

Bioquímica Estrutural:

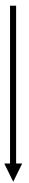
Estudo da estrutura das moléculas biológicas e dos princípios que a regem.

(~ Biologia Estrutural)

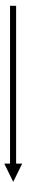
Macromoléculas biológicas

- **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

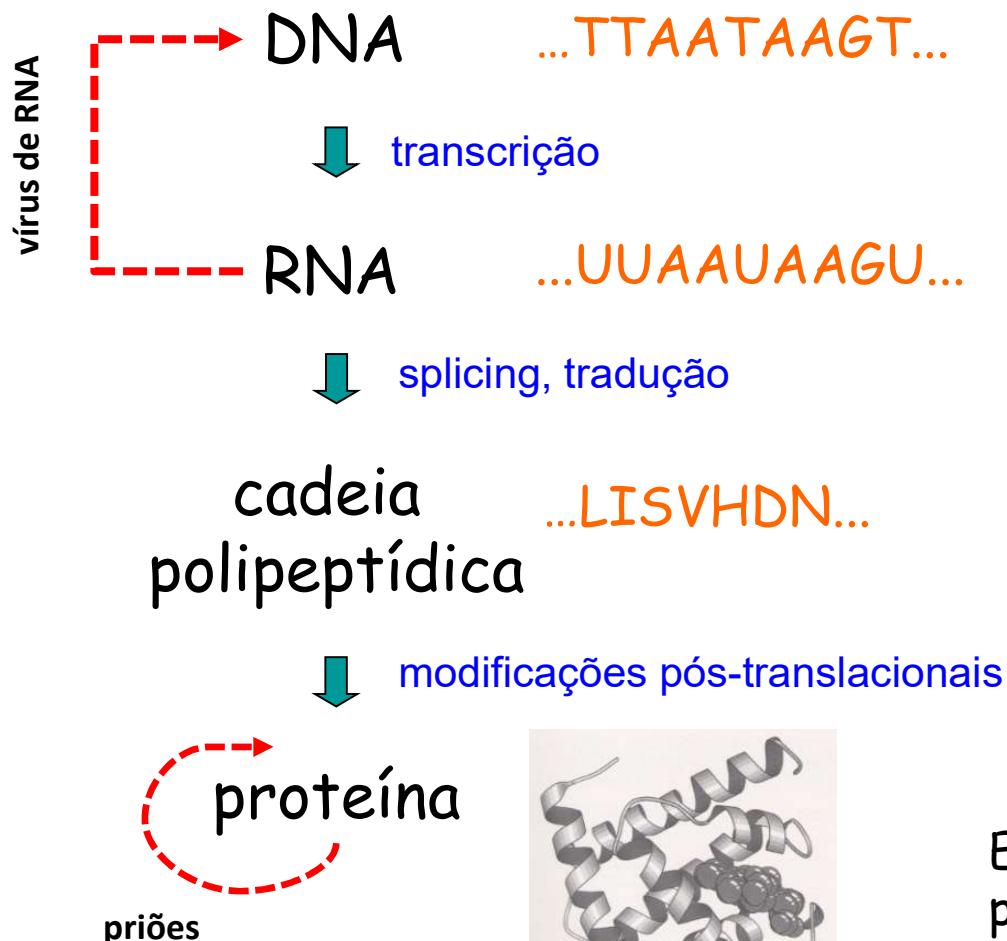


Estrutura

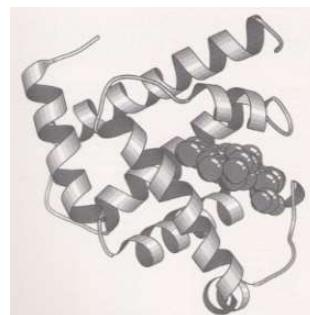


Função

Fluxo de informação biológica



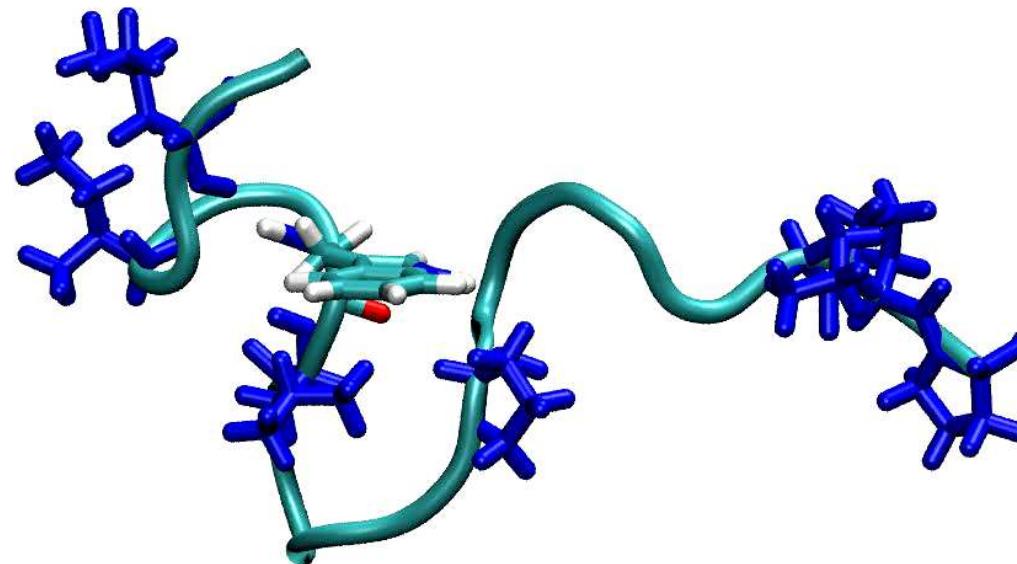
Dogma central da biologia molecular



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

Sequência->Estrutura

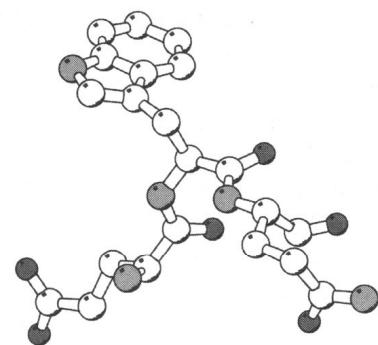
Folding da mini-proteína Trp-cage em solução aquosa:



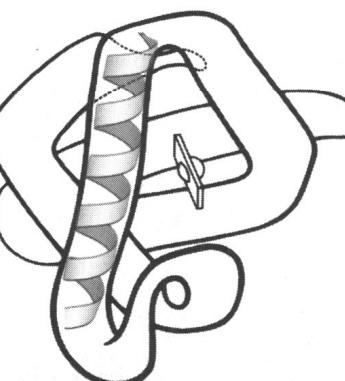
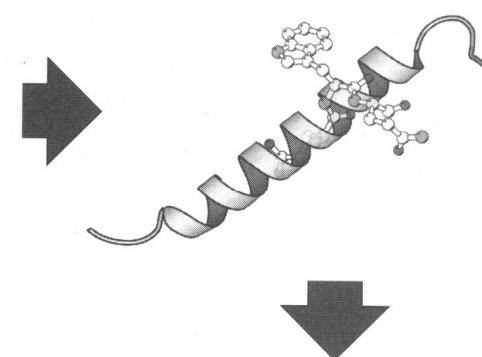
Muitas protéinas adquirem a sua estrutura tridimensional espontâneamente (*folding*)

Níveis de organização da estrutura das proteínas

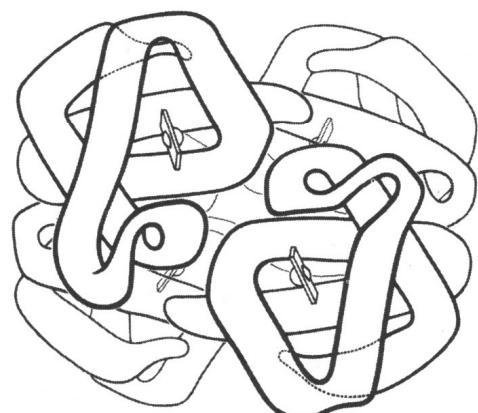
Estrutura primária



Estrutura secundária

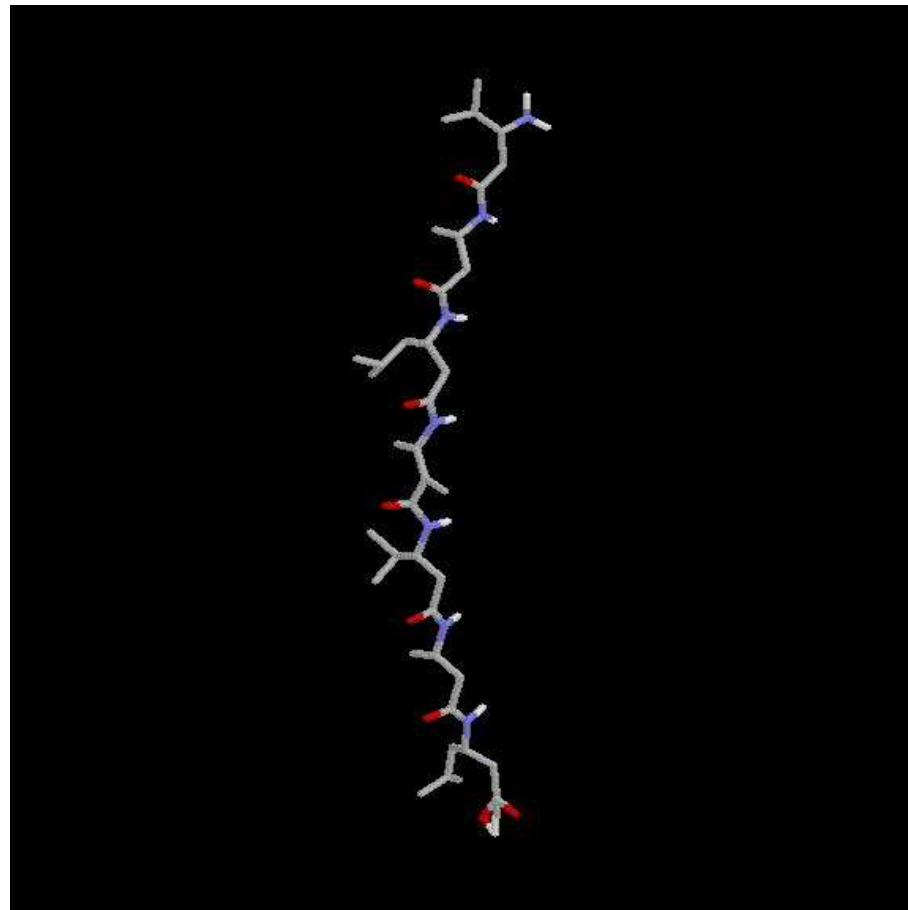


Estrutura quaternária



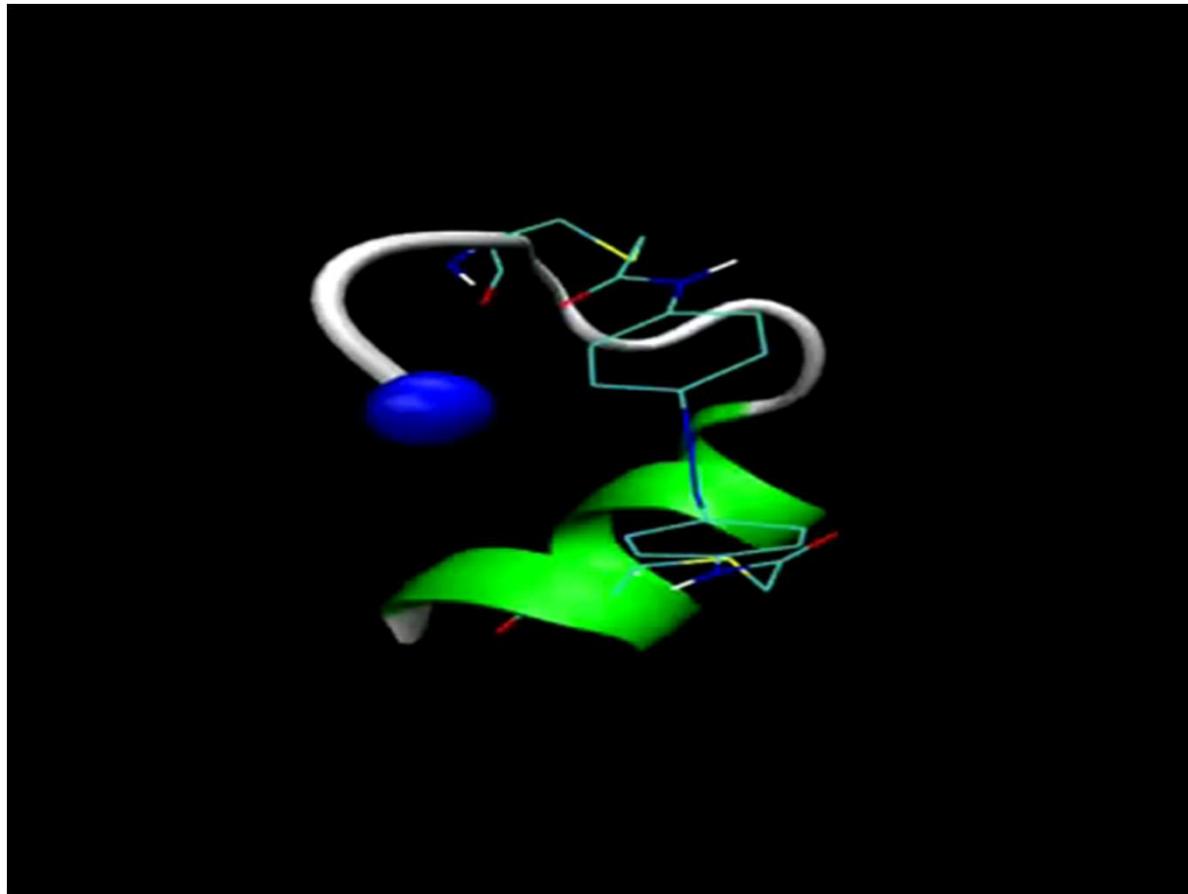
Estrutura terciária

Formação hierárquica da estrutura



Formação espontânea de uma hélice α
(simulação)

