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Phase locking in integrate-and-fire models with refractory periods and modulation

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Abstract. It is known [8, 11, 16, 26] that phase locking can entrain frequency information when the leaky integrate-and-fire (IF) model of a neuron is forced by a periodic function. We show that this is still the case when the IF model is made more biologically realistic. We incorporate into our model spike dependent threshold modulation and refractory periods. Consecutive firing times from this model and their respective interspike intervals are related by an annulus map. We prove a general theorem concerning orientation reversing annulus twist homeomorphisms, which shows that our map admits a unique rotation number. This implies, in particular, that chaotic behaviour is not possible in our model and phase locking is predicted.

1. Introduction

One of the central questions in neuroscience is how the brain represents and processes information. This process involves very large collections of highly interconnected neurons and is difficult to tackle in this generality. A simpler version of this question asks how this same process is performed by a single neuron. It is not clear to what extent it is reasonable to expect that the behaviour of a single neuron can give insight into the function of a large ensemble of neurons. However, since only the measurements from single neurons were technologically possible until relatively recently, neuroscientists have studied single neurons extensively and a great deal is known about them. One of the phenomena observed on this level is that of *phase locking*. In neuroscience, what is often meant by this term is a stable matching of a post-stimulus time histogram (PSTH) of spikes to peaks in the input signal. A PSTH can be interpreted as an approximation of the probability of a spike following the stimulus. This notion does not require periodic input, but does require a repeated stimulus, so that one can form the PSTH.

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One mathematical model of this phenomena requires periodic input and a deterministic model which produces spikes. Different models [8,11,15,17,21,36,26,20] give rise to different maps which relate consecutive spikes, but for all these maps one can define a *rotation number*, ρ, that counts average phase rotation per spike. If this number is unique and rational $\left(\rho = \frac{p}{q}\right)$, then the map admits a stable q-periodic point, whose period is completed in p periods of the driving input. When the system settles to such a stable periodic point it fires q times per p periods, thus exhibiting matching frequency of firing to the frequency of the input. Further, since these periodic points are stable, they will persist under small perturbations and so this behaviour is "locked" under small changes in parameters. Such phase locking has been shown to exist for periodic input to the integrate-and-fire model of a neuron [26,16,17,33].

The leaky integrate-and-fire (IF) model of a neuron, introduced by Lapicque [29] almost hundred years ago, is one of the simplest models of a spiking neuron. In this model, the state of the neuron is modelled by the variable $u(t)$. The model is forced by some stimulus $s(t)$ and integrated until $u(t)$ reaches a constant threshold Θ. The time t such that $u(t) = \Theta$ is considered a *firing time*, at which the variable $u(t)$ is reset to zero and integration begins anew. To model the permeability of real neurons, a leak parameter $\sigma \geq 0$ is included. We denote $\{\tau_n\}_{n=0}^{\infty}$ to be the set of discrete times at which the model fires, not to be confused with the continuous time t. The model is then described by a linear differential equation with a threshold

$$\begin{aligned} \frac{du}{dt} &= -\sigma u + s(t) \\ u(t) = \Theta &\Rightarrow u(t^+) = 0 \end{aligned} \tag{1}$$

Keener *et. al* [26] investigated the behaviour of the IF model with constant threshold when forced by a periodic input. Following their lead we will consider a periodic input of the form

$$s(t) = S(1 + B\cos(t))$$

where S and B are non-negative scaling parameters. We will ignore the case $S = 0$ since this is equivalent to the input $s(t) = 0$ for which firing never occurs. Also, we consider only the 2π periodic case since for any other period a simple transformation of time in (1) can transform the system into a 2π periodic one.

When the IF model (1) is forced by this input, it is possible to construct an implicit function that relates consecutive firing times. This map was originally introduced in [38] and was subsequently studied extensively in Keener *et. al* [26]. In the latter paper, it was shown that given certain invertibility criterion this function could be solved explicitly in the form

$$\tau_{n+1} = f(\tau_n).$$

For this map, they found that $f(\tau + 2\pi) = f(\tau) + 2\pi$ and thus f is a lift of a degree one circle map. For such a map the rotation number ρ can be defined

$$\rho(f) = \lim_{n\to\infty} \frac{f^n(\tau)}{2\pi n}.$$

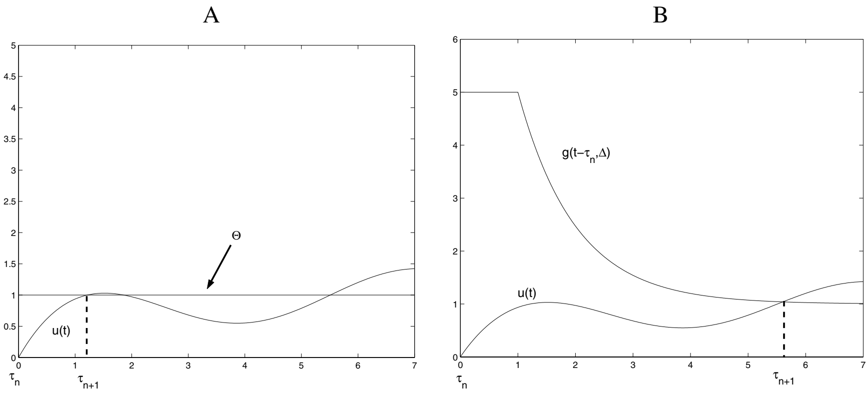


Fig. 1. Representative examples of A) the classic IF model with constant threshold and B) the modified version used in this paper. Note that the next firing time is the first intersection of the two variables.

In their case, the rotation number is independent of the initial condition τ [26]. Consequently, when the rotation number of the induced mapping is rational, $\rho = \frac{p}{q}$, then the corresponding IF model is $q : p$ phase locked.

The IF model can be thought of as a reduction of more biologically realistic models such as the Hodgkin-Huxley model [1]. Like any model, despite its similarities the IF model fails in many ways to mimic the behaviour of real neurons. This is to some extent caused by the simplicity of the integrating mechanism, but also by the simple form of the threshold.

The goal of this paper is to include additional features into the IF model which better model the behaviour of a real neuron. In the first part, we will incorporate both absolute and relative refractory periods and in the second we add modulation of the threshold by the length of previous interspike interval. To define these terms, recall that during the *absolute refractory period* a neuron cannot fire [28] . After this period, during the *relative refractory period* the neuron can fire, but only if the input is very large. *Interspike interval threshold modulation* [28] is a phenomena where the threshold is lowered if there was no spiking for a long time (i.e. the preceding interspike interval is large) and the threshold is increased if the preceding interspike interval was short. This characteristic can also be thought of as a simplified version of adaptation. Adaptation is a well established and long known characteristic of neural cells that dates back to Adrian and Zotterman [2]. Recently, Azouz and Gray [4] performed in vivo experiments demonstrating a relationship between the firing threshold and previous firing times that is qualitatively similar to the interspike interval threshold modulation studied in this paper.

Different combinations of these features have been used in integrate-and-fire models previously. In particular, adaptation has been modelled via dynamic thresholds extensively in the past [13, 19, 34, 35, 39].

We approach this topic with a model as general as possible and focus on the phase locking properties inherent to this model. However, it is important to note that our goal is not to create a quantitative model of refractory periods and adaptation.

Instead, we will focus on the behaviour of the IF model when it is constrained to exhibit the qualitative nature of these features.

We begin modelling this behaviour by considering a non-constant threshold function, $g(t, \Delta_n)$ where $\Delta_n = \tau_n - \tau_{n-1}$ is the length of the preceding interspike interval. This threshold function will be reset after each spike and therefore it takes the form $g = g(t - \tau_n, \Delta_n)$. We assume that:

1. There is a $\Delta_{abs} > 0$ such that the function $g(t)$ for $t \in [\tau_n, \tau_n + \Delta_{abs}]$ is sufficiently large so that no firing can occur during this time period.
2. After $\tau_n + \Delta_{abs}$, the threshold function will decrease monotonically to some base value Θ. We will not define relative refractory period precisely, as we will not use this notion mathematically. Roughly, it corresponds to an interval after which the threshold has decreased to values comparable to Θ. Thus,
$$g' = \frac{\partial g}{\partial t} < 0$$
$$\lim_{t \to \infty} g(t) = \Theta \tag{2}$$
For the remainder of this paper, we denote g' to be the partial derivative of g with respect to t.
3. To model interspike interval threshold modulation we assume that
$$\frac{\partial g}{\partial \Delta_n} < 0 \tag{3}$$
so that "large" previous interspike intervals lead to lowered threshold values and consequently quicker spiking and vice versa.
4. We assume that when evaluated at the time of fire τ_{n+1} we have
$$\left| \frac{\partial g}{\partial t} \right|_{t=\tau_{n+1}} > \left| \frac{\partial g}{\partial \Delta_n} \right| \tag{4}$$
Notice that at $t = \tau_{n+1}$ we have
$$g = g(\tau_{n+1} - \tau_n, \Delta_n) = g(\Delta_{n+1}, \Delta_n).$$
Therefore we can interpret the assumption (4) as the requirement that the effect on the threshold function due to the most recent interspike interval should be greater than that of previous interspike intervals.

These assumptions are quite general. We do not assume a particular form of the threshold function g and all assumptions are biologically motivated. Once again, we emphasise that the ambiguity concerning the threshold function g allows our results more flexibility and breadth in their application.

Our main goal is to study the behaviour of the model (1) with the new threshold function g when it is forced by a periodic input. We want to emphasise that one should not expect that the results of Keener *et. al.* [26] would automatically generalise to our problem with a non-constant threshold function. For instance, the standard IF model can only fire when $\frac{du}{dt} \geq 0$. Due to the dynamic nature of the threshold function g, this is not true in our case. As a result, the set of eligible firing times is larger in magnitude and unique rotation number is not necessarily guaranteed. Furthermore, inclusion of interspike interval threshold modulation requires a second variable which transforms our problem from the circle map f to an annulus map F. This is also a non-trivial extension of the work of Keener *et. al* [26].

For a circle map f, recall that when f is not monotone, then it is possible that the rotation number depends on initial condition [25]. A similar fact is known for area-preserving annulus maps satisfying a *twist condition* [25]. In these cases, all such rotation numbers belong to a closed interval called a rotation interval [25, 30]. For every rational rotation number the corresponding map on the circle has a q-periodic point, and to each irrational rotation number corresponds a non-periodic trajectory. The presence of a nontrivial rotation interval has been used as an indicator of a chaotic dynamics [27] and is often referred to as *rotational chaos*. The presence of such chaos has been observed in the Hodgkin-Huxley model [3], the Van-der Pol Oscillator [18], a leaky IF model with threshold fatigue [14] as well as in certain live neurons [22]. Intuitively, mathematical phase locking is not compatible with chaotic dynamics.

In the first part of this paper we will show that the map f for a non-constant threshold with refractory periods still admits a unique rotation number. Thus, a non-trivial rotation interval and rotational chaos are not possible. In the process of revising this paper we have learned of recent results due to Brette [8], where the monotonicity of the function f was established under a quite general set of assumptions. We discuss the relationship between these results and our results in the conclusion.

In the second part of the paper we study a general threshold function that incorporates interspike interval threshold modulation in addition to refractory periods. In this case, the model will give rise to an annulus map. Again, we show that if the annulus map arising from the IF model is continuous, then the map admits a unique rotation number. Therefore chaos is ruled out and phase-locking is predicted. We prove the last result using a novel theorem about orientation reversing annulus maps, whose second iteration satisfies the twist condition.

2. Preliminaries

In this section, we will consider a threshold function $g(t - \tau_n, \Delta_n)$ which satisfies the assumptions stated in the previous section.

Note that the alteration of the threshold function g does not affect integration of the IF equation (1) and as a consequence its solution is (see Keener *et. al* [26])

$$u(t) = \frac{S}{\sigma}(1 - e^{-\sigma(t-\tau_N)}) + \frac{SB}{\sigma}\sin\beta\{\sin(t+\beta) - \sin(\tau_N+\beta)e^{-\sigma(t-\tau_N)}\} \quad (5)$$

where

$$\sin\beta = \frac{\sigma}{\sqrt{1+\sigma^2}}.$$

The threshold function is reset at each firing time and therefore it takes the form $g(t - \tau_N, \Delta_n)$. The next firing time occurs for the smallest value of $t = \tau_{n+1}$ for which

$$u(\tau_{n+1}) = g(\tau_{n+1} - \tau_n, \Delta_n)$$

Thus, the condition for firing is an implicit function of three variables (τ_{n+1}, τ_n, Δ_n). We consider solutions of

$$g(\tau_{n+1} - \tau_n, \Delta_n) - u(\tau_{n+1}) = 0. \tag{6}$$

Setting $t = \tau_{n+1}$ in (5), and multiplying (6) by $\frac{\sigma}{S}e^{\sigma\tau_{n+1}}$ yields

$$\frac{\sigma}{S}g(\tau_{n+1} - \tau_n, \Delta_n)e^{\sigma\tau_{n+1}} - e^{\sigma\tau_{n+1}} + e^{\sigma\tau_n} - e^{\sigma\tau_{n+1}}B\sin\beta\sin(\tau_{n+1} - \beta) \\ + e^{\sigma\tau_n}B\sin\beta\sin(\tau_n + \beta) = 0,$$

from which we will define an implicit function H that relates τ_{n+1}, τ_n, and Δ_n, as

$$H(\tau_{n+1}, \tau_n, \Delta_n) = \frac{\sigma}{S}g(\tau_{n+1} - \tau_n, \Delta_n)e^{\sigma(\tau_{n+1})} - h(\tau_{n+1}) + h(\tau_n) = 0, \tag{7}$$

where

$$h(t) = e^{\sigma t}(1 + B\sin\beta\sin(t + \beta)).$$

The equation (7) implicitly relates a firing time τ_n to the next firing time, τ_{n+1}. It is possible that there is a set of distinct triples $(\tau^i, \tau_n, \Delta_n)$ such that $H(\tau^i, \tau_n, \Delta_n) = 0$ for all i. In such a case we take τ_{n+1} to be the minimum of all such τ^i.

Our first observation is that the function H is invariant under the transformation:

$$\tau_{n+1} \to \tau_{n+1} + 2\pi, \qquad \tau_n \to \tau_n + 2\pi \qquad \tau_{n-1} \to \tau_{n-1} + 2\pi \tag{8}$$

Indeed, $h(t+2\pi) = e^{2\sigma\pi}h(t)$, $g(\tau_{n+1}+2\pi-\tau_n-2\pi, \Delta_n) = g(\tau_{n+1}-\tau_n, \Delta_n)$ and $\Delta_n = \tau_n + 2\pi - \tau_{n-1} - 2\pi = \Delta_n$. Therefore, following the transformation (8) both sides of equation (7) will be multiplied by a factor $e^{2\sigma\pi}$.

Lemma 2.1. *If a function of three variables $H(\tau_{n+1}, \tau_n, \Delta_n)$ is invariant under the transformation (8) and the equation $H(\tau_{n+1}, \tau_n, \Delta_n) = 0$ can be implicitly solved as*

$$\tau_{n+1} = f(\tau_n, \Delta_n) \tag{9}$$

then

$$f(\tau + 2\pi, \Delta) = f(\tau, \Delta) + 2\pi.$$

Proof. The invariant transformation (8) together with $H(\tau_{n+1}, \tau_n, \Delta_n) = 0$ gives

$$H(\tau_{n+1} + 2\pi, \tau_n + 2\pi, \Delta_n) = H(\tau_{n+1}, \tau_n, \Delta_n) = 0.$$

Since the first component can be explicitly solved as a function of the second we have

$$\tau_{n+1} + 2\pi = f(\tau_n + 2\pi, \Delta_n).$$

□

If this function f exists, we can relate the new firing time and new interspike interval $(\tau_{n+1}, \Delta_{n+1})$ to the old pair (τ_n, Δ_n). Let $G : \mathbf{R} \times \mathbf{R} \to \mathbf{R} \times \mathbf{R}$ be defined by

$$G(\tau_n, \Delta_n) = (f(\tau_n, \Delta_n), f(\tau_n, \Delta_n) - \tau_n). \tag{10}$$

Then

$$(\tau_{n+1}, \Delta_{n+1}) = G(\tau_n, \Delta_n).$$

By Lemma 2.1 the function $G(\tau, \Delta)$ is a lift of an annulus map $F : S^1 \times I \to S^1 \times I$ where $\tau_n \mod 2\pi \in S^1$ and the interspike interval $\Delta_n \in I$ for $I = [\Delta_{abs}, \infty)$.

We will now turn our attention to the conditions under which the function f exists. By the Implicit Function Theorem, f exists locally whenever the partial derivative

$$H_{\tau_{n+1}} := \frac{\partial H}{\partial \tau_{n+1}} \neq 0.$$

This condition on the derivative $H_{\tau_{n+1}}$ will appear many times throughout the paper. We begin by computing the derivative explicitly and proving some lemmas related to it.

Lemma 2.2. *The function $H(\tau_{n+1}, \tau_n, \Delta_n)$ is continuously differentiable and*

$$H_{\tau_{n+1}}(\tau_{n+1}, \tau_n, \Delta_n) = \frac{\sigma}{S} e^{\sigma\tau_{n+1}} \left(\frac{g'(\tau_{n+1}, \Delta_n) + \sigma g(\tau_{n+1}, \Delta_n)}{S} - 1 - B\cos(\tau_{n+1})\right) \tag{11}$$

Proof. We will expand the $\sin(\tau + \beta)$ before differentiation. In this way

$$\begin{aligned} h(\tau) &= e^{\sigma\tau}(1 + B\sin\beta\sin(\tau+\beta)) \\ &= e^{\sigma\tau}(1 + B\sin\beta(\sin(\tau)\cos(\beta) + \cos(\tau)\sin(\beta))) \end{aligned}$$

By product rule, we can differentiate so that,

$$\begin{aligned} h'(\tau) &= \sigma e^{\sigma\tau}(1 + B\cos\beta\sin\beta\sin\tau + B\sin^2\beta\cos\tau) \\ &\quad + e^{\sigma\tau}(B\cos\beta\sin\beta\cos\tau - B\sin^2\beta\sin\tau) \end{aligned}$$

Since $\sin\beta = \frac{\sigma}{\sqrt{1+\sigma^2}}$ it follows that $\cos\beta = \frac{1}{\sqrt{1+\sigma^2}}$. Using this information we get,

$$h'(\tau) = \sigma e^{\sigma\tau}\left(1 + \frac{B\sigma\sin\tau}{1+\sigma^2} + \frac{B\sigma^2\cos\tau}{1+\sigma^2}\right) + e^{\sigma\tau}\left(\frac{B\sigma\cos\tau}{1+\sigma^2} - \frac{B\sigma^2\sin\tau}{1+\sigma^2}\right)$$

Note that both the second and fifth terms cancel, leaving the derivative only in terms of $\cos(\tau)$.

$$h'(\tau) = \sigma e^{\sigma\tau} + \frac{B\sigma^3 e^{\sigma\tau}\cos\tau}{1+\sigma^2} + \frac{B\sigma e^{\sigma\tau}\cos\tau}{1+\sigma^2}$$

We factor a $B\sigma e^{\sigma\tau}\cos\tau$ term and cancel $1+\sigma^2$ to get

$$h'(\tau) = \sigma e^{\sigma\tau} + B\sigma e^{\sigma\tau}\cos\tau = \sigma e^{\sigma\tau}(1 + B\cos\tau). \tag{12}$$

With $h'(\tau)$ computed we finish the proof of the Lemma by straightforward differentiation of (7) with respect to τ_{n+1}. □

Corollary 2.3. *The partial derivative of H with respect to τ_n has the following form.*

$$H_{\tau_n} = \sigma e^{\sigma\tau_n}(1 + B\cos(\tau_n)) - \frac{\sigma}{S} g' e^{\sigma\tau_{n+1}} \tag{13}$$

Proof. Using (12) we arrive at,

$$H_{\tau_n} = \sigma e^{\sigma\tau_n}(1 + B\cos(\tau_n)) + \frac{\sigma}{S}\frac{\partial g}{\partial T}\frac{\partial T}{\partial \tau_n} e^{\sigma\tau_{n+1}},$$

where T denotes the first component in $g(t-\tau_n, \Delta_n)$. To finish the proof of the Lemma, we note that,

$$\frac{\partial g}{\partial T}\frac{\partial T}{\partial \tau_n} = -\frac{\partial g}{\partial T} = -\frac{\partial g}{\partial t} = -g'.$$ □

Now we investigate the domain of f. We show that the triples $(\tau_{n+1}, \tau_n, \Delta_n)$ at which $H = 0$, satisfy a certain condition, which restricts the image of f and consequently the domain of the higher iterate maps, f^n.

Lemma 2.4. *If $g(\tau_{n+1} - \tau_n, \Delta_n)$ is the value of the threshold function at the first firing time τ_{n+1} after τ_n, then the following inequality must be satisfied:*

$$1 - \frac{\sigma g(\tau_{n+1} - \tau_n, \Delta_n)}{S} + B\cos(\tau_{n+1}) \geq \frac{g'(\tau_{n+1} - \tau_n, \Delta_n)}{S} \tag{14}$$

Proof. Let τ_{n+1} be the first instance after a firing time τ_n such that $g(\tau_{n+1} - \tau_n, \Delta_n) = u(\tau_{n+1})$. Since both of these functions are continuous and from the definition of firing, $g(\tau_{n+1} - h - \tau_n, \Delta_n) > u(\tau_{n+1} - h)$ for all sufficiently small h. Subtracting the value of both functions at τ_{n+1} from each side, and then dividing by $-h$, we are left with

$$\frac{g(\tau_{n+1} - h - \tau_n, \Delta_n) - g(\tau_{n+1} - \tau_n, \Delta_n)}{-h} < \frac{u(\tau_{n+1} - h) - u(\tau_{n+1})}{-h}.$$

Taking limits on both sides we see that $g'(\tau_{n+1} - \tau_n, \Delta_n) \leq \frac{du}{dt}(\tau_{n+1})$. In other words,

$$-\sigma u + S(1 + B\cos(\tau_{n+1})) \geq g'(\tau_{n+1} - \tau_n, \Delta_n).$$

At τ_{n+1}, $u = g(\tau_{n+1}, \Delta_n)$, so substituting and then dividing by S, we derive the stated result. □

Corollary 2.5. *The partial derivative $H_{\tau_{n+1}}$ must be negative or zero at all firing times.*

Proof. Notice that by moving everything to the right hand side in (14), we get

$$\frac{g' + \sigma g}{S} - 1 - B\cos(\tau_{n+1}) \leq 0.$$

Comparing to (11) we see that

$$H_{\tau_{n+1}} \leq 0$$

at all values $(\tau_{n+1}, \tau_n, \Delta_n)$. □

3. Threshold function with refractory periods

In this section we simplify the function g defined above by not including threshold modulation by Δ_n. Thus in this section $g = g(t - \tau_n)$.

Our main result for this threshold function is similar to that of Keener *et. al* [26] where the (σ, S, B) parameter space was sub-divided into three parameter regions. In each region the function f had different properties: in one region, f was monotone and continuous, in second f was piecewise continuous and monotone on its image and in the third f was not defined. Despite these differences Keener *et.al* [26] showed that for all parameter values either spiking stops or there is a unique rotation number.

In our case, in addition to the parameters (σ, S, B), the threshold function g is also a parameter. Let $\mathcal{G}$ be the set of continuous functions $g : \mathbf{R}^+ \to \mathbf{R}^+$ satisfying assumptions (2)-(4). Hence, our parameter space $\mathbf{R}^+ \times \mathcal{G}$ is infinite dimensional.

Our main result in this section is the following Theorem.

Theorem 3.1. *Assume that a threshold function g satisfies (2)-(4) (i.e. $g \in \mathcal{G}$). Then for all values of parameters $(\sigma, B, S, g) \in \mathbf{R}^{3+} \times \mathcal{G}$ either firing stops or the function f relating firing times through $\tau_{n+1} = f(\tau_n)$ exists and admits a unique rotation number. Consequently, chaotic behaviour is not possible.*

In order to prove this Theorem we need to investigate all possible functions f which arise from our model and how different forms of f affect their rotation set. To this end we divide the set of possible functions f into four classes. Let

$$\mathbf{D} := \{f : \mathcal{D} \to \mathbf{R} : f(x + 2\pi) = f(x) + 2\pi\}$$

be the set of lifts of a degree one circle maps where the domain $\mathcal{D}$ may be a proper subset of $\mathbf{R}$ (we allow $\mathcal{D} = \emptyset$ as well). Let

A Let $\mathbf{A} := \{f \in \mathbf{D} \mid f$ is continuous and monotone increasing$\}$;
B Let $\mathbf{B} := \{f \in \mathbf{D} \mid f$ is piecewise continuous and monotone increasing$\}$;
C Let $\mathbf{C} := \{f \in \mathbf{D} \mid f$ is piecewise continuous$\}$;

From this we note that,

$$\mathbf{A} \subset \mathbf{B} \subset \mathbf{C} \subset \mathbf{D}.$$

We first observe that by results of Herman [23] and Keener [27], if $f \in \mathbf{B}$, then f admits a unique rotation number. We address the cases when $f \in \mathbf{C}$ or $f \in \mathbf{D}$ next.

Lemma 3.2. *Assume that f is defined as in (9) and $f \in \mathbf{D} \setminus \mathbf{C}$. Then the domain of f^2 is an empty set. In other words, the firing stops after at most one fire.*

Proof. First, we note that the lemma is trivially true if the domain of f is an empty set. Assume now that f is defined on a strict, non-empty subset of $\mathbf{R}$. We compute $\limsup_{t\to\infty} u(t)$ from (5):

$$LS := \limsup_{t\to\infty} u(t) = \frac{S}{\sigma} + \frac{SB}{\sigma}\sin\beta. \tag{15}$$

Observe that if $LS > \Theta$ then for all τ_n there exists a time $\tau_{n+1} > \tau_n$ when the system fires again. In other words, if $LS > \Theta$ then $f \in \mathbf{C}$ and the mapping is defined everywhere. Therefore, for $f \in \mathbf{D} \setminus \mathbf{C}$ we must have

$$LS \leq \Theta,$$

and whether the system fires depends on the initial condition τ_n and its relation to the period of the input. In order for the system to fire, there must exist a time t such that the function $u(t)$ is equal to g. Then, by (2), $u(t)$ must be greater or equal Θ at such a firing time. Combining this with $LS \leq \Theta$ we get that at the firing time τ_{n+1},

$$u(\tau_{n+1}) \geq \frac{S}{\sigma} + \frac{SB}{\sigma}\sin\beta. \tag{16}$$

Recall from (5) that the solution $u(t)$ has the form

$$u(t) = \frac{S}{\sigma}(1 - e^{-\sigma(t-\tau_n)}) + \frac{SB}{\sigma}\sin\beta\{\sin(t+\beta) - \sin(\tau_n+\beta)e^{-\sigma(t-\tau_n)}\}.$$

Since $0 < e^{-\sigma(t-\tau_n)} < 1$ for all t greater than τ_n, we see that in order to satisfy (16) we must have

$$\sin(\tau_{n+1}+\beta) - \sin(\tau_n+\beta)e^{-\sigma(\tau_{n+1}-\tau_n)} > 1. \tag{17}$$

Therefore in order for τ_{n+1} to exist, the previous firing time τ_n must satisfy

$$-\sin(\tau_n+\beta) > 0. \tag{18}$$

This equation defines a superset of the domain $D \subset [0, 2\pi]$ of the map f. In other words, if $\tau_n \in D$ then (18) holds. We rearrange terms in (17) to get

$$\sin(\tau_{n+1}+\beta) > 1 + \sin(\tau_n+\beta)e^{-\sigma(\tau_{n+1}-\tau_n)}.$$

Since $\sin(\tau_n+\beta) < 0$ and $e^{-\sigma(\tau_{n+1}-\tau_n)} < 1$, we get that $\sin(\tau_{n+1}+\beta) > 0$. Therefore, as a consequence of (18) $\tau_{n+1} \notin D$. □

As a result of this lemma, if f is undefined for some value in its domain, then the rotation number is not defined for any value of its domain. Next, we investigate what happens when f is non-monotone.

Lemma 3.3. *Let f be given by (9) and let $f \in \mathbf{C} \setminus \mathbf{B}$. Then f is monotone on its image.*

Proof. We define a set Q to be all τ_n for which the map f is decreasing and the set P to be the set of τ_{n+1} for which the model does not fire. We will show that $Q \subset P$; in other words $\tau_n \in Q$ implies $\tau_{n+1} \notin P$, which implies the statement of the Lemma.

We begin by defining Q. By Lemma 2.4, $H_{\tau_{n+1}}$ is always non-positive at firing times. Then f is decreasing ($f' = \frac{H_{\tau_n}}{H_{\tau_{n+1}}} \leq 0$) if and only if $H_{\tau_n} < 0$. Using (13) this means

$$H_{\tau_n} = \sigma e^{\sigma \tau_n}(1 + B\cos(\tau_n)) - \frac{\sigma}{S} g' e^{\sigma \tau_{n+1}} < 0$$

Dividing by $\sigma e^{\sigma \tau_n}$ and solving for $B\cos(\tau_n)$ yields,

$$B\cos(\tau_n) < \frac{g'(\tau_{n+1} - \tau_n)}{S} e^{\sigma(\tau_{n+1} - \tau_n)} - 1 \tag{19}$$

Let U_1 be the right hand side of (19). Then the set Q has the form

$$Q := \{x \mid B\cos(x) < U_1\}.$$

This implicitly defines the set Q as all the values of τ_n at which $f(\tau_n)$ is decreasing.

To define the set P we return our attention to Lemma 2.4. The converse of Lemma 2.4 provides a set of potential τ_{n+1} where the model can not fire, defined by the condition,

$$B\cos(\tau_{n+1}) < \frac{g'(\tau_{n+1} - \tau_n) + \sigma g(\tau_{n+1} - \tau_n)}{S} - 1. \tag{20}$$

If we denote the right hand side of (20) by U_2 then P has the form

$$P := \{x \mid B\cos(x) < U_2\}.$$

This condition implicitly defines the set P.

Clearly, $Q \subset P$ if and only if $U_1 \leq U_2$. To demonstrate the latter inequality, notice that $e^{\sigma(\tau_{n+1} - \tau_n)} > 1$, $g' < 0$ and consequently $U_1 \leq U_2$ even without the positive σg term in (20). Thus, we conclude $Q \subset P$ which implies that although the map f may not be monotone on its domain D, it is monotone on $f(D)$. □

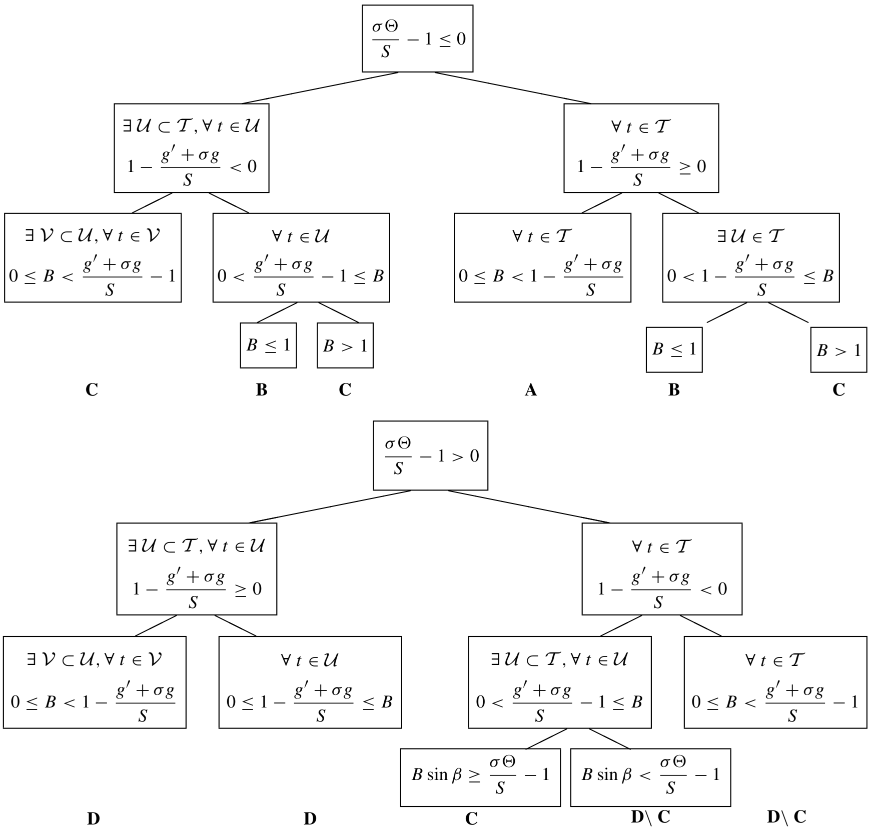
Proof of Theorem 3.1. If $f \in \mathbf{A}$ or $f \in \mathbf{B}$ results of [23] and [27] respectively show existence of a unique rotation number.

If $f \in \mathbf{D} \setminus \mathbf{B}$ then either $f \in \mathbf{D} \setminus \mathbf{C}$ or $f \in \mathbf{C} \setminus \mathbf{B}$. In the first case Lemma 3.2 shows that firing will stop, in the second case Lemma 3.3 implies that after one iteration f is monotone. Since the rotation number is defined in terms of a limit where the number iterations go to infinity, in this case rotation number will still be unique. As a consequence, it is known that f either has a unique rotation number or no rotation number at all, i.e. the firing stops. □

Remark 3.4. We remark on the size of the parameter set where phase locking occurs. For any fixed threshold function g let $X_g := \{(\sigma, B, S) \mid f = f(\sigma, B, S, g) \in C \setminus A\}$ and $Y_g := \{(\sigma, B, S) \mid f = f(\sigma, B, S, g) \in A\}$. By results of Keener [27] and Herman [23], there is a Cantor set C_X of measure 0 in X_g, and a Cantor set C_Y with positive measure in Y_g, such that if $(\sigma, B, S) \in C_*$ then $f(\sigma, B, S)$ has an irrational rotation number. It follows that there is a full measure subset of X_g, and there is a positive, but not full, measure subset of Y_g where phase locking occurs.

The following theorem indicates which set (**A**, **B**, **C** or **D**) the function f belongs to, based on the parameter values (σ, B, S) and the threshold function g.

Theorem 3.5. *The parameter space* $(\sigma, B, S, g) \in \mathbf{R}^{3+} \times \mathcal{G}$ *can be subdivided into* 11 *regions according to the figure below. On the bottom of each decision path is the set that the corresponding function* f *belongs to.*



3.1. Proof of Theorem 3.5

Parameter region $\frac{\sigma\Theta}{S} - 1 \le 0$.

In this region of parameter space, our first observation is that for any τ_n, a successive firing time τ_{n+1} always exists. To see this, observe that our definition of the parameter region gives

$$\frac{S}{\sigma} \geq \Theta. \tag{21}$$

We also find that as $t \to \infty$ the solution $u(t)$ approaches

$$\frac{S}{\sigma}(1 + B \sin\beta \sin(t + \beta)).$$

This function oscillates around the value $\frac{S}{\sigma}$. By (21) this value is super-threshold. Consequently, in this parameter region, the model will fire again, regardless of when the previous fire τ_n was. In other words, the mapping f is well-defined on the set $[0, 2\pi]$ and $f \notin \mathbf{D}$.

For any τ_n, let T be the set of all possible firing times $T = \{t \mid t > \tau_n + \Delta_{abs}\}$. The limit

$$\lim_{t\to\infty} 1 - \frac{g' + \sigma g}{S} = 1 - \frac{\sigma\Theta}{S} \geq 0$$

by the definition of this region. As a consequence, the term $1 - \frac{g'+\sigma g}{S}$ cannot be negative for all values of $t \in T$. Therefore, either $1 - \frac{g'+\sigma g}{S} \geq 0$ for all $t \in T$ or there is a subset of T where the opposite inequality holds true. According to this criterion, we further subdivide this region.

3.1.1. $1 - \frac{g'+\sigma g}{S} \geq 0 \quad \forall t \in T$

Again, we further subdivide this region into two cases:

Case 1. $0 \leq B < 1 - \frac{g'+\sigma g}{S} \quad \forall t \in T$.

