Biochemistry

2.1) Biomolecules

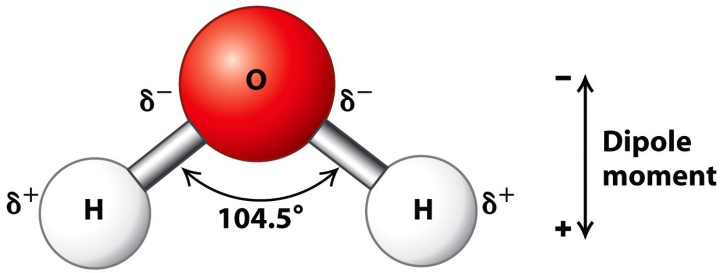
Prof. Dr. Klaus Heese

Biochemistry

- Bio-Molecules,
- Amino Acids,
- Peptides / Proteins

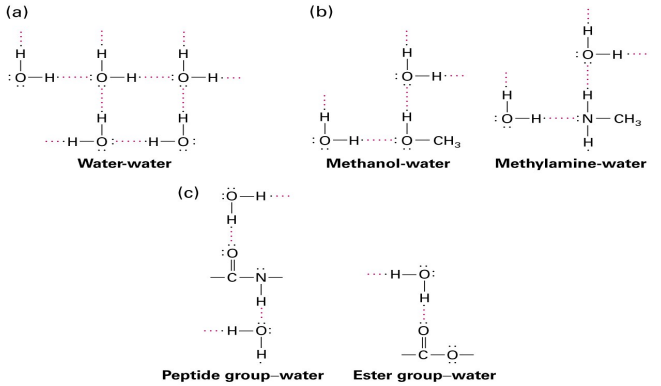
Prof. Dr. Klaus Heese

Water – H_2O

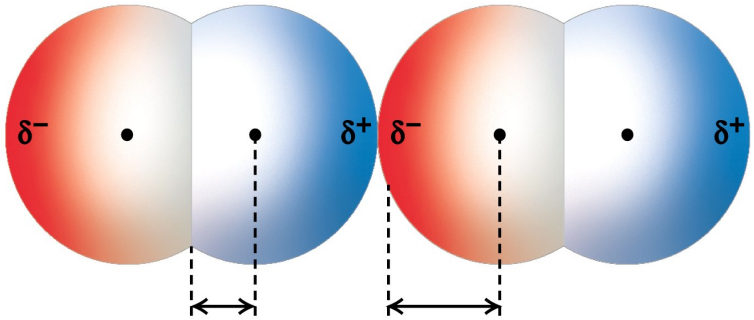


Bio-Molecules – Interactions

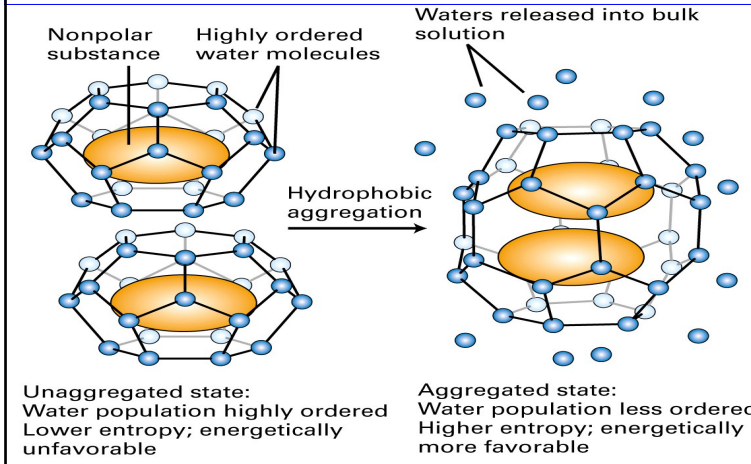
Hydrogen Bonds



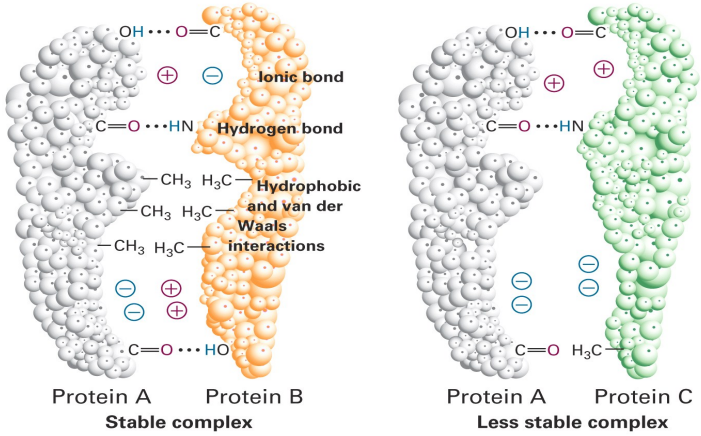
Range / radius of charges and influences for molecule-molecule interactions



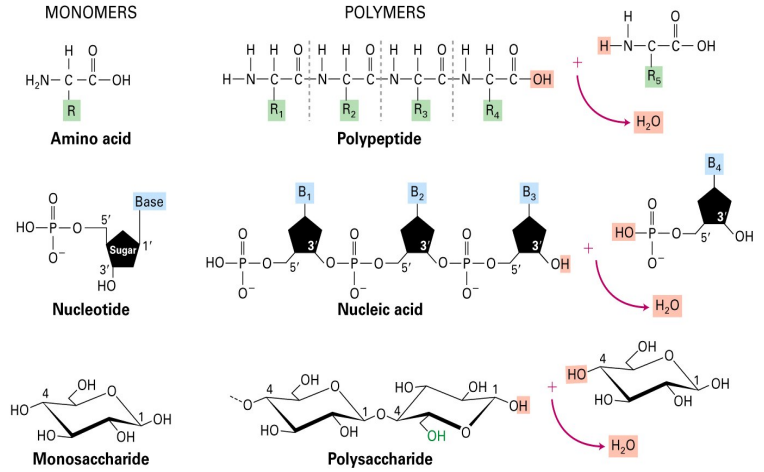
Water molecules modulate molecule interactions / behavior / functions



Various non-covalent protein-protein interactions



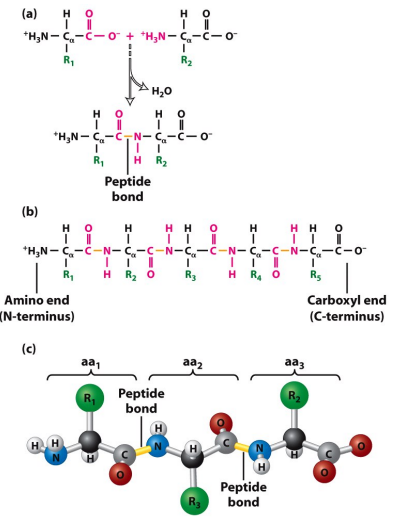
Essential Bio-Energy-related Bio-Molecules



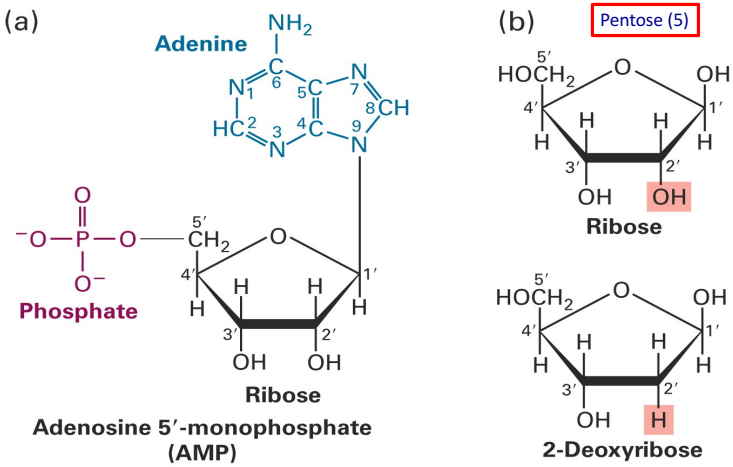
Amino acids

Peptides

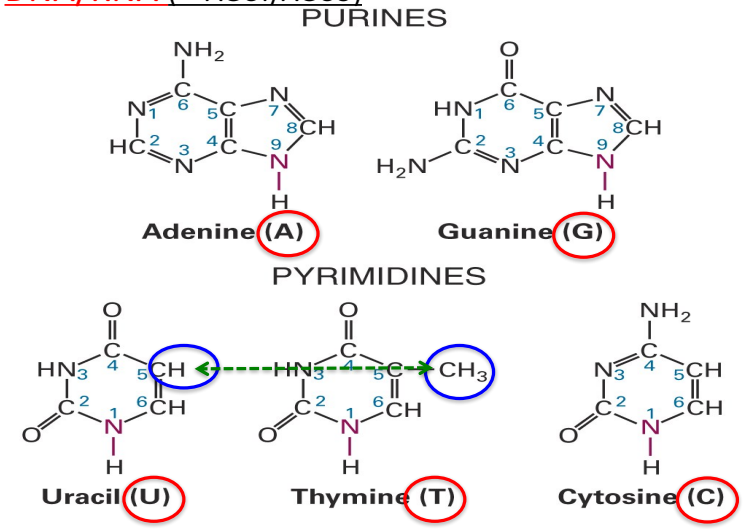
Proteins

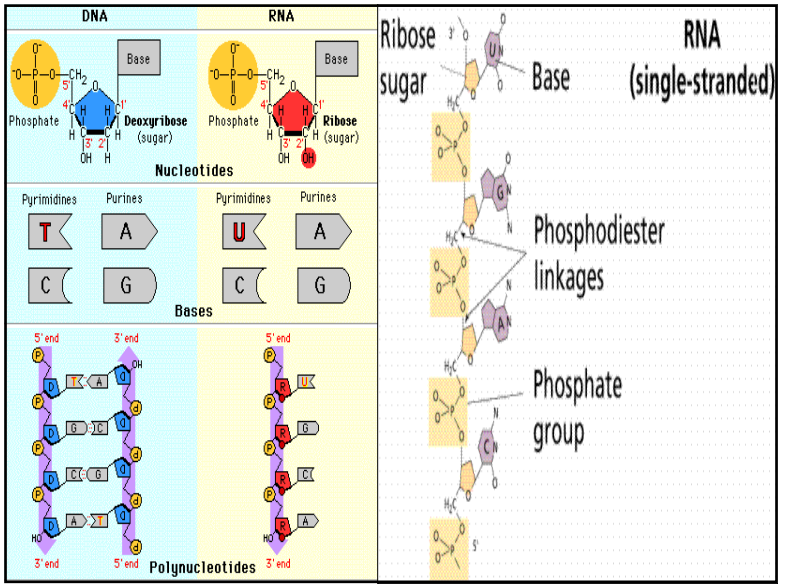


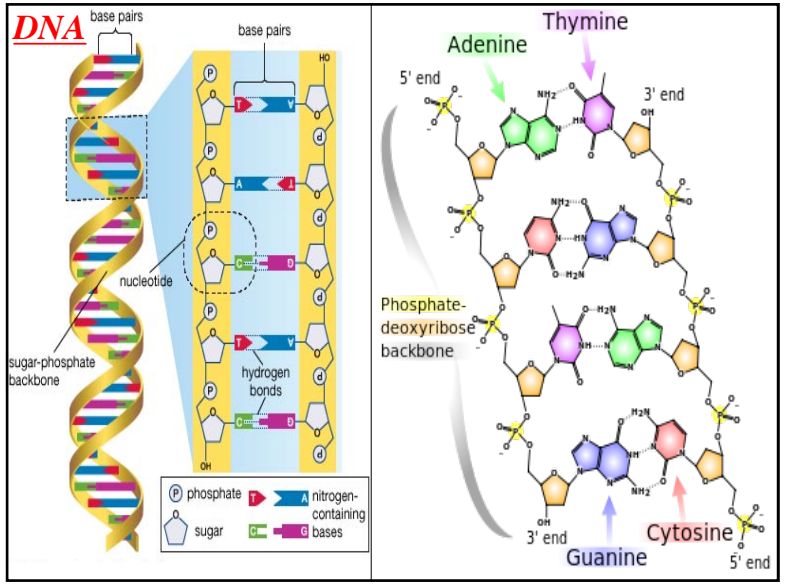
THE Bio-Energy Molecule ATP



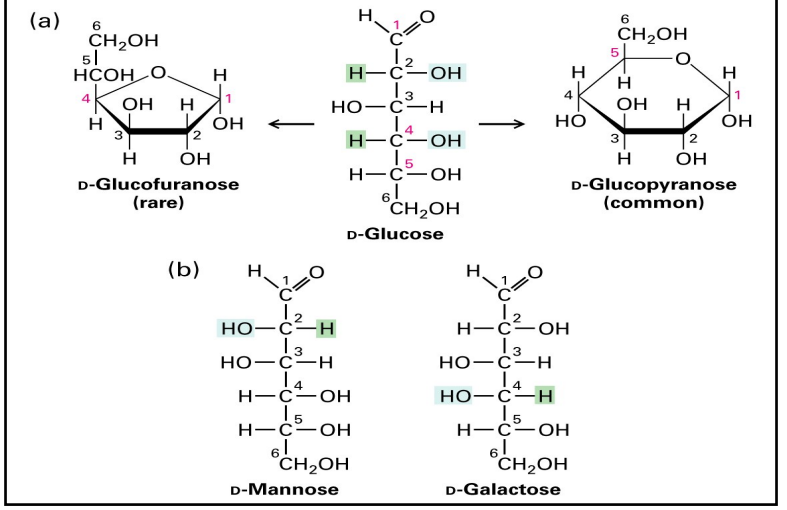
DNA/RNA (= AGCT/AGCU)





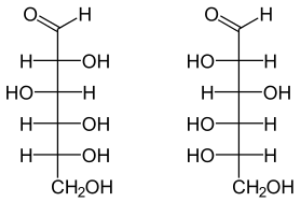


Bio-Energy: Chemical Structure of Hexoses ($C_6H_{12}O_6$)



Enantiomers - Steroisomers

D-/L-forms



D-Glucose

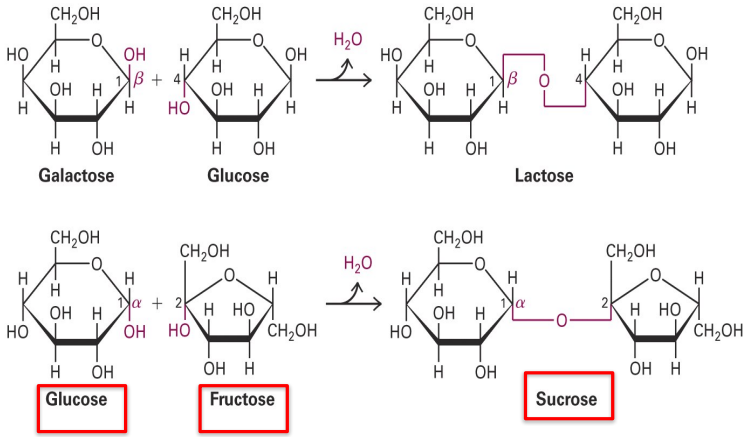
L-Glucose

(natural)

only synthetic, good for diabetic patients but expensive as gold

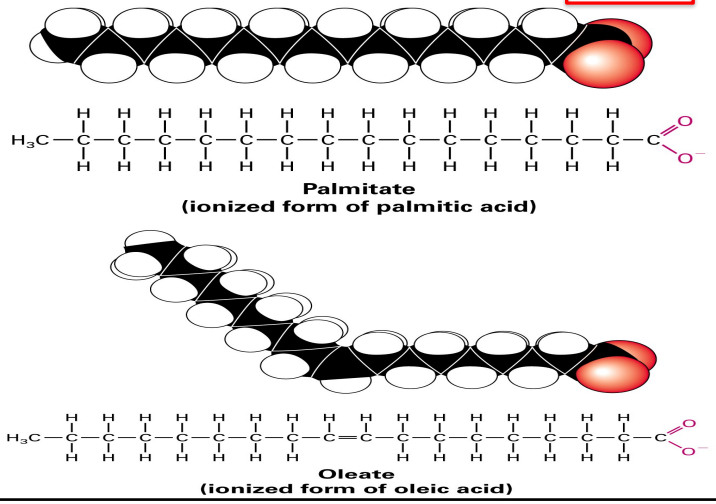
Bio-Energy: Chemical Structure of Hexoses ($C_6H_{12}O_6$)

Di-Saccharides Lactose and Sucrose



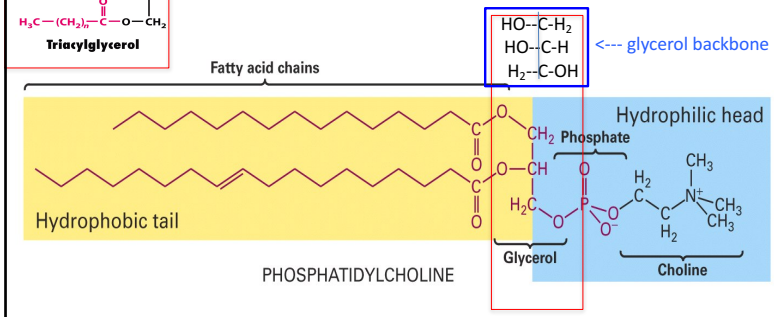
Lipids – Cell Membrane and Cell Metabolism etc

The effect of a double bond on the shape of fatty acids



Phosphatidylcholine, a typical phosphoglyceride

Lipids

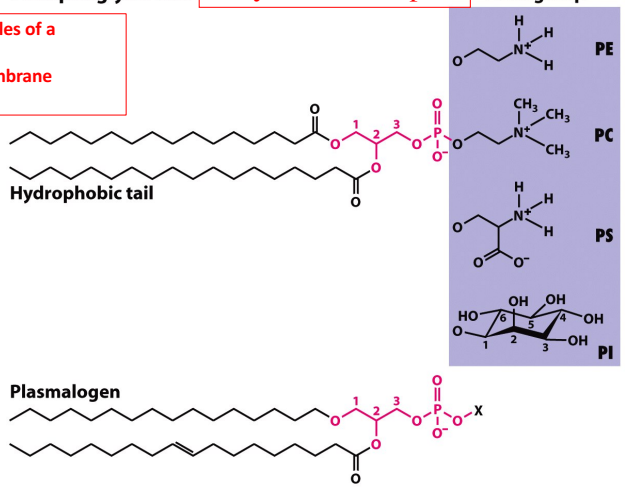


All phosphoglycerides are amphipathic – having a hydrophobic tail (yellow) and a hydrophilic head (blue) in which glycerol is linked via a phosphate group to an alcohol. Either of or both the fatty acyl side chains in a phosphoglyceride may be saturated or unsaturated. In phosphatidic acid (red), the simplest phospholipid, the phosphate is not linked to an alcohol.

Phosphoglycerides

Fatty Acids & Lipids

Molecules of a Biomembrane

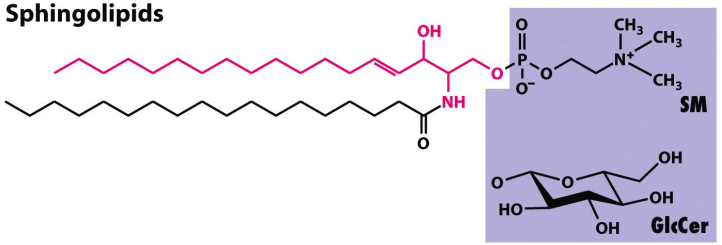


PC = phosphatidylcholine; PE = phosphatidylethanol; PS = phosphatidylserine; SM = sphingomyelin; PI = phosphoinositol

Sphingolipids

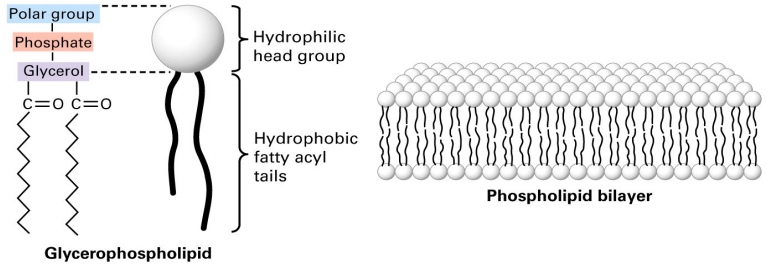
Fatty Acids & Lipids

Molecules of a Biomembrane

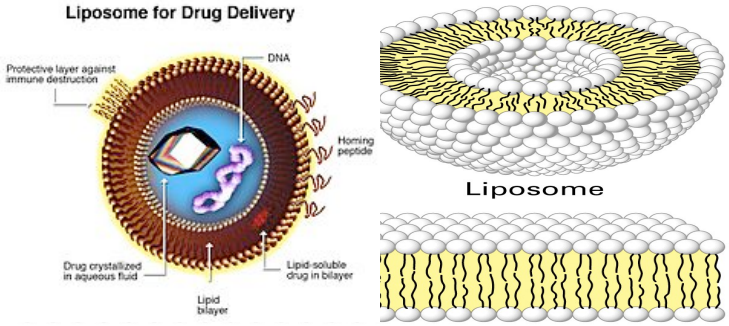


PC = phosphatidylcholine; PE = phosphatidylethanol; PS = phosphatidylserine; SM = sphingomyelin; PI = phosphoinositol

Essential Cell Membrane Molecules



Cross-sectional views of the three structures formed by phospholipids in aqueous solutions



The white spheres depict the hydrophilic heads of the phospholipids, and the squiggly black lines (in the yellow regions) represent the hydrophobic tails. Shown are a spherical micelle with a hydrophobic interior composed entirely of fatty acyl chains; a spherical liposome, which has two phospholipid layers and an aqueous center; and a two-molecule-thick sheet of phospholipids, or bilayer, the basic structural unit of bio-membranes.

Biochemistry

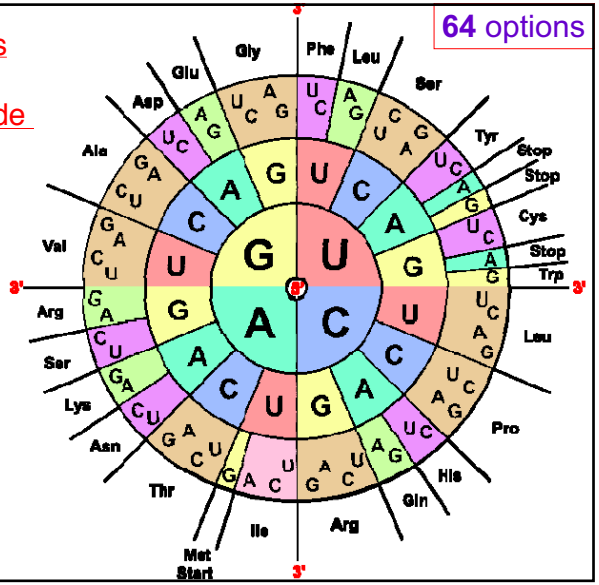
2.2) Amino Acids

Prof. Dr. Klaus Heese

Amino Acids

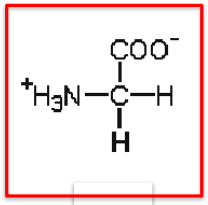
Genetic Code

64 options



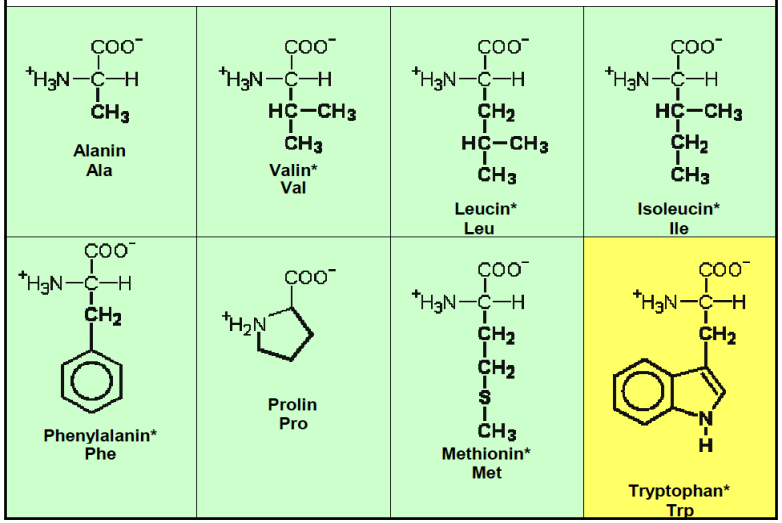
read 5' ---> 3'

20 Proteinogen Amino Acids = amino acids determined in the genetic code

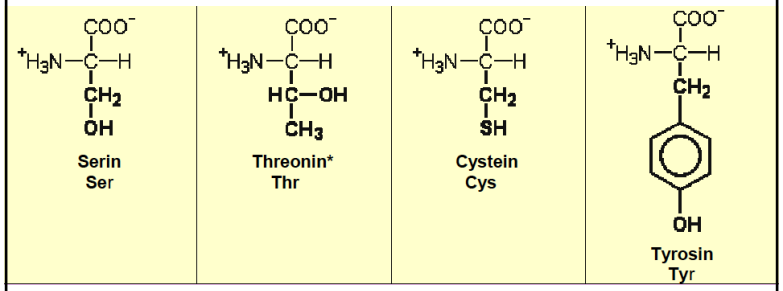


Gly

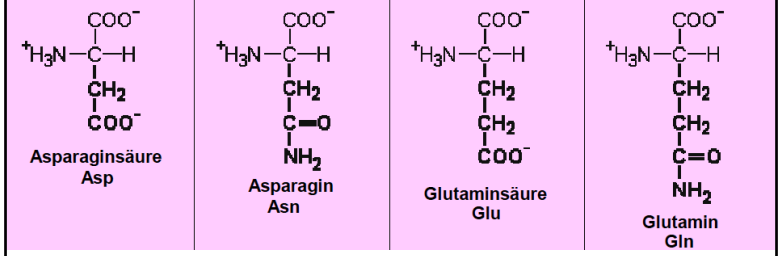
Hydrophobic Amino Acids



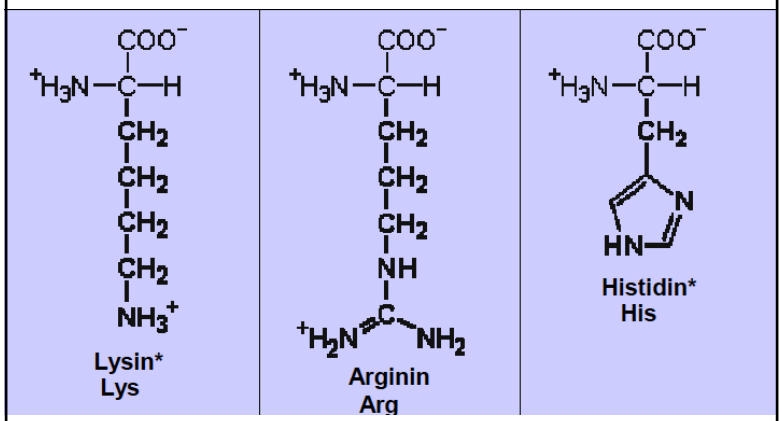
Amino Acids with polar side chains



Acidic Amino Acids

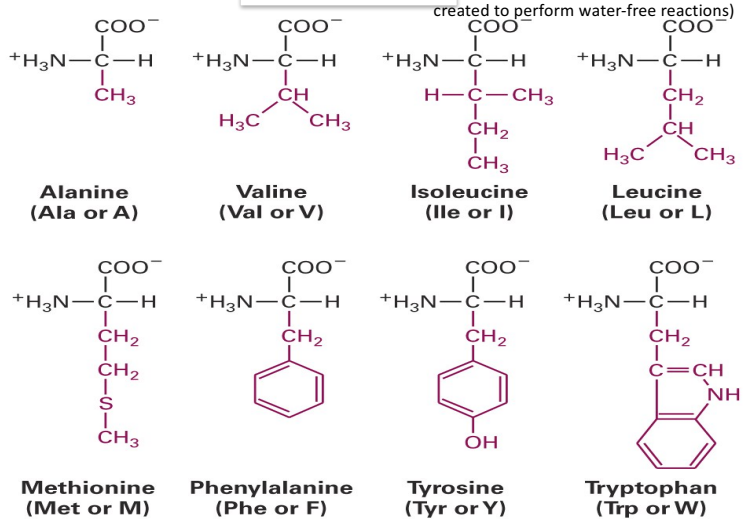


Basic Amino Acids

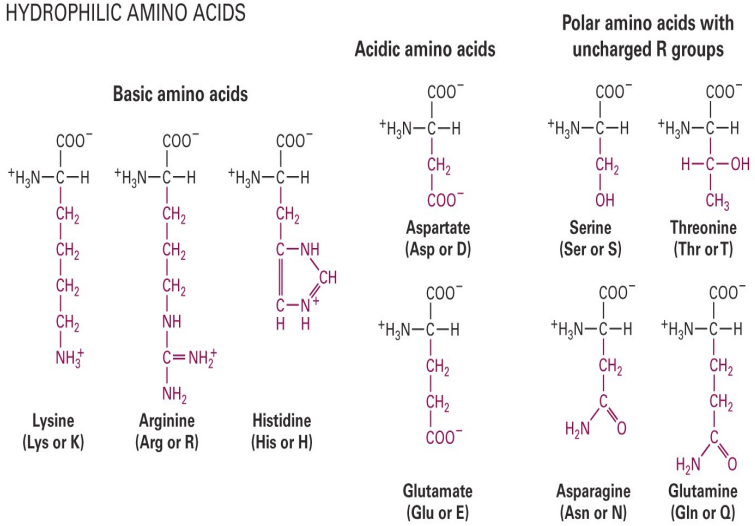


HYDROPHOBIC AAs

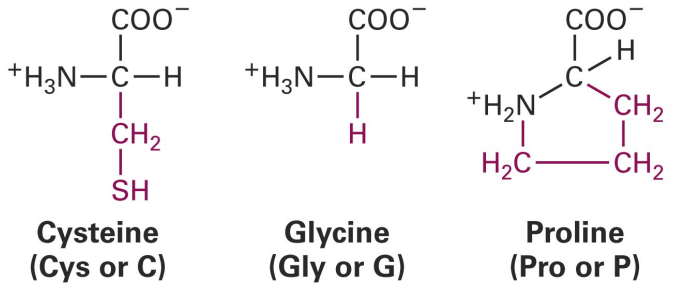
(lipophil, apolar, upon association of lipophilic groups a water-free space is created to perform water-free reactions)



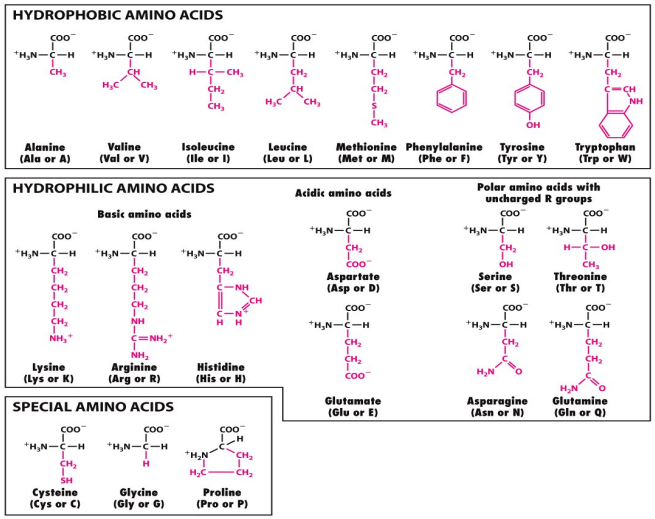
HYDROPHILIC AMINO ACIDS

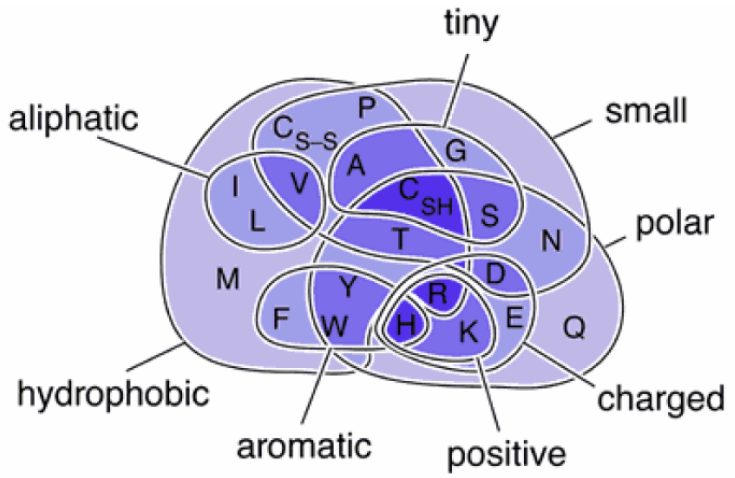


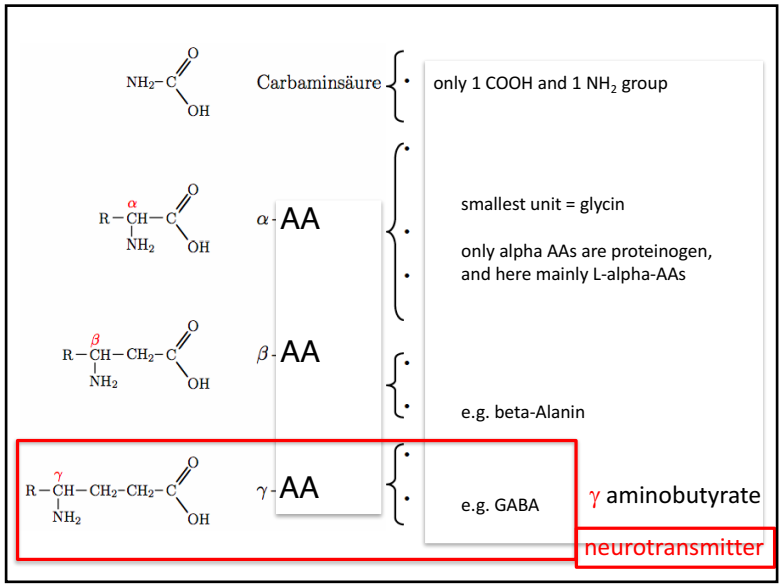
SPECIAL AMINO ACIDS

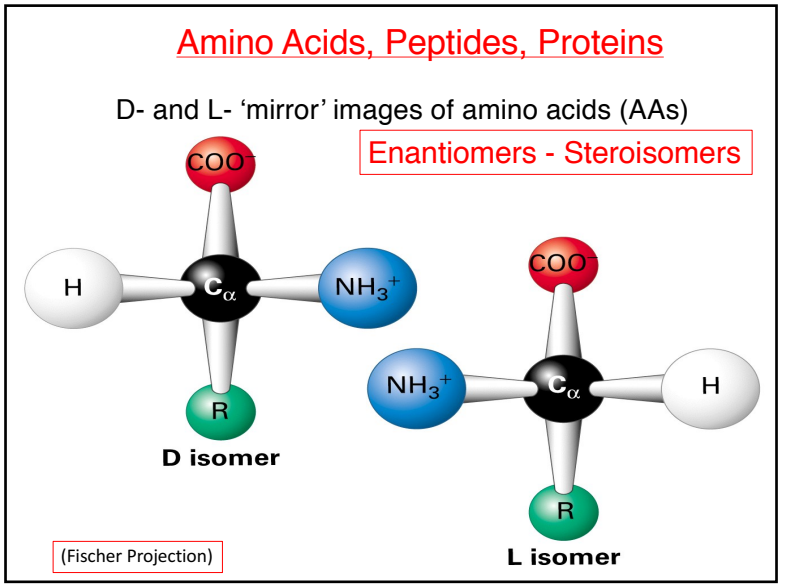


Amino Acids


HYDROPHOBIC AMINO ACIDS
Alanine (Ala or A)
Valine (Val or V)
Isoleucine (Ile or I)
Leucine (Leu or L)
Methionine (Met or M)
Phenylalanine (Phe or F)
Tyrosine (Tyr or Y)
Tryptophan (Trp or W)
HYDROPHILIC AMINO ACIDS
Basic amino acids
Lysine (Lys or K)
Arginine (Arg or R)
Histidine (His or H)
Acidic amino acids
Aspartate (Asp or D)
Glutamate (Glu or E)
Polar amino acids with uncharged R groups
Serine (Ser or S)
Threonine (Thr or T)
Asparagine (Asn or N)
Glutamine (Gln or Q)
SPECIAL AMINO ACIDS
Cysteine (Cys or C)
Glycine (Gly or G)
Proline (Pro or P)