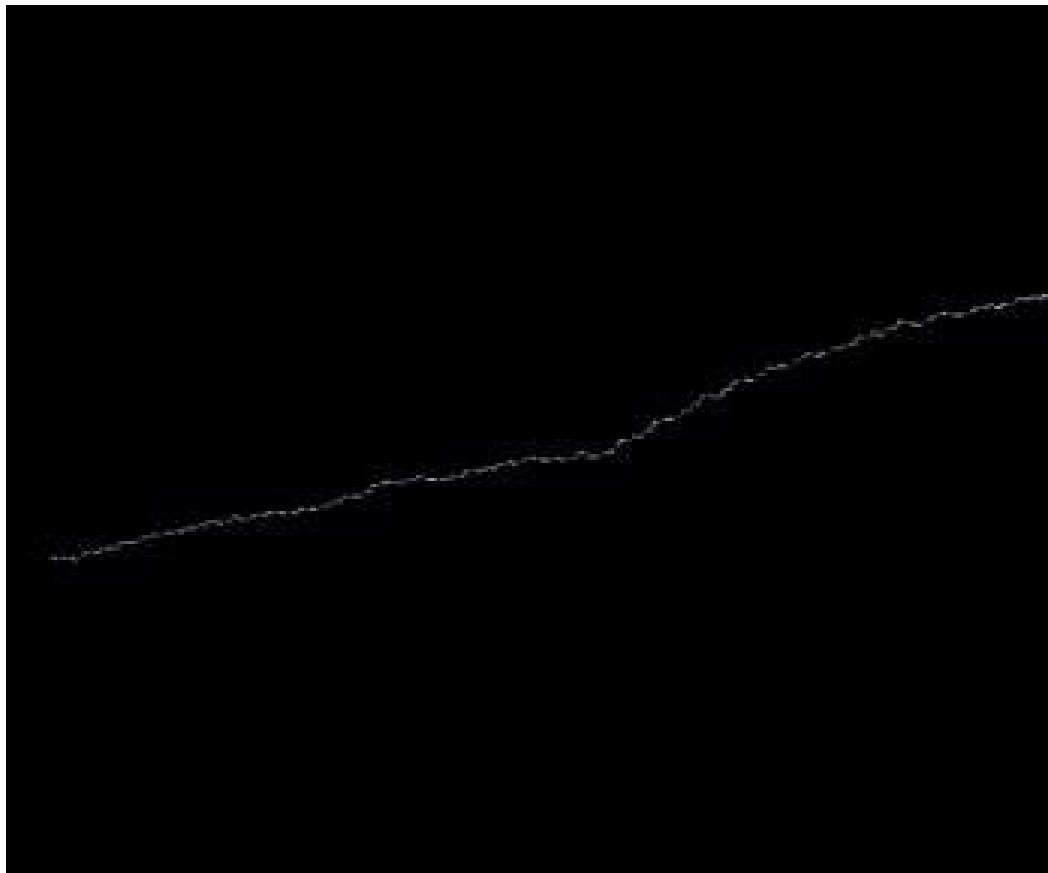
Formação hierárquica da estrutura



Formação espontânea de uma hélice α
(simulação)

Paoli *et al.* (2009) J.Chem.Phys. B 113:4335-4442

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:
 - ❖ Cristalografia de raios X
 - ❖ Ressonância Magnética Nuclear (NMR)
 - ❖ Outros métodos (microscopia electrónica, difracção de neutrões, etc...)

Que informação temos disponível ?

(dados do Protein Data Bank em **28/03/2021**)

Número de estruturas tridimensionais (coordenadas atómicas):

- Proteínas: 154160
- Ácidos Nucleícos: 3581
- Complexos ácido nucleíco-proteína: 9170
- Proteína/Oligossacárido: 8861
- Outros: 205

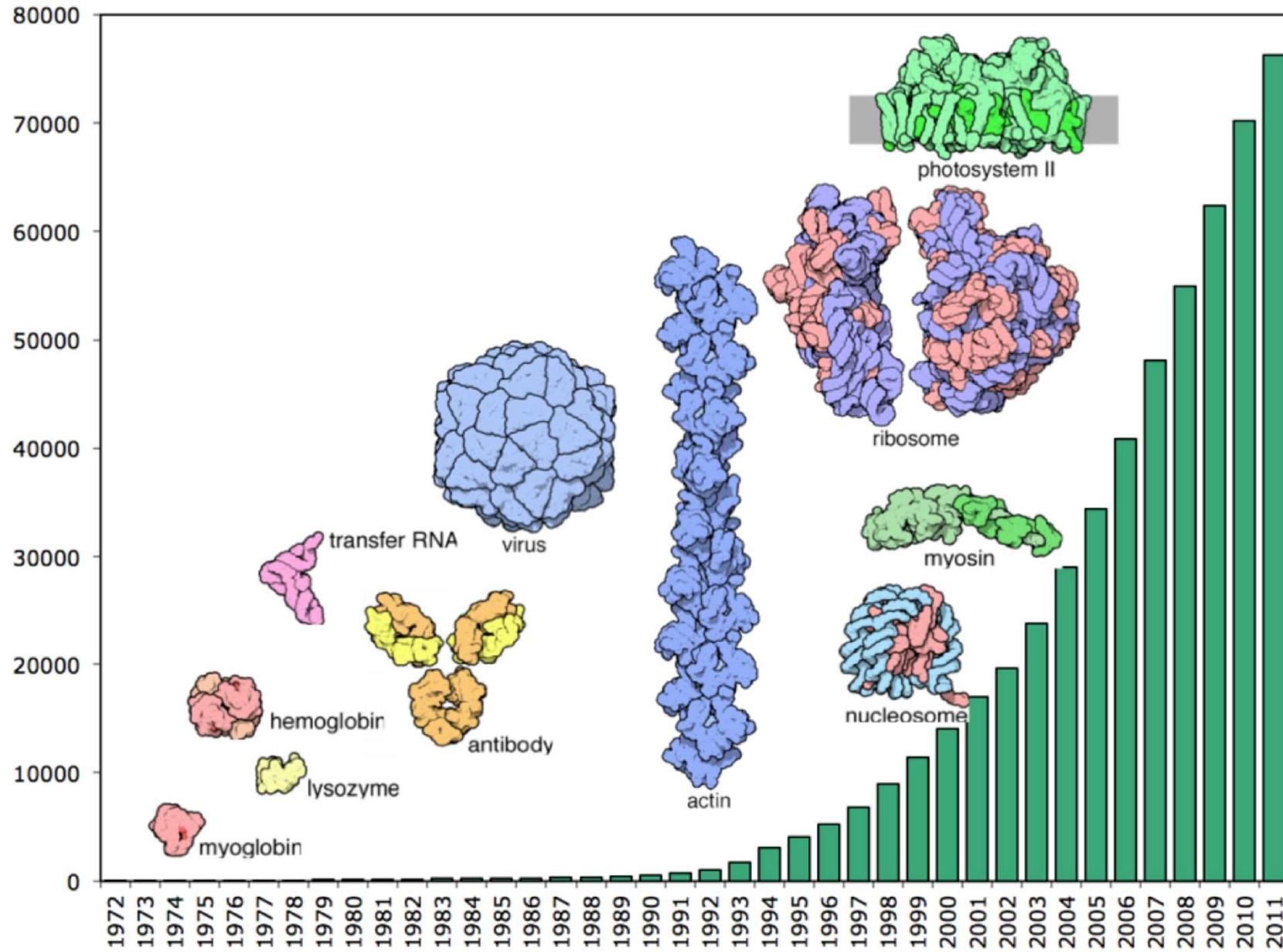
Total: 175977 estruturas

Métodos experimentais de determinação da estrutura:

- Cristalografia de raios X: 155122
- NMR em solução aquosa: 13326
- Microscopia electrónica: 7239
- Métodos híbridos: 184
- Outros: 106

<http://www.rcsb.org>

Progresso na determinação das estruturas



RCSB Protein Data Bank

www.rcsb.org/pdb/home/home.do

Apps Bookmarks D pmartel UALG Acad Drug Design Programming Bioinformatics Science Enzymology Other bookmarks

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RCSB PDB An Information Portal to 126447 Biological Macromolecular Structures

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PDB-101 Worldwide Protein Data Bank EMDDataBank NDB Structural Biology Knowledgebase Worldwide Protein Data Bank Foundation

f t y q

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A Structural View of Biology

This resource is powered by the Protein Data Bank archive-information about the 3D shapes of proteins, nucleic acids, and complex assemblies that helps students and researchers understand all aspects of biomedicine and agriculture, from protein synthesis to health and disease.

A Molecular View of HIV Therapy

2016 FASEB BioArt Wiener

January Molecule of the Month

Contact Us

Princípios que regem a
estrutura das biomoléculas

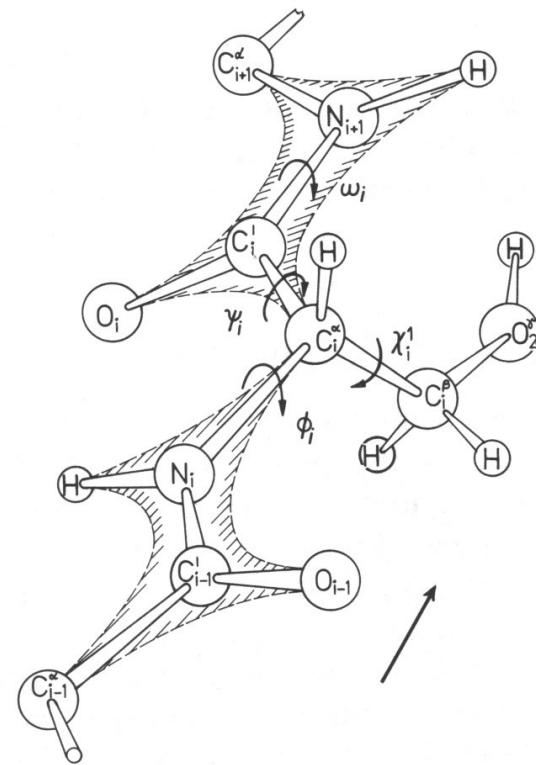
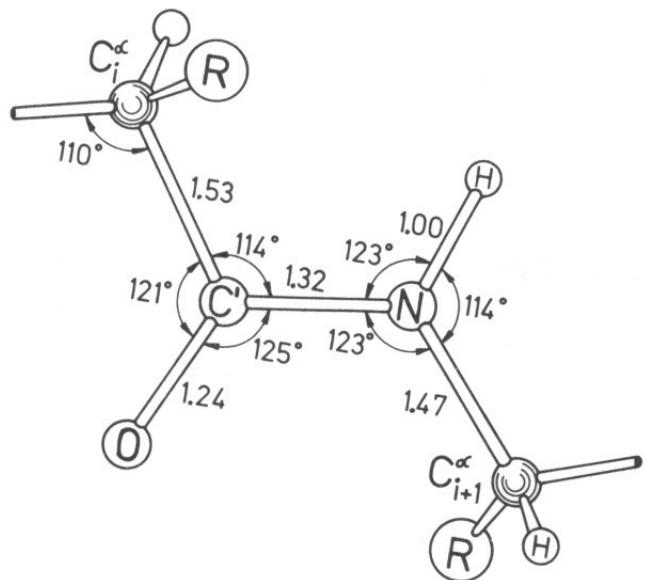
"Perhaps the most remarkable features of the molecule are its complexity and lack of symmetry. The arrangement seems to be almost totally lacking the kind of regularities which one instinctively anticipates and it is more complicated than has been predicted by any theory of protein structure"

J.C. Kendrew et al., 1958

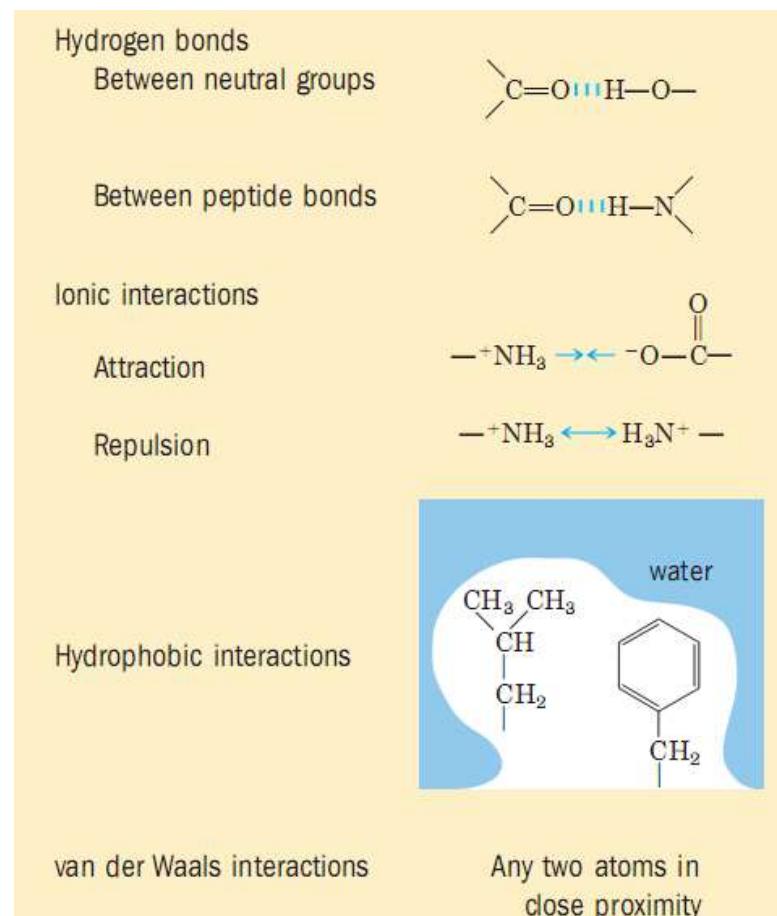


- As macromoléculas biológicas parecem, numa primeira análise, distanciar-se dos princípios simples de geometria e simetria que sabemos reger a estrutura das moléculas pequenas.

