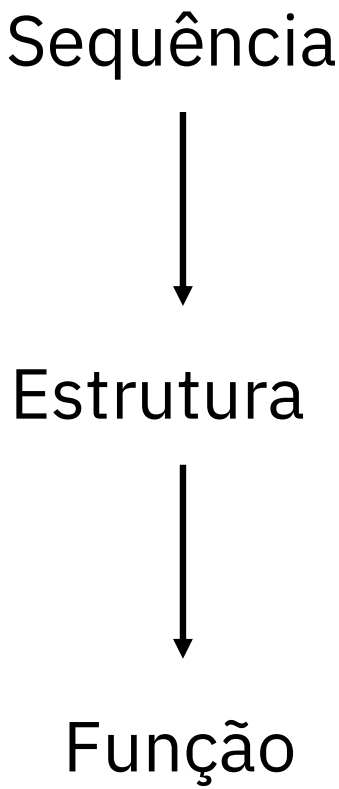
Bioquímica Estrutural:

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

vírus de RNA

DNA ...TTAATAAGT...

transcrição

RNA ...UUAAUAAGU...

splicing, tradução

cadeia polipeptídica ...LISVHDN...

modificações pós-translacionais

proteína

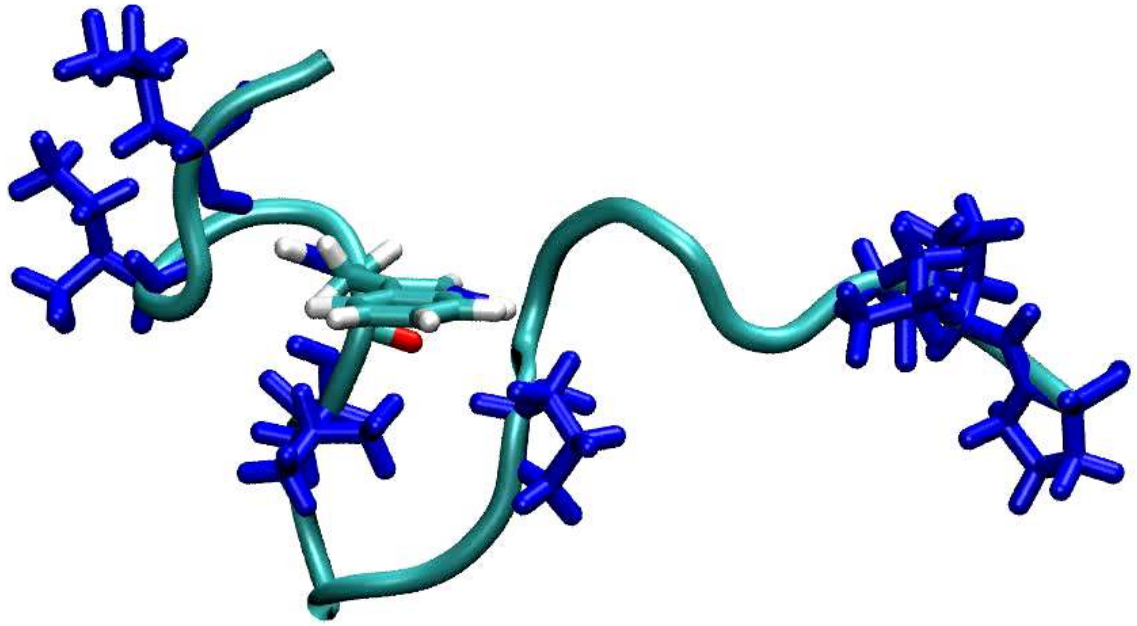
priões

Dogma central da biologia molecular

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

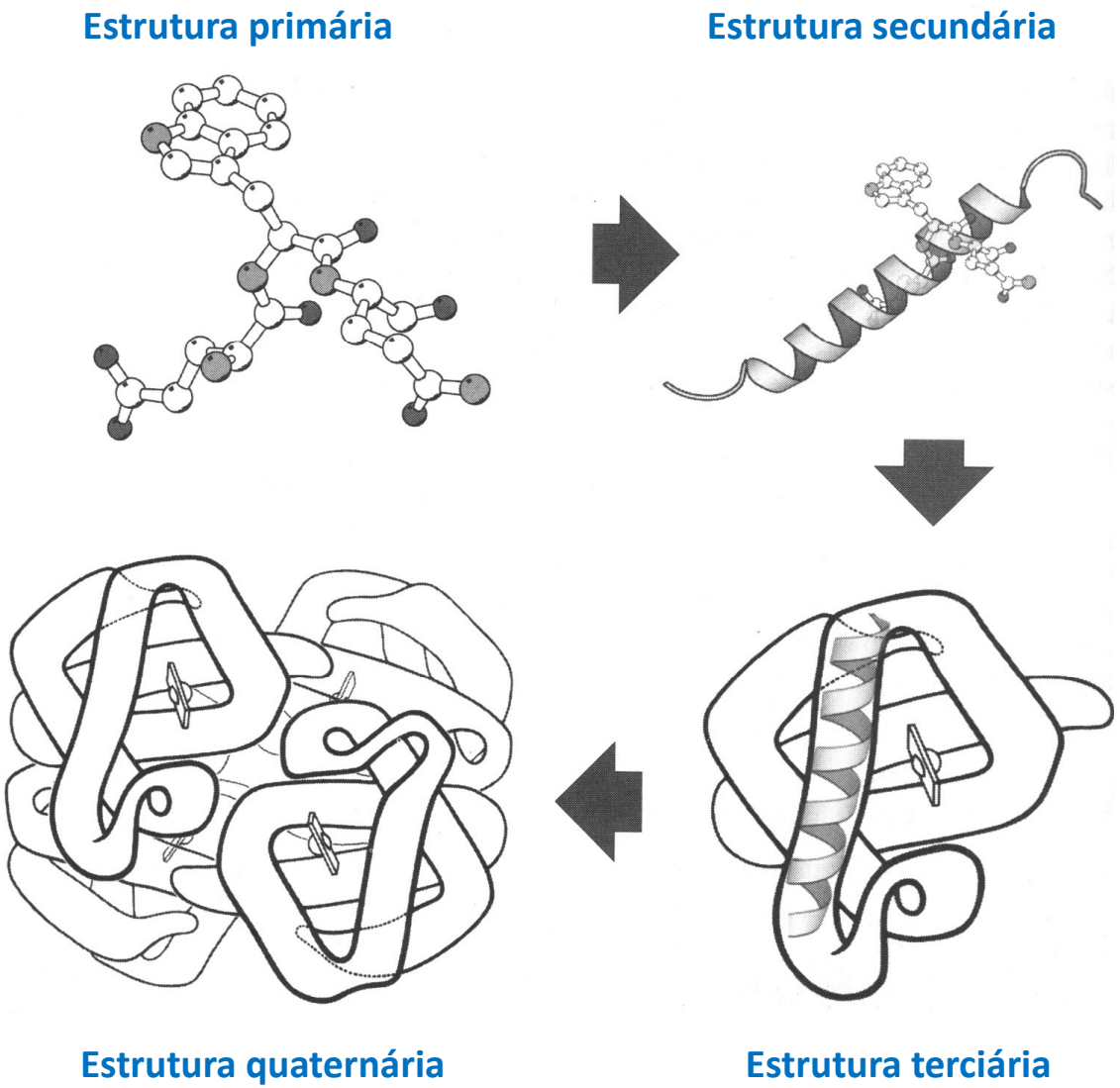
Sequência->Estrutura

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



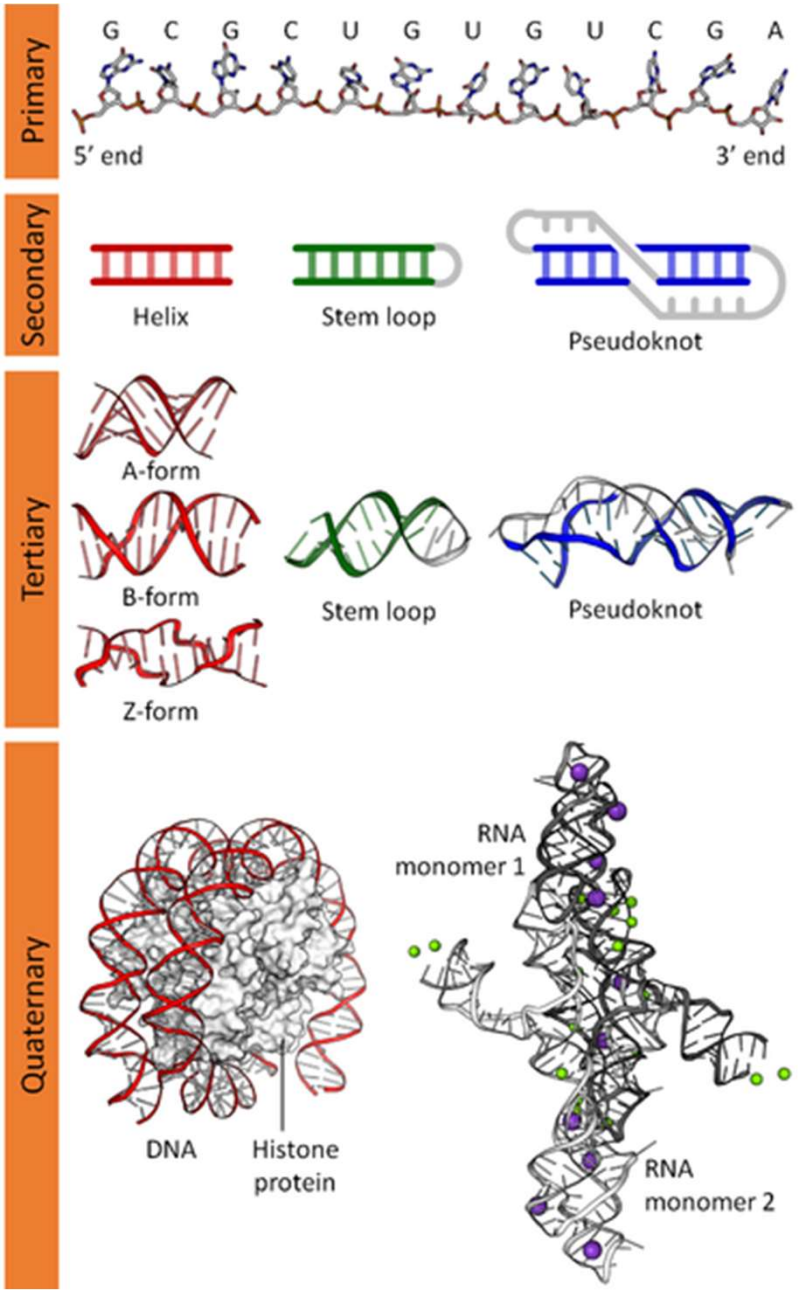
Muitas protéinas adquirem a sua estrutura tridimensional *espontâneamente (folding)*

Níveis de organização da estrutura das proteínas

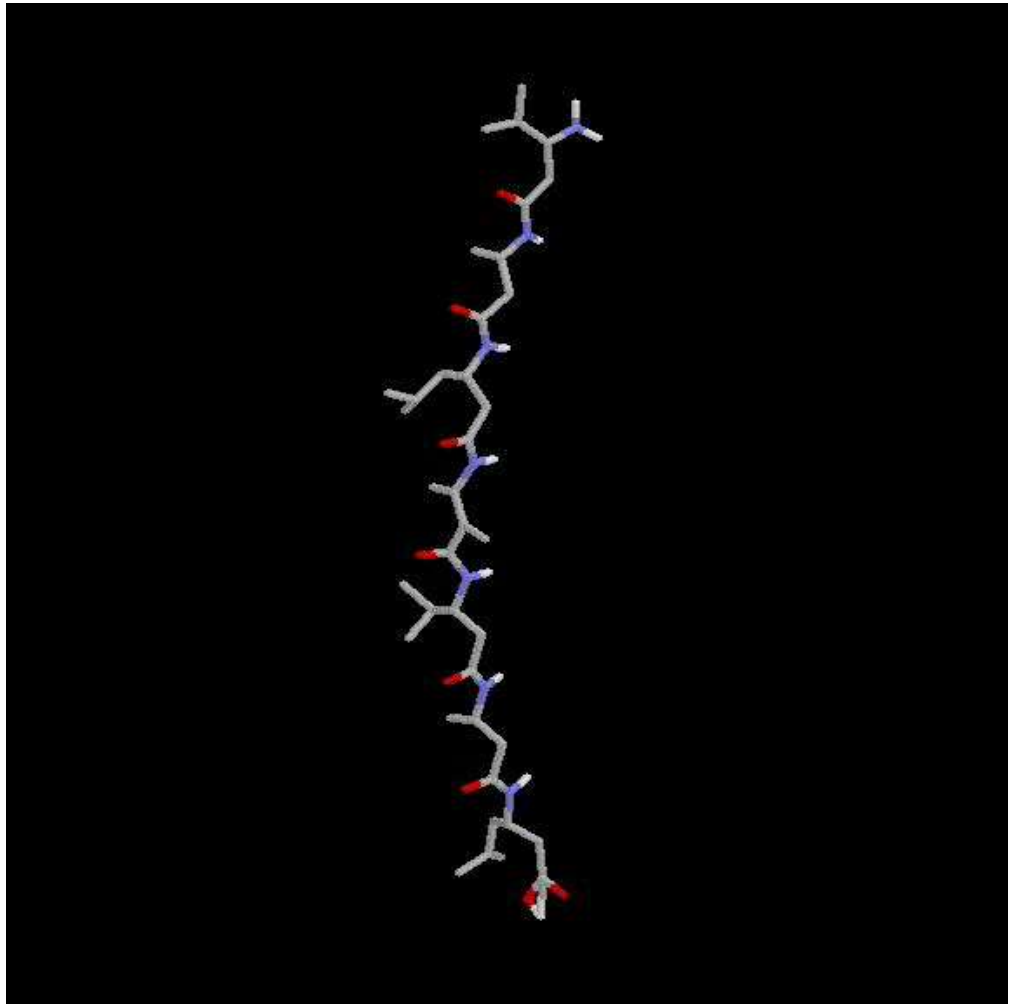


Níveis de organização da estrutura de ácidos nucleícos

Estrutura quaternária pode envolver moléculas de proteína

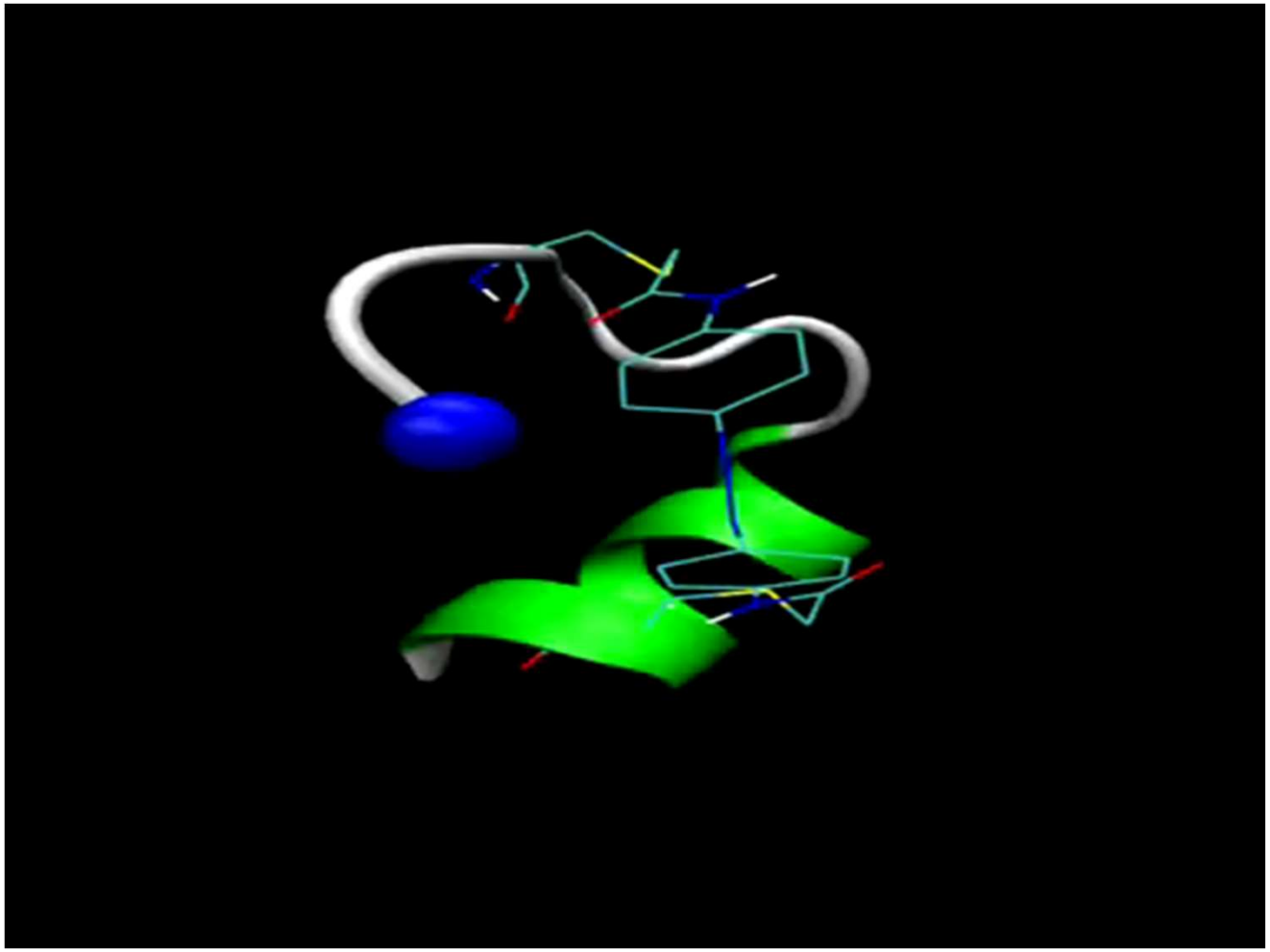


Formação hierárquica da estrutura



Formação espontânea de uma hélice α
(simulação)

