

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



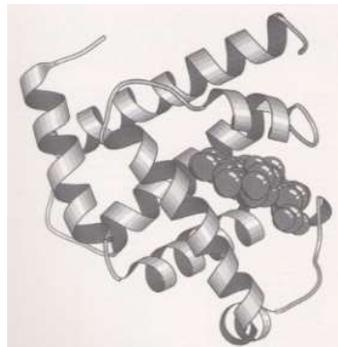
Função

Fluxo de informação biológica

vírus de RNA



priões

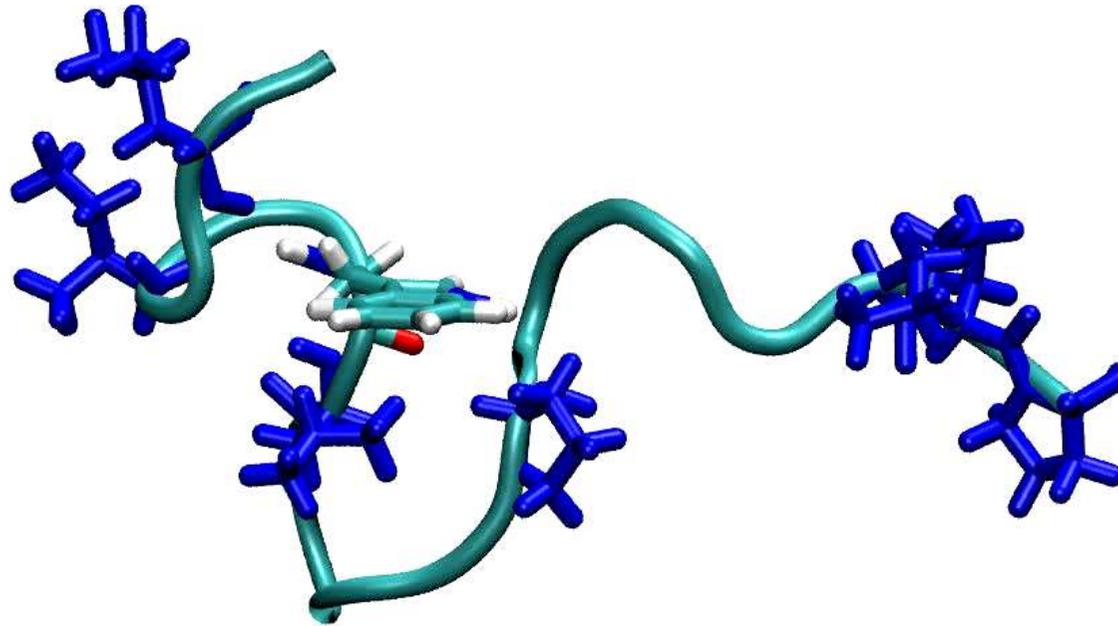


Dogma central da biologia molecular

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

Sequência->Estrutura

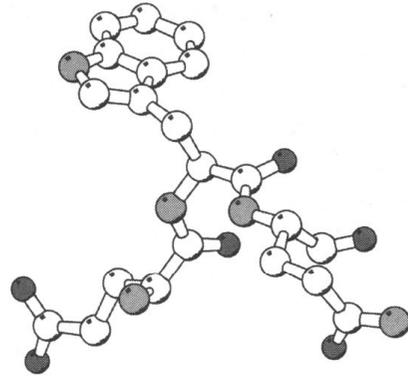
Folding da mini-proteína Trp-cage em solução aquosa:



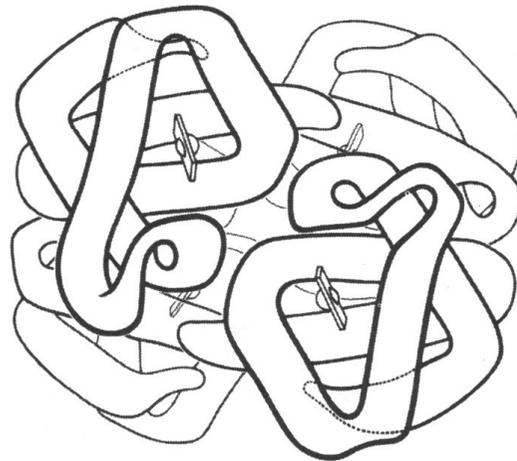
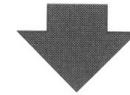
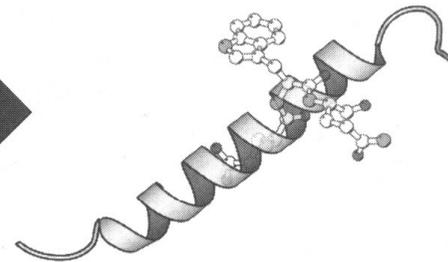
Muitas proteínas adquirem a sua estrutura tridimensional *espontaneamente (folding)*

Níveis de organização da estrutura das proteínas

Estrutura primária



Estrutura secundária



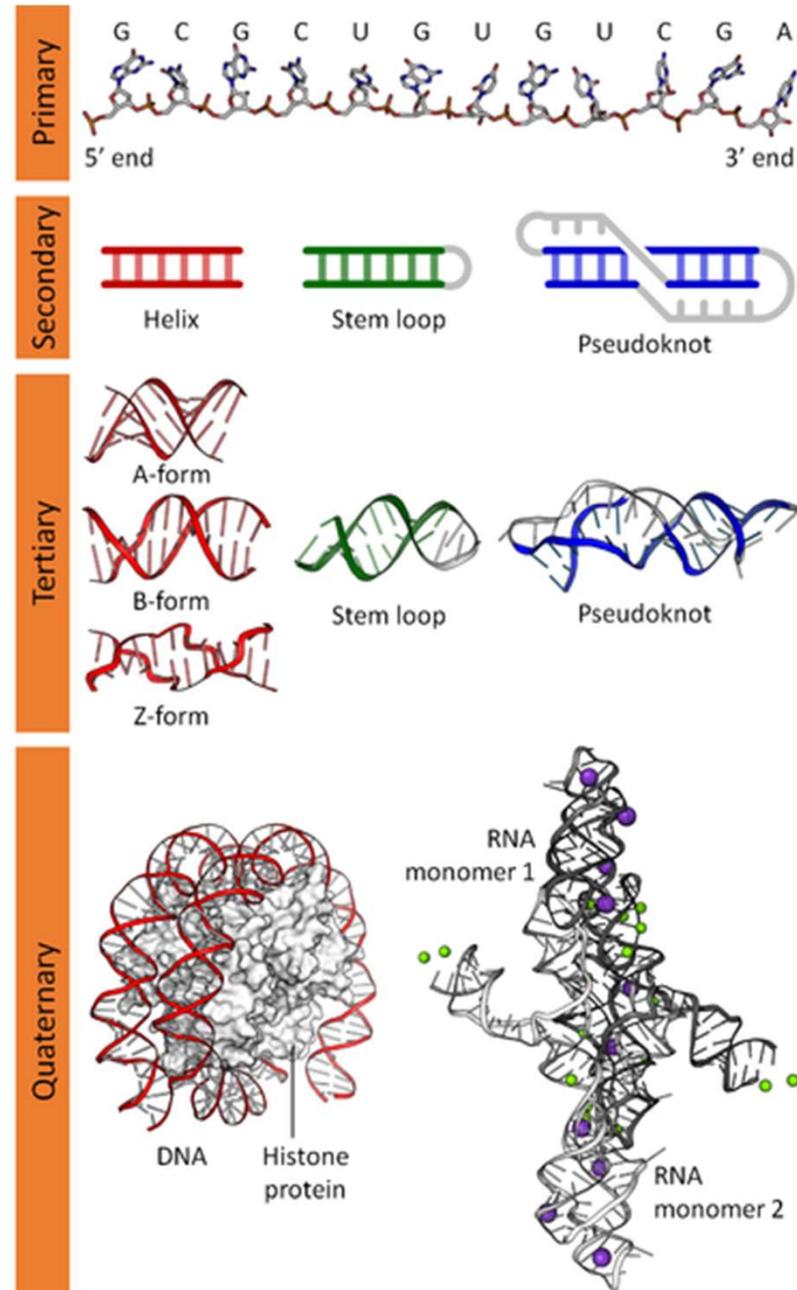
Estrutura quaternária



Estrutura terciária

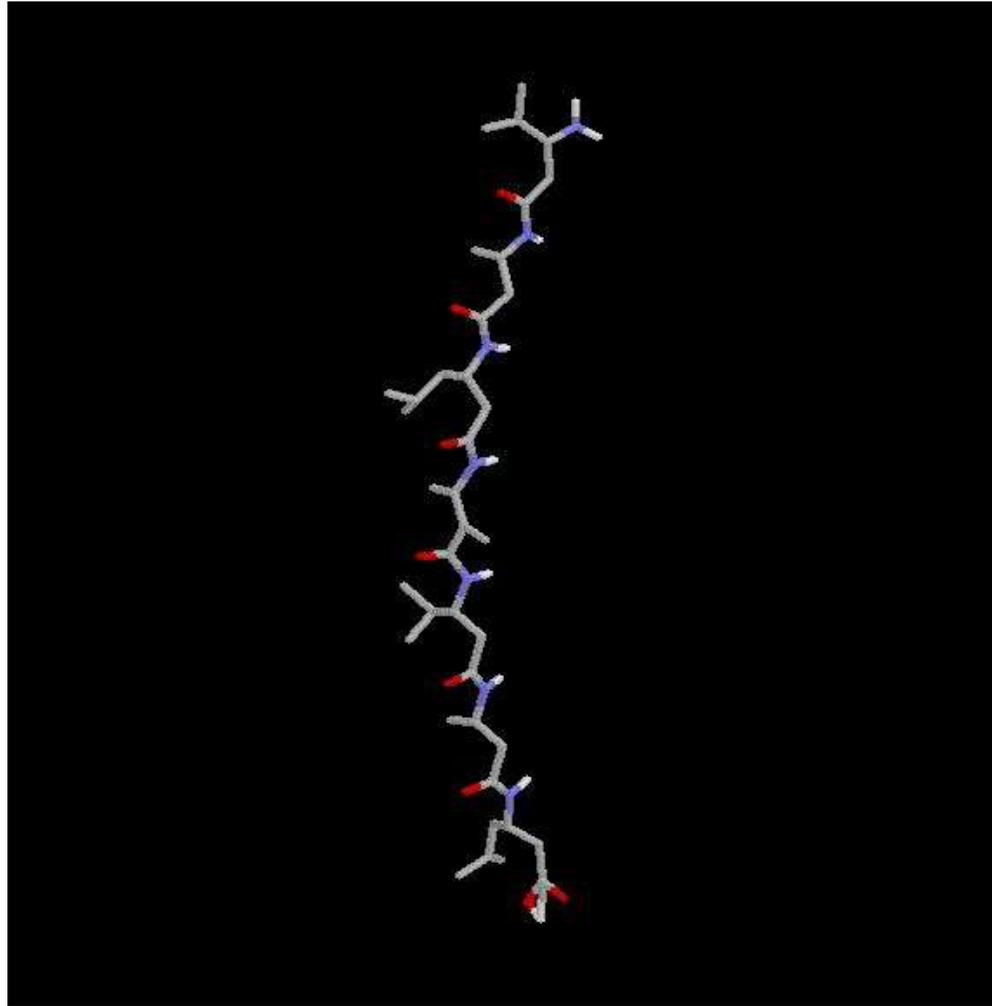


Níveis de organização da estrutura de ácidos nucleicos



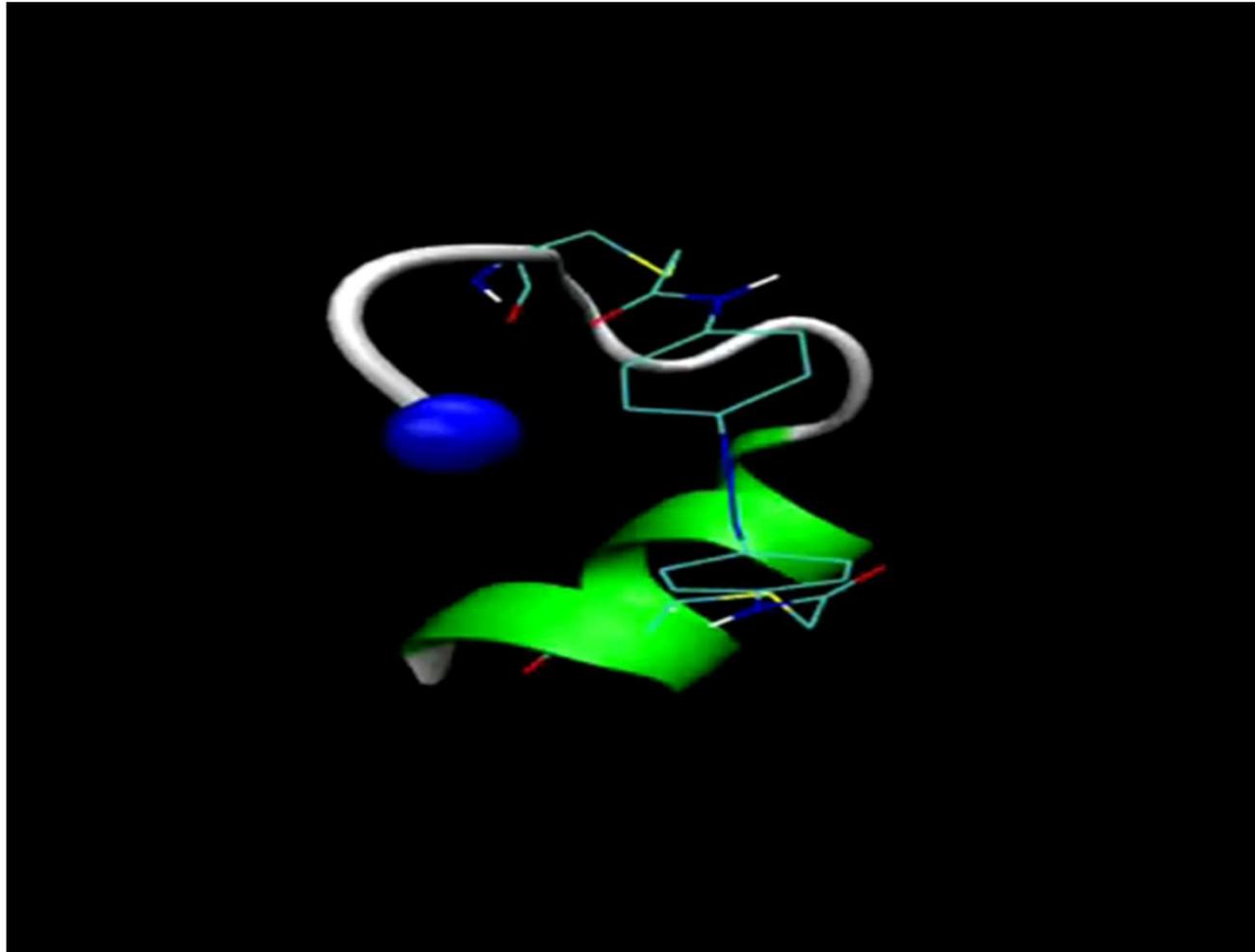
Estrutura quaternária
pode envolver moléculas
de proteína

Formação hierárquica da estrutura



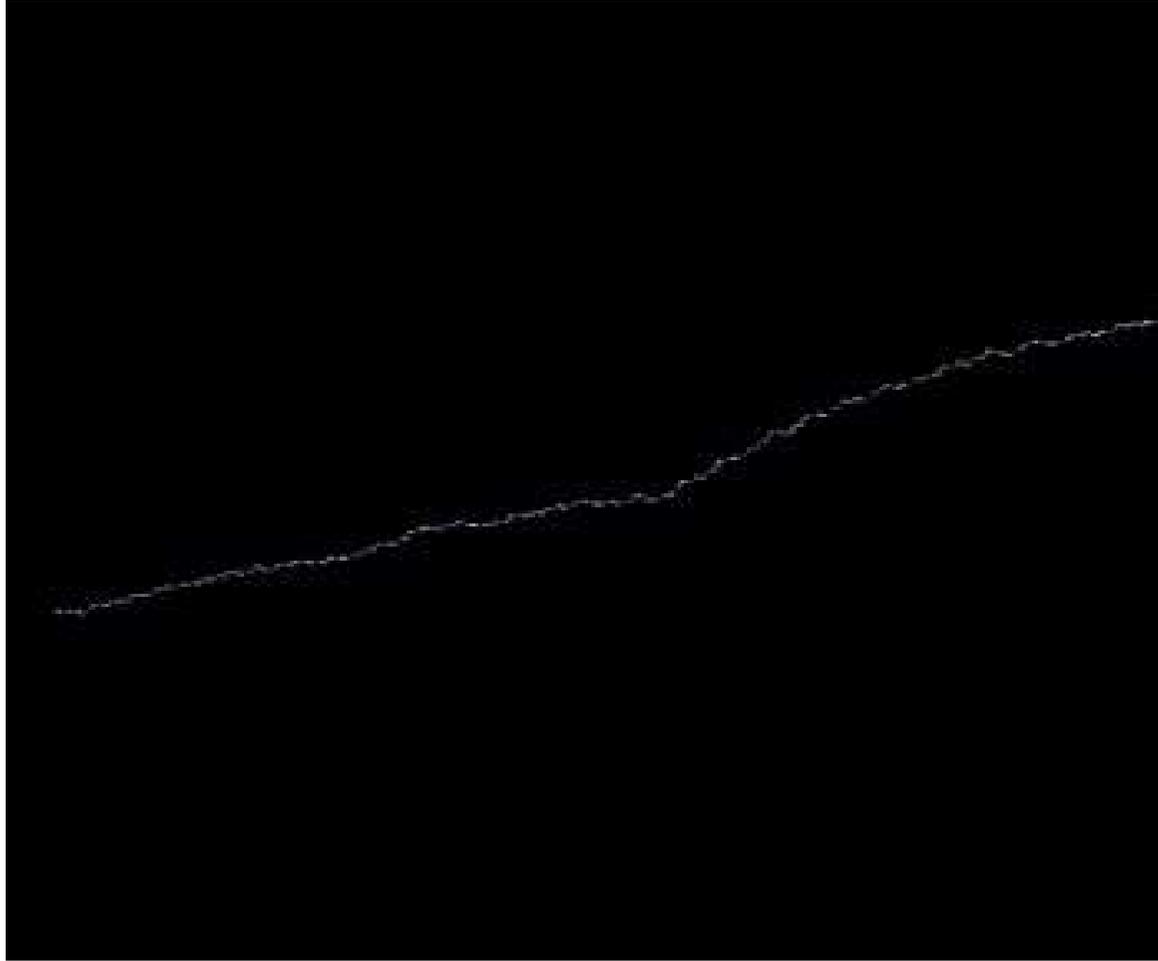
Formação espontânea de uma hélice α
(simulação)