- Ligações covalentes, geometria molecular:



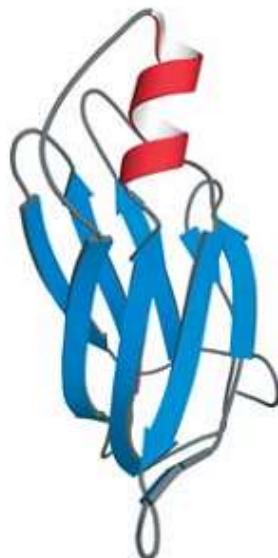
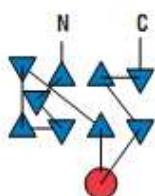
•Interacções não-covalentes:



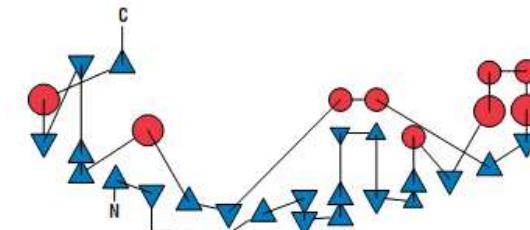
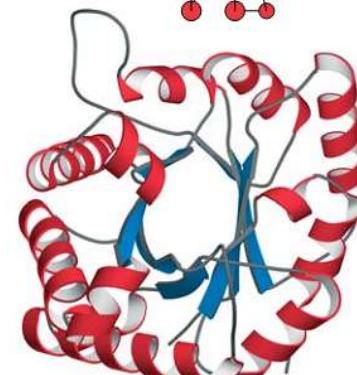
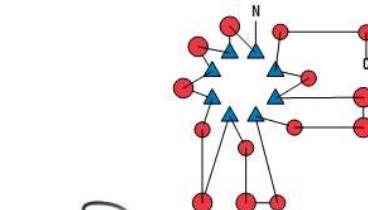
- Princípios arquitectónicos



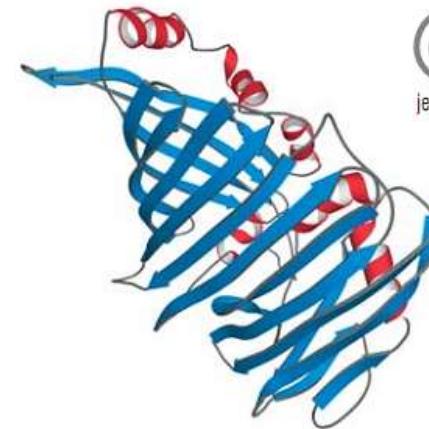
Greek key



...

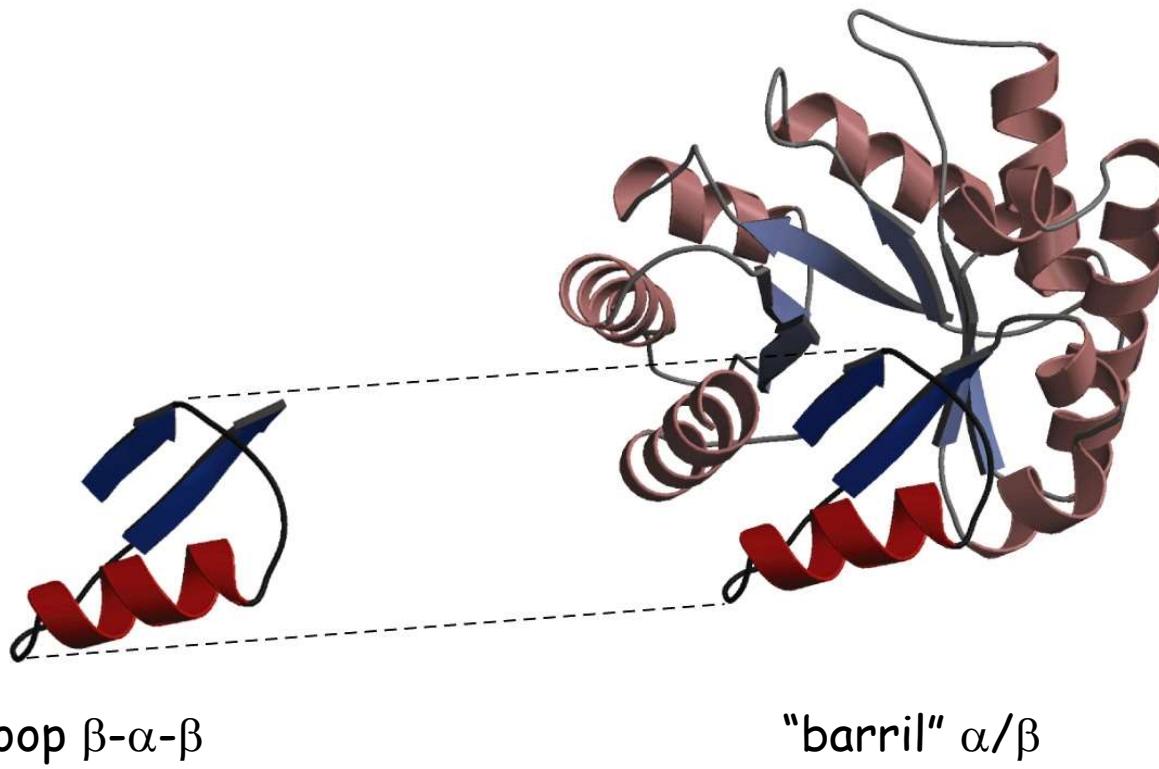


jelly roll



Recorrência de padrões estruturais na arquitectura das biomoléculas.

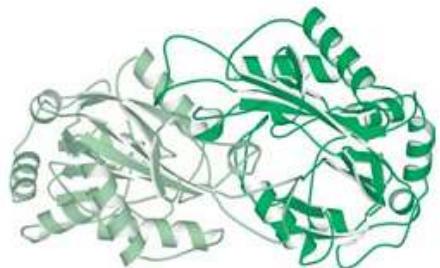
- Princípios arquitectónicos (cont.):



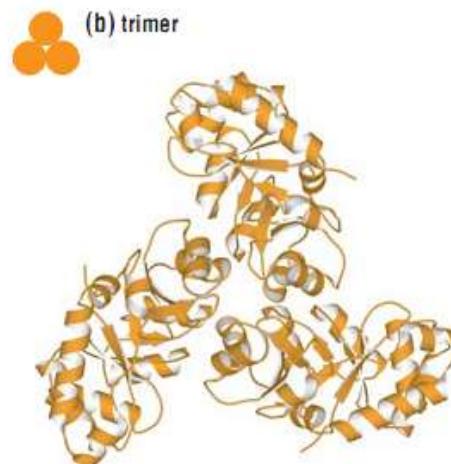
Formação de estruturas a partir da associação de unidades estruturais

- Oligomerização:

(a) dimer



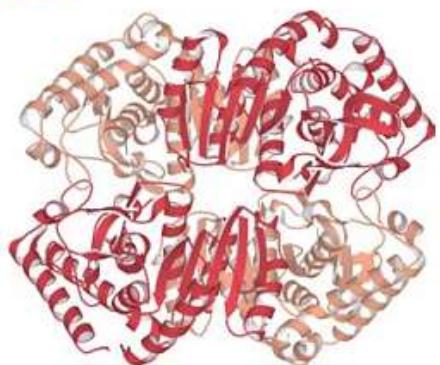
(b) trimer



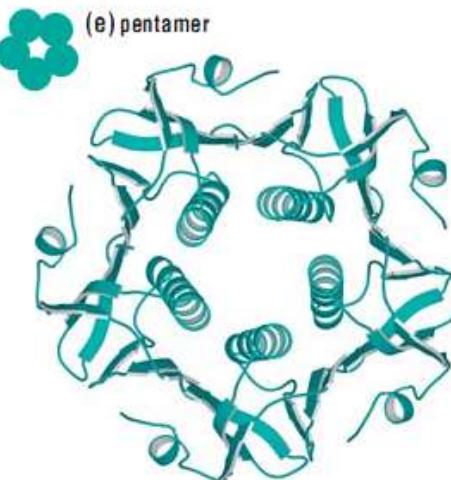
(c) planar tetramer



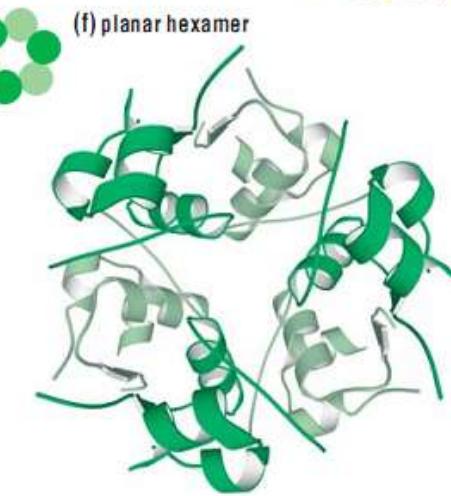
(d) tetramer



(e) pentamer



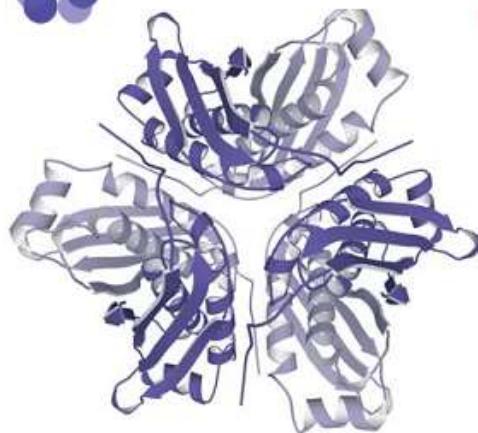
(f) planar hexamer



- Oligomerização(cont.):



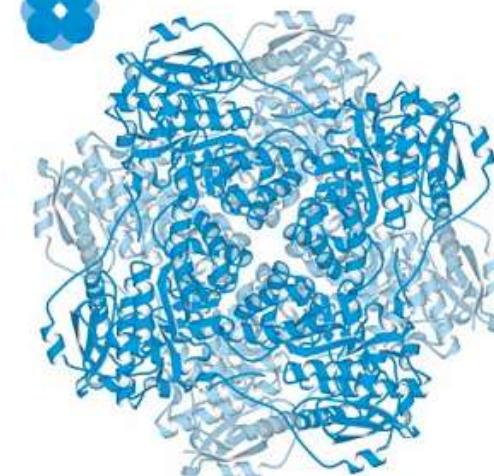
(g) hexamer (trimer of dimers)



