

# **NUCLEIC ACIDS and PROTEINS** **structure and function**

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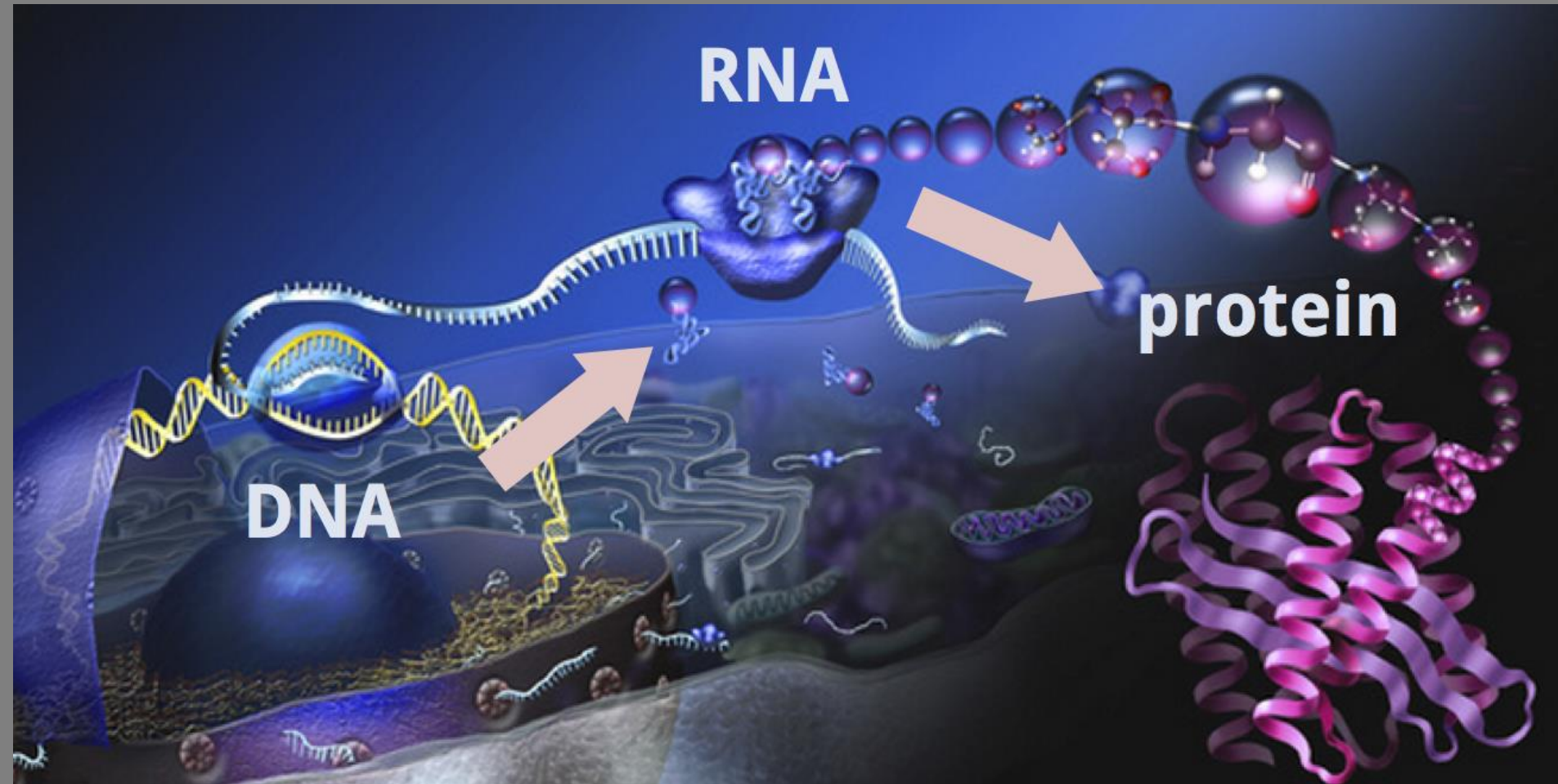


# Learning Goals

Theoretical knowledge on;  
Nucleic acids and proteins;

1. Structure and biosynthesis  
(polymerization)
2. Structure and function relation
3. Basics of genome anatomy
4. Protein structure

# Central Dogma



# Genetic Material

- F. Griffith: 1928 – Describes heritable genetic properties (phenotype).



Experiments on *S. pneumoniae*:

# Genetic Material

- T.H. Morgan: 1933 - Nobel prize



Inheritance and chromosome  
What is the genetic material?

A. Protein

B. DNA

C. Protein + DNA

# Genetic Material

- Avery, McCharty ve McLeod: 1944



Courtesy of the Rockefeller Archive Center.  
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Reproducing Griffith's experiments  
DNA is the inherited biomolecule.



# Genetic Material

- Martha Chase and Alfred Hershey - 1953: DNA is the material responsible for the inheritance. (1968 Nobel candidate).



# Genetic Material



Francis Harry  
Compton Crick

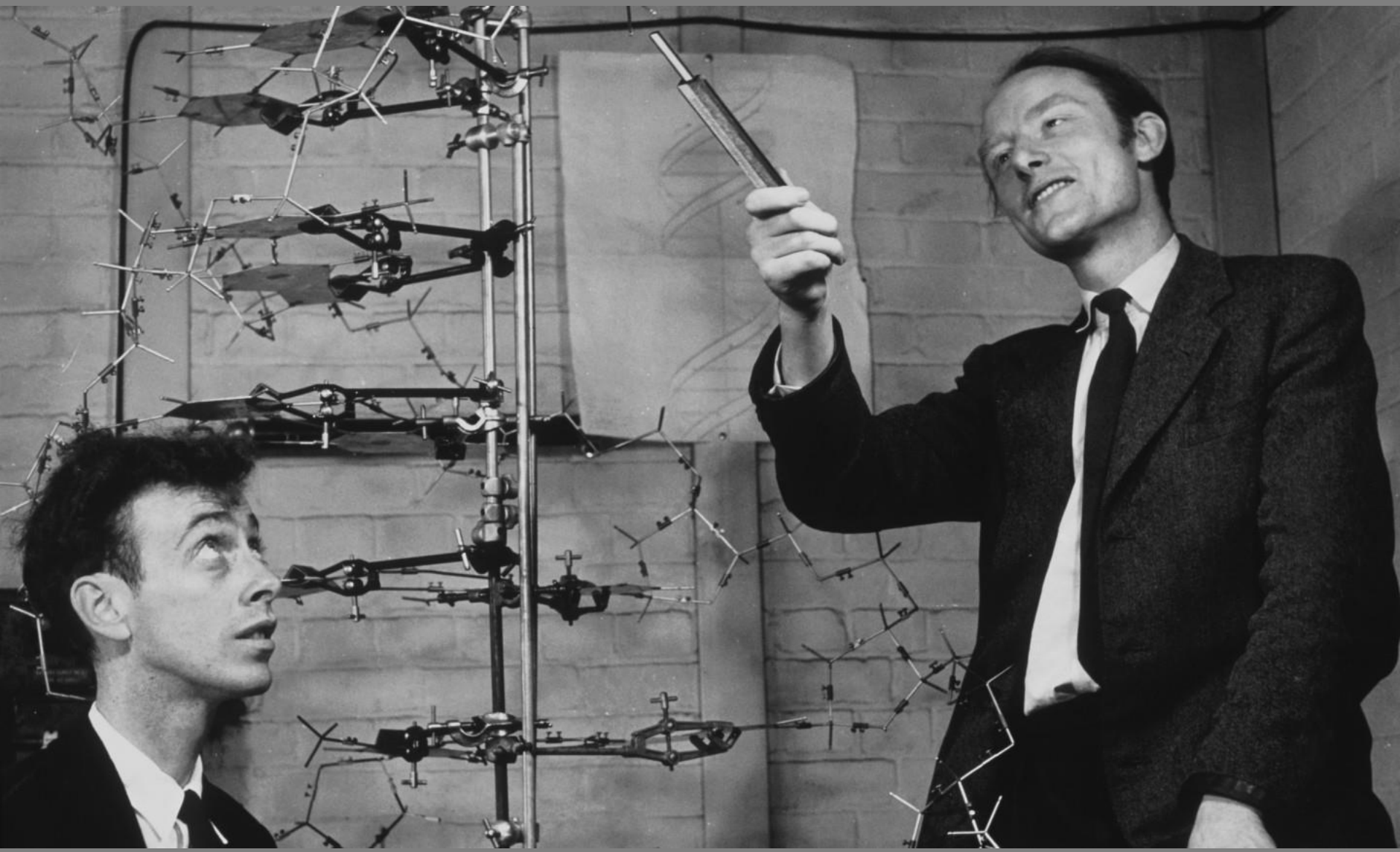


James Dewey  
Watson

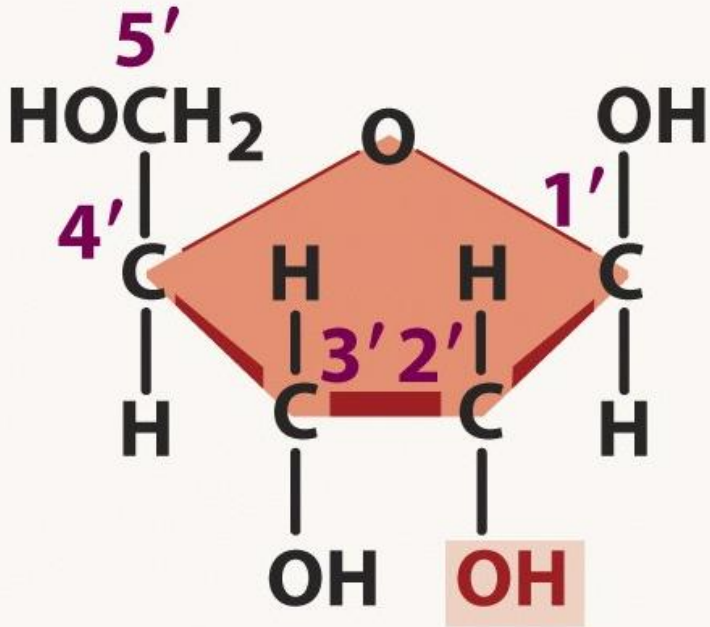


Maurice Hugh  
Frederick Wilkins

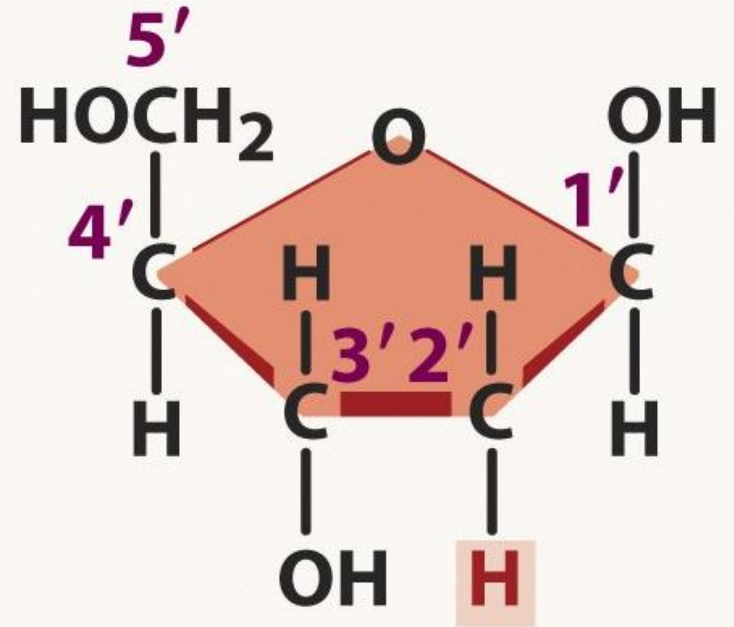
Double helix structure with an antiparallel  
orientation (1954)  
Nobel prize (1962)



