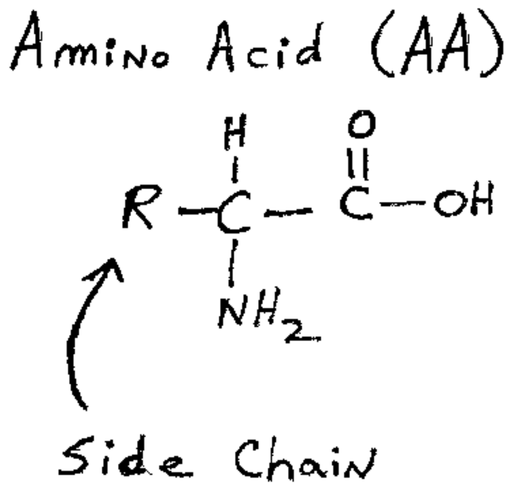
BL 4010 Lecture #4

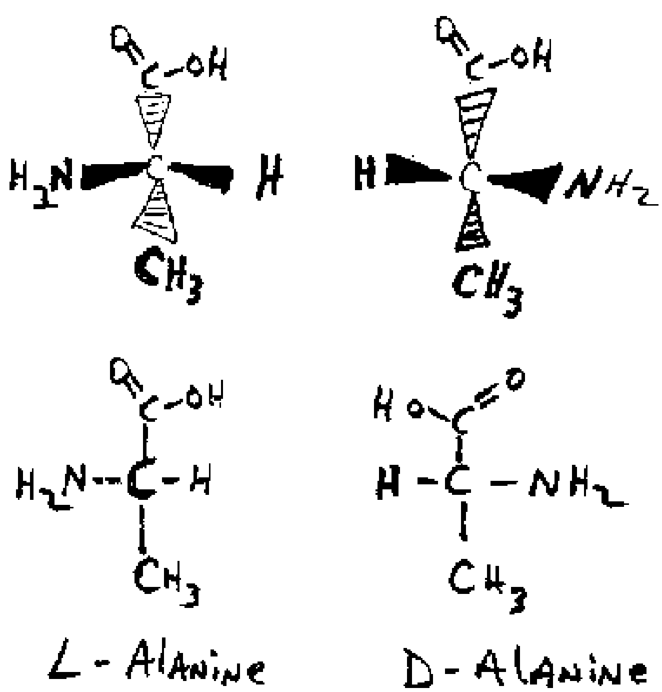
Amino Acid Structures

General structure of an Amino Acid (abbreviated AA):



{*Figure 1*}

Most Amino Acids are asymmetric or chiral - illustrated here with alanine:



{*Figure 2*}

All Amino Acids found in proteins are in the L-form.

If you were to eat large quantities of D-amino acids, it would kill you.

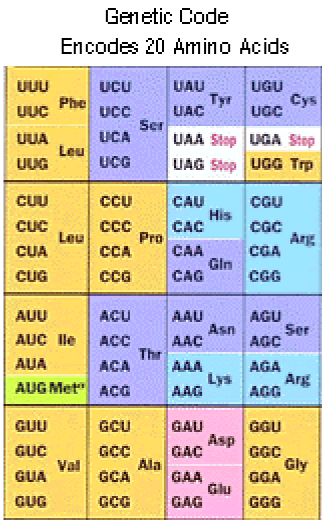
Types of Amino Acids based on side-chain chemical character:

I. Non-Polar or hydrophobic (water hating)

II. Flexible

III. Polar or hydrophilic (water loving)

There are 20 Amino Acids encoded by codons in the genetic code:



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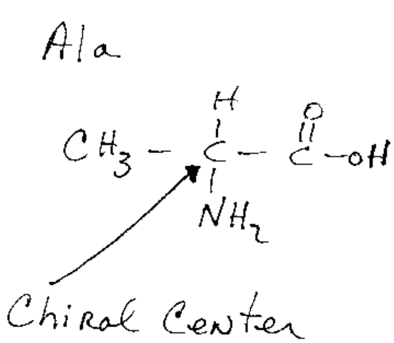
When there are more than 100 AAs found in nature, why only 20 AAs in proteins? Because these 20 AAs provide all the chemical and size groups needed to make a very large number of proteins. Plus many of these amino acids become modified after translation into proteins, which increases the available chemical character of amino acid side chains.

