

Research Article

Development of Neuron Ion Channel Model using Colored Noise Terms in the Conductance

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Abstract: The aim of this study is the ion channel model with noise variance as approximations to the Hodgkin-Huxley model proposed, due to the Hodgkin-Huxley model affected when inserting some colored noise terms inside the conductances, where those effects captured by colored noise because of the gate multiplicity. Firstly, it introduces the comparison of ion channel based on Fox, Lu and Linaro models. Additionally, in order to overcome the limitations of other parameter estimation methods, the proposed method fully constrains their models and obtains all model's capabilities of reproducing the data. Finally, the relationship between the sequence of colored noise and the spike frequency are simulated efficiently each gate compared with microscopic simulations of the stochastic Markov process method. In simulation results, the spiking rate generated from the proposed model very close to microscopic simulations and doesn't effect by the membrane size.

Keywords: Colored noise, hodgekin-huxley, ion channel, microscopic, noise variance, spike frequency

INTRODUCTION

The nerve cell theoretical foundation in the building block of the nervous system was introduced by Hodgkin and Huxley (1952). It processes information and sends, receives the ultimate control signal as control functions such as our breathing, complex memory and different body activity (Andersen *et al.*, 2007). Although all neurons share the same basic structure still the neuron in nervous system has many different forms depending on its occupied area and its function. The ideas of the patch-clamp technique permitted to determine experimental approaches of the possibility of measuring ion currents through individual ion channels which development by Sakmann and Neher (1995). If the numbers of ion channels are large, the channel fluctuations can become also critically close to the action potential threshold (Schneidman *et al.*, 1998; Rubinstein, 1995), in the action potential threshold that has small numbers of ion channels and that are open, the timing accuracy was determined. In addition, the bursting or spiking in the ion channels in the numerical simulations and theoretical investigations of channel dynamics caused by the internal noise (DeFelice and Isaac, 1993; Fox and Lu, 1994; Chow and White, 1996; Rowat, 2007; Diba *et al.*, 2004). Channel noises in the patch-clamp experiments are producing large voltage fluctuations to affect the propagation of action potentials and timing, initiation (Dorval and White, 2005; Jacobson *et al.*, 2005; Kole

et al., 2006; Kienker, 1989). The membrane channel dynamics which have represented by Markov models was utilized (Rudy and Silva, 2006; Mino *et al.*, 2002). Many researchers work on this field to provide enough statistics of spike generation in the stochastic HH (Zeng and Jung, 2004; Bruce, 2009; Sengupta *et al.*, 2010; Linaro *et al.*, 2011). According to these studies that Fox and Lu (1994) stochastic extension to the Hodgkin and Huxley equations may not be suitable for accurately simulating channel noise, even with large numbers of ion channels in simulations. The method that proposed using more stochastic terms and avoids the expense, complex matrix operations (Orio and Soudry, 2012). The gating variables that contain Gaussian white noise in the stochastic HH equation was proposed (Güler, 2013; Bédard and Destexhe, 2009). However, a complete, comprehensive analysis of spike generation in the stochastic HH this model is needed, that additionally includes the generation of the database on the estimation.

In this study, the proposed model directly determines a set of maximal functions of voltage parameters to fit the model neuron from the Hodgkin-Huxley equations. The behaviors of the theoretical relationship between neural behavior and the parameters that specify a neuronal model are described in detail. The simulation model doesn't only depend on the fluctuations in the number of open gates, but additionally on the existence of several numbers of gates in the single ion channels.

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THEORETICAL BACKGROUND

The Hodgkin-Huxley equations: Hodgkin and Huxley (1952) deduced that the ionic membrane conductances are variable with time and voltage-dependent and gave the form of this voltage-dependence. By treating a segment of the axon as a simple electric circuit, Hodgkin and Huxley (1952) arrived at equations describing the electric activity of the axon. The cell membrane, which separates the extracellular medium from the cytoplasm of the cell, acts as a capacitor with capacitance C (Hodgkin and Huxley used a value, based on laboratory measurement, of $10 \text{ } \mu\text{F}/\text{cm}^2$ for C). The ion current channels offer parallel pathways by which charge can pass through the cell membrane. Hodgkin and Huxley use three ionic currents in their description of the squid giant axon; potassium current I_K , sodium current I_{Na} and a leakage current I_L . The potassium and sodium currents have variable resistances that represent the voltage gated conductances associated with the membrane ion channels. The total current I is the sum of the ionic currents and the capacitive current which represents the rate of accumulation of charge on opposite sides of the cell membrane. The capacitive current, from electrical circuit theory, is $\frac{dV}{dt}$, where v is the membrane potential. Hodgkin and Huxley take $v=0$ to represent the neuron's resting potential and the equations below follow this convention:

$$\frac{dV_m}{dt} + I_{ion} = I_{ext} \quad (1)$$

$$I_{ion} = \sum_i I_i \quad (2)$$

$$I_i = g_i(V_m - E_i) \quad (3)$$

$$I = \bar{g} m^p h^q (V - V_{rev}) \quad (4)$$

The number of independent activation gates was represented by the integer power p in the Eq. (4), which was introduced by Hodgkin and Huxley (1952). In addition, they measured a time delay in the rise of the potassium and sodium currents when stepping from hyperpolarized to depolarize potentials, but when the axon is depolarized but falls alongside no appreciable inflection after it is depolarized. If g_k , is utilized as a variable the end of the record can be fitted alongside a first-order equation, but a third- or fourth-order equation is needed to describe the beginning. A functional simplification is achieved by presuming that g_k , is proportional to the fourth manipulation of a variable that obeys a first-order equation. In this case, the rise of potassium conductance from zero to a finite value is delineated by $1 - \exp(-t)$ ⁴, while the fall is given by $\exp(-4t)$. The rise in conductance consequently displays a marked inflection, while the fall is a simple. A comparable assumption employing a

cube instead of a fourth power describes the early rises of sodium conductance.

The ionic currents are given by Ohm's law ($I = gV$):

$$I_{ion} = I_{Na} + I_K + I_L \quad (5)$$

$$I_{Na} = g_{Na}(V_m - E_{Na}) \quad (6)$$

$$I_K = g_K(V_m - E_K) \quad (7)$$

$$I_L = g_L(V_m - E_L) \quad (8)$$

where,

E_{ion} = The reversal potential

g_{ion} = The ionic membrane conductance

These conductance's, in the case of the sodium and potassium currents, are variable and voltage-dependent, representing the voltage-gating of the ion channels. Hodgkin and Huxley (1952) deduced from experiment the following forms for the ionic membrane conductances:

$$g_k = \bar{g}_k n^4 \quad (9)$$

$$g_{na} = \bar{g}_{na} m^3 h \quad (10)$$

where, (n, m, h) , are ion channel gate variables dynamics, \bar{g}_i , is a constant with the dimensions of behavior per cm^2 (mention that n between 0 and 1).

In order to normalize the result, a maximum value of conductance (\bar{g}_i), is required.

The n , m and h dynamic are listed below:

$$\dot{n} = \frac{dn}{dt} = \alpha_n(1 - n) - \beta_n n \quad (11)$$

$$\dot{m} = \frac{dm}{dt} = \alpha_m(1 - m) - \beta_m m \quad (12)$$

$$\dot{h} = \frac{dh}{dt} = \alpha_h(1 - h) - \beta_h h \quad (13)$$

where, α_x and β_x , are rate constant that the changes happened with voltage changes, but not affected by time, while the value of dimensions' variable n can take place between 0 and 1, also its stand for of a single gate probability that is in permissive state.

Hodgkin and Huxley measured constantly $\alpha_i \beta_i$ as functions of V in the following:

$$\alpha_i = \frac{x_i(V)}{\tau_n(V)} \quad (14)$$

$$\beta_i = \frac{1 - x_i(V)}{\tau_n(V)} \quad (15)$$

Dynamics of the membrane: The HH model was considered in this study. The analysis is applicable to each conductance based model with ion channels

governed by linear, voltage dependent kinetics. The equation below described the membrane potential of the neuron.

$$C \frac{dV}{dt} = -g_K \psi_K (V_m - E_K) - g_{Na} \psi_{Na} (V_m - E_{Na}) - g_L (V_m - E_L) + I \quad (16)$$

V above is the transmembrane voltage and ψ_K is the dynamic variable in the formula represents the ratio of open channel from potassium which is the proportional number of open channels to the complete number of potassium channel in the membrane; also ψ_{Na} is the dynamic variable in the formula represents the ratio of open sodium channel and I is externally current. All of the two channel variables ψ_K and ψ_{Na} in the Hodgkin-Huxley equations is taken as their approximated deterministic value, $\psi_K = n^4$ and $\psi_{Na} = m^3 h$; while the potassium channel has four $n_{_}gates$ and sodium channel have three $m_{_}gates$ and one $h_{_}gate$. In case the channel is considered open, all the gates of that channel have to be open and the gating variable for potassium is n and for sodium is m and h.

