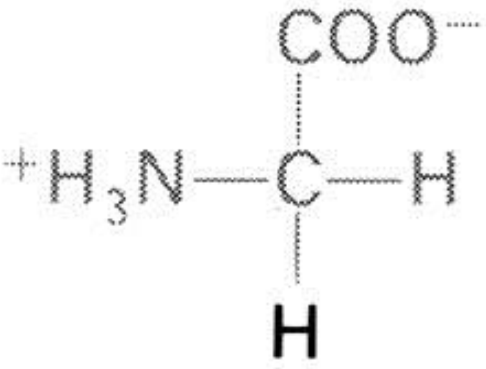
Lecture #2

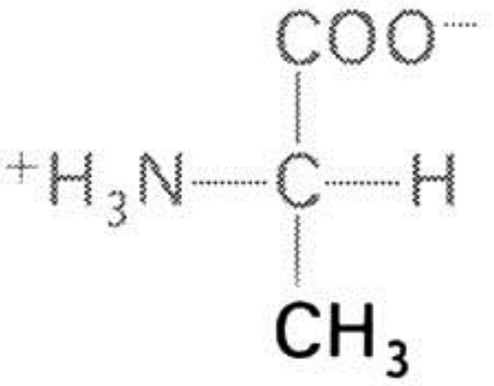
- The 20 amino acids
  - Names
  - Structures
  - Properties
- pH and acid basics
- Forces stabilizing protein structures

Amino acids having aliphatic side chains



no sidechain, not optically active

Glycine
Gly
G

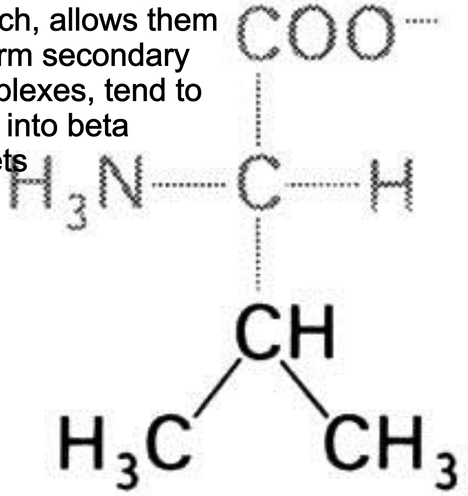


zwitterionic at neutral group

"in the middle" in terms of hydrophilicity, methyl group is mildly hydrophobic

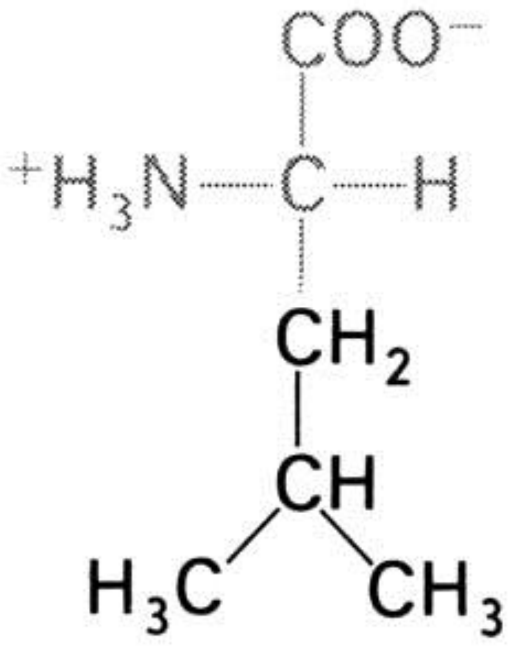
Alanine
Ala
A

aliphatic chain, beta branch, allows them to form secondary complexes, tend to form into beta sheets



Valine
Val
V

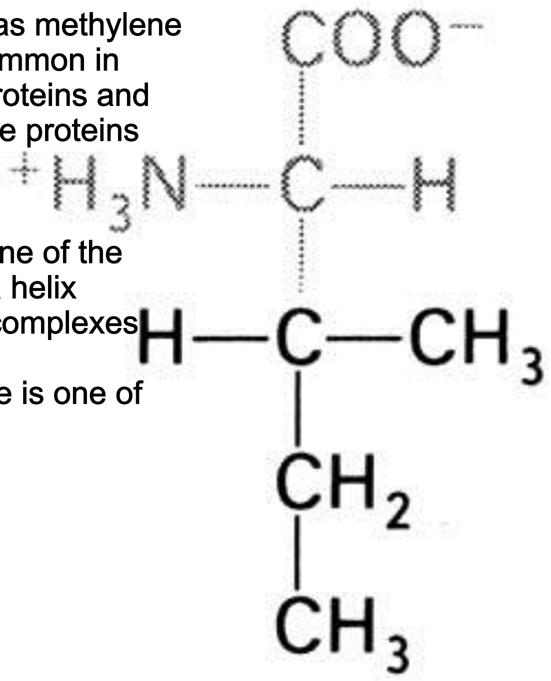
Amino acids having aliphatic side chains



isomers
leucine has methylene group, common in soluble proteins and membrane proteins

leucine one of the best beta helix forming complexes

isoleucine is one of the worst

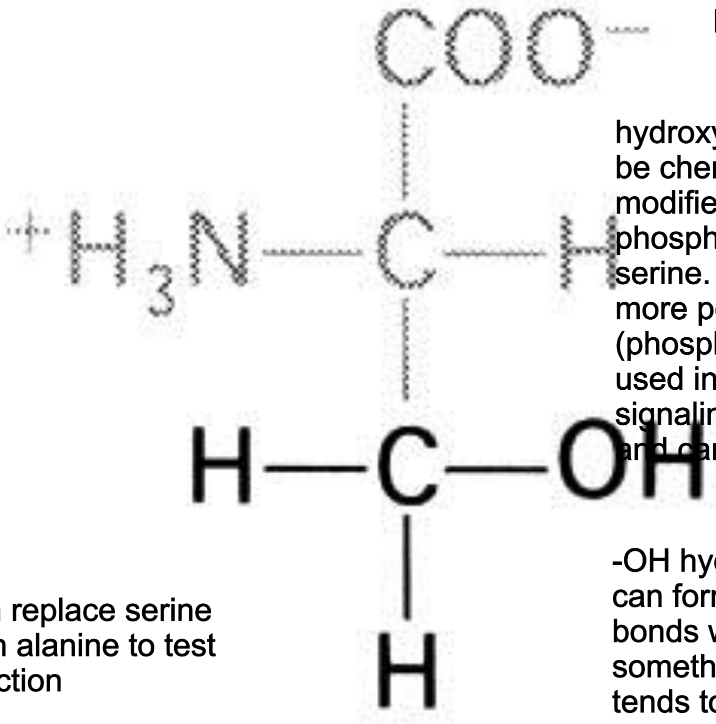


Leucine
Leu
L

Isoleucine
Ile
I

Serine and threonine have aliphatic hydroxyl side chains

polar

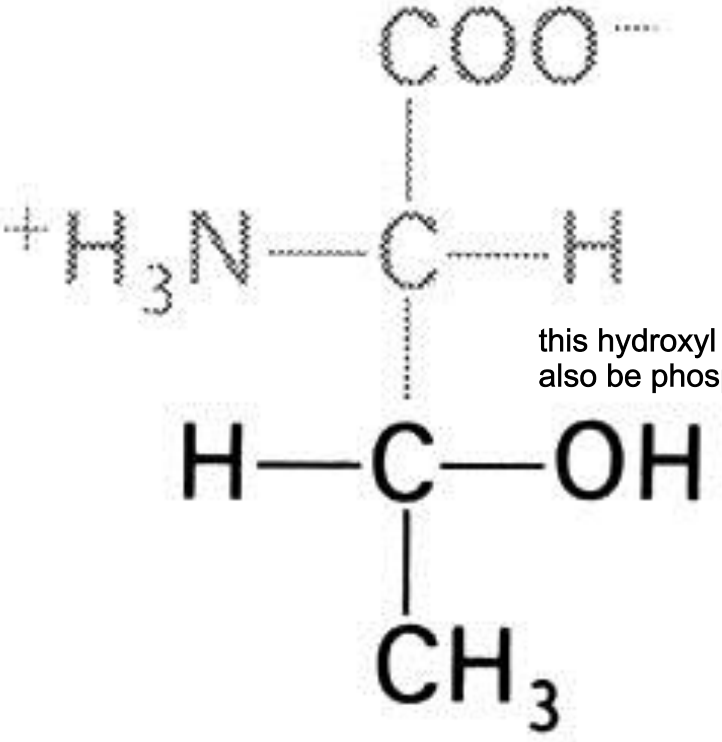


hydroxyl group can be chemically modified, ATP can phosphorylate serine. making it more polar (phosphoserine: used in cell signaling, hormones, and cancer

