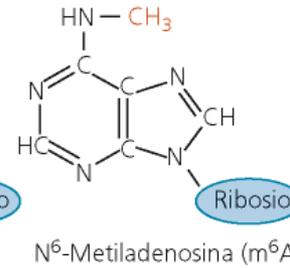
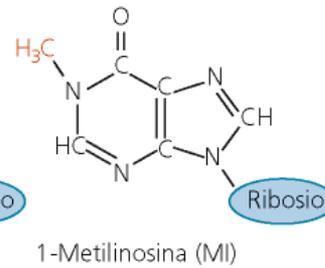
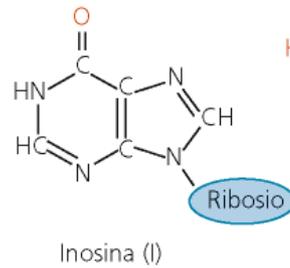
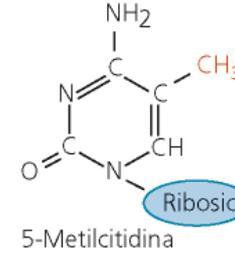
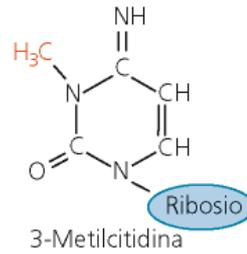
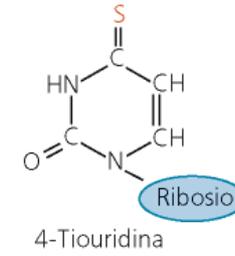
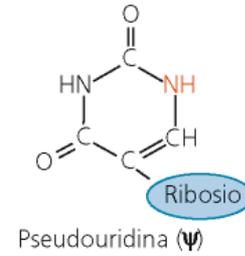
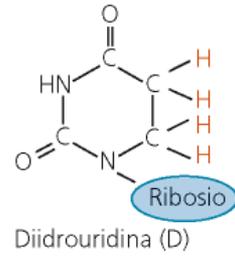


ACG ammino-carbonile;
Watson-Crick

**Nucleosidi
con basi normali**



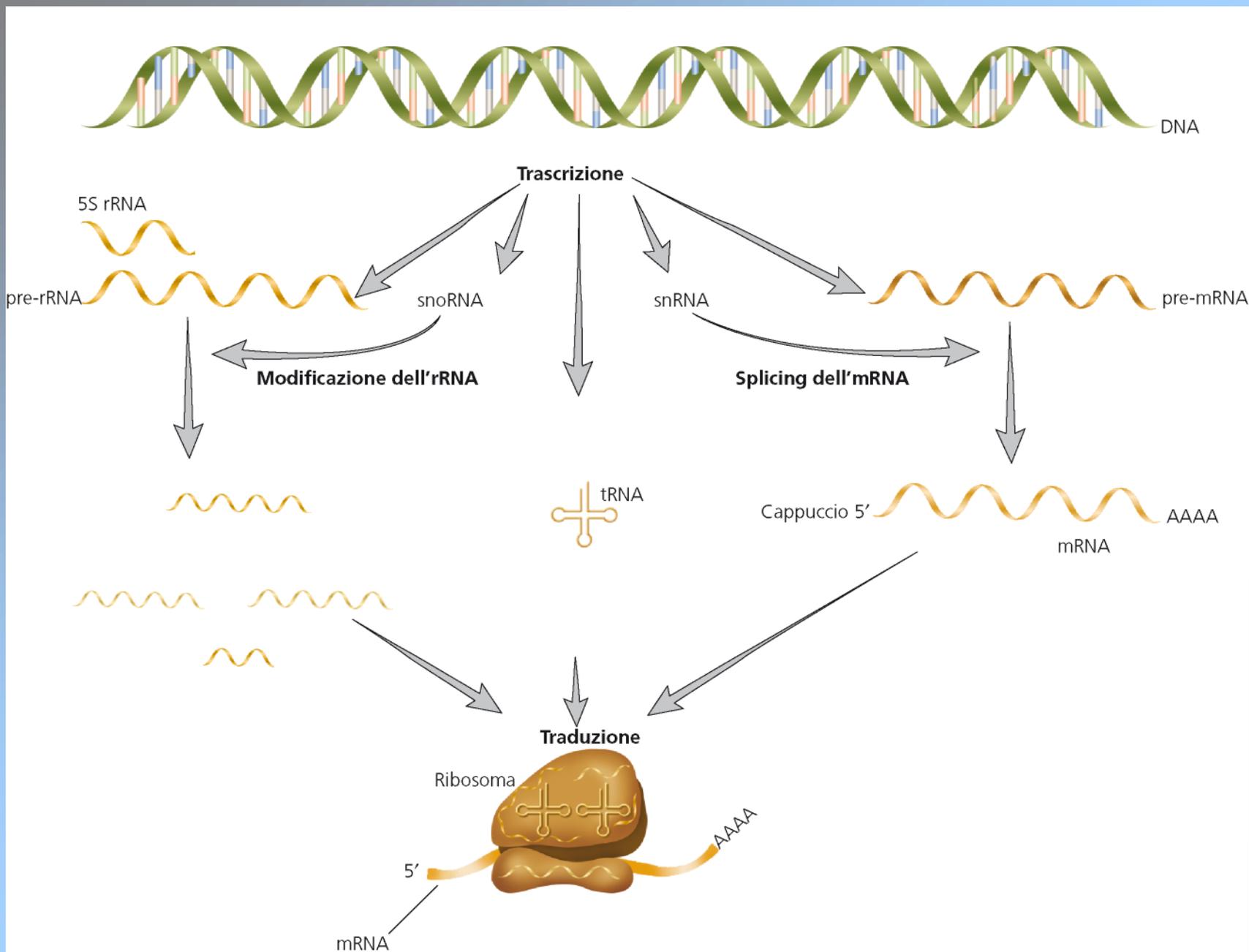
