A scalar Poincaré map for struggling in *Xenopus* tadpoles

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Abstract

Synaptic plasticity is widely found in many areas of the central nervous system. In particular, it is believed that synaptic depression can act as a mechanism to allow simple networks to generate a range of different firing patterns. The simplicity of the locomotor circuit in hatchling *Xenopus* tadpoles provides an excellent place to understand such basic neuronal mechanisms. Depending on the nature of the external stimulus, tadpoles can generate two types of behaviours: swimming when touched and slower, stronger struggling movements when held. Struggling is associated with rhythmic bends of the body and is accompanied by anti-phase bursts in neurons on each side of the spinal cord. Bursting in struggling is thought to be governed by a short-term synaptic depression of inhibition. To better understand burst generation in struggling, we study a minimal network of two neurons coupled through depressing inhibitory synapses. Depending on the strength of the synaptic conductance between the two neurons, such a network can produce symmetric $n - n$ anti-phase bursts, where neurons fire n spikes in alternation, with the period of such solutions increasing with the strength of the synaptic conductance. Using a fast/slow analysis, we reduce the multidimensional network equations to a scalar Poincaré burst map. This map tracks the state of synaptic depression from one burst to the next, and captures the complex bursting dynamics of the network. Fixed points of this map are associated with stable burst solutions of the full network model, and are created through fold bifurcations of maps. We prove that the map has an infinite number of stable fixed points for a finite coupling strength interval, suggesting that the full two-cell network also can produce $n - n$ bursts for arbitrarily large n . Our findings further support the hypothesis that synaptic depression can enrich

the variety of activity patterns a neuronal network generates.

Keywords: *Xenopus*, Synaptic depression, Poincaré map, Dynamical system

1. Introduction

Short-term synaptic plasticity may have a role in burst activity in central pattern generators (CPGs). Short-term synaptic depression is commonly found in neuronal networks involved in the generation of rhythmic movements, such as in the pyloric CPG of the spiny lobster (Rabbah and Nadim, 2007), or in the lumbosacral cord of the chick embryo (Donovan et al., 1998). Synaptic depression modulates the strength of synapses in response in changes to the presynaptic firing frequency. At a high neuronal firing frequency, depression weakens the strength of synapses and therefore reduces the magnitude of the respective postsynaptic response. At low firing frequency, in contrast, it allows sufficient time for the synapse to recover from depression between spikes, leading to a stronger postsynaptic response. In reciprocal networks, synaptic depression has been shown to act as a “switch”, giving rise to a wide range of network dynamics such as synchronous and multi-stable rhythms, as well as fine tuning the frequency of network oscillations (Nadim and Manor, 2000; Nadim et al., 1999; Bose and Booth, 2011).

A switch between two CPG rhythms that is guided by synaptic depression can be observed in hatchling *Xenopus* tadpoles. Tadpoles select between two main behaviours in response to different types of skin stimuli. Swimming occurs in response to a brief touch or a single electrical pulse to the trunk (Clarke et al., 1984), and is accompanied by low-amplitude 12 to 25 Hz alternating left and right bending moves that progress from head to tail (Kahn et al., 1982). Alternatively if held, tadpoles produce struggling, with slower 2 to 10 Hz bending moves of the whole body that spread in the opposite direction, from the tail to the head (Kahn and Roberts, 1982). The switch from swimming to struggling is associated with a change from a pattern of low-frequency alternating single spikes in swimming at 12 – 25 Hz (Kahn et al., 1982), to one of alternating high-frequency bursting in struggling, with bursts occurring at periods ranging from 100 to 500 ms (Kahn and Roberts, 1982; Soffe, 1993). The synaptic depression substantially weakens synapses and guides the network rhythm during the high-frequency bursts in struggling. Both swimming and struggling are produced by two overlapping

33 spinal cord CPG networks that share some types of individual neurons. One
34 such shared class of neurons are the inhibitory commissural interneurons
35 (cINs), which have reciprocal depressing inhibitory synapses with neurons
36 on the opposite site of the spinal cord (Li et al., 2007).

37 It has been proposed that this synaptic depression of reciprocal inhibition
38 can act as a burst termination mechanism during struggling: while one side
39 of the spinal cord is firing, inhibition from cINs prevents the other side from
40 firing. Weakening of inhibition as a result of synaptic depression allows the
41 antagonistic side to be released, start firing, and terminate the ongoing burst.
42 This periodic process is believed to produce the rhythmic anti-phase bursts
43 found in tadpole struggling. Such anti-phase bursty rhythms have been previ-
44 ously replicated in a small half-centre neuronal network model that contains
45 the four main types of neurons active during struggling (Li et al., 2007):
46 ascending interneurons, repetitive firing descending interneurons, motoneu-
47 rons, and cINs. In this model each neuron population is approximated by
48 three biophysical neurons, so there are 18 cells in the network. In line with
49 Brown’s (1911) hypothesis of rhythmogenesis in the spinal cord, the model
50 relies on depression of reciprocal inhibition between cINs to act as a burst
51 termination mechanism. While the model in Li et al. (2007) reproduces the
52 struggling-like burst patterns qualitatively, burst rhythm generation in this
53 model has not been investigated systematically, nor does the model provide
54 a description for how depression controls the network dynamics.

55 To address these questions we reduce the complexity of the struggling net-
56 work to a simpler formulation of Brown’s (1911) rhythmogenesis hypothesis.
57 We study the mechanisms of burst generation in struggling using a generic
58 half-centre CPG that consists of two identical, tonically active neurons that
59 are coupled through inhibitory depressing synapses. Each neuron represents
60 a population of cINs on either side of the tadpole spinal cord. Our model re-
61 duction is based on the approach previously taken by Bose and Booth (2011),
62 where the dynamics of a similar two-cell reciprocal inhibitory network with
63 depression has been analysed. Bose and Booth (2011) relied on the methods
64 from geometric singular perturbation theory to separate the timescales of
65 the fast membrane, and the slow synaptic dynamics of the network to de-
66 rive one-dimensional conditions for the existence of stable anti-phase burst
67 solutions. While these conditions justify the existence of bursting, they do
68 not explain how such solutions are created nor what shapes their parameter
69 space. Here, we extend the analysis by Bose and Booth (2011) by construct-
70 ing a scalar Poincaré map which tracks the evolution of depression from one

burst to the next, and whose fixed points correspond to stable burst solutions of the two-cell network. Our map construction is motivated by the burst length map of a T-type calcium current, utilised in Matveev et al. (2007), which approximates the anti-phase bursting dynamics of a network of two coupled Morris-Lecar (Morris and Lecar, 1981) neurons. This network does not contain short-term synaptic depression, and burst termination is instead accomplished through the dynamics of a slow T-type calcium current which makes the single cells bursty, even in absence of network interactions.

This paper is organised as follows. First, we introduce the network of two neurons, and describe the properties of the single cell and synapse dynamics. We use numerical simulations of the network to provide an intuition for the range of possible burst dynamics the system can produce. Next, we state the simplifying assumptions and perform a fast-slow analysis of the single cell equations, resulting in an algebraic equation that uniquely determines the type of burst solution a network displays. Then, we analytically derive the first return map of the depression variable, first assuming that solutions consist of n spikes, and later relaxing this assumption. We end this work with a conclusion.

2. Model

2.1. Model Description

For numerical simulations we consider a pair of identical Morris-Lecar neurons (Morris and Lecar, 1981), with parameters adopted from Bose and Booth (2011). The source code is available at https://gitlab.com/bursting_map. The Morris-Lecar model is a set of two first-order differential equations that describe the membrane dynamics of a spiking neuron. The depolarisation is modelled by an instantaneous calcium current, and the hyperpolarisation by a slow potassium current and a leak current. The membrane potential v_i and potassium activation w_i of neuron i ($i, j = 1, 2$) is described by:

$$\dot{v}_i = f(v_i, w_i) - \bar{g}s_j(v_i - v_s), \quad (1)$$

$$\dot{w}_i = h(v_i, w_i). \quad (2)$$

Here v_s is the inhibitory reversal potential, and $\bar{g}$ and s_j are the maximal synaptic conductance and the synaptic gating, respectively, constituting

the total inhibitory conductance $\bar{g}s_j$ from neuron j to neuron i . Function $f(v_i, w_i)$ describes the membrane currents of a cell that include a constant current I , and three ionic currents: an instantaneous calcium current, a potassium current, and a leak current, with respective reversal potentials v_{Ca} , v_K , and v_L , as well as maximum conductances g_{Ca} , g_K , and g_L :

$$f(v_i, w_i) = -g_{Ca}m_\infty(v_i)(v_i - v_{Ca}) - g_Kw_i(v_i - v_K) - g_L(v_i - v_L). \quad (3)$$

The function $h(v_i, w_i)$ models the kinetics of the potassium gating variable w_i , and is given by

$$h(v_i, w_i) = \frac{w_\infty(v_i) - w_i}{\tau_w}. \quad (4)$$

The asymptotic functions m_∞ and w_∞ for the calcium and potassium conductances, respectively, are given by

$$m_\infty(v_i) = \frac{1}{2} (1 + \tanh((v_i - v_A)/v_B)), \quad (5)$$

$$w_\infty(v_i) = \frac{1}{2} (1 + \tanh((v_i - v_C)/v_D)). \quad (6)$$

All model parameters are given in Table 1.

