Amplitude-modulated spiking as a novel route to bursting: Coupling-induced mixed-mode oscillations by symmetry breaking

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Mixed-mode oscillations consisting of alternating small- and large-amplitude oscillations are increasingly well understood, and are often caused by folded singularities, canard orbits or singular Hopf bifurcations. We show that coupling between identical nonlinear oscillators can cause mixed-mode oscillations because of symmetry breaking. This behavior is illustrated for diffusively coupled FitzHugh-Nagumo oscillators with negative coupling constant, and we show that it is caused by a singular Hopf bifurcation related to a folded saddle-node (FSN) singularity. Inspired by earlier work on models of pancreatic beta-cells [A. Sherman, Bull Math Biol 56, 811 (1994)], we then identify a new type of bursting dynamics due to diffusive coupling of cells firing action potentials when isolated. In the presence of coupling, small-amplitude oscillations in the action potential height precede transitions to square-wave bursting. Confirming the hypothesis from the earlier work that this behavior is related to a pitchfork-of-limit-cycles bifurcation in the fast subsystem, we find that it is caused by symmetry breaking. Moreover, we show that it is organized by a FSN in the averaged system, which causes a singular Hopf bifurcation. Such behavior is related to the recently studied dynamics caused by so-called torus canards.

Many neurons and endocrine cells exhibit so-called bursting electrical activity consisting of episodes of action potential firing interspersed with silent phases. The transition from simple spiking electrical activity to such complicated dynamics has been studied theoretically in several model systems. In this work we present a novel route to bursting due to electrical cell-to-cell coupling, where the amplitude of action potentials exhibit small-amplitude oscillations before the transition to bursting. We dissect the mathematical structure underlying the transition, first for a simpler system of coupled FitzHugh-Nagumo units and then for the coupled bursters using averaging and geometric singular perturbation theory. Our results should be of interest for the study of mixed-mode oscillations in other biological and physical oscillators in the presence of coupling, and suggest new theoretical studies related to torus canards and slow transitions through cusp catastrophes.

I. INTRODUCTION

Many neurons and other excitable cell types exhibit non-trivial bursting activity, where active phases of rapid action potential firing are interspersed with periods of quiescence, besides simple action potential generation. Such patterns have been the subject of a series of biophysical modelling studies and related analyses1–6 and are of biological relevance since bursting for example has been suggested to cause greater hormone release than simple spiking electrical activity7–9.

Complex electrical activity is caused by cellular mechanisms operating on different time scales. Thus, the mathematical concepts of slow-fast dynamical systems and geometric singular perturbation theory provide insight into the dynamics of the mathematical models5,6,10. In particular, mixed-mode oscillations11,12 consisting of alternating small- and large-amplitude oscillations occur in many models of electrical activity13–16. Such behavior is increasingly well understood, and is often caused by folded singularities, canard orbits or singular Hopf bifurcations, which typically occur when the fast subsystem possesses a saddle-node bifurcation when treating the slow variables as parameters11,12,17.

Torus-canards, which underlie amplitude-modulated bursting, are the most recent kind of mixed-mode oscillations that has been investigated10,18–21. This behavior occurs when the fast subsystem presents a saddle-node-of-periodic-orbits bifurcation such that the related fold has a folded singularity21, and is typically happening at the transitions from spiking to bursting behavior, where the envelope amplitude of action potentials oscillate for parameter values near the transition19,21.

Coupling of spiking cells can introduce bursting22–27. In a model of electrical activity in pancreatic beta-cells, complicated dynamics occurs at the coupling-induced transition between spiking and bursting. Here, the cells may exhibit a number of synchronized full action potentials before settling into a square-wave burst with anti-phase oscillations23. This behavior was suggested to be related to a pitchfork-of-limit-cycles (PFLC) bifurcation, but was not studied in detail23. Here we study this scenario in greater detail and find that the amplitudes of the action potentials show small-amplitude oscillations24–26, and that they exhibit bursts of synchronized full action potentials before settling into a square-wave burst with anti-phase oscillations27.

Thus, the study of mixed-mode oscillations in biological systems, especially those exhibiting bursting, is a rich field of research. In this work, we focus on the role of coupling in generating mixed-mode oscillations, with a particular emphasis on the transition from spiking to bursting.
II. AMPLITUDE-MODULATED SPIKING AS A ROUTE TO BURSTING

The same behavior as seen by Sherman\textsuperscript{23} is seen in a polynomial model of square-wave bursting representative of most conductance-based biophysical models of bursting electrical activity\textsuperscript{28,29}. We modified the model slightly and coupled two cells. The model can be written in Lienard form\textsuperscript{28,29} as

\begin{align}
    u'_i &= y_i , \\
    y'_i &= -F(u_i)y_i - G(u_i) - z_i - \varepsilon(u_i - c) \\
    &\quad + g_c(u_j - u_i) + g_c(y_j - y_i), \quad j \neq i, \\
    z'_i &= \varepsilon(u_i - c),
\end{align}

where $u_i$ is the transformed membrane potential of cell $i = 1, 2$, and $z_i$ is a slow variable. The coupling term involving $y_i$ results from the transformation from a biophysically inspired model to Lienard form\textsuperscript{28}. The coupling constant $g_c$ corresponds biophysically to the gap junction conductance between the two cells, and in conductance-based models it would only appear once (in the equation for the membrane voltage). The nonlinear functions are given by $F(u) = a((u - \bar{u})^2 - \eta^2)$ and $G(u) = u^2 - 3(u + 1)$.

We observe that this polynomial model can produce a number of synchronized action potentials before switching to bursting (Fig. 1A), similar to the case in\textsuperscript{23}. Importantly, the switch from spiking to bursting is preceded by oscillations in the amplitude of each spike (Fig. 1B), which we interpret as small-amplitude oscillations (SAOs). The same behavior as seen by Sherman\textsuperscript{23} is also present in biophysical models such as the one used by Sherman\textsuperscript{23} (not shown). At the end of a burst, the cells near-synchronize during the silent phase, which may allow the system to reenter spiking and the scenario repeats such that a new episode of bursting is preceded by a variable number of action potentials. We note that the averages of the two cells over each action potential begin oscillating in anti-phase around the nullcline for the slow variables (Fig. 1C), suggesting that symmetry breaking plays an important role, and that averaging can provide insight into the dynamics. We will show that this amplitude-modulated route to bursting is related to a singular torus bifurcation, the equivalent of a singular Hopf bifurcation, as a result of a folded saddle-node in the averaged system, similar to the mechanism underlying torus canards and amplitude-modulated bursting.

III. MIXED-MODE OSCILLATIONS AS A RESULT OF SYMMETRY BREAKING

To understand how symmetry breaking, related to the PFLC bifurcation in the fast subsystem, can cause mixed-mode oscillations, we first study a simpler system that has a similar bifurcation structure but with a pitchfork bifurcation of equilibria rather than of limit cycles. We consider two identical coupled FitzHugh-Nagumo (FHN) oscillators\textsuperscript{31–33}:

\begin{align}
    \varepsilon \dot{x}_i &= -x_i^3 + 3x_i - y_i + \gamma(x_j - x_i), \quad j \neq i, \\
    \dot{y}_i &= x_i - c,
\end{align}

It is convenient to change to the coordinates $x_i$ is the transformed membrane potential of cell $i = 1, 2$, and $z_i$ is a slow variable. The coupling term involving $y_i$ results from the transformation from a biophysically inspired model to Lienard form\textsuperscript{28}. The coupling constant $g_c$ corresponds biophysically to the gap junction conductance between the two cells, and in conductance-based models it would only appear once (in the equation for the membrane voltage). The nonlinear functions are given by $F(u) = a((u - \bar{u})^2 - \eta^2)$ and $G(u) = u^2 - 3(u + 1)$.

\begin{align}
    \varepsilon \dot{x}_{i\parallel} &= -x_{i\parallel}^3 + 3x_{i\parallel} - y_{i\parallel} - 3x_{i\parallel}x_{i\perp}^2, \\
    \varepsilon \dot{x}_{i\perp} &= -x_{i\perp}^3 + 3x_{i\perp} - y_{i\perp} - 3x_{i\perp}x_{i\perp}^2 - 2\gamma x_{i\perp}, \\
    \dot{y}_{i\parallel} &= x_{i\parallel} - c, \\
    \dot{y}_{i\perp} &= x_{i\perp}.
\end{align}

For $c > 1$ and in the absence of coupling, each FitzHugh-Nagumo system has a globally stable equilibrium. Moderate coupling with negative coupling constant $\gamma < 0$ can destabilize this symmetric equilibrium and introduce mixed-mode oscillations where a number of small-amplitude oscillations are present before the system exhibits a large-amplitude oscillation (Fig. 2). Negative coupling thus results in behavior similar to the averaged, coupled system of bursting cells (1)-(3), see Fig. 1, as will be further clarified below (Section IV). The scenario with $\gamma < 0$ was previously studied numerically and for very weak coupling in a regime where so-called leapfrogging, consisting of alternating spiking order between the two oscillators, occurs e.g. as a result of alternating SAOs.\textsuperscript{33} Krupa et al.\textsuperscript{32} performed a detailed analysis of mixed-mode oscillation in heterogeneous coupled FitzHugh-Nagumo systems, but in the presence of attracting coupling and where one of the cells was oscillatory when uncoupled.
Differentiating this equation gives

To study the dynamics on $S$ we multiply by the cofactor matrix of $D_x\Phi$ and get

By rescaling time we can drop $\det D_x\Phi$ and obtain the desingularized system

We focus first on equilibria in the symmetric subspace defined by $x_\perp = 0$. These satisfy

The equilibrium $(x_\parallel, x_\perp) = (c, 0)$ is also an equilibrium of the original system (6)-(9), and is hence an ordinary equilibrium. The other equilibria $(x_\parallel, x_\perp) = (\pm x_\parallel, 0) = (\pm (\sqrt{1 - \frac{2}{3}\gamma})0)$ lie on the fold, satisfy Thm. 6.2 in Brøns, Krupa, and Wechselberger, and are thus folded singularities. Note that these correspond to the pitchfork bifurcations observed in the layer problem for $\gamma < 0$, and to the singular Hopf bifurcation in the full system.

Evaluated at the ordinary singularity $(c, 0)$, the Jacobian of (15) becomes

FIG. 2. Small-amplitude oscillation precede large-amplitude excursions in the FHN model. Simulation of system (4)-(5) with $\gamma = -0.2$, $\varepsilon = 0.01$ and $c = 1.06 < \sqrt{1 - \frac{2}{3}\gamma} \approx 1.06458$. The inset shows a zoom on the small-amplitude oscillations.

It is easily seen that the only equilibrium of the full system is $(x_\parallel, x_\perp, y_\parallel, y_\perp) = (c, 0, -c^3 + 3c, 0)$. The Jacobian evaluated at the equilibrium has eigenvalues

Note that $\lambda_{3,4}$ are purely imaginary ($\pm i/\sqrt{\varepsilon}$) for $c = \mp \sqrt{1 - \frac{2}{3}\gamma}$, where a singular Hopf bifurcation occurs if we treat $c$ as a bifurcation parameter. The first Liapunov number is $\frac{3(\gamma - 3)}{4\varepsilon^{3/2}} + O(\varepsilon^{-1/2})$, which is positive for $\gamma < 0$ and small positive $\varepsilon$. Hence, we have a singular subcritical Hopf bifurcation.

Studying the symmetric fast subsystem with $y_\perp = 0$ and $y_\parallel$ as parameter, we find that this layer problem has a pitchfork bifurcation at $\lambda = \sqrt{1 - \frac{2}{3}\gamma}$ (Fig. 3AC). For $y_\perp \neq 0$, we have the typical behavior for the cusp catastrophe with imperfect pitchfork bifurcations where the pitchfork present for $x_\perp = 0$ splits into two separate branches with one of them showing a saddle-node bifurcation (Fig. 3BD).

The critical manifold $S$ for system (6)-(9) is found by setting $\varepsilon = 0$, which yields a 2d-manifold in $\mathbb{R}^4$ parameterized by $x := (x_\parallel, x_\perp)^T$ with

Differentiating this equation gives

Note that fold curves on $S$ are given by $\det D_x\Phi = 0$, where the system is singular.

FIG. 3. Equilibria of the fast subsystem (6)-(7) treating $y_\parallel$ as a bifurcation parameter for $y_\perp = 0$ (panels A and C, which shows a zoom of panel A) and $y_\perp = 0.1$ (B and D (zoom)). Red, respectively black, points indicate unstable, respectively stable, equilibria. Pitchfork and saddle-node bifurcations are indicated by PF and SN, respectively.
whereas the Jacobian at the symmetric folded singularity \((x^*_s, 0)\) is
\[
\begin{pmatrix}
-6x^*_s(x^*_s - c) & 0 \\
0 & 2\gamma + 6x^*_s(x^*_s - c)
\end{pmatrix}
\] (18)
\[
= \begin{pmatrix}
-6x^*_s(x^*_s - c) & 0 \\
0 & 3 + x^*_s(3x^*_s - 6c)
\end{pmatrix} \quad \text{(19)}
\]
Thus, treating \(c\) as a bifurcation parameter, we see that the ordinary equilibrium is stable for \(c > x^*_s > 1\) where the folded singularity is a saddle. At \(c = x^*_s\) the equilibria meet in a transcritical bifurcation (Fig. 4A), which corresponds to a folded saddle-node (FSN), and a singular Hopf bifurcation in the full system as discussed above. For \(x^*_s > c > \left(1 + x^*_s^2\right)/2x^*_s\) (\(\approx 1.002\) for \(\gamma = -0.2\)) the folded singularity is a folded node, and the SAOs appear as the system passes through the folded singularity (Fig. 4BC).

For \(x^*_s \neq 0\), it can be shown by straightforward calculations that the only two equilibria of (15) are given by \((\bar{x}_l, \pm \bar{x}_r)\) with \(\bar{x}_l = \gamma c/(3c^2 + \gamma - 3)\) and \(\bar{x}_r^2 = \bar{x}_l^2 - 2c\bar{x}_l + 1\). These equilibria lie outside the region of interest near \((x^*_s, 0)\) for \(c \approx x^*_s\), and are not studied further. We note that they do not satisfy the criteria that guarantees that they are folded singularities, see Thm. 6.2 in Brons, Krupa, and Wechselberger.\(^11\)

### IV. ANALYSIS OF AMPLITUDE-MODULATED SPIKING

We now return to amplitude-modulated spiking at the transition to bursting in the model given by (1)-(3) (see Fig. 1). Changing coordinates, as done for the FHN system above to \(u_l = (u_1 + u_2)/2\) and \(u_\perp = (u_1 - u_2)/2\) (and similarly for \(y_l\) and \(z_l\)), the model becomes
\[
u^*_l = y^*_l, \quad (20)
u^*_l = y^*_l, \quad (21)
y^*_l = -F(u_l)y^*_l - G(u_l) - z^*_l - \varepsilon(u_l - c) - (-u_\perp + ay^*_l + 2ay^*_l(u_l - \bar{u})u_\perp)u_\perp \quad (22)
y^*_l = -u^*_l - ay^*_l u^*_l - z^*_l - (F(u_l) + 2g_\perp)y^*_l \quad (23)
\]
\[
y^*_l = -3u^*_l + 2ay^*_l(u_l - \bar{u}) - 3 + 2g_\perp u_\perp - \varepsilon u_\perp \quad (24)
z^*_l = \varepsilon(u_l - c) \quad (25)
\]
Clearly, the symmetric subspace produced by \(u_\perp = y_\perp = z_\perp = 0\) is invariant. For the parameters producing SAOs in the spike amplitude before bursting, the fast subsystem has a bifurcation structure similar to the one observed by Sherman.\(^23\). In particular, for \(z_\perp = 0\), spiking occurs on a short stable part of the in-phase (IP); \(u_\perp = y_\perp = 0\) periodic branch, which loses stability in a pitchfork of limit-cycles (PFLC) bifurcation, located at \((z_{\text{PFLC}}, \bar{u}_{\text{PFLC}})\), which appears to coincide with the point where the system transits into bursting due to a stable antiphase periodic branch emerging from another (upper) PFLC (Fig. 5A).

#### A. Averaging

As mentioned above and motivated by Fig. 1C, we perform averaging to analyze this system and the origin of SAOs in the spike amplitude further. By standard averaging theory, \(z' = \bar{u} - c, z'_\perp = \bar{u}_\perp\). Here and elsewhere, \(\bar{x} = \frac{1}{T} \int_0^T x(t) dt\), where \(T\) is the period of the limit cycle. Thus, the averaged \((z_\perp, z_\perp)\) subsystem has equilibria where \((u_l, u_\perp) = (c, 0)\), which appear from Fig. 1C to be organizing the SAOs. The bifurcation diagram for \(\bar{u}_l\) (Fig. 5BC) shows that the \(z_\perp\) nullcline intersects the average IP branch just above the PFLC bifurcation, where the averaged fast subsystem is unstable, and this point is thus a saddle equilibrium for the full averaged system. In addition, \(\bar{u}_\perp\) performs small oscillations around the \(z_\perp\) nullcline (Fig. 5C), as already noted in Fig. 1C.

At the PFLC, two unstable branches are born. When projected onto the \((z_\perp, \bar{u}_\perp)\) plane, these are located symmetrically around the stable IP branch for \(z_\perp = 0\) (Fig. 5D). When the symmetry of the averaged fast subsystem is broken by \(z_\perp \neq 0\), an imperfect pitchfork bifurcation is present, and in particular we observe a saddle-node of limit cycles (SNLC). Similarly, when projecting the location of the limit cycles onto the \((z_\perp, u_\perp)\) plane for different values of \(z_\perp\) (Fig. 5E), we see that SNLCs are present for \(z_\perp > z_{\text{PFLC}}\). For \(z_\perp < z_{\text{PFLC}}\), only an unstable branch with \(u_\perp\) a decreasing function of \(z_\perp\) is present. The locations of the SNLCs depend on \((z_\perp, z_\perp)\) as seen from the two-parameter bifurcation diagram (Fig. 5F), which presents a cusp at \((z_{\text{PFