

# Response to the reviewers

We are very grateful to the reviews for their comments. We are, of course, very pleased that Reviewer 2 was so supportive of our manuscript and that they have endorsed publication. We were equally pleased that Reviewer 1 has engaged so fully with our work, that they saw value in our results and have provided such thoughtful and valuable suggestions. We are sorry it has taken a long time to reply; we wanted to give careful consideration to these suggestions and have made a number of substantial extensions to the work which we believe has made it stronger; we are very grateful for the help the referee comments provided in this.

The biggest changes in the revised manuscript came as a result of points P2.1.1 and P2.3.8, which led us to revert our model to the original equations and parameter values used in Bose and Booth (2011). The motivation behind a slightly different model in our original manuscript, as well as the consequence of the latest changes in the revised manuscript, are explained in section 1.2. Both reviewers also pointed out that some of our notation and terminology is unclear. As a result we renamed many of the terms, an overview of the most important terms is given in section 1.1. We will refer to the first version of the manuscript that was submitted to the journal as the “original manuscript” (M0), and we will call the latest submitted version the “revised manuscript” (M1). If not otherwise stated, the equations numbers, figures, and line numbers refer to the revised manuscript. This response is structured as follows: Section 1 contains the terminology as well as summarises the main model changes in the revised manuscript. In section 2 we address the concerns raised by Reviewer 1, and in section 3 the concerns raised by Reviewer 2.

## 1 Summary of changes

### 1.1 Terminology and notation

Notation and terminology in this field is surprisingly controversial; different authors use different terms for the same thing and the same terms for things that are different, sometimes subtly different. We have tried to follow the referees suggestions as much as possible, but would be grateful for any further guidance. Below we briefly define the controversial terms. In the context of a spiking limit cycle of an uncoupled Morris-Lecar (ML) cell we have:

- $T_a$ : The time interval when the voltage is above firing threshold, i.e. when  $v > v_\theta$ .
- $T_s$ : The time interval when the voltage is below firing threshold, i.e. when  $v < v_\theta$ .

In the context of a stable  $n : n$  solution we have:

- **Active cell**: Cell that is currently firing.
- **Silent cell**: Cell that is currently suppressed and does not fire.

- **Active phase:** Time interval between the start of the limit cycle and the time when the voltage of the active cell falls below firing threshold after the  $n$ th spike, i.e. for  $t \in [0, (n-1)T + T_a]$ .
- **Silent phase:** Time interval after the end of the active phase and the cycle period, i.e. for  $t \in ((n-1)T + T_a, P]$
- **Active phase map:** Map  $F_n$  that models the evolution of  $d$  during the active phase.
- **Recovery phase map:** Map  $Q_n$  that models the evolution of  $d$  during the silent phase.
- **Left and right branch borders:** The left and right branch borders of stable  $n : n$  solutions are denoted by  $\bar{g}_{\mathcal{L}}(n)$  and  $\bar{g}_{\mathcal{R}}(n)$ , respectively.

## 1.2 Model changes

In this section we first explain the model differences between the Bose and Booth (2011) paper and our original manuscript. We will then outline a short motivation for these changes. Finally the model of the revised manuscript is discussed. There are two main differences in the model equations and parameters between the original manuscript and Bose and Booth (2011): First, the value of the applied current  $I$  is different: In Bose and Booth (2011) they have  $I = 3.8 \mu\text{A}/\text{cm}^2$ , in the original manuscript we had  $I = 6 \mu\text{A}/\text{cm}^2$ . Second, the original manuscript uses step-wise resets of  $d$  and  $s$  to simplify the dynamics of the active state of the spike (when  $v > v_\theta$ ).

