

UFABC

Bacharelado em Ciência & Tecnologia

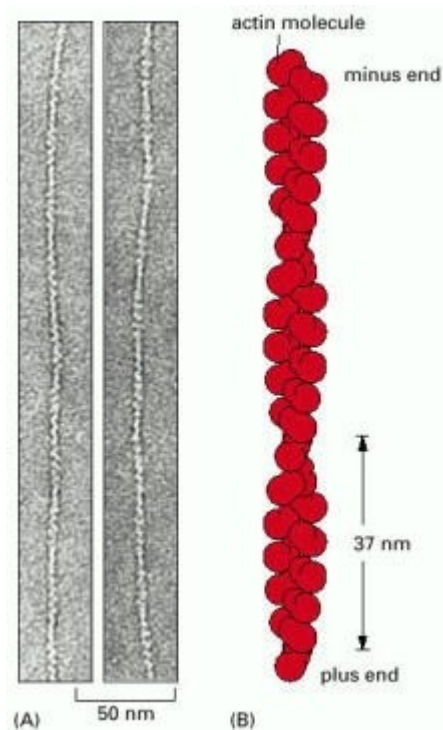
Proteínas recombinantes

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Universidade Federal do ABC

O que são proteínas ?



Actina

Contração Muscular

(A) Transmission [electron](#) micrographs of negatively stained [actin](#) filaments. (B) The helical arrangement of actin molecules in an actin filament. (A, courtesy of Roger Craig.)

