Quantum Tunnelling in Glycine Receptors: A Mathematical Model

Andrew Davison Email: a.davison5@ncl.ac.uk

Posters in Parliament

Introduction

Glycine receptors (GlyRs) are pentameric (composed of five subunits) ligand-gated ion channels. The binding of the neurotransmitter glycine to the receptor protein opens a chloride-permeable pore, allowing the hyperpolarization of the membrane potential through the influx of negatively charged chloride ions (figure 1). These receptors are involved in several important physiological processes: pain perception, brain development and motor control[1,2].

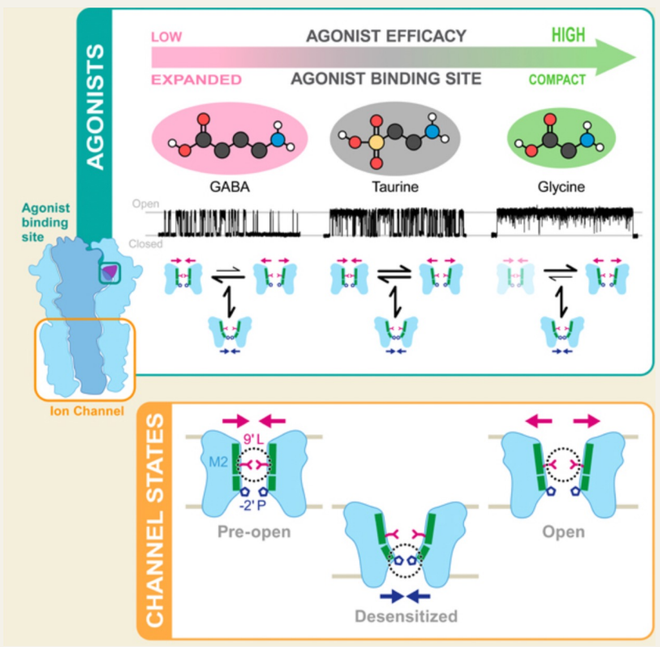

Figure 1: the opening and closing of glycine receptors in response to glycine or related agonists. Taken from Yu et al[2].

Quantum tunnelling (QT) is a process whereby a particle can move through a potential energy barrier despite having less kinetic energy than the barrier itself (figure 2). The role of quantum tunnelling across ion channels has previously been studied and modelled for sodium, potassium and GABA receptors. This has provided solutions for problems in fields such as neurophysiology and pharmacokinetics[3].

In this project, the mathematical model developed by Alali et al[3] will be applied to glycine receptors to determine if QT of chloride ions could depolarise the cell membrane to a physiologically relevant extent.

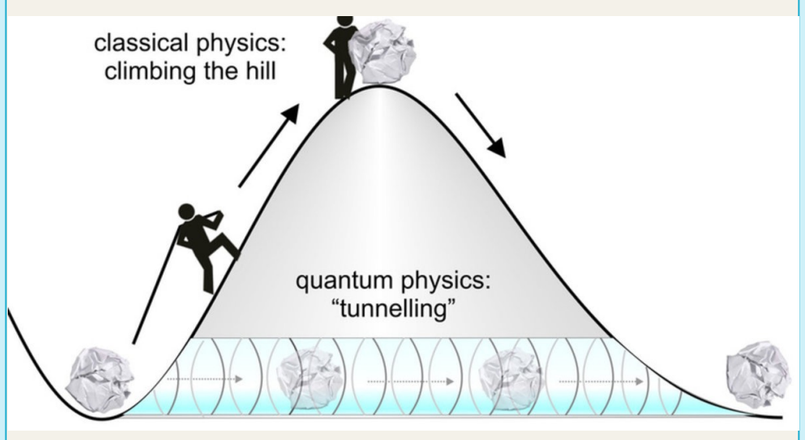

Figure 2: a comparison of quantum tunnelling and classical mechanics in the movement of a particle through and over a potential energy barrier respectively. Figure taken from the Max Planck Society[4].

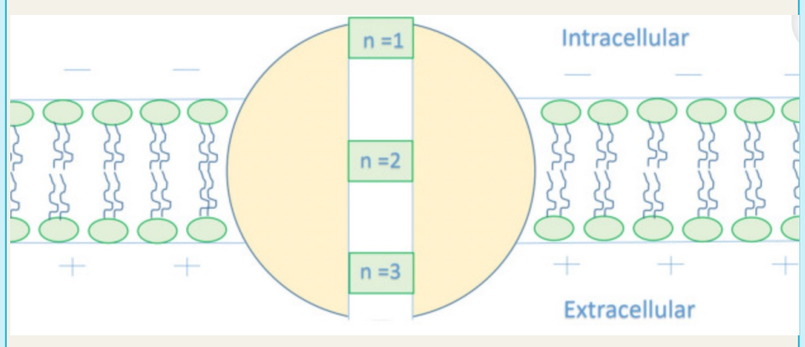

Figure 3: various locations of the gate in a glycine receptor ranging from n = 1 being located more intracellularly, n = 2 being found in the middle of the receptor, and n = 3 being located more extracellularly. Figure taken from Alali et al[3].

Methods

The probability of QT can be modelled by the following equation:

$$T_Q = e^{\frac{-\sqrt{8m}}{h} \times \frac{2w}{3g}\sqrt{(g-KE)^3}}$$

Where T_Q is the probability of tunnelling, *m* is the mass of chloride ion (5.9×10^{-26} kg), *g* is the height of the energy barrier of the closed gate in the GABA receptor, *w* is the length of the gate, *KE* is the kinetic energy of the chloride ion and h represents the reduced Planck's constant (1.054×10^{-34}Js).

As Cl^- are present both extracellularly (EC) and intracellularly (IC), different kinetic energies are expected depending upon location. As the IC cell membrane is negatively charged relative to the EC membrane, it is expected that IC chloride ions will gain kinetic energy as they move extracellularly, whereas the extracellular ions will lose kinetic energy. The location of the gate will be represented by n, and the kinetic energy of extracellular ions will decrease by $\frac{qV_m}{n}$, whilst the energy of intracellular ions will increase by $qV_m\left(1-\frac{1}{n}\right)$, where q represents the charge of the chloride ion (1.6×10^{-19} C) and V_m represents the membrane voltage (figure 3). The kinetic energy of intracellular and extracellular chloride ions can be decomposed into two components: thermal and electrical potential energy.

$$KE(Cl_I) = \frac{3}{2}K_BT + qV_m(1-\frac{1}{n})$$

$$KE(Cl_E) = \frac{3}{2}K_BT - \frac{qV_m}{2n}$$

Here, $KE(Cl_I)$ and $KE(Cl_E)$ represent the kinetic energy of intracellular and extracellular Cl^- ions respectively; T represents temperature in Kelvin and K_B represents Boltzmann's constant (1.381×10^{-23}J/K). In the second equation, the electrical potential energy component is halved to produce positive KE values.

These equations for KE were incorporated into the equation for the probability of quantum tunnelling. This produced two equations that describe the probability of QT for intracellular and extracellular ions respectively:

$$T_Q(Cl_I) = e^{\frac{-\sqrt{8m}}{h} \times \frac{2w}{3g}\sqrt{(g-\left(qV_m\left(1-\frac{1}{n}\right)\right)+\frac{3}{2}K_BT)^3}}$$

$$T_Q(Cl_I) = e^{\frac{-\sqrt{8m}}{h} \times \frac{2w}{3g}\sqrt{(g-(\frac{3}{2}K_BT-\frac{qV_m}{2n}))^3}}$$

These equations were then used to graph the probability of quantum tunnelling for intracellular and extracellular chloride ions at certain physiological parameters (see figure 4). Namely, a membrane potential (V_m) of 0.07V, modelling the gate as being closest to the intracellular region of the cell, rather than in the middle (n = 1), a temperature of 37°C (human body temperature) and assuming a gate length (w) equal to 1×10^{-10}m.

Results

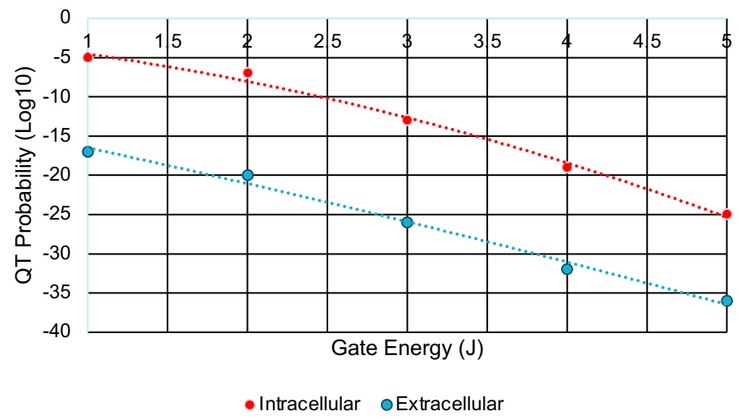

Figure 4: the probability of quantum tunnelling at increasing heights of the energy barrier. Note: gate energies on this graph are multiplied by a factor of 10^{10}, so when G = 2J, the true energy of the gate is 2×10^{-10} joules (J).

As shown in Figure 1, as gate energy increases, the probability of QT for both intracellular and extracellular ions decreases. Overall, even at minute gate energies, the probability of QT for chloride ions is minuscule, but the probability would increase when greater quantities of receptors are considered.

Discussion

This research has demonstrated the theoretical possibility of quantum tunnelling across glycine receptors under standard physiological conditions. Further work could concentrate upon measuring the density with which glycine receptors are packed in cell membranes, as this information could be used to calculate the conductance of glycine receptors with regards to QT, or how well they conduct charges. This will determine if QT is physiologically relevant to membrane depolarization or not.

Understanding the behaviour of ions and their respective channels at the quantum level may also be useful for informing gene therapies. The use of gene therapy to correct defective ion channels is under consideration for treating several conditions[5]. Therefore, knowing how channels behave in healthy individuals will enable researchers to tailor gene edits and new channels for patients with greater accuracy and precision.

References

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