# Maximum Likelihood Parameter Estimation in a Stochastic Resonate-and-Fire Neuronal Model

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***Abstract*—Recent work has shown that resonate-and-fire model is both computationally efficient and suitable for large network simulations. In this paper, we examine the estimation problem of a resonate-and-fire model with random threshold. The model parameters are divided into two sets. The first set is associated with subthreshold behavior and can be optimized by a nonlinear least squares algorithm. The other set contains threshold and reset parameters and its estimation is formulated in terms of maximum likelihood formulation. We evaluate such a formulation with detailed Hodgkin-Huxley model data.**

***Keywords*-resonate-and-fire; parameter estimation; maximum likelihood; simulated annealing.**

## I. Introduction

One essential issue in computational neuroscience is to characterize the relationship between neural output recording and the input current to the cell, [1]. To reproduce the behavior of neurons, the spiking neuron model has been widely used. Although a detailed Hodgkin-Huxley [2] neuron model could mimic the neuronal dynamics more accurately, it is computationally inefficient in parameter estimation and model simulation. Therefore, spiking model is the first choice for large network simulation. In [3], a second order model is introduced to be able to reproduce almost all types of firing patterns *in-vivo* and keep the computation efficient at the same time. In authors' previous work, a linear-in-the-parameters presentation of aforementioned quadratic model is developed and allows us to identify experimentally obtained data. However, a small flaw in the assumptions prevents us from further research. Although the quadratic model is proven to be biologically meaningful, it can only qualitatively reproduce the firing pattern, i.e., the model can not quantitatively represent the upstroke of the spike unless it is assumed that the parameters are voltage-dependent [4]. To address this issue, a modification is made to this model. Instead of assuming voltage-dependent parameters, we remove the quadratic term in the model and consider it to be a representation only for subthreshold dynamics. Since now we narrow our interest zone down to the subthreshold region, the mismatch in the upstroke does not affect our identification any more. Another reason to consider simplifying the model instead of additional assumption is, by the removal, the model dynamics become linear and can be treated analytically, without hurting the ability to replicate multiple firing patterns.

In order to match the experimentally observed data to a particular parametric model , many parameter estimation methods have been introduced for estimating parameter values from the recorded voltage trace. In [5], an adaptive exponential integrate-and-fire neuron model is manually hand-tuned to fit a detailed Hodgkin-Huxley based model. Although the result in [5] shows good match between the proposed model and the detailed Hodgkin-Huxley based model, such trial-and-error approach depends mainly on researcher's experience and thus is labor-intensive. In [6], a database of single-compartment model neurons is constructed by exploring the entire parameter space – this approach is only practical when the parameter space has a low dimension. In [1], a maximum likelihood problem is formulated with a stochastic integrate-and-fire model. The maximum likelihood formulation can be also found in other literature, e.g., [7].

In this paper, we consider a resonate-and-fire model with stochastic threshold which is assumed to be a Gaussian random variable. By assuming that the threshold is the only component that has a stochastic property, the membrane potential is therefore deterministic and solvable. Here, we

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assume that both the input to the cell and the voltage recording trace are known for characterization. A nonlinear least squares method is first applied to fit the subthreshold dynamics. Then, the second characterization problem consists of estimating of parameters that associate with the initiation of the firing event and the reset. Considering the interspike interval as only reference in this level of estimation, we optimize the parameters by finding the maximum of the likelihood of the obtained firing data through simulated annealing. We apply this formulation on detailed Hodgkin-Huxley model data and show preliminary results.

The remainder of this paper is organized as follows. In Section II, we present the resonate-and-fire neuron model with random threshold. Technical details for the identification mechanism are provided in Section III. Section IV provides preliminary results followed by discussion in Section V. Appropriate conclusions are drawn in Section VI.

## II. Problem Definition

A two dimensional quadratic neuron model is introduced in [3]. Compared to the integrate-and-fire model, the additional variable, accounting for the activation of $K^+$ ionic currents and inactivation of $Na^+$ ionic currents, allows the model to present many types of firing patterns that are common in biological systems. However, the nonlinearity introduced by the quadratic term prevents one from treating the model analytically. Meanwhile, it also requires variable parameters to reproduce the exact spike shape [4]. Therefore, we remove the quadratic term and make the model as resonate-and-fire type, as follows

$$\frac{dv}{dt} = k_1 v + k_2 - k_3 u + k_3 i \tag{1}$$

$$\frac{du}{dt} = a(bu - v) \tag{2}$$

when $i$ is the input/synaptic current. Whenever the potential $v$ hits the threshold, the neuron is said to fire a spike, and the variables are reset according to

$$if\ v = V_t,\ then \begin{cases} v \to c \\ u \to u + d \end{cases} \tag{3}$$

where $V_t$ is the threshold. Although it is in a different formulation, the model present here is the same as the one discussed in [8] or [9].