Formação hierárquica da estrutura



Formação espontânea de uma hélice α
(simulação)

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):

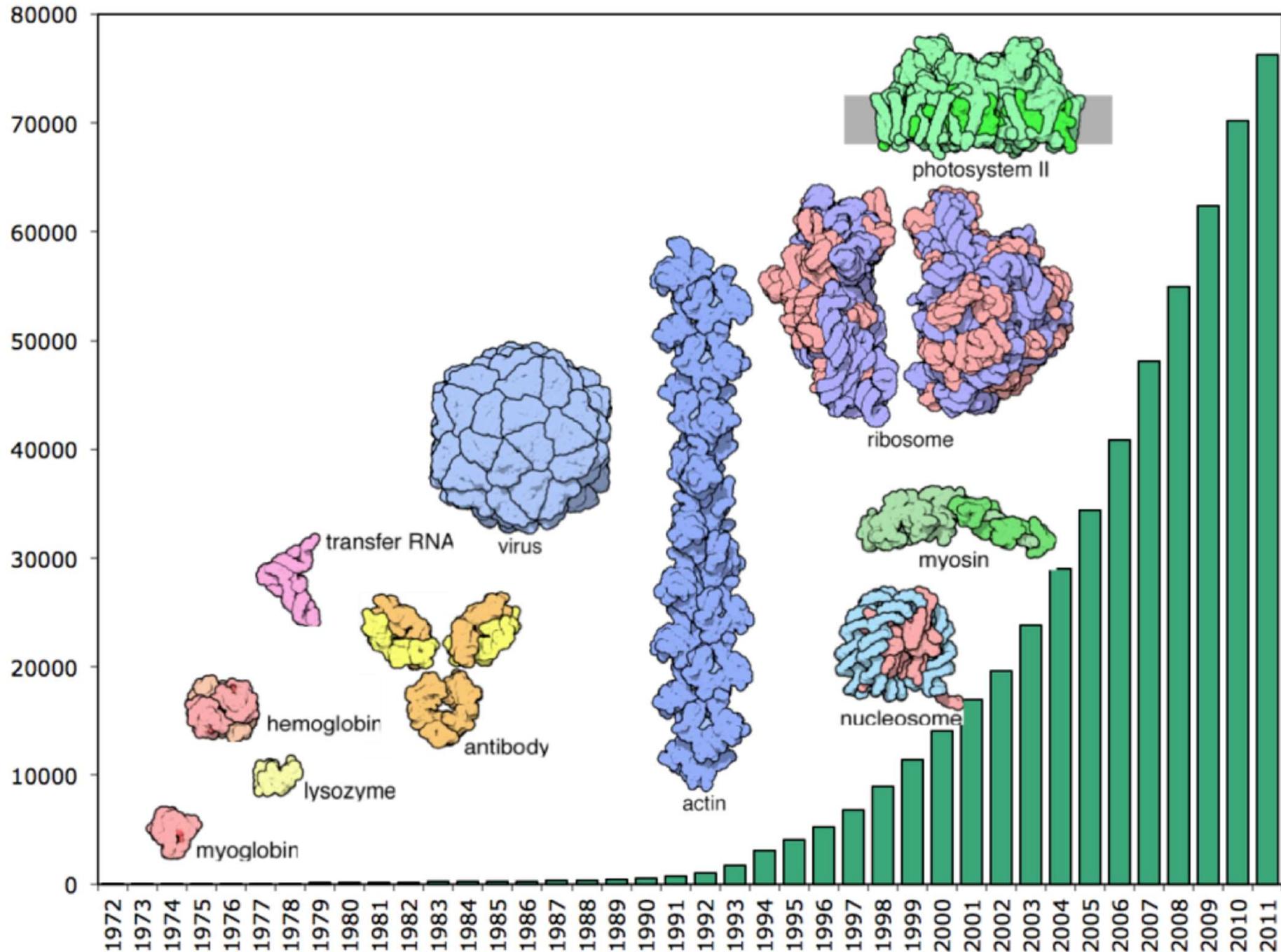
- Proteínas: 186680
- Ácidos Nucleicos: 4373
- Complexos ácido nucleico-proteína: 12606
- Proteína/Oligossacárido: 11514
- Outros: 228

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

Progresso na determinação das estruturas



- Welcome
- Deposit
- Search
- Visualize
- Analyze
- Download
- Learn

RCSB Protein Data Bank (RCSB PDB) enables breakthroughs in science and education by providing access and tools for exploration, visualization, and analysis of:

- Experimentally-determined 3D structures from the Protein Data Bank (PDB) archive
- Computed Structure Models (CSM) from AlphaFold DB and ModelArchive

These data can be explored in context of external annotations providing a structural view of biology.



February Molecule of the Month

Nanowires

Latest Entries

As of Tue Jan 30 2024

8GLK
The Type 9 Secretion System dGidL peak II, NucA substrate bound complex

Features & Highlights

- Register for the February 5 RCSB.org Office Hour**
Have questions about how to use RCSB.org? Join us for a virtual Office Hour.
- Notice: NGL Viewer Depreciation**
As of June 28, 2024, the NGL molecular viewer will be removed from RCSB.org. Users are encouraged to use Mol* for 3D visualization.
- Take the CSM User Survey and Win**
Please take this brief survey about Computed Structure Models at RCSB.org to be entered into a drawing for a set of Bound Playing Cards.

News

Publications

- February 4 is World Cancer Day**
PDB structures reveal how cell growth is normally controlled, and how cancer cells circumvent these essential controls
02/01/2024
- Register for VIZBI 2024 (March 13–15)**
Learn the latest data visualization methods and techniques
01/30/2024
- Register for the February 13 Mol* Webinar**
Join RCSB PDB to learn how to Visualize Biomolecular structures with Mol*: From Atoms to Movies
01/19/2024

PDB at a Glance	66,758 Structures of Human Sequences	17,179 Nucleic Acid Containing Structures	More Statistics
CSM at a Glance	999,251 AlphaFoldDB	69,326 ModelArchive	

Princípios que regem a estrutura das biomoléculas

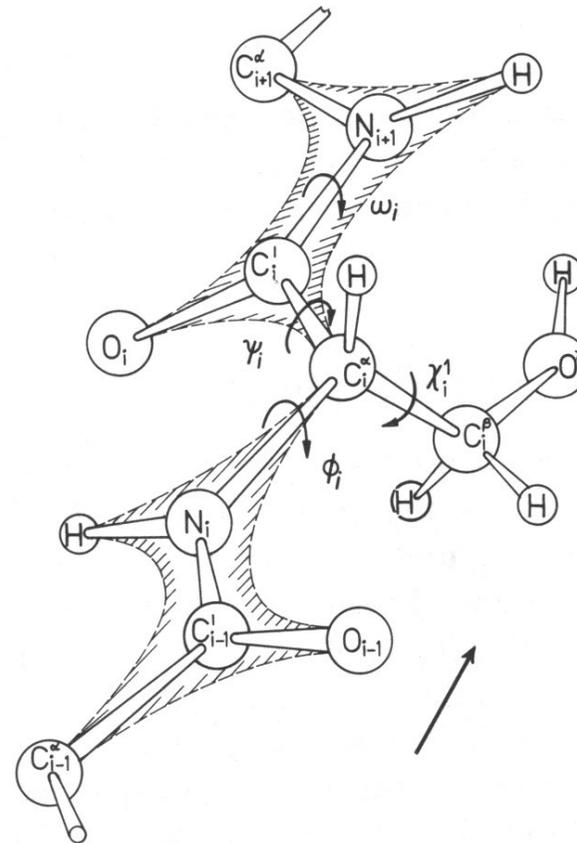
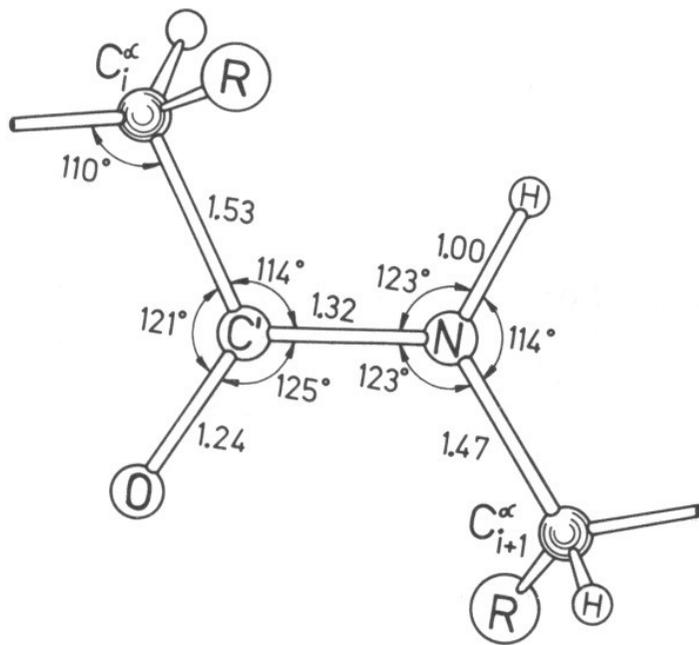
“Perhaps the most remarkable features of the molecule are its *complexity* and *lack of symmetry*. The arrangement seems to be almost totally lacking the kind of regularities which one instinctively anticipates and it is more complicated than has been predicted by any theory of protein structure”

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

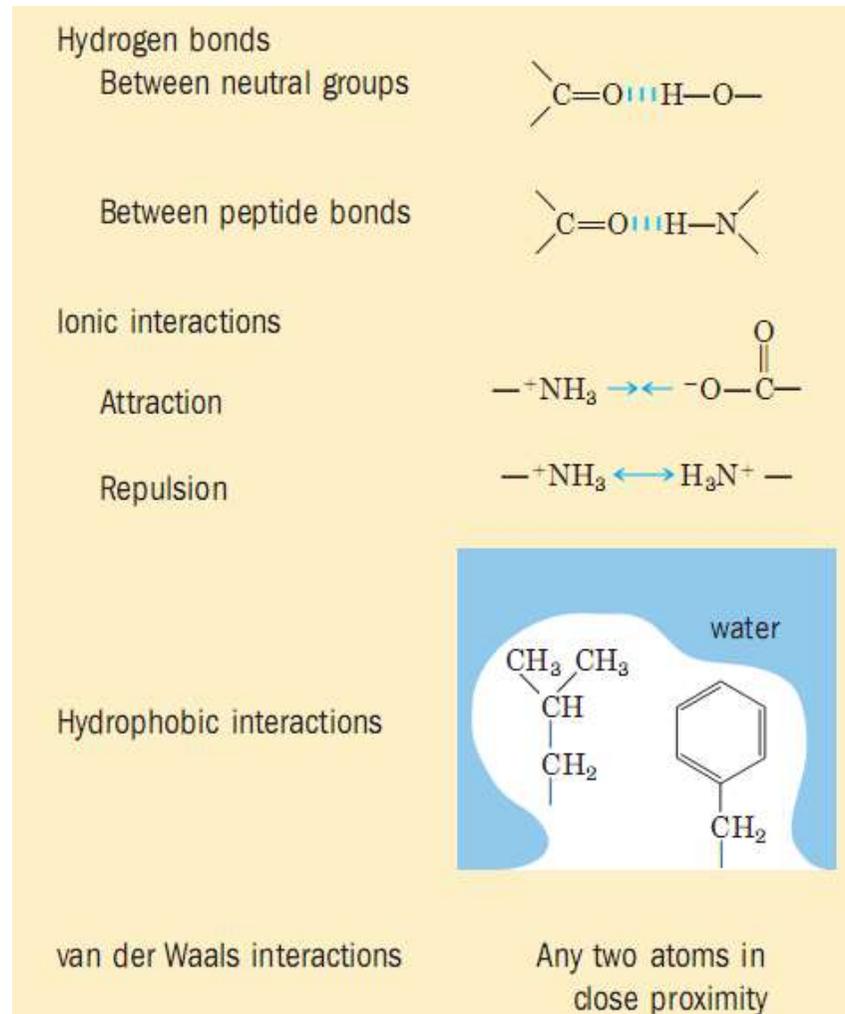


- As macromoléculas biológicas parecem, numa primeira análise, distanciar-se dos princípios simples de geometria e simetria que sabemos reger a estrutura das moléculas pequenas.

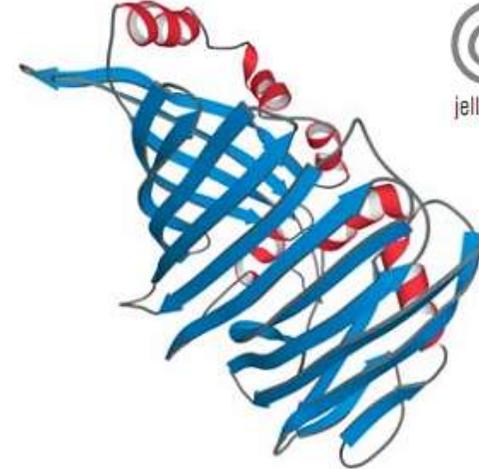
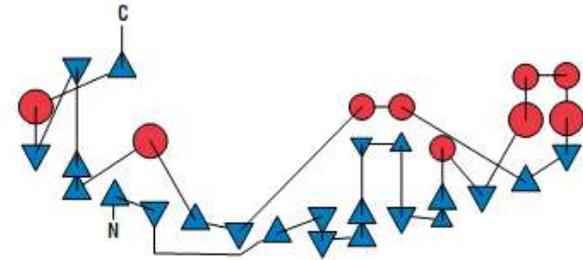
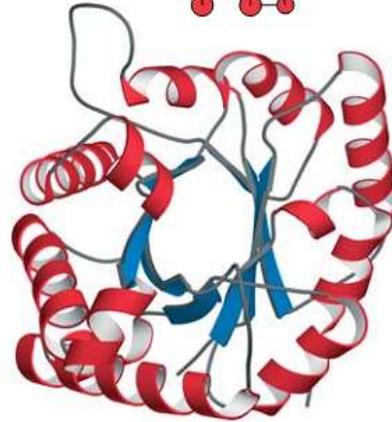
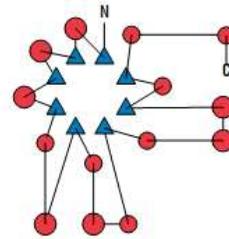
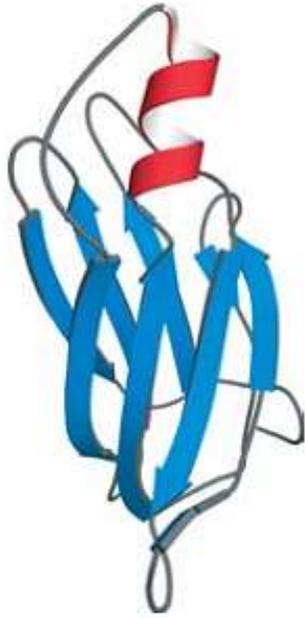
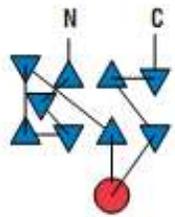
- Ligações covalentes, geometria molecular:



•Interações não-covalentes:



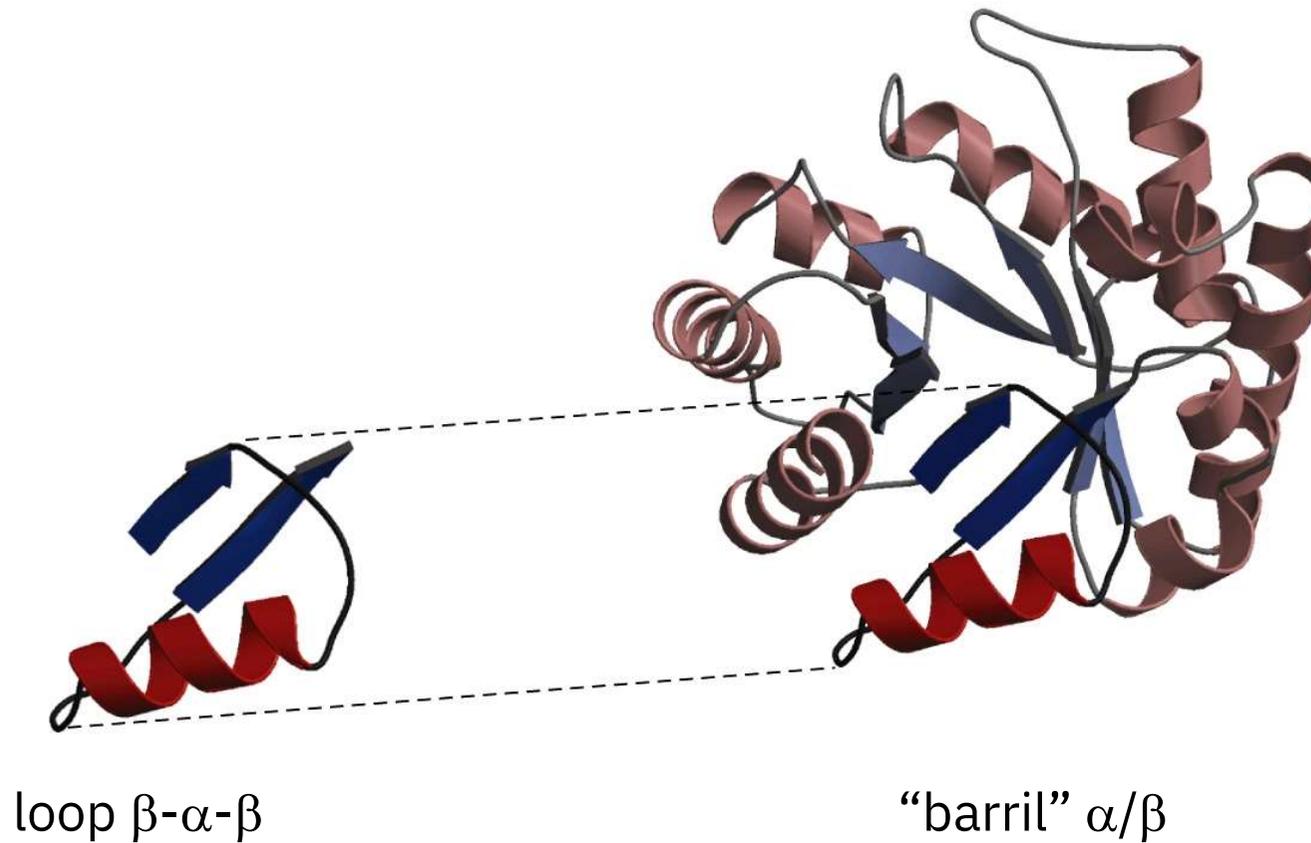
- Princípios arquitectónicos



...