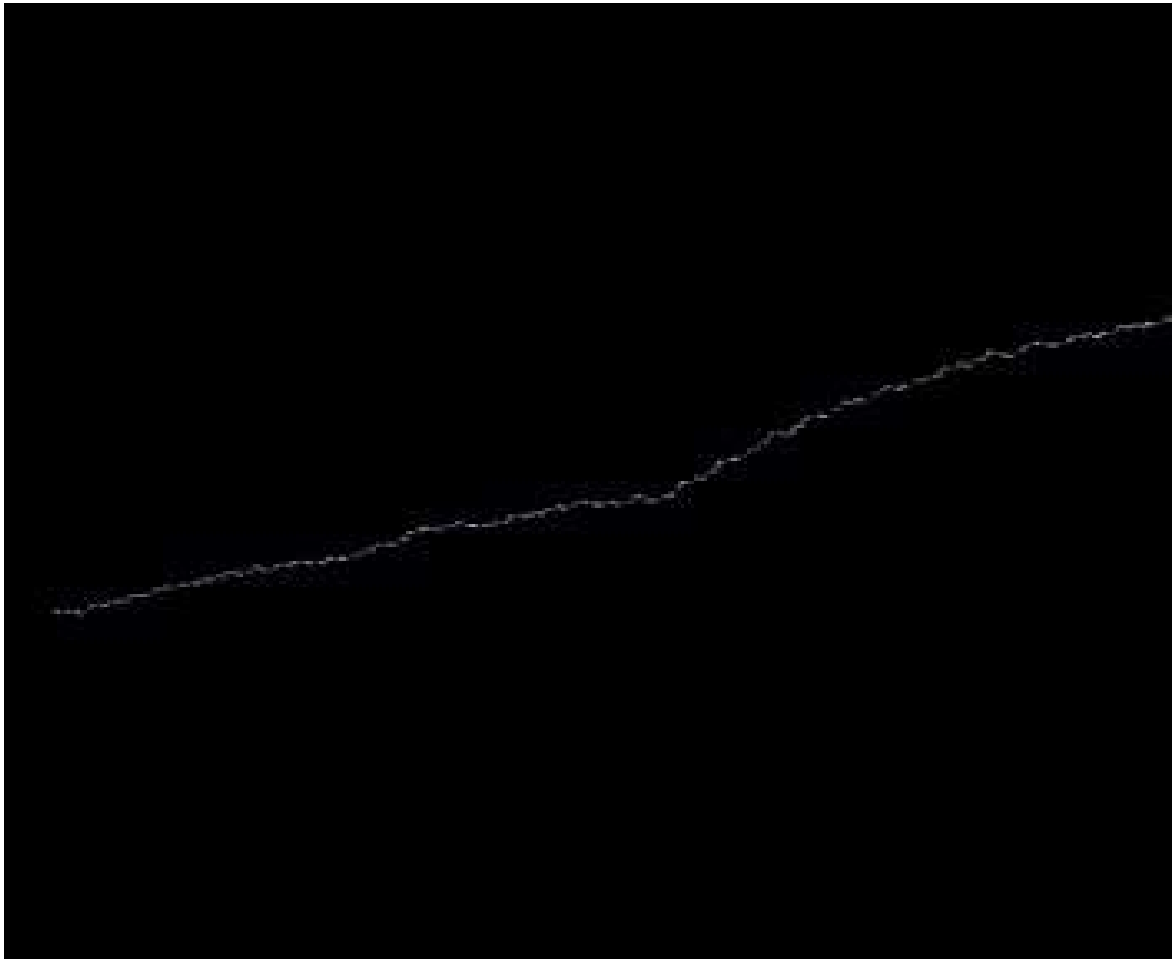
Formação hierárquica da estrutura



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)
  - ❖ Microscopia Electrónica
  - ❖ Outros métodos (difração de neutrões, SAXS, etc)

Que informação temos disponível ?

(dados do Protein Data Bank em 5/02/2024)

Número de estruturas tridimensionais (coordenadas atómicas):

- Proteínas: 186680
- Ácidos Nucleícos: 4373
- Complexos ácido nucleíco-proteína: 12606
- Proteína/Oligossacárido: 11514
- Outros: 228

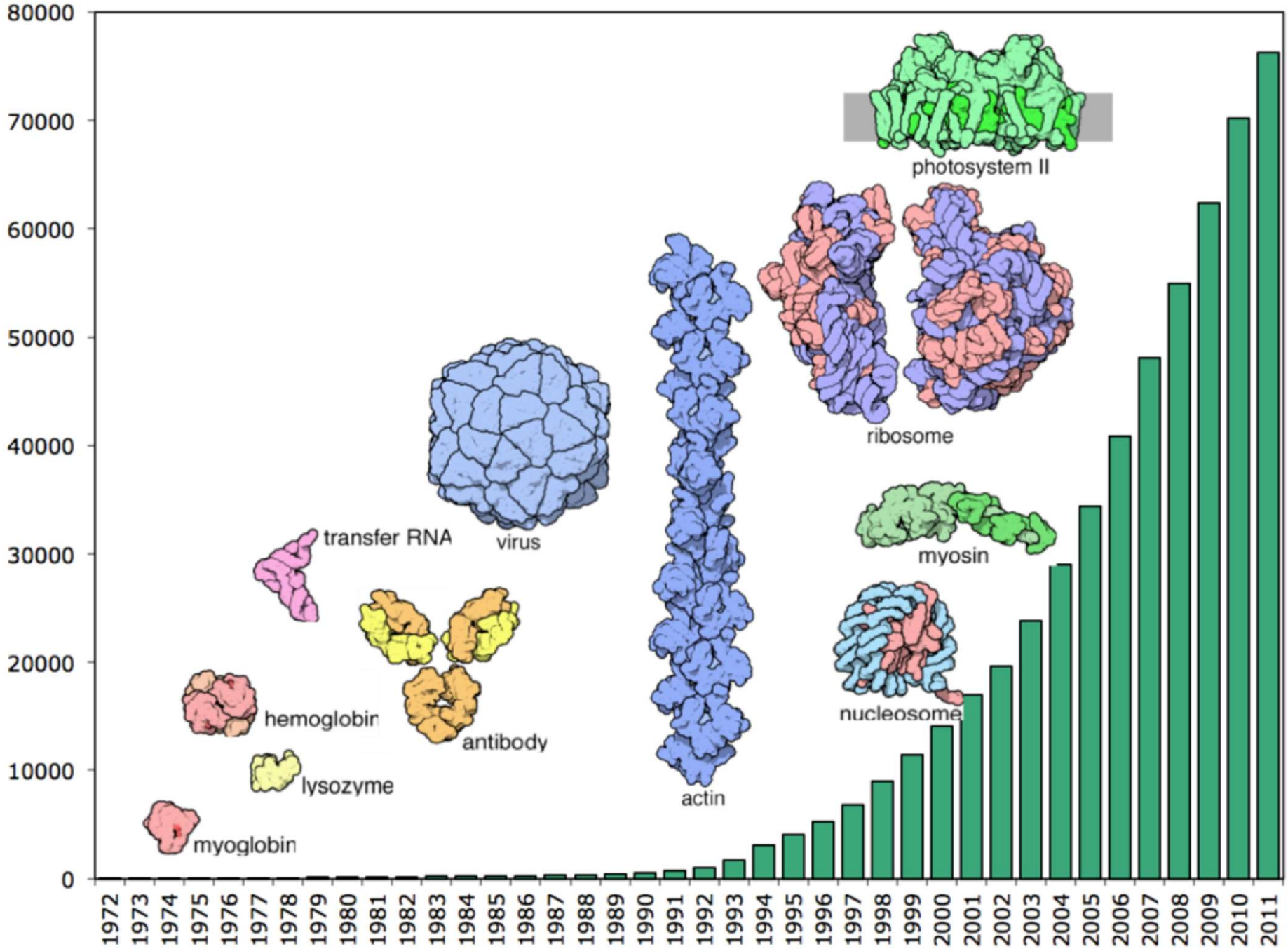
Total: 215401 estruturas

Métodos experimentais de determinação da estrutura:

- Cristalografia de raios X: 181272 (**84.6%**)
- Microscopia electrónica: 18720 (8.69%)
- NMR em solução aquosa: 14164 (6.58%)
- Métodos híbridos: 229
- Outros: 116

http://www.rcsb.org

Progresso na determinação das estruturas



http://www.rcsb.org

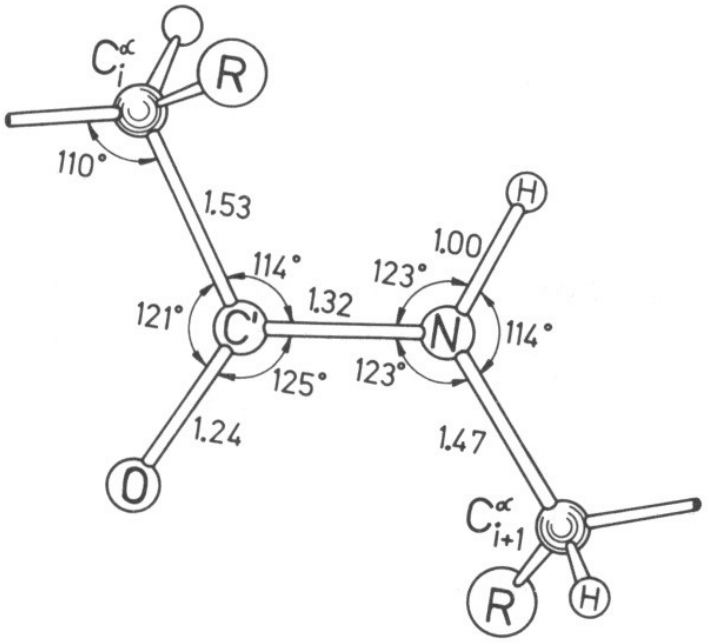
Princípios que regem a estrutura das biomoléculas

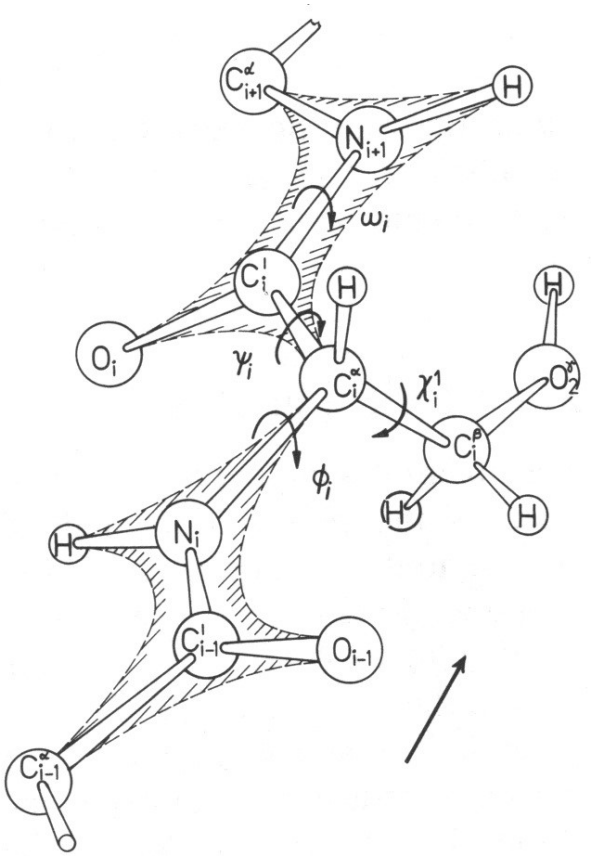
“Perhaps the most remarkable features of the molecule are its *complexity* and *lack of symmetry*. The arrangement seems to be almost totally lacking the kind of regularities which one instinctively anticipates and it is more complicated than has been predicted by any theory of protein structure”

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

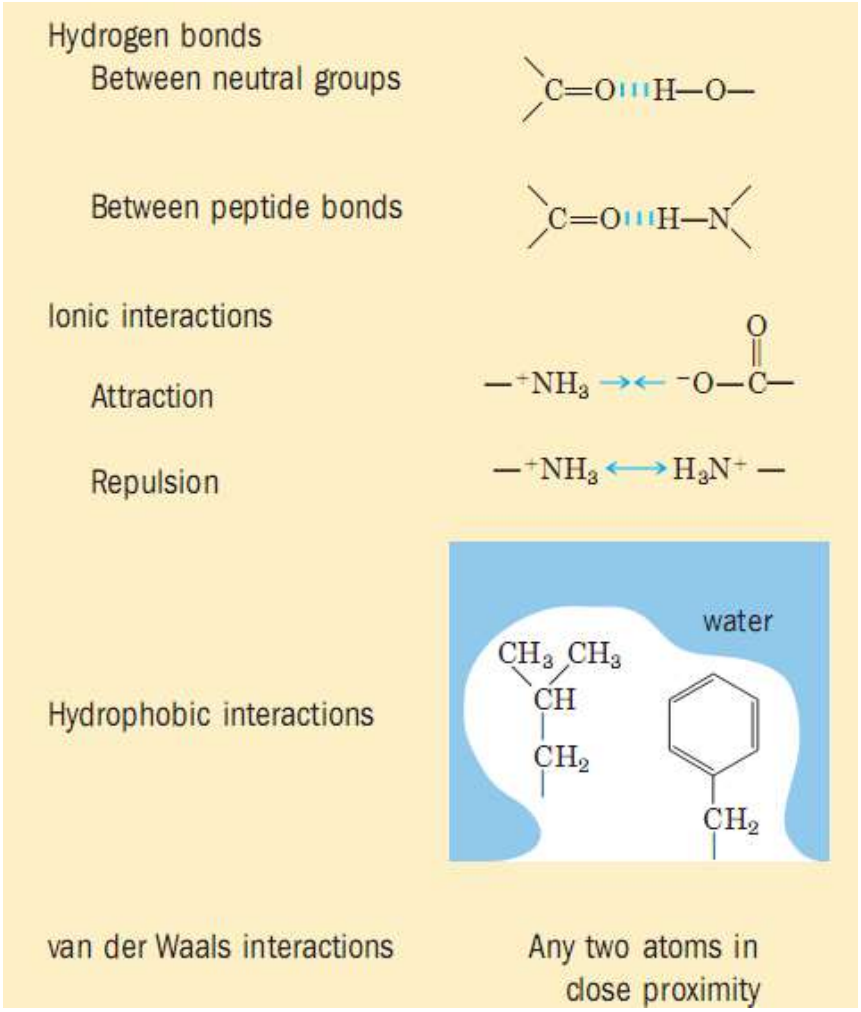
• As macromoléculas biológicas parecem, numa primeira análise, distanciar-se dos princípios simples de geometria e simetria que sabemos reger a estrutura das moléculas pequenas.

- Ligações covalentes, geometria molecular:

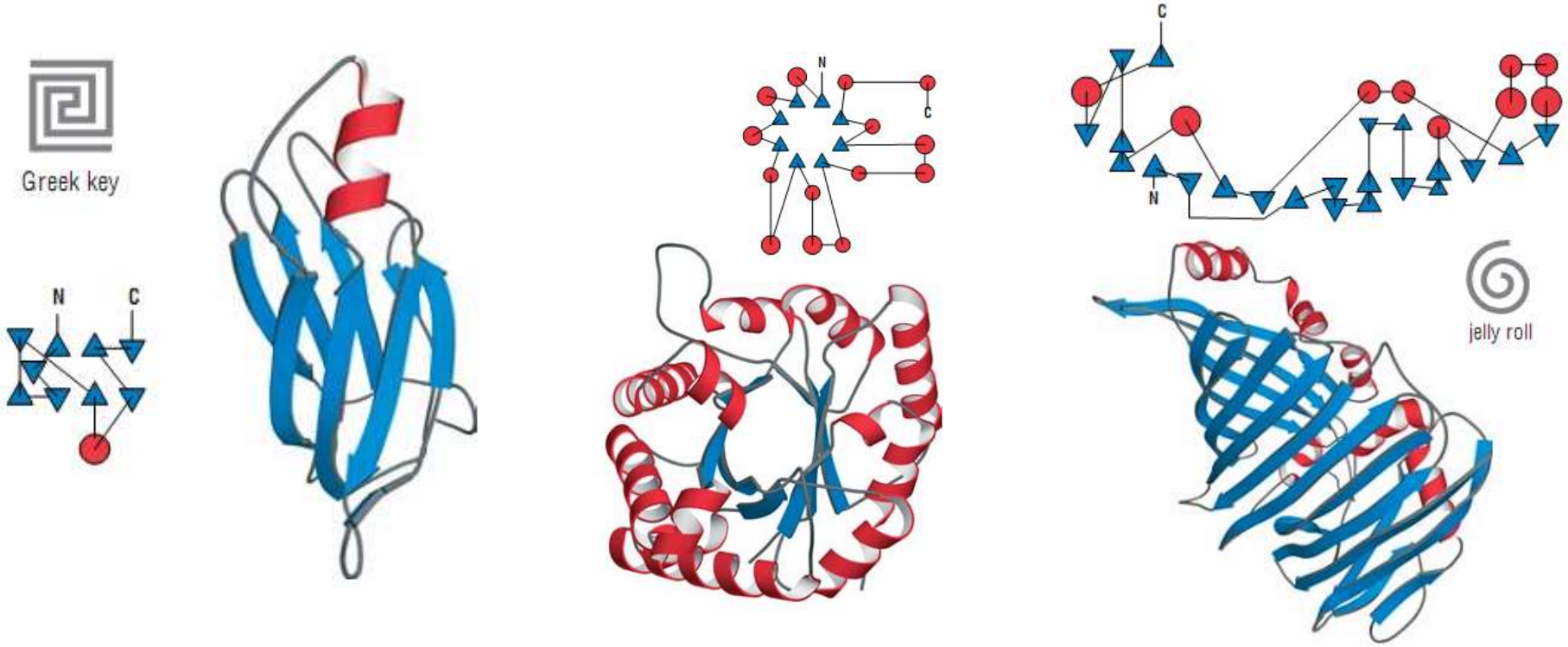




•Interações não-covalentes:



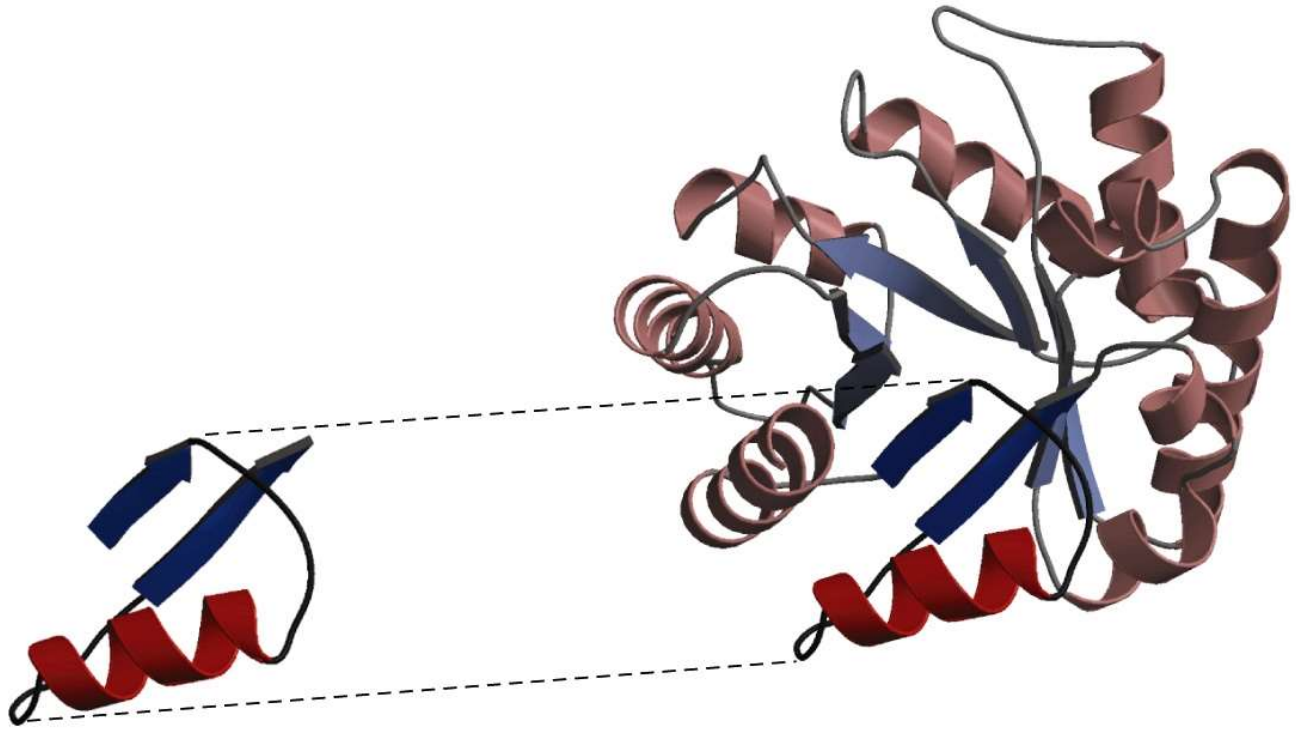
- Princípios arquitectónicos



...

Recorrência de padrões estruturais na arquitectura das biomoléculas.

- Princípios arquitectónicos (cont.):

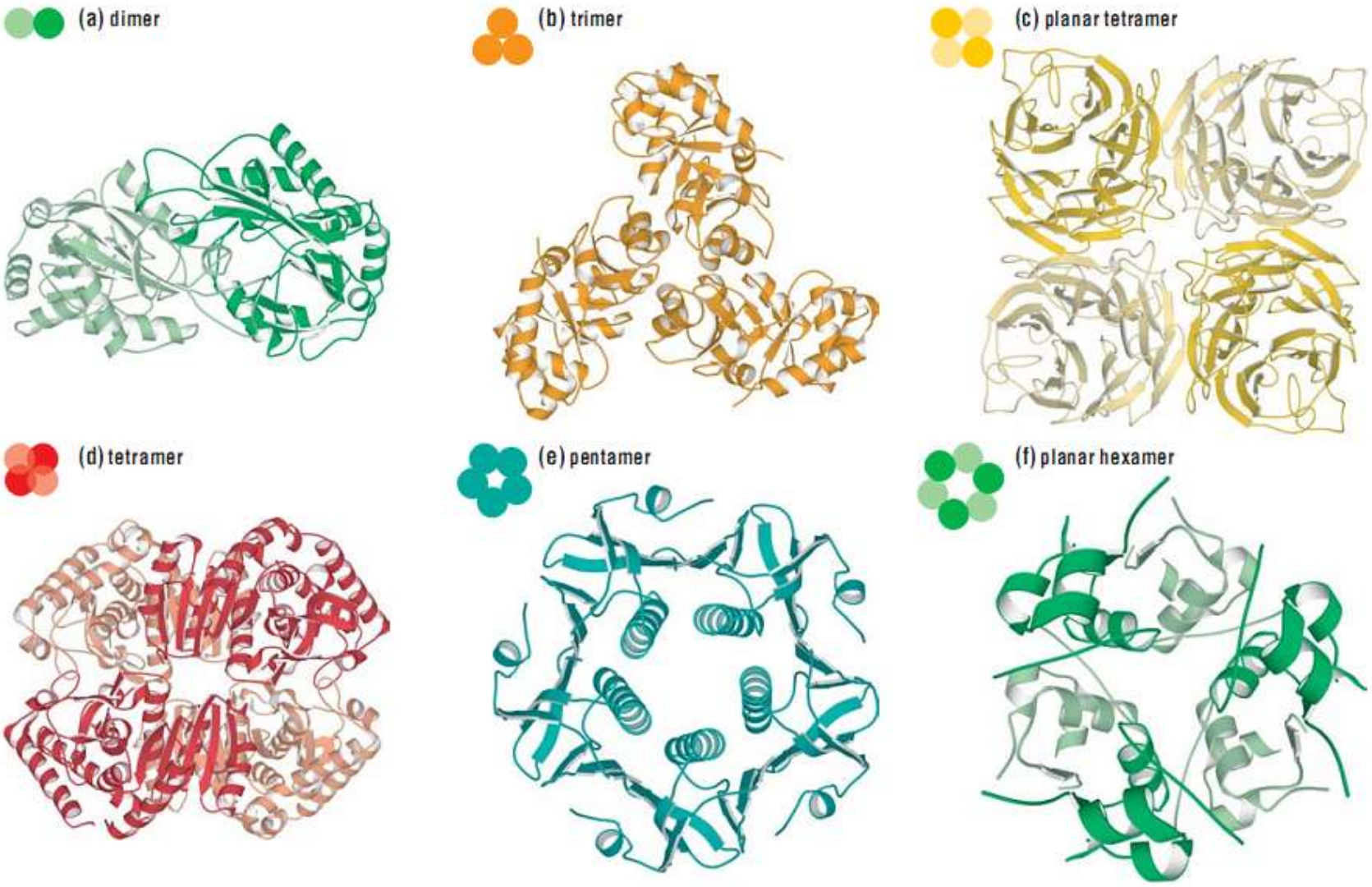


loop β-α-β

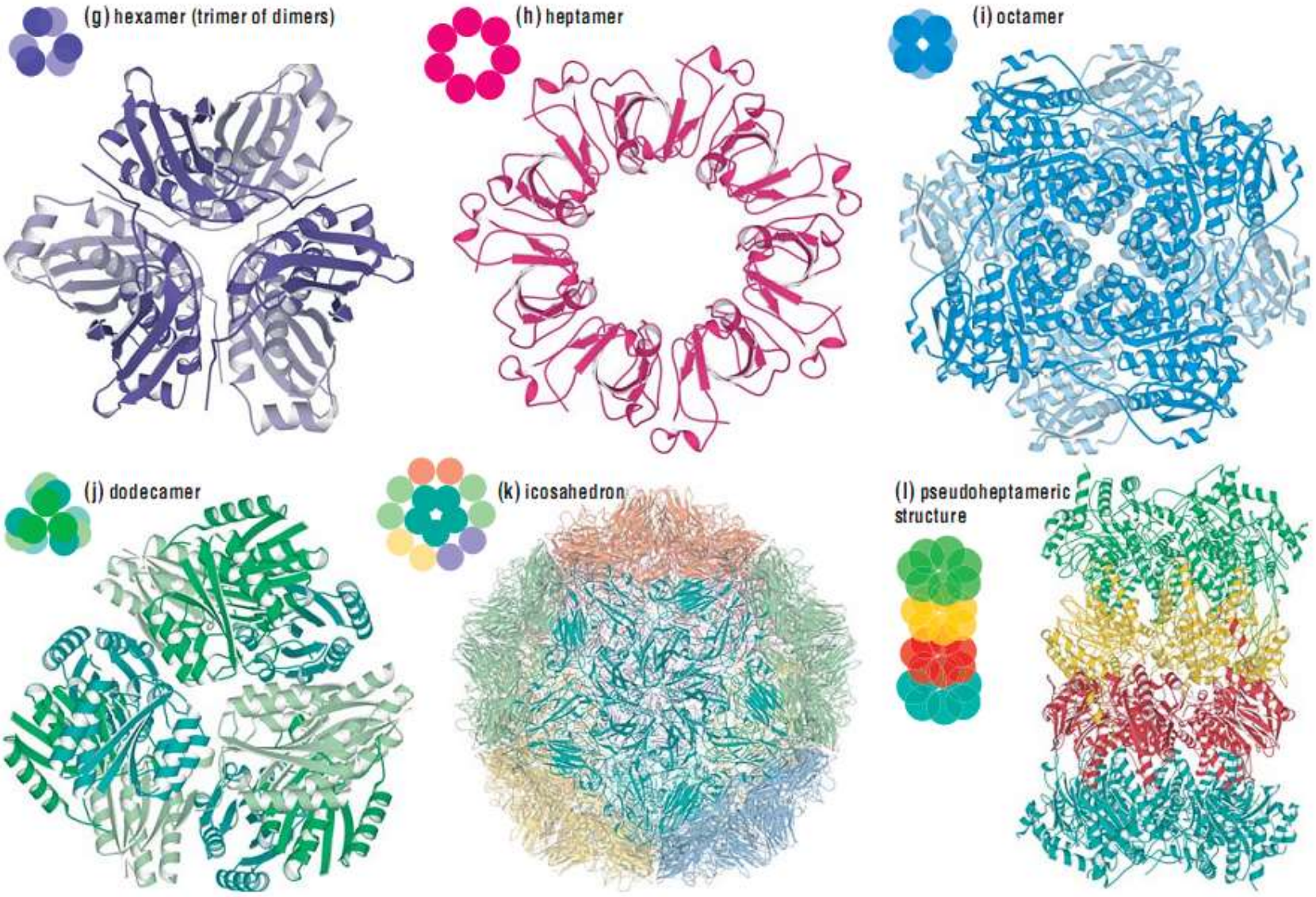
“barril” α/β

Formação de estruturas a partir da associação de unidades estruturais

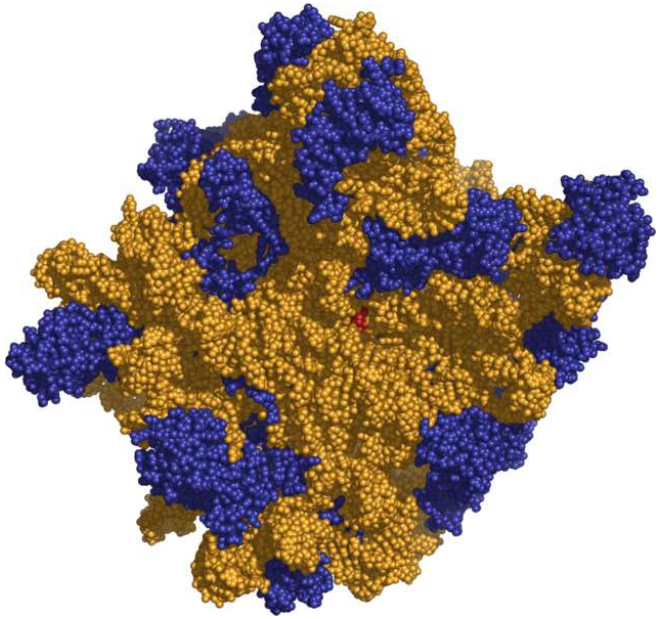
- Oligomerização:



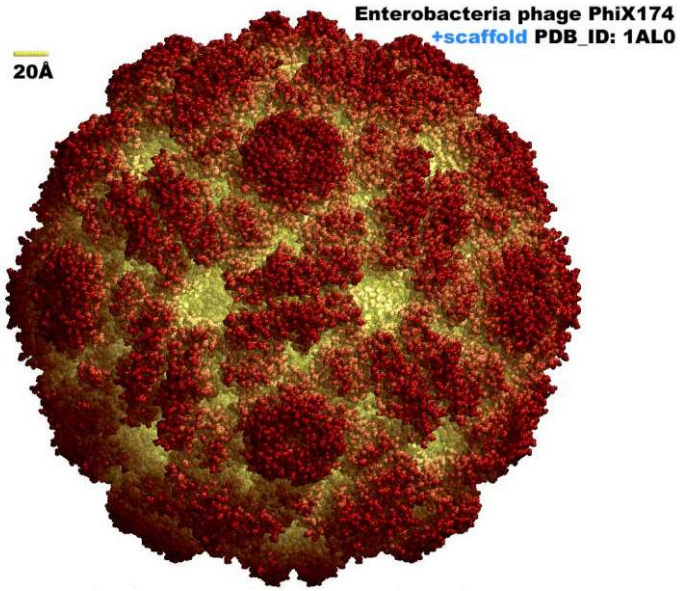
- Oligomerização(cont.):



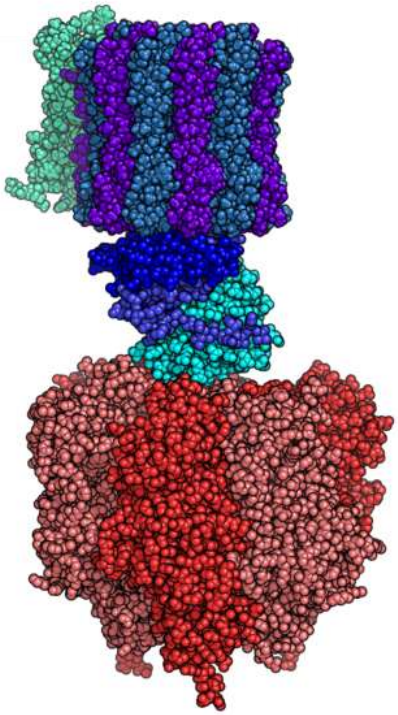
- Formação de estruturas supramacromoleculares