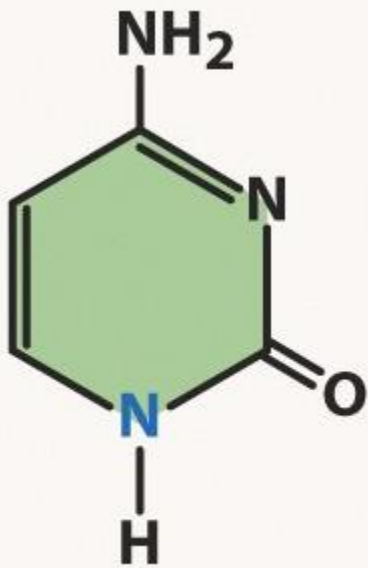
# 5 carbon sugar



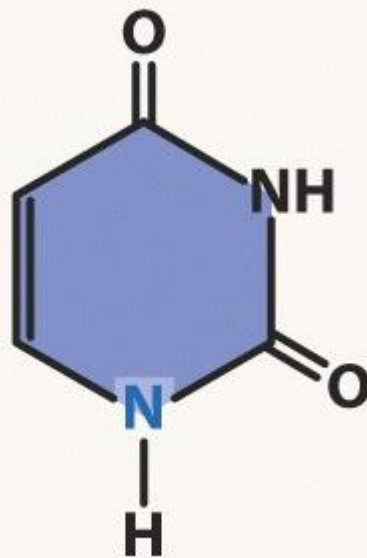
Ribose



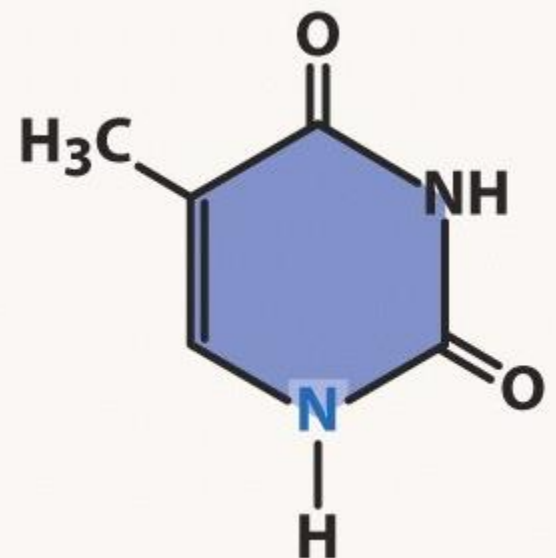
Deoxyribose



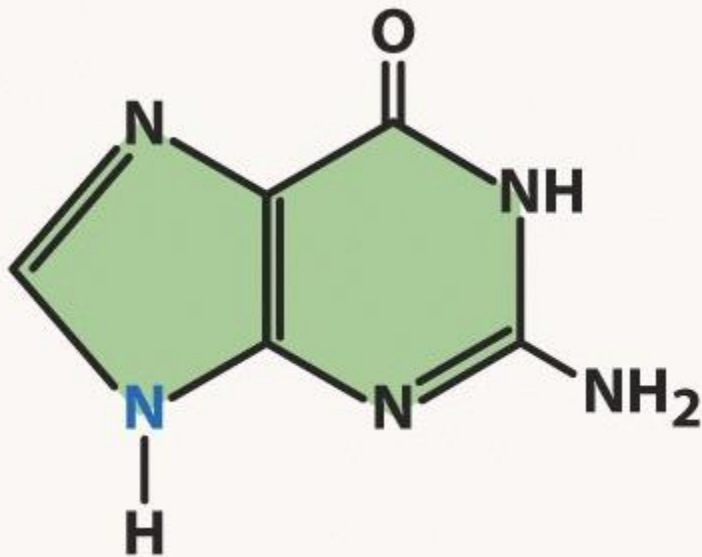
Cytosine



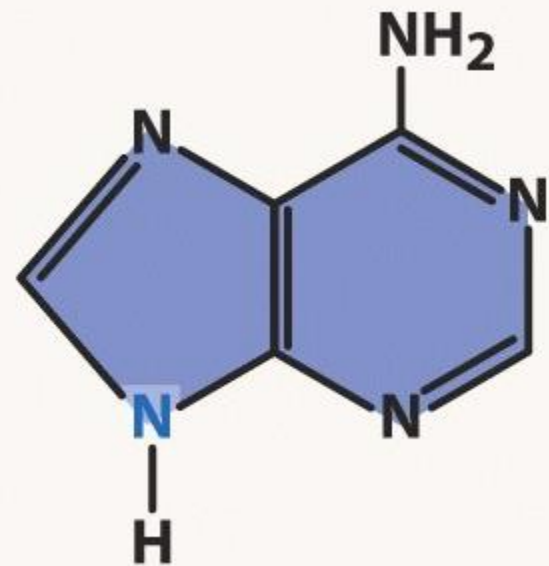
Uracil



Thymine



Guanine

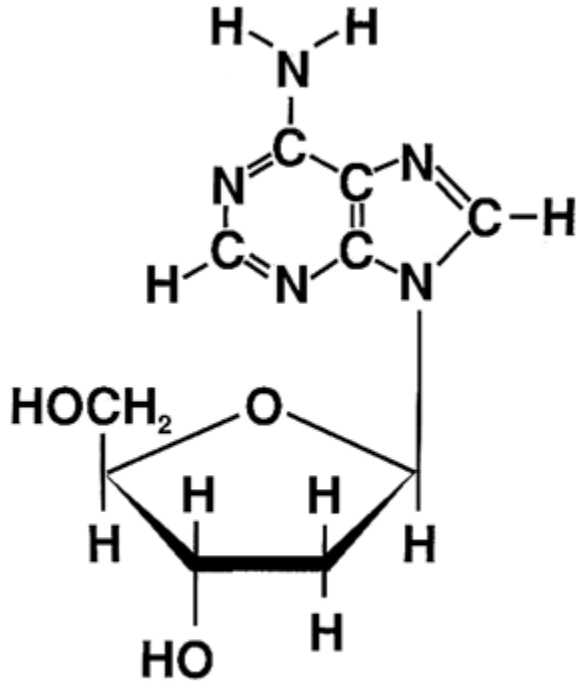


Adenine

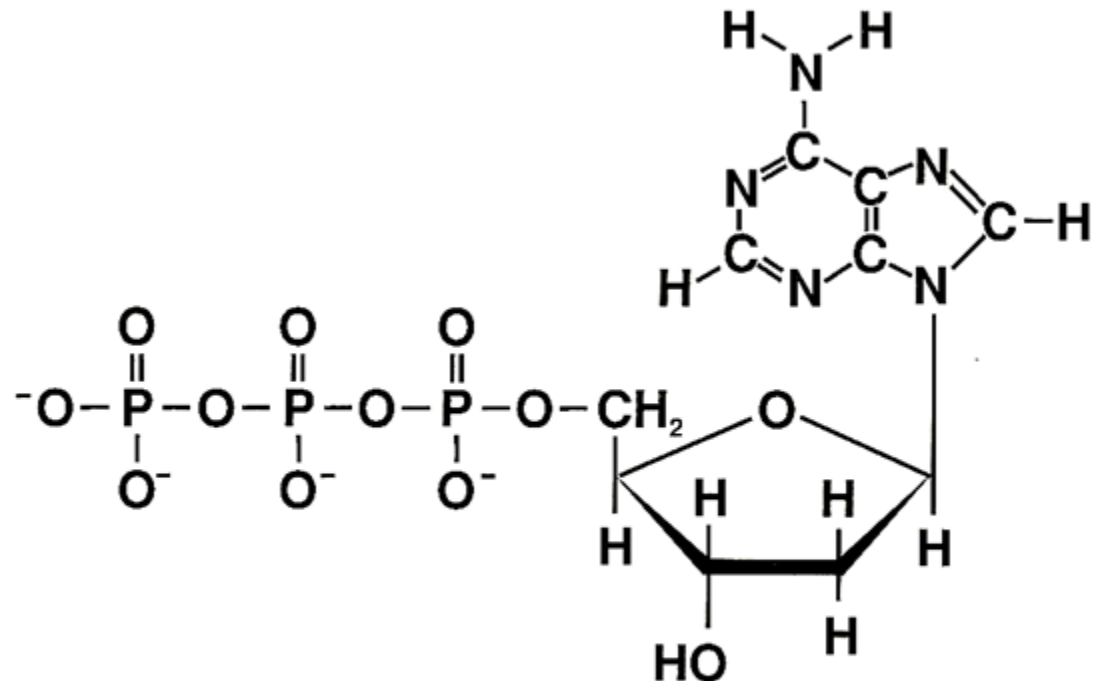
Base + Sugar = Nucleoside

Base + Sugar + Phosphate = Nucleotide

# Nucleotide ve Nucleoside

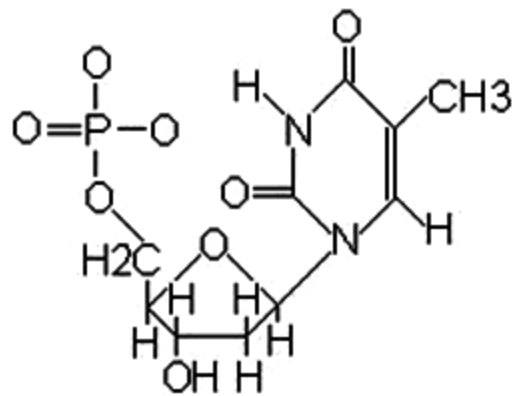
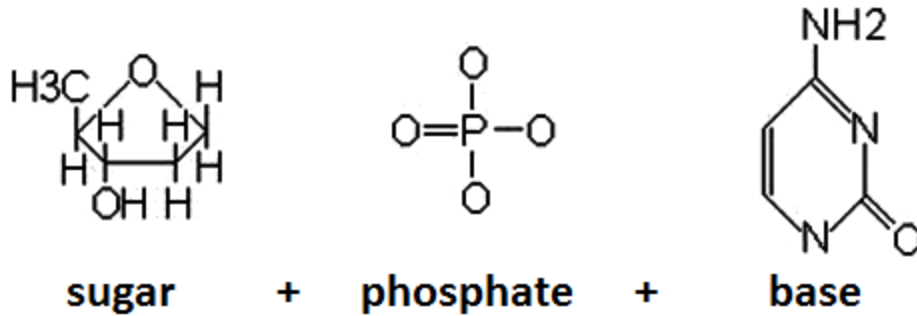


**Deoksyadenosine  
(nucleoside)**

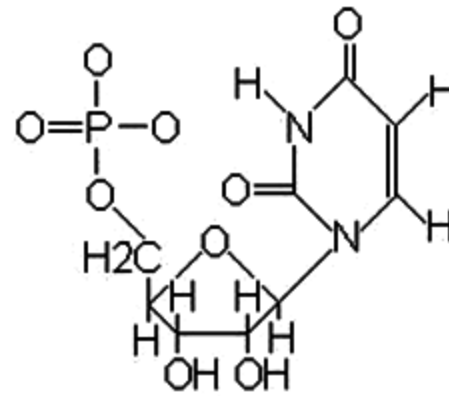


**Deoksyadenosine triphosphate  
(nucleotide)**

# Nucleic Acids



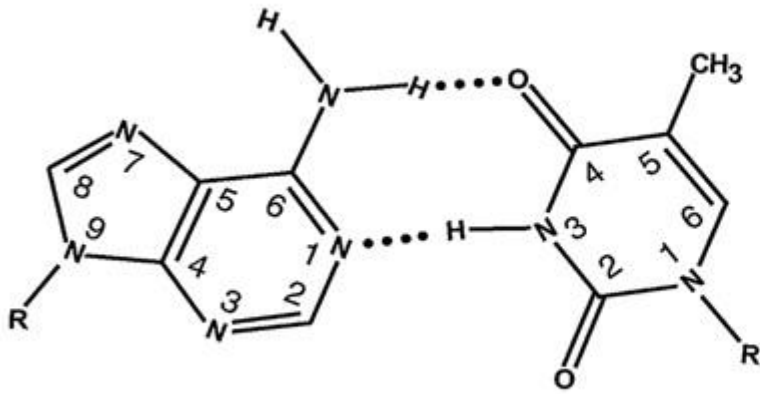
**deoxythymidine  
monophosphate**



**thymidine  
monophosphate**

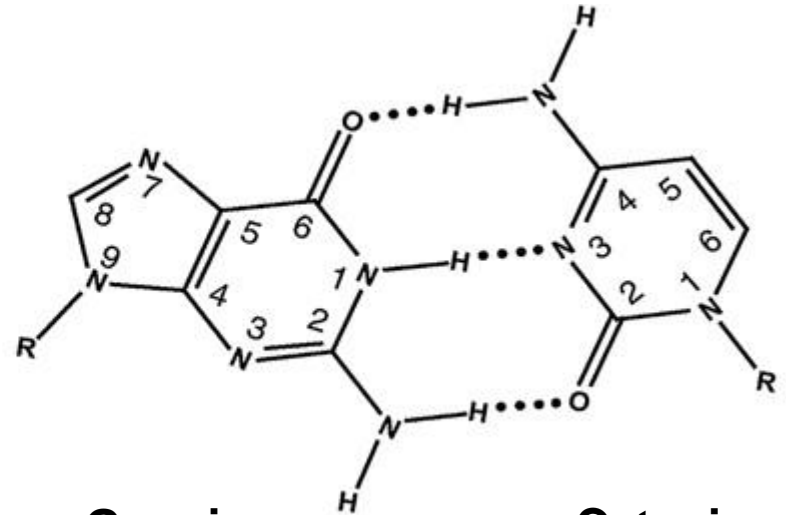


# Watson-Crick base pairing



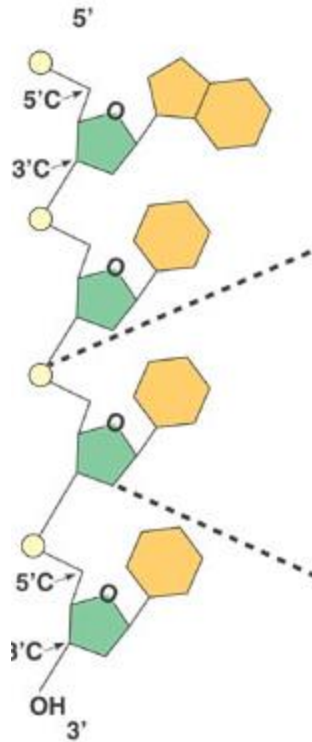
**Adenine**

**Thymine**

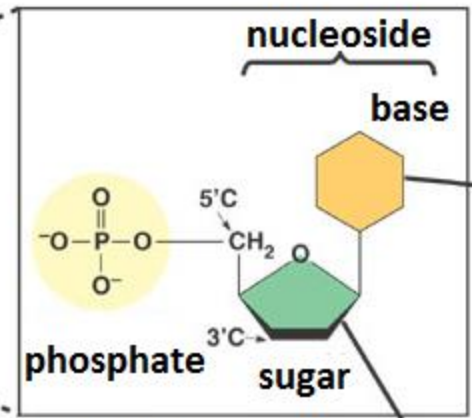


**Guanine**

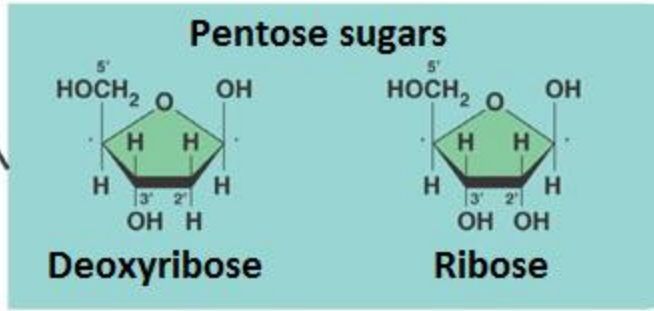
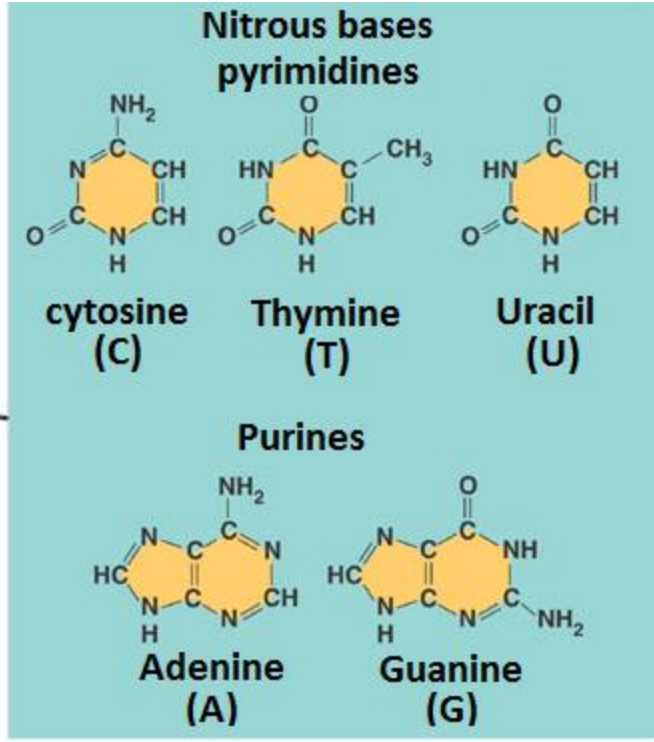
**Cytosine**



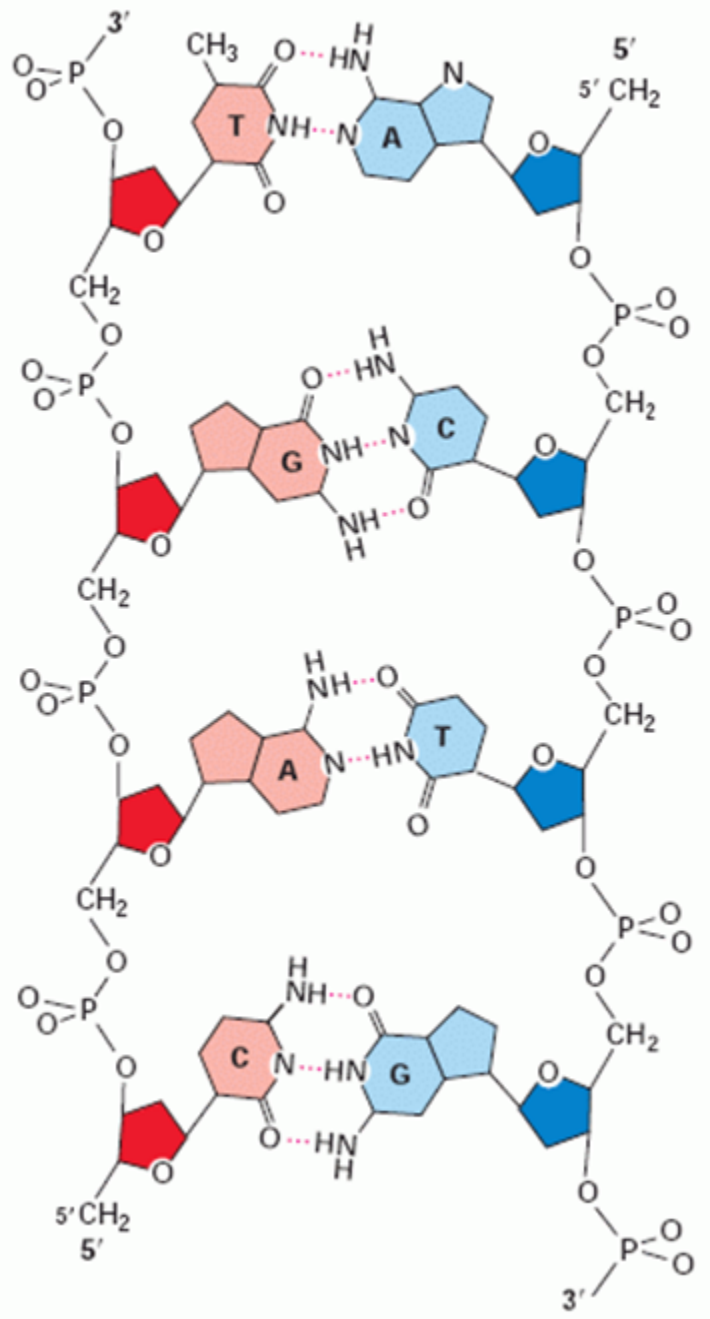
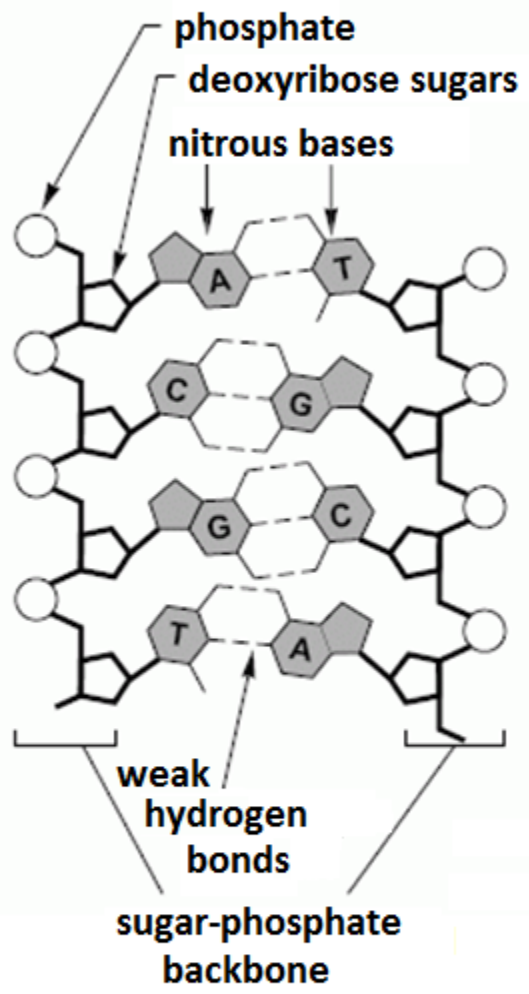
**polynucleotide  
(nucleic acid)**



