

# **Interações Intermoleculares – papel da água**

## **Aminoácidos, peptídeos e proteínas**

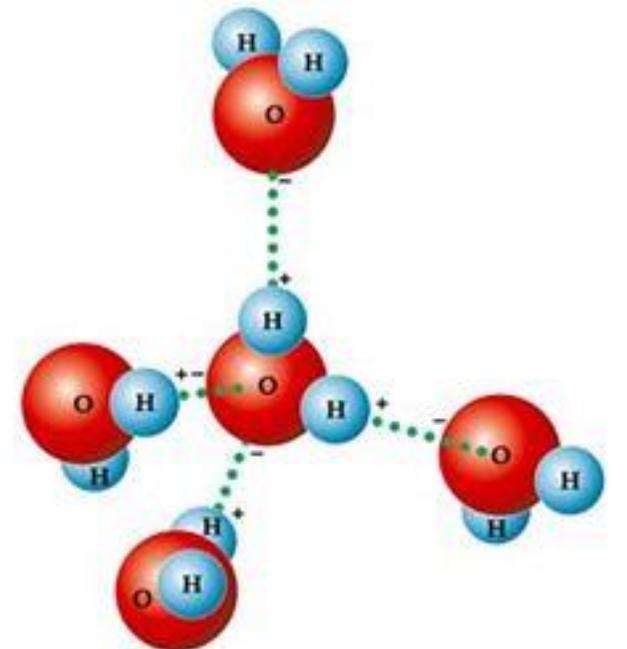
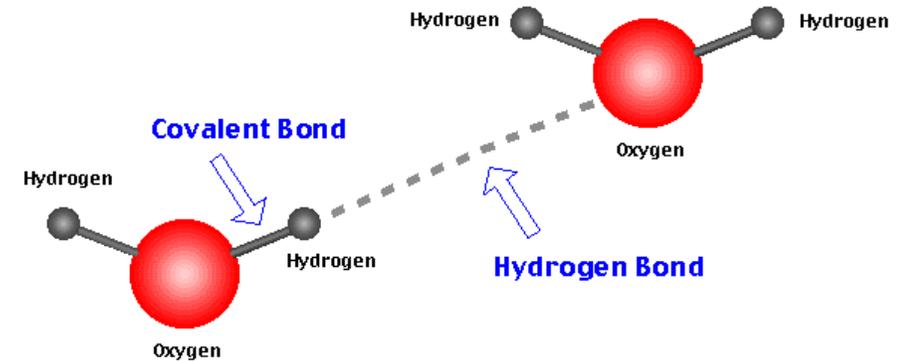
**Prof Marcio Dias**  
**[mvbdias@usp.br](mailto:mvbdias@usp.br)**

**Por que estudar a água????**

A molécula de água e seus produtos iônicos –  $H^+$  e  $OH^-$  influenciam a estrutura, auto-organização e propriedades dos componentes celulares

# Ligação de hidrogênio

- responsável pela força coesiva que faz a água ser líquida em temperatura ambiente
- Responsável pela água apresentar altamente ordenada em cristais
- Biomoléculas polares são prontamente dissolvidas em água pelas energeticamente favoráveis interações entre moléculas de água e soluto



## Geometria da molécula de água

- Oxigênio atrai elétrons mais fortemente que hidrogênio, portanto os elétrons são mais frequentes na vizinhança com o oxigênio
- Resultado: formação de dois dipolos na molécula de água.

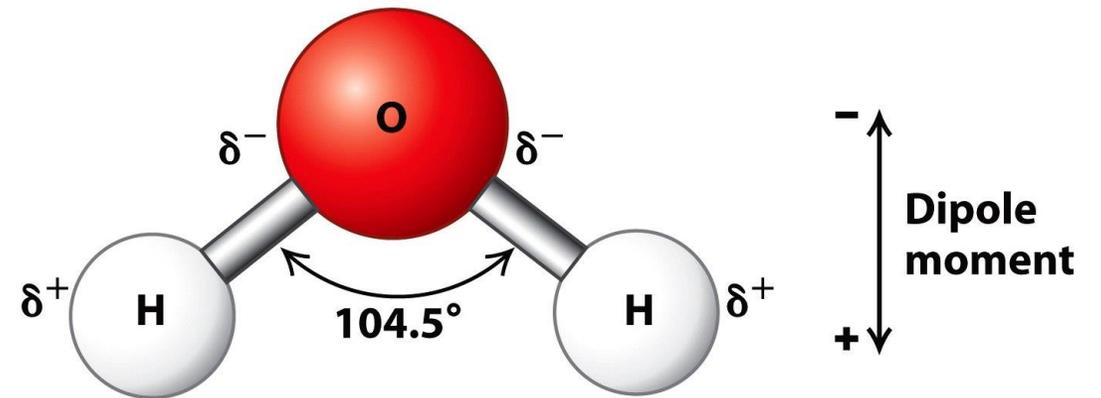
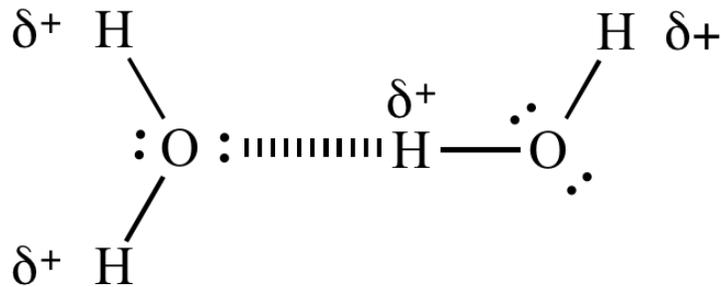
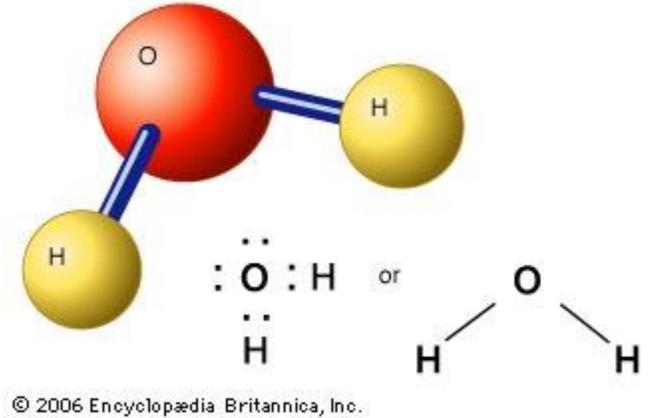
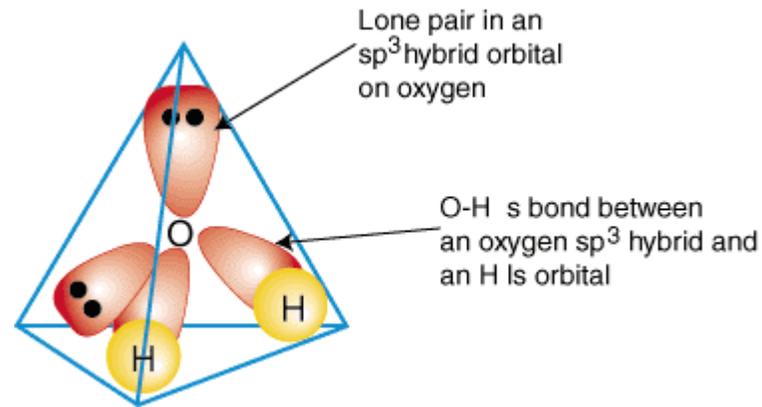
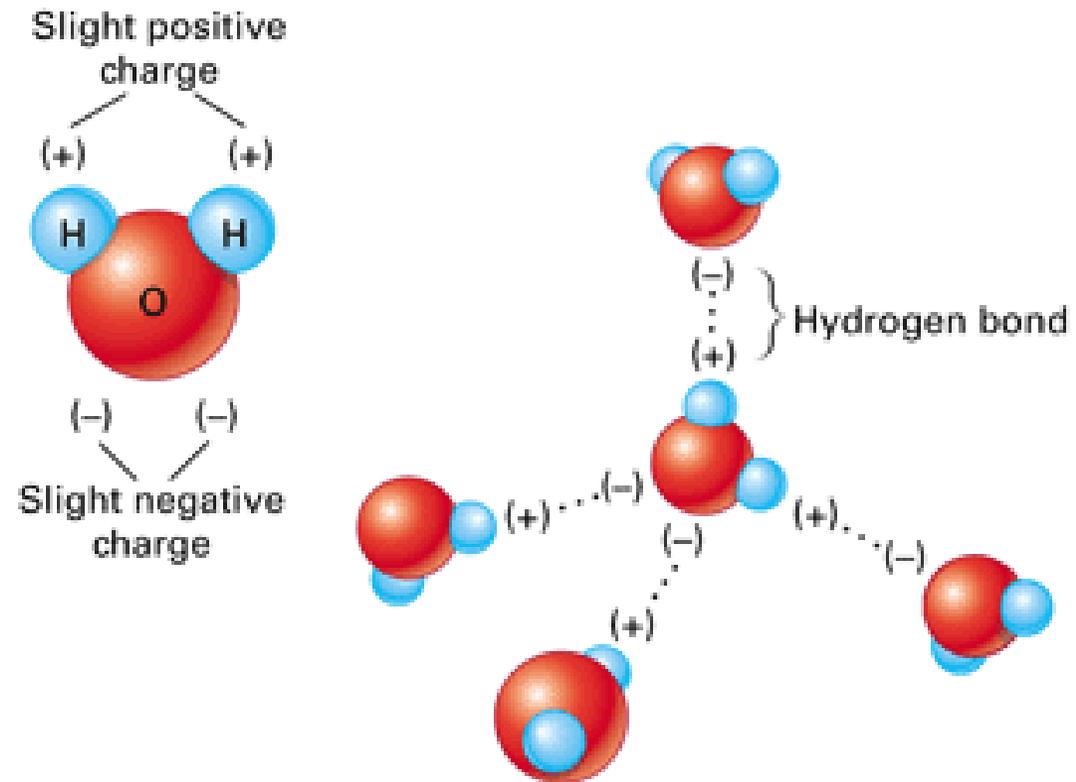


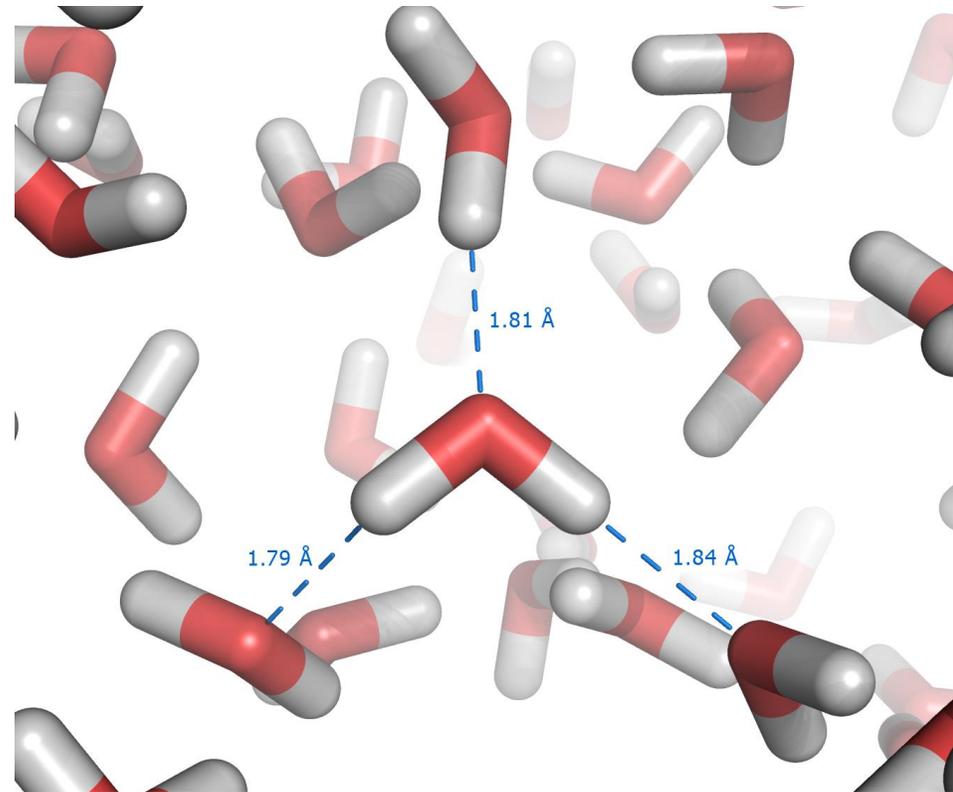
Figure 2-5  
Molecular Cell Biology, Sixth Edition  
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## Ligação de hidrogênio: resultado da formação de dipolos da molécula de água

- Ligações de hidrogênio são relativamente fracas (energia de dissociação da ligação é de 23KJ/mol em comparação com 470 KJ/mol da ligação O-H).