Ribossoma



Vírus

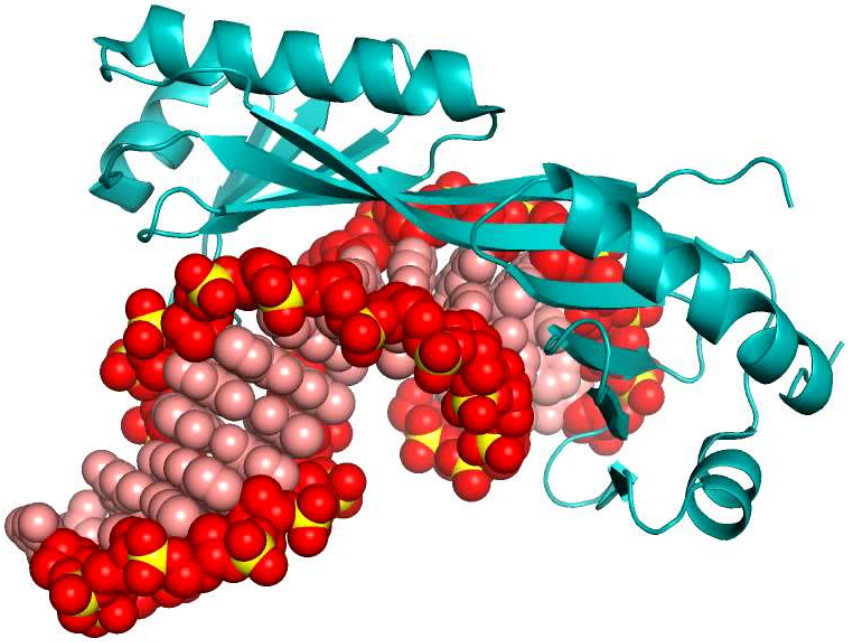


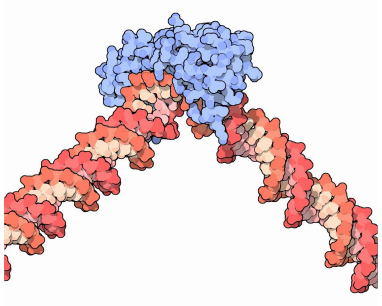
ATPase

Função

Associação a ligandos

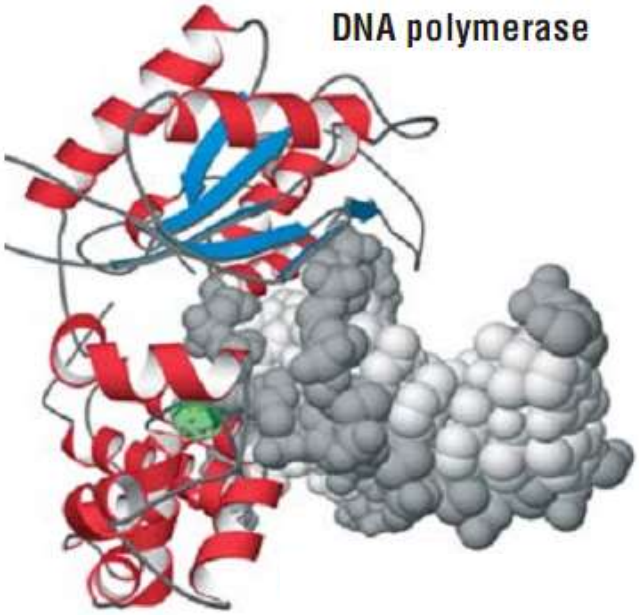
TATA-binding protein

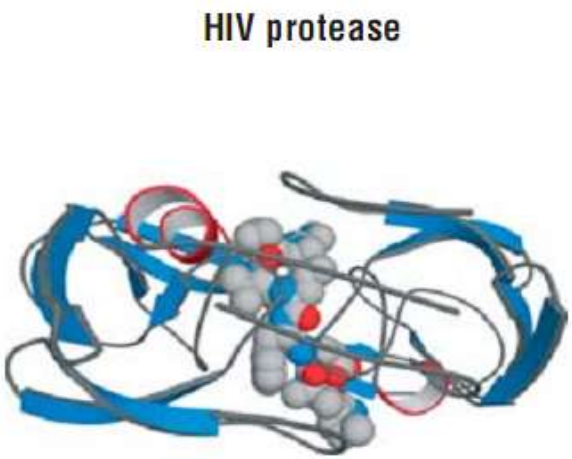




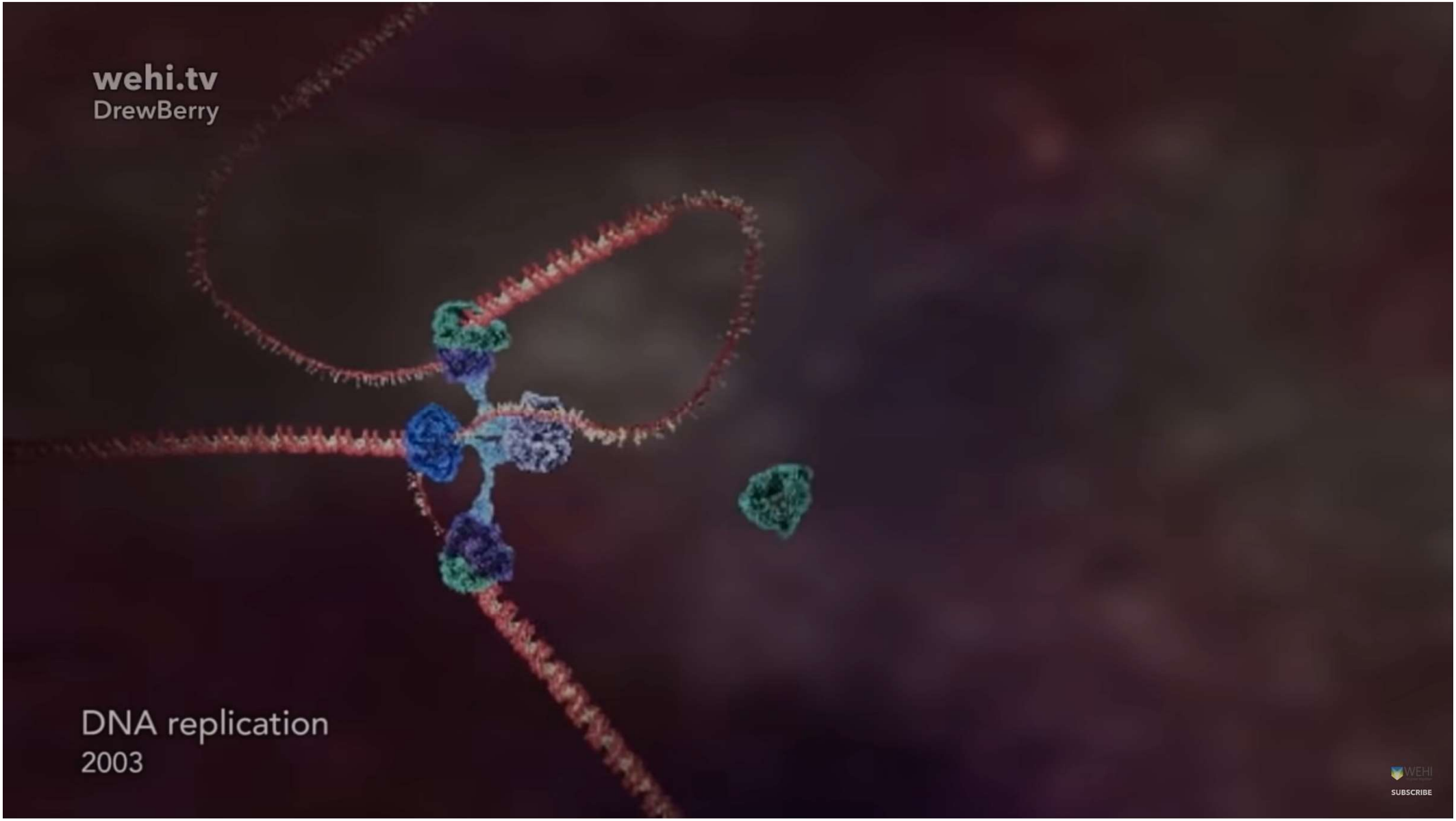
Myoglobin

Catálise



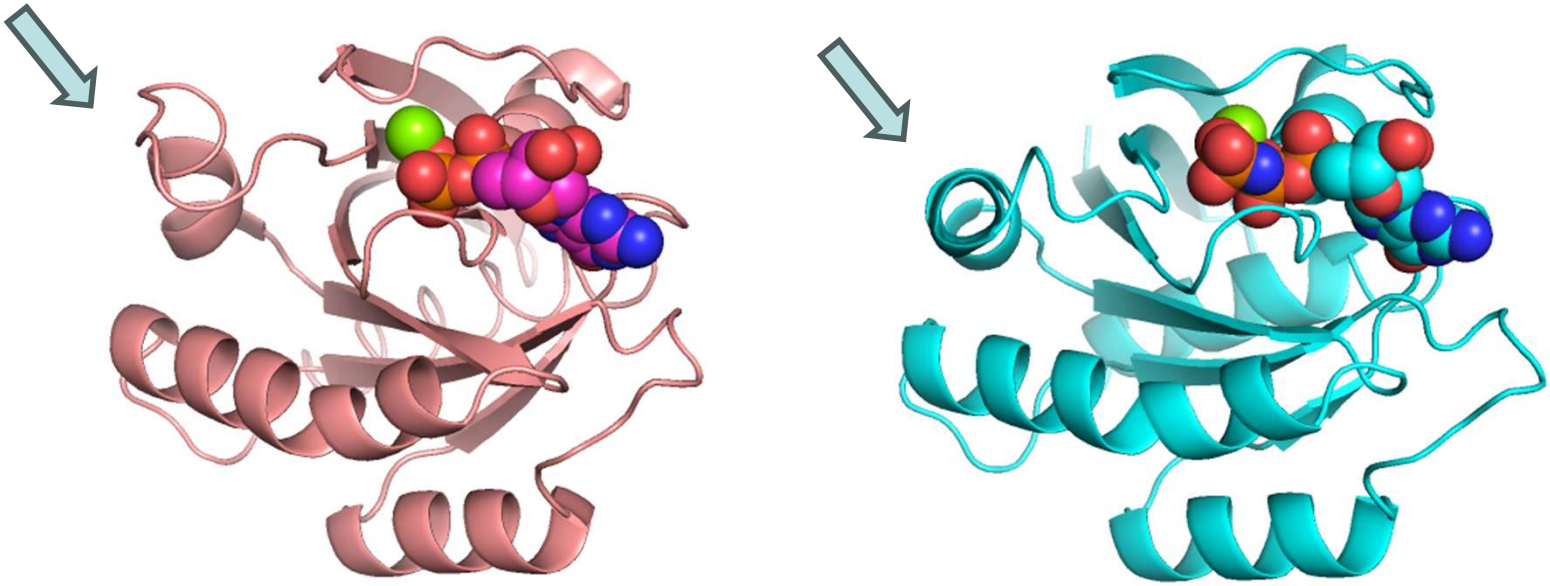


A molecular copying machine



Sinalização

ras protein

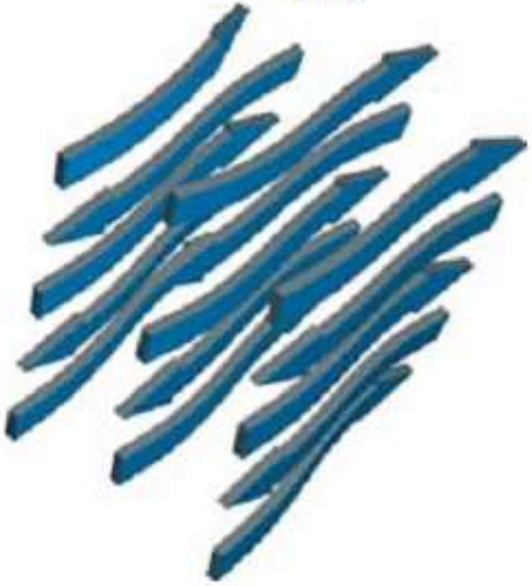


On **Off**

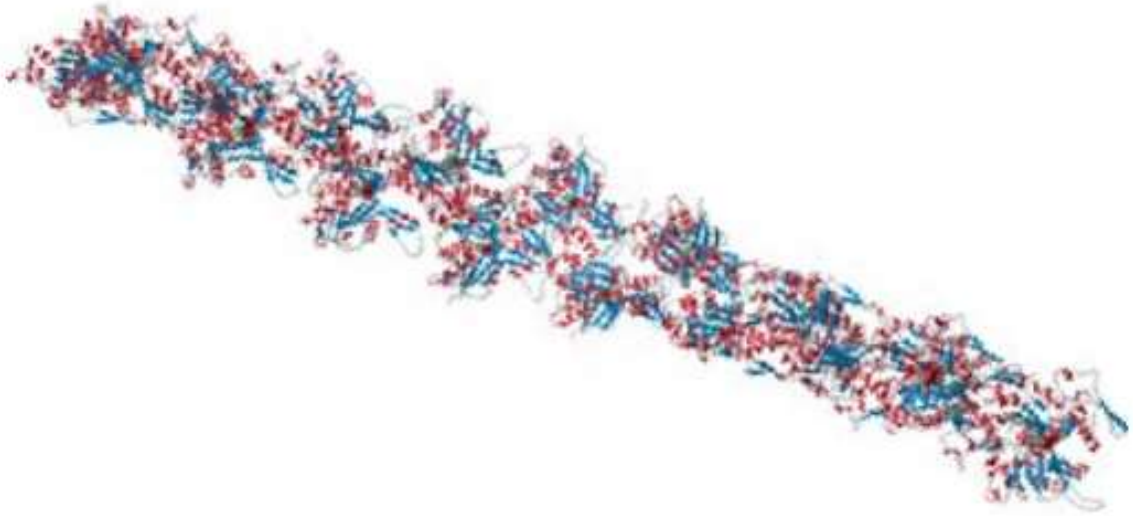
PDB: 5p21, 4q21

Estrutura

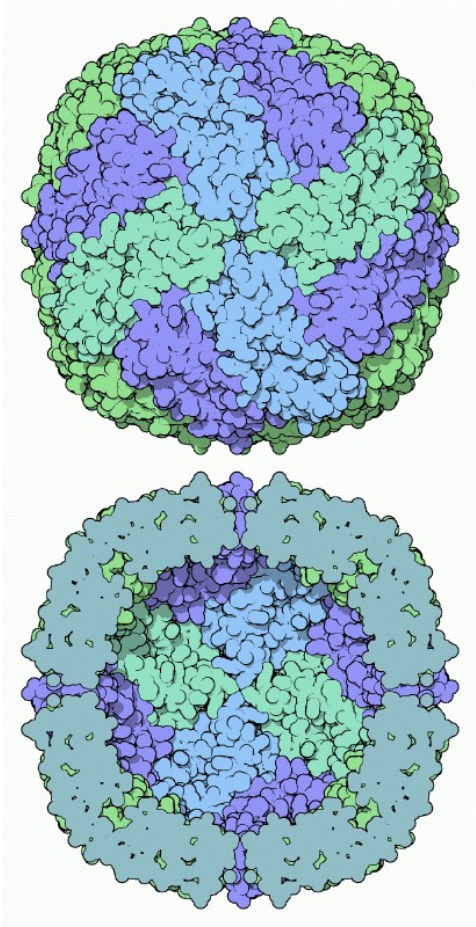
Silk



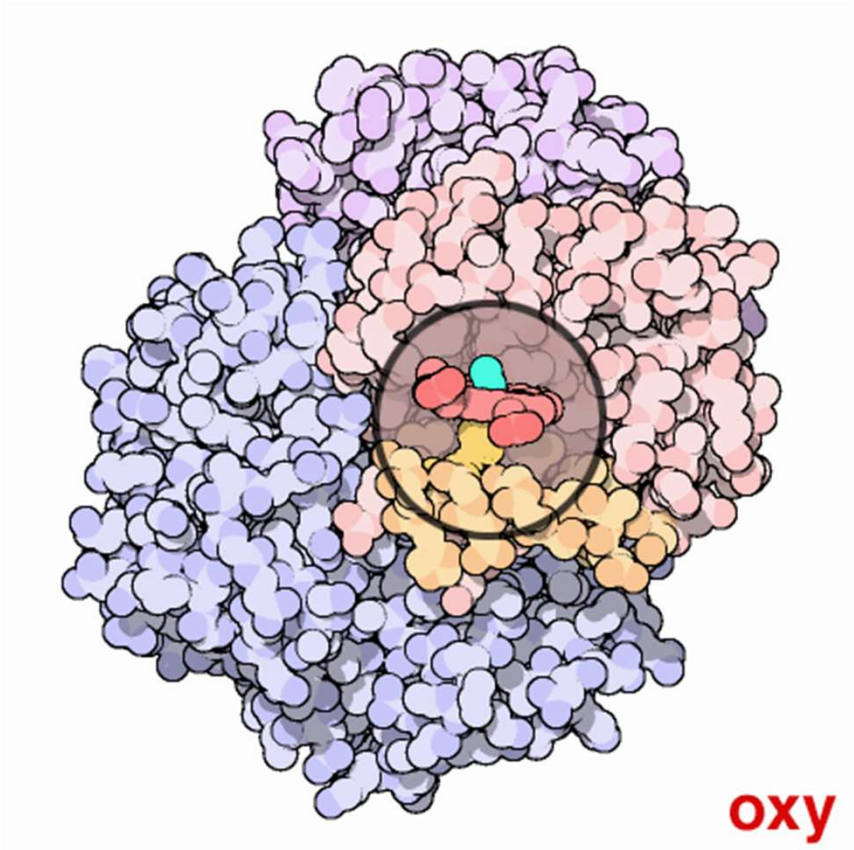
F-actin



Transporte

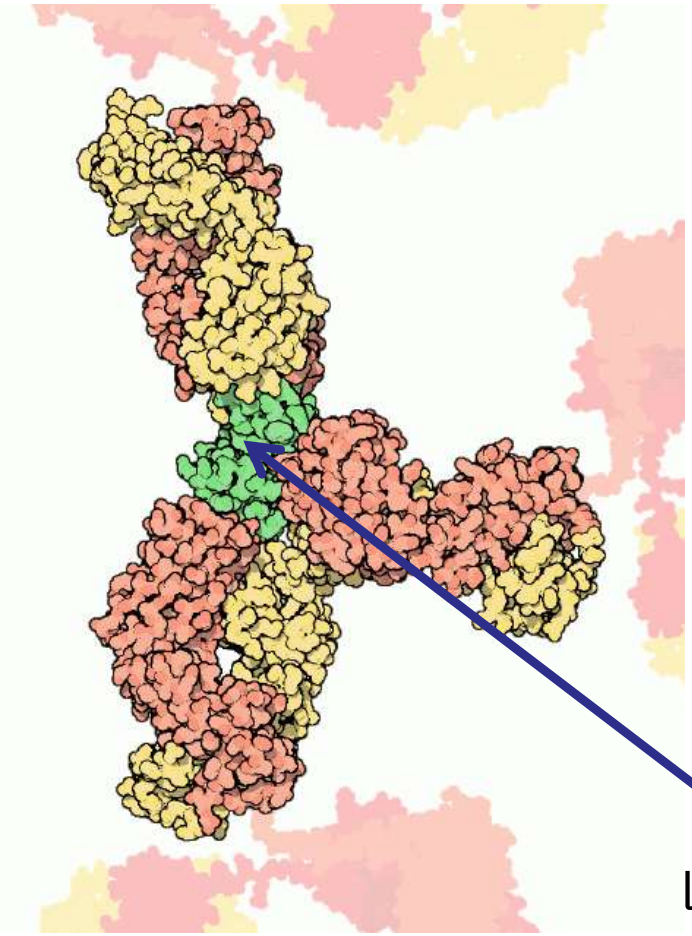


Ferritina (ferro)

