UNIT 1: METABOLIC PROCESSES

Enzymes

ACTION

- enzymes are **catalysts** – these are chemicals that speed up a chemical reaction without being used up in the process
- catalytic reactions involve the recycling of the enzyme once it has done its job
- almost all biochemical reactions, whether they involve the transfer of protons, the transfer of electrons, or transfer of entire atoms, require the help of enzyme molecules
- most biological processes involve the successful collision between reactant molecules in order for products to form
- not all collisions are successful
- to ensure the success of such collisions, and in order for the transition complex to occur, thus the product molecules to be produced, enzymes need to become involved
- in living systems, enzymes actually hold reactant molecules in place, in the correct 3-dimensional orientation in space, so collisions age successful, and products are made
- Figure 1, p. 69 illustrates the effect that enzymes have on the ease with which a reaction occurs
- these catalyst molecules allow for a greater percentage of reactant molecules to possess the necessary orientation so as to successfully collide with each other
- note that enzyme have no effect on the free energy that goes into or is released in any reaction
- they only lower the activation energy, thereby allowing more reactant molecules to possess the minimum amount of energy necessary to collide successfully and make products
- the molecule that the enzyme acts on is called the **substrate** molecule
- each enzyme binds to its substrate molecule in a unique manner, thereby activating it, or making it more reactive
- enzymes are very specific for the substance to which they bind
- even isomers of substrates won't bind to the enzyme
- most enzyme name have the same root as their substrates, but end in "ase" – for example, amylase breaks down amylose, maltase breaks down maltose, etc.
- the site where the enzyme binds to the substrate is called the **active site**
- the active site on an enzyme is usually an actual notch or groove in the protein's 3-dimensional structure
- the notch in the protein is compatible with the shape of the substrate, such that they "fit" together
- as the substrate approaches the active site of a protein, the R-groups in the polypeptide chain of the protein interact with the functional groups of the substrate, and the protein changes its shape slightly so as to improve the "fit" and better

accommodate the substrate – this is called the **induced-fit model** of enzyme-substrate interaction

- click on the following link to see an animation of the induced-fit model: http://scholar.hw.ac.uk/site/biology/activity6.asp
- when the two are attached, this creates the **enzyme-substrate complex** (see Figure 2, p. 70)
- Figure 3, p. 70 illustrates how maltase catalyzes the hydrolysis of maltose into two separate α-glucose molecules
- during the enzyme-substrate complex, the 1-4 glycosidic linkage between the two glucose molecules is weakened
- the bond breaks, water reacts at this point, and the shape of the enzyme is slightly altered, which results in a loss of affinity for the product molecules, thus releasing them
- upon release, the protein reforms its original structure and is now ready to bind to another maltose
- to see an animation of this action click on the following web site: http://web.ukonline.co.uk/webwise/spinneret/other/anenz.htm

LIMITATIONS

- it is important to note that any enzyme-catalyzed reaction can be **saturated** – all available specific enzymes are bound to their substrates
- there are a limited number of enzyme molecules that can be used at any one time
- both temperature and pH affect enzyme activity
- Figure 5a, p. 72 illustrates how enzymatic activity can vary with environmental temperature changes
- however, above or below a certain range of tolerance for the enzyme, the activity decreases
- this is because thermal agitation disrupts protein structure, resulting in the **denaturation** of the enzyme, thus loss of enzyme function
- every enzyme has an optimal temperature at which it is the most effective
- most human enzymes work best at 37˚ C temperatures
- enzymes also have an optimal pH at which they most efficiently bind to substrates
- Figure 5b, p. 72 illustrates how pH affects the operation of pepsin and trypsin, two human digestive enzymes

ENZYME "HELPERS"

- some enzymes require the presence of certain substances before they can work properly – these behave like "switches" that turn an enzyme on and off
- such agents can be inorganic – **cofactors**, or organic – **coenzymes**

- they may covalently bind to active sites on the protein structure, or they may bind to the substrate itself
- some examples of cofactors are Zn^{2+}, and Mn^{2+} ions
- coenzymes include derivatives of vitamins such as:
    - NAD^+ (nicotinamide adenine dinucleotide), a derivative of vitamin B_3 (niacin) -- acts as an electron carrier in cellular respiration
    - $NADP^+$ (nicotinamide adenine dinucleotide phosphate) – acts as an electron carrier in photosynthesis

ENZYME INHIBITION

- a variety of substances can inhibit enzyme action:
    - **competitive inhibitors**
        - act as substrate "mimics" since they are very similar in structure
        - bind to active sites and block the normal substrate from binding (see Figure 6a and b, p. 73)
        - if the concentration of the normal substrate is increased this inhibition can be overcome
    - **noncompetitive inhibitors**
        - these do not compete with the substrate for the active site – instead they attach to another site on the enzyme, causing a change in the enzyme's shape, as seen in Figure 6c, p. 73)
        - this changes the active site in such a way that it no longer "fits" the substrate
        - an example of such an inhibitor is DDT – a poison that inhibits enzymes of the nervous system
        - some enzyme inhibitors are actually useful in the controlling of enzyme activity

ALLOSTERIC REGULATION

- enzyme activity must be controlled in cells, otherwise unwanted or unnecessary catalytic reactions may result, wasting a cell's energy
- there are two ways that a cell can reduce enzyme activity:
    - restricting the production of a particular enzyme, thereby reducing its activity
    - inhibiting the action of existing cellular enzymes
- some enzymes actually produce a second site (at some distance away from its substrate active site), called **allosteric sites**
- a substance that binds to an allosteric site may inhibit or stimulate an enzyme's activity

- most allosteric proteins are globular and have allosteric sites and active sites in each of their tertiary structures that make up the protein
- **activators** that bind to allosteric sites help keep the active sites in a conformation that “fits” its particular substrate
- **allosteric inhibitors** stabilizes the inactive form of the enzyme
- Figure 7, p. 73 illustrates allosteric regulation

FEEDBACK INHIBITION

- this very common form of protein inhibition involves a series of sequential reactions, each catalyzed by a specific enzyme, where desired product at the end of the series is in fact an allosteric inhibitor of an enzyme that catalyzes at the beginning of the series (see Figure 8, p. 74)
- when too much of the product is made, it feeds back as an inhibitor an binds to the enzyme, changes its shape, thus inhibiting its function
- this causes the chain of reactions to stop and reduces the production of the final product
- as the product gets used up, its concentration decreases, causing a reduction of allosteric inhibition, thus making the enzyme exist in the active form more often, and the production of the inhibitor product increases again
- this feedback inhibition process keeps the amount of product made in check and prevents the over-enzymatic activity

COMPARTMENTAL INHIBITION

- some cells control metabolic processes by restricting the location of enzymes and enzyme complexes to certain locations within the cell
- for example, some enzymes for cellular respiration are contained in the mitochondria, whereas others are dissolved in the cytoplasm
- therefore metabolic activity of mitochondrial enzymes can be indirectly controlled if the movement of substrate molecules across the mitochondrial membrane is controlled

PRACTICAL USES OF ENZYMES

- amylases for the enzymatic hydrolysis of starch (amylose and amylopectin) in industry to make syrup from starch to sweeten foods
    - this involves α amylase to break starch into maltose, then glucomylase (maltase) to break maltose into glucose
    - the reaction is seen on p. 75
- proteases – protein-hydrolyzing enzymes – used to coagulate milk for the manufacture of cheese
    - common one that is used is *rennet*, which is derived from chymosin
- amylases and proteases are also used in the dry cleaning industry to break down protein and carbohydrate stains on fabrics
    - enzymes are used in the cleaning of dirt on clothing – they break down stains and remove them with less agitation and at lower temperatures than soaps or detergents do
- α galactosidase (lactase) is used to help break down lactase into glucose and galactose for people who are lactose-intolerant
- lipases – fat-hydrolyzing enzymes – are used in making Italian cheeses like Romano and Parmesan
    - the lipases break up the fat in the milk to free up the fatty acids
        - the type and concentration of the fatty acids gives the cheeses their unique flavour
- additional uses of enzymes are outlined in Table 1, p. 76.

Homework: p. 77, 1-8.