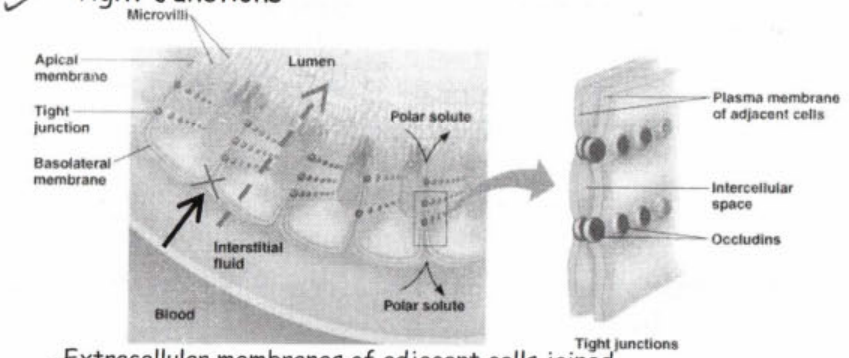
Biology 2A03
Lecture # 3

Protein activity

Jan 6, 11

Cell - cell contact (adhesions)

✓ Tight Junctions



-Extracellular membranes of adjacent cells joined

-Transport pathway between cells (extracellular) blocked

-Most substances must therefore go transcellularly

- Forms a selective barrier

Fig 2.26

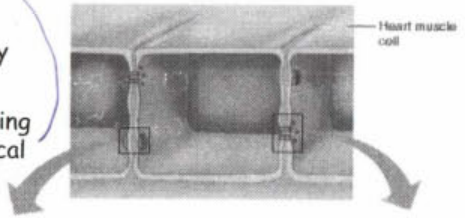
-E.g. most epithelial cells

✓ Desmosomes

-Hold adjacent cells tightly together

-found in areas of stretching (e.g. skin) or high mechanical stress (cardiac cells)

→ b/c of pumping of heart



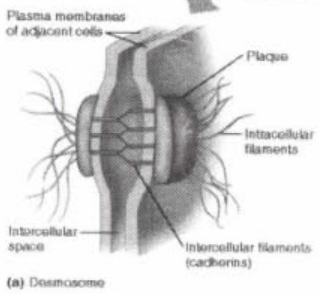
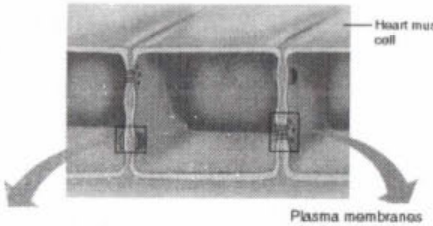


Fig 2.27

✓ Gap Junctions



→ found in ventricle & atrium

- Protein channels (connexons) linking cytosols of adjacent cells

- channels are very small (1.5nm diameter) & limits what can pass

- concentrated in cardiac cells at intercalated disks & important for passage of electrical signals (Fig 14.8)

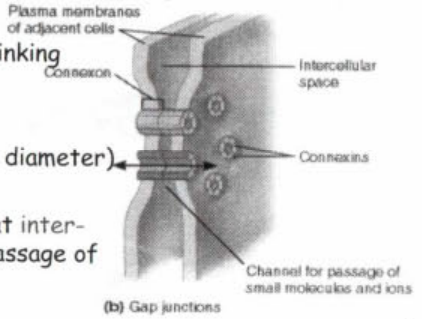


Fig 2.27

Protein activity

Proteins and protein function central to physiology

Protein activity is controlled by:

1) Rates of synthesis and/or degradation
2) Changes in 3D conformation (shape). → i.e. temperature
(Determined by amino acid composition)

-Important for ligand binding to active binding site

The shape of proteins and therefore ligand binding modified by:

1) **Allosteric modulation:** Non-covalent binding of factors to other regulatory sites results in a change in shape of the active site

↳ changes the way the ligand binds to the active site.

Protein activity (cont)

2) **Covalent modulation:** Covalent binding of -ve PO_4^{2-} to amino acid side chains by protein kinases
(e.g. serine, threonine, tyrosine)

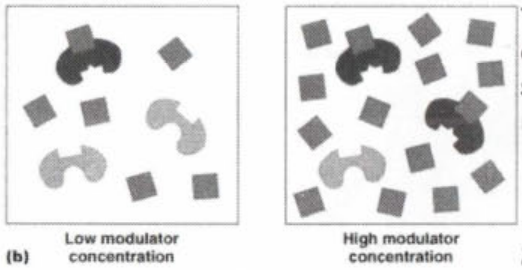
-Changes protein conformation and distribution of -ve charges

Protein kinases add PO_4^{2-} from ATP to proteins
PO_4^{2-} can be removed by protein phosphatases

-Kinases can be controlled allosterically demonstrating that the 2 systems can interact

-Both allosteric and covalent modification affect the binding affinity of enzyme for substrate (ligand) or a binding site can be turned off or on

See Fig 3-9, 3-10

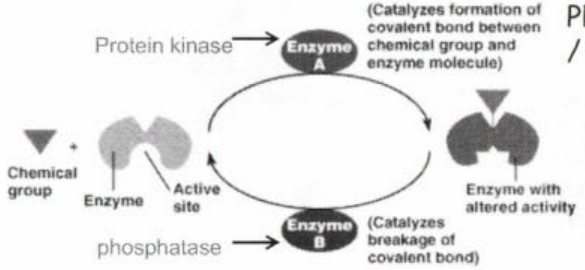


1) **Allosteric modulation:**

e.g. substrate for fat synthesis inhibits enzyme in fat oxidation

2) **Covalent modulation:**

Phosphorylation / dephosphorylation



Allosteric regulation is the regulation of an enzyme or other protein by binding an effector molecule at the protein's allosteric site (that is, a site other than the protein's active site). Effectors that enhance the protein's activity are referred to as allosteric activators, whereas those that decrease the protein's activity are called allosteric inhibitors.