Note that (1) and (2) only describe the subthreshold approximation, and the post threshold dynamics of cell does not form part of the model: the upstroke/downstroke are drawn by hand. Unlike [10] in which a triangular pulse is used to mimic the shape of the spike, here we ignore the whole spiking behavior, only using a straight line to mark the spike arrival.

Therefore, a threshold is needed to indicate the initiation of the spike. In [11], a fixed threshold is exploited for this purpose. However, the voltage threshold for a spike depends not only on the instant voltage value, but also on the rate of voltage change preceding each spike, which indicates that a variable threshold is more realistic. The variation of spike threshold could also be a function of instantaneous firing rate [12]. Fig. 1 shows the probability of firing for specific voltage value, from which we can see there is no obvious "jump" in firing probability so that we can define it as "threshold". Data used to generate Fig. 1 is obtained from a detailed ion-channel based spiking model of [13]. Actually, the stochastic property of spike threshold has been proposed and proved in literature [14], [15]. This randomness could be a consequence of signal noise or the aforementioned factors affecting the spike threshold. Others may use a stochastic term in membrane dynamics to present the signal noise, as in [7]. In fact, this is computationally identical to subtracting the noise from the potential and adding it to the threshold [16]. In this paper, we consider the threshold to be the random component in the neuron model and assume its distribution is a Gaussian and i.i.d. That is,

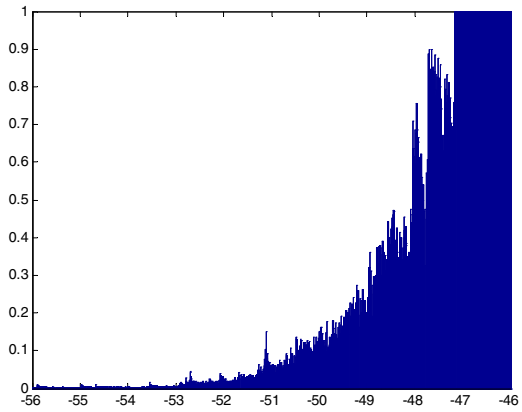


Figure 1. Firing probability of voltage shows there is no clear value could be defined as "threshold". For each voltage value, if there are $N$ points at this value in the database and $n$ of them directly followed by a spike, the the firing probability is defined as $n/N$.

$$V_t \sim N(m, \sigma) \tag{4}$$

## III. The Estimation Problem

Our problem now is to estimate the parameters $(k_1, k_2, k_3, a, b, c, d, m, \sigma)$. Generally, two types of data can be used for the identification, interspike intervals (ISIs) and membrane potential depolarization recording. For the first type, the estimation problem would be more complicated and need additional assumptions to succeed [7]. Therefore, we investigate the second kind of data here. We divide the parameters into two sets: $\theta_l = (k_1, k_2, k_3, a, b)$ is associated with linear dynamics while $\theta_t = (c, d, m, \sigma)$ is linked to after-spike resetting and threshold variation. Thus, the

estimation problem consists of both matching the voltage recording to find $\theta_l$ and maximizing the likelihood to find $\theta_t$.

### A. Subthreshold Estimation

Linear system given by (1) and (2) can be analytically treated and solved. This is useful when we want to use gradient based or least squares based estimation technique, which requires the derivative of the objective function with respect to the parameters. The solution of (1) and (2) can be presented as

$$v = f\left(i, t; \theta_l\right). \tag{5}$$

Given the input $i$, $f$ is a nonlinear function on parameter set $\theta_l$. In fact, $v$ also depends on $c$ and $d$ which we do not identify in this stage. The effect of $c$ and $d$ will be excluded by choosing data beyond the transient period immediately following a spike. Thus in the subthreshold region, the voltage dynamic is independent of $\theta_t$, depending only on $\theta_l$. The estimate for $\theta_l$ is therefore given by nonlinear least squares estimation [17]. Non-linear least squares is a form of least squares used to fit observations to a model that is nonlinear in parameters. The algorithm is run iteratively. If the reference data is a $n \times 1$ vector, then the objective function to be minimized is

$$S = \sum_i \left(v_i - \hat{v}_i\right)^2 \tag{6}$$

and the update law is given by

$$\theta_l^{k+1} = \theta_l^k + \Delta\theta_l \tag{7}$$

$$\Delta\theta_l = \left(J'J\right)^{-1} J'\Delta v \tag{8}$$

where $\Delta v = v - \hat{v}$ is a $n \times 1$ vector defining the error between actual and estimate; and $J$ is the $n \times j$ Jacobian matrix, with elements given by

$$J_{ik} = \frac{\partial \hat{v}_i}{\partial \theta_{l_k}}. \tag{9}$$

Note that Jacobian matrix $J$ is a function of estimated parameters and updates from one iteration to the next.

### B. Maximum Likelihood Estimation

In this step, we assume the interspike intervals are the only output recording from the cell. The spike time $\{t_j\}$ is defined to be the time of the peak of each spike. During interval $t \in (t_{j-1}, t_j)$, the cell is not firing. Since the data we examine here are discrete-time sample data, we denote all data points during interval $(t_{j-1}, t_j)$ as $\{t_i\}$. The likelihood for parameter $\theta_t$ can therefore be defined as the probability that the noisy threshold $V_t$ is under the membrane potential $v$ at spike time $\{t_j\}$ and over $v$ at non-spike time $\{t_i\}$, which can be written as

$$\begin{aligned} L\left(\theta_t\right) &= \log\left(\prod_i \int_{v_i}^{\infty} G\left(V_t; m, \sigma\right) dV_t \right. \\ &\qquad \left. * \prod_j \int_{-\infty}^{v_j} G\left(V_t; m, \sigma\right) dV_t \right) \\ &= \sum_i \log \int_{v_i}^{\infty} G\left(V_t; m, \sigma\right) dV_t \\ &\quad + \sum_j \log \int_{-\infty}^{v_j} G\left(V_t; m, \sigma\right) dV_t \end{aligned} \tag{10}$$

where $G\left(V_t; m, \sigma\right)$ is the Gaussian probability density function of threshold $V_t$ with mean $m$ and variance $\sigma^2$. Technically, the term "log-likelihood" would be more appropriate to denote $L\left(\theta_t\right)$, but in this paper we use "likelihood" for simplicity. Note that since $v$ is a function of $c$ and $d$, since $\theta_l$ is considered fixed at this stage, we still need to generate a new voltage trace for each set of parameter $\theta_t$.

Based on the likelihood function (10), the estimated parameter set is thus given by

$$\hat{\theta}_t = \arg\max L\left(\theta_t\right). \tag{11}$$

### C. Simulated Annealing

In this paper we use simulated annealing (SA) technique [18], [19] to find the maximum of the previously formulated likelihood. Unlike gradient based law or least squares which might be stuck with local maxima, simulated annealing is designed for global optimization. The name "simulated annealing" comes from the annealing technique in metallurgy, which involves heating and controlled cooling of a material to minimize the internal energy of its crystals. Fig. 2 shows the SA algorithm. In each iteration, a point $s'$ in the neighborhood of the old point $s$ is randomly selected. The decision to consider or reject the new point as a "better" point depends on the probability function $P$

$$P = \begin{cases} 1 & \text{if } L\left(s'\right) > L\left(s\right) \\ e^{-1/T} & otherwise \end{cases} \tag{12}$$

where $T$ is called "temperature." The possibility to accept the worse point allows the algorithm to move along the opposite direct and thus get rid of local maximum.

The SA algorithm begins with a large temperature value $T_0$, allowing the algorithm to move randomly in the parameter space. Then the parameter gradually decreases. The "cooling" algorithm for the temperature $T$ used here is given by

$$T = T_0\left(1 - r\right)^2 \tag{13}$$

where $r$ is the ratio of current iteration $n$ to the maximum allowed iteration $N$. The algorithm stops after the maximum iteration is reached. A detailed description of the algorithm follows.