**Nucleosidi
con basi modificate**



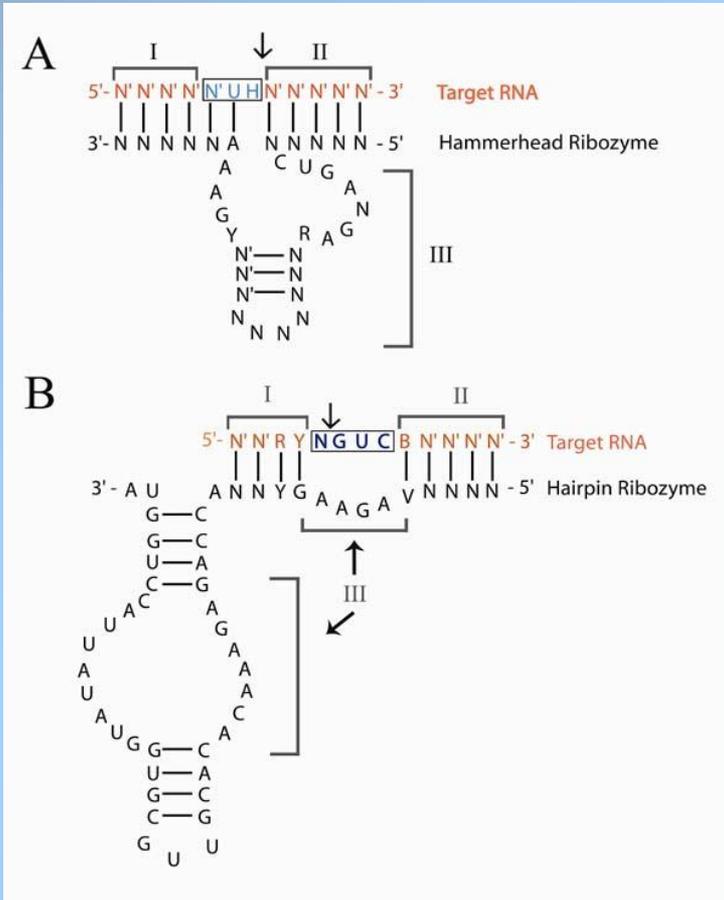
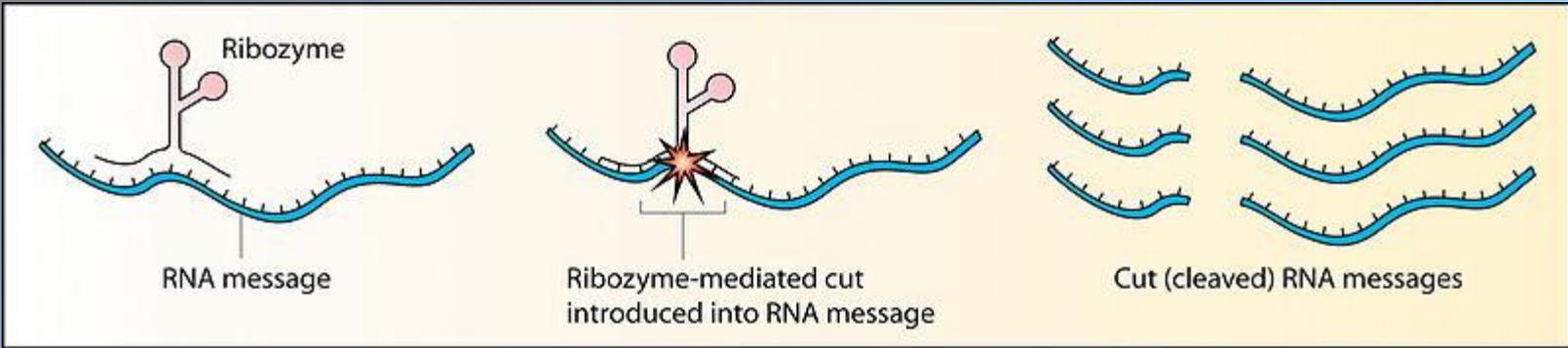
7-Metilguanosina (MG)