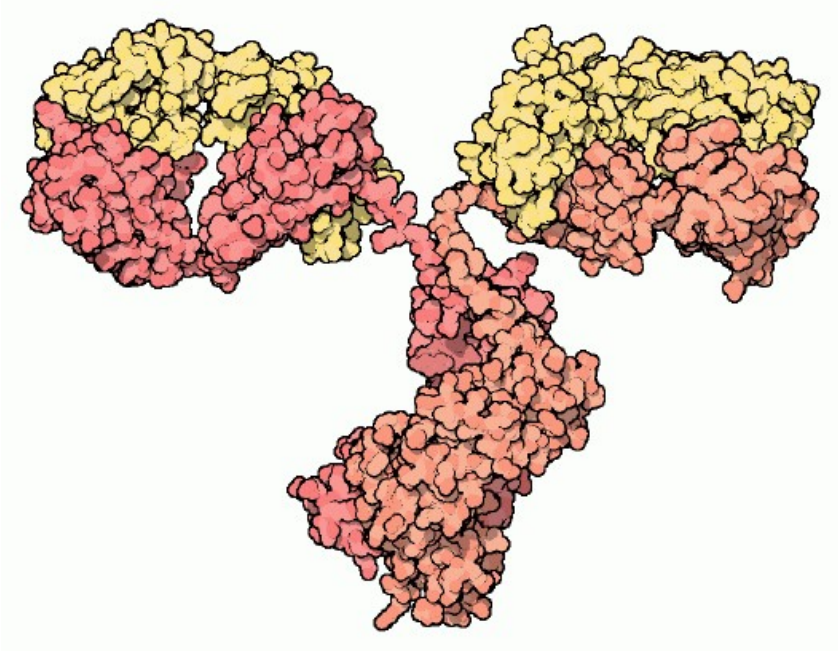


Hemoglobina (oxigénio)