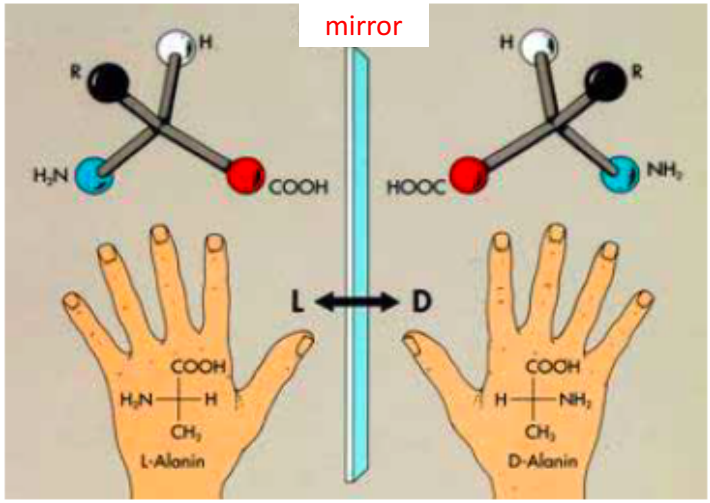

tiny
aliphatic
small
polar
hydrophobic
aromatic
positive
charged
P
G
A
S
T
N
D
E
Q
K
R
H
W
Y
F
M
L
V
I


Carbaminsäure
only 1 COOH and 1 NH2 group
α-AA
smallest unit = glycin
only alpha AAs are proteinogen, and here mainly L-alpha-AAs
β-AA
e.g. beta-Alanin
γ-AA
e.g. GABA
γ aminobutyrate
neurotransmitter

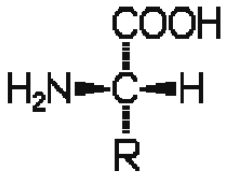

Amino Acids, Peptides, Proteins
D- and L- 'mirror' images of amino acids (AAs)
Enantiomers - Steroisomers
D isomer
L isomer
(Fischer Projection)

Enantiomers - Steroisomers

All but Glycine

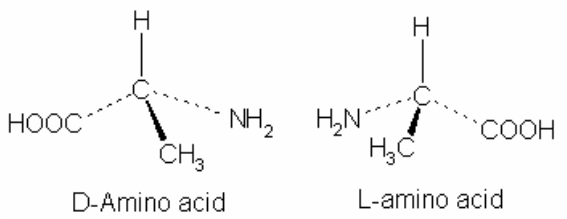


Amino Acids

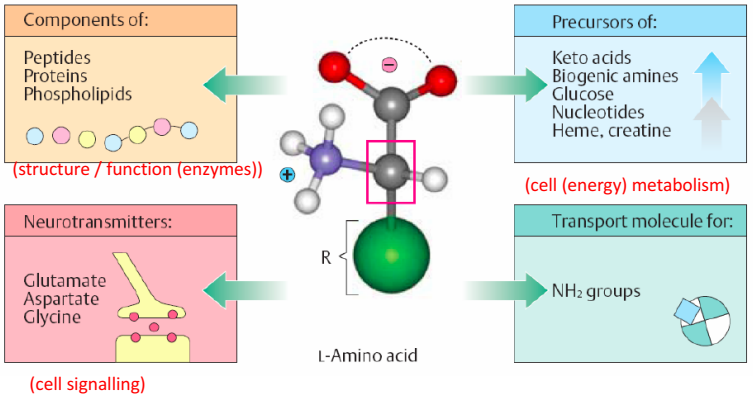


All α-amino acids, except glycine, chiral (= at least 1 asymetric C atom)

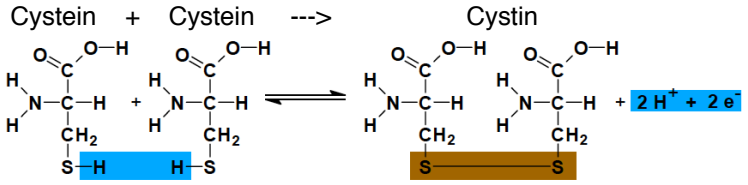
That means, there exist D- and L-form, only L-form is proteinogen !

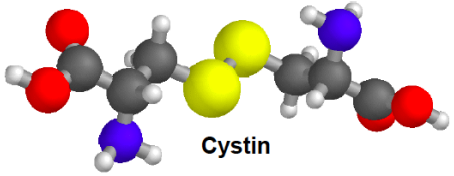


Amino Acids are:



Disulfid (S-) -bridges





Essential Amino Acids

9 amino acids that must be taken up by food because your body cannot synthesize these AAs:

- die verzweigtkettigen (**Valin, Leucin, Isoleucin, Threonin**) und die
- aromatischen Aminosäuren (**Phenylalanin, Tryptophan**
- Außerdem sind die Aminosäuren **Methionin** und **Lysin** essentiell, für Kleinkinder zusätzlich **Histidin**

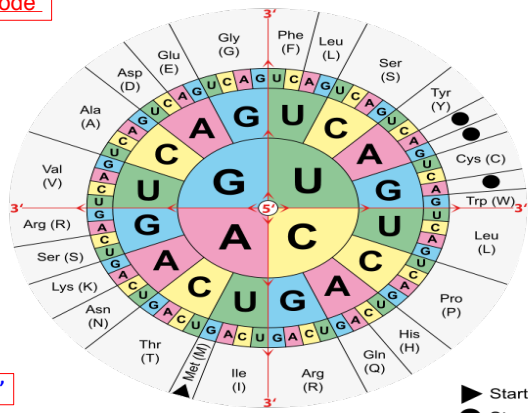
An essential amino acid or indispensable amino acid is an amino acid that cannot be synthesized de novo (from scratch) by the organism, and thus must be supplied in its diet. The nine amino acids humans cannot synthesize (but encode for !) are phenylalanine, valine, threonine, tryptophan, methionine, leucine, isoleucine, lysine, and histidine (i.e., F V T W M L I K H).

from genes to proteins – the genetic code

64 options

Amino Acids

Genetic Code



read 5' ---> 3'

Cracking the Code

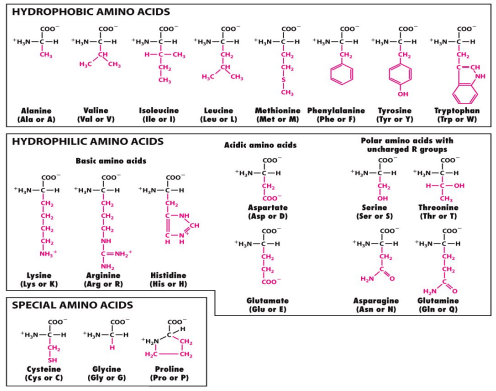
64 options

- A codon in messenger RNA is either translated into an amino acid or serves as a translational stop signal
- Codons must be read in the correct reading frame for the specified polypeptide to be produced
- The genetic code is nearly universal shared by organisms from the simplest bacteria to the most complex animals

Second mRNA base

First mRNA base (5′end)	U	C	A	G	Third mRNA base (3′end)
U	UUU Phe	UCU Ser	UAU Tyr	UGU Cys	U
	UUC Phe	UCC Ser	UAC Tyr	UGC Cys	C
	UUA Leu	UCA Ser	UAA Stop	UGA Stop	A
	UUG Leu	UCG Ser	UAG Stop	UGG Trp	G
C	CUU Leu	CCU Pro	CAU His	CGU Arg	U
	CUC Leu	CCC Pro	CAC His	CGC Arg	C
	CUA Leu	CCA Pro	CAA Gln	CGA Arg	A
	CUG Leu	CCG Pro	CAG Gln	CGG Arg	G
A	AUU Ile	ACU Thr	AAU Asn	AGU Ser	U
	AUC Ile	ACC Thr	AAC Asn	AGC Ser	C
	AUA Ile	ACA Thr	AAA Lys	AGA Arg	A
	AUG Met or start	ACG Thr	AAG Lys	AGG Arg	G
G	GUU Val	GCU Ala	GAU Asp	GGU Gly	U
	GUC Val	GCC Ala	GAC Asp	GGC Gly	C
	GUA Val	GCA Ala	GAA Glu	GGA Gly	A
	GUG Val	GCG Ala	GAG Glu	GGG Gly	G

20 Proteinogenic Amino Acids

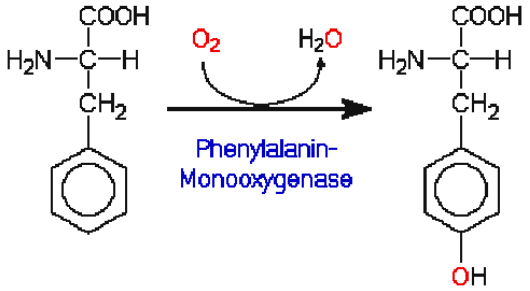


Non-Essential Amino Acids	Essential Amino Acids
Alanin Arginin Asparagin Aspartat Cystein Glutamat Glutamin Glycin Histidin Prolin Serin Tyrosin	Leucin (L) Phenylalanin (F) Tryptophan (W) Methionin (M) Isoleucin (I) Lysin (K) Valin (V) Threonin (T) (Bei Kindern: Arginin (R))

Merksatz für essentielle Aminosäuren (L-F-W-M-I-K-V-T)
Leider fehlen wichtige Moleküle im Körper vieler Tiere.

Phenylketonurie (PKU) - "Fölling Disease"

(lack of Phenylalanin-Monooxygenase)

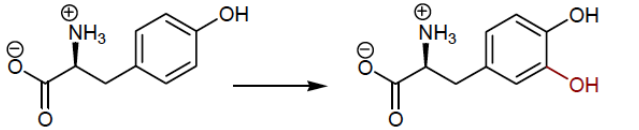


Phenylalanin Tyrosin

Non-Proteinogen Amino Acids

3,4-Dihydroxyphenylalanin (DOPA) (Neurotransmitter)

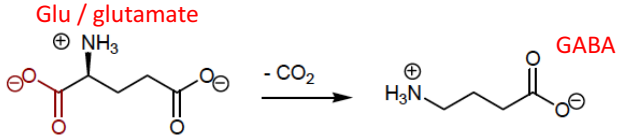
(Dopamine-Precursor)



Tyrosin 3,4-Dihydroxyphenylalanin

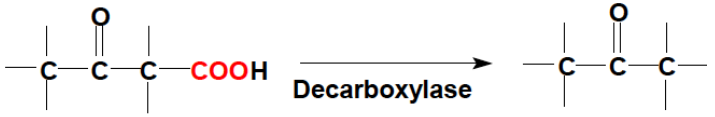
γ-Aminobutyrat (inhibitorischer Neurotransmitter)

Glu / glutamate

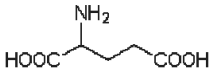


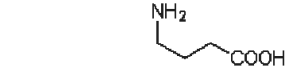
Glutamat γ-Aminobutyrat

Biogene Amine



Glu / E

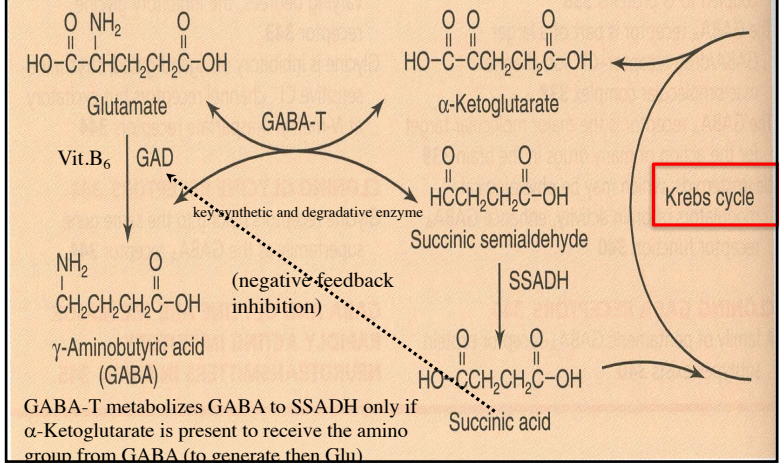




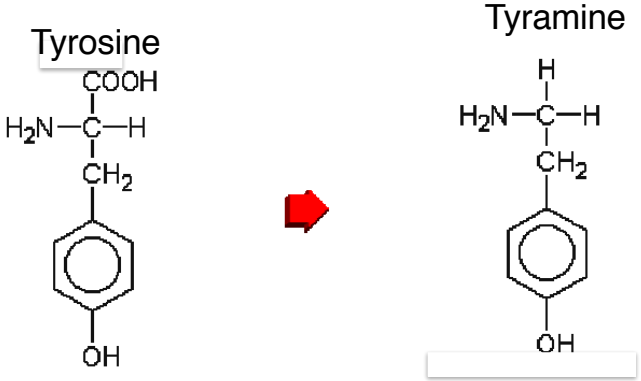
γ-Aminobuttersäure (GABA),
γ aminobutyrate

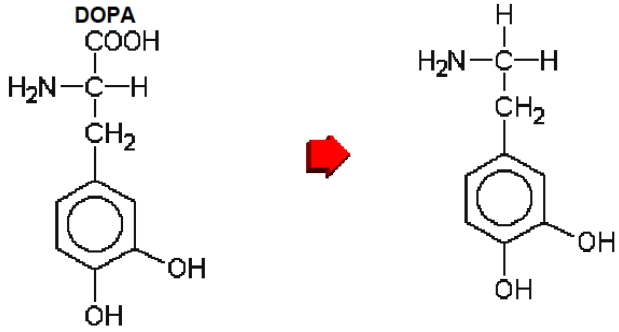
neurotransmitters

Major difference between catecholamines and amino acid neurotransmitters
the latter are derived from glucose metabolism and
are taken up by glia and neurons



GABA-T metabolizes GABA to SSADH only if α-Ketoglutarate is present to receive the amino group from GABA (to generate then Glu)



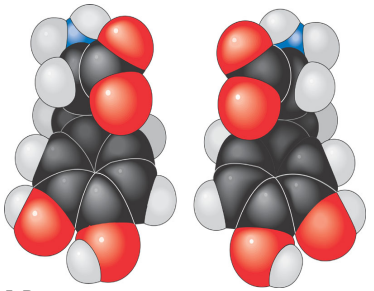


Dopamine
catecholamine

neurotransmitter

---> Parkinson Disease

- Enantiomers
  - are important in the pharmaceutical industry



L-Dopa
(effective against Parkinson's disease)

D-Dopa
(biologically inactive)

Neurotransmitter synthesis

Phenylalanine (dietary) (essential AA) -----> (Phenylalanine-hydroxylase) (in liver)

Tyrosine (usually high conc. in brain TH is saturated by Tyr)

Rate-limiting step — Tyrosine hydroxylase

Phenethylamine (PEA)

DOPA (does cross BBB)

DOPA decarboxylase (L-AADC) (very fast!)

Dopamine (does not cross BBB)

Dopamine β-hydroxylase (DBH)

Noradrenaline

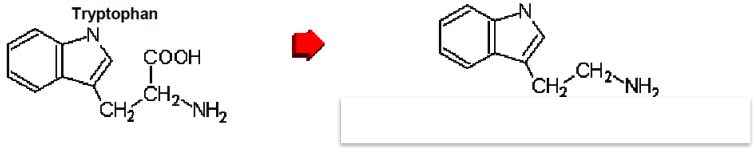
Phenylethanolamine N-methyl transferase (PNMT, in adrenal gland regulated by glucocorticoids and NGF)

Adrenaline

L-Tyrosine → (Tyrosine hydroxylase (Tetrahydrobiopterin, O_2)) → L-DOPA → (DOPA decarboxylase (Pyridoxal phosphate)) → Dopamine → (Dopamine β-hydroxylase (Ascorbate, O_2)) → Norepinephrine → (Phenylethanolamine N-methyltransferase (S-adenosylmethionine)) → Epinephrine

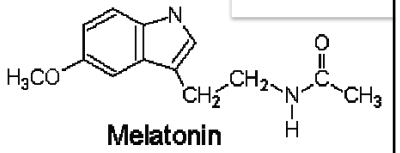
Biosynthetic pathway for cate-

Tryptophan → Tryptamine



Neurotransmitter Serotonin / 5HT

Serotonin



Melatonin

neurotransmitter

5-HT:

1% in brain;
In the blood (in platelets) and induces contractions of smooth muscle organs; high concentration in intestinal mucosa where it causes contraction of intestinal smooth muscle

(essential AA) — **Tryptophan** — in Neurons (limited, can cross BBB)

tryptophan hydroxylase (rate-limiting step)

5-hydroxytryptophan

Neurotransmitter synthesis

aromatic amino acid decarboxylase (L-AADC) (fast)

Serotonin (5-HT) (cannot cross BBB)

monoamine oxidase + aldehyde dehydrogenase → **5-hydroxyindoleacetic acid**

Pineal: 5-HT *N*-acetyl-transferase → **N-Acetyl serotonin**

5-hydroxyindole-*O*-methyltransferase → **Melatonin**

(PEA)

Phenylethylamine (PEA) is found in abundance in cacao. Because PEA is heat sensitive, much of the PEA in conventional cooked and processed chocolate is missing. PEA is the chemical that we produce in our bodies when we fall in love. This is likely one of the main reasons why love and chocolate have such a deep connection. PEA also plays a role in increasing focus and alertness.

The biosynthesis and catabolism of serotonin. Note that in the pineal gland, serotonin is converted enzymatically to melatonin.

Amino acids

–

Acid – Base Equilibrium

pH, buffers, etc.

Introduction: acid-base equilibrium

$CH_3COOH \rightleftharpoons CH_3COO^- + H^+$

$NH_4^+ \rightleftharpoons NH_3 + H^+$

$H_2O \rightleftharpoons OH^- + H^+$

$H_3O^+ \rightleftharpoons H_2O + H^+$

donor - acceptor

Acid: electron-pair acceptor or proton donor
Base: electron-pair donor or proton acceptor

Strong acid: pH = -log (n [acid]) with n = number of protons that can dissociate)
Strong base: pH = 14 + lg [base]
Equations are valid for concentrations less than 0.1 M.

For weak acids / base:

$HA \rightleftharpoons A^- + H^+$

$$K_S = \frac{[H^+] \bullet [A^-]}{[HA]}$$

e.g. in water, then for each A^- one H^+ is formed ---> $[A^-] = [H^+]$

$$[H^+]^2 = K_S \bullet [HA]$$

$$\rightarrow [H^+] = \sqrt{K_S \bullet c_{gesamt}}$$

$$\rightarrow pH = 0.5\ (pK_S - \lg [HA_{total}])$$

If HA is only partially (a little bit) dissociated then $[HA] = [HA_{total}]$

if $[A^-] > [H^+]$, e.g. in a buffer system --->

$$pH = pK_S + \lg \frac{[A^-]}{[HA]} \quad = \quad pH = pK_S + \lg \frac{[Base]}{[Acid]}$$

Henderson-Hasselbach Equation

Acid Base

Standard reaction $HA + H_2O \rightleftharpoons A^{\ominus} + H_3O^{\oplus}$

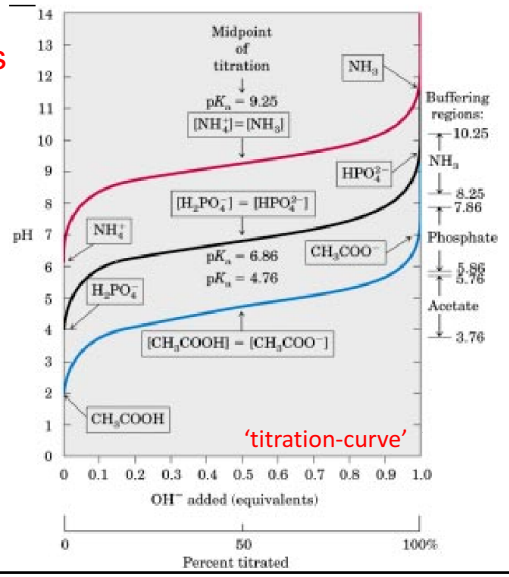
Law of mass action $K = \frac{[A^{\ominus}] \cdot [H_3O^{\oplus}]}{[HA] \cdot [H_2O]}$

Simplified $K_a = \frac{[A^{\ominus}] \cdot [H^{\oplus}]}{[HA]}$

Henderson–Hasselbalch equation $pH = pK_a + \log \frac{[A^{\ominus}]}{[HA]}$

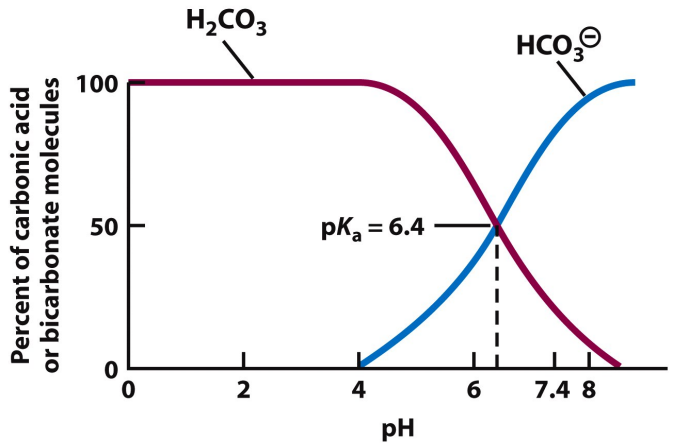
Measure of proton transfer potential

Amino acids – acid-base systems



Buffers

$H_2CO_3 \rightleftharpoons HCO_3^- + H^+$

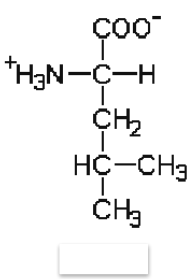


O_2 / CO_2 transport (respiration)

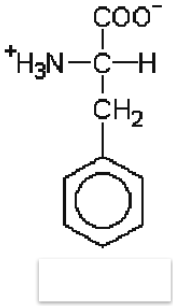
Amino acids – acid-base systems

Example of neutral amino acids, isoelectric point (Hybrid Ion) around pH 5.5-7.5

Characterized e.g. by unpolar side-chain

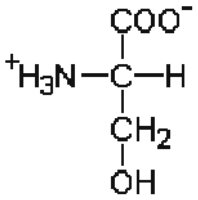


Leucine

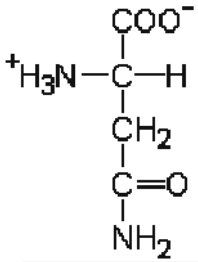


Phenylalanine

Example of neutral amino acids with functional (not acid, not basic) groups; e.g hydroxyl group or acid-amid/carboxyl-amid
These AAs are polar-neutral

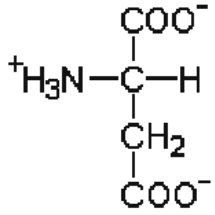


Serine



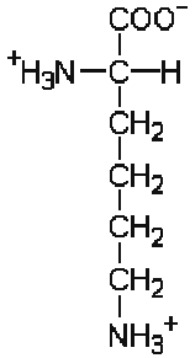
Asparagine, Asn, N

Example of acidic amino acids with functional carboxyl group



Aspartate, Asp, D

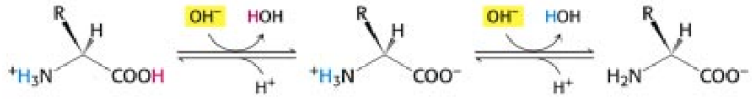
Example of basic amino acids with functional amino group (can easily catch protons)

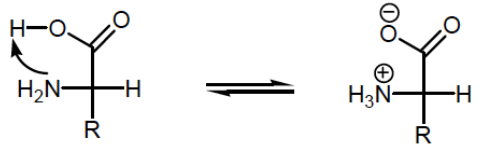


Lysine

Dissociation of Amino Acids

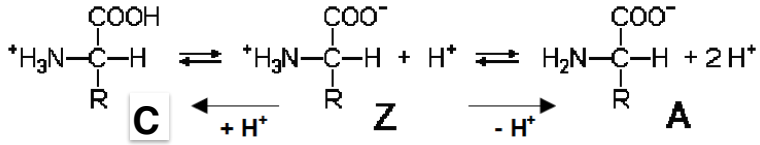
Amino Acids are ampholytes





Hybrid / Zwitterion (Z)

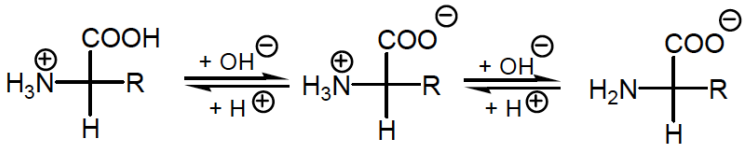
Dissociation of Amino Acids



Cation (C) 'Zwitter' (hybrid) Anion (A)

At isoelectric point (pH_{IP}) the AA is neutral (net charge = 0) and in most cases as 'Zwitter'/hybrid form
In a similar way – each protein has a pH_{IP} where it is neutral (uncharged).

Glycine



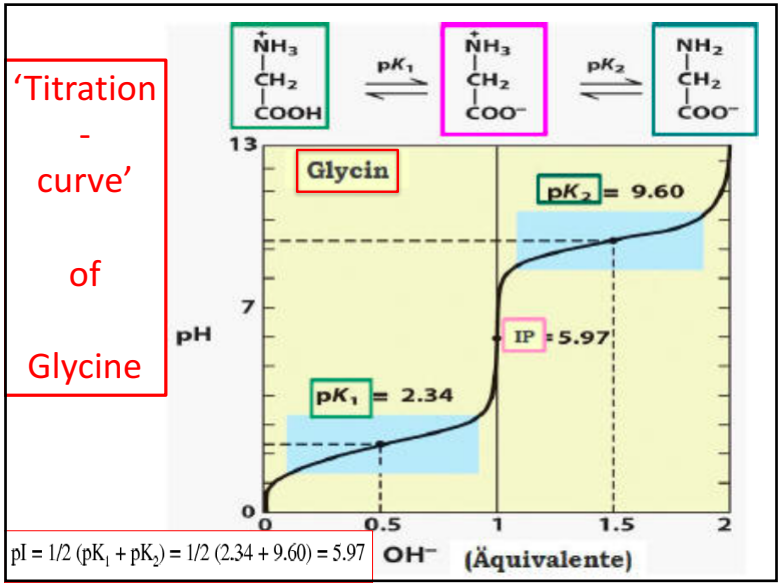
pH< 1 pH = 6 pH > 13

(Hybrid-Ion)

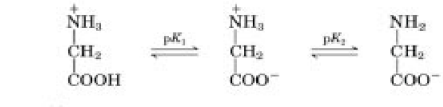
IP or IEP (Isoelectric Point)

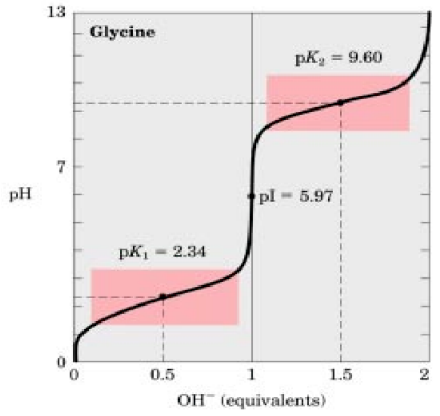
pH (IEP) or pH (IP) or pI or pIP

'Titration - curve' of Glycine



$pI = 1/2\ (pK_1 + pK_2) = 1/2\ (2.34 + 9.60) = 5.97$

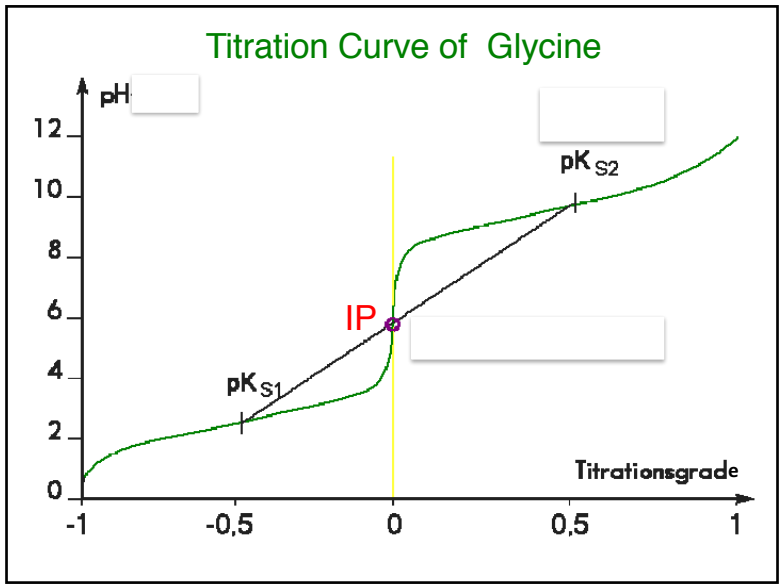




Both the buffer ranges are from a physiological point of view (pH around 7) not relevant

'Titration-curve'

$pI = 1/2\ (pK_1 + pK_2) = 1/2\ (2.34 + 9.60) = 5.97$



Glycine has maximum buffer activity at pK_{S1} and pK_{S2}

at pK_{S1} [C] = [Z] and at pK_{S2} [A] = [Z]

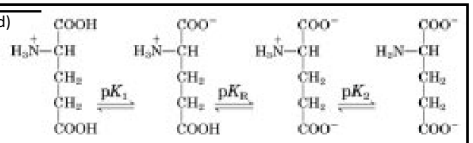
Isoelectric point:
pH_{IP} = (pK_{S1} and pK_{S2}) / 2

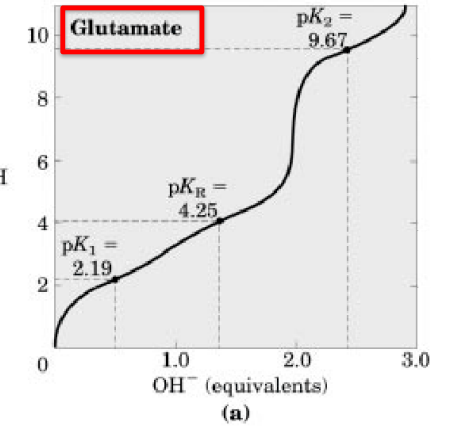
(the value in the basic area will be excluded)

Glu/E: $pH(IEP) = \frac{pK_{S1} + pK_{SR}}{2}$

= (2.19+4.25)/2

= 3.22





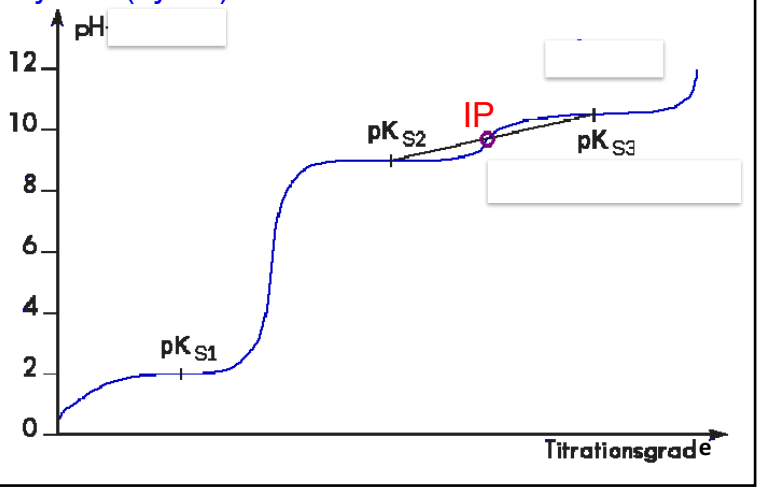
$pI = 1/2\ (pK_n + pK_{n+1})$

pK_n and pK_{n+1} refer to the specie with the netto-charge = 0; means here, the H+ reaction that makes from the neutral specie a positive specie and the de-H+ reaction that makes from the neutral specie a negative specie.

pK_R is the pK value of the side group R

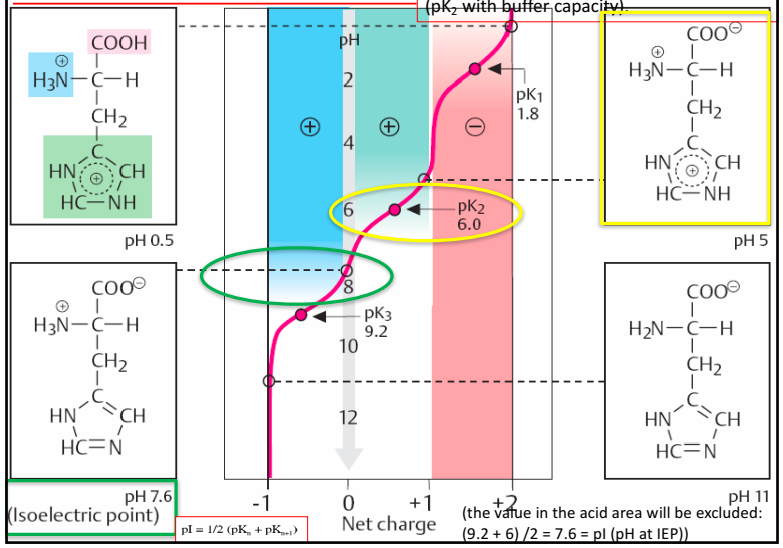
Also here the buffer ranges are from a physiological point of view (pH around 7) not relevant

Titration Curve of a basic amino acid such as Lysine (Lys/K)



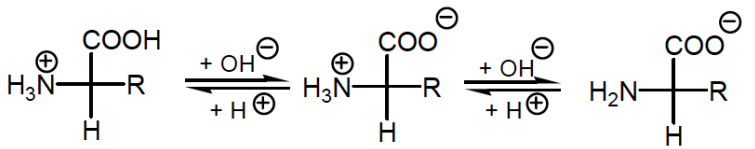
Titration Curve of Histidine

the only AA with a pK in physiological range (pK_2 with buffer capacity).



