

Key information to know about amino acids & tips for remembering

Much more and downloadable version: <https://thebumblingbiochemist.com/lets-talk-science/amino-acids/>

For all amino acids, know their 1 letter and 3 letter abbreviations. Also, know which have special features.

Amino acid abbreviation memory tricks

Focus on the exceptions (tips on these below) and what remains are the ones that make your life easier! (Their 1-letter abbreviations match their first letters, and their 3-letter abbreviations match their first 3 letters (except Isoleucine))

- **Alanine: Ala, A**
- **Cysteine: Cys, C**
- **Glycine: Gly, G**
- **Histidine: His, H**
- **Isoleucine: Ile, I** (*caution, Ile, not Iso*)
- **Leucine: Leu, L**
- **Methionine: Met, M**
- **Proline: Pro, P**
- **Serine: Ser, S**
- **Threonine: Thr, T**
- **Valine: Val, V**

These have 1 letter abbreviations that are different from their first letter, but are phonetically based and/or their second letter:

- **Arginine: Arg, R** (*Beware the pirate jokes*)
- **Glutamine: Gln, Q** (*Glu sounds like Q (just remember Glu isn't a Q...); Also, you can remember gluatmiNe has a (nitrogen-containing) amide group, whereas glutamic acid doesn't.*)
- **Phenylalanine: Phe, F**
- **Tryptophan: Trp, W** (*Think of how Tweety bird would say it, and if you put Try, try again...*)
- **Tyrosine: Tyr, Y**

The leftovers... Let's go back through the alphabet and see what's left we can use

- **Asparagine: Asn, N** (*You can remember asparagiNe has a (nitrogen-containing) amide group, whereas aspartic acid doesn't.*)
- **Aspartic acid/Aspartate: Asp, D** (*Sounds kinda like asparDate?*)
- **Glutamic acid/Glutamate: Glu, E** (*G is after A and E is after D; Glu's side chain is also longer than that of Asp*)
- **Lysine: Lys, K** (*K is close to L, so might as well . . .*)

Shapely suggestions...

- **Valine, V:** Its side chain is helpfully shaped like a V
- **Leucine, L:** Think of a V at the end of a linker, which looks a bit like an L
- **Threonine, T:** There are 3 “groups” in its side chain, and one of them has an oxygen (O)
- **Lysine, K:** There are 4 “points” on a K and 4 carbons in Lys’ side chain
- **Proline, P:** Proline’s side chain loops back on itself, making it look a bit like a P.
- **Tryptophan, W:** W’s big and bulky and so’s Tryptophan!
- **Phenylalanine, F:** If you think of that F being a benzene ring...

Main amino acid groupings to know

“Acidic” and “basic” amino acids

Note: Each of the amino acids in this category has an ionizable side chain that can give and take protons. The pK_R of an amino acid is the pH at which half the copies of the side chain of these amino acids are protonated and the other half are deprotonated. The lower the pH, the more protons are available to take. Thus, at a pH below an amino acid’s pK_R , most of the copies of the amino acid are protonated. At a pH above the pK_R , most of the copies are deprotonated. Whether or not the amino acid is *charged* depends on whether the protonated or deprotonated form is the neutral form, and this is what we use to classify amino acids as “basic” or “acidic”.

- **Acidic amino acids (typically negatively charged)** – these are acids (proton donators) in their neutral (uncharged) form and thus negatively charged in their deprotonated, conjugate base forms. *Note: the “acid” and “-ate” forms are just the conjugate acid (neutral, protonated form) and the conjugate base (negatively charged deprotonated form) respectively.*
 - **Aspartic acid/aspartate (Asp, D)**
 - **Glutamic acid/glutamate (Glu, E)**
- **Basic amino acids (frequently positively charged)** – these are bases (proton acceptors) in their neutral (uncharged) form and thus positively charged in their protonated, conjugate acid forms.
 - **Arginine (Arg, R)**
 - **Lysine (Lys, K)**
 - **Histidine (His, H)**
 - *Note: unlike, Arg & Lys, which have high pK_R s and are thus usually positively charged, His has a lower pK_R (~6), and is thus more often neutral than charged in the body (where the pH is ~7.4 or so). But, when it is charged, it is positively charged.*