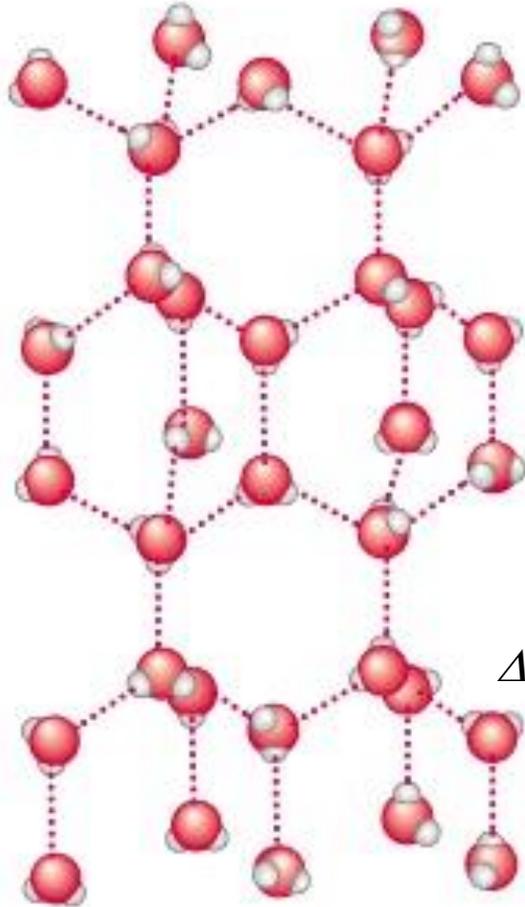


Dinâmica das moléculas de água em solução = tempo da ligação de hidrogênio = 1-20 picosegundos e outra ligação é formada em 0.1 ps



A soma de todas as ligações de hidrogênio em moléculas de água cria uma alta coesão interna ou água líquida

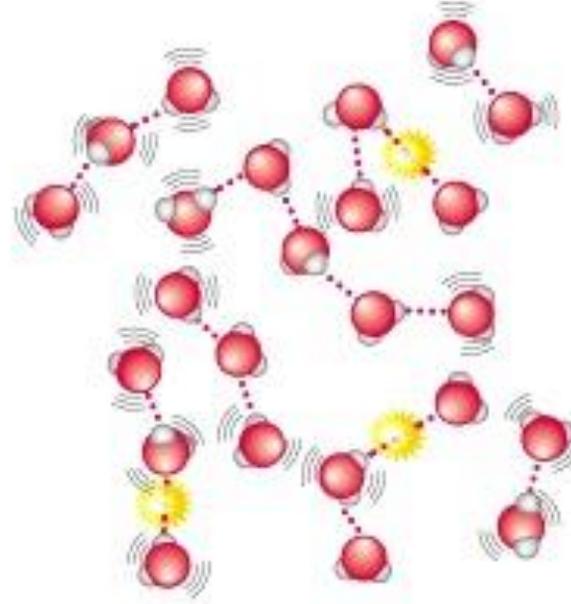
(a) Solid water (ice)



$$\Delta H = +5.9 \text{ KJ/mol}$$

4 ligações

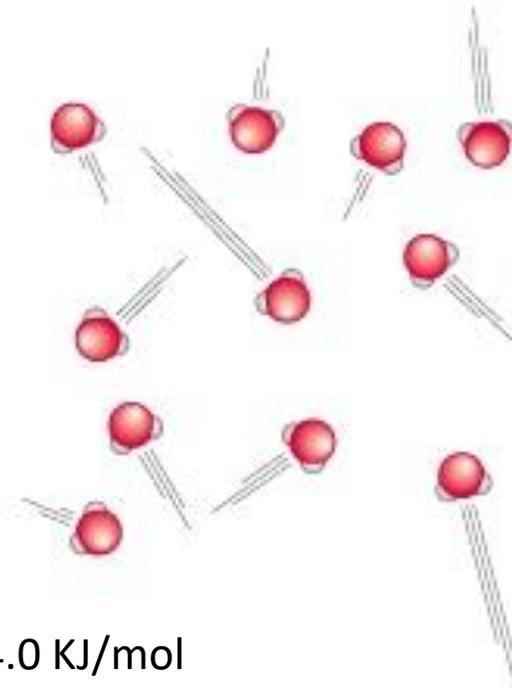
(b) Liquid water



$$\Delta H = +44.0 \text{ KJ/mol}$$

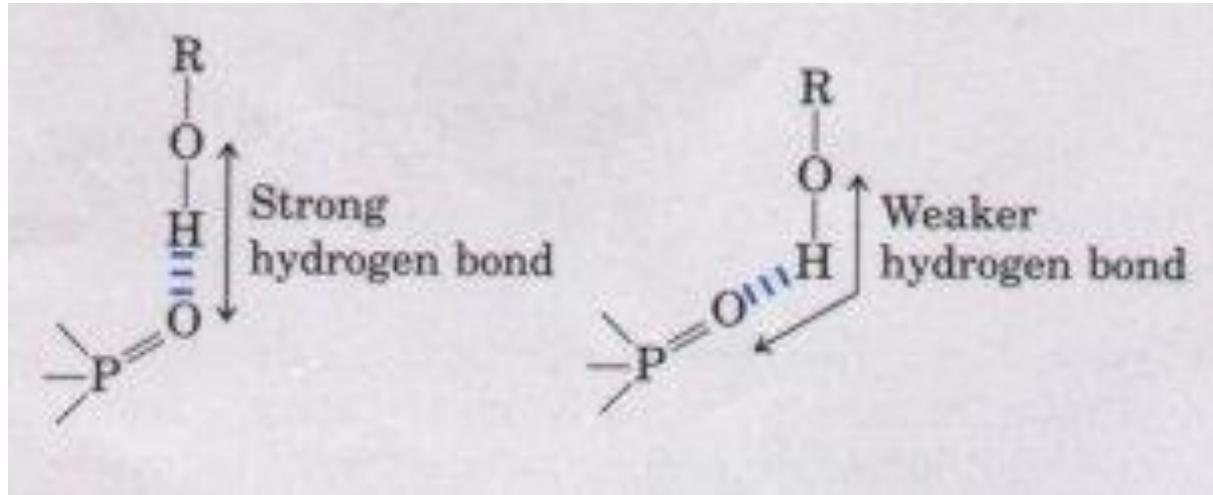
3.4 ligações

(c) Gaseous water (steam)

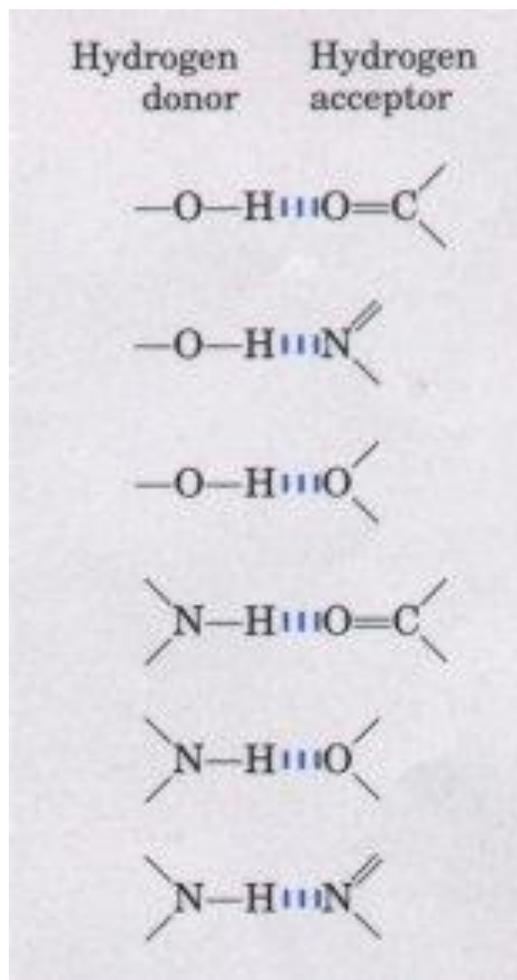
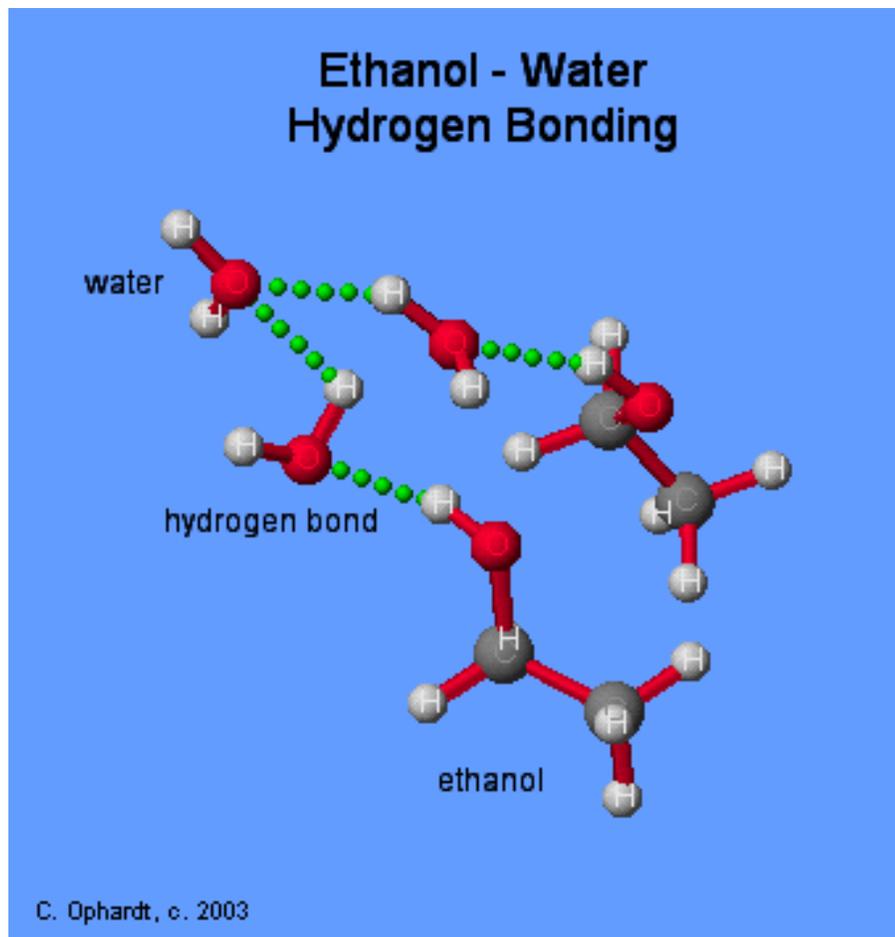


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Interações em linha reta maximizam a interação eletrostática



## Água pode formar ligações de hidrogênio com solutos polares



C-H não forma ligação de hidrogênio

Ponto de ebulição butanol = 117°C

Ponto de ebulição butano = 0,5°C

Substâncias não carregadas como açúcares, compostos contendo O-H e N-H tendem a ser solução em água devido a formação de ligações de hidrogênio