**nucleotide**



**Nucleoside components**



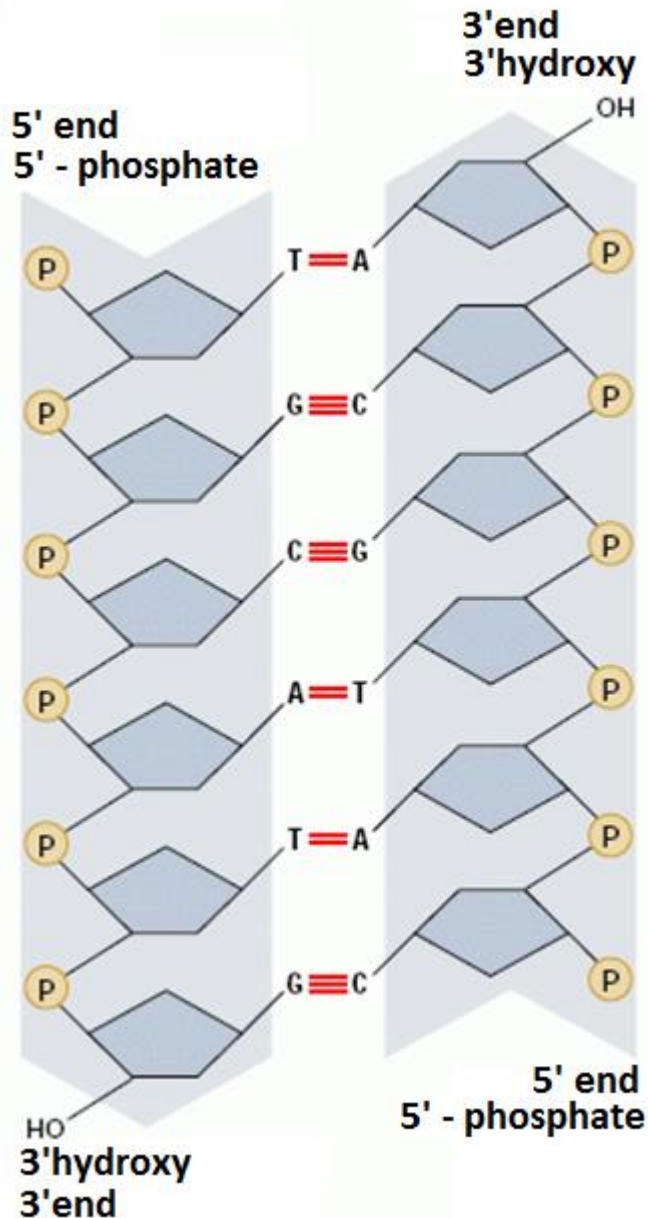
# DNA Structure

- two antiparallel strands are linked by w the weak hydrogen bonds.
- Base pairing occurs between purines and pyrimidines by hydrogen bonds  
Adenine = Thymine  
Guanine ≡ Cytosine
- In any double stranded DNA molecule, the number of A = T, G =C.
- DNA exhibits a helical structure.

# DNA HELIX

- DNA strand orientation is depicted by the sugar residue.
- DNA strand elongates from the 5' end.
- DNA polymerizes in 5' → 3' direction.
- DNA is written in 5' → 3' direction.
- Phosphate (P) resides in the 5' end.
- Hydroxy residue (OH) is on the 3' end.

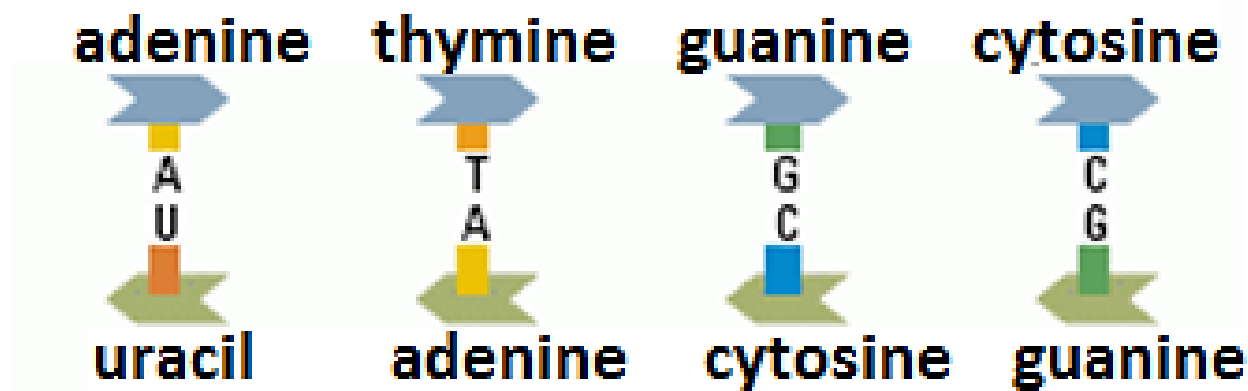
# DNA Structure



- A pairs T
- G pairs C
- A=T - two H bonds
- G≡C - three H bonds
- A = T, G=C
- A+G = T+C
- ANTIPARALLEL strands

# Bases residing in DNA and RNA

## Base residue in the template DNA



## Base residue in the transcribed RNA

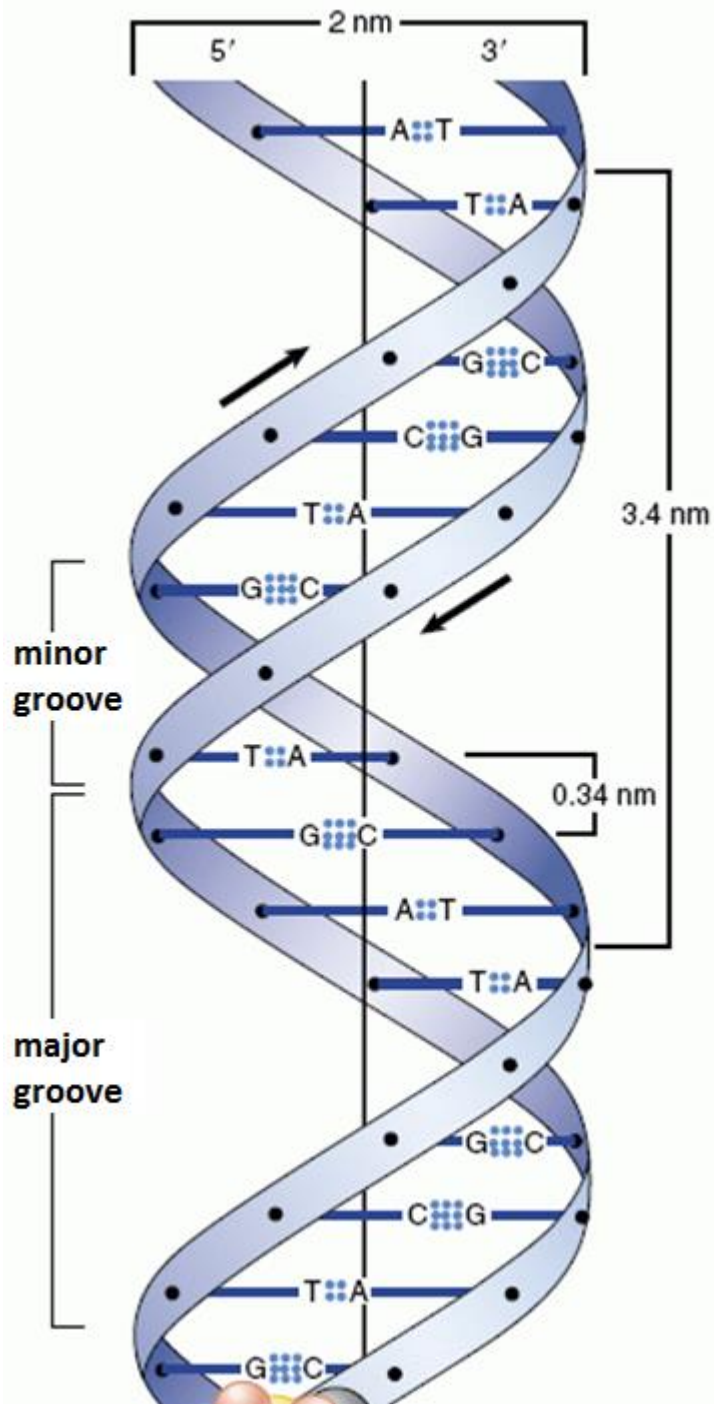
Uracil (U) replaces thymine (T) in RNA





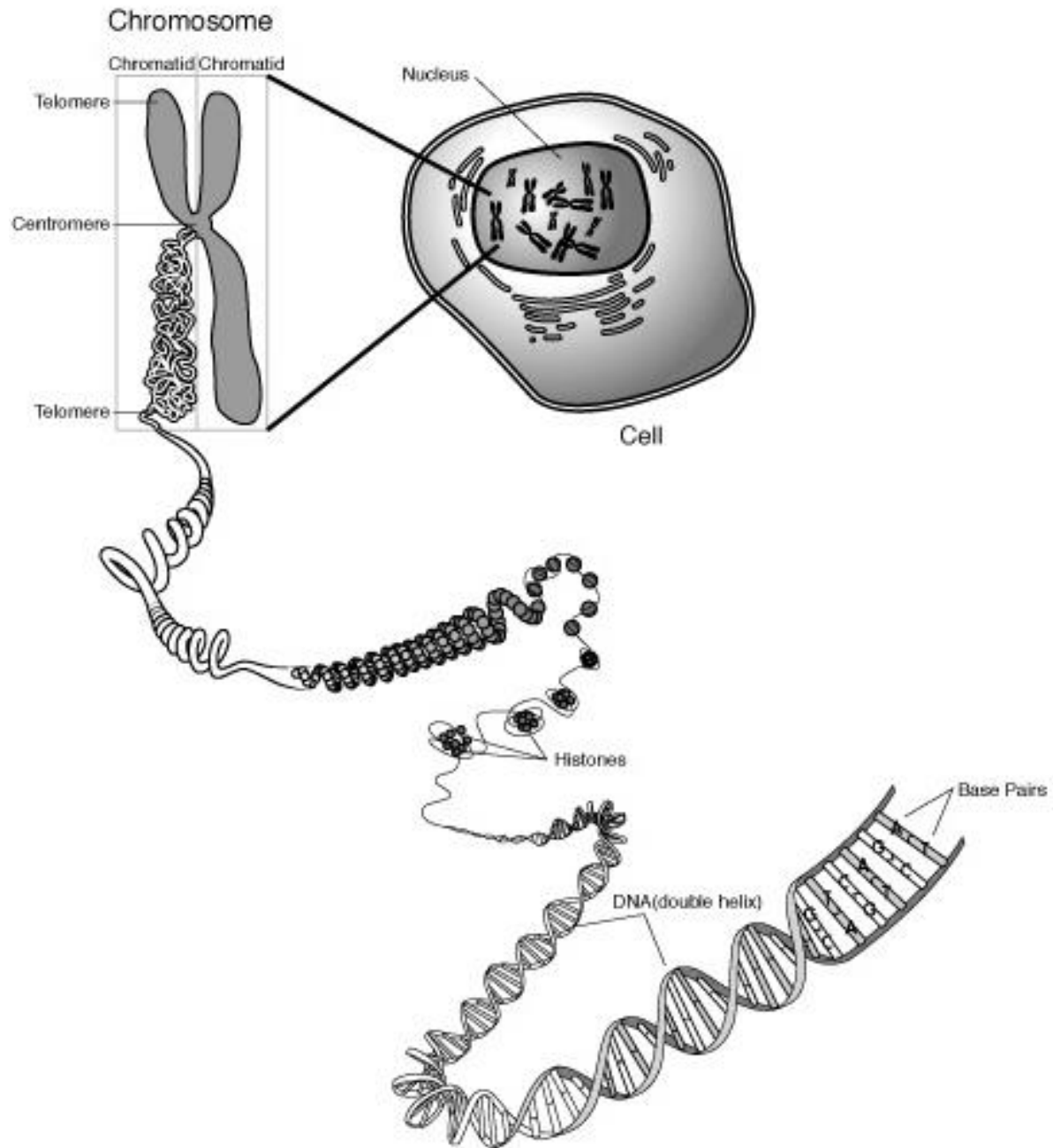
# DNA HELIX

- Radius = 2 nm
- One round = 3.4 nm
- One round = 10 base
- Two bases = 0.34 nm
- Major groove and minor groove

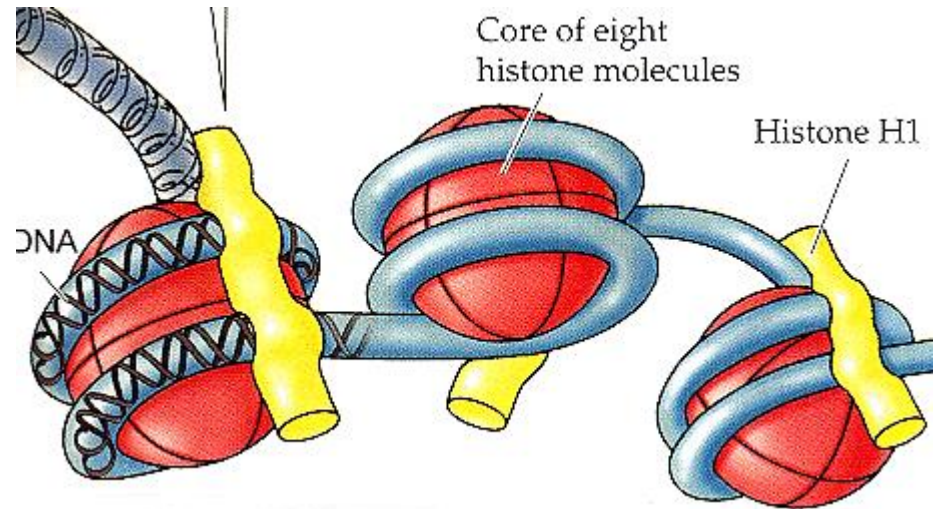
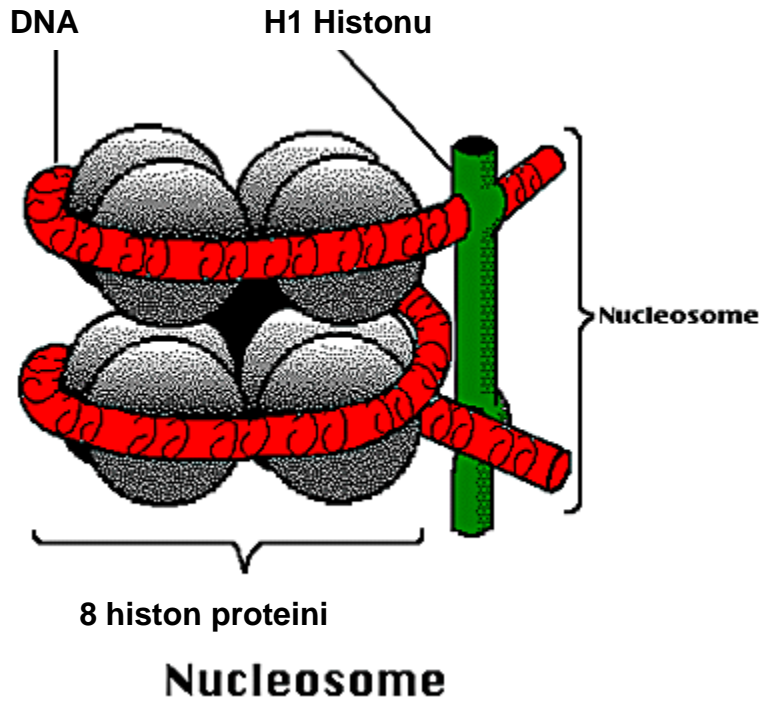