Defesa

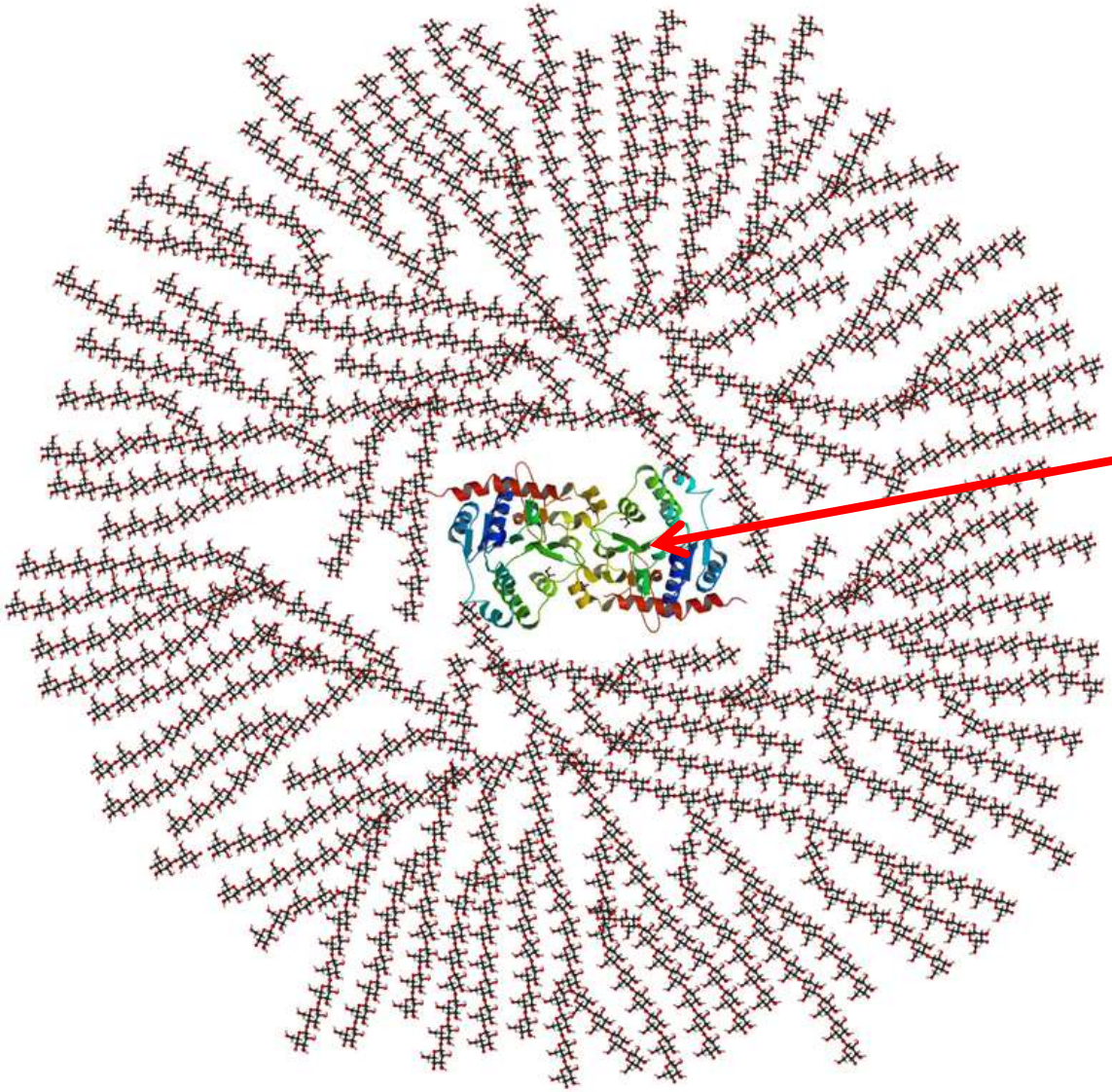


lisozima



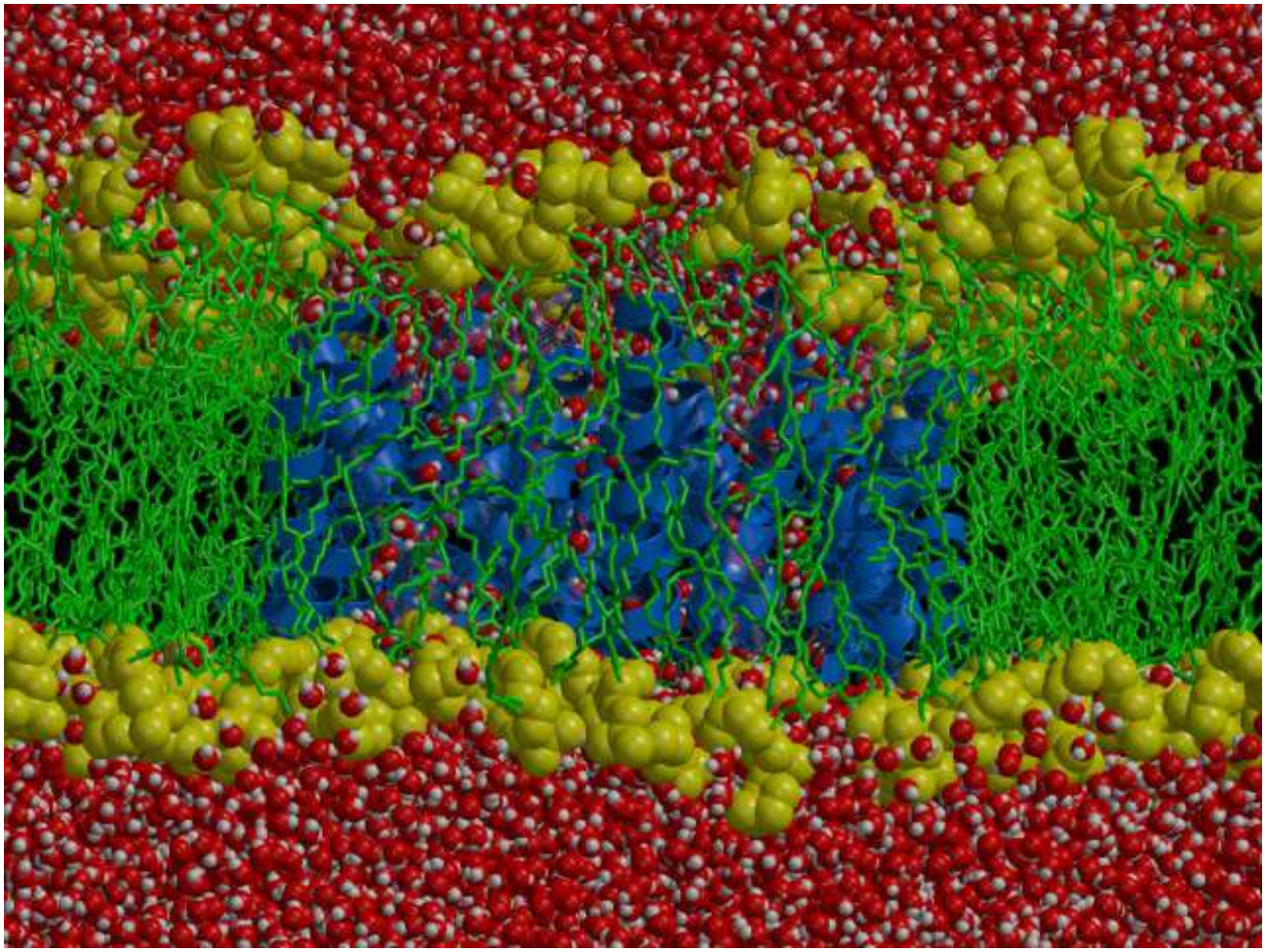
imunoglobulina

Armazenamento



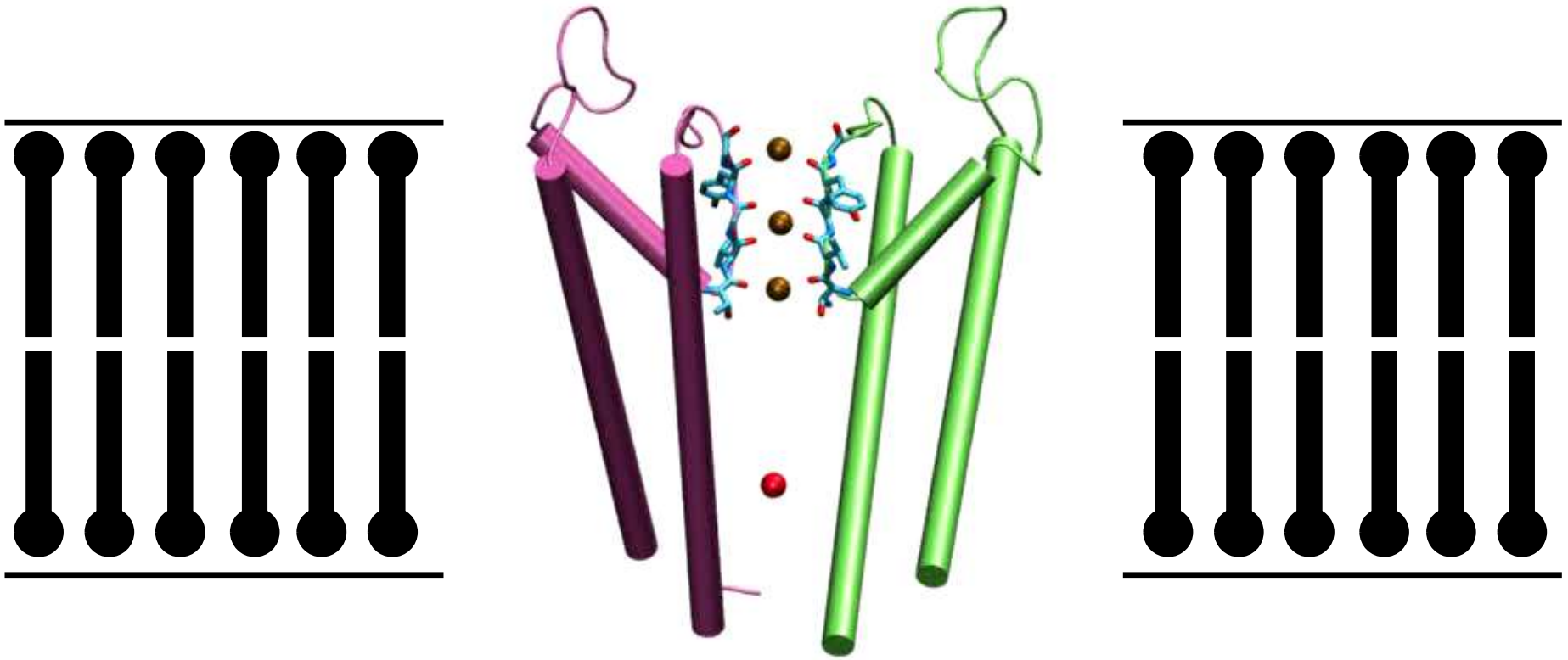
Glicogénio

Compartimentação



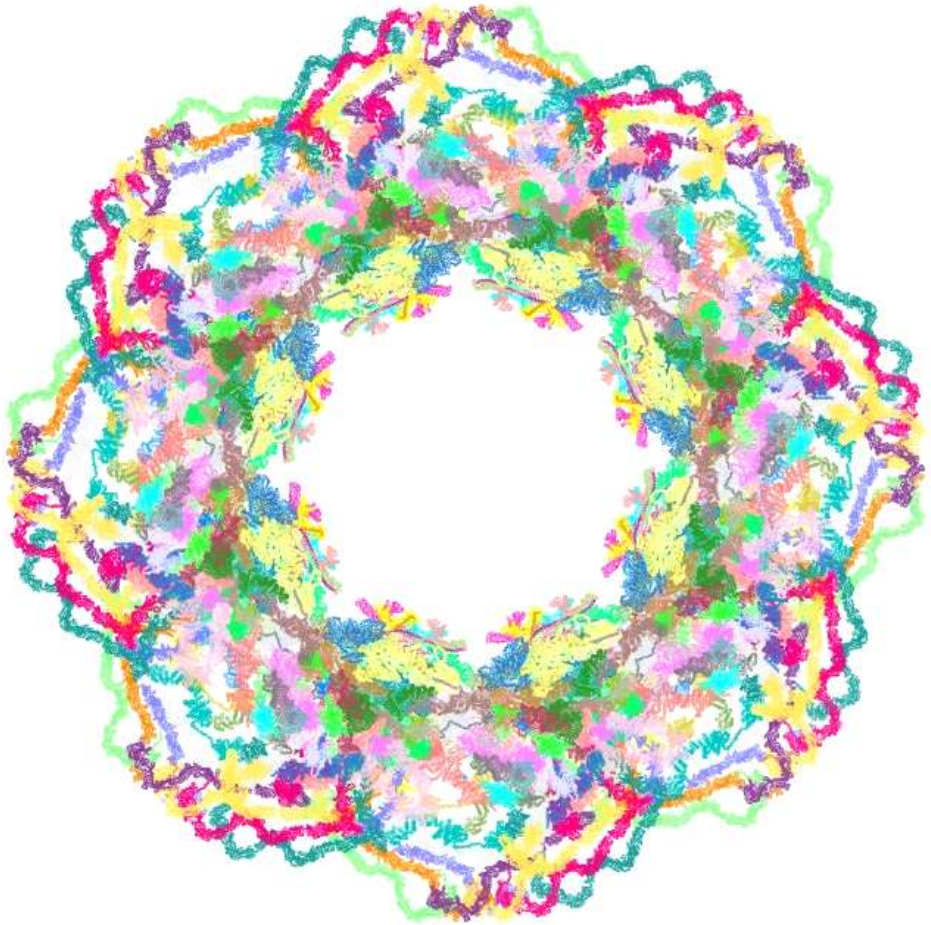
Membrana+aquaporina

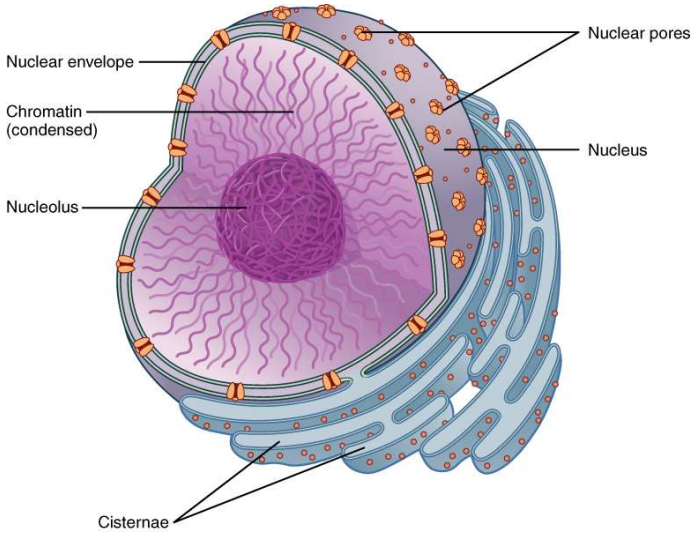
Permeabilidade e transporte

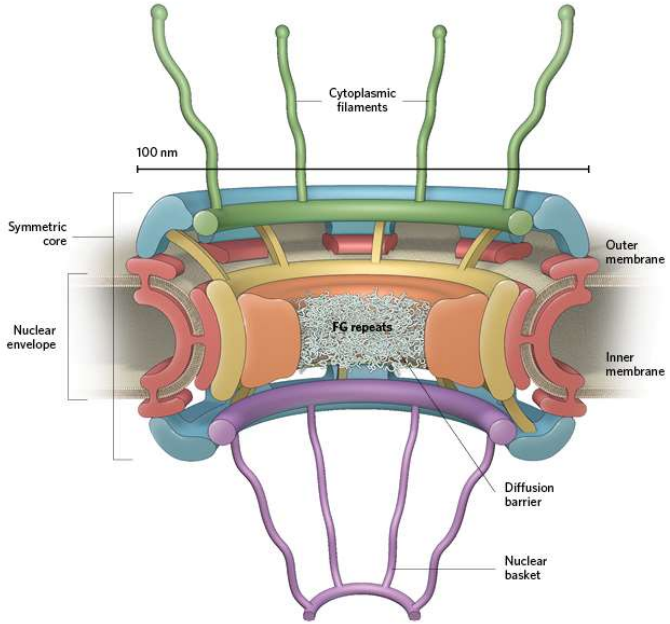


As macromoléculas biológicas funcionam como máquinas moleculares

Estrutura de um poro nuclear



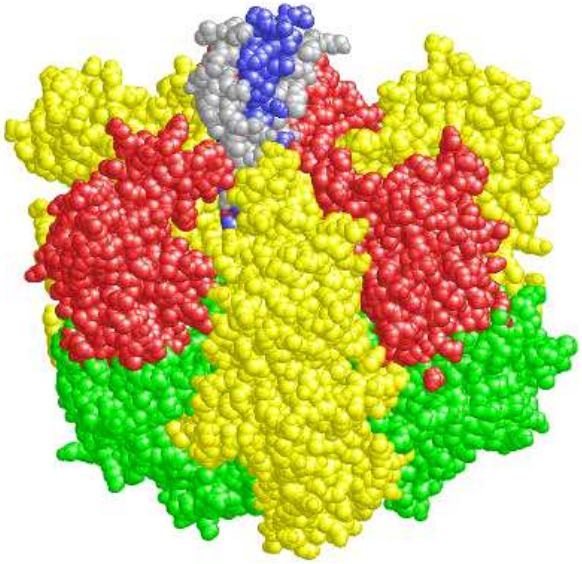


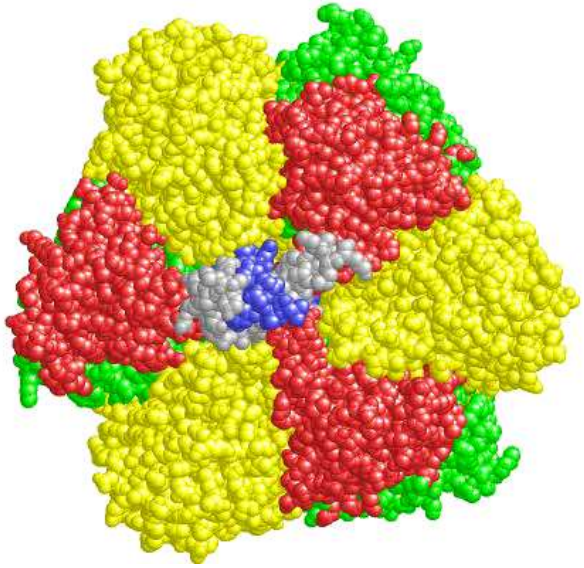


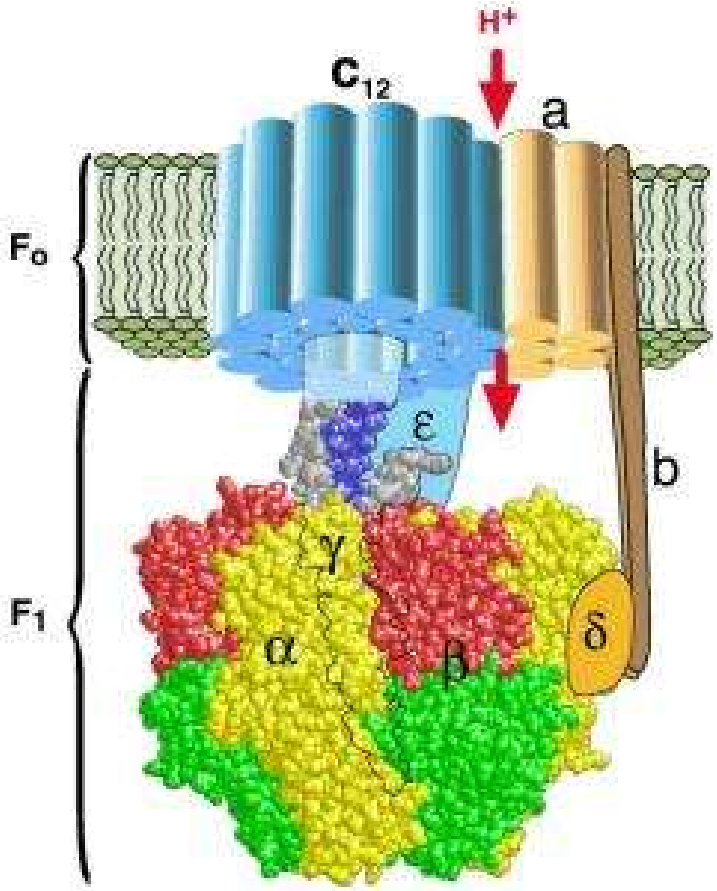
PDB: 7r5j

Conversão de energia

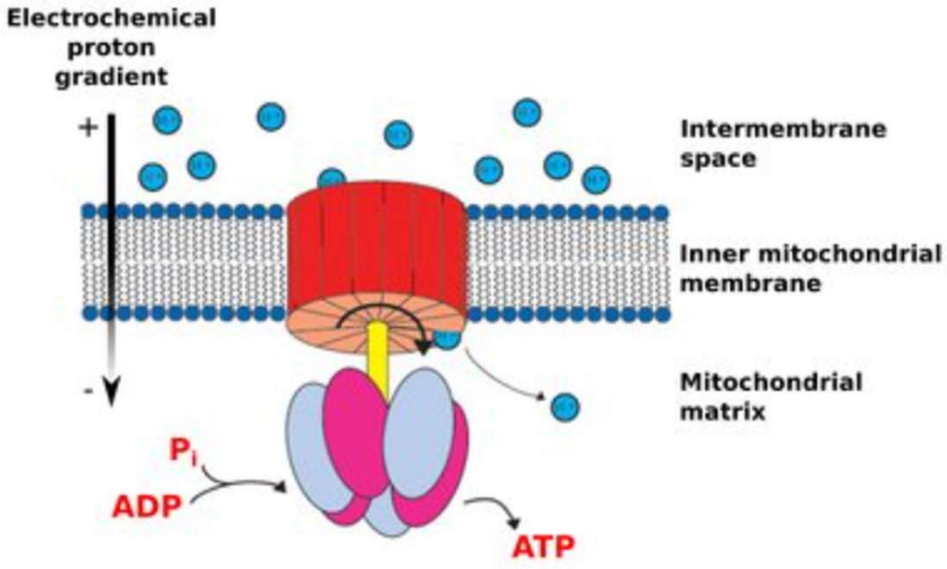
ATPsintase



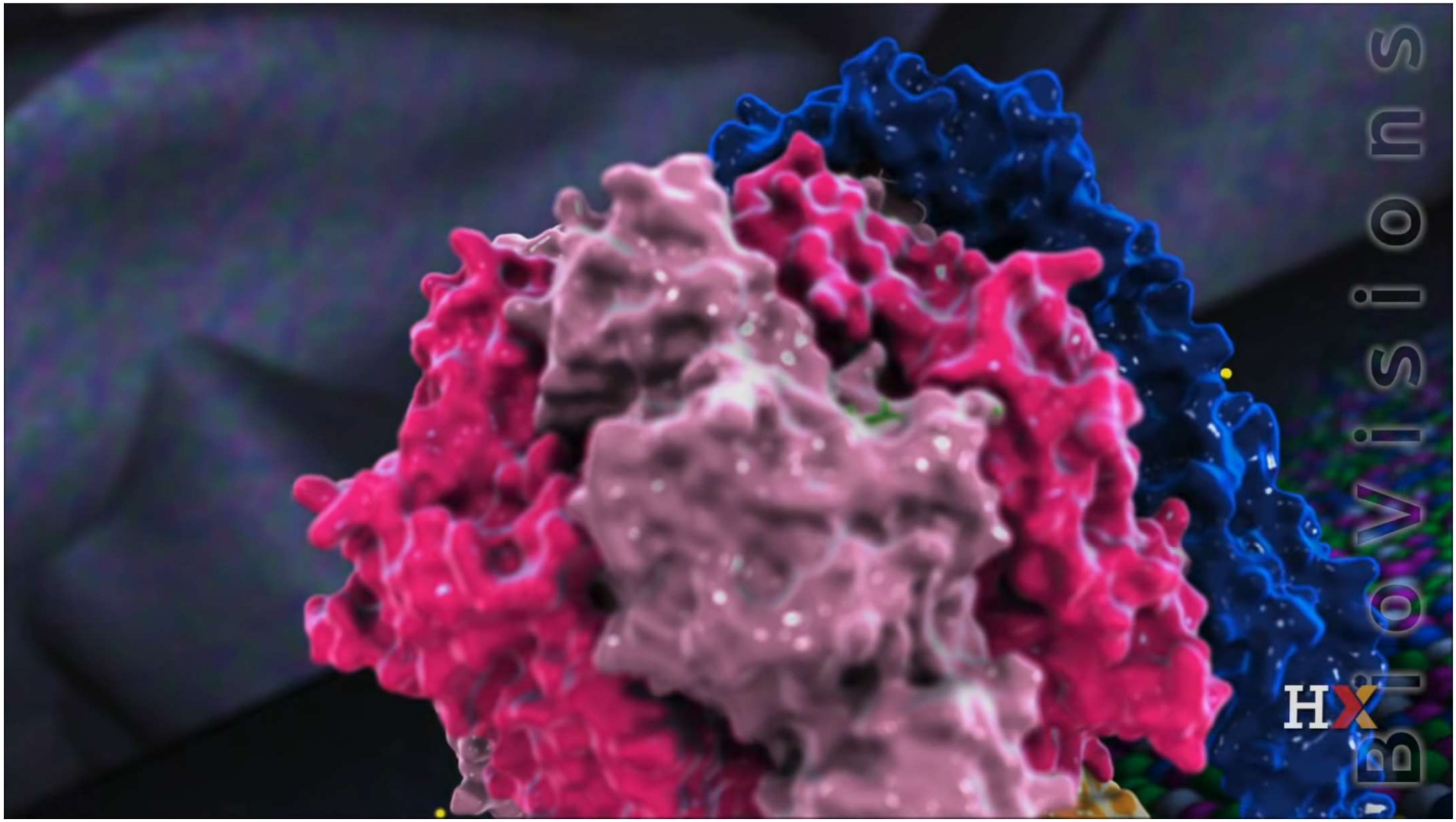




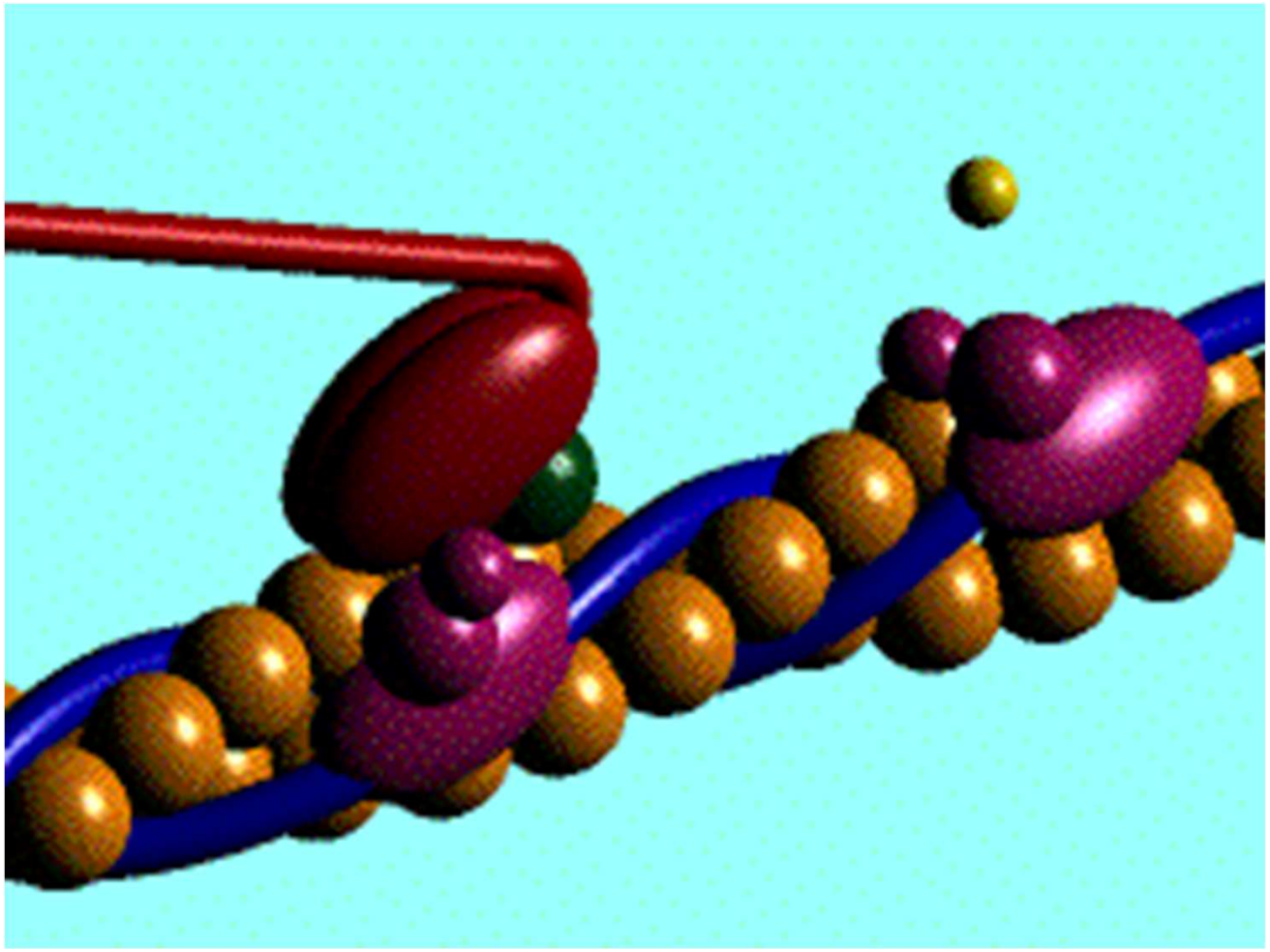
H. Wang and G. Oster (1998). Nature 396:279-282.