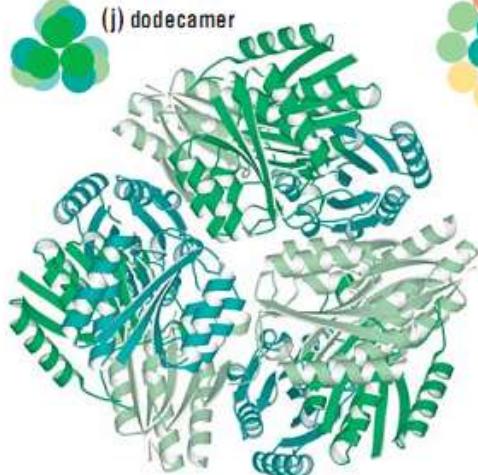
(h) heptamer



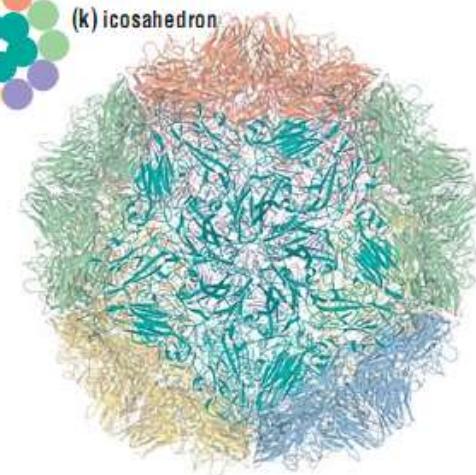
(i) octamer



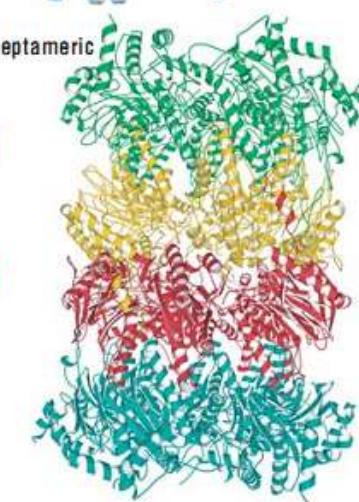
(j) dodecamer



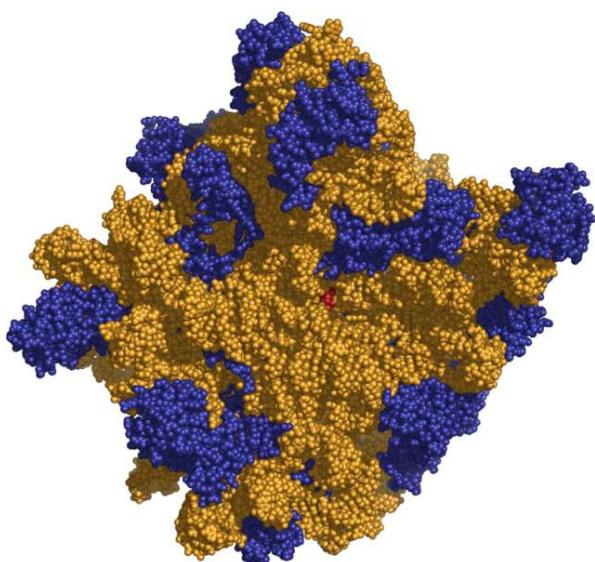
(k) icosahedron



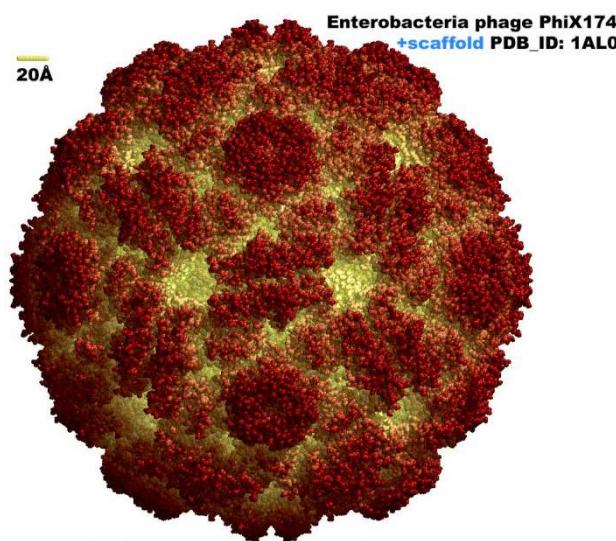
(l) pseudoheptameric structure



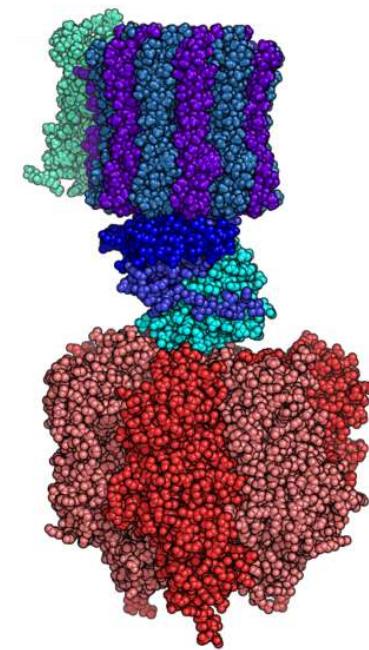
- Formação de estruturas supramacromoleculares



Ribossoma



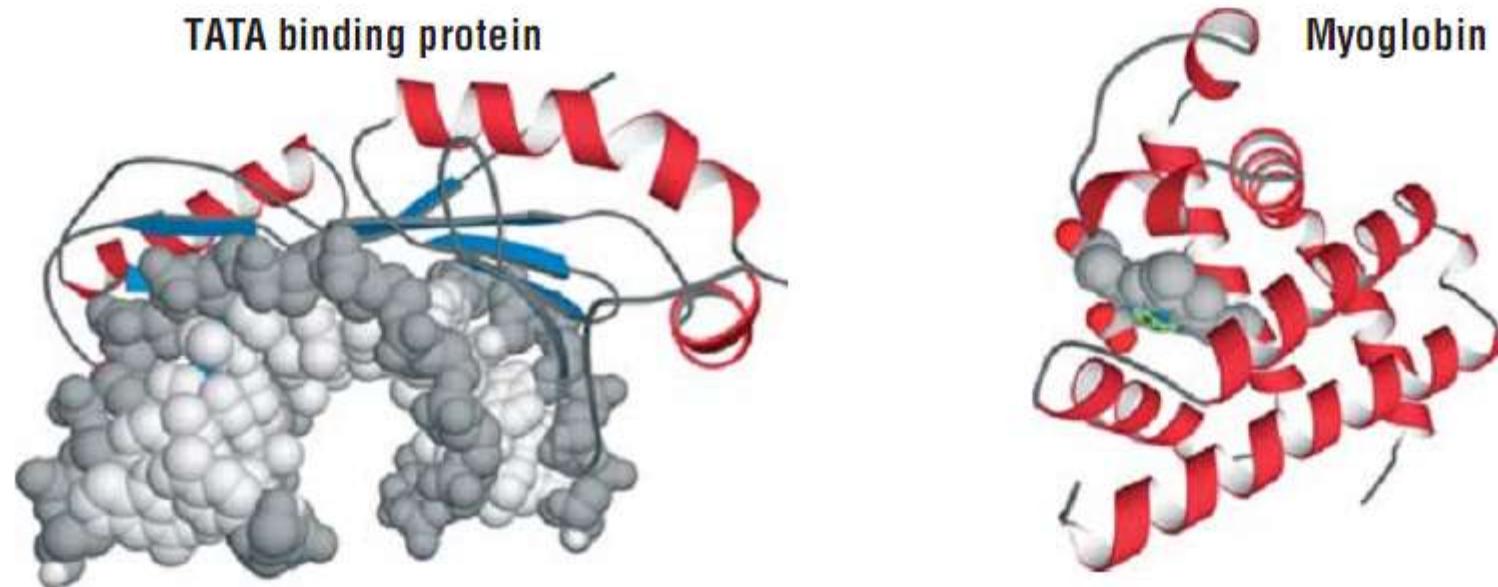
Vírus



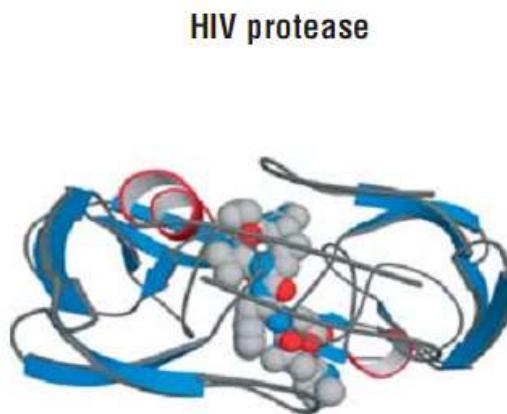
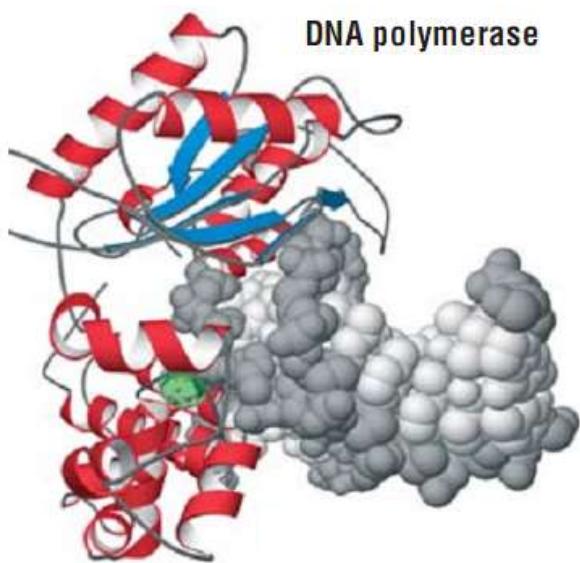
ATPase

Função

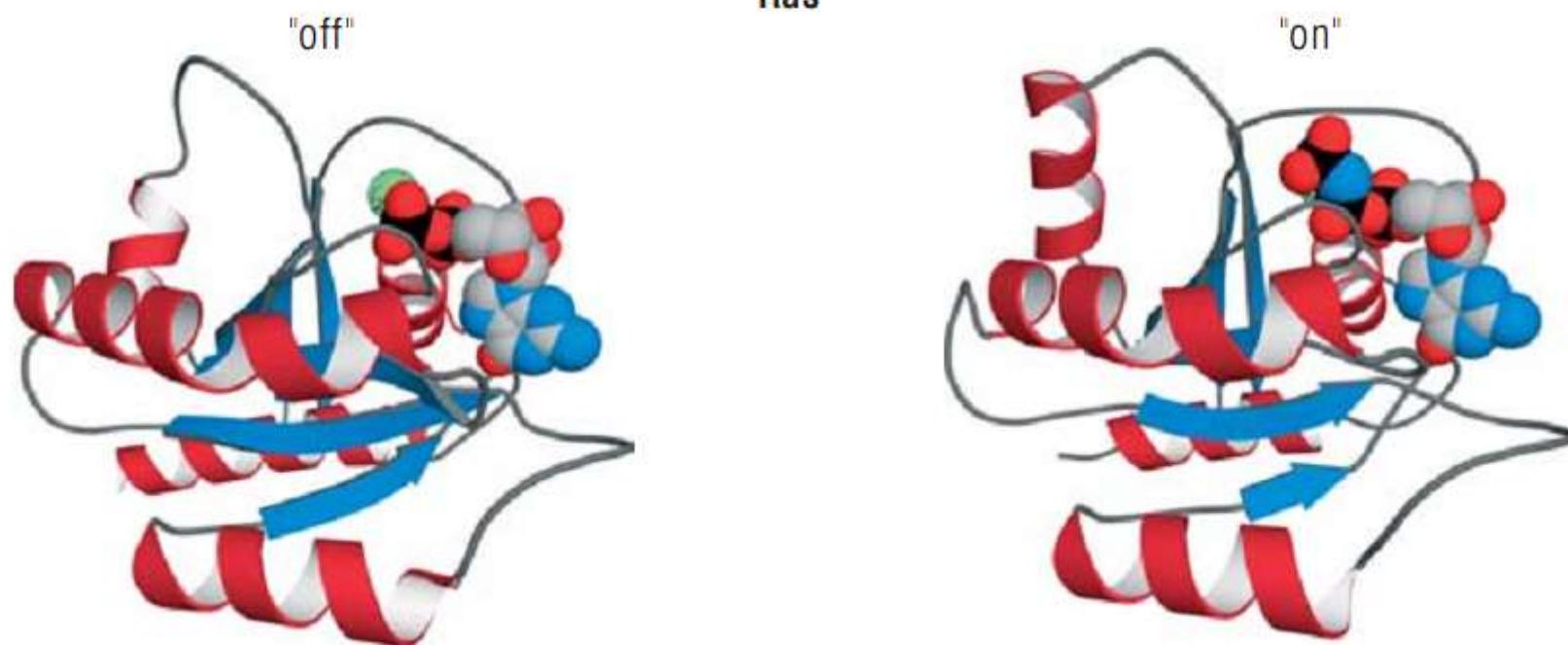
Associação a ligandos



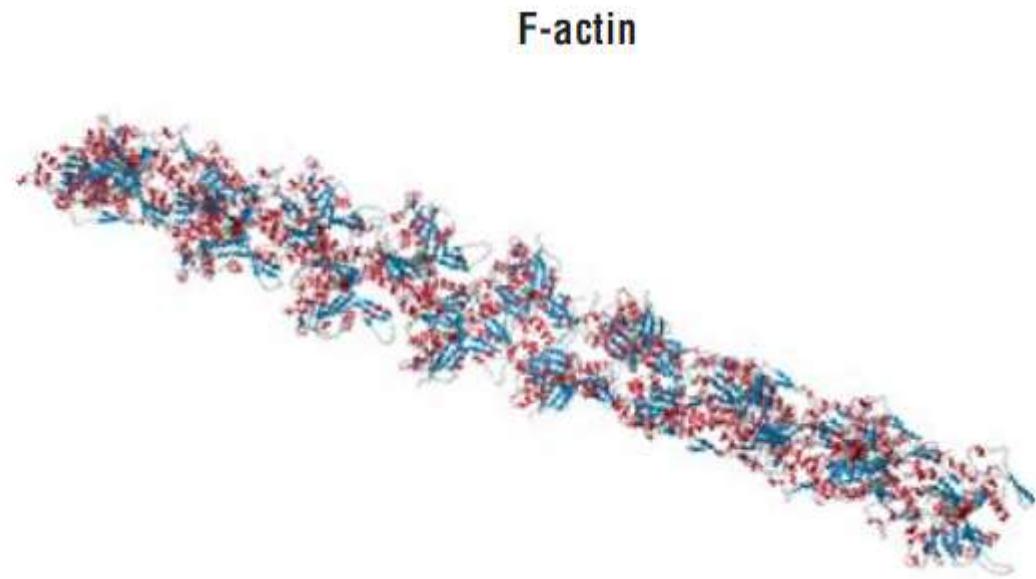
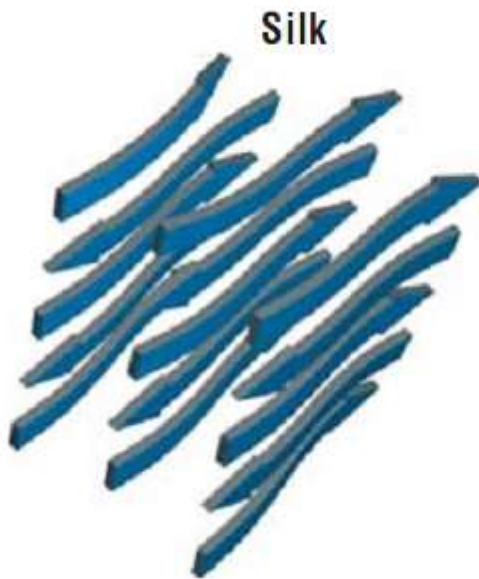
Catálise