The rate functions that found to be as:

$$\alpha_n(V) = \frac{0.01(10-V)}{\exp(\frac{10-V}{10}) - 1}, \quad (17)$$

$$\beta_n(V) = 0.125 \exp\left(-\frac{V}{80}\right), \quad (18)$$

$$\alpha_m(V) = \frac{0.1(25-V)}{\exp(\frac{10-V}{10}) - 1}, \quad (19)$$

$$\beta_m(V) = 4 \exp\left(-\frac{V}{18}\right), \quad (20)$$

$$\alpha_h(V) = 0.07 \exp\left(-\frac{V}{20}\right), \quad (21)$$

$$\beta_h(V) = \frac{1}{\exp(\frac{30-V}{10}) + 1} \quad (22)$$

The functions α_V and β_V have dimensions of [1/time] and govern the rate at which the ion channels transition from the closed state of the open state (α) and vice versa (β).

Fox and Lu model: In (Fox & Lu) model, the ϕ_K , ϕ_{Na} noise terms, do not take place and they are similar to zero:

$$\phi_K^F = \phi_{Na}^F = 0, \quad (23)$$

where, the Gaussian white noise with the mean squares are η_n , η_m , η_h and the high F is used to clarify the case of the model:

$$\langle \eta_n(t) \eta_n(t') \rangle^F = \frac{\alpha_n(1-n) + \beta_n n}{N_K} \delta(t - t') \quad (24)$$

$$\langle \eta_m(t) \eta_m(t') \rangle^F = \frac{\alpha_m(1-m) + \beta_m m}{N_{Na}} \delta(t - t') \quad (25)$$

$$\langle \eta_h(t) \eta_h(t') \rangle^F = \frac{\alpha_h(1-h) + \beta_h h}{N_{Na}} \delta(t - t') \quad (26)$$

Linaro model: In this model (Linaro *et al.*, 2011), the proportions of open channels with the diffusions obtained from the covariances of n^4 and $m^3 h$ is determined by the competent powers of the inevitability gating variables. The potassium conductance, ϕ_K^L , in the noise term reads as:

$$\phi_K^L = \sum_{i=1}^4 z_{K,i}, \quad (27)$$

where, the stochastic variables are $z_{K,i}$:

$$\tau_{K,i} z'_{K,i} = -z_{K,i} + \sigma_{K,i} \sqrt{2} \tau_{K,i} \xi_{K,i}, \quad (28)$$

$\tau_{K,i}$ and $\sigma_{K,i}$, are the opening, closing rates of n-gates. $\xi_{K,i}$, are Gaussian White Noise (GWN) with zero means. Similarly, the sodium conductance, ϕ_{Na}^L , in the noise term reads as:

$$\phi_{Na}^L = \sum_{i=1}^7 z_{Na,i}, \quad (29)$$

where, the stochastic variables are $z_{Na,i}$:

$$\tau_{Na,i} z'_{Na,i} = -z_{Na,i} + \sigma_{Na,i} \sqrt{2} \tau_{Na,i} \xi_{Na,i} \quad (30)$$

$\tau_{Na,i}$, $\sigma_{Na,i}$, are the opening, closing rates of both m-gates and h-gates. $\xi_{Na,i}$, are Gaussian white noise (GWN) with zero means and unit variances. In the differential equations for the gating variables, the noise terms are similar zero:

$$\eta_n^L = \eta_m^L = \eta_h^L = 0 \quad (31)$$

THE PROPOSED MODEL

The proposed model in Eq. (32, 34, 35), is a new modification of the Hodgkin-Huxley equations by development and adding GWN with the mean zero ($\xi(t)$) to the equations. In addition, it calculates the potassium and sodium channels when there are more than one n-gate and m-gate, in the dynamic variable by considering the membrane potential to have a large number of channels and that's enough to satisfy both ψ_K and ψ_{Na} . The differential equations for the activation and inactivation variables in the proposed model can be solved at any instant in time and the values of all the activation; inactivation variables are known at any instant by inspection of the voltage trace. This proposed model allows for estimation all parameters and

functions of voltage precisely. More specifically, the numbers of the gating variables, the conductance and the steady states and time constant estimated as functions of voltage. The regular states are using mathematical modifications on data collected using four voltage clamp protocols. The equations that describe the proposed model shown as follows:

$$C\dot{V} = -g_K \sum_i n^4 (V - E_K) - g_{Na} \sum_i m^3 h (V - E_{Na}) - g_{Ca} \psi_{Ca} (V - E_{Ca}) - g_L (V - E_L) + I + \xi(t) \quad (32)$$

where,

$\psi_K = n^4$ is an open potassium channels ratio

$\psi_{Na} = m^3 h$ is an open sodium channels, ratio

If we have more than one channel the dynamic variable (ψ_K), will be as follows:

$$\psi_K = \sum_i n^4$$

$$\psi_{Na} = \sum_i m^3 h, \quad i = \text{number of channels.}$$

ψ_{Ca} , is an open calcium channels, ratio depends on the concentration of Ca^{+2} :

$$[\psi_{Ca}] = \begin{cases} \frac{[Ion_{Ca}]_{out}}{[Ion_{Ca}]_{in}}, & \text{if } Ion_{Ca} \geq 1mV \\ 0, & \text{otherwise} \end{cases} \quad (33)$$

If the concentration of the calcium is high the channel will open otherwise close.

Here $[\psi_K], [\psi_{Na}]$, is the ratio of open (potassium and sodium channels), computed across all achievable order of the membrane getting $4X_K n, 3X_{Na} m, X_{Na} h$, open n- gates, as shown below:

$$[\psi_K] = \begin{cases} \frac{(4X_K n)^3 (4X_K n)^2 (4X_K n)^1 n}{(4X_K)^3 (4X_K)^2 (4X_K)^1}, & \text{if } X_K n \geq 1 \\ 0, & \text{otherwise} \end{cases} \quad (34)$$

$$[\psi_{Na}] = \begin{cases} \frac{(3X_{Na} m)^2 (3X_{Na} m)^1 m}{(4X_{Na})^2 (4X_{Na})^1} h, & \text{if } X_{Na} n \geq 1 \\ 0, & \text{otherwise} \end{cases} \quad (35)$$

If the membrane size is small then $\psi_K = n^4$ and $\psi_{Na} = m^3 h$, the proposed model's value $\psi_K = [\psi_K] = n^4$ and $\psi_{Na} = [\psi_{Na}] = m^3 h$, applies at any times.

where, $[\psi_K], [\psi_{Na}]$, reads as:

$$\psi_K = n^4 + \sigma_K q_K$$

$$\psi_{Na} = m^3 h + \sigma_{Na} q_{Na}$$

The equations that describe the dynamics of q_K are:

$$\tau \dot{q}_K = p_K \quad (36)$$

$$\tau p_K = -\gamma_K p_K - w_K^2 [\alpha_n (1 - n) + \beta_n n] g_K + \xi_K \quad (37)$$

The equations that describe the dynamics of q_{Na} are:

$$\tau \dot{q}_{Na} = p_{Na} \quad (38)$$

$$\tau p_{Na} = -\gamma_{Na} p_{Na} - w_{Na}^2 [\alpha_m (1 - m) + \beta_m m] g_{Na} + \xi_{Na} \quad (39)$$

In which (D_n, D_m), is identical to:

$$\alpha_n (1 - n) + \beta_n n \quad \text{and} \quad \alpha_m (1 - m) + \beta_m m \quad (40)$$

The standard deviation of ψ_K, ψ_{Na} , will be as follows:

$$\sigma_K = \sqrt{\frac{n^4 (n^4)^{-1}}{X_K}} q_K \quad (41)$$

$$\sigma_{Na} = \sqrt{\frac{m^3 (m^3)^{-1}}{X_{Na}}} h q_{Na} \quad (42)$$

The complete model for the dynamic variable (ψ_K), (ψ_{Na}), is:

$$\psi_K = n^4 + \sqrt{\frac{n^4 (n^4)^{-1}}{X_K}} q_K \quad (43)$$

$$\psi_{Na} = m^3 h + \sqrt{\frac{m^3 (m^3)^{-1}}{X_{Na}}} h q_{Na} \quad (44)$$

The gate noise model is:

$$\dot{n} = \frac{dn}{dt} = \alpha_n (1 - n) - \beta_n n + \xi_K \quad (45)$$

$$\dot{m} = \frac{dm}{dt} = \alpha_m (1 - m) - \beta_m m + \xi_{Na} \quad (46)$$

$$\dot{h} = \frac{dh}{dt} = \alpha_h (1 - h) - \beta_h h + \xi_h \quad (47)$$

Markov process (microscopic): The traditional way of modelling the transient sodium current has been using the HH formalism, according to expressions similar to Eq. (32). The theoretical interpretation of this model, made by Hodgkin and Huxley is similar to that commented for the potassium current. In the case of the sodium channel, there should be four gating particles, three m particles controlling activation and one h particle for inactivation, each one undergoing first-order transitions between two forms:

$$"1 - m" \rightleftharpoons "m": \frac{dm}{dt} = \alpha_m (1 - m) - \beta_m m \quad (48)$$

$$"1 - h" \rightleftharpoons "h": \frac{dh}{dt} = \alpha_h (1 - h) - \beta_h h \quad (49)$$

