

Random Walk Model for Spontaneous Neural Firing

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EE 508

1 Abstract

A random walk model of spontaneous activity in neurons is analyzed using the theory of discrete time, discrete space Markov chains. The model has been shown to replicate some observed behavior in neurons in the cochlear nucleus of cats. Here, we compute limiting probabilities and the distribution of first passage times to model firing rate and interspike interval histograms, respectively. These theoretical results are then compared to the outcomes of numerical simulations of the random walk process.

2 Introduction

The behavior of a nerve cell can be analyzed in terms of the voltage difference between the intra- and extracellular media. This quantity is referred to as the transmembrane (or membrane) potential and typically fluctuates around some resting potential of $\sim -70\text{mV}$. Stimulation that further decreases the membrane potential is called inhibitory and the membrane is said to be hyperpolarized. Alternatively, stimulation that increases the membrane potential is called excitatory and the membrane is said to be depolarized.

An essential feature of the dynamics of membrane potential in neurons is the generation of action potentials, also known as spikes. If a nerve cell is sufficiently depolarized to a so-called threshold value, the ionic content of the cell undergoes rapid changes that leads to sudden and further depolarization of the cell until it reaches a maximum value of $\sim 100\text{mV}$ and returns to its resting potential. When this process happens we say an action potential or spike has been generated or that the neuron has fired. Neuronal firing is the mechanism by which signals are passed through the nervous system, allowing the brain to process incoming stimuli, regulate bodily functions, and perform more sophisticated cognitive processing. Understanding neural dynamics is therefore of considerable interest to many scientists.

There is a rich history of mathematical modeling of the dynamics of membrane potentials. Much early work is based on the Nobel Prize winning work of Hodgkin and Huxley. These models are typically nonlinear ordinary differential equations and therefore are completely deterministic descriptions of the cell membrane, see for instance [1] for a description of the Hodgkin-Huxley approach. These models have proven extremely useful for furthering our understanding of firing neurons but they neglect the stochastic nature of neurons. Typical sources of stochasticity in membrane potentials include synaptic noise (whereby other neurons excite and/or inhibit a neuron in some seemingly random fashion) and membrane noise (due to Brownian motion of ions, random conformational changes of ion channels, and other factors). See for instance [5] for a review of analyzing the stochastic activity of neurons. As a result, a neuron, even in the absence of any apparent stimulus, will have some fluctuating membrane potential and may even produce action potentials. This is defined as the spontaneous activity of the neuron.

A significant early contribution to the application of stochastic methods to neural dynamics was the formulation of a random walk model for spontaneous activity in a neuron by Gerstein and Mandelbrot [2]. The approach in this paper was to assume some incoming random sequence of inhibitory and excitatory stimuli would cause the membrane potential to fluctuate about its resting potential. The trajectory of the membrane potential over time was

assumed to follow a random walk. Depending on the ratio of excitatory to inhibitory stimuli, the random walk would be biased and therefore drift toward or away from the threshold potential. An important result from this model is that the bias in the random walk could be tuned so that the model can fit interspike interval data of spontaneous activity of several neurons in the cochlear nucleus of anesthetized cats. While many more sophisticated stochastic models of neural activity have since been developed, the relative simplicity of this random walk model enables some analysis using the tools developed in this course for discrete time, discrete space Markov chains.

3 Markov Chain Model

Following the approach of Gerstein and Mandelbrot [2], transmembrane potential and firing dynamics of a neuron are modeled as a discrete time, discrete and finite space Markov chain model. This approach assumes that the dynamics of a nerve cell's membrane potential can be modeled as a random walk, as described below:

- Let the transmembrane potential be described by a discrete and finite set of numbers v_1, v_2, \dots, v_k . These define the states of the Markov chain.
- For states $i = 2, 3, \dots, k - 1$ the probability of transitioning in one time step from v_i to v_{i+1} is p and the probability of transitioning from v_i to v_{i-1} is $q = 1 - p$.
- State v_1 is a reflecting boundary representing some limit to the amount the nerve cell can hyperpolarize. Thus v_1 transitions to v_2 with probability 1.
- State v_k represents the threshold potential for the neuron. When v_k is reached, an action potential is said to have been generated and the random walk returns to a resting potential, denoted v_r ($1 < r < k$), with probability 1.

The above assumptions define a $k \times k$ probability transition matrix P that fully characterizes the Markov chain.

$$P = \begin{bmatrix} 0 & 1 & 0 & \cdots & \cdots & \cdots \\ q & 0 & p & & & \\ & \ddots & \ddots & \ddots & & \\ & & & q & 0 & p \\ \cdots & 0 & 1 & 0 & \cdots & \end{bmatrix} \quad (3.1)$$

P has the familiar structure of a transition probability matrix for a random walk except for the last row where the 1 is meant to be in the r^{th} column to effect the return to v_r after the voltage reaches threshold at v_k .

The undetermined parameters in the model are k (the number of states), r (the resting potential), and the transition rate p . The parameter p determines the bias, or drift, in the random walk. The biological significance of p is that higher values correspond to greater excitatory input and therefore higher levels of spontaneous activity. The number of voltage states and the position of the resting potential will affect the model outcomes. For the simulations in this paper k and r are set to 160 and 128, respectively, to be consistent with parameter values used in [2].

The above model is an extremely simplified description of neural dynamics. The Markov assumption (that the next value of membrane potential depends only on the current value) is likely inappropriate because the membrane potential depends on chemical and electrical gradients across the membrane, the state of thousands of ion channels distributed along the cell membrane, the history of stimuli provided to the cell, and many other factors. Despite these simplifications, the model has been successfully fitted to interspike interval data from the nerve cells in the cat cochlear nucleus [2]. Furthermore, its relative simplicity enables some analysis using the tools developed in this course.

Two important characterizations of neural firing that we can analyze with this model are firing rate and interspike intervals. The model was originally formulated based on neurons in the auditory system and it is well known that different neurons in the auditory pathway

fire spontaneously with a range of rates. This range of spontaneous behavior is thought to help the auditory system encode sound intensity. Interspike intervals can potentially encode sound frequency in cases where the firing pattern of a neuron is synchronous with the frequency of the stimulus. See, for instance [6] for a discussion of the neural responses in the auditory system.

4 Analysis

4.1 Firing Rate

The firing rate is defined as the number of action potentials generated by a neuron in a given period of time. In terms of the random walk model formulated in Section 3, firing rate can be defined as the proportion of time spent in the threshold state v_k . It is clear from the construction of the random walk model that all states communicate and therefore the Markov chain is irreducible. Furthermore, since there are only a finite number of states ($k < \infty$), it follows that all states are recurrent (see [4], page 197). Finally, since all recurrent states in a finite state Markov chain are positive recurrent ([4], page 204), the proportion of time spent in state i is precisely the limiting probability π_i which can be computed by finding the unique solution to ([4], page 205):

$$\pi_j = \sum_{i=1}^k \pi_i P_{ij}, \text{ for } 1 \leq j \leq k, \quad (4.1)$$

$$\sum_{j=1}^k \pi_j = 1. \quad (4.2)$$

It follows from the biological definition of the firing rate and the mathematical properties of π_k that the firing rate of the modeled neuron is π_k . We now develop a method for computing the limiting probabilities by exploiting the tridiagonal structure of the transition probability

matrix P .