These 20 AAs can be divided into the above 3 groups (non-polar, flexible and polar) and then subdivided by their chemical character:

Group I = Non-Polar -- 8 AAs

Hydrocarbon NON-POLAR AMINO ACIDS -- 5 AAs -- Ala Val Leu Ile Pro:

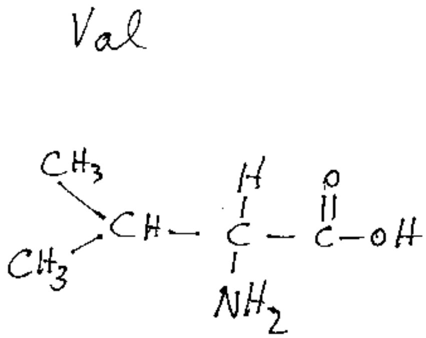
Non-Polar -- Hydrocarbon -- Ala (Alanine) - in computers Ala = A



{*Figure 3*}

The chiral Carbon of Ala is emphasized here! All amino acids are derivatives of Ala, except Gly (see below).

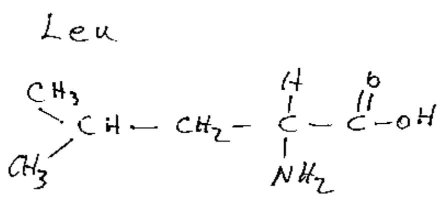
Non-Polar -- Hydrocarbon -- Val (Valine) - in computers Val = V



{*Figure 4*}

Val has to methyl groups added to Ala to make an isopropyl group.

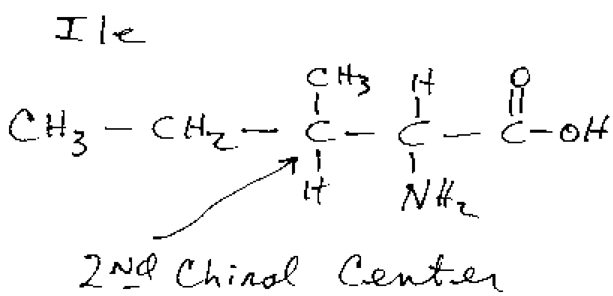
Non-Polar -- Hydrocarbon -- Leu (Leucine) - in computers Leu = L



{*Figure 5*}

Leu adds an isopropyl group to Ala so that Leu has 4 carbons in its side chain.

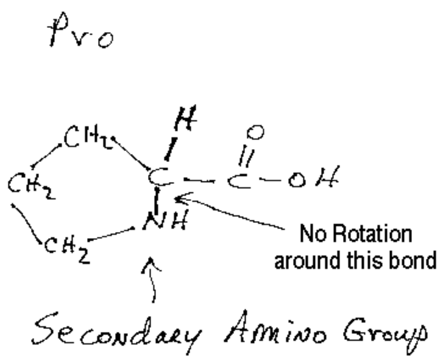
Non-Polar -- Hydrocarbon -- Ile (Isoleucine) - in computers Ile = I



{*Figure 6*}

Ile is a structural isomer of Leu so it also has 4 carbons in its side chain. But Ile is bulkier than Leu near the base of the side chain, while Leu is bulkier than Ile farther out on the side chain (size/shape of side chains is important). Ile has a 2nd chiral center which is emphasized in the Ile drawing above (Fig. 6). Why does Ile have a chiral center and Leu not?

