Interações Intermoleculares – papel da água

Aminoácidos, peptídeos e proteínas

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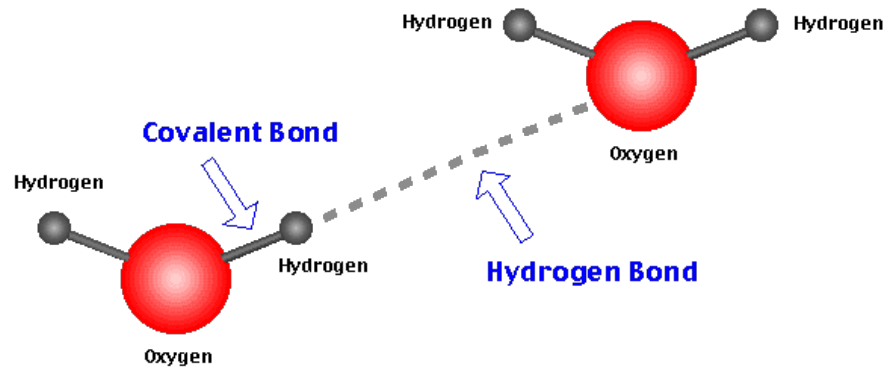
Por que estudar a água????

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

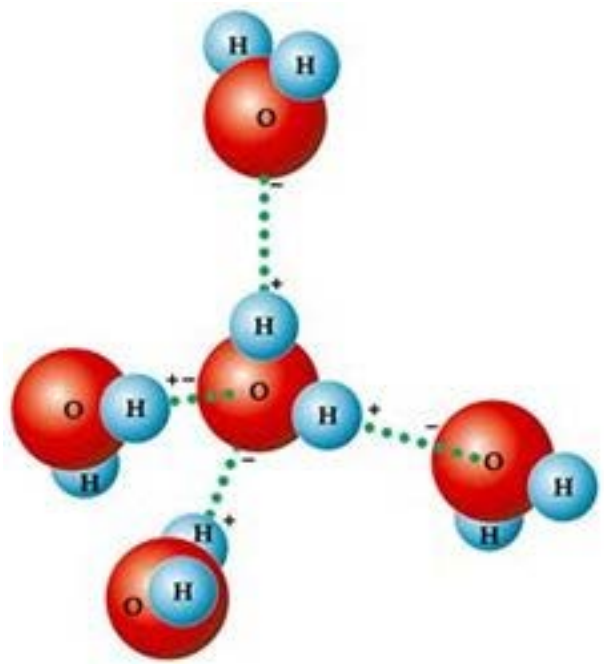
Ligação de hidrogênio



- responsável pela força coesiva que faz a água ser líquida em temperatura ambiente

- Responsável pela água apresentar altamente ordenada em cristais

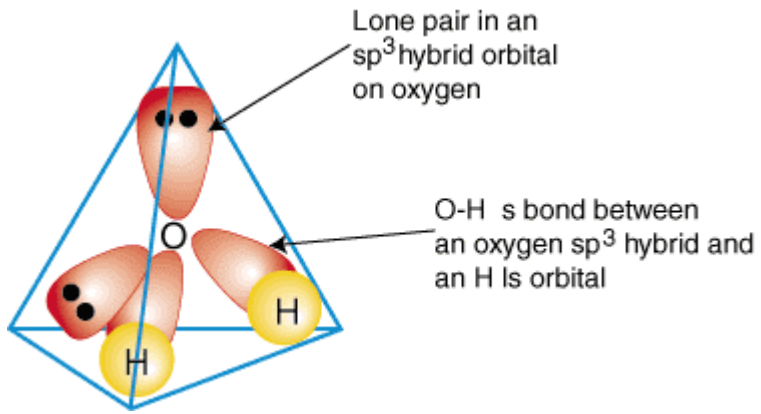
- Biomoléculas polares são prontamente dissolvidas em água pelas energeticamente favoráveis interações entre moléculas de água e soluto

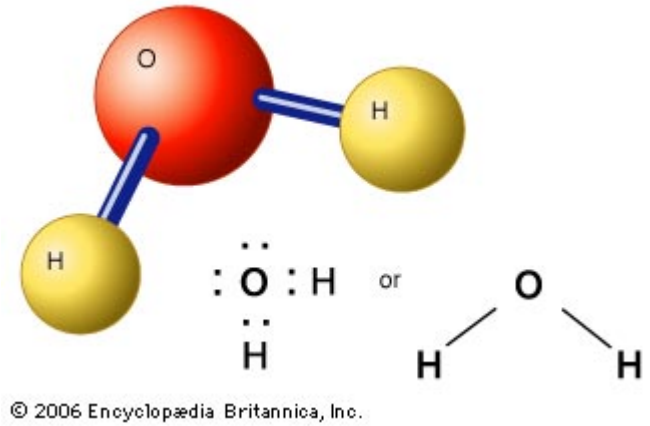


Geometria da molécula de água

- 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.





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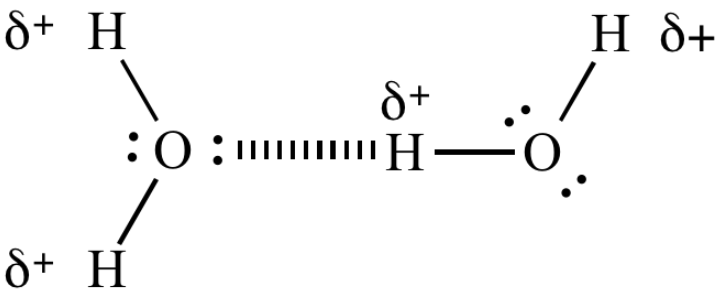

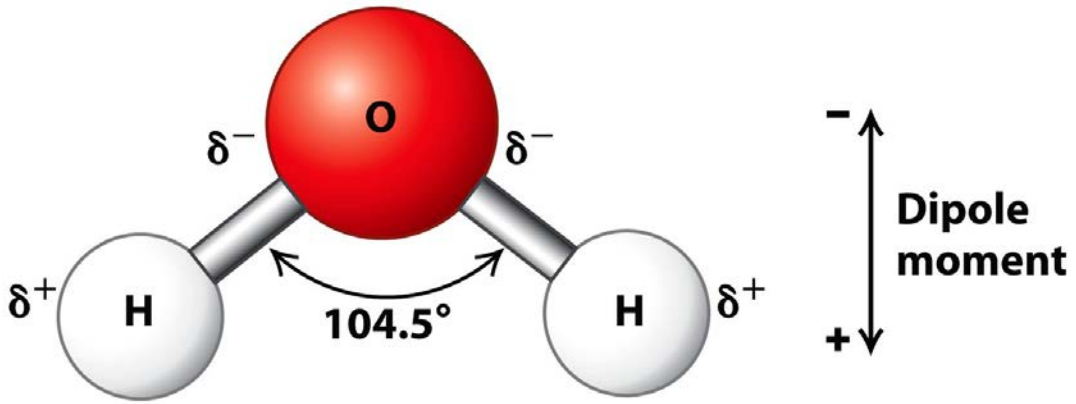

Figure 2-5
Molecular Cell Biology, Sixth Edition
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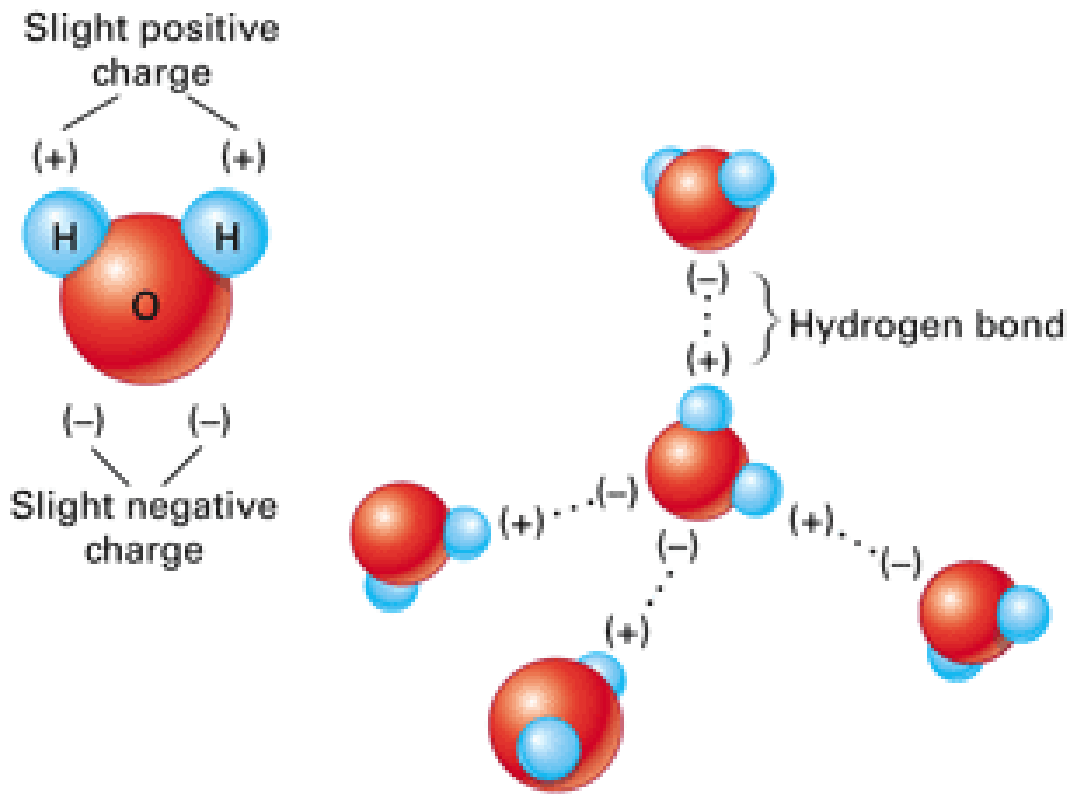
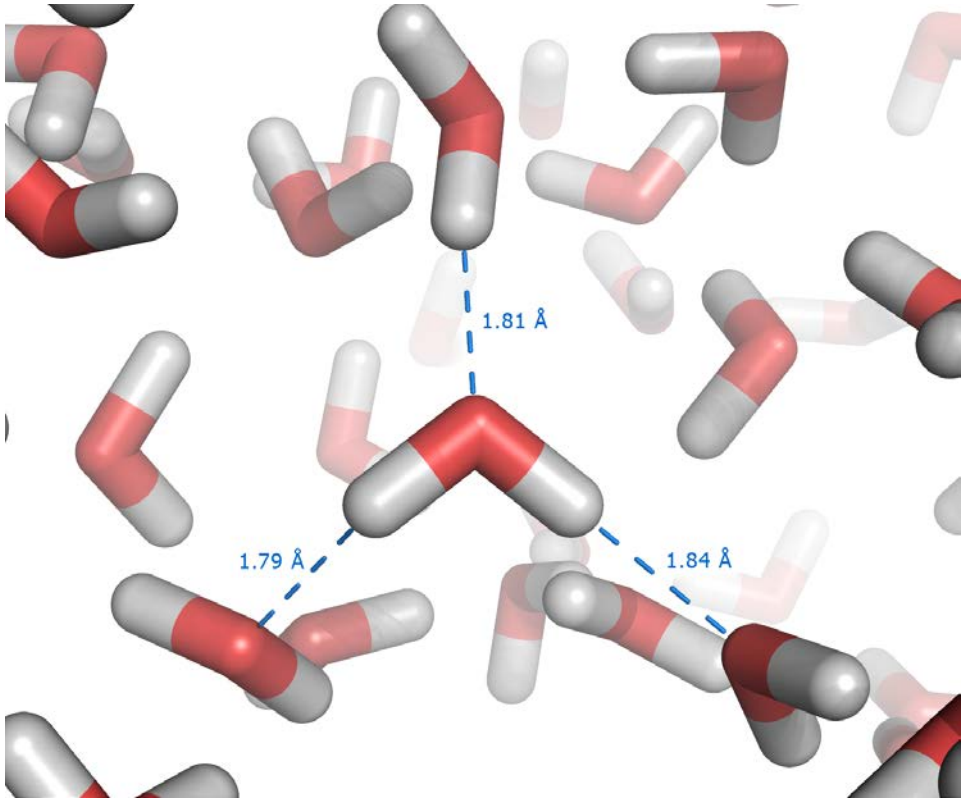
Ligação de hidrogênio: resultado da formação de dipolos da molécula de água

- 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.

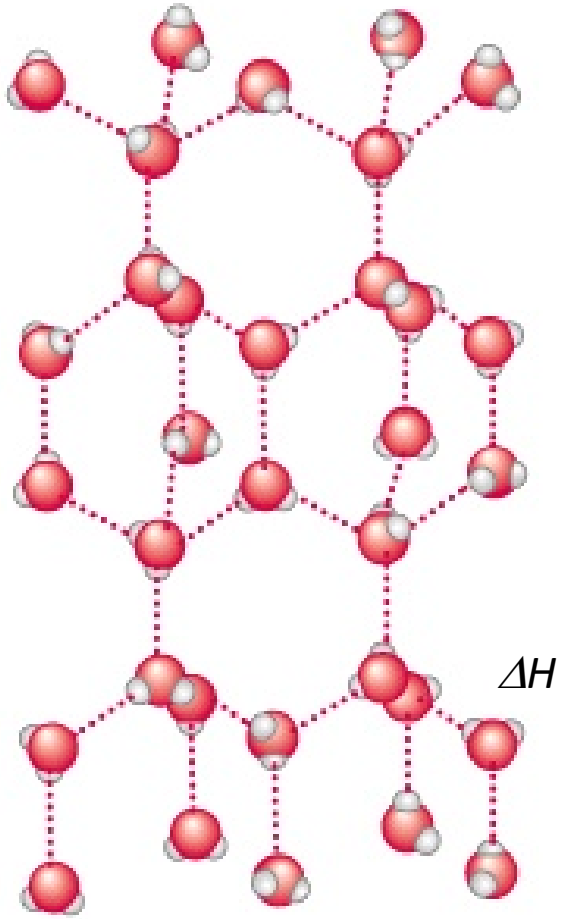


Dinâmica das moléculas de água em solução = tempo da ligação de hidrogênio = 1-20 picosegundos e outra ligação é formada em 0.1 ps