Polypeptide
chain

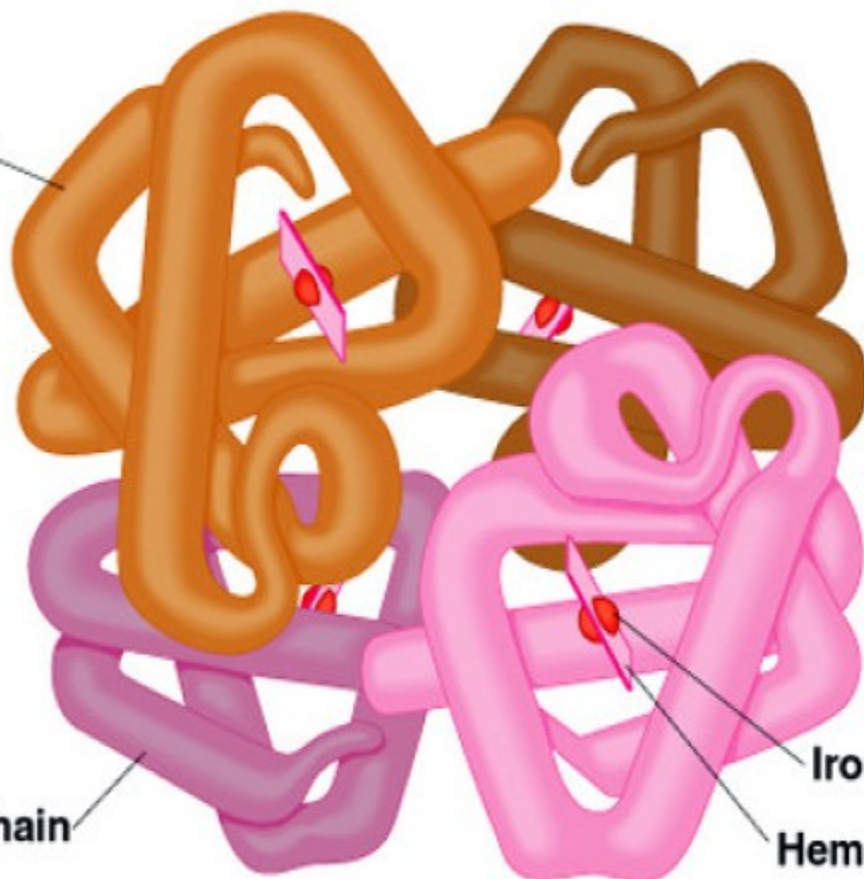
β chain

α chain

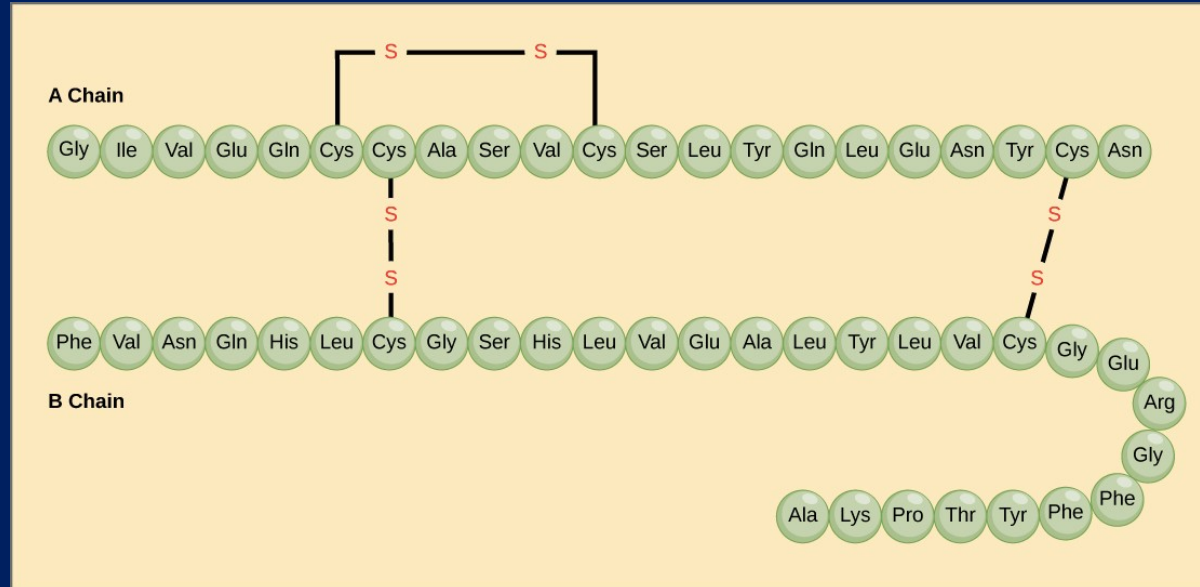
Iron **Fe**

Heme

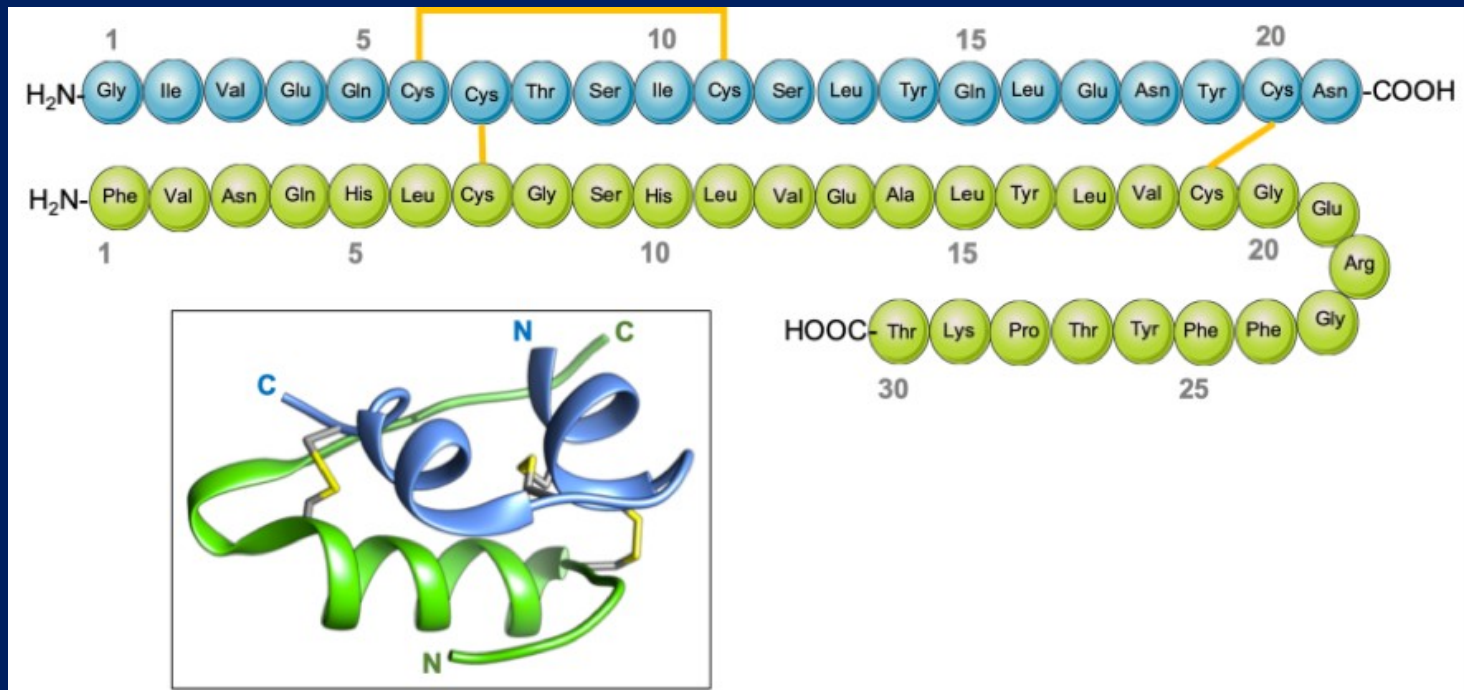
Hemoglobin



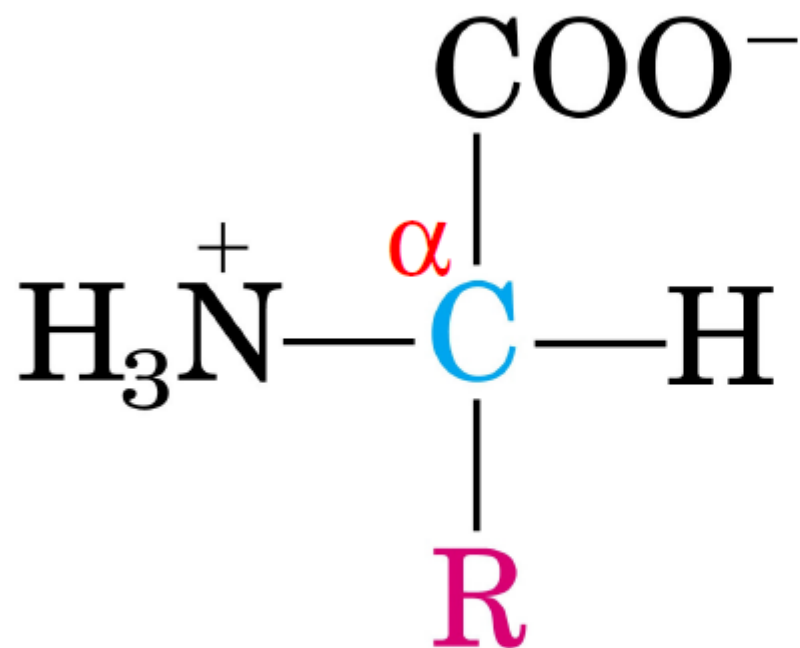
Insulina



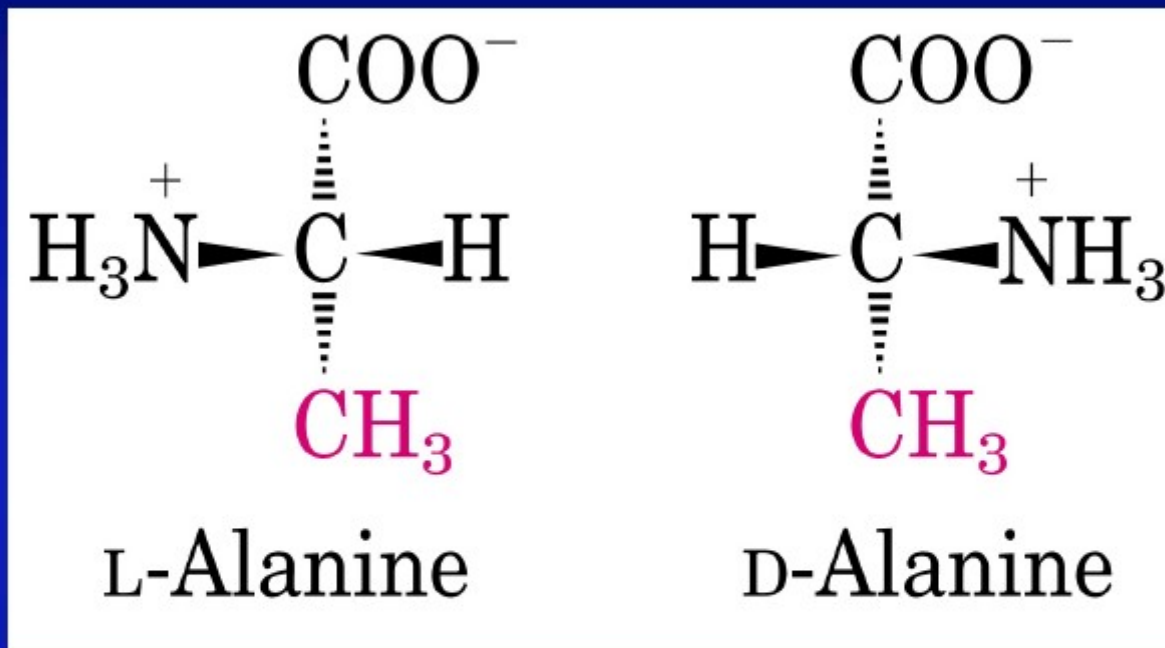
Insulina



***Qual a molécula base
para as proteínas ?***



O carbono α apresenta 4 ligantes diferentes, com exceção da glicina, apresentando assim estereoquímica.

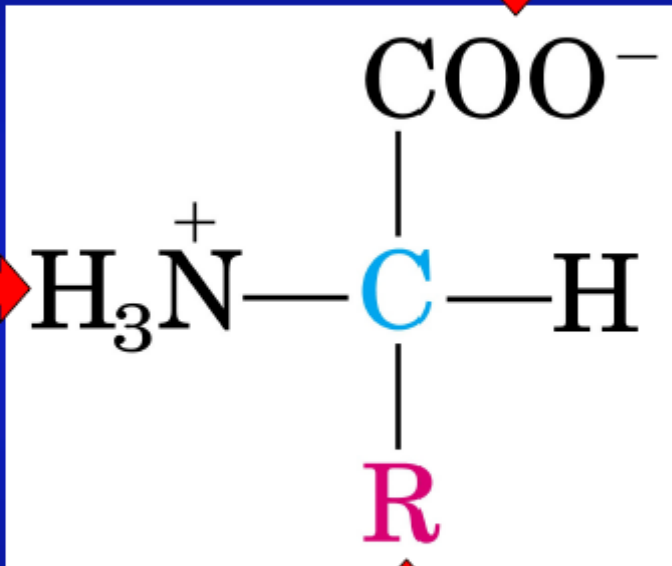


Todas as proteínas encontradas nos seres vivos são formadas por **L-aminoácidos.**

**GRUPO
CARBOXILA**



**GRUPO
AMINO**



**CADEIA
LATERAL**

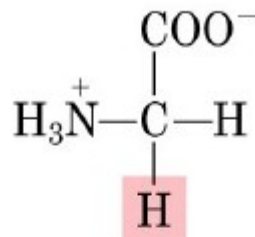
Os aminoácidos diferem entre si pela estrutura da cadeia lateral (R).

A classificação dos 20 aminoácidos é feita por meio de sua cadeia lateral (R) e podem ser divididos em:

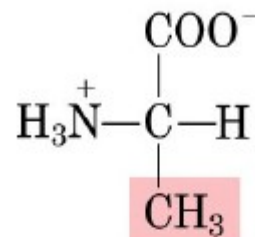
- **apolares** (hidrofóbicos);
- **polares** (hidrofílicos);

Os aminoácidos polares ainda são divididos em polares **sem carga**, polares **carregados positivamente** e polares **carregados negativamente**.