Non-Polar -- Hydrocarbon -- Pro (Proline) - in computers Pro = P

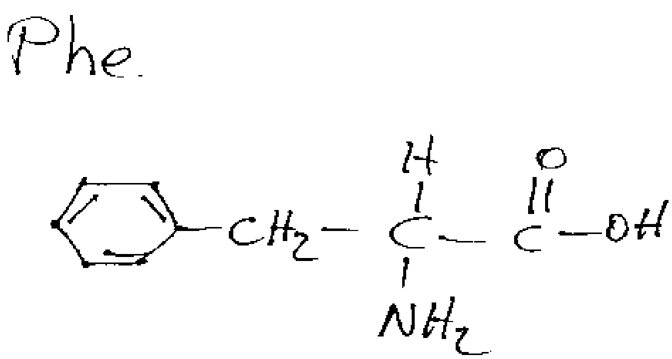


{*Figure 7*}

Pro is a very special amino acid due to its inflexible character!!! Pro is inflexible because its side chain bonds to alpha-amino group in a ring structure which can not twist around the bond between alpha-amino group and alpha carbon, which all other AAs can. Also Pro, thus, has a secondary amino group (notice the single hydrogen on its Nitrogen atom) with different chemical character than the primary amino groups in all other amino acids, which have two hydrogens on them. Try to draw Pro or make a model if you have a model set (left over from a chemistry course).

Aromatic NON-POLAR AMINO ACIDS -- 2 AAs --Phe Trp:

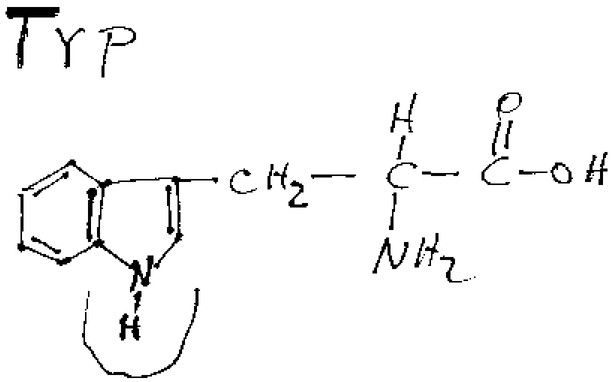
Non-Polar -- Aromatic -- Phe (Phenylalanine) -- in computers Phe = F



{*Figure 8*}

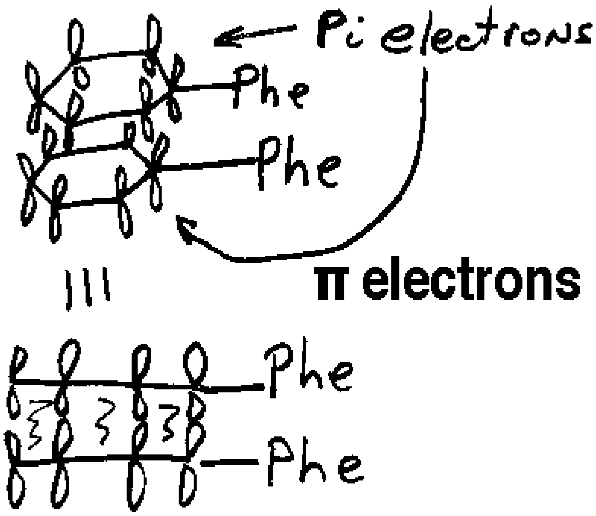
Phe adds a benzene ring to Ala!

Non-Polar -- Aromatic -- Trp (Tryptophan) -- in computers Trp = W



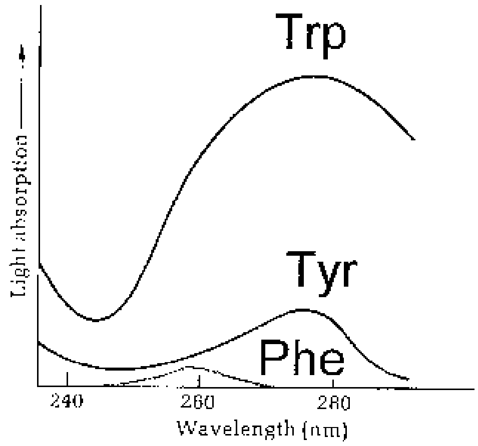
{*Figure 9*}

Trp has a heterocyclic aromatic group with an aromatic amine in it. Aromatic amines (emphasized in Fig. 9) like in Trp do not ionize since the Nitrogen has its free electrons tied up in the Pi cloud with the electrons of the Carbon-Carbon aromatic double bonds. Aromatic Pi clouds allow them to bond together via interaction of the Pi electrons. The planar character of aromatic side chains helps the Pi cloud bonding.