# Genome in Numbers

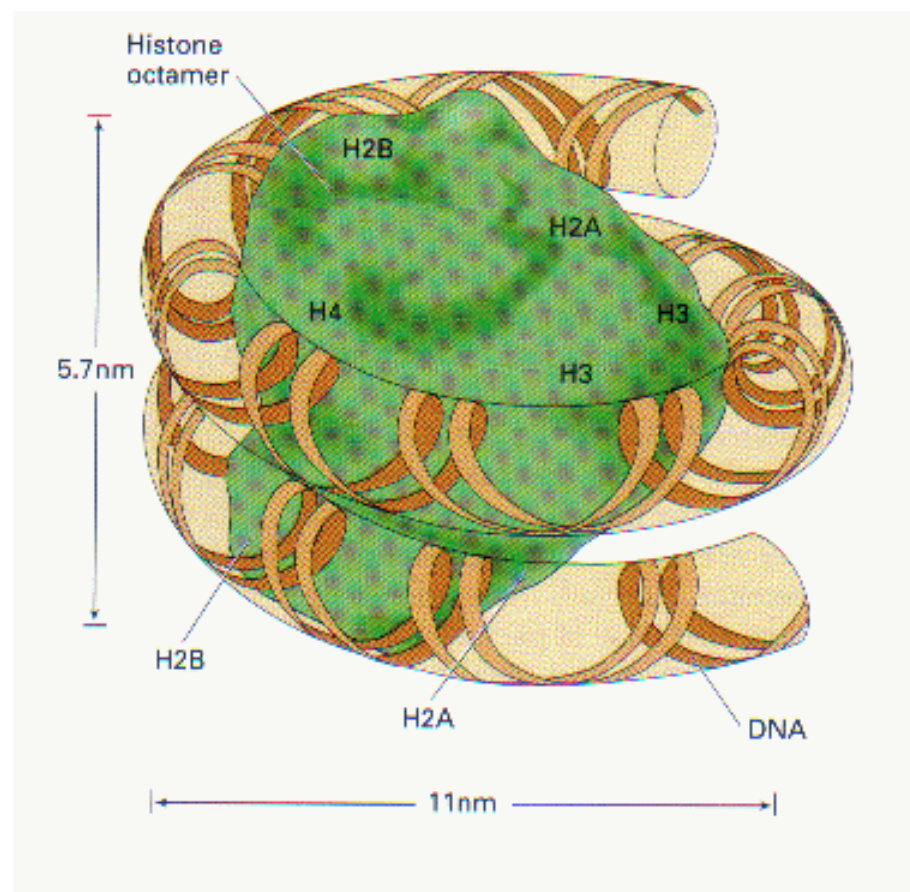
E.coli genome	4.6 million base
Yeast genome	15 million base
Smallest human chromosome (Y)	50 million base
Largest human chromosome (1)	250 million base
Total human genome	3.2 billion base



# Nucleosome structure



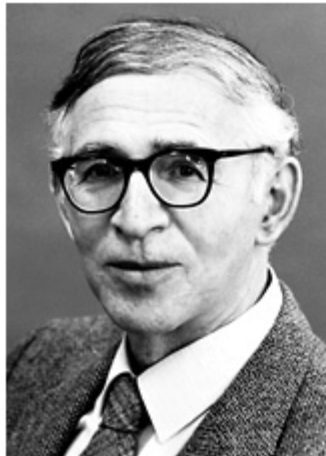
# Nucleosome Structure





## The Nobel Prize in Chemistry 1982

"for his development of crystallographic electron microscopy and his structural elucidation of biologically important nucleic acid-protein complexes"



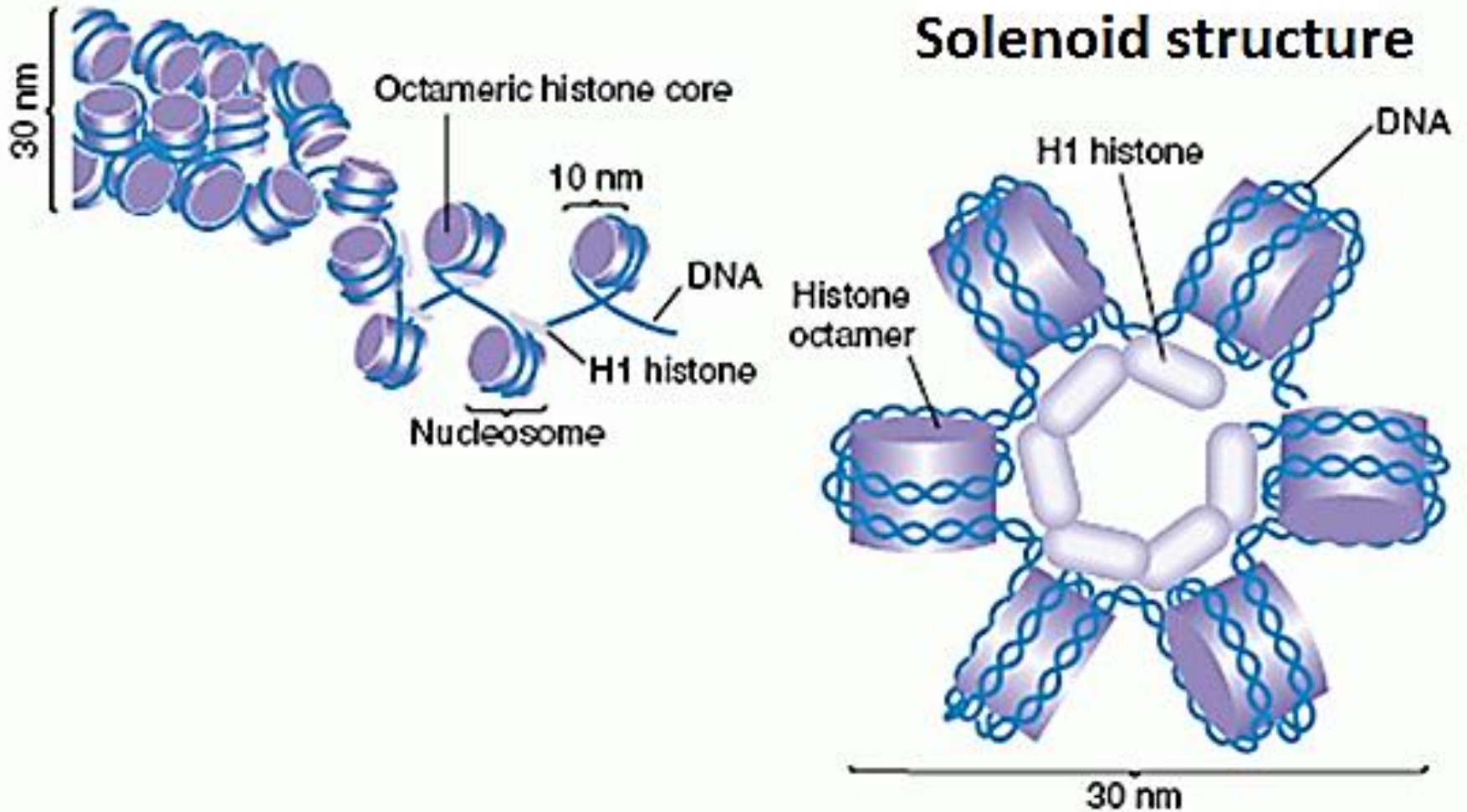
**Aaron Klug**

United Kingdom

MRC Laboratory of  
Molecular Biology  
Cambridge, United  
Kingdom

b. 1926  
(in Zelvas, Lithuania)

# Solenoid Structure



# Chromosome packaging

DNA helix



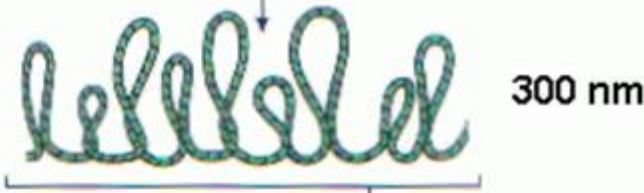
Nucleosome structure



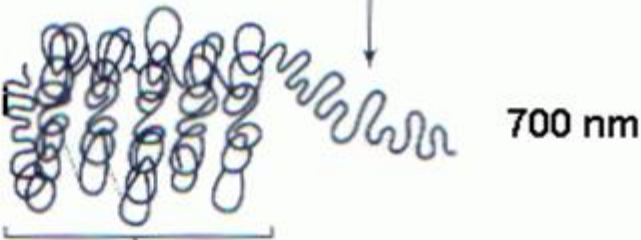
Nucleosome packaging (solenoid structure)



Chromatin loops



Chromosome condensation



Metaphase chromosome



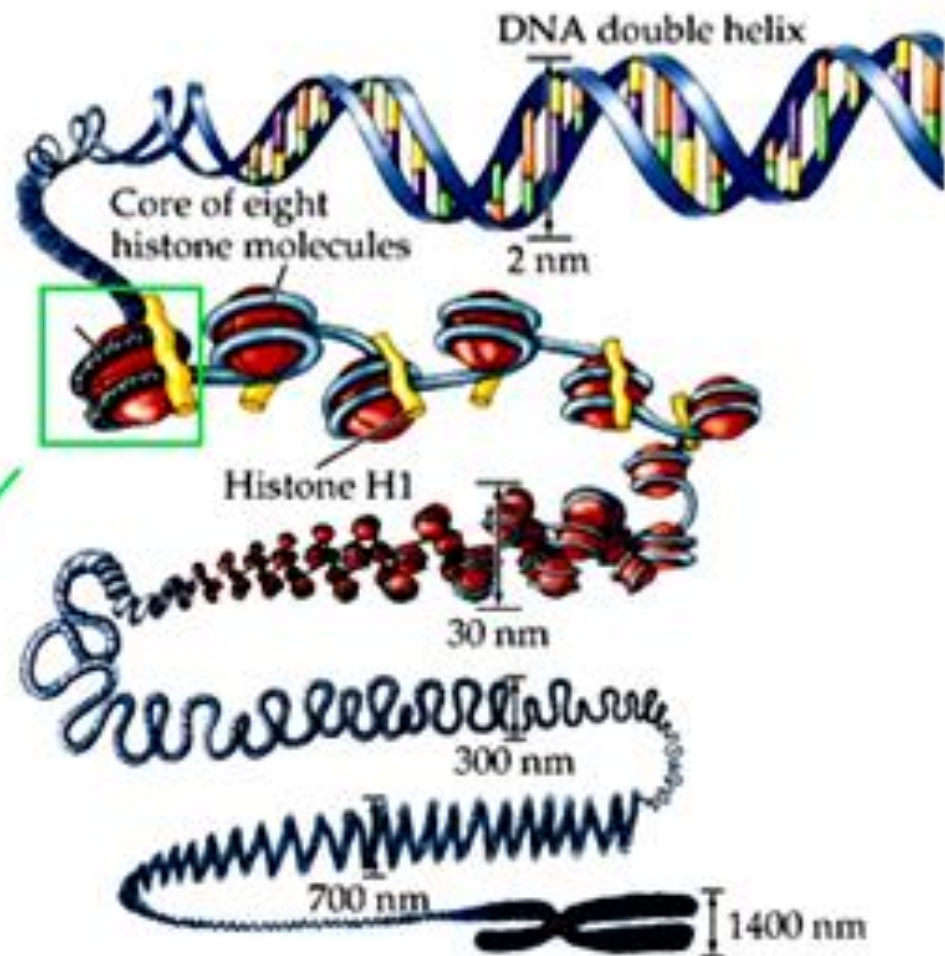


# DNA packaging

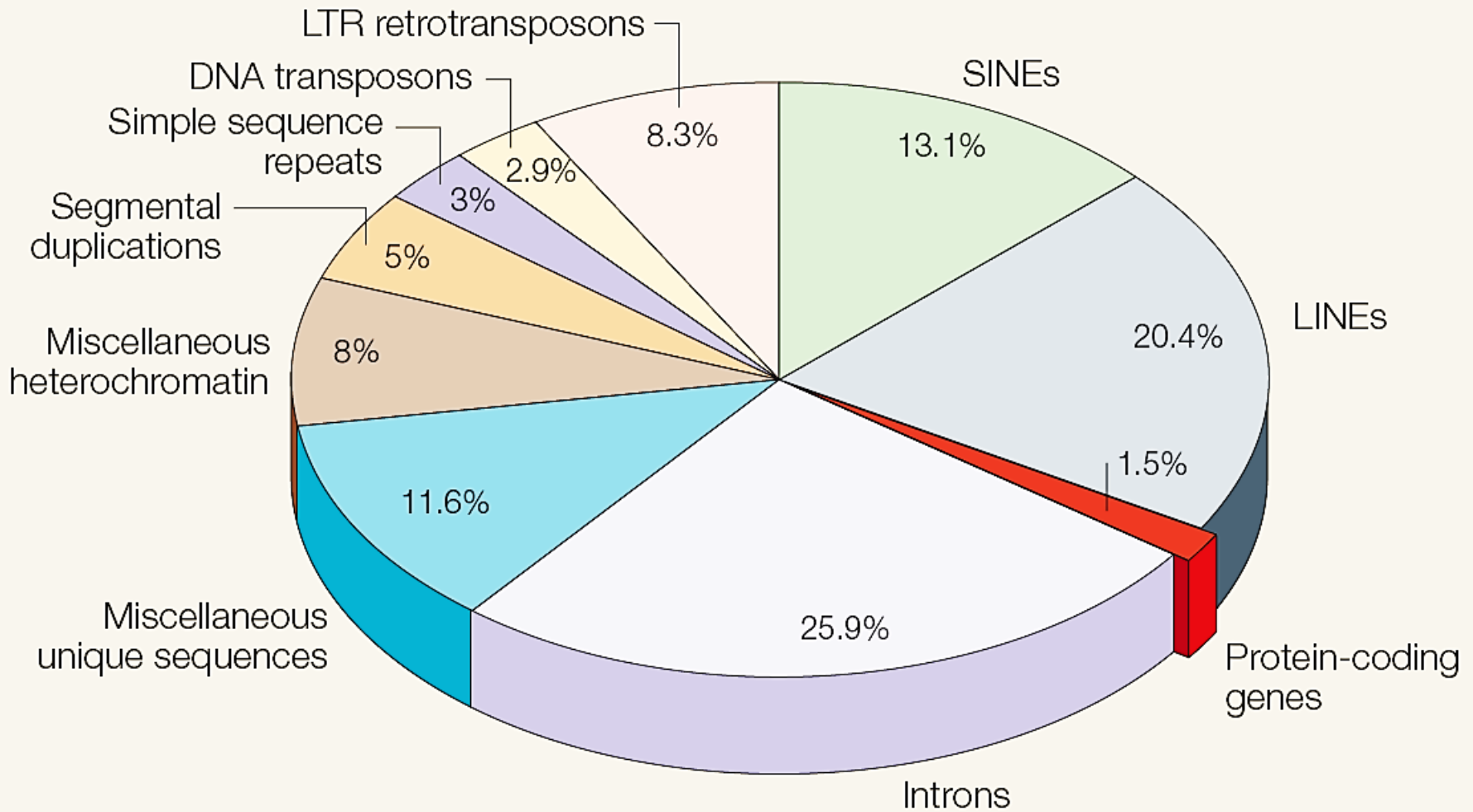
<b>STRUCTURE</b>	<b>radius</b>
Helix structure	2 nm
Nucleosome structure (histone)	11 nm
Solenoid structure of nucleosomes	30 nm
Chromatin loops	300 nm
Chromosomal condensation	700 nm
Metaphase chromosome	1400 nm