Memory tips for acidic & basic amino acids:

- You’re **DE**ad if you drink acid
- Baseball is played in the pa**HRK**

- Aspartic acid/Aspartate: Asp, D (*Sounds kinda like asparDic acid/asparDate? Just be careful not to then misspell it!*)
- Aspartate comes before Glutamate alphabetically.
 - This matches D being before E in the alphabet (i.e., G is after A and E is after D) and Aspartate's side chain being shorter than Glutamate's.

Structurally strange amino acids – don't expect to find these in common secondary structures like alpha helices & β -sheets!

- **Proline (Pro, P)** – its side chain folds back on itself in a ring, restricting movement of the peptide bond around it and preventing hydrogen bonding with its backbone nitrogen.
- **Glycine (Gly, G)** – its side chain is just a hydrogen; basically, it doesn't have a side chain. This makes the peptide bond around it very flexible, as more angles are possible without causing atoms to hit one another (i.e., sterically clash).

Memory tips for structurally strange amino acids:

- Despite its name, proline is actually anti-“lines”
- Glycine (Gly) may make you think all you were taught about amino acids was a lie! (because it acts differently than the others thanks to its tininess)

Amino acids with hydroxyl groups (Thus subject to post-translational modifications (PTMs) like phosphorylation as well as frequently being directly involved in enzymatic reactions as nucleophiles, acting as “catalytic” residues):

- **Serine (Ser, S)**
- **Threonine (Thr, T)**
- **Tyrosine (Tyr, Y)**

Memory tips for amino acids with hydroxyl groups:

- These **STY**-lish amino acids often wear accessories (i.e., PTMs) and catalyze trends!

Aromatic amino acids (Among other superpowers, these absorb UV280 light (especially Trp))

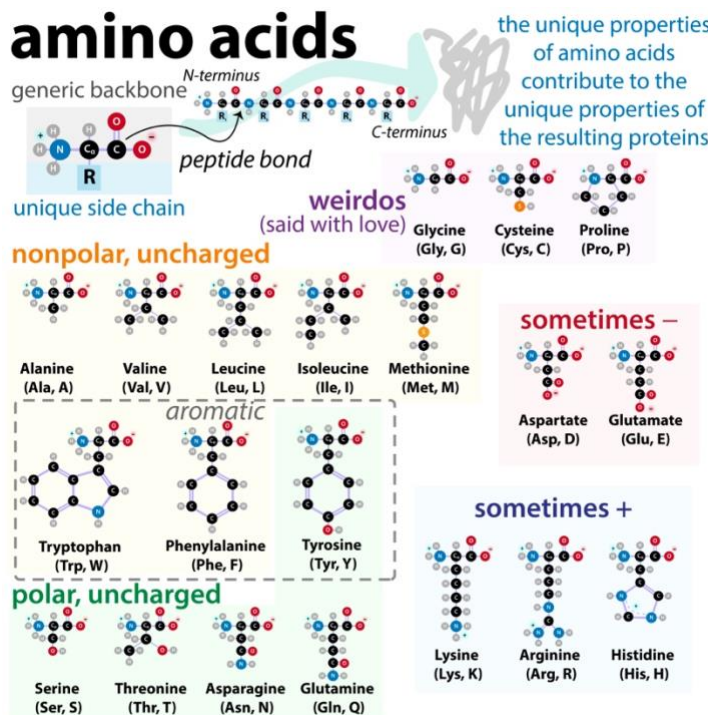
- Tryptophan (Trp, W)
- Phenylalanine (Phe, F)
- Tyrosine (Tyr, Y)
- Histidine (His, H)
 - *Note: although it's aromatic, it's often left out of discussions of aromatic amino acids because its status as a basic amino acid typically gets more attention, and its more hydrophilic than the other aromatic amino acids.*

