Bioquímica Estrutural:

Estudo da estrutura das moléculas biológicas e dos princípios que a regem.

(~ **Biologia Estrutural**)

Macromoléculas biológicas

- **DNA:** repositório da informação genética na maioria dos organismos vivos
- **RNA:** transferência (e repositório) de informação genética, matriz para a síntese proteica, funções estruturais, etc...
- **Proteínas:** componentes estruturais (pele, ossos, músculo, cabelo, etc...), catálise de reacções bioquímicas (enzimas), transmissão de sinais, regulação, transdução de energia, etc.,etc., etc.!..
- **Lípidos:** componentes essenciais das membranas biológicas, sinalização
- **Polissacáridos:** armazenamento de energia, função estrutural

Sequência

Estrutura

Função

Fluxo de informação biológica

Gene ...TTAATAAGT...

⇩ transcrição

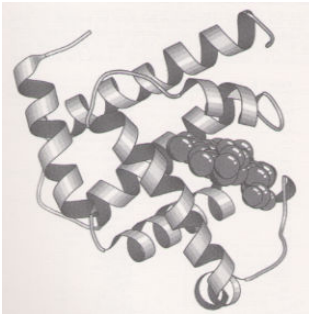
m-RNA ...UUAAUAAGU...

⇩ splicing, tradução

cadeia polipeptídica ...LISVHDN...

⇩ modificações pós-translacionais

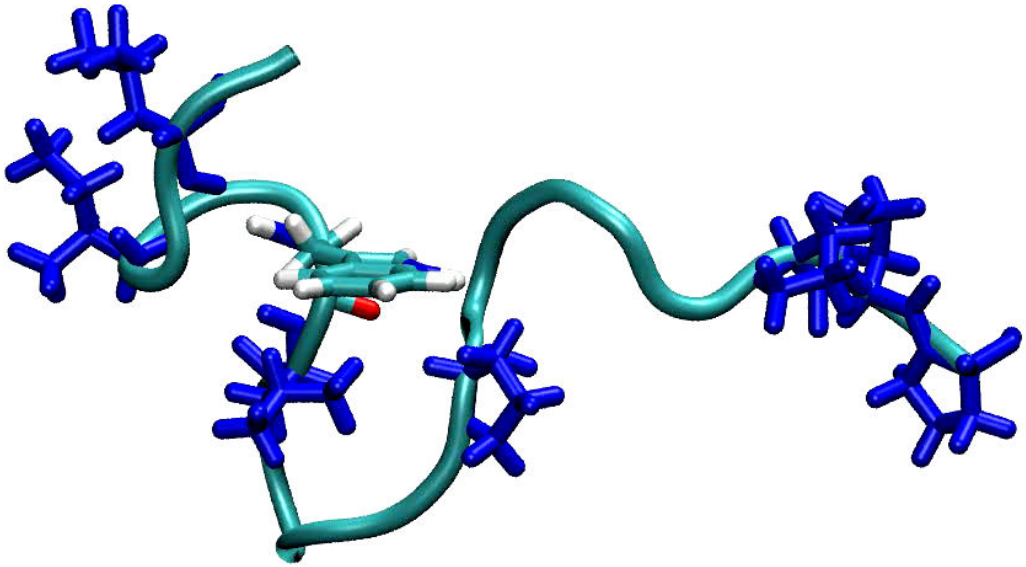
proteína



Dogma central da biologia molecular

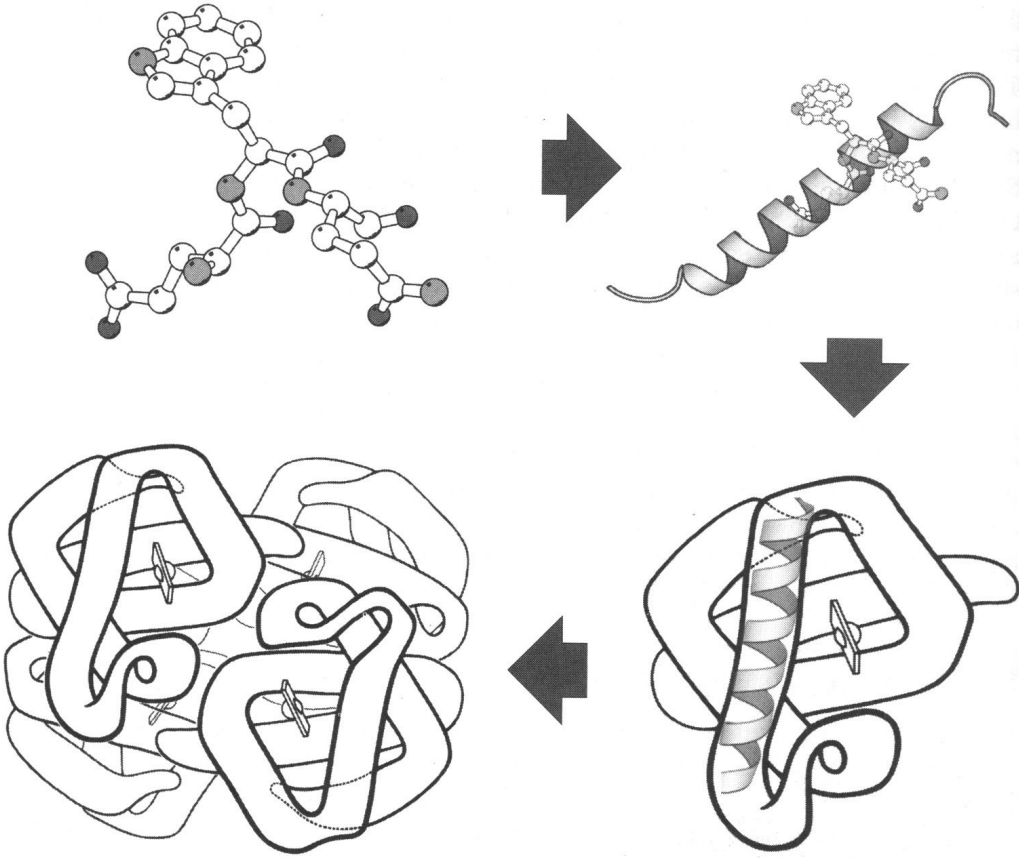
Excepções: vírus de RNA, priões, ribozimas (?)

Sequência->Estrutura

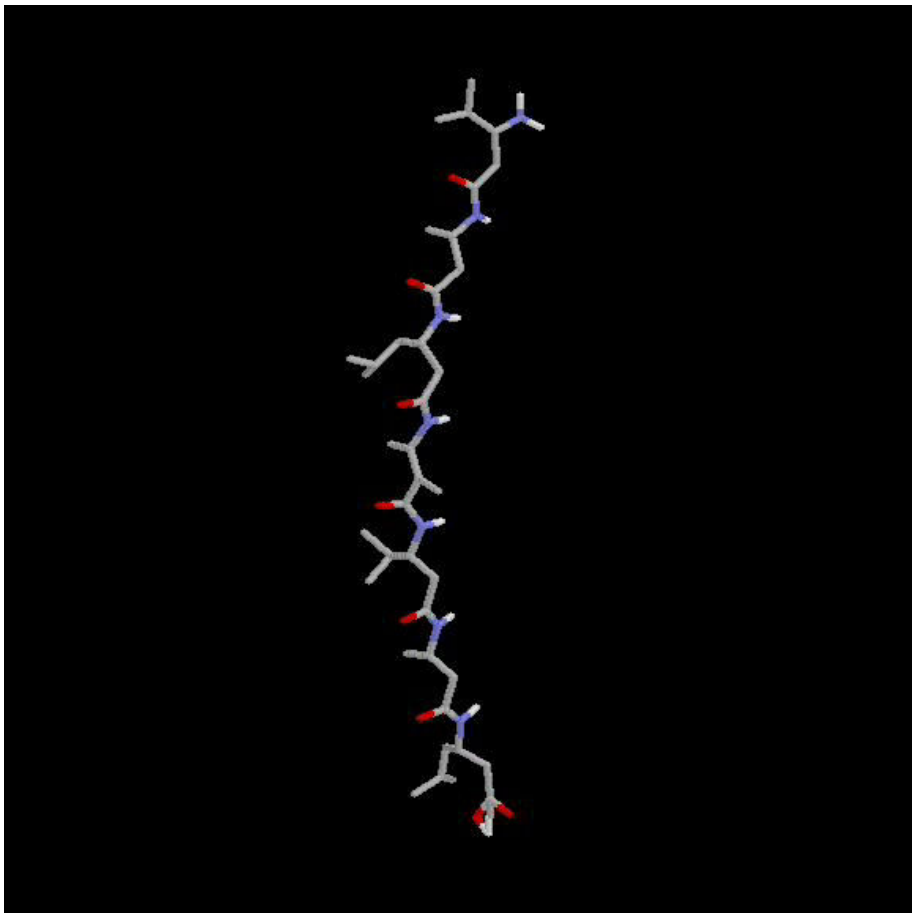


Muitas protéinas adquirem a sua estrutura tridimensional *espontâneamente (folding)*