A água dissolve sais como NaCl

Gases não são solúveis em água

# Compostos anfipáticos

Proteínas, pigmentos, vitaminas, hormônios esteroidais

Formação de interações hidrofóbicas

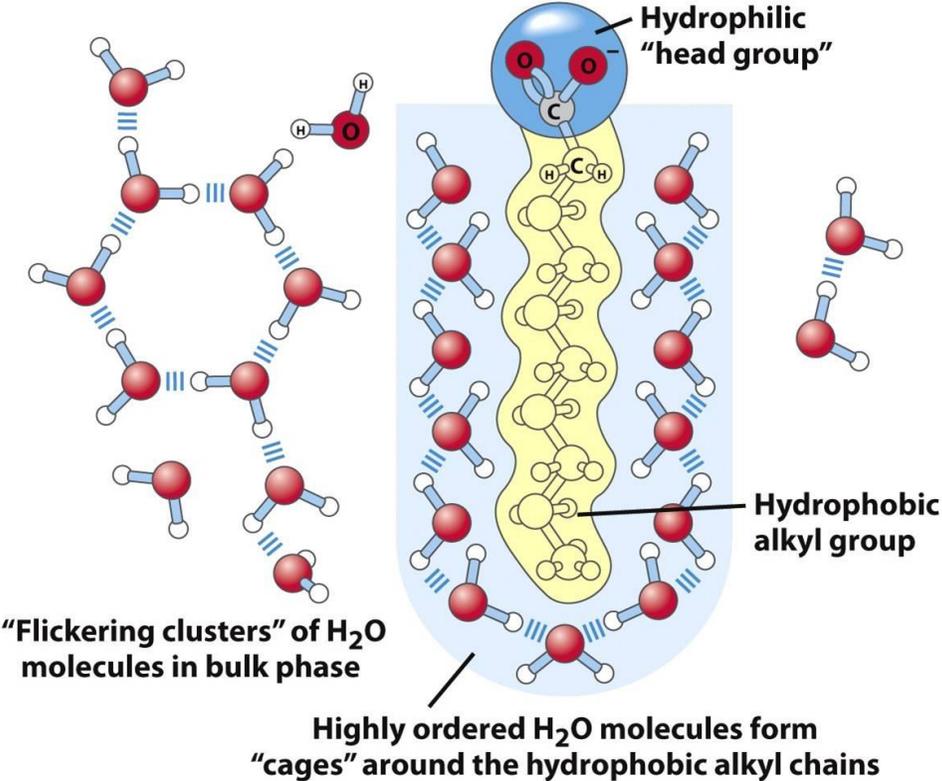
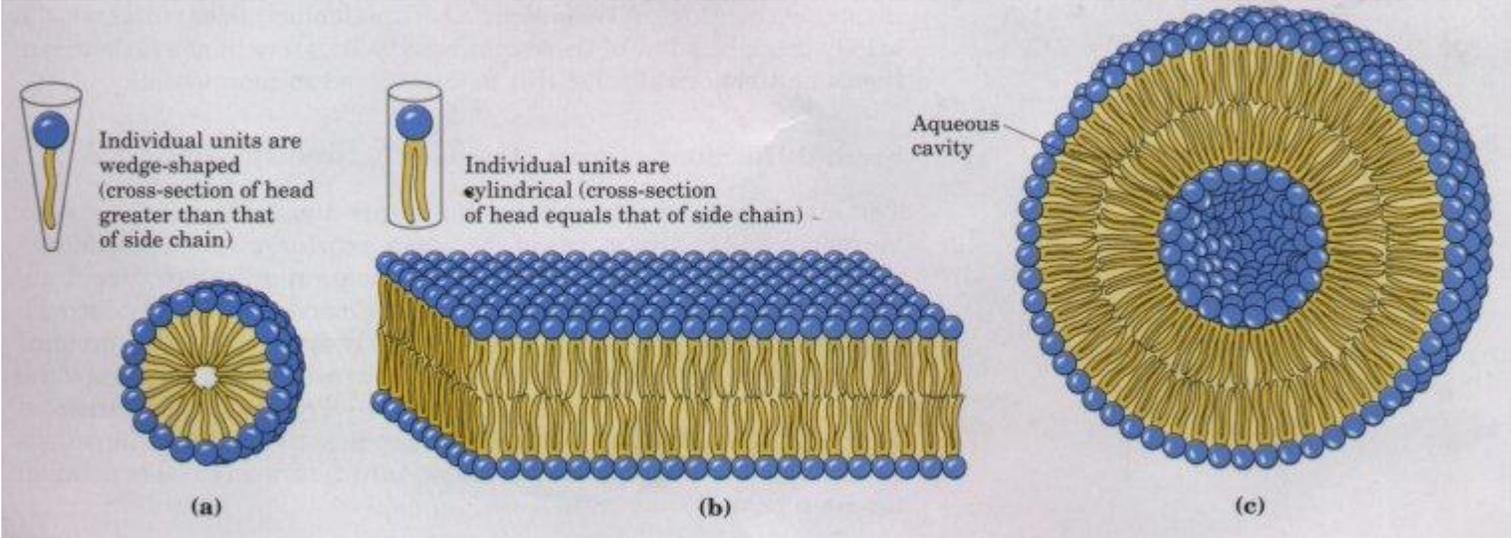


Figure 2-7a  
Lehninger Principles of Biochemistry, Fifth Edition  
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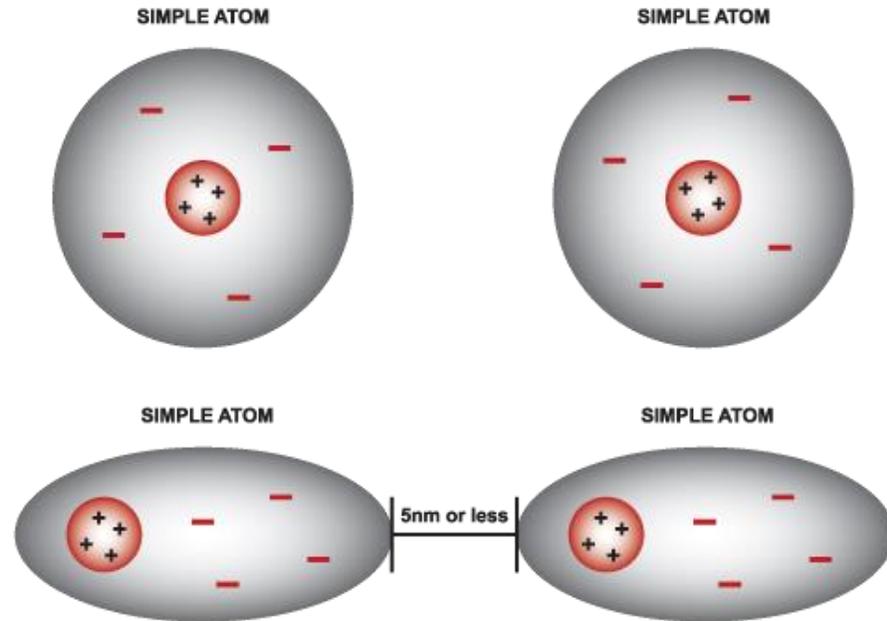
# Interações de van der Waals ou forças de London

## VAN DER WAALS' FORCES (VDW) DIAGRAM

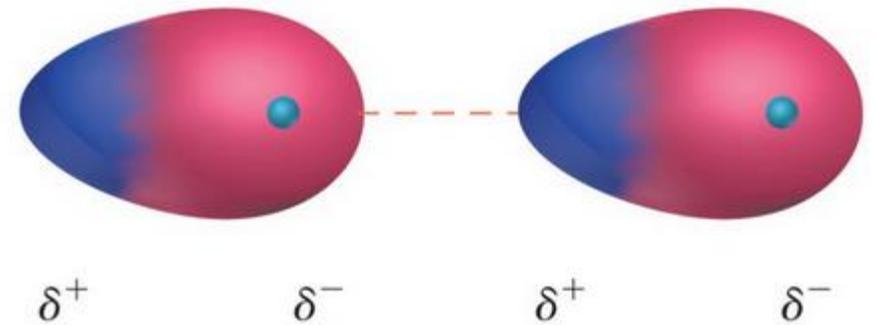
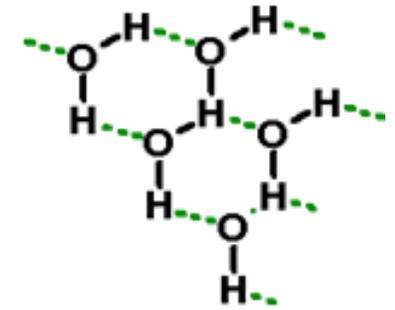
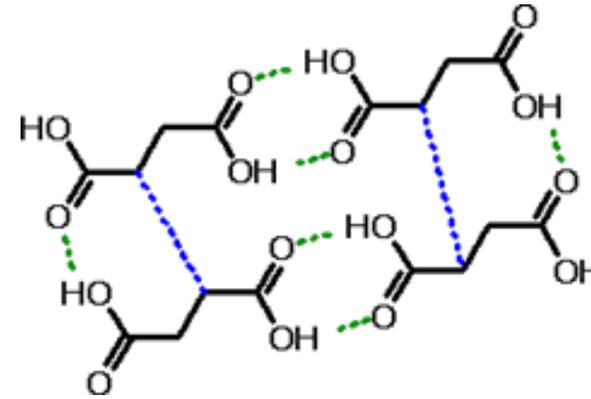
### KEY

+ POSITIVE NUCLEUS

- NEGATIVE CHARGED ELECTRON CLOUD

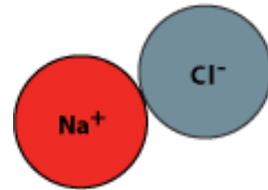


When two atoms come within 5 nanometers of each other, there will be a slight interaction between them, thus causing polarity and a slight attraction.

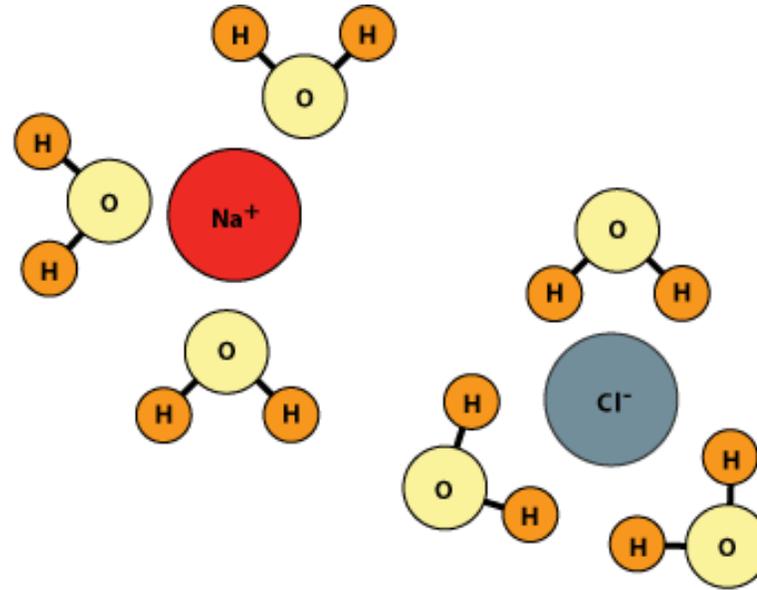


## Interações iônicas

Interação que ocorre entre dois compostos que apresentam cargas opostas e portanto ocorre em íons.

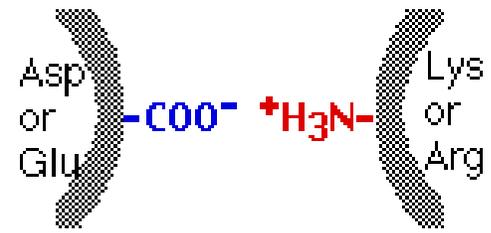


Sodium Chloride ( $\text{NaCl}$ ) in air

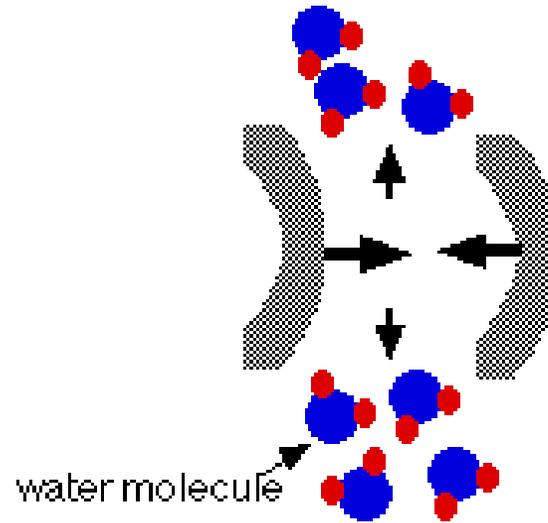


Sodium Chloride ( $\text{NaCl}$ ) in water ( $\text{H}_2\text{O}$ )

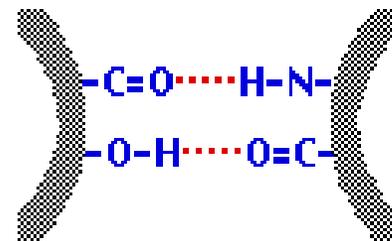
Hidratação



### Ionic Interactions



### Hydrophobic Interactions



### Hydrogen Bonds

## Efeito de moléculas de água na estrutura e função de proteínas

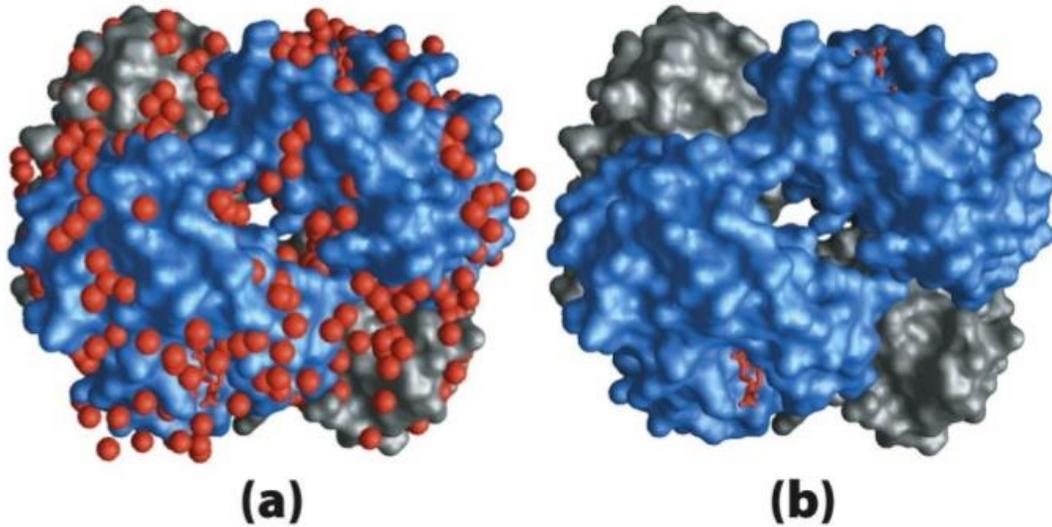


Figure 2-9  
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Water binding in hemoglobin. (PDB ID 1A3N) The crystal structure of hemoglobin, shown (a) with bound water molecules (red spheres) and (b) without the water molecules. The water molecules are so firmly bound to the protein that they affect the x-ray diffraction pattern as though they were fixed parts of the crystal. The two  $\alpha$  subunits of hemoglobin are shown in gray, the two  $\beta$  subunits in blue. Each subunit has a bound heme group (red stick structure), visible only in the  $\beta$  subunits in this view.

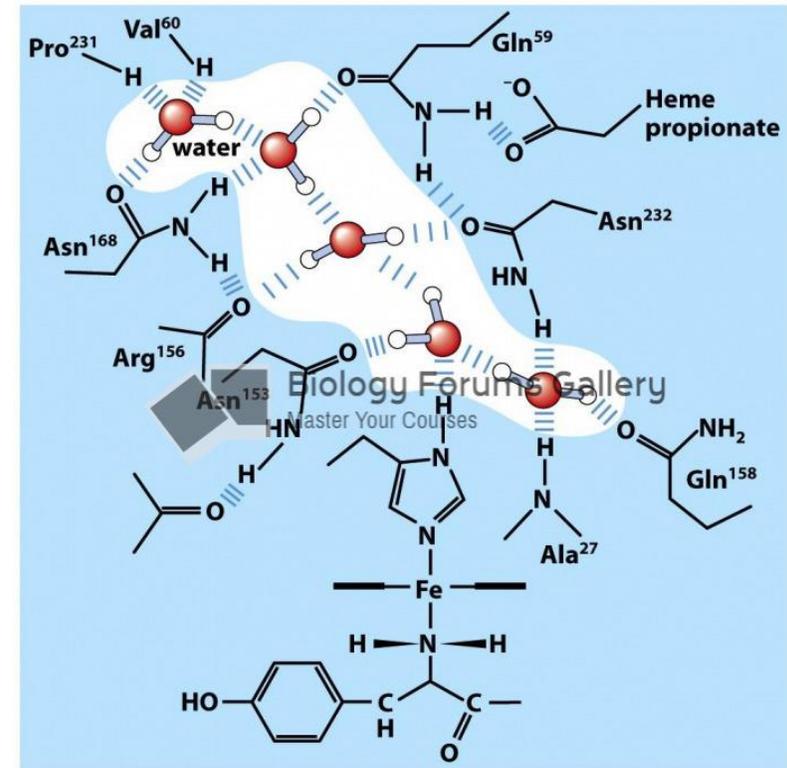
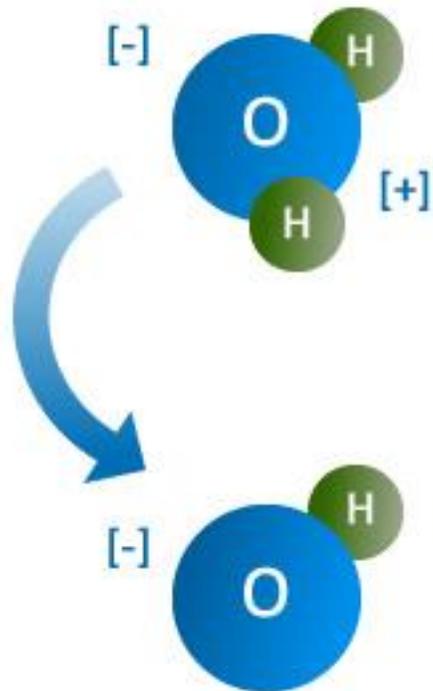


Figure 2-10  
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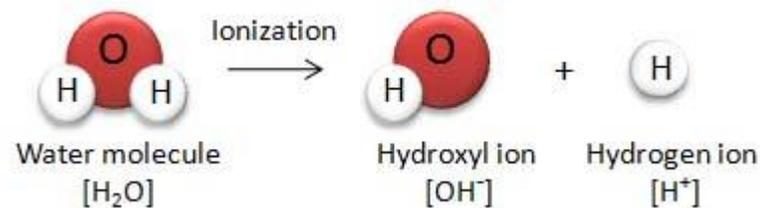
# Ionização da água

## How Ionized Water is Made

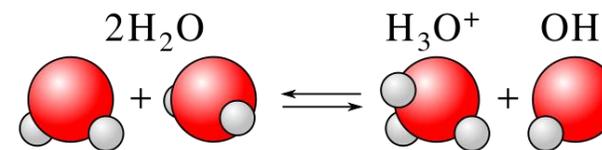


Ionization dissociates the water molecules to form one hydroxyl ion [OH<sup>-</sup>] (alkaline), and one hydrogen ion [H<sup>+</sup>] (acidic).

A água tem uma leve tendência a sofrer ionização e liberar um íon de hidrogênio (rapidamente sofre hidratação e forma um íon hidrônio, (H<sub>3</sub>O<sup>+</sup>) e um íon hidróxido



Entretanto, a ionização da água é reversível



# **Aminoácidos - propiedades**

# As proteínas são constituídas por 20 diferentes aminoácidos

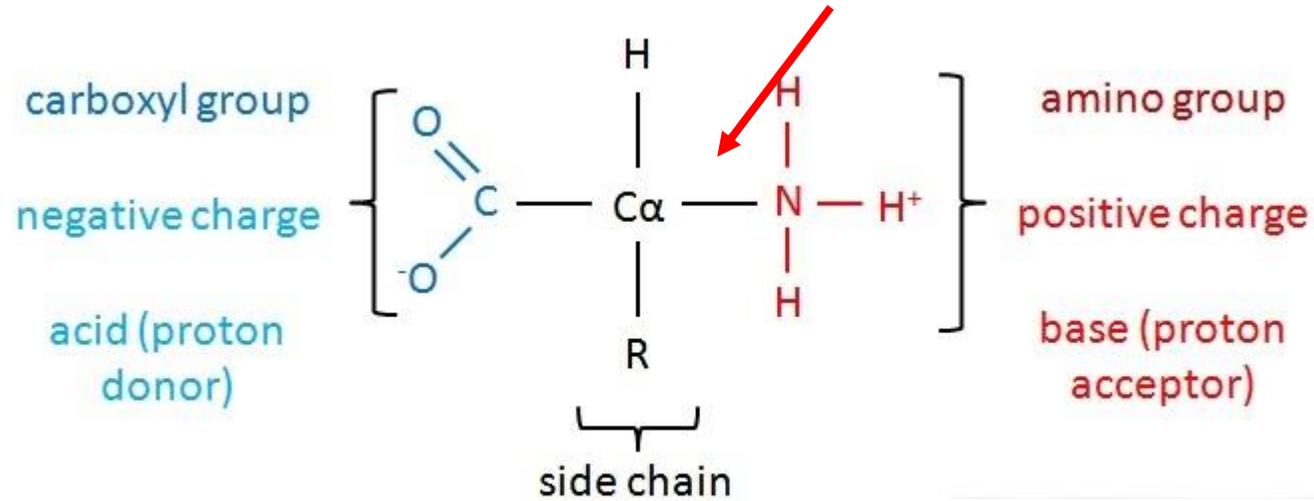
O nome dos aminoácidos foram dados pela fonte que eles foram encontrados pela primeira vez:

Asparagina = aspargos , in 1806

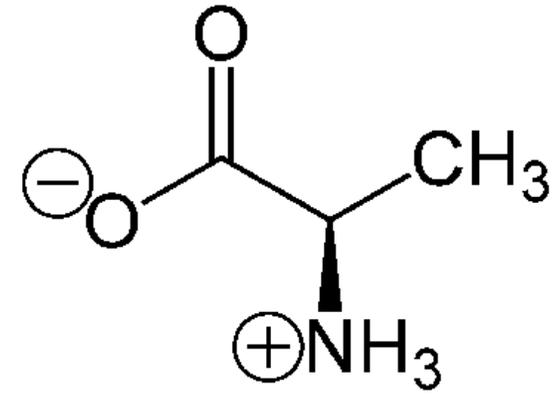
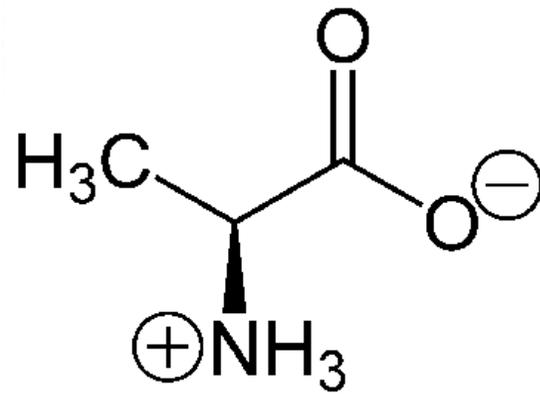
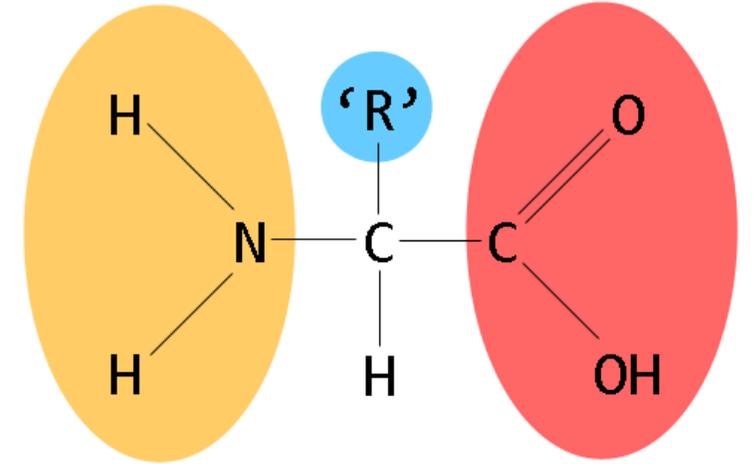
- Tirosina = queijo (do grego *tyros*)
- A treonina foi o último a ser identificado, 1938



# Os 20 aminoácidos mais comuns são $\alpha$ -aminoácidos

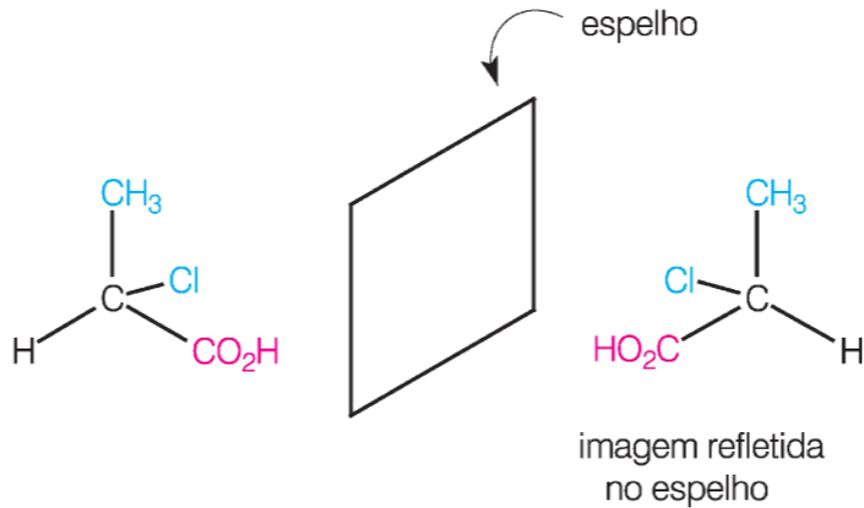


Amino Group      Acid Group

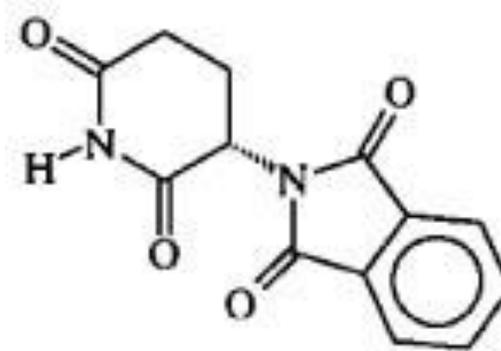
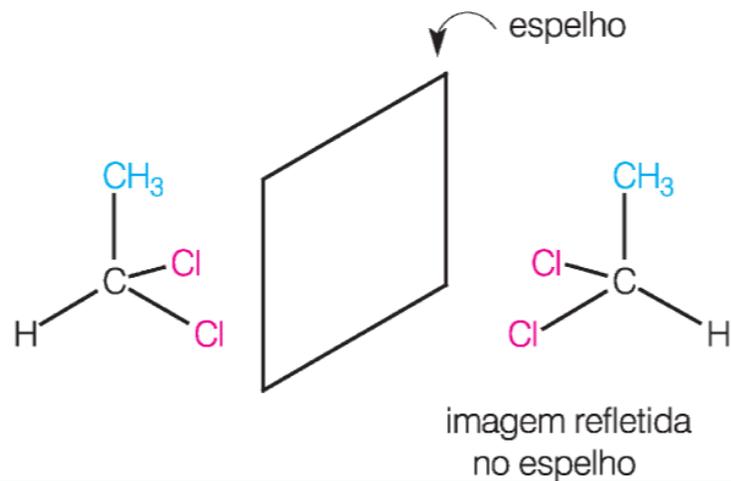


# Os Aminoácidos apresentam quiralidade

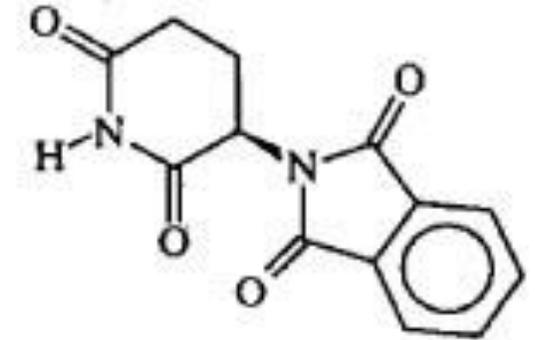
MOLÉCULA QUIRAL



MOLÉCULA AQUIRAL

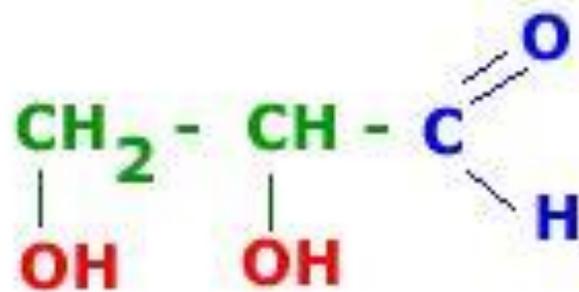


**(S)-Talidomida**  
Teratogênico

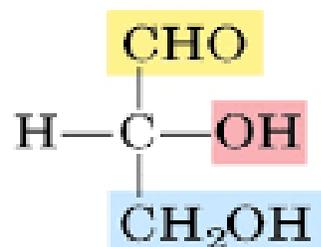


**(R)-Talidomida**  
Sedativo e hipnótico

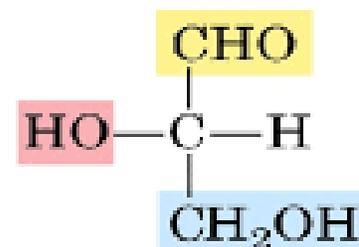
Onde está a quiralidade neste composto (gliceraldeído)?



aldeído glicérico

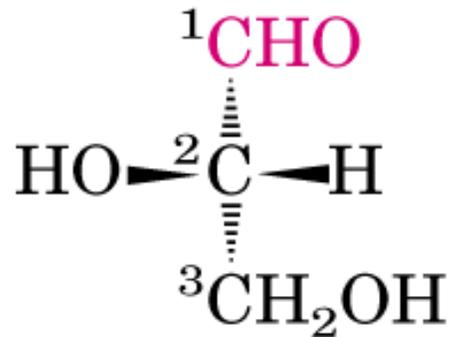


(*R*)-(+)-gliceraldeído  
D-gliceraldeído

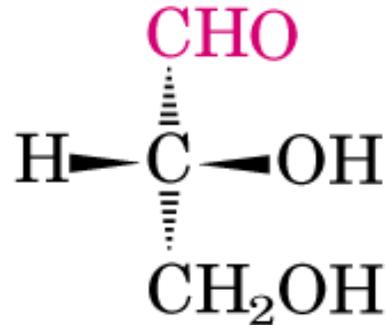


(*S*)-(-)-gliceraldeído  
L-gliceraldeído

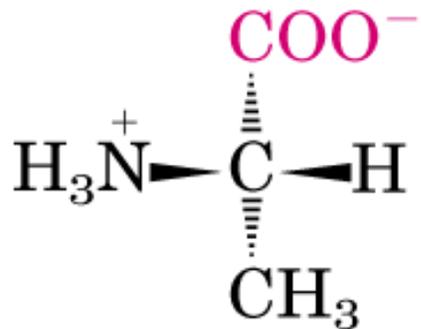
# Os Aminoácidos apresentam quiralidade



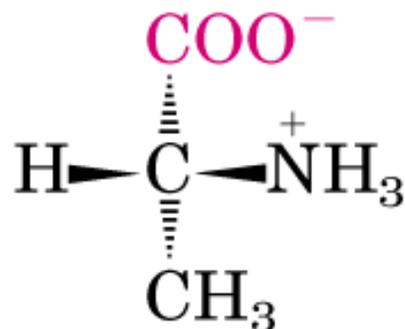
L-Glyceraldehyde



D-Glyceraldehyde

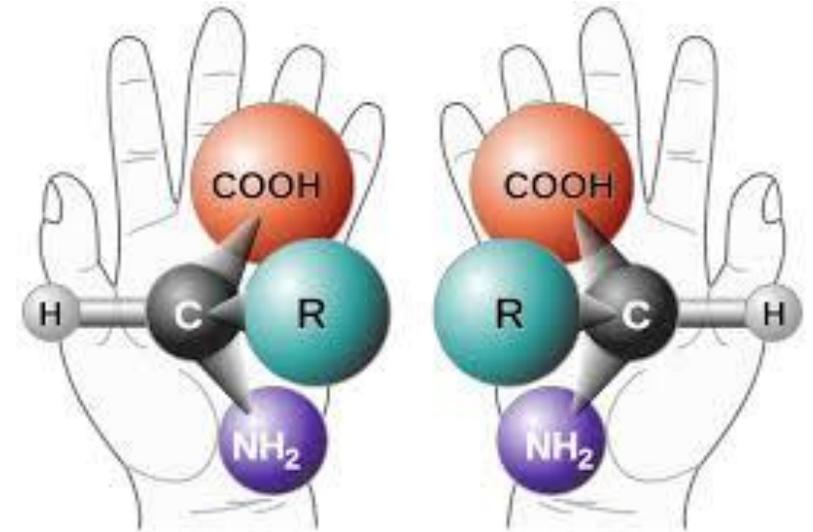


L-Alanine



D-Alanine

Proposto por Emil Fischer em 1891 e para todos os compostos quirais relacionados com o gliceraldeído tem a sua configuração



**L** e **D** refere-se **somente** a configuração absoluta dos carbonos quirais, e não as propriedades ópticas da molécula, que é diferente do sistema (*R* e *S*) usado na química orgânica

# Os aminoácidos proteínogênicos são estereoisômeros L

Código de 1 letra = Margaret O. Dayhoff, 1925-1983)

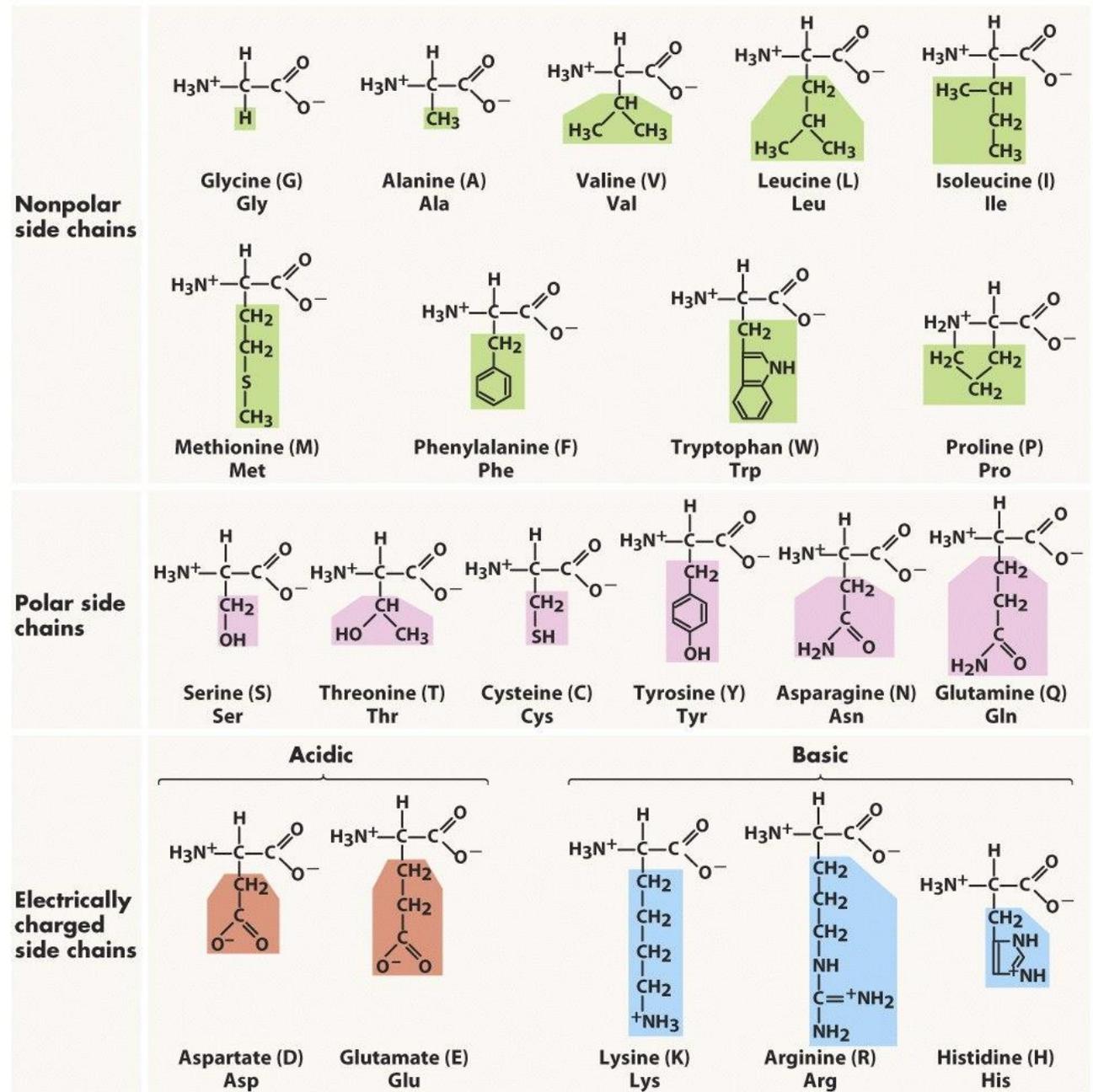


Figure 3-5 Biological Science, 2/e

Qual o impacto da quiralidade na função das enzimas?