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

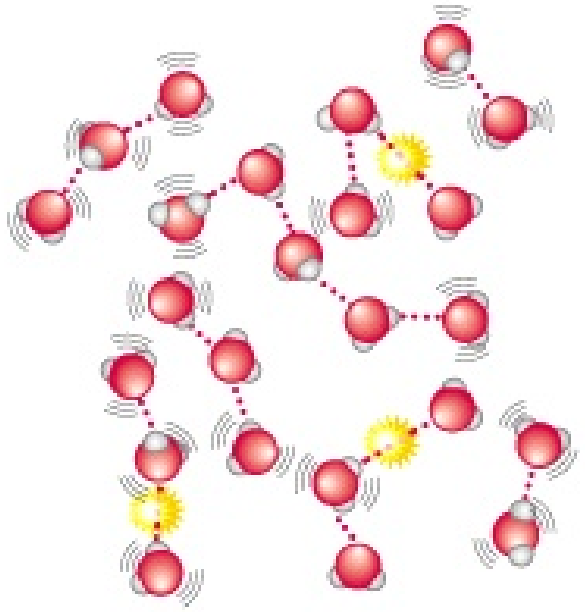
(*a*) **Solid water (ice)**



4 ligações

ΔH = +5.9 KJ/mol

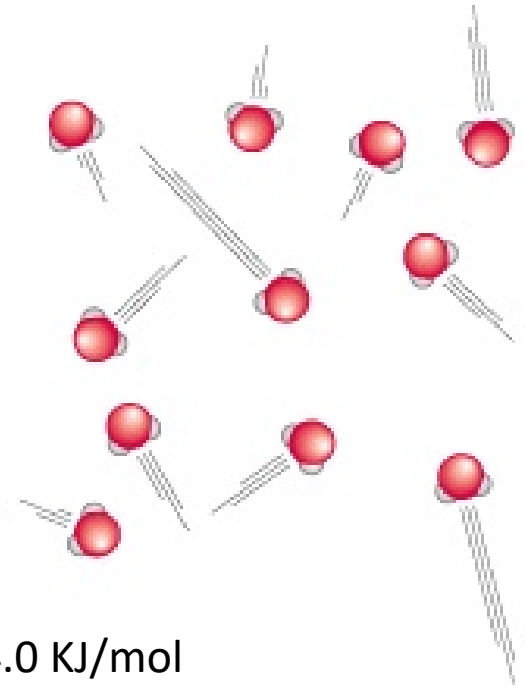
(*b*) **Liquid water**



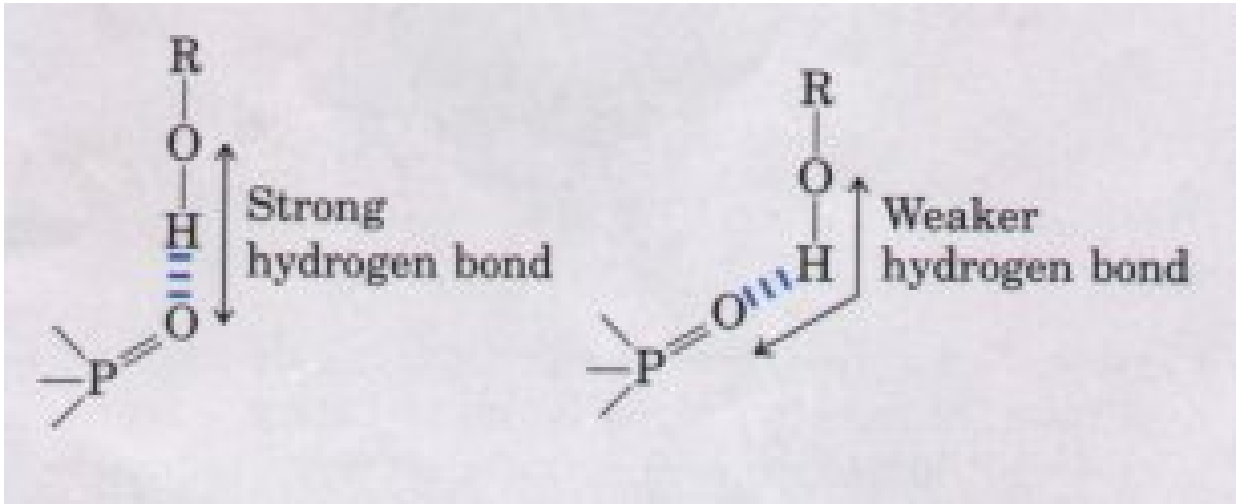
3.4 ligações

ΔH = +44.0 KJ/mol

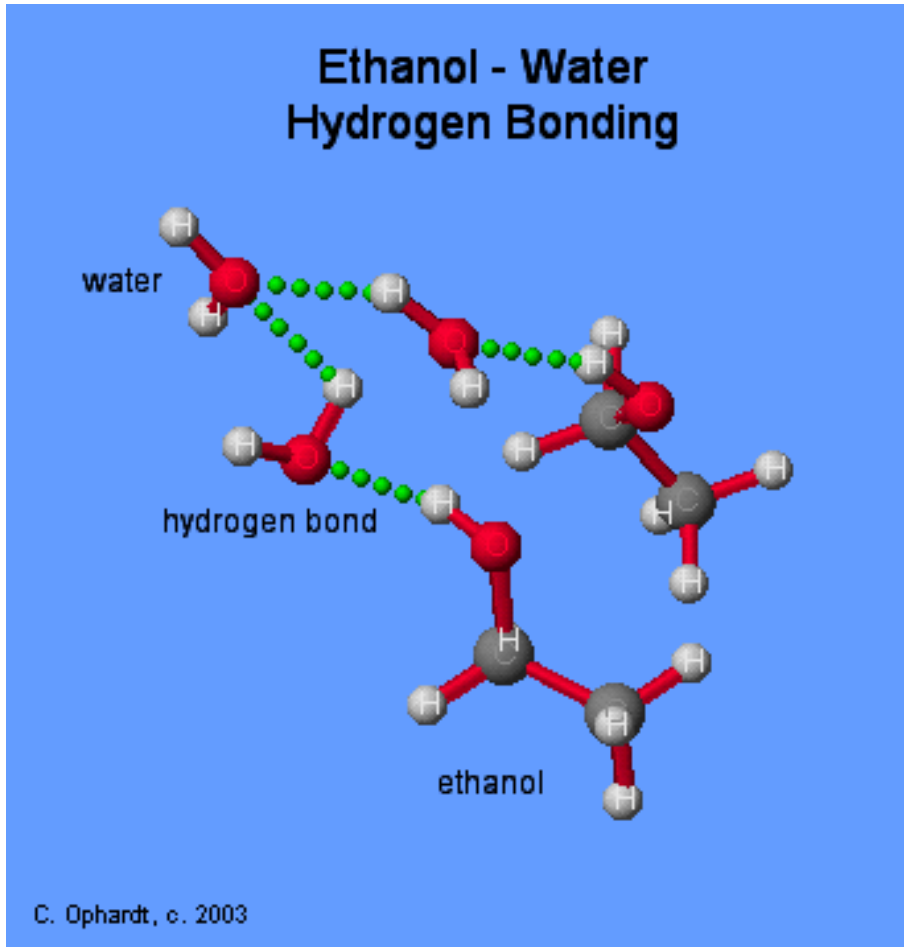
(*c*) **Gaseous water (steam)**

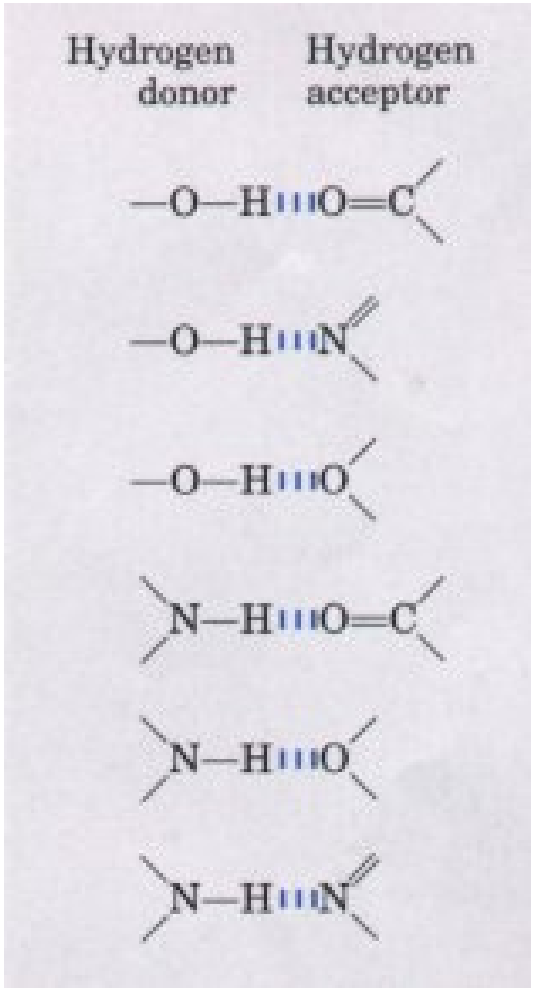


Interações em linha reta maximizam a interação eletrostática



Água pode formar ligações de hidrogênio com solutos polares





C-H não forma ligação de hidrogênio

Ponto de ebulição butanol = 117ºC

Ponto de ebulição butano = 0,5ºC

Substâncias não carregadas como açucares, 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

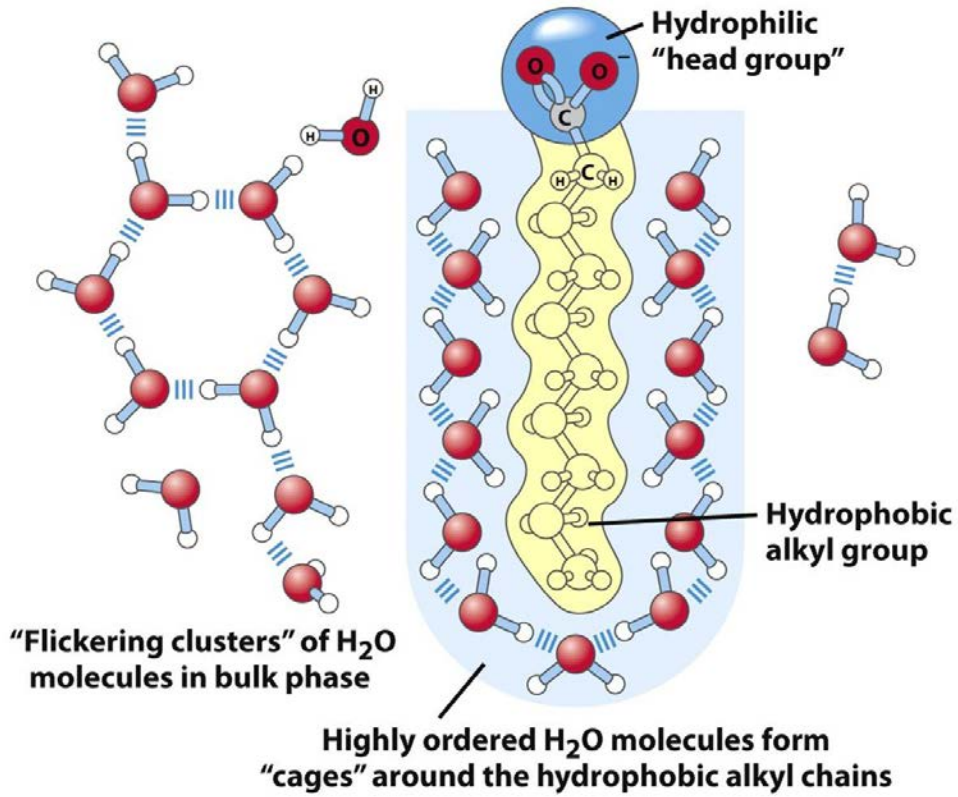
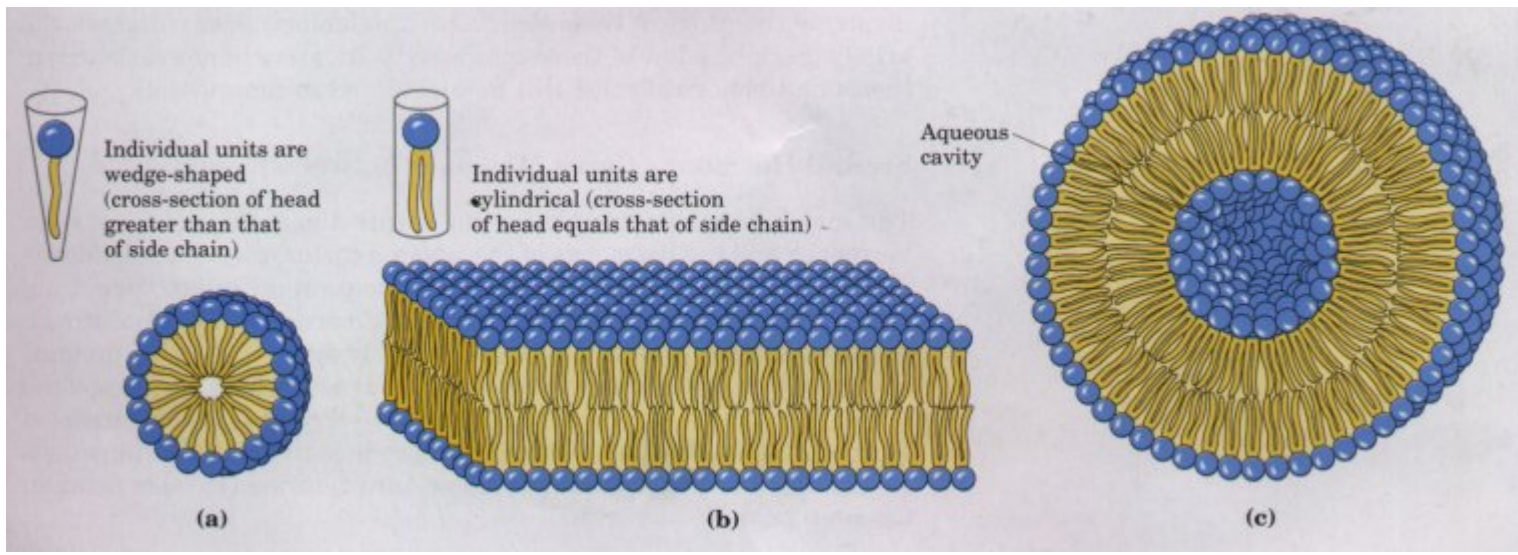


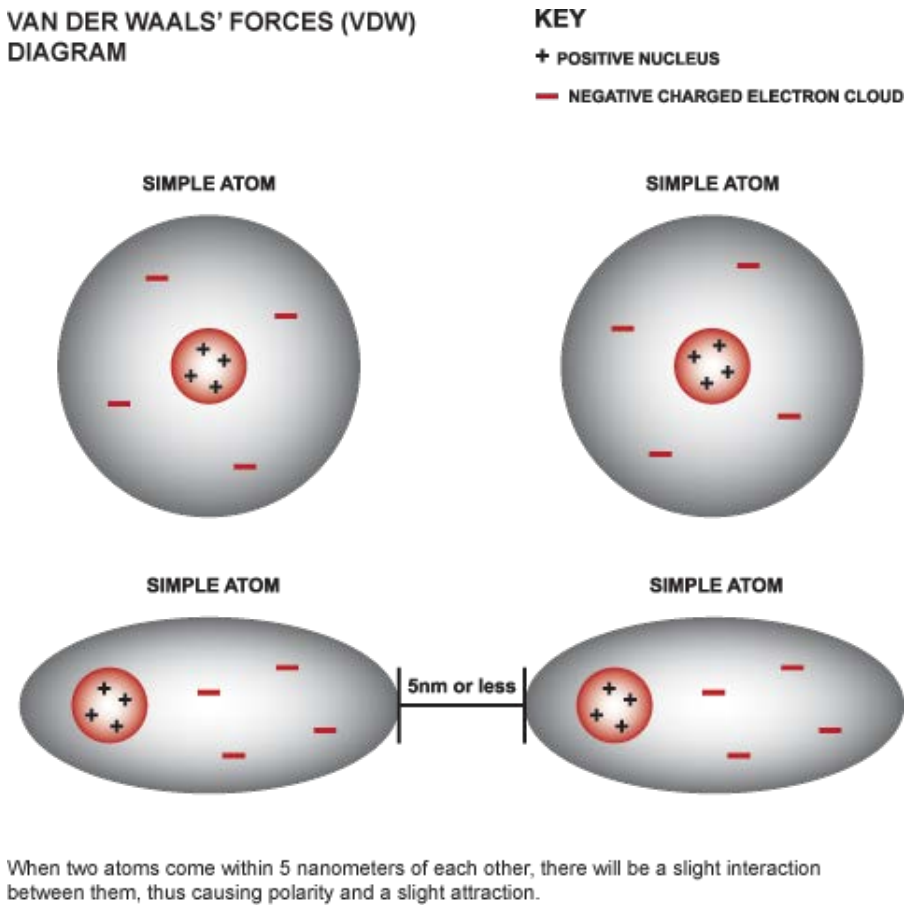
Figure 2-7a
Lehninger Principles of Biochemistry, Fifth Edition

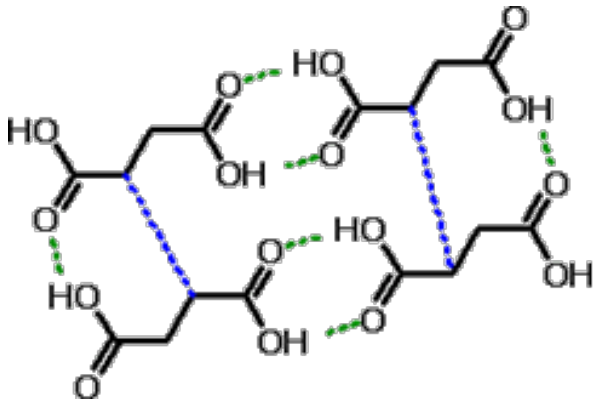
Proteínas, pigmentos, vitaminas, hormônios esteroidais