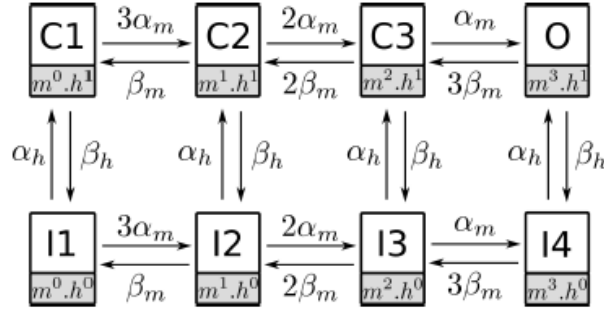


Fig. 1: Kinetic representation of the HH model for the sodium channel

where, the kinetic rates $\alpha_{m,h}$ and $\beta_{m,h}$ depend on the membrane potential V .

The HH model for the sodium current can be also represented by the kinetic model shown in Fig. 1, with three closed states C1, 2, 3, four inactivated I1,2,3,4 and only one open O. All the inactivated states have zero h gates, but a different number of m ones. Similarly, the difference between the closed states and the open one is the same, but all of them have one h gate. Vertical rates from (to) inactivated states I1, 2, 3, 4 are equal, because they all represent the same conformational change: a gate h becomes available (unavailable). On the other hand, horizontal rates are not equal, because they represent interactions between states with different m gates. For example, the transition from the farthest closed state C1 to C2 happens if only one in three (kinetically undistinguishable) mgates become available: that is the reason of the $3\alpha_m$ rate. However, going from C3 to O implies that the remaining unavailable m gate of C3 becomes available, leading to the α_m rate. The same can be said for the reverse transitions: O goes to C3 by dropping only one of its three m gates.

For example, O indicates the probability of the channel to be in the open state. Consequently, the rates represent the transition probability from one state to another. The occupancy of each state can be found by solving the corresponding master equation, like this one for the Ostate:

$$\frac{dO}{dt} = \alpha_m C3 + \alpha_h I4 - (3\beta_m + \beta_h) O \quad (50)$$

Another outcome of the stochastic model is that the sum of the state's occupancies must be one. For the model in Fig. 1, that means: $C1 + C2 + C3 + I1 + I2 + I3 + I4 + O = 1$. Therefore, a Markov model with N states may have only $N - 1$ independent master equations.

The deterministic HH model can be interpreted as the Markov model in the limit of a large number of channels (whole cell recordings), where each state becomes the fraction of channels occupying it (Zeng and Jung, 2004). In this case, a macroscopic current can be expressed as:

$$I = \gamma \cdot N \cdot O(V - E_K) \quad (51)$$

where, γ is the single channel conductance and N the number of channels.

Conceptually, Markov models are closer than HH models to the real operation of ionic channels, given that it would be possible to map each state to a conformational form of the proteins, determined by molecular dynamics.

RESULTS AND DISCUSSION

In this section, we assess our model's effectiveness in numerical experiments. The assessment develops computations and statistics from the microscopic simulations, FL, linaro equations and proposed model in a comparative manner. As the microscopic simulation scheme, we employ the method known as the simple stochastic method see (Mino *et al.*, 2002) in which all the gates are simulated individually using the Markov scheme. Once the numbers of open channels are known, the voltage is integrated to the next time of gate update using Eq. (32). In the numerical implementation of our model equations, it is necessary to check, after each time step, whether or not the noise terms in Eq. (45, 46, 47) have taken n, m, or h outside the range of [0, 1]. If so, the step must be repeated with new random numbers for ξ_K , ξ_{na} , or ξ_h . We compare the mean spiking rates obtained from the microscopic simulations, proposed model and the FL, linaro equations, using the above semi-deterministic dynamics. The simulation model in Eq. (43, 44) numerically was developed by using C++ programming language, MATLAB and GraphPad Prism. The input current was time independent, which was modified based on the program to handle time dependent current and the noise variance in this simulation were a periodic sin wave under noise variance, as shown below:

$$I(t) = I_{base} + \xi(t) \quad (52)$$

where, I_{base} indicates the current situation and the (GWN) with mean zero is $(\xi(t))$. A series of

Table 1: Constant parameters of the models

Constant parameters	Value
γ_K	10
w_K^2	150
T_K	400
γ_{Na}	10
w_{Na}^2	200
T_{Na}	200

Table 2: Parameter values of the membrane

Ionic current	Reflection potential (mV)	The conductance (mS/cm ²)
Sodium (Na ⁺)	$E_{Na} = -115$	$x1 = 120$
Potassium (K ⁺)	$E_K = 12$	$x2 = 36$
Leakage (L)	$E_L = -10.613$	$x3 = 0.3$
Calcium (Ca ²⁺)	$E_{Ca} = 136$	$x4 = 40$

experiments has been used to examine the effectiveness of the noise in the proposed model in a relative manner with the Microscopic simulation, as mentioned above.

The experiments applying by using parameter values of the membrane with including Gaussian white noise in the proposed model and in the Fox and Lu (1994) and Linaro equations as described in formula (52). Hence, it can be seen that the performance of the proposed model was quite similar to the microscopic simulations. Thus, whatever Figures have been driven out as a result, there is a difference between the spike frequency of the Fox and Lu (1994) and Linaro equations and the proposed model, which is actually containing the spikes from microscopic simulation. In addition, the difference between spike frequencies becomes smaller when the noise variance increases.

The Gaussian White Noise terms (GWN) with zero means which used in the numerical experiments shown below:

$$\langle \xi_K(t) \xi_K(t') \rangle = \gamma_K T_K [\alpha_n(1-n) + \beta_n n] \delta(t-t') \quad (53)$$

$$\langle \xi_{Na}(t) \xi_{Na}(t') \rangle = \gamma_{Na} T_{Na} [\alpha_m(1-m) + \beta_m m] \delta(t-t') \quad (54)$$

$$\langle \xi_K(t) \xi_K(t') \rangle = \frac{\alpha_n(1-n) + \beta_n n}{4X_K} \delta(t-t') \quad (55)$$

$$\langle \xi_{na}(t) \xi_{na}(t') \rangle = \frac{\alpha_m(1-m) + \beta_m m}{3X_{Na}} \delta(t-t') \quad (56)$$

$$\langle \Xi_H(T) \Xi_H(T') \rangle = \frac{A_H(1-H) + B_H H}{X_{Na}} \Delta(T-T') \quad (57)$$

The phenomenological methods through numerical experiments estimate the values of the parameters. Both these values can calculate an approximation by phenomenological means, as given in Table 1.

The parameter's value of the membrane in Eq. (32) shows in the Table 2. Where X_K , X_{Na} , X_{Ca} corresponds for potassium and sodium and calcium complete numbers of channels and multiplied the X_K by $4n$ for potassium to get $4X_K n$ and also for sodium, calcium

resulting $3X_{Na} m$, $X_{Na} h$ to get open channels with the total number. In addition, the Markov process has been put into the gate's dynamics. The probability of the time t and time $t+\Delta t$ is exponential ($-\alpha_n \Delta t$), which means the n-gate is closed or becomes open and the probability of time t and time $t + \Delta t$ is exponential ($-\beta_n \Delta t$) which means the n-gate is open and the all of the parameters α_n , β_n are the rate of voltage get at the opening and closing of n-gates. Furthermore, the same process is applied for the m-gate and h-gate.

We observe from the Figs that the firing statistics from our equations are in good agreement with the corresponding statistics from the microscopic simulations. That is, our equations capture the gate noise effectively. FL equations, on the other hand, evoke spiking rates significantly larger than the rates of the microscopic scheme. The reason for this discrepancy is that the variances of the noise terms n and m in the FL formulation do not really correspond to the gate noise. It is in fact beneficial to the FL formulation to have noise variances larger than needed to model the gate noise, when the completely stochastic actual dynamics, rather than the semi-deterministic dynamics, is taken into consideration. The differences in performance of the Linaro model and the proposed model in response to noise in the rates are rather striking. Why does the Linaro model undergo such a conspicuous loss of accuracy in its statistics when the noise variance is used despite the fact that the proposed model's adequacy remains intact? we interpret this as follows. In its derivation, the Linaro *et al.* (2011) formulation draws on the covariance function of the fraction of open channels at the steady state. Therefore, the validity of the formulation becomes questionable when the number of open gates changes rapidly. With the use of noise variance, rapid changes occur in the values of rates, which can result in fast changes in the number of open gates; therefore, the Linaro *et al.* (2011) model undergoes a loss of accuracy in its statistics with the use of noise variance.

Figure 2 represents the comparison between the three curves used different noise variance, it can be seen that the proposed model was quite close to the microscopic simulations and the spike frequency increase and will be more accurate when the noise variance increasing as investigated by Fox and Lu (1994). Where the membrane size for potassium is 300, for sodium is 1000 and $I_{base} = 0$, threshold = 0.005 and the averages are computed in 30 sec' time window. The numbers of the sodium channel calculated as follows:

Number of sodium channel = Number of potassium channel/3*10.

The comparison between the three curves used different noise variance in the simulations as shown in Fig. 3. In addition, the difference between spike frequencies becomes smaller after the noise variance increases as mentioned by Linaro *et al.* (2011). Where

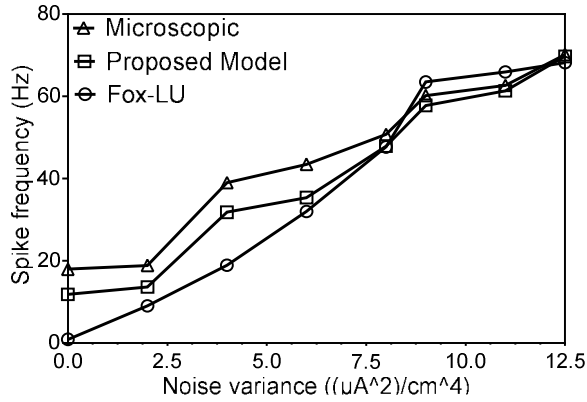


Fig. 2: Mean spiking rates against the noise variance

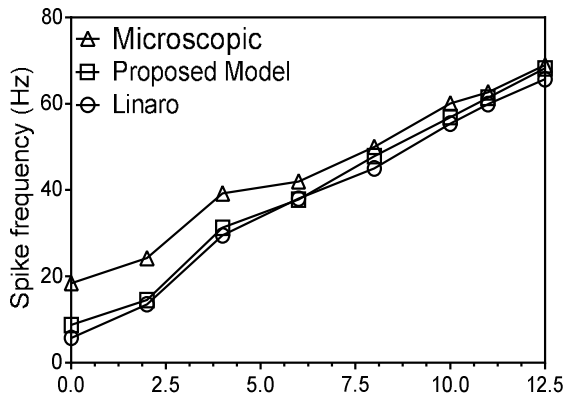


Fig. 3: The mean spiking rates against the noise variance

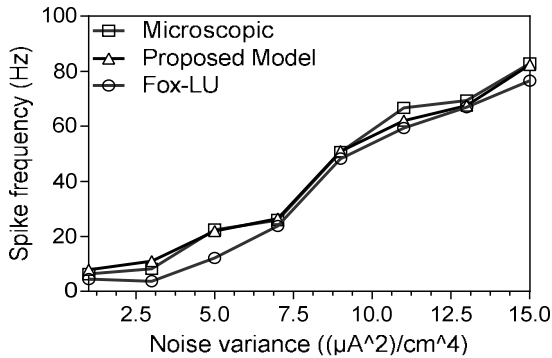


Fig. 4: Mean spiking rates against the noise variance

the membrane size for potassium is 300, for sodium is 1000, for calcium is 150 and $I_{base} = 0$. Furthermore, the averages are computed in 30 sec' time window.

The mean spiking rates against the noise variance at different noise variance used to show the comparison between the three curves as shown in Fig. 4. The proposed model was quite close to the microscopic simulations. In addition, after the noise variance increases, the difference between spike frequencies becomes smaller. Where the membrane size for potassium is 1710, for sodium is 5700, for calcium is 1520 and $I_{base} = 3$. The averages are computed in 30 sec'

Table 3: Different parameter values of the membrane

Ionic current	Reflection potential (mV)	The conductance (mS/cm ²)
Sodium (Na ⁺)	$E_{Na} = 110$	$x1 = 130$
Potassium (K ⁺)	$E_K = -15$	$x2 = 40$
Leakage (L)	$E_L = 10.5$	$x3 = 0.2$
Calcium (Ca ²⁺)	$E_{Ca} = 126$	$x4 = 36$

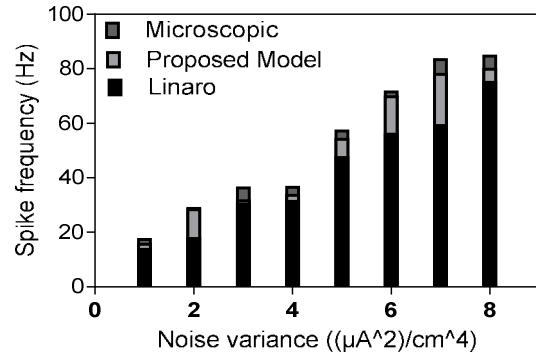


Fig. 5: The mean spiking rates against the noise variance

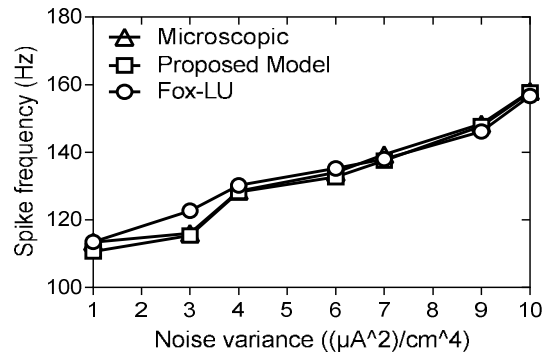


Fig. 6: The relationship between noise variance and the spike frequency

time window. Table, 3 illustrate different parameter's values of the membrane used in Fig. 4.