Our mathematical analysis is performed on the equations of a single cell, which is why we will omit the subscripts i, j from here on. When the cells are uncoupled ($\bar{g} = 0$), the membrane dynamics are determined by the cubic v -nullcline ($v_\infty(v)$) with

$$v_\infty(v) = \frac{-g_{ca}m_\infty(v)(v - v_{ca}) - g_l(v - v_l) + I}{g_K(v - v_k)}, \quad (7)$$

and the sigmoid w -nullcline $w_\infty(v)$, satisfying $\dot{v} = 0$ and $\dot{w} = 0$, respectively. The two curves intersect along the middle branch of v_∞ , creating an unstable fixed point p_f with a surrounding stable limit cycle of period T (Figure 1A). Trajectories along that limit cycle have the familiar shape of the action potential (Figure 1B). The trajectory of an action potential can be dissected into four phases: (1) a silent phase, (2) a jump up, (3) an active phase, and (4) a jump down (see e.g. Ermentrout and Terman, 2010). During the silent phase the trajectory evolves along the left branch ($v < v_\theta$) of the cubic v -nullcline. Once the trajectory reaches the local minimum of v_∞ at (v_L, w_L) ,

Table 1: Parameter for coupled Morris-Lecar model.

Parameter	value
g_l	0.15 mS/cm ²
g_{Ca}	0.3 mS/cm ²
g_K	0.6 mS/cm ²
v_K	-70 mV
v_L	-50 mV
v_{Ca}	100 mV
v_A	1 mV
v_B	14.5 mV
v_C	4 mV
v_D	15 mV
I	6 μ A/cm ²
τ_w	100 ms
τ_d	1000 ms
τ_s	100 ms
v_θ	0 mV
v_s	-80 mV
λ	0.5
T	217 ms

125 it “jumps up” to the right branch, crossing the firing threshold v_θ . During
126 the active phase the trajectory then evolves along the right branch of the
127 cubic until it arrives at the local maximum (v_R, w_R) , where it “jumps down”
128 to the left branch.

129 Applying a constant inhibitory conductance $\bar{g}s > 0$ moves the cubic v_∞
130 with the ensuing unstable fixed point down the sigmoid w_∞ in the $(v - w)$ -
131 plane. When the synaptic conductance $\bar{g}s$ is large enough, p_f becomes stable
132 and all periodic trajectories relax into an equilibrium (see Figure 2). There
133 exists a unique value $\bar{g}s = g^*$ when the fixed point lies exactly on the left
134 local minimum of v_∞ . This is where the fixed point changes stability via
135 a sub-critical Andronov-Hopf bifurcation and the stable limit cycle vanishes
136 via a fold bifurcation of limit cycles (e.g. see Ermentrout and Terman, 2010).
137 Thus, when a constant inhibitory conductance is applied, g^* acts as a *release*
138 *conductance*: a cell is prevented from tonic spiking when $\bar{g}s > g^*$ and it will
139 fire spikes when $\bar{g}s < g^*$ (Bose and Booth, 2011).

Figure 1: Periodic solution of relaxation-oscillator model neuron. **A**: Projection of limit cycle onto (v, w) -phase plane with v -nullcline (blue, v_∞) and w -nullcline (orange, w_∞). Unstable fixed point p_f is indicated by an orange dot. **B**: Corresponding voltage trace of an action potential.

140 The dynamics of the synaptic interactions between the neurons is gov-
 141 erned by a synaptic gating variable s , and a depression variable d .

$$\dot{s} = -s/\tau_s, \quad (8)$$

$$\dot{d} = (1 - d)/\tau_d. \quad (9)$$

142 Variable d describes a firing rate dependent depletion mechanism that governs
 143 the amount of depression acting on the synapse; our model is agnostic with
 144 respect to the exact mechanism of this depletion, be it pre- or post-synaptic.
 145 At spike time when the voltage v crosses a synaptic threshold v_θ , the synaptic
 146 gating variable s is reset to the current value of the depression variable d ,
 147 and d is scaled down by the depression strength parameter λ ($0 < \lambda < 1$).
 148 This results in the following discontinuous reset rule on spike time:

$$s \leftarrow d, \quad (10)$$

$$d \leftarrow \lambda d. \quad (11)$$

Figure 2: Nullclines v_∞ (blue) and w_∞ (orange) in (v, w) -phase plane for different values of the total synaptic conductance $\bar{g}s$. For small $\bar{g}s < g^*$, fixed point p_f is unstable (orange point). Larger values of $\bar{g}s$ move v_∞ down in the (v, w) -plane until p_f changes stability (half orange, half blue point) at some critical total conductance value $\bar{g}s = g^*$, and becomes stable (blue point) for $\bar{g}s > g^*$.

149 The equations for the depression model were adapted from Bose et al. (2001).
 150 These equations are a mathematically tractable simplification of the estab-
 151 lished phenomenological depression model previously described by Tsodyks
 152 and Markram (1997). The original equations in Bose et al. (2001) include an
 153 exponential decay of d throughout the active phase of the action potential,
 154 that is

$$\dot{d} = -d/\tau_\beta, \quad (12)$$

155 while $v > v_\theta$ for a decay time constant τ_β . To simplify the mathematical
 156 analysis we have reduced these dynamics to a single-reset event at spike time
 157 according to (11). It is easy to see that this simplification is natural given
 158 a constant duration of the active phase of an action potential, and it will

159 become evident from our results that this simplification does not qualitatively
160 change the dynamics of the network compared to the original equations with
161 depression dynamics described by (12).

162 2.1.1. Anti-Phase Bursting Solutions

163 Short-term synaptic depression of inhibition in a half-centre oscillator acts
164 as a *burst termination* mechanism and is known to produce $n - n$ anti-phase
165 burst solutions of varying period. Such $n - n$ solutions consist of cells firing
166 bursts of n spikes in alternation (see Figure 3A). While one cell is firing a
167 burst it provides an inhibitory conductance to the other cell thus preventing
168 it from firing. Therefore, at any given moment one cell is spiking while the
169 other is inhibited. Consistent with Bose and Booth (2011) we will refer to
170 the currently firing cell as “free” and we will call the inhibited cell “quiet”.
171 Additionally, we will distinguish between two phases of a $n - n$ solution: We
172 will refer to the burst duration of a cell as the “free phase”, and we will
173 call the remaining duration of a cycle, when a cell is not spiking, the “quiet
174 phase”.

175 With each action potential of the free cell, short-term depression leads to
176 a step-wise decrease of d , and consequently of s . If d depresses faster at spike
177 time than it can recover in the inter-spike-intervals (ISIs), the total synaptic
178 conductance $\bar{g}s$ will eventually become sufficiently small to allow the quiet
179 cell to be released and start firing, thus inhibiting the previously free cell.
180 While a cell is quiet its associated depression variable can recover. Once the
181 quiet cell is released its inhibition will be sufficient to terminate the burst of
182 the previously free cell and commence a new cycle. Figure 3B depicts the
183 depression and recovery of d as well as the discontinuous resets of s in a 4 – 4
184 burst.

185 As previously demonstrated by Bose and Booth (2011), the coupling
186 strength $\bar{g}$ plays a crucial role in the generation of burst solutions in a two-
187 cell reciprocally inhibitory network with synaptic depression. In particular,
188 they found that increasing $\bar{g}$ produces longer $n - n$ bursts. Figure 4 shows
189 numerically stable $n - n$ solutions for varying values of $\bar{g}$. For small values
190 of $\bar{g}$ the network produces anti-phase spiking (1 – 1). As $\bar{g}$ is increased the
191 network generates solutions of increasing n , that is 2 – 2, 3 – 3, and so on.
192 When the coupling strength $\bar{g}$ is sufficiently large, that is $\bar{g} > \bar{g}_{sup} \approx 1.016$
193 mS/cm², (bottom of Figure 4), one of the cells continuously spikes at its
194 uncoupled period T while the other cell is fully suppressed.

195 We numerically compute the bifurcation diagram of stable $n - n$ solutions

Figure 3: Solution profiles of a 4 – 4 burst. **A**: Membrane potentials of cell 1 (v_1 , blue), and cell 2 (v_2 , orange). **B**: Synaptic variables d_1 (blue) and s_1 (grey) of cell 1.

with the control parameter $\bar{g}$ (see Appendix for algorithm description). Figure 5A depicts the period P of $n - n$ solutions as $\bar{g}$ is varied. Stable $n - n$ solutions have a period that lies some interval $(2(n - 1)T, 2nT)$. Therefore, $n - n$ solutions are created at some period $P > 2(n - 1)T$ and destroyed at exactly $P = 2nT$. Moreover, stable $n - n$ solutions of longer period occur on increasingly smaller intervals of $\bar{g}$. In particular, large period $n - n$ solutions exist between the 5 – 5 and the suppressed solutions (region between dotted lines in Figure 5A, solution branches not displayed).

2.2. Mathematical Analysis of Two-Cell Network

The goal of the following mathematical analysis will be to reduce the complexity of the eight-dimensional system to some easily tractable quantity. As we will see later this quantity is the value of the depression variable d of one of the two cells. We will then construct the evolution of d for the free and quiet phases of the cycle separately. Having a description of the full cycle in

Figure 4: Stable $n-n$ solutions for increasing values of the coupling strength $\bar{g}$ (increasing top to bottom).

210 terms of d will allow us to explore the parameter space and understand *how*
 211 these $n-n$ burst solutions are created. The main arguments in the following
 212 two sub-sections 2.2.1 and 2.2.2 were first explored in Bose and Booth (2011)
 213 and will be explained in more detail below. However, while Bose and Booth

Figure 5: Numerically computed bifurcation diagrams of stable $n-n$ solutions for increasing coupling strength $\bar{g}$. **A:** Period P of stable solutions. Dashed lines show the interval between the 5-5 and the suppressed solutions, where higher period $n-n$ solutions occur on increasingly smaller ranges of $\bar{g}$. **B:** ISIs corresponding to $n-n$ solutions in A. Long ISIs are associated with the quiet phase of a burst, short ISIs with the free phase. During the free phase, ISIs are of approximately constant duration T .

(2011) used these arguments to derive algebraic conditions that guarantee the periodicity of the depression variable for different $n-n$ solutions, we will use these arguments to construct a Poincaré map of d , which will provide an intuition for the dynamics of d .

2.2.1. Assumption $ISI=T$

The following mathematical analysis is greatly simplified by assuming that the ISIs during the free phase are of constant duration T . That is to say, once a cell becomes free, it fires at its uncoupled period T . This assumption seems reasonable given that (1) the inhibitory conductance decays exponentially to zero during the quiet phase of a cycle, and (2) the fact that many biophysical neuron models, such as the Morris-Lecar model, will fire at approximately their uncoupled period T once released from inhibition.

It is evident from the burst solutions presented in Figure 4 that the respective ISIs in the free phase are nearly constant. We further verify this observation by computing the associated ISIs of stable solutions found in Figure 5A. Figure 5B illustrates the bifurcation diagram of ISIs for varying

230 $\bar{g}$. Naturally, burst solutions with $n > 1$ contain two types of ISIs: Long ISIs
 231 during the quiet phase, and short ISIs in the free phase. Note that in the
 232 latter ISIs are nearly constant, $ISI \approx T$, affirming the above assumption.
 233 The assumption $ISI = T$ allows us to ignore the membrane dynamics of the
 234 free cell, and construct the evolution of its synaptic variables iteratively from
 235 spike to spike. By tracking the exact values of d and s of the free cell we
 236 will determine when the quiet cell is released and becomes free, terminating
 237 the burst of the previously free cell. In the next section we will define such a
 238 “release condition” by exploiting the discrepancy in timescales between the
 239 fast voltage dynamics, and the slow potassium and synaptic dynamics.

240 2.2.2. Fast/Slow Analysis of Single Cell Model

241 Neuronal membrane dynamics typically involve mechanisms that evolve
 242 on very different timescales. In the case of a single Morris-Lecar neuron (Fig-
 243 ure 1) the trajectory spends a lot of time in the silent and active phases, while
 244 the voltage jumps up and down occur seemingly instantaneously. Geometric
 245 singular perturbation theory provides methods to utilise such discrepancy in
 246 timescales (Fenichel, 1979). Consider equations (1) and (2) for an uncoupled
 247 Morris-Lecar neuron with $\bar{g} = 0$. By rescaling $f = \tilde{f}/\epsilon$ we obtain the generic
 248 equations of a fast/slow system:

$$\epsilon \dot{v}_i = \tilde{f}(v_i, w_i), \quad (13)$$

$$\dot{w}_i = h(v_i, w_i). \quad (14)$$

249 By analysing these equations in the limit $\epsilon \rightarrow 0$, we will find an explicit
 250 description of the action potential that is of a lower dimension than the
 251 original system. Consider two timescales: a slow timescale t that describes
 252 the evolution of v and w in the silent and active phases, and a fast timescale
 253 τ that is used to describe the jumps up and down. We initially inspect the
 254 fast timescale τ : By first substituting $t = \epsilon\tau$, and then setting $\epsilon = 0$ we
 255 acquire the singularly perturbed system of equations

$$v' = \tilde{f}(v, w), \quad (15)$$

$$w' = 0. \quad (16)$$

256 Here the prime symbol “ $'$ ” represents the derivative with respect to τ . The
 257 first equation describes the evolution of the voltage as $t \rightarrow \infty$ during the

up- and down jumps, that is from the local extrema (v_L, w_L) and (v_R, w_R) respectively to the opposite branch. The second equation implies that during those jumps the slow variable w is constant. For the jump up we have $w = w_L$ while for the jump down $w = w_R$. In the singular limit we can therefore simplify the jump dynamics to the scalar equation:

$$v' = \tilde{f}(v, w_{L,R}). \quad (17)$$

Now, consider the slow timescale t by setting $\epsilon = 0$:

$$0 = \tilde{f}(v, w), \quad (18)$$

$$\dot{w} = h(v, w). \quad (19)$$

The first equation describes the v -nullcline and the second equation models the evolution of the slow variable w along the left and right branches of that v -nullcline during the silent and active phases respectively. Here we can use the implicit function theorem to express this evolution of w as a scalar equation by replacing v with its associated asymptotic value. Let $v_L(w)$ and $v_R(w)$ describe the v -nullcline on the left and right branches, that is for $v < v_L$ and $v > v_R$ respectively. Then the slow timescale dynamics are given by:

$$\dot{w} = h(v_{L,R}(w), w). \quad (20)$$

In sum, geometric singular perturbation theory allows us to reduce the two-dimensional uncoupled Morris-Lecar model to two scalar differential equations for the fast and slow phases of an action potential respectively, at least in the limit $\epsilon \rightarrow 0$. In the above analysis we assumed *uncoupled* cells, that is $\bar{g} = 0$. In the following section we will extend the analysis to include synaptic interaction in the network when $\bar{g} > 0$.

2.2.3. Release Condition

Our assumption for the free cell states that it fires at its uncoupled period ($ISI = T$). We can therefore disregard weak inhibition ($\bar{g}s < g^*$) in our analysis. Instead, we concentrate on the dynamics of the quiet cell under strong inhibition, when $\bar{g}s - g^*$ is sufficiently large. In this case, the v - and w -nullclines intersect to the left of v_L creating a stable fixed point p_f at some

(v_{p_f}, w_{p_f}) (Figure 2). Each time the free cell produces a spike, p_f jumps down along the w -nullcline and becomes stable. The inhibitory conductance $\bar{g}s$ then decays exponentially according to equation (8), and p_f moves back up the $(v - w)$ -plane. For $\bar{g}$ sufficiently large, our previous fast-slow analysis can be extended to include these piecewise-continuous synaptic dynamics.