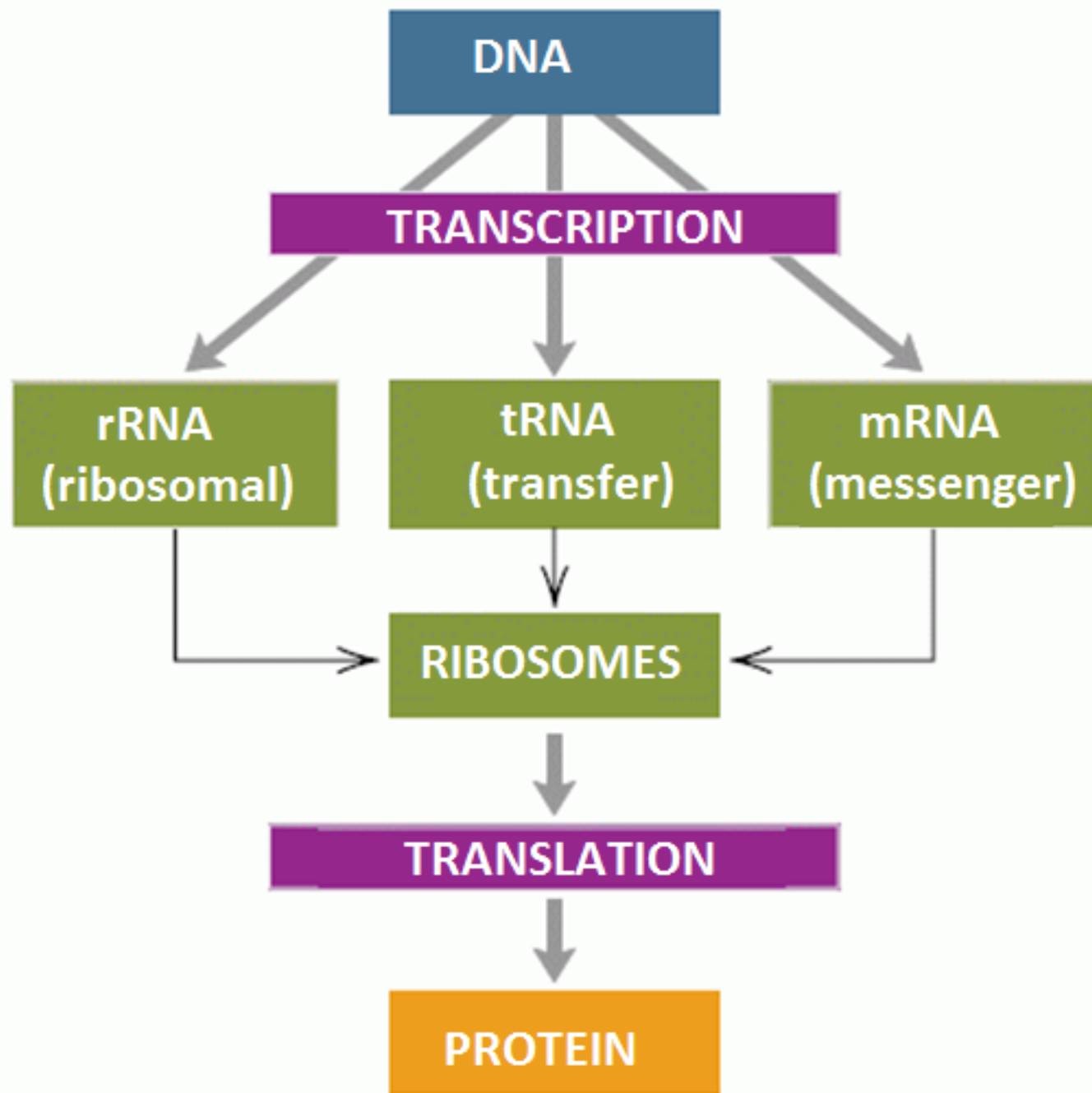
# 2m DNA

NUCLEUS  $\varnothing 10 \mu\text{m}$

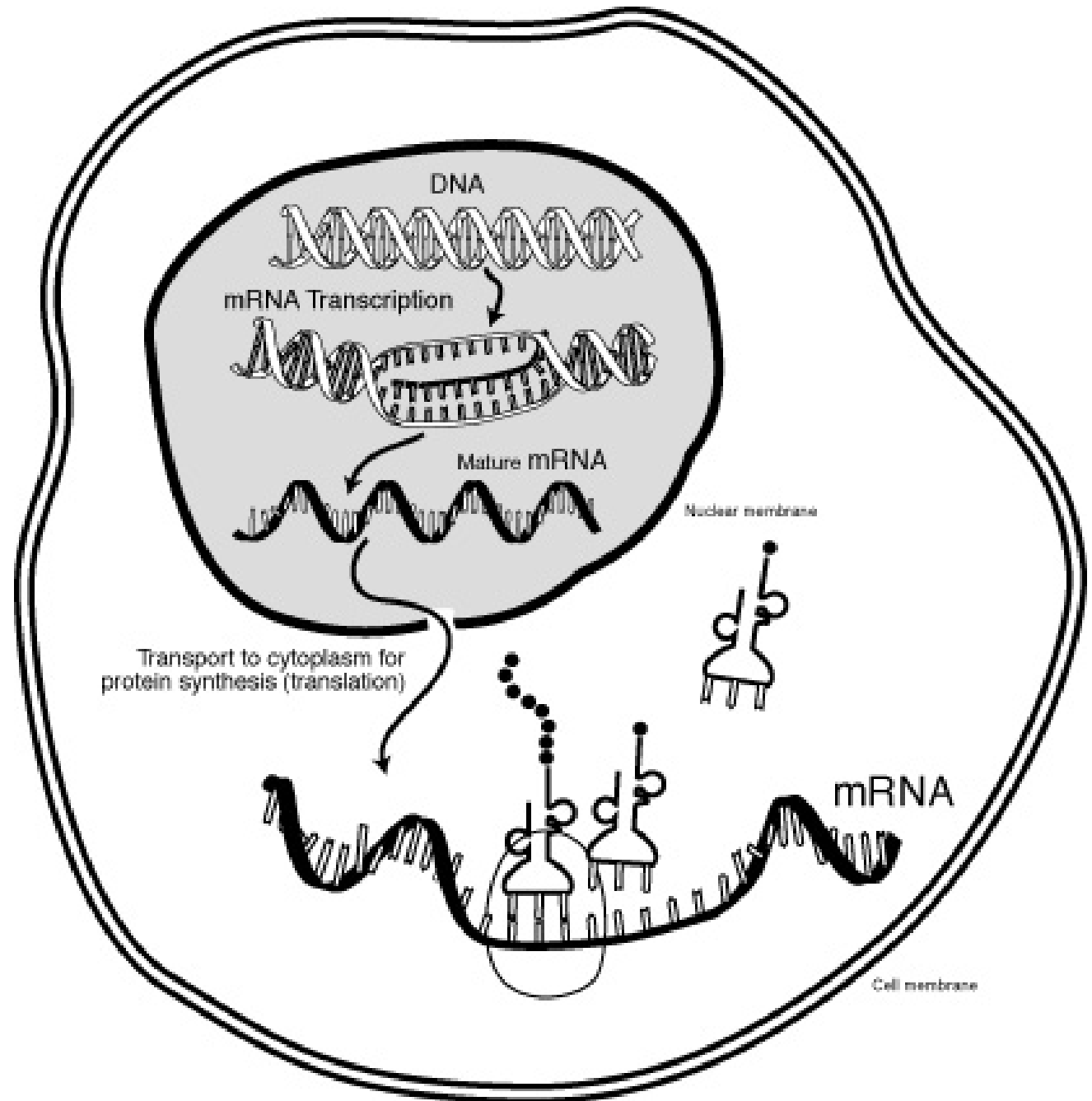


# Human Genome

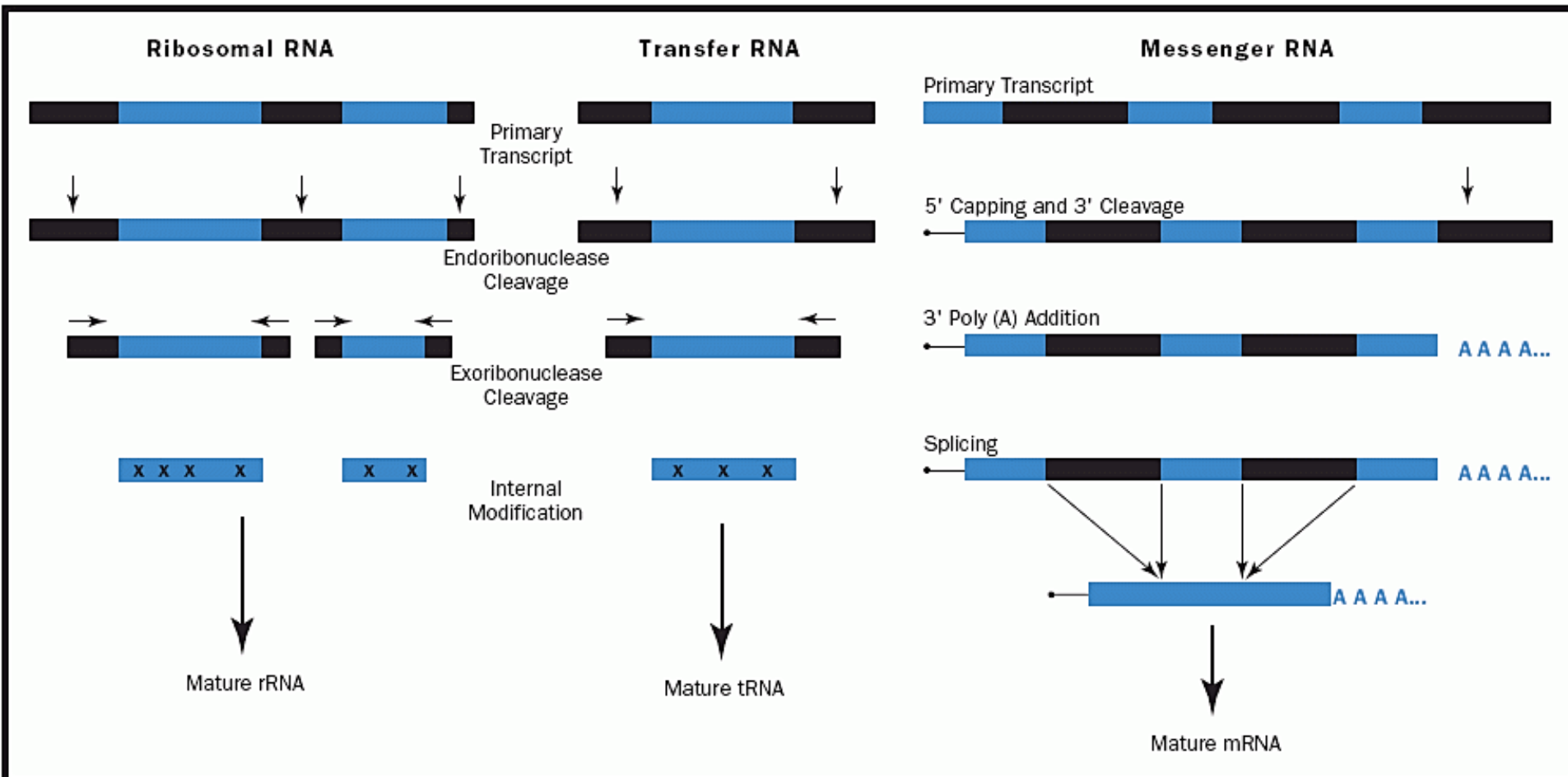




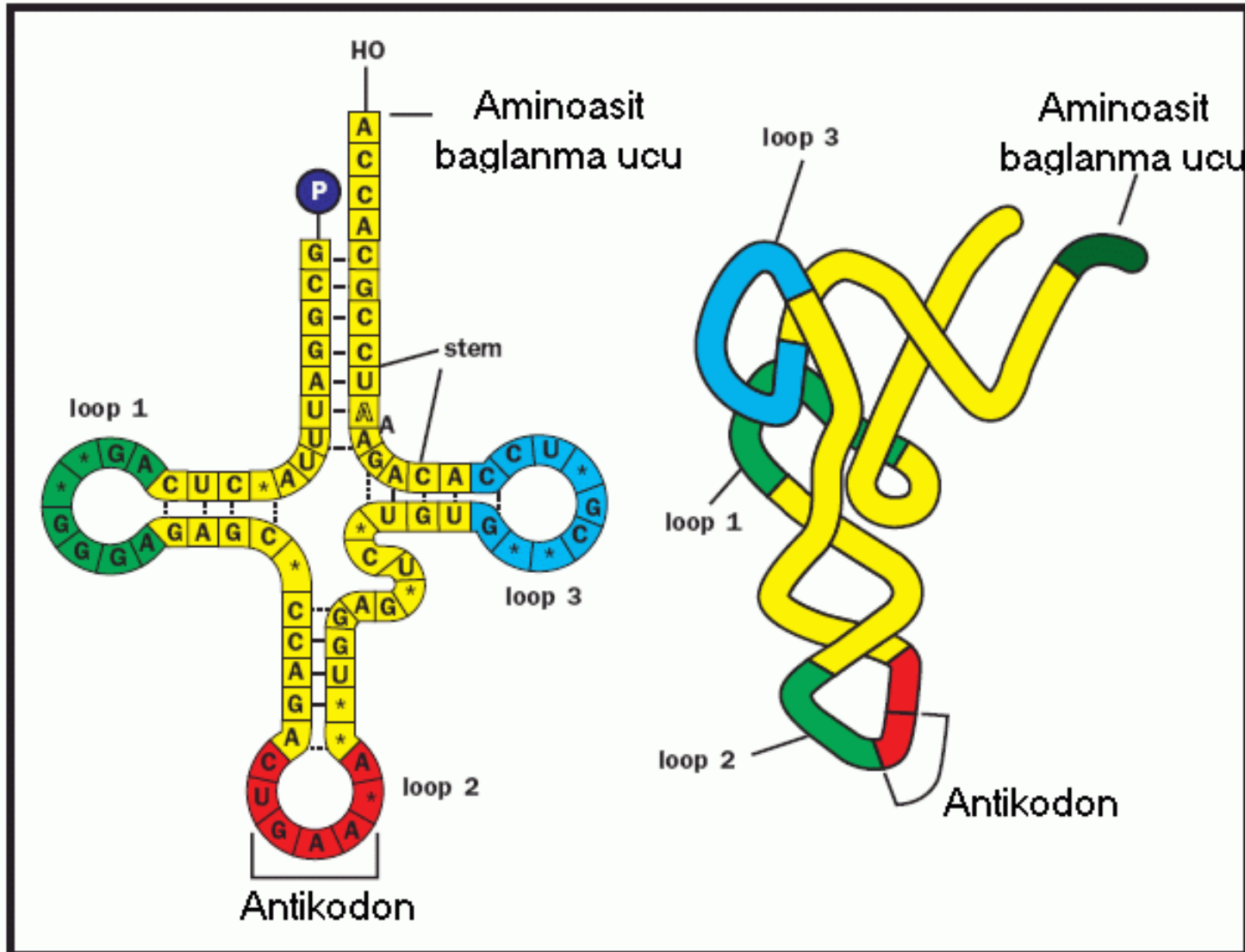
# mRNA



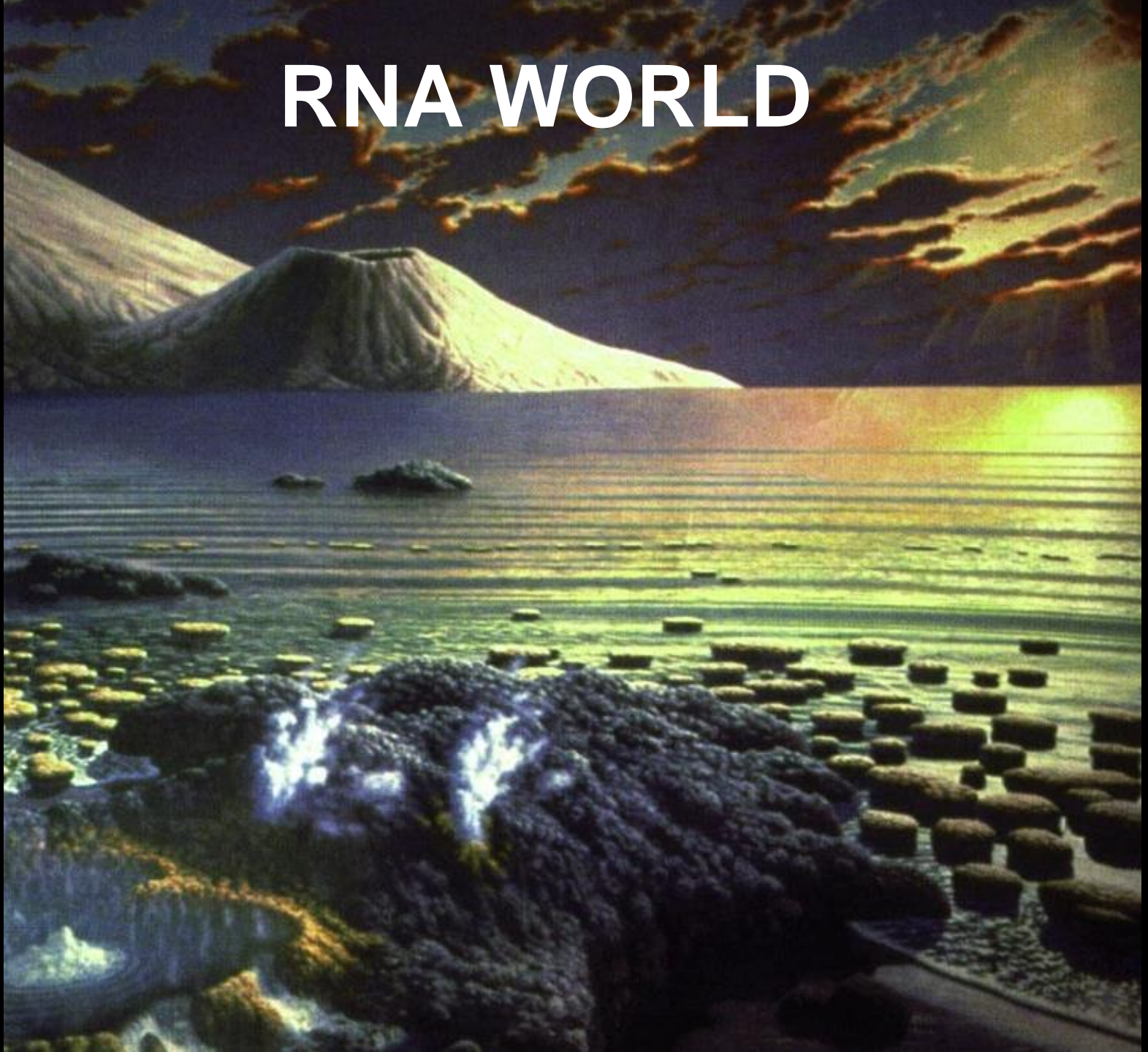
# RNA processing and modifications



# tRNA structure

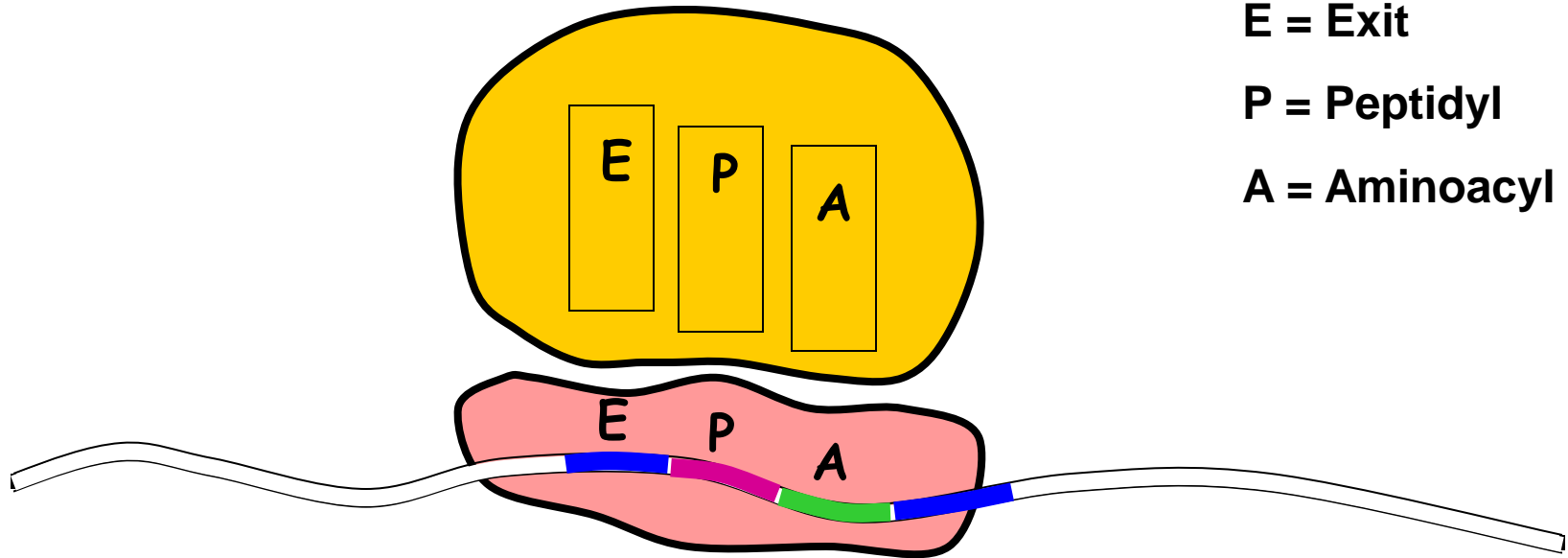


# RNA WORLD





# Functional Structure of the Ribosome

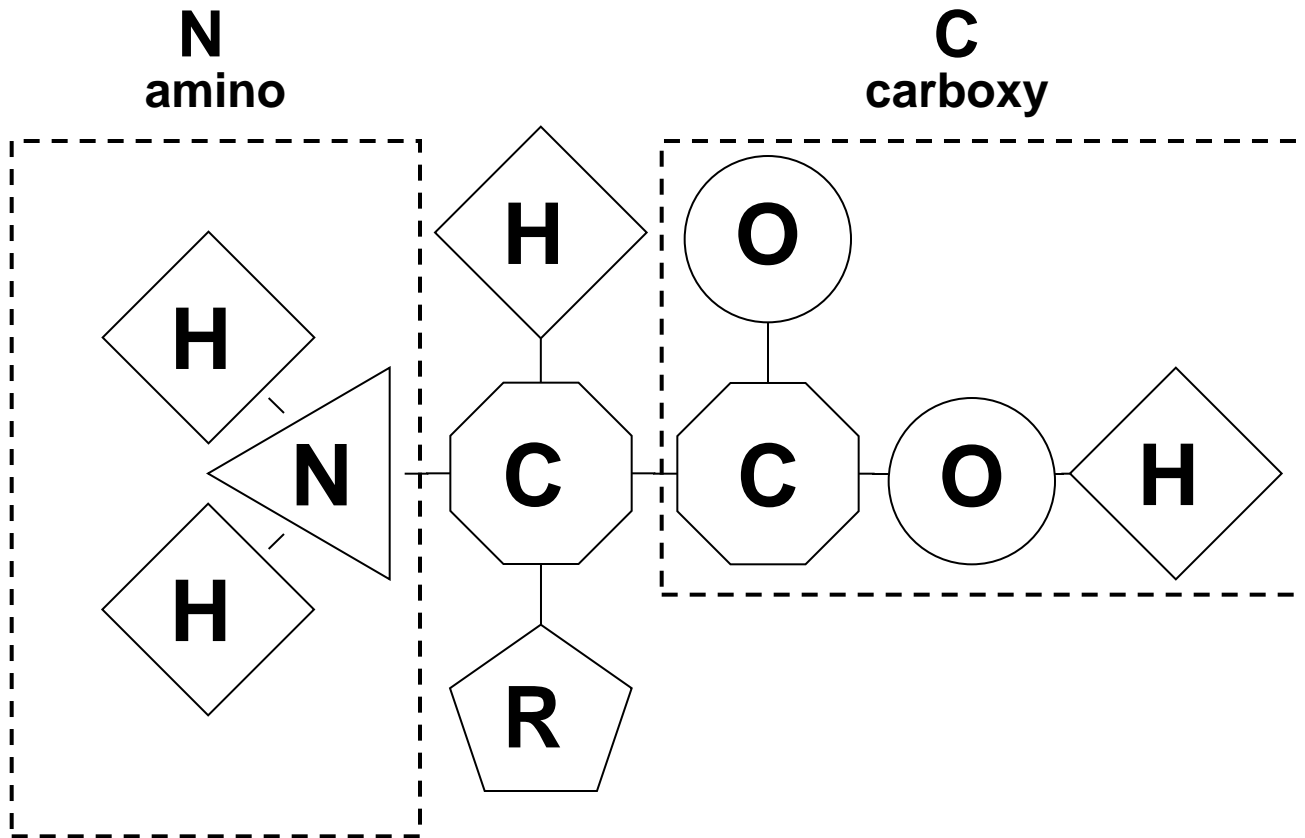


E = Exit

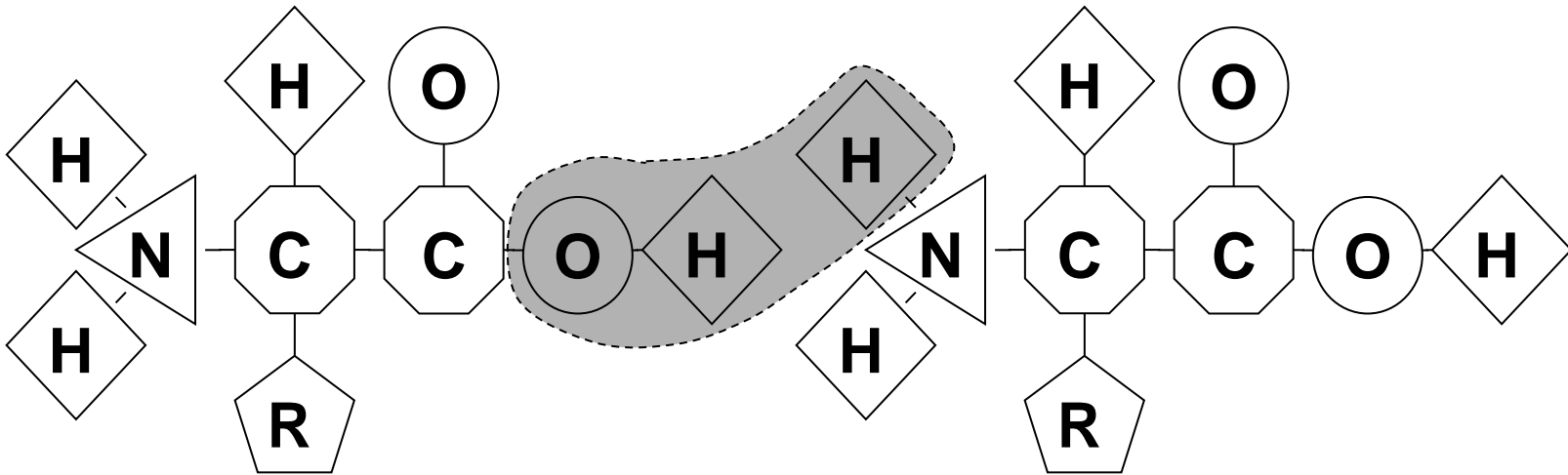
P = Peptidyl

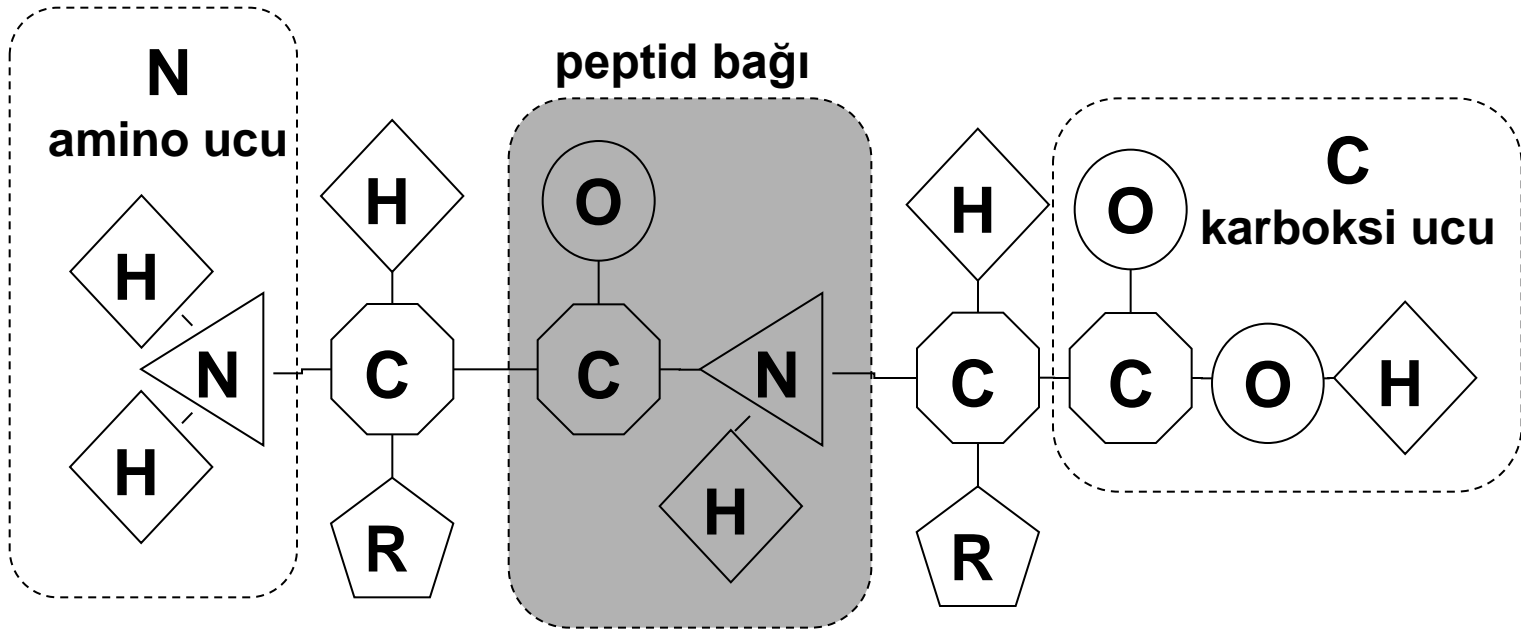
A = Aminoacyl

# Aminoacid

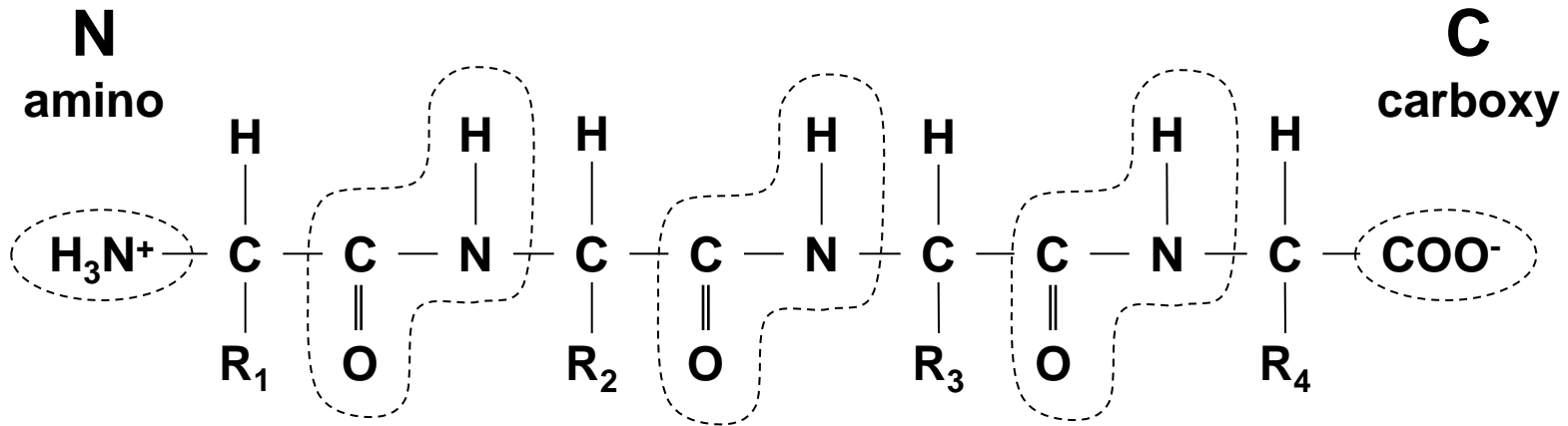