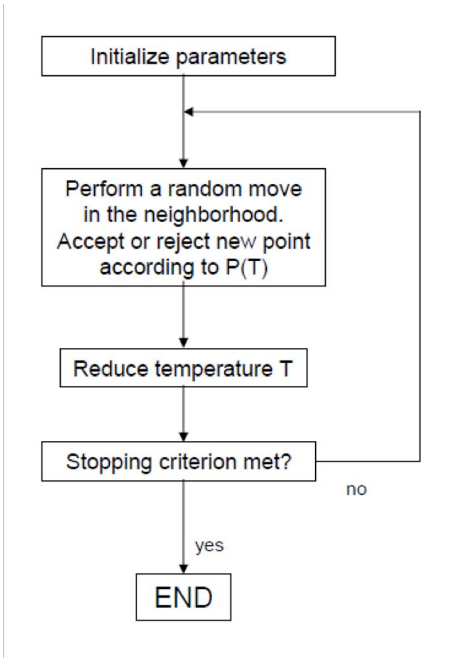


Figure 2. The simulated annealing algorithm

- *Step 0*. Choose a starting point $s_0$, a starting temperature $T_0$, and maximum iteration $N$. Set boundary for each direction if needed. Compute the likelihood of the initial point.
- *Step 1*. Generate a new point $s'$ from the neighborhood of point $s$. Projection applies if the new point exceeds the preset boundary.
- *Step 2*. Compute the likelihood of the new point. Call probability function (12), and replace $s$ with $s'$ if $P$ is larger than a randomly picked up number between 0 and 1. Otherwise, $s$ remains untouched.
- *Step 3*. Increase the current iteration $n$ and update the temperature $T$.
- *Step 4*. If $n < N$, go to step 1; else, stop the search.

## IV. Preliminary Results

We applied the aforementioned approach on two types of data, resonate-and-fire model data and detailed Hodgkin-Huxley model data. The detailed model data is generated in *NEURON* environment [20], by using a detailed ion-channel based spiking model of [13] with parameters from [21] (code for this model available at [22]). The model could simulate three types of spiking cell. In this paper we investigate the regular spiking cell. We used the current clamp simulation and injected pre-generated white noise current to stimulate the cell. Output data were sampled at 50kHz.

### A. Resonate-and-fire Model Data

We first apply proposed method on reference data generated by the exact model - this is to testify the correctness

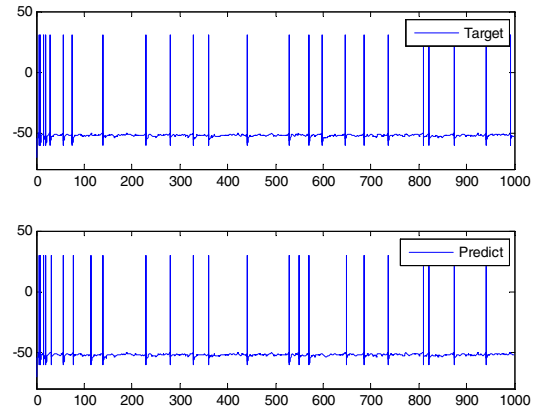


Figure 3. Comparison of spike train. Target data is generated by the exact model.

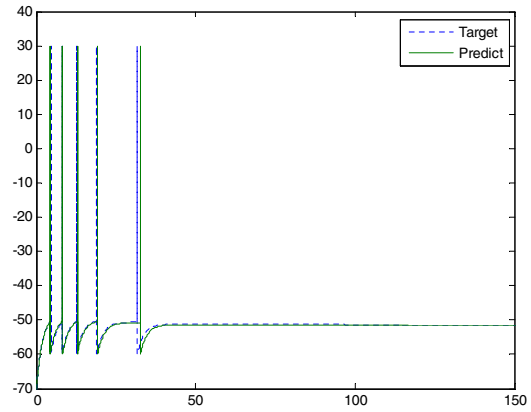


Figure 4. Comparison of spike train. Target data is generated with step input.

of the proposed formulation. Parameters for the reference model are chosen to simulate a rapidly adapting receptor (i.e., receptor initially responds and then quickly stops firing in response to steady input). Fig. 3 shows the evaluation result under noisy input. In Fig. 4, the estimated parameters successfully replicate the quick adapting firing pattern.

### B. Detailed Hodgkin-Huxley Model Data

Now,we present results on detailed Hodgkin-Huxley model data. After the estimation process, the estimated parameters are evaluated by comparing the predicted output of the model to unseen data. Fig. 5–6 show the evaluation results. From fig 5 one can see that the subthreshold traces are very close to each other, showing that dynamics (1) and (2) yield good approximation in the linear zone. Fig 6 shows part of the spike trains, in which the predicted train closely

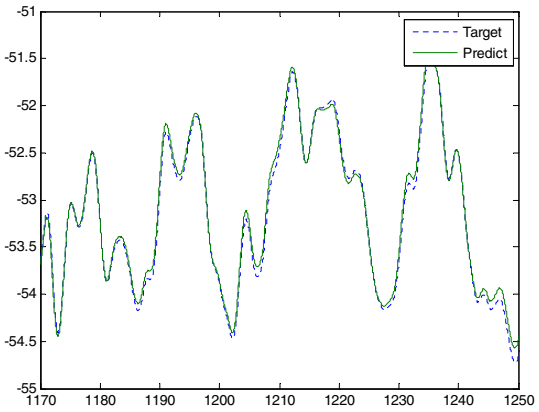


Figure 5. Comparison of subthreshold dynamics. Target data is generated under the same type of input as the one used in the reference data generation.