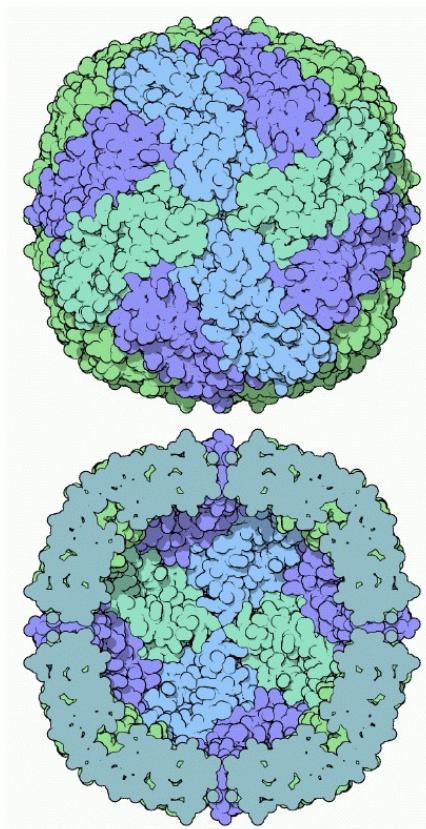
Sinalização



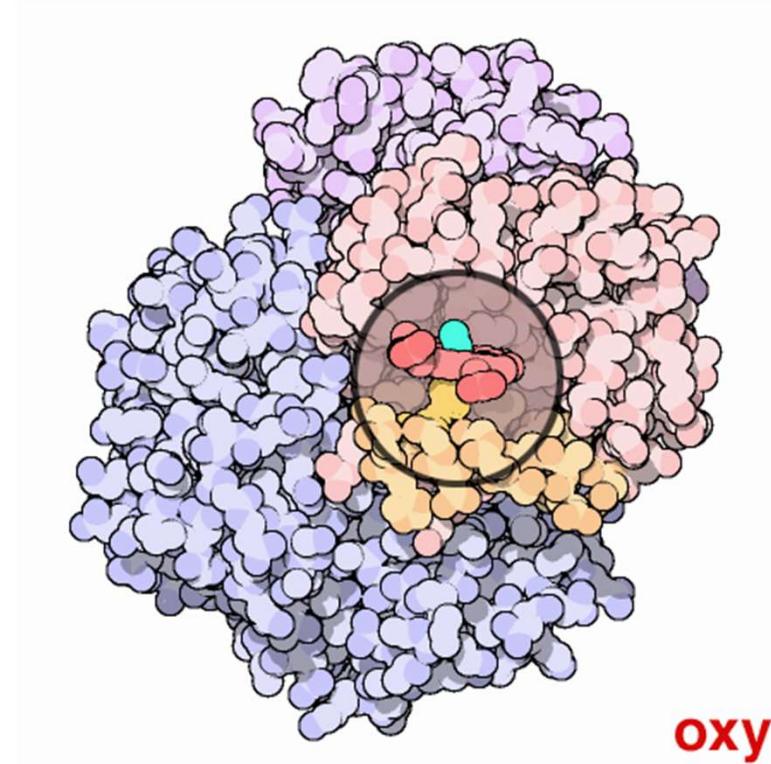
Estrutura



Transporte

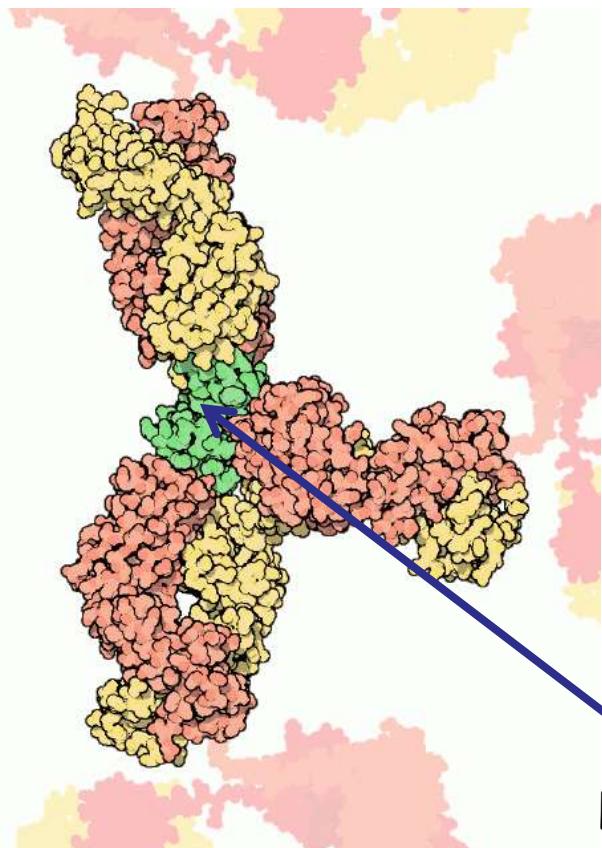


Ferritina (ferro)

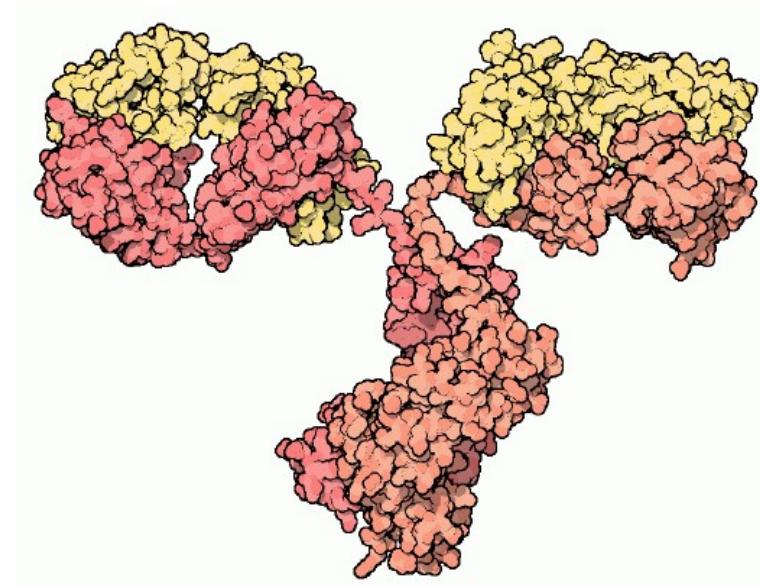


Hemoglobina (oxigénio)

