***Abstract***

1. ***Introduction***
2. ***Methods***
   1. **Input current**
   2. **Ion channels**

The current through the sodium channel was modelled using a Markovian scheme developed by Raman and Bean (2001). This scheme models the dynamics of both the transient and resurgent gate.

**Diagram, schematic

Description automatically generated with medium confidence**

Where

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* 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*.

( 4 )

where *I* is the total membrane current per unit area, *Cm* is the membrane capacitance per unit area, *gK* and *gNa* are the potassium and sodium conductances per unit area, respectively, *VK*and *VNa* are the potassium and sodium reversal potentials, respectively, and *gl* and *Vl* are the leak conductance per unit area and leak reversal potential, respectively. The time dependent elements of this equation are *Vm*, *gNa*, and *gK*, where the last two conductances depend explicitly on voltage as well.

The Hodgkin and Huxley developed a model in which the properties of an excitable cell are described by a set of four ordinary differential equations. Together with the equation for the total current mentioned above, these are:

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where *I* is the current per unit area, and α{\displaystyle \alpha \_{i}} and {\displaystyle \beta \_{i}}β are rate constants for the *i*-th ion channel, which depend on voltage but not time. There are three gating variables: n for the Potassium channel activation, m for the Sodium channel activation (opening) and h for the Sodium channel inactivation (closing). The value of a gating variables is dimensionless and will vary between 0 and 1; 0 indicates that the channel is closed, whereas 1 indicates that the channel is open. The gating variable fraction is an indication of the conductance of a certain ion at a given time and membrane voltage

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(n,m,h)∞ are the steady state values for activation and are usually represented as a function of Vm.

Chart, histogram

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Figure 1: Potassium and Sodium channels as function of time

{\displaystyle V\_{m}}

The Hodgkin–Huxley model can be thought of as a differential equation system with four state variables, {\displaystyle V\_{m}(t),n(t),m(t)}V(t), n(t), m(t) and h(t){\displaystyle h(t)}, that change with respect to time{\displaystyle t}. The system is difficult to study because it is a nonlinear system and cannot be solved analytically. However, there are many numerical methods available to analyze the system. Certain properties and general behaviors, such as limit cycles, can be proven to exist. A picture containing chart

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Figure 2: Limit cycles of the gating variables as a function of Voltage

Channel kinetics are described with the usual Hodgkin-Huxley channel equations and constants with, α, β being the forward and backwards rate in ms-1, respectively.

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One other technical note is that certain function forms can become indeterminate at certain voltage values. Given a specific voltage, an(Vm) and am (Vm) may evaluate to the indeterminate form 0/0. The solution to this problem is to apply L’Hospital’s rule2, 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.

|  |  |
| --- | --- |
| ***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 1: Constants defined in Python based on range of values defined in the Hodgkin-Huxley mode

Chart, line chart

Description automatically generated

Figure 3: Neuron potential as a function of time

Simulations were run in Python 3.9.10, 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.

1. **Results**
2. **Discussion**

***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***

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3. *Raman and B. P. Bean. Inactivation and recovery of sodium currents in cerebellar Purkinje neurons: evidence for two mechanisms. Biophysical Journal, 80:729–737, 2001.*