Queosina (Q)

Wyosina (Y)

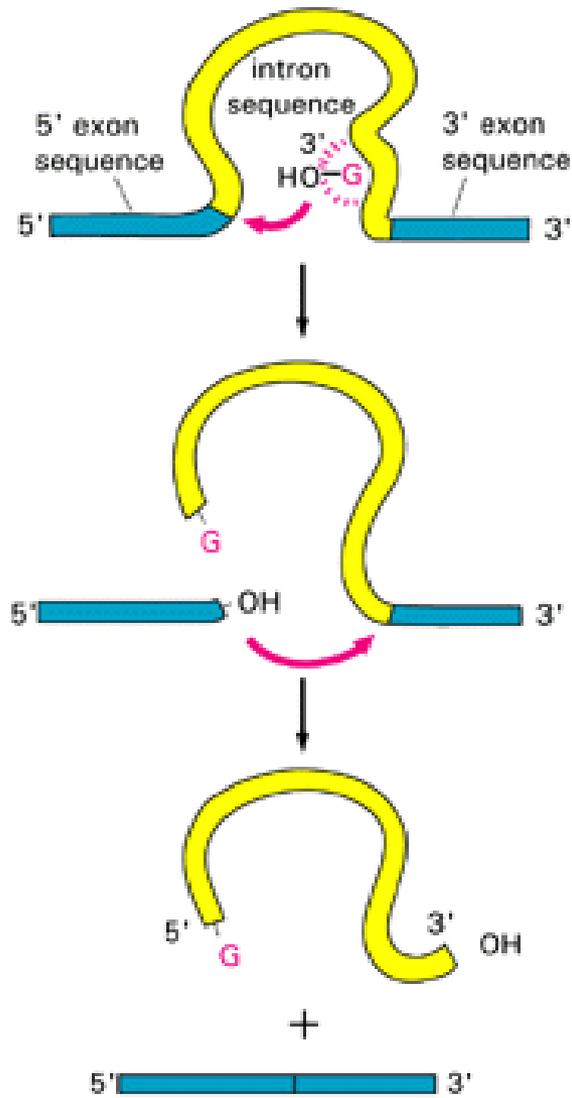


RNA CATALITICO RIBOZIMI

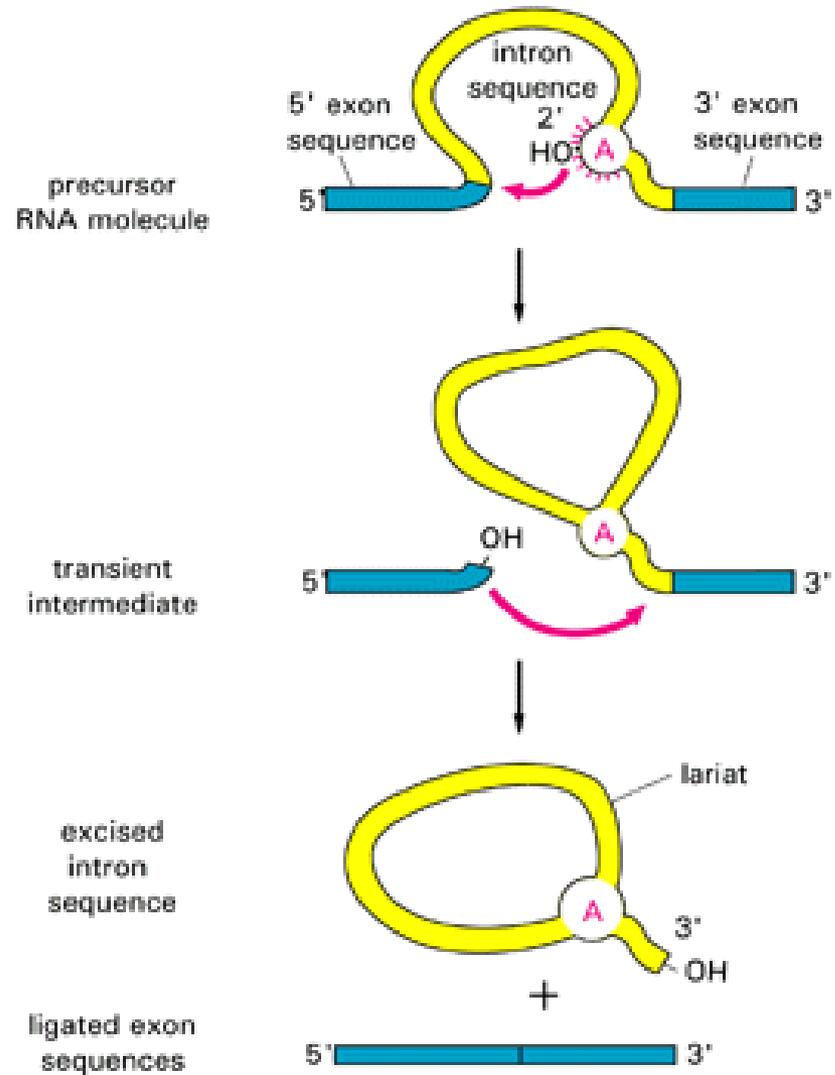


RIBOZIMI

Group I self-splicing intron sequences