Recall from Lemma 2.2 that the sign of $H_{\tau_{n+1}}$ depends on the sign of the expression $\frac{g'+\sigma g}{S} - 1 - B\cos(\tau_{n+1})$. We use the assumption for case 1 to get

$$\frac{g' + \sigma g}{S} - 1 - B\cos(\tau_{n+1}) \leq \frac{g' + \sigma g}{S} - 1 + B < 0. \tag{22}$$

It now follows that the partial derivative $H_{\tau_{n+1}} < 0$ is always negative in this region. Therefore by the Implicit Function Theorem applied to the function $H(\tau_{n+1}, \tau_n) = 0$ there is a continuous function f with $\tau_{n+1} = f(\tau_n)$ satisfying

$$H(f(\tau_n), \tau_n) = 0.$$

The derivative of f is

$$f'(\tau) = -\frac{H_{\tau_n}}{H_{\tau_{n+1}}}$$

Since $H_{\tau_{n+1}} < 0$ for this case, we turn our attention to the sign of H_{τ_n} to compute the derivative of f. From Corollary 2.3 we know that that,

$$H_{\tau_n} = \sigma e^{\sigma\tau_n}(1 + B\cos(\tau_n)) - \frac{\sigma}{S} g' e^{\sigma\tau_{n+1}}.$$

Using the fact that $1 + B\cos(\tau) \geq 1 - B$ we place a lower bound on H_{τ_n},

$$H_{\tau_n} = \sigma e^{\sigma\tau_n}(1 + B\cos(\tau_n)) - \frac{\sigma}{S}g' e^{\sigma\tau_{n+1}} \geq \sigma e^{\sigma\tau_n}(1 - B) - \frac{\sigma}{S}g' e^{\sigma\tau_{n+1}}$$

By manipulating the condition defining case 1 we get $1-B > \frac{g'(\tau-\tau_n)+\sigma g(\tau-\tau_n)}{S}$ and after substitution this yields,

$$H_{\tau_n} > \sigma e^{\sigma\tau_n}(\frac{g' + \sigma g}{S}) - \frac{\sigma}{S}g' e^{\sigma\tau_{n+1}}.$$

After rearranging terms,

$$H_{\tau_n} > \frac{\sigma}{S}g'(e^{\sigma\tau_n} - e^{\sigma\tau_{n+1}}) + \frac{\sigma^2}{S}e^{\sigma\tau_n}g.$$

The first term is the product of two negative terms and the second is always positive. Thus, the partial derivative of H with respect to τ_n is always positive. Since $H_{\tau_{n+1}} < 0$ and thus non-zero $f(\tau)$ is continuous. Since $H_{\tau_n} > 0$, f is monotonically increasing and continuous. Thus, $f \in \mathbf{A}$.

Case 2. $\exists U \subset T$ such that for all $t \in U$ we have $B \geq 1 - \frac{g'+\sigma g}{S} \geq 0$

In this region the partial derivative, $H_{\tau_{n+1}}$ may be zero and as a consequence the Implicit Function Theorem is not always applicable. Therefore, f may not be defined for all τ_n. However, it can still be defined on subintervals of the interval $[0, 2\pi]$ where $H_{\tau_{n+1}} < 0$. Let (τ_{d+1}, τ_d) be a point such that $H(\tau_{d+1}, \tau_d) = 0$ and $H_{\tau_{n+1}}(\tau_{d+1}, \tau_d) = 0$, and where τ_{d+1} is the minimal value of t satisfying these conditions. Since $H_{\tau_{n+1}}(\tau_{d+1}, \tau_d) \leq 0$ for all (τ_{d+1}, τ_d) the points τ_d are isolated for a generic choice of parameters by Lemma 2.2. Since $H_{\tau_{n+1}} = 0$ at this point, the function f is not defined via Implicit Function Theorem at τ_d. To rectify this we specify

$$f(\tau_d) = \tau_{d+1}.$$

Now we turn our attention to the behaviour of f at τ_d. Towards this end, we recall (see (6) and (7)) that the function $H(\tau_{n+1}, \tau_n)$ has the following form

$$H(\tau_{n+1}, \tau_n) = \frac{\sigma}{S}e^{\sigma\tau_{n+1}}(g(\tau_{n+1} - \tau_n) - u(\tau_{n+1})). \tag{23}$$

From this we get,

$$H_{\tau_{n+1}}(\tau_{n+1}, \tau_n) = \frac{\sigma^2}{S}e^{\sigma\tau_{n+1}}(g(\tau_{n+1} - \tau_n) - u(\tau_{n+1})) + \frac{\sigma}{S}e^{\sigma\tau_{n+1}}(\frac{dg}{d\tau_{n+1}} - \frac{du}{d\tau_{n+1}}). \tag{24}$$

At (τ_{d+1}, τ_d), both $H(\tau_{d+1}, \tau_d) = 0$ and $H_{\tau_{n+1}}(\tau_{d+1}, \tau_d) = 0$ are equal to zero. By (23) and (24), at the discontinuity

$$g(\tau_{d+1} - \tau_d) = u(\tau_{d+1}) \quad \text{and} \quad \frac{dg}{d\tau_{n+1}}(\tau_{d+1} - \tau_d) = \frac{du}{d\tau_{n+1}}(\tau_{d+1}).$$

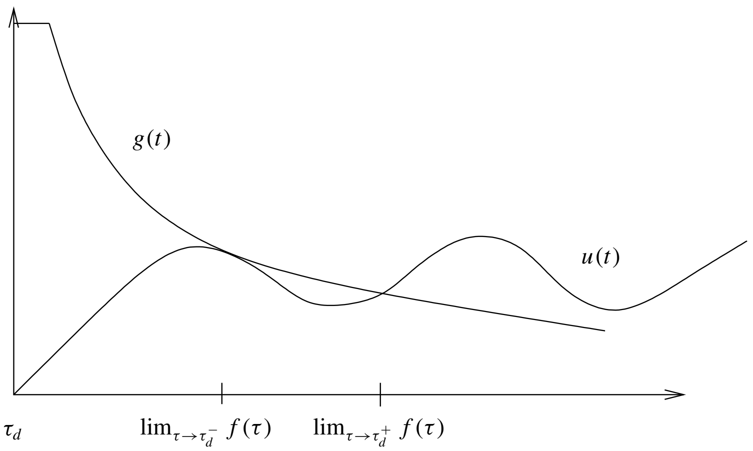


Fig. 2. The source of a discontinuity of the function f; the threshold $g(t)$ touches the solution $u(t)$.

Therefore at $t = \tau_{d+1}$ the threshold function $g(t - \tau_n)$ and the solution $u(t)$ have a contact of order at least 1. It is easy to see that if the order of contact is even, then the two functions cross each other, and if the order of the contact is odd, then the intersection is "one-sided"(as shown in Figure 2). In the first case, the intersection time τ_{d+1} depends continuously on the initial time τ_d. It follows that f has at τ_d a removable singularity for the even order case.

The case when g and u have a contact of odd order at τ_{d+1} is illustrated in Figure 2. Here, an arbitrarily small increase in the initial condition τ_d will have a large impact on the intersection time of g and u. More precisely, following τ_{d+1} there exists an interval I such that for $t \in I$,

$$1 - \frac{g' + \sigma g}{S} > -B\cos(t)$$

or equivalently,

$$g'(t - \tau_d) > u'(t).$$

By to Lemma 2.4, no value of $t \in I$ is eligible to be a firing time. Thus, when τ_d is increased the resulting effect upon the next consecutive firing time must be greater than the length of I. As a result,

$$\lim_{t\to\tau_d^-} f(\tau_d) < \lim_{t\to\tau_d^+} f(\tau_d)$$

and at τ_d the function f has a jump discontinuity.

We further subdivide case 2 into

- $\{ B \leq 1.\}$ In this case it follows from (13) that the partial derivative $H_{\tau_n} < 0$. As a consequence, f is monotone and piecewise continuous. Thus, for case 2 if $B \leq 1$ then $f \in \mathbf{B}$.
- $\{B > 1\}$ When $B > 1$ the function f may be non-monotone since $H_{\tau_n} \geq 0$. However, by the previous argument it is still piecewise continuous. This means that if $B > 1$ then $f \in \mathbf{C}$.

In case 2, it is impossible to state explicitly whether the function f belongs to $\mathbf{A}$ or $\mathbf{B} \setminus \mathbf{A}$ (for $B < 1$). Since the condition defining case 2 is time dependent, it follows that making a distinction between the continuous and discontinuous case ($\mathbf{A}$ or $\mathbf{B} \setminus \mathbf{A}$) would require advance knowledge concerning the precise location of future firing times (to assure that the condition for case 2 is satisfied *at* the firing time and not just for some possible firing time after the absolute refractory period). Such an assumption is impractical to the point that the more ambiguous representation presented here is preferable. The moral is that the existence condition defining case 2 does not imply a discontinuity, only that it is possible there could be one. Regardless, the rotation number remains well-defined and unique for all possible parameters within this case.

Recall that we still assume $\frac{\sigma\Theta}{S} - 1 \leq 0$. Now instead of assumption (3.1.1) we assume

3.1.2. $\exists U \subset T$ *such that* $1 - \frac{g'+\sigma g}{S} < 0 \quad \forall t \in U$
We again consider two cases.

