CHEM 191
Module 4
Structures and reactions of biological molecules

Lecture 6
Amino acids

Lecturers: Dr Andrea Vernall andrea.vernall@otago.ac.nz
Dr Eng Wui Tan ewtan@chemistry.otago.ac.nz

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Module 4 Lecture 6
Learning objectives

Learning Objectives:

- Interpret Fischer projections of amino acids and designate as *L* or *D*
- Assign the chiral centre of an amino acid as *R* or *S*
- Understand that amino acid chemistry is dominated by acid-base chemistry
- Define the term isoelectric point
- Draw the structure(s) of an amino acid that predominate(s) at a specified pH based on amino acid p*K*a information

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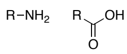
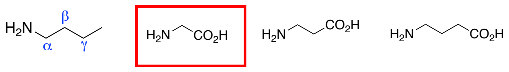
Amino acid structure

- Also covered in Module 1, lecture 9, amino acids contain **amino** and **carboxylic acid** functional groups in the same molecule



- Amino acids can be classified according to how far apart the **amine** and **carboxylic acid** functional groups are from each other



Alpha (α) amino acids are what we will just call 'amino acids' in CHEM 191

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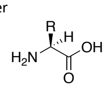
Different amino acids

- Amino acids are named based on the 'side-chain', R
- All natural amino acids in humans are the 'L' enantiomer



- There are 20 'common' amino acids

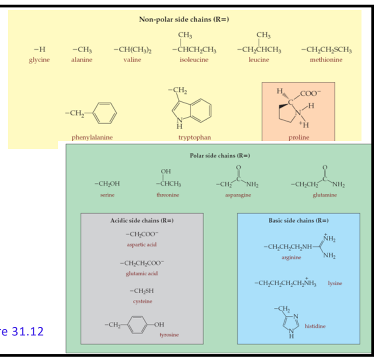


Figure 31.12

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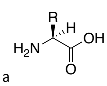
Amino acid stereochemistry



- All except for glycine (R = H) have a carbon atom with 4 different groups attached i.e. have a **chiral** or **stereogenic centre** (also called a **stereocentre**)
- Thus they are **chiral** molecules - each can exist as a pair of enantiomers (glycine is achiral and has only 1 form)

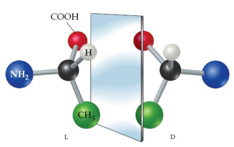


Figure 31.11, alanine enantiomer

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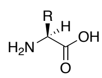
Amino acid stereochemistry

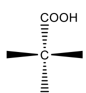


- All natural amino acids are the *L*-isomer and have the same relative 3D arrangement of functional groups
- As we did for carbohydrates, **Fischer projections** can be used to represent the 3D structure of amino acids

The COOH is drawn at the top, the 'R' group (side chain) at the bottom and chiral carbon is represented as a cross piece.

In this orientation:

- bonds up and down project into the page
- bonds to the side project out from the page



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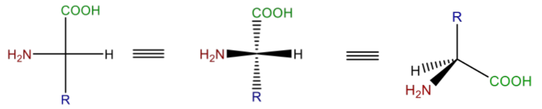
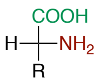
Amino acid stereochemistry

- The **Fischer project** for a natural amino acid (the *L* isomer) always has the NH_2 group on the left



L-amino acid, naturally occurring form



D-amino acid

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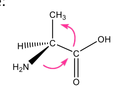
Amino acid stereochemistry

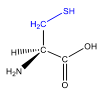
- We can also define amino acid stereochemistry based on the *R*, *S* system
- Even though all *L*-amino acids have the **same** relative 3D arrangement, **not all are the *S* isomer….**

Alanine:



- The priority sequence is NH_2 > COOH > CH_3 > H
- View from the side opposite H
- The trace NH_2 → COOH → CH_3 is anticlockwise
- The **stereochemistry is (*S*)**

Cysteine:



- –CH_2-SH group has higher priority than COOH (NH_2 > –CH_2-SH > COOH >H)
- Same arrangement in space for cysteine and alanine but ***L*-cysteine is the R stereoisomer**

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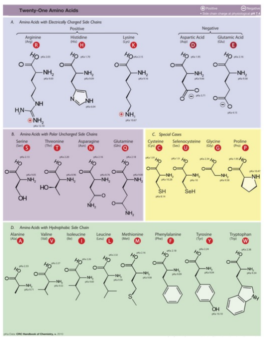
Amino acid short-hand naming

- You don't need to memorise these shorthands, but we will use this format on slides in the next few lectures.

