First Draft Research Paper

Abstract:

Bursting oscillations are prevalent in the Nervous System. Phase Response Curves (PRCs) are studied and utilized to explain the oscillatory behavior of neurons involved in the Nervous System of complicated organisms found in nature. We study the oscillatory bursting behavior of the *Cancer borealis* and exploit the properties of a square bursting model to describe the phenomena of periodic bursting. We break up the bursting dynamics within a period and analyze them separately and independently to predict the next burst. Standard spike analysis and PRCs are used to construct the full PRC of the bursting oscillation. We derive conditions for which addition, subtraction, and truncation regularly occur, and modify our method for these special cases. The method described in this paper is beneficial because it utilizes the construction of standard spike PRCs to develop more complicated bursting oscillatory PRCs.

Introduction:

Oscillators and periodic behavior are frequently found in nature. Neurons are known to exhibit a variety of oscillatory dynamics. Our studies involve the rhythmic motor patterns in the crustacean Stomatogastric Nervous System (STNS). Periodic bursting was found in the AB - PD coupled neuronal oscillator of the *Cancer borealis*. This coupled neuron is the pacemaker of the pyloric rhythm recorded from the Stomatogastric Ganglion (STG), located in the STNS of the *Cancer borealis*. The STG consists of an intricate network of neurons responsible for the sorting of food particles before they are further digested. Data is collected from recording the PD neuron in the STG using standard laboratory procedures of dissection and electro-physiological recordings.

Bursting oscillations are characterized by an active phase of condensed spikes, and a silent phase of steady resting behavior as shown in figure 1. These bursts occur with a constant period which makes it convenient to study the periodic behavior using Phase Plane Theory and the Phase Response Curve (PRC). The PRC is a plot displaying phase shifts of period due to a singular perturbatory stimulus along the period. With the knowledge of the PRC we can predict future states of the oscillation given certain input stimulus along its period. This can be accommodating when describing more complicated neuronal networks and coupled neurons, where there are multiple stimuli from linked neurons.
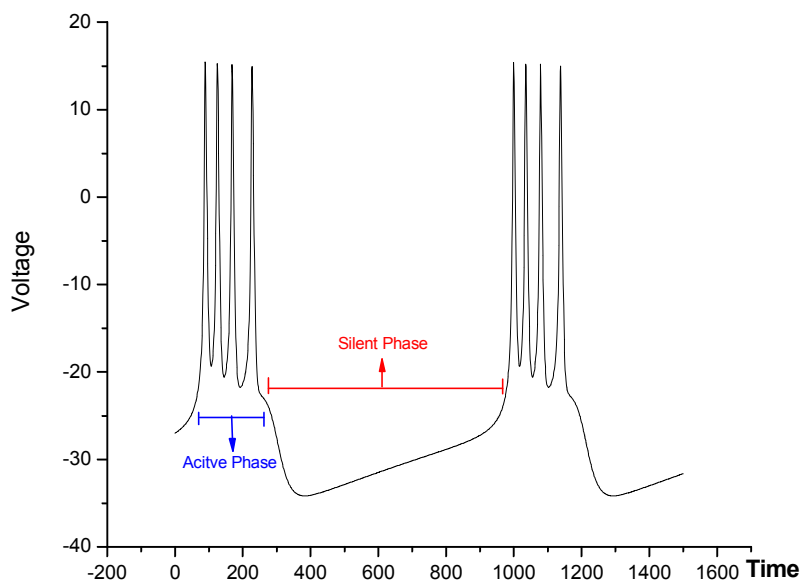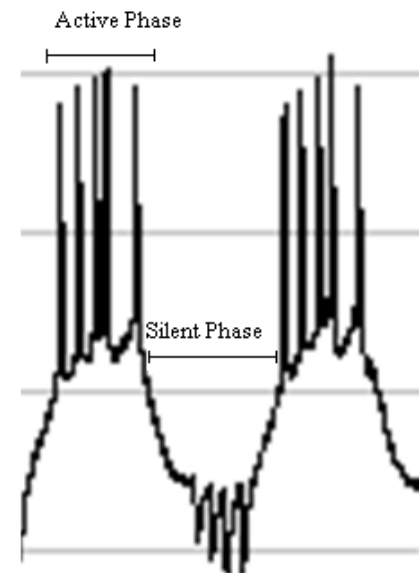
Model Voltage Trace

Fig. 1. Voltage trace of a bursting period is shown of the model (above) and the PD recording (right). The active phase composed of rapid, condensed spikes. The silent phase consists of steady, resting behavior.

Mathematical models are often used in understanding bursting oscillations. We used a square bursting oscillator with similar properties to the PD neuron. This is a modified Morris – Lecar Model associated to a slow variable calcium current. This model is governed by a set of differential equations with a stable periodic solution. This is a crucial element that exists in both the model and the neuron, which guarantees that a solution will always tend to this periodic solution. In this paper we will discuss some of the dynamic properties found in periodic bursting

from studying the PRC of recordings taken from the PD neuron of the *Cancer borealis* and the model described with similar relevant properties.

The goal and objective of our research is to develop a simple method of constructing the PRC of a bursting oscillator. A bursting oscillation is complicated to analyze and involves many anomalies. The spiking PRC is relatively standard and simple to create and interpret. We take a spike – to – spike approach to the burst and construct coherent PRCs. We consider the PRC over sections of the period in an attempt to describe the full PRC. We break up the period into the active phase or fast dynamics and silent phase or slow dynamics, and then try to understand them independently. We can then patch them together to understand the full dynamics. Another phenomenon we discovered was the addition and subtraction of spikes within the burst. Under certain conditions on the parameters of the model we see an extra or the loss of a spike. With further investigations we try to generalize these conditions. Concepts of the adjoint theory, the infinitesimal PRC, are utilized. We apply basic phase plane analysis and geometric aspects to Ermentrout's *Chapter 7 Neural Oscillators 1 Weak Coupling* **[1]** model in examining the spikes within the burst. For these special circumstances we modify our method of constructing the full PRC to incorporate the extra or missing spike.