Enzymes

Cell metabolism: Sum of all chemical reactions that occur in cells

1) Anabolism (synthesis)
2) Catabolism (breakdown)

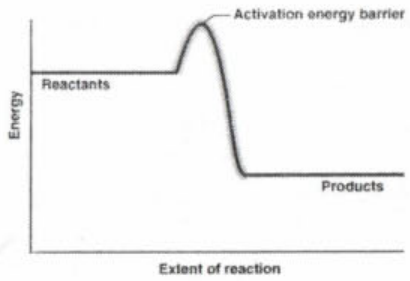
Virtually every chemical reaction in the body catalyzed by enzymes

Often need cofactors (trace metals such as Mg, Fe, Cu, zinc) or coenzymes derived from vitamins (e.g. NAD^+, FAD^+, and Coenzyme A from B vitamins)

A **cofactor** is a non-protein chemical compound that is bound to a protein and is required for the protein's biological activity.

Covalent modulation is the alteration of a protein's shape and function by covalent bonding of chemical groups to it.

Coenzymes and cofactors serve the same function. They cause or regulate the speed of chemical reactions. The difference between the two is that coenzymes are organic substances, while cofactors are inorganic.

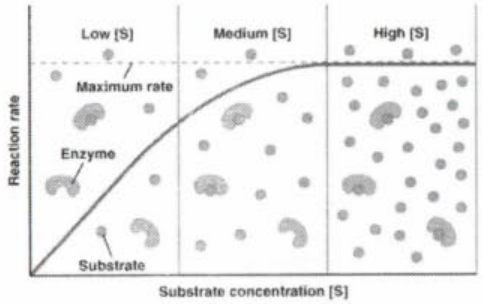


(a)

Uncatalyzed they occur at too slow a rate (years in some cases) due to high activation energy

Enzymes decrease the activation energy and increase reaction rates by a factor of 10^5 to 10^{17}

Fig 3.4a



Increasing ES complexes

Enzyme 100% saturated w/ S

Fig 3-7

Enzyme Kinetics – studying the rate of reactions

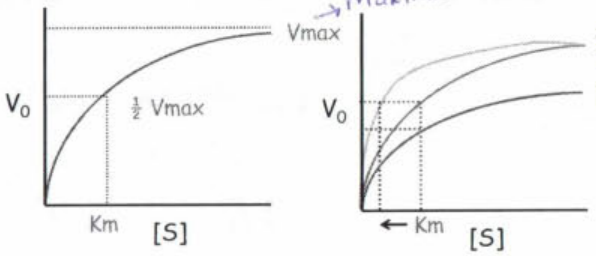
$$S + E \rightleftharpoons ES \rightarrow P + E$$

most important step.

Rates of enzyme reactions depend upon:

1) Substrate [S] or product [P] (Law of mass action)
2) Enzyme concentration [E]
3) Enzyme activity (catalytic rate)

Km = inverse of enzyme affinity.



See Fig 3-3
Fig 3-7
Fig 3.8

Decrease in Km indicates increase in affinity as it takes a lower conc of substrate to reach ½ Vmax.

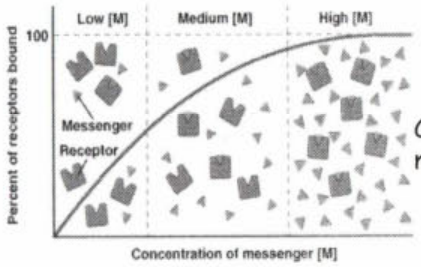
Fig 5-9
Fig 5-10

Receptors

Show characteristics very similar to enzymes

The magnitude of a cell's response depends on:

1) The messenger's concentration
2) The # of receptors present
3) Affinity of receptor for messenger



Can become saturated with messenger

Relationship between [S] and reaction rate

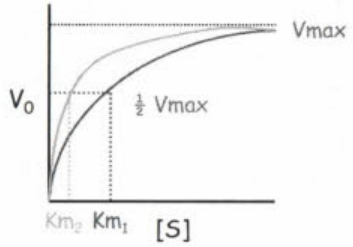
The quantitative description of enzyme reaction rates to [S], constants Vmax and Km occurs by the:

Michaelis-Menten equation: $V_0 = \frac{[S]\,V_{max}}{K_m + [S]}$

Km = substrate concentration ([S]) at which $V_0 = \frac{1}{2}$ Vmax

If affinity increases then the # of ES complexes increase at any given [S] or the same # of [ES] at lower [S] (i.e. Km decreases)

In other words at high affinities $\frac{1}{2}$ Vmax occurs at a lower [S]

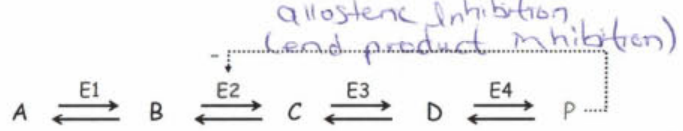


Km can be determined from this plot.

1/Km = affinity

Metabolic pathways

A sequence of enzyme-mediated reactions leading to a specific product



Specific reaction steps may be regulated to control flux through the entire pathway.

Classically these are called "rate limiting" steps but modern control theory does not use this term

Looks at the relative control at each enzymatic step.

End product inhibition is negative feedback used to regulate the production of a given molecule.

The initial substrate is a molecule that is altered in three steps by enzymes E1, E2, E3, and E4. The end product will combine with E2 to stop the reaction so there will not be an excess production of the end product.