Defesa

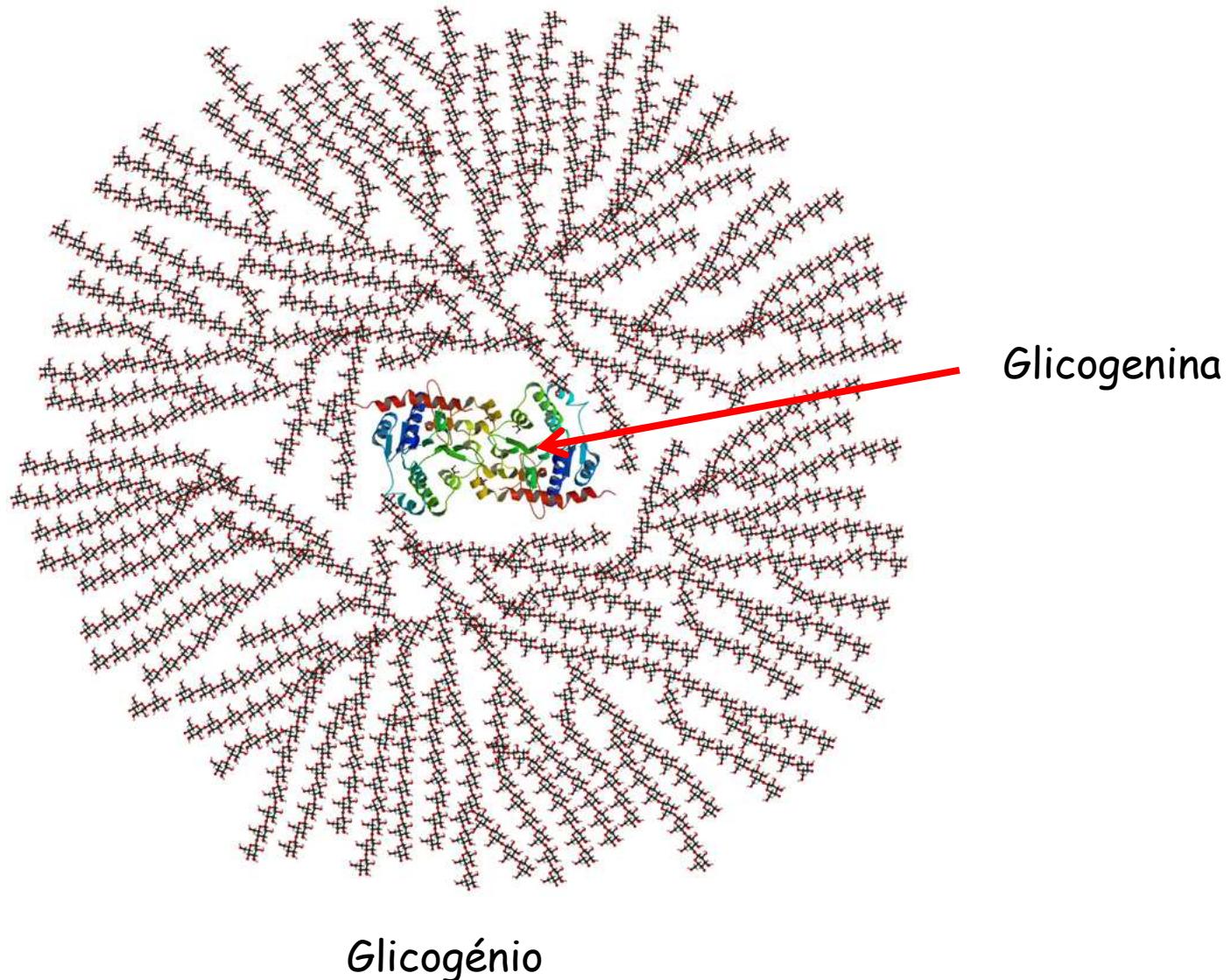


lisozima

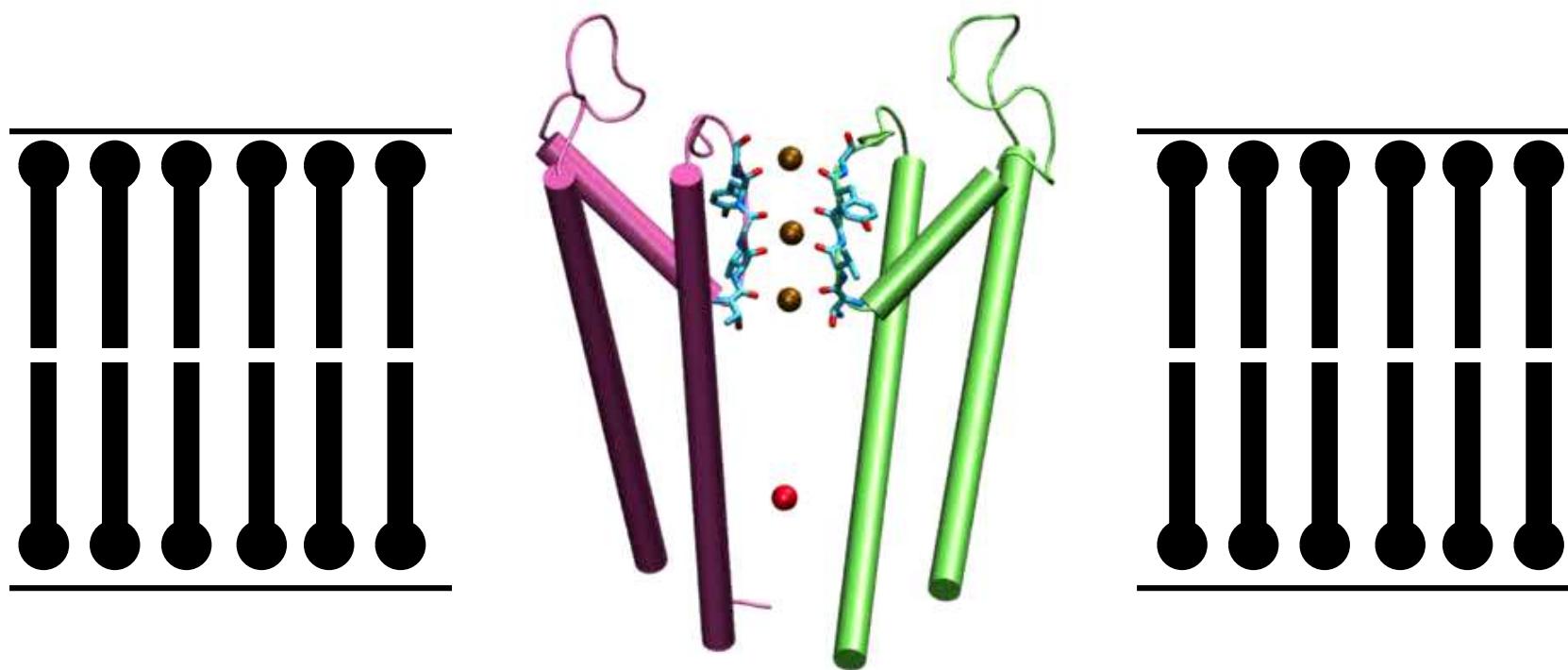


imunoglobulina

Armazenamento



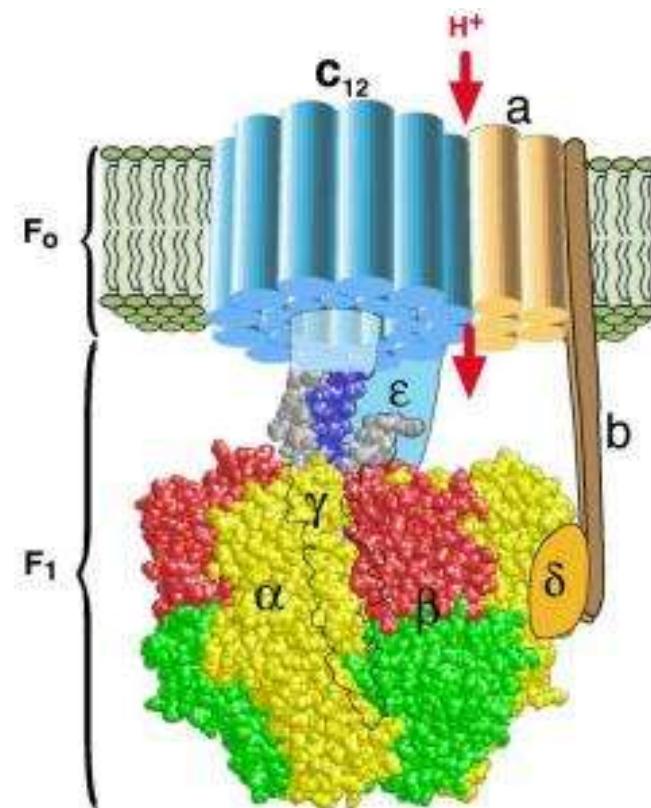
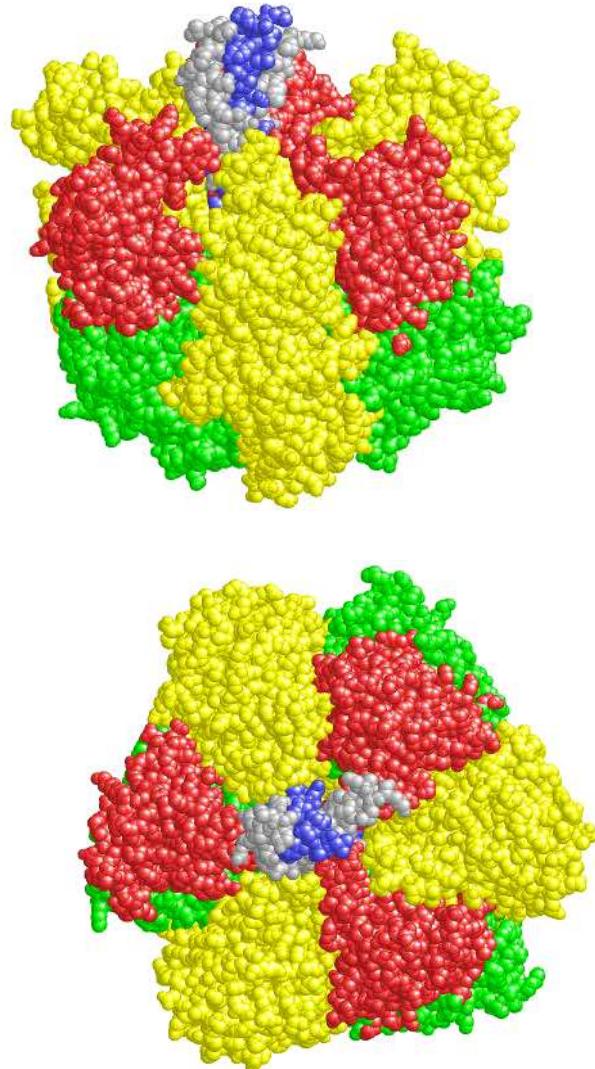
Permeabilidade



As macromoléculas biológicas funcionam como máquinas moleculares

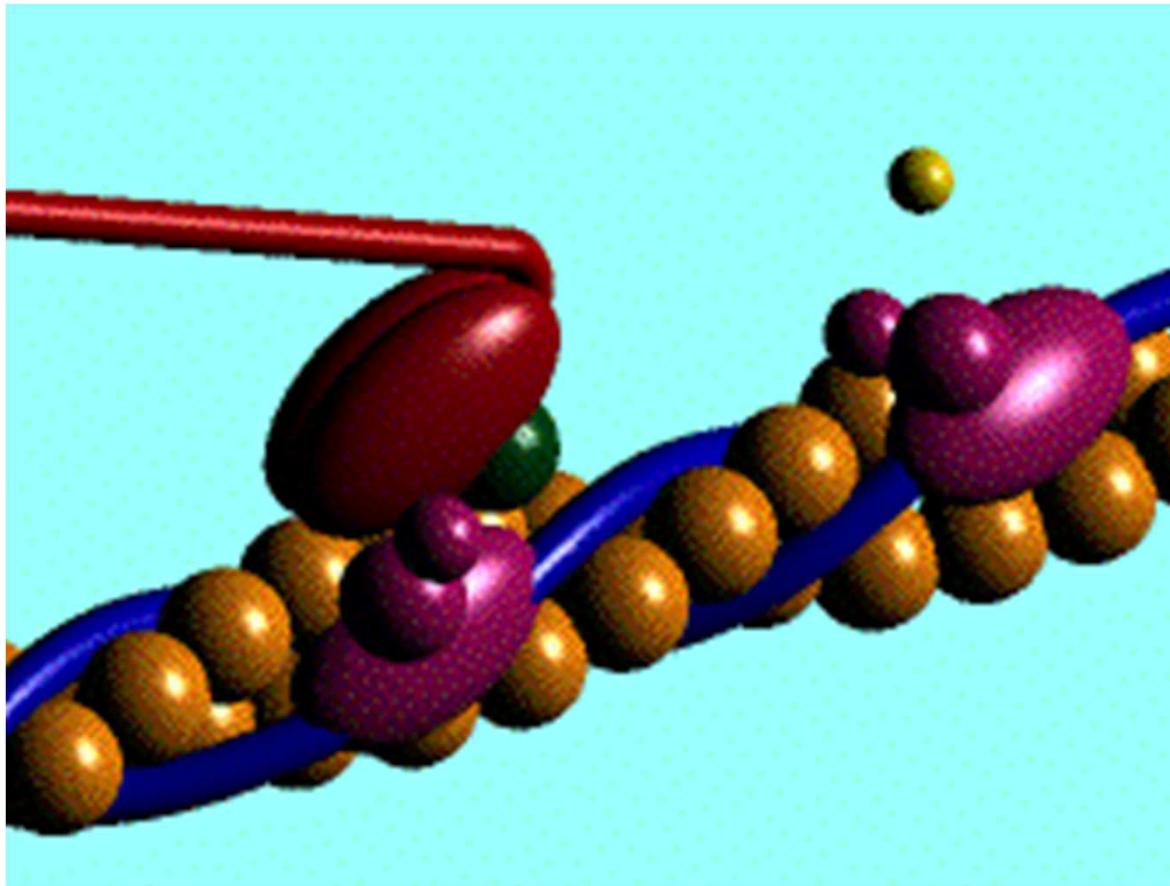
Conversão de energia

ATPsintase



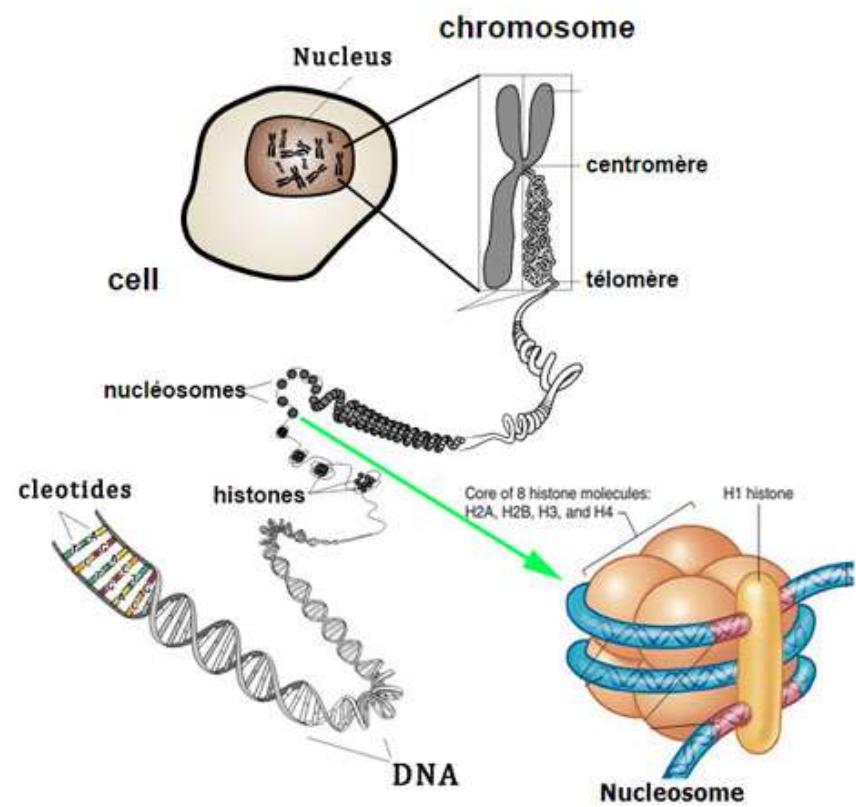
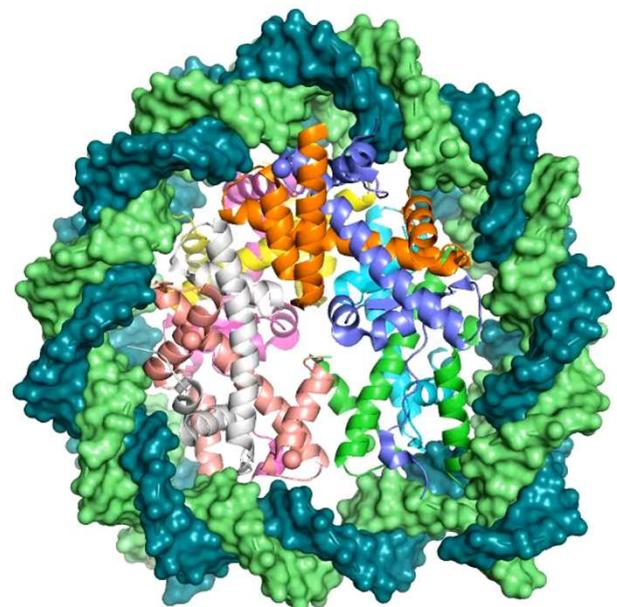
H. Wang and G. Oster (1998). Nature 396:279-282.