Experimental estimation of pK values

Glycine



pH< 1 pH = 6 pH > 13

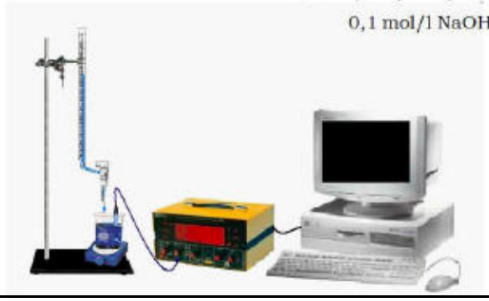
(Hybrid-Ion)

Experiment:

Preparation of a solution consisting of HCl and Glycine (each 0,1 mol·l-1). Titration with 20 ml NaOH (c = 0,1 mol·l-1) by adding first 1 ml and later 0,5 ml drop by drop.

0,1 mol/l Glycinhydrochlorid

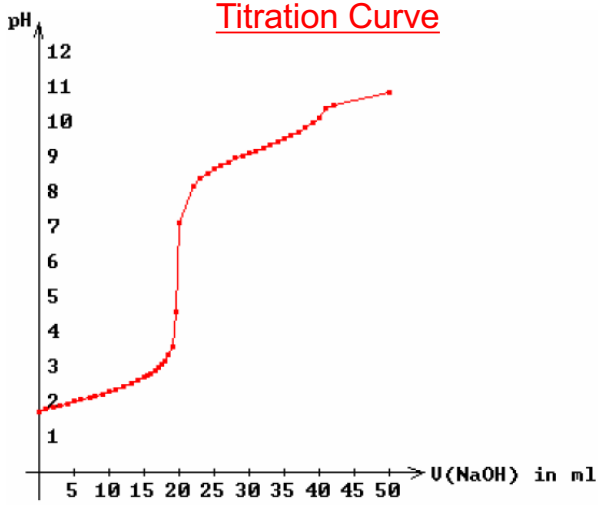
0,1 mol/l NaOH



c(HCl)=0,1 mol/L
c(NaOH)=0,1 mol/L
c(Glycin)=0,1 mol/L
H_2O

V(NaOH) in ml	pH-Wert	V(NaOH) in ml	pH-Wert
0	1,75	19,5	4,57
1	1,8	20	7,14
2	1,85	22	8,2
3	1,9	23	8,4
4	1,97	24	8,54
5	2,03	25	8,68
6	2,08	26	8,78
7,3	2,15	27	8,87
8	2,2	28	8,98
9	2,25	29	9,03
10	2,31	30	9,13
11	2,38	31	9,2
12,1	2,45	32	9,28
13,1	2,55	33	9,36
14	2,62	34	9,44
15	2,71	35	9,53
15,5	2,78	36	9,62
16	2,83	37	9,71
16,5	2,9	38	9,85
17	2,98	39	10
17,5	3,09	40	10,15
18	3,2	41	10,4
18,5	3,35	42	10,5
19	3,6	50	11,1

Titration Curve

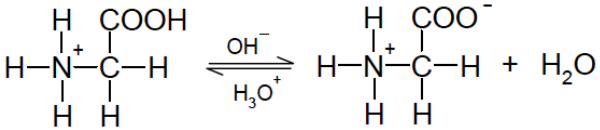


Analysis of the titration curve

Volume (AA) = 20 ml
Concentration (AA) = 0,1 mol·l^{-1}
Concentration (NaOH) = 0,1 mol·l^{-1}

Henderson-Hasselbach Equation: $pH = pK_s + \lg\left(\frac{c(A^-)}{c(AH)}\right)$

At the beginning:



AS^+

$AS^{+/-}$ = Z (Zwitterion) (hybrid-ion)

After adding 10 ml NaOH the $[AS^+] = [AS^{+/-}] = [Z]$ ---->

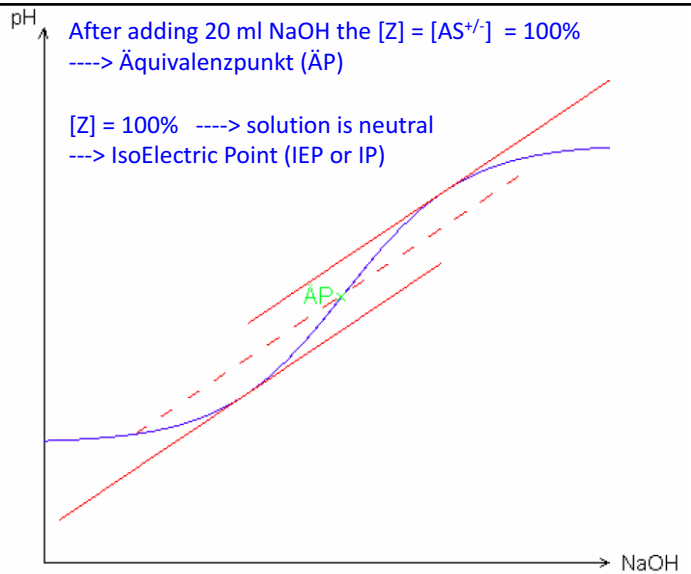
$$pH = pK_s + \lg\left(\frac{50\%}{50\%}\right)$$

$$pH = pK_s + \lg(1)$$

$$pH = pK_s \rightarrow HÄP_1$$

$pH = pK_{S1} = 2.35$ (Halbäquivalenzpunkt-1)

After adding 20 ml NaOH the $[Z] = [AS^{+/-}] = 100\%$
----> Äquivalenzpunkt (ÄP)

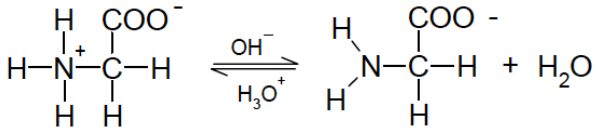


After adding 20 ml NaOH the $[Z] = [AS^{+/-}] = 100\%$
----> Äquivalenzpunkt (ÄP)

[Z] = 100% ----> solution is neutral
---> IsoElectric Point (IEP or IP)

After adding 30 ml NaOH the $[Z] = [AS^{+/-}] = [AS^-]$

Equilibrium:



$[Z] = [AS^{+/-}]$ = $[AS^-]$

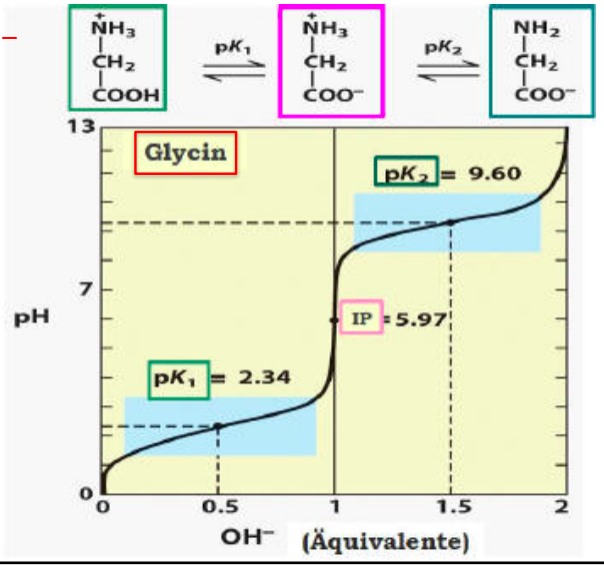
$$pH = pK_s + \lg\left(\frac{50\%}{50\%}\right)$$

$$pH = pK_s + \lg(1)$$

$$pH = pK_s \rightarrow HÄP_2$$

$pH = pK_{S2} = 9.78$ (Halbäquivalenzpunkt-2)

Experiment – summary



pI or pIP or $pH(IEP) = \frac{pK_{s1} + pK_{s2}}{2}$

Examples:

Leu/L (pK_{s1} = 2,36, pK_{s2} = 9,60)

$$pH(IEP) = \frac{pK_{s1} + pK_{s2}}{2} = \frac{2,36 + 9,60}{2} = 5,98$$

acidic AA (the value in the basic area will be excluded)

Asp/D (pK_{s1} = 1,88, pK_{s2} = 9,60, pK_{sR} = 3,60)

$$pH(IEP) = \frac{pK_{s1} + pK_{sR}}{2} = \frac{1,88 + 3,60}{2} = 2,74$$

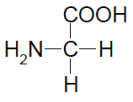
basic AA (the value in the acidic area will be excluded)

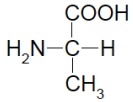
Lys/K (pK_{s1} = 2,18, pK_{s2} = 8,95, pK_{sR} = 10,53)

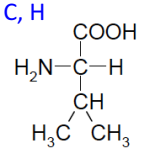
$$pH(IEP) = \frac{pK_{s2} + pK_{sR}}{2} = \frac{8,95 + 10,53}{2} = 9,75$$

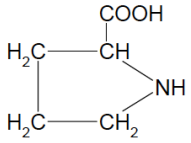
IEPs of AAs:

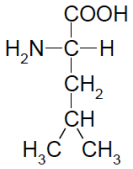
1. Neutral AAs with side chain R = C, H

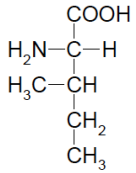

Glycin (Gly)
IEP = 6,0

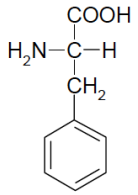

Alanin (Ala)
IEP = 6,1


Valin (Val)
IEP = 6,0

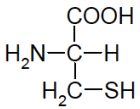

Prolin (Pro)
IEP = 6,3

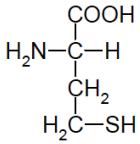

Leucin (Leu)
IEP = 6,0

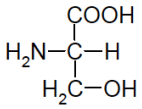

Isoleucin (Ile)
IEP = 6,0

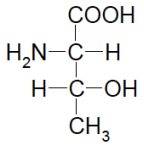

Phenylalanin (Phe)
IEP = 5,5

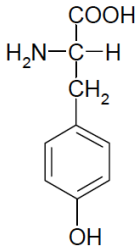
2. Neutral AAs with side chain R = O, S, N

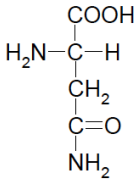

Cystein (Cys)
IEP = 5,0

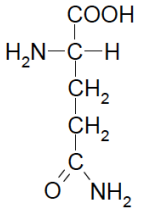

Methionin (Met)
IEP = 5,7

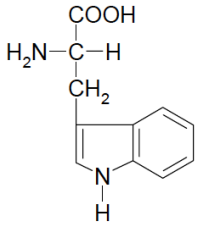

Serin (Ser)
IEP = 5,7


Threonin (Thr)
IEP = 5,6

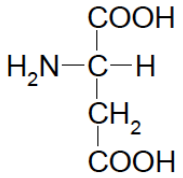

Tyrosin (Tyr)
IEP = 5,6

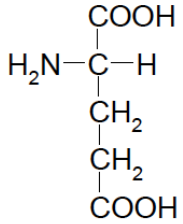

Asparagin (Asn)
IEP = 5,4


Glutamin (Gln)
IEP = 5,7

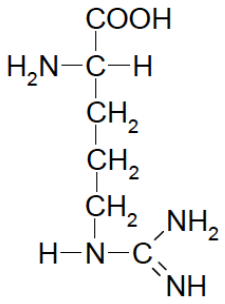

Tryptophan (Trp)
IEP = 5,9

3. Acidic AAs:

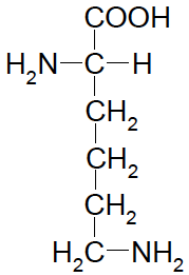

(Asp)
IEP = 2,9


(Glu)
IEP = 3,2

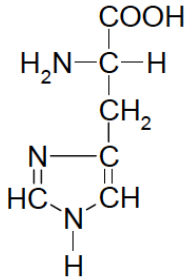
4. Basic AAs:



(Arg)
IEP = 10,8



(Lys)
IEP = 9,7



(His)
IEP = 7,6

	pK_1 -COOH	pK_2 α-NH_2	pK_3 side-chain (pK_R)
Alanin	2,3	9,7	
Threonin	2,6	10,4	
Glutamin	2,2	9,1	
Asp	2,1	9,8	3,9
Glut	2,2	9,7	4,3
Histidin	1,8	9,2	6,0
Cystein	1,7	10,8	8,3
Tyrosin	2,2	9,1	10,1
Lysin	2,2	9,0	10,5
Arginin	2,2	9,0	12,5

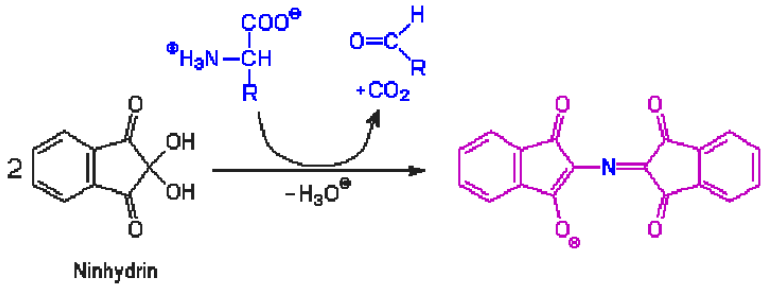
Amino acid	Abbreviation/ symbol	M_r	pK_a values: pK_1 (—COOH)	pK_2 ($—NH_3^+$)	pK_R (R group)	pI	Hydropathy index*	Occurrence in proteins (%)†
Nonpolar, aliphatic R groups								
Glycine	Gly G	75	2.34	9.60		5.97	−0.4	7.2
Alanine	Ala A	89	2.34	9.69		6.01	1.8	7.8
Proline	Pro P	115	1.99	10.96		6.48	1.6	5.2
Valine	Val V	117	2.32	9.62		5.97	4.2	6.6
Leucine	Leu L	131	2.36	9.60		5.98	3.8	9.1
Isoleucine	Ile I	131	2.36	9.68		6.02	4.5	5.3
Methionine	Met M	149	2.28	9.21		5.74	1.9	2.3
Aromatic R groups								
Phenylalanine	Phe F	165	1.83	9.13		5.48	2.8	3.9
Tyrosine	Tyr Y	181	2.20	9.11	10.07	5.66	−1.3	3.2
Tryptophan	Trp W	204	2.38	9.39		5.89	−0.9	1.4
Polar, uncharged R groups								
Serine	Ser S	105	2.21	9.15		5.68	−0.8	6.8
Threonine	Thr T	119	2.11	9.62		5.87	−0.7	5.9
Cysteine	Cys C	121	1.96	10.28	8.18	5.07	2.5	1.9
Asparagine	Asn N	132	2.02	8.80		5.41	−3.5	4.3
Glutamine	Gln Q	146	2.17	9.13		5.65	−3.5	4.2
Positively charged R groups								
Lysine	Lys K	146	2.18	8.95	10.53	9.74	−3.9	5.9
Histidine	His H	155	1.82	9.17	6.00	7.59	−3.2	2.3
Arginine	Arg R	174	2.17	9.04	12.48	10.76	−4.5	5.1
Negatively charged R groups								
Aspartate	Asp D	133	1.88	9.60	3.65	2.77	−3.5	5.3
Glutamate	Glu E	147	2.19	9.67	4.25	3.22	−3.5	6.3

Determination of NH_2-group in AAs:

$$R-NH_2 \xrightarrow{NaOH} NH_3\uparrow \qquad NH_3 + H_2O \rightarrow NH_4^+ + OH^-$$

boiling AAs with NaOH , NH_3 gas forms and reacts on wet pH paper with the water. The OH^- is then coloring the pH paper (e.g. blue)

Amino Acid Identification using Ninhydrin



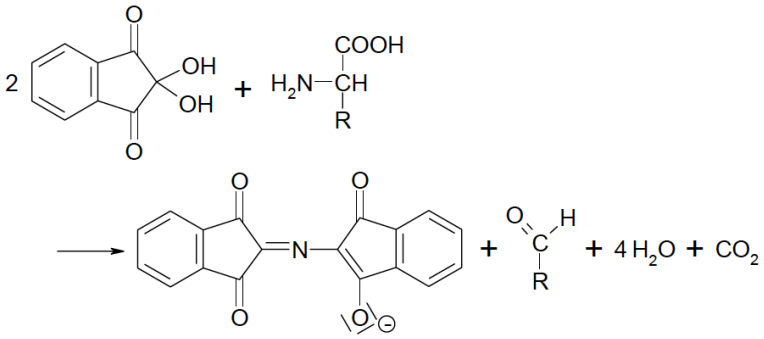
Ninhydrin

✔ -Amino Acids react with Ninhydrin forming the blue violet – red-brown dye. The AA will be decarboxylated and oxidized to form an aldehyde with 1 less C-atom.