Níveis de organização da estrutura

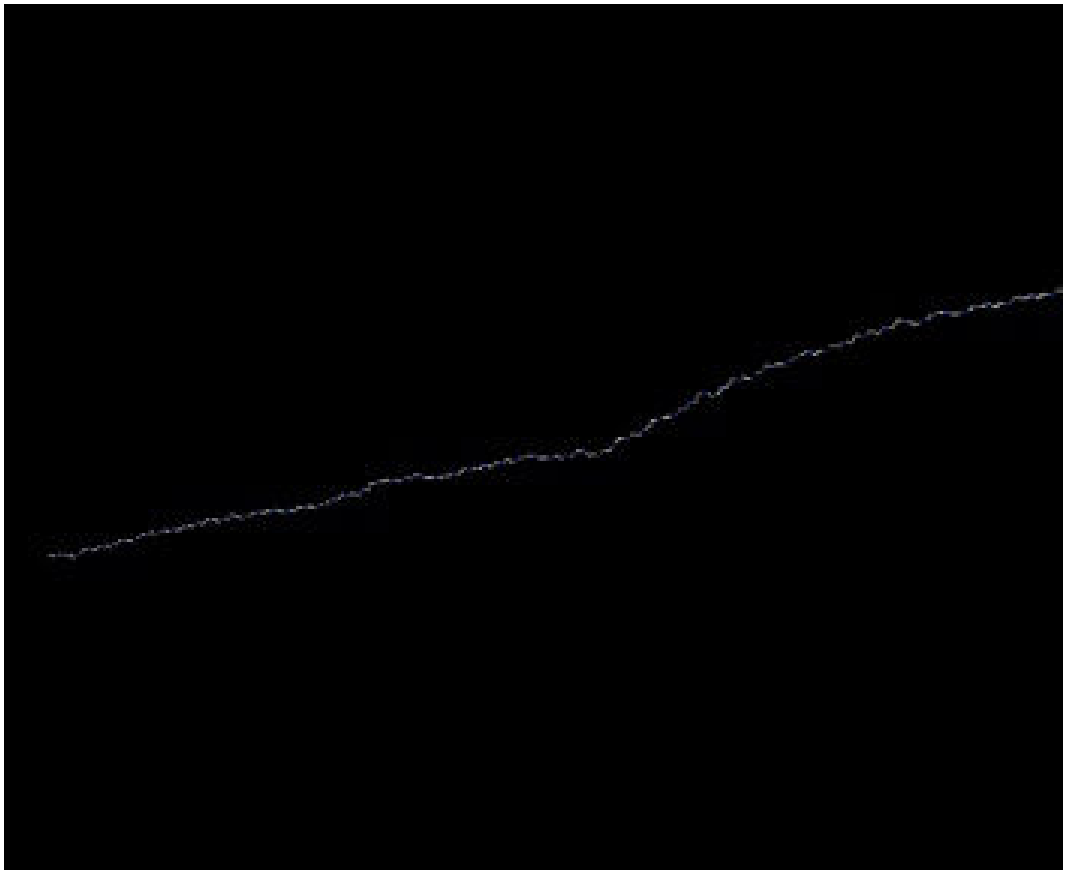


Formação hierárquica da estrutura



Formação espontânea de uma hélice α
(simulação)

Formação hierárquica da estrutura



"Simulação" do *folding* ubiquitina

De onde provêm a informação estrutural ?

Combinação de vários tipos de conhecimento:

- Teoria da ligação química

- Geometria de moléculas pequenas

- Métodos experimentais para a determinação da estrutura de biomoléculas:
    - Cristalografia de raios X
    - Ressonância Mag. Nuclear
    - Outros métodos

Que informação temos disponível ?

Número de estruturas tridimensionais (coordenadas atómicas):

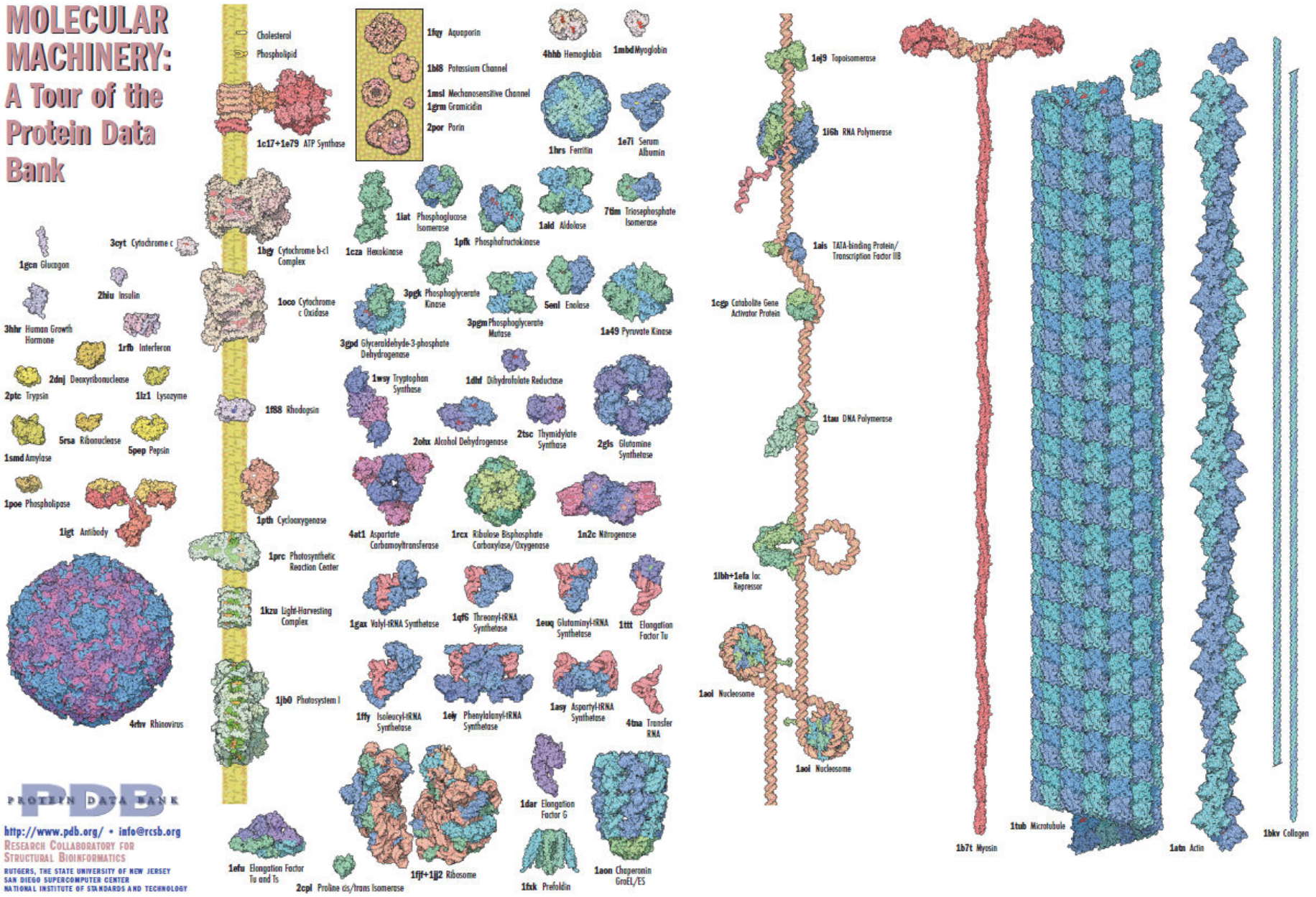
- 35767 proteínas
- 1579 complexos ácidos nucleíco-proteína
- 1671 ácidos nucleícos
- 18 glícidos

Total: 39051 estruturas

Métodos experimentais de determinação da estrutura:

- X-ray: 33126
- NMR: 5707
- Microscopia: 134
- Outros: 84

MOLECULAR MACHINERY: A Tour of the Protein Data Bank



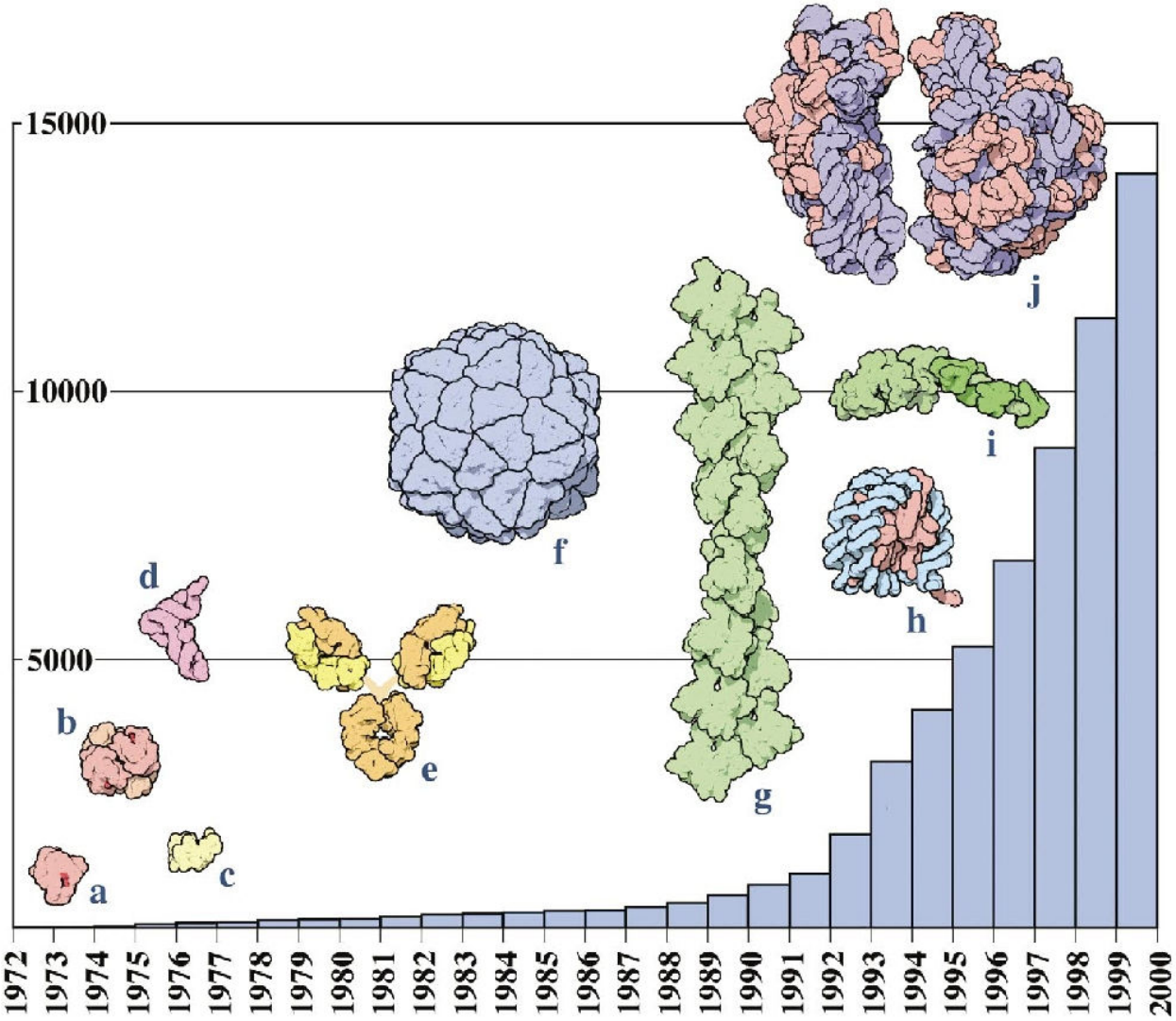
PROTEIN DATA BANK

http://www.pdb.org/ • info@rcsb.org

RESEARCH COLLABORATORY FOR STRUCTURAL BIOINFORMATICS

RUTGERS, THE STATE UNIVERSITY OF NEW JERSEY
SAN DIEGO SUPERCOMPUTER CENTER
NATIONAL INSTITUTE OF STANDARDS AND TECHNOLOGY

Crescimento do Protein Data Bank



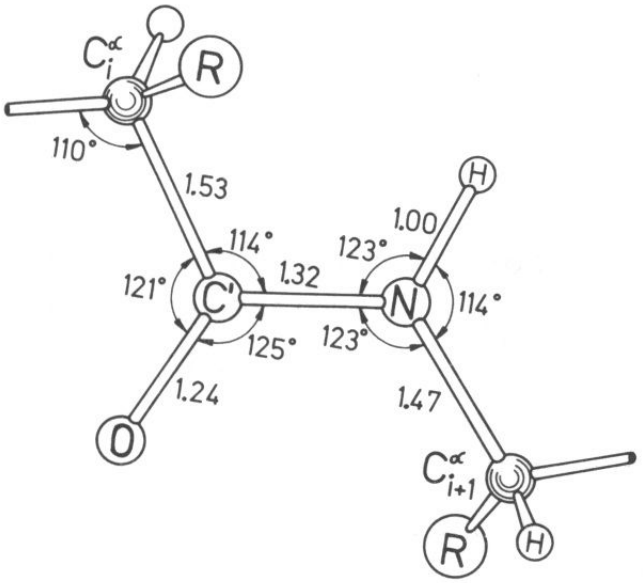
Princípios que regem a estrutura das biomoléculas

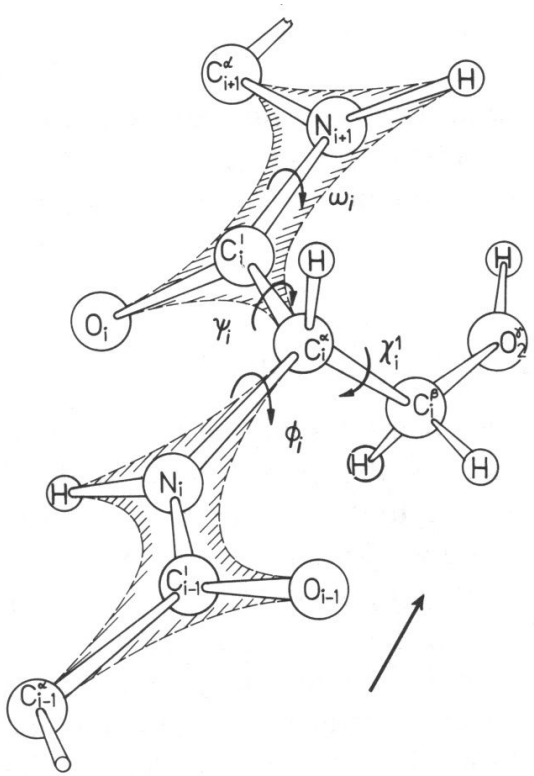
"Perhaps the most remarkable features of the molecule are its *complexity* and *lack of symmetry*. The arrangment seems to be almost totally lacking the kind of regularities wich one instinctively antecipates and it is more complicated than has been predicted by any theory of protein protein structure"

J.C. Kendrew *et al.*, 1958

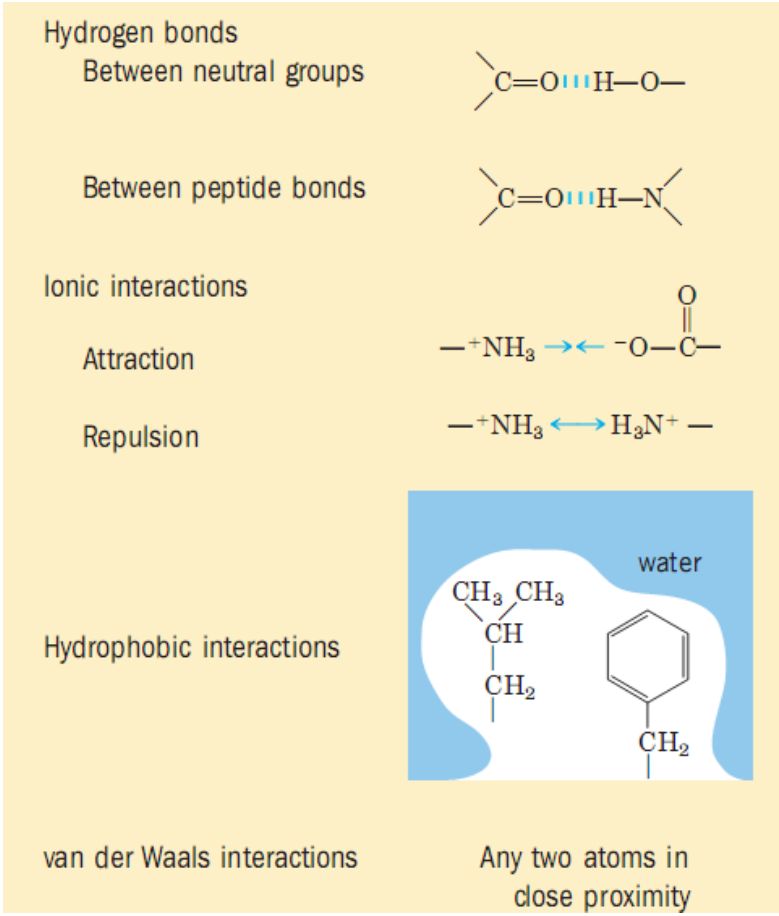
• As macromoléculas biológicas parece, numa primeira análise, distanciar-se dos princípios simples de geometria e simetria que sabemos reger a estrutura das moléculas pequenas.