Case 3. $B \geq \frac{g'+\sigma g}{S} - 1 > 0 \quad \forall t \in U.$

Recall that in this parameter region $\lim_{t\to\infty} 1 - \frac{g'+\sigma g}{S} \geq 0$ and firing is always guaranteed regardless of τ_n. In other words, although $1 - \frac{g'+\sigma g}{S}$ is negative for $t \in U$, the set U must be bounded and thus U is a strict subset of T. Rearranging the condition for case 3, we find that

$$-B \leq 1 - \frac{g' + \sigma g}{S} < 0. \tag{25}$$

With this condition we have an analog of case 2 where

$$B \geq 1 - \frac{g' + \sigma g}{S} > 0 \tag{26}$$

since $B\cos(t)$ oscillates around the origin. However, there remains a key distinction between case 2 and the present case 3. In the present case, the restriction $B \geq \frac{g'+\sigma g}{S} - 1 > 0$ only applies to the set U. Outside the set U, B could be less than or greater than $\frac{g'+\sigma g}{S} - 1$. If the time of the next fire falls within U, then by (25) and (26) the system behaves analogously to case 2. If the time of the next fire falls within the subset of T where $B < \frac{g'+\sigma g}{S} - 1$, the system behaves analogously to case 1. Since it is possible that some of the firing times can fall into one set and other times to another set, we must consider a worst case scenario. This implies that $f \in \mathbf{B}$ or $f \in \mathbf{C}$ depending on whether $B \leq 1$ or $B > 1$ respectively.

Case 4. $\exists V \subset U$ such that $0 \leq B < \frac{g'+\sigma g}{S} - 1 \quad \forall t \in V$

Moving the B term to the left hand side of the expression in case 4 yields,

$$0 < \frac{g' + \sigma g}{S} - 1 - B < \frac{g' + \sigma g}{S} - 1 + B\cos(\tau_{n+1})$$

Referring to Lemma 2.4 we see that the model cannot fire for any $t \in V$. Once again, recalling that $\lim_{t\to\infty} 1 - \frac{g'+\sigma g}{S} \geq 0$ implies that $V \subsetneq U \subsetneq T$. Since τ_{n+1} cannot be in V the set of eligible firing times is reduced to those within $T \setminus V$. Other than this difference, the same conclusions from case 3 hold here and $f \in \mathbf{C}$ or $\mathbf{B}$ depending on $B \leq 1$ or $B > 1$.

Parameter region $\frac{\sigma\Theta}{S} - 1 > 0$

We will leave the definition of T unchanged and note that firing is not necessarily guaranteed in this regime as it was in the previous one. Therefore, we are presented with the possibility that f may not be well-defined for some values of τ_n.

3.1.3. $1 - \frac{g'+\sigma g}{S} < 0 \quad \forall t \in T$

Case 5. $0 \leq B < \frac{g'+\sigma g}{S} - 1 \quad \forall t \in T$

By Lemma 2.4, if $B < \frac{g'+\sigma g}{S} - 1$ is true for all t, then there is no τ_{n+1} at which the system can fire. Hence, the model is unable to fire and for parameters in this region we have $f \in \mathbf{D} \setminus \mathbf{C}$.

Case 6. $\exists U \in T$ such that for all $t \in U$ we have $B \geq \frac{g'+\sigma g}{S} - 1 > 0$.

There are two distinctions to be made for parameters within this region. We will take the limsup of $u(t)$ as $t \to \infty$

$$\limsup_{t\to\infty} u(t) = \frac{S}{\sigma} + \frac{SB}{\sigma}\sin\beta. \tag{27}$$

If the right hand side is super-threshold ($B > \frac{1}{\sin\beta}(\frac{\sigma\Theta}{S} - 1)$), then for all τ_n a successive τ_{n+1} exists and the map f can be defined for all τ_n . Therefore, the same results as in section 3.1.2 apply and $f \in \mathbf{B}$ or $\mathbf{C}$. Since $\mathbf{B} \subset \mathbf{C}$ we conclude only that $f \in \mathbf{C}$.

On the other hand, if the right hand side is eventually sub-threshold then whether the model fires or not is a function of τ_n. Recalling the form of $u(t)$ (see (5)), we regroup it as follows,

$$u(t) = \{\frac{S}{\sigma}(1 - e^{-\sigma(t-\tau_n)}) + \frac{SB}{\sigma}\sin\beta\sin(t+\beta)\}$$
$$-\frac{SB}{\sigma}\sin\beta\sin(\tau_n+\beta)e^{-\sigma(t-\tau_n)}$$

The bracketed portion of this expression or the left side must be less than Θ and hence g by (27). Therefore, the model can only fire if the right most term is positive. Namely, $\sin(\tau_n + \beta) < 0$ must be true in order for the model to elicit firing and hence the domain of f is restricted to a subset of $[0, 2\pi]$. Therefore, by Lemma 3.2 $f \in \mathbf{D} \setminus \mathbf{C}$.

3.1.4. $\exists U \subset T$ *for which* $1 - \frac{g'+\sigma g}{S} \geq 0$
Case 7. $0 \leq 1 - \frac{g'+\sigma g}{S} \leq B \quad \forall t \in U$

Once again, existence of a set U does not imply that the model will fire within U for all τ_n. If that were the case, then the results from Case 2 would be directly applicable here and the model would give rise to an $f \in \mathbf{B}$ or $\mathbf{C}$, whose behaviour would depend upon the value of B. However, it is also possible that the next firing time will fall outside this set U, or will not exist at all. This means that the model would be firing according to either Case 5 or Case 6. Thus, we can only conclude $f \in \mathbf{D}$.

Case 8. $\exists V \subset U$ for which $0 \leq B < 1 - \frac{g'+\sigma g}{S} \quad \forall t \in U$

This is again an expansion of what was described in Case 7. If the model fires in V for all τ_n, then the results are analogous to those in Case 1 and the model will induce a map, $f \in \mathbf{A}$. However, if this is not true, then from Case 7 we know that the model will give rise to a map $f \in \mathbf{D}$.

This completes the proof of Theorem 3.5.

□

4. Interspike interval threshold modulation

In this section we will add dependence of the threshold function on the preceding interspike interval Δ_n. Recall from section 2 that if the implicit equation $H(\tau_n, \tau_{n+1}, \Delta_n) = 0$ can be solved for τ_{n+1} as $\tau_{n+1} = f(\tau_n, \Delta_n)$ then the function f gives rise to a function

$$G = (f(\tau_n, \Delta_n), f(\tau_n, \Delta_n) - \tau_n). \tag{28}$$

Furthermore, G covers an annulus map $F : A \to A$, with $A = S^1 \times [\Delta_{abs}, \infty)$. Our goal is to show that if the map f is continuous, then the map F admits a unique rotation number. This is rather surprising since, in general, homeomorphisms of an annulus may have rotation sets with non-empty interior [25].

4.1. Annulus maps

In this section, we introduce some theorems and constructions concerning general annulus maps. We will use the notion of prime ends, introduced by Carathéodory [10] and used previously in similar settings by [5–7,12,31,32].

Let S be a continuum in an annulus A, separating the annulus into two parts, A^{out} and A^{in}. This means that both A^{out} and A^{in} are open, A^{out}, A^{in} and S are mutually disjoint and their union is A. A simple arc $Q \subset cl(A^{out})$ with distinct endpoints q_1, q_2 on the boundary ∂S and $Q \setminus \{q_1, q_2\} \subset \text{int}A^{out}$, is a *cross cut*. Consider a sequence $\{Q_n\}$ of disjoint cross cuts such that Q_n separates Q_{n-1} from Q_{n+1}. There is a corresponding sequence of domains $\{D_n\}$, where D_n is a subdomain of A^{out} bounded by the crosscut Q_n and the continuum S, which contains Q_{n+1}, except its end points. Then $D_1 \supset D_2 \supset \ldots$. We call e, a sequence of such domains $\{D_n\}$, an *chain* of A^{out}.

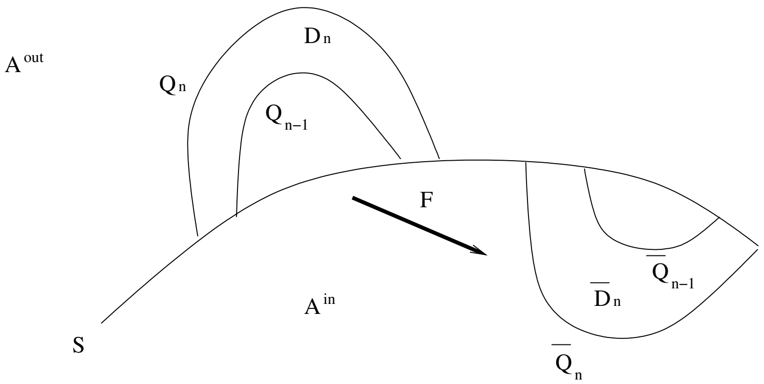


Fig. 3. End in A^{out} is mapped by the map F to an end in A^{in}.

A domain D' contains a chain e if $D_n = D_n(e)$ lies in D' for all $n > n_0(D')$. If e_1 and e_2 are two chains such that for every n, $D_n(e_1) \supset D_m(e_2)$ for $m = m(n)$, then we say that e_1 contains e_2 (or that e_1 is divisible by e_2). Two chains are *equivalent* if they divide each other. An equivalence class of chains is called an *end*. A *prime end p* is an end, such that for any chain $e \in p$ and any chain e' such that e' divides e, we have $e' \in p$.

We now specify a topology on the set of prime ends of the set A^{out}. Take an arbitrary cross cut Q and its domain D. Let $\tilde{D}$ be the set of all prime ends contained in the domain D. Let $\mathcal{B} := \{\tilde{D} \,|\, D$ is a domain for a crosscut $Q\}$. Carathéodory [10] has proved that with this topology the set of prime ends of A^{out} is homeomorphic to a circle S^1. We call the circle defined by the prime ends of A^{out} a *circle of prime ends of* A^{out} and denote it by S^1_{out}.