Our singular equations for the fast system predict that v will be at its equilibrium value of v_{p_f} immediately after the pre-synaptic spike and will remain at the fixed point as the v -nullcline moves. What about w ? If the change in w -direction is significantly faster than the change in s direction, w will quickly approach w_{p_f} after the pre-synaptic spike. As the synaptic conductance decays and p_f moves up, w will remain in close proximity to w_{p_f} . Throughout the ISI of the free cell the attraction towards p_f will then be sufficient to prevent the trajectory of the quiet cell from jumping up. Next, the trajectory of the quiet cell can only leave the neighbourhood of the stable fixed point p_f , if p_f becomes unstable. This, however, requires that the total synaptic conductance $\bar{g}s$ acting on the quiet cell drops below the release conductance g^* discussed in section 2.1, that is

$$\bar{g}s < g^*. \quad (21)$$

The fast time-scale reduction then guarantees that on the slow timescale the trajectory of the quiet cell will jump up instantaneously, becoming free and firing an action potential. As will become evident in the next section, $\dot{w} \gg \dot{s}$ indeed holds for relaxation oscillator type models and fast inhibitory synapses, such as our configuration of the Morris-Lecar model.

In summary: The release condition

$$\bar{g}s = g^* \quad (22)$$

is sufficient to predict when the quiet cell is released. Due to the symmetry of $n - n$ solutions the release occurs at exactly half the period of the full cycle, that is at $P/2$. The release time therefore uniquely determines the solution. Furthermore, computation of the release time does not depend on the membrane nor the synaptic dynamics of the quiet cell. Instead, the solution of the synaptic variable s of the free cell is sufficient to predict when $\bar{g}s = g^*$ is satisfied. Finally, s is solely determined by the evolution of the depression variable d of the free cell. Constructing a solution $d(t)$ of d during the free phase of either cell will therefore uniquely determine the solution of the full eight-dimensional network. However, finding the solution $d(t)$

requires us to know the initial value $d(0)$ at the start of a cycle at $t = 0$. In the next section we will construct a scalar return map that tracks these initial values $d(0)$ from cycle to cycle of stable $n - n$ solutions.

2.3. Explicit burst map $\Pi_n : \mathbf{d}_k \mapsto \mathbf{d}_{k+1}$

2.3.1. Rationale

In this section we construct the scalar Poincaré map $\Pi_n : \mathbf{d}_k \mapsto \mathbf{d}_{k+1}$. Here the discrete variable $\mathbf{d}_k$ tracks the values of the continuous depression variable d at the beginning of each $n - n$ burst. The map Π_n therefore describes the change of d , of either of the two cells, from the beginning of one cycle to the beginning of the next cycle. Following the analysis approach taken in Bose and Booth (2011), for now we will assume that the number of spikes in the free phase is known and given by n . Later we will relax this assumption. We will construct Π_n by evolving d first during the free phase and then during the quiet phase of the $n - n$ limit cycle. First, let us give explicit definitions of the free and quiet phases. A schematic illustration of both phases is given in Figure 6.

Suppose that at $t_1 = 0$ cell 1 becomes free with some initial $d(0)$. Cell 1 then fires n spikes at the uncoupled period T . Let $s(t)$ and $d(t)$ be corresponding solutions of the synapse variables of cell 1. After n spikes the total conductance $\bar{g}s(t)$ acting on the quiet cell 2 has decayed sufficiently to satisfy the release condition (22): that is at some time $t = (n - 1)T + \Delta t$ we have $\bar{g}s(t) = g^*$. Cell 2 is then released and prevents cell 1 from further spiking. Here Δt is the *inter-burst-interval*, or the time between the last spike of cell 1 and the first spike of cell 2 (Bose and Booth, 2011). Once released, cell 2 also fires n spikes until cell 1 becomes free once again at time

$$t = 2(\Delta t + (n - 1)T) \equiv P, \quad (23)$$

thus commencing a new cycle. We can now define the free and quiet phases of cell 1 explicitly: The free phase of cell 1 is the time interval between the first and last spikes of the burst, that is for time $0 < t < (n - 1)T$. During the free phase of cell 1, the quiet cell 2 is inhibited sufficiently strong to prevent it from firing, hence $\bar{g}s > g^*$. The quiet phase of cell 1 is the remaining duration of the cycle when cell 2 is bursting, that is when $(n - 1)T < t < 2(\Delta t + (n - 1)T)$. Note that only the quiet phase depends on Δt .

The quantity Δt will play a central role in the construction of Π_n . From equation (23) it follows that for any given n and $\bar{g}$, Δt is uniquely associated with the period P , and therefore also with the release time of the quiet cell:

Figure 6: Schematic diagram of the free and quiet phases for a 3-3 solution. **A:** Membrane potentials of cell 1 (v_1) and cell 2 (v_2). The grey patches depict the two inter-burst-intervals Δt . **B:** Total synaptic conductance of cell 1 ($\bar{g}s_1$) as it crosses the release conductance g^* . **C:** Solution $d(t)$ of depression variable of cell 1, during free (blue) and quiet phases (orange).

$$\Delta t = \frac{1}{2}P - (n - 1)T. \quad (24)$$

352 We can use (24) and the numerically computed bifurcation diagram of P
 353 in Figure 5A to obtain the graph of Δt as a function of $\bar{g}$ (Figure 7). The
 354 quantity $\Delta t(\bar{g})$ is monotonically increasing: stronger coupling $\bar{g}$ increases
 355 the total synaptic conductance $\bar{g}s$ that acts on the quiet cell, thus delaying
 356 its release. It is easy to see that $\Delta t < T$: once Δt crosses T , the free
 357 cell can "squeeze in" an additional spike and the solutions bifurcate into
 358 $(n + 1) - (n + 1)$.

Figure 7: Numerically computed bifurcation diagram of Δt for varying $\bar{g}$. Each continuous branch is associated with a stable $n - n$ burst solution. Increasing $\bar{g}$ increases Δt until the solutions bifurcate at $\Delta t = T$.

359 Distinguishing between the free and quiet phases of a cycle allows us to
 360 describe the dynamics of the depression variable d explicitly for each phase.
 361 As can be seen from Figure 6C, during the free phase d depresses at spike
 362 times and recovers in the ISIs. In contrast, during the quiet phase d only

recovers and does not depress. Given the initial $\mathbf{d}_k = d(0)$ at the beginning of the cycle and the number of spikes in the free phase n , we can now construct the burst map Π_n . The map $\Pi_n(\mathbf{d}_k) = Q_n(F_n(\mathbf{d}_k))$ is a composition of two maps. Map $F_n : \mathbf{d}_k \mapsto \Delta t$ models the evolution of d in the free phase. F_n takes an initial value $\mathbf{d}_k = d(0)$ and predicts the inter-burst-interval Δt . Map $Q_n : \Delta t \mapsto \mathbf{d}_{k+1}$ models the recovery of d in the quiet phase given some Δt .

2.3.2. Free Phase Map $F_n : \mathbf{d}_k \mapsto \Delta t$

Let us start with map F_n : At each spike time t_k , variable d depresses with the reset $d(t_k) \leftarrow \lambda d(t_k^-)$ (equation (11)). For the duration of the subsequent ISI ($t_k < t < T + t_k$), the recovery of d is described by the solution to (9):

$$d(t) = 1 - (1 - \lambda d(t_k))e^{-t/\tau_d}. \quad (25)$$

By substituting $t = T$ we can build a linear map that models the depression of d from spike time t_k to the subsequent spike time t_{k+1} during the free phase:

$$\mathbf{d}_{k+1} = \lambda \rho \mathbf{d}_k + (1 - \rho), \quad (26)$$

where to keep the notation simple we let $\rho = e^{-T/\tau_d}$ in (26). Since $0 < \lambda, \rho < 1$, the map (26) is increasing and contracting, with a fixed point at

$$d_{sup} = \frac{1 - \rho}{1 - \lambda \rho}, \quad (27)$$

where $0 < d_{sup} < 1$. As we will see later, d_{sup} is associated with fixed points of the burst map Π_n corresponding to the suppressed solution (see Figure 4E). Solving (26) gives us the linear map $\delta_n : \mathbf{d}_1 \mapsto \mathbf{d}_n$, that for some initial $\mathbf{d}_1 = d(0)$ at $t = 0$ computes $\mathbf{d}_n$ at the n th spike time t_n :

$$\delta_n(\mathbf{d}_1) = \alpha(n)\mathbf{d}_1 + \beta(n), \quad (28)$$

where

$$\alpha(n) = (\lambda \rho)^{n-1}, \quad (29)$$

$$\beta(n) = (1 - \rho) \sum_{i=0}^{n-2} (\lambda \rho)^i. \quad (30)$$

Figure 8: Linear map $\delta_n : d_1 \mapsto d_n$ for $n = 1, 2, 3, 4$ with fixed point at d_{sup} .

383 Note that $0 < \alpha, \beta < 1$. Figure 8 shows $\delta_n(d_1)$ for varying n . Since $\lambda < 1$,
 384 function δ_n is a linearly increasing function of d_1 , decreasing with n . Natu-
 385 rally, δ_n has a fixed point at d_{sup} for all n . Having identified d after n spikes,
 386 we can now use the release condition $\bar{g}s = g^*$ (equation (22)) to find Δt . At
 387 the last spike of the free phase at time $t_n = (n - 1)T$, synapse variable s is
 388 reset according to equation (10):

$$s(t_n) \leftarrow d(t_n^-). \quad (31)$$

389 Here $d(t_n^-) = \delta_n(d(0))$, and t_n^- is the time just before the n th spike. After
 390 the last spike s decays exponentially according to equation (8). Setting the
 391 initial value to $d(t_n^-)$ yields:

$$s(t) = d(t_n^-)e^{-\Delta t/\tau_s}, \quad (32)$$

392 where $\Delta t < T$. Now, our fast-slow analysis guarantees that the quiet cell
 393 2 will spike and become free when $\bar{g}s - g^*$ crosses zero. We can therefore

394 formulate the release condition as:

$$\bar{g}d(t_n^-)e^{-\Delta t/\tau_s} = g^*. \quad (33)$$

395 Finally, solving for Δt and substituting $\delta_n(\mathbf{d}_k)$ from the equation (28), which
 396 relates $\delta_n(d)$ to d and ρ , for $d(t_n^-)$ gives the map F_n :

$$F_n(\mathbf{d}_k) := \tau_s \ln \left(\frac{\bar{g}}{g^*} \delta_n(\mathbf{d}_k) \right) = \Delta t. \quad (34)$$

Figure 9: Map $F_n : \mathbf{d}_k \mapsto \Delta t$ for $n = 1, 2, 3, 4$ and $\bar{g} = 0.6$ with corresponding vertical asymptotes at $d_a(n)$ (dotted vertical lines). d_{sup} is indicated by a dashed vertical line.

397 Figure 9 shows F_n for varying n .

398 To elucidate the properties of F_n we will consider negative values of d .
 399 However, it is important to note that values $d < 0$ are biologically impossible
 400 as d models a finite pool of neurotransmitter, and therefore must be positive.
 401 Moreover, the reset of d at spike time in the full system of ODEs according to
 402 $d \leftarrow \lambda d$ will always guarantee $d > 0$ since $\lambda > 0$. We will also accept negative

values of Δt , interpreting them as $n - n$ solutions with partially overlapping bursts. As will become evident, $\Delta t < 0$ is only a formal violation of the biological realism of the map Π_n , as stable $n - n$ solutions of the full system of ODEs system only exist for $\Delta t > 0$.

It is easy to show that F_n is a strict monotonically increasing function of $\mathbf{d}_k$. Larger values of $\mathbf{d}_k$ at burst onset cause stronger inhibition of the quiet cell, and therefore prolong its release time and the associated Δt . Map F_n is defined on $(d_a, 1)$, where d_a is a vertical asymptote for $\delta_n = 0$ with

$$d_a(n) = -\frac{\beta(n)}{\alpha(n)} < 0. \quad (35)$$

The curves F_n for all $n > 0$ intersect at d_{sup} . We can now use the release condition (22) to find the corresponding minimal coupling strength $\bar{g}_{sup}$ that will produce full suppression solutions. We write $\bar{g}_{sup}$ as a function of the depression strength λ :

$$\bar{g}_{sup}(\lambda) = \frac{g^* e^{T/\tau_s}}{d_{sup}}. \quad (36)$$

$$(37)$$

Substituting (27) for d_{sup} yields:

$$\bar{g}_{sup}(\lambda) = g^* e^{T/\tau_s} \frac{1 - \lambda\rho}{1 - \rho}. \quad (38)$$

Note that the above dependence of $\bar{g}_{sup}$ on λ is linear and monotonically decreasing. A biological interpretation of the monotonically decreasing $\bar{g}_{sup}(\lambda)$ is easy to find: Increasing λ reduces the strength of the depression of the free cell. This in turn allows the free cell to fully suppress the quiet cell at smaller values of $\bar{g}$.

2.3.3. Quiet Phase Map $Q_n : \Delta t \mapsto \mathbf{d}_{k+1}$

We now turn to the construction of map $Q_n : \Delta t \mapsto \mathbf{d}_{k+1}$. Q_n describes the recovery of d during the quiet phase. As we have identified earlier, the recovery in the quiet phase lasts for $2\Delta t + (n - 1)T$. Substituting that into the recovery equation (25) yields the map Q_n :

$$Q_n(\Delta t) := 1 - (1 - \lambda \mathbf{d}_n) e^{-(2\Delta t + (n-1)T)/\tau_d}. \quad (39)$$

Figure 10: Quiet phase map $Q_n : \Delta t \mapsto \mathbf{d}_{k+1}$ for $n = 1, 2, 3, 4$ and $\bar{g} = 0.6$. Intersection of curves Q_n for all n occurs at $\Delta t = \ln \frac{\bar{g}}{\lambda g^*}$ (dashed line).

426 Here $\mathbf{d}_n$ is the value of the depression variable at the last spike t_n of the free
427 phase. Given Δt , we solve the release condition (22) for $\mathbf{d}_n$:

$$\mathbf{d}_n = \frac{g^*}{\bar{g}} e^{\Delta t / \tau_s}. \quad (40)$$

428 Map Q_n is shown in Figure 10 for various values n . Map $Q_n(\Delta t)$ is monoton-
429 ically increasing as larger values Δt imply a longer recovery time, and hence
430 Q_n grows without bound. All curves Q_n intersect at some $\Delta t = \tau_s \ln \left(\frac{\bar{g}}{g^* \lambda} \right)$
431 where

$$Q_n \left[\tau_s \ln \left(\frac{\bar{g}}{g^* \lambda} \right) \right] = 1. \quad (41)$$

432 As we will show in the next section, all fixed points of the full map Π_n occur
433 for $\mathbf{d}_k < 1$. We will therefore restrict the domain of Q_n to $(-\infty, \ln \left(\frac{\bar{g}}{g^* \lambda} \right) \tau_s)$

434 and the codomain to $(-\infty, 1)$.

435 2.3.4. Composition Map $\Pi_n : d_k \mapsto d_{k+1}$

Figure 11: Map $\Pi_n : d_k \mapsto d_{k+1}$. **A:** Π_n for $n = 1, 2, 3, 4$ at $\bar{g} = 0.6$. **B:** Π_2 with $n = 2$ for varying $\bar{g} \approx 0.01, 0.034, 0.3$. Identity function is illustrated by a diagonal line.

436 Having found F_n and Q_n , we can now construct the full map $\Pi_n(d_k) =$
 437 $Q_n[F_n(d_k)]$:

$$\Pi_n(d_k) := 1 - \frac{\rho^{n-1} g^{\star\tau} \delta_n^{-\tau}(d_k)(1 - \lambda \delta_n(d_k))}{\bar{g}^\tau}, \quad (42)$$

438 where we substituted $\tau = 2\tau_s/\tau_d$. Since d is the slowest variable and $\tau_d > \tau_s$,
 439 we assume $\tau < 1$. Figure 11A depicts Π_n for various n . Just as F_n , map
 440 Π_n is defined on $(d_a(n), 1)$. Intersections of Π_n with the diagonal at some $d^\star$
 441 with $\Pi_n(d^\star) = d^\star$ are fixed points of the map. Varying the synaptic strength
 442 $\bar{g}$ moves the curves Π_n up and down the (d_k, Π_n) -plane. Figure 11B shows
 443 Π_2 with $n = 2$. For $\bar{g} < 0.03$ map Π_2 has no fixed points. As $\bar{g}$ is increased
 444 to $\bar{g} \approx 0.03$, Π_2 coalesces with the diagonal tangentially. When $\bar{g} > 0.03$, a
 445 pair of fixed points emerge, a stable $d_-^\star$ and an unstable $d_+^\star$, indicating the
 446 occurrence of a fold bifurcation of maps.