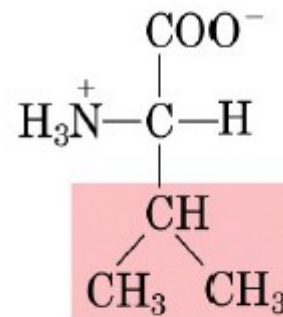
AMINOÁCIDOS APOLARES ALIFÁTICOS



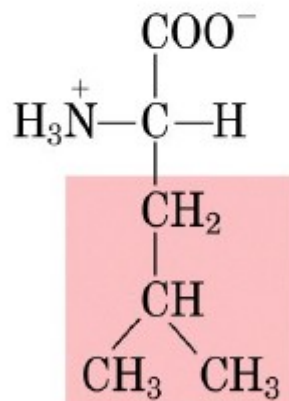
Glycine



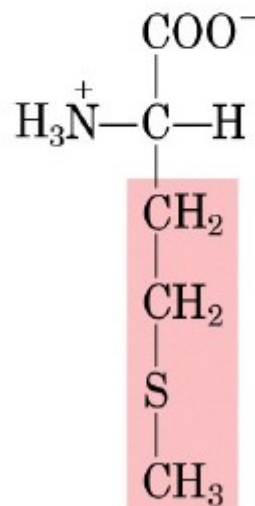
Alanine



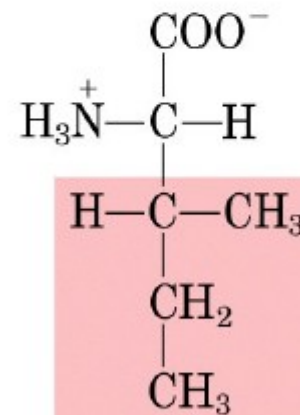
Valine



Leucine

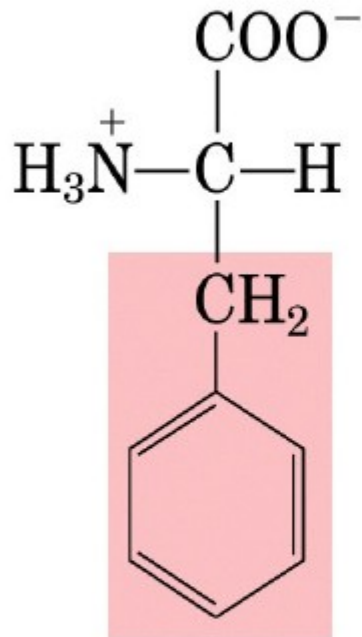


Methionine

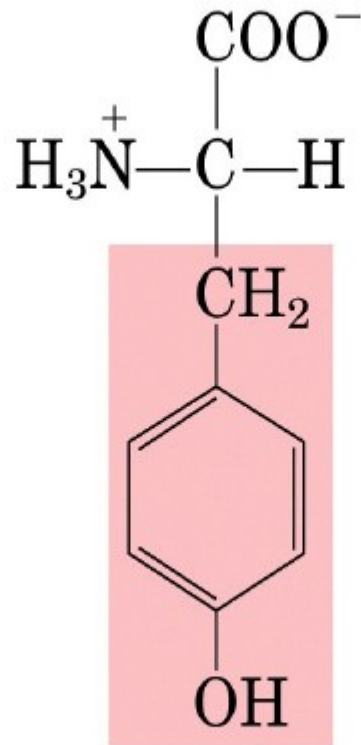


Isoleucine

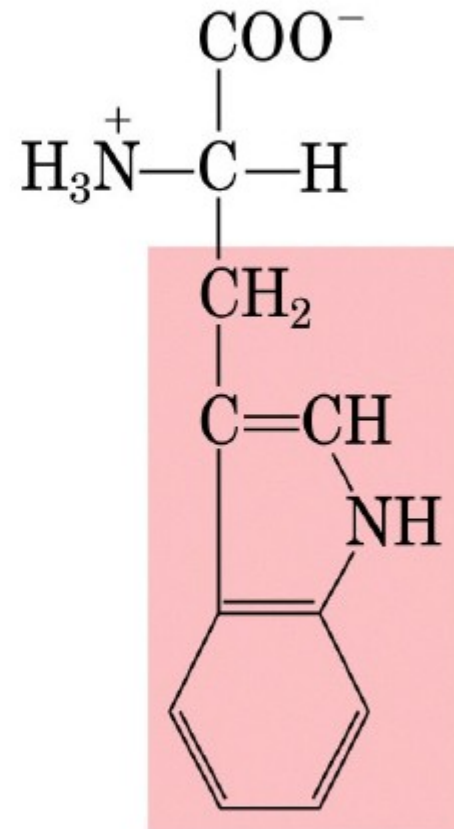
AMINOÁCIDOS APOLARES AROMÁTICOS



Phenylalanine

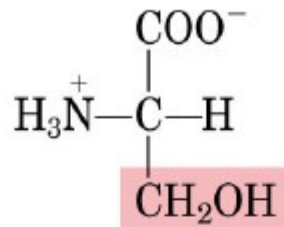


Tyrosine

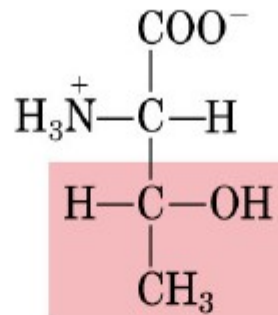


Tryptophan

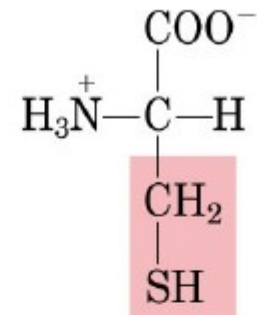
AMINOÁCIDOS POLARES SEM CARGA



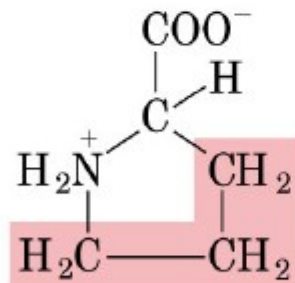
Serine



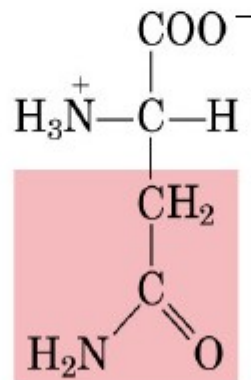
Threonine



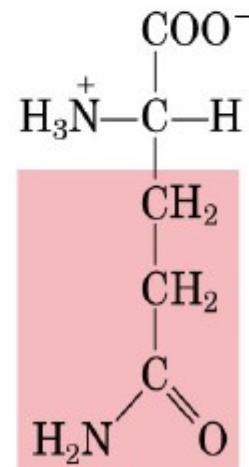
Cysteine



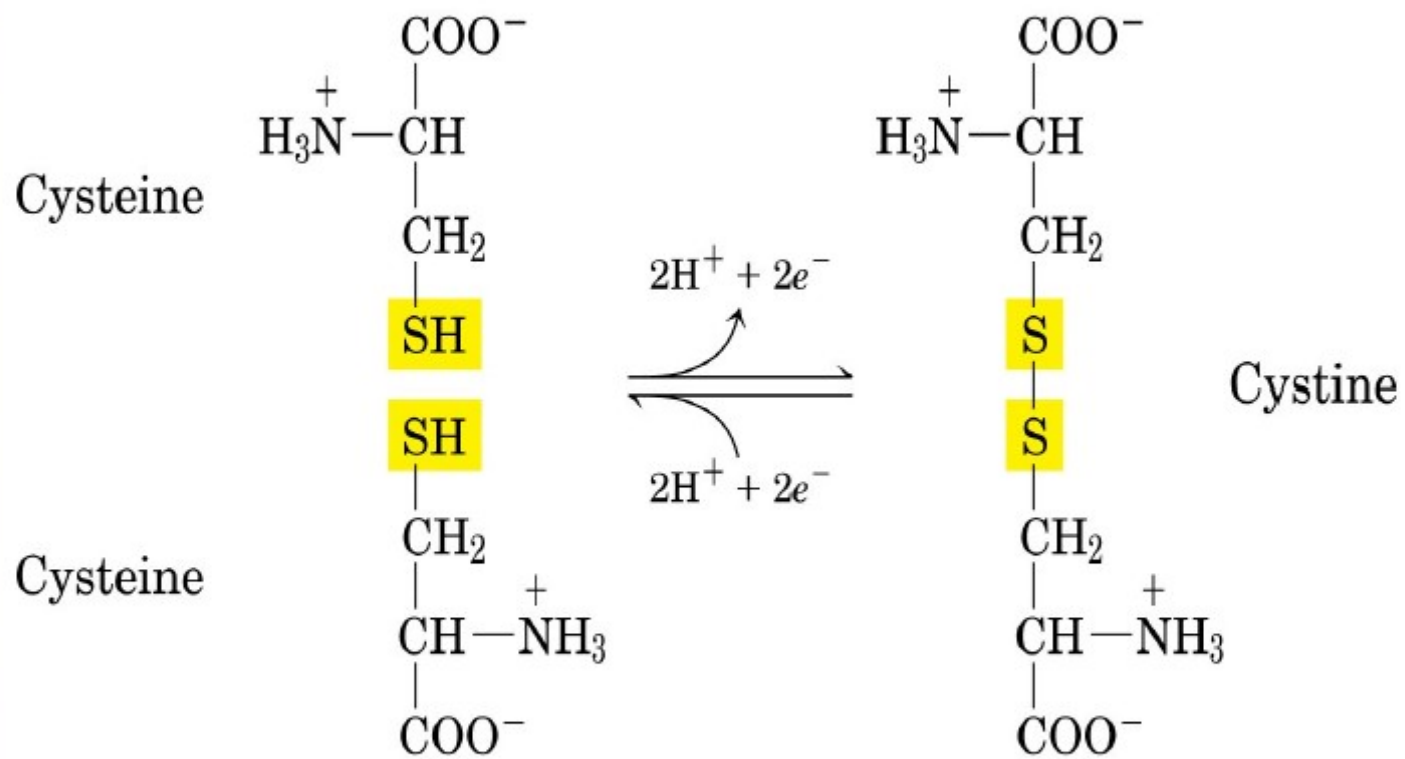
Proline



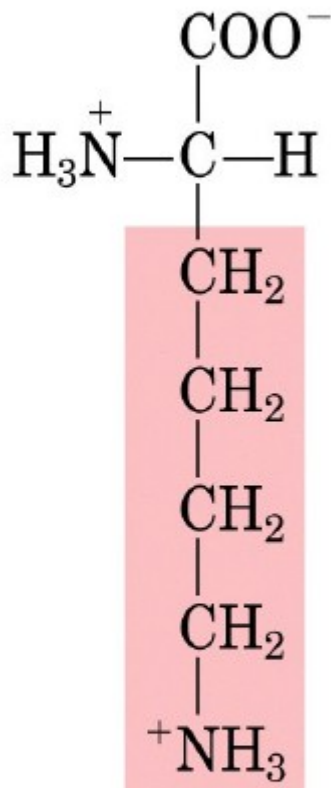
Asparagine



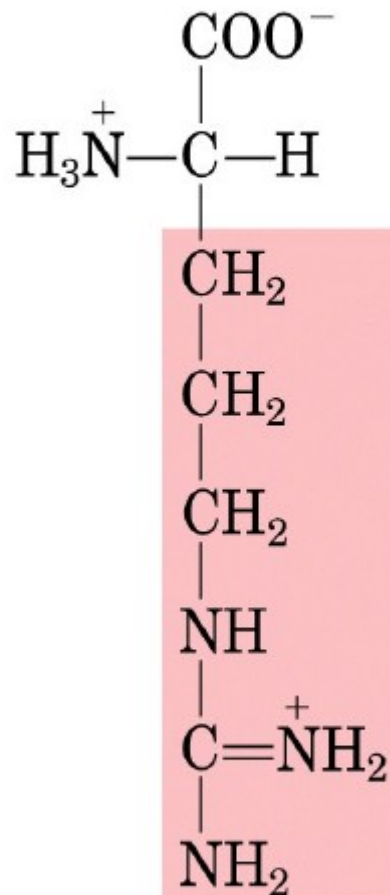
Glutamine



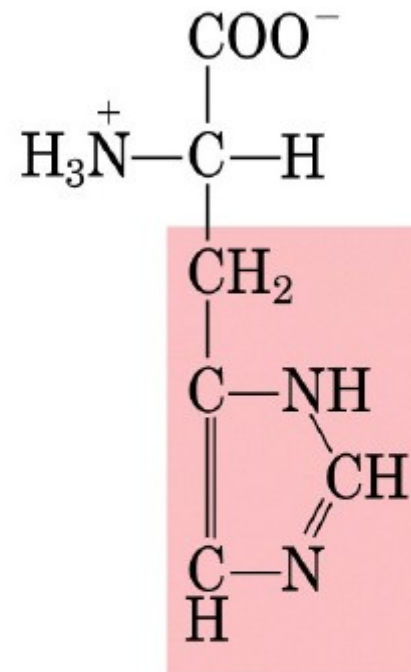
AMINOÁCIDOS POLARES CARREGADOS POSITIVAMENTE