- Ligações covalentes, geometria molecular:

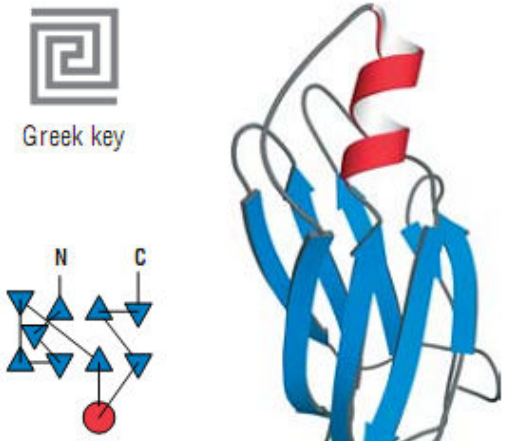


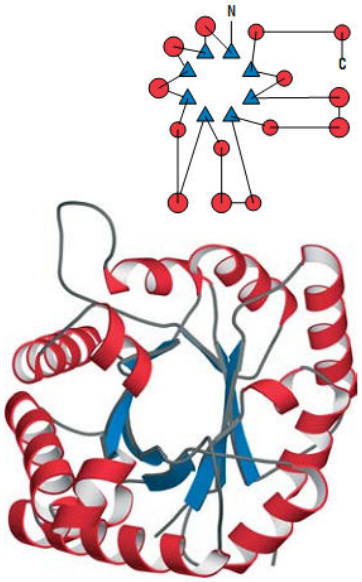


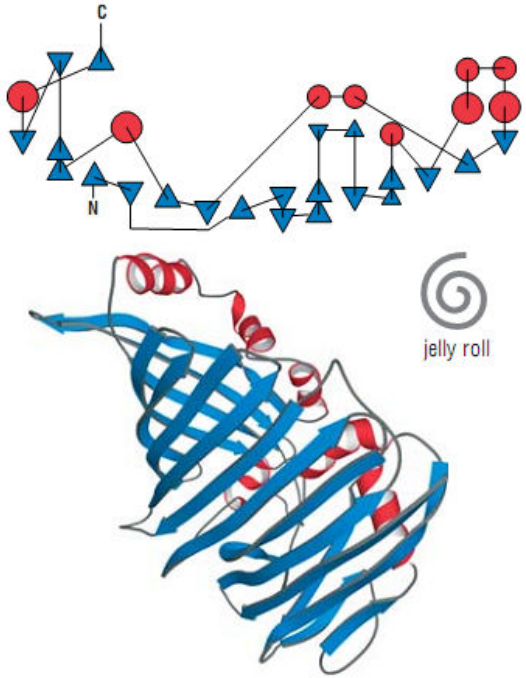
- Interacções não-covalentes:



- Princípios arquitectónicos



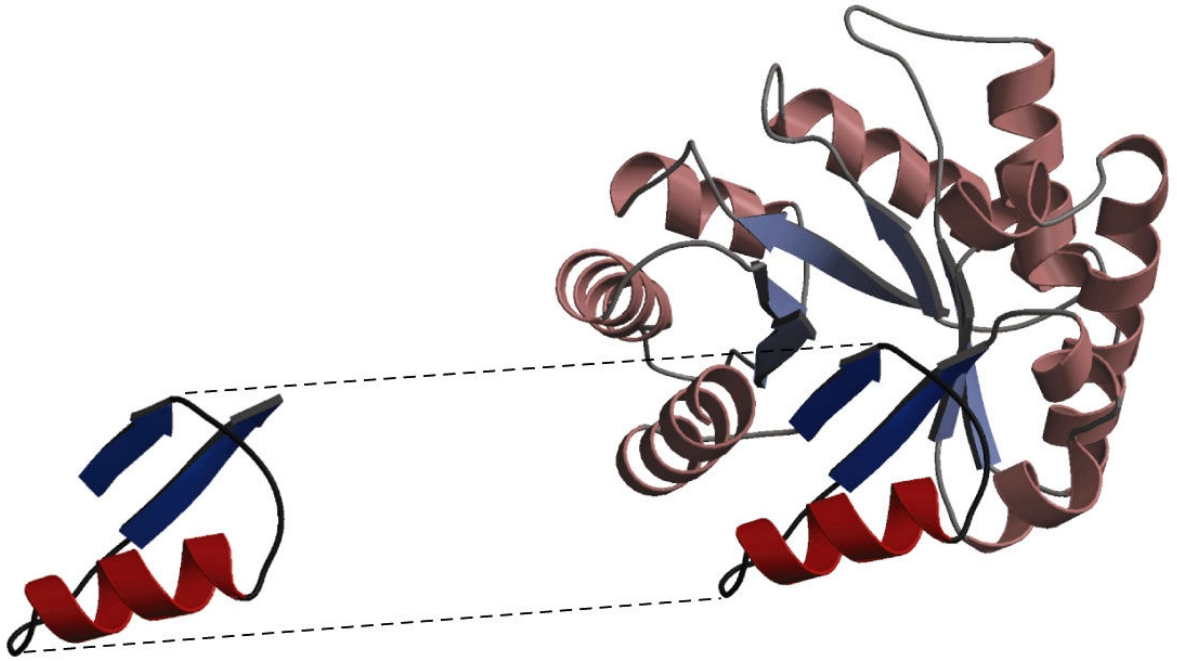




...

Recorrência de padrões estruturais na arquitectura das biomoléculas.

- Princípios arquitectónicos (cont.):