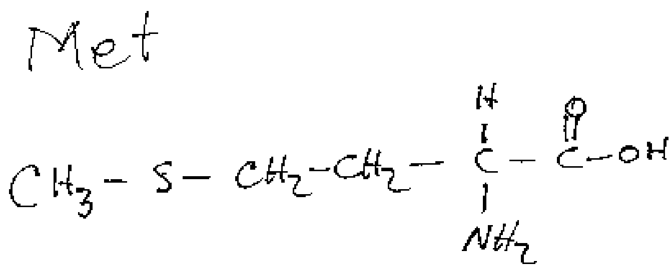
{*Figure 9a}

Pi electrons physically lie above and below the plane of the aromatic ring. Because of Pi electrons aromatic AAs absorb light in the UV!



Thiol Ether NON-POLAR AMINO ACID -- 1 AA -- Met:

Non-Polar -- Thiol Ether -- Met (Methionine) -- in computers Met = M

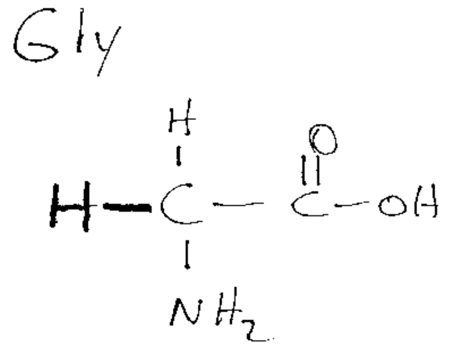


{*Figure 10*}

Met introduces the important Sulfur element into proteins which is found in Cys also (see below). Met contains a thiol ether (R-S-R) in its side chain, which is much less polar than an oxy-ether (R-O-R) like the compound we call ether, which is an polar organic solvent. Met is a very hydrophobic AA.

Group II = Flexible -- 1 AA -- Glycine is the Flexible Amino Acid

Flexible -- Gly (Glycine) -- in computers Gly = G



{*Figure 11*}

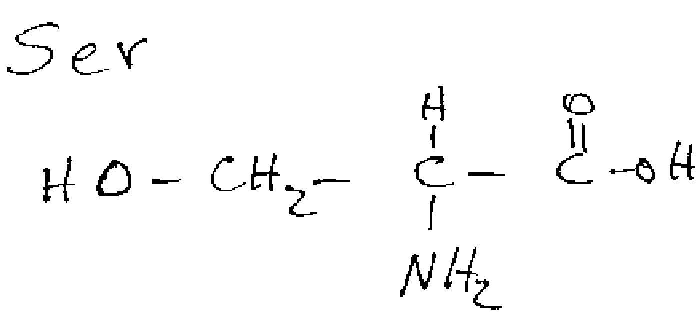
Gly is a unique AA with no chiral center -- but it is prochiral since it has two groups the same (ie H) on the central carbon -- so it still has sidedness - try making a model of Gly. Most important since Gly has no side chain it is very flexible and can easily twist around its alpha-amino Nitrogen bond to the alpha-Carbon. Several Gly connected together in a protein can make a swivel joint like structure. Gly is the opposite of Pro - Gly is flexible while Pro is inflexible. Finally, Gly makes a transition from the non-polar AAs to the polar AAs. Gly is neither non-polar or polar ....or maybe it is either non-polar or polar!

Group III = Polar -- 11 AAs THE POLAR AMINO ACIDS

Polar AAs are important since they provide chemical groups for interaction with water. Thus, the hydrogen bonding character of polar AAs is key in forming protein structures. While the ionic bonding character of charged polar AAs is also important in protein structure. Also the polar side chains in these AAs provide the chemically reactive groups in proteins.