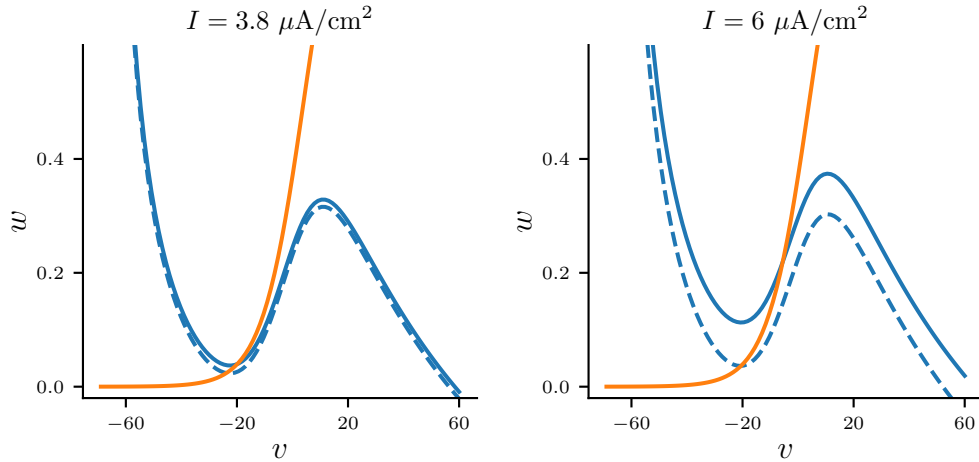


Figure R1: Nullclines of the Bose and Booth (2011) ML model with  $I = 3.8 \mu\text{A}/\text{cm}^2$  (left), and the model from our original manuscript with  $I = 6 \mu\text{A}/\text{cm}^2$  (right). The solid blue lines are the  $v$ -nullclines when  $\bar{g}s = 0$ . The dashed blue lines are the  $v$ -nullclines when  $\bar{g}s$  is near the respective bifurcation point where the fixed point changes stability.

49 The main motivation for increasing  $I$  in the original manuscript had to do with the “excitability”  
 50 of a silent ML cell, and was to simplify the explanation of the concept of the “release conductance”.  
 51 Figure R1 shows the  $v$ - and  $w$ -nullclines for  $I = 3.8 \mu\text{A}/\text{cm}^2$  (left) and for  $I = 6 \mu\text{A}/\text{cm}^2$  (right)  
 52 when no inhibition is applied and  $g = 0$  (let  $g := \bar{g}s$ ). The dashed lines indicate the  $v$ -nullcline at  
 53 the bifurcation point when the total synaptic conductance  $g$  is at the respective bifurcation value,  
 54  $g = g_{bif}$ . In case of  $I = 3.8 \mu\text{A}/\text{cm}^2$  we have  $g_{bif} \approx 0.007 \mu\text{A}/\text{cm}^2$ , whereas for  $I = 6 \mu\text{A}/\text{cm}^2$  we  
 55 have  $g_{bif} \approx 0.03804 \mu\text{A}/\text{cm}^2$ . Hence for  $I = 3.8 \mu\text{A}/\text{cm}^2$  and  $g = 0$ , the unstable fixed point is  
 56 “closer” in phase space to the stable fixed point at bifurcation when  $g = g_{bif}$ , than in case of  $I = 6$   
 57  $\mu\text{A}/\text{cm}^2$ . In other words, a silent cell with  $I = 3.8 \mu\text{A}/\text{cm}^2$  is “easier to excite” than a silent cell  
 58 with  $I = 6 \mu\text{A}/\text{cm}^2$ .

In contrast to the  $I = 6 \mu\text{A}/\text{cm}^2$  scenario, when  $I = 3.8 \mu\text{A}/\text{cm}^2$  the bifurcation at  $g = g_{bif}$  is  
 not sufficient to accurately predict the release time of the silent cell, as the silent cell can produce  
 a first spike despite  $g > g_{bif}$ . Why this happens is interesting but not trivial, and we believe that  
 at this stage it is not important. However, when  $I = 6 \mu\text{A}/\text{cm}^2$  the condition  $g > g_{bif}$  becomes  
 sufficient to accurately predict the release time of the silent cell, that is assuming  $n > 1$  and with  
 the exception of the 2 : 2 outliers in fig. 6 (M0). When  $g > g_{bif}$  is sufficient for predicting the  
 release time, the definition of the release conductance  $g^*$  becomes straightforward, that is  $g^* = g_{bif}$ .  
 Moreover, the value of  $g^*$  can be computed numerically, for example using AUTO. The downside  
 of using  $I = 6 \mu\text{A}/\text{cm}^2$  is that finding  $g^*$  analytically becomes difficult. Because Reviewer 1 asked  
 for an analytic derivation of  $g^*$  in point P2.3.8, and to avoid more confusion by using a different  
 model than Bose and Booth (2011), we have followed the referee’s suggestion and moved the model  
 to  $I = 3.8 \mu\text{A}/\text{cm}^2$  in the revised manuscript; all the analysis and numerical computation has been  
 redone with this revised value. As explained above, however, this complicates the definition and  
 explanation of  $g^*$ : Now the actual value of the release conductance (as defined by the value of  $g$  at  
 the first spike time of the silent cell) depends on both  $n$  and  $\bar{g}$ , as we illustrate in fig. 4A. But as the  
 graph also shows, the dashed line appears to be a good approximation for the numerically computed  
 release conductances. This line marks the value of  $g$  of a suppressed and  $\bar{g} = \bar{g}_s$ , at the end of a cycle;  
 recall that  $\bar{g}_s$  is the minimum coupling strength that will produce the full suppressed solution. And  
 this values is easy to express analytically:

$$\bar{g}_s d_s \lambda e^{-T_s/\tau_\kappa} = g^* \approx 0.0068 \text{ mS}/\text{cm}^2.$$