# Peptide Bond

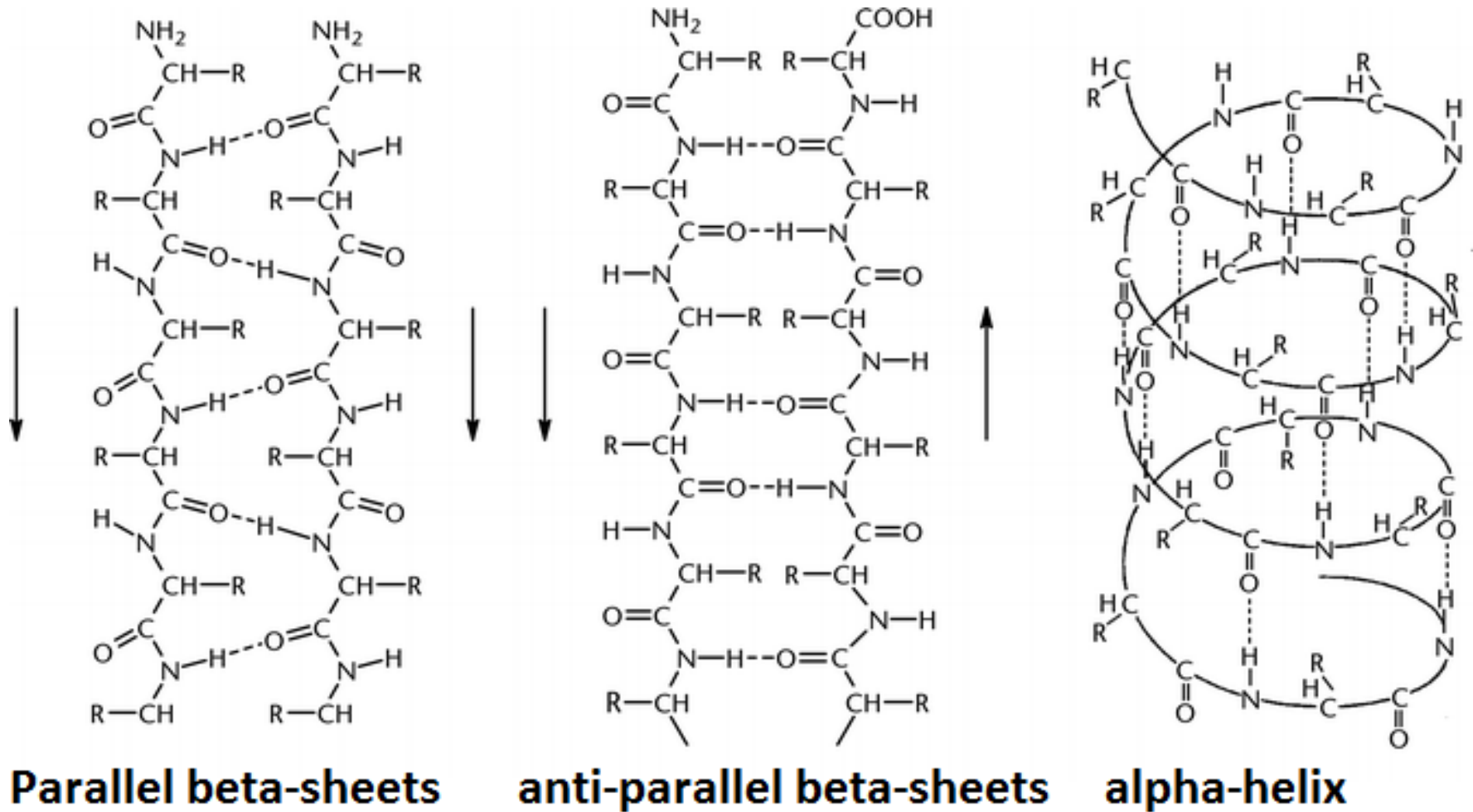




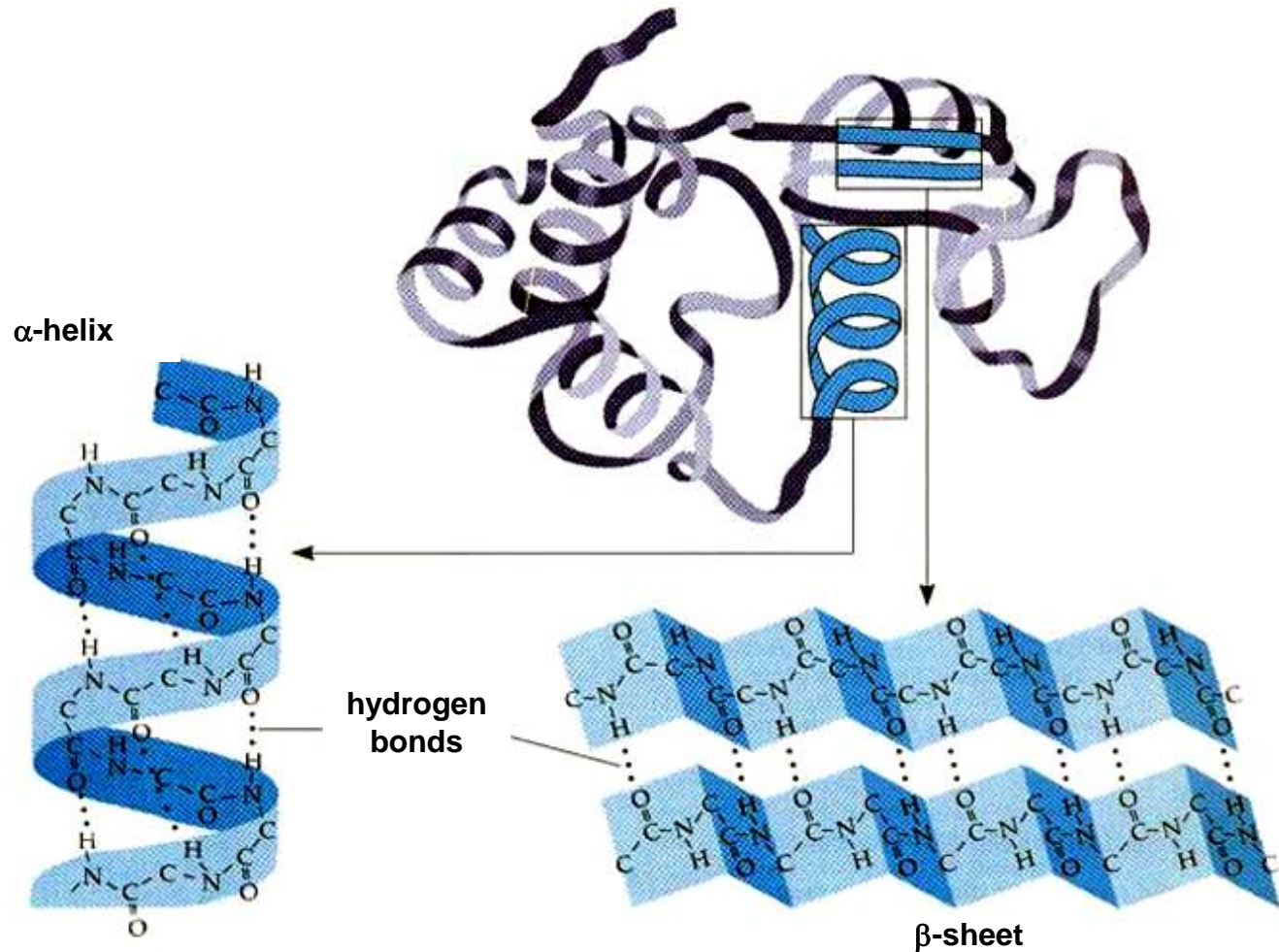
# Polypeptide chain



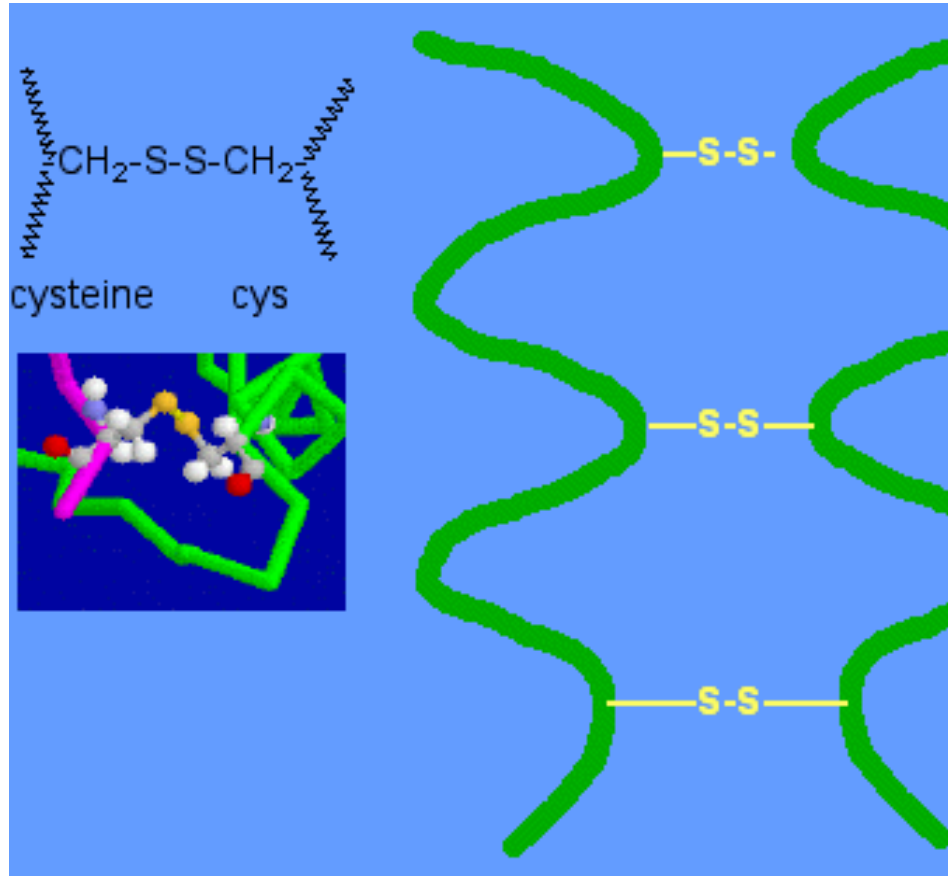
# Secondary Structure



# Secondary Structure

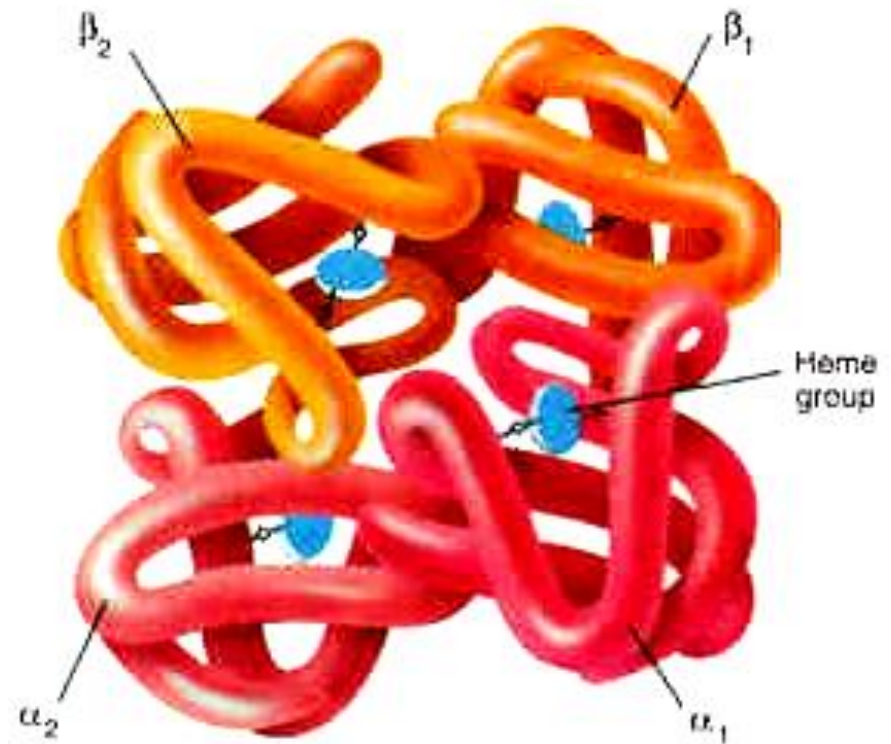
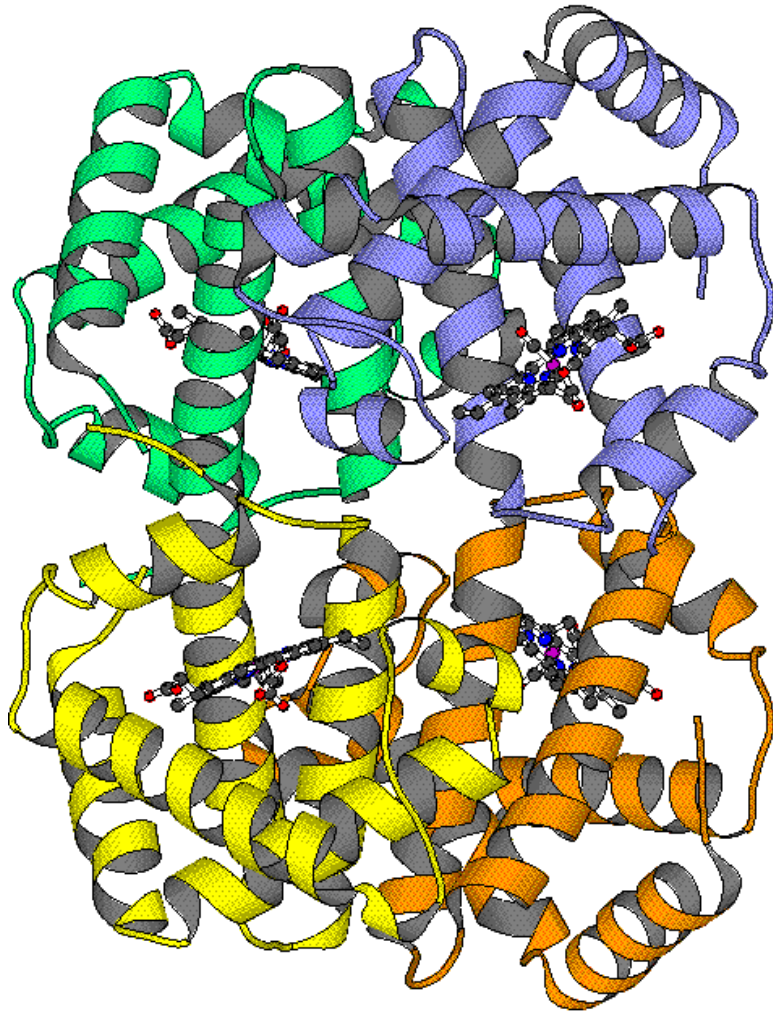