447 Finding fixed points $d^\star$ explicitly for all $n > 0$ is not trivial. However,
 448 we can use equation (42) to determine $d^\star$ *implicitly*, utilising the implicit
 449 function theorem. Let Φ_n describe the fixed points of Π_n :

$$\Phi_n(d^*) := \Pi_n(d^*) - d^* = 0. \quad (43)$$

Then the derivative with respect to $\bar{g}$ is calculated as

$$D_{\bar{g}}\Phi_n(d^*) = \tau \frac{\rho^{n-1} g^{*\tau} \delta_n^{-\tau}(d^*) (1 - \lambda \delta_n(d^*))}{\bar{g}^{\tau+1}}. \quad (44)$$

We can see that the sign of $D_{\bar{g}}\Phi_n$ is determined by the sign of $1 - \lambda \delta_n(d^*)$. Solving $1 - \lambda \delta_n(d^*) = 0$ for d^* by applying the definition of δ_n in equation (28) yields

$$d^* = \frac{\lambda^{-1} - \beta(n)}{\alpha(n)} =: d_\phi(n). \quad (45)$$

Simple calculations reveal that $d_\phi(n)$ is strictly increasing with n :

$$d_\phi(n+1) - d_\phi(n) = \frac{\lambda^{-1} - 1}{(\lambda\rho)^n} > 0 \text{ for all } n > 0. \quad (46)$$

Since $d_\phi(n=1) = \lambda^{-1} > 1$ for $\lambda \in (0, 1)$, we can conclude that $D_{\bar{g}}\Phi_n > 0$ for all $d^* < 1$ and all $n > 0$. This allows us to utilise the implicit function theorem to express $\bar{g}$ as a function of d^* , and solving equation (43) for $\bar{g}$ we then get the synaptic coupling strength $\bar{g}(d^*)$ that corresponds to the fixed point d^* :

$$\bar{g}(d^*) = g^* \left(\frac{\rho^{n-1} \delta_n^{-\tau}(d^*) (1 - \lambda \delta_n(d^*))}{1 - d^*} \right)^{1/\tau}. \quad (47)$$

The graph of the inverse of $\bar{g}(d^*)$ is shown in Figure 12 (orange line). Note the typical quadratic shape of a fold bifurcation. It is also evident from Figure 11B that for $\lambda = 0.5$ the fold bifurcations occur for increasingly smaller $\bar{g}$ as n is increased. In the remaining part of this section we will show that all fixed points d^* for all $n > 1$ are indeed created via fold bifurcations of maps. To show that our derivation of $\bar{g}(d^*)$ works we also compute the curves numerically using the conventional Newton-Raphson method (Press, 2007) (blue circles). As we will show below, map $\Pi_n(d_k)$ is monotonically increasing, and the root-finder is therefore guaranteed to converge (with at least quadratic rate) to the two roots (if any exist) if initialised at $d_a(n)$ and 1.

Figure 12: Bifurcation diagrams of Π_n for $n = 1, 2, 3$: analytically (orange line) and numerically (blue circles) computed fixed points d^* of map Π_n for varying $\bar{g}$ and $n = 1, 2, 3$.

2.3.5. Fold Bifurcations of Π_n

The derivative of $\Pi_n(d_k)$ is given by

$$D\Pi_n(d_k) = \frac{\tau_s \alpha \rho^{n-1} g^{\star\tau} \left(\frac{2}{\tau_{d_k}} \delta_n^{-(\tau+1)}(d_k) + \frac{\tau_{d-2\tau_s}}{\tau_d \tau_s} \lambda \delta_n^{-\tau}(d_k) \right)}{\bar{g}^\tau} \quad (48)$$

It is straightforward to show that Π_n is strictly monotonous with $D\Pi_n > 0$ and $D^2\Pi_n < 0$. In the limit $d_k \rightarrow d_a$ the slope $D\Pi_n$ is unbounded, and since $D^2\Pi_n < 0$ there exists a unique d^* for any $\bar{g} > 0$ such that $D\Pi_n(d^*) = 1$. For $d_k < 1$, it is also evident that $D_{\bar{g}}\Pi_n > 0$. Since $\lim_{\bar{g} \rightarrow 0} \Pi_n$ is unbounded and $\lim_{\bar{g} \rightarrow \infty} \Pi_n = 1$ for $d > d_a$ and any $n > 0$, it follows then by the intermediate value theorem that there exists some $\bar{g}_c > 0$ and $d_c \in (d_a, 1)$ such that $\Pi_n(d_c)|_{\bar{g}=\bar{g}_c} = d_c$, and $D\Pi_n(d_c) = 1$. That is, every curve Π_n undergoes a fold bifurcation by intersecting the diagonal tangentially at some d_c and

481 creating two fixed points, one stable and one unstable. Here $D^2\Pi_n(\mathbf{d}_k) < 0$
 482 and $D_{\bar{g}}\Pi_n > 0$ constitute the nondegeneracy conditions (e.g. see Kuznetsov,
 483 2004) indicating that in a neighbourhood of $(d_c, \bar{g}_c)$, map $\Pi_n(\mathbf{d}_k)$ has the
 484 topological normal form of a codimension-1 fold bifurcation, that is $y \mapsto$
 485 $\beta + y - y^2$, where $y \in \mathbb{R}$ and $\beta \in \mathbb{R}$.

486 The above conclusion not only signifies that all fixed points of Π_n are
 487 created via fold bifurcations of maps, but most importantly, that for n and $\bar{g}$
 488 large enough, maps Π_n have a stable fixed point. In fact, we can show that
 489 for any finite coupling strength $\bar{g} > 0$, there exists some $N > 0$, such that
 490 for all $n > N$ the map Π_n has a stable fixed point. Consider the fixed point
 491 $\mathbf{d}_k = d_{sup}$ (equation (27)) of δ_n , where $\delta_n(d_{sup}) = d_{sup}$ for any $n > 0$. Then
 492 from equations (42) and the fact that $\rho^n > \rho^{n+1}$ it is straightforward to show
 493 that for all $n > 0$

$$\Pi_n(d_{sup}) < \Pi_{n+1}(d_{sup}). \quad (49)$$

494 In the limit $n \rightarrow \infty$ we have

$$\lim_{n \rightarrow \infty} \Pi_n(d_{sup}) = 1 > d_{sup}. \quad (50)$$

495 Since $\Pi_n(d_{sup})$ is monotonically increasing with n , it follows that for any
 496 $\bar{g} < \bar{g}_{sup}$ there exists some $N > 0$ such that $\Pi_n(d_{sup}) > d_{sup}$ for any $n > N$.
 497 The monotonicity of Π_n and $D\Pi_n$ with respect to $\mathbf{d}_k$ then implies that such
 498 maps Π_n have a pair of fixed points on $(d_a, 1)$. In other words, for any finite
 499 interval of $\bar{g}$ on $(0, \bar{g}_{sup})$ there exists an infinite number of maps Π_n that have
 500 a stable fixed point and are associated with a burst limit cycle of the full
 501 network. In other One example of a long-cyclic 11 – 11 burst can be seen
 502 in Figure 13. Note that while the map predicts stable $n - n$ solutions for
 503 any $\bar{g} < \bar{g}_{sup}$ sufficiently large, these solutions occur on increasingly small
 504 parameter intervals of $\bar{g}$, which makes identifying them in the ODE system
 505 numerically challenging.

506 Deriving the exact $\bar{g}$ for each n associated with the fold bifurcations is
 507 cumbersome. However, in the limit $\lambda \rightarrow 1$ the equations (48) and (42) be-
 508 come more manageable. To provide a better intuition for the map we will
 509 therefore demonstrate the fold bifurcations in the theoretical case of total ab-
 510 sence of depression, that is when $\lambda = 1$. This scenario can be associated with
 511 a full suppressed solution. In this case $\Pi_n|_{\lambda=1}$ simply models the exponential
 512 recovery of d according to equation (9) for $0 < t < 2(\Delta t + (n - 1)T) = P$:

Figure 13: Long-cyclic 11 – 11 burst solution with $\bar{g} = 1.015$. **A**: Membrane potentials v_1 and v_2 of the two cells. **B**: Synaptic variables d_1 and s_1 of first cell.

$$\Pi_n(\mathbf{d}_k)|_{\lambda=1} = 1 - (1 - \mathbf{d}_k)e^{-2\Delta t/\tau_d}\rho^{2(n-1)}. \quad (51)$$

Equation (51) has a fixed point at $d^* = 1$ for all $n > 0$, which allows us to find $\Delta t = F_n(1)$. We obtain:

$$\Pi_n(\mathbf{d}_k = 1)|_{\lambda=1} = 1 - (1 - \mathbf{d}_k)\left(\frac{\bar{g}}{g^*}\right)^{-\tau}\rho^{2(n-1)}. \quad (52)$$

Parameter values $\bar{g}$ that are associated with the fold bifurcations satisfy equation $D\Pi_n(d = 1)|_{\lambda=1} = 1$, solving for $\bar{g}$ gives

$$\bar{g}_f(n) = g^*\rho^{2(n-1)/\tau} = g^*\exp\left(\frac{-(n-1)T}{\tau_s}\right), \quad (53)$$

where $\bar{g}_f(n)$ denotes the fold bifurcation value of $\bar{g}$ as a function of n . Figure 14 depicts the values of $\bar{g}_f(n)$ for increasing n in the limit $\lambda \rightarrow 1$ (orange),

as well when $\bar{g}_f(n)$ is numerically computed for $\lambda = 0.5$ (blue) using a conventional Simplex minimisation (Nelder and Mead, 1965) of $\bar{g}(d^*)$ (equation (47)).