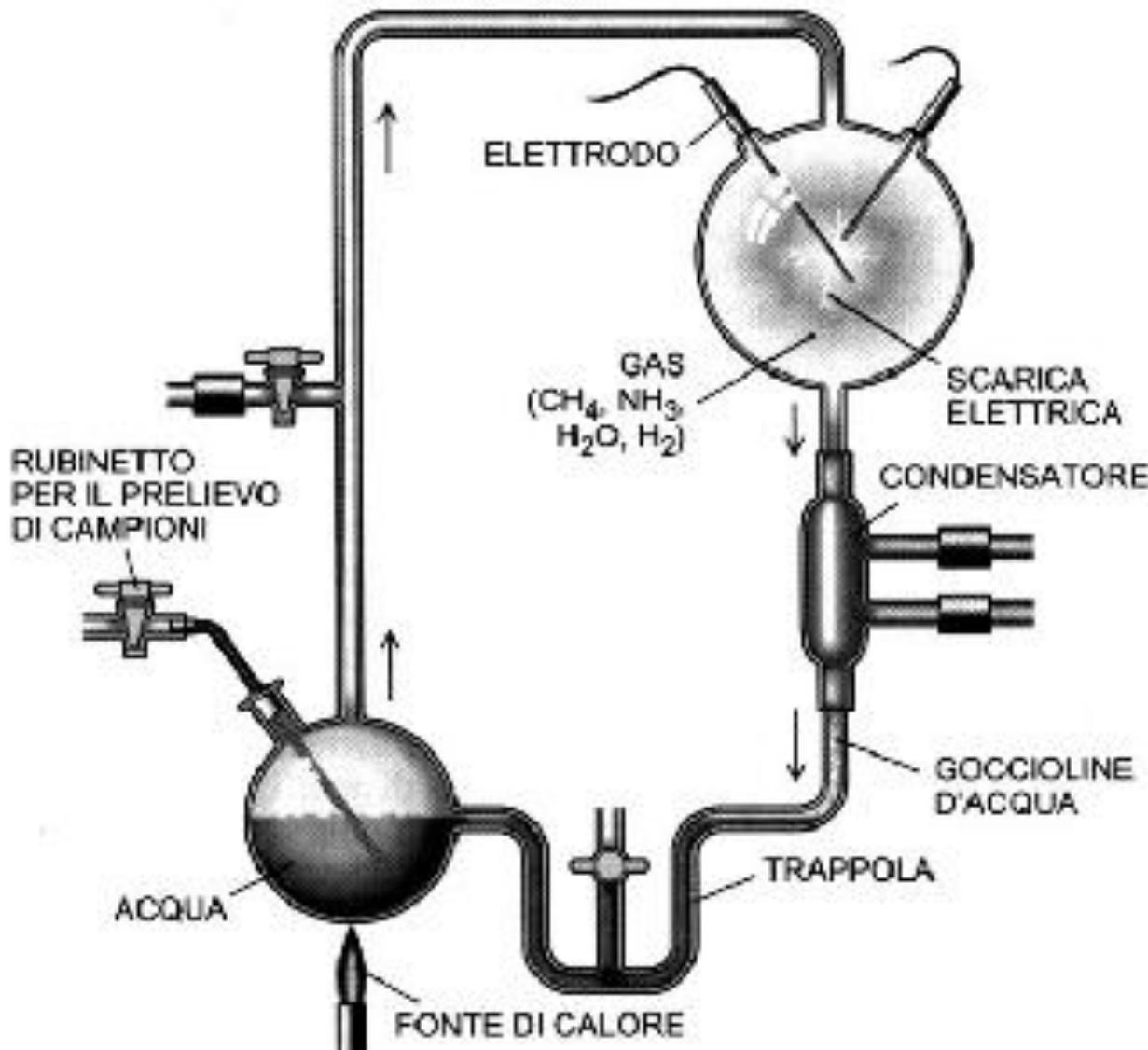


Group II self-splicing intron sequences



IL MONDO A RNA

ESPERIENZA DI MILLER



Carboxylic Acids

Formic, Acetic, Propionic, Straight and branched C4 - C10, Glycolic, Lactic, Succinic

Purine and Pyrimidine Bases

Adenine, Guanine, Xanthine, Hypoxanthine, Cytosine, Uracil

Sugars

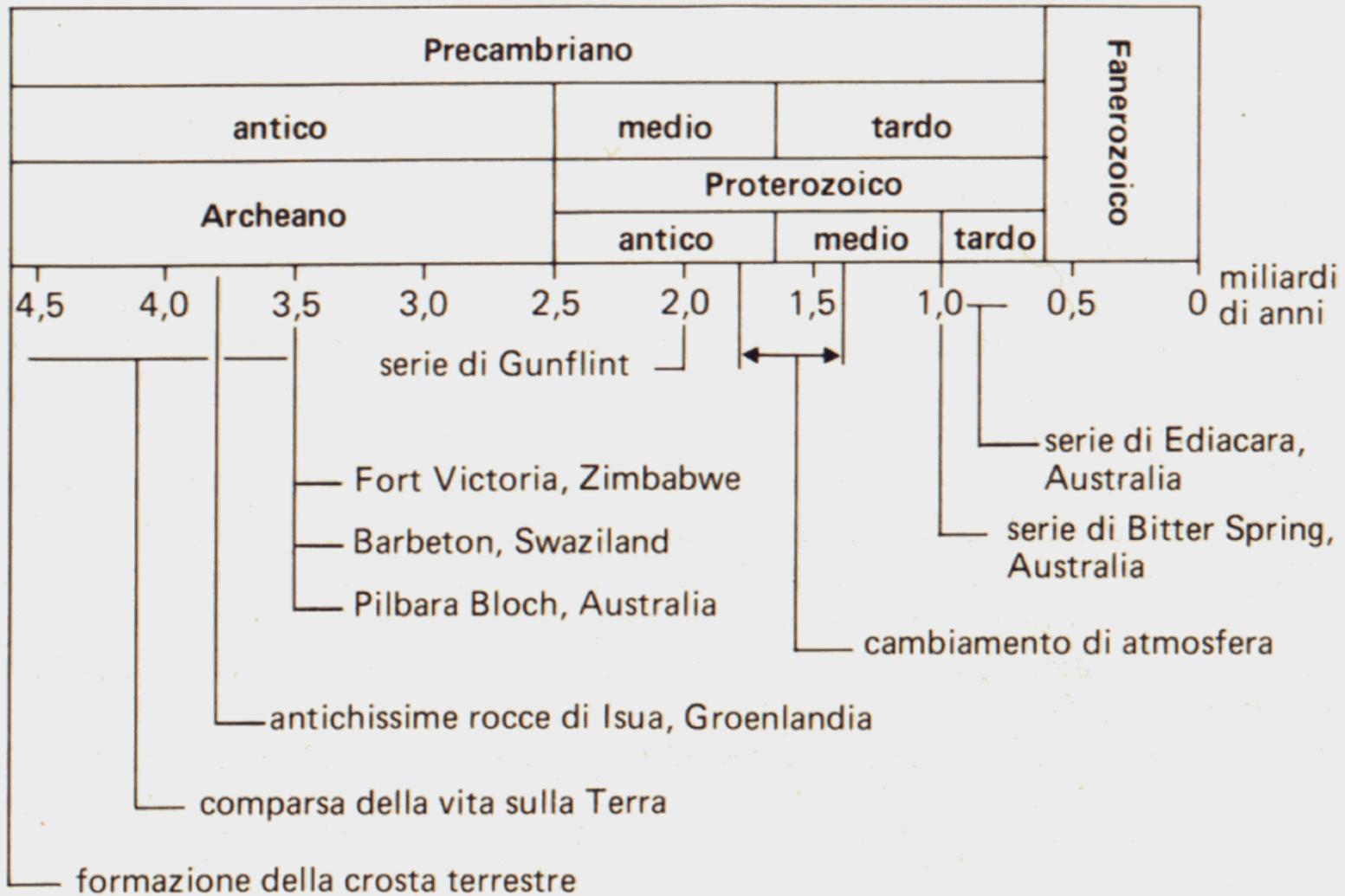
Pentoses (especially ribose), hexoses, both straight and branched chain

Amino Acids

Glycine, Alanine, 2-Aminobutyric, Valine, Leucine, Isoleucine, Proline, Aspartic, Glutamic, Serine, Threonine

Miscellaneous

Formaldehyde, HCN



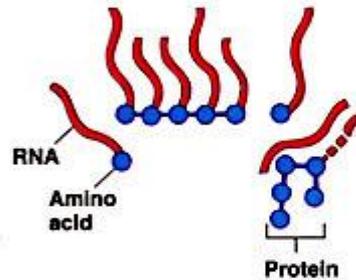
154 Proposed RNA world origins



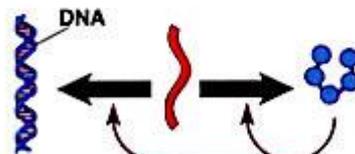
[A] RNA forms



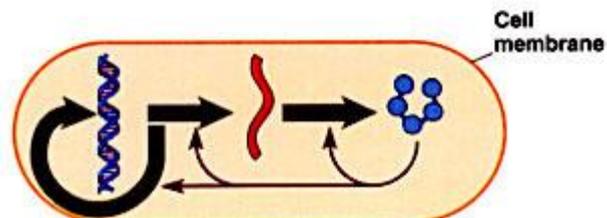
[B] Ribozymes catalyze RNA replication



[C] RNA catalyzes protein synthesis



[D] RNA encodes both DNA and protein



[E] Proteins catalyze cell activities