59 Another advantage of using  $I = 3.8 \mu\text{A}/\text{cm}^2$  is that all release delays are on the millisecond scale,  
 60 and there are no more outliers such the branch B in fig. 6 (M0); or at least none that we could find  
 61 numerically. We had not anticipated this advantage and are pleased that Reviewer 1 prompted us to  
 62 use this new value of  $I$ .

63 The main motivation for changing the synapse model was mathematical convenience, as it made  
 64 the  $\Pi_n$ -map formulation more readable. This change does not appear to affect the overall picture,  
 65 i.e. the period bifurcation diagram has a similar shape even after our change, e.g. compare fig. 4A

(M0) to fig. 3 (M1). However, the biological realism of the step-wise resets of  $s$  and  $d$  in the original manuscript were correctly questioned by Reviewer 1 in P2.1.1. We trust that reverting to the original equations used in Bose and Booth (2011) solves this concern.

To sum up the model changes: The revised manuscript has  $I = 3.8 \mu\text{A}/\text{cm}^2$ , and synaptic dynamics are modelled by

$$\dot{d} = \begin{cases} (1-d)/\tau_a & \text{if } v < v_\theta, \\ -d/\tau_b & \text{if } v > v_\theta, \end{cases}$$

$$\dot{s} = \begin{cases} -s/\tau_\kappa & \text{if } v < v_\theta, \\ 0 & \text{if } v > v_\theta, \end{cases}$$

and we set  $s = d$  while  $v > v_\theta$ . All equations and derivation in the process of the construction of  $\Pi_n$  were modified accordingly. It is important not note that  $\lambda$  is a *derived* parameter in the revised manuscript:

$$\lambda := \exp(-T_s/\tau_a). \quad (1)$$

Naturally all the data for all figures was recomputed with the new model. Fig. 5 (M0) that showed the nullclines for various  $\bar{g}s$  was removed; because  $g^*$  is not defined by the Hopf-bifurcation in the revised manuscript, an illustration of the nullclines as  $\bar{g}s$  is varied seems to be of minor importance. The “release delay” fig. 6 (M0) was replaced by fig. 4A and B (M1).

### 1.3 Other minor changes

- In Fig. 1 (M0) we removed the four phases of a spike (“active”, “silent”, “jump up”, “jump down”). We did this to reduce the terminology confusion regarding “free”/“quite” vs “active”/“silent”, pointed out by Reviewer 1 in P2.2.1. As suggested by the reviewer, in the revised manuscript we use “active”/“silent” to refer to the two phases of burst only.
- Fig. 4B (M0) was removed, as  $IBI$  is not clearly defined and is confusing.
- $T_{act}$  and  $T_{inact}$  were renamed to  $T_a$  and  $T_s$ , respectively.
- $\bar{g}_+$  and  $\bar{g}_-$  were renamed to  $\bar{g}_\mathcal{L}$  and  $\bar{g}_\mathcal{R}$ , as a response to point P2.3.19 raised by Reviewer 1.
- Synaptic time constant  $\tau_s$  was renamed to  $\tau_\kappa$ , the original notation used in Bose and Booth (2011).

## 2 Reviewer 1

## 2.1 Major Comments

**Point P2.1.1** — I don't see the justification for assuming  $\dot{d} = (1 - d)/\tau_d$  when a neuron is ACTIVE (see below for "active" meaning). Can the authors provide some biological justification that the available synaptic resources actually increase during a spike? If not, it seems critical that they give some other justification that this assumption is OK.

Reply: We agree with the reviewer's criticism. Beyond mathematical convenience there was no biological justification for making the assumption that the depression variable recovers when  $v > v_\theta$ . In the original model from Bose and Booth (2011)  $d$  decays when  $v > v_\theta$ :

$$\dot{d}_i = \begin{cases} (1 - d_i)/\tau_a & \text{if } v_i < v_\theta, \\ -d_i/\tau_b & \text{if } v_i > v_\theta, \end{cases}$$

which is now also used in the revised manuscript, see eq. (5) and (6).

**Point P2.1.2** — The authors assume that each spike has duration  $T$ . But that can only be true exactly if the  $s$  variable from the silent neuron is 0, which is never the case. The authors should compute how fast  $s$  has to decay to make period= $T$  a reasonable approximation even in the first spike of a burst, and some commentary about this should be given.