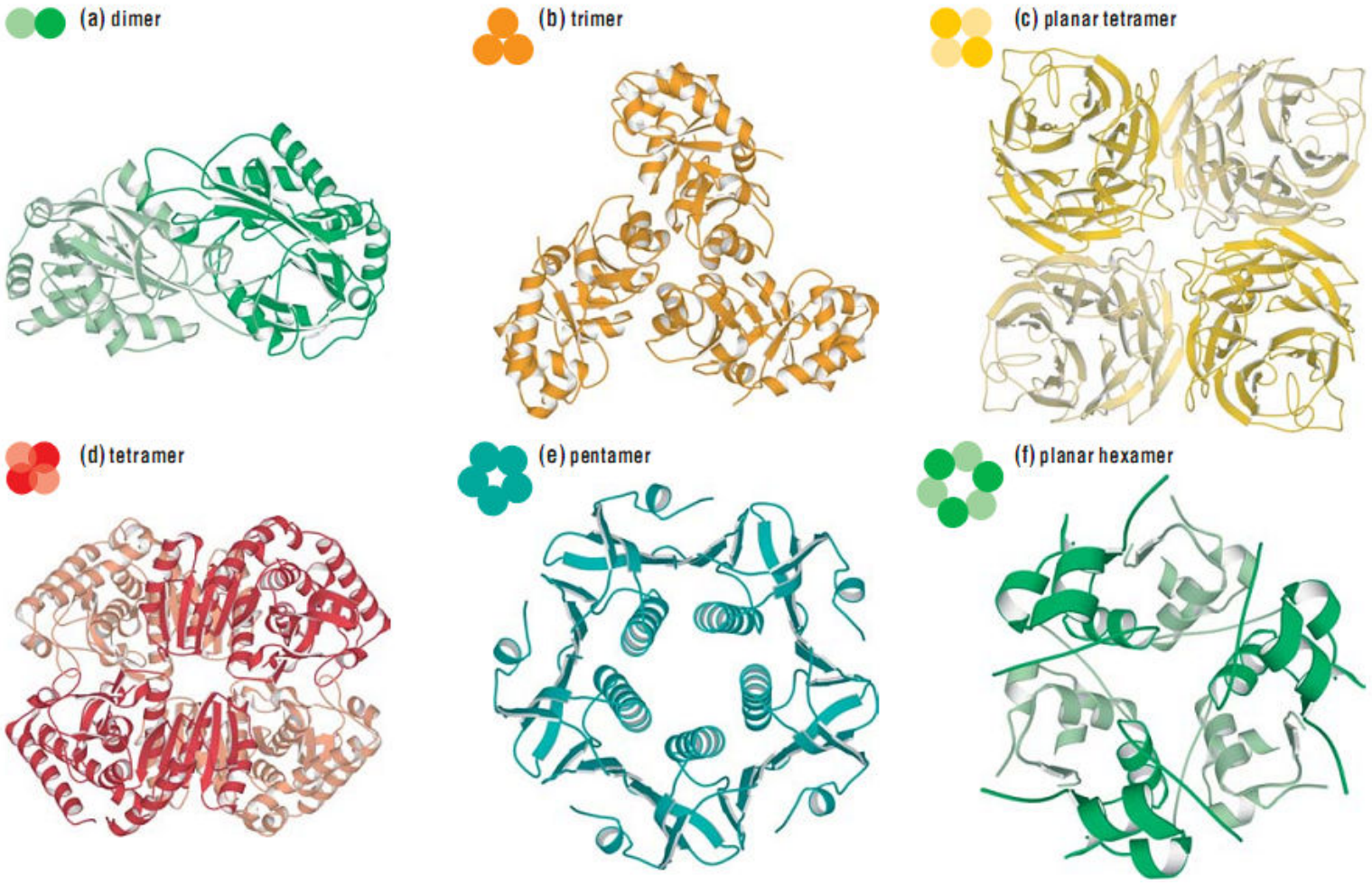


loop β-α-β

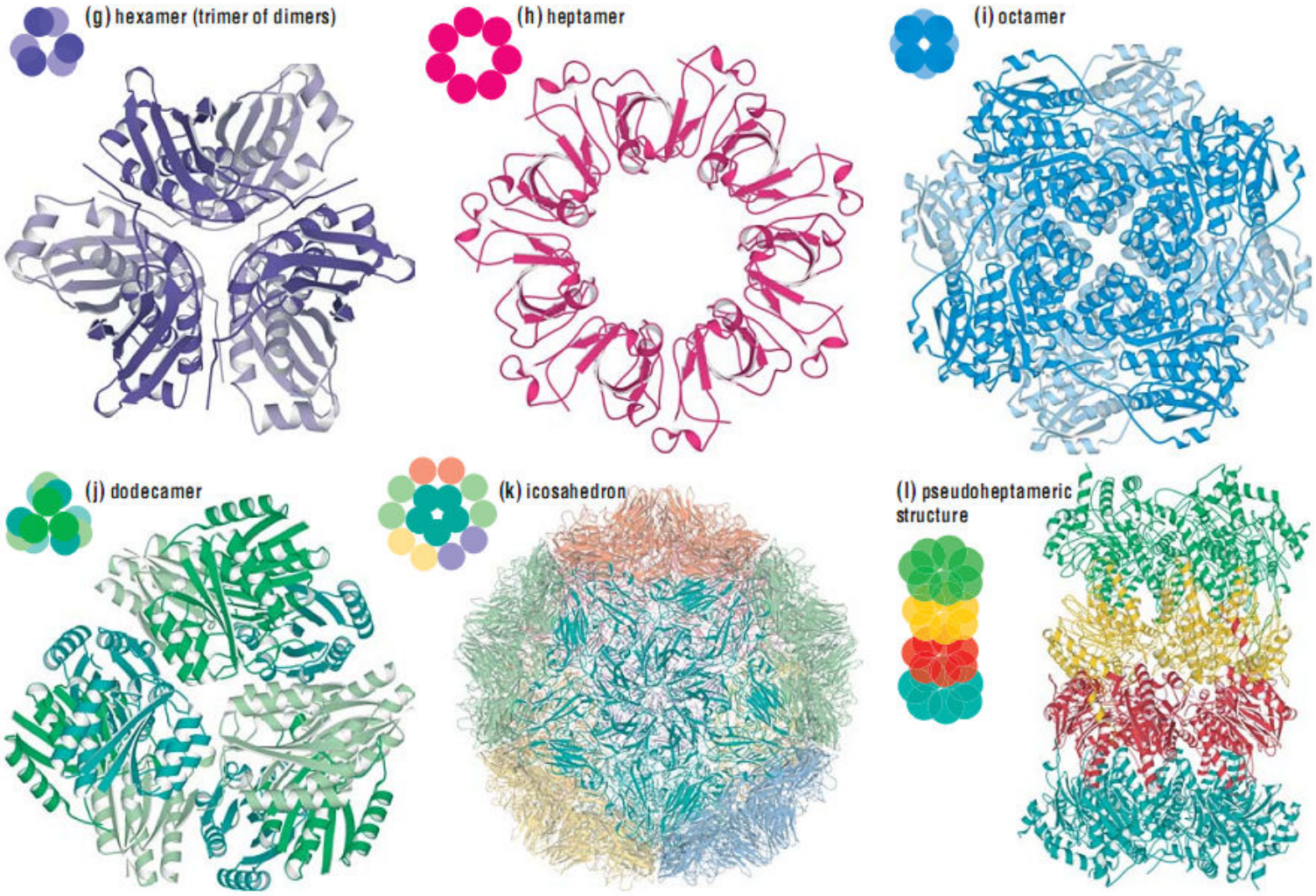
"barril" α/β

Formação de estruturas a partir da associação de unidades estruturais

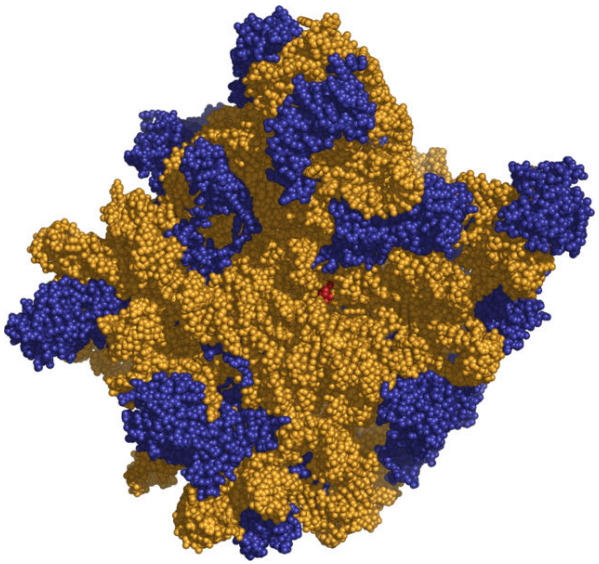
- Oligomerização:



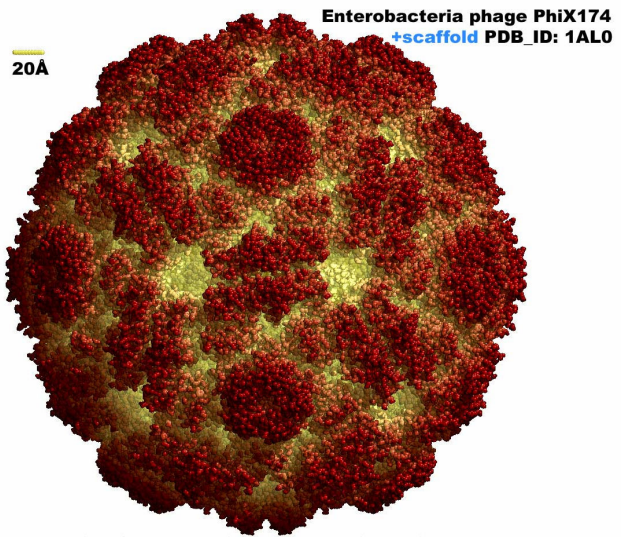
- Oligomerização(cont.):



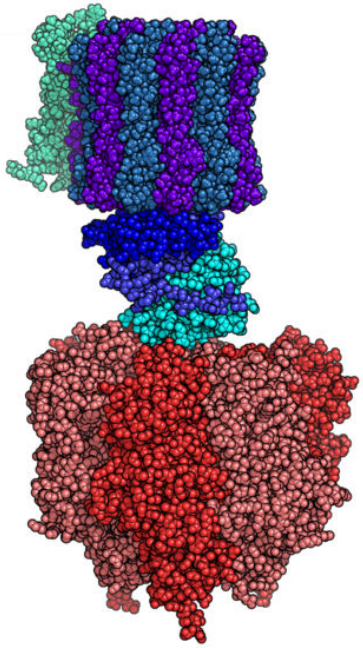
- Formação de estruturas supramacromoleculares



Ribossoma



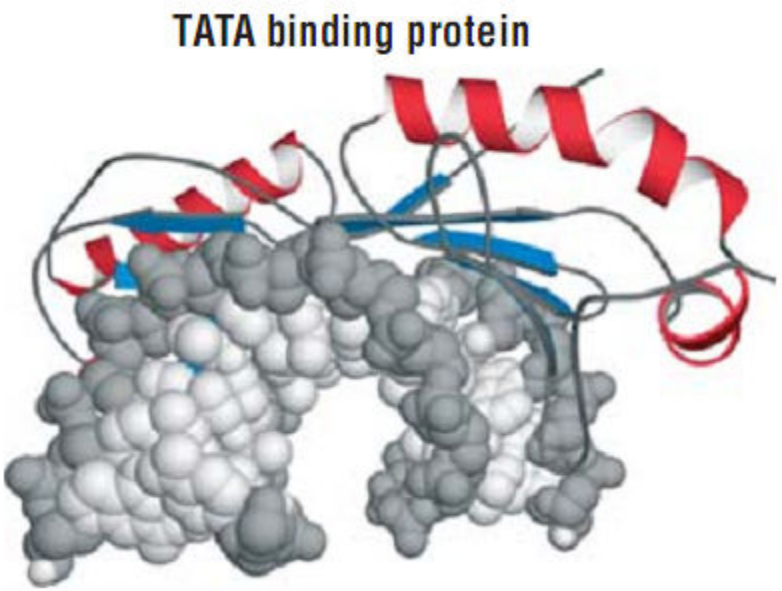
Vírus

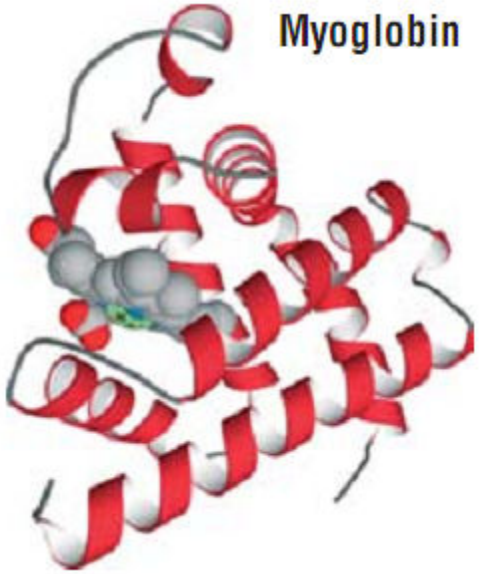


ATPase

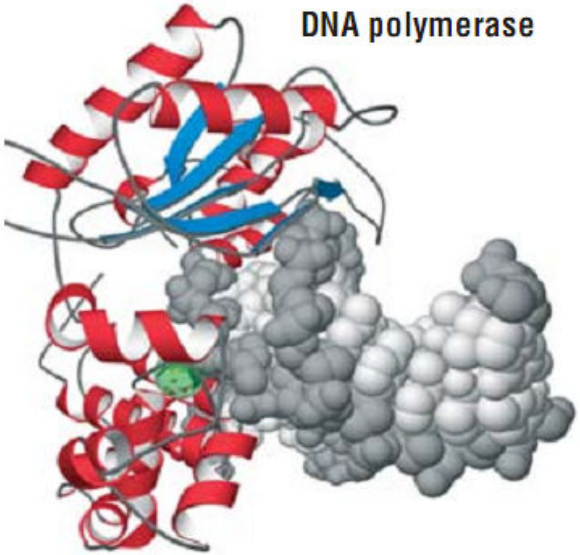
Função

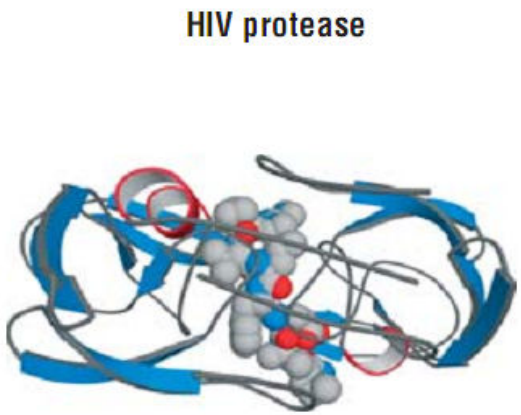
"Binding"



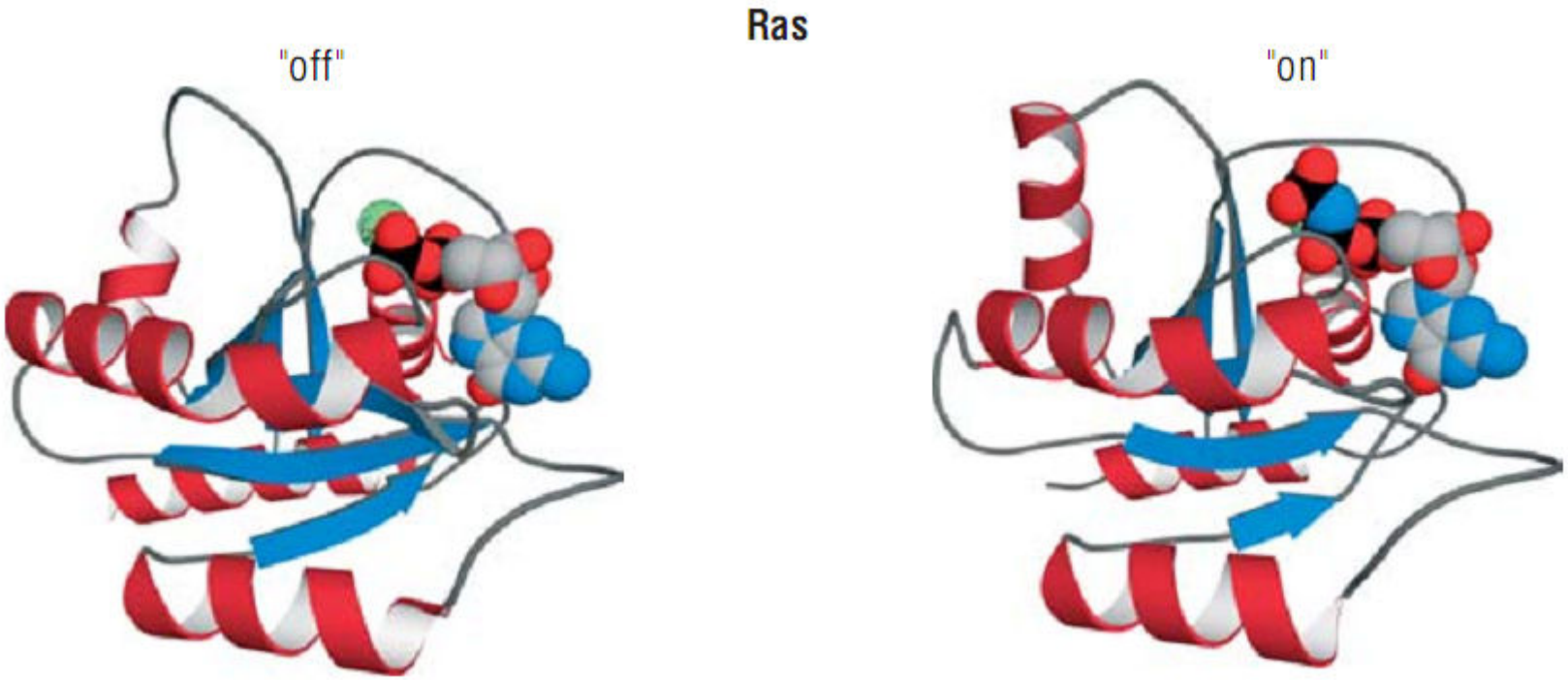


Catálise



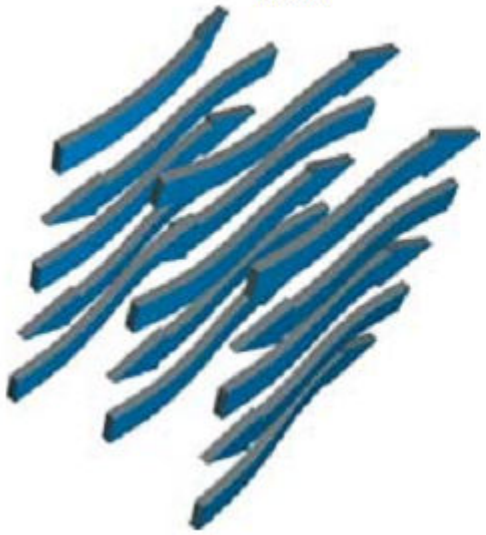


"Switching"