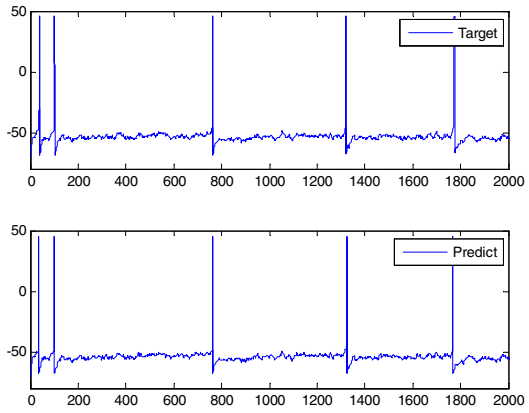


Figure 6. Comparison of spike train. Target data is generated under the same type of input as the one used in the reference data generation.

follows the target with the same adaptation rate. We ran the evaluation ten times, the statistics are listed in Table I. The estimated parameters lead to a averagely 16.3 spikes while the target has 15 spikes under the input stimulus.

Table I. Evaluation on HH Model

| No. of evaluations | Target spikes | Mean error |
|---|---|---|
| 10 | 15 | 1.3 |

Fig. 7 shows the evaluation result under step current. The prediction nicely follows the first three spikes, but misses the fourth one. However, the prediction still successfully replicates the spike adaptation encoded in the target train.

## V. Discussion

In our formulation, we assume that the subthreshold trace could be defined as a "linear zone" where the dynamics (1) and (2) are a good approximation. This subthreshold area is upperbounded by the variable threshold. Results shown in last section indicate the validity of this assumption, since the error between the predicted and target in Fig. 5 is under 5%. Since the linear model is capable of replicating only the subthreshold dynamics, the reference voltage trace used for the first-step nonlinear least squares estimation should not contain any supra-threshold activity. This is done by choosing piecewise traces between each spikes, with starting point and ending points far away from the nearest spike.

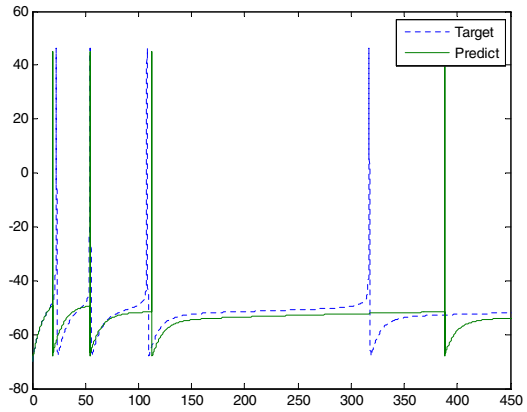


Figure 7. Predicted and target are under constant current input.

Another assumption we made in this formulation is that we assumed all the stochastic components in the system, including system noise and the variability of threshold, are presented by the threshold distribution. Our results suggest that such simplification leads to over prediction of the firing rate. However, the results are still acceptable - the errors are small in percentage and the predicted spike trains have similar patterns as the target. We believe that a model with more sophisticated assumption or component could address the over prediction issue, yet this would result in larger computation cost.

The computation of the likelihood function (10) is the major cost of computation. The original likelihood function is defined over all the time instants. The reference data is sampled at 50kHz, which results in a large size of $\{t_i\}$. Actually, considering the fact that $G(V_t; m, \sigma)$ is the Gaussian probability density function which is zero beyond $3\sigma$ distance from the mean $m$, thus the voltage trace was processed to make $\{t_i\}$ only contains points that are not too far away from the mean. This requires us to have some knowledge about the parameters before the estimation, which is acceptable since by looking at the reference train, one can easily draw a reasonable boundary for $m$ and $\sigma$.

## VI. Conclusion

In this paper, we studied a resonate-and-fire model with stochastic threshold. Considering the fact that a quadratic neuronal model is not capable of replicating the shape of spike, we removed the quadratic term from this model and made the model resonate-and-fire. Also considering the fact that channel noise exists in almost all cell systems, we assumed the threshold for the resonate-and-fire model to be random and normal. By formulating the parameter estimation problem into a two-stage problem, an estimation mechanism based on nonlinear least squares and maximum likelihood was presented. Reference data generated by a detail Hodgkin-Huxley model was fed to the estimation mechanism. Estimated parameters were evaluated by data that are not used in the estimation process. Results show good match between the prediction and the target.

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