Reply: We agree that  $\tau_\kappa$  is important for the  $ISI = T$  assumption. The paragraph outlining the is assumption in section 3.2 of the main text has been edited to highlight the importance of  $\tau_\kappa$  for the validity of that assumption. We have also added section 3 to the Supplementary Material where we numerically explore how changing the value of  $\tau_\kappa$  affects the first, second, and third  $ISI$ . There we come to the conclusion that for  $\tau_\kappa \leq 100$  ms the effect of a non-zero  $s$  at the start of the active phase is negligible for the first, and naturally the subsequent,  $ISIs$ .

## 2.2 Terminology

**Point P2.2.1** — First, the authors refer to the neurons as "free" or "quiet" and refer to the "free phase" and "quiet phase". They say that they follow Bose and Booth in doing so. But I have read (and written) MANY papers on bursting/CPGs/multi-phase solutions, and they always refer to "active" and "silent" rather than "free" and "quiet". The authors should switch their word use as well to avoid confusing the field.

Reply: We agree that the "free"/"quiet" terminology is uncommon in the field. When referring to a cell in the context of  $n : n$  limit cycles, apart from being consistent with Bose and Booth (2011), our original intent was to use the "free"/"quiet" terms to distinguish them from the phases of the action potential, where we used the more common "active"/"silent" terms. However, as

Reviewer 1 has pointed out, using “active”/“silent” to refer to both the phases of a spiking limit cycle (Ermentrout and Terman, 2010, e.g. p. 250), and the bursting limit cycle (Ermentrout and Terman, 2010, e.g. p. 103) (at least in the context of “bursty” single cells) appears to be more common in the field. For the construction of  $\Pi_n$  only the distinction between the active ( $v > v_\theta$ ) and quiet ( $v < v_\theta$ ) states of an action potential, and the associated times intervals  $T_a$  and  $T_s$ , are essential. To reduce confusion we have therefore removed the mention of the “four phases of a spike” (lines 112-118 in M0), such that in the new version of the manuscript “active” and “silent” refer exclusively to the phases of a  $n : n$  solution. We hope that this clarification is sufficient to be consistent with the field, but if this is still confusing we are open for further naming suggestions.

**Point P2.2.2** — Second, the authors use *ISI* and *IBI* incorrectly. The *ISI* is the inter-spike interval. This is the period BETWEEN spikes, NOT the entire period  $T$  of a spiking event (see e.g., line 181). The *IBI* is the inter-burst interval. In this paper, that would be the silent phase duration for one neuron. It is NOT the entire period of a bursting event, nor is it the delay from the end of one neuron’s active phase to the start of the other neuron’s active phase (e.g., line 266). These need to be corrected throughout the paper.

Reply: We agree with the reviewer that the *IBI* notation is misleading, and it has been completely removed from the manuscript. For the inter-spike-interval *ISI* we have used what we believe is the standard definition (e.g. see Ermentrout and Kopell, 1998; Bose and Booth, 2011; Matveev et al., 2007): The *ISI* is the time interval between successive spike times, where a spike time is the time when the voltage crosses the firing threshold upwards, i.e. the time when  $v$  changes from being below the firing threshold to being above it. In the case of an uncoupled ML cell we have  $ISI = T$ .

**Point P2.2.3** — Third, in the Results, the authors state the signs of various derivatives without proof. Some are obvious (e.g., eqn. (30)) but others, such as eqn. (31), are not. Some brief justification is needed.

Reply: Agreed. We have added a brief explanation regarding the monotonicity of  $\Pi_n$  w.r.t.  $d^*$  (line 331), which follows from the monotonicity of both  $Q_n$  and  $F_n$ . Showing  $dQ_n/d\Delta t > 0$  and  $dF_n/dd^* > 0$  for our model parameters is uncomplicated.

**Point P2.2.4** — Fourth, Fig. 11A seems to contrast with Fig. 4A. Fig. 11A seems to show massive multistability of solutions for different  $n$ , whereas Fig. 4A only has bistability. Some clarification is needed

Reply: Figure 11A (M0) shows stable fixed points of  $\Pi_n$  for different  $n$ . Figure 4A (M0) shows the period of stable  $n : n$  solutions for the flow system. The map  $\Pi_n$  relies on the assumption that the active phase contains exactly  $n$  spikes. This assumption is only valid on certain intervals of  $\bar{g}$ , namely those defined by  $\bar{g}_{\mathcal{L}}(n)$  and  $\bar{g}_{\mathcal{R}}(n)$ . We have added some additional clarification in line 375.

146 **Point P2.2.5** — And fifth, the notation  $n - n$  is non-ideal, as it looks like  $n$  minus  $n$ . In my opinion,  
147  $n : n$  is more standard and clearer.

148 Reply: Thank you for this suggestion, as it especially makes the  $(n + 1) : (n + 1)$  easier to read. As  
149 suggested, we have replaced the  $n - n$  notation with  $n : n$  everywhere in the revised manuscript.

## 150 **2.3 Minor Comments**

151 **Point P2.3.1** — Line 31: It’s a CPG composed of reciprocally inhibitory neurons; referring to a  
152 “reciprocally inhibitory CPG” is misleading.

153 Reply: Agreed. We changed “reciprocally inhibitory CPG” to “CPGs composed of reciprocally  
154 inhibitory neurons” in line 30.

155 **Point P2.3.2** — The par. starting on line 38 is unclear: The  $1 - d$  conditions for  $n : n$  solutions in  
156 [6] are stated to be for  $n \leq 2$  (line 43); the authors should clarify if  $n : n$  in line 48 also refers to  
157  $n \leq 2$  or not.

158 Reply: Agreed. We added a clarification that the scalar conditions are valid only for  $n \leq 2$  (line 47).

159 **Point P2.3.3** — Results line 130: It is important to note that both neurons inhibit each other at  
160 all times.  $s$  may get small but it’s nonzero. Thus, “inhibited” cell is not really well-defined.

161 Reply: Agreed. We changed “inhibited cell” to “suppressed cell”, and added a short explanation, see  
162 lines 120–123.

163 **Point P2.3.4** — Line 137: Wang & Rinzel, 1992 (and perhaps Skinner et al. from 1993 or 1994)  
164 should be cited in reference to release.

165 Reply: Added the Wang and Rinzel (1992) and Skinner et al. (1994) references when “release” is  
166 mentioned in line 126.

167 **Point P2.3.5** — I don’t understand Fig. 4B. The ISI is less than the IBI, so how can their ratio be  
168 bigger than 1? Or perhaps the axis label “ISI/IBI” does not refer to ISI divided by IBI? Clarification  
169 is needed.

170 Reply: The *IBI* notation was indeed unclear, and did not help in explaining our model assumptions,  
171 thank you for pointing this out. All mentions of *IBI*, as well as Fig. 4B (M0), have been removed  
172 from the revised manuscript. Instead, we provide a more straightforward numerical argument for

the  $ISI = T$  assumption in lines 172–182: For every stable  $n : n$  solution in the period bifurcation diagram (fig. 3 in the revised manuscript), we compute all  $ISIs$  and find that they all fall within the interval  $[376, 377]$  ms.

**Point P2.3.6** — Line 200: “revolve” should be replaced by “evolve”.

Reply: The whole paragraph formerly starting at line 194 (M0) has been rewritten.

**Point P2.3.7** — Line 213 is incorrect: It’s not the decay of  $d$  that matters but the decay of  $s$  before the next spike occurs. Correction needed - except now I realize that lines 207-219 can be cut, as they add nothing relative to the previous paragraph.

Reply: Definition of  $g^*$  was changed due to the change in equations, consequently the paragraph formerly starting in line 207 (M0) was removed.

**Point P2.3.8** — It seems like the authors should be able to analytically compute or at least approximate  $g^*$  and should give some explanation for the delay in Fig. 6A, left branch. This must relate to the silent cell spending too short of a time in the silent phase. Fig. 4 is certainly relevant.

Reply: Thank you for this remark. Due to the aforementioned model changes and redefinition of  $g^*$  we can now express  $g^*$  explicitly in eq. (21).

**Point P2.3.9** — Lines 246-7: The authors should revise because  $s$  is determined by  $d$  and by  $\tau_s$ .

Reply: Agreed. In line 214 we clarify that the value of  $s$  “at each spike time” of the active cell depends only on  $d$ . This is because in the revised synapse model (eq. (8))  $s$  is set to the value  $d$  when  $v > v_\theta$ .

**Point P2.3.10** — Line 270: It seems like the active phase ends at time  $(n - 1)T + \Delta t$ , yet the authors say it ends at  $(n - 1)T$ . This may be more convenient for their analysis but it’s not correct usage of the phase terminology, so clarification is needed.

Reply: It is indeed misleading when we let the active phase end at  $(n - 1)T$ , since this time is the beginning of the last spike of the active cell. The change of the model to Bose and Booth (2011) original equations, where  $T = T_a + T_s$ , and the according redefinition of the active phase hopefully clarifies this issue. In the revised manuscript the active phase ends at  $(n - 1)T + T_a$ , which is also the time when the previously active cell becomes silent.

