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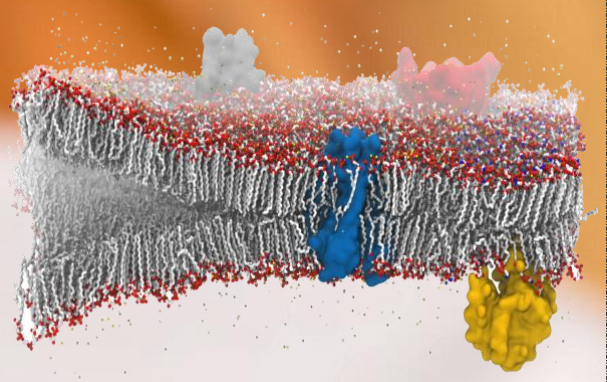
The Pharmacology of Lock and Key Receptors

Pharmacology describes a receptor to be any molecule with a biological significance to which a drug can bind and generate a quantifiable response. Hence structural proteins and enzymes are classed under pharmacological receptors. The most abundant pharmacological receptors that can be exploited with therapeutics are proteins responsible for transmitting extracellular into intracellular responses.

The Building Blocks of Cellular Transmissions



[1]

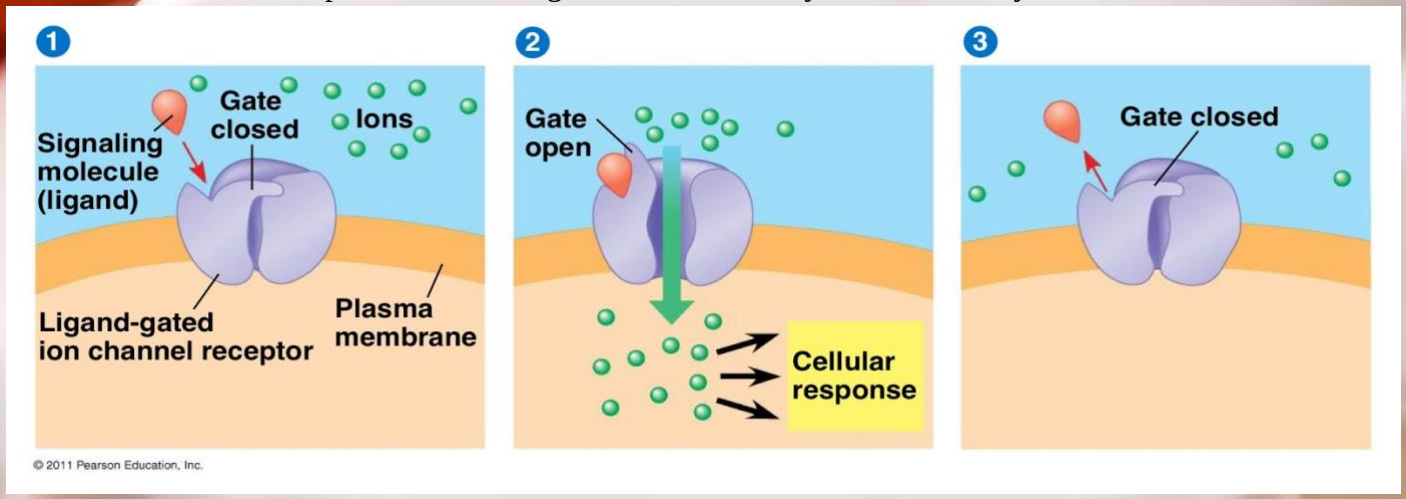
Lipid membranes are recognised to be the minimum requirement for the basic structure of a cell membrane [1]. Though all good things have their limits so does the permeability of the lipid membrane. Many essential molecules that keep our body in tune are hydrophilic, meaning they're irresistibly attracted to water. Hence hydrophilic molecules or charged ions, as Sodium (Na^+) and Calcium (Ca^{2+}); encounter difficulties when demanding to cross the 'water repelling' lipid membrane. Though basis of our existence is based on the movement ions in and out of the cell.

The movement of ions brands ion channels as a key piece in the game of equilibrium [1]. Ion channels are elemental for the survival of any organism because of the essentiality of controlling ion equilibrium [1,2]. They are typically crucial to the transmission of signals throughout the brain and have multiple systems to open and close. Chemical messengers bind to LGICs at synapses transmitting chemical signals into electrical signals in the neurons. You can think of it as a locked room and getting in without a key is impossible [5].