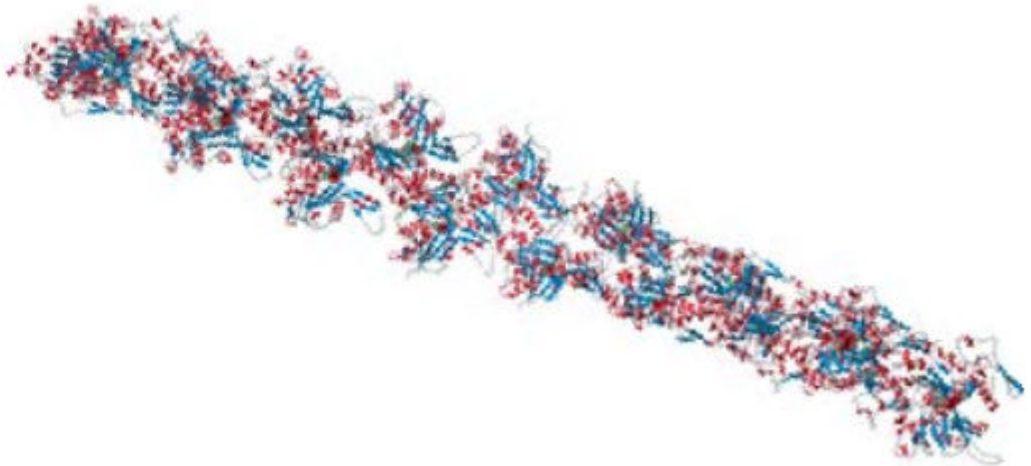


Estrutura

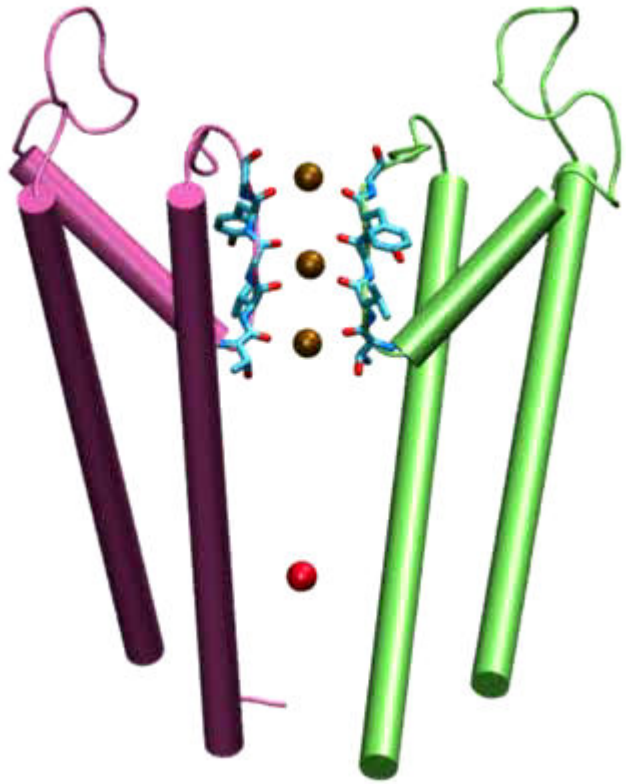
Silk



F-actin



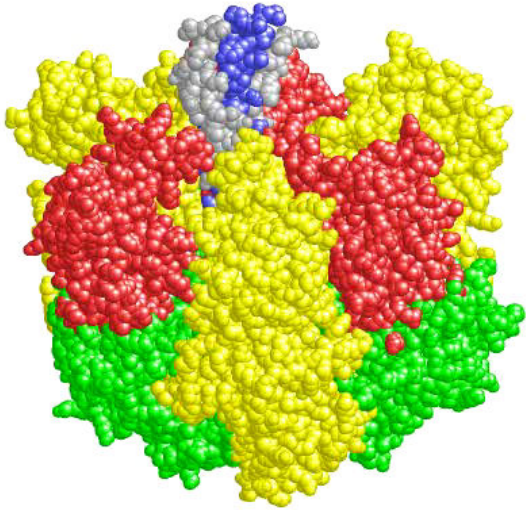
Permeabilidade

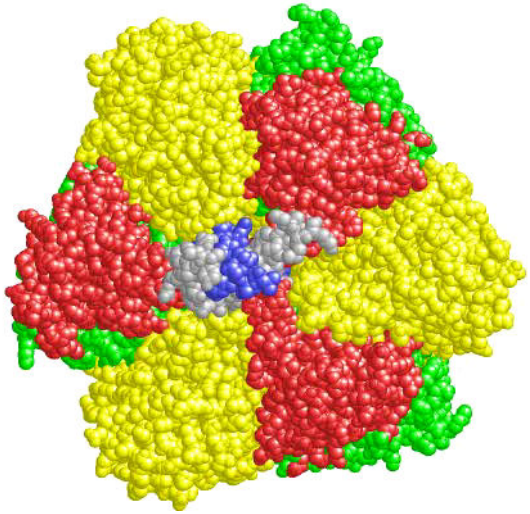


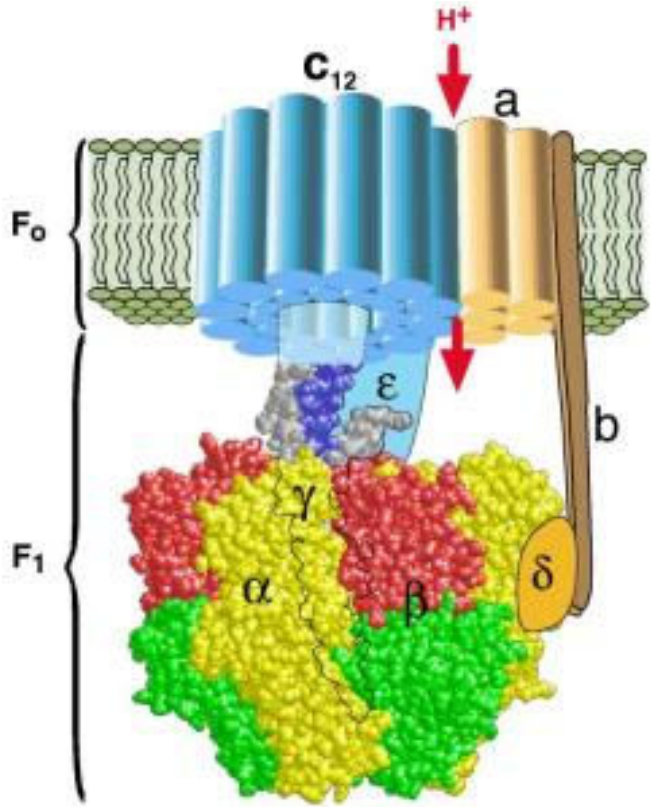
As macromoléculas biológicas funcionam como máquinas moleculares

Conversão de energia

ATPsintase

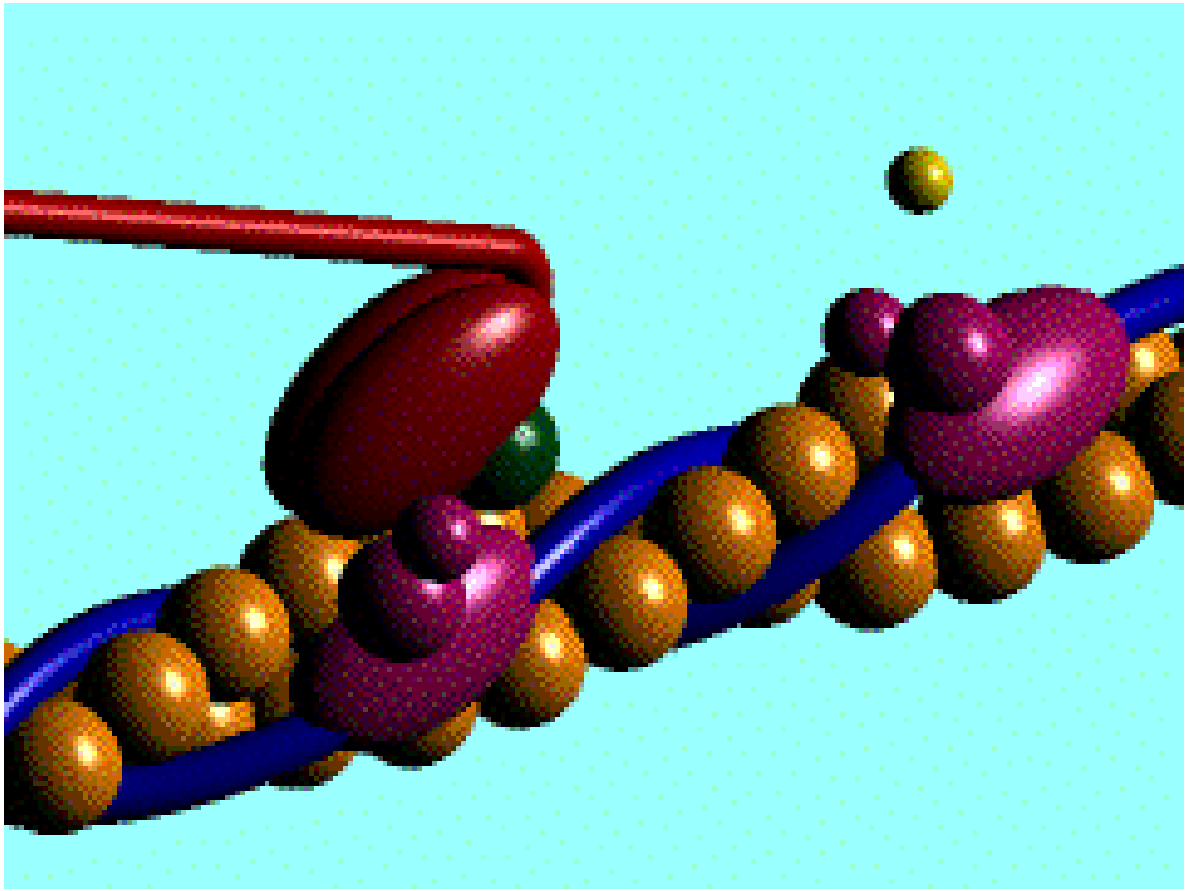






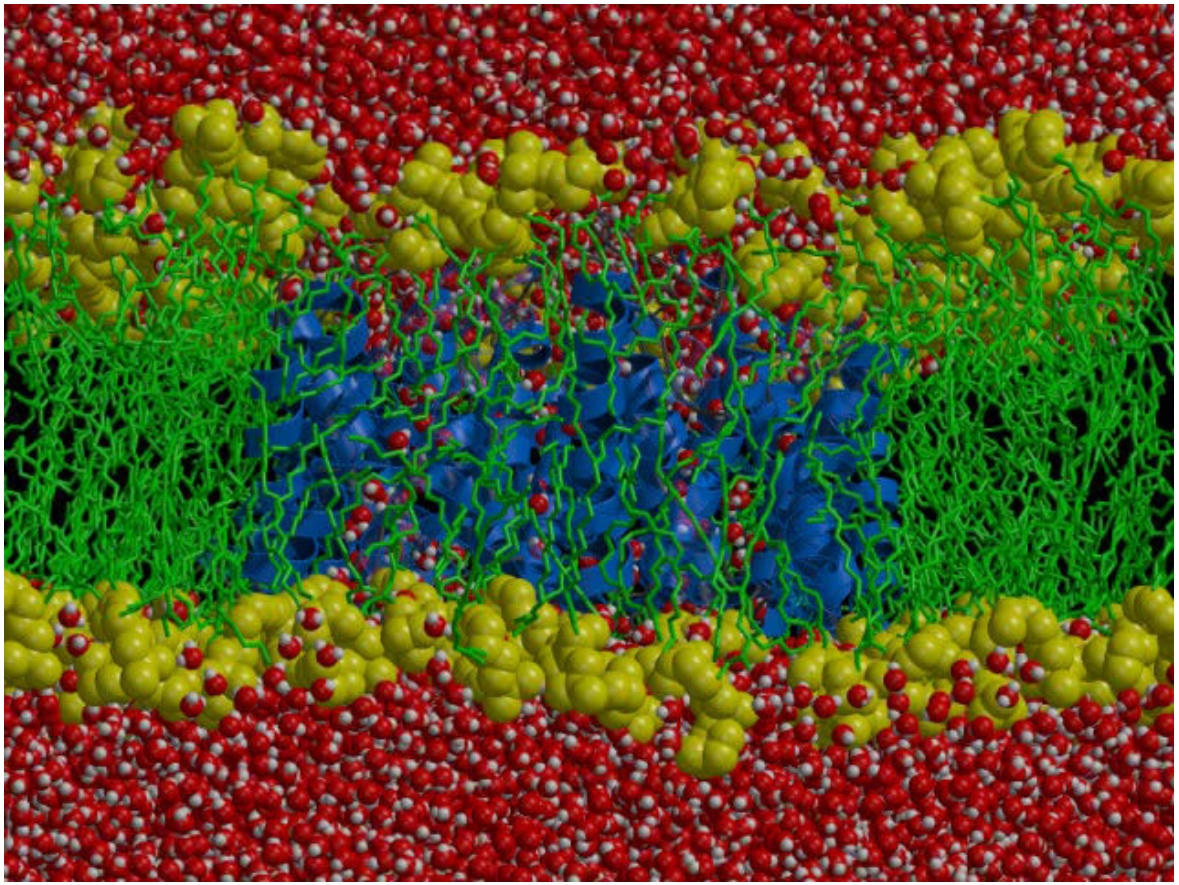
H. Wang and G. Oster (1998). Nature 396:279-282.

Motilidade



Actina+Miosina

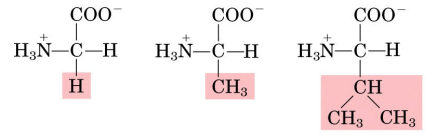
Compartimentação



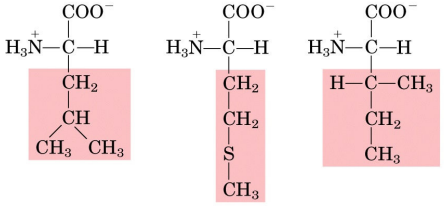
Membrana+aquaporina

Proteínas

Nonpolar, aliphatic R groups

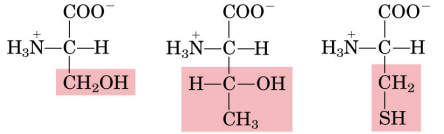


Glycine Alanine Valine

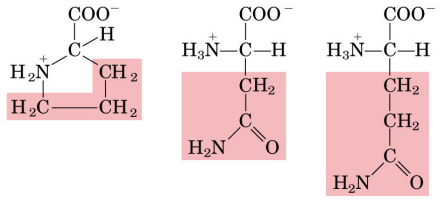


Leucine Methionine Isoleucine

Polar, uncharged R groups

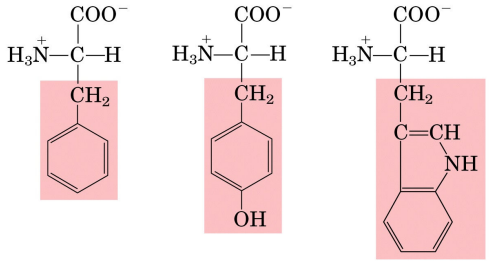


Serine Threonine Cysteine



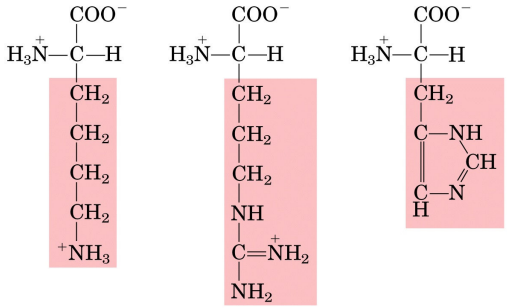
Proline Asparagine Glutamine

Aromatic R groups



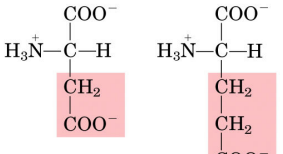
Phenylalanine Tyrosine Tryptophan

Positively charged R groups

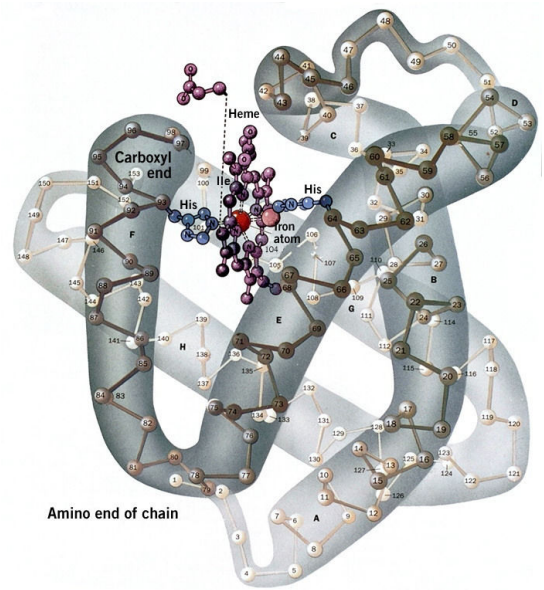


Lysine Arginine Histidine

Negatively charged R groups

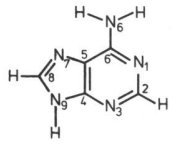


Aspartate Glutamate

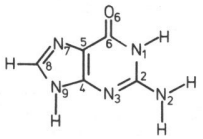


Mioglobina

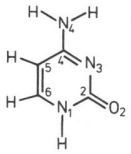
Ácidos nucleícos



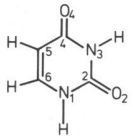
Adenine
Ade



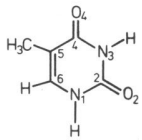
Guanine
Gua



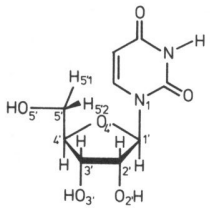
Cytosine
Cyd



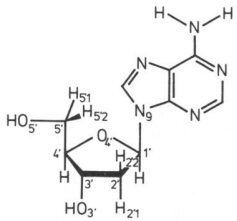
Uracil
Ura



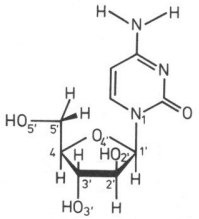
Thymine
Thy



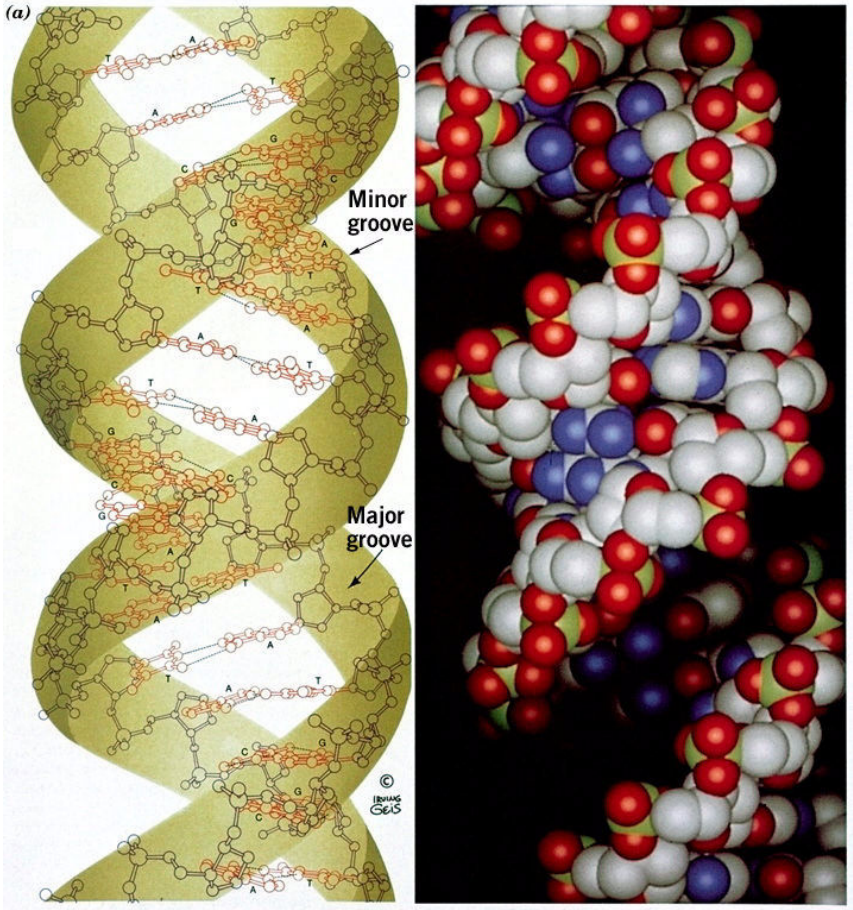
Uridine
Urd, U



Deoxyadenosine
dAdo, dA



Arabinocytidine
araCyd, araC



B-Dna