Lysine

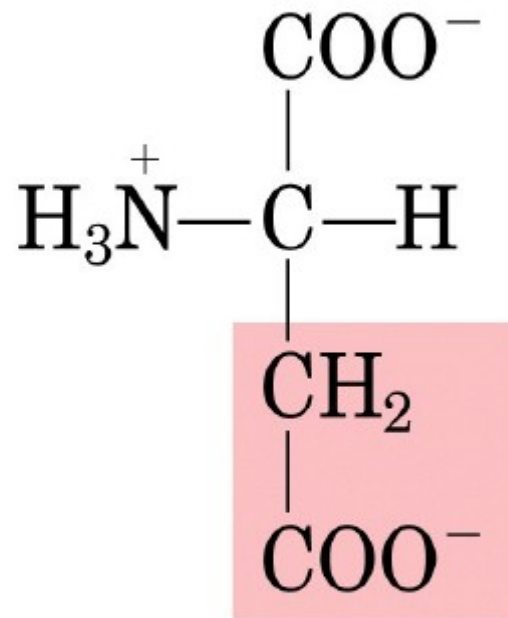


Arginine

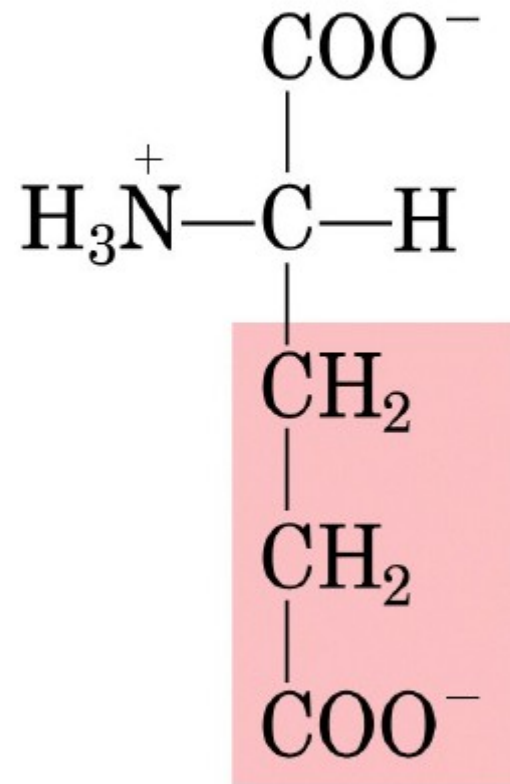


Histidine

AMINOÁCIDOS POLARES CARREGADOS NEGATIVAMENTE



Aspartate



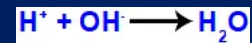
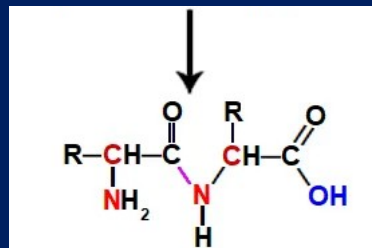
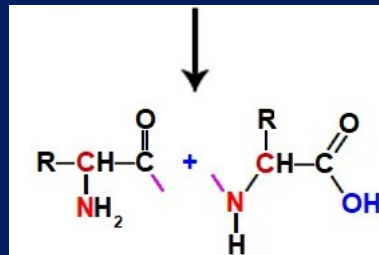
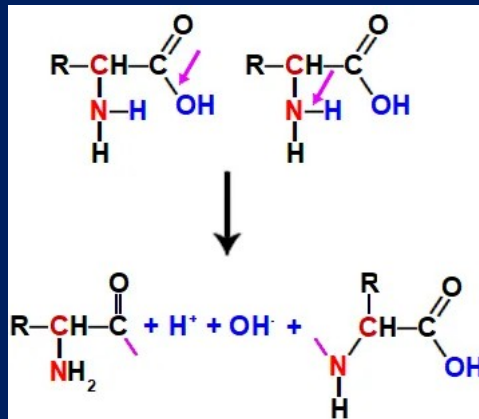
Glutamate

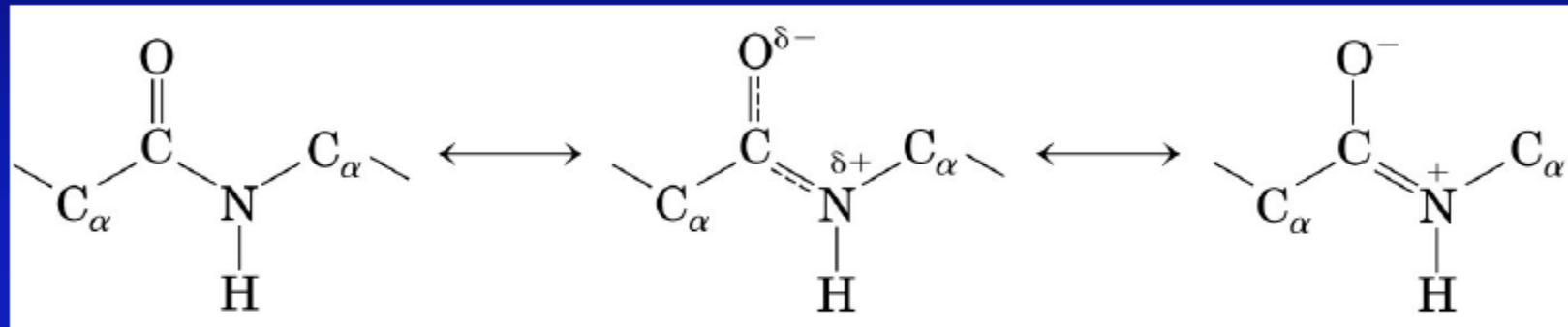
A LIGAÇÃO PEPTÍDICA

O grupo carboxílico de um aminoácido 1 pode se ligar covalentemente ao grupamento amino de um aminoácido 2, com perda de uma molécula de H_2O , formando uma ligação amida.

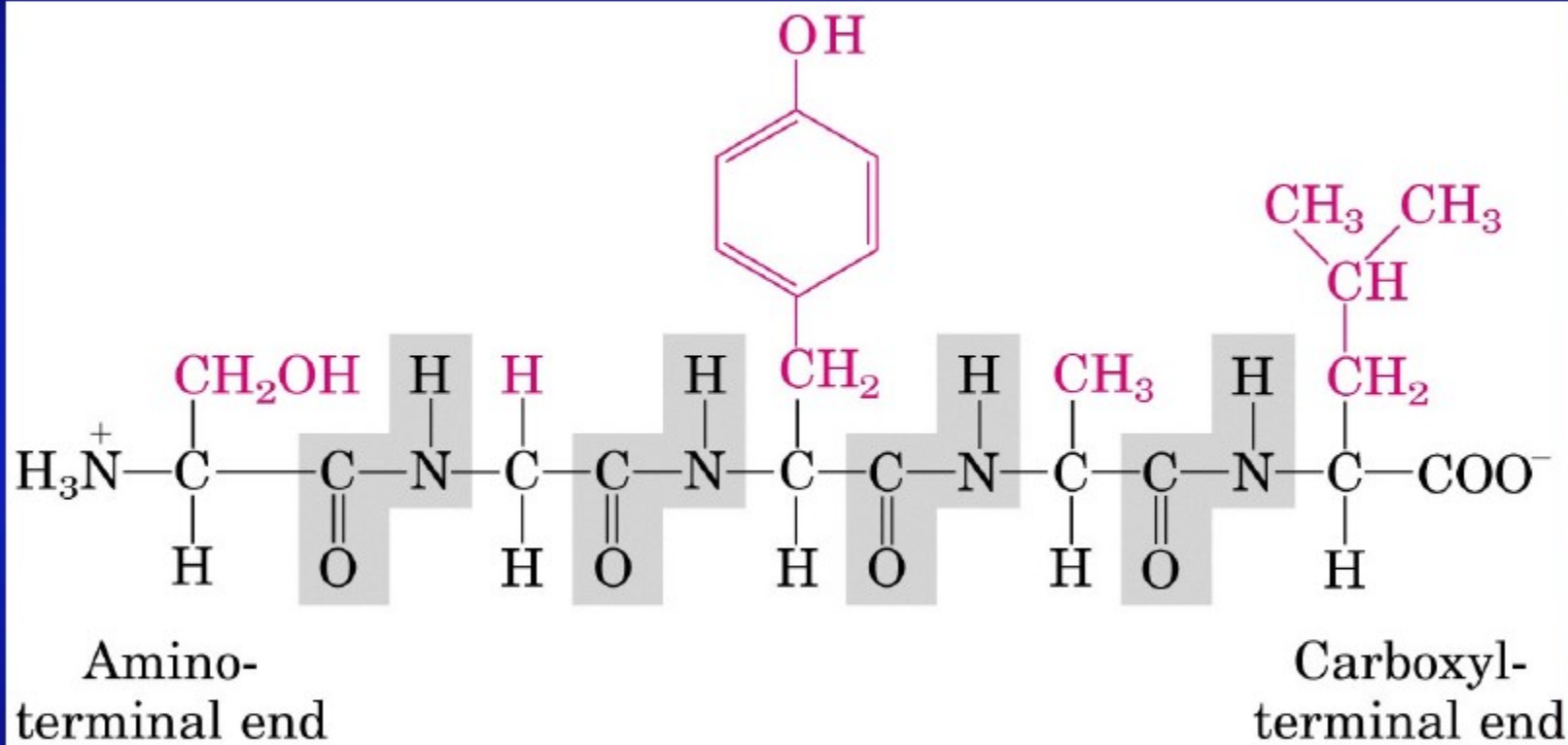
- dipeptídeos;**
- tripeptídeos;**
- oligopeptídeos;**
- polipeptídeos (proteínas);**