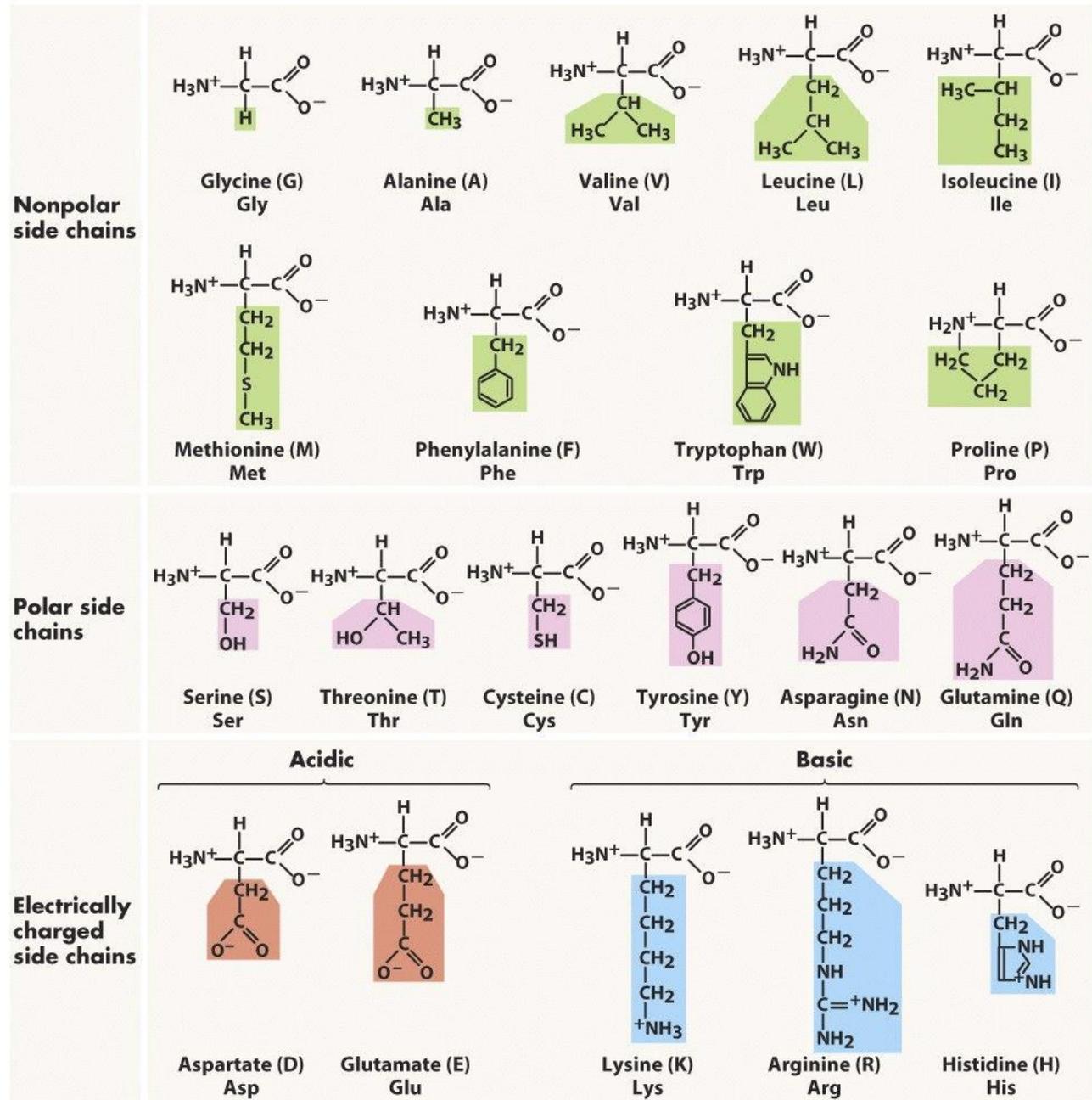
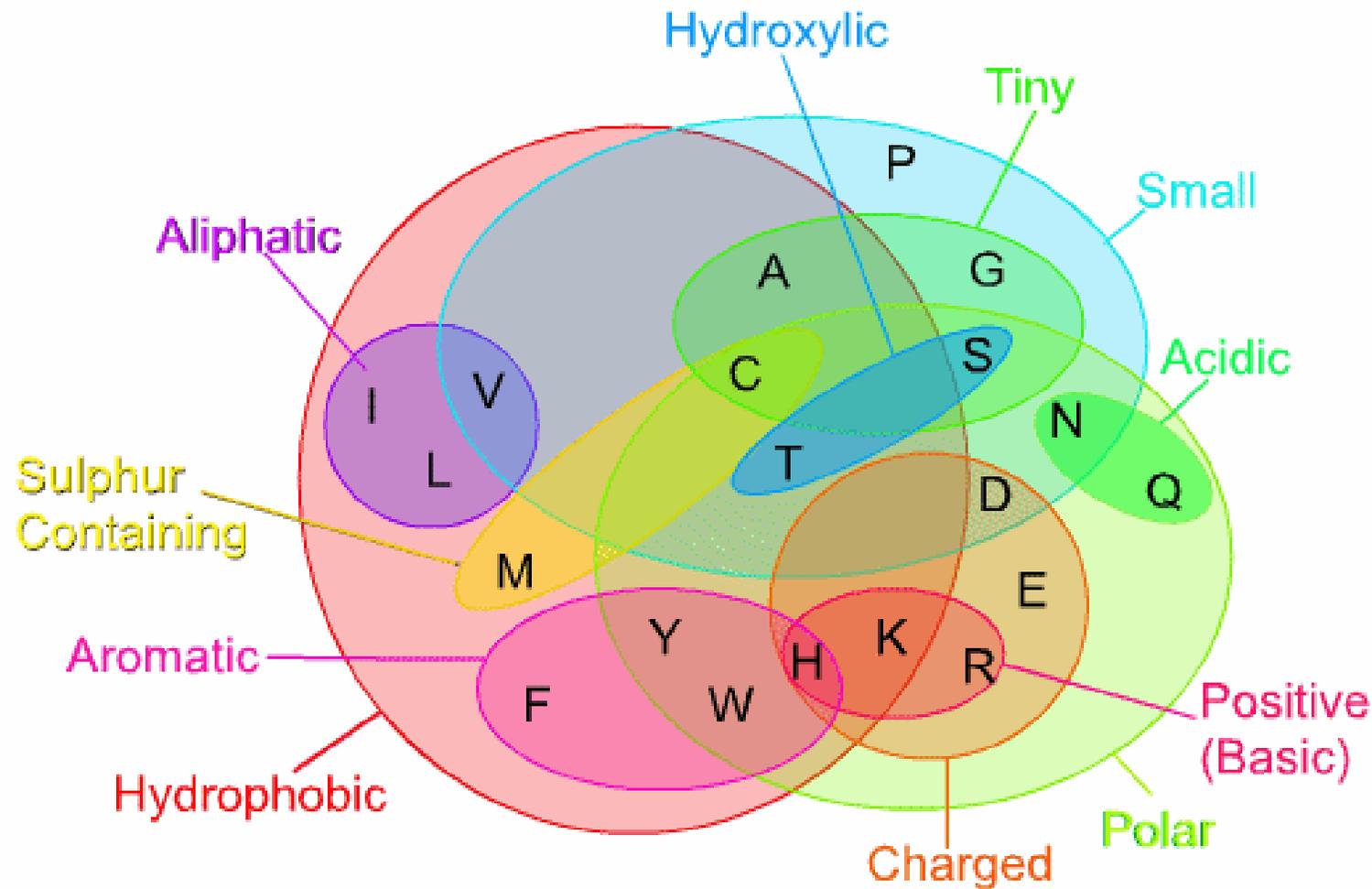
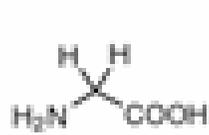


Figure 3-5 Biological Science, 2/e

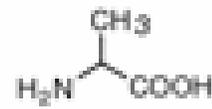


## Amino Acids

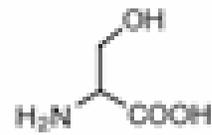
- A** alanine (ala)
- R** arginine (arg)
- N** asparagine (asn)
- D** aspartic acid (asp)
- C** cysteine (cys)
- Q** glutamine (gln)
- E** glutamic acid (glu)
- G** glycine (gly)
- H** histidine (his)
- I** isoleucine (ile)
- L** leucine (leu)
- K** lysine (lys)
- M** methionine (met)
- F** phenylalanine (phe)
- P** proline (pro)
- S** serine (ser)
- T** threonine (thr)
- W** tryptophan (trp)
- Y** tyrosine (tyr)