A similar construction using prime ends in A^{in} defines a *circle of prime ends of* A^{in} and will be denoted by S^1_{in}.

Theorem 4.1. *Assume that the annulus $A := S^1 \times I$, where I is an interval, admits a homeomorphism onto the image $F : A \hookrightarrow A$, satisfying the following conditions:*

1. *there is a globally attracting invariant set $S \subset A$ which separates A into two open sets A^{out} and A^{in};*
2. *F maps A^{out} to A^{in} and A^{in} to A^{out};*
3. *$F^2(x, y) = (F_1(x, y), F_2(x, y))$ satisfies the twist condition*

$$\frac{\partial F_1}{\partial y} < 0. \tag{29}$$

Then for any $z \in A$ the rotation number $\rho(z) = \rho$ independent of z.

Proof. As a first step we define the dynamics induced by F^2 on the sets of prime ends S^1_{out} and S^1_{in}. We observe that given a chain of cross-cuts $\{Q_n\} \subset A^{out}$ the image $\{F^2(Q_n)\} \subset A^{out}$ is a chain of cross-cuts. Furthermore, since F^2 is a homeomorphism, the division property of chains is preserved by F^2. Thus a chain representing a prime end maps by F^2 to a chain representing another prime end. Therefore, if e is a prime end in A^{out} then $F^2(e)$ is another prime end, and this notation is unambiguous. Since F^2 is a homeomorphism it induces a homeomorphism $g_{out} : S^1_{out} \to S^1_{out}$. A similar construction shows that F^2 induces a homeomorphism $g_{in} : S^1_{in} \to S^1_{in}$. Since these maps are homeomorphisms, there is a unique rotation number ρ^{out} for the map g_{out} and a unique rotation number ρ^{in} for the map g_{in}. Since F^2 satisfies the twist condition, the result of LeCalvez [30], following earlier results of Birkhoff [7], shows that for any $z \in A$ the rotation number $\rho(z) \in [\rho^{in}, \rho^{out}]$. To finish the proof we will show that $\rho^{in} = \rho^{out}$.

Indeed, we notice that the homeomorphism F maps a chain of cross cuts $\{Q_n\} \subset A^{out}$ to a chain of cross cuts $\{Q'_n\} \subset A^{in}$. Since F is a homeomorphism, it maps prime ends of A^{out} to prime ends of A^{in}. Thus, there is a commutative diagram

$$\begin{array}{ccc} S^1_{out} & \overset{g_{out}}{\to} & S^1_{out} \\ \downarrow F & & \downarrow F \\ S^1_{in} & \overset{g_{in}}{\to} & S^1_{in} \end{array}.$$

It follows that the maps g_{out} and g_{in} are conjugate and thus their rotation numbers ρ^{out} and ρ^{in} are the same. □

4.2. Annulus Map for the IF model

We now wish to apply Theorem 4.1 to the annulus map that arises from the IF model with refractory periods and interspike interval threshold modulation included. With the function G defined by (28) and covering the annulus map F, we have the following theorem.

Theorem 4.2. *Consider the threshold function $g = g(t - \tau_n, \Delta_n)$ in the IF model (1) which satisfies assumptions (2)-(4). Assume that the f defined in (9) is continuous.*

Then there is an annulus $A_0 \subset A$, with $f(A) \subset A_0$, such that the restriction of the annulus map F to A_0 has the following properties

1. *F is a homeomorphism onto the image;*
2. *there exists an attracting invariant set $\mathcal{S}$ which separates the annulus A into A^{out} and A^{in};*
3. *F maps A^{out} to A^{in} and A^{in} to A^{out};*
4. *F^2 satisfies the twist condition (29).*

Remark 4.3. The assumption that f is continuous is restrictive since it requires, roughly, that the circle maps $f(\tau_n, \Delta_n)$ with Δ_n fixed, belong to set $\mathbf{A}$ for all Δ_n. This set has non-empty interior and its size depends on the particular choice of the threshold function g. As is clear from Theorem 4.1 however, this assumption needs to be satisfied only in some small neighbourhood of the set $\mathcal{S}$. Since we do not know where the set $\mathcal{S}$ is located, this sharper condition is hard to verify, but we expect that it will be satisfied for most choices of parameters. The results from the previous section give a way to verify the continuity of f for a given form of the threshold function g by checking that all circle maps $f(\tau_n, \Delta_n)$, with Δ_n fixed, belong to the set $\mathbf{A}$.

Proof of Theorem 4.2. We first list some consequences of the continuity assumption on f. By Corollary 2.5 at the time of fire we must have $H_{\tau_{n+1}}(\tau_{n+1}, \tau_n, \Delta_n) \leq 0$. However, since $f(\tau_n, \Delta_n)$ is continuous for all (τ_n, Δ_n) we must have that

$$H_{\tau_{n+1}}(\tau_{n+1}, \tau_n, \Delta_n) < 0.$$

On the other hand, by assumption (3)

$$\frac{\partial H}{\partial \Delta_n} = \frac{\sigma}{S} e^{\sigma \tau_{n+1}} \frac{\partial g}{\partial \Delta_n} < 0.$$

Finally, from the Implicit Function Theorem we get

$$\frac{\partial f}{\partial \Delta_n} = -\frac{\frac{\partial H}{\partial \Delta_n}}{H_{\tau_{n+1}}} < 0. \tag{30}$$

1. F **is homeomorphism onto the image** We have assumed that the map f is continuous. Since G has the form $G = (f, f - \tau_n)$, it is continuous as well and the induced annulus map F is also continuous.
   We show that F is injective. Consider an arbitrary element of $(\tau', \Delta') \in A_0$. We seek the values (τ, Δ) such that

   $$(\tau', \Delta') = G(\tau, \Delta) = (f(\tau, \Delta), f(\tau, \Delta) - \tau).$$

   First we note that comparing second components we get

   $$\Delta' = f(\tau, \Delta) - \tau = \tau' - \tau$$

   from which we solve $\tau = \tau' - \Delta'$. Since τ' is only determined up to multiples of 2π, the same holds for τ. With the τ value determined, we need to solve

   $$\tau' = f(\tau, \Delta)$$

   for Δ. By (30) and the Implicit Function Theorem there is a function q such that $\tau' = f(\tau, q(\tau', \tau))$. In other words $\Delta = q(\tau', \tau)$. By Lemma 2.1 this solution is unique, even if we change τ and τ' to $\tau + 2\pi$ and $\tau' + 2\pi$ respectively.
2. F **is orientation reversing:** Computing the Jacobian of F yields:

   $$DF = \begin{bmatrix} \frac{\partial F}{\partial \tau_n} & \frac{\partial F}{\partial \Delta_n} \\ \frac{\partial F}{\partial \tau_n} - 1 & \frac{\partial F}{\partial \Delta_n} \end{bmatrix}$$

   and the determinant is,

   $$det\ DF = \frac{\partial f}{\partial \tau_n}\frac{\partial f}{\partial \Delta_n} - (\frac{\partial f}{\partial \tau_n} - 1)\frac{\partial f}{\partial \Delta_n} = \frac{\partial f}{\partial \Delta_n}$$

The last expression is negative by (30), which implies that the determinant is always strictly negative and thus the map F is orientation reversing. It follows that F^2 is orientation preserving.

3. **There exists an invariant set** S **which separates** A **to** A^{out} **and** A^{in} **and** F **maps** A^{out} **to** A^{in} **and** A^{in} **to** A^{out} We first define annulus A_0. Let

$$\alpha := 2 \sup_{\tau_n}(f(\tau_n, \Delta_{abs}) - \tau_n).$$

By (30)

$$\frac{\partial \Delta_{n+1}}{\partial \Delta_n} = \frac{\partial f(\tau_n, \Delta_{abs}) - \tau_n}{\partial \Delta_n} = \frac{\partial f}{\partial \Delta_n} < 0$$

and so the second component of the image $G(A)$ is always less than or equal to $\alpha/2$. Since the inequality above is strict it follows that the second component $G(\tau, \alpha)$ is strictly bigger than Δ_{abs} for all τ. We define $A_0 := S^1 \times [\Delta_{abs}, \alpha]$. For notational convenience, we set $U_0 := A_0$ and we let $U_n := F^n(U_0)$. By the previous argument about the covering map G,

$$U_1 \subsetneq U_0$$

is a strict subset of U_0. Clearly $U_1 \supset U_2 \supset U_3 \supset \ldots$ is a nested sequence of compact, connected, non-empty subsets of A. Therefore the set

$$S := \bigcap_{i=1}^{\infty} U_i$$

is a non-empty, compact and connected set; in other words, a continuum. Since U_1 is a homeomorphic image of an annulus U_0, that separates $S^1 \times \Delta_{abs}$ from $S^1 \times \alpha$, the set $A \setminus U_1$ has two components, A_1 and B_1, such that

$$S^1 \times \Delta_{abs} \subset A_1 \text{ and } S^1 \times \alpha \subset B_1.$$

Let A_i be the component of $U_0 \setminus U_i$ containing A_1, and let B_i be the component of $U_0 \setminus U_i$ containing B_1. Since F^2 is orientation preserving it is easy to see that

$$F^2(A_i) = A_{i+2} \quad \text{and} \quad F^2(B_i) = B_{i+2}. \tag{31}$$

Let $A^{in} = \bigcup_{i=i}^{\infty} A_i$ and $A^{out} := \bigcup_{i=1}^{\infty} B_i$. Since A_i and B_i are open, so are A^{out} and A^{in}. Since F^2 is a homeomorphism $A^{in} \cap A^{out} = \emptyset$. Indeed, if $x \in A^{in} \cap A^{out}$, then $x \in A_i \cap B_j$ for some i and some j. Assume without loss of generality that $i \geq j$. Using (31) we get, depending on the parity of i, either $F^{-i+1}(x) \in A_1 \cap B_{j-i+1}$ or $F^{-i+1}(x) \in B_1 \cap A_{j-i+1}$. Since $B_{j-i+1} \subset B_1$ and $A_{j-i+1} \subset A_1$, and $A_1 \cap B_1 = \emptyset$ we arrive at a contradiction. Therefore $A^{in} \cup A^{out} \cup S = A$ and these sets are mutually disjoint.

It remains to show that S separates A^{out} and A^{in}. Assume, by contradiction, that S does not separate A^{out} and A^{in} and so there exists a path $\gamma : [0, 1] \to A_0$ with $\gamma(0) \in A^{in}$, $\gamma(1) \in A^{out}$ and $\gamma([0, 1]) \cap S = \emptyset$. Let $P_{in} \subset [0, 1]$ be the set of all t such that $\gamma(t) \in A^{in}$ and let $P_{out} \subset [0, 1]$ be the set of all t such that $\gamma(t) \in A^{out}$. We first note that since $\gamma([0, 1]) \cap S = \emptyset$ we have $P_{in} \cup P_{out} = [0, 1]$. Furthermore, both A^{in} and A^{out} are open and thus the sets P_{in} and P_{out} are open. Finally, $\gamma(0) \in A^{in}$ and $\gamma(1) \in A^{out}$, and so both P_{in} and P_{out} are non-empty. Since P_{in} and P_{out} are disjoint, they form a separation of a connected set [0, 1]. This is a contradiction.

4. **F^2 satisfies the twist condition**
To show that F^2 satisfies the twist condition we consider the second iteration of F (see (10)).

$$\begin{aligned}(\tau_{n+2}, \Delta_{n+2}) &= (F_1(\tau_n, \Delta_n), F_2(\tau_n, \Delta_n)) \\ &= (f(\tau_{n+1}, \Delta_{n+1}), f(\tau_{n+1}, \Delta_{n+1}) - \tau_{n+1})).\end{aligned}$$

Differentiating F_1 with respect to Δ_n yields

$$\frac{\partial F_1}{\partial \Delta_n} = \frac{\partial f}{\partial \tau_{n+1}} \frac{\partial \tau_{n+1}}{\partial \Delta_n} + \frac{\partial f}{\partial \Delta_{n+1}} \frac{\partial \Delta_{n+1}}{\partial \Delta_n}$$

Given the form of (10) we get

$$\frac{\partial \tau_{n+1}}{\partial \Delta_n} = \frac{\partial f}{\partial \Delta_n} \quad \text{and} \quad \frac{\partial \Delta_{n+1}}{\partial \Delta_n} = \frac{\partial f}{\partial \Delta_n}.$$

Therefore, we can factor out $\frac{\partial f}{\partial \Delta_n}$ and are left with

$$\frac{\partial F_1}{\partial \Delta_n} = \frac{\partial f}{\partial \Delta_n}(\tau_n, \Delta_n) \left(\frac{\partial f}{\partial \tau_{n+1}}(\tau_{n+1}, \Delta_{n+1}) + \frac{\partial f}{\partial \Delta_{n+1}}(\tau_{n+1}, \Delta_{n+1}) \right). \tag{32}$$

By (30) the first term is negative. We turn our attention to the remaining partial derivatives. These can be calculated explicitly from the function H and yield,

$$\begin{aligned}&\left(\frac{\partial f}{\partial \tau_{n+1}} + \frac{\partial f}{\partial \Delta_{n+1}} \right) (\tau_{n+1}, \Delta_{n+1}) \\ &= \sigma e^{\sigma \tau_{n+1}} (1 + B \cos(\tau_{n+1})) - \frac{\sigma}{S} \frac{\partial g}{\partial \tau} e^{\sigma \tau_{n+2}} + \frac{\sigma}{S} \frac{\partial g}{\partial \Delta_{n+1}} e^{\sigma \tau_{n+2}} \\ &= \sigma e^{\sigma \tau_{n+1}} (1 + B \cos(\tau_{n+1})) - \frac{\sigma}{S} e^{\sigma \tau_{n+2}} \left(\frac{\partial g}{\partial \tau} - \frac{\partial g}{\partial \Delta_{n+1}} \right).\end{aligned}$$

The assumption (4) implies that the last bracket is negative and hence

$$\left(\frac{\partial f}{\partial \tau_{n+1}} + \frac{\partial f}{\partial \Delta_{n+1}} \right) (\tau_{n+1}, \Delta_{n+1}) > 0.$$

This implies that the twist condition (32) holds.. Therefore, F^2 is an orientation preserving twist map.

□

Corollary 4.4. *Under the assumptions of Theorem 4.2 the map $F : A_0 \to A_0$ admits a unique rotation number.*

Proof. Theorem 4.2 verifies the assumptions of Theorem 4.1. □

5. Conclusions

We generalised the integrate-and-fire model of a neuron by modifying the threshold function to include absolute and relative refractory periods and the effects of adaptation. We modelled the latter by assuming that a long interspike interval tends to lower the threshold and a short interspike interval increases the threshold. The assumptions on the threshold functions are very general and biologically justified. In particular, we do not assume a particular functional form of the threshold and the class of thresholds satisfying our assumptions is quite broad.

Our first result is a generalisation of the work of Keener *et. al.* [26]. In contrast to the constant threshold considered in Keener *et. al.* [26], we assume that the threshold function is very large immediately following a spike and then decreases monotonically to a constant value Θ. This models absolute and relative refractory periods. Even with the more general threshold function we obtain an analogous result to that of Keener *et. al.* [26]. For all parameter values and all threshold functions satisfying the assumptions above and when forced by a periodic stimulus, either the model stops firing or the function relating consecutive spike times is monotone on its image. As a consequence, the rotation number associated to this function is always unique and chaotic behaviour (chaotic spiking) is ruled out. In the process of revising this paper we have learned of a recent paper by R. Brette [8], which overlaps considerably with this result. Contrasting our model with the more general one presented there, it is seen that our model is leaky (assumption (H1) in [8]), but it does not satisfy assumption (H2) in [8], since we allow the constant B to be greater than one. The Theorem 3 of [8] is analogous and more general to our Lemma 3.3 and it is proved under either assumption (H1) or the assumption (H2). As corollary of Theorem 3 of [8] one can obtain the result of our Theorem 3.1. The analog in our paper to Theorem 2 of [8], which is a key result needed to prove Theorem 3, is Lemma 2.4. The only advantage of our result over a more general result of [8] is the Theorem 3.5, which shows explicit regions in parameter space in which the resetting function f is continuous and monotone, piecewise continuous and monotone, and non-monotone respectively.

Our second result concerns modelling adaptation of the threshold function in addition to modelling refractory periods. With the threshold depending on two variables, the map relating consecutive spikes depends not only on the previous spike time, but also on the previous interspike interval. This map is a covering map for an annulus map. We prove that this map, under biologically justified assumptions, is orientation reversing and its second iterate satisfies the twist condition. We prove a general result for annulus homeomorphisms with these properties, which states that such a homeomorphism admits a unique rotation number. We then apply this general result to our map stemming from the integrate-and-fire model.

The fact that the integrate-and-fire model with both refractory periods and adaptation always admits a unique rotation number is surprising. The dynamics of general annulus maps can be quite complicated [7,30] and rotation numbers may form nontrivial intervals in which case chaotic behaviour is present [24].

The second reason why this result is interesting is that Chacron *et. al.* [13, 14] studied the integrate-and-fire model with threshold adaptation, which they modelled using threshold fatigue. They provide convincing numerical evidence and some analytical evidence that the annulus map in their model exhibits chaotic dynamics. In their analysis they also construct an annulus map, which uses fatigue as a radial variable. Our annulus map uses the previous interspike interval as the radial variable and in both cases the phase variable is the phase of the fire. It seems that the key aspect of our model, which may be responsible for a lack of chaos, is the monotone dependence of the radial variable with respect to phase variable. This difference is more subtle when considered on the level of the differential equations defining these two IF models. In our model the reset value of the threshold depends monotonically on the last interspike interval and the form of threshold function decaying towards steady state is arbitrary. The level of the threshold (fatigue) in Chacron *et. al.* [13, 14] after the spike depends monotonically on the level of the fatigue before the spike and afterwards the threshold decays exponentially towards its steady state value. The key difference between the two models is that the reset value of the threshold in Chacron *et. al.* [13, 14] also depends on the value of voltage $u(t)$ at the time of spike, while in our model the threshold reset value depends only on the time since the last spike. Thus, in both cases the threshold reset value is state-dependent, but the state of the neuron is defined differently.

Given the nature of these findings and others which cite chaos as being intrinsic to neural cells [37, 3, 22, 18], our results suggest that this chaotic behaviour may not be due to refractoriness or threshold adaptation which depends only on the time since the last spike.

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