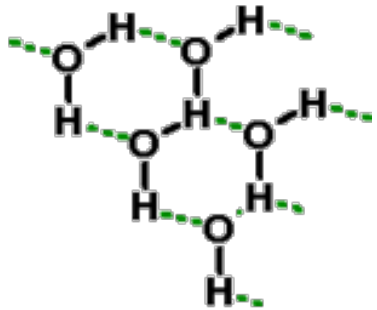
Formação de interações hidrofóbicas

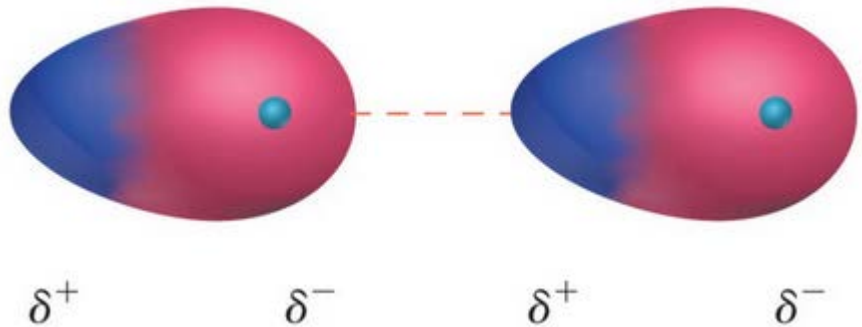


Interações de van der Waals ou forças de London





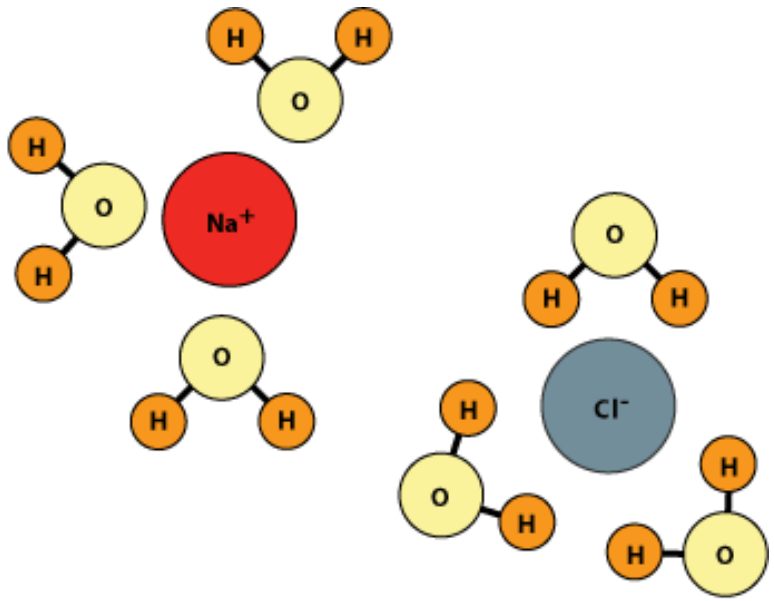




Interações iônicas

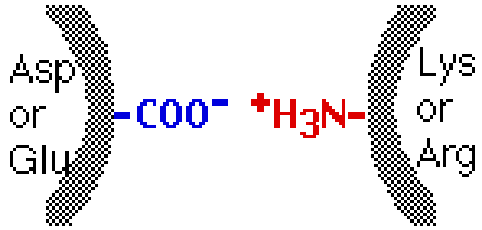
Interação que ocorre entre dois compostos que apresentam cargas opostas e portanto ocorre em íons.

Sodium Chloride (NaCl) in air

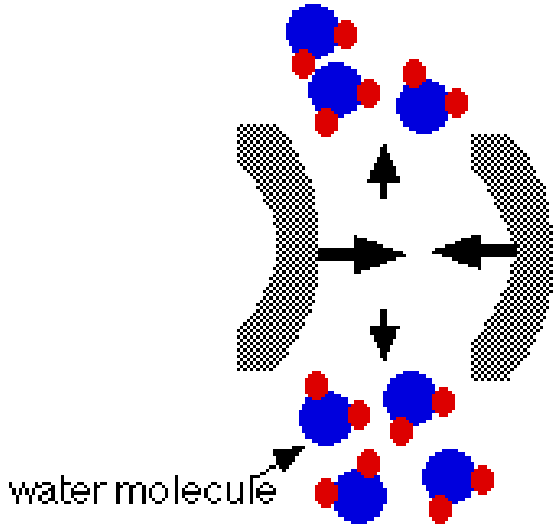


Sodium Chloride (NaCl) in water (H_2O)

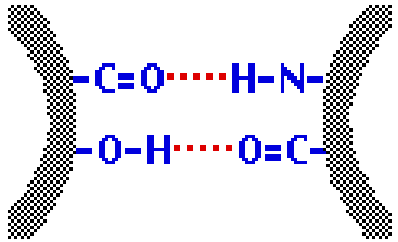
Hidratação



Ionic Interactions



Hydrophobic Interactions



Hydrogen Bonds

Efeito de moléculas de água na estrutura e função de proteínas

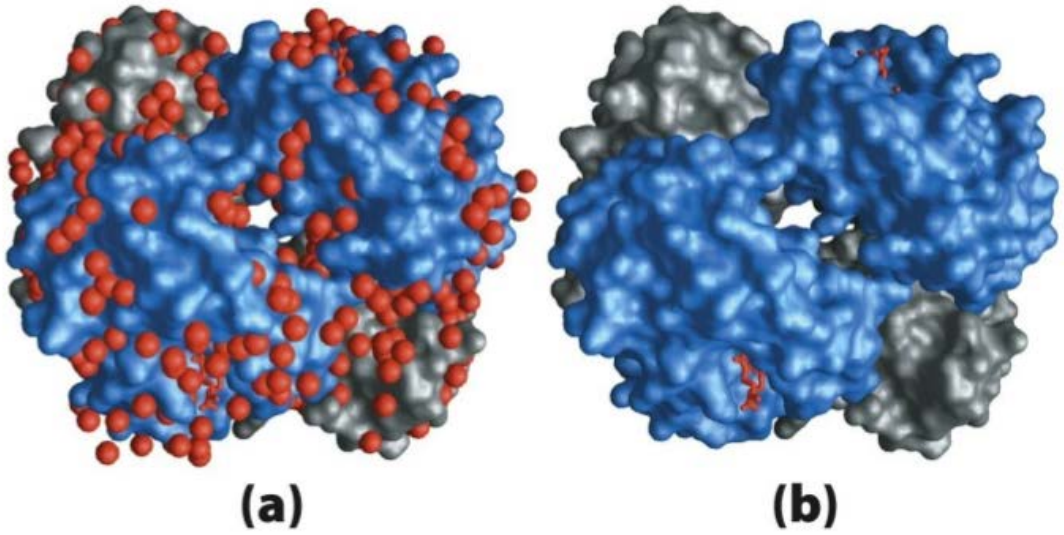


Figure 2-9
Lehninger Principles of Biochemistry, Fifth Edition

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 α subunits of hemoglobin are shown in gray, the two β subunits in blue. Each subunit has a bound heme group (red stick structure), visible only in the β subunits in this view.

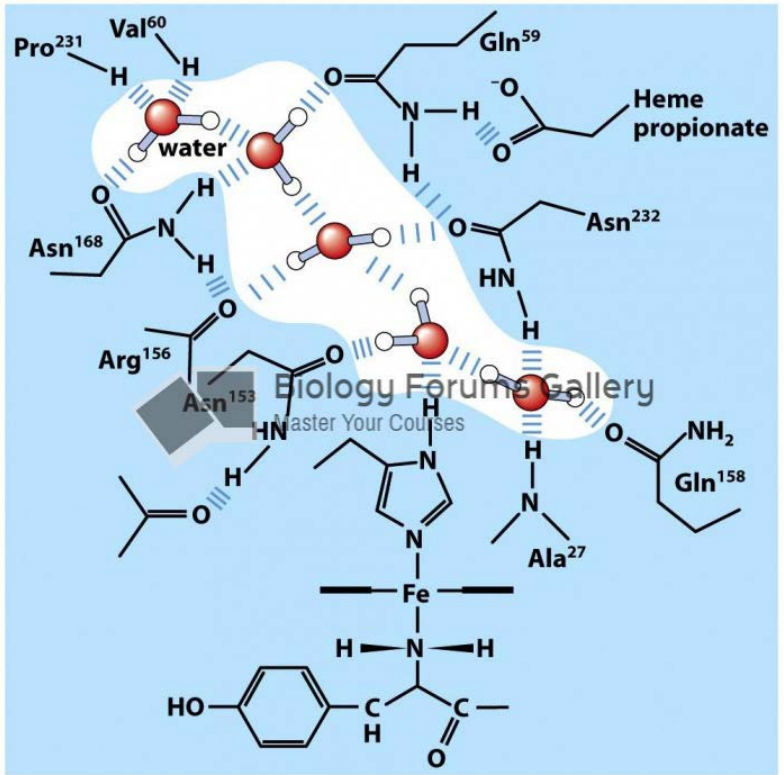
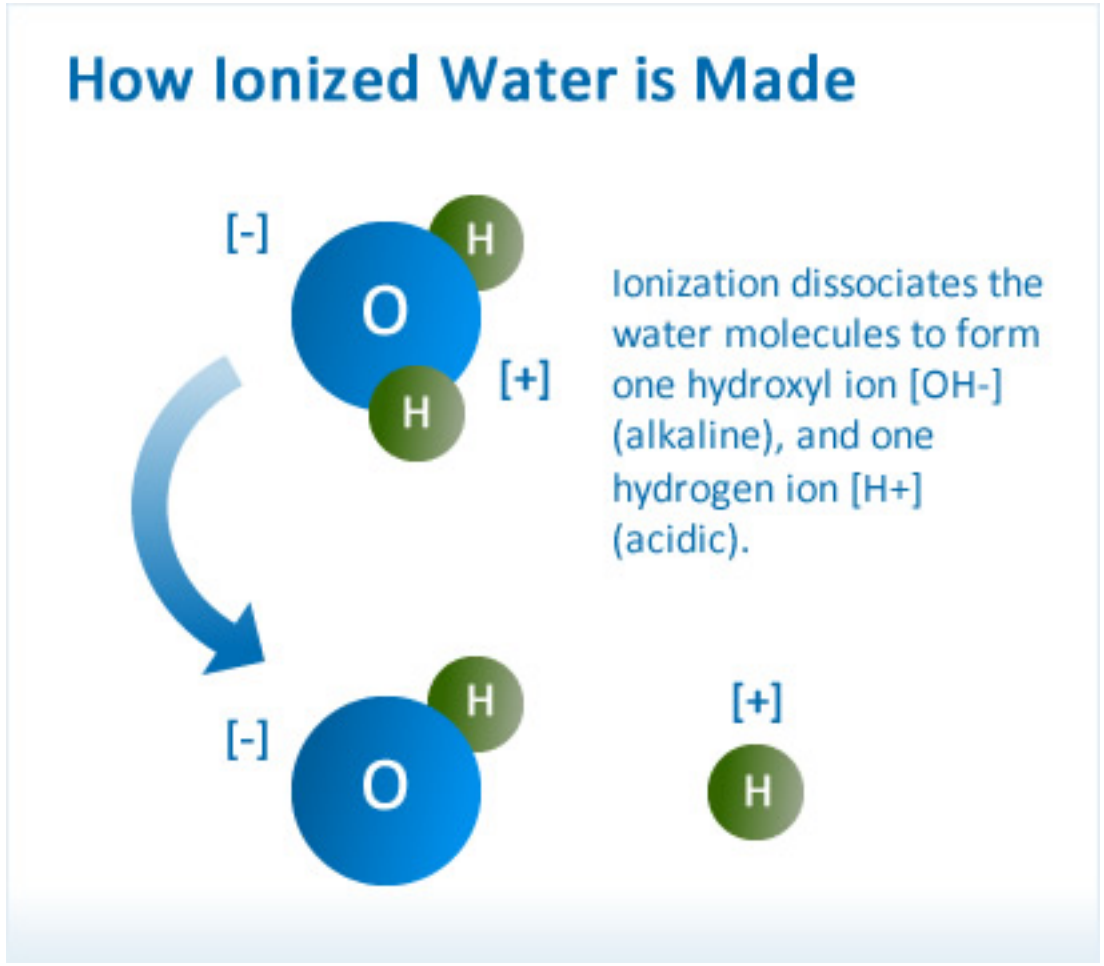
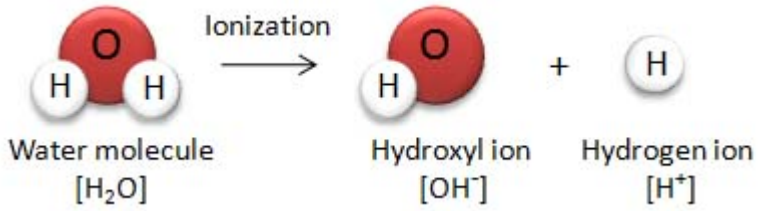


Figure 2-10
Lehninger Principles of Biochemistry, Fifth Edition

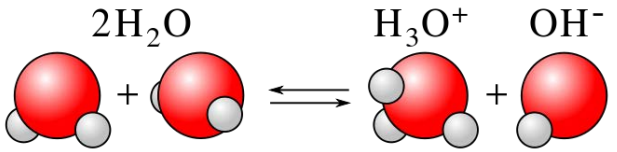
Ionização da água



A água tem uma leve tendência a sofrer ionização e liberar um íon de hidrogênio (rapidamente sofre hidratação e forma um íon hidrônio, (H_3O^+) e um íon hidróxido



Entretanto, a ionização da ága é reversível



Aminoácidos - propriedades

As proteínas são constituídas por 20 diferentes aminoácidos

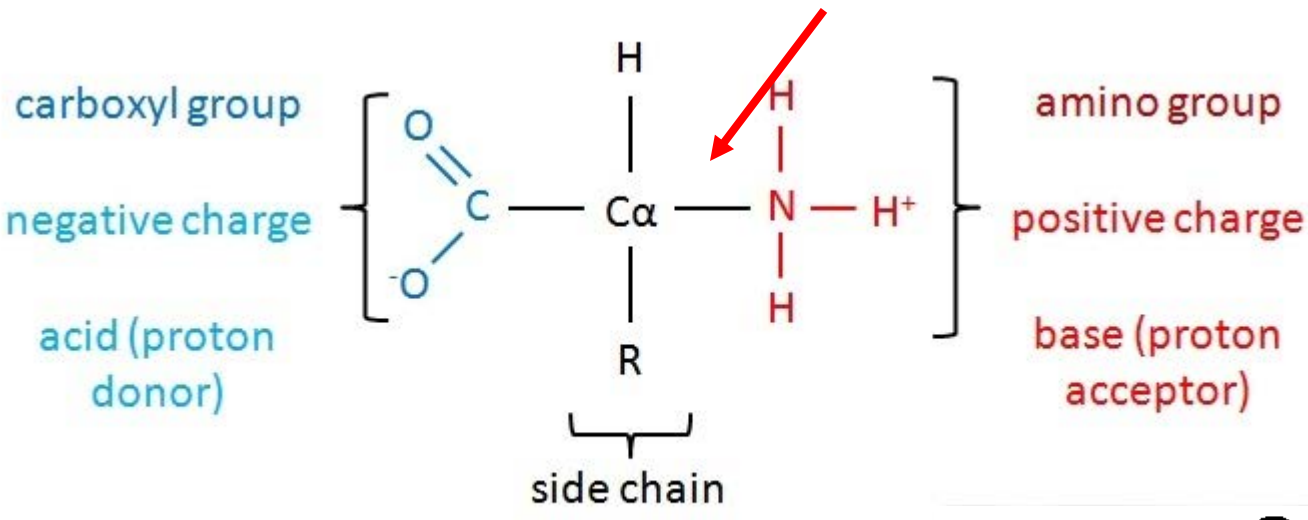
O nome dos aminoácidos foram dados pela fonte que eles foram encontrados pela primeira vez:

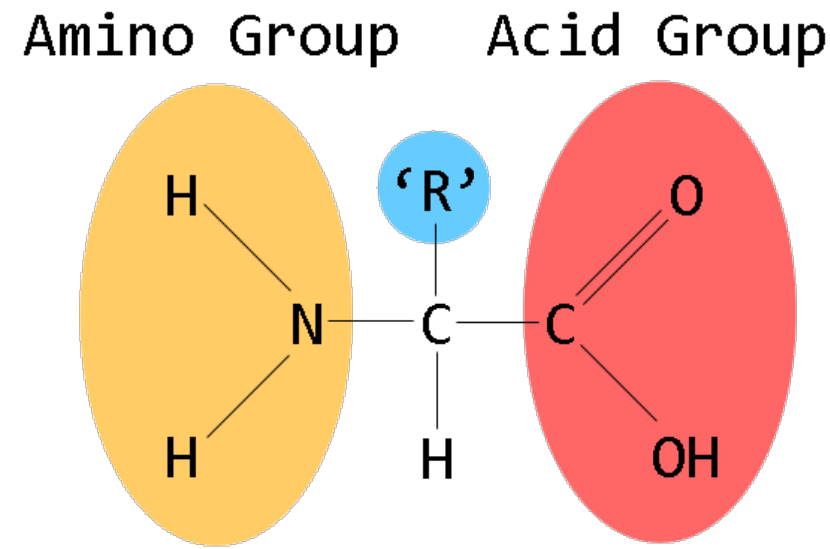
Asparagina = aspargos , in 1806

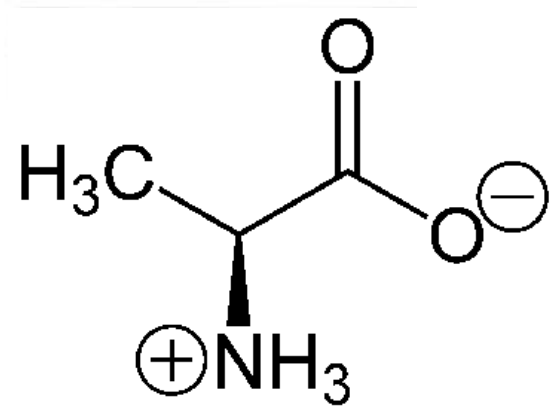
- Tirosina = queijo (do grego *tyros*)