Crosslinkable amino acids

- **Cysteine (Cys, C)**
 - Forms disulfide bridges/disulfide crosslinks under oxidizing conditions.
 - The form in disulfide bridges is referred to as cystine
 - Memory trick: you lose an e in the name when you lose an e⁻ in the molecule (get oxidized)
- **Lysine (Lys, K)**
 - Rather than forming crosslinks through sulfurs (which lysine doesn't have), Lys uses its amine group nitrogen to form Schiff bases that can do things like allow for various covalent modifications, holding of enzymatic cofactors, and crosslinking reactions in the lab.

At this point, most of the “leftovers” are nonpolar, “hydrophobic” amino acids with unreactive (but not unimportant) side chains.

Once you've mastered these main groupings, take time to memorize what functional groups **each** amino acid has or doesn't have. And how this relates to their position on the polar/nonpolar spectrum, where the more heteroatoms (atoms other than carbons or hydrogens) a side chain contains, the more polar it is and thus the more likely it is to be acceptable on the surface of a protein hanging out with solvent, compared to less polar amino acids which are typically found in a protein's interior.



Learn your amino acid abbreviations!

These ones make your life simpler

Alanine: Ala, **A**

Cysteine: Cys, **C**

Glycine: Gly, **G**

Histidine: His, **H**

Isoleucine: Ile, **I**

Careful! It's Ile, not Iso

Leucine: Leu, **L**

Methionine: Met, **M**

Proline: Pro, **P**

Serine: Ser, **S**

Threonine: Thr, **T**

Valine: Val, **V**

These at least are “sound”

Arginine: Arg, **R**

Beware the pirate jokes

Glutamine: Gln, **Q**

Glu sounds like Q (just remember Glu isn't a Q...);

Also, you can remember glutamine has a (Nitrogen-containing) amide group

Phenylalanine: Phe, **F**

Tryptophan: Trp, **W**

Think of how Tweety bird would say it

And, if you put “Try”; try again ...

Tyrosine: Tyr, **Y**

And here are the ones

still left around

Asparagine: Asn, **N**

Remember asparagine has a (Nitrogen-containing) amide group

Aspartate: Asp, **D**

Sounds kinda like asparDate?

Glutamate: Glu, **E**

G is after A and E is after D

Lysine: Lys, **K**

K is close to L, so might as well ...

Remember your **acidic (often negative)** and **basic (often positive)** amino acids

You're **DEad** if you drink acid



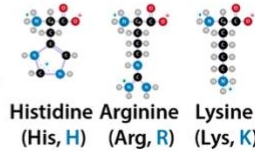
Aspartate comes before Glutamate alphabetically.
This matches D being before E in the alphabet.
And Aspartate's side chain being shorter than Glutamate's.

Well, that's pretty negative . . .

Let's be positive!

Baseball is played in the pa**HRK**

His majesty Histidine is very wishy-washy charge-wise (he's more often neutral)– but, when he's charged, he's positive!



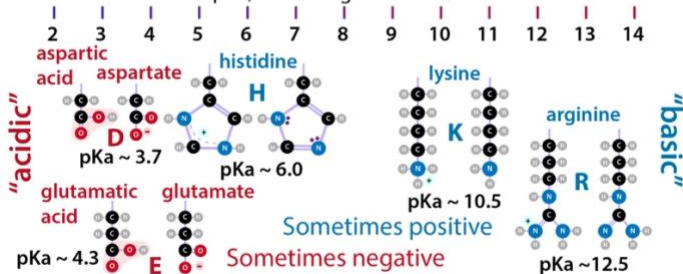
Some amino acids are often charged

The **pKa** (aka pK_a for a side chain) is the pH at which 1/2 the copies of something are protonated **acidic pH** lots of free protons **basic pH** not many free protons

At a **LOWER pH (acidic conditions)**, there are more protons around so there are more opportunities to take one. Whether or not a molecule takes the opportunity depends on how much it wants it & is reflected in the pKa.