Alcohols - Neutral Polar Amino Acids -- 3 AAs -- Ser Thr & Tyr:

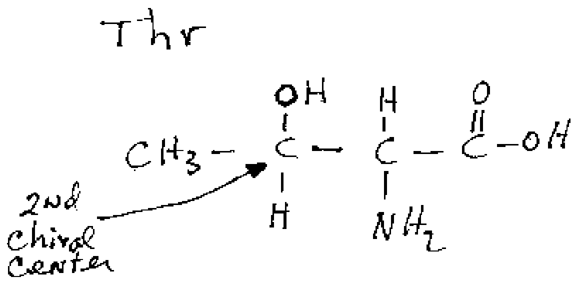
Polar -- Neutral -- Alcohols -- Ser (Serine) -- in computers Ser = S



{*Figure 12*}

Ser contains one -OH group and so it is essentially hydroxy-Ala. The hydroxyl group on Ser does not normally ionize, so it is not charged in proteins - its neutral. Ser is the smallest AA of the polar amino acids and is very polar. The hydroxyl group on Ser provides enzymes a very good nucleophilic group for doing chemistry. Another important function of Ser is to form esters with phosphate, making phospho-ester proteins. Phosphorylation of proteins/enzymes is very important in regulation of activity.

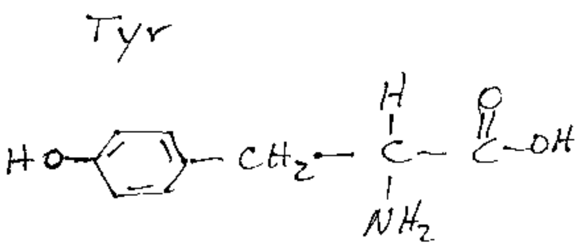
Polar -- Neutral -- Alcohols -- Thr (Threonine) -- in computers Thr = T



{*Figure 13*}

Thr adds a Carbon on to Ser, which makes the hydroxyl group less accessible in Thr than Ser. Thr serves more often in a structural role in proteins and is usually not as chemically active as Ser. Thr can form esters with phosphoric acid and phospho-Thr is often found in proteins.

Polar -- Neutral -- Alcohols -- Tyr (Tyrosine) -- in computers Tyr = Y

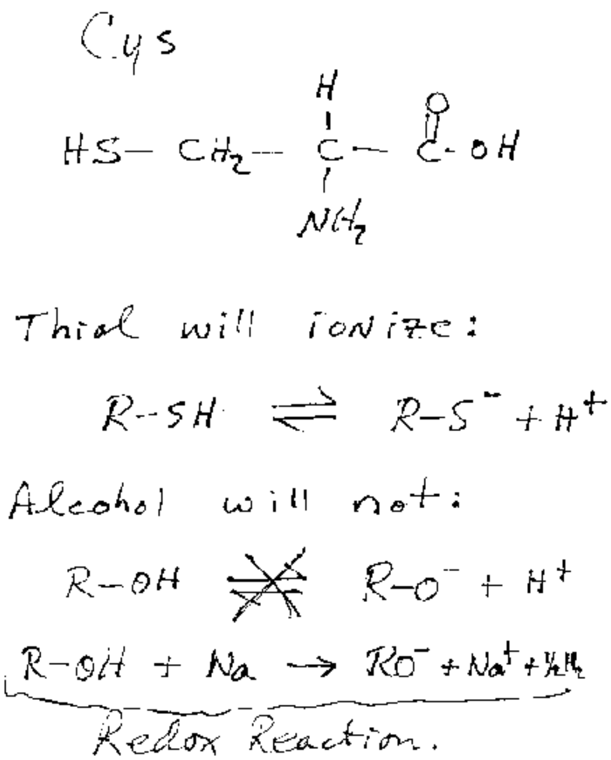


{*Figure 14*}

Tyr is an aromatic alcohol and so it has both aromatic character and polar character. The hydroxyl of Tyr is like the hydroxyl in phenol, so at high pH it can ionize. Tyr can also form phospho-esters like Ser and Thr. Phospho-Tyr is very important in proteins/enzymes involved in regulating the cycle cell.

Thiol - Neutral Polar Amino Acid -- 1 AA -- Cys:

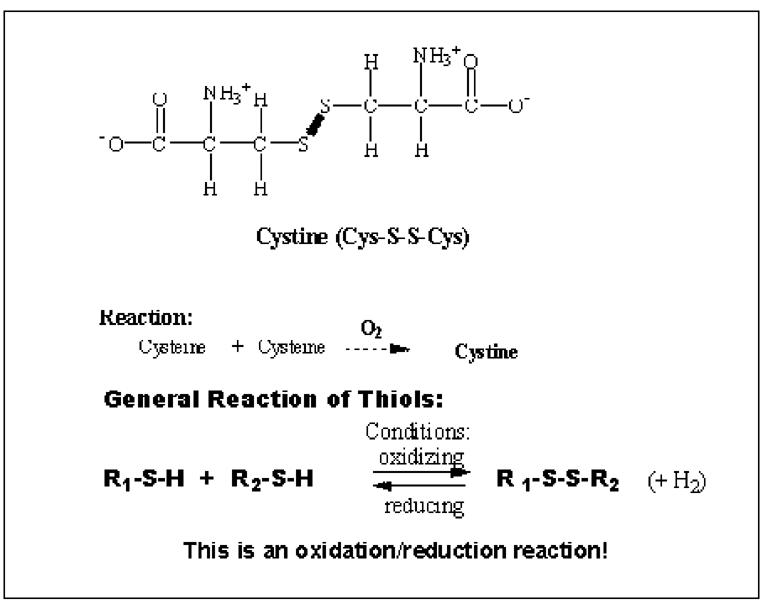
Polar -- Neutral -- Thiol -- Cys (Cysteine) -- in computers Cys = C



{*Figure 15*}

Cys is essentially thiol-Ala. The thiol (-SH) group of Cys can ionize as shown in graphic. Thiols ionize at about pH 8 and so usually they are protonated at biological pH. Hydroxyl groups like in Ser have pK about 15 or so and do not ionize normally (emphasized in Fig. 15). To make a hydroxyl group in a compound like methanol ionize requires an oxidation/reduction reaction.

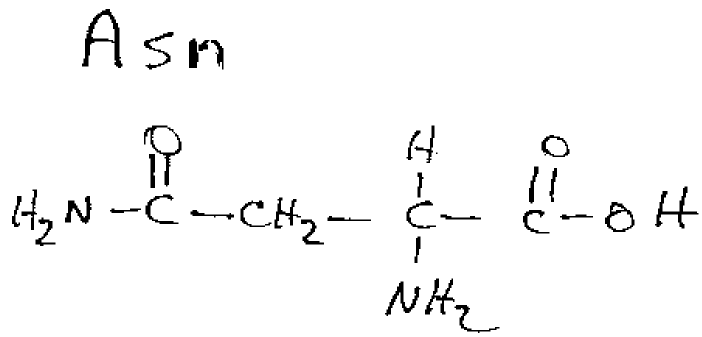
A Special Feature of Cys is that it can oxidize (in the presence of oxygen) and react with another Cys to form Cystine or what we can a disulfide bond:



The formation of "Cystine" can take place between 2 polypeptide chains to make a cross-link between them. This is actually an enzyme catalyzed reaction which takes place in the lumen of ER in cells when proteins are being exported from the cell. A very good example is the production of antibodies by cells in the immune response - antibody proteins contain many Cys-Cys or disulfide bonds. Excellular proteins often contain Cys-Cys bonds, while cellular proteins do not usually contain the Cys-Cys since the conditions in the cell are reducing. In the second part of the graphic above, the general reaction of 2 thiols is shown. In the presence of oxygen or oxidizing conditions, the 2 thiols react to form a disulfide bond between them. Since this is a redox reaction, the hydride ion released by each thiol is usually coupled to an electron acceptor reaction or in simple oxidiation with oxygen, hydrogen peroxide is usually formed with further reduction to water.

Amides - Neutral Polar Amino Acids -- 2 AAs -- Asn & Gln:

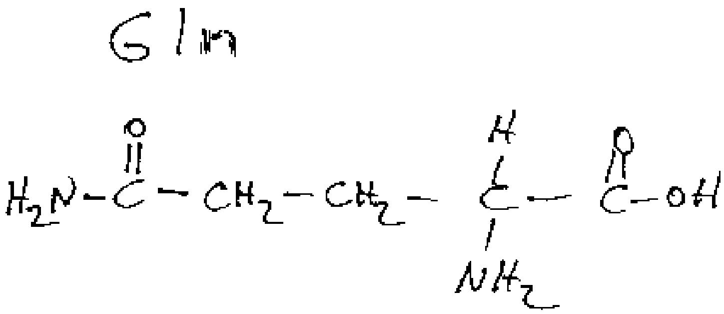
Polar -- Neutral -- Amides -- Asn (Asparagine) -- in computers Asn = N