For $1 \leq j \leq r$, Equation 4.1 yields the following equations:

$$q\pi_2 = \pi_1 \text{ for } j = 1 \quad (4.3)$$

$$\pi_1 + q\pi_3 = \pi_2 \text{ for } j = 2 \quad (4.4)$$

$$p\pi_{j-2} + q\pi_j = \pi_{j-1} \text{ for } 3 \leq j \leq r \quad (4.5)$$

These equations can be solved successively as $\pi_j = a_j\pi_1$ for $j = 2, 3, \dots, r$. A recursion relation can be established and we find that

$$\pi_2 = \frac{1}{q}\pi_1 \quad (4.6)$$

$$\pi_3 = \frac{1}{q}(\pi_2 - \pi_1) = \frac{p}{q^2}\pi_1 \quad (4.7)$$

$$\pi_j = \pi_{j-1} + \frac{p}{q}(\pi_{j-1} - \pi_{j-2}) \text{ for } 4 \leq j \leq r. \quad (4.8)$$

The tridiagonal structure of P is broken in the r^{th} column by the presence of the 1 in the final row which represents the return to resting potential after generation of an action potential. The forward solution of π_j as a multiple of π_1 is not possible for $j > r$, but we can work backward from $j = k$ to find b_j where $\pi_j = b_j\pi_k$. This procedure yields:

$$\pi_{k-1} = \frac{1}{p}\pi_k \quad (4.9)$$

$$\pi_{k-2} = \frac{1}{p}\pi_{k-1} = \frac{1}{p^2}\pi_k \quad (4.10)$$

$$\pi_j = \pi_{j+1} + \frac{q}{p}(\pi_{j+1} - \pi_{j+2}) \text{ for } r \leq j \leq k-3. \quad (4.11)$$

Now use the r^{th} equation to rewrite π_k as a multiple of π_1 :

$$p\pi_{r-1} + q\pi_{r+1} + \pi_k = \pi_r \quad (4.12)$$

$$\Rightarrow \pi_k = \left(\frac{a_r - pa_{r-1}}{1 + qb_{r+1}} \right) \pi_1. \quad (4.13)$$

All limiting probabilities π_j have now been determined as scalar multiples of π_1 . The final step is to compute π_1 by normalizing the sum of all π_j to be 1.

This method has been implemented in MATLAB (m-file is included in Appendix 7.1). Figure 1 shows π_k as a function of the transition probability p . For $p < \frac{1}{2}$, the random walk is biased away from the threshold state and the firing rate, as represented by π_k , appears to be nearly zero. π_k appears to be approximately linear as a function of p for $p > \frac{1}{2}$, but this has not been verified analytically.

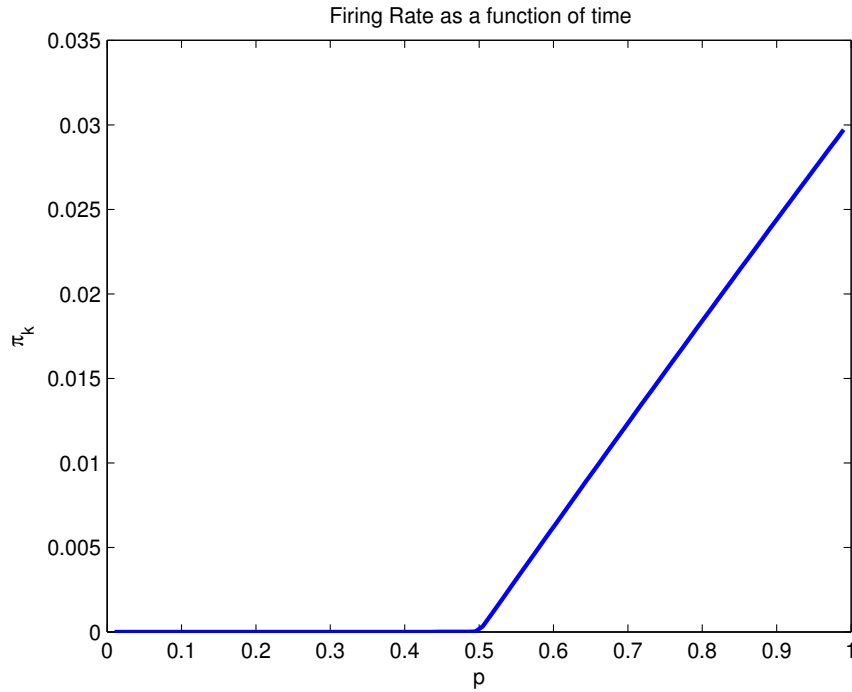


Figure 1: Limiting Probability π_k as function of random walk transition probability p . $p = 0.5$ is an unbiased random walk. $0.5 < p < 1$ is biased toward the threshold state v_k .