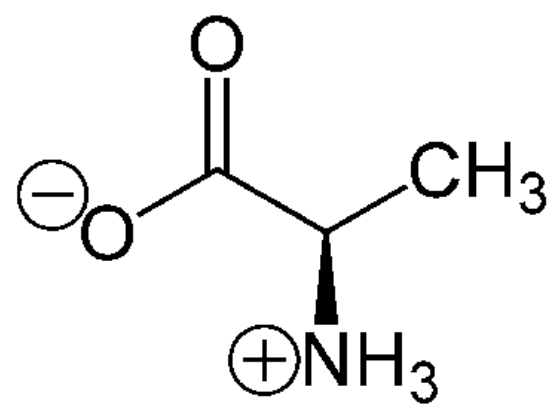
- A treonina foi o último a ser identificado, 1938

Os 20 aminoácidos mais comuns são α-aminoácidos

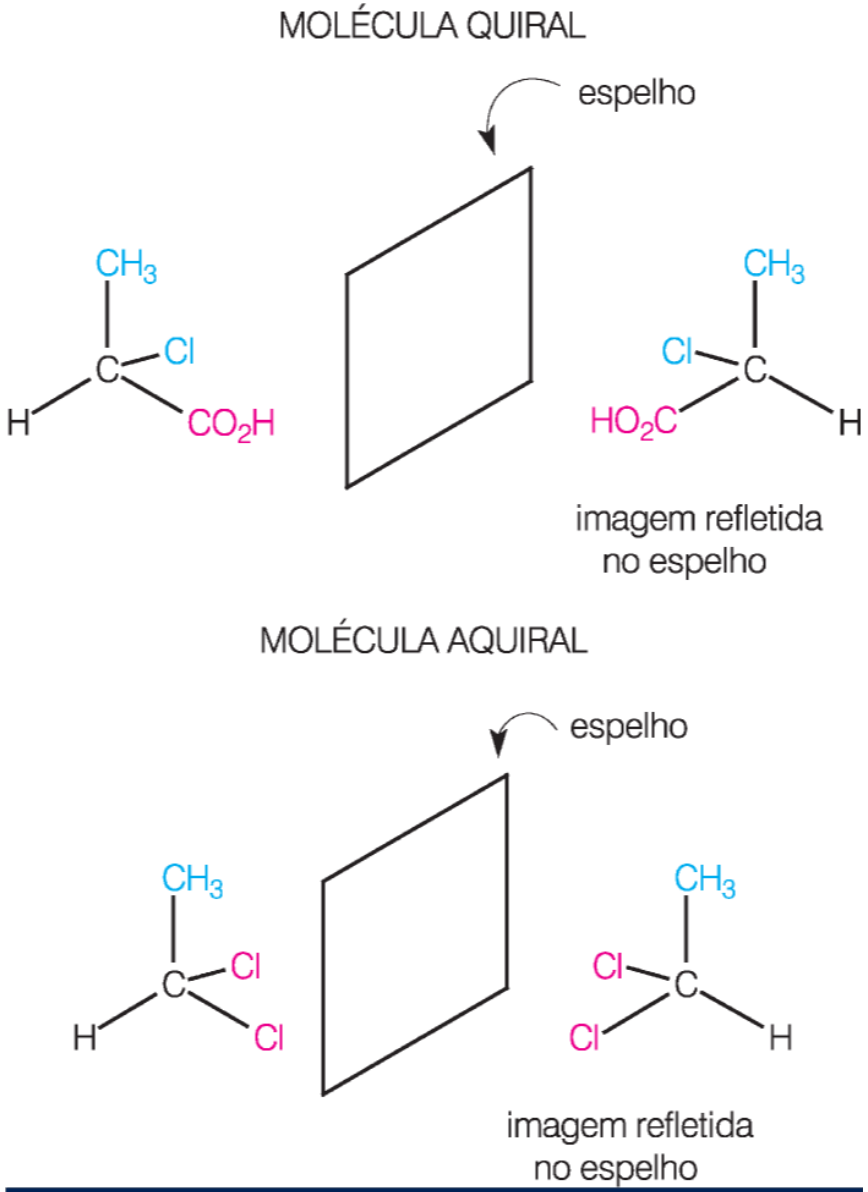


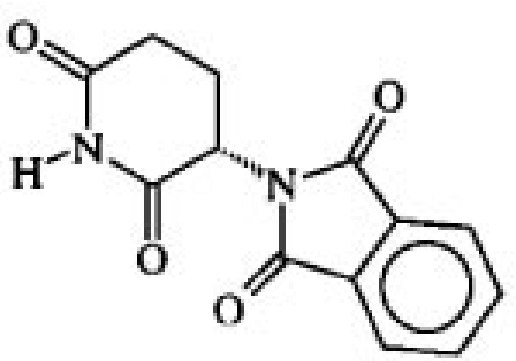




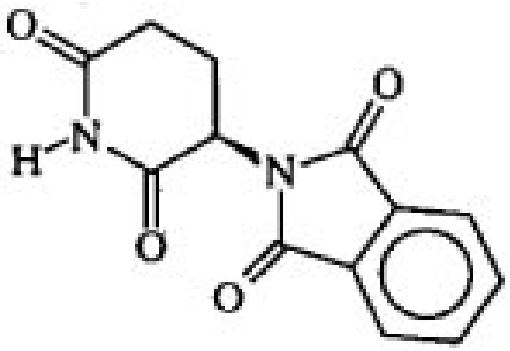


Os Aminoácidos apresentam quiralidade



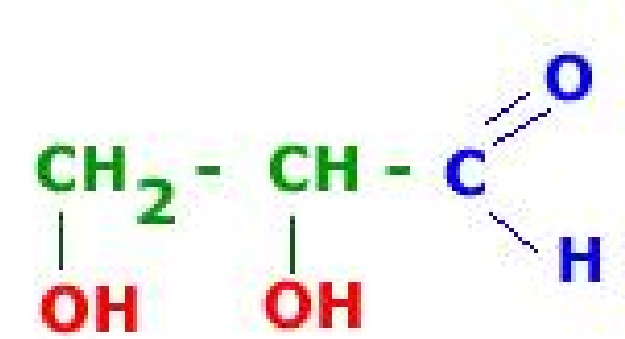


(S)-Talidomida
Teratogênico

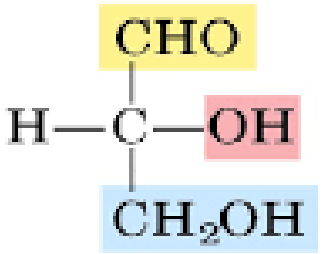


(R)-Talidomida
Sedativo e hipnótico

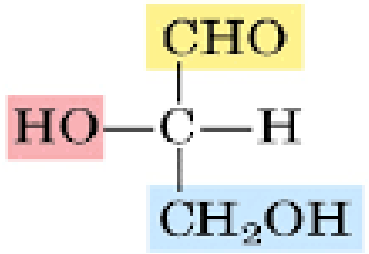
Onde está a quiralidade neste composto (gliceraldeído)?



aldeido glicérico

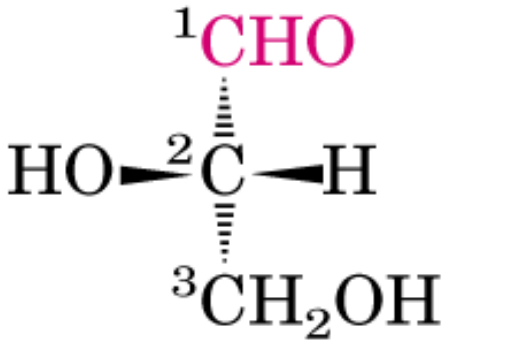


(*R*)-(+)-gliceraldeído
D-gliceraldeído

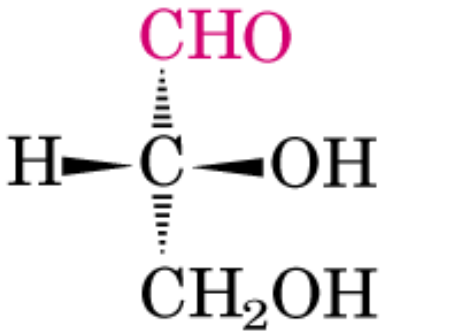


(*S*)-(-)-gliceraldeído
L-gliceraldeído

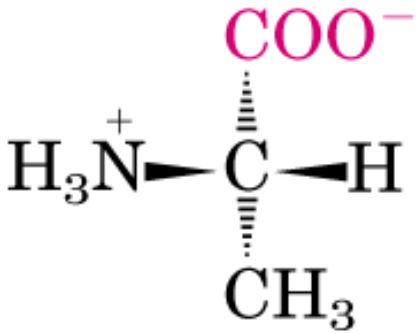
Os Aminoácidos apresentam quiralidade



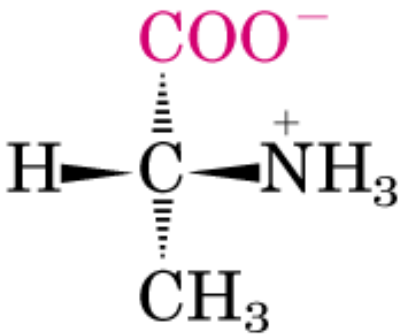
L-Glyceraldehyde



D-Glyceraldehyde

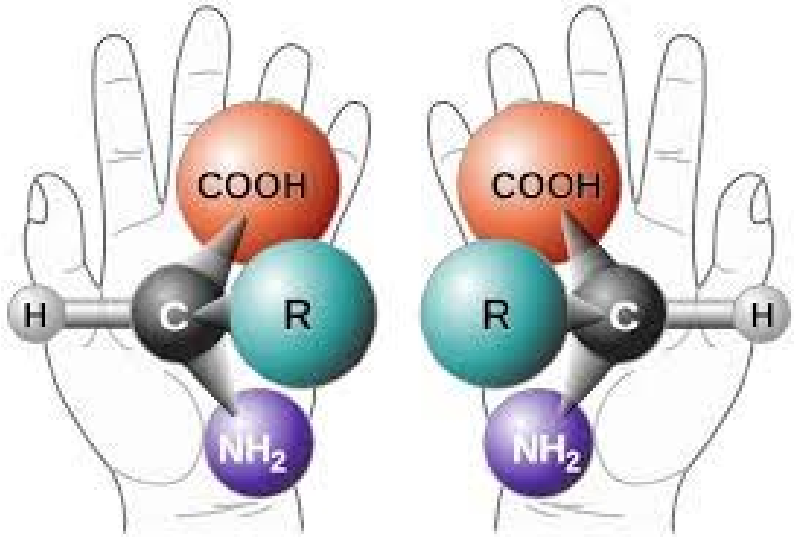


L-Alanine



D-Alanine

Proposto por Emil Fischer em 1891 e para todos os compostos quirais relacionados com o gliceraoldeído 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 proteinogênicos são estereoisômeros L

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

Qual o impacto da quiralidade na função das enzimas?

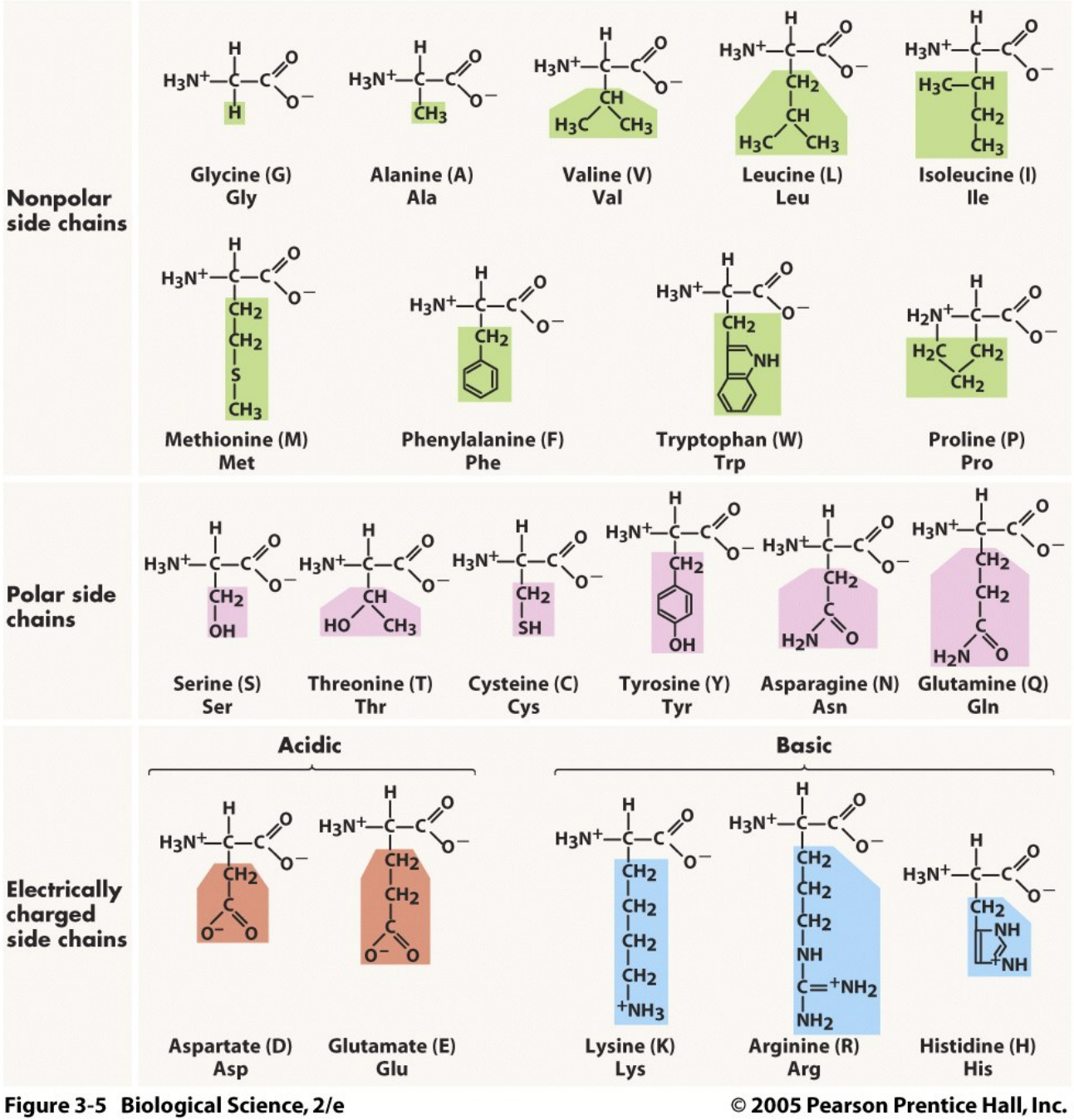
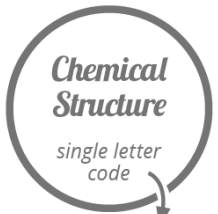


Figure 3-5 Biological Science, 2/e

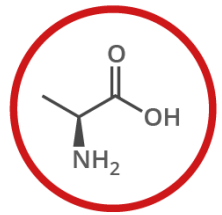
A GUIDE TO THE TWENTY COMMON AMINO ACIDS

AMINO ACIDS ARE THE BUILDING BLOCKS OF PROTEINS IN LIVING ORGANISMS. THERE ARE OVER 500 AMINO ACIDS FOUND IN NATURE - HOWEVER, THE HUMAN GENETIC CODE ONLY DIRECTLY ENCODES 20. 'ESSENTIAL' AMINO ACIDS MUST BE OBTAINED FROM THE DIET, WHILST NON-ESSENTIAL AMINO ACIDS CAN BE SYNTHESISED IN THE BODY.

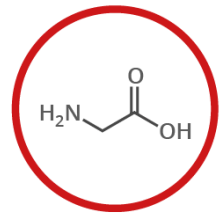
Chart Key: ALIPHATIC · AROMATIC · ACIDIC · BASIC · HYDROXYLIC · SULFUR-CONTAINING · AMIDIC · NON-ESSENTIAL · ESSENTIAL



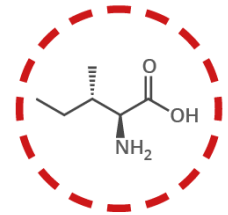
NAME **A**
three letter code
DNA codons



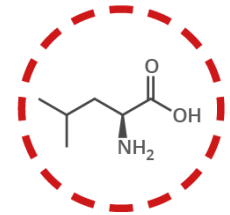
ALANINE A
Ala
GCT, GCC, GCA, GCG



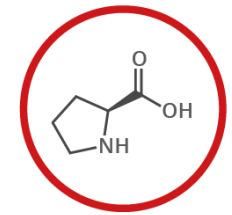
GLYCINE G
Gly
GGT, GGC, GGA, GGG



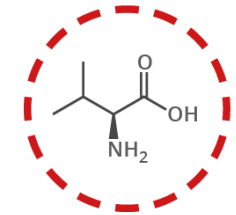
ISOLEUCINE I
Ile
ATT, ATC, ATA



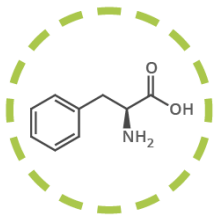
LEUCINE L
Leu
CTT, CTC, CTA, CTG, TTA, TTG



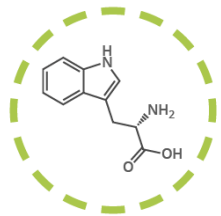
PROLINE P
Pro
CCT, CCC, CCA, CCG



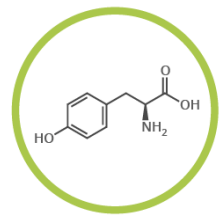
VALINE V
Val
GTT, GTC, GTA, GTG



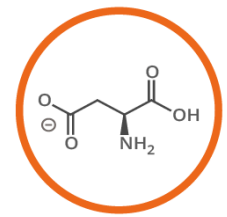
PHENYLALANINE F
Phe
TTT, TTC



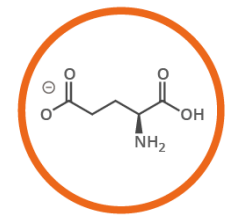
TRYPTOPHAN W
Trp
TGG



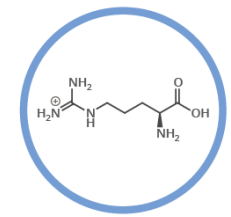
TYROSINE Y
Tyr
TAT, TAC



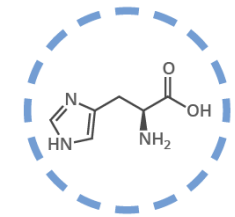
ASPARTIC ACID D
Asp
GAT, GAC



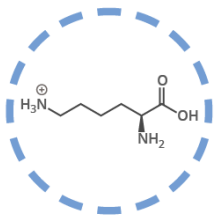
GLUTAMIC ACID E
Glu
GAA, GAG



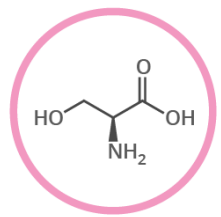
ARGININE R
Arg
CGT, CGC, CGA, CGG, AGA, AGG



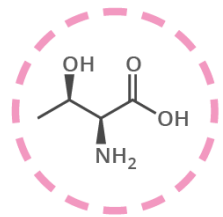
HISTIDINE H
His
CAT, CAC



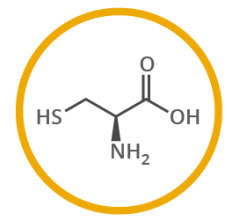
LYSINE K
Lys
AAA, AAG



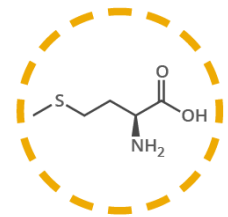
SERINE S
Ser
TCT, TCC, TCA, TCG, AGT, AGC



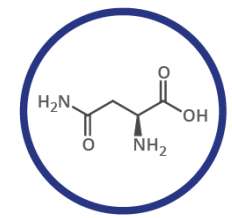
THREONINE T
Thr
ACT, ACC, ACA, ACG



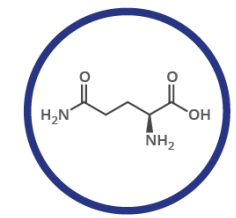
CYSTEINE C
Cys
TGT, TGC



METHIONINE M
Met
ATG



ASPARAGINE N
Asn
AAT, AAC



GLUTAMINE Q
Gln
CAA, CAG

Note: This chart only shows those amino acids for which the human genetic code directly codes for. Selenocysteine is often referred to as the 21st amino acid, but is encoded in a special manner. In some cases, distinguishing between asparagine/aspartic acid and glutamine/glutamic acid is difficult. In these cases, the codes asx (B) and glx (Z) are respectively used.

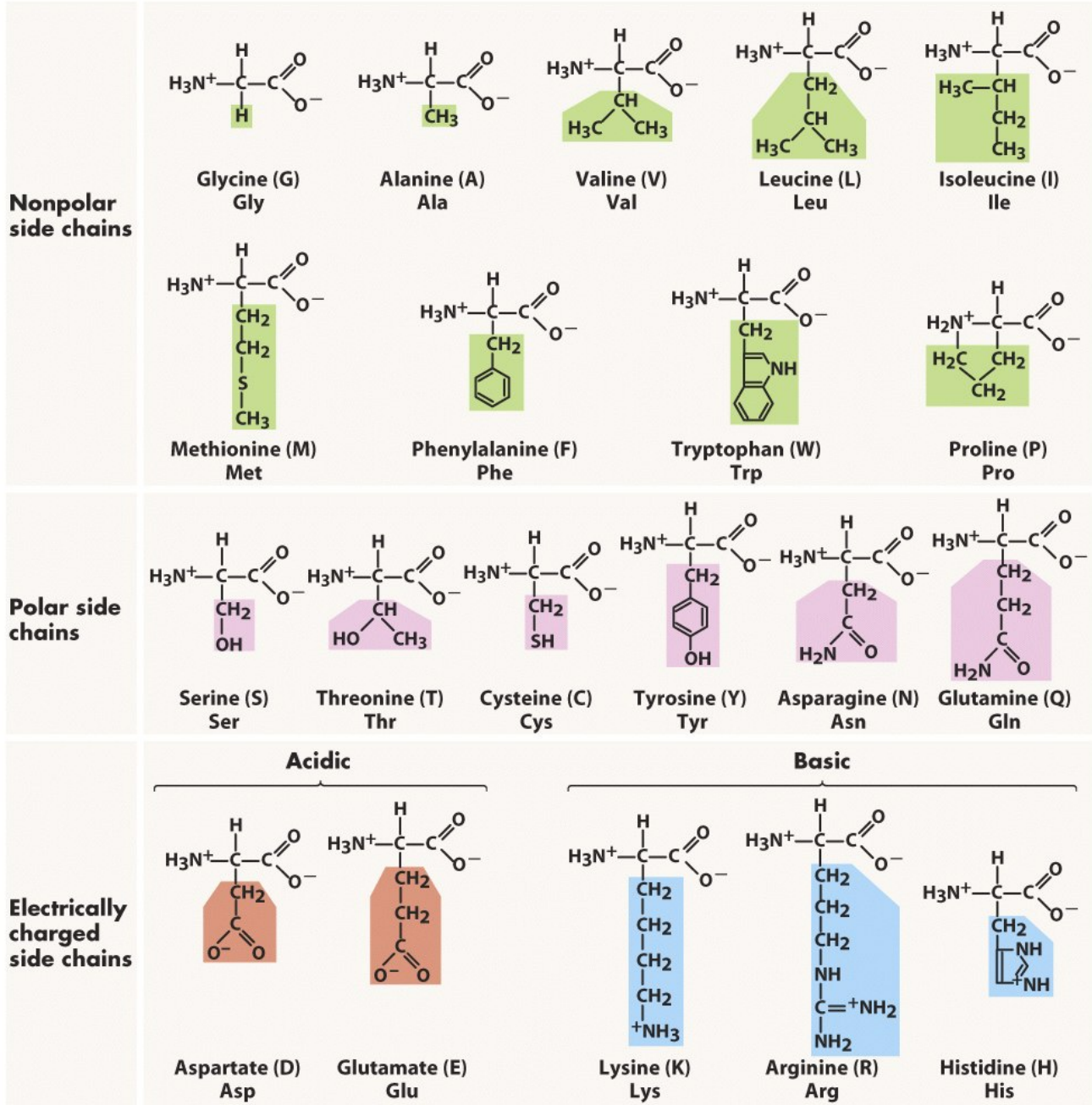
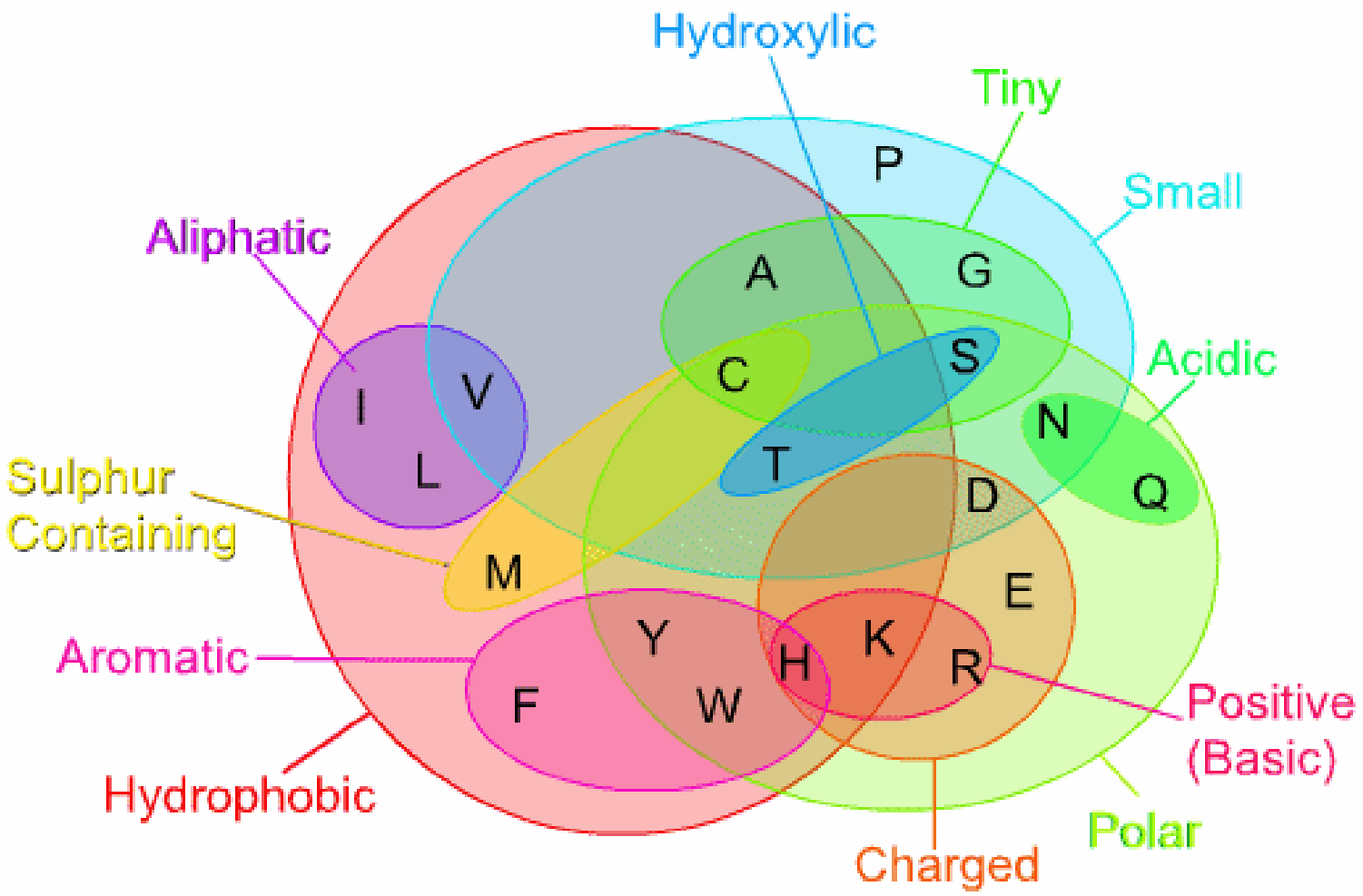


Figure 3-5 Biological Science, 2/e

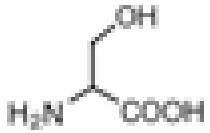


Amino Acids

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 metioneine (met)
F phenyalanine (phe)
P proline (pro)
S serine (ser)
T threonine (thr)
W trytophan (trp)
Y tyrosine (tyr)