Recorrência de padrões estruturais na arquitectura das biomoléculas.

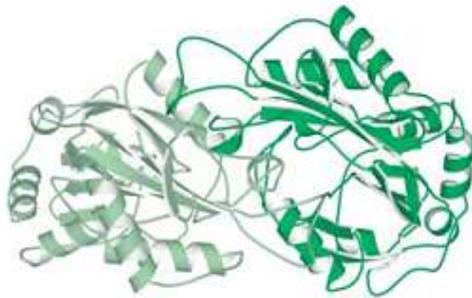
- Princípios arquitectónicos (cont.):



Formação de estruturas a partir da associação de unidades estruturais

- Oligomerização:

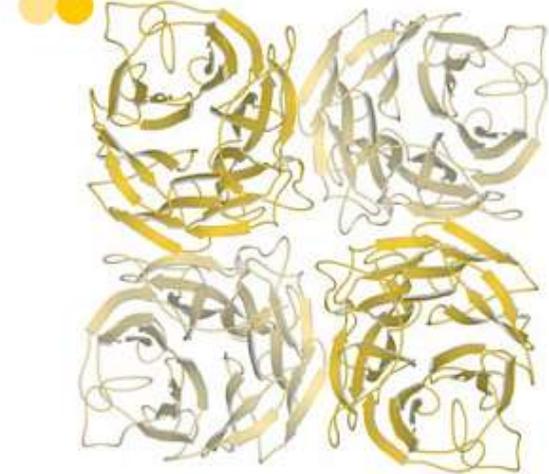
(a) dimer



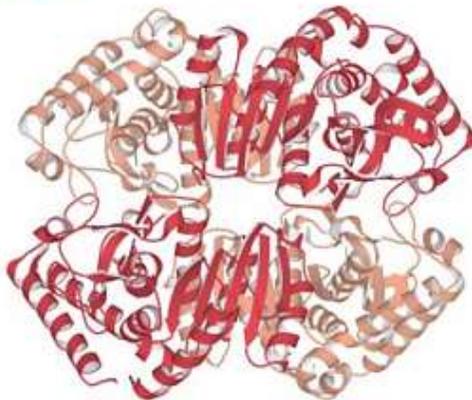
(b) trimer



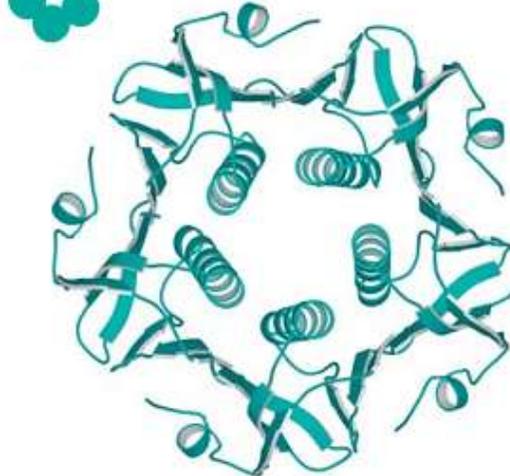
(c) planar tetramer



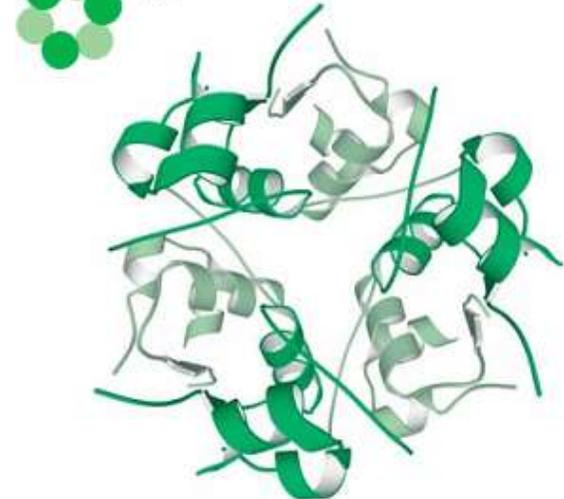
(d) tetramer



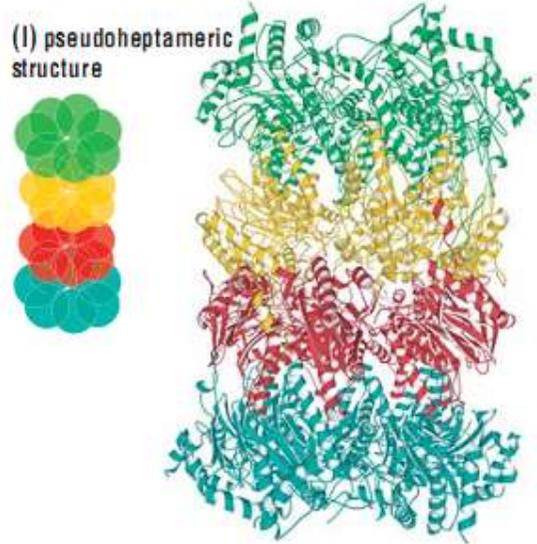
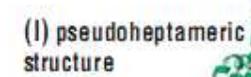
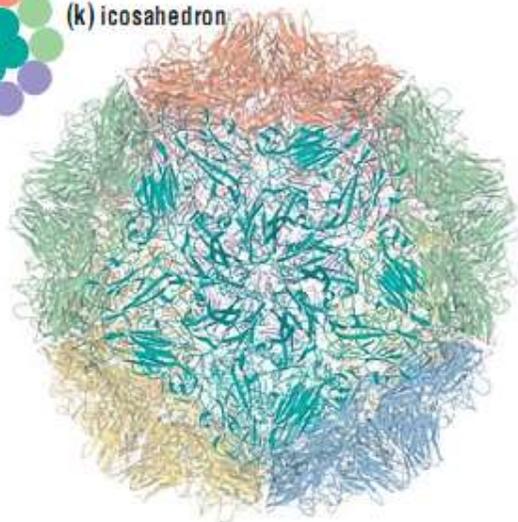
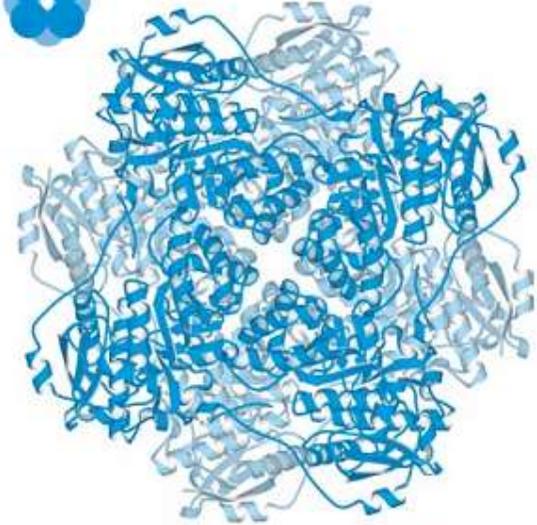
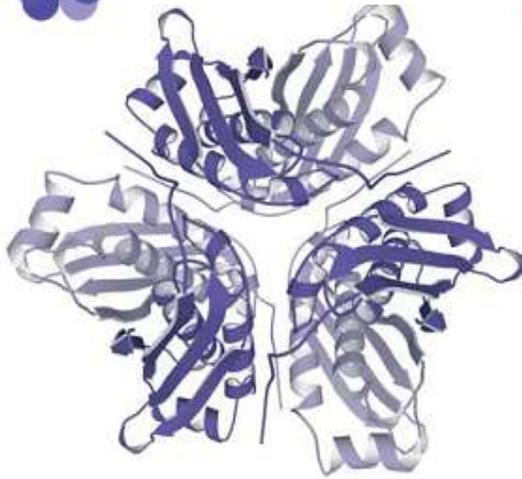
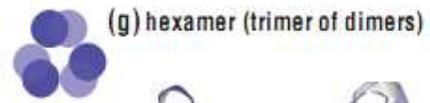
(e) pentamer



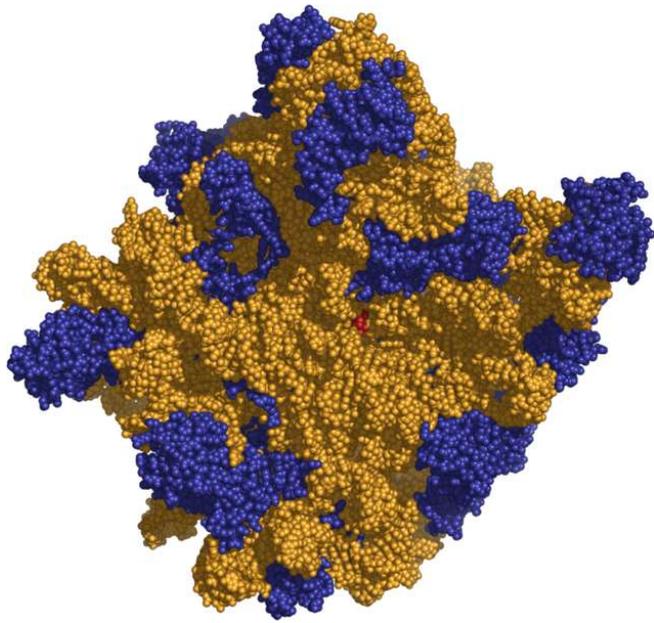
(f) planar hexamer



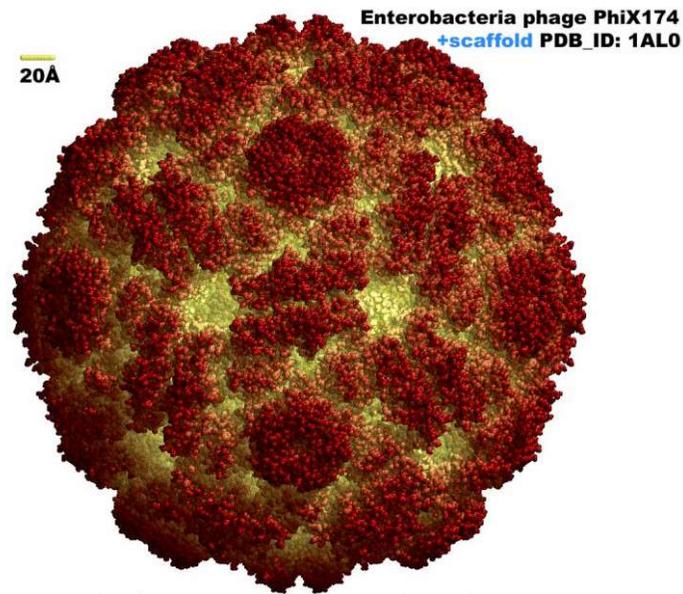
- Oligomerização(cont.):



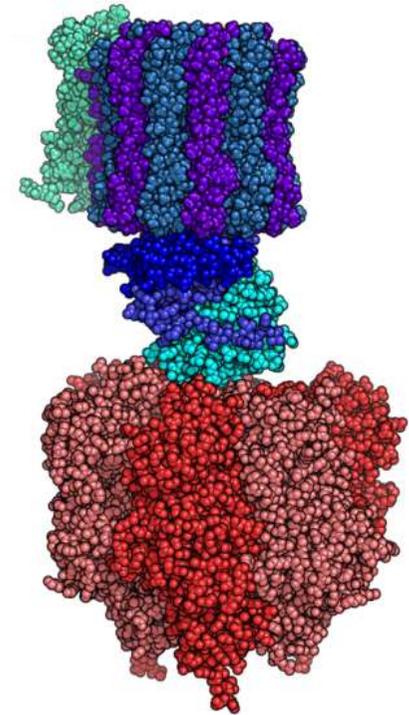
- Formação de estruturas supramacromoleculares



Ribossoma



Vírus

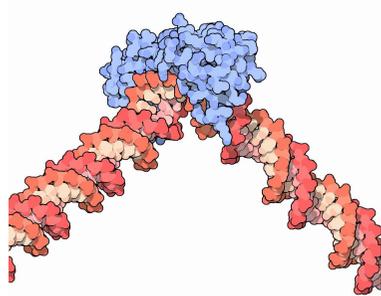
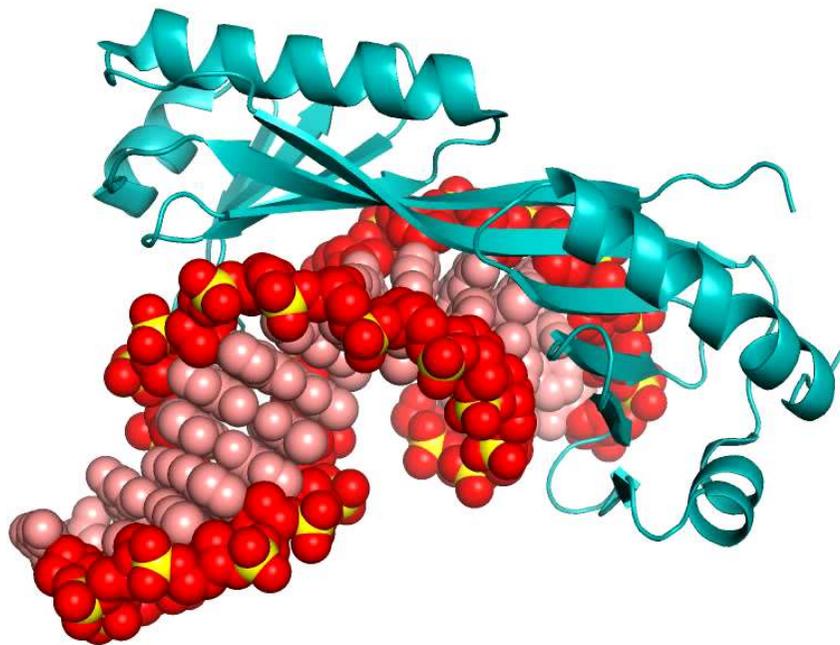


ATPase

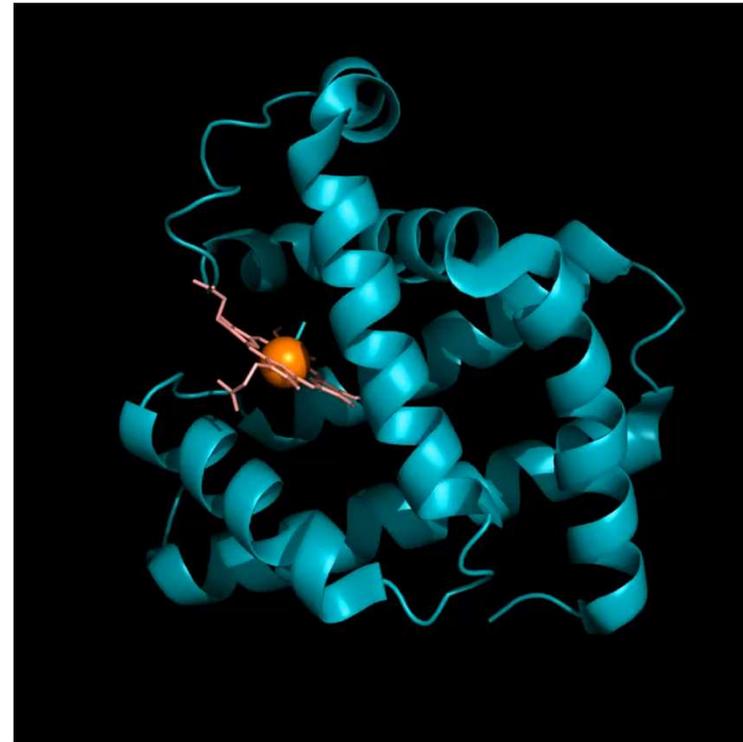
Função

Associação a ligandos

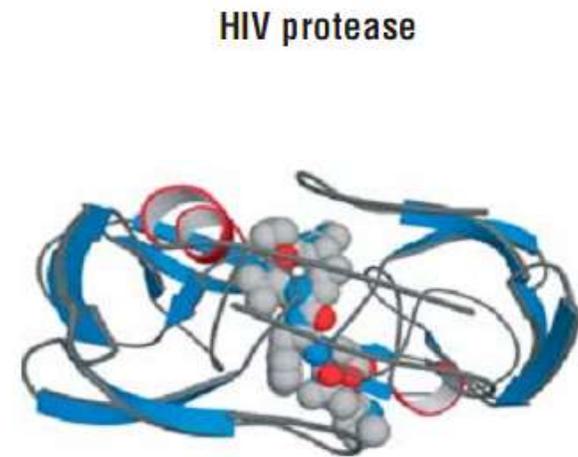
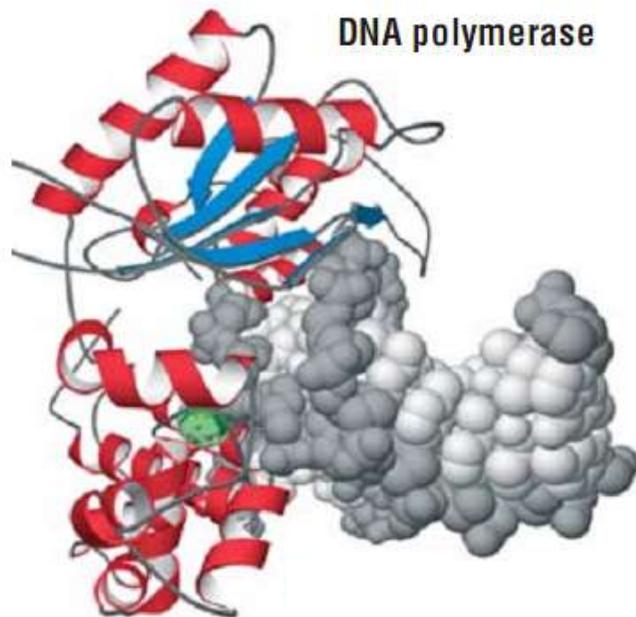
TATA-binding protein