Figure 14: Values of $\bar{g}$ associated with fold bifurcations computed numerically for $\lambda = 0.5$ (blue) and found explicitly in the limit $\lambda \rightarrow 1$ (orange) for increasing n .

2.4. Recursive burst map $\Pi : \mathbf{d}_k \mapsto \mathbf{d}_{k+1}$

2.4.1. Rationale

Having now gained an understanding of how different $n - n$ solutions are created and what determines the shape of the bifurcation diagram, let us remove the assumption that the free phase of a cycle contains exactly n spikes. The main effect of removing this assumption is that now n has to be found explicitly for any $\mathbf{d}_k = d(0)$ at the cycle start. We will find n recursively by iterating through the spike times of the free cell until the release condition (22) predicts the firing of the previously quiet cell. This will yield the recursive map $F : \mathbf{d}_k \mapsto L$, that now returns the burst length

532 L given some initial $\mathbf{d}_k = d(0)$. Given L , variable d can be easily evolved
 533 during the quiet phase with the map $Q : L \mapsto \mathbf{d}_{k+1}$. In analogy to the
 534 previous section, we define the composite burst map as $\Pi(\mathbf{d}_k) = Q[F(\mathbf{d}_k)]$
 535 (without subscripts).

536 2.4.2. Free Phase Map $F : \mathbf{d}_k \mapsto L$

Figure 15: Recursive map $F : \mathbf{d}_k \mapsto L$ (blue) in comparison to the map $F_n : \mathbf{d}_k \mapsto \Delta t$ (orange) for $n = 1, 2, 3$ and $\bar{g} = 0.6$. The output of $F_n(\mathbf{d}_k)$ has been transformed to $(n-1)T + F_n(\mathbf{d}_k)$ in order to match $F(\mathbf{d}_k)$.

537 Let us start with the map $F : \mathbf{d}_k \mapsto L$ that models the depression of d
 538 during the free phase. At each spike time, we will test whether the total
 539 synaptic conductance is sufficient to allow cell 1 to fire another spike, or
 540 whether cell 2 becomes free and terminates the burst of cell 1. As in the
 541 previous section, let us assume that cell 1 becomes free and produces an
 542 action potential at $t = 0$ with some initial $\mathbf{d}_k = d(0)$ and, naturally, a
 543 $L(0) = 0$. This means that the total synaptic conductance acting on the
 544 quiet cell 2 is given by $\bar{g}\mathbf{d}_k e^{-t/\tau_s}$ (equation (32)). The release condition (22)

determines whether cell 2 becomes free after some $t = \Delta t$, or whether cell 1 fires at least another spike at $t = T$. If there exists a $t < T$ such that

$$\bar{g}\mathbf{d}_k e^{-t/\tau_s} < g^*. \quad (54)$$

then cell 2 becomes free before cell 1 can fire another spike. The exact time Δt can be found by solving the release condition (22) for Δt with the substitution $s = \mathbf{d}_k e^{-\Delta t/\tau_s}$:

$$\Delta t = \tau_s \ln \left(\frac{\bar{g}}{g^*} \mathbf{d}_k \right). \quad (55)$$

In contrast, if the inhibitory conductance is sufficient to keep cell 2 quiet for at least $t = T$, then

$$\bar{g}\mathbf{d}_k e^{-T/\tau_s} > g^* \quad (56)$$

holds, and cell 1 can produce one more spike. In this case, L will be at least of length T and we set:

$$L = L(0) + T. \quad (57)$$

We can find the value of the depression variable at the next spike of cell 1 at time $t = T$ by evolving d according to equation (25):

$$d(T^-) = 1 - (1 - \lambda \mathbf{d}_k) e^{-T/\tau_d}. \quad (58)$$

Now we are in a position to repeat the preceding procedure and test once more whether the quiet cell will remain quiet for a duration T . Assume that after n spikes d will be sufficiently depressed to release the quiet cell before the subsequent spike of the free cell. The exact time of that release will be then given by the previously accumulated burst duration L and the inter-burst-interval Δt . For a free phase consisting of n spikes the release time L of the quiet cell is given by

$$L = (n - 1)T + \tau_s \ln \left(\frac{\bar{g}}{g^*} \mathbf{d}_n \right). \quad (59)$$

This iterative procedure allows us to define F recursively. Given some initial $F_0 = L(0) = 0$, we define

$$F(\mathbf{d}_k) := \begin{cases} T + F(1 - (1 - \lambda \mathbf{d}_k)e^{-T/\tau_d}) & \text{if } \bar{g}\mathbf{d}_k e^{-T/\tau_s} > g^*, \\ \tau_s \ln \frac{\bar{g}\mathbf{d}_k}{g^*} & \text{otherwise.} \end{cases} \quad (60)$$

565 Note that as we update the input of the recursive call to F with

$$\mathbf{d}_{k+1} \leftarrow 1 - (1 - \lambda \mathbf{d}_k)e^{-T/\tau_d}, \quad (61)$$

566 we also implicitly track the evolution of d . Figure 15 shows the partially
567 continuous map F , and the previously constructed continuous map F_n for
568 various n . Since F_n returns Δt and not L , we have added $(n-1)T$ to each
569 curve of F_n to have matching axes. This way it becomes evident that each
570 continuous interval of F corresponds to a release time L consisting of n spikes,
571 and therefore overlaps with the respective curve F_n .

572 *2.4.3. Quiet Phase Map $Q : L \mapsto \mathbf{d}_{k+1}$*

573 Given the release time of the quiet cell L , determining the recovery from
574 depression of cell 1 via the map $Q : L \mapsto \mathbf{d}_{k+1}$ is straightforward. The
575 duration of the quiet phase is given by $(n-1)T + 2\Delta t = L + \Delta t$. We can
576 find Δt directly from the definition of L in (59):

$$L = (n-1)T + \Delta t. \quad (62)$$

577 Since n is unknown, we can use the remainder to find Δt :

$$\Delta t = L \bmod T \text{ for } L > 0. \quad (63)$$

578 Then map Q is defined by:

$$Q(L) = 1 - (1 - \lambda \mathbf{d}_n)e^{-(L+\Delta t)/\tau_d}. \quad (64)$$

579 Here $\mathbf{d}_n$ is the value of the depression variable at the last spike of the free
580 phase. We can find $\mathbf{d}_n$ as in equation (40), that is

$$\mathbf{d}_n = \frac{g^*}{\bar{g}} e^{\Delta t/\tau_s}. \quad (65)$$

581 Figure 16 shows the partially continuous map $Q : L \mapsto \mathbf{d}_{k+1}$ and the con-
582 tinuous map $Q_n : \Delta t \mapsto \mathbf{d}_{k+1}$ for $n = 1, 2, 3, 4, 5$. To match the axes of
583 both maps Q and Q_n , we have transformed the domain of Q_n according to

Figure 16: Partially continuous map $Q : L \mapsto \mathbf{d}_{k+1}$ (blue) in comparison to the continuous map $Q_n : \Delta t \mapsto \mathbf{d}_{k+1}$ (orange) for $n = 1, 2, 3, 4, 5$ and $\bar{g} = 0.6$. To match the axis of both maps, the domain of Q_n has been transformed according to $\Delta t = L - (n - 1)T$.

584 $\Delta t = L - (n - 1)T$. Just as with F , each continuous interval of Q corresponds
585 to a recovery duration consisting of n spikes, and therefore overlaps with the
586 associated curve Q_n .