**Point P2.3.11** — It’s disorienting to see  $\delta_n(d^*)$  in eqn. (20) when just above (line 320) the same quantity is called  $d_n = d(t_n^-)$ . The authors should pick one notation for both places.

Reply: Agreed. We have removed the  $d_n$  notation completely.



203 **Point P2.3.12** — Cut line 339 and equation (27). These add a bit of confusion and nothing else.

204 Reply: We believe that line 339 (M0) and eqn. (27) (M0) (eq. (30) in M1) are central to understanding  
205 the derivation of map  $Q_n$ . Eqn. (27) (M0) implies that if we know  $\Delta t$ , then we can predict the value  
206 of the depression variable of the active cell after  $n$  spikes. This statement is not trivial because when  
207 computing  $Q_n$  we have no knowledge of the initial  $d^*$ . We have added some additional explanation  
208 in line 312 and would suggest to leave eqn. (27) (M0) as it is.

209 **Point P2.3.13** — Fig. 9 caption: mention where the  $Q_n$  curves intersect.

210 Reply: Added intersection to caption in fig. 7.

211 **Point P2.3.14** — Eqn. (29): remind the reader that  $\delta_n(d^*)$  comes from eqn. (20) and that  $g^*$  is  
212 obtained numerically.

213 Reply: Added reminder in line 323.

214 **Point P2.3.15** — Lines 364-6 including eqn. (36) should be cut – they are neither new nor helpful  
215 here.

216 Reply: Agreed. Lines have been removed as suggested.

217 **Point P2.3.16** — Eqns. (37),(38) can and should be combined.

218 Reply: Combined as suggested.

219 **Point P2.3.17** — Eqn. (44) is confusing: here the authors want  $d_f^* = \phi_h(\bar{g})$ , so it's strange to  
220 express it as a function of  $d_f^*$  again.

Reply: The  $d_f^*$  in eqn. (44) (M0) was a typo, thank you for pointing this out. It should be

$$\phi_n(\bar{g}) := G^{-1}(\bar{g}). \quad (2)$$

221 Corrected accordingly in eq. (45).

222 **Point P2.3.18** — Fig. 11B needs more explanation, such as a reminder that the orange curves are  
223 only computed over small intervals of  $\bar{g}$  where the solution branch is stable.

224 Reply: Agreed. Added reminder in the fig. 10 caption that the orange curves are computed from  
225 stable  $n : n$  solutions that come from numerical integration of the system.

226 **Point P2.3.19** — The notation  $\bar{g}_+(n) < \bar{g}_-(n)$  seems strange – seems like these should be reversed  
227 (the math is fine, I’m questioning the choice of notation).

228 Reply: We changed the  $\bar{g}_+(n) < \bar{g}_-(n)$  notation to  $\bar{g}_{\mathcal{L}}(n) < \bar{g}_{\mathcal{R}}(n)$ , where the  $\mathcal{L}$  and  $\mathcal{R}$  subscripts  
229 stand for “left” and “right” branch borders.

230 **Point P2.3.20** — Line 415: [21] is cited twice.

231 Reply: Corrected.

232 **Point P2.3.21** — Rather than stating eqn. (54), it would be clearer just to reference eqn. (47)  
233 there.

234 Reply: Agreed. We removed eqn. (54) (M0) and referenced eqn. (47) (M0), see line 391.

235 **Point P2.3.22** — A better explanation of what is shown in Fig. 12 is needed. Is this  $\bar{g}_+(n)$  and  
236  $\bar{g}_-(n)$  for various  $n$ , computed numerically from (56) and (58)?

237 Reply: Agreed. A short clarification was added in the text and captions to fig. 10.

238 **Point P2.3.23** — Discussion lines 459-462: Please explain what such “light” has been shed here. If  
239 none, as it appears, that’s OK for this math paper, but then this comment doesn’t really belong in  
240 the discussion.

241 Reply: Agreed, our formulation was indeed misleading. This paper does not provide much insight  
242 on the underlying biological mechanisms in anti-phase burst generation. Instead, by “underlying  
243 mechanisms” we were referring to the “mathematical principles”, e.g. importance of model parameters  
244 for the rhythm etc. A clarification was added in the text, line 431.

245 **Point P2.3.24** — I’m confused about lines 534-6. I have never heard of learning in a CPG. Please  
246 clarify what is meant.