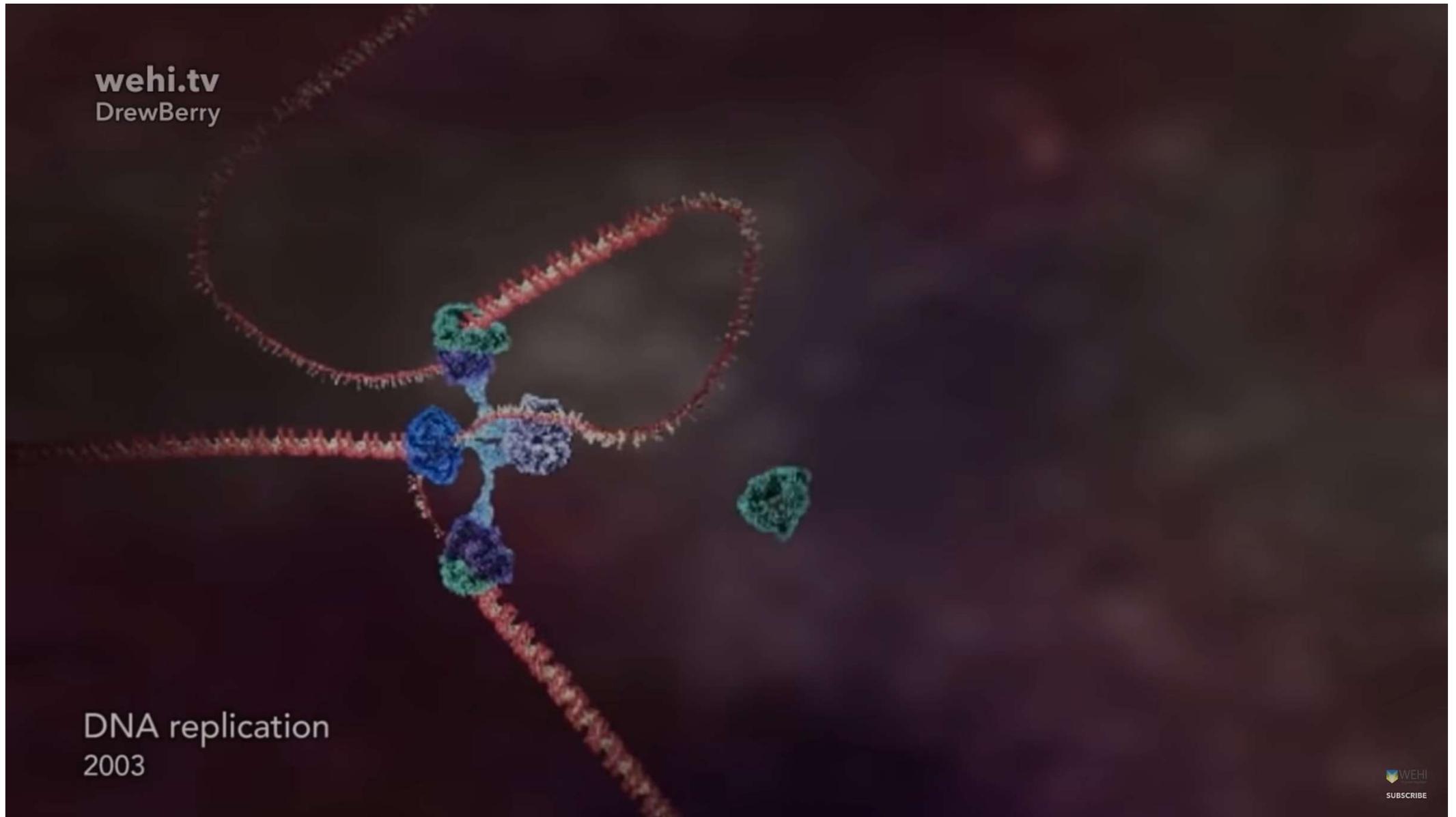
Myoglobin



Catálise

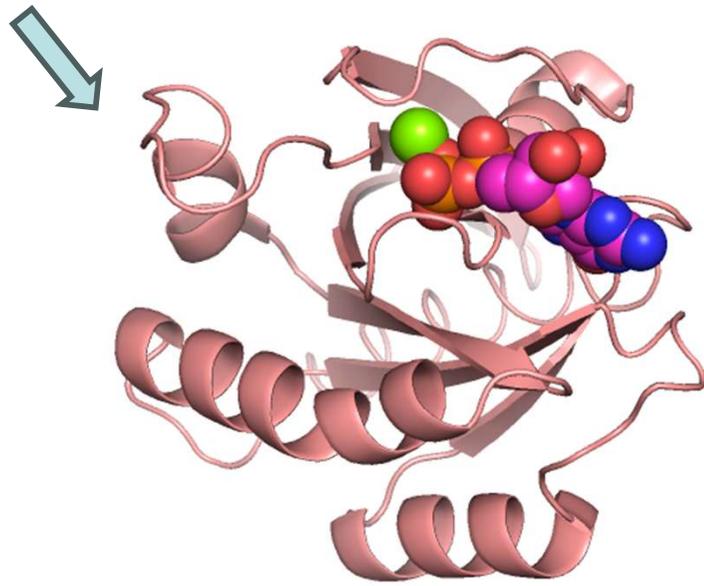


A molecular copying machine

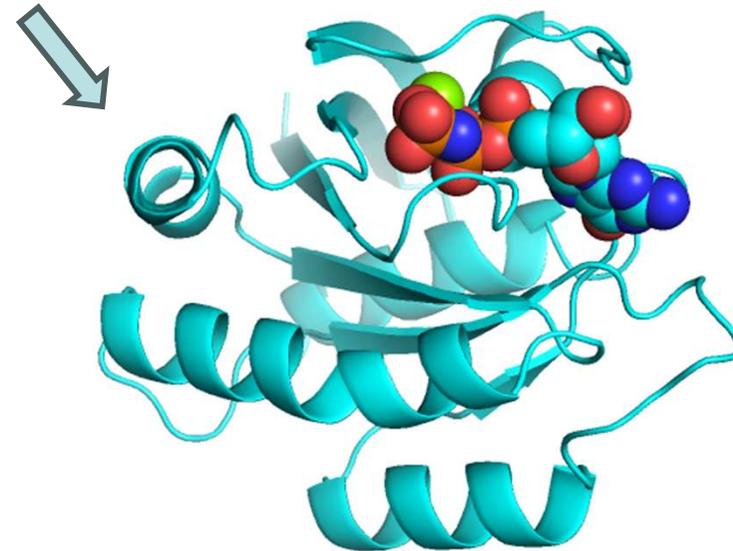


Sinalização

ras protein



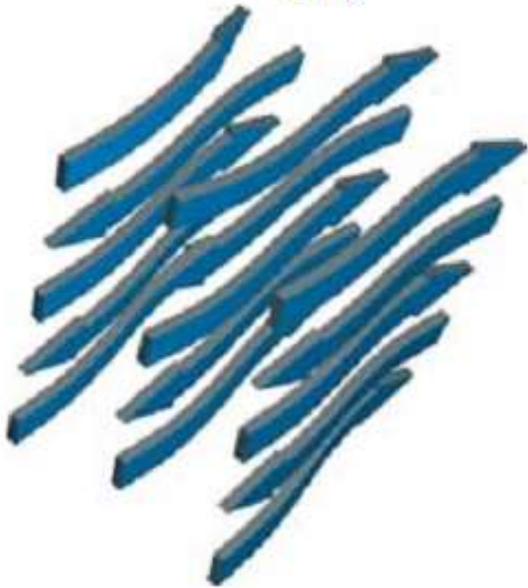
On



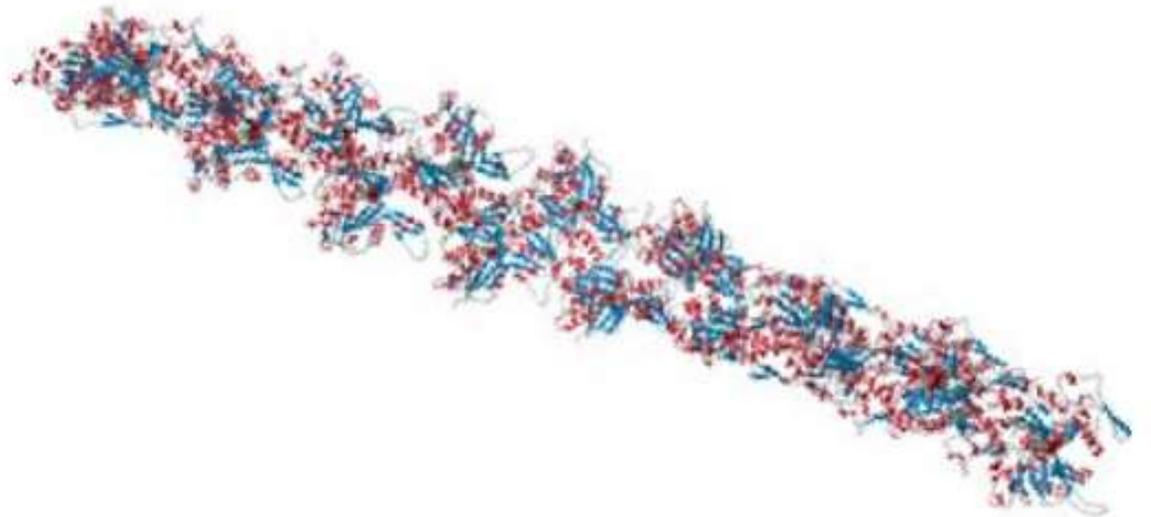
Off

Estrutura

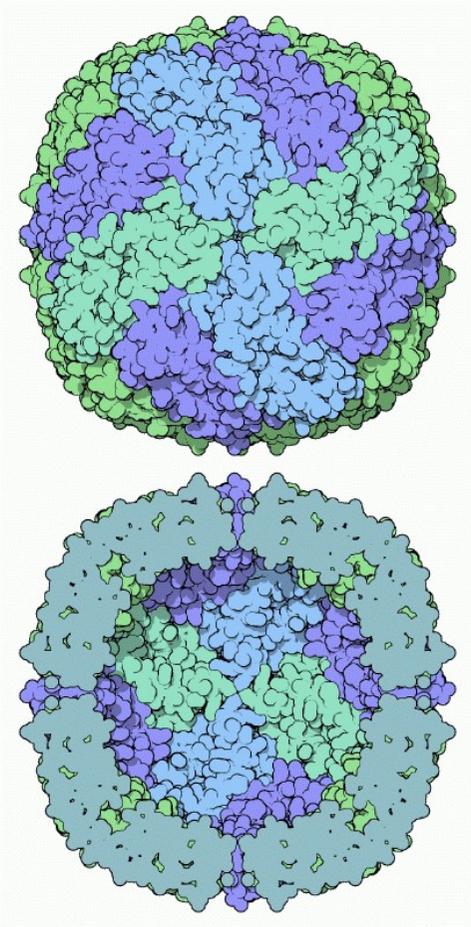
Silk



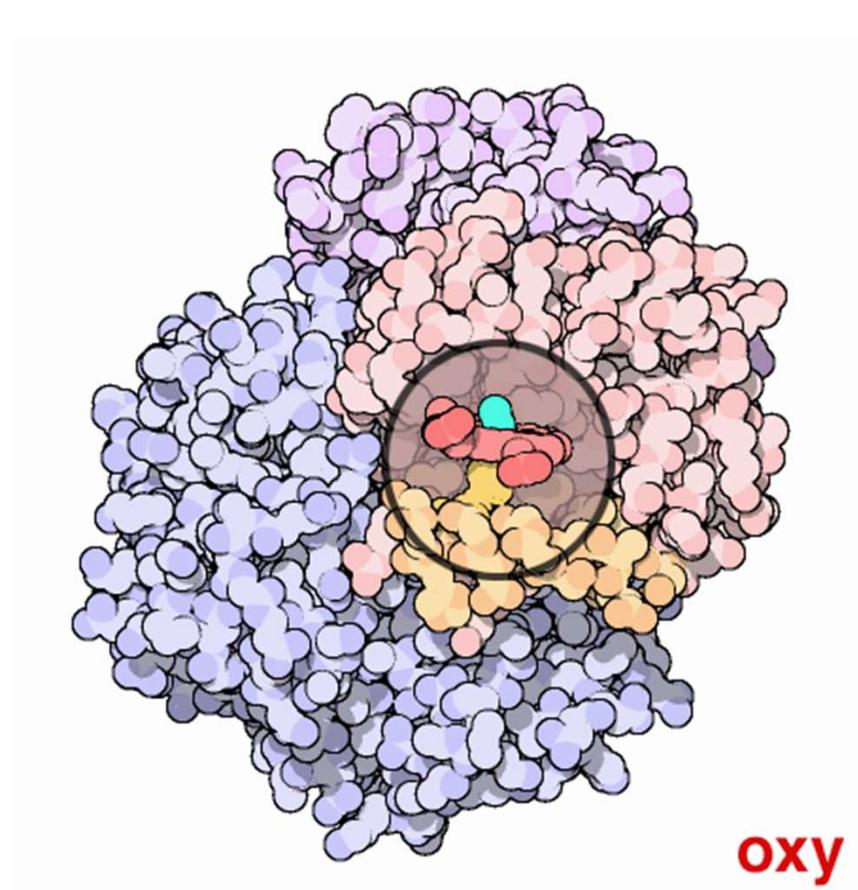
F-actin



Transporte

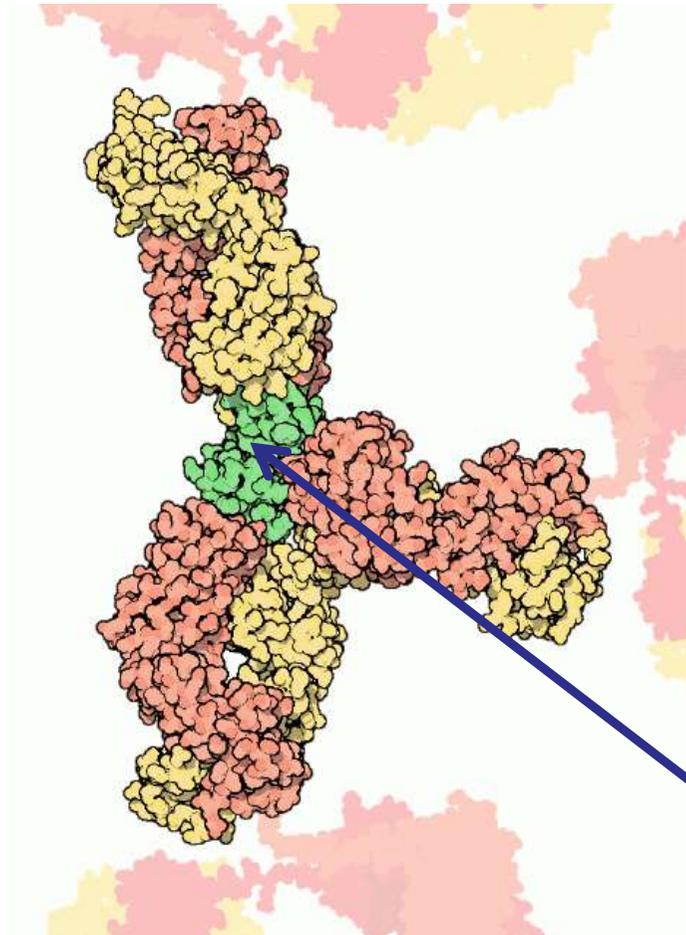


Ferritina (ferro)

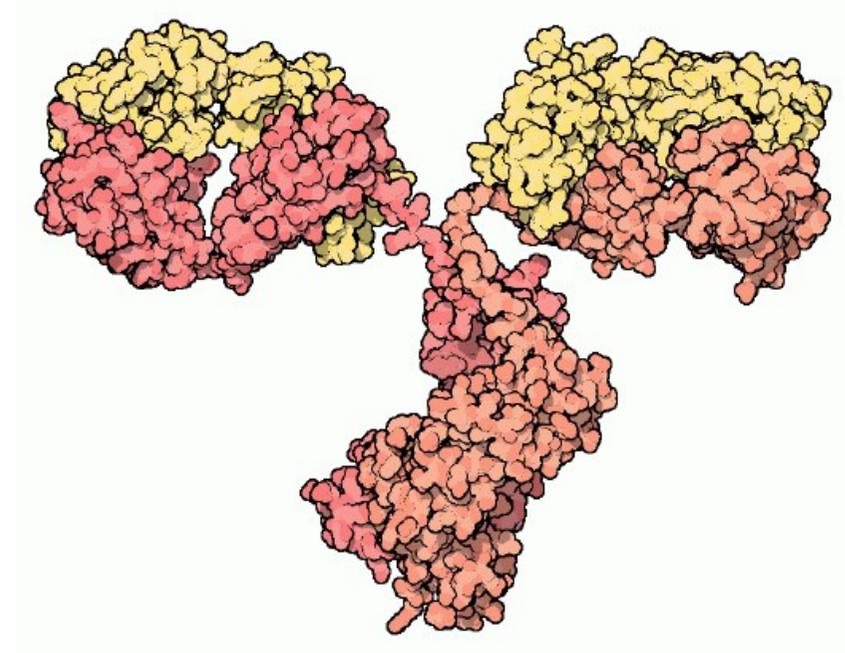


Hemoglobina (oxigênio)

Defesa

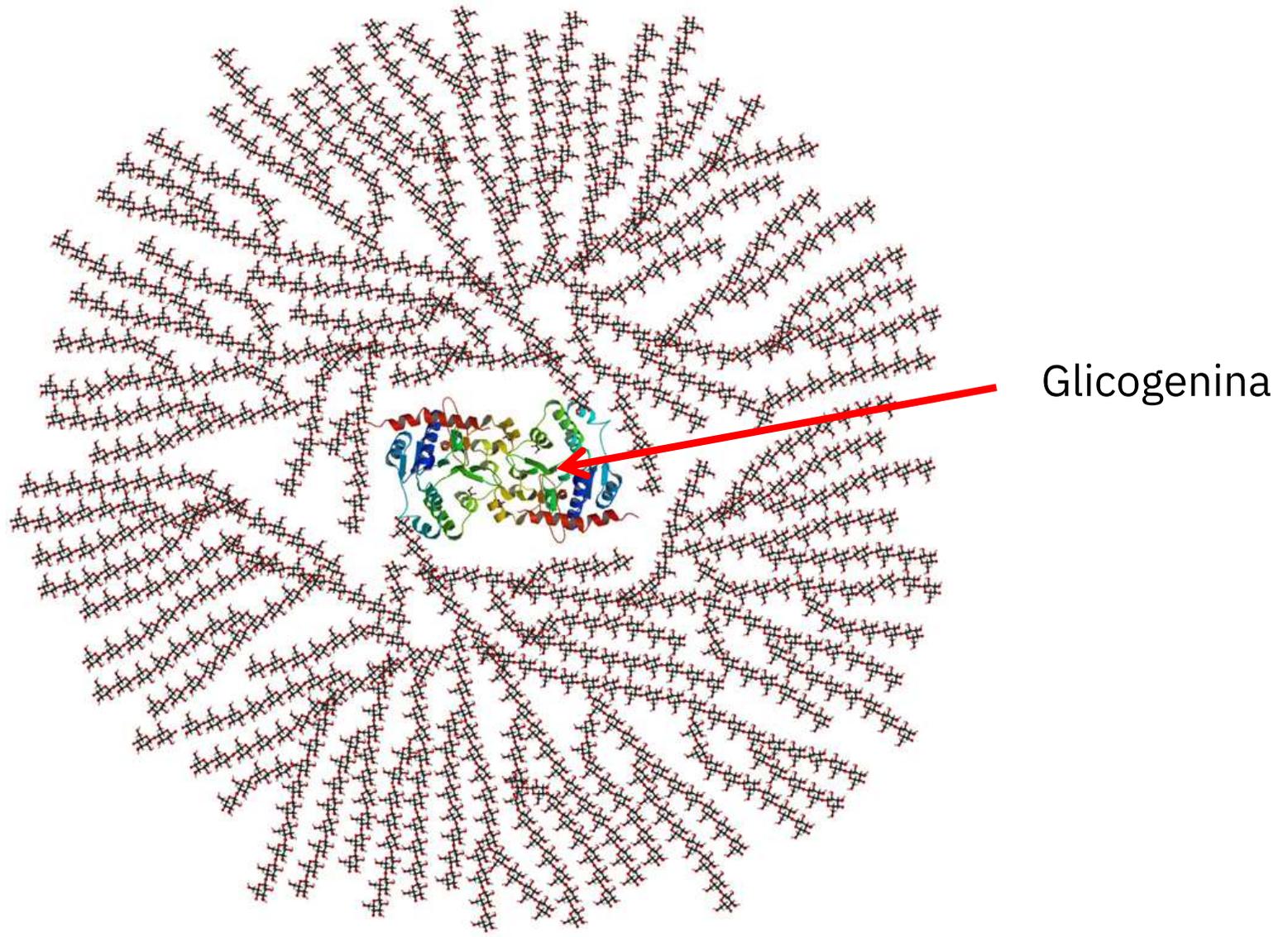


lisozima



imunoglobulina

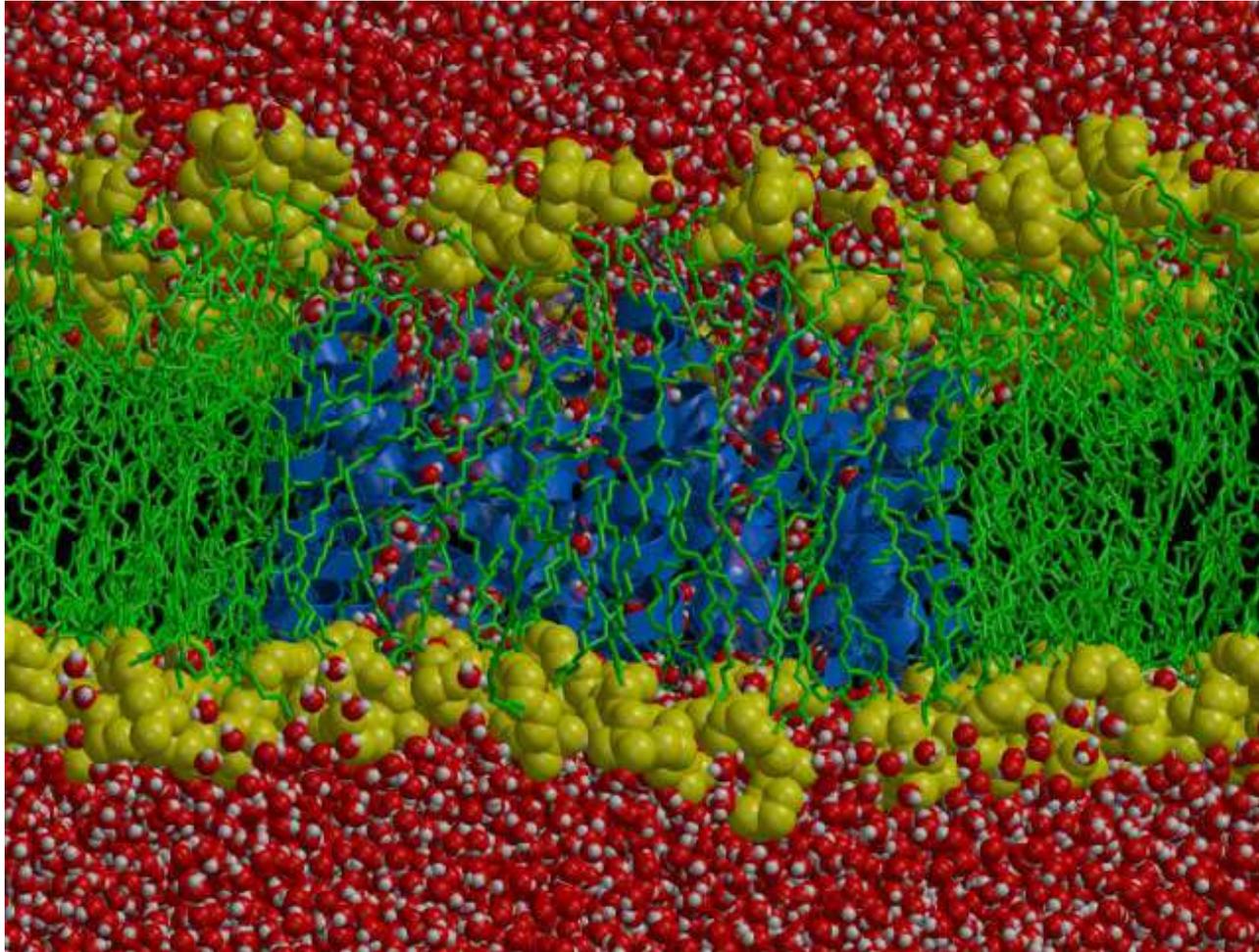
Armazenamento



Glicogenina

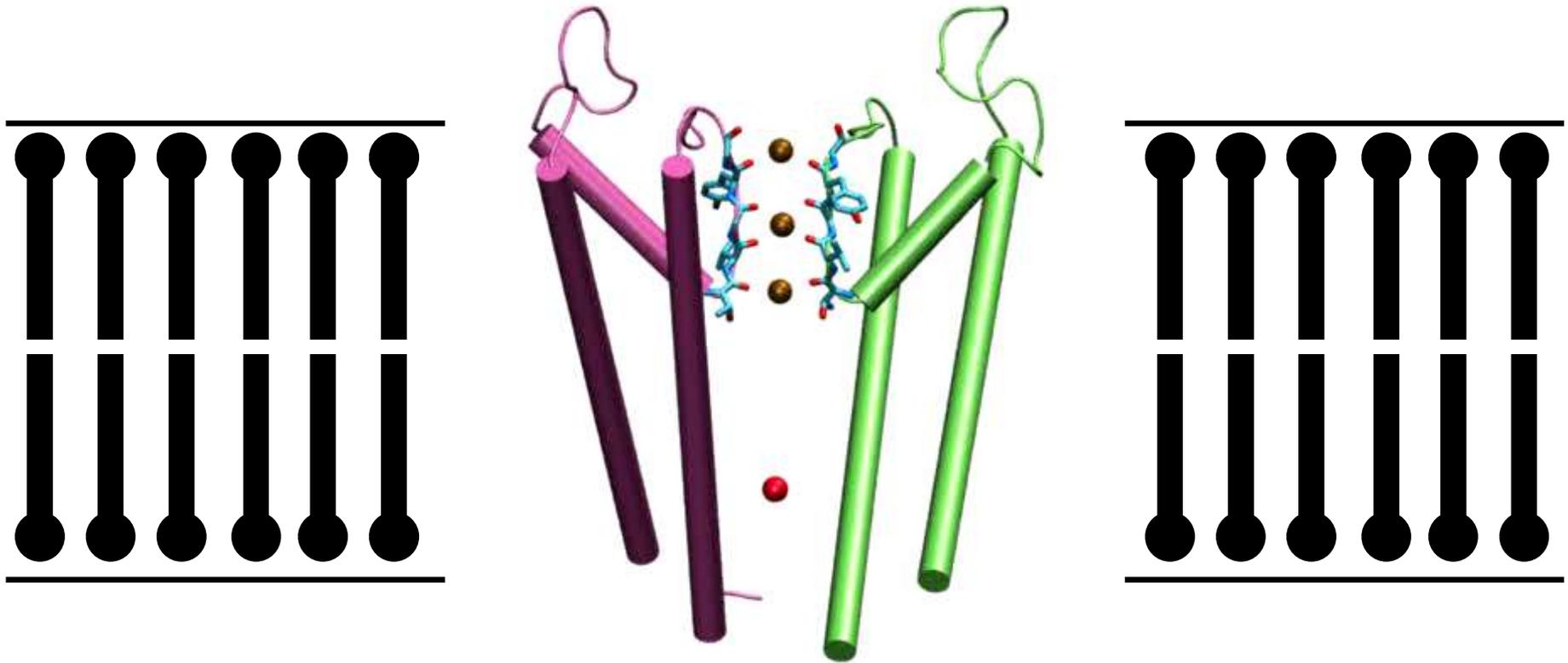
Glicogénio

Compartimentação



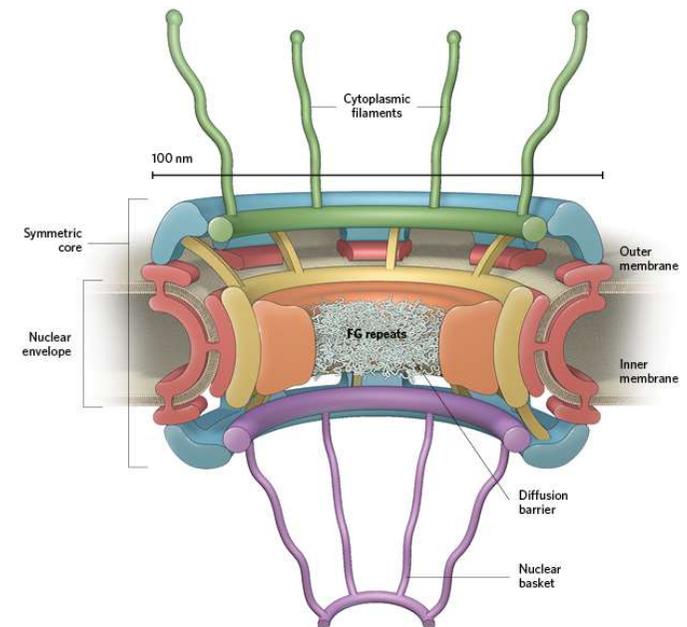
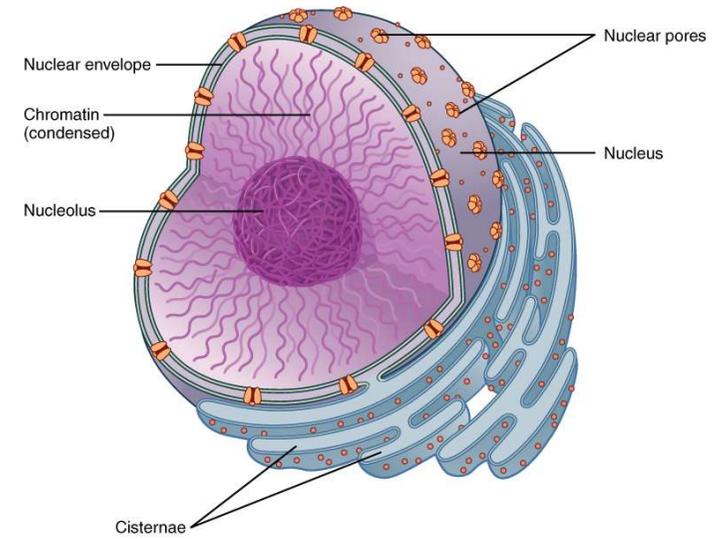
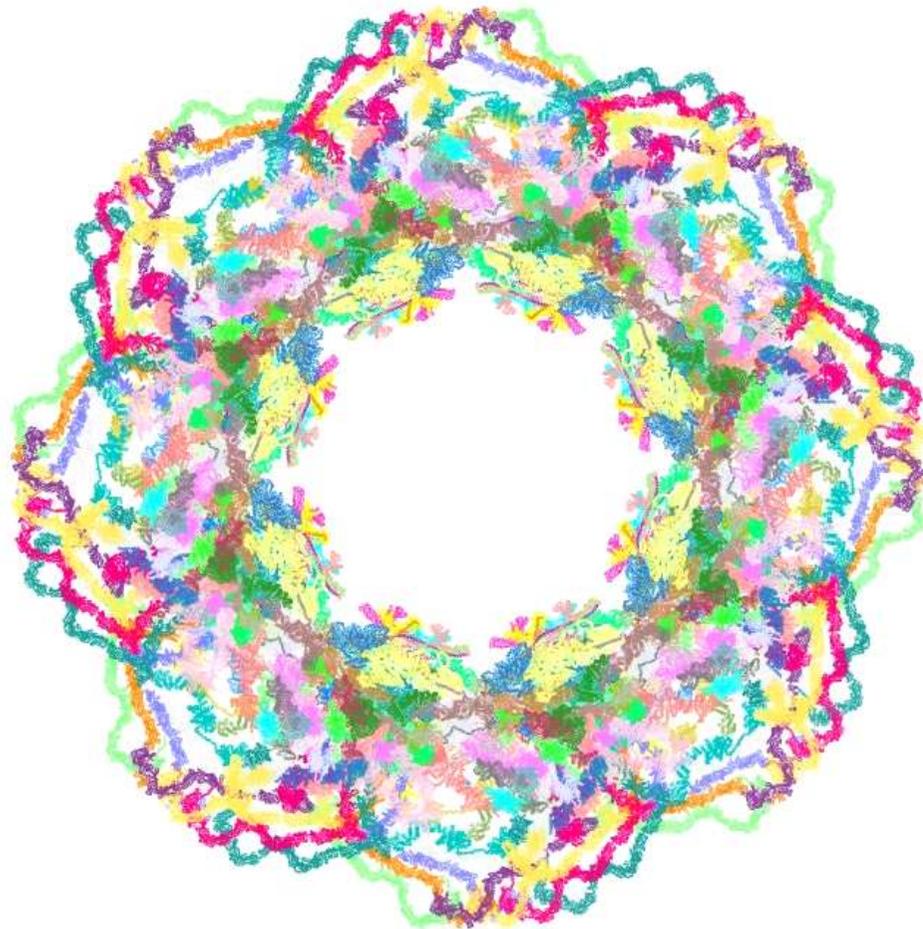
Membrana+aquaporina

Permeabilidade e transporte



As macromoléculas biológicas funcionam como máquinas moleculares

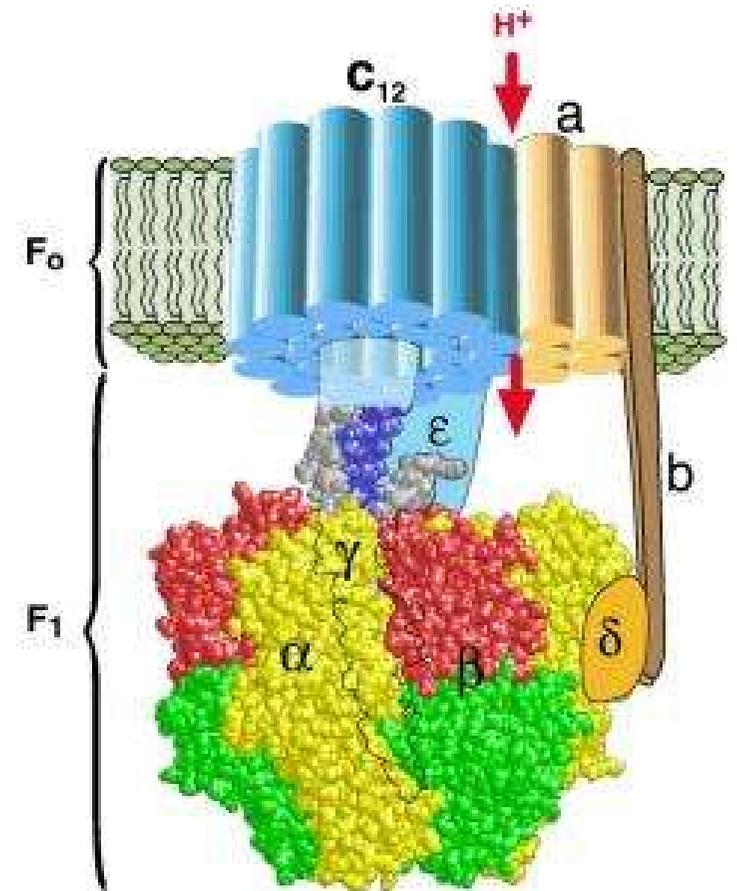
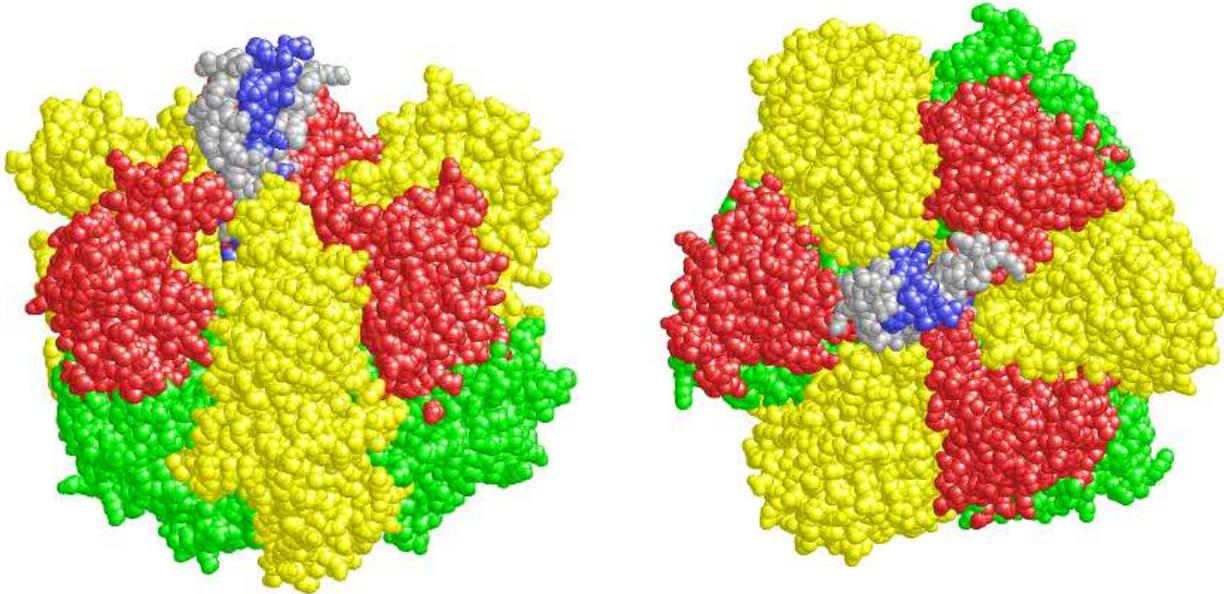
Estrutura de um poro nuclear



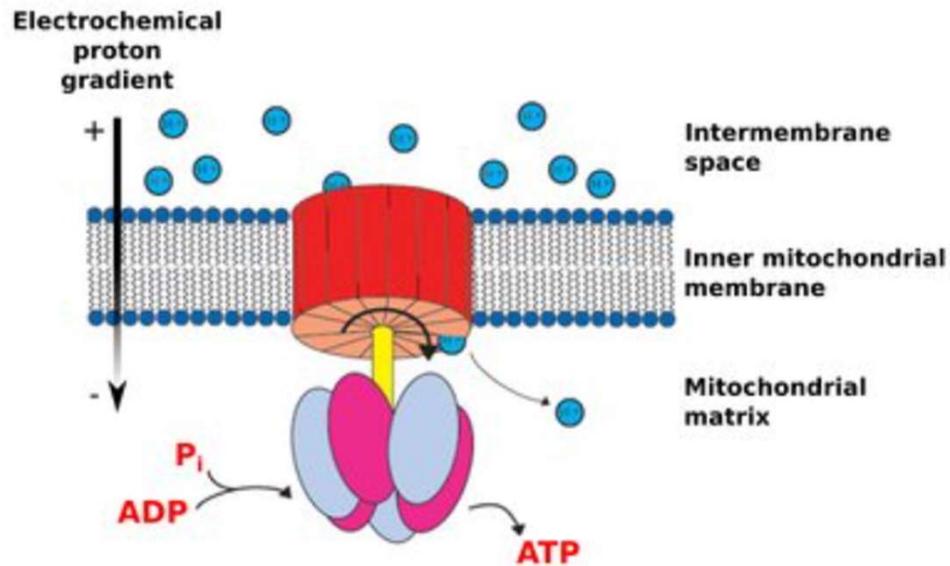
PDB: 7r5j

Conversão de energia

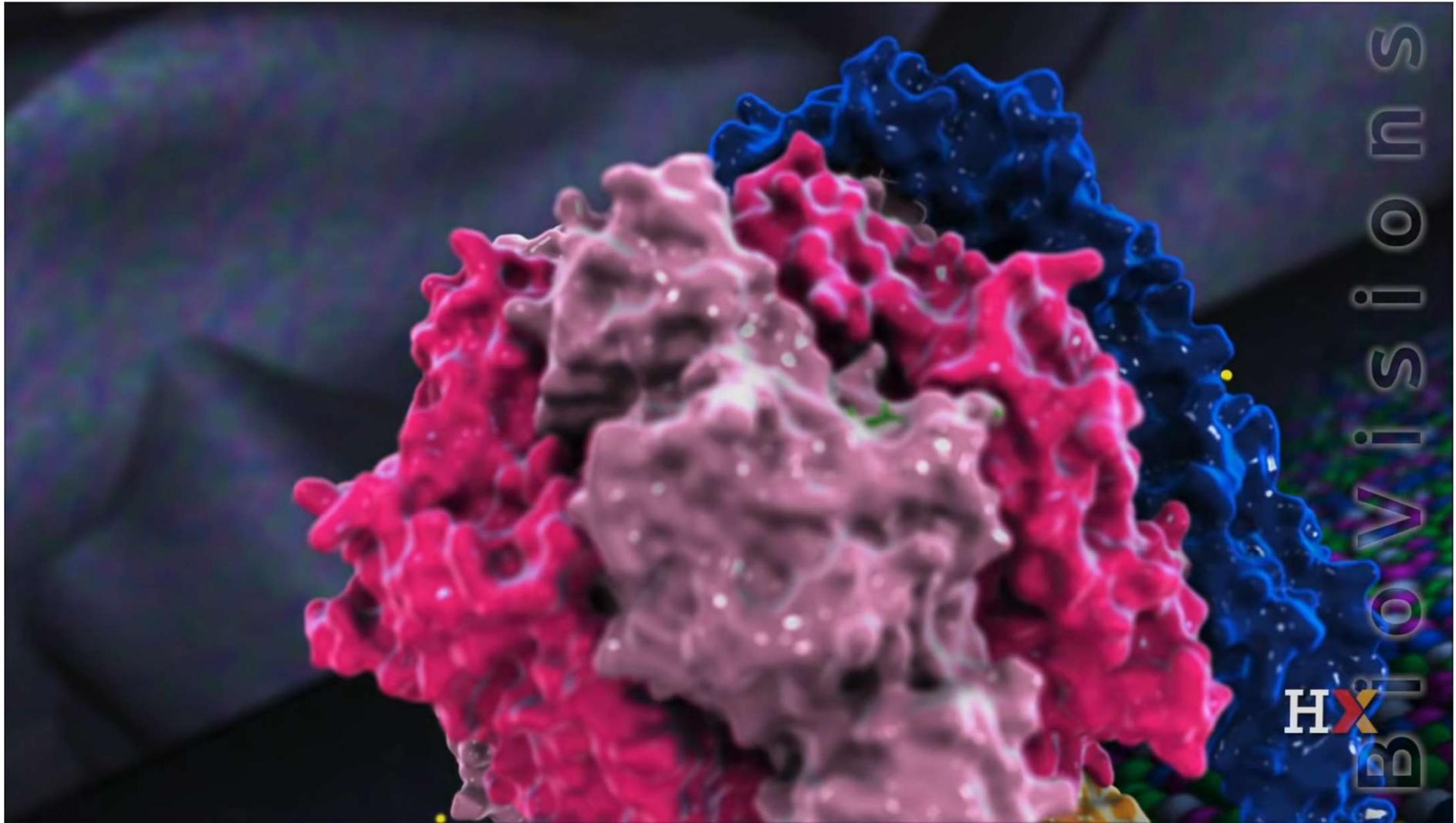
ATPsintase



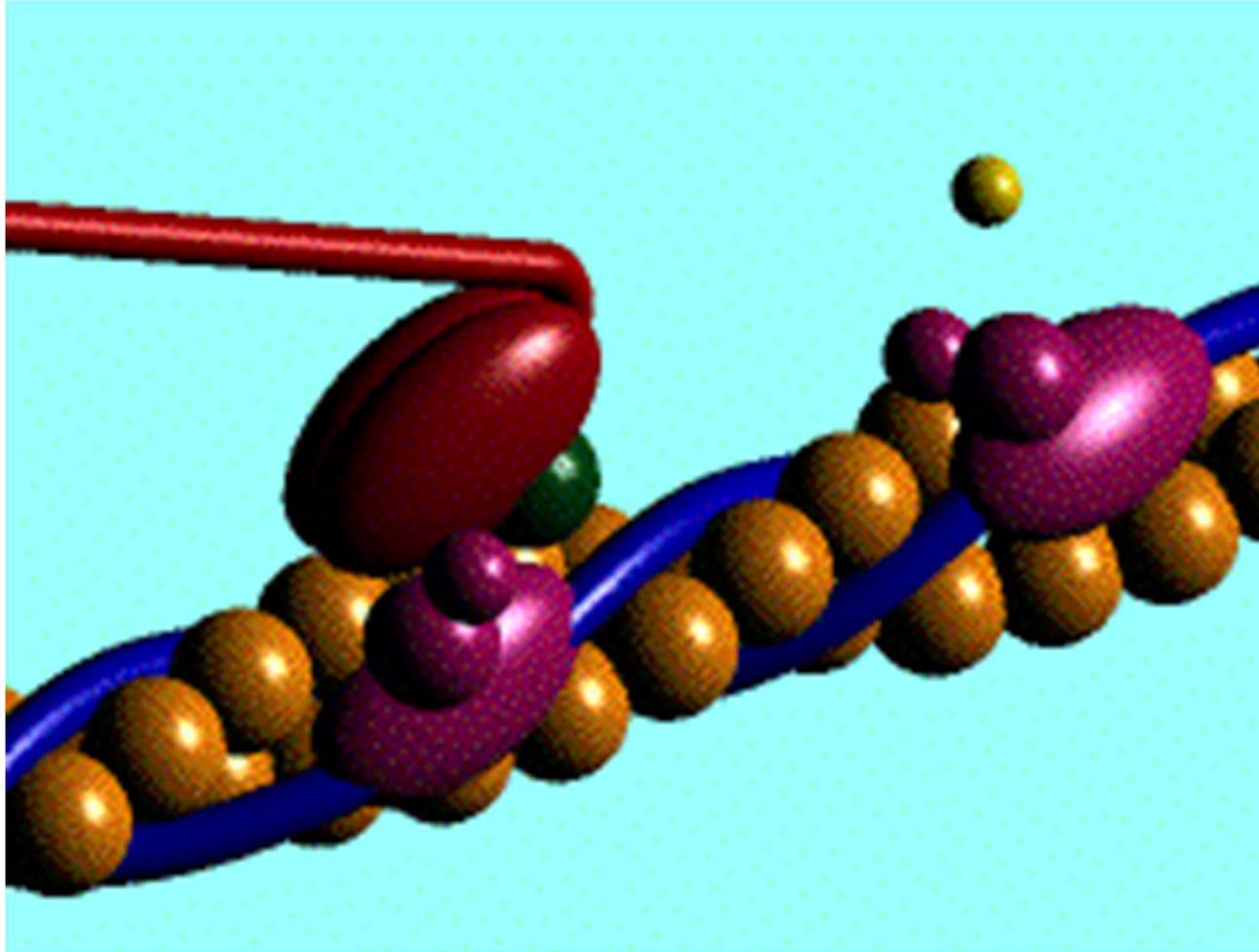
H. Wang and G. Oster (1998). Nature 396:279-282.



A molecular power generator

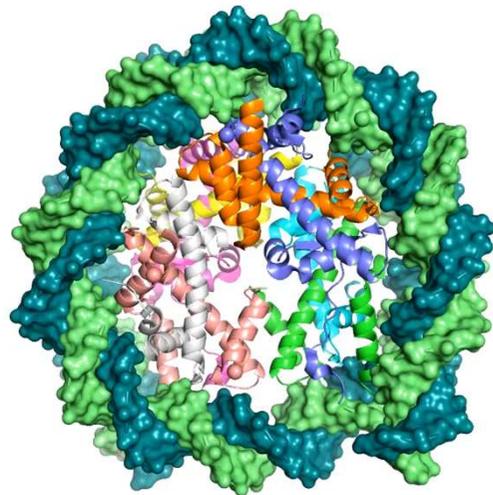
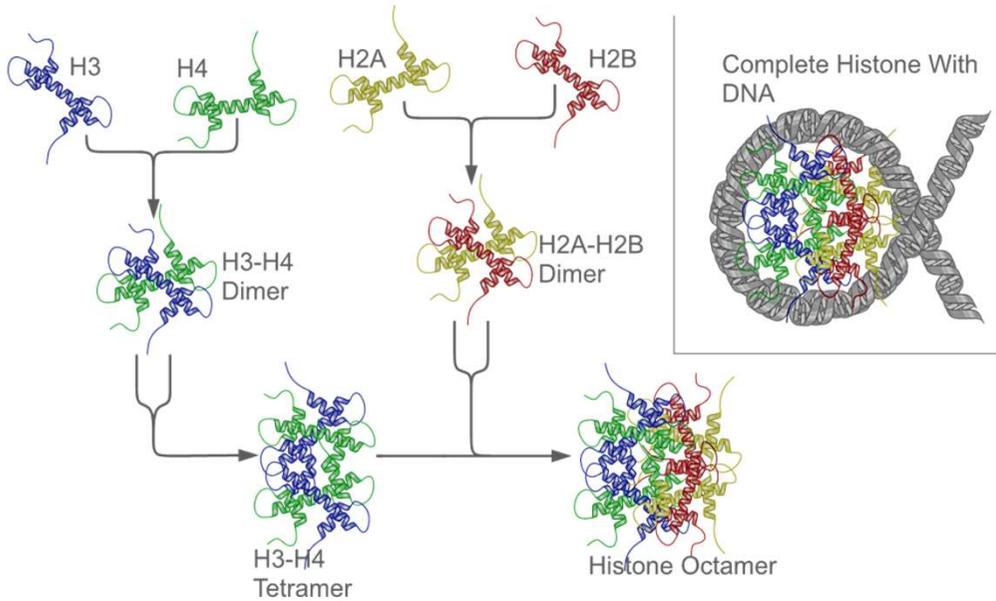


Motilidade

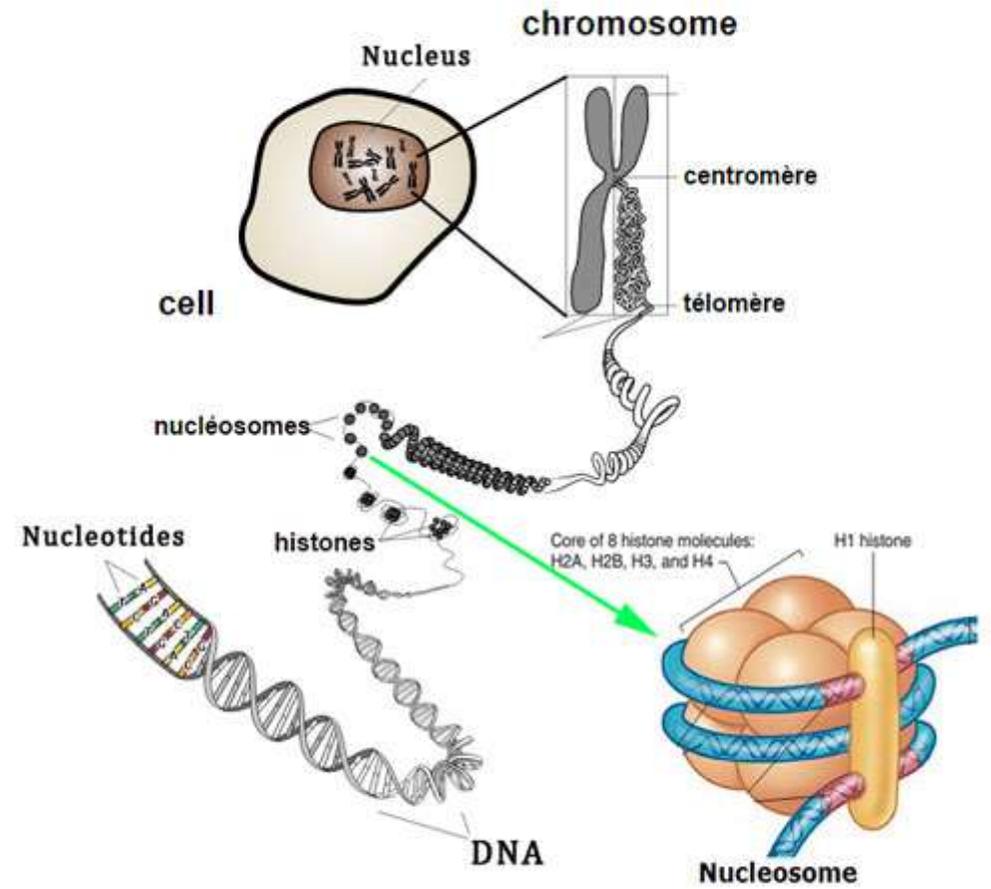


Actina+Miosina

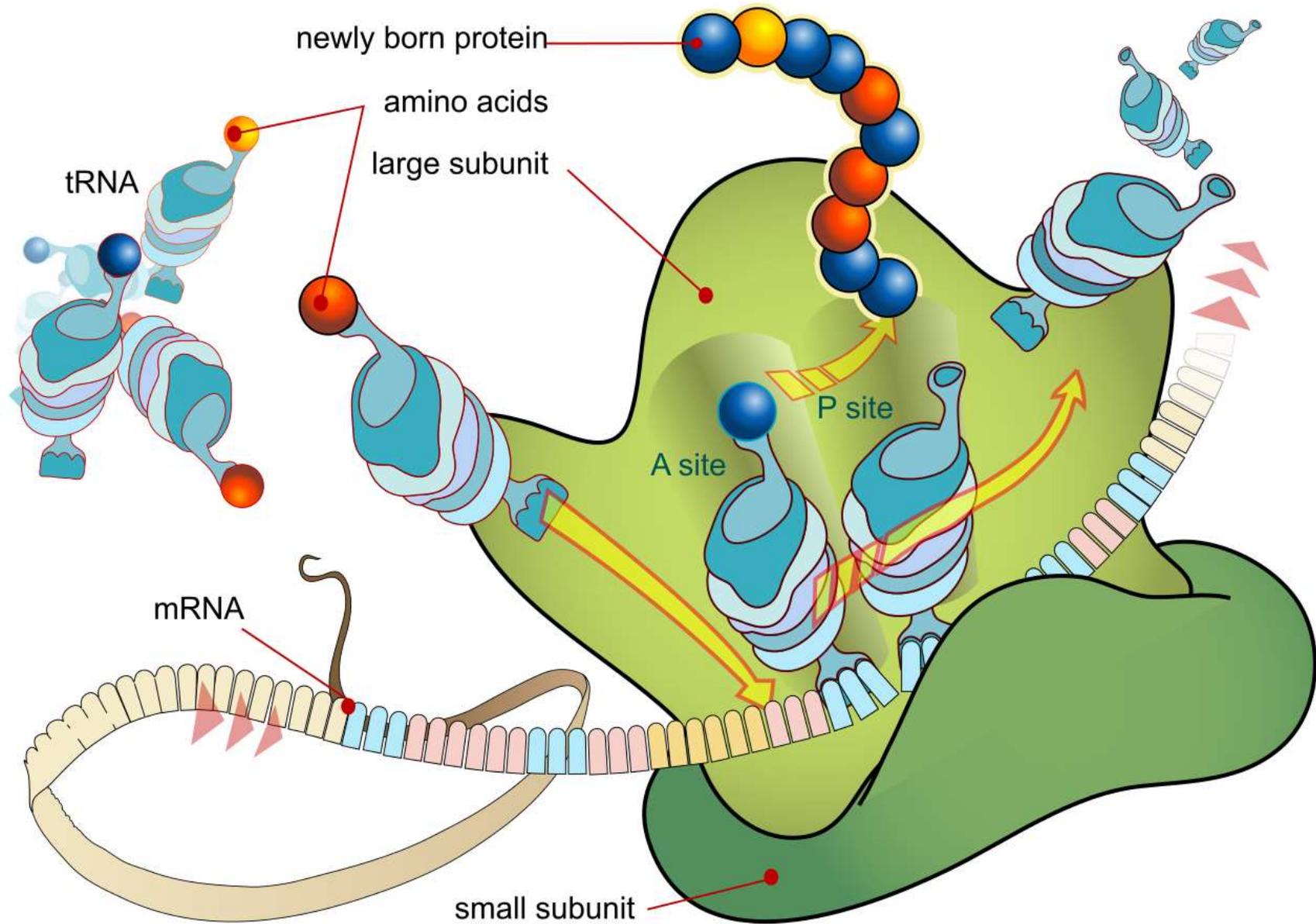
Informação



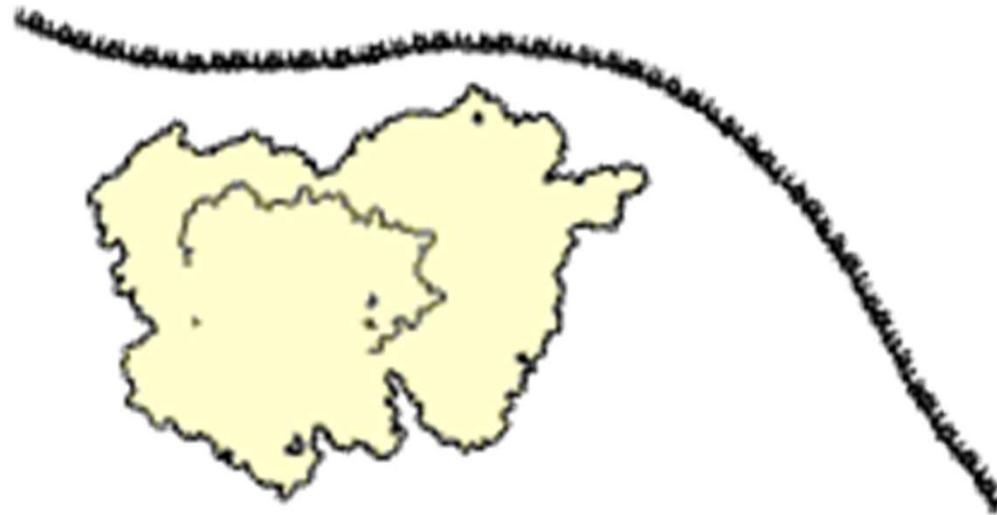
Nucleossoma



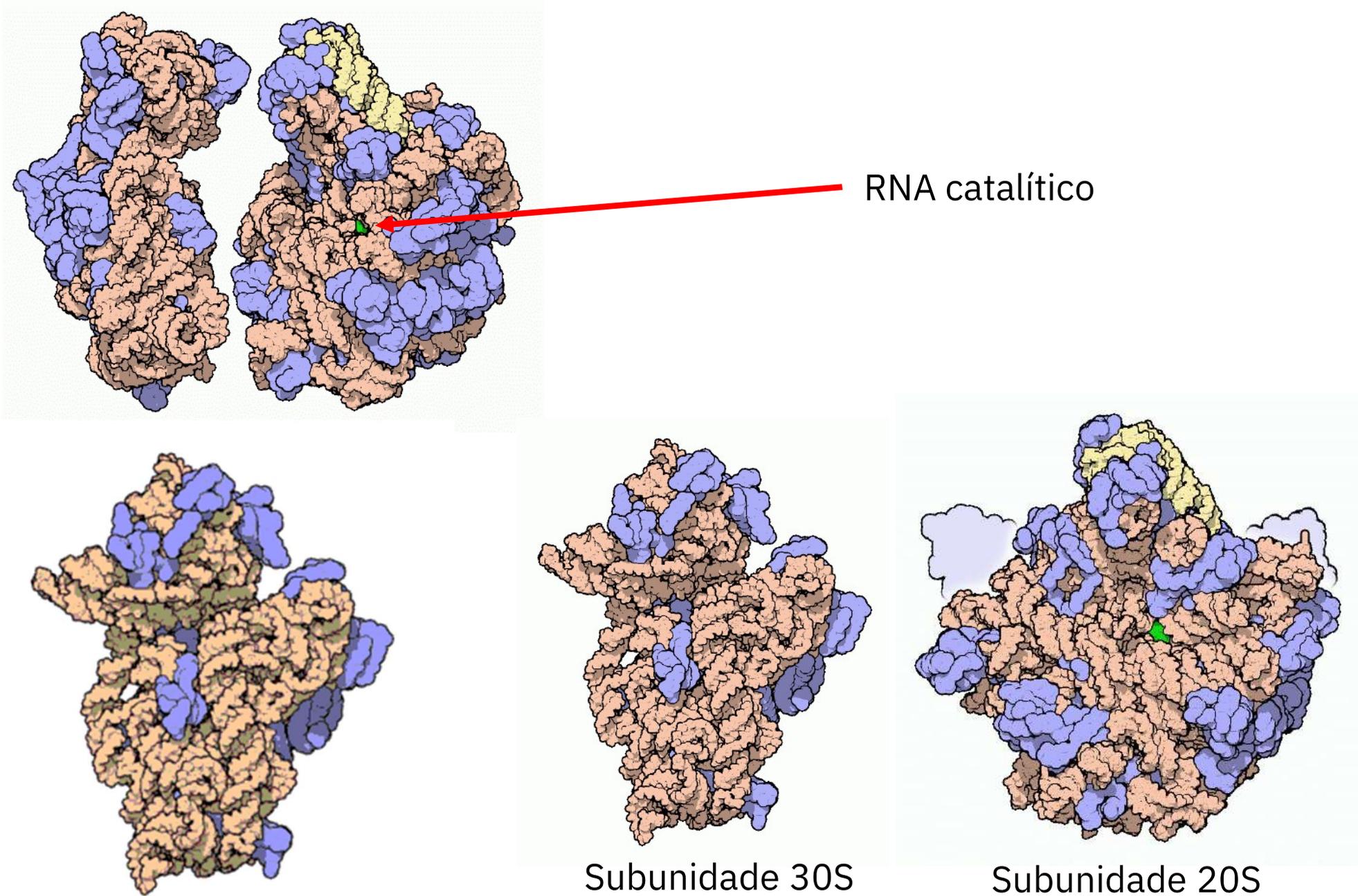
Síntese proteica



Síntese proteica (animação)

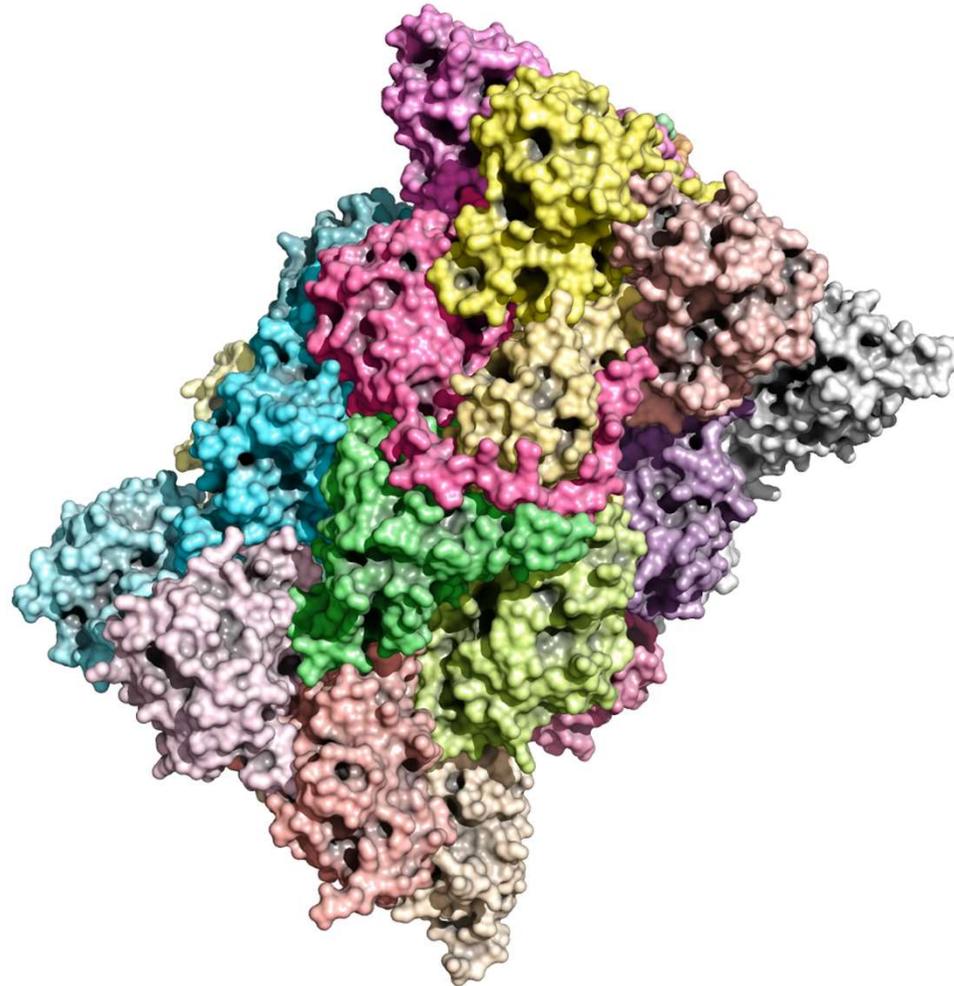


Estrutura do ribossoma bacteriano



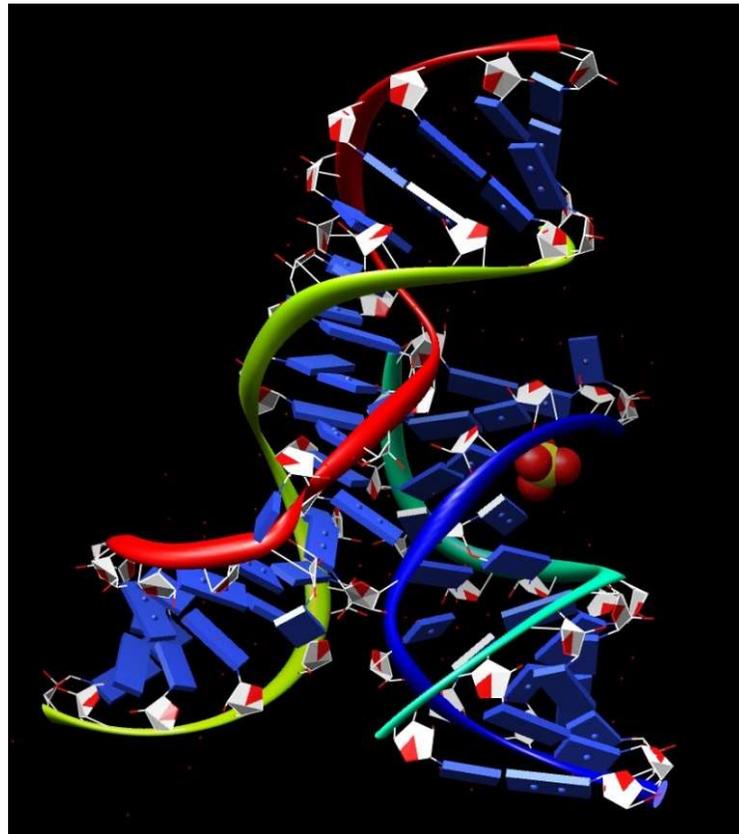
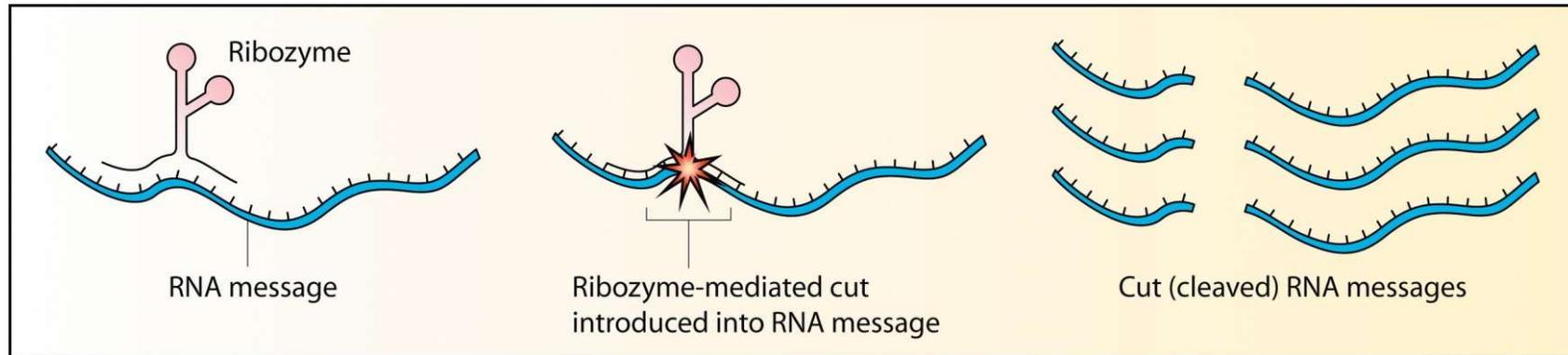
Reciclagem de proteínas

Proteassoma

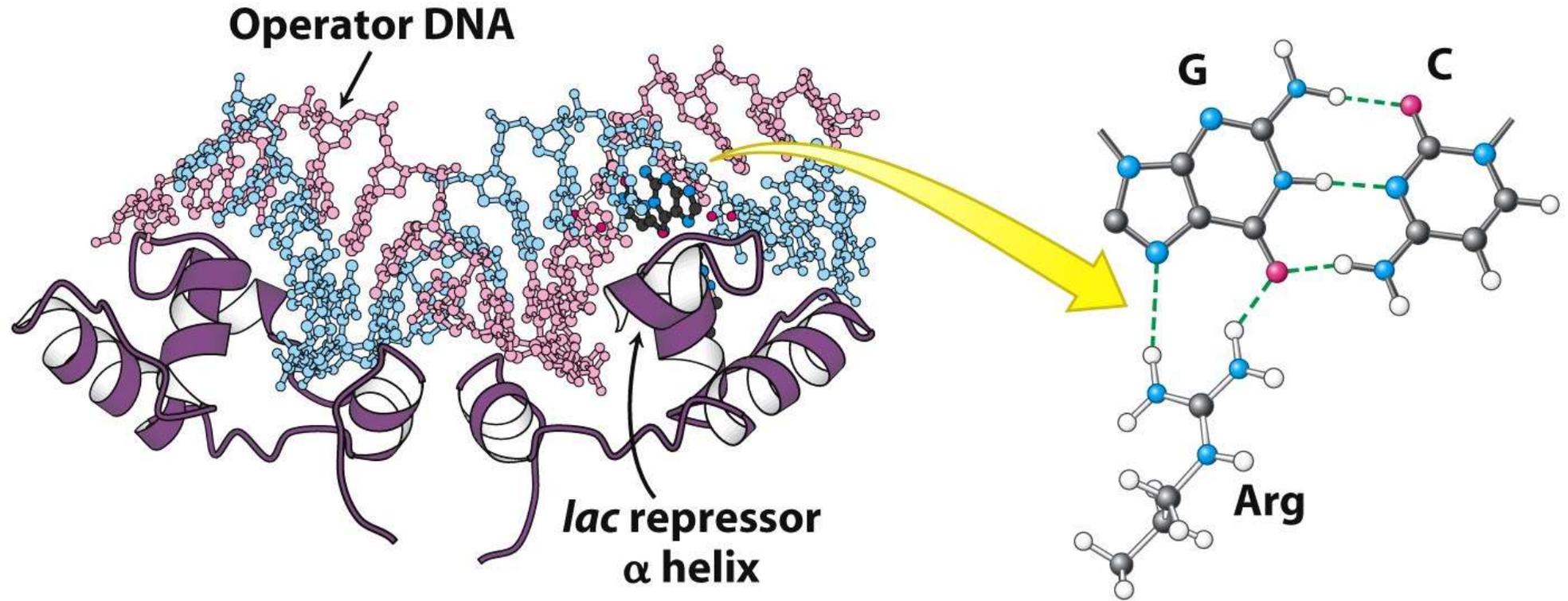


Assemblagem de máquinas moleculares

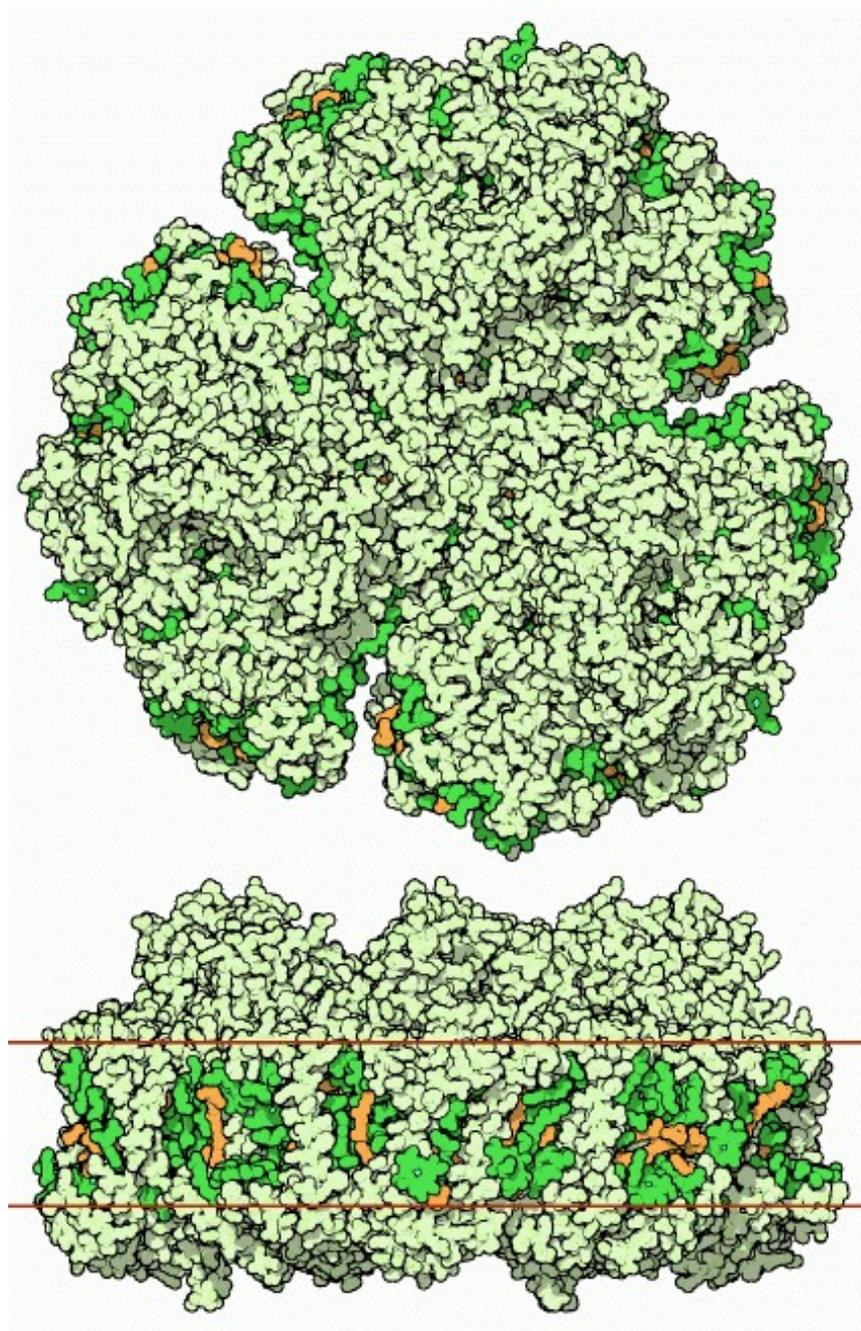
Ribozimas



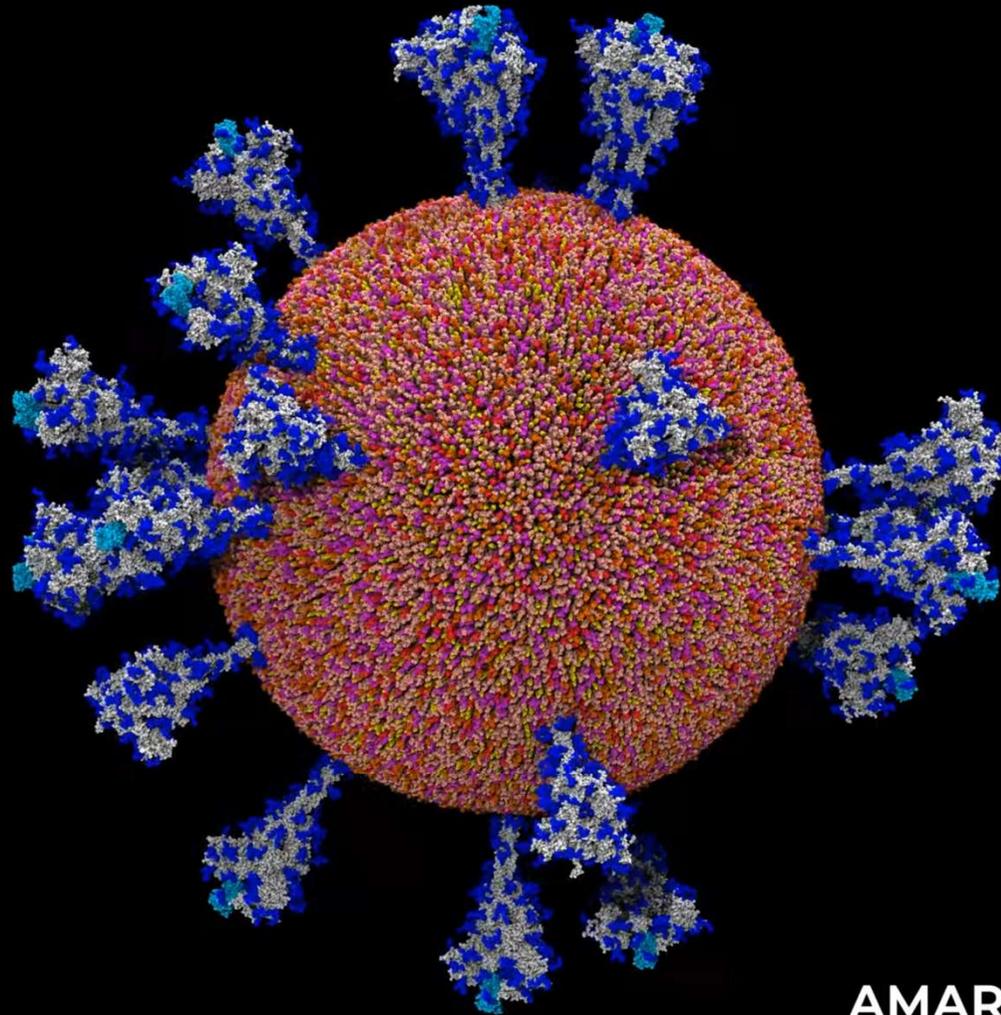
Regulação da transcrição



Fotossistema I

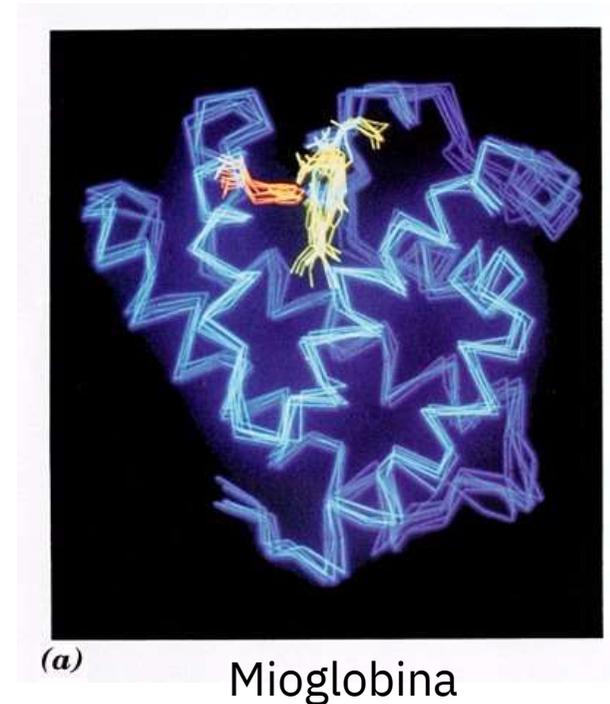
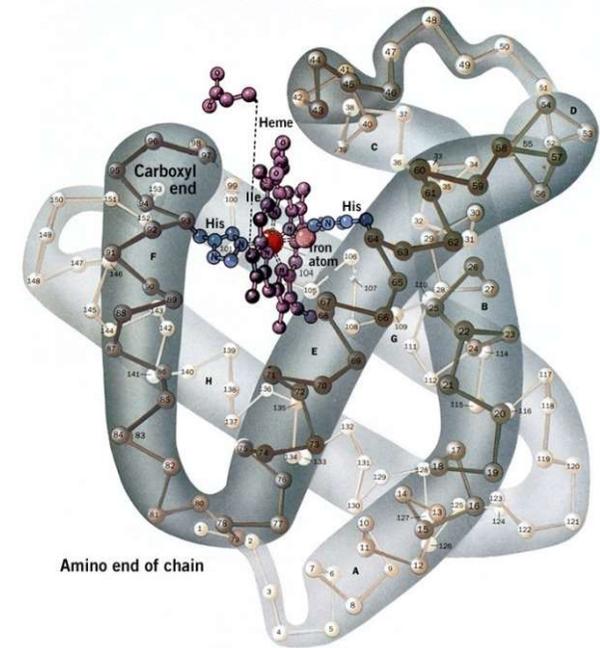
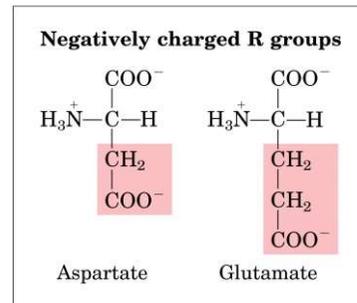
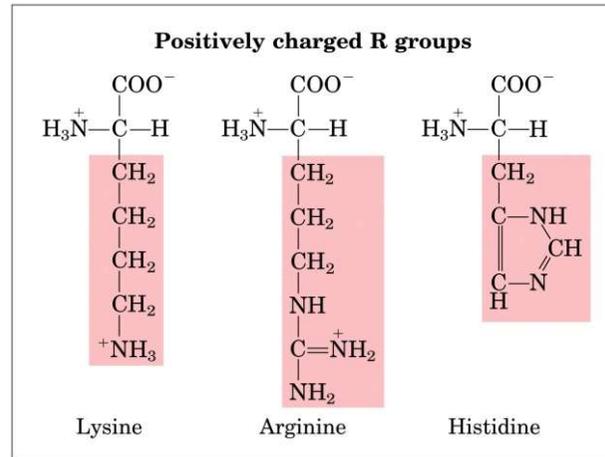
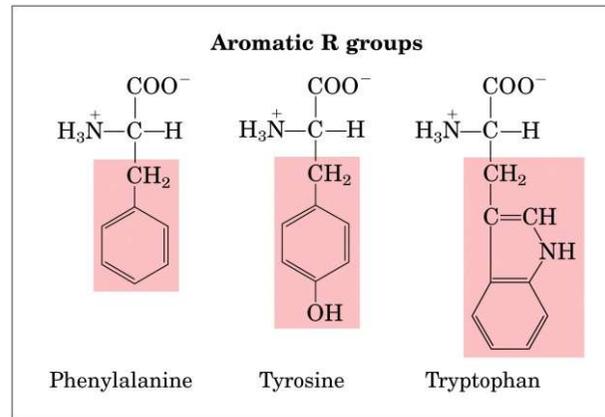
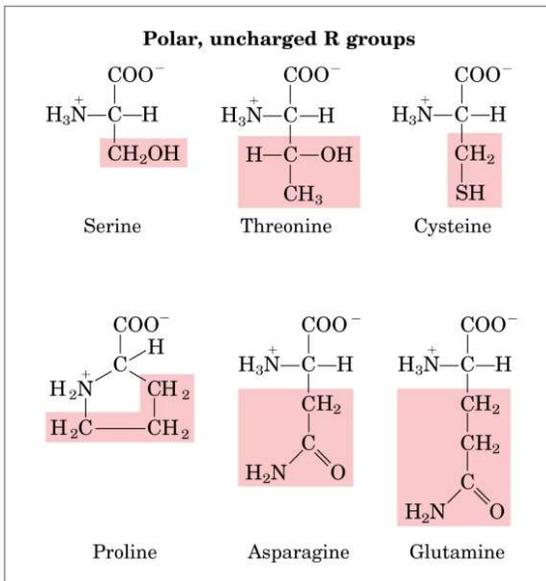
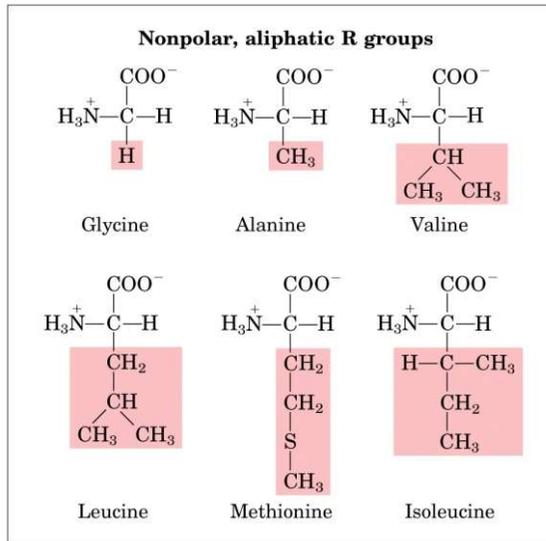


3.5M-atom model of SARS-CoV-2

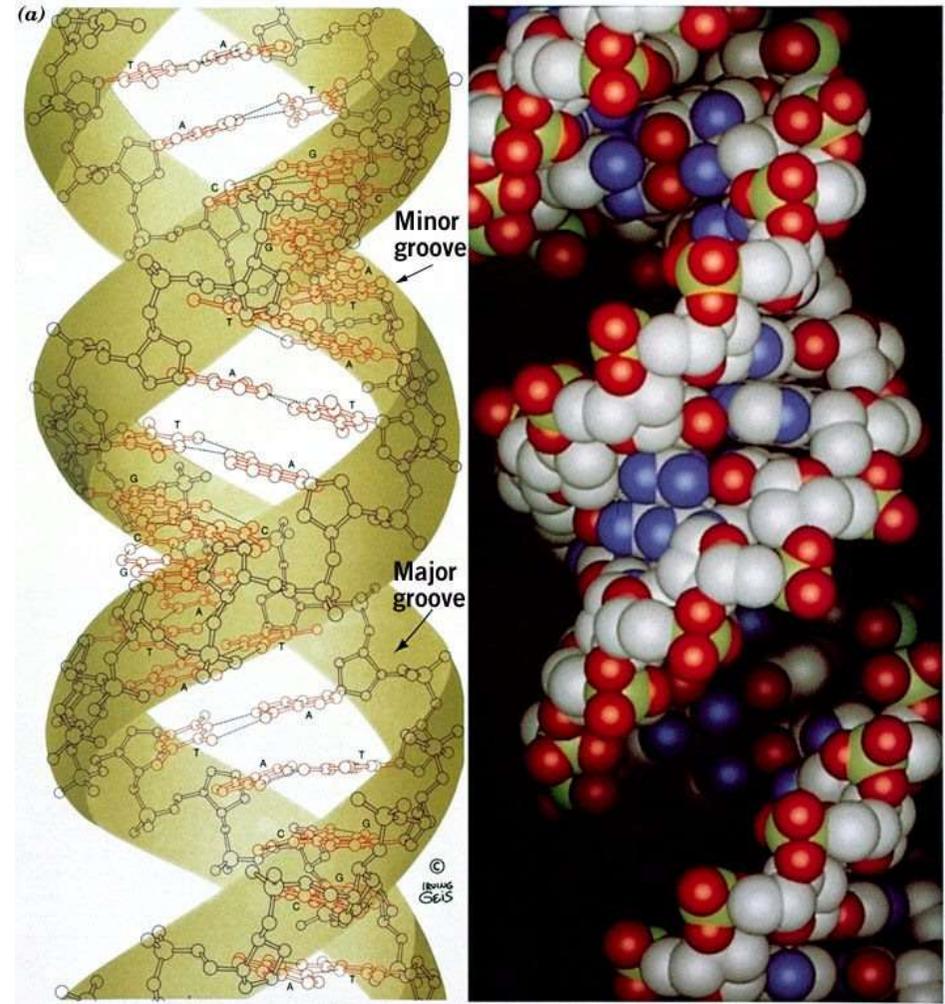
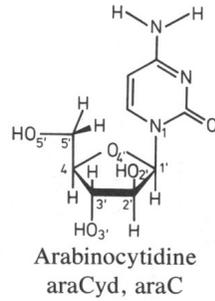
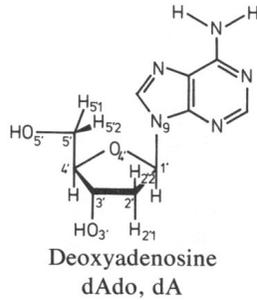
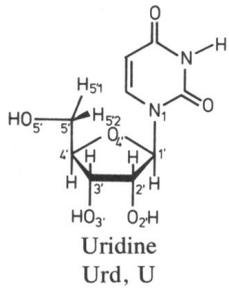
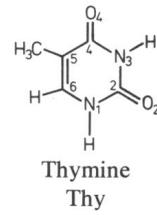
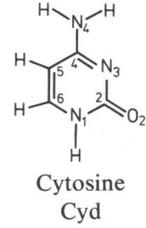
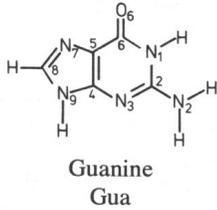
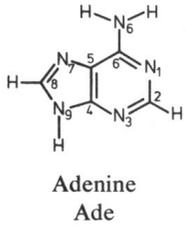


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Proteínas



Ácidos nucleicos



B-Dna