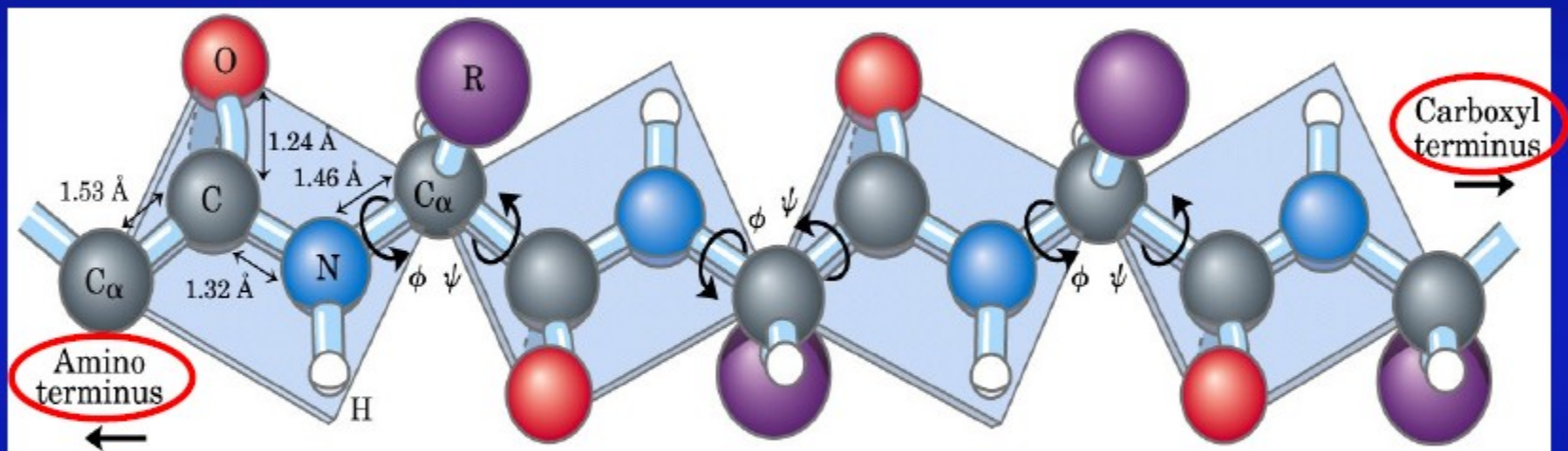
Ligação peptídica

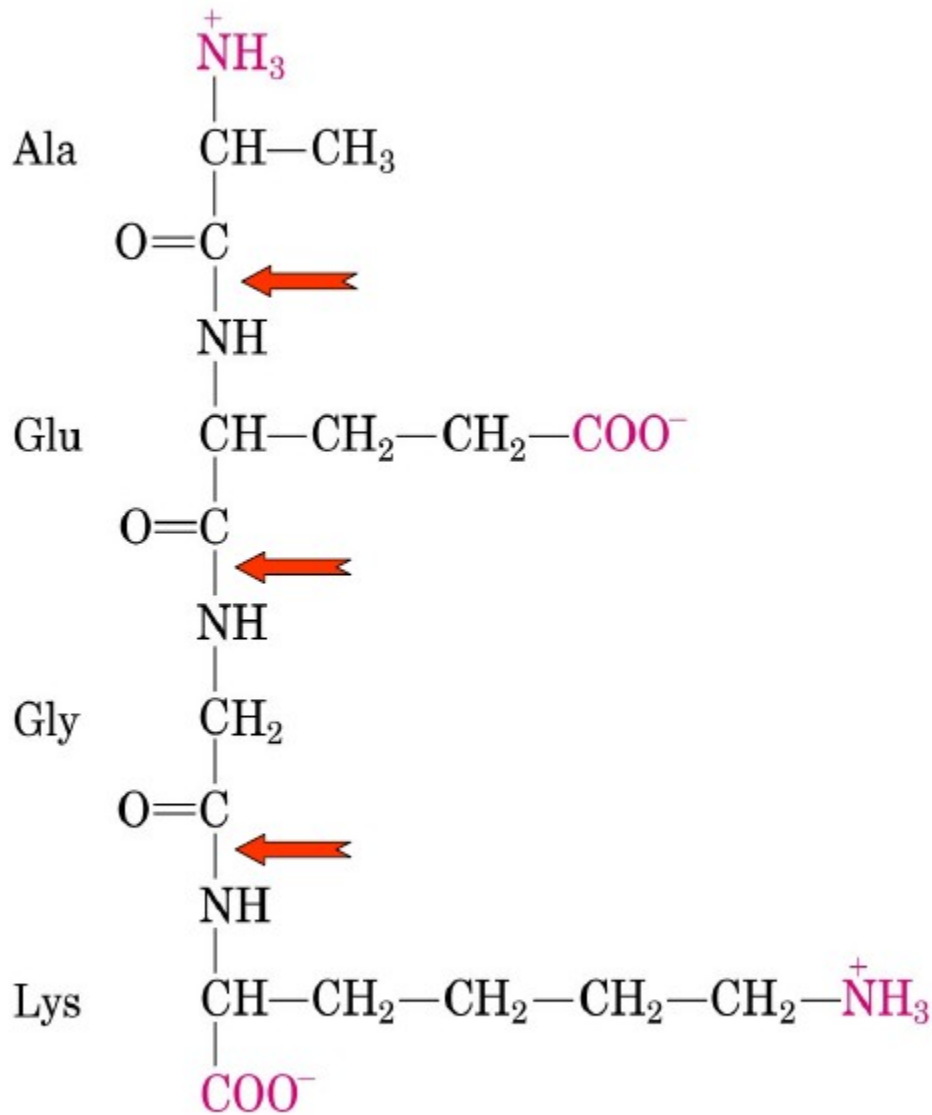




A ligação peptídica tem caráter de ligação dupla (sp^2), ou seja, são planares e rígidas, sendo que somente a ligação simples do carbono α permite rotação.



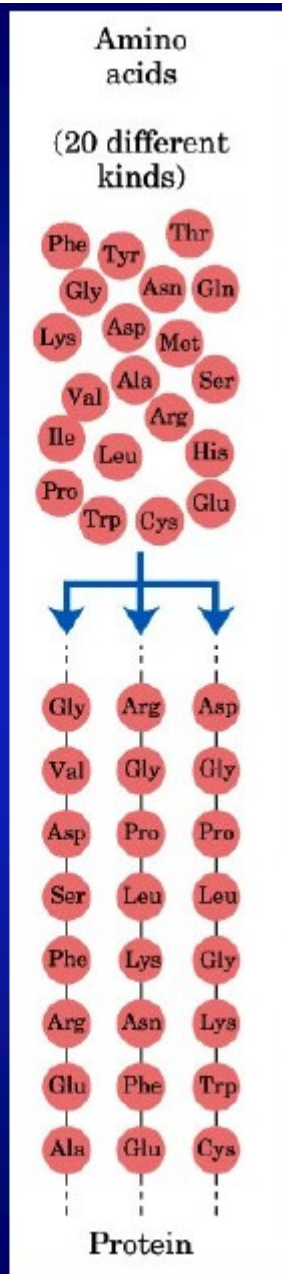




4 aa



**3 ligações
peptídicas**



AMINOÁCIDOS são
as unidades
monoméricas que
formam as
PROTEÍNAS

***ESTRUTURA
DE
PROTEÍNAS***

table 5-3

Amino Acid Composition of Two Proteins*

Amino acid	Number of residues per molecule of protein	
	Bovine cytochrome c	Bovine chymotrypsinogen
Ala	6	22
Arg	2	4
Asn	5	15
Asp	3	8
Cys	2	10
Gln	3	10
Glu	9	5
Gly	14	23
His	3	2
Ile	6	10
Leu	6	19
Lys	18	14
Met	2	2
Phe	4	6
Pro	4	9
Ser	1	28
Thr	8	23
Trp	1	8
Tyr	4	4
Val	3	23
Total	104	245

*Note that standard procedures for the acid hydrolysis of proteins convert Asn and Gln to Asp and Glu, respectively. In addition, Trp is destroyed. Special procedures must be employed to determine the amounts of these amino acids.

table 5-2

Molecular Data on Some Proteins

	Molecular weight	Number of residues	Number of polypeptide chains
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	609	1
Hexokinase (yeast)	102,000	972	2
RNA polymerase (<i>E. coli</i>)	450,000	4,158	5
Apolipoprotein B (human)	513,000	4,536	1
Glutamine synthetase (<i>E. coli</i>)	619,000	5,628	12
Titin (human)	2,993,000	26,926	1

A estrutura das proteínas pode ser descrita em quatro níveis:

1. Estrutura primária

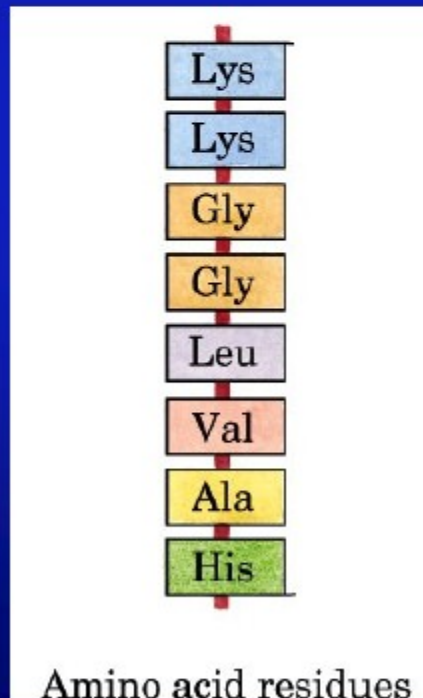
2. Estrutura secundária

3. Estrutura terciária

4. Estrutura quaternária

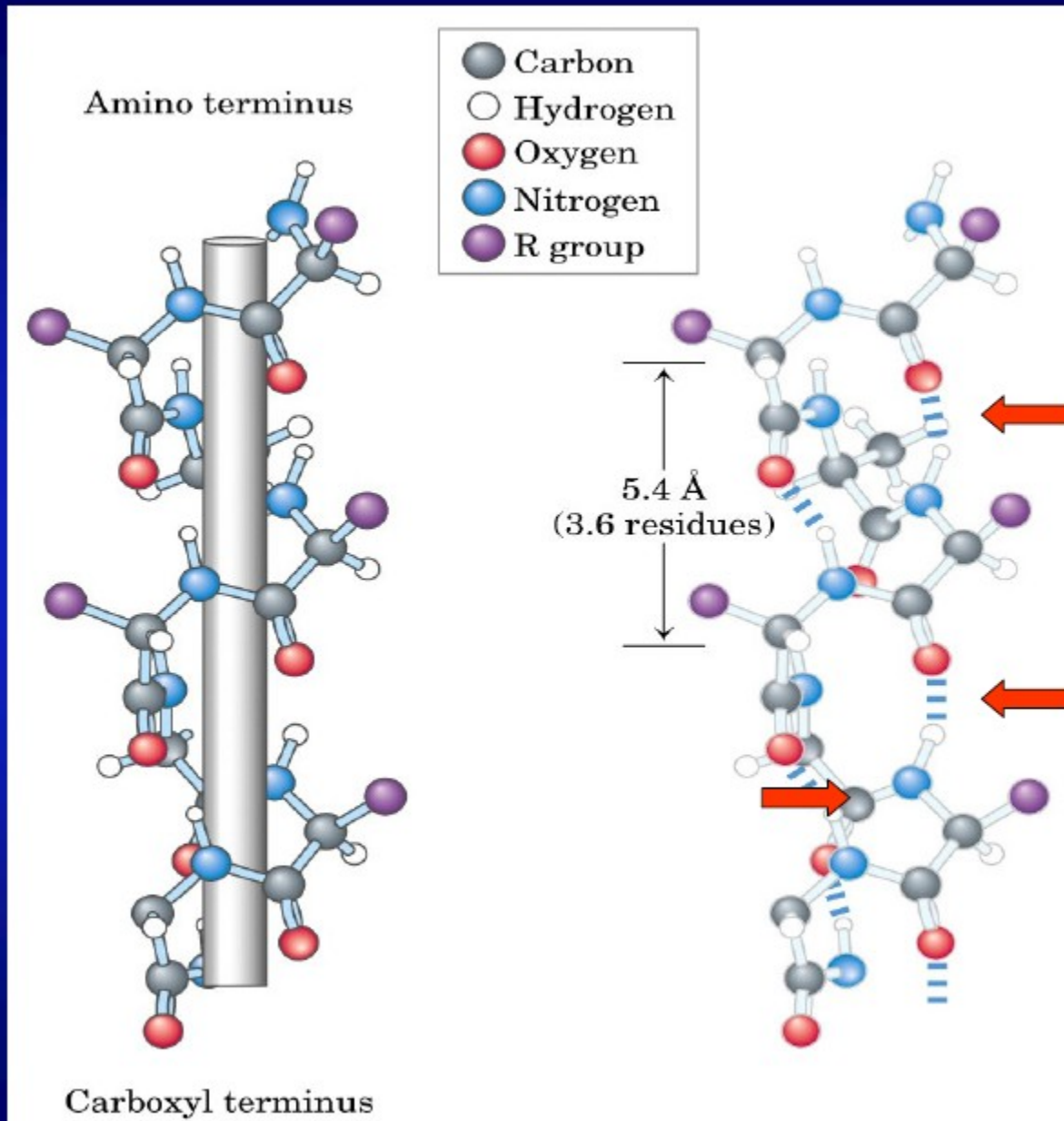
1. Estrutura primária

Refere-se à sequência de aminoácidos ao longo da cadeia polipeptídica, mantida por **ligações covalentes**, que é determinada geneticamente, sendo específica para cada proteína;

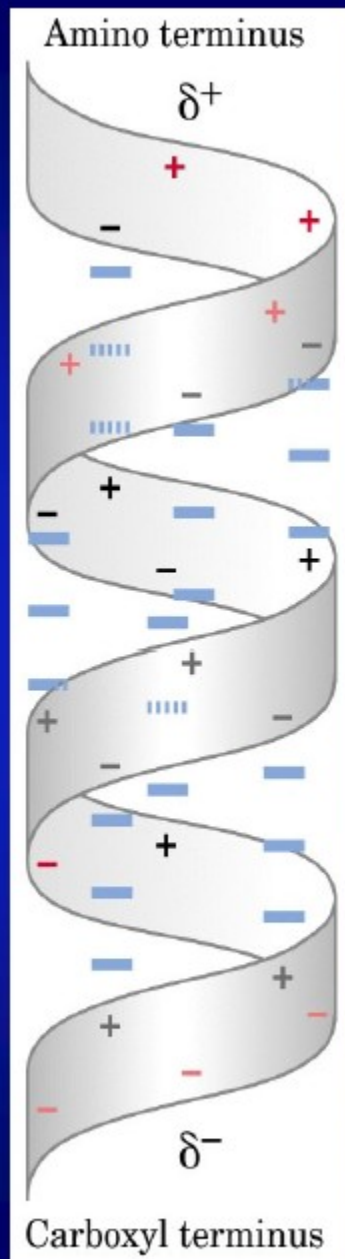


2. Estrutura secundária

Refere-se à conformação adquirida por segmentos da cadeia polipeptídica. Normalmente, apresenta-se como α -hélice ou folha β -pregueada e esses dois tipos de estrutura secundária podem ocorrer nas proteínas em proporções variáveis;