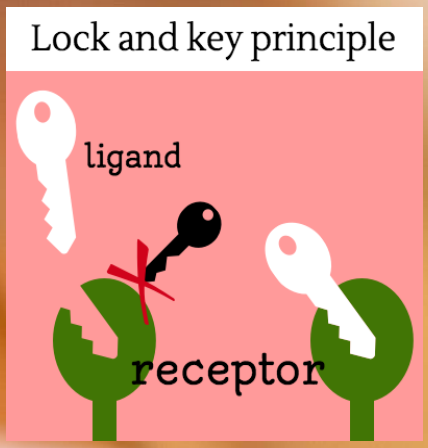
LGICs transport ions across the membrane only using the force generated by a concentration gradient or so called 'passive' diffusion [1]. Like everything in life ion concentrations try to follow equilibrium. Ion channels open like flood gates sanctioning the abundance of ions to forcefully rush through, allowing the ions to move from high to low concentrations.

The Lock and Key Receptor

LGICs are a class of ion channels and yet again make them utterly crucial for normal bodily functions, everything from the generation of mere thought to your autonomic heartbeat [1,3]. It's quite mind boggling to think that these microscopic channels instigate all our voluntary and involuntary actions. [15]



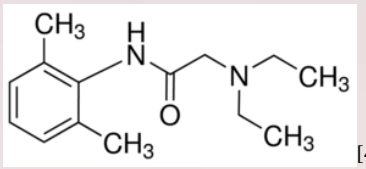
A ligand binds to the ligand binding site on the receptor. The attachment of the ligand transforms the receptor causing conformational changes that open the channel, thus allowing ions to gush in and trigger meticulous pathways. The receptor closes when the ligand detaches from the binding site inactivating the receptor [6]. The sequence of events customarily follow the steps exhibited in the images above.



[3]

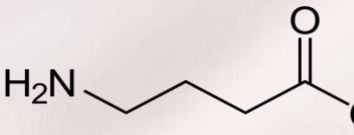
These multifaceted microscopic units are like Lego by having at least two domains, in which one spans the total width of the membrane facilitating the movement of ions (the transmembrane ion pore domain), and the second that tasks as a binding site for the chemical messenger (the extracellular domain) [1,5].

Lidocaine and Diazepam Molecular Interactions



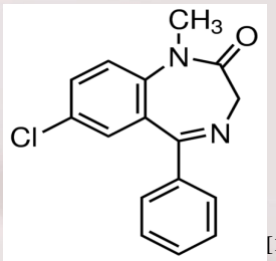
[4]

Lidocaine is a typical numbing agent used as a cardiac depressant and to desensitize a specific area of tissue from pain [9]. The drug works by binding to a specific site of the LGIC - known as the allosteric site, an additional binding site to active binding site; and blocks sodium ions from rushing into the cell [9,12]. Ultimately, this prevent depolarisation. The impeded channels prevent the initiation and propagation of signals along the neuron, stopping the transmission of any signals [9,10]. The effect of lidocaine on LGICs can be thought of as though there was a locked train door to an empty train, as the influx of people at the station are unable to enter, they cannot continue their journey. Alongside this, lidocaine is an anaesthetic as it stops the initiation and transmission of any signals of sensation to the central nervous system to later be perceived [10,12].



[7]

γ-aminobutyric acid (GABA) is the main inhibitory amino acid neurotransmitter in the vertebrate central nervous system [13]. GABA binds to synaptic receptors permitting the efflux of potassium (K^+) or influx of negatively charged chloride ions (Cl^-) and thus hyperpolarizing the cell or moving it away from the threshold 'transmission trigger'. GABA receptors require a ligand to open and allow the bidirectional flow of ions [10,13].



[13]

Benzodiazepines like are diazepam are notorious to have muscle relaxation, sedative and aesthetic properties, by augmenting the effect γ-aminobutyric acid (GABA) has on its own receptor [9,13]. Diazepam. It increases the affinity of GABA for its receptor, so diazepam increases the binding strength of GABA to its ligand receptor [11,13]. GABA on its own opens the flood gates and hyperpolarizes the cell. With the addition of a benzodiazepines like a diazepam they hold the chloride (Cl^-) channels open longer dramatically increase in the amount of negatively charged ions into the cell and hence extending the hyperpolarization which inhibits additional excitation of the cell leading to tissue desensitization [9,11].

Reference:

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