Glycine

Alanine

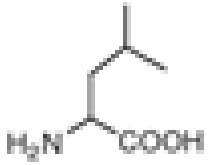


Serine

Threonine

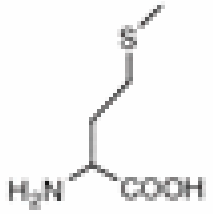
Cysteine

Valine



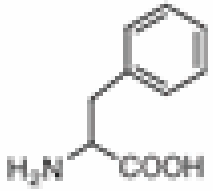
Leucine

Isoleucine

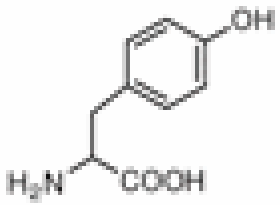


Methionine

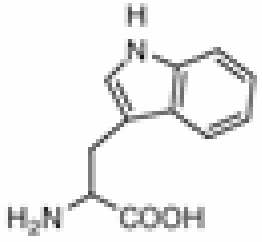
Proline



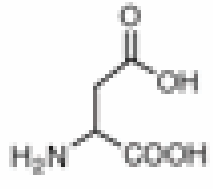
Phenylalanine



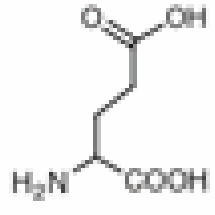
Tyrosine



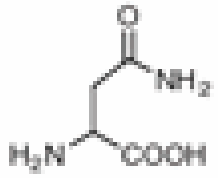
Tryptophan



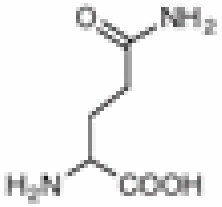
Apartic Acid



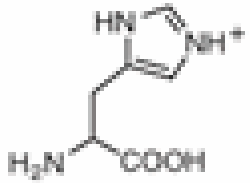
Glutamic Acid



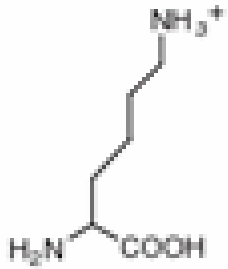
Asparagine



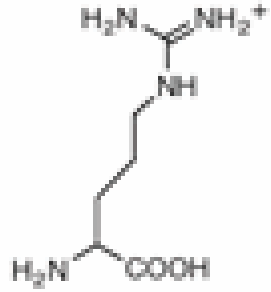
Glutamine



Histidine

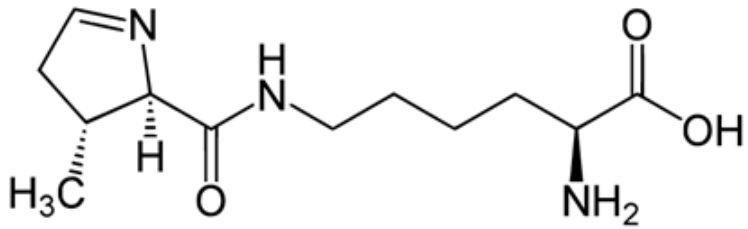


Lysine

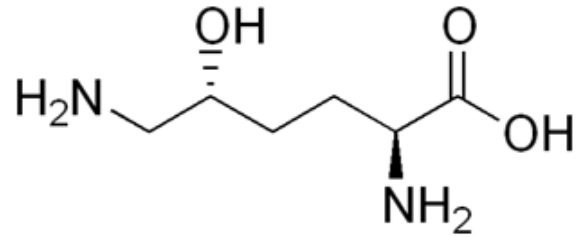


Arginine

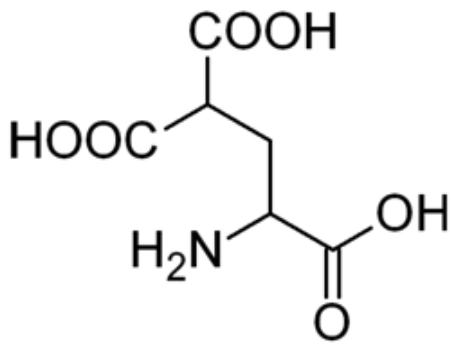
Outros Aminoácidos incomuns



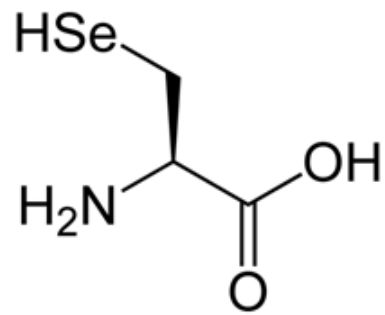
Pyrrolysine



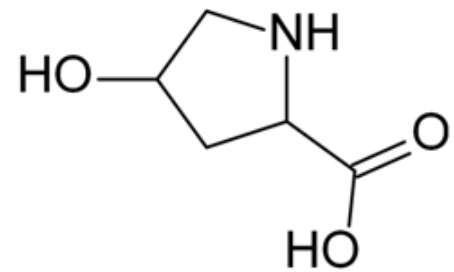
Hydroxylysine



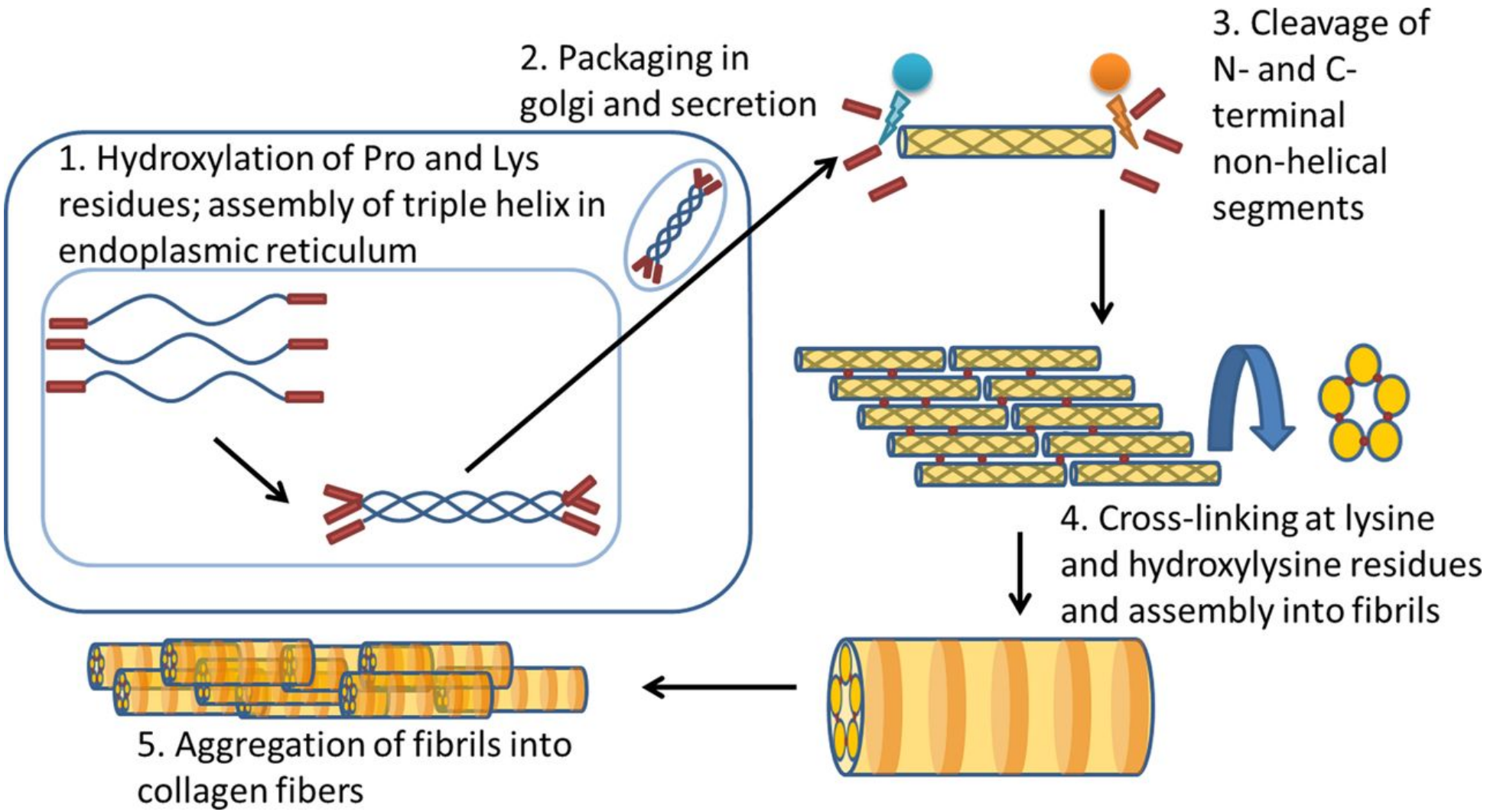
γ-carboxyglutamic acid



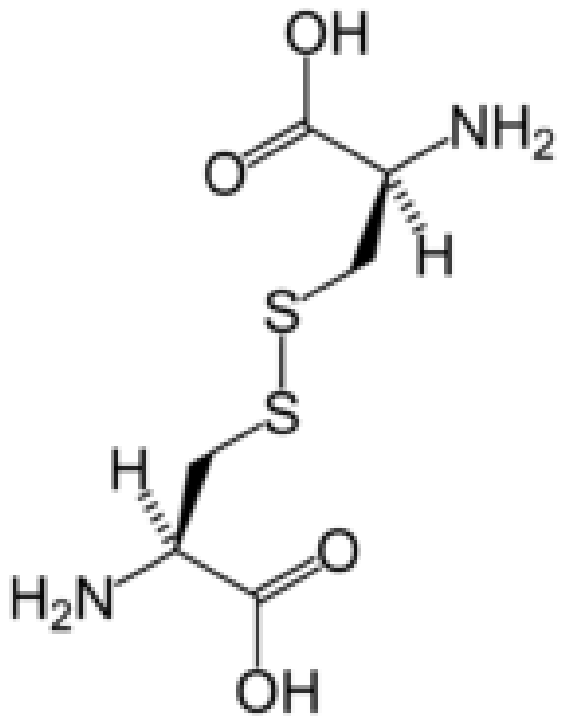
Selenocysteine



Hydroxyproline


1. Hydroxylation of Pro and Lys residues; assembly of triple helix in endoplasmic reticulum
2. Packaging in golgi and secretion
3. Cleavage of N- and C-terminal non-helical segments
4. Cross-linking at lysine and hydroxylysine residues and assembly into fibrils
5. Aggregation of fibrils into collagen fibers

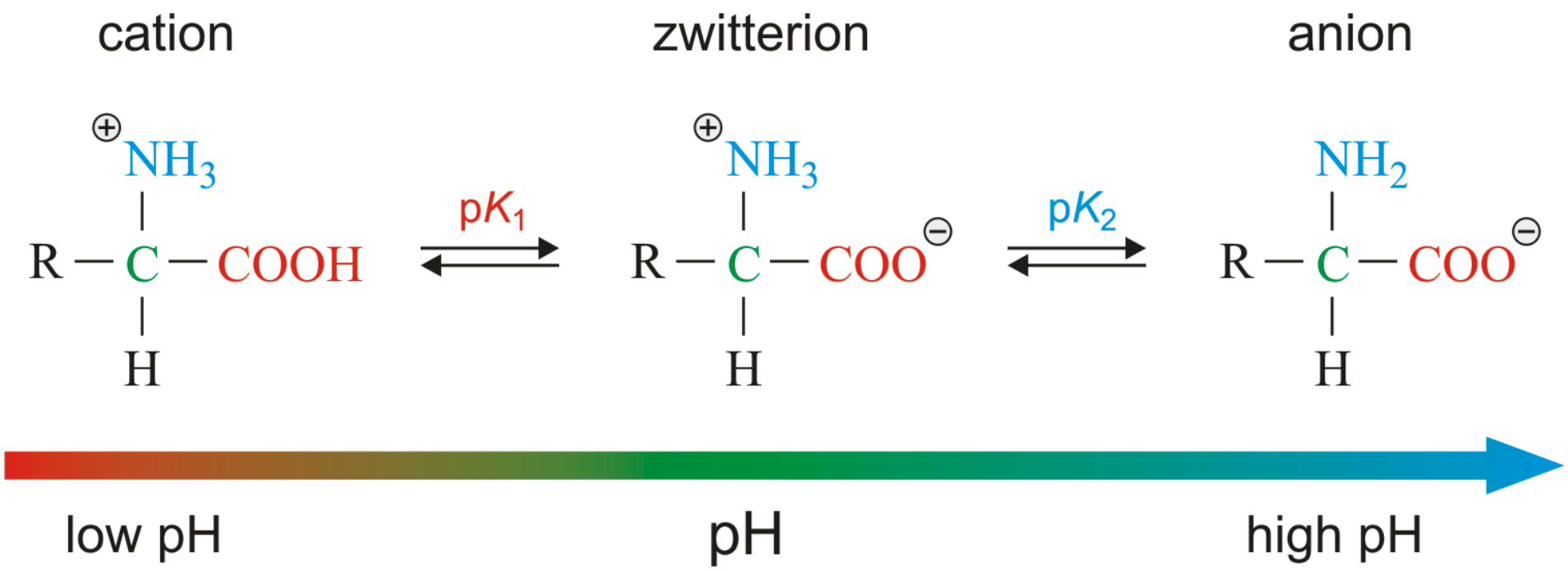
As cisteínas são capazes de formar pontes disulfeto



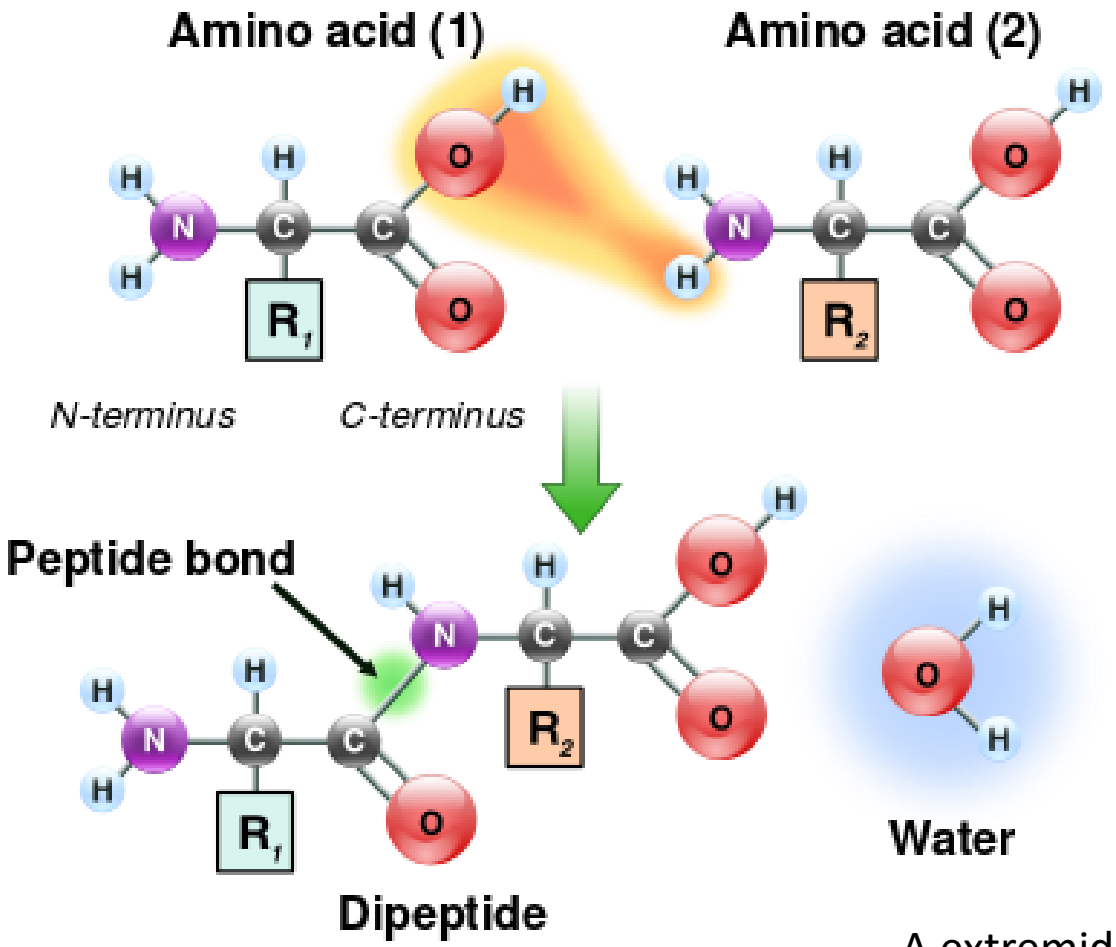
Os aminoácidos são moléculas zwitteriônicas

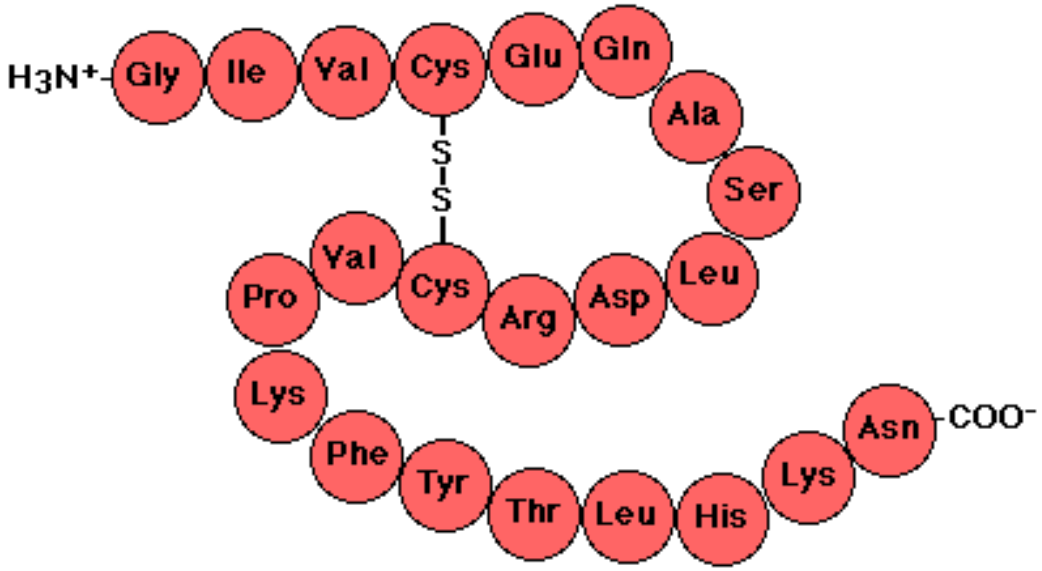
Eles podem ser tanto ácidos ou bases por causa dos seus grupos amino e ácido carboxílico

Os aminoácidos também pode ser chamados de anfólitos por causa da sua natureza ácido-base