---> finger print

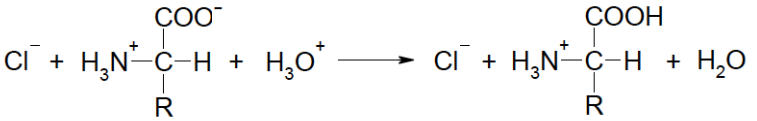
Boiling of AAs with Ninhydrin in 2-Propanol

---> Identification of AA or NH-group in AAs

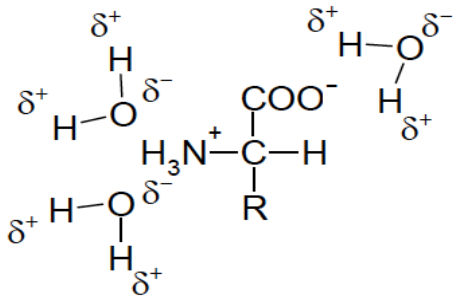


practical (forensic) application: finger prints

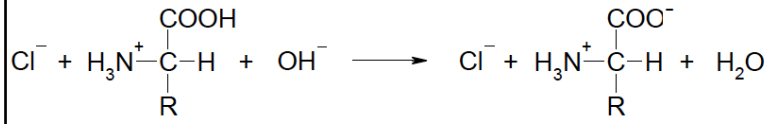
AA (Tyrosine) plus water plus HCl ---> soluble



After adding NaOH, precipitation because Z (Zwitter-ion) is not soluble due to oposing hydrate-covers, no uniform hydrate-cover possible;



after adding NaOH, the AAs becomes insoluble.

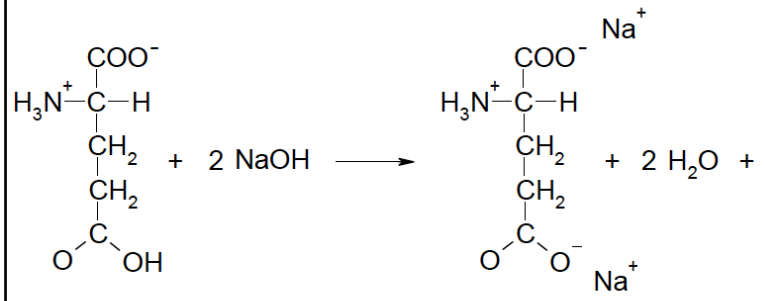


after adding more NaOH, the AAs becomes again soluble.

A substance is only water soluble
if a uniform hydrate cover can be formed

Synthesis of Natrium glutamate:

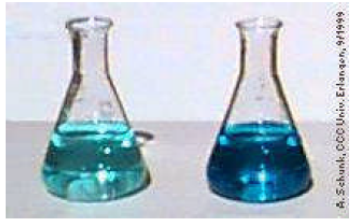
Glutamine (Gln) plus NaOH (drop-wise), then evaporation of the water)



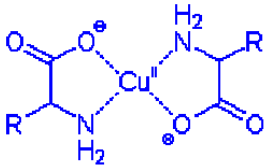
Dinatriumglutamat

Chelat complex with Amino Acids

Amino acids easily form complexes with metal ions (those with 2 valences) such as Cu^{2+} = Biuret-reaction



$[Cu(H_2O)_4]^{2+}$-complex $[Cu(Gly)_2]$-complex



AAs in RedOx Reactions

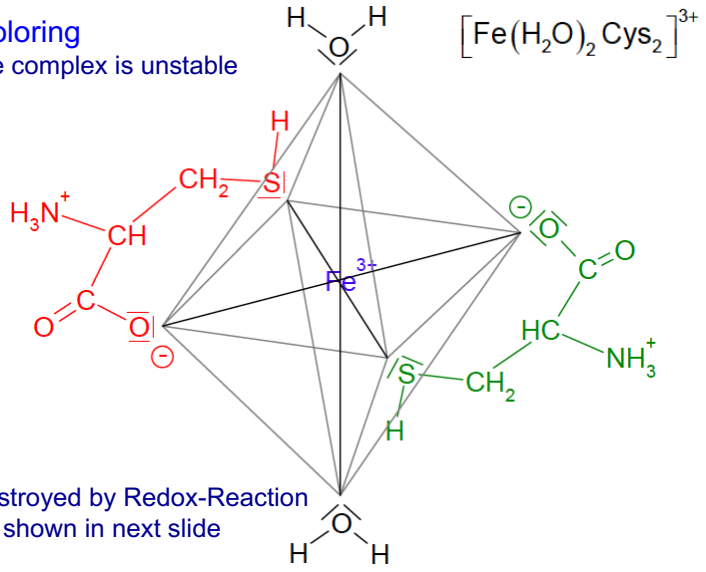
Oxydation of Cysteine:

5ml cysteine (1%) plus 1 ml $Fe(III)Cl_3$, then shake.

After shaking, the solution becomes blue; upon leaving the flask quietly alone the blue color disappears; and re-shaking is required for blue coloring

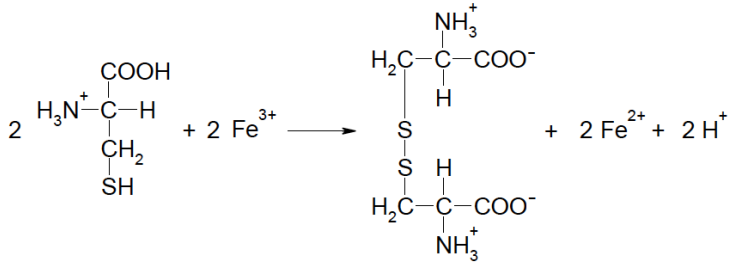
Coloring

the complex is unstable



destroyed by Redox-Reaction as shown in next slide

De-coloring:



Oxidation: $2 \cdot Rest\text{-}SH \rightarrow Rest\text{-}S\text{-}S\text{-}Rest + 2e^-$

Reduktion: $Fe^{3+} + 1e^- \rightarrow Fe^{2+}$ $\quad | \cdot 2$

Redox: $2S^{-II} + 2Fe^{3+} \rightarrow 2S^{-I} + 2Fe^{2+}$

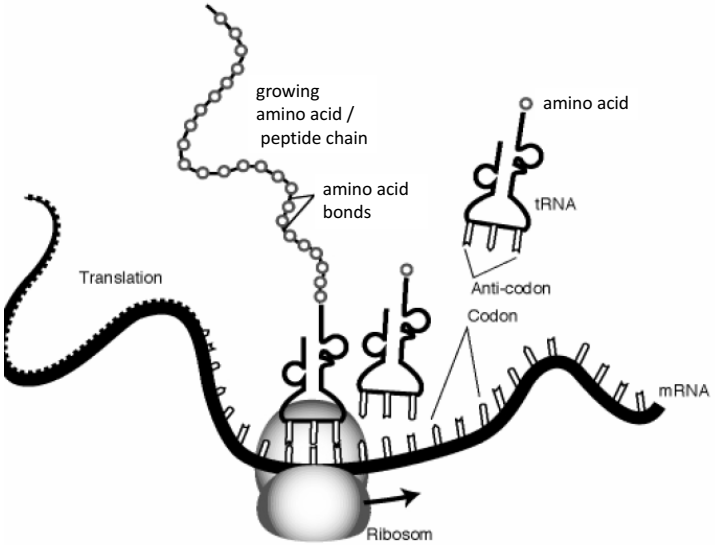
Re-Coloring
after shaking, O_2 (Oxygen) enters the solution to form fresh Fe^{3+}
The unstable complex is reformed, but soon destroyed again

Oxidation:	Fe^{2+}	$\rightarrow Fe^{3+} + 1e^-$	$\mid \cdot 2$
Reduktion:	$\frac{1}{2}O_2 + 2e^-$	$\rightarrow O^{2-}$	
Redox:	$Fe^{2+} + \frac{1}{2}O_2$	$\rightarrow O^{2-} + 2Fe^{3+}$	

Biochemistry

2.3) Peptides / Proteins

Prof. Dr. Klaus Heese

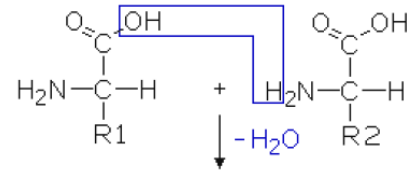


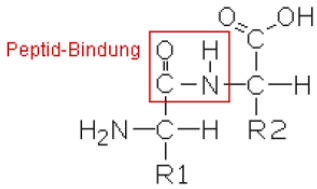
Amino acids

Peptides

Proteins

Peptide Bonds

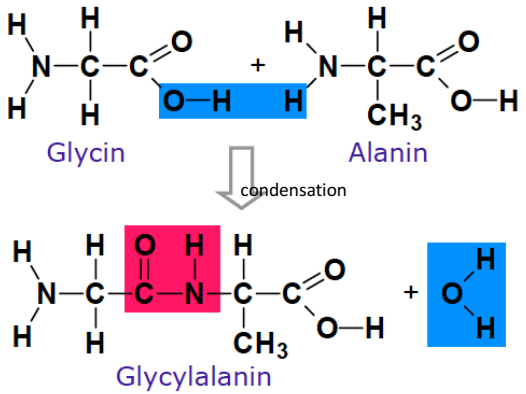




Amino acids

Peptides

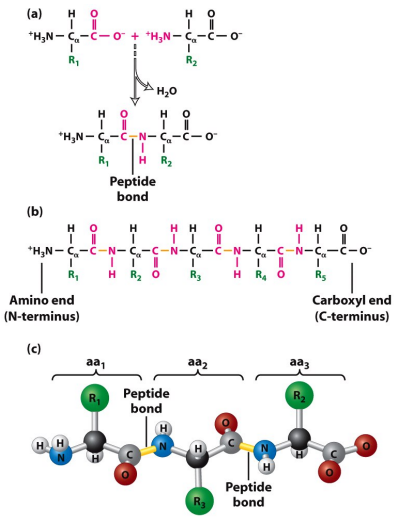
Proteins

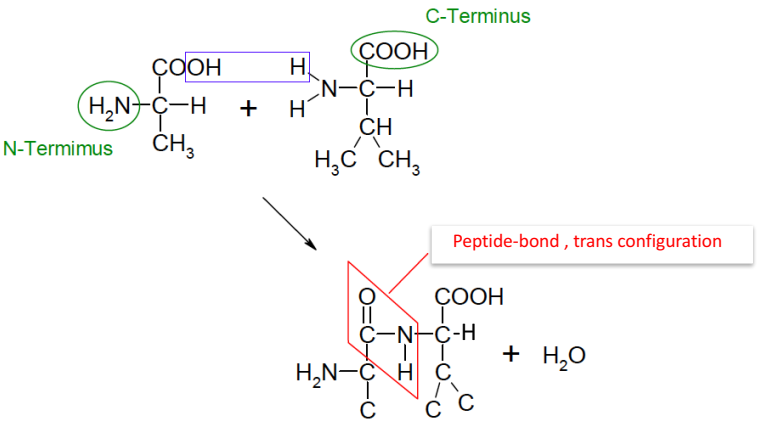


Amino acids

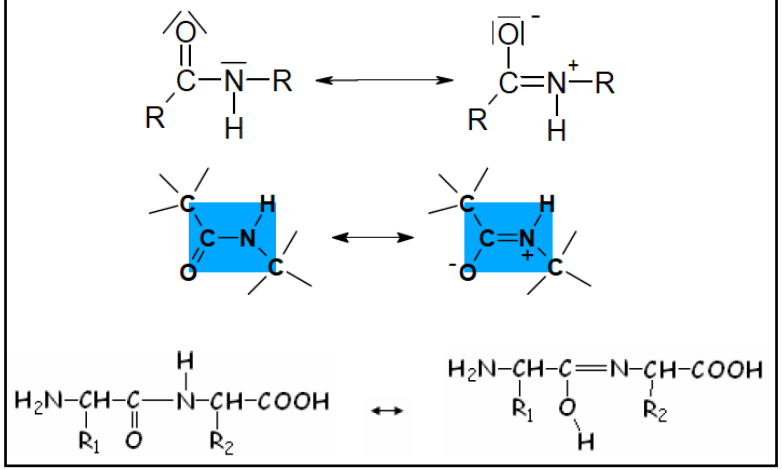
Peptides

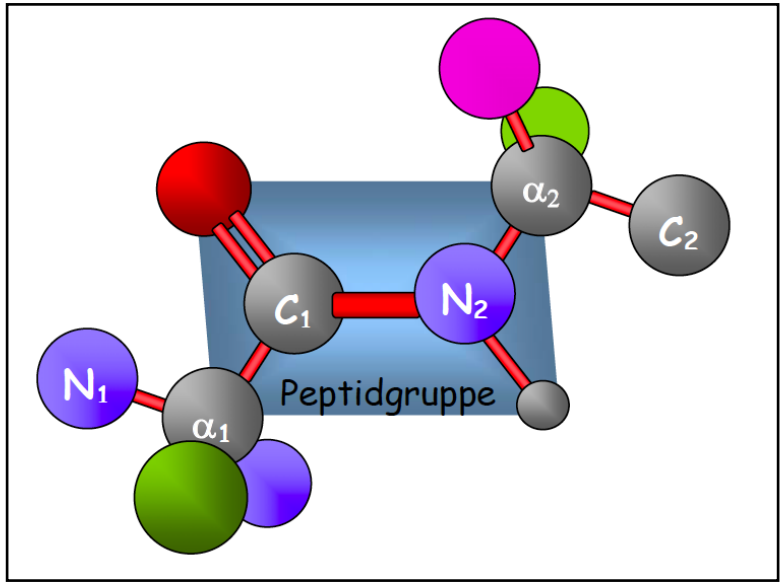
Proteins

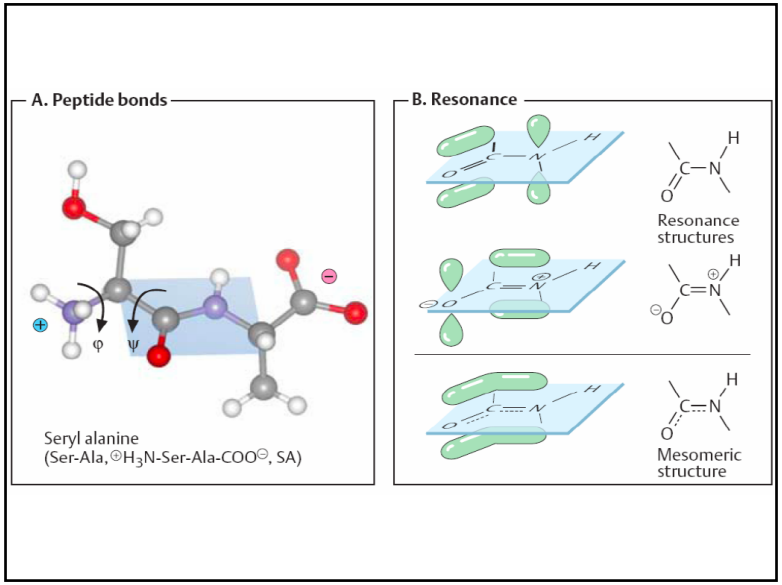


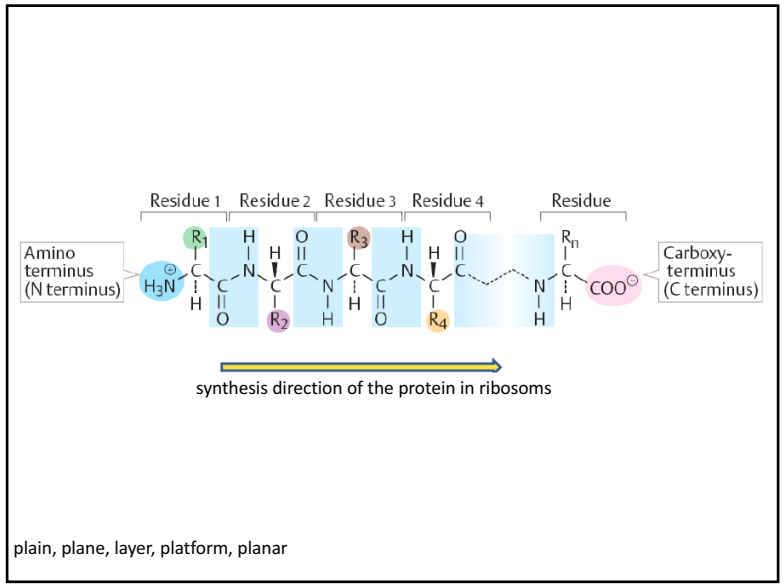


Peptide bond is planar due to:

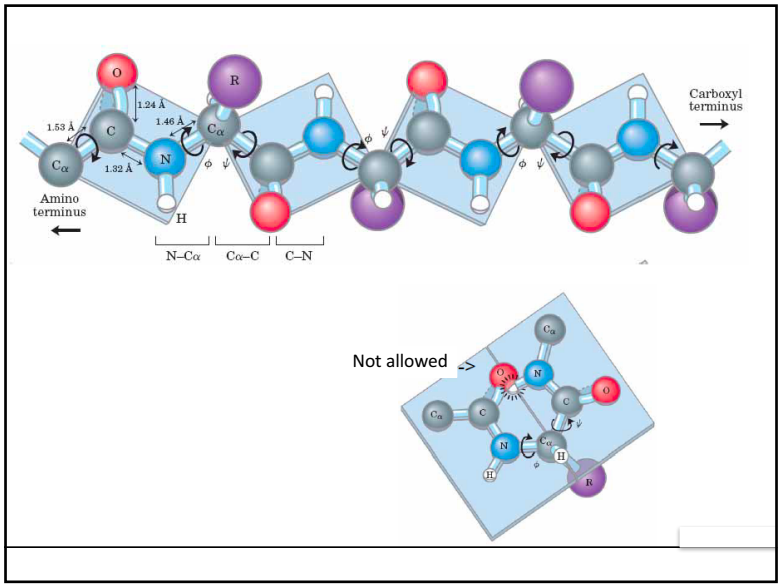




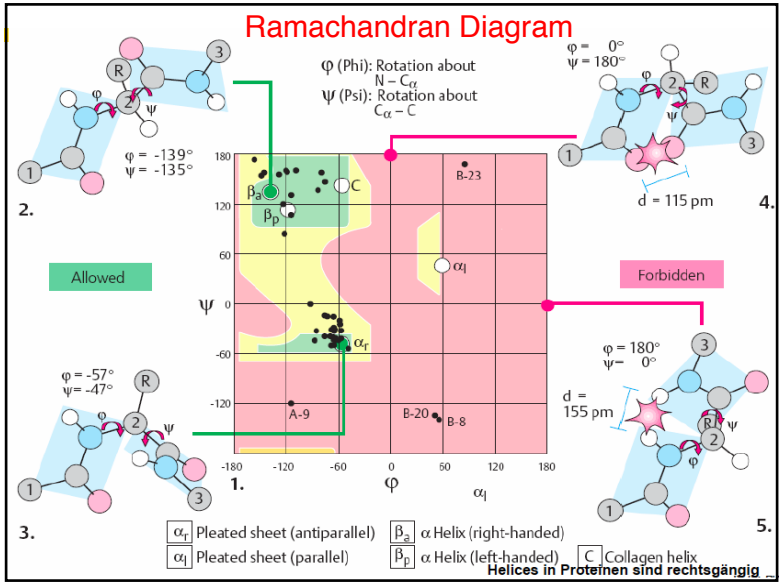




plain, plane, layer, platform, planar



Ramachandran Diagram



Dipeptide benennt man im Allgemeinen nach ihren Bestandteilen. Dabei Beginnt man mit einem H (für das N-terminale Ende) und endet mit einem OH (für das C-terminale Ende). Für Alanin und Valin hieße das:

H – Ala – Val – OH

Da ohne Zusatzstoffe nicht festgelegt werden kann, welche Enden miteinander reagieren, kann auch folgendes Dipeptid entstehen:

H – Val – Ala – OH

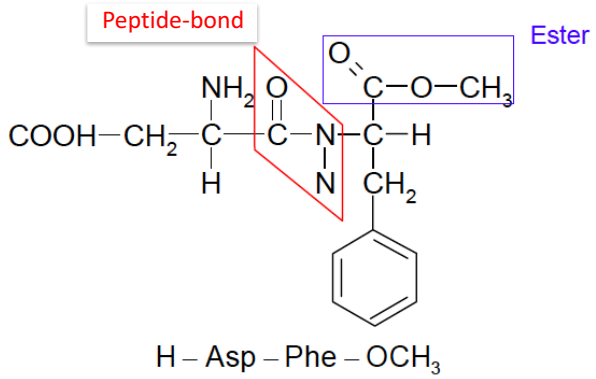
Außerdem können noch die Fälle auftreten, in denen zwei gleiche Moleküle miteinander reagieren:

H – Ala – Ala – OH und H – Val – Val – OH

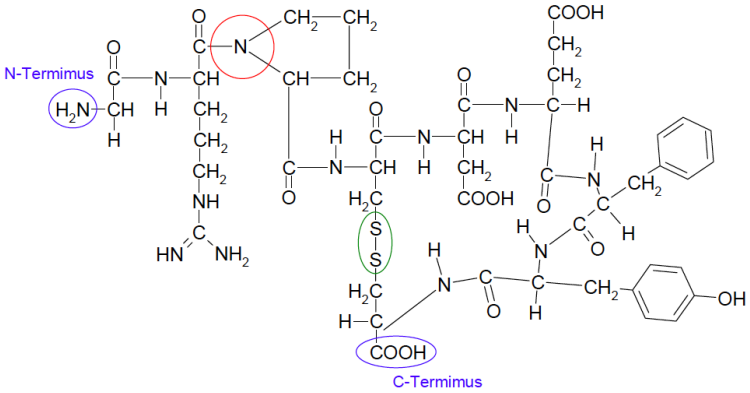
Dipeptide (2)
Tripeptide (3)
Oligopeptide (2-9)
Polypeptide (10-100)

>100AAs ---> Proteins

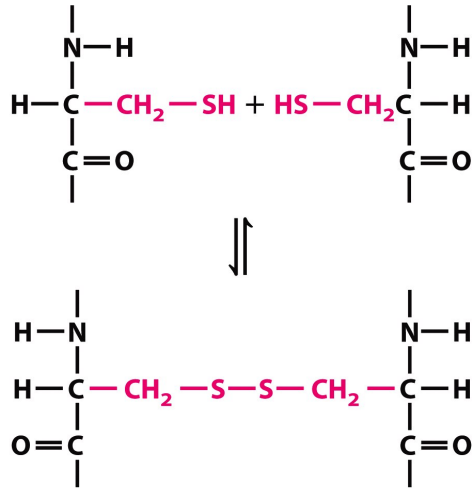
Oligo-peptides



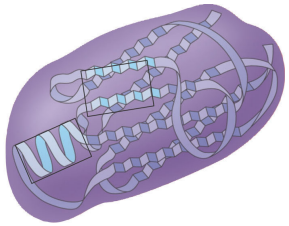
Vasopressin

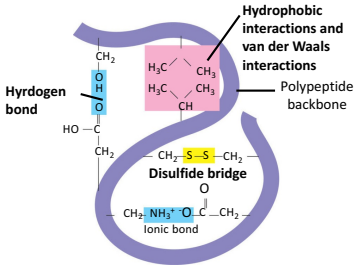


Cysteine in Proteins

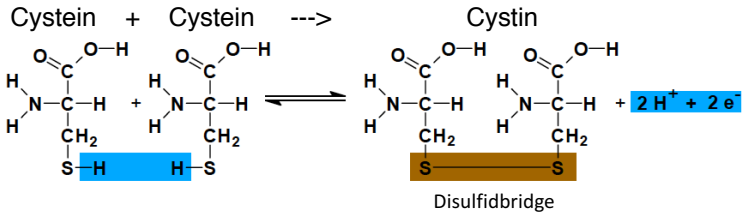


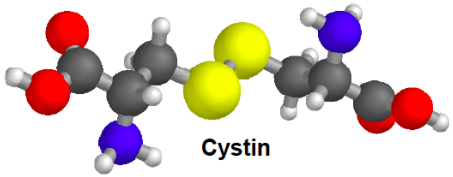
- Tertiary structure
  - is the overall three-dimensional shape of a polypeptide
  - results from interactions between amino acids and R groups



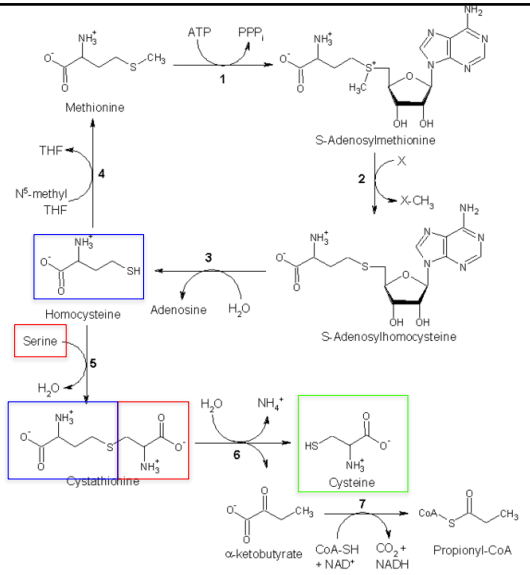


Disulfid-bridges





Biosynthesis of Cystein



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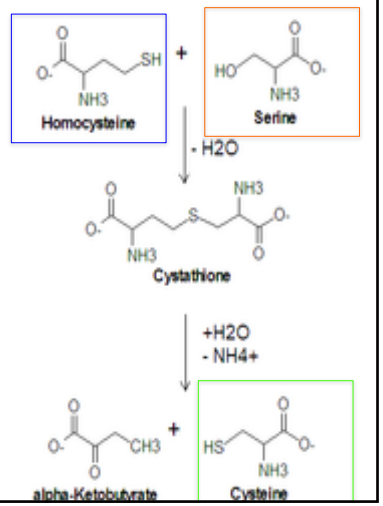
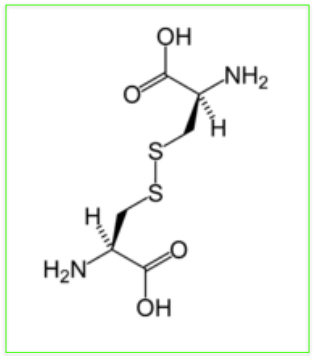


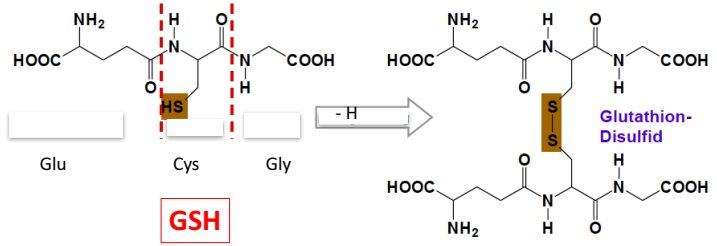
http://en.wikipedia.org/wiki/Homocysteine

http://en.wikipedia.org/wiki/Cysteine



Cystine (shown here in its neutral form), two cysteines bound together by a disulfide bond.

Biological Important Peptides



GSH

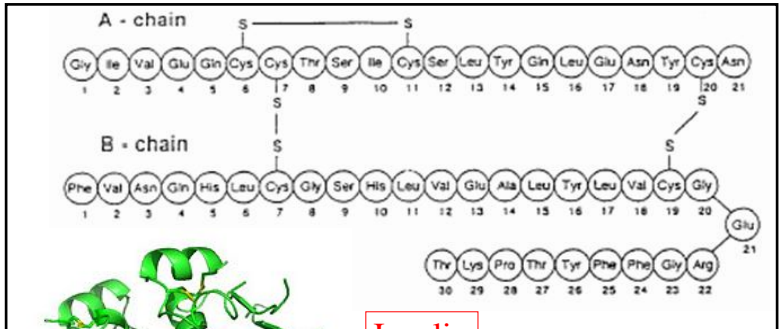
Glutathion: Tri-peptide:

Glu-Cys-Gly

GSSG

The thiol group (-SH) is easy to be oxidized to form disulfide bridges to a 2nd Glutathione molecule under cleavage of H.

This is an important Redox-system in the blood and muscles.



Insulin

(controls blood glucose level)

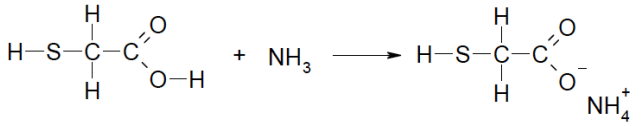
http://reddymed.com/insulin.htm

practical application: hairdresser / coiffeur

Disulfide (S-S) bridges between the hairs need to be cleaved

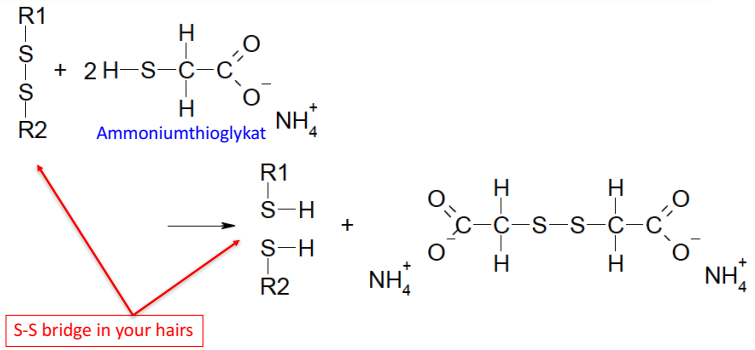
Vorgänge bei der Dauerwelle

Soll eine Dauerwelle gemacht werden, müssen die Disulfidbrücken zwischen den Haaren gespalten werden, damit die Haare eine neue Form annehmen können. Zum Spalten dieser Disulfidbrücken wird Ammoniumthioglykat benutzt. Es wird wie folgt synthetisiert:



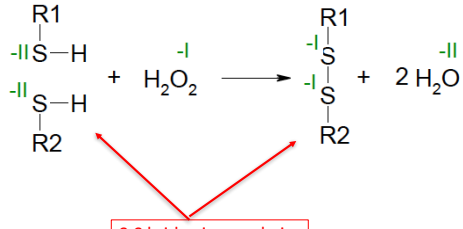
This is the activation reaction to form Ammoniumthioglykat

Cleavage of S-S bridges by Ammoniumthioglykat



After the hairdresser has made the new hairstyle, the S-S bridges will be recovered with H_2O_2

Nachdem die Disulfidbrücken gespalten und die Frisur fertig gestellt ist, werden die Disulfidbrücken wiederhergestellt. Die Fixierung erfolgt mit Wasserstoffperoxid (H_2O_2):



Cysteine in RedOx Reactions

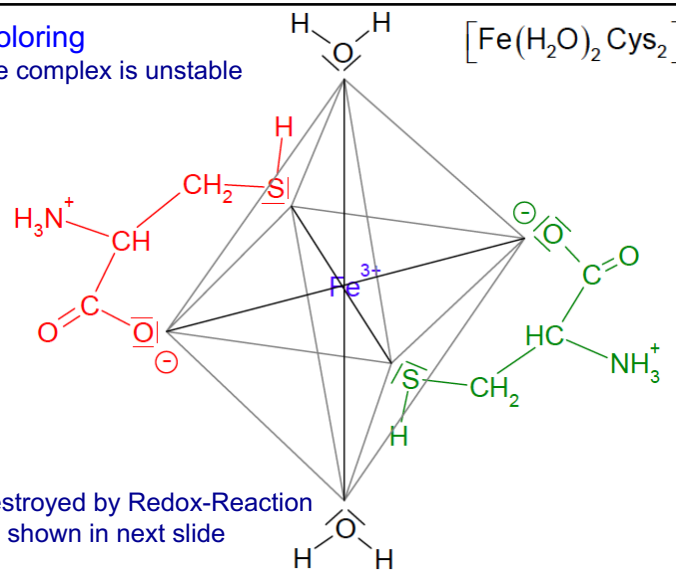
Oxydation of Cysteine:

5ml cysteine (1%) plus 1 ml $Fe(III)Cl_3$, then shake.

After shaking, the solution becomes blue; upon leaving the flask quietly alone the blue color disappears; and re-shaking is required for blue coloring

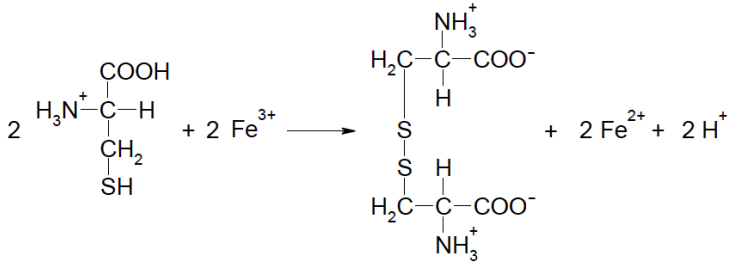
Coloring

the complex is unstable



destroyed by Redox-Reaction as shown in next slide

De-coloring:



Oxidation:	$2 \cdot Rest\text{-}SH$	$\rightarrow Rest\text{-}S\text{-}S\text{-}Rest + 2e^-$	
Reduktion:	$Fe^{3+} + 1e^-$	$\rightarrow Fe^{2+}$	$\mid \cdot 2$
Redox:	$2S^{-II} + 2Fe^{3+}$	$\rightarrow 2S^{-I} + 2Fe^{2+}$	

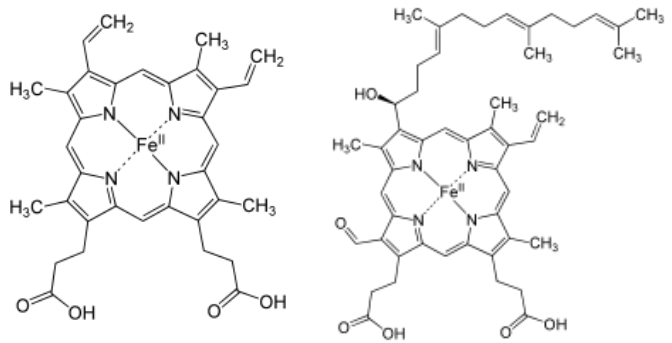
Re-Coloring

after shaking, O_2 (Oxygen) enters the solution to form fresh Fe^{3+}
The unstable complex is reformed, but soon destroyed again

Oxidation:	Fe^{2+}	$\rightarrow Fe^{3+} + 1e^-$	$\mid \cdot 2$
Reduktion:	$\frac{1}{2}O_2 + 2e^-$	$\rightarrow O^{2-}$	
Redox:	$Fe^{2+} + \frac{1}{2}O_2$	$\rightarrow O^{2-} + 2Fe^{3+}$	

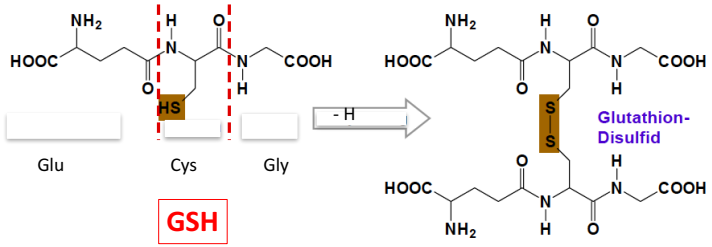
http://en.wikipedia.org/wiki/Heme

A haem (British English) or heme (American English) is a chemical compound of a type known as a prosthetic group consisting of an Fe2+ (ferrous) ion contained in the centre of a large heterocyclic organic ring called a porphyrin, made up of four pyrrolic groups joined together by methine bridges. Not all porphyrins contain iron, but a substantial fraction of porphyrin-containing metalloproteins have heme as their prosthetic group; these are known as hemoproteins. Hemes are most commonly recognized as components of hemoglobin, the red pigment in blood, but are also found in a number of other biologically important hemoproteins such as myoglobin, cytochrome, catalase, and endothelial nitric oxide synthase.