Meanwhile, the mean spiking rates against the noise variance at different noise variance used in the simulations to show the comparison between the three curves as clarified in Fig. 5. The result showed that the proposed model was affected by noise variance more than the Linaro model. Where the membrane size for potassium is 1710 and for sodium is 5700, $I_{base} = 5$, threshold = 0.005 and the averages are computed in 30 seconds' time window.

Additionally, the relationship between noise variance and the spike frequency at different noise variance used to show the comparison between the three curves as illustrated in Fig. 6. Where the membrane size for potassium is 3525, calcium is 3525, sodium is 11750 and $I_{base} = 12$, threshold = 0.005. And the simulation time window is 30 sec

Figure 7 shows how the speed of spike frequency as the noise variance increases for both the proposed model and Linaro model. Furthermore, different noise

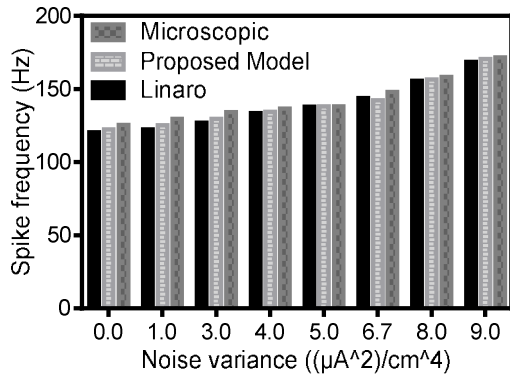


Fig. 7: Spike frequency against noise variance for the proposed model and Linaro model

variance with large membrane size used to show the comparison between the three curves. Whoever, the membrane patch composed of 3525 of potassium channels and 11750 of sodium channels and $I_{base} = 14$, threshold = 0.005. As well as the averages are computed in 30 sec' time window.

A series of experiments has been used to examine the effectiveness of the colored noise terms in the proposed model in a relative manner with the Microscopic simulation, as mentioned above. Hence, it can be seen that the performance of the proposed model was quite similar to the microscopic simulations. Thus, whatever Figs. have been driven out as a result, there is a difference between the spike frequency of the HH, Fox-Lu and Linaro equations and the proposed model, which is actually containing the spikes from microscopic simulation.

In addition, the difference between spike frequencies becomes smaller when the noise variance increases. If the colored noise is included in the equations, it is noticeable that the spike frequency is very consistent with the microscopic simulation.

CONCLUSION

The Hodgkin-Huxley type models accept a set of parameters as input and generate voltage data describing the behavior of the neuron. Proposed model solving the Hodgkin-Huxley equations for a set of input parameters refers to integrating the equations in order to obtain the resulting simulated Gaussian noise and the voltage (potassium, sodium) channels. In addition, the channel noise neuron model was studied well under the influence of varying input signal and it has been discovered that to be the main cause in the unusual increases in the cell excitability and in spontaneous firing membrane size should be small enough. Moreover, it was discovered that the proposed model keeps on advancing the spontaneous firing even if membrane size is larger, wherever the gate of noise is insufficient for activating the cell. According to the

experimental results, the spiking rate generated from the model is extremely close to the one from the actual simulation, doesn't effect by the membrane size. In difference, the rate generated through an increase in noise variance, the Fox-Lu and Linaro equation was almost similar as compared to the spikes from the model and it will be more accurate. Experimental results also highlight the mean spiking rates against noise, which was introduced by a different membrane size I_{base} and noise variance, in which three curves represent the competition between the microscopic simulation with the proposed model and Fox-Lu and Linaro equation, which showed that the proposed model has worked quite similar to the microscopic simulations. Overall, the motivation for this study is to clarify a proposed model, deliberative and rigorous methodology for parameter estimation for the Fox-Lu and Linaro models that overcomes all the limitations of current parameter estimation methodologies. An important outcome of this methodology is that the proposed model allows researchers to study hypotheses that could not have been studied using any other parameter estimation method.

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