This paper contains a brief description of the Cancer borealis and the PD neuron, and includes an explanation of relevant procedures used in the laboratory. We show methods of construction for our different PRC plots. There is a brief discussion of the model and the phase plane analysis. The concept and method used in developing the full PRC using the analysis of the pieces is introduced and fully explained. Then evidence of spike addition and subtraction is shown and general conditions are derived. Modifications to our method are shown to incorporate the addition and subtraction of spikes within the burst. We then relate this and earlier results to describe the full PRC and its properties.

Methods:

Biological Aspect and Laboratory Procedures: The stomatogastric ganglion (STG) consists of a network of neurons which control the muscles of the stomach. We focus on the pyloric rhythm, one of the rhythms produced by the STG. The pyloric rhythm is a three part cycle consisting of a large sized burst of impulses from the LP neuron, followed by a small burst of impulses from the PY neuron, and end in a medium burst of impulses from the PD neuron. This recording is usually taken from the *lvn* of the nerve. After we extract the STG from the *Cancer borealis* and keep it in a Petri dish under physiological saline of low temperature and certain pH (It should look like Figure 2), we isolate the *lvn* with a vaseline well. A potential difference is created between the neighborhood surroundings of the *lvn* inside the well and the outside of the well. An electrode is placed inside the well and the voltage difference is recorded. The recording obtained by the procedures above is called an extra – cellular recording. The *stn* is the section of the ganglion where the pyloric neurons can be found. To get an intra – cellular recording of individual neurons we must desheath the *stn*. All neurons are then exposed and we are free to take readings by positioning an electrode proximate to the neuron. To identify the PD neuron we fit the bursting intra – cellular recording to the PD complex of the extra – cellular pyloric rhythm. This will reveal the PD neuron because it is easy to identify the PD impulse from the pyloric rhythm; the simultaneous intracellular burst is the PD nerve (Figure 3). We isolated the PD neuron to prevent interference and input stimuli from synaptic neurons by adding pharmaceutical agents such as Tetrodotoxin (TTX) or Picrotoxin. Another more time consuming method is to find the LP neuron (which is the only synaptic linked neuron) and hyperpolarize it to suppress it from spiking. These procedures allowed the PD neuron to oscillate with minimal natural external inputs.
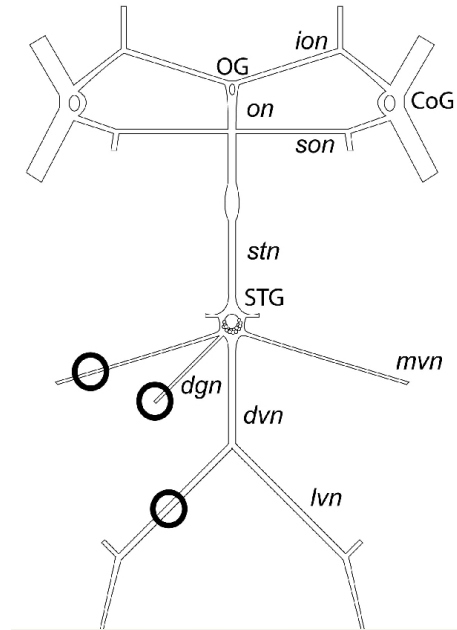
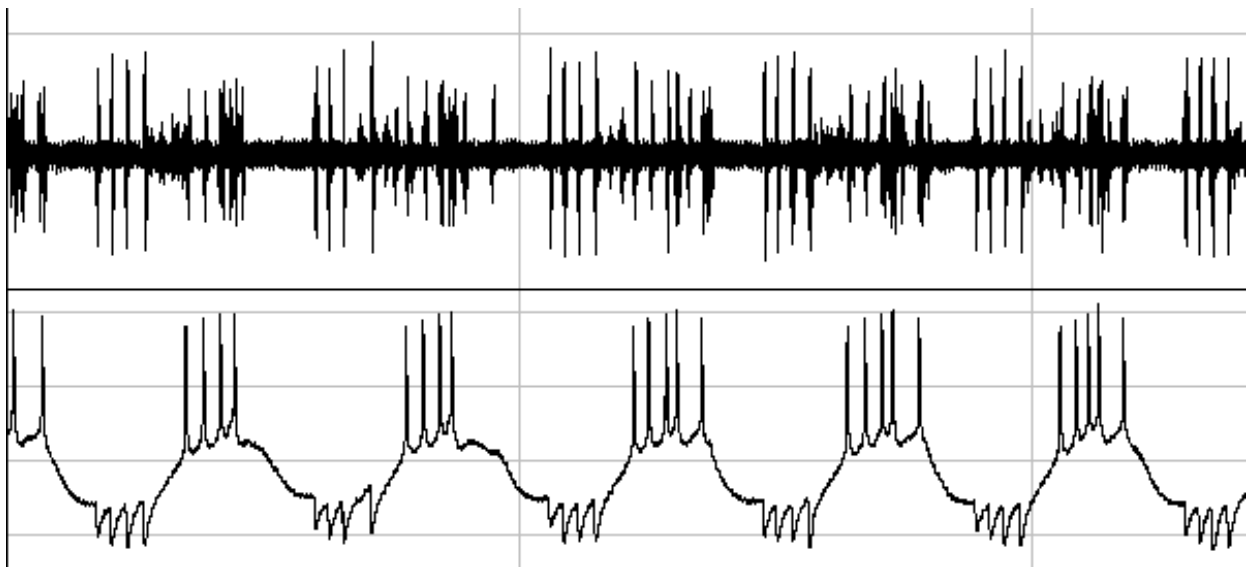**Fig. 2.** Architecture of the Stomatogastric Ganglion (STG) **[2]**

Fig. 3. The intra – cellular PD burst is shown above and it occurs simultaneously with the medium sized PD impulse from the pyloric rhythm on the bottom. The pyloric rhythm consist of the LP (large impulse), PY (small impulse), and PD (medium impulse) tri – phasic rhythm. These recordings are time scaled.

Mathematical Concepts and General Definition of PRC: The PRC is a plot of the period shift due to a perturbation. If we normalize by the period we can describe points along a period by its phase. Given perturbations along the phases of the period we can record the time shift of the next burst. Let's call P_o the period of the unperturbed oscillator, this will include the time duration between the start of a spike to the start of the next spike. The perturbation or stimulus input is measured from the start of the spike (P_p) and is normalized to represent the phase of perturbation, P_p/P_o. The new period after an input stimulus P' is measured, in the same way, from the start of the spike (These definitions are portrayed in Figure 4a). Using these definitions we can call the period shift or difference $\Delta P = P_o - P'$. We normalize this for our plot of the PRC ($\Delta P/P_o$ vs. P_p/P_o). By definition of period shift we can see immediate qualitative information. If ΔP is positive we have an advance in period due to the perturbation. Likewise if ΔP is negative we see a delay in period. In short if $\Delta P > 0$ we should see an advance in period of the next spike, where as if $\Delta P < 0$ there would be a delay in the period. The qualitative information held in the plot of a PRC describes approximate cycle delay or advance due to the perturbation applied. This can be applied to a bursting oscillator measuring a period from the start of a burst to the start of the next burst as shown in figure 4b. These general definitions and methods were applied in the construction of PRCs for the biological recordings of the *Cancer borealis* and the Modified Morris – Lecar Model.
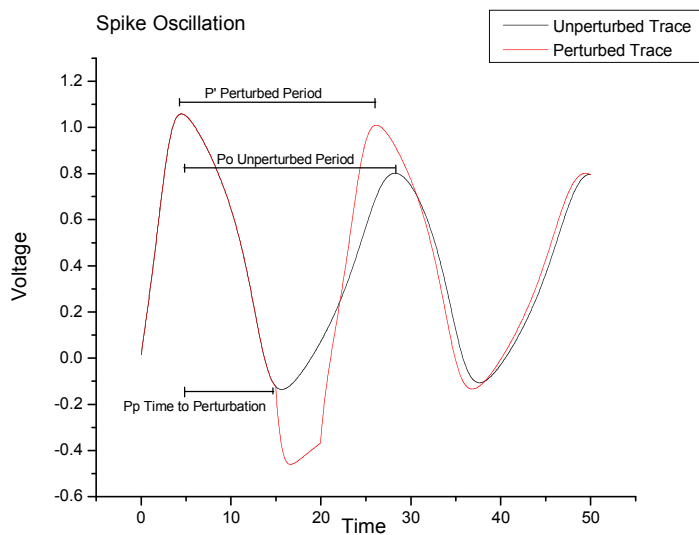

Fig. 4a. Voltage trace illustrating characteristics used in defining the spike PRC
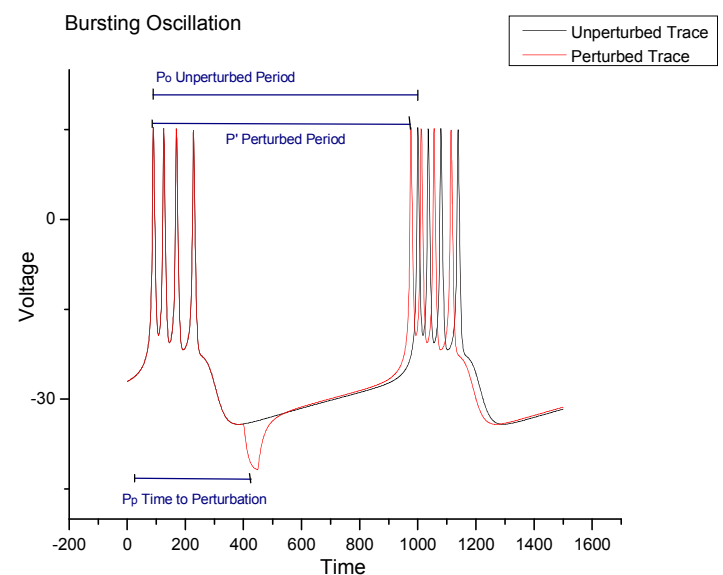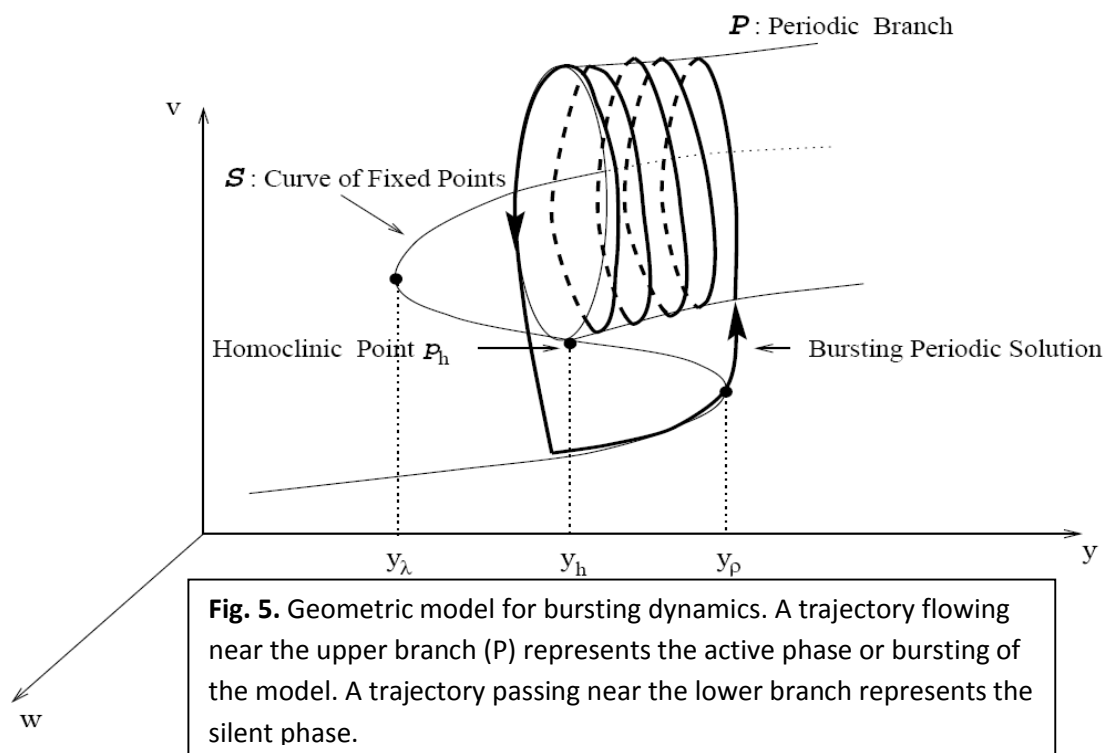

Fig. 4b. Voltage trace illustrating characteristics used in defining the burst PRC

Software and PRC of Biological Recordings: Phase Response, a lab software created by Farzan Nadim, was used to calculate the PRC of the *Cancer borealis*. This software records the period of a selected cycle, and normalizes it to calculate the phase of points along the cycle. It then injects a given amplitude of current to the next cycle at a given phase calculated from the previous cycle. We defined the phase from 0 (the beginning of the burst) to 1 (the beginning of the next burst) and injected current at 0.1 intervals. We waited a minimum of 4 to 5 cycles in between inputs to give the oscillator time to return to steady state, and stabilize its period. The signals were recorded, saved, and later analyzed for the construction of the PRC. The signals were analyzed using Clampex, a widely-used data acquisition and analysis program for the control and recording of current-clamp experiments developed by Axon CNS Molecular Devices [3]. The PRC constructed here uses the same definitions given above. An obstacle we came across was the variability of the biological oscillator. Due to external conditions such as temperature of saline or other external frequencies the period was dynamic. To account for this we repeated the procedures several times and averaged them.

Model: The model we adopted, as mentioned earlier, is a modified Morris – Lecar **[Appendix]** with a slow variable calcium current. The 3 dimensional square burster model is comprised of the following ordinary differential equations as described in Lee & Terman's *Uniqueness and Stability of Periodic Bursting Solutions* **[4]**:

$$C\frac{dv}{dt} = f_1(v,w,Ca) = -\sum I_n + ms(t-\tau)$$

$$\frac{dw}{dt} = f_2(v,w,Ca) = \frac{\phi(w_\infty(v)-w)}{\tau_w(v)} \qquad (1)$$

$$\frac{dCa}{dt} = \varepsilon f_3(v,w,Ca) = \varepsilon(-\mu I_{Ca} - Ca)$$

Depicted above are the general equations of the 3D Morris – Lecar where *v* represent voltage potential, *w* represents the behavior of gated channels within the cell, and *Ca* represents the intracellular calcium. *C* is the capacitance, and *Σ I* represents the sum of current. *ms(t-τ)* represents the stimulus properties of the model, where *m* is the amplitude, *s* is composed of the product of two heavy side step functions giving impulse like behavior, and *t-τ* gives the duration of the perturbation. Notice the *ε* in the calcium differential equation, this is the "slow variable" of the calcium dynamics [ε ∈ (0,1)]. Figure 5 depicts a geometric model for bursting dynamics. The S shaped curve represents the set of fixed points. The lower branch consists of stable fixed points, and the middle branch of saddle points. The cylindrical surface of the upper branch represents the limit cycle behavior of periodic solutions. This is the essence of the burst. When a trajectory passes near the lower branch of stable fixed points it is attracted to a neighborhood moving to the right. This represents the silent or resting phase. The slow dynamics push the trajectory to the periodic branch at the right most point of the S shaped curve. The trajectory now passes near and around the periodic branch representing the rapid spike of the burst. This is the active phase. The trajectory must now pass through the homoclinic orbit to fall back to the silent phase. This represents one cycle of the bursting solution. A more formal and extensive description is given in David Terman's *An Introduction to Dynamical Systems and Neuronal Dynamics* [5].

Fig. 5. Geometric model for bursting dynamics. A trajectory flowing near the upper branch (P) represents the active phase or bursting of the model. A trajectory passing near the lower branch represents the silent phase.

Results and Dicussion:

PRC Piece By Piece: It is generally simpler to construct the PRC of a spike oscillation than it is for periodic bursting. We break our bursting oscillation into pieces to ease the effort of constructing the PRC of the full bursting oscillation. We use a spike analysis to describe the active phase. In figure 6 you will find how the period of a full burst is dissected. The period between spikes are labeled P_n where $n=1, 2, 3$. The period of the silent phase is P_{silent}. The period of the full burst is P_{full} and is obviously the sum of the periods that make it up:

$$P_{full} = P_1 + P_2 + P_3 + P_{silent} \qquad (2)$$

A Few Necessary Assumptions: It is reasonable to assume that the corresponding unperturbed periods are roughly constant through phase plane theory and concepts of limit cycles. One assumption that has to be made is that perturbations applied to the oscillator during a certain period duration will only cause a shift in the following spike without drastically affecting the oscillation as a whole. Given a perturbation we will have a change in the period of the full burst, P'_{full}. This is composed of the sum of the other periods but we will need to account for the change in period depending on location of perturbation. For example a perturbation in P_1 causes an advance or delay in the second spike and the other spikes shift accordingly without a change in their periods. Therefore a perturbation in P_1 causes a shift in the second spike changing the period to P'_1 and the period of the entire burst to P'_{full}. Here we will have $P'_{full} = P'_1 + P_2 + P_3 + P_{silent}$. An advance or delay in the second spike has caused a change in the corresponding period, P_1, and the period of the full burst P_{full}; the other periods (P_2, P_3, P_{silent}) remain the same but shift correspondingly. This is shown in figure 7 where Δt is the same for each shift.

Another assumption we make is that our perturbations do not cause an addition or subtraction of a spike; the number of spikes are constant. For perturbations that cause addition or subtraction of spikes complications are aroused that must be accounted for. This phenomenon of addition or subtraction of spikes will be addressed later. Intuitive conditions for which addition and subtraction will be derived and certain adjustments to the method will be made accordingly.
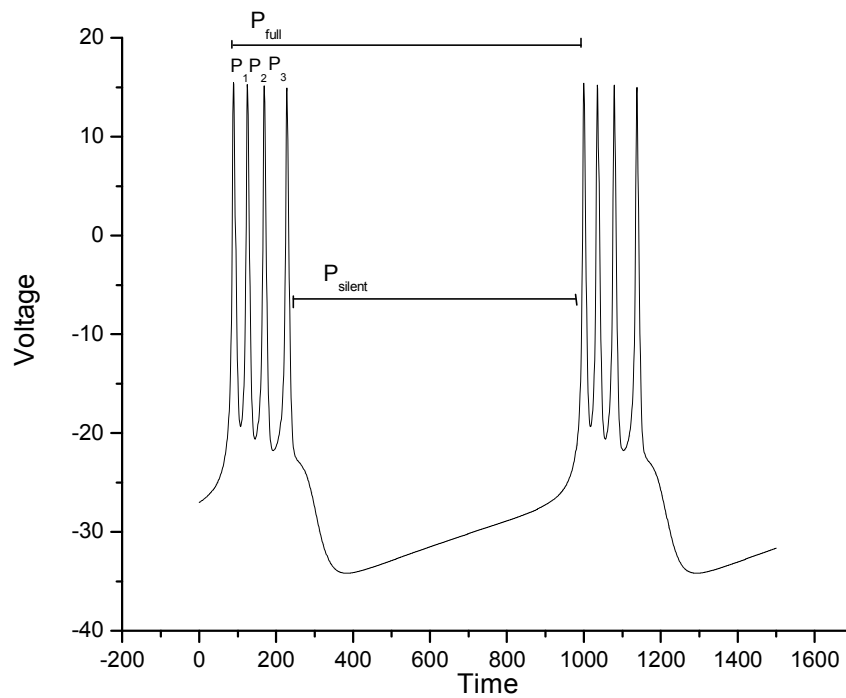
Fig. 6. Voltage trace illustrating the method of breaking up the full period of a burst. P_1 corresponds to the period between spikes 1 and 2. P_2 and P_3 are defined in the same way respectively. P_{silent} is the period of the silent phase. These periods sumed together are P_{full}, the period of the full burst.
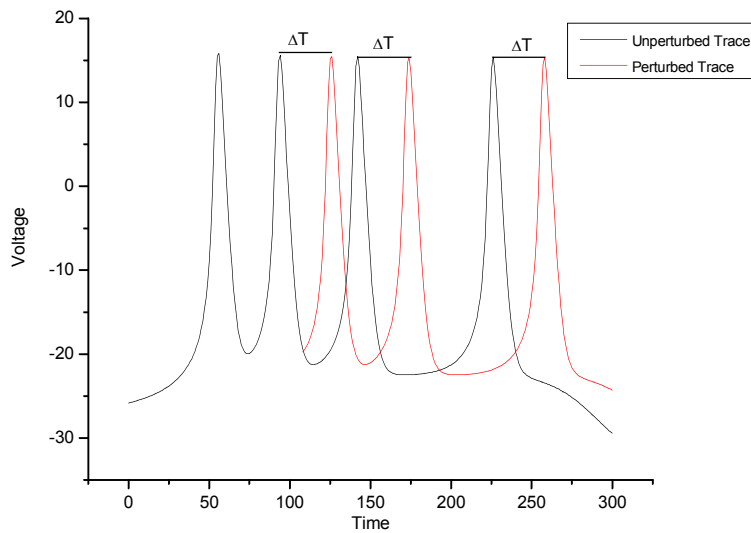

Fig. 7. A perturbation in between spike 1 and 2 causes a delay in the second spike by ΔT, but leaves the other spikes unaffected. They shift accordingly, this is shown where ΔT is the same. By comparison we can tell that P_2 and P_3 are unaffected.

As a reminder, the goal here is to predict the next burst just by the knowledge of the occurrences of the smaller piece. So far we have discussed the unperturbed periods P_1, P_2, P_3, P_{silent}, and P_{full}. These are easily attainable. With a perturbation we have P'_{full}, a shift in the full period. The location of the perturbation is also necessary and we have a corresponding shift P'_i, where $i = 1, 2, 3,$ or $silent$ depending on the location of the perturbation. We can calculate the PRCs of the broken periods easily since it is a spike PRC. These values are shown by $\varphi_i(\theta)$, the phase response as a function of the input phase and defined as:

$$\varphi_i(\theta) = \frac{P_i - P'_i}{P_i} \qquad i = 1, 2, 3, silent \qquad (3)$$

Knowing the corresponding PRCs we can obtain the shift of the pertaining period, P'_i. With simple algebra we find:

$$P'_i = P_i(1 - \varphi_i(\theta)) \qquad (4)$$

This allows us to get the shift in the next burst P'_{full}:

$$P'_{full} = \sum_n P_n + P'_i = \sum_n P_n + P_i(1 - \varphi_i(\theta)) \qquad (5)$$

Here *i* symbolizes the period which was perturbed and n symbolizes the unperturbed periods. Notice P'_{full}, "the unknown", is solved for "the knowns;" the smaller periods it is composed of P_n and P_i, and the PRC of the perturbed period $\varphi_i(\theta)$.

A More General Approach: We can solve for the PRC of the bursting oscillator in a general manner using a similar approach. All definitions and assumptions made above apply in this approach as well. We use a backwards approach to solve for the PRC of the bursting oscillator. Let us start with the definition of the PRC and assume the perturbation was applied between the first two spikes advancing or delaying P_1 to P'_1.

$$\varphi_{full}(\theta) = \frac{P_{full} - P'_{full}}{P_{full}} \tag{6}$$

Where
$$P_{full} = P_1 + P_2 + P_3 + P_{silent}$$

And
$$P'_{full} = P'_1 + P_2 + P_3 + P_{silent}$$

We can apply the definition to these and we are left with:

$$\varphi_{full}(\theta) = \frac{P_1 - P'_1}{P_{full}}$$

We can manipulate $\varphi_{full}(\theta)$ by dividing the top and bottom by $\frac{1}{P_1}$. Let $\frac{P_{full}}{P_1} = \hat{P_1}$ for convenience.

$$\varphi_{full}(\theta) = \frac{\varphi_1(\theta)}{\hat{P}_1}$$

We get an equation for the bursting oscillator's PRC in terms of the PRC of the first two spikes. Similarly we can derive an equation for a perturbation between the second and third spikes, third and fourth spikes, and in the silent phase. We will have the following respectively:

$$\varphi_{full}(\theta) = \frac{\varphi_2(\theta)}{\hat{P}_2} , \varphi_{full}(\theta) = \frac{\varphi_3(\theta)}{\hat{P}_3} , \varphi_{full}(\theta) = \frac{\varphi_{silent}(\theta)}{\hat{P}_{silent}}$$

This is easily generalized where the PRC of the full bursting oscillator is proportional to the PRC of the sectional period the perturbation is applied divided by $\hat{P}_i = \frac{P_{full}}{Pi}$:

$$\varphi_{full}(\theta) = \frac{\varphi_i(\theta)}{\hat{P}_i}$$

> Where *i (1, 2, 3, silent)* represents the location of the perturbation

(7)

Sufficient Conditions of Spike Addition and Spike Deletion: There are rarities when an additional spike appears in the burst or there is the loss of a spike. Complications occur with addition and subtraction of spikes, obviously amendments must be made in these cases. To consider this problem the conditions of their occurrence should be known. Under the conditions derived, our methods of construction will be modified to incorporate the extra or loss of spikes.

The trajectory depicted in figure 5 is a solution to the equations (1). We can call this trajectory Γ and is a stable manifold. We adopt the standard definition for the phase map $\Theta : M \rightarrow S^1$ where S^1 is the unit circle and Θ defines the phase or asymptotic phase of a point in M depending on whether the point is on Γ or in an appropriately defined neighborhood of Γ. The unit circle S^1 is depicted in figure 8, and points along S^1 represent phase of a point along the stable manifold Γ. We depict $\Theta = 0$ as the phase at which our burst begins and $\Theta = eb$ is the phase at which the burst ends. The spikes within our burst occur at phases between $\Theta = 0$ and $\Theta = eb$.
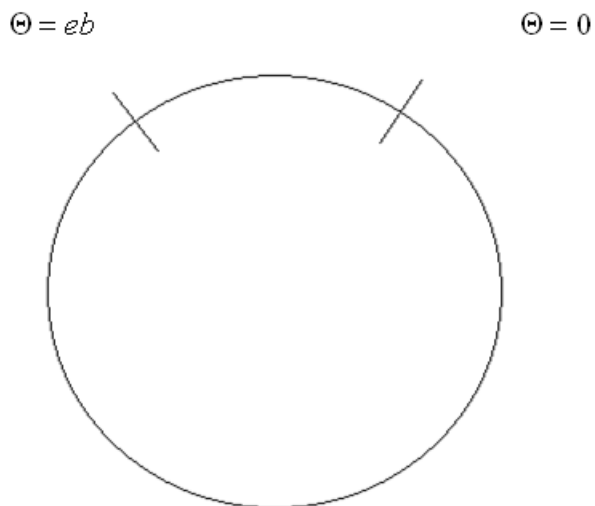
$$\Theta = eb \qquad\qquad\qquad \Theta = 0$$

Fig. 8. We show the unit circle S^1 that we have mapped our solution onto. $\Theta = 0$ is where we define our burst to begin and $\Theta = eb$ is where we define our burst to end. In our model we have four spikes which we can show with points along S^1.

We adopt the phase equation as Ermentrout **[ref]**: $\dot{\theta} = 1 + Z(\theta)I_p(\theta)$. Here $\dot{\theta}$ represents the flow of phase and $Z(\theta)$ is the adjoint or infinitesimal PRC and $I_p(\theta)$ is the perturbatory input. Notice with no input $I_p(\theta)$ is 0 and our equation describes a unit circle. Let θ_p be the phase of perturbation and θ_f be the phase point after perturbation and $\theta_p \in [0, \theta_{eb}]$, θ_{eb} being the phase at the end of a burst without any perturbation. If we are going to have spike addition, it is necessary that $\dot{\theta} < 0$ so that the phase point traces out old values again and allows the possibility of tracing the older spikes again. To rule out the possibility of spike addition we could require that $\dot{\theta} > 0$ for $\theta \in [0, \theta_{eb}]$. This requirement implies that $Z(\theta)I_p(\theta) > -1$. If we assume that the adjoint is strictly positive in some relevant region, we see that positive input or excitatory perturbations cannot cause spike addition since they satisfy the restriction. Notice that only negative input or inhibitory perturbations with strong values violate this restriction and cause spike addition; whereas small magnitude inhibitory input cannot cause spike addition. These conditions were reflected in our model.

To show conditions for the inputs which cause spike deletion we continue with our analysis. Let $0 < \theta_p < \theta_f < \theta_{eb}$ and define $\zeta = \dfrac{ISI_{max}}{T}$, where ISI_{max} is the maximum interval between two spikes within the burst. Define *T* as the period of the entire oscillation. To guarantee spike deletion we require that $\displaystyle\int_{\theta_p T}^{\theta_p T + \tau} \dot{\theta} dt = \zeta$, where τ is the duration of the perturbation. This is the same as saying $\theta_f - \theta_p = \zeta$, or that the phase point has been taken to a phase point that is at least equal to the maximum "phase length." We make substitutions and manipulate the interval to get:

$$\int_{\theta_p T}^{\theta_p T + \tau} (1 + Z(\theta)I_p(\theta))dt = \zeta \Rightarrow \int_{\theta_p T}^{\theta_p T + \tau} (Z(\theta)I_p(\theta))dt = \zeta - \tau \qquad (8)$$

Multiplying both sides by τ^{-1} and using the average value theorem of calculus we obtain:

$$\langle I_p Z \rangle = \frac{\zeta - \tau}{\tau} \tag{9}$$

Here we have given a constant measureable value to the average product of I_p and Z. The perturbation is usually a predetermined constant applied square pulse; this allows us to rearrange the equation like so:

$$I_p = \frac{\zeta - \tau}{\tau \langle Z \rangle} \tag{10}$$

We now have sufficient conditions on our perturbation or input current which cause spike deletion for when the perturbation duration, τ, is arbitrarily small. With a few modifications to our derivation we can derive similar conditions on the input current for spike addition. These conditions do not define all occurrences of spike addition and deletion; this is just an intuitive mechanism where spike addition and deletion can be seen.

Modifications Incorporating Addition and Subtraction: Now that we have an idea of when addition and subtraction occurs we can describe the changes that must be made to use our method of predicting the next burst. We can demonstrate this modification for addition with the following:

$$P'_{full} = \sum_n P_n + P'_i + P_a \tag{11}$$

This is a simple to concept where $\sum_{n} P_n$ represents the sum of the inter-spike periods which do not contain a perturbation; P'_i represents the inter-spike period with a perturbation; P_a is the new period due to a spike addition. The period due to an added spike is not always known, so a naïve but sufficient approach for spike addition is to measure the period created due to an addition and substitute this value for P_a. You can then continue the analysis as usual, and calculate P'_{full}. From this value, $\varphi_{full}(\theta)$ is calculated through simple algebra for the given input.

This can be a bit tricky for spike deletion because we don't know which spike has been deleted. Since our model only deals with four spikes, this can be managed easily by case. We will describe case 1 if a perturbation is applied in P_1 and a spike is deleted afterwards, equation (5) can be modified as follows:

$$P'_{full} = P'_1 + P_d + P_{silent}$$

The second case will occur if we perturb in P_2 causing spike deletion will result in only one remaining spike, (leaving P_1 and P'_2). We can use the above equation where $P_d = P'_2$. The third case is a perturbation applied in P_3 this can only cause burst truncation in which the burst ends abruptly. In a case of truncation we should measure the changed P_{silent}, and take the sum of the inter-spike periods to get P'_{full}.

In the cases of spike addition and deletion we obtain the phase response using the definition of a PRC, equation (6), with the value of P'_{full} calculated.

Concluding Remarks:

There are limitations to the technique described above. This approach is a good approximation for first order PRCs. First order oscillations are described as a perturbation where the trajectory comes back to steady state or before the trajectory reaches zero-phase (usually marks the start of a spike). Whereas a higher order perturbation occurs when the trajectory passes zero-phase before it comes back to steady state. These are depicted in a two dimensional model where the solution is represented by a stable limit – cycle.
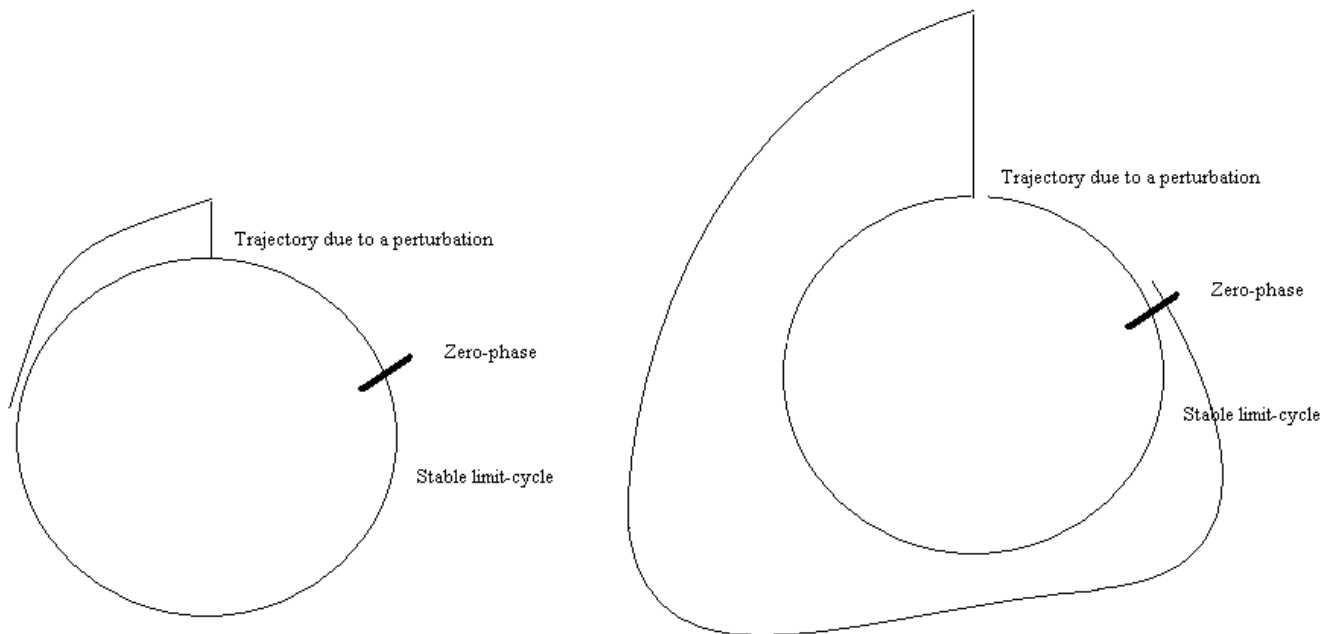

Fig. 9. The right picture shows a first order PRC where the trajectory returns to the limit-cycle before zero-phase. The left is a higher order PRC where the trajectory returns to limit-cycle after zero-phase.

We can improve upon the approach described by taking into account the changes on the other inter-spike periods due to earlier perturbations. We assumed the only period affected is the perturbation containing period. If we can come up with a way to consider the affects of perturbation due to all inter-spike periods following a perturbation, we can construct the full PRC more accurately and realistic. A way to do this is to fit a well defined function onto the PRCs of the inter-spike periods. I can apply this function to the second and third inter-spike periods taking into account the shift of the previous periods. This will give the new periods after a perturbation, and the sum of these gives a more accurate and realistic full period shift. This will result in a better approximation for the full PRC. This requires further research.

We have shown the construction of the full PRC described by breaking the period into parts and using spike PRCs is a beneficial technique because of the simplicity in calculate spike PRCs. The construction of spike PRCs are standard as opposed to the complexity of a burst PRC. It is also helpful when applying oscillatory perturbations within the period where there is a single perturbation in the inter-spike periods. This can be found in a neural network such as the *stg* when the active phases of two bursting oscillations are not in phase. Here the spikes of the active phases act as perturbations acting upon the others period so long as there is one perturbation in each inter-spike period. Our model gives a first ordered PRC approximation to any perturbed oscillation with a restriction upon the number of perturbations between each spike.

Appendix

Model Code used on XPP:

```
dv/dt = ( I - ICa-(gk*w+gkca*z)*(V-VK)-gl*(V-Vl)+m*(s(t-tau)))/c
dw/dt = phi*(winf(V)-w)/tauw(V)
dca/dt=pert*eps*(-mu*Ica-ca)
tau'=0
Ica=gca*minf(V)*(V-Vca)
z=Ca/(Ca+Ca0)
v(0)=-18.7
w(0)=.071
ca(0)=10.39
minf(v)=.5*(1+tanh((v-v1)/v2))
winf(v)=.5*(1+tanh((v-v3)/v4))
tauw(v)=1/cosh((v-v3)/(2*v4))
s(t)=heav(t)*heav(sigma-t)
param vk=-84,vl=-60,vca=120
param i=45,gk=8,gl=2,c=20
param v1=-1.2,v2=18,pert=1
param m=0,sigma=50 t0=931
#param_fig1-3 v3=2,v4=30,phi=.04,gca=4.4
param v3=12,v4=17.4,phi=.06666667,gca=4
param v3=12,v4=17.4,phi=.23,gca=4
param mu=.2,ca0=10,eps=0.005,gkca=.25
aux zbar=z
aux icaa=ica
aux vprime=( I - ICa-(gk*w+gkca*z)*(V-VK)-gl*(V-Vl)+m*(s(t-tau)))/c
aux prc=1-t/t0
aux phase=tau/t0
aux amp=m
@ xp=zbar,yp=v,xlo=0,xhi=1,ylo=-75,yhi=20,total=2000,dt=1,meth=gear,toler=1e-5
@ dtmax=5,dtmin=1e-10,bound=1000
@ back=white
Done
```

<u>References:</u>

[1] Ermentrout, *Chapter 7. Neural Oscillators* 1. *Weak Coupling,*

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