-OH hydroxyl group. can form hydrogen bonds with water or something else tends to be on surface of proteins, but can also hydrogen bond to other parts of the protein.
serine can be deprotonated, commonly in active site of enzymes

can replace serine with alanine to test function

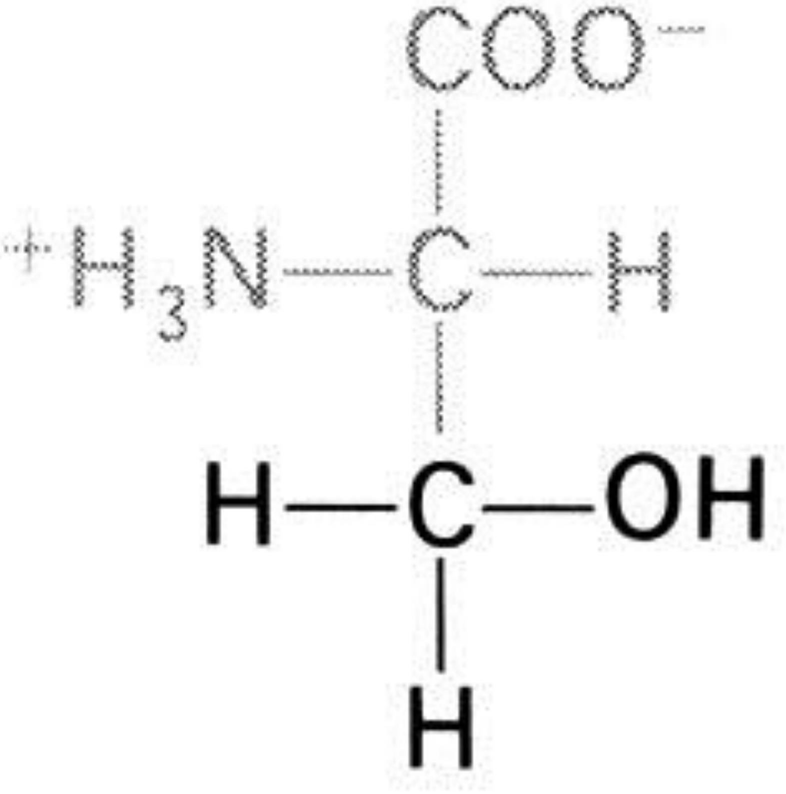
Serine
Ser
S



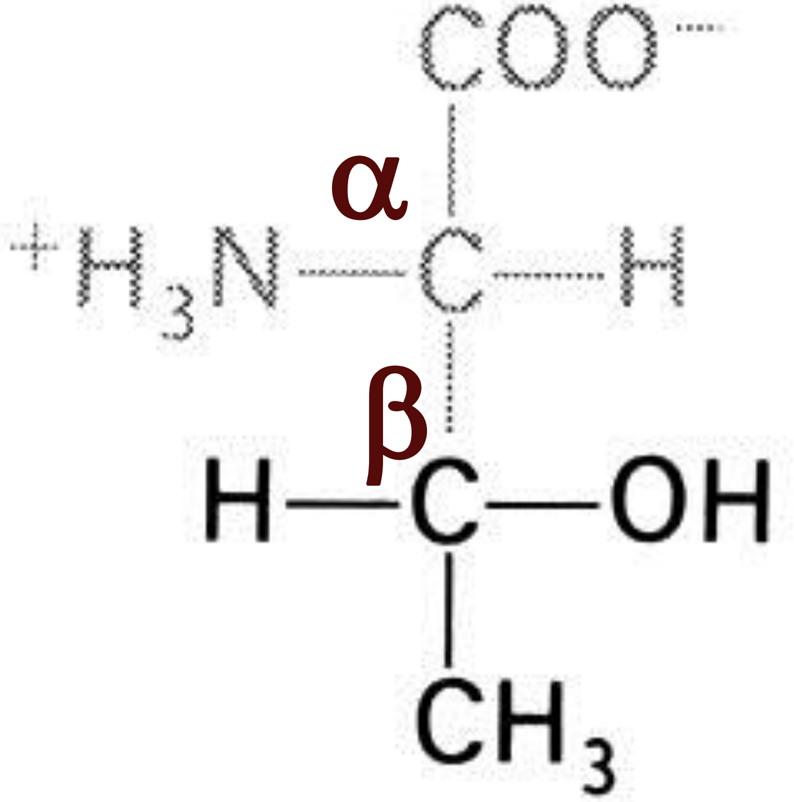
this hydroxyl group can also be phosphorylated

Threonine
Thr
T

Threonine has a β-branched side chain

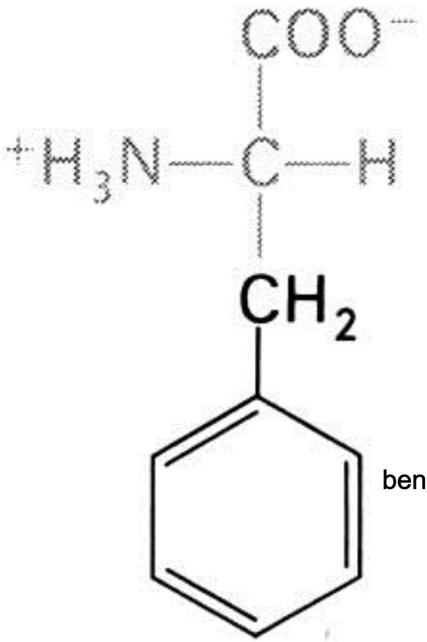


Serine



Threonine

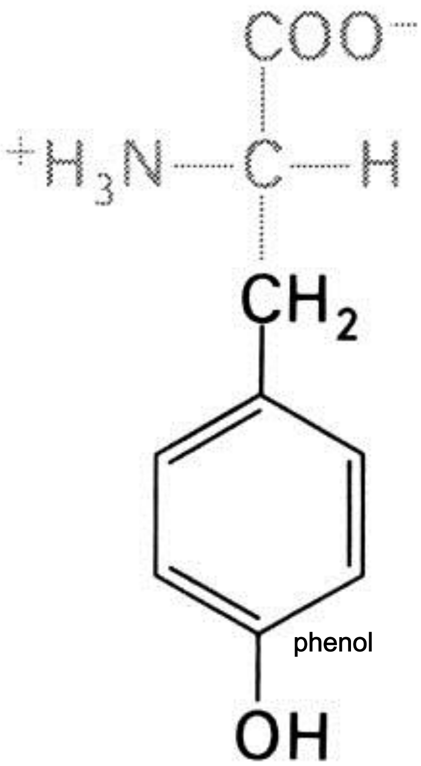
Phenylalanine, tyrosine, and tryptophan have aromatic side chains