Heme B **Heme A**

Biological Important Peptides



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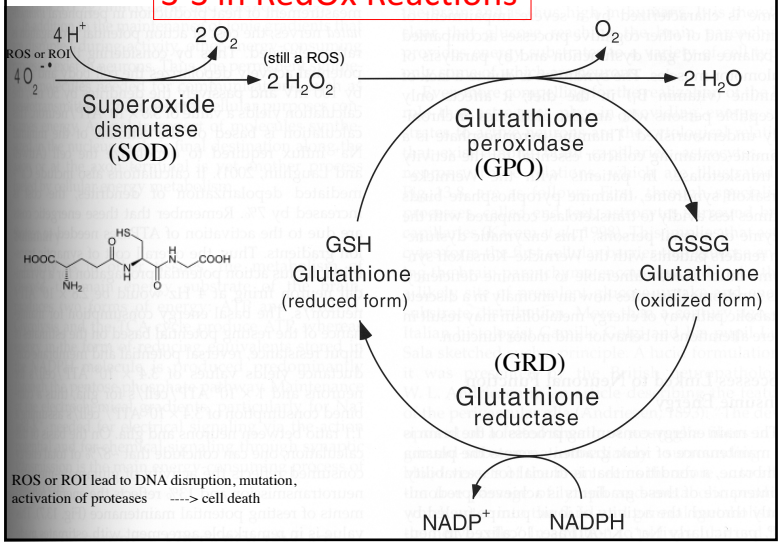
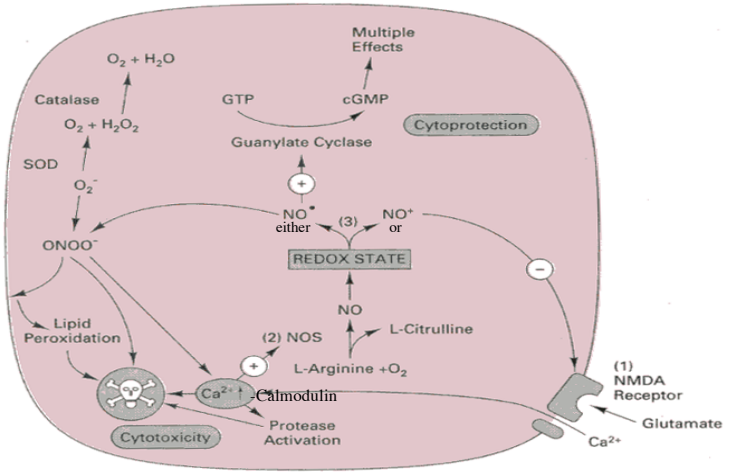
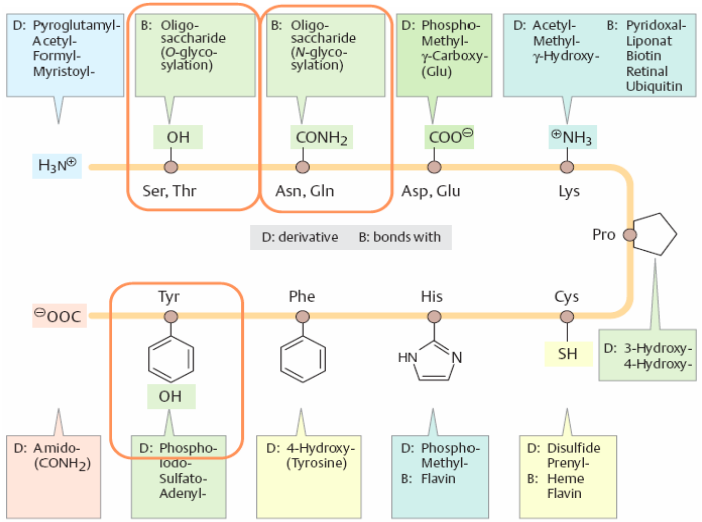
S-S in RedOx Reactions



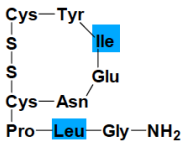
Postulated mechanism whereby NO causes cytotoxicity or cytoprotection in nervous tissue

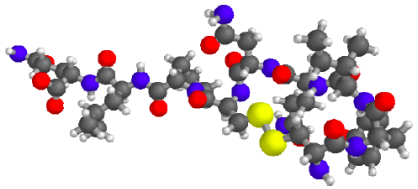


Post-translational modifications of Amino Acids



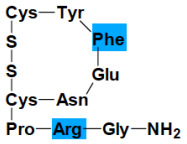
Biological Important Peptides





Ocytocin:

Ring-form peptide hormone with intra-molecular disulfide bridge , causing contraction of muscles in mammary gland and uterus.



Vasopressin:

peptide hormone, only 2 AAs are different to Ocytocin, causes water reabsorption in kidney; and blood-pressure increase.

Significance of Peptides

Synthesized as proteins/peptides based on DNA codons

Multi-functions:

as hormones

Anti inflammation

anti-viral

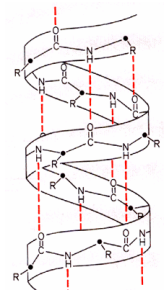
Antibiotic

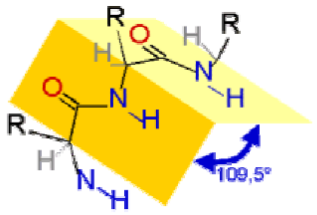
Opioid peptides

Epo (Erythropoetin) / sports

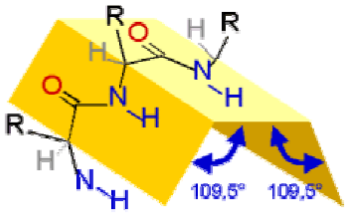
Proteins & Structure

✔ -Helix

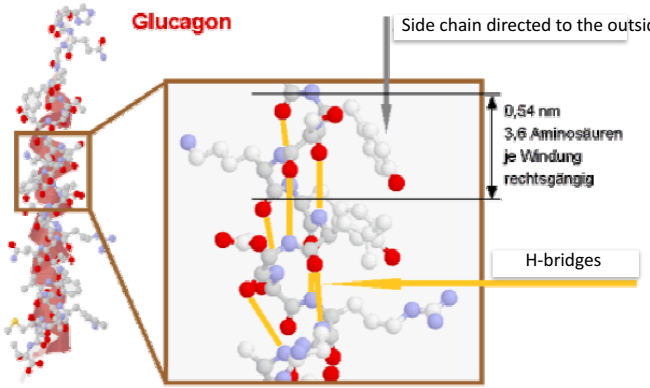


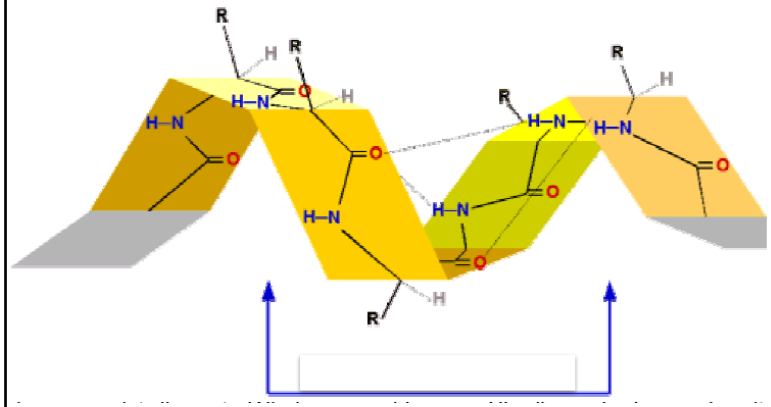


2 amid bonds



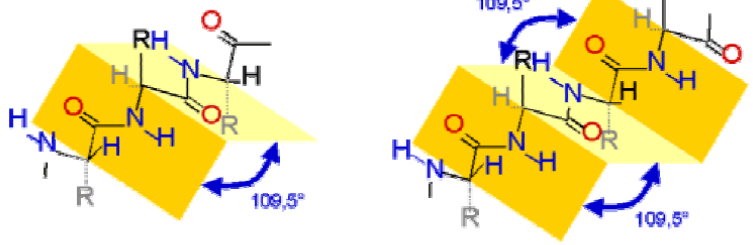
3 amid bonds





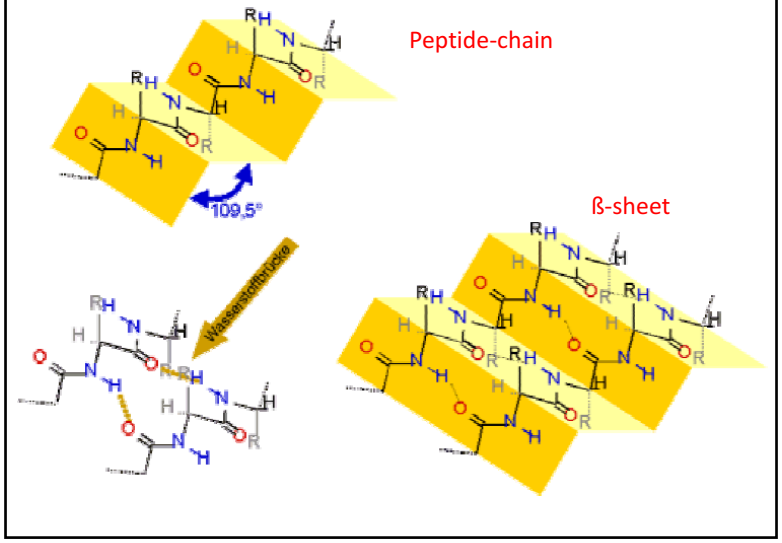
3.6 amino acids per 'turn' (Windung)

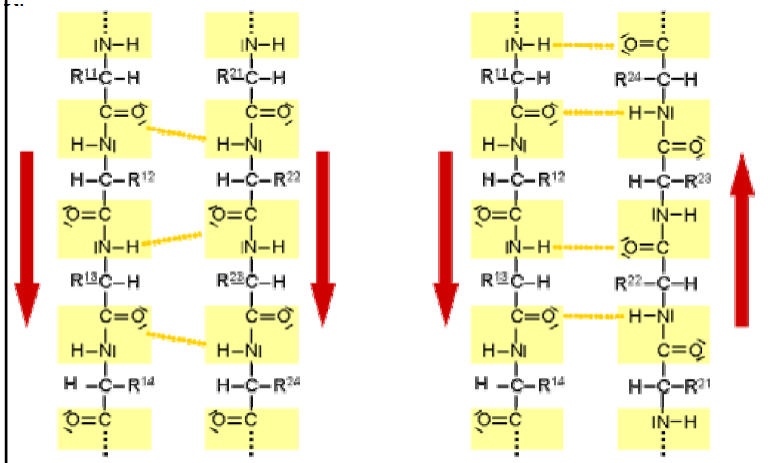
ß-sheet:



2 amid bonds

3 amid bonds





parallel ß-sheet

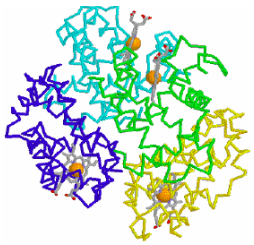
anti-parallel ß-sheet

The Tertiary Structure of Proteins

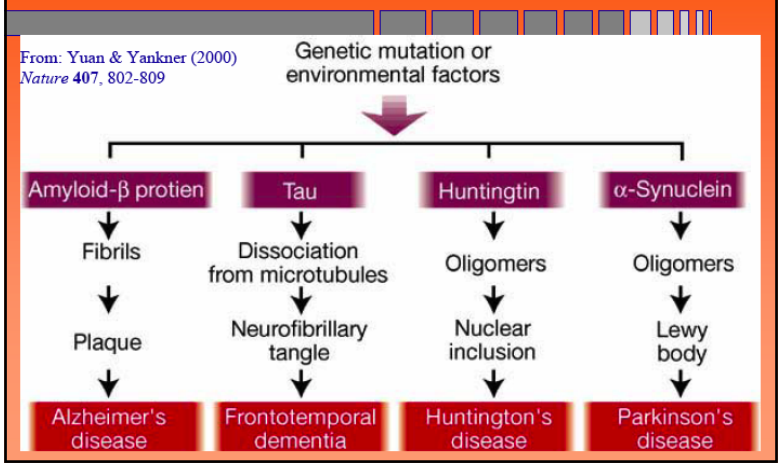
The tertiary structure describes the spatial arrangement of a protein e.g. as alpha-helix or beta-sheet using also disulfide-bridges, ion-bonds, Van-der-Vaals forces, etc

The Quaternary Structure of Proteins

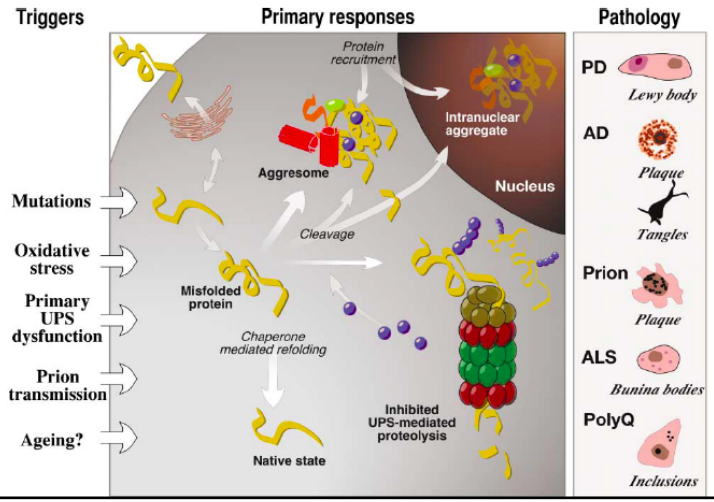
In the quaternary structure several protein chains form a globular structure by arranging themselves around ions such as Fe^{2+}, Mg^{2+}, etc…

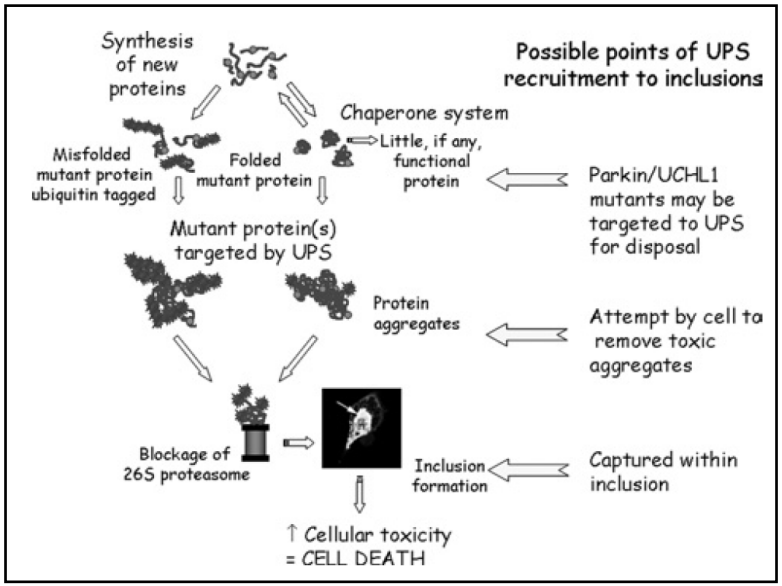


Abnormal protein structures in the pathogenesis of neurodegenerative diseases

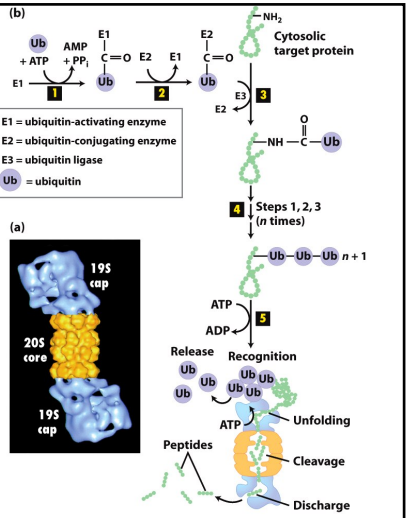


Abnormal Protein Folding and Neurodegenerative / Brain diseases





The unfolded protein response (UPR), ubiquitin proteasome system (UPS) activation and its correlation with autophagy system



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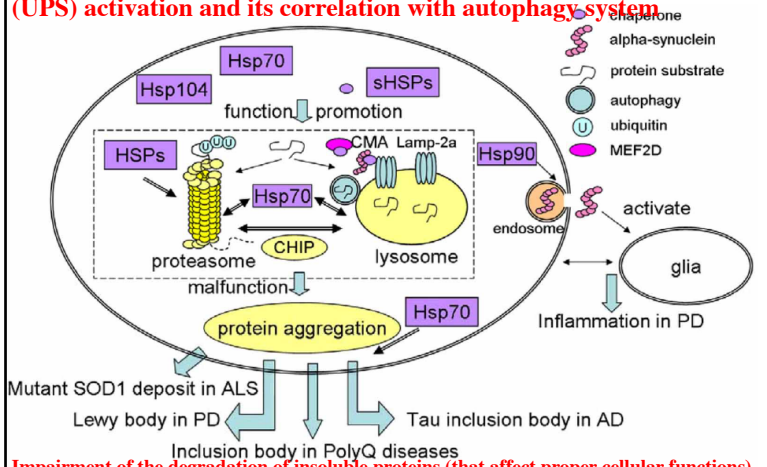

Impairment of the degradation of insoluble proteins (that affect proper cellular functions) leads to NDs such as PD

CHIP: C terminal of molecular chaperone interaction protein; MEF2D: myocyte enhancer factor 2D; CMA: chaperone mediated autophage

END