4.2 Interspike Interval

An important validation of this random walk model is that, by adjusting the transition probability p , the distribution of simulated interspike intervals can be fit to observed interspike interval from neurons in the cochlear nucleus of anesthetized cats [2]. That fitting procedure, however, relies on a diffusion approximation to the random walk process to compute a probability density function for the first passage time from resting potential to the threshold potential state. Rather than relying on this approximation, we show below how it is possible to compute the probability mass function of the transition from v_r to v_k directly from the transition probability matrix P .

Define the random variable T to be the number of time steps it takes the random walk process to first arrive at v_k , when starting from v_r . T is the first passage time of v_r to v_k and represents the time between spikes of a firing neuron. This time is referred to as the interspike time or interspike interval (ISI). The probability mass function of T is

$$f_T(n) = P \{ \text{First passage time from } v_r \text{ to } v_k \text{ is } n \text{ steps} \}. \quad (4.14)$$

This probability is equivalent to the sum of the probabilities of a random walk moving from v_r to v_j ($1 \leq j < k$) without going through v_k in $n-1$ steps, followed by a transition from v_j to v_k on the n^{th} step. To determine these probabilities, it is useful to redefine the threshold state as an absorbing state. Then we have a new transition probability matrix:

$$\bar{P} = \begin{bmatrix} 0 & 1 & 0 & \cdots & \cdots & \cdots \\ q & 0 & p & & & \\ & \ddots & \ddots & \ddots & & \\ & & & q & 0 & p \\ \cdots & \cdots & \cdots & \cdots & 0 & 1 \end{bmatrix} \quad (4.15)$$

Since v_k is absorbing in this Markov chain, the (r, j) element of \bar{P}^{n-1} is equal to the prob-

ability of transitioning from state v_r to v_j in $n - 1$ time steps and not entering v_k at any time prior to $n - 1$. By the Markov property, the probability of transitioning to v_k on the n^{th} step is independent of the path taken in the previous $n - 1$ steps and is given by the one step transition probabilities from the original matrix P . So we have

$$f_T(n) = \sum_{j=1}^{k-1} \overline{P}_{r,j}^{n-1} P_{j,k} \quad (4.16)$$

$$\Rightarrow f_T(n) = \overline{P}_{r,k-1}^{n-1} p. \quad (4.17)$$

The last equality is obtained by inspecting the form of P in Equation 3.1 and observing that the only nonzero transition probability from v_j to v_k is if $j = k - 1$. The probability in this case is $P_{k-1,k} = p$. This method for computing $f_T(n)$ has been implemented in MATLAB (m-file is included in Appendix 7.2)

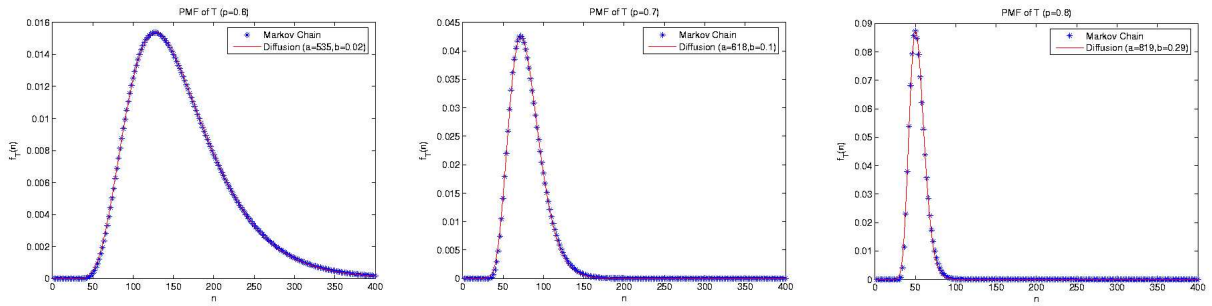


Figure 2: ISI probability mass functions for $p = 0.6$ (left panel), $p = 0.7$ (center), and $p = 0.8$. Solid red line shows a fit using the functional form $Kn^{-\frac{3}{2}} \exp(-\frac{a}{n} - bn)$ obtained from the diffusion approximation used in [2].