benzene ring

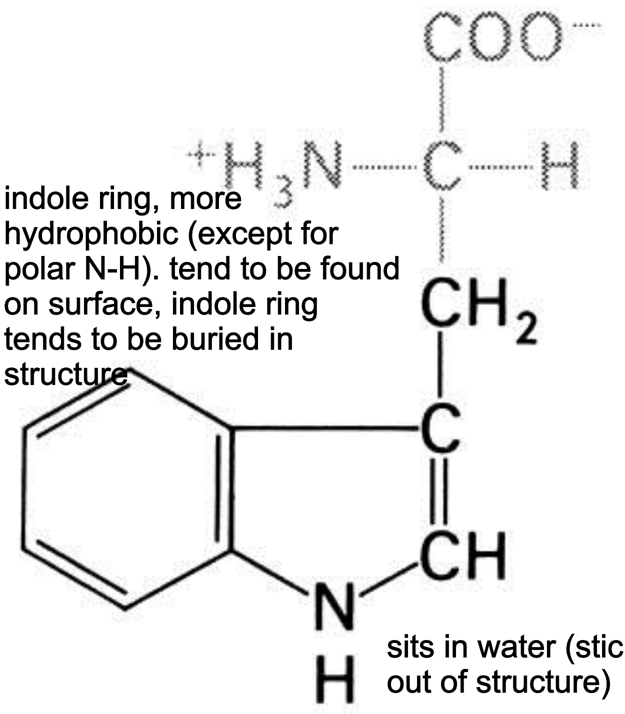
hydrophobic amino acid

Phenyl-alanine
Phe
F



phenol

Tyrosine
Tyr
Y

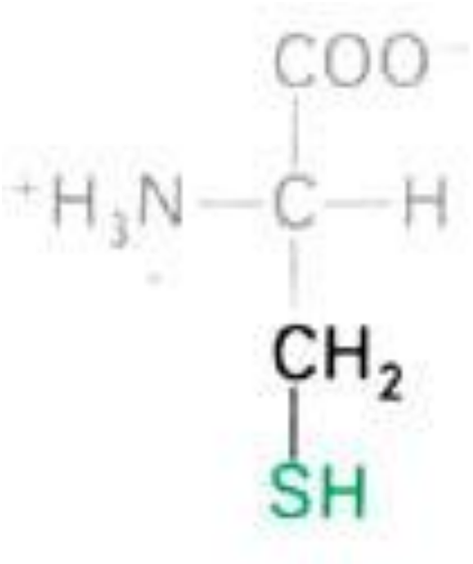


indole ring, more hydrophobic (except for polar N-H). tend to be found on surface, indole ring tends to be buried in structure

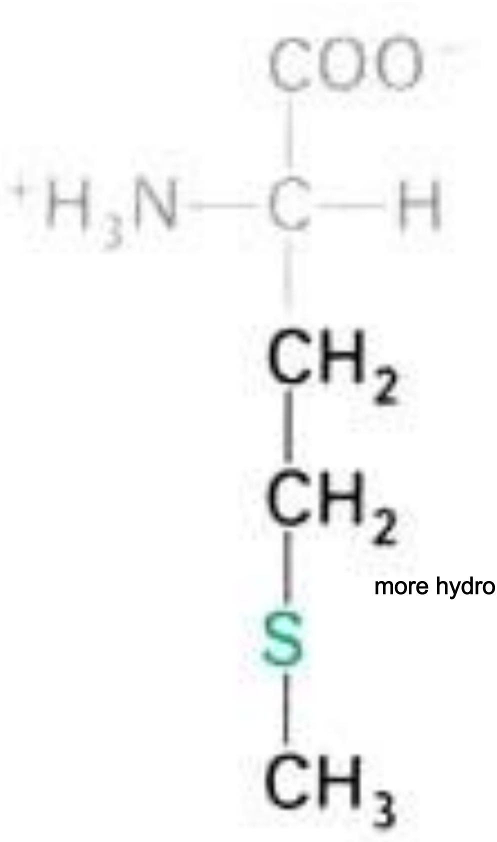
sits in water (sticking out of structure)

Tryptophan
Trp
W

Sulfur - containing amino acids



very short chain, polar group, can hydrogen bond



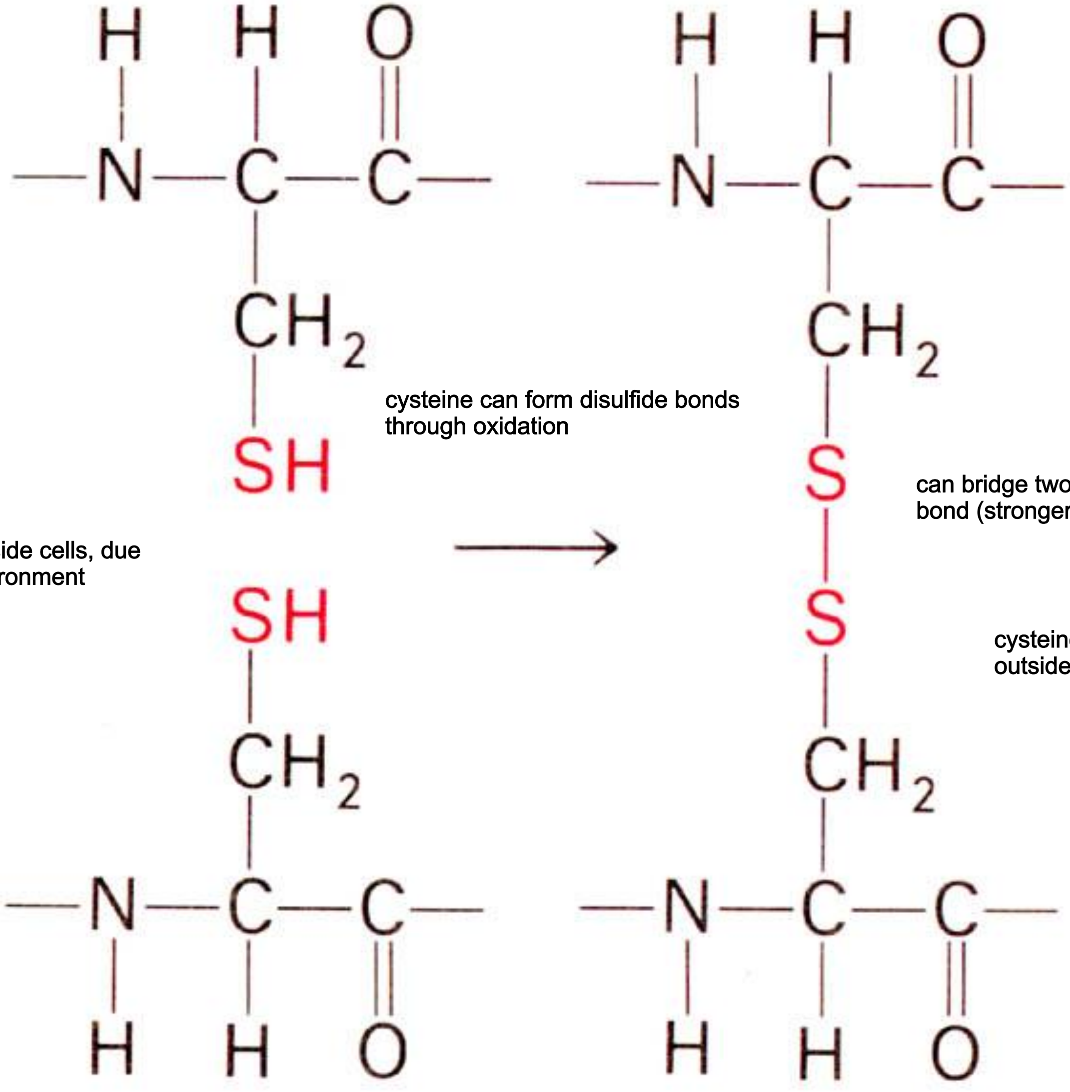
more hydrophobic than cysteine

Cysteine
Cys
C

Methionine
Met
M

initiator codon

Disulfide bond



cysteine can form disulfide bonds through oxidation

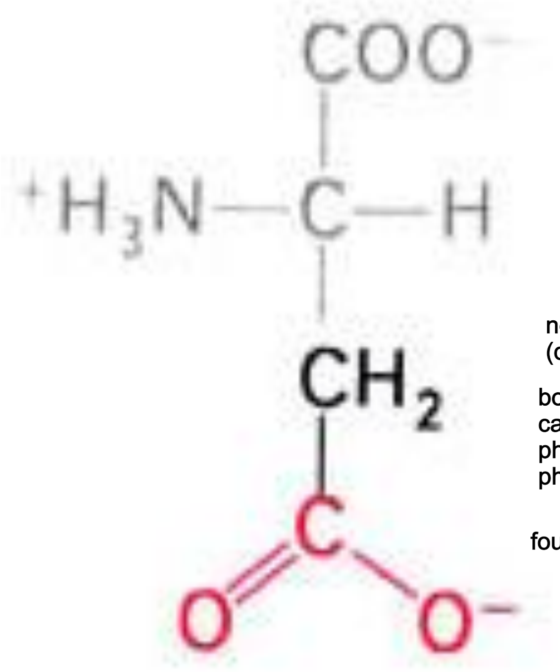
cysteine exists inside cells, due to a reducing environment

can bridge two parts of a protein with a covalent bond (stronger) and at a longer distance

cysteine is found in proteins secreted outside of cells (like insulin)

Cysteine **Cystine**

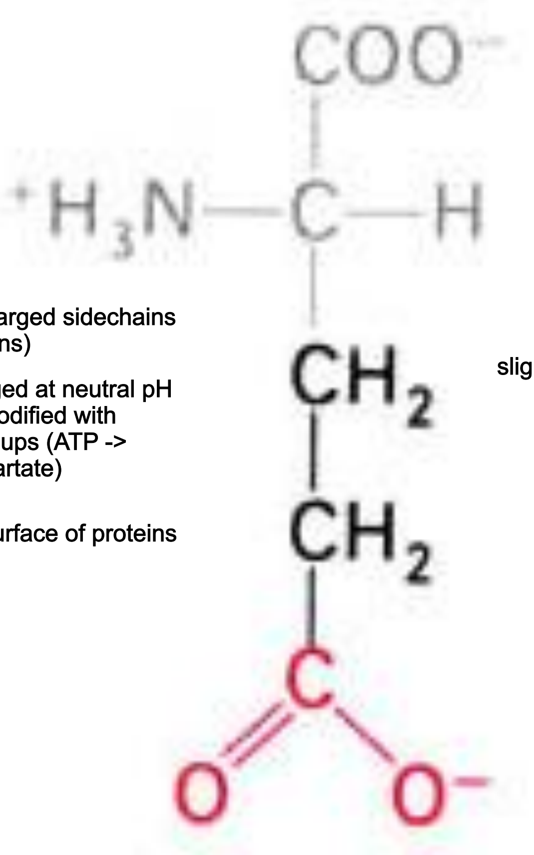
Acidic amino acids



negatively charged sidechains
(donate protons)

both are charged at neutral pH
can also be modified with
phosphate groups (ATP ->
phosphor aspartate)

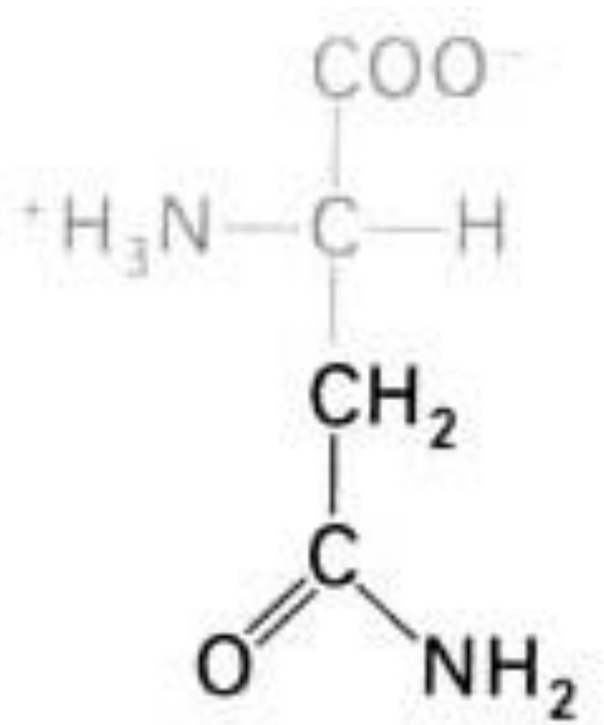
found on the surface of proteins



slightly more hydrophobic

Aspartate
Asp
D

Glutamate
Glu
E

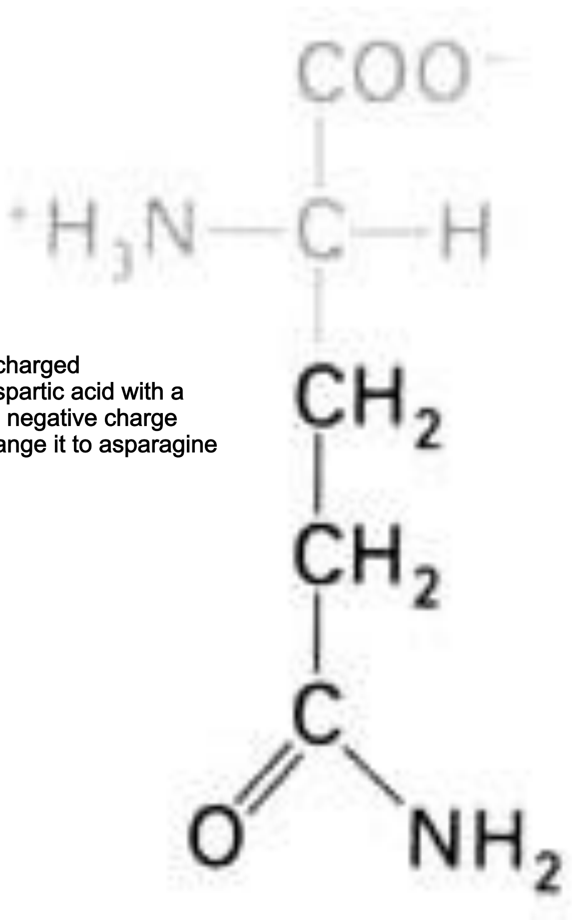


amine bond. don't have a negative charge, but still very polar

carbohydrates are attached covalently to asparagine, like carbohydrates (glycoproteins)

Glycoproteins are on membrane proteins are secreted

polar, but not charged
experiment: aspartic acid with a charge - is the negative charge important? change it to asparagine and examine