{*Figure 16*}

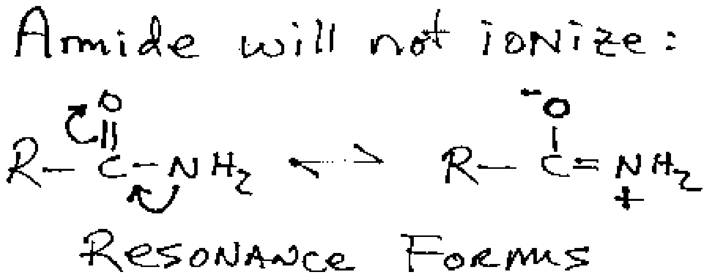
Asn is a very small amino acid as well as being very polar. Amides are neutral and do not ionize nor do they accept protons (see graphics below; ie Fig. 18 & 19)

Polar -- Neutral -- Amides -- Gln (Glutamine) -- in computers Gln = Q



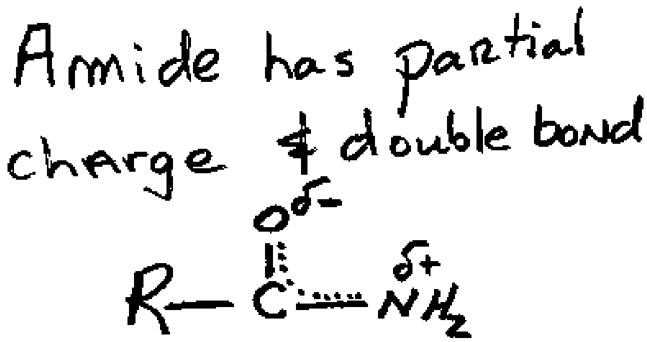
{*Figure 17*}

Gln is a bit larger amide than Asn because it has a longer side chain string of Carbons. Both the amide AAs are neutral derivatives of the corresponding acid AAs (Asp & Glu - see below) Understanding the chemical character of the amide is very important, since the peptide bond of proteins is an amide bond, which will be discussed in the next lecture (see Lecture 5).



{*Figure 18*}

Amides have a partial double bond character and also a partial charge character because of the resonance forms shown in the above graphic (Fig. 18).

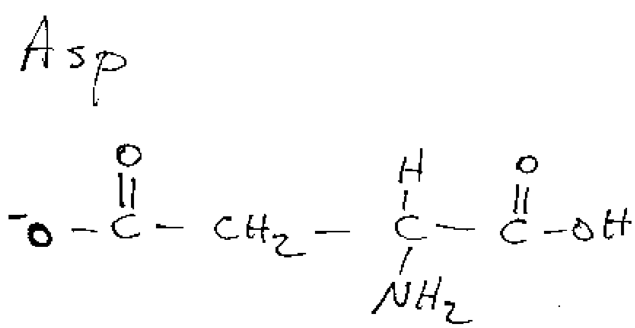


{*Figure 19*}

Another way to look at the partial charge and double bond of an amide is shown above. Since the free electrons of the Nitrogen atom are tied up in forming the partial double bond, the Nitrogen can not accept a proton (H+). This Nitrogen also has a partial positive charge, which tends to repel the proton (H+) and prevents it from binding to the nitrogen.

Acids - Negatively Charged Amino Acids -- 2 AAs -- Asp & Glu:

Polar -- Charged -- Acids -- Asp (Aspartic acid or Aspartate) -- in computers Asp = D

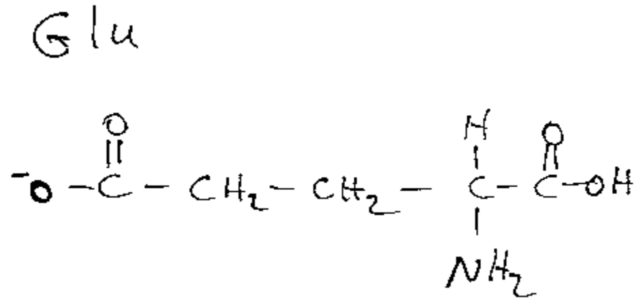


{*Figure 20*}

Asp has a second carboxylic acid group in addition to its alpha-carboxylic acid group. The Asp side chain carboxyl group is normally ionized at biological pH; Asp a negatively charged AA. Asp is a rather small AA and is very polar.