587 2.4.4. Composition Map $\Pi : \mathbf{d}_k \mapsto \mathbf{d}_{k+1}$

588 We can compute the full map $\Pi : \mathbf{d}_k \mapsto \mathbf{d}_{k+1}$ numerically, by first cal-
589 culating the burst length $L = F(\mathbf{d}_k)$, and then finding the return value
590 $\mathbf{d}_{k+1} = Q(L)$:

$$\Pi(\mathbf{d}_k) = Q[F(\mathbf{d}_k)]. \quad (66)$$

591 Figure 17A shows map Π (blue) and the curves Π_n (orange) for $\bar{g} = 0.65$
592 and $n = 1, 2, 3$, and Figure 17B depicts Π for increasing values of $\bar{g}$. Π is
593 a partially continuous map, where each continuous interval associated with
594 some n is described by a curve Π_n . Therefore, all qualitative descriptions

Figure 17: **A:** Partially continuous and recursive map Π (blue) in comparison to the continuous map Π_n (orange) for $n = 1, 2, 3$ and $\bar{g} = 0.6$. Π is bistable with two stable fixed points. **B:** Map Π for increasing parameter values $\bar{g}$.

of Π_n regarding monotony, slope, and dependence on $\bar{g}$ also hold for Π on the respective continuous intervals. Most importantly, it follows that for $\bar{g}$ sufficiently large, Π has at least two fixed points, one of which is stable. Stable fixed points d^* of Π are associated with stable $n - n$ solutions of the flow system, and can be interpreted as the maximum values of d at the start of the cycle (see Figure 18B).

We have previously shown that for any finite range of coupling strengths with $\bar{g} < g_{sup}$, there exists an infinite number of maps Π_n that have a stable fixed point. This also means that Π has stable fixed points linked to stable $n - n$ solutions for any n sufficiently large. In other words, given that our reduction assumptions hold, a two-cell reciprocally inhibitory network with depression can produce an infinite number of anti-phase burst patterns (of increasing period) on the coupling strength interval $(0, \bar{g}_{sup})$.

We also observe that there exist some values of $\bar{g}$, such as $\bar{g} = 0.76$ in Figure 17A, where Π has two stable fixed points. Figure 18A shows a numerically computed cobweb plot of Π for $\bar{g} = 0.76$ with initial values at 0.1 (blue lines) and 1.0 (orange lines) respectively. Both sequences approach the respective stable fixed points (blue and orange dots) after a number of iterations of Π . Figure 18B depicts the associated 3 - 3 (top, orange) and

Figure 18: **A**: Cobweb diagram of $\Pi : d_k \mapsto d_{k+1}$ for $\bar{g} = 0.76$. Numerical iterations are initialised at $d_1 = 0.1$ and $d_1 = 1.0$ and quickly converge to the two stable fixed points (blue and orange dots) respectively. **B**: Corresponding solution profiles acquired from numerically integrating the system of ODEs. Orange and blue dots represent values d_k in close neighbourhood to the fixed points of Π , corresponding to 3 – 3 (top) and 2 – 2 (bottom) bursts respectively.

2 – 2 (bottom, blue) solutions of the depression variable from numerical simulations of the full ODE system. Bose and Booth (2011) have previously shown the existence of bistability in a very similar network for $n < 3$.

We compute these fixed points numerically to derive the full bifurcation diagram. Figure 19 illustrates two bifurcation diagrams: One diagram that has been used in Figure 5 (blue lines) and computed by simulating the original system of ODEs. The other diagram has been found by numerically identifying stable fixed points of Π (orange). Note that our reduction approach relies on the assumption that the total synaptic conductance $\bar{g}s$ is sufficiently large. This may explain the better match between the two diagrams for larger values of $\bar{g}$. However, even for large $n - n$ burst solutions there is a mismatch between the curves, in particular at the left and right boundaries close to the period increments. Presumably our assumptions on the time scales of w and s dynamics do not hold here and can only be captured by more complex approximations.

Figure 19: Numerically computed bifurcation diagram (blue) of period P as a function of $\bar{g}$, in comparison to curves found from stable fixed points of map Π (orange).

629 2.5. Conclusion

630 To study the mechanisms of burst generation in tadpole struggling we
631 have analysed a neuronal network that consists of a pair of inhibitory neurons
632 that undergo a frequency dependent synaptic depression. We have shown
633 that when the strength of inhibition between the neurons is varied, such a
634 simple network can display a range of different struggling-like $n - n$ burst
635 patterns. We have applied methods of geometric singular perturbation theory
636 to reduce a network model of eight ODEs to a scalar first return map Π of
637 the slow depression variable d . This map Π is a composition of two maps,
638 F and Q , that model the evolution of d during the free and quiet phases of
639 $n - n$ solutions respectively. Both F and Q maps are constructed by using the
640 dynamics of single uncoupled neurons. We have then proved the existence
641 and stability of fixed points of Π , which are created in pairs through a fold
642 bifurcation of maps, where the stable fixed point correspond to stable $n - n$

burst solutions of the full two-cell system of ODEs. The results from our one dimensional map match excellently with numerical simulation of the full struggling network.

We have studied anti-phase $n - n$ solutions, assuming that the synaptic coupling $\bar{g}$ between the two cells is symmetrical. However, Bose and Booth (2011) have shown that asymmetrical coupling can result in network solutions of type $m - n$, where one cell fires m spikes, while the other n . It is conceivable that our map construction can be extended to also describe $m - n$ solutions. Remember, in the case of symmetrical coupling and assuming $n - n$ solutions, we had to build one map F_n for the free phase, and another map Q_n for the quiet phase. With asymmetrical coupling, one would have to account for solutions of both the $m - n$ and $n - m$ types. To do that, one could construct a two-dimensional map that tracks the depression variables d_1 and d_2 of both cells. Generally speaking, our map construction approach is applicable to any small network, even with more than two neurons. The main obstacle lies in identifying all combinations of different solutions. Another drawback of our reduction approach is the strictness of assumptions about the time-scale disparity in the system. That is, the method is only applicable to neuronal models with membrane dynamics that are not too slow, e.g. such as the slow calcium-dependent T-current analysed in Matveev et al. (2007). A network with synaptic depression and neurons with slow membrane currents would possibly involve dynamics that occur on at least three timescales. In theory, however, the methods of singular perturbation can also be applied to systems with more than two timescales (e.g. Kuehn, 2015).

While we have identified the bifurcations of the reduced map, we have not found the corresponding bifurcations of the flow system. However, our results are reminiscent of a saddle homoclinic orbit bifurcation, where a stable periodic orbit collides with a saddle equilibrium, and its period becomes infinite. A number of theoretical studies have investigated such a *homoclinic tangency to a periodic orbit* in higher-dimensional systems (e.g. Gavrilov and Shilnikov, 1972; Gaspard and Wang, 1987), and a next step would be to provide a rigorous explanation of not only the map dynamics, but also of the flow dynamics.

We have shown that with varying coupling strength synaptic depression of inhibition can enable a half-centre network to produce an infinite number of stable burst solutions of arbitrarily long period. This result is in line with the idea that one role of synaptic depression in the nervous system may be to allow a finite size neuronal network to participate in different tasks by

681 producing a large number of rhythms (Bose and Booth, 2011; Jalil et al.,
682 2004; Li et al., 2007). To change from one rhythm to another would only
683 require a reconfiguration of the network through changes in synaptic coupling
684 strength, which can occur through the process of learning. Thus short-term
685 synaptic depression of inhibition may provide means for a network to adapt
686 to environmental challenges without changing its topology, that is without
687 the introduction or removal of neurons, or the development of new, and
688 destruction of old synaptic connections.

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696 2.7. Appendix: Computing bifurcation diagram numerically

697 The bifurcation diagram of stable $n - n$ solutions of the two-cell network
698 in Figure 5 is obtained numerically as follows: We initialise the coupling
699 strength at parameter values associated with one type of $n - n$ solution,
700 that is we choose the values $\bar{g} = 0.4, 0.7, 0.8, 0.9, 0.98$ for the $1 - 1$, $2 - 2$,
701 $3 - 3$, $4 - 4$, and $5 - 5$ solutions respectively. For each $\bar{g}$ the system is then
702 numerically integrated sufficiently long for any transients to fully subside.
703 We then identify one period of the solution by finding the first return of the
704 depression variable d_1 . That is, we choose some value $\mathbf{d}_k$ at a spike time t_k ,
705 and by iterating from spike to spike find some subsequent value $\mathbf{d}_{k+1}$ at spike
706 time such that $|\mathbf{d}_{k+1} - \mathbf{d}_k| < \epsilon$. If a periodic solution of type $n - n$ is found
707 in such way, $\bar{g}$ is step-wise increased/decreased, and the above algorithm
708 is repeated. Otherwise, the set of all previously found solutions and the
709 corresponding values $\bar{g}$ are returned.

710 Note that applying conventional methods of numerical continuation is not
711 straightforward for our model, as the discontinuous resets in equations (10)
712 and (11) make the root finding challenging (e.g. see Kuznetsov, 2004, for
713 continuation methods).

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