A molecular power generator

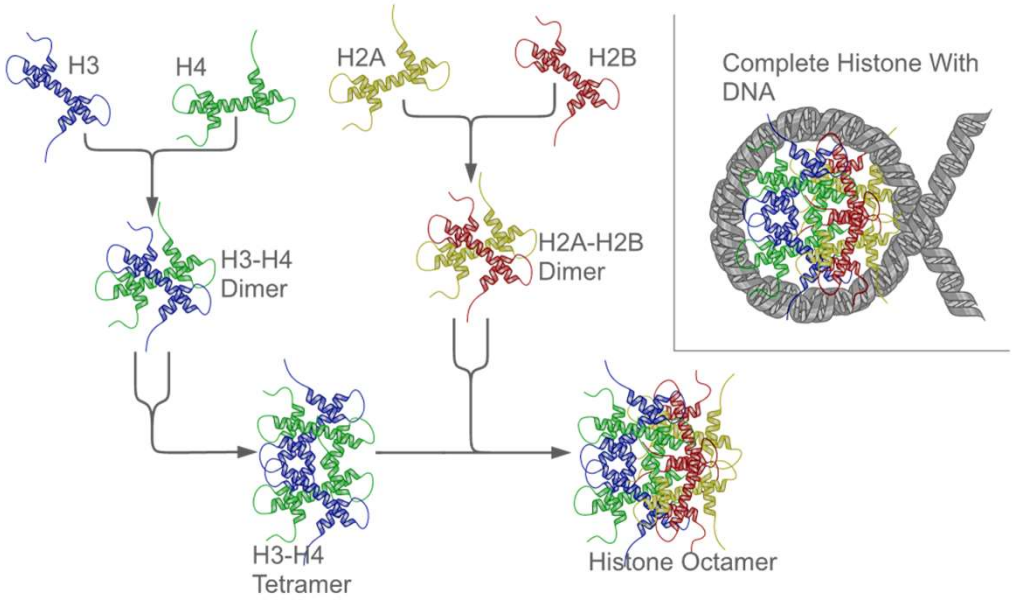


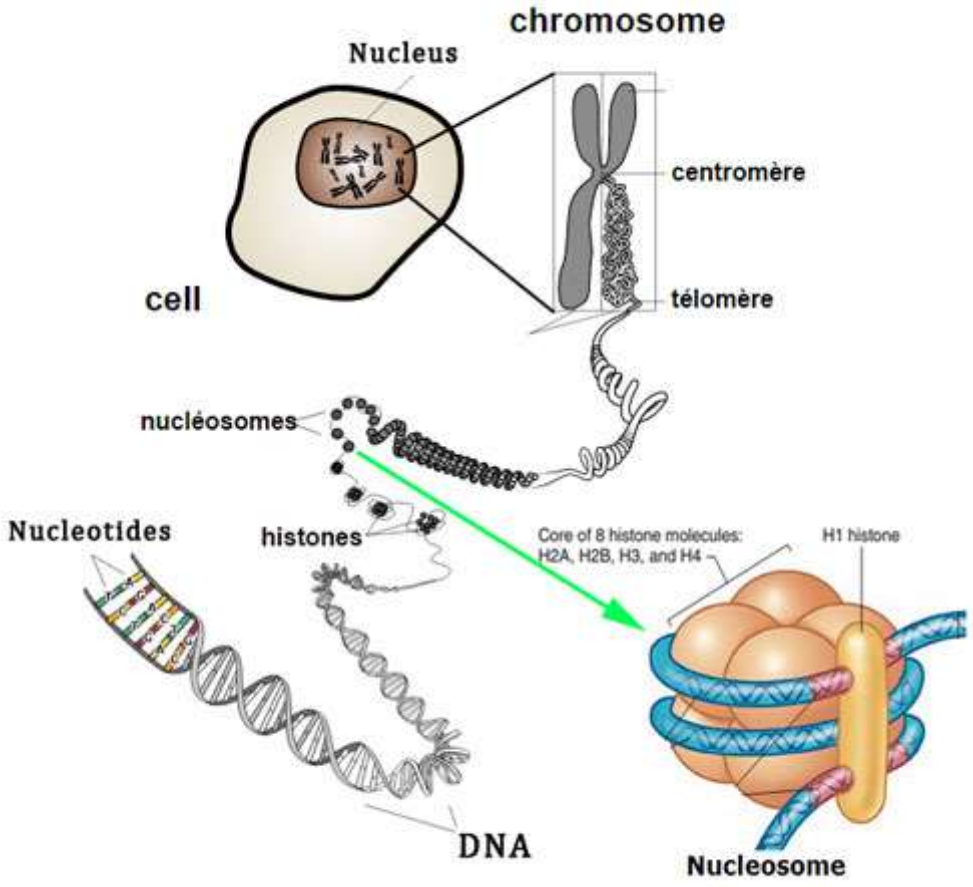
Motilidade

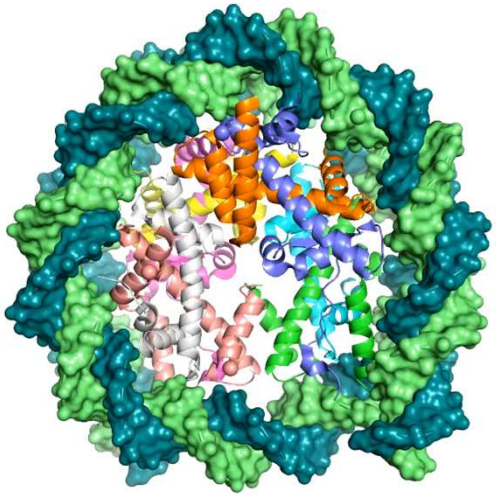


Actina+Miosina

Informação

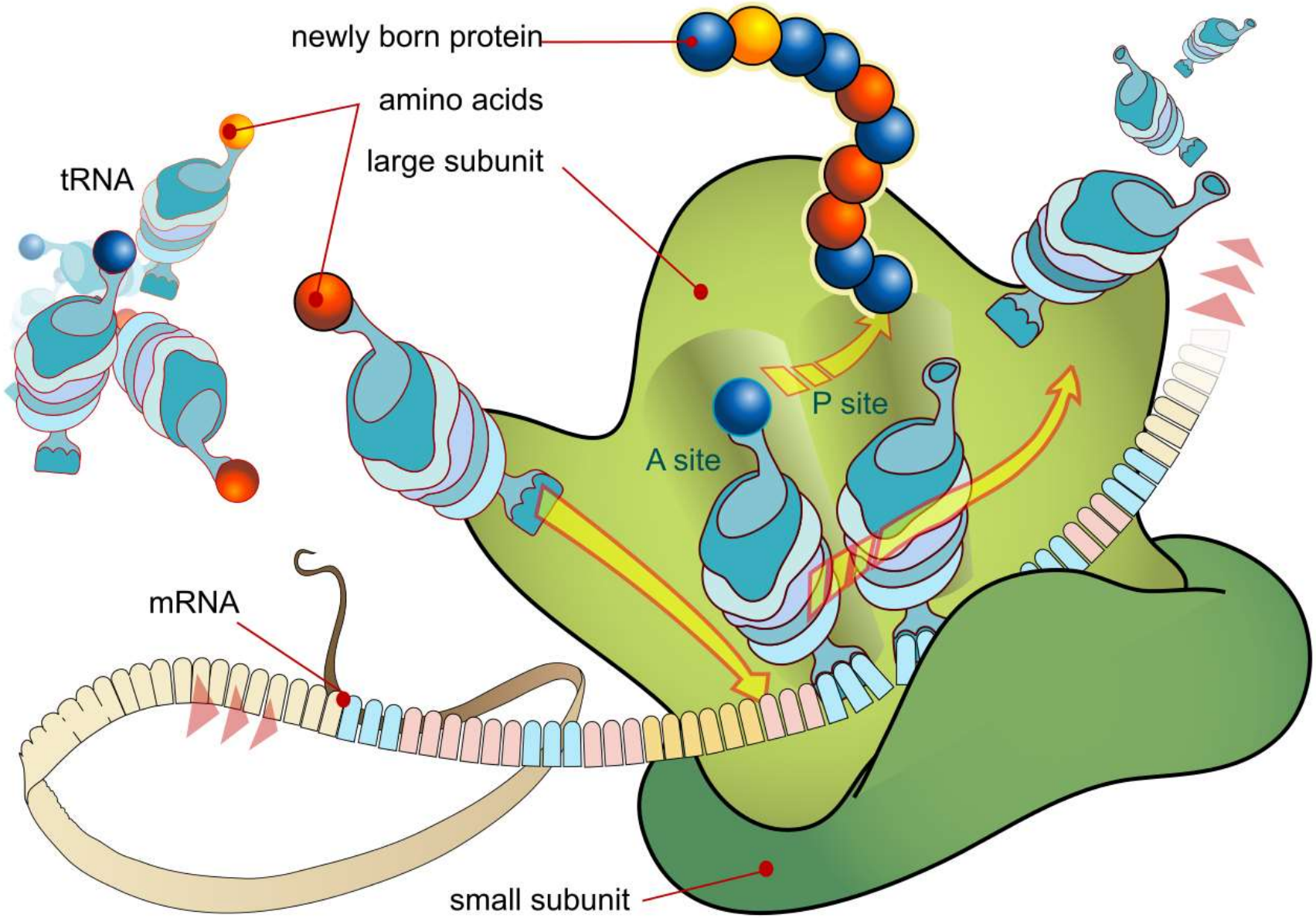




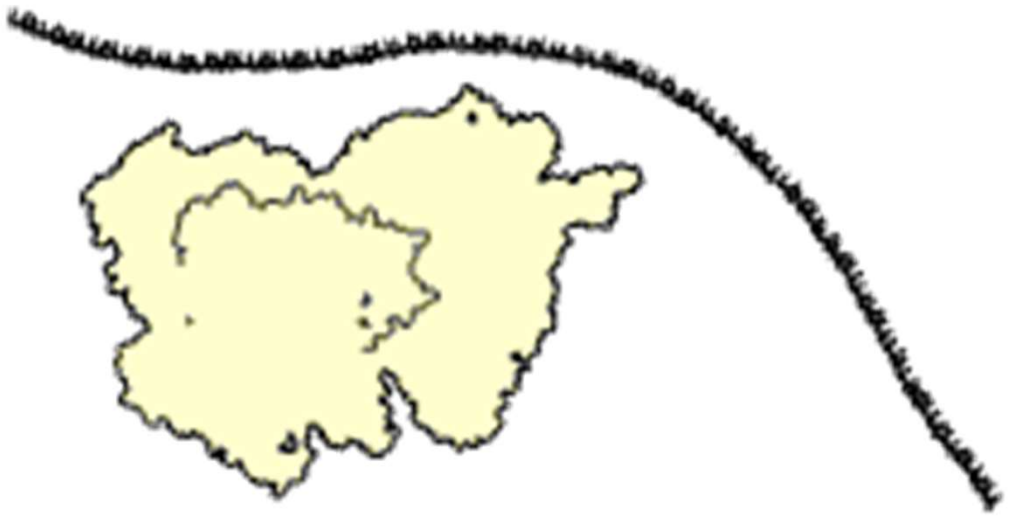


Nucleossoma

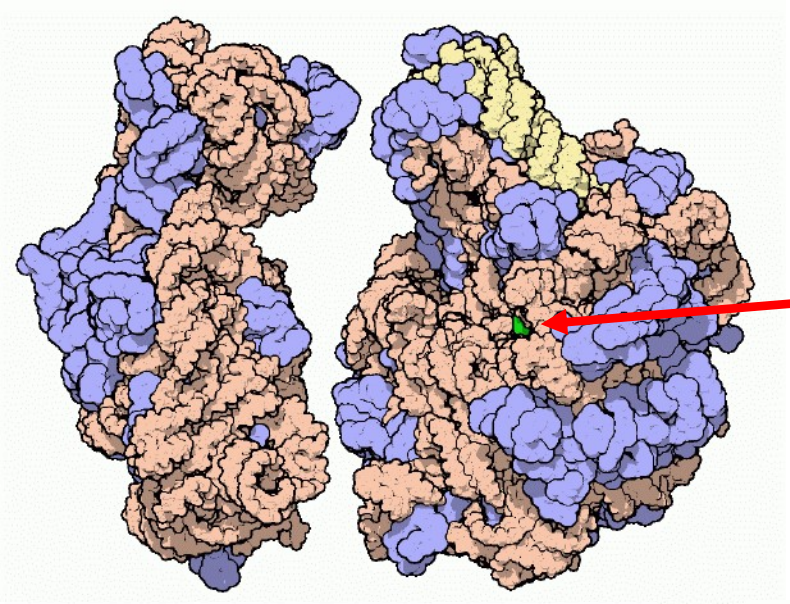
Síntese proteíca



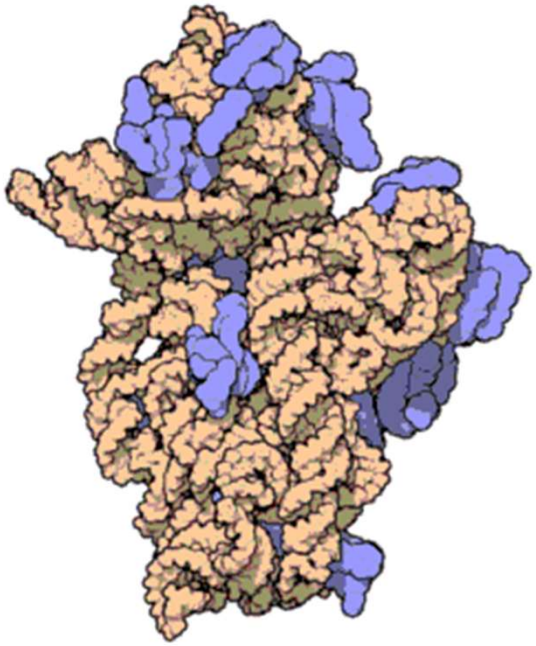
Síntese proteíca (animação)

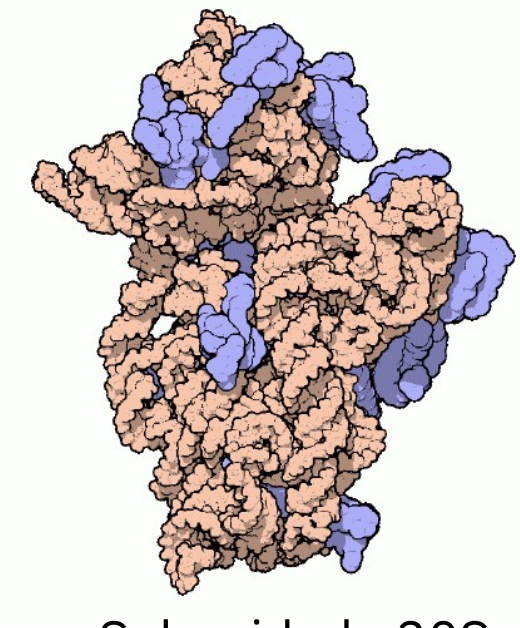


Estrutura do ribossoma bacteriano

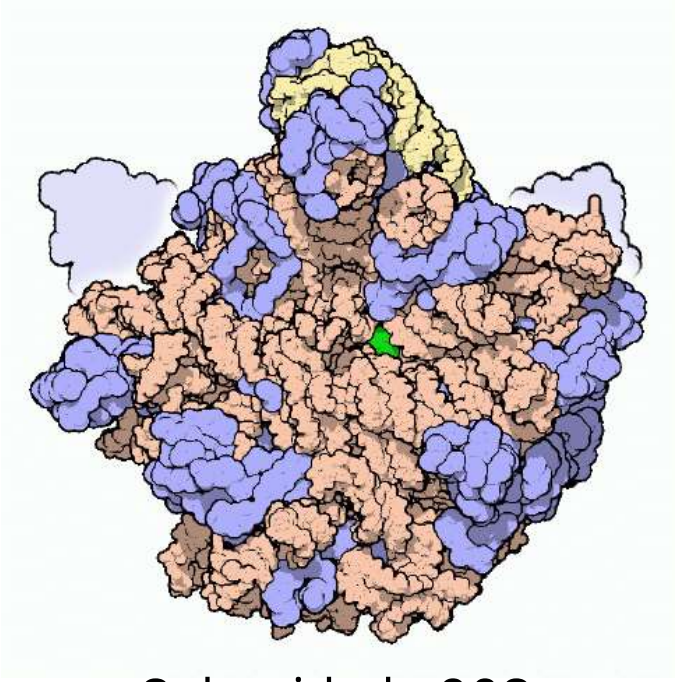


RNA catalítico





Subunidade 30S



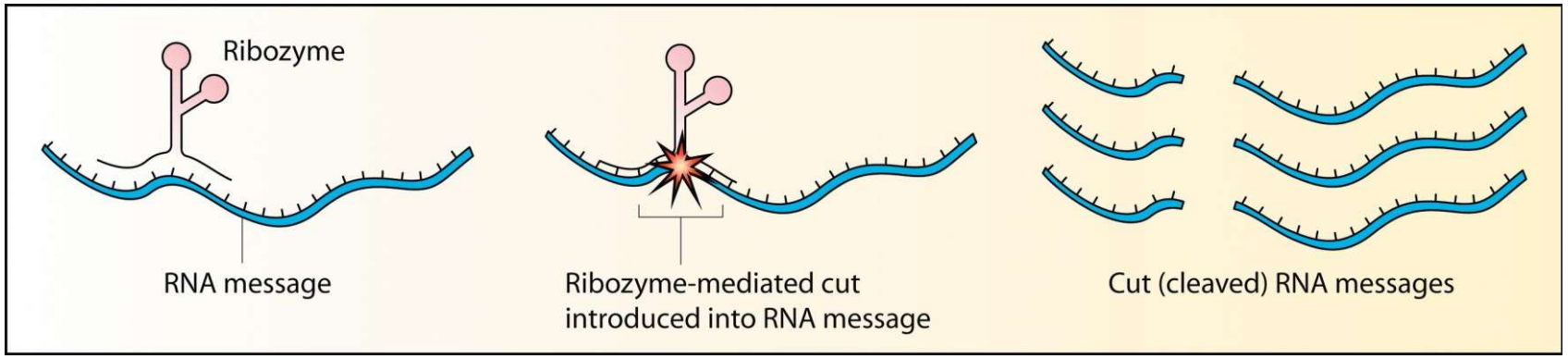
Subunidade 20S

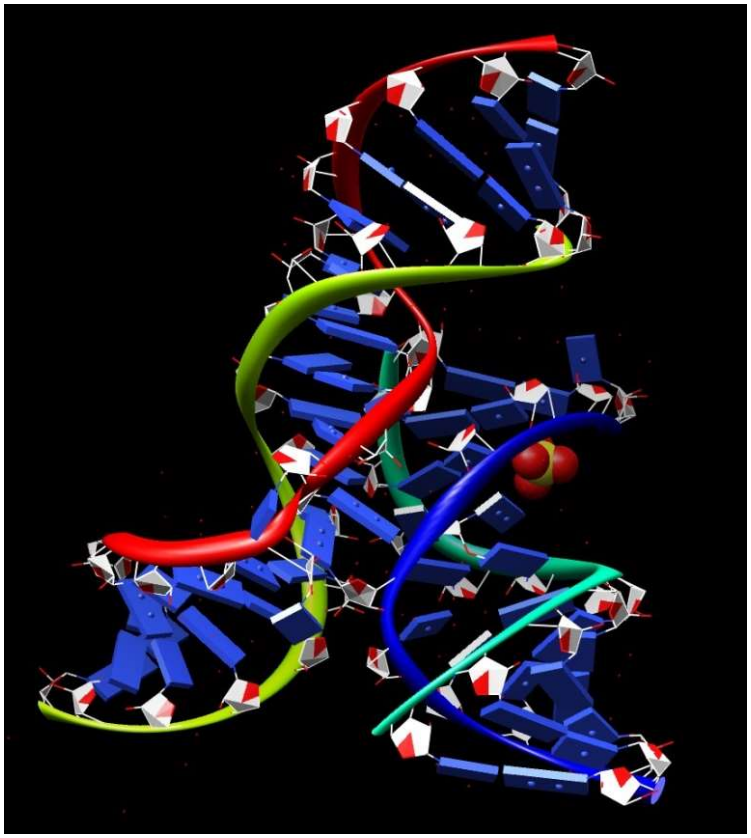
Reciclagem de proteínas

Proteassoma

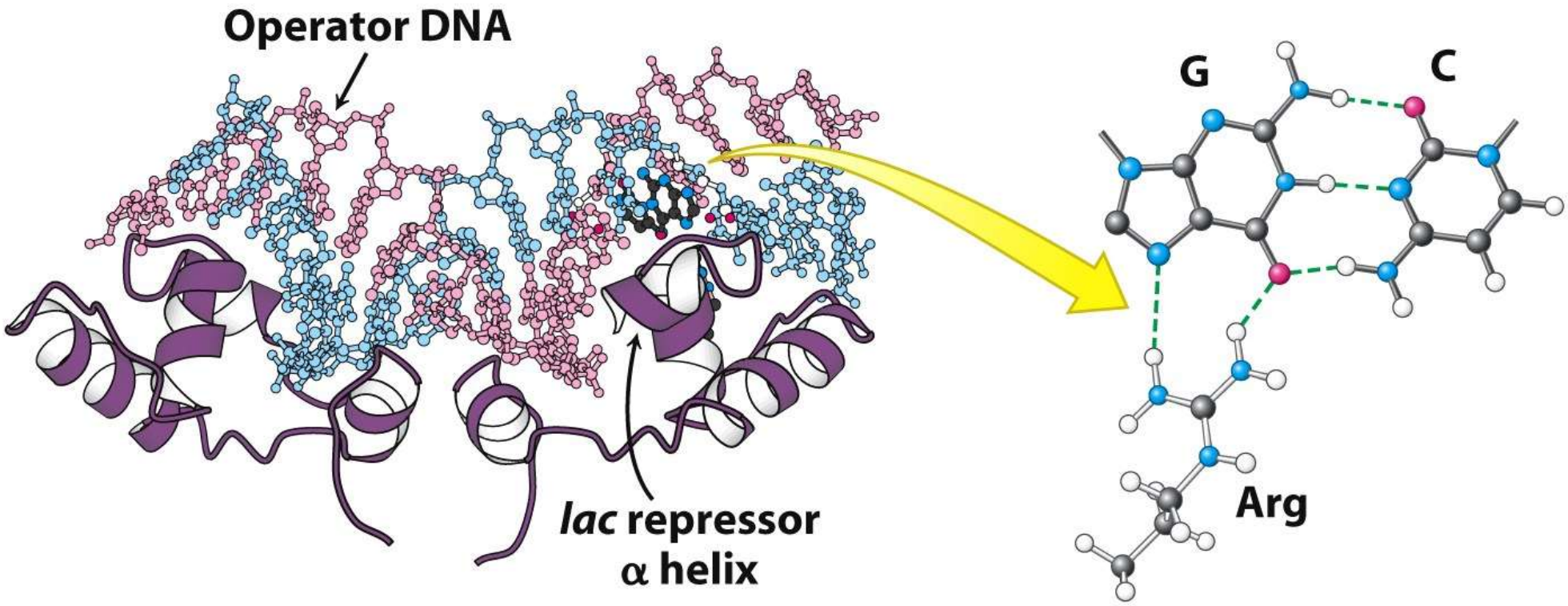
Assemblagem de máquinas moleculares

Ribozimas

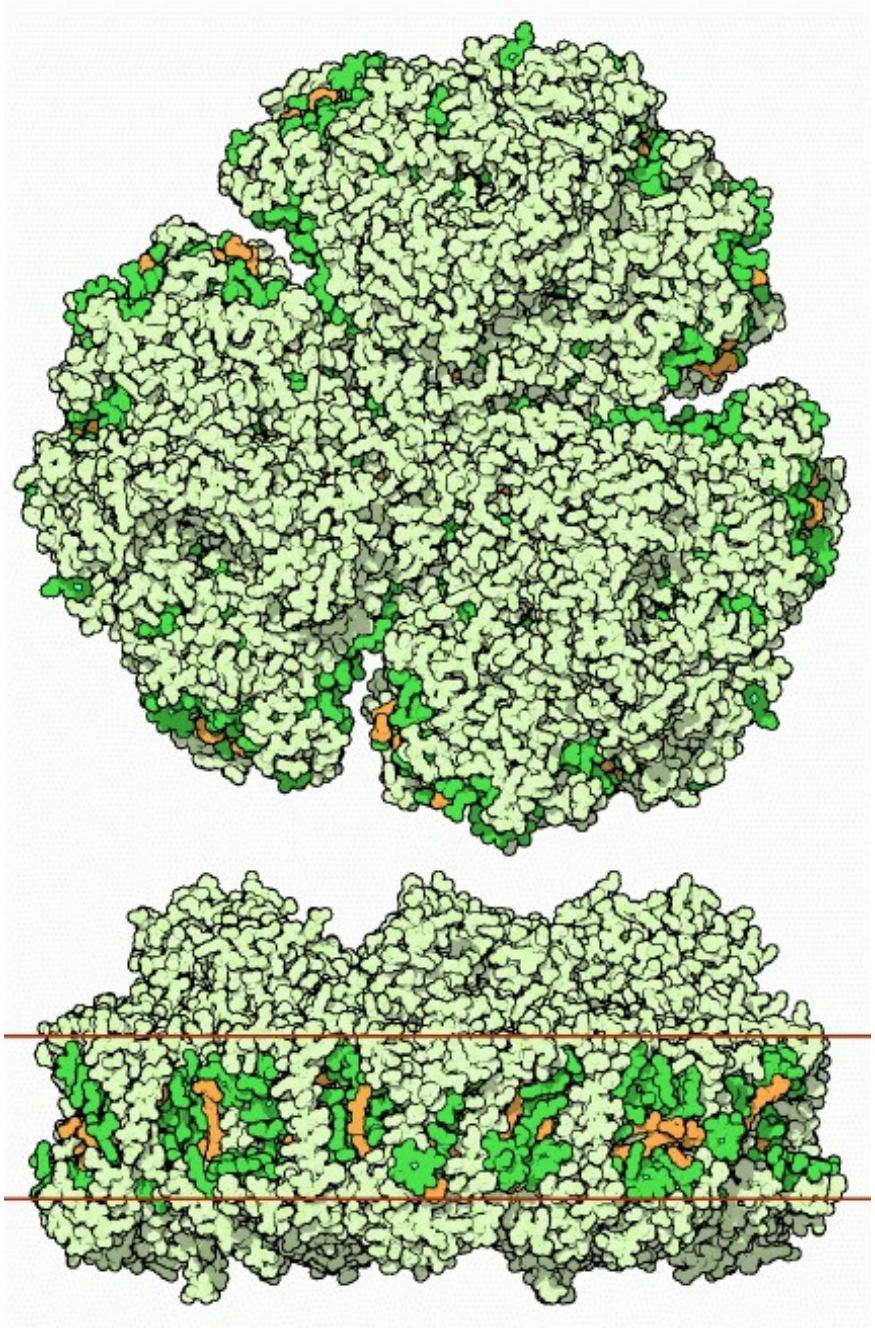

Ribozyme
RNA message
Ribozyme-mediated cut
introduced into RNA message
Cut (cleaved) RNA messages



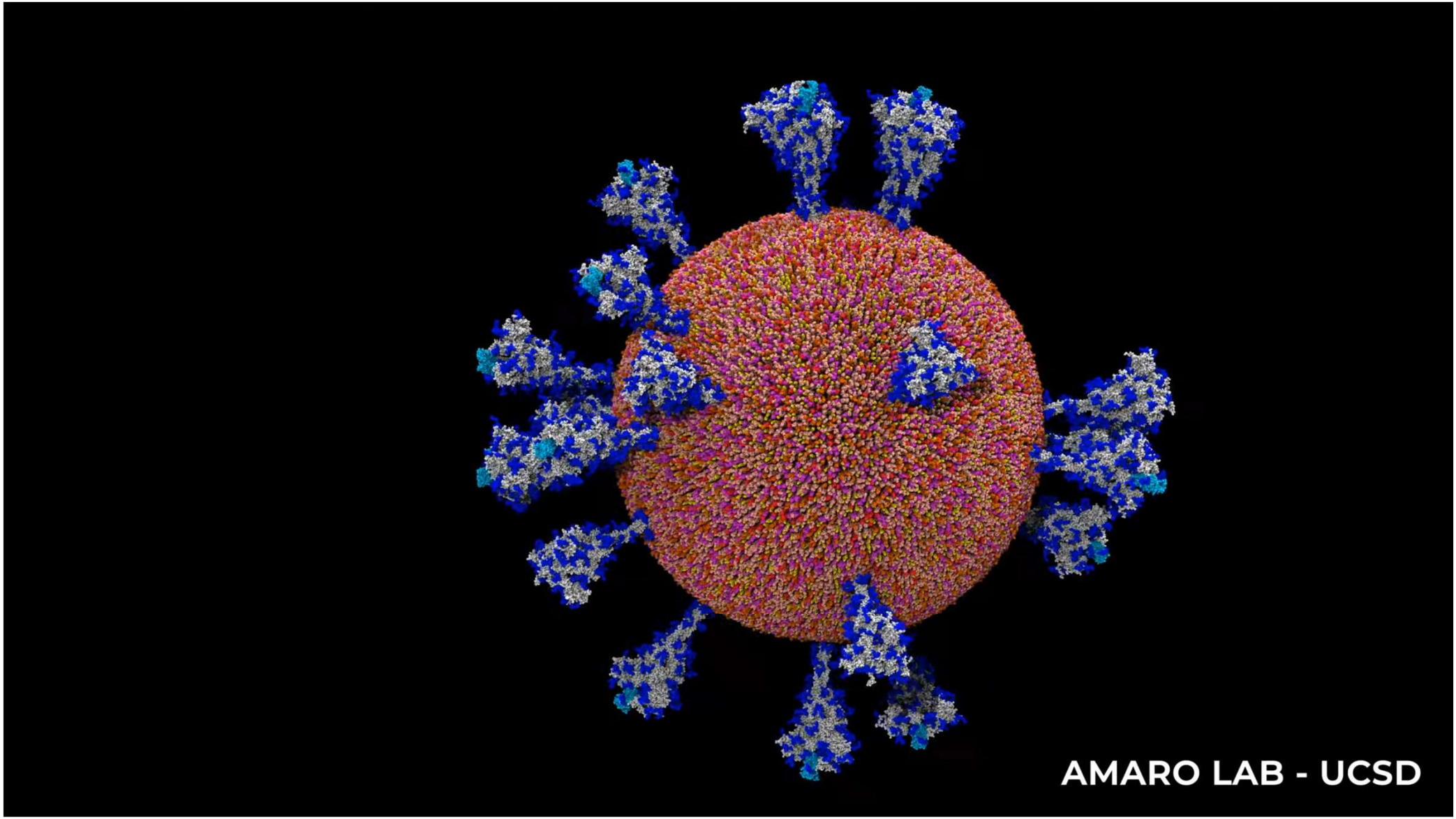
Regulação da transcrição



Fotossistema I

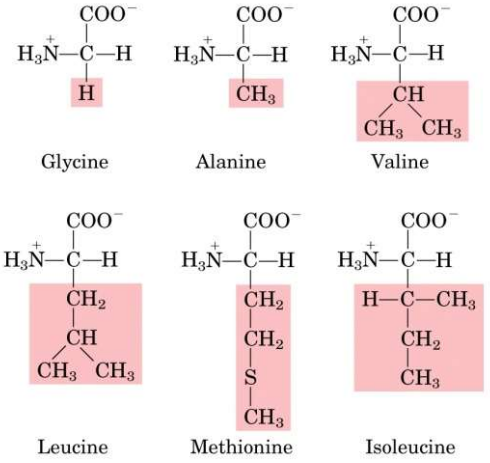


3.5M-atom model of SARS-CoV-2

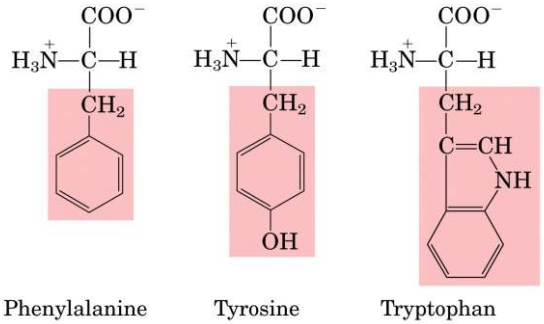


Proteínas

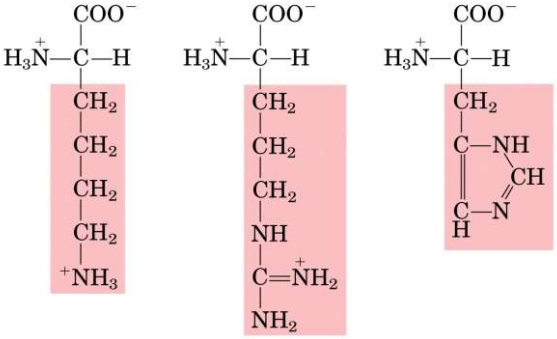
Nonpolar, aliphatic R groups



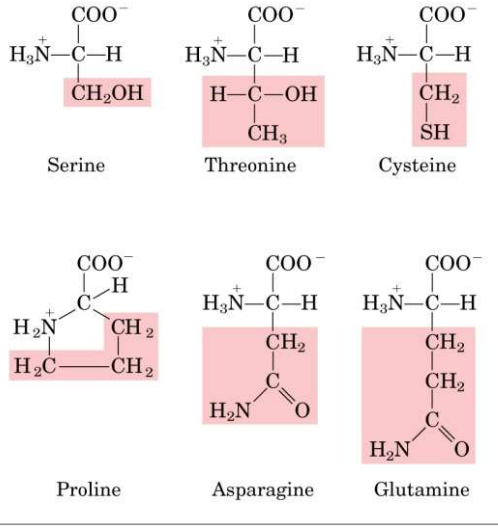
Aromatic R groups



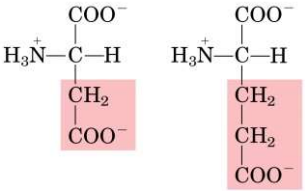
Positively charged R groups

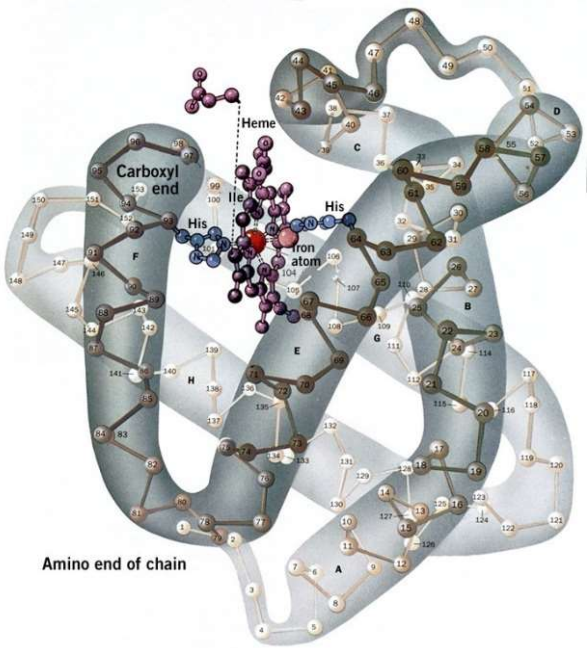


Polar, uncharged R groups



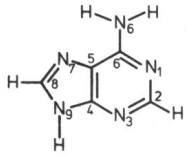
Negatively charged R groups



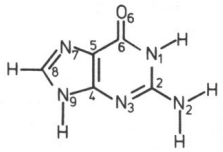


Mioglobina

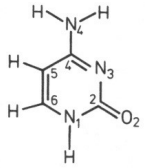
Ácidos nucleícos



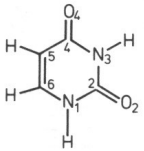
Adenine
Ade



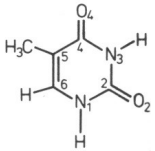
Guanine
Gua



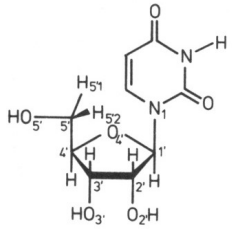
Cytosine
Cyd



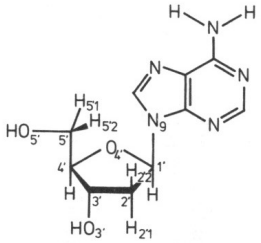
Uracil
Ura



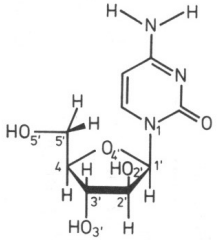
Thymine
Thy



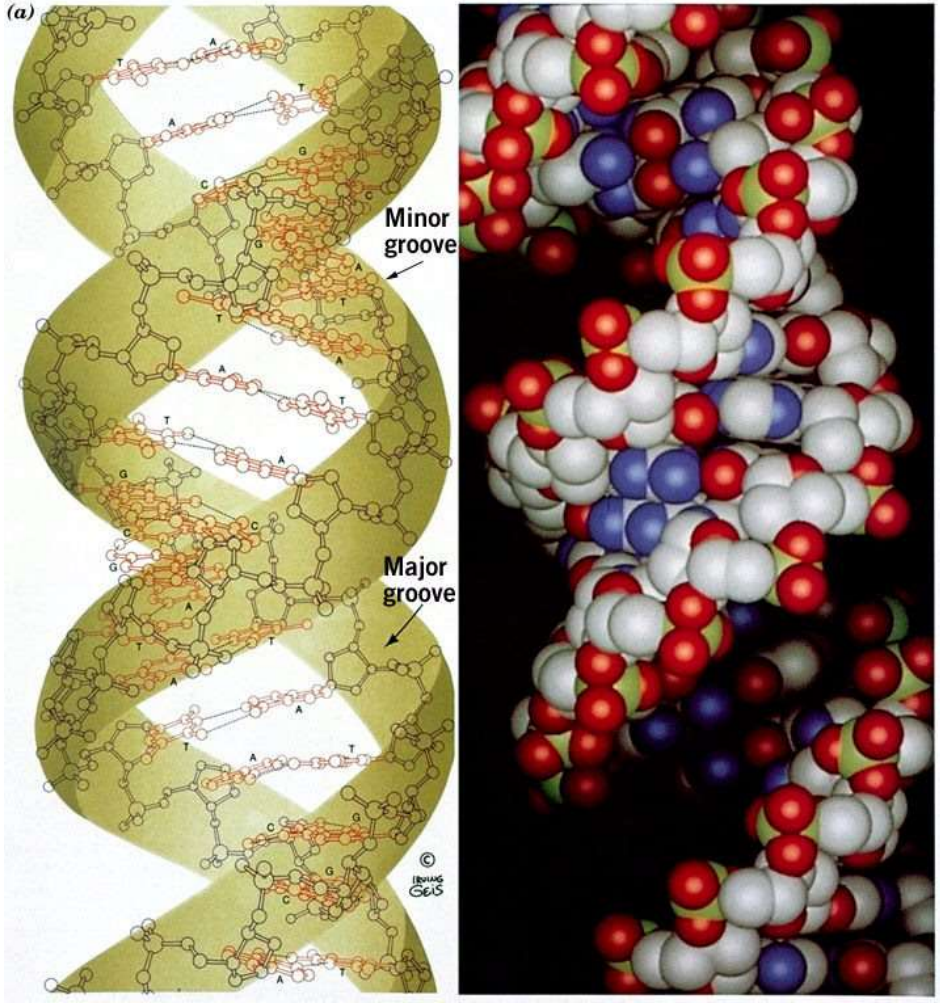
Uridine
Urd, U



Deoxyadenosine
dAdo, dA



Arabinocytidine
araCyd, araC



B-Dna