# OPTIMIZATION AND IMPROVEMENT OF HODGKIN-HUXLEY MODEL UNDER THE INFLUENCE OF ION CHANNEL NOISE IN NEURONS

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**SUPERVISOR'S DECLARATION**

We hereby declare that We have checked this thesis and in our opinion, this thesis is adequate in terms of scope and quality for the award of the degree of Doctor of Philosophy in Engineering Technology.

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I hereby declare that the work in this thesis is based on my original work except for quotations and citations which have been duly acknowledged. I also declare that it has not been previously or concurrently submitted for any other degree at Universiti Malaysia Pahang or any other institutions.

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# DEDICATION

*"Our brains keep working despite frequent failures of their component neurons, and this 'fault-tolerant' characteristic is of great interest to engineers who wish to make computers more reliable."*

*TO MY FATHER MAHMOOD KHUDHUR SALMAN*

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## LIST OF SYMBOLS

| | |
|---|---|
| A | number of activation gates per channel. |
| B | number of inactivation gates per channel. |
| C | concentration potential |
| C | capacitance on the Hodgkin-Huxley equations |
| $Ca^{+2}$ | calcium |
| $Cl^{-}$ | chloride |
| CV | coefficient of variation |
| $C_m$ | membrane capacitance |
| D | diffusion coefficient |
| E | reversal potential of the current |
| $E_m$ | membrane potential |
| Eion | equilibrium potential |
| F | Faraday’s constant |
| $f_1(x)$ | cubic function |
| | maximal conductance of the population |
| $g_{ion}$ | ionic membrane conductance |
| $g_1(x)$ | linear function |
| h | ion channel gate variable dynamics for sodium |
| $h_\infty(V)$ | steady-state inactivation function |
| $I_k$ | potassium current |
| $I_{na}$ | sodium current |
| $I_l$ | leakage current |
| I(t) | externally applied current |
| $K^+$ | potassium |
| m | ion channel gate variable dynamics for sodium |
| $m_\infty(V)$ | steady-state inactivation function |
| n | ion channel gate variable dynamics for potassium |
| $Na^+$ | sodium |
| P | average proportion of channels |
| $P_{ion}$ | permeability for that ion |
| R | universal gas constant |
| $R_m$ | membrane resistance |
| Ri | indicator of the ability of charges |

| | |
|---|---|
| T | absolute temperature |
| ⟨T⟩ | mean interspike interval |
| ⟨T^2⟩ | mean squared interval |
| V | membrane potential |
| Vm | function of input current |
| $v_{thresh}$ | threshold voltage |
| $\tau_m$ | rates of change for the respective variables. |
| $\tau_n$ | rates of change for the respective variables. |
| $\tau_h$ | rates of change for the respective variables. |
| $\tau(V)$ | inactivation time constant |
| ξ (t)) | Gaussian white noise terms |
| $^y$and $^z$ | Gaussian white noises with zero means |
| $\psi_K$ | an open potassium channels ratio |
| $\psi_{Na}$ | an open sodium channels, ratio |
| Π | corresponds to the expectation value of a momentum |
| $\varepsilon_m^y$ | correction coefficients |
| $\varepsilon_u^z$ | correction coefficients |
| $\varepsilon_u^y$ | correction coefficients |
| $\varphi_K^L$, | potassium conductance |
| $\varphi_{Na}^L$ | sodium conductance |
| $\tau_{K,i}$ | opening of n-gates. |
| $\sigma_{K,i}$ | closing rates of n-gates. |

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# ABSTRAK

Dalam beberapa tahun kebelakangan ini, ia telah diperdebatkan dan ditunjukkan secara eksperimen bahawa hingar saluran ion di neuron boleh menyebabkan kesan asas pada sifat dinamik neuron. Kebanyakannya, bunyi saluran ion dilihat mampu menyebabkan tembakan spontan dan resonans stokastik. Walau bagaimanapun, model Hodgkin-Huxley terjejas apabila beberapa istilah hingar berwarna dimasukkan ke dalam konduktansinya, di mana kesan-kesan yang ditangkap oleh hingar berwarna disebabkan oleh banyaknya pintu. Mengenai kedudukan turun naik voltan trans-membran, dan unsur turun naik saluran terbuka dikaitkan dengan kepelbagaian pintu. Tambahan pula, fenomena itu didapati dengan ketara meningkatkan spike coherence. Dalam tesis ini, model yang dicadangkan secara langsung dapat menentukan satu set fungsi maksimum bagi parameter voltan agar sesuai dengan model neuron dari persamaan Hodgkin-Huxley. Statistik akan diperolehi menggunakan saiz membran yang berbeza dan nilai arus masuk yang berlainan. Ia pertama kali diperkenalkan kesan (tanpa, dengan) hingar berwarna, pada model yang dicadangkan dan perbandingan saluran ion berdasarkan model HH, Fox-Lu, dan Linaro. Di samping itu, untuk mengatasi batasan kaedah penganggaran parameter lain, kaedah yang dicadangkan sepenuhnya dapat menghalang model mereka dan memperoleh semua keupayaan model untuk menghasilkan semula data. Persamaan stokastik Hodgkin-Huxley berwarna dipelajari apabila arus masuk ke neuron adalah [arus input tanpa hingar dan arus bising]. Kadar puncak dan puncak koheren diperiksa, dan coefficient of variation yang didapati dari model bunyi berwarna akan dijelaskan melalui urutan eksperimen dengan membandingkan model yang dicadangkan dengan simulasi mikroskopik. Khususnya, peranan yang dimainkan oleh kehadiran istilah bunyi berwarna dalam konduktif telah difokuskan dalam peperiksaan. Akhirnya, nsekali, perangkaan generik puncak, koordinat puncak, kecekapan menembak, latensi, dan jitter dari set persamaan yang diartikulasikan didapati sangat tepat berbanding dengan statistik yang sama dari simulasi Markov mikroskopik yang tepat. Keputusan simulasi mendedahkan bahawa di atas nilai kritikal kekerapan input dan juga di bawah nilai amplitud tertentu, istilah berwarna memainkan peranan yang sangat menonjol pada statistik menembak. Di samping itu, kadar pakuan yang dihasilkan dari model yang dicadangkan sangat sama dengan simulasi mikroskopik dan tidak mempengaruhi saiz membran. Di samping itu, Kaedah Pengoptimuman Swarm Partikel biasanya digunakan untuk mengoptimumkan parameter model petak, dengan menggunakan fungsi objektif yang merangkumi kedua-dua voltan (V) dan arus (I) dengan dinamik pembolehubah pintu saluran ion (n untuk saluran kalium dan mh untuk saluran natrium) berdasarkan formalism Hodgkin-Huxley dalam paksi gergasi squid, untuk model titik-neuron. Sementara itu, perkembangan persamaan regresi digunakan dalam data eksperimen, untuk pemboleh ubah anggaran get lojik dalam arus membran. Hasil simulasi mendedahkan bahawa potensi tindakan yang lebih besar, yang mana saiz dikawal oleh perbezaan antara voltan dan arus dengan memilih pemboleh ubah optimum get lojik untuk (dalam) pengaktifan saluran membran boleh terjejas lebih cepat, bergerak pada kelajuan yang lebih cepat daripada yang lebih kecil.

# ABSTRACT

In recent years, it has been argued and shown experimentally that ion channel noise in neurons can cause fundamental effects on the neuron's dynamical behavior. Most profoundly, ion channel noise was seen to be able to cause spontaneous firing and stochastic resonance. However, Hodgkin-Huxley model affected when inserting some colored noise terms inside the conductance's, where those effects captured by colored noise due to the gate multiplicity. Regarding the position of the trans-membrane voltage fluctuations, and the element of open-channel fluctuations is attributed to gate multiplicity. Furthermore, the phenomenon was found to significantly enhance the spike coherence. In this thesis, the proposed model directly determines a set of maximal functions of voltage parameters to fit the model neuron from the Hodgkin-Huxley equations. The statistic will be obtained using different membrane size and different input current values.  Firstly, introduced the effect of (without, with) colored noise on the proposed model and the comparison of ion channel based on HH, Fox- Lu, and Linaro models. Additionally, in order to overcome the limitations of other parameter estimation methods, the proposed method fully constraints their models and obtains all models capabilities of reproducing the data. The colored stochastic Hodgkin-Huxley equations were studied when the input current to the neuron is (noise-free input currents and noisy currents). The spiking rates and the spike coherence were examined, and the coefficient of variation to be extracted from the colored noise model will be explained through a sequence of experiments by comparing the proposed model with the microscopic simulations.  In particular, the role played by the presence of the colored noise terms in the conductances was focused on in the examination. Finally, statistics of spike generation, spike coherence, firing efficiency, latency, and jitter from the articulated set of equations are found to be highly accurate in comparison with the corresponding statistics from the exact microscopic Markov simulations. The simulation results revealed that above a critical value of the input frequency and also below a certain amplitude value, the colored terms play a very prominent role in the firing statistics. In addition, the spiking rate generated from the proposed model is very close to microscopic simulations and does not affect the membrane size. On the other hand, Particle Swarm Optimization (PSO) methods are commonly used to optimize compartment model parameters, by using an objective function that includes both voltage (V) and current (I) with ion channel gate variables dynamics (n for potassium channel and m h for sodium channel) based on Hodgkin–Huxley formalism in the squid giant axon, for a point-neuron model. Meanwhile, the development of regression equations was used for the estimation gating variables in the membrane current.  The simulation results revealed that the larger action potentials, whose size is controlled by the difference between the voltage and current with choosing optimal gating variables for activation and inactivation membrane channels can be affected more rapidly, travel at a faster speed than smaller ones.

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