***2. Methods***

**2.1 Hodgkin-Huxley model**

The **Hodgkin–Huxley model**, or **conductance-based model**, is a mathematical model that describes how action potentials in neurons are initiated and propagated. It is a set of nonlinear differential equations that approximates the electrical characteristics of excitable cells such as neurons and cardiac myocytes. It is a continuous-time dynamical system.

The typical Hodgkin–Huxley model treats each component of an excitable cell in this case a Purkinje cell as an electrical element. The lipid bilayer is represented as a capacitance (Cm). Voltage-gated ion channels are represented by electrical conductances (*gn*, where *n* is the specific ion channel) that depend on both voltage and time. Leak channels are represented by linear conductances (*gL*). Finally, the membrane potential is denoted by *Vm*.

Channel kinetics are described with the usual Hodgkin-Huxley channel equation and constants with, α, β being the forward and backwards rate, respectively.

( 1 )

( 2 )

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( 6 )

Where n is the Potassium channel, m is the opening Sodium channel and h is the closing Sodium channel.

One other technical note is that certain function forms can become indeterminate at certain voltage values. Given a specific voltage, an(V) may evaluate to the indeterminate form 0/0. The solution to this problem is to apply L’Hospital’s rule, which states that if f(x) and g(x) approach 0 as x approaches a, and f ‘(x)/ g’(x) approaches L as x approaches a, then the ratio f (x)/ g(x) approaches L as well. Using this rule, it can be shown that an(10) = 0.1 and am(25) = 0.430825375 .Hence, the limits for every case are hardcoded for simplicity and efficiency.

All of the constants listed in Table 1, are defined in Python. These numbers fall into the range of experimental values provided in the original Hodgkin and Huxley model.

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| ***Constant*** | ***Chosen Value*** |
| Cm (μF/cm2) | 1.0 |
| GNa (mmhos/cm­­2) | 120.0 |
| GK (mmhos/cm­­2) | 36.0 |
| Gl (mmhos/cm­­2) | 0.3 |
| Vm (mV) | 0.0 |
| VNa (mV) | 115.0 |
| VK (mV) | -12.0 |
| Vl (mV) | 10.613 |
| VThresh (mV) | 55.0 |
| Iinj (μA/cm2) | 10.0 |
| Tmin (ms) | 0.0 |
| Tmax (ms) | 35.0 |

Table : Constants defined in Python based on range of values defined in the Hodgkin-Huxley mode

Simulations were run in Python 3.9, OS on a CPU. Models were simulated as ordinary differential equations and integration was performed explicitly using the scipy.integrate.odeint package suitable for stiff problems or non-stiff problems of first order ode-s.

Optimization was performed using a mixture of error minimization and hand-tuning techniques.

***CONFLICT OF INTEREST STATEMENT***

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

***References***