R= H	glycine	gly	(G)
R= CH_3	alanine	ala	(A)
R = CH_2OH	serine	ser	(S)
R = CH_2SH	cysteine	cys	(C)
R = CH_2COOH	aspartic acid	asp	(D)
R = $(CH_2)_4$-NH_2	lysine	lys	(K)



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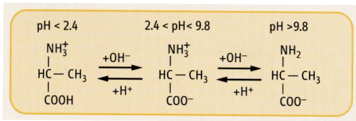
Chemistry of amino acids

- Governed by the amino group, the carboxylic acid group, and any functional groups in the side chain (R)
- All amino acids have an acidic and basic functional group in close proximity
- As covered in Module 1, lecture 9, the **amino** and **carboxylic acid** functional groups will be ionised, depending on the pH, e.g. for Ala



pK_{a1} = 2.4
pK_{a2} = 9.8

An α-amino group is *protonated* when charged (+ve)

An α-carboxyl acid group is *deprotonated* when charged (-ve)

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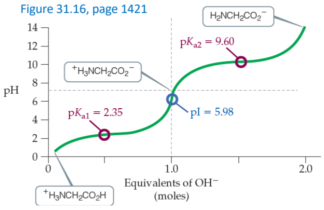
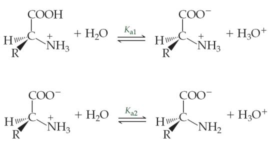
Acid-base properties of glycine

- We can measure and visualize this via a titration, as shown in Module 1, Lecture 9

Figure 31.16, page 1421



[31.21, 31.22], page 1420



- pI is the **isoelectric point** ……

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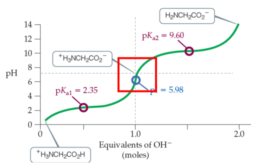
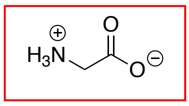
Zwitterions and the isoelectric point (pI)

- A zwitterion is overall neutral as contains positive and negative charges that cancel each other out
- When the pH equals the pI, the amino acid zwitterion is at its maximum concentration and is the predominate species in the solution.





Glycine zwitterion

The isoelectric point of an amino acid is the point at which the amino acid has no net electrical charge

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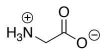
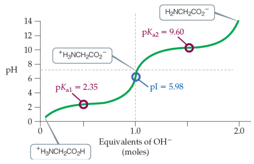
Zwitterions and the isoelectric point (pI)

- For all amino acids with a side chain functional group that can't be ionised, then the isoelectric point (pI) is the average of the amino and carboxylic acid p*K*a values

Glycine pI = (2.35 + 9.60) / 2 = 5.98

At a pH of 5.98, glycine exists predominantly as a zwitterion

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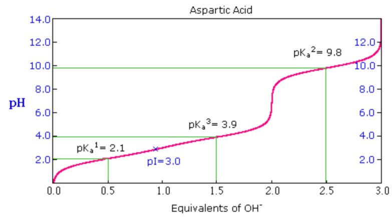
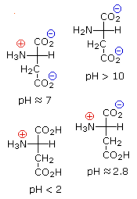
Isoelectric point (pI) with different side chains (R)

- For amino acids with side chains that have **acidic** or **basic** functional groups, there are **three** functional groups that can easily ionise depending on the pH, e.g. Asp





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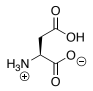
Isoelectric point (pI) with different side chains (R)

- For an amino acid with an acidic or basic R group, the pI is the average of the two p*K*a values that are more similar



The Asp **zwitterion** predominates at **pH 2.98**

Amino Acid	pK_{a1}	pK_{a2}	pK_a of side chain group	pI
COOH CH$_2$ H–C–COOH NH$_2$ *Aspartic acid*	2.10	9.82	3.86	(2.10 + 3.86)/2 = 2.98
NH$_2$ (CH$_2$)$_4$ H–C–COOH NH$_2$ *Lysine*	2.18	8.95	10.53	(8.95 + 10.53)/2 = 9.74

- What's so important about ionisation at different pH?
- The pH can be different in different parts of the body, therefore the ionisation of these functional groups can change, therefore so can solubility and activity …..

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Determine dominant amino acid form at a given pH

- We can approximate how much ionisation there is at a given pH
- Recap from Module 1, lecture 9
  - If p*K*a = pH of environment, then half (50%) of the functional group corresponding to that p*K*a is ionised
  - When pH and p*K*a are approximately 1 unit different – approx. a 90/10% ratio
  - When pH and p*K*a are approximately 2 units different – approx. 99/1% ratio
- Let's approximate the ionisation of an amino acid in the

Stomach, pH = 2

Plasma, pH = 7.4

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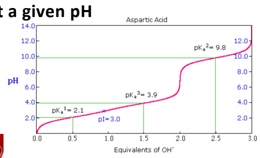
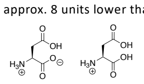
Determine dominant amino acid form at a given pH

Amino Acid	pK_{a1}	pK_{a2}	pK_a of side chain group
COOH CH$_2$ H–C–COOH NH$_2$ *Aspartic acid*	2.10	9.82	3.86



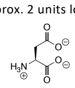
Stomach, pH = 2

- pH is approx. equal to p*K*a1
- pH is approx. 2 units lower than p*K*a3
- pH is approx. 8 units lower than p*K*a2



Plasma, pH = 7.4

- pH is approx. 5 units higher than p*K*a1
- pH is approx. 4 units higher than p*K*a3
- pH is approx. 2 units lower than p*K*a2



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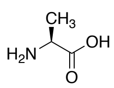
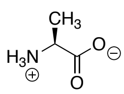
Drawing amino acids in neutral form

- It is convention to draw out the chemical structures of amino acids in neutral form



- But remember that the ionised form(s) actually almost always exist in solution, and the ionised form(s) often dominate the chemistry of amino acids



Alanine, in a pH = 7.4 solution, e.g. plasma

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