Motilidade



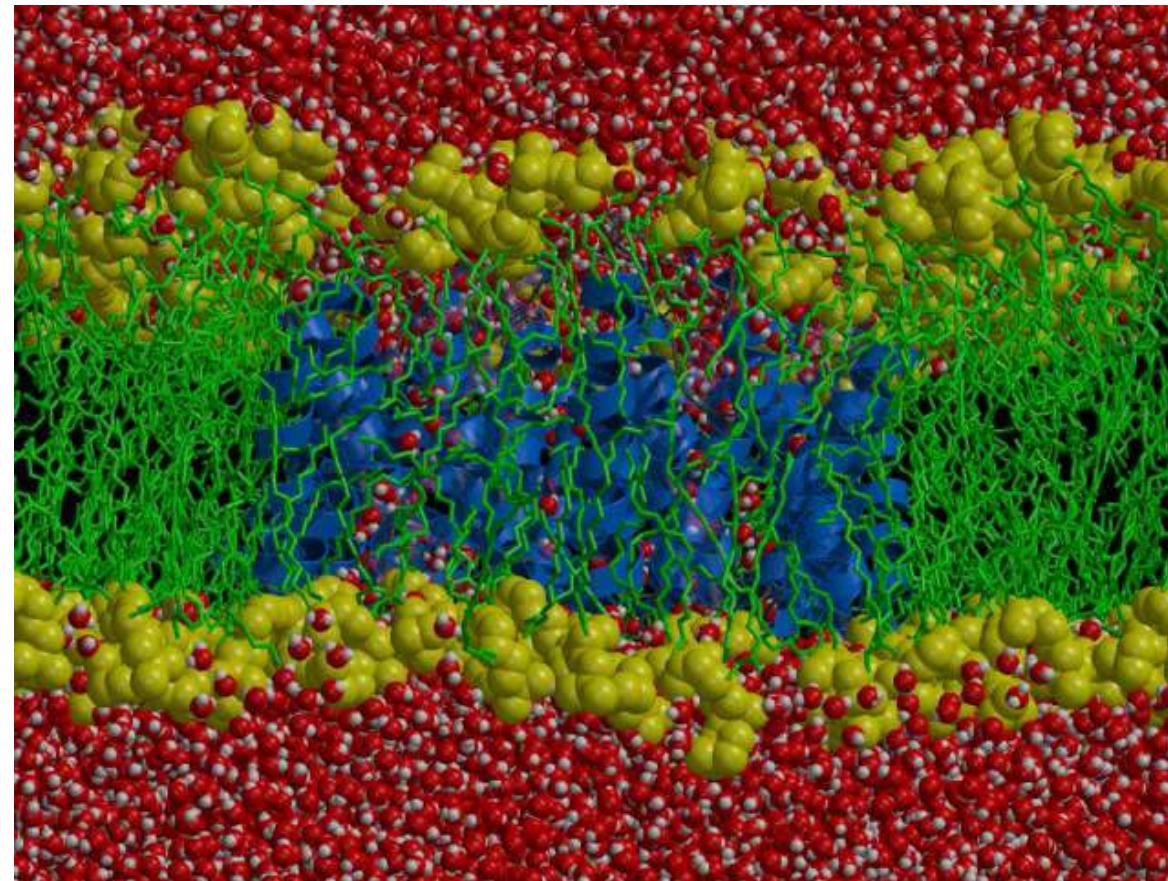
Actina+Miosina

Informação



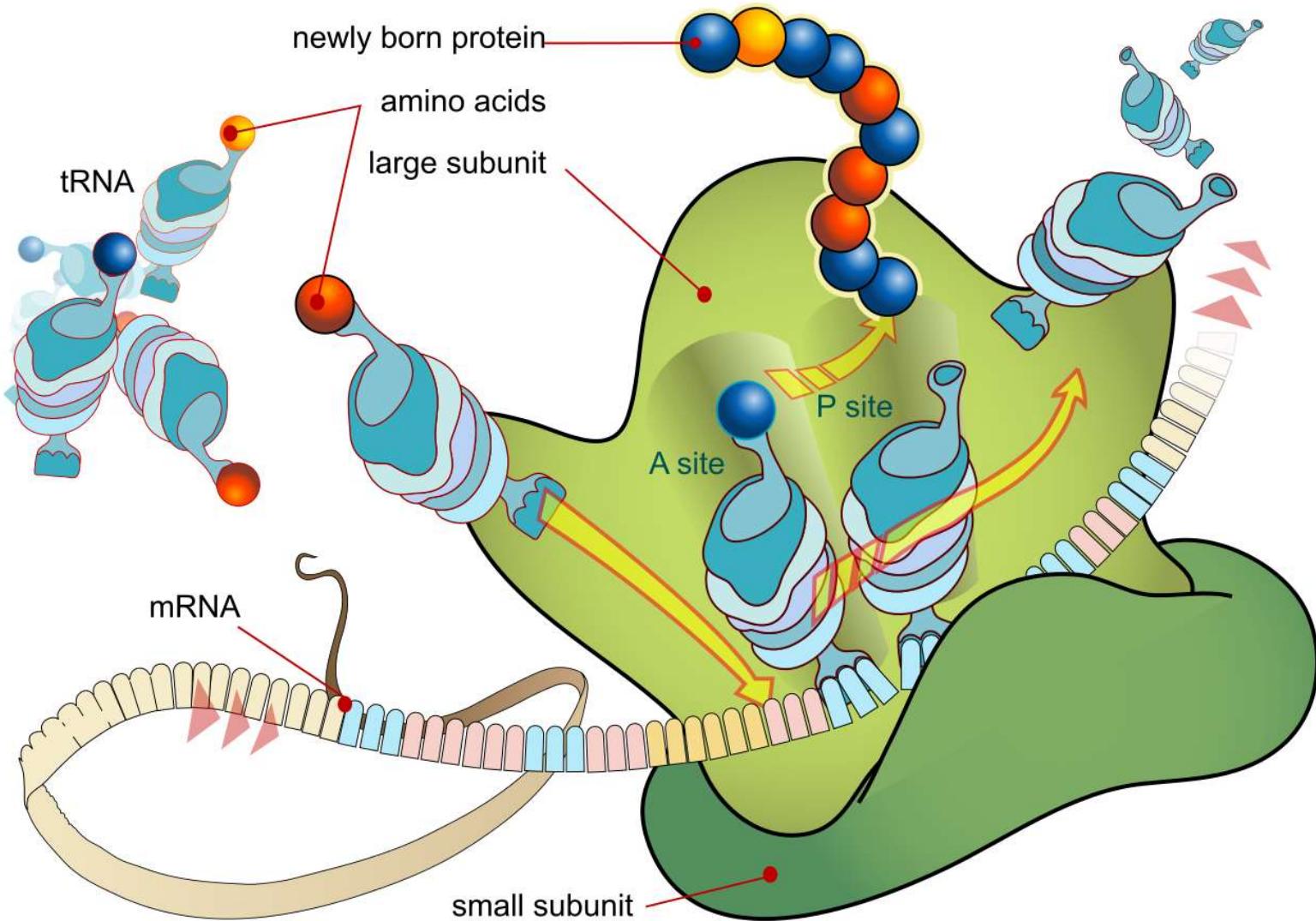
Nucleossoma

Compartimentação

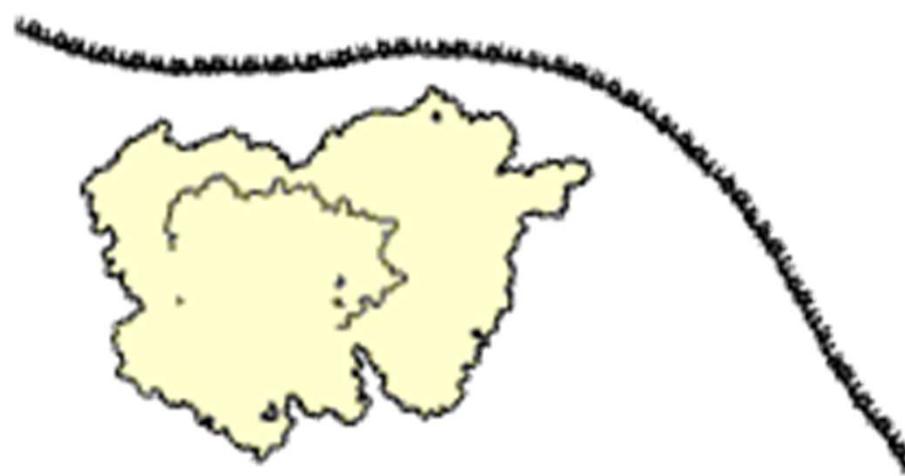


Membrana+aquaporina

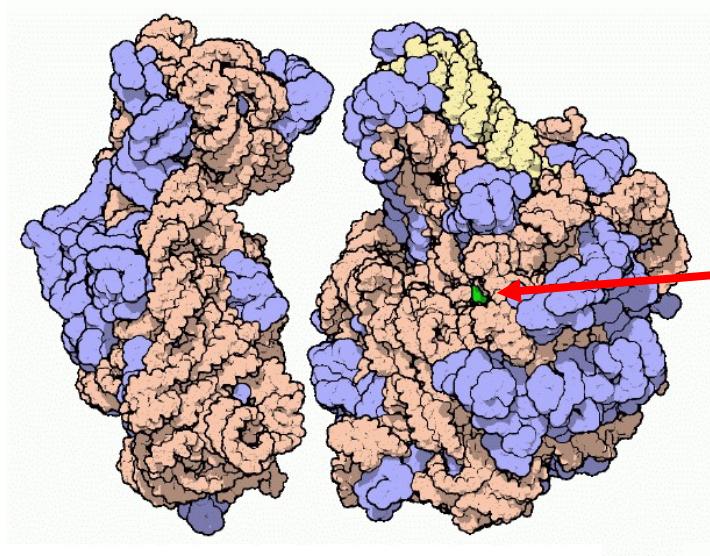
Síntese proteíca



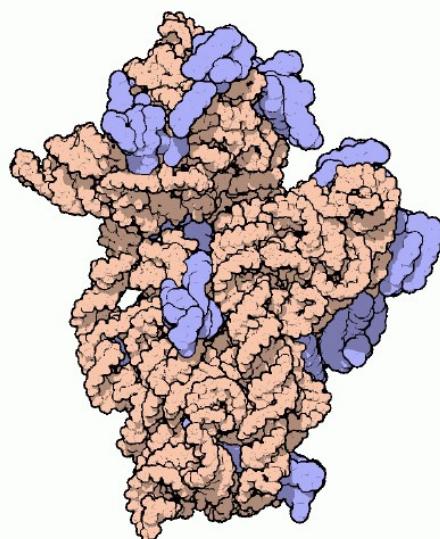
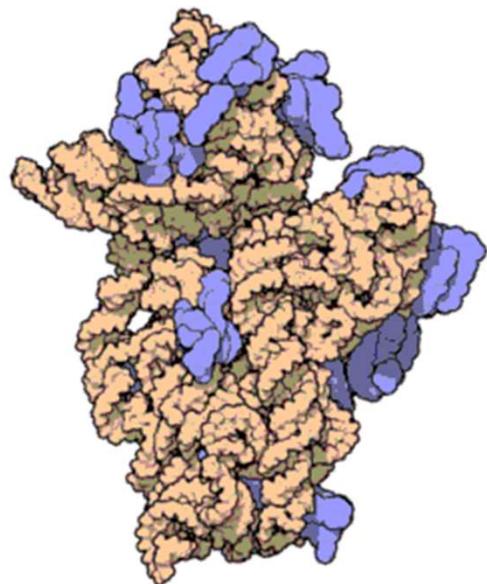
Síntese proteíca (animação)



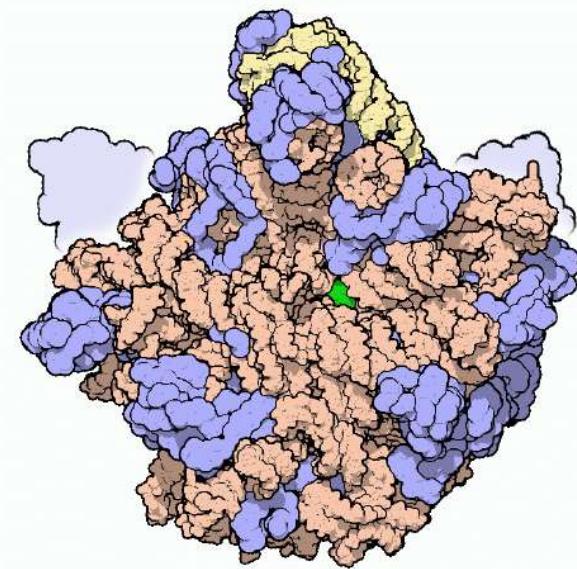
Estrutura do ribossoma bacteriano



RNA catalítico

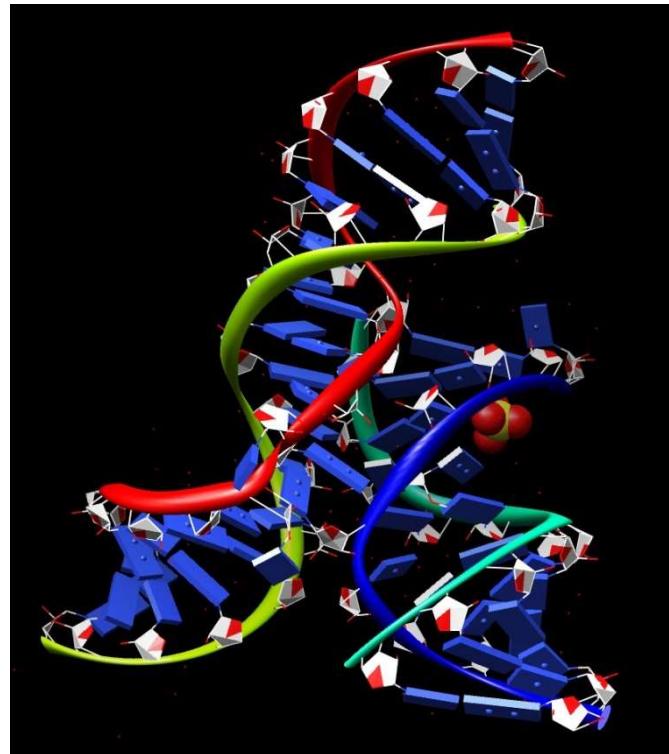
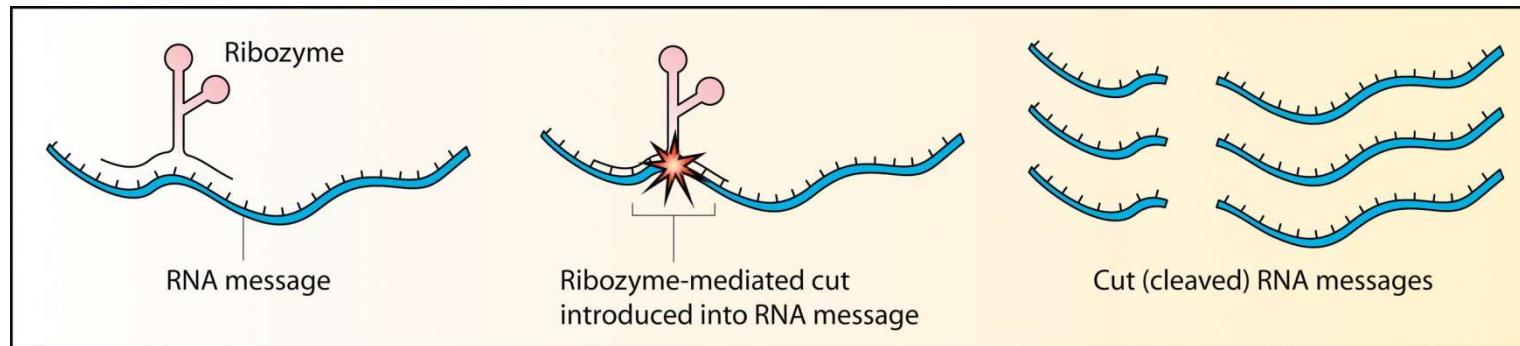