247 Reply: An elaborate explanation of learning in CPGs seems to be beyond the scope of this paper,  
248 and we have removed the learning reference. If the reviewer is interested the topic “learning in  
249 CPGs”, please consider Lukowiak and Syed (1999), where the authors experimentally study learning  
250 through operant conditioning in the respiratory CPG of the *Lymnaea stagnalis* snail, which consists  
251 of three inter-neurons. Interestingly, they show that in this CPG learning seems to occurs on both  
252 the synaptic level (change in connection strength), and cell-intrinsic level (changes in membrane  
253 properties).

## 3 Reviewer 2

### 3.1 Major Comments

**Note on terminology and notation for Reviewer 2:** In our replies to Reviewer 2 we used the same terminology as used in the original manuscript. This is because the majority of the terminology changes were suggested by Reviewer 1. In the following replies we wanted to focus on the content of the points raised by Reviewer 2, instead of burdening them with new terminology.

**Point P3.1.1** — My major concern is about a few inaccuracies in the terminology. The authors several times repeat that  $n - n$  solution “bifurcates” to  $(n + 1) - (n + 1)$  one (page 3, line 78; page 8, line 281; page 11, line 346; page 14, lines 3-4 of Sec. 3.6; page 14, line 423). I cannot fully agree with such a formulation, since (as follows, e. g., from Eqs. (51) and (52)) there are ranges of the bifurcation parameter (coupling strength)  $\bar{g}$  where two subsequent solutions coexist. When one says that solution A “bifurcates” to solution B, it usually means that before the bifurcation only solution A exists and after the bifurcation only solution B exists, which is not the current case. The authors should revise this point to avoid confusion.

Reply: We agree with the reviewer’s formulation of “bifurcation”, i.e. before the bifurcation point only solution A exists and after only solution B, and that bistability between  $n - n$  and  $(n + 1) - (n + 1)$  solutions should not be referred to as “bifurcation”. However, doesn’t the loss of stability at the left and right branch borders qualify for the reviewer’s definition of bifurcation? That is, near the right border  $\bar{g}_-(n)$  of a  $n - n$  branch, as  $\bar{g}$  is increased beyond  $\bar{g}_-(n)$  the  $n - n$  solution “bifurcates” into a  $(n + 1) - (n + 1)$  solution when the  $n - n$  solution loses stability (similarly near the left branch border as  $\bar{g}$  is decreased). This use of the term “bifurcates” is consistent with Bose and Booth (2011), e.g. see p. 48: “..., we will analytically explain why the bifurcation from a  $n - n$  solution occurs at periods of  $2nT$ ” or p. 49: “Further, the condition also implies that a  $1 - 1$  solution bifurcates to another solution when ...”. The lines in the original manuscript that were pointed out by the reviewer use the term “bifurcates” to refer to these branch borders. Unless we are misunderstanding the reviewer, we would suggest to leave these lines unchanged. However, we are open for an alternative terminology that more accurately describes what is happening at the branch borders.

**Point P3.1.2** — By the same reason, I suggest the authors to avoid the term “period increment bifurcation” (page 1, line 15; page 2, line 69; page 14, lines 408, 413, 416 and 419; page 17, lines 509 and 516), and moreover, such term does not exist. The confusion could have been appeared because of the title of Ref.[23]. The authors of that reference meant a particular type of the big bang bifurcation, where the latter is a codim-2 bifurcation, an organizing center. On the other hand, one can refer to the period increment bifurcation structure (or scenario), which consists of the parameter regions corresponding to periodic dynamics (periodicity regions) that are organized in the parameter space according to a particular principle. However, the bifurcations defining the

boundaries of these periodicity regions may be different. For instance, in works by Avrutin et al. the boundaries of such regions were associated with boundary collision bifurcations, since the map there considered was discontinuous. In the current work, it is not clear which bifurcation is responsible for appearance/disappearance of the  $n - n$  solution. It is not a trivial question and certainly requires deeper analysis, but it is incorrect to call it “period increment bifurcation”.

Reply: This comment is very helpful, thank you. The reviewer is correct, the term “period increment bifurcation” does not exist, Avrutin and colleagues indeed only use the terms “period increment scenario” or “structure”. Throughout the revised manuscript we have replaced the term “period increment bifurcation” by one of the following: “period increment scenario”, “period increment dynamics”, or simply “bifurcation”. The changed lines in the revised manuscript are: line 14, line 384, line 390, and lines 480–491. The section 3.6 title was changed to “Stable solution branch borders”.

### 3.2 Minor Comments

**Point P3.2.1** — Page 2, line 36: change “explaination” to “explanation”.

Reply: Corrected.

**Point P3.2.2** — Page 5, line 158: insert “as” between “well” and “irregular”.

Reply: Corrected.

**Point P3.2.3** — Page 5, line 158: It is claimed that in the certain range of the parameter  $\bar{g}$  (marked in fig. 4A), there exist non-symmetric  $n - m$  and even irregular solutions. Non-symmetric solutions are mentioned once more in Sec. 4 in connection with an asymmetric coupling. Can such solutions indeed appear in the symmetric version of the system? If yes, could the authors provide an example? Or alternatively, the respective sentence in line 158 can be developed a bit concerning this point.

Reply: Figure R2 shows an example of the aforementioned “irregular” solutions. The figure was produced with strong symmetric coupling  $\bar{g} = 0.581$  (mS/cm<sup>2</sup>), which is close to the  $\bar{g}_s$  associated with the left border of the branch of suppressed solutions. An integration time step of  $dt = 0.5$  ms was used. To get rid of transients the system was integrated for 500,000 ms, and fig. R2 shows the last 20,000 ms. It would be interesting to explore how chaotic the system is for large  $\bar{g}$ , but this would likely distract from the main story of the paper, which is also the main reason why we have not included this graph in the paper.

**Point P3.2.4** — Page 6, line 183: The authors probably meant “fig. 4B” instead of “fig. 4A”, as the latter does not show ISI (only for the suppressed solution when it is equal to the period).

Reply: Fig. 4 (M0) was removed from the paper.

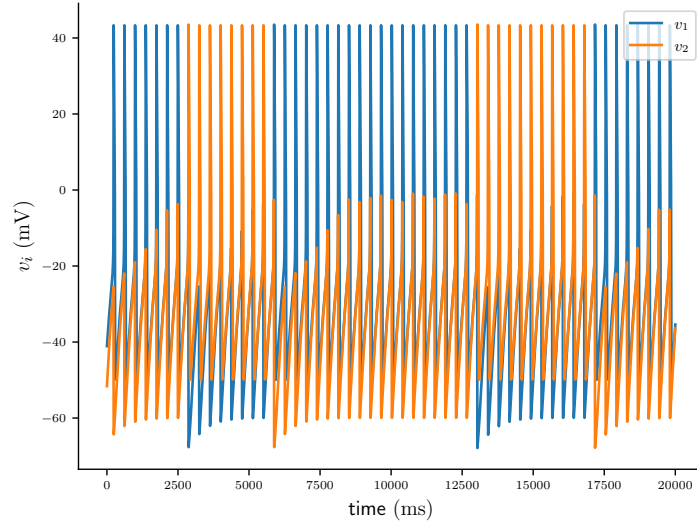


Figure R2: Voltage traces of an “irregular” solution with  $\bar{g} = 0.581$  (mS/cm<sup>2</sup>).

320 **Point P3.2.5** — Page 7, line 235: Did the authors mean “ $\bar{g}s$  crosses  $g^*$ ”?

321 Reply: Corrected.

322 **Point P3.2.6** — Page 7, line 246: It should be “ $g^*$ ” instead of “ $g^*$ ” like throughout the manuscript.

323 Reply: Corrected.

324 **Point P3.2.7** — Page 12, line 371: It should be “is not trivial”.

325 Reply: Corrected.

326 **Point P3.2.8** — In Eq. (44) the function  $G_n^{-1}$  cannot depend on  $d^*$ , please revise.

327 Reply: Indeed, thank you for spotting this.  $G_n^{-1}$  depends on  $\bar{g}$ . Changed accordingly.

328 **Point P3.2.9** — Page 13, line 383: Please remove the word “we”.

329 Reply: Corrected.

330 **Point P3.2.10** — Page 14, line 415: Ref. [21] is written twice.

331 Reply: Corrected.

332 **Point P3.2.11** — Page 17, line 511: In “Avrutin et al. and colleagues” either “et al.” or “and  
333 colleagues” should be removed.

334 Reply: Corrected.

335 **Point P3.2.12** — Fig. 1A: Marking the threshold  $v_\theta$  would be helpful.

336 Reply: Added  $v_\theta$  indicators. to fig. R1.

337 **Point P3.2.13** — Fig. 4: The regions of overlapping (bistability) are obviously distinguishable.  
338 However, it would be helpful if they are highlighted, for instance, by vertical lines or colored vertical  
339 stripes, so that one can easier guess the approximate critical values of  $\bar{g}$ .

340 Reply: Good idea. This will be done in the next iteration of the review process (if there is one).

341 **Point P3.2.14** — Caption of Fig.10: It should be  $\Pi_n : d^\star \mapsto d^\star$ .

342 Reply: Corrected.

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