Proteins and amino acids

Proteins are biological polymers

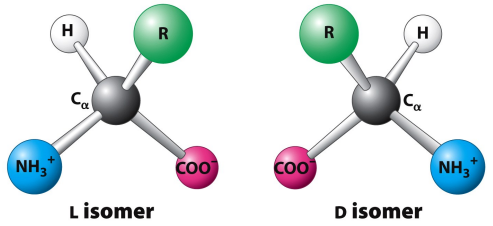
Monomeric building blocks: **α-amino acids**
- 20 used in nature (actually more, but we'll go with 20…)
- Same backbone
- Differ in their "R" group, or "side chain"

R groups contain many types of **functional groups**
- Wide variety of chemical purposes

Can interact with many types of molecules
- e.g. Other amino acids, other biological molecules, small organic molecules, metal ions, etc.

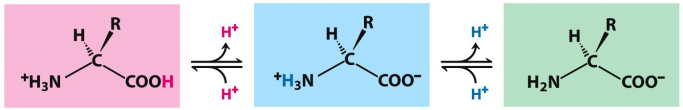
Amino acids

Chiral
- The α-carbon is a stereocenter!
- Almost all biological amino acids are:
  - Often, but not always, *S* instead of *R*

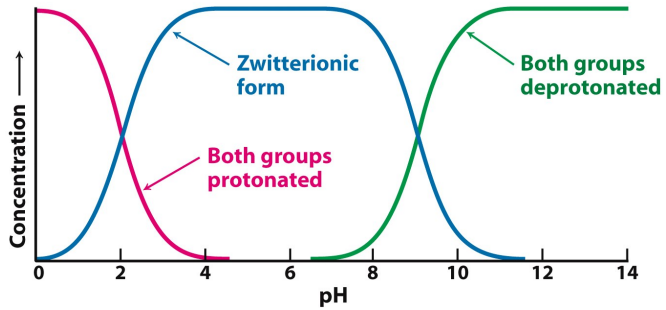


Amino acids

At physiological pH, amino acids are **zwitterions**



$pK_a \approx$ _____ $pK_a \approx$ _____



Amino acids

20 amino acids, each has **one-letter** and **three-letter** abbreviations

Several ways of classifying amino acids by R group, basis of:
- Charged/uncharged
- Polarity
- Hydrophobicity
- Aromaticity

We will use:
1. Non-polar (hydrophobic)
2. Polar (neutral)
3. Positively charged
4. Negatively charged

Hydrophobic, nonpolar amino acids

Glycine
Alanine
Valine
Leucine
Isoleucine*
Methionine
Proline
Phenylalanine
Tryptophan

Neutral, polar amino acids

Serine
Threonine*
Cysteine
Asparagine
Glutamine
Tyrosine

Charged amino acids

Positively charged
Lysine
Arginine
Histidine

Negatively charged
Aspartate
Glutamate

Amino acids

Seven of the 20 amino acids have **ionizable side chains**

Aspartate and **glutamate**: pK_a ≈
(aspartic acid and glutamic acid)

Lysine: pK_a ≈

Arginine: pK_a ≈

Histidine: pK_a ≈

Cysteine: pK_a ≈

Tyrosine: pK_a ≈

Amino acids

What you need to know

- Full names
- One-letter abbreviations
- Three-letter abbreviations

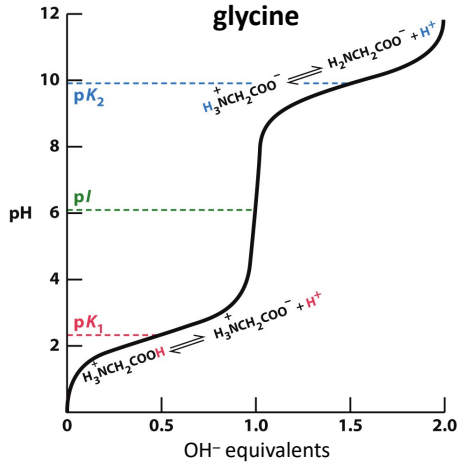
- Structures, including all stereochemistry

- pK_a of all ionizable groups
  - Titration curves

(The alphabet can help you learn!)

Titration curves

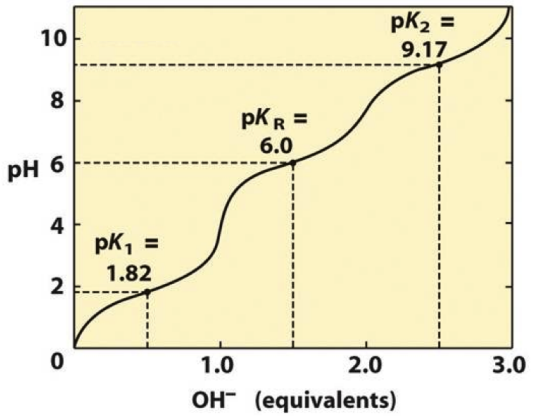
For amino acids without ionizable side chains:



- pK_as are at every 0.5 equivalents of OH⁻. ***Why?***

Titration curves

pK_{a1} 1.8 pK_{a2} 6.0 pK_{a2} 9.2



What amino acid?

What is the p*I*?

Titration curves

Exercise:

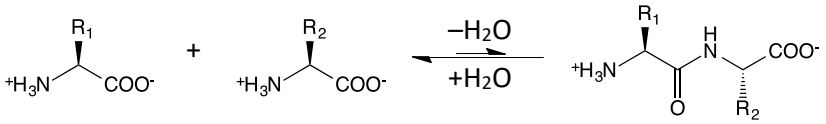
1. What does the **titration curve for tyrosine** look like?
- carboxyl: pK_a is 2.20
- amino: pK_a is 9.21
- OH (phenol): pK_a is 10.46

2. Draw the predominant **structures of tyrosine** at:
- pH 1.0
- pH 6.0
- pH 10.0
- pH 12.0

3. What is the **p*I* of tyrosine**?

Peptides and polypeptides

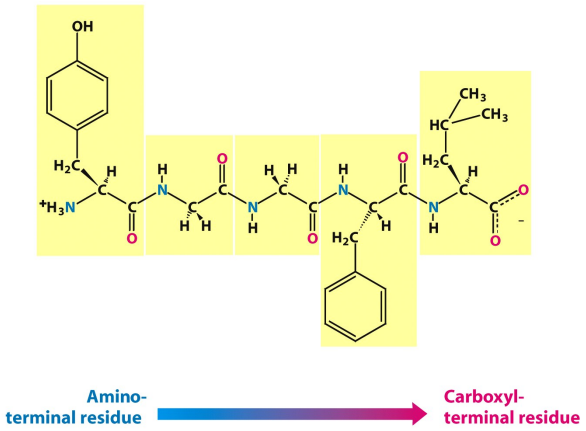
Amino acids are linked together by peptide/amide bonds



- Equilibrium favors individual amino acids
- But kinetically, peptides are very stable

Peptides and polypeptides

Directionality



Peptides, polypeptides, and proteins

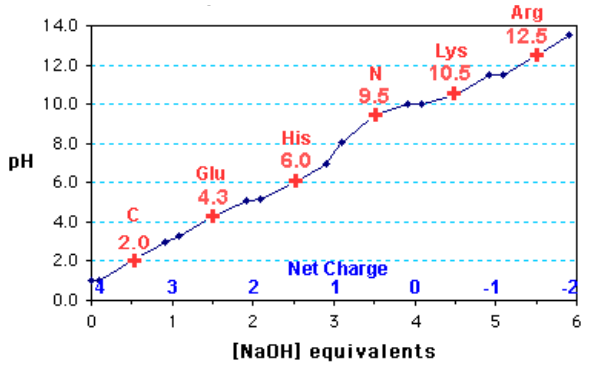
Peptides
Short… How short? Ambiguous… <20? <50?

Polypeptides
Longer…

Protein
A polypeptide…
- Usually: 50–2000+ amino acids
- Average amino acid: 110 g/mol (Daltons, Da)
- So proteins: 5,500–220,000+ Da
  - 5.5 – 220+ kDa
- Have *a precise sequence*, determined by the genetic code

Peptides, polypeptides, and proteins

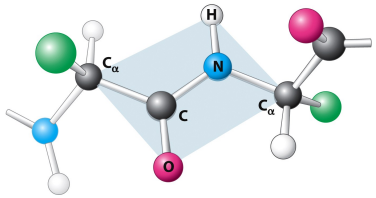
Titration curves



p*I*:
Still the average of pK_as on either side of neutral species!
What is the p*I* here?

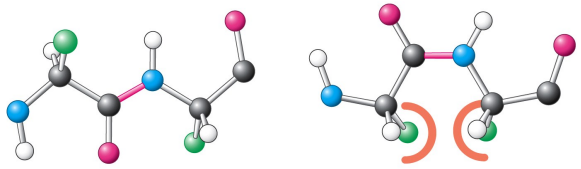
Polypeptide structure

Peptide bonds are planar, due to resonance



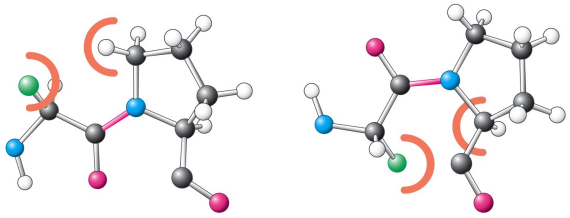
Polypeptide structure

Peptide bonds are planar, due to resonance
- Almost always *trans* (some exceptions…)



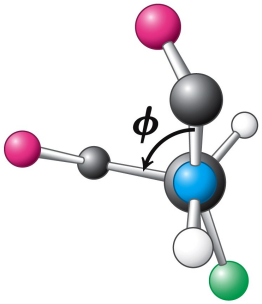
Trans **Cis**

Most common exception: **proline** (10-40% are *cis*)

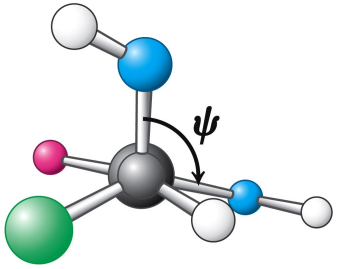


Polypeptide structure

Torsion angles (a.k.a. dihedral angles) and conformational flexibility
- ϕ, ψ angles



$\phi = -80°$



$\psi = +85°$

In proteins, not all possible ϕ, ψ angles are observed!!

Ramachandran plot