Polar -- Charged -- Acids -- Glu (Glutamic acid or glutamate) -- in computers

Glu = E

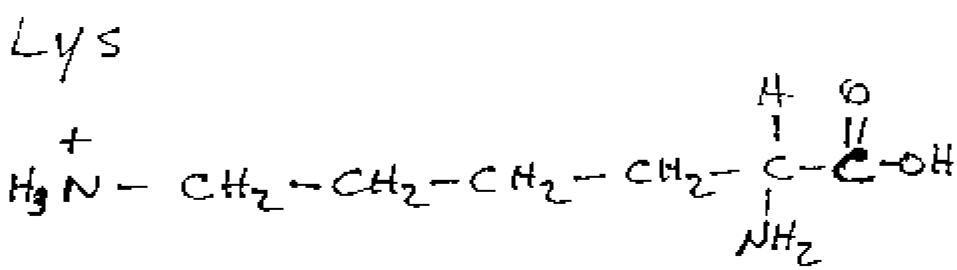


{*Figure 21*}

Glu also has a second carboxylic acid group in addition to its alpha-carboxylic acid group. The Glu side chain carboxyl group is normally ionized at biological pH; Glu is negatively charged.

Bases - Positively Charged Amino Acids -- 3 AAs -- Lys Arg & His:

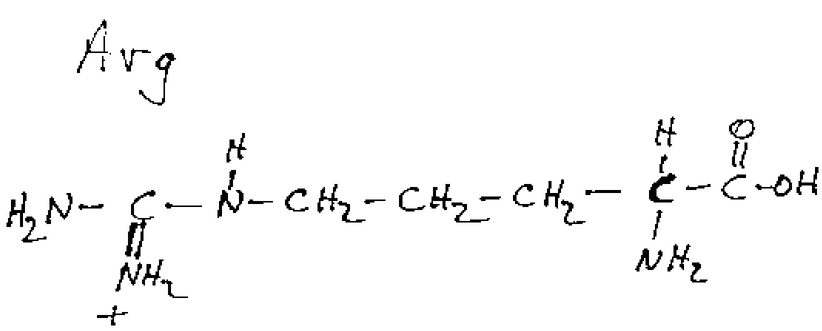
Polar -- Charged -- Bases -- Lys (Lysine) -- in computers Lys = K



{*Figure 22*}

Lys has a primary amino group at the end of a 4 Carbon side chain and it can be positively charged. Since the Lys side chain amino group has a high pK (see lecture 3), it is often charged at biological pH.

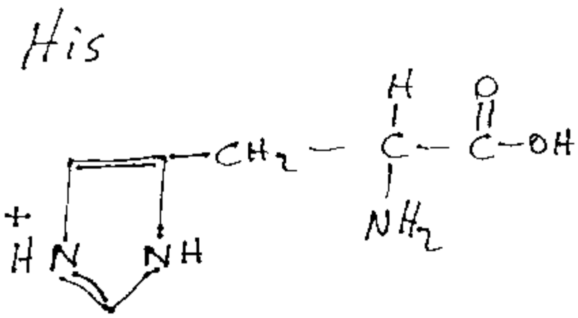
Polar -- Charged -- Bases -- Arg (Arginine) -- in computers Arg = R



{*Figure 23*}

Arg has a complex side chain containing 3 Nitrogen groups, which work as a unit to give a positive charge. Since the Arg side chain group has a very high pK (see lecture 3), it is always charged at biological pH. Arg provides proteins/enzymes with essentially a fixed positive charge.

Polar -- Charged -- Bases -- His (Histidine) -- in computers His = H



{*Figure 24*}

His has an aromatic-like pair of amino groups, making His a unique AA with a positive charge -- sometimes. His with a pK for its side chain near neutrality, means that it can either be charged or not at biological pH. His, when not charged, is a very strong nucleophile and is very important in enzyme chemistry. His is also very important as a proton acceptor and donor in biochemical reactions.