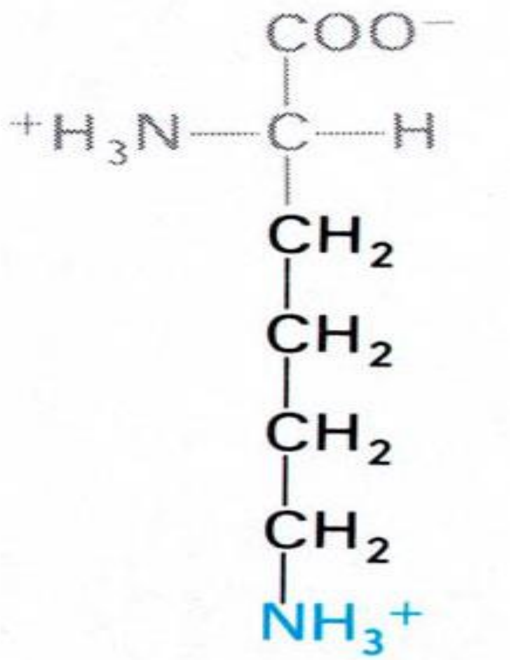


Asparagine
Asn
N

sugars on asparagine are not found inside the cell

Glutamine
Gln
Q

Basic amino acids



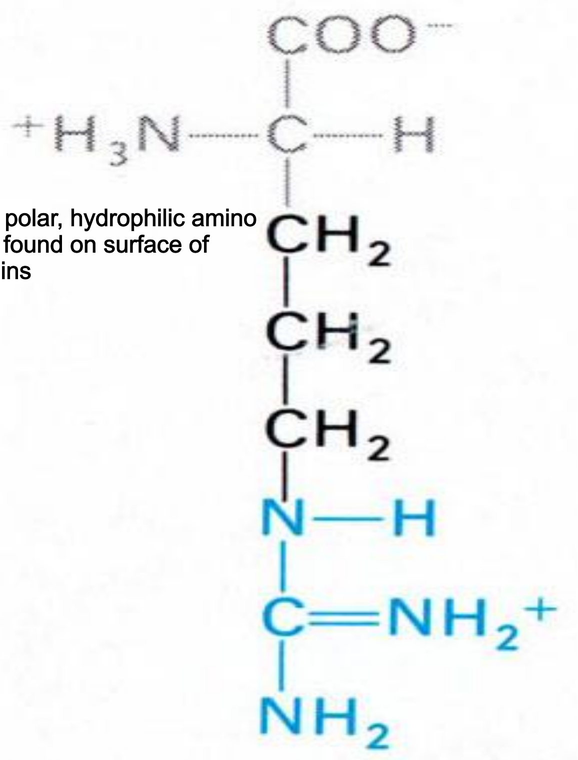
very charged and very polar. tend to be found on surface of proteins. aliphatic chain is very hydrophobic, NH3+ is on the surface of the protein, and the chain is buried. similar to tryptophan

Lysine

Lys

K

most polar, hydrophilic amino acid. found on surface of proteins



Guanidinium group

Arginine

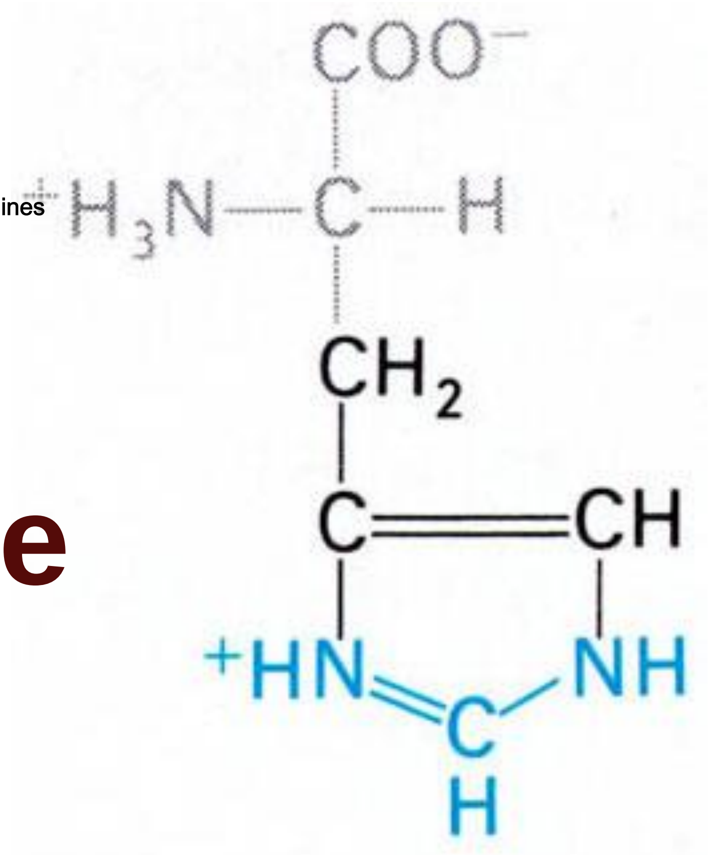
Arg

R

essential for catalysis, usually found on active site of enzymes.
has imidazole ring, can be positively charged under certain pH conditions.
functions as a proton acceptor or donator

histidine can bind metal ions like iron or copper (chelator)

albumin protein: end terminus has a bunch of histamines which bind copper, etc



Imidazole ring

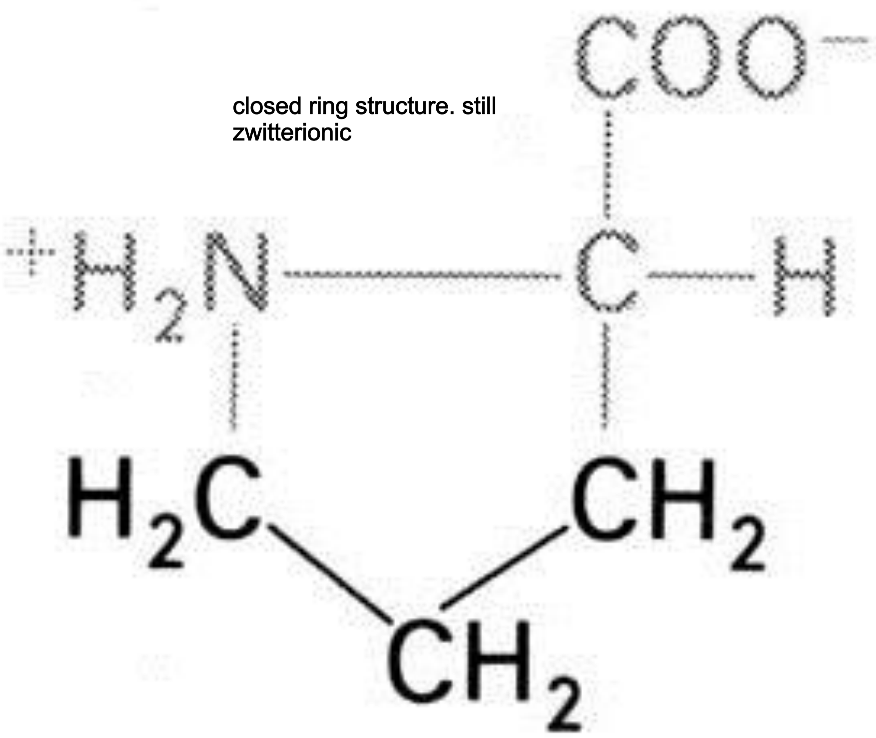
Histidine
His
H

Proline

can still form amide bonds in proteins
tends to put a kink or bend in the protein chain
commonly found in U-turns/reverse chains
usually found near the beginning of a helix chain
not usually involved in catalysis

Proline
Pro
P
imino acid

Side chain is cyclic ring via a covalent bond with the backbone nitrogen atom



closed ring structure. still zwitterionic

Hydrophobic (non-polar) amino acids

Ala, Gly*

Val, Ile, Leu, Met

Phe

Pro*

* polar due to the proton, not super hydrophobic

Hydrophilic (polar) amino acids

Polar: Asn, Gln

Ser, Thr

Cys*

* often present at the surface of the protein. cystine is more hydrophobic and tends to be buried in the protein structure