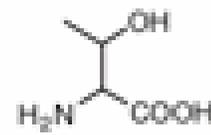
**Glycine**



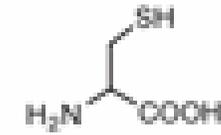
**Alanine**



**Serine**



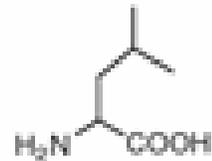
**Threonine**



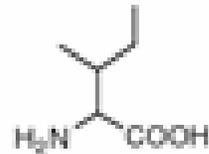
**Cysteine**



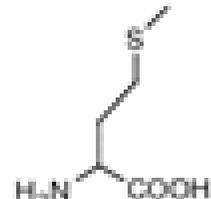
**Valine**



**Leucine**



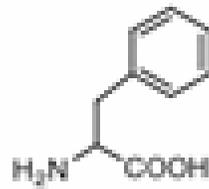
**Isoleucine**



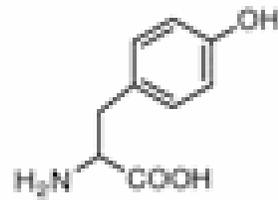
**Methionine**



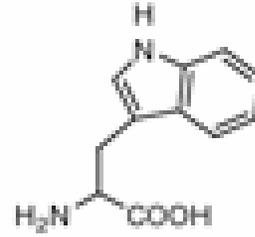
**Proline**



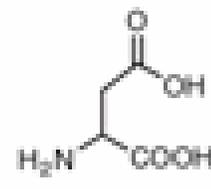
**Phenylalanine**



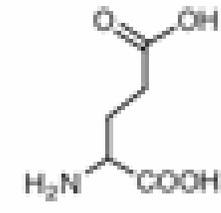
**Tyrosine**



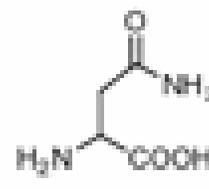
**Tryptophan**



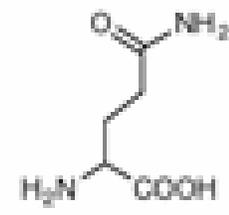
**Aspartic Acid**



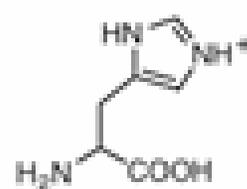
**Glutamic Acid**



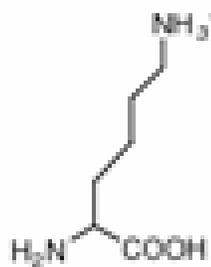
**Asparagine**



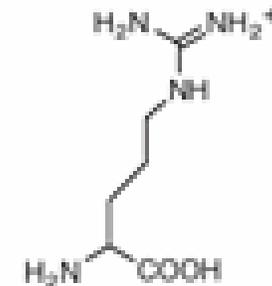
**Glutamine**



**Histidine**

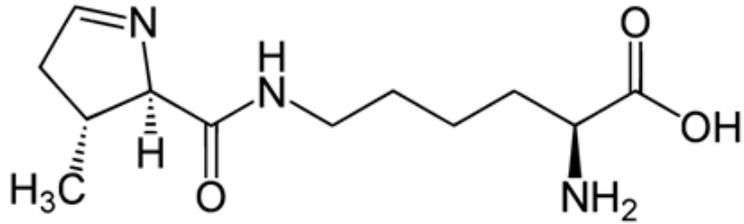


**Lysine**

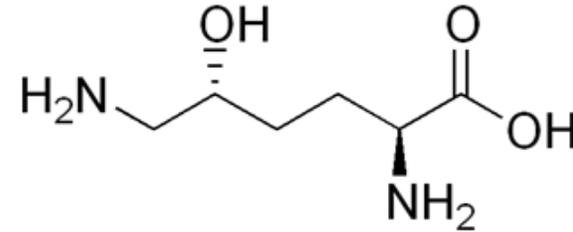


**Arginine**

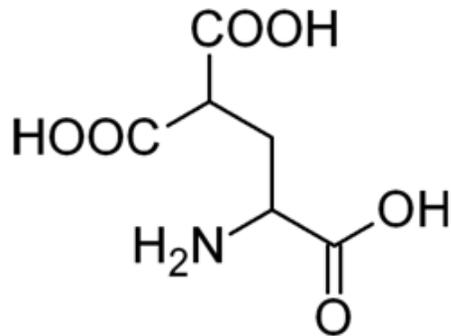
# Outros Aminoácidos incomuns



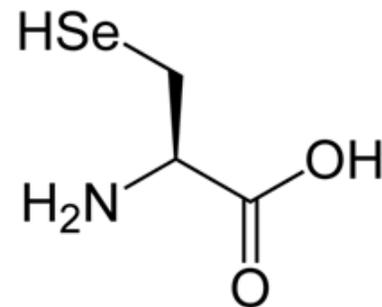
Pyrrolysine



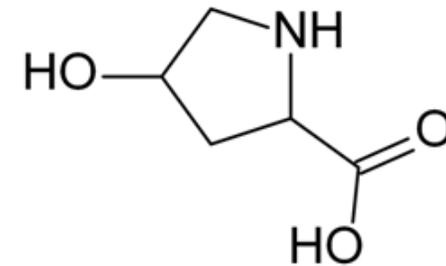
Hydroxylysine



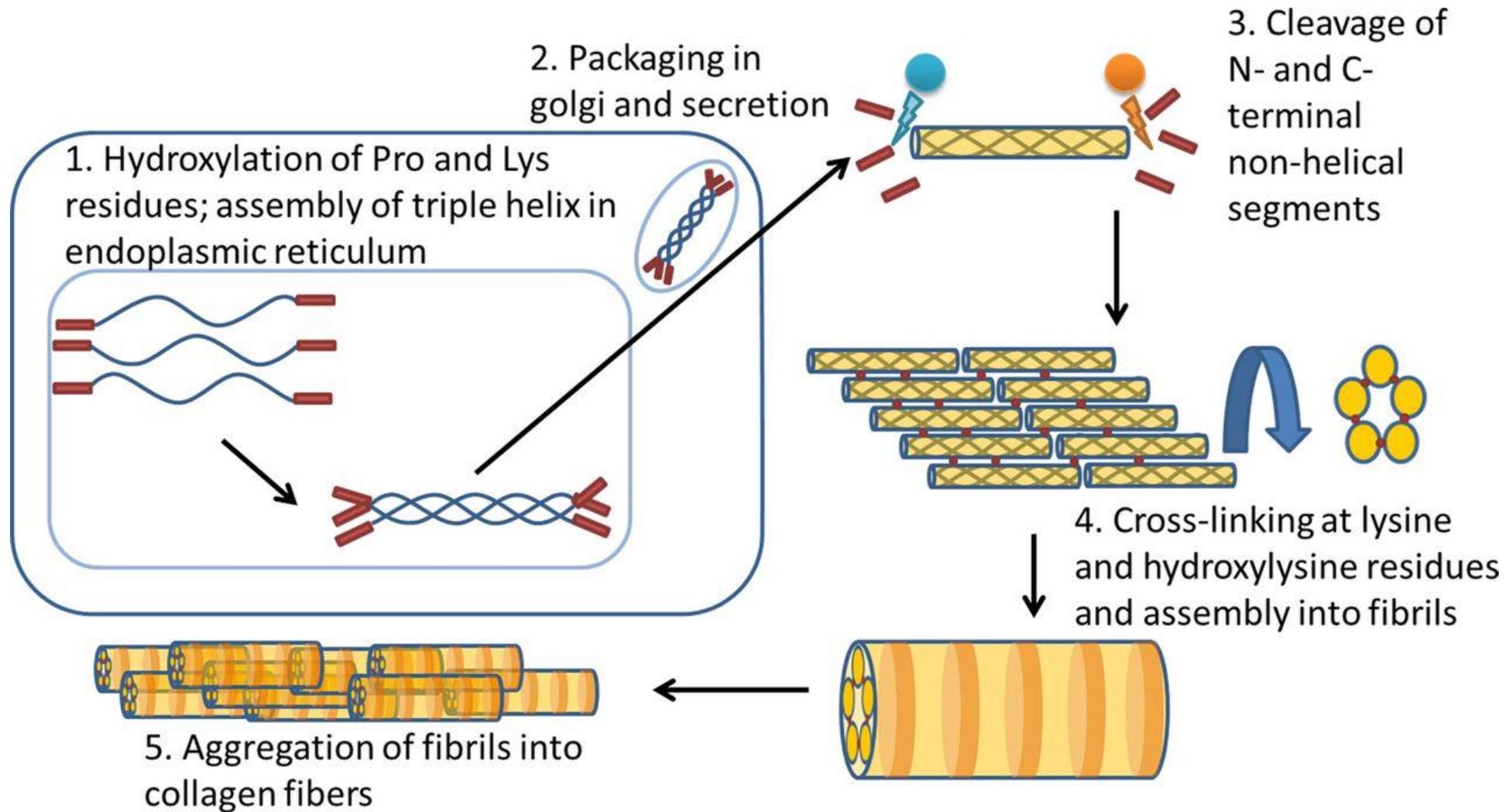
γ-carboxyglutamic acid



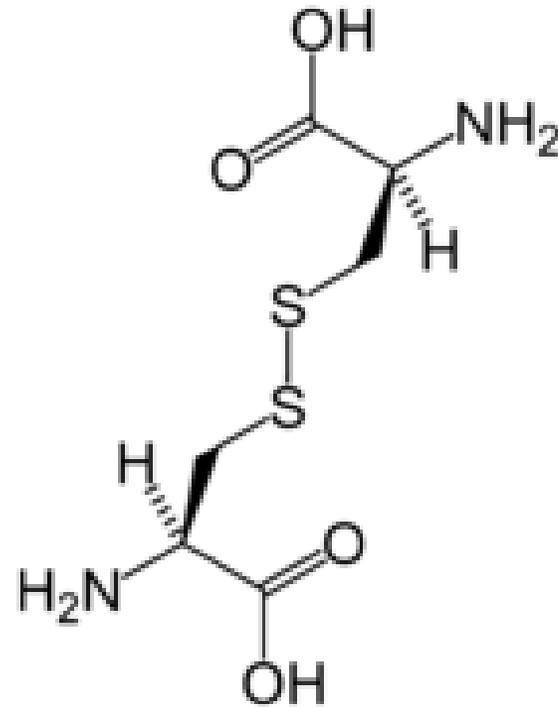
Selenocysteine



Hydroxyproline

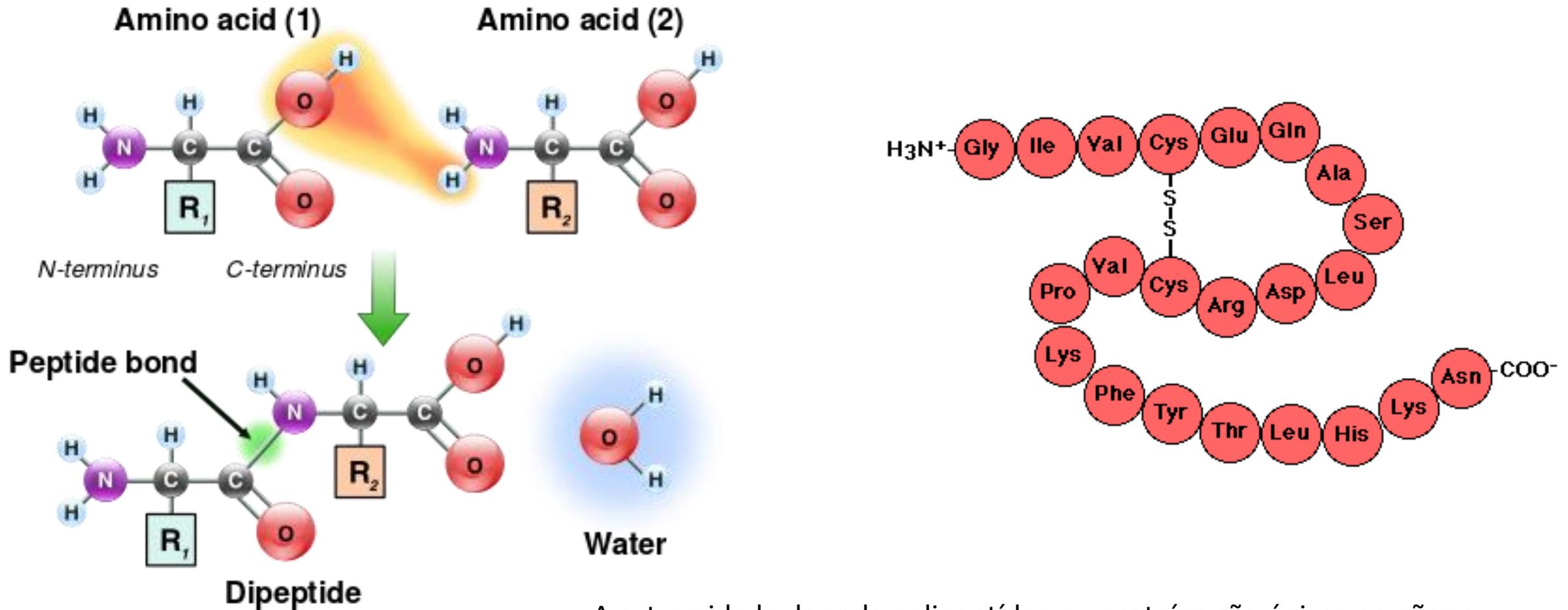


**As cisteínas são capazes de formar pontes disulfeto**





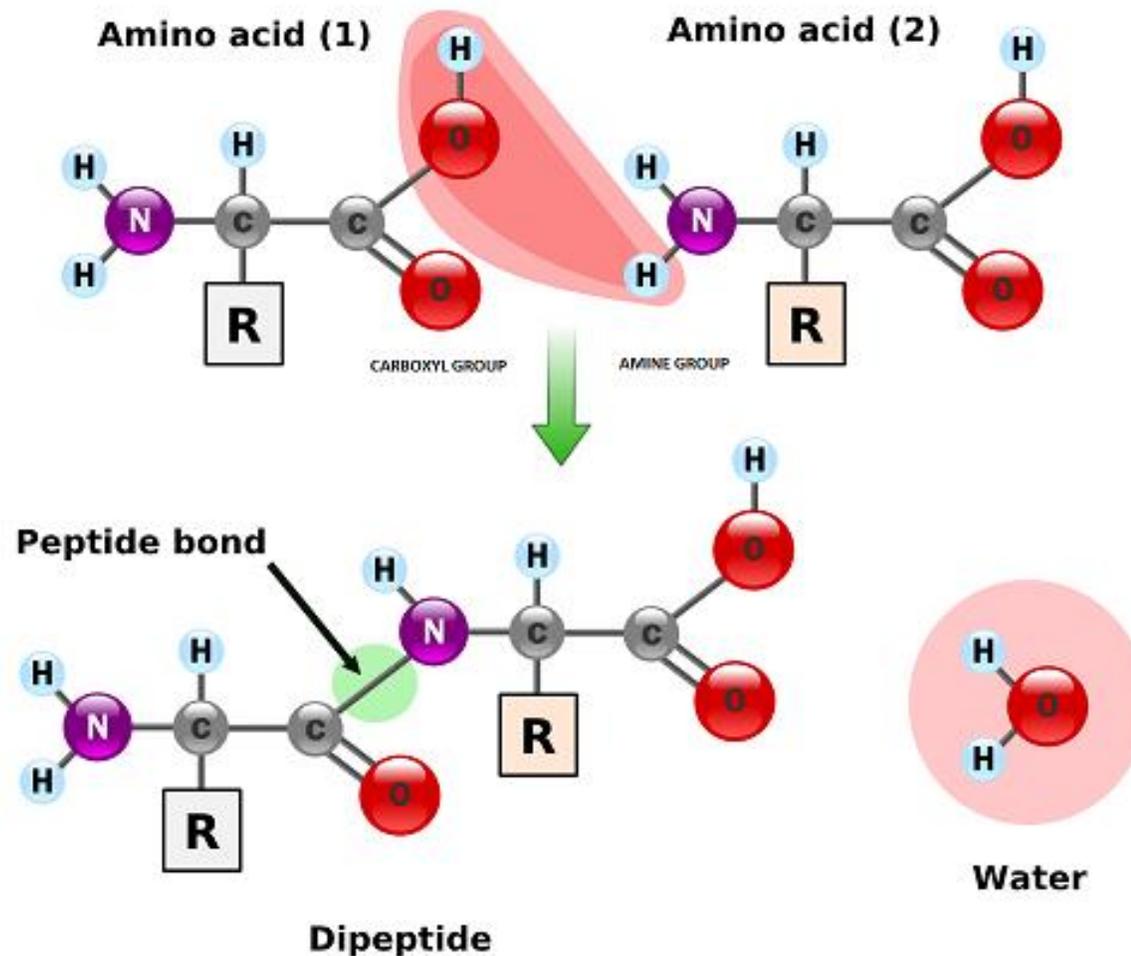
## As proteínas são formados por aminoácidos



A extremidade de cada polipeptídeo ou proteína são únicas porções  $\alpha$ -amino and  $\alpha$ -carboxi ionizável, embora os grupos também possam ser ionizáveis em alguns aminoácidos

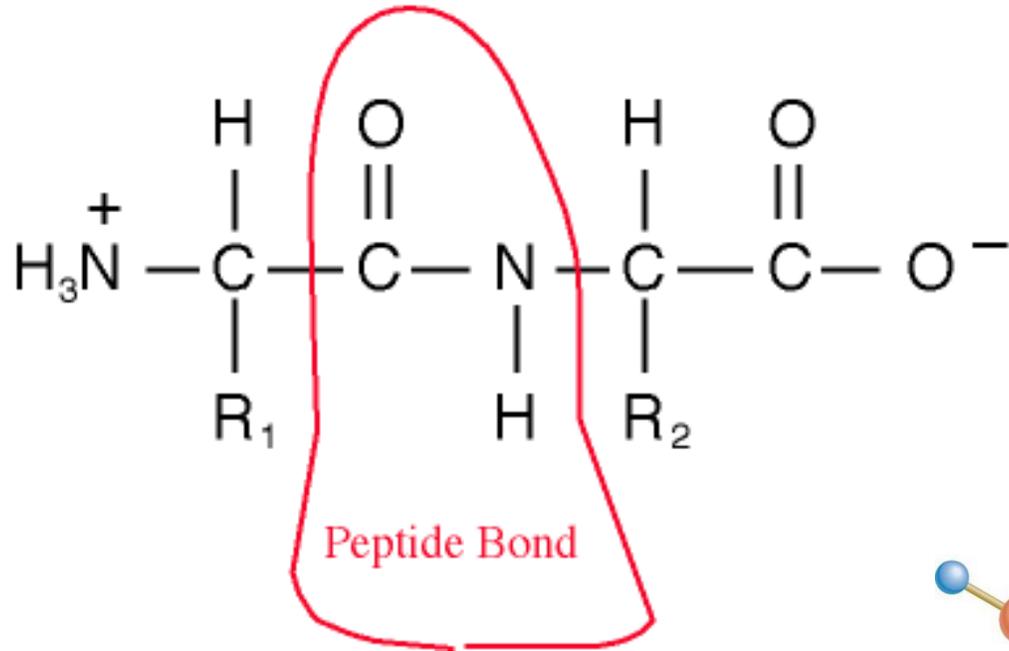
# Peptídeos e proteínas

Dois aminoácidos são covalentemente juntados por uma reação de **condensação** realizado pelo ribossomo. Essa ligação é chamada de ligação peptídica