Subunidade 30S

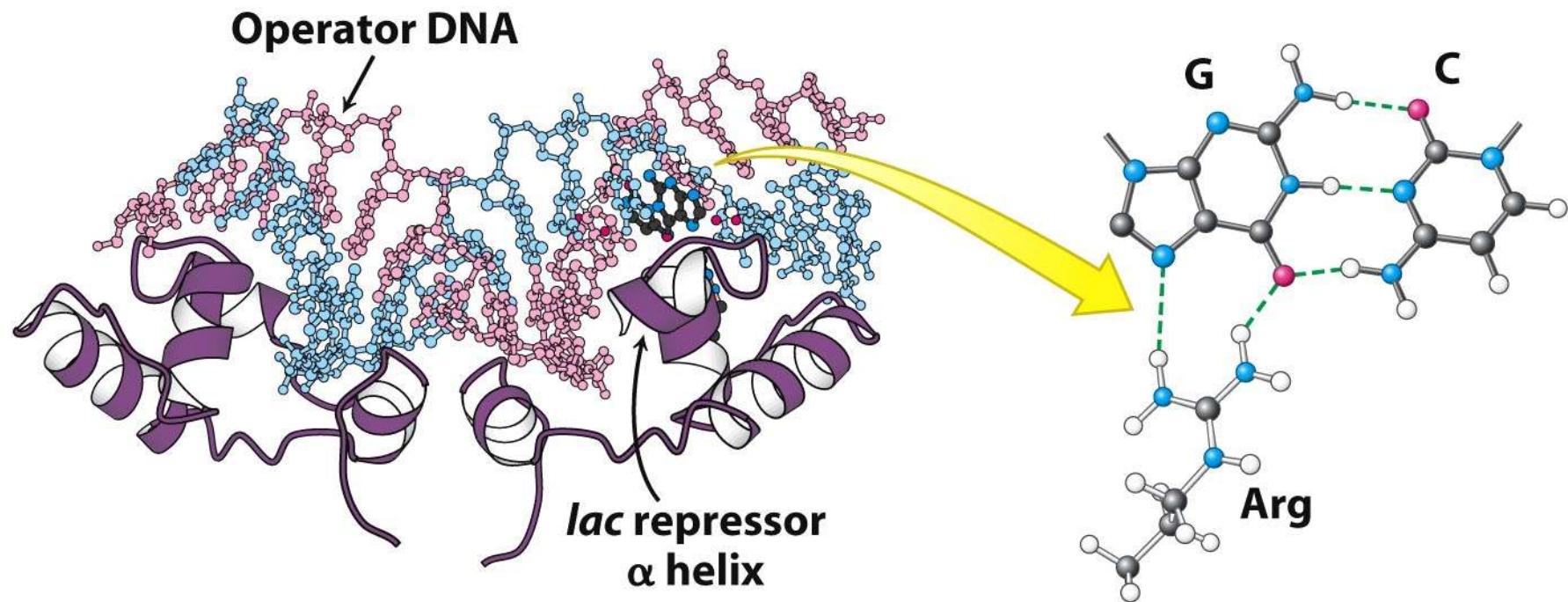


Subunidade 20S

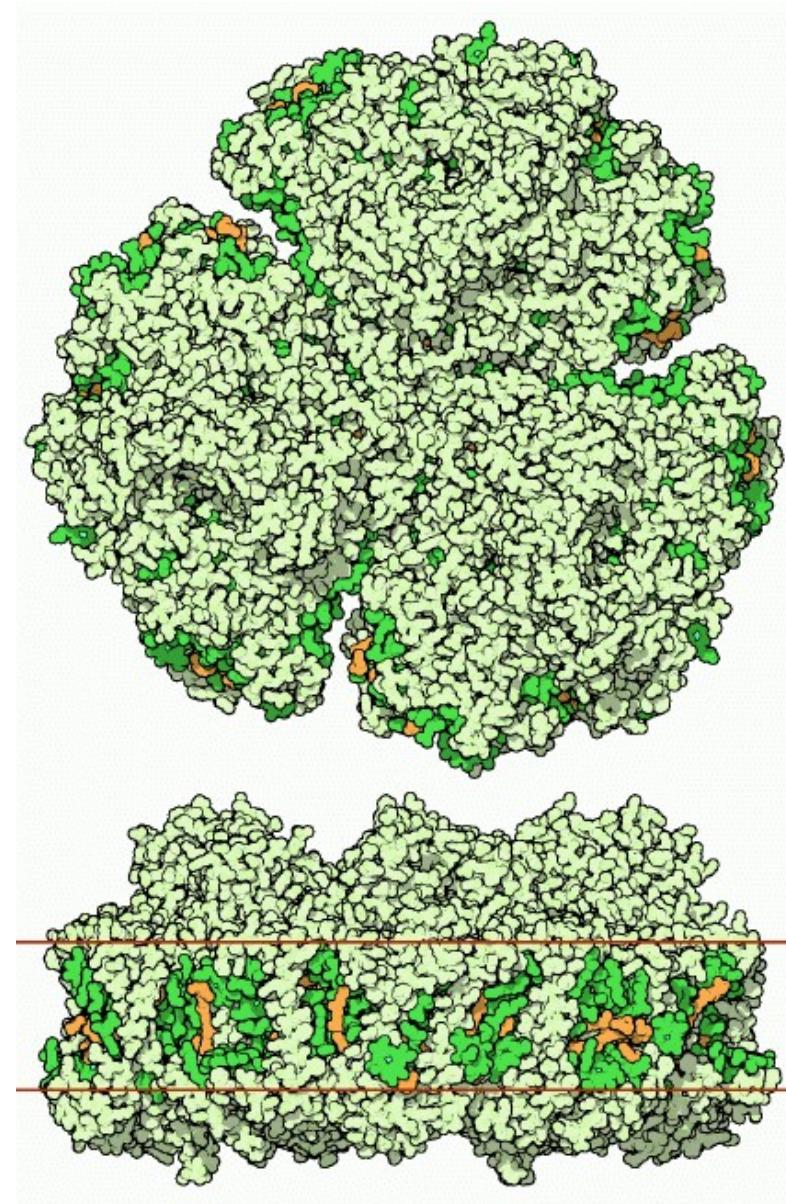
Ribozimas



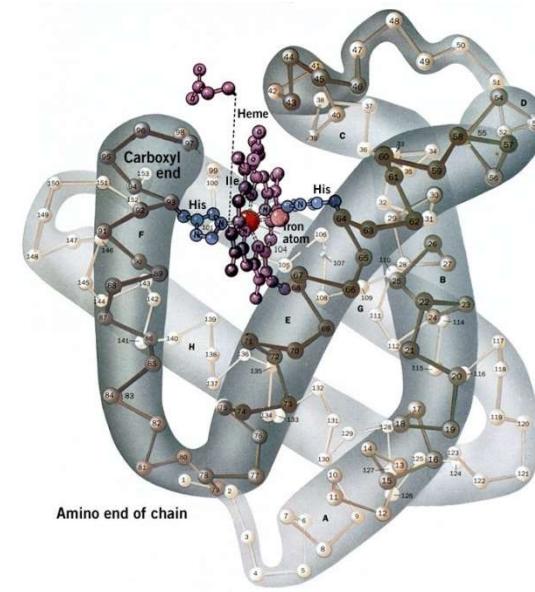
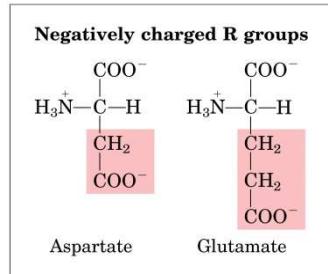
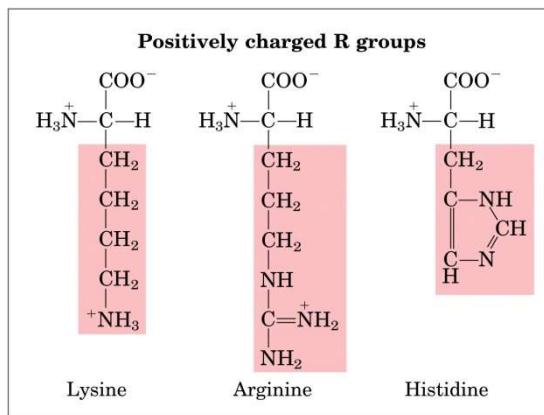
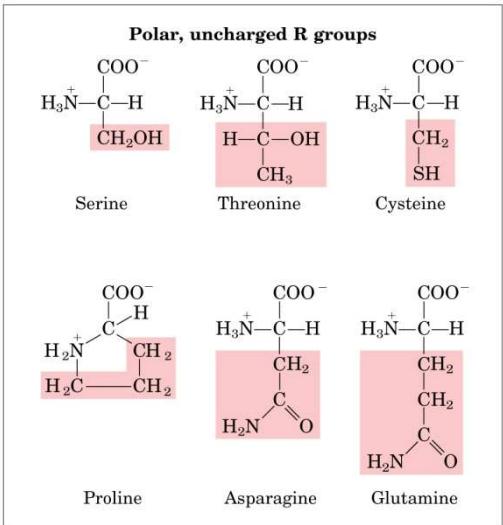
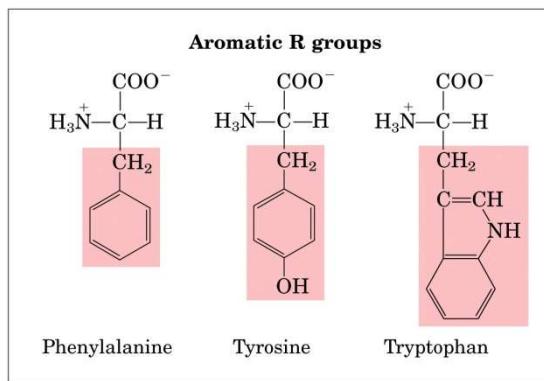
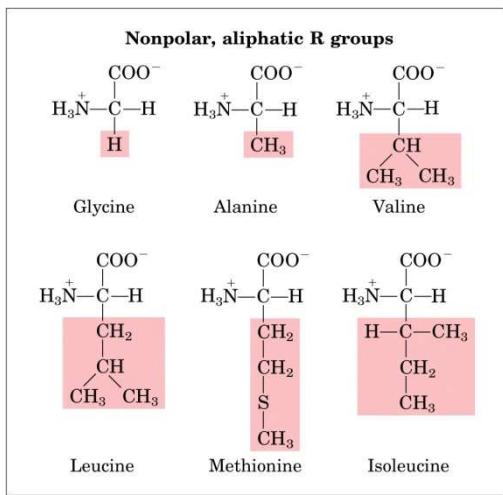
Regulação da transcrição



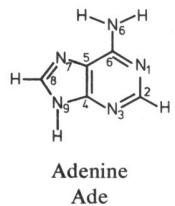
Fotossistema I



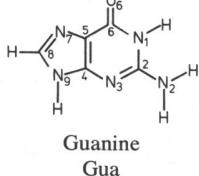
Proteínas



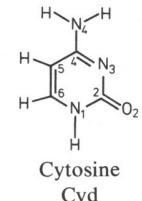
Ácidos nucleicos



Adenine Ade



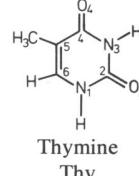
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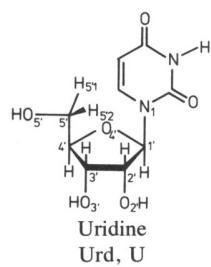
Cytosine Cyd



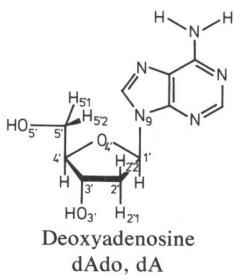
Uracil



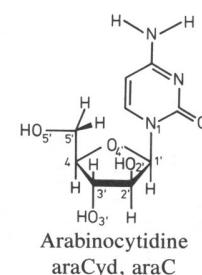
Thymine



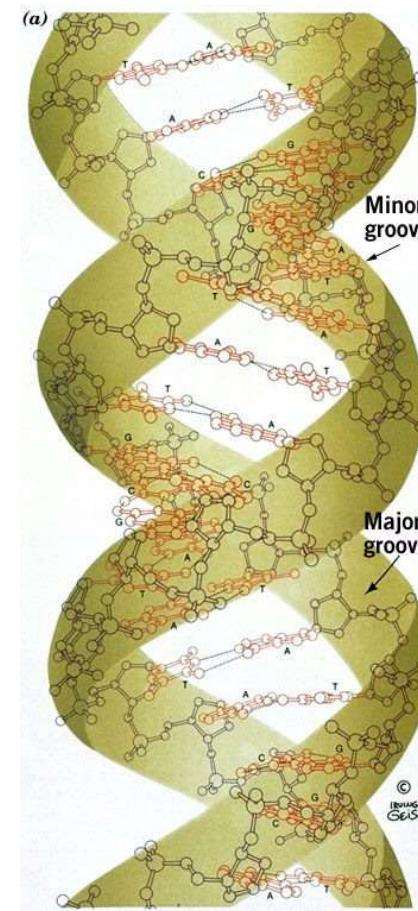
Uridine
Urd, U



Deoxyadenosine
dAdo, dA



Arabinocytidine
araCyd, araC



B-Dna