Below the pKa, the protonated form dominates **Above the pKa**, the deprotonated form dominates

The lower the pKa, the stronger the acid/weaker the base



We call these amino acids "acidic" because their neutral (uncharged) forms act as acids (donate protons).

"Acidic" amino acids are often –

We call these amino acids "basic" because their neutral (uncharged) forms act as bases (take protons).

"Basic" amino acids are often +

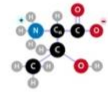
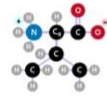
Side-chain shapely suggestions

Valine: Val, V **Leucine: Leu, L** **Threonine: Thr, T**

Side chain is helpfully shaped like a V

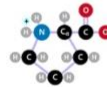
Think of a V at the end of a linker

There are 3 "groups" in its side chain, and one of them has an oxygen (O)



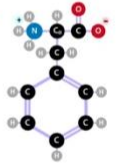
Proline: Pro, P

Proline's side chain loops back on itself, kinda like a P



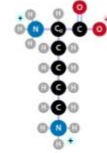
Phenylalanine: Phe, F

If you think of that F being a benzene ring...



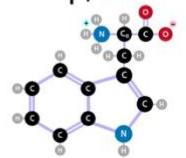
Lysine: Lys, K

There are 4 "points" on a K and 4 carbons in Lys' side chain

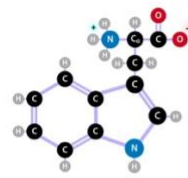


Tryptophan: Trp, W

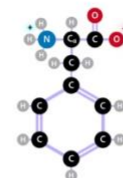
W's big and bulky and so's Tryptophan!



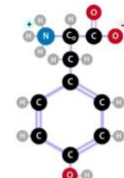
Aromatic amino acids



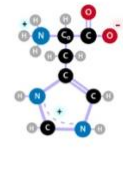
Tryptophan (Trp, W)



Phenylalanine (Phe, F)



Tyrosine (Tyr, Y)



Histidine (His, H)

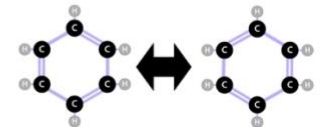
In aromatic molecules, atoms in a flat ring share electrons all the way around the ring

Delocalized pi bonds



This can be represented with resonance structures

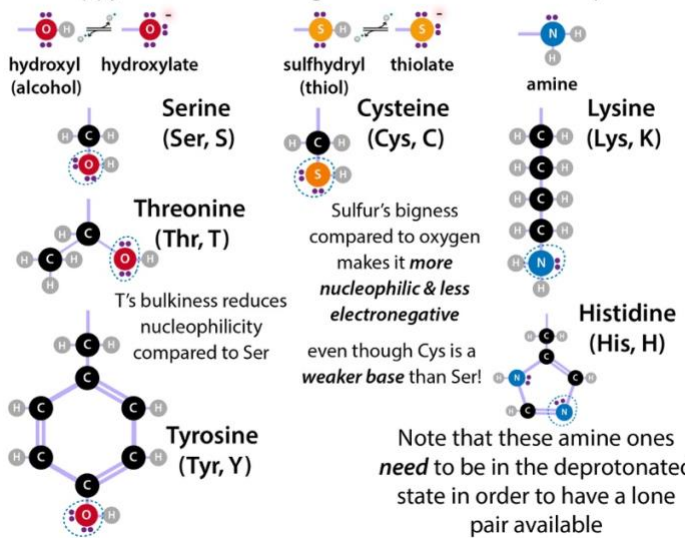
These don't really switch back & forth, the reality is just something in the middle!



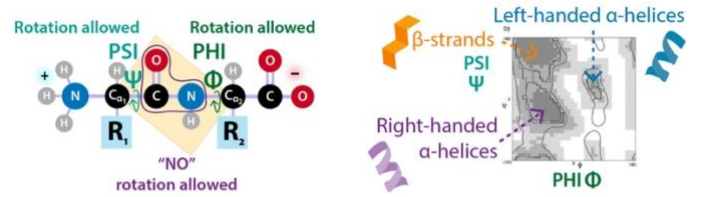
Some nucleophilic amino acids

Look for a lone pair of electrons to share!

Especially in the deprotonated state! Electronegative atoms like electrons, but don't like concentrated charge. Charge makes them unhappy and thus more eager to react with an electrophile.



Ramachandran plots show peptide backbone dihedral angles



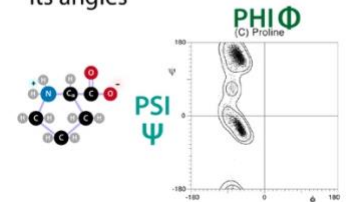
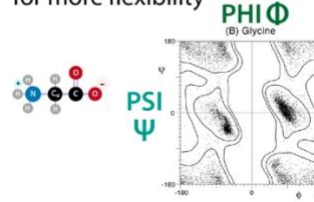
There are places you do & don't expect most amino acids to be

Dark: core Light: generous!
Medium: allowed allowed

And then there are exceptions...

Glycine's smallness allows for more flexibility

Proline's awkwardness limits its angles

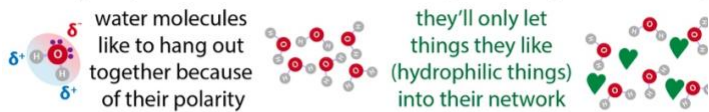


Plots from Lovell et al. 2003, *Protein*

Hydropathy

whether an amino acid & water get along helps determine where you'll find it

the hydrophobic effect is a main driving force of protein folding

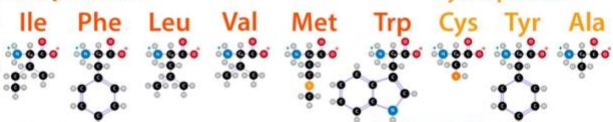


so if you stick in hydrophobic things, the water molecules gang up around them to maximize their water-water contacts and minimize water-hydrophobe contacts

this forces hydrophobic things to gather together - for proteins this means hydrophobic amino acids huddling in the center of proteins (for cytoplasmic proteins - the opposite holds for membrane proteins)

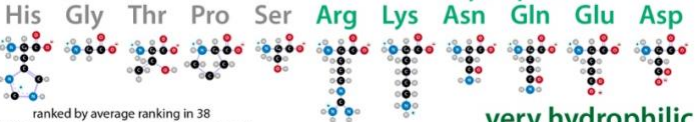
very hydrophobic

typically found buried in proteins



hydrophobic

neither



hydrophilic

very hydrophilic

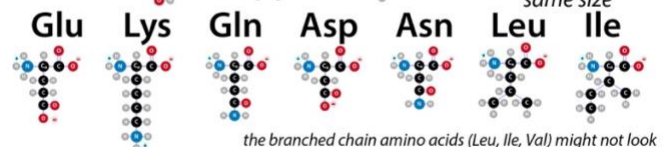
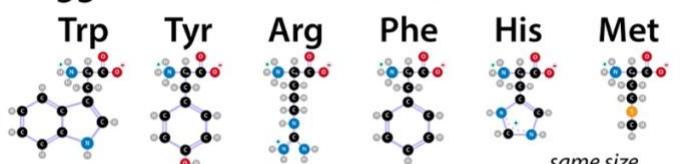
often found on the surface of water-soluble protein

ranked by average ranking in 38 hydrophobicity scales, *Proteins: Structure and Molecular Properties* by Thomas E. Creighton

Size

all peptide bonds have limited rotation, but big R groups are harder to accommodate - so steric hindrance further limits rotation ranked by decreasing molecular weight

biggest



the branched chain amino acids (Leu, Ile, Val) might not look that big, but the branching near the backbone limits movement



proline is the most restricted

smallest

Much more on amino acids: <https://thebumblingbiochemist.com/lets-talk-science/amino-acids/>

Video walk-through of this guide: <https://youtu.be/duIF1N57Q6M>