Hydrophilic (charged) amino acids

can also be neutral
depending on pH

Basic: Arg, Lys*, His

Acidic: Asp, Glu

Amphipathic aromatic amino acids

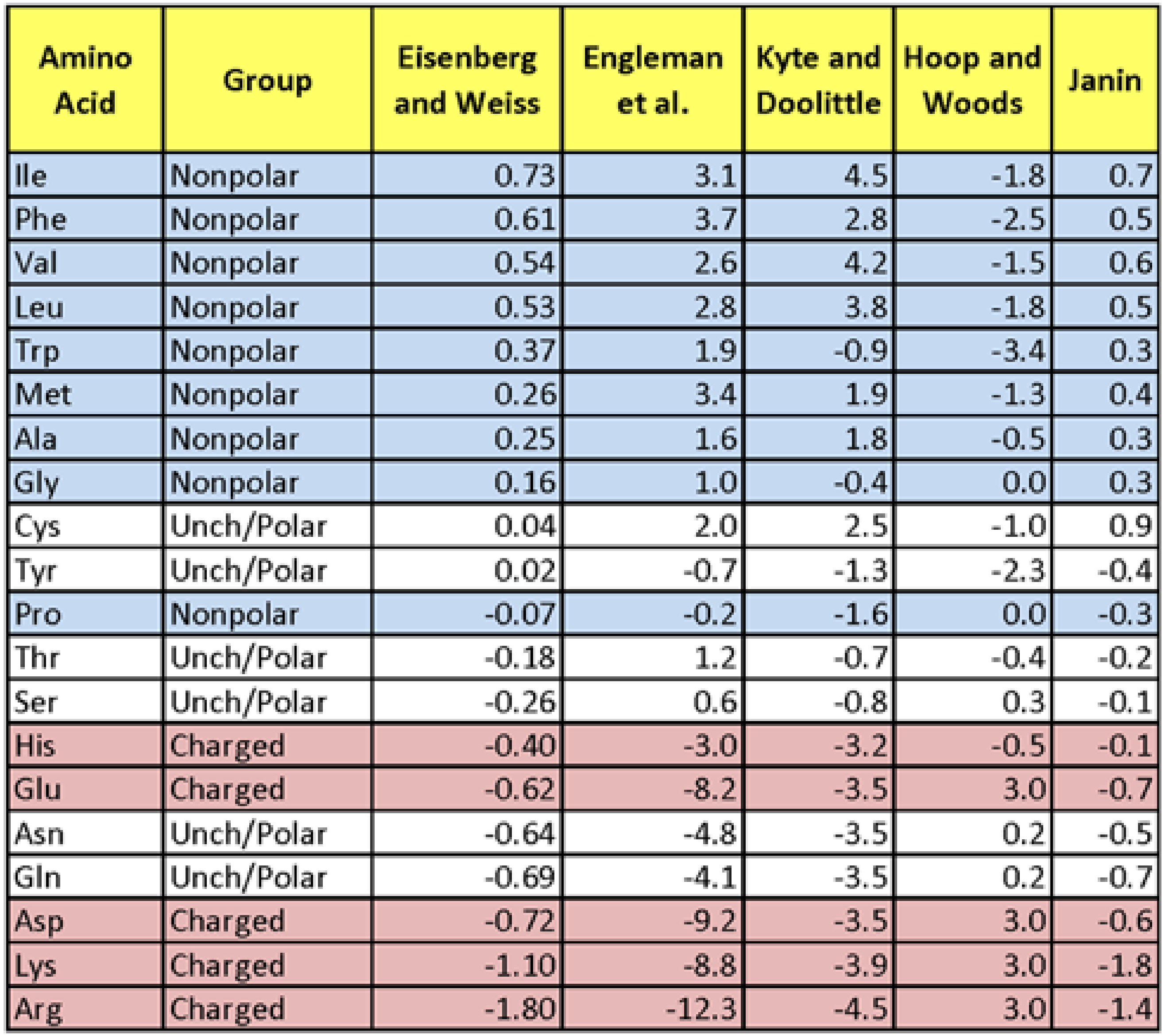
benzene ring

indole ring

Tyr, Trp

Hydrophobicity scales

Kyte + Doolittle is most
commonly used scale



Amino Acid	Group	Eisenberg and Weiss	Engleman et al.	Kyte and Doolittle	Hoop and Woods	Janin
Ile	Nonpolar	0.73	3.1	4.5	-1.8	0.7
Phe	Nonpolar	0.61	3.7	2.8	-2.5	0.5
Val	Nonpolar	0.54	2.6	4.2	-1.5	0.6
Leu	Nonpolar	0.53	2.8	3.8	-1.8	0.5
Trp	Nonpolar	0.37	1.9	-0.9	-3.4	0.3
Met	Nonpolar	0.26	3.4	1.9	-1.3	0.4
Ala	Nonpolar	0.25	1.6	1.8	-0.5	0.3
Gly	Nonpolar	0.16	1.0	-0.4	0.0	0.3
Cys	Unch/Polar	0.04	2.0	2.5	-1.0	0.9
Tyr	Unch/Polar	0.02	-0.7	-1.3	-2.3	-0.4
Pro	Nonpolar	-0.07	-0.2	-1.6	0.0	-0.3
Thr	Unch/Polar	-0.18	1.2	-0.7	-0.4	-0.2
Ser	Unch/Polar	-0.26	0.6	-0.8	0.3	-0.1
His	Charged	-0.40	-3.0	-3.2	-0.5	-0.1
Glu	Charged	-0.62	-8.2	-3.5	3.0	-0.7
Asn	Unch/Polar	-0.64	-4.8	-3.5	0.2	-0.5
Gln	Unch/Polar	-0.69	-4.1	-3.5	0.2	-0.7
Asp	Charged	-0.72	-9.2	-3.5	3.0	-0.6
Lys	Charged	-1.10	-8.8	-3.9	3.0	-1.8
Arg	Charged	-1.80	-12.3	-4.5	3.0	-1.4

Roles of the side chains

- **Hydrophobic** (non-polar) amino acids (F, L, I, V)occur usually in the interior of globular proteins
- **Hydrophilic** (charged/polar) amino acids (R, K, E, D, Q, N, S, T) occur on the protein surface, interact with water

Amino acid % composition in soluble proteins

Common

Leu	9.4 %	great alpha helix former
Ala	7.5	less hydrophobic than leucine. good helix former, and in extended strands
Ser	7.2	
Gly	6.8	
Val	6.6	beta branch, great beta sheet former and helix former

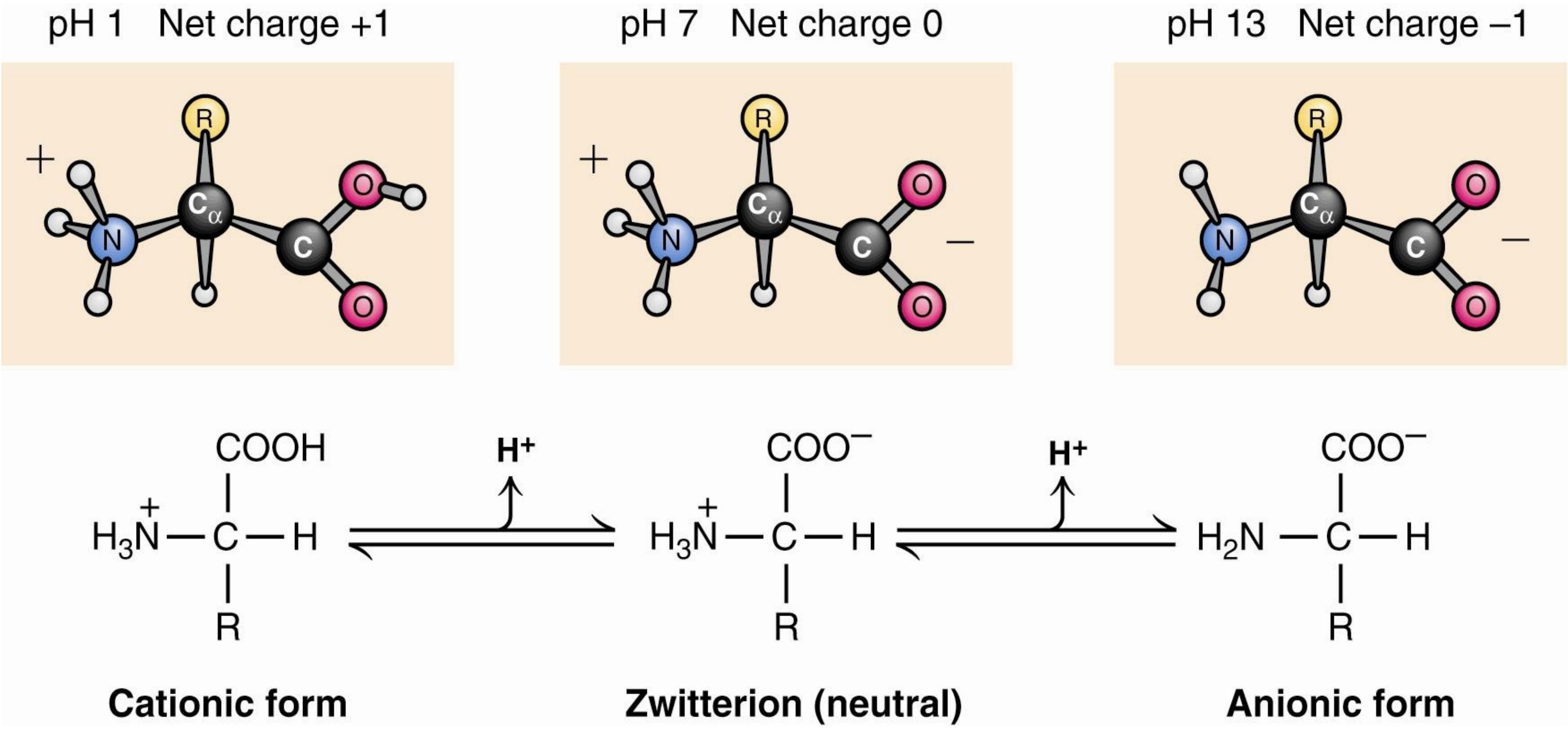
Rare

Trp	1.2 %	fluroescence
Cys	1.6	
His	1.8	

pH

- $pH = 7.0$
- $[H^+] = 10^{-7.0}$
- $[H^+] = 0.1\ \mu M$

Zwitterion form of amino acids



also function as amino acids. glutamic acid and glycine

pK_a of amino acid side-chains

pKa: pH value at which group is half protonated and half unprotonated

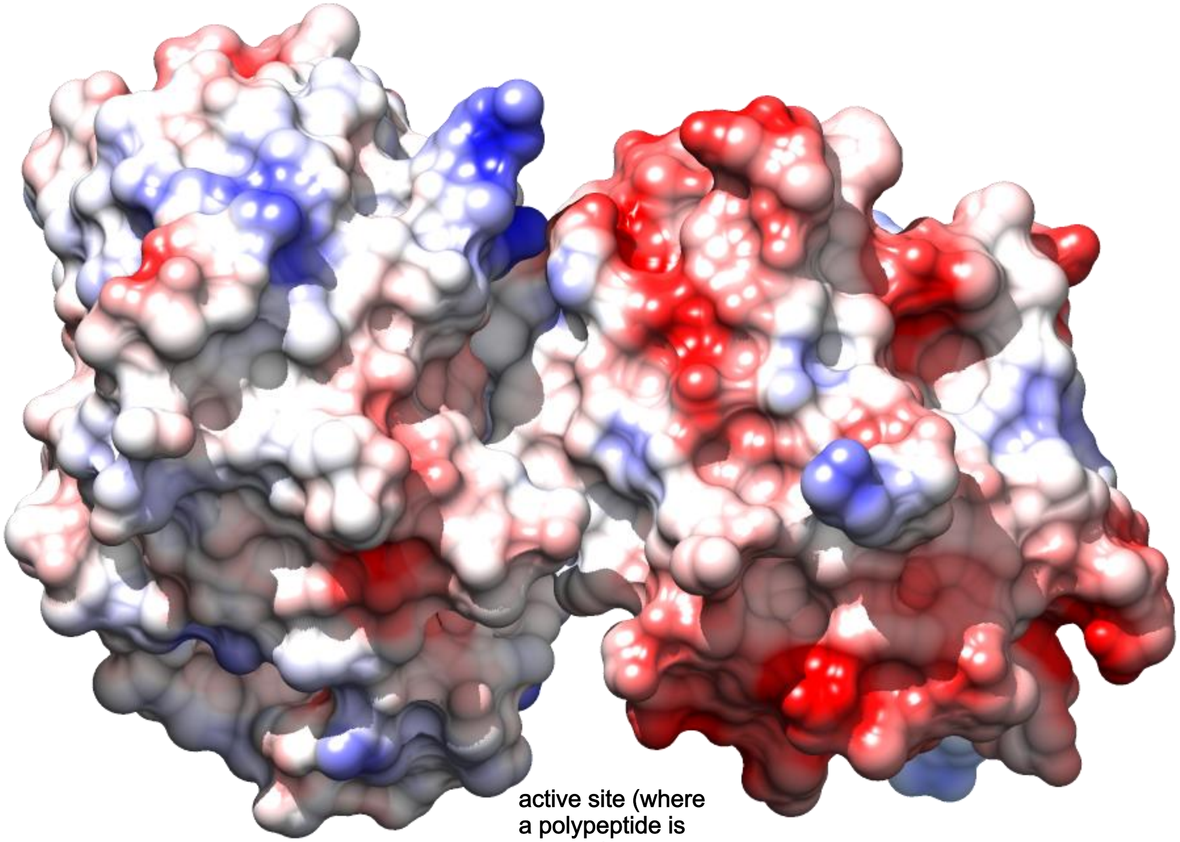
- **Arginine, Arg, R: $pK_a = 12.5$**
- **Lysine, Lys, K: $pK_a = 10.5$**
- **Cysteine, Cys, C: $pK_a = 8.3$**

can lose a proton depending on environment

- **Histidine, His, H: $pK_a = 6.0$**
- **Glutamic Acid, Glu, E: $pK_a = 4.3$**
- **Aspartic Acid, Asp, D: $pK_a = 3.9$**

aspartic acid's pka can be different depending on the environment (buried in protein)

Trypsin surface charge
Basic (blue), acidic (red)



active site (where a polypeptide is cleaved)

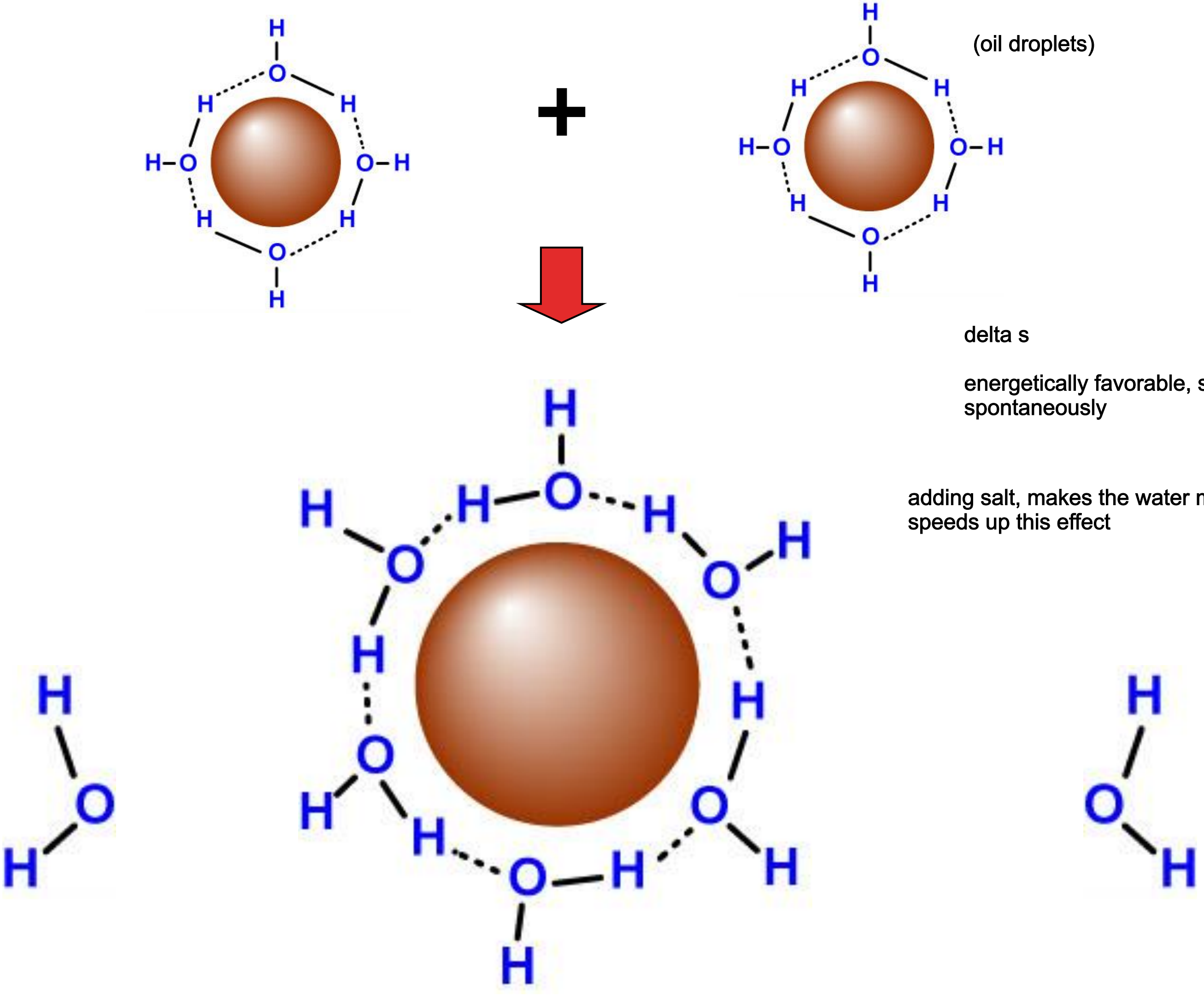
Interactions stabilizing protein structures