As proteínas são formados por aminoácidos

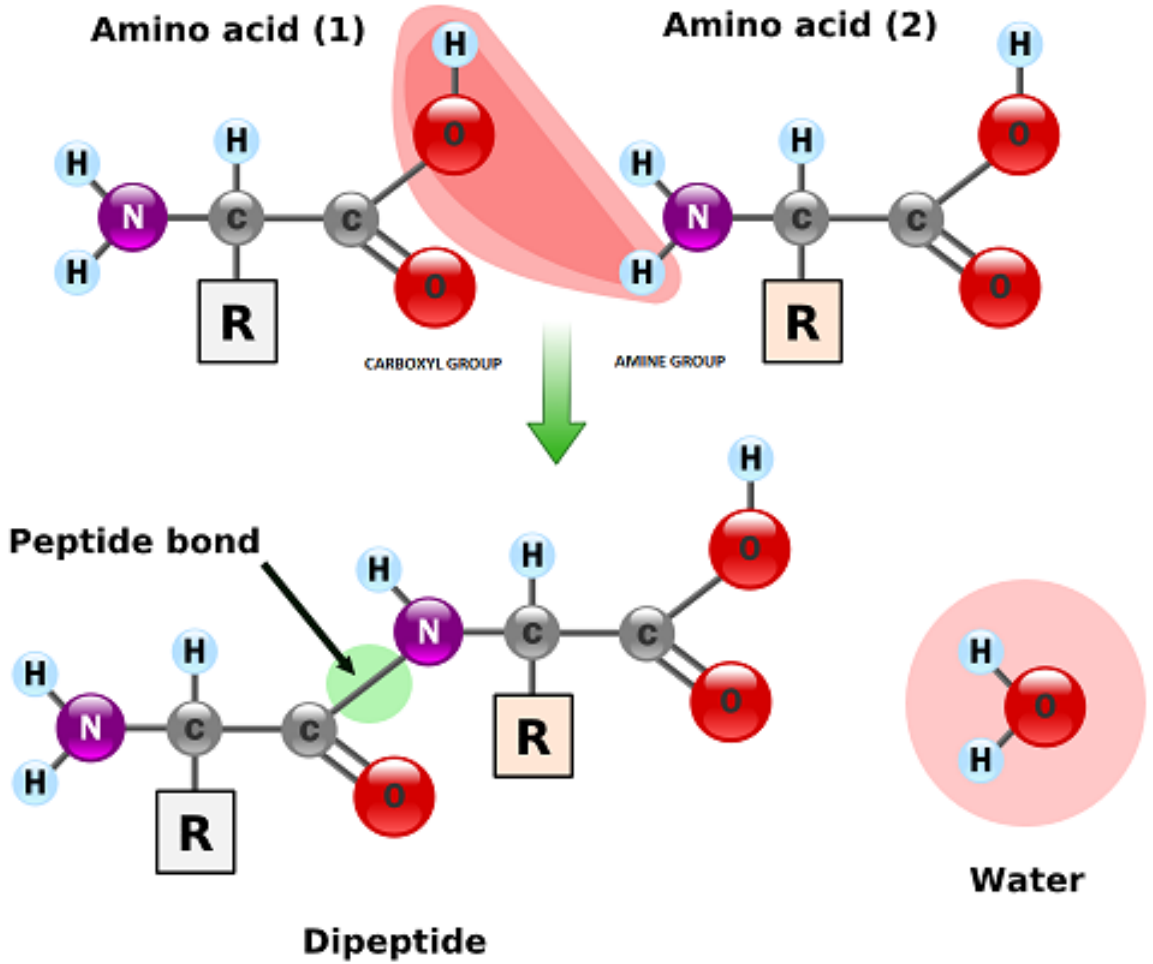




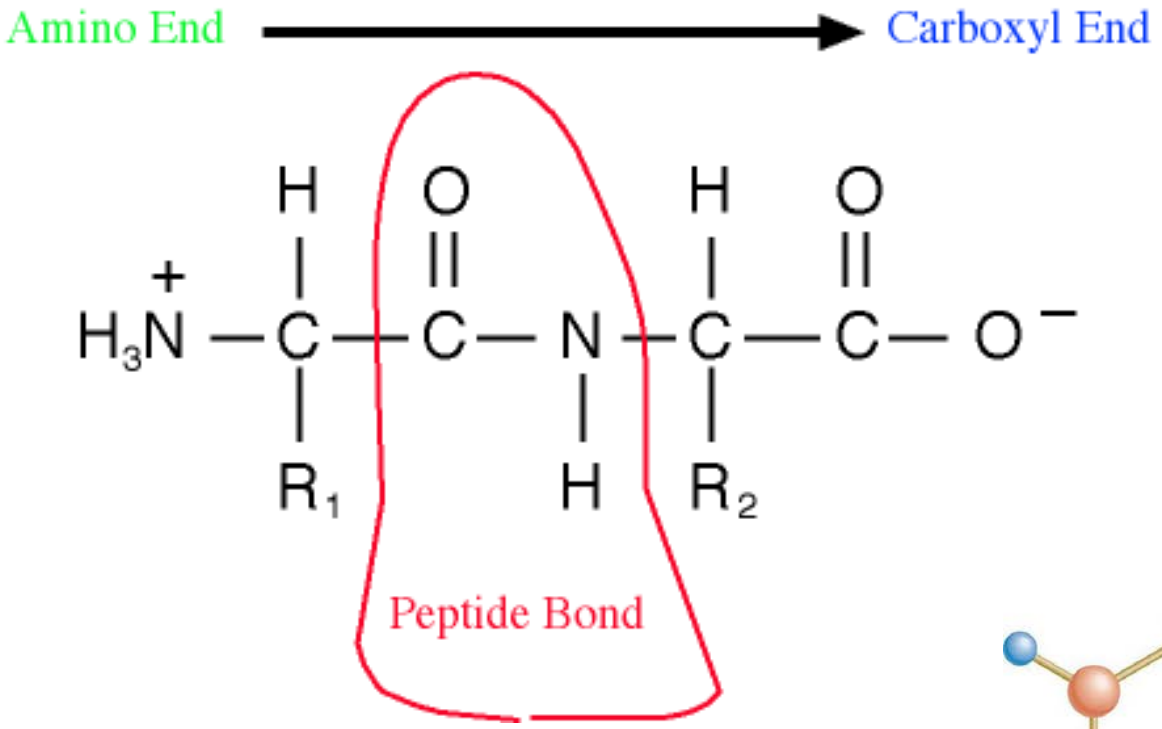
A extremidade de cada polipeptídeo ou proteína são únicas porções α-amino and α-carboxi ionizável, embora os grupos também possam ser ionizáveis em alguns aminoácidos

Peptídeos e proteínas

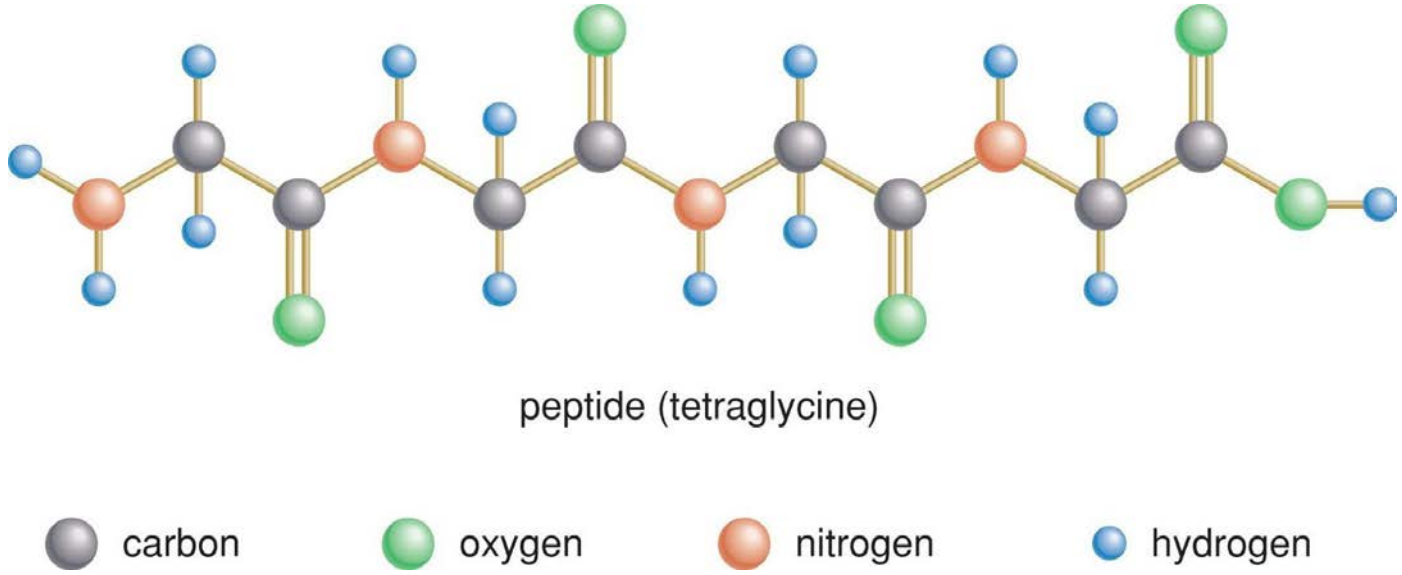
Dois aminoácidos são covalentemente juntados por uma reação de **condensação** realizado pelo ribossomo. Essa ligação é chamada de ligação peptídica



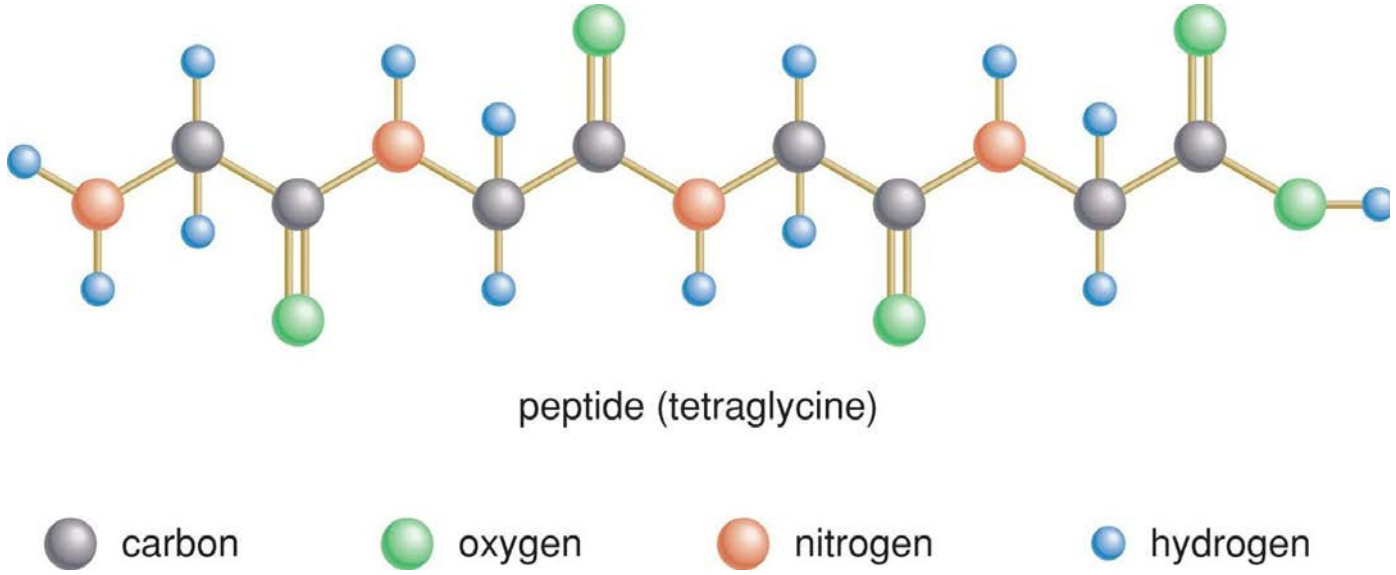
A ligação peptídica



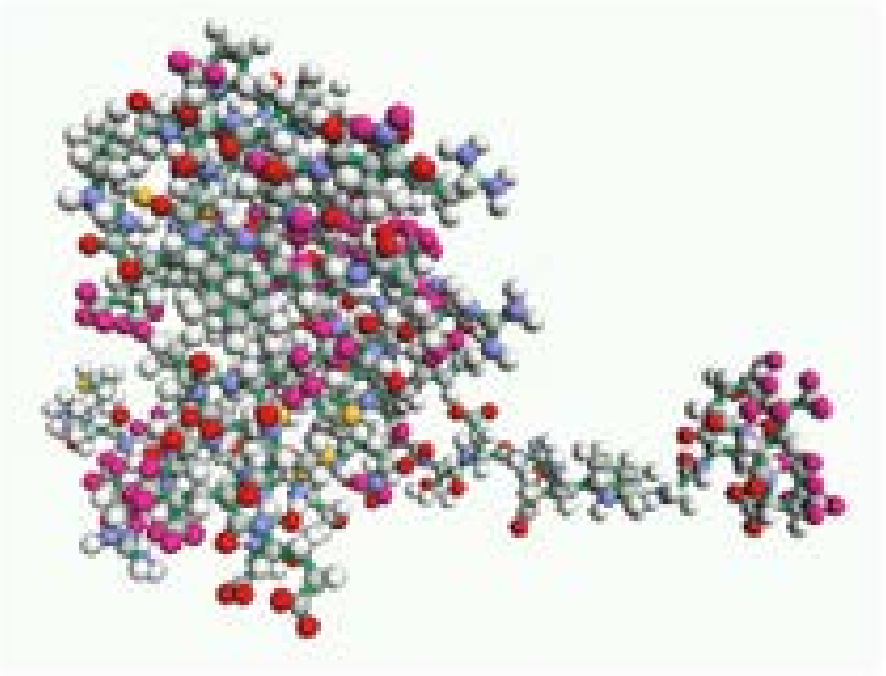
A ligação peptídica é altamente estável



Oligopeptídeos = poucos aminoácidos
Polipeptídeos = muitos aminoácidos

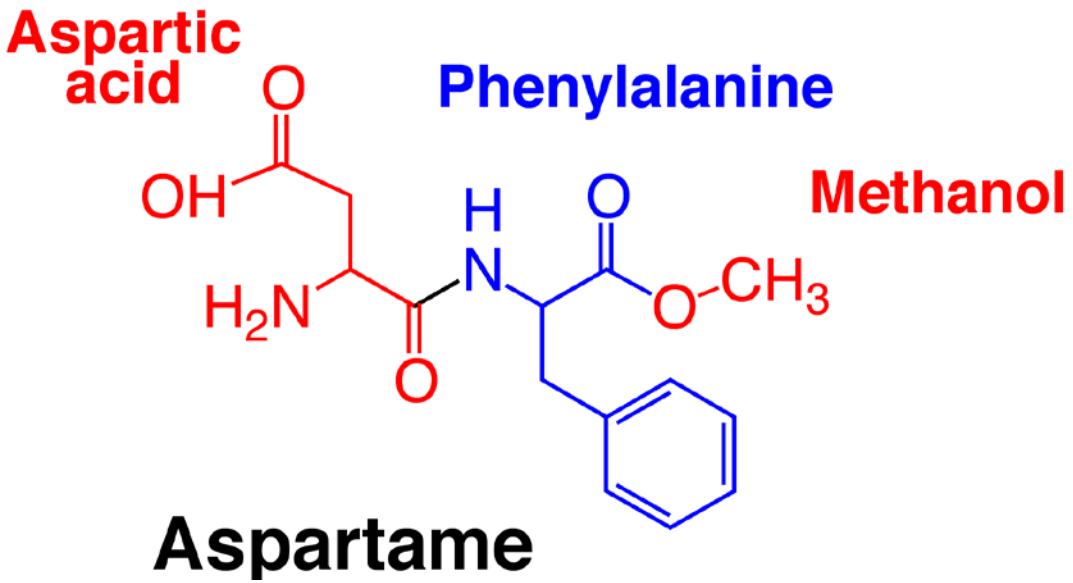


Polipeptídeos = peso molecular < 10,000 Da
Proteínas = peso molecular > 10,000 Da