Figure 2 shows $f_T(n)$ for three different values of p . In addition, the solid lines show best fits of the functional form $Kn^{-\frac{3}{2}} \exp(-\frac{a}{n} - bn)$ which is the probability density function for first passage time in the diffusion approximation to a biased random walk used in [2]. A natural consequence of the construction of the random walk is that there is a zero probability of reaching threshold from v_r on every other time step. These zero values are omitted from the plotted figures and the fitting procedure. The diffusion approximation seems to be valid for these parameter choices. Note that as p increases the random walk becomes more biased.

As a consequence, $f_T(n)$ shifts leftward and narrows. For the limiting value of $p = 1$, the motion through state space is deterministic. The associated $f_T(n)$ would be a delta function centered at $k - r$ indicating guranteed spiking every $k - r$ time steps.

By determining how $f_T(n)$ varies with p we see the limits on when the model can potentially be used to describe observed ISI data. The original goal of the model as proposed by Gerstein and Mandelbrot was to describe spontaneous activity in neurons in the cochlear nucleus of cats. The observed ISI histograms for these neurons have been roughly classified and include a variety of shapes including both unimodal, asymmetric distributions with exponential decay; unimodal (symmetric and asymmetric) with non-exponential decay; and bimodal [3]. It is clear from Figure 2 that, at best, the model potentially can be used to interpret data from neurons with spontaneous firing patterns characterized by ISI histograms which are unimodal, asymmetric, and exhibit exponential decay but that it cannot describe many of the other observed firing patterns in the data set.

5 Numerical Results

The random walk model for the membrane potential of a neuron introduced in Section 3 has been implemented in MATLAB (m-file is included in Appendix 7.3). Using this program we can simulate the activity of a neuron to differing ratios of excitatory and inhibitory stimuli by varying p to control the bias of the random walk.

A sample path of the stochastic process is pictured in Figure 3. The trajectory is shown for the first 1000 time steps with $p = 0.6$. During this time the random walk reaches the threshold potential at v_{160} six times. The simulated firing rate in this case is For this choice of parameter values, the algorithm outlined in Secton 4.1 predicts that $\pi_k \approx 0.0621$.

Figure 4 shows the convergence of the simulated firing rate (computed as number of visits to v_k divided by the number of time steps that have elapsed) to the exact firing rate represented by the limiting probability π_k . It is evident that the simulated firing rate has not

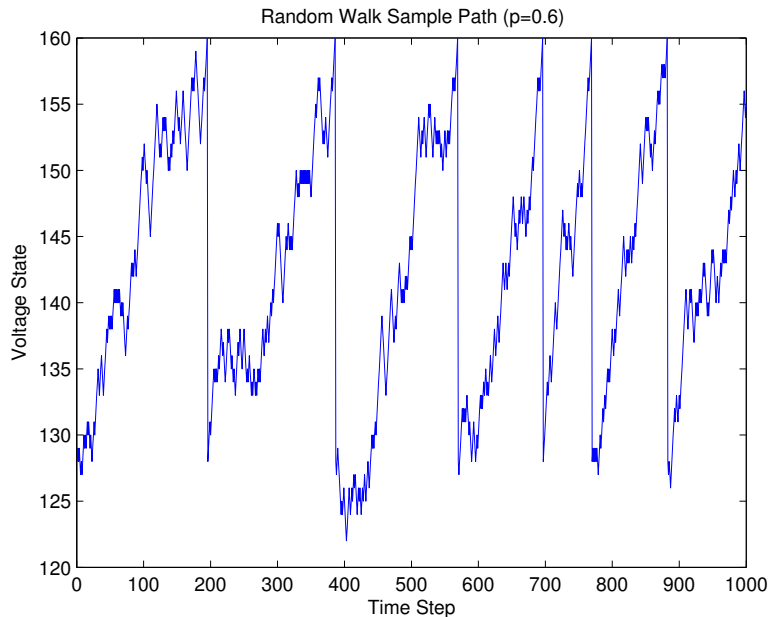


Figure 3: A realization of the random walk model for membrane potential. This trajectory features 6 spikes in the first 1000 time steps. Resting potential state is $r = 128$, threshold state is $k = 160$, and $p = 0.6$.