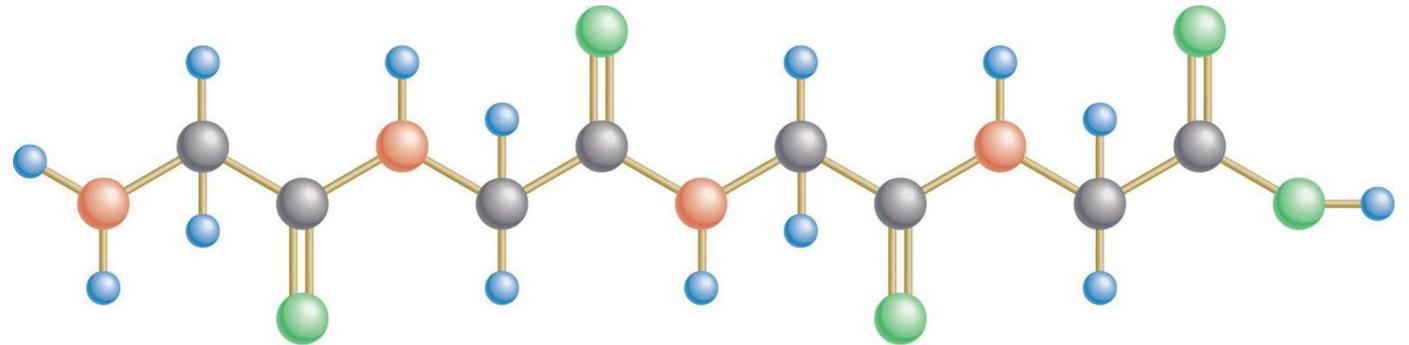


# A ligação peptídica

Amino End  Carboxyl End



A ligação peptídica é altamente estável



peptide (tetraglycine)

 carbon

 oxygen

 nitrogen

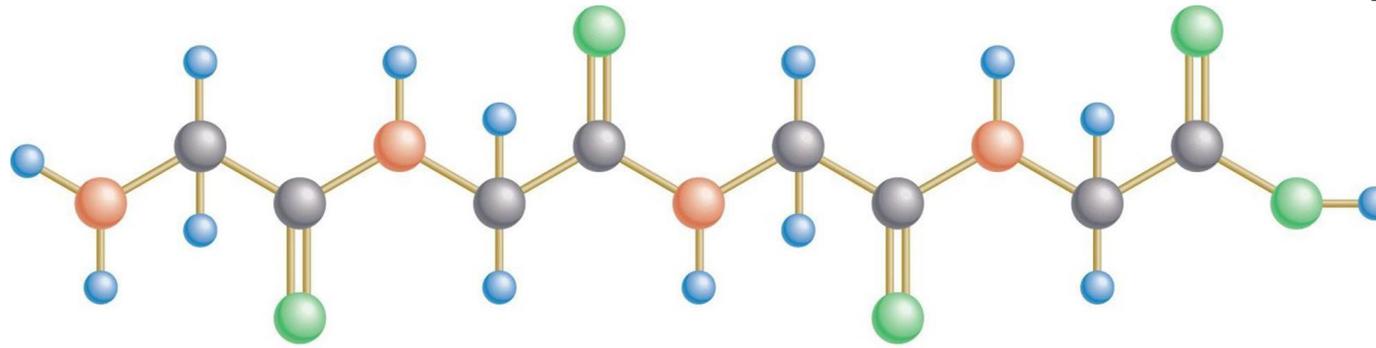
 hydrogen

**Oligopeptídeos = poucos aminoácidos**

**Polipeptídeos = muitos aminoácidos**

**Polipeptídeos = peso molecular < 10,000 Da**

**Proteínas = peso molecular > 10,000 Da**



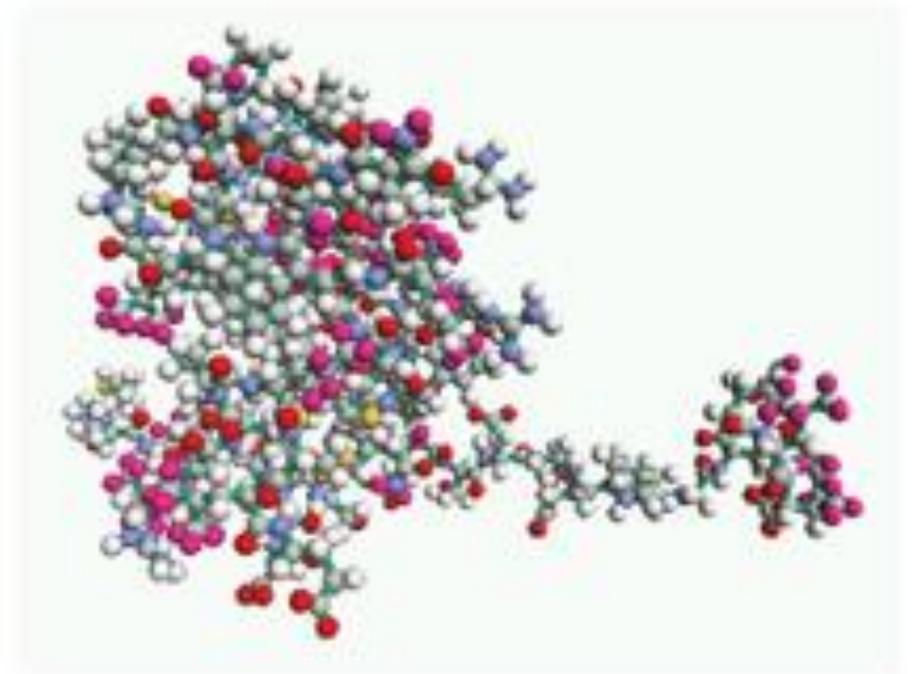
peptide (tetraglycine)

● carbon

● oxygen

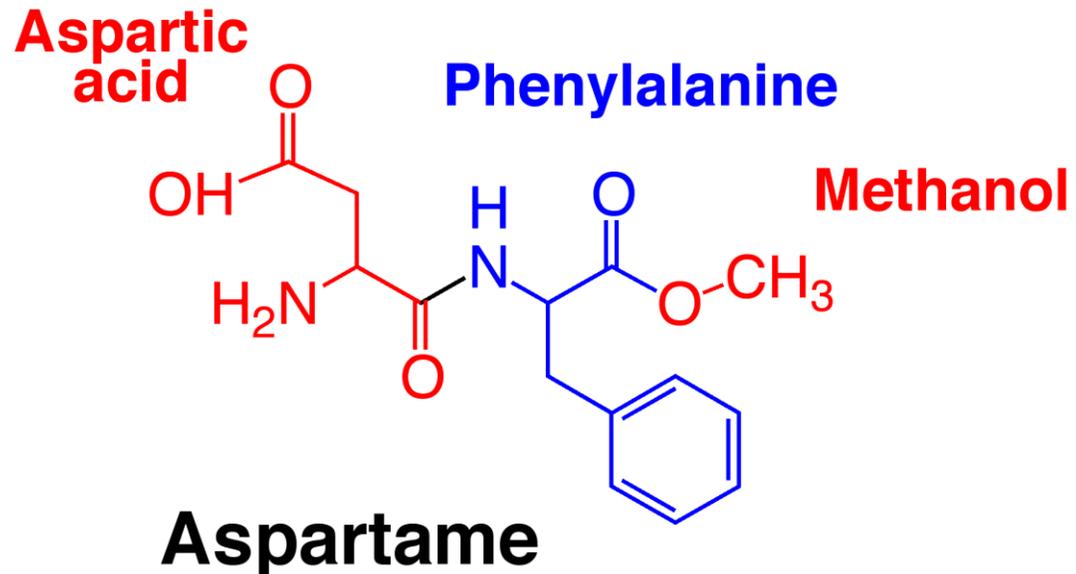
● nitrogen

● hydrogen



# Peptídeos biologicamente ativos

Não há generalizações para o tamanho e o peso molecular de peptídeos ativos e proteínas



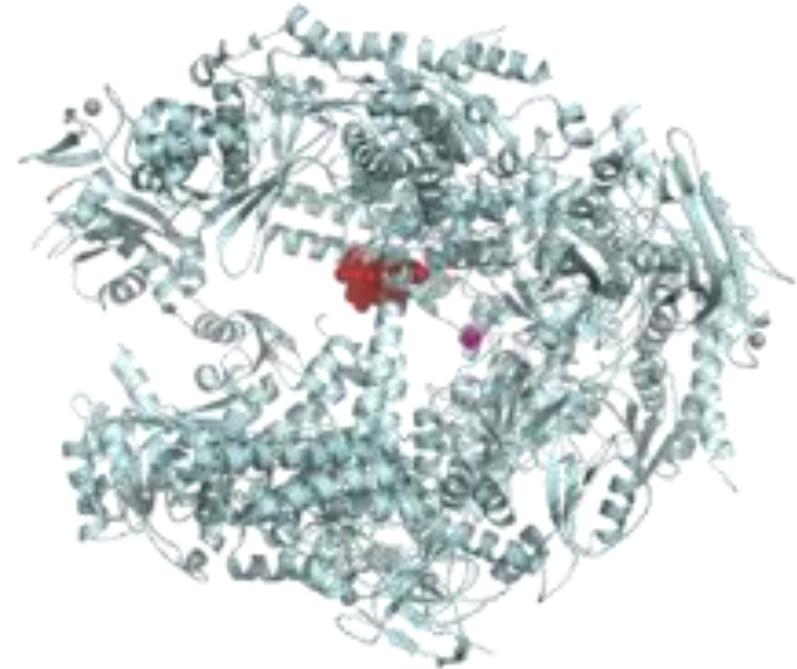
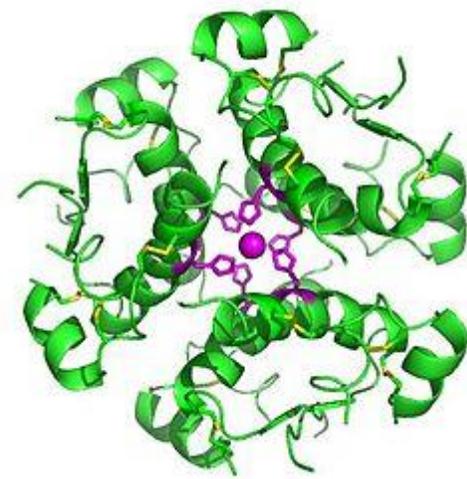






**Table 6-1 Molecular data on some proteins**

	Molecular weight	Number of residues	Number of polypeptide chains
Insulin (bovine)	5,733	51	2
Cytochrome <i>c</i> (human)	13,000	104	1
Ribonuclease A (bovine pancreas)	13,700	124	1
Lysozyme (egg white)	13,930	129	1
Myoglobin (equine heart)	16,890	153	1
Chymotrypsin (bovine pancreas)	21,600	241	3
Chymotrypsinogen (bovine)	22,000	245	1
Hemoglobin (human)	64,500	574	4
Serum albumin (human)	68,500	~550	1
Hexokinase (yeast)	102,000	~800	2
Immunoglobulin G (human)	145,000	~1,320	4
RNA polymerase ( <i>E. coli</i> )	450,000	~4,100	5
Apolipoprotein B (human)	513,000	4,536	1
Glutamate dehydrogenase (bovine liver)	1,000,000	~8,300	~40



## Questões?

- Por que boa parte das proteínas são solúveis em água?
- Qual o papel da água na manutenção da forma de uma proteína?
- Por que as proteínas de membrana não são solúveis em água?
- Qual a importância das interações de hidrogênio e interações hidrofóbicas na estrutura e funcionamento do DNA?
- Qual a relação que existe em uma sequência de nucleotídeos com a sequência de aminoácidos e conseqüentemente com a função de uma proteína? Ou seja quem dita a função de uma proteína?