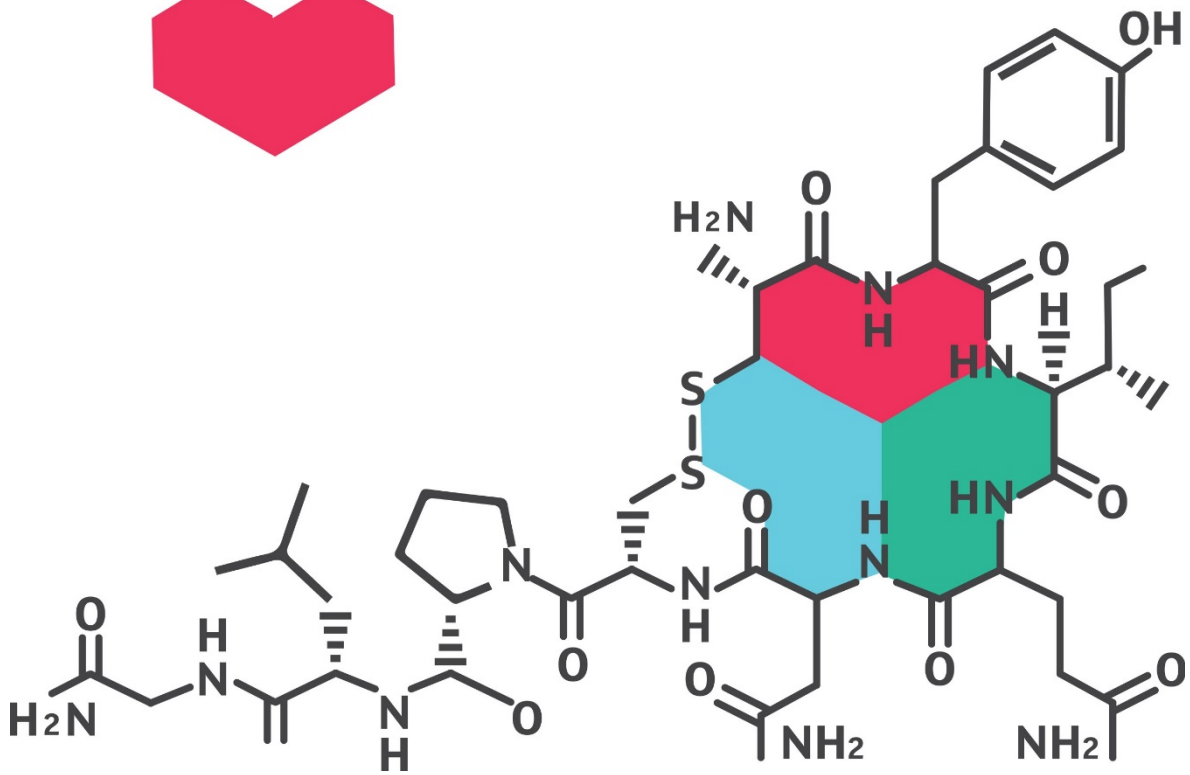
Peptídeos biologicamente ativos

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

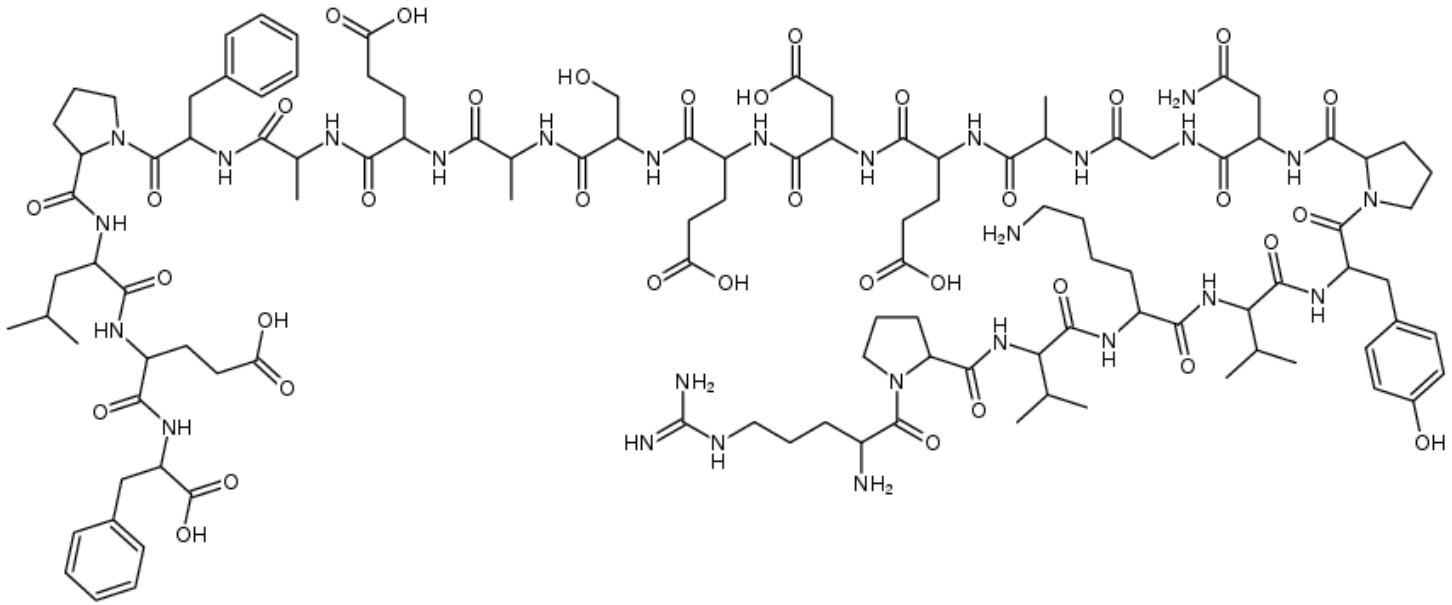


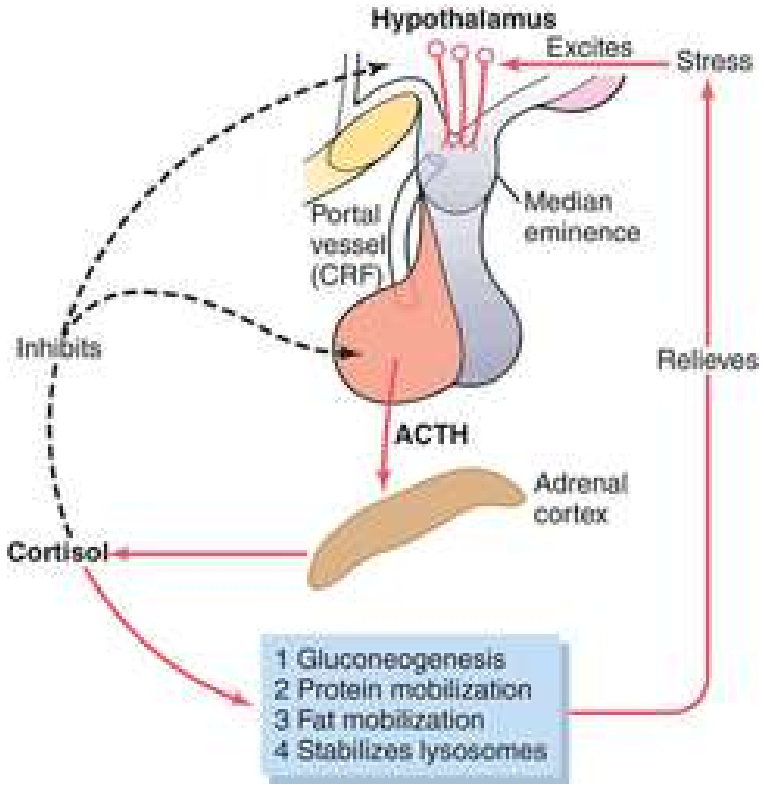
No amor, no PARTO,
na amamentação,
nos melhores momentos da vida:

OCITOCINA

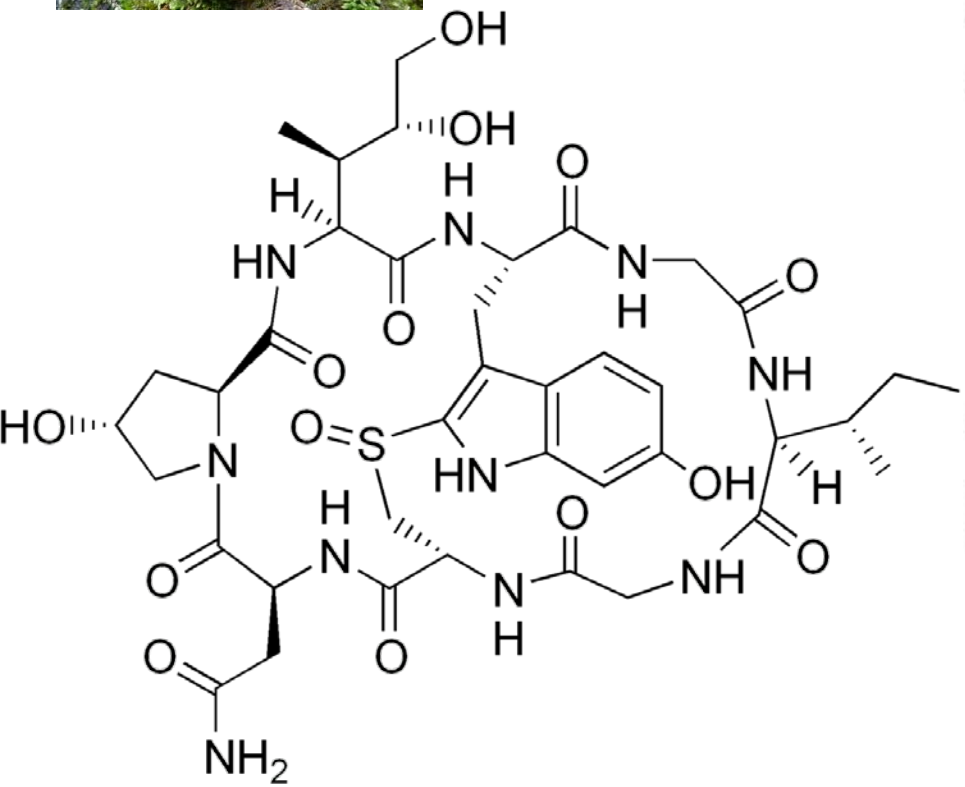


ACTH



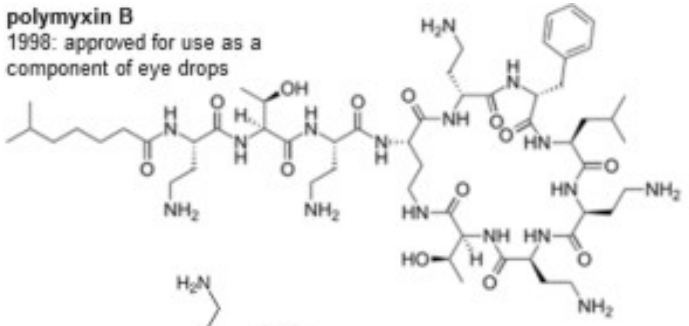

Hypothalamus
Excites
Stress
Portal vessel (CRF)
Median eminence
Inhibits
Relieves
ACTH
Adrenal cortex
Cortisol
1 Gluconeogenesis
2 Protein mobilization
3 Fat mobilization
4 Stabilizes lysosomes

Toxinas/antibióticos

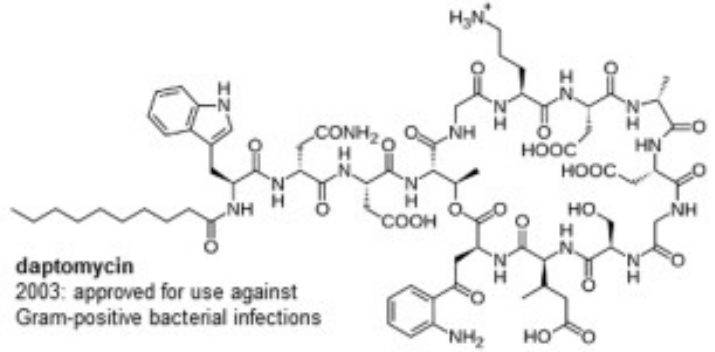


Amanitin

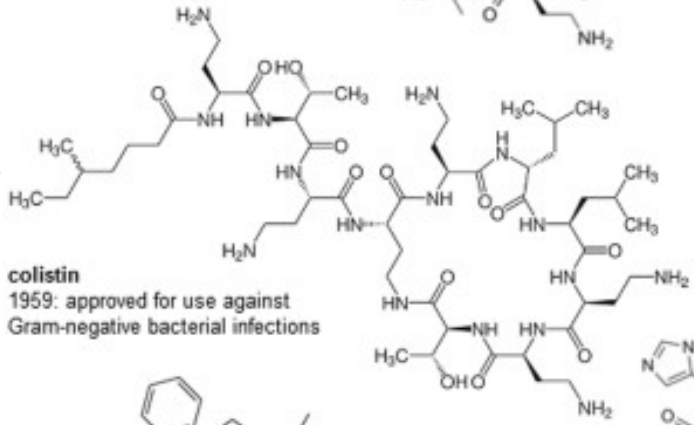
polymyxin B
1998: approved for use as a component of eye drops



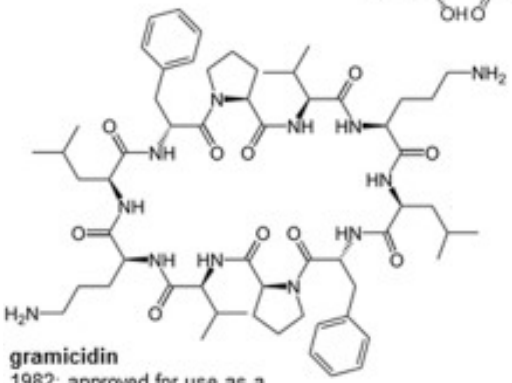
daptomycin
2003: approved for use against Gram-positive bacterial infections

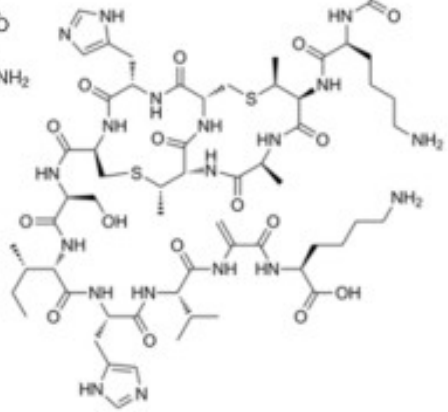


colistin
1959: approved for use against Gram-negative bacterial infections



gramicidin
1982: approved for use as a component of eye drops





nisin
1988: approved for use as a food preservative

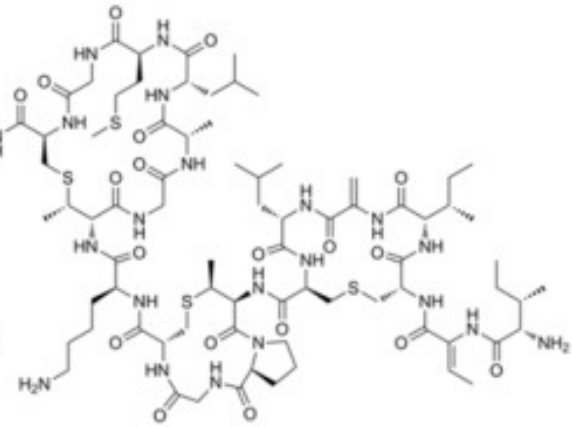
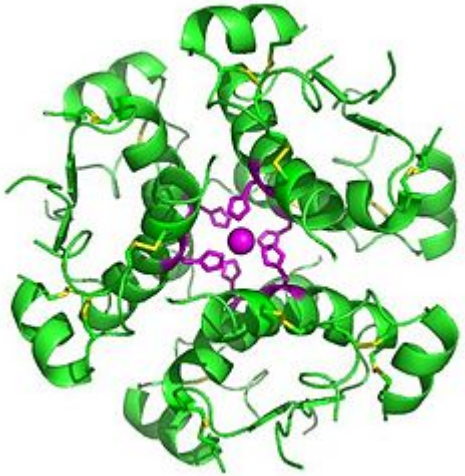
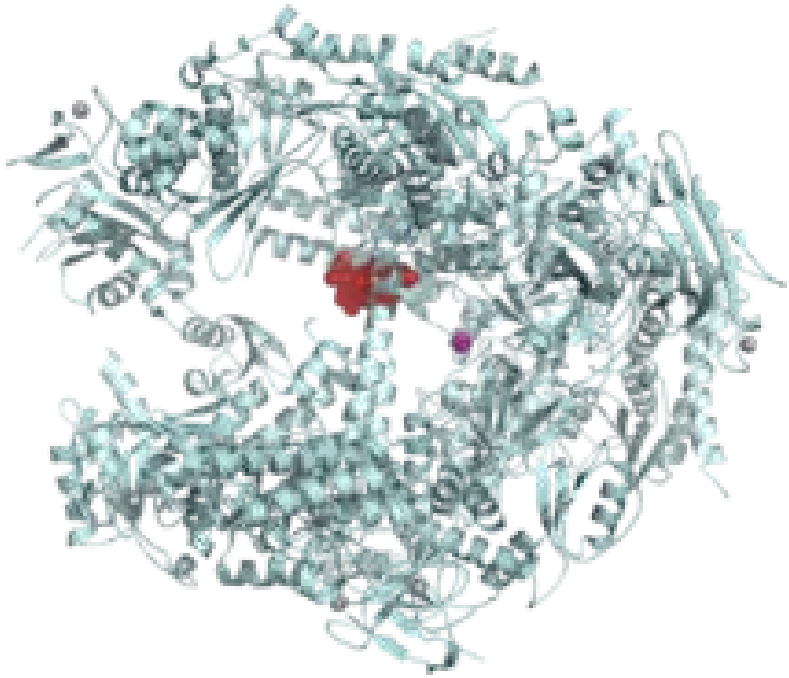


Table 6–1 Molecular data on some proteins

	Molecular weight	Number of residues	Number of polypeptide chains
Insulin (bovine)	5,733	51	2
Cytochrome *c* (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 (*E. coli*)	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 da 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 consequentemente com a função de uma proteína? Ou seja quem dita a função de uma proteína?