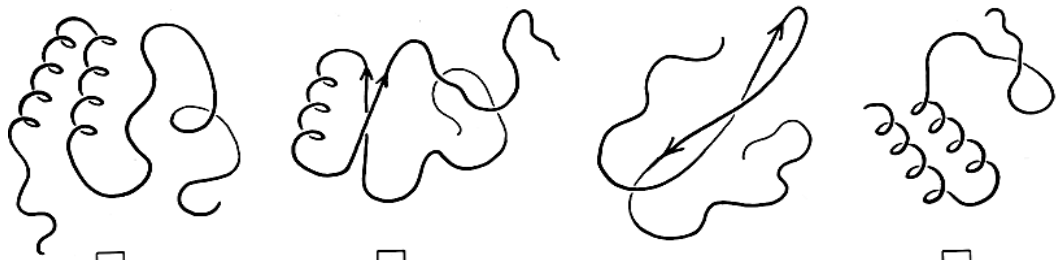
# Tertiary Structure





# Quaternary Structure





I. Nucleation



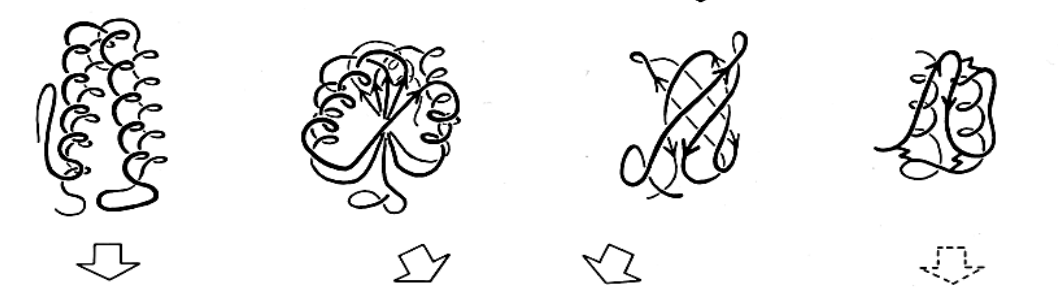
II. Growth and coalescence



to form



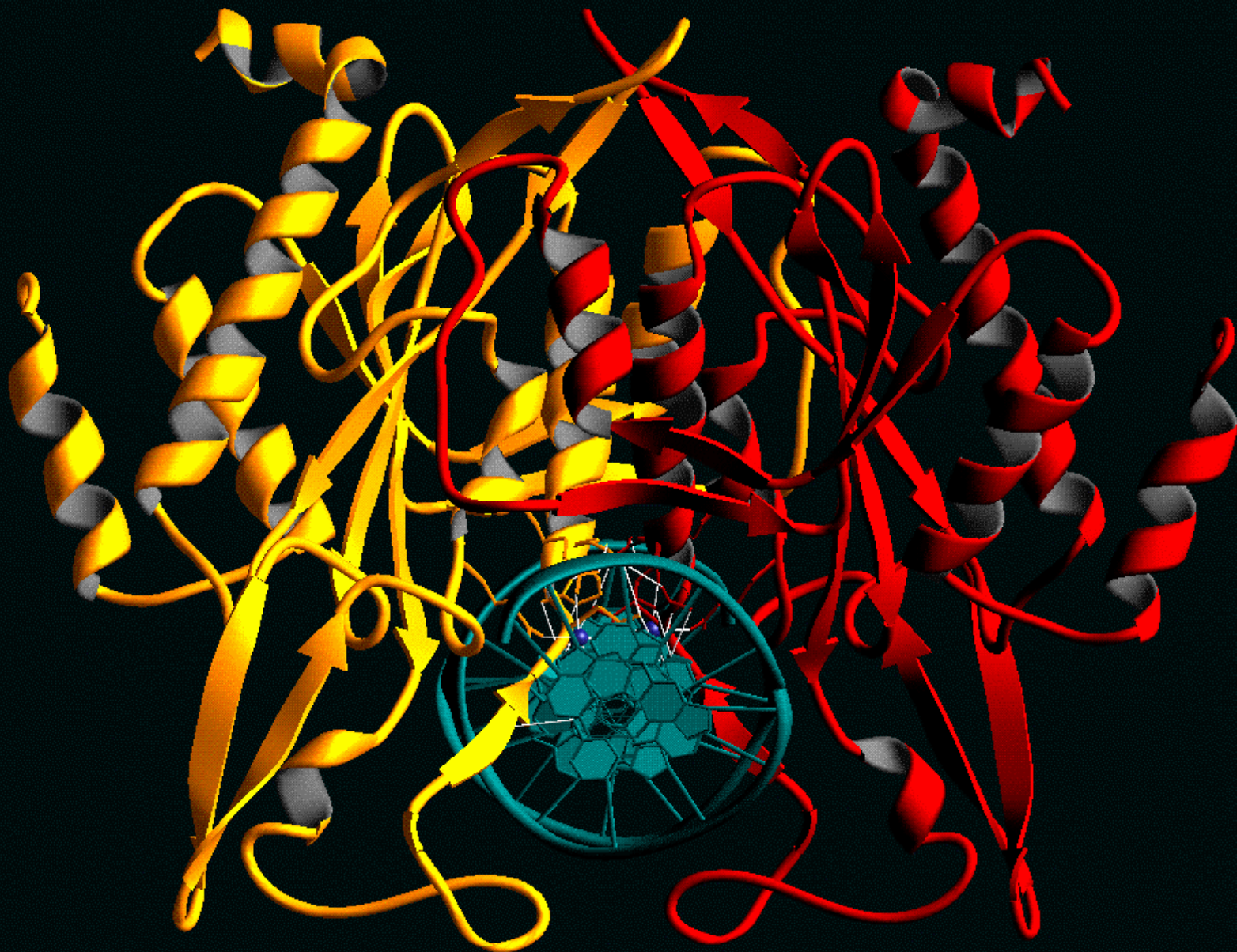
regular secondary structure

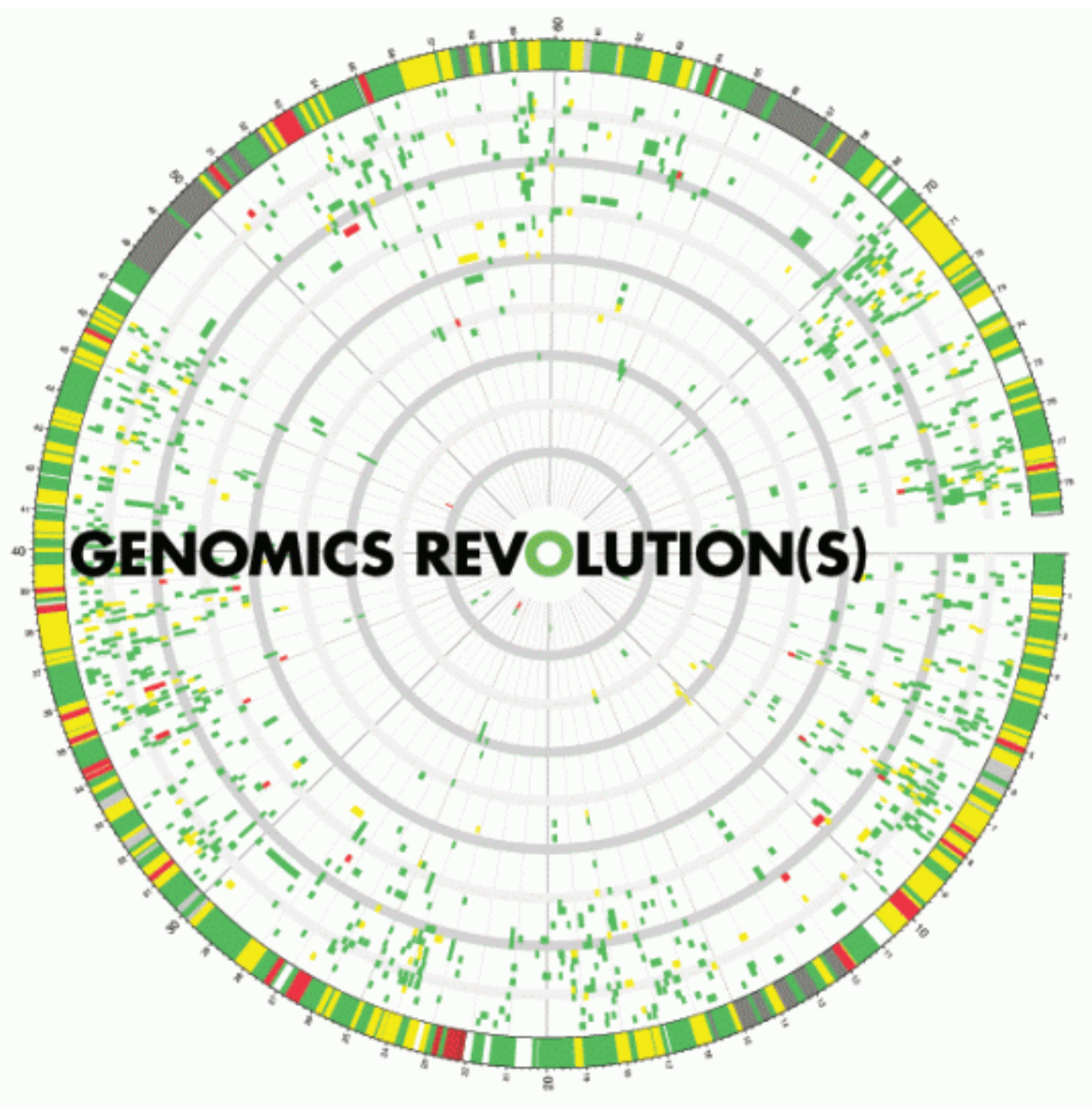


III. Readjustment for maximum overall stability



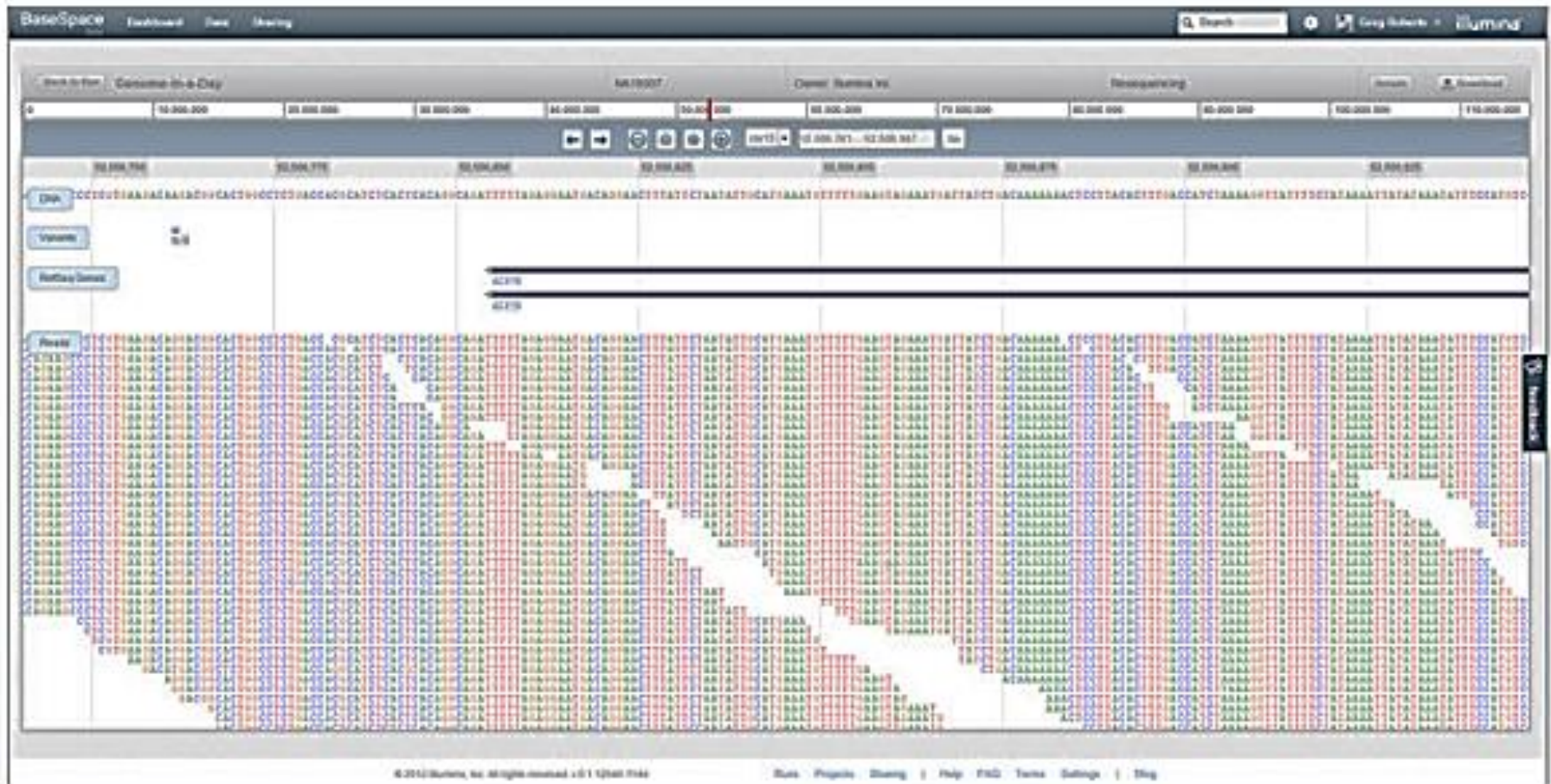
IV. Quaternary association



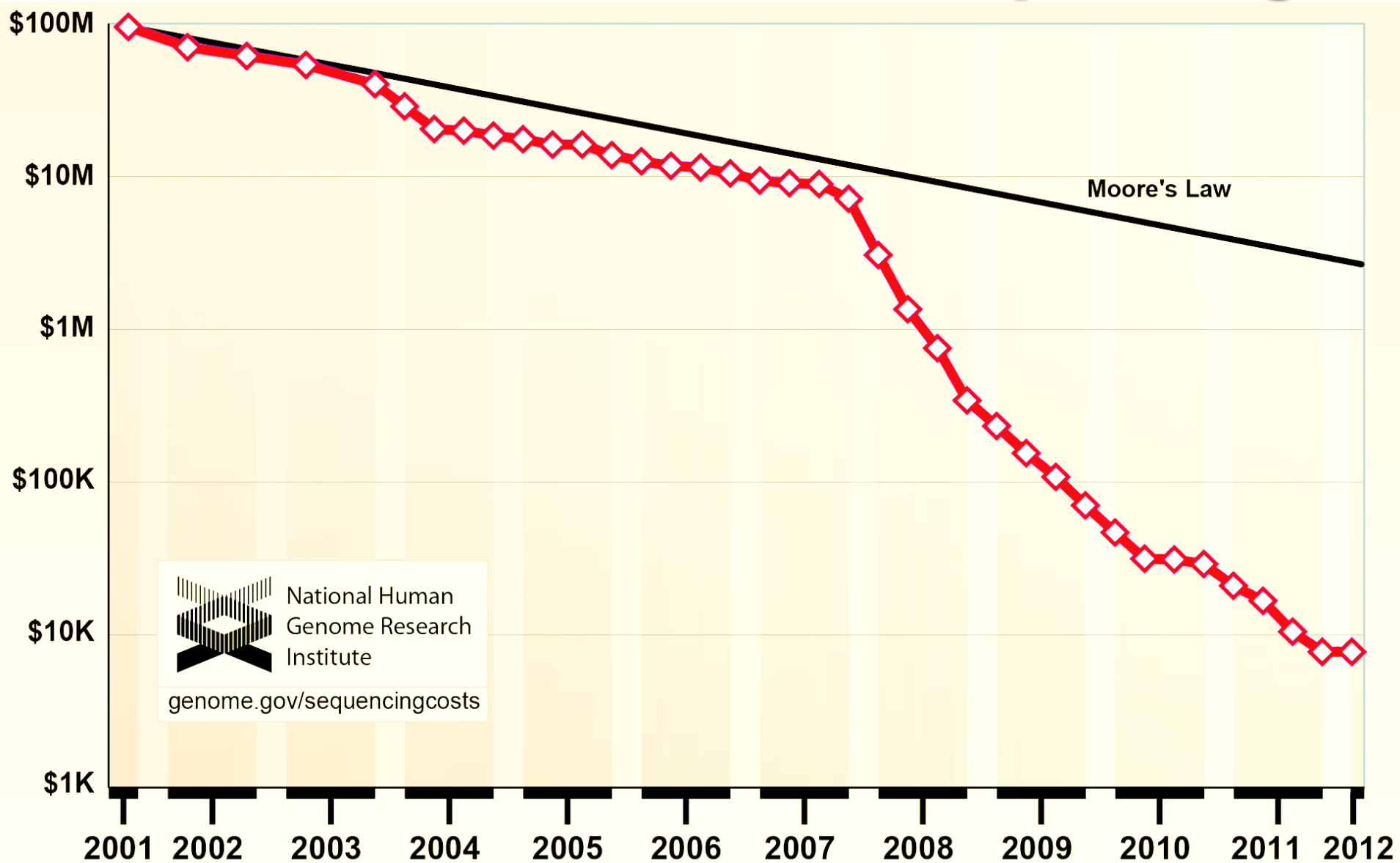


# High-Throughput Sequencing (Deep sequencing)

## Genome-in-a-day dataset



# Cost of Whole Genome Sequencing



## LETTERS

# The complete genome of an individual by massively parallel DNA sequencing

David A. Wheeler<sup>1\*</sup>, Maithreyan Srinivasan<sup>2\*</sup>, Michael Egholm<sup>2\*</sup>, Yufeng Shen<sup>1\*</sup>, Lei Chen<sup>1</sup>, Amy McGuire<sup>3</sup>, Wen He<sup>2</sup>, Yi-Ju Chen<sup>2</sup>, Vinod Makhijani<sup>2</sup>, G. Thomas Roth<sup>2</sup>, Xavier Gomes<sup>2</sup>, Karrie Tartaro<sup>2†</sup>, Faheem Niazi<sup>2</sup>, Cynthia L. Turcotte<sup>2</sup>, Gerard P. Irzyk<sup>2</sup>, James R. Lupski<sup>4,5,6</sup>, Craig Chinault<sup>4</sup>, Xing-zhi Song<sup>1</sup>, Yue Liu<sup>1</sup>, Ye Yuan<sup>1</sup>, Lynne Nazareth<sup>1</sup>, Xiang Qin<sup>1</sup>, Donna M. Muzny<sup>1</sup>, Marcel Margulies<sup>2</sup>, George M. Weinstock<sup>1,4</sup>, Richard A. Gibbs<sup>1,4</sup> & Jonathan M. Rothberg<sup>2†</sup>

The association of genetic variation with disease and drug response, and improvements in nucleic acid technologies, have given great optimism for the impact of 'genomic medicine'. However, the formidable size of the diploid human genome<sup>1</sup>, approximately 6 gigabases, has prevented the routine application of sequencing methods to deciphering complete individual human genomes. To realize the full potential of genomics for human health, this limitation must be overcome. Here we report the DNA sequence of a diploid genome of a single individual, James D. Watson, sequenced to 7.4-fold redundancy in two months using massively parallel sequencing in picolitre-size reaction vessels. This

ditional genomic sequencing. This is the first genome sequenced by next-generation technologies. Therefore it is a pilot for the future challenges of 'personalized genome sequencing'.