reached π_k after 1000 time steps, but that eventually the simulated firing rate will converge to π_k . The rate of convergence of simulated firing rate to π_k increases with p .

The proportion of time spent in the threshold state is of most interest because of its biological interpretation as the firing rate. But the limiting probability solution obtained in Section 4.1 is valid for all voltage states. Figure 5 compares the proportion of time spent in each state up to the time at which the 100th spike to the limiting probability solution.

Lastly, we compare the probability mass function $f_T(n)$ for the interspike time to interspike times computed from a realization of the random walk. The results for $p = 0.7$ after 1000 spikes are pictured in Figure 6. Not pictured is the fact that every odd interspike time has probability zero of occurring because of the choice of r and k in the random walk definition. It is clear from the figure that the realized histogram matches the computed probability mass function and displays the skewed profile with exponential tail observed in many neurons in the cochlear nucleus of cats [3].

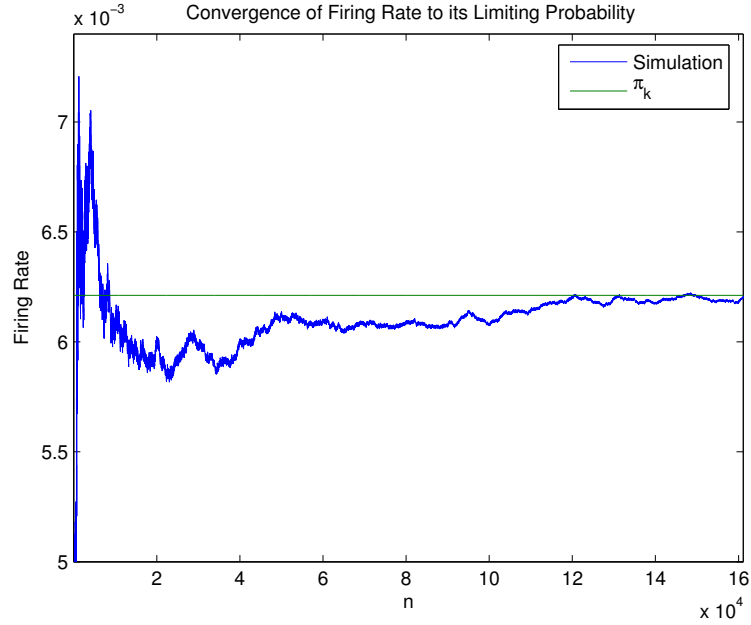


Figure 4: Simulated firing rate from the random walk model (blue) converges to its limiting probability (green).

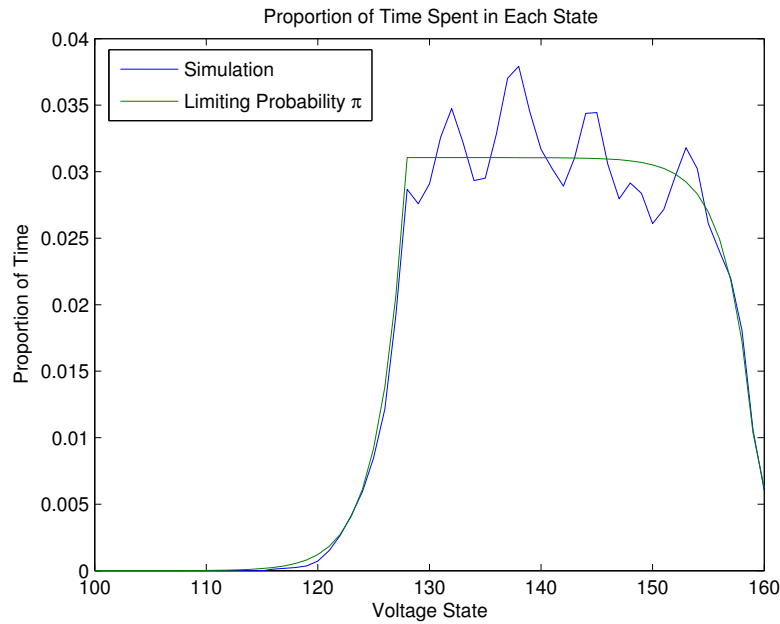


Figure 5: Proportion of time in each voltage state for random walk model after 100 spikes ($n = 16636$) (blue) compared to limiting probability π (green).

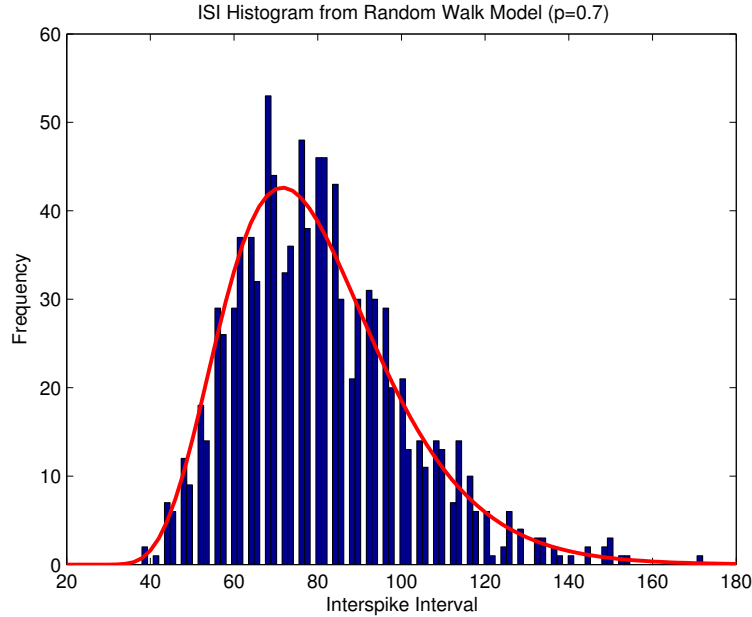


Figure 6: ISI Histogram for a realization of the random walk model ($p=0.7$, 1000 spikes) compared to $f_T(n)$ scaled by number of spikes (red line). For ease of visualization, only nonzero values of $f_T(n)$ are included in the plot.

6 Conclusion

In this paper we have revisited a random walk model of spontaneous neural activity. Although the model grossly simplifies the biological reality of actual neurons, it has been successfully fitted to ISI histograms obtained from neurons in the cochlear nucleus of cats. The model defines a discrete space, discrete and finite time Markov chain model and can therefore be analyzed with the theory developed in this course. We have analyzed the long term behavior of the model by deriving its limiting probabilities. We have also computed a probability mass function representing the ISI histogram that is derived directly from the transition probability matrix of the Markov chain. These results have been verified by comparing theoretical predictions to outcomes from a simulated random walk. Although the model has limited biological application, it is rewarding to analyse it using the methods we have studied this quarter.

References

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- [2] George L. Gerstein and Benoit Mandelbrot. Random walk models for the spike activity of a single neuron. *Biophys. J.*, 4:41–68, 1964.
- [3] R. R. Pfeiffer and N. Y.-S. Kiang. Spike discharge patterns of spontaneous and continuously stimulated activity in the cochlear nucleus of anesthetized cats. *Biophys. J.*, 5:301–316, 1965.
- [4] Sheldon M. Ross. *Introduction to Probability Models*. Academic Press, San Francisco, 9 edition, 2007.
- [5] Henry C. Tuckwell. *Introduction to Theoretical Neurobiology: Volume 2 Nonlinear and Stochastic Theories*. Cambridge University Press, New York, 1988.
- [6] William A. Yost. *Fundamentals of Hearing: An Introduction*. Academic Press, New York, 5 edition, 2007.

7 Appendix

MATLAB files used for this project are in the following subsections.

7.1 Limiting Probabilities

```
% This is limitprob.m
% Computes limiting probabilities for random walk model of neuron
%
% Joshua Goldwyn
% EE 508 Final Project

rest = 128; % index of resting potential
thresh = 160; % index of threshold

% Random Walk transition probabilities
p = 0.6;
q = 1-p;

% forward solve for coefficients as a function of v_1
a(1) = 1; % v_1
a(2) = 1/q;
a(3) = (1/q)*(a(2)-1);
for i=4:rest;
    a(i) = a(i-1) + (p/q)*(a(i-1)-a(i-2));
end;

% backward solve for coefficients as function of v_thresh
b(thresh) = 1;
b(thresh-1) = 1/p;
b(thresh-2) = 1/(p^2);
for i=thresh-3:-1:rest;
    b(i) = b(i+1) + (q/p)*(b(i+1)-b(i+2));
end;

% solve for v_thresh coefficient re: v_1
c = (a(rest) - p*a(rest-1)) / (q*b(rest+1)+1);
%rescale coefficients
a = a/c;

% normalize using sum=1
b(thresh) = 1 / sum([a b(length(a)+1:length(b))]);

% Recompute using normalized vectors
eqp = b(thresh) * [a b(length(a)+1:length(b)-1) 1];
```

7.2 Interspike Interval Probability Mass Function

```
% This is interspike.m
% Computes pmf for ISI. f_T(n) in the notation of the paper.
%
% Joshua Goldwyn
% EE 508 Final Project

% Transition probabilities
p = 0.6;
q = 1-p;

rest = 128; % Resting potential
thresh = 160; % Threshold Boundary

% Define Probability Transition Matrix
P = p*diag(ones(thresh-1,1),+1) + q*diag(ones(thresh-1,1),-1);
P(1,2) = 1;
P(thresh,:) = 0;
P(thresh,rest)=1;

% Define alternate matrix with absorbing threshold state
PP = P;
PP(thresh,:) = 0;
PP(thresh,thresh) = 1;

% Prepare for for loop
tempP = eye(thresh);
tempPP = eye(thresh);

isi(1) = P(rest,thresh);

% Loop over time steps
for n=2:1E3;

    tempP = tempP*P;
    tempPP = tempPP*PP;

    isi(n) = tempPP(rest,thresh-1)*p; %*(1-tempPP(rest,thresh));

end;
```

7.3 Random Walk Simulation

```
% This is rw.m
% Random Walk Model for Membrane Potential of a Neuron
% Based on Gerstein and Mandelbrot, Biophys J. Vol. 4, 1964.
%
% Joshua Goldwyn
% EE 508 Final Project

p = 0.6; % Probability of advancing one step
q = 1-p; % Probability of moving back one step

rest = 128; % Resting potential
thresh = 160; % Threshold Boundary
N = 1E3; % Number of spikes to observe

v(1) = rest; % initial condition
t = 0; % Time counter
count = 1; % spike counter
rand('seed',41); %initialize randomization so can replicate

while count <= N;
    t = t + 1;
    if v(t) == 1; % Reflecting boundary
        v(t+1) = 2;
    elseif v(t) == thresh % spike
        v(t+1) = rest;
        s(count) = t; % record spike time
        count = count + 1; % advance spike counter
    else
        if rand < p % advance one step
            v(t+1) = v(t) + 1;
        else % move back one step
            v(t+1) = v(t) - 1;
        end;
    end; % end if
end; % end while loop

% Compute ISI
ispike = s(2:N) - s(1:N-1) - 1;

% Compute proportion of time in each state
for i = 1:thresh
    limprob(i) = length(find(v == i)) / (t + 1);
end;
```