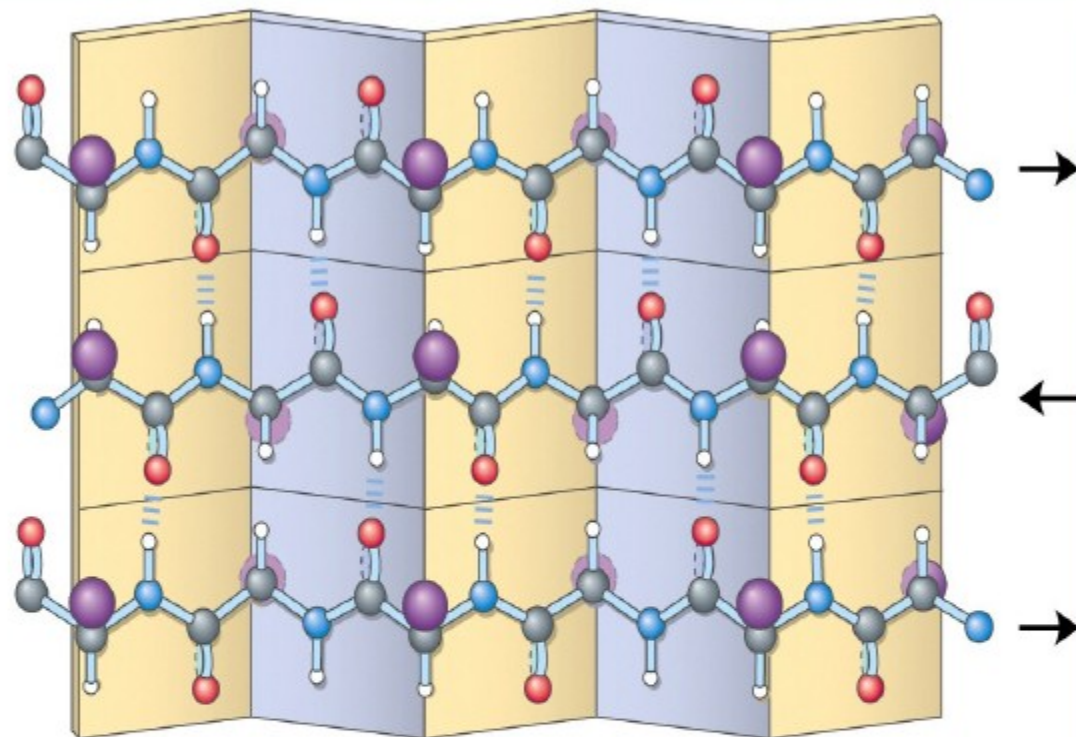
**pontes
de
hidrogênio
INTRACADEIA**



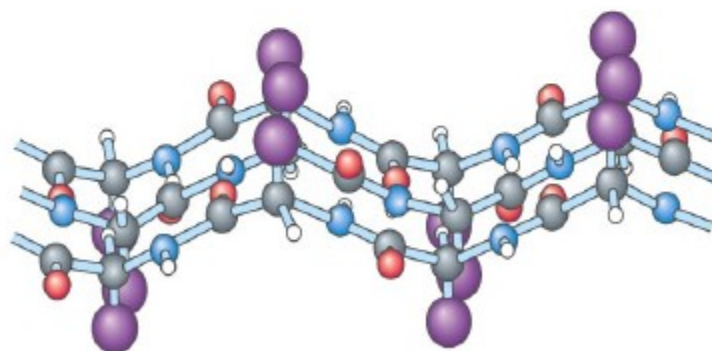
**interações
eletrostáticas**

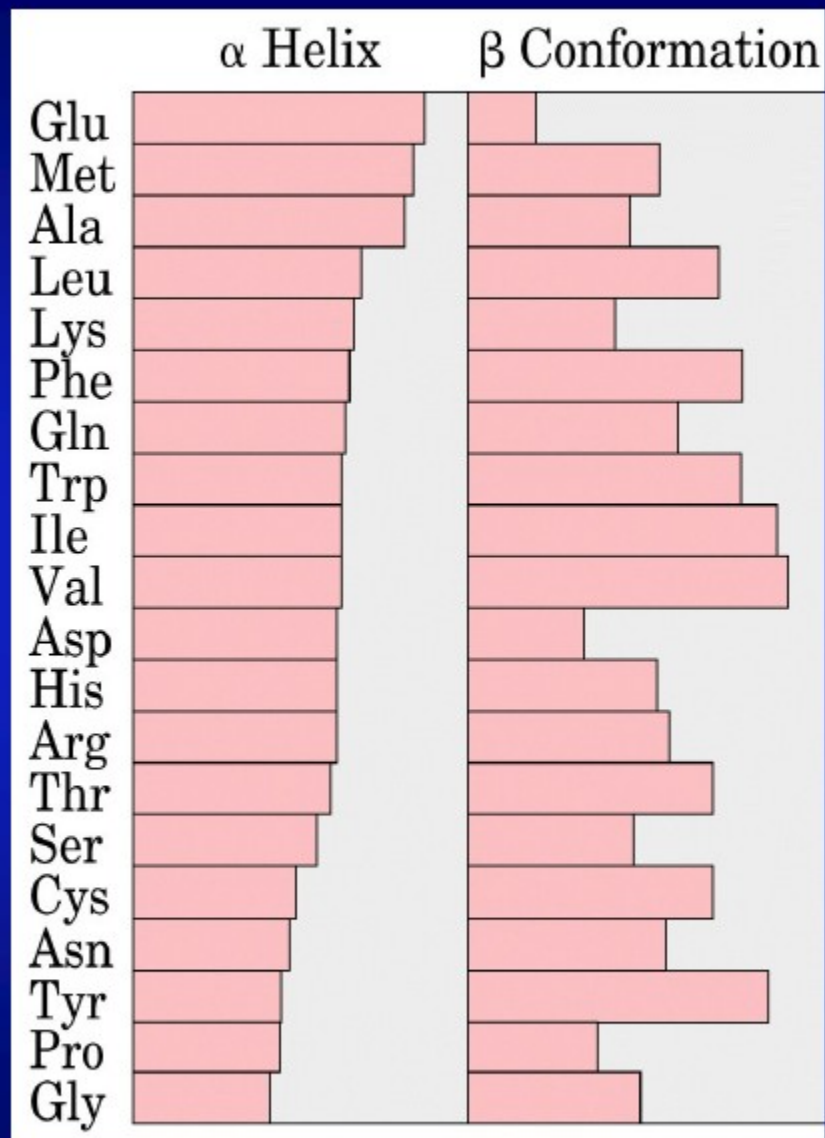
**pontes
de
hidrogênio
INTERCADEIAS**

Top view

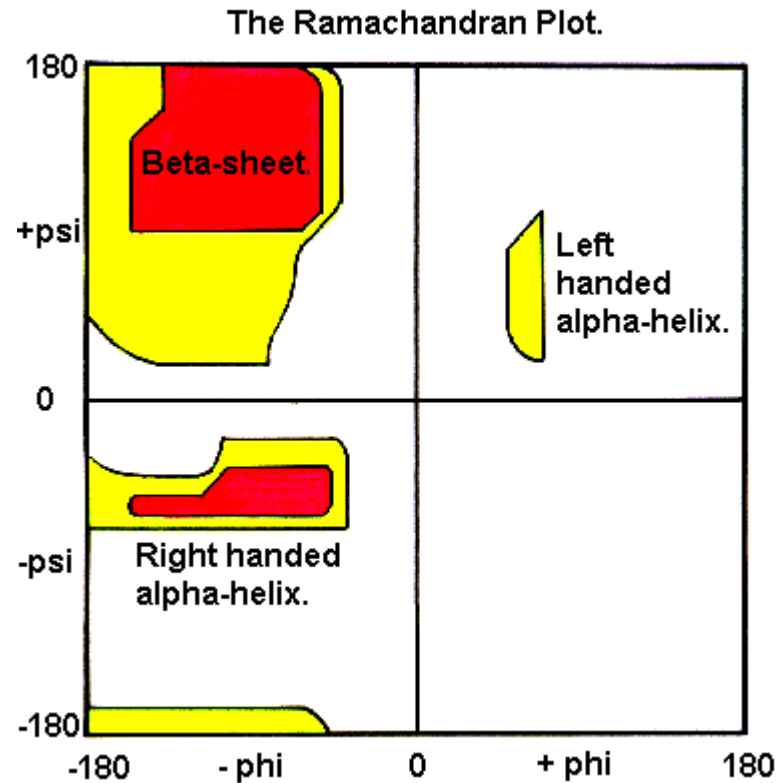


Side view



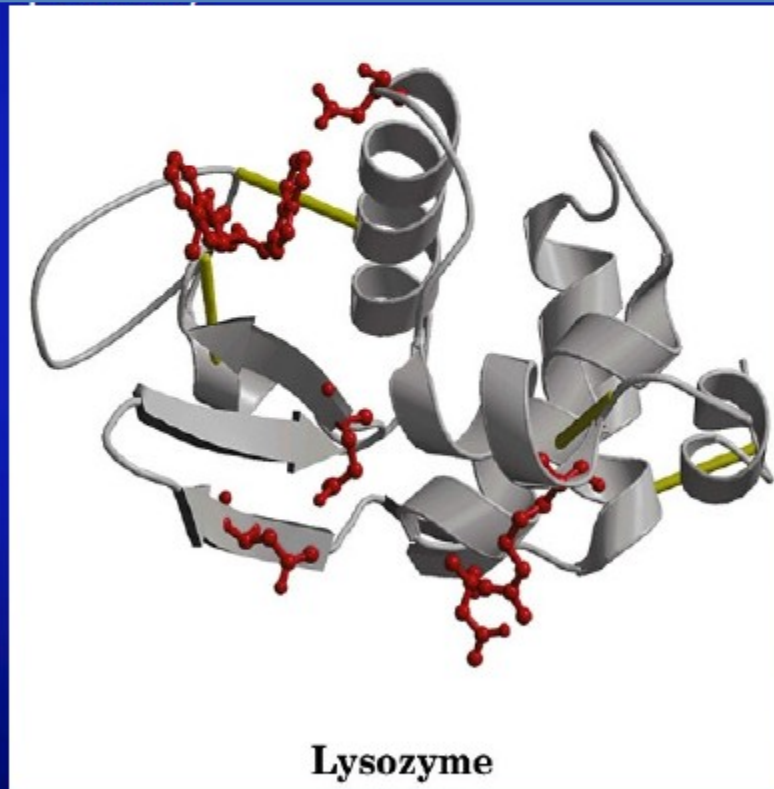


Plot de Ramachandran



3. Estrutura terciária

Estrutura tridimensional de uma proteína constituída por apenas uma cadeia polipeptídica



4. Estrutura quaternária

Estrutura tridimensional de uma proteína constituída por mais de uma cadeia polipeptídica

