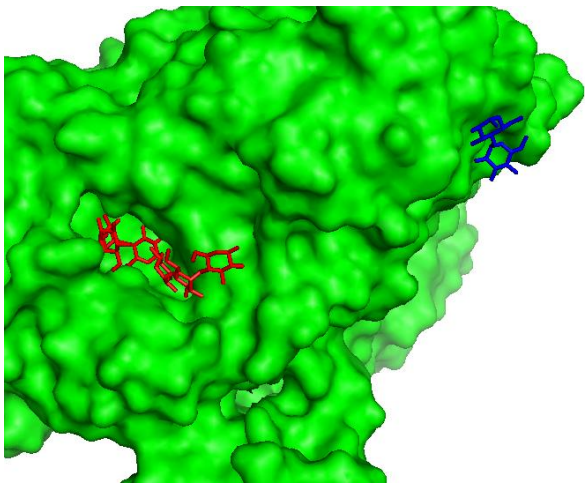
TA6 – Enzyme and Inhibitors

ENZYMES

Enzymes are types of **proteins** which act as **biological catalysts** on a **substrate**. Each human will have many thousands of chemical reactions occurring in the body simultaneously. These will be breaking down food and old cells, forming new cells, storing carbohydrates as glycogen, and repairing our bodies. Whilst this is going on, your body will be releasing hormones and neurotransmitters, and pumping ions across membranes. Your body is made entirely from chemicals, and the chemistry involved allows you to exist as you do today. Because there are so many reactions going on, it is important that your body can speed up some of them, to help regulate your body, such as in homeostasis. Classic examples of human enzymes include the digestive ones. It takes a while for the carbohydrates in bread to break down into glucose, as you can see by looking at the bread in supermarkets, you'll never see it convert into sugar, even when it's gone stale and mouldy! However, when you eat bread, the enzyme **amylase** which is in your saliva breaks it down rapidly into sugars, as you can taste if you hold a piece of bread in your mouth for a couple of minutes.

These enzymes are vital, because they allow reactions to occur very fast, acting as a biological catalyst. Catalysts are species which help to speed up a reaction without being used up themselves.

Enzymes work using an **active site** which is **stereospecific**. The active site is part of the enzyme which actively catalyses a reaction, such as breaking down carbohydrates. It is said to be stereospecific because the 3D structure of the substrate is important. The active site is biologically designed to be **complementary** to the substrate. This means that the substrate fits well in the active site, so that the reaction occurs much easier. It also stops the enzyme from catalysing other side reactions as easily. For the enzyme amylase, you want it to break down polysaccharides, but you don't want it to break down everything it sees!



1qho_active_site. This shows an amylase enzyme bound to a hexasaccharide, which is visible in red. There is a clear indentation in the surface of the enzyme. This is the active site.

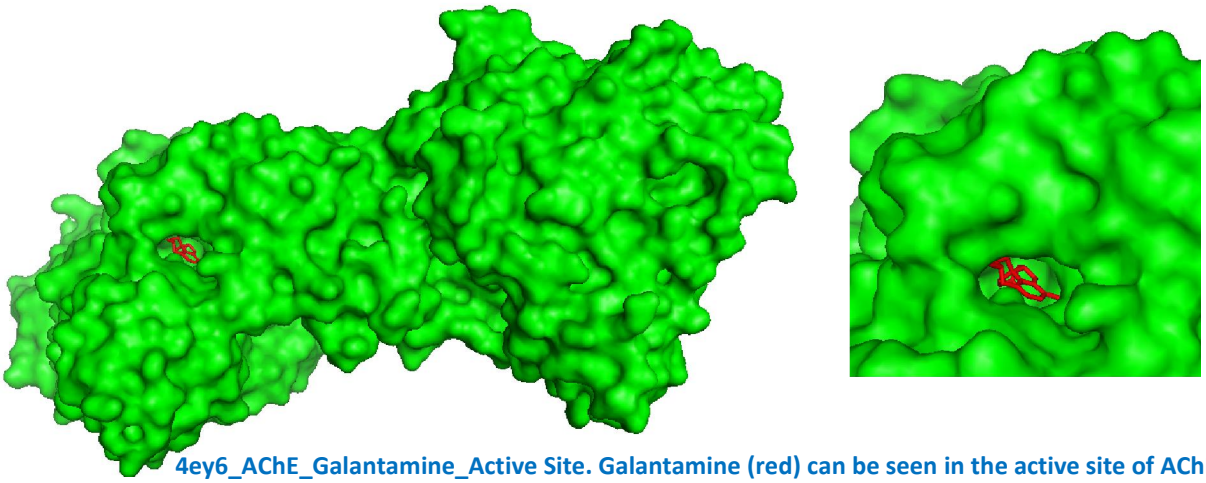
ENZYME INHIBITORS

Because the active site is where the main chemistry happens, it is crucial to the overall function of an enzyme. If an active site is changed slightly, or blocked, then the enzyme will not work. An **inhibitor** is a molecule which stops a catalyst from working by blocking the active site.

Acetylcholine (ACh) is a very important neurotransmitter. It is released by neurons, and travels to the next neuron in the pathway via a neural synapse. This allows nerves to interact with each other, and is vital in transmitting nerve signals across the body. In the body, there is an enzyme called

acetylcholine esterase (AChE), which breaks down acetylcholine, stopping it from building up and saturating the nerve cells – your nerve signals have to be turned off at some point, or your body could never relax your muscles!

In most humans, the amount of the enzyme AChE balances the amount of the neurotransmitter ACh, so that nerve signals are sent around the body without any problems. However, in some cases there are problems with the nerve transmissions, such as in Alzheimer's disease. In Alzheimer's, there isn't enough of the neurotransmitter ACh in the brain, which makes it difficult for nerve signals to pass effectively, and this reduces the function of the brain. One treatment for Alzheimer's is to reduce the activity of AChE. If this can be done, then there will be more ACh in the brain, and the brain can work more effectively, as it used to. To do this, an inhibitor is used, to stop AChE from working, and therefore stop ACh from being broken down. This increases the concentration of ACh in the brain, helping to reduce the effects of Alzheimer's disease. This is done using the inhibitor drug **galantamine**, which can be found in snowdrops and daffodils. Galantamine blocks the active site of AChE, stopping ACh being broken down, and slows down Alzheimer's.



4ey6_AChE_Galantamine_Active Site. Galantamine (red) can be seen in the active site of AChE. This acts as an inhibitor by blocking the active site, stopping the enzyme from working.

ALLOSTERIC MODULATORS

It is useful to be aware that molecules can bind away from the active site, and still affect the enzymes efficiency. These are called **allosteric modulators**. Allosteric modulators bind to the enzyme at a location other than the active site. By doing this, they interact with part of the protein, and cause a **conformational change.** So, they may bind near the active site, and cause the polypeptide chain to deform slightly, indirectly changing the shape of the active site. This can make the active site more, or less complementary to a substrate molecule. If it makes the active site less complementary to a substrate, then the enzyme's rate of reaction will decrease, and may even stop altogether.