- Hydrophobic
- Electrostatic
- Hydrogen bonds
- van der Waals

The hydrophobic effect

- **Non-polar groups are driven together not so much because they have a high affinity for each other, but <u>because water hydrogen bonds strongly to itself.</u>**

Structured water is released and entropy increases



(oil droplets)

delta s

energetically favorable, so happens spontaneously

adding salt, makes the water more polar and speeds up this effect

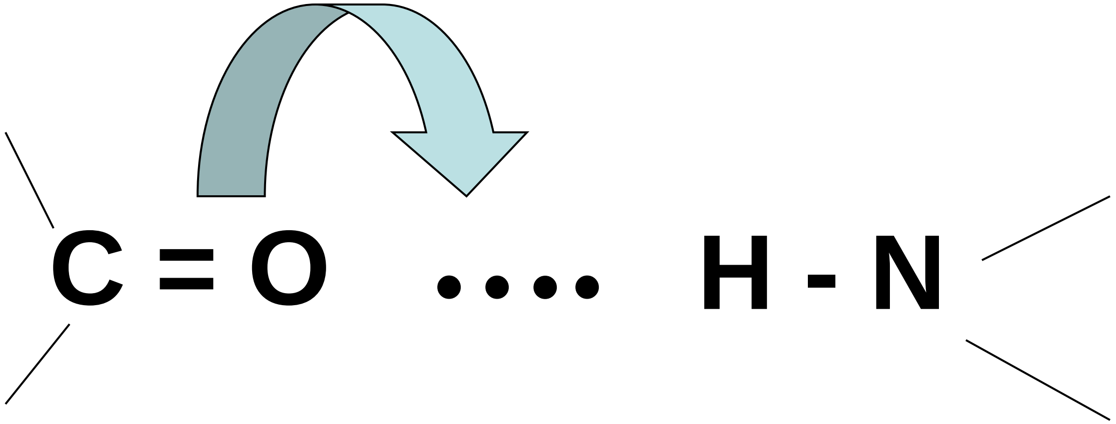
Electrostatic forces

- Attraction between oppositely-charged species (+, -), especially protonated amino and ionized carboxylate groups.
- Arg (+ve) … Asp (-ve)

Hydrogen bonds

- **Stabilizing, attractive interaction between a proton (often part of a polarizable bond such as -NH, -OH, or -SH) and an electron-donating species (often C = O)**
- **Important for protein structure such as the alpha-helix**

Electron density donated from carbonyl group to form H-bond



C = O …. H - N

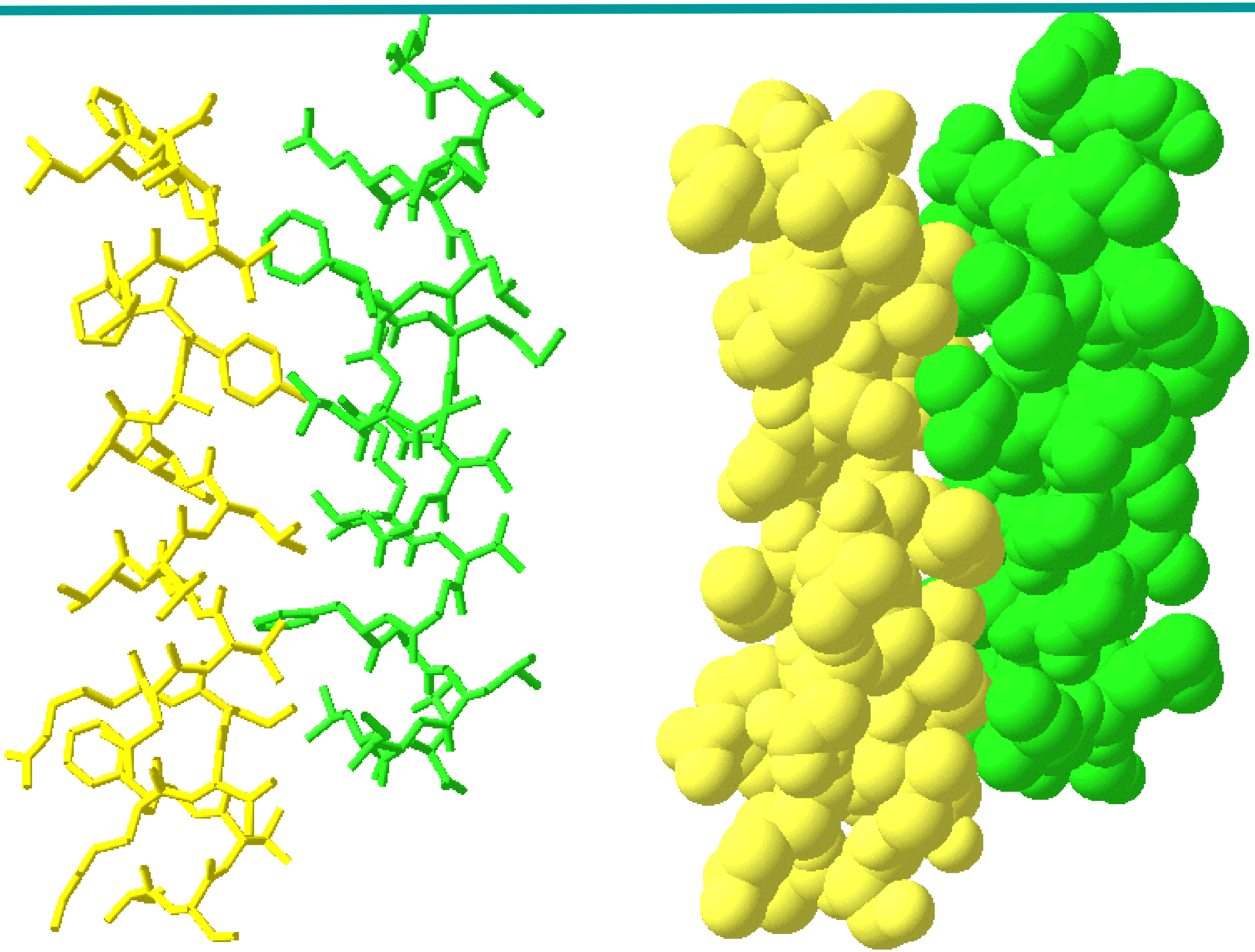
The C=O bond is the donor of electrons, the N-H proton is the acceptor

van der Waals interactions

- Stem largely from favorable (non-repulsive) interactions between side chains, based on proximity and packing - at, but not closer than - the ‘van der Waals contact distance’

further distance = repulsive forces (London dispersion forces)

van der Waals PACKING: Close contacts occur between protein segments (“ridges into grooves”)



Summary

- 20 amino acids make up proteins
- Hydrophobic residues are buried inside proteins
- Charged/polar residues on the protein surface
- What effect would substitution of a charged residue for a buried hydrophobic residue have on protein structure?