Polypeptide
chain

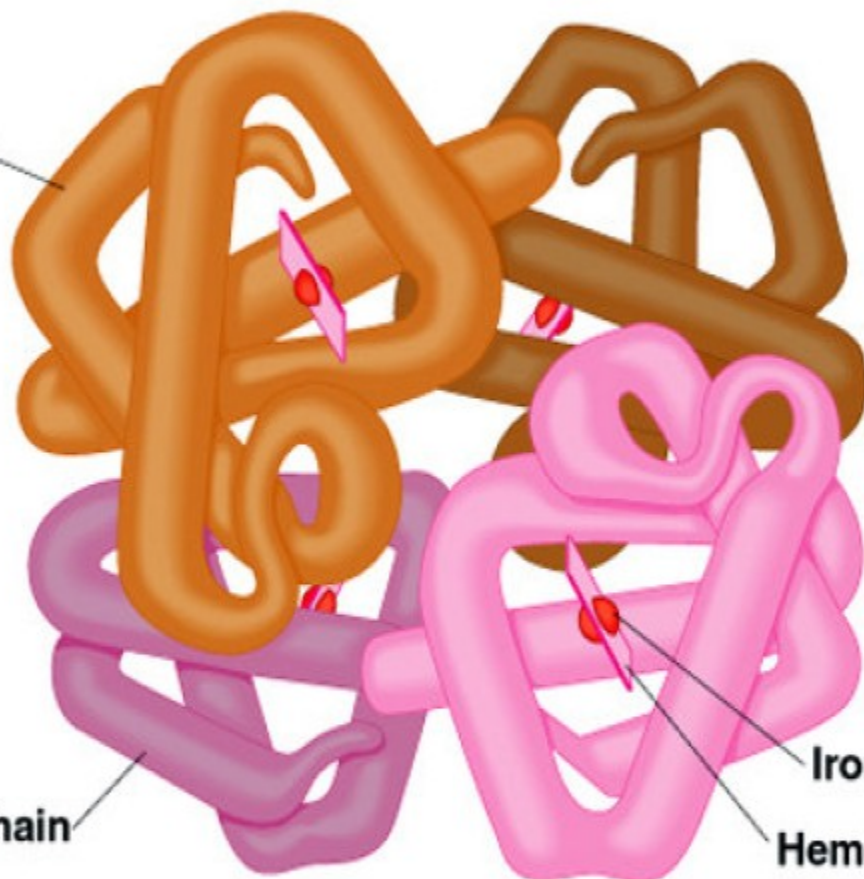
β chain

α chain

Iron **Fe**

Heme

Hemoglobin

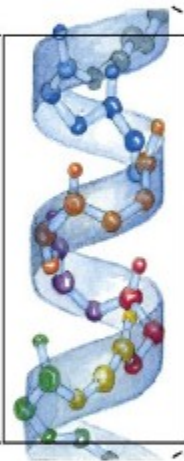


**Primary
structure**



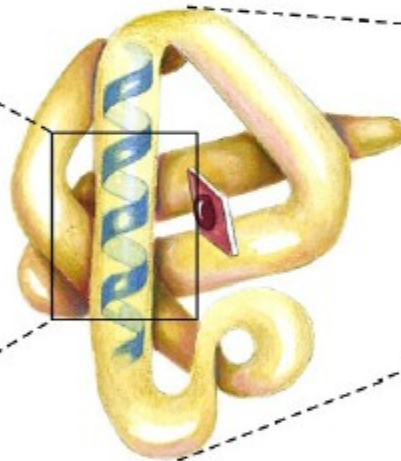
Amino acid residues

**Secondary
structure**



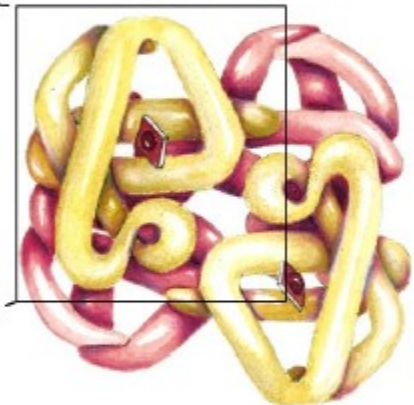
α Helix

**Tertiary
structure**



Polypeptide chain

**Quaternary
structure**



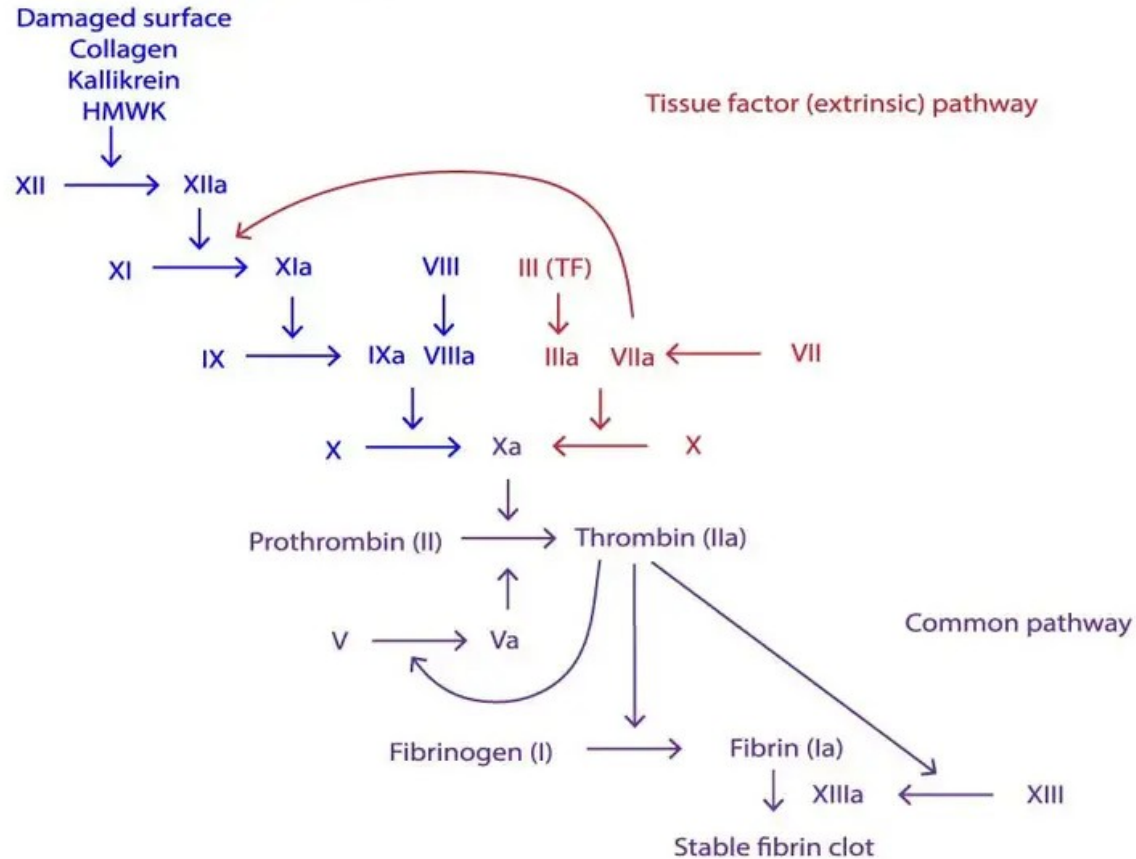
Assembled subunits

Proteínas recombinantes

aplicações

Cascata da coagulação sanguínea

Contact activation (intrinsic) pathway



Hemofilia

Tipos de Hemofilia:

A hemofilia é classificada nos tipos A e B. Pessoas com Hemofilia tipo A são deficientes de fator VIII (oito).

Já as pessoas com hemofilia do tipo B são deficientes de fator IX (nove).

Os sangramentos são iguais nos dois tipos, porém a gravidade dos sangramentos depende da quantidade de fator presente no plasma (líquido que representa 55% do volume total do sangue).

Tratamento:

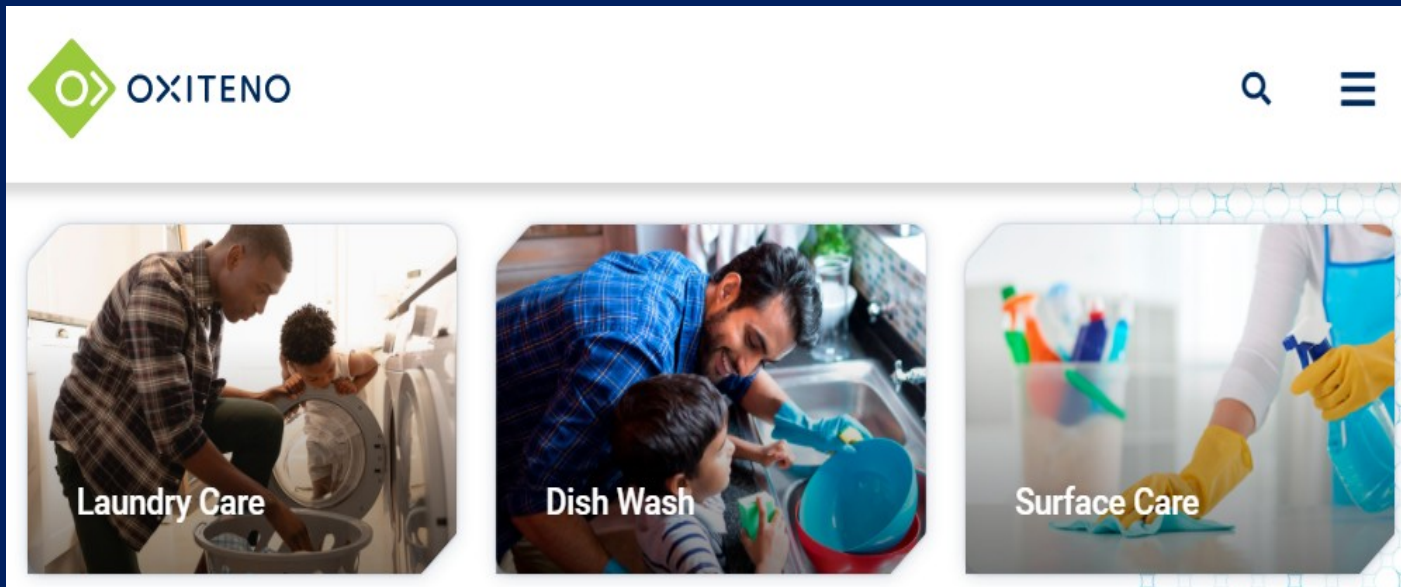
O tratamento é feito com a reposição intra-venal (pela veia) do fator deficiente, mas para que o tratamento seja completo, o paciente deve fazer exames regularmente e jamais utilizar medicamentos que não sejam recomendados pelos médicos.

Proteínas recombinantes - uso médico-farmacológico

Some Recombinant Proteins Were Produced and Commercialized in Medicine				
Brand	Generic	Company	Therapeutic category	Indications
THE FIRST GENERATION OF THERAPEUTIC PROTEINS				
Humulin	Insulin	Eli Lilly	Diabetes	Diabetes
Hematrope	Recombinant somatropin	Eli Lilly	Hormones	Growth failure
Genotropin	Somatropin	Pfizer	Hormones	Growth failure
Intron A	Interferon alpha 2b	Schering-Plough	Anti-infective	Viral infections
Avonex	Interferon beta-1a	Biogen Idec	Multiple sclerosis	Chronic inflammatory demyelinating polyneuropathy
Betaseron/Betaferon	Interferon beta-1b	Schering AG	Multiple sclerosis	Multiple sclerosis
NeoRecormon	Epoetin beta	Roche	Blood modifier	Anemia
Kogenate	Factor VIII	Bayer	Blood modifier	Hemophilia
NovoSeven	Factor VIIa	Novo Nordisk	Blood modifier	Hemophilia
Benefix	Factor IX	Wyeth	Blood modifier	Hemophilia
Fabrazyme	Agalsidase beta	Genzyme	Enzymes	Fabry disease
Replagal	Agalsidase alfa	TKT Europe	Enzymes	Fabry disease
Pulmozyme	Dornase alpha	Genetech	Enzymes	Cystic fibrosis
Actimmune/Asithone	Alteplase	Genetech	Blood factor	Myocardial infarction

Proteínas recombinantes – indústria de detergentes

- Lipases, proteases, glicosidases



Desejo a todos um excelente
quadrimestre, que consiga agregar
algum conhecimento a vocês!