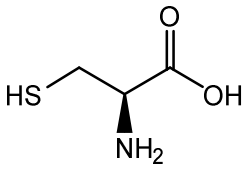
Name:
Date:

QA4 - Tertiary Structure and Specificity

1. <u>The amino acid cysteine is shown below. How can cysteine contribute to the overall tertiary structure of a polypeptide?</u>



By forming **hydrogen bonds**, it can help manipulate how the **protein folds in 3D**. Uniquely, it can form **disulfide bonds** to other cysteine residues. These bonds form, and this forces the polypeptide chain to adopt a unique **3D arrangement** – this is called the tertiary structure.

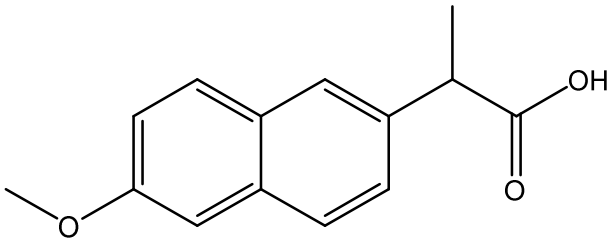
2. <u>How does the tertiary structure, and protein folding relate to the complementary of an enzyme's active site?</u>

As the amino acid residues in a polypeptide begin to interact, they form bonds such as hydrogen bonds and disulfide bridges. This causes the protein to fold into its tertiary structure. This **protein folding creates an active site within the protein**, by folding in a specific way, generating a **complementary site for a ligand to bind**.

3. <u>The catalytic triad is a set of three amino acids in the active site which often catalyses a desired chemical reaction. Explain why it is useful to have amino acids in the triad which have very different side chains.</u>

Different amino acids can have very **different side chains**, with **different chemical properties**. These 'R-groups', are incredibly important, and allow each amino acid residue to react differently. For example, one may have a **basic** side chain, one an **acidic** one, and one a **nucleophilic** one. These **different side chains allow different chemical reactions to occur**, and this allows the **enzyme to act as a catalyst**, by reacting with the substrate.

4. <u>Naproxen, shown below, is a non-steroidal anti-inflammatory drug, which is used for pain relief. By using naproxen as an example, explain why it is important to consider stereospecificity in active sites.</u>



Naproxen, like many drugs, is a **chiral molecule**, with a **chiral carbon centre**. It therefore has **two different enantiomers**, R-naproxen, and S-naproxen. These two images, which are **mirror images** of each other, will **react differently with the amino acids in an enzymes active site**. This is because the **amino acids are chiral**, and can **differentiate between two different enantiomers**. Although one of the

enantiomers will bind well to the desired enzyme, because **the active site is stereospecific**, the other may not bind quite so well. In fact, the other one may bind elsewhere and have **unexpected side effects**, which could be dangerous.

5. How does a drug which shows specificity differ from one which shows selectivity towards an enzyme?
   Specificity: Will only bind to **one particular active site** of an enzyme
   Selectivity: **Prefers to bind to a specific active site**, but **can bind to others**, especially if there is a high concentration of the drug.

6. Describe how the lock and key model of an enzyme differs from the induced fit model, and explain the advantage of each model.
   The lock and key model assumes that there is **only one specific active site (lock) for each drug (key)**. It is a **good approximation** and explains the complementarity of active sites and ligands.
   The induced fit model **allows some flexibility in the structure of the active site**. Polypeptides naturally have a small amount of flexibility, which means that the active site can adapt very slightly, to give a **complementary fit** to the substrate. This model is **more accurate** than the lock and key one.

7. Proteins can be categorised into two different groups, based on their tertiary/quaternary structures, as either globular or fibrous. Explain the structural differences between them, and describe how this relates to their functions.
   Globular proteins are globe-like structures, which are **roughly spherical**. They often function as **enzymes**. The primary and secondary structures of the polypeptides fold themselves into a ball shape, and create an **active site** – a nook in the structure – into which a **substrate can bind**. This allows the enzyme to **efficiently catalyse a particular reaction.**
   Fibrous proteins are fibre-like, often having **long thin strands** woven in some manner. These are used as **structural proteins**, giving **overall strength** to biological structures, such as the protein keratin in hair and nails.