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# Stochastic resonance, coherence resonance, and spike timing reliability of Hodgkin–Huxley neurons with ion-channel noise

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## HIGHLIGHTS

- Stochastic dynamics of a single Hodgkin–Huxley neuron with ion-channel noise is studied.
- The variability of neural spontaneous spikes attains a minimum for an optimal membrane area.
- Channel noise induces stochastic resonance to response to external periodic input.
- The reliability of neuronal responses to repeated stimulus is modulated by membrane area.
- Arnold tongues of high reliability arise from the resonance effect of spike timing reliability.

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## ABSTRACT

The random transitions of ion channels between open and closed states are a major source of noise in neurons. In this study, we investigate the stochastic dynamics of a single Hodgkin–Huxley (HH) neuron with realistic, physiological channel noise, which depends on the channel number and the voltage potential of the membrane. Without external input, the stochastic HH model can generate spontaneous spikes induced by ion-channel noise, and the variability of inter-spike intervals attains a minimum for an optimal membrane area, a phenomenon known as coherence resonance. When a subthreshold periodic input current is added, the neuron can optimally detect the input frequency for an intermediate membrane area, corresponding to the phenomenon of stochastic resonance. We also investigate spike timing reliability of neuronal responses to repeated presentations of the same stimulus with different realizations of channel noise. We show that, with increasing membrane area, the reliability of neuronal response decreases for subthreshold periodic inputs, and attains a minimum for suprathreshold inputs. Furthermore, Arnold tongues of high reliability arise in a two-dimensional plot of frequency and amplitude of the sinusoidal input current, resulting from the resonance effect of spike timing reliability.

## 1. Introduction

Noise is ubiquitous in biological neural systems. In a single neuron, it originates from stochastic ion-channel gating, random neurotransmitter release, and its diffusion and binding to synaptic receptors [1,2]. Particularity, the random

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transitions of individual ion channels between open and closed states generate an internal source of noise, known as channel noise, which adds stochastic fluctuations to ionic conductance [3]. Over the last decade much effort has been devoted to the modeling of channel noise and investigating its effects on the stochastic dynamics of neural systems. It has been demonstrated that this physiological noise may alter the firing threshold [4,5], spike timing [6,7], and the reliability [8] of single neurons, as well as the spatiotemporal pattern and firing coherence in neuronal networks [9,10].

The activity of ion channels is governed by random transitions among a number of possible channel conformations of gates or subunits, which accounts for channel noise. Accordingly, the mathematical modeling of physiological noise is well established in terms of Markov Chain (MC) models, which assume that the state of an ion channel is described by a discrete-state, continuous-time Markov chain [3,11–14]. Each state in the chain represents a particular configuration of the ion channel and the transition from one state to the next depends on the voltage potential of the membrane. MC models have been widely used to study the effects of channel noise on stochastic dynamics of neurons [4,6,8], but these models are computationally expensive to simulate, which limits its applicability to investigate the role of physiological noise in the network level. As a result, Fox et al. proposed simpler channel-based and subunit-based models that use stochastic differential equation to approximate the stochastic spiking activity produced by MC models [15–17]. These models have been applied to investigate the impact of ion channel noise on the spiking pattern of small-world neural networks [9,10]. Recently, the stochastic-shielding approximation is also applied to Markov chains to simulate random gating process of ion channels [18]. With other simplified forms of channel noise, such as white Gaussian noise, its effects on stochastic neuronal dynamics at the single-cell level and network level were extensively investigated [19–23].

Noise from ion channels and synapses plays an important role in the stochastic neural dynamics and induce many complex behaviors, such as stochastic resonance [24–26], coherence resonance [27–29], and synchronization [30,31]. The most representative one is stochastic resonance (SR), which refers to a phenomenon that the response of a nonlinear dynamical system to a weak periodic signal can be amplified and optimized by a moderate intensity of additive noise [32–34]. SR phenomenon has been observed in many biological experiments, showing that the ability of sensory neurons to process weak input signals can be significantly enhanced by adding noise to the system [35–37]. Theoretically, the generation mechanism of stochastic resonance has been studied in excitable neuron models, and a bell-shaped curve in the signal-to-noise ratio or mutual information is obtained by tuning external noise [24,38,39]. It is also suggested that noise can facilitate the information detection and transmission in complex neuronal networks via stochastic resonance [40–46].

Robustness of neuronal spike timing to physiological noise is a prerequisite for a spike timing-based coding strategy. The reliability of neural responses, which refers to the neuron's ability to generate the same spike patterns in different repetitions of the same stimulus, depends on the properties of inputs [47]. Previous studies have shown that the spike timing reliability can be enhanced with increasing stimulus amplitude [48] and reach maximal when the driving frequency matches the intrinsic frequency of the neuron or its harmonics [49,50]. Spike timing is highly unreliable for repeated direct current inputs, whereas fluctuating current inputs can significantly improve the firing reliability [8,48]. Galan et al. further demonstrated an optimal time scale of the input fluctuations for maximal spike timing reliability [51]. In addition, the intrinsic properties of neurons can also determine the firing reliability. Different types of neurons are sensitive to different stimuli. For example, cortical interneurons show maximum reliability in response to higher-frequency sinusoidal stimuli, whereas pyramidal cells respond more reliably to lower-frequency sinusoidal inputs [52]. Ionic conductance of cortical neurons affects their reliability in response to suprathreshold rhythmic inputs [53]. Moreover, inherent noise in ion channels plays a critical role in determining the reliability of neuronal firing in single neurons and enables them to act as "smart" encoders [8,54].

In this paper, to simplify the numerical simulation, we use a simplified realistic model of channel noise proposed by Yu et al. [55] to investigate the effects of this physiological noise on the stochastic dynamics of a single Hodgkin–Huxley (HH) neuron driven by periodic external inputs. In particularly, we explore the phenomenon of noise-induced stochastic resonance and spiking time reliability. Accordingly, the rest of this paper is organized as follows: Section 2 is devoted to introducing the mathematical model of channel noise and expanding the deterministic HH neuronal model to include realistic, physiological noise. Section 3 shows the simulation results of stochastic neuronal dynamics induced by channel noise. Finally, a brief conclusion of this paper is given in Section 4.

## 2. Mathematical models

### 2.1. Channel noise

The states of an ion channel are determined by the configuration of its constitutive gates, which must be all in an open state for the channel to be conducting. The kinetics of an individual gate can be described by a two-state process [11,14]:

$$\text{Closed} \underset{\beta(V)}{\overset{\alpha(V)}{\rightleftarrows}} \text{Open} \tag{1}$$

where $V$ is membrane potential of the neuron; $\alpha(V)$ and $\beta(V)$ are the voltage-dependent transition rates. The probability, $p$, of a gate to be in the open state satisfies the differential equation

$$\frac{dp}{dt} = \alpha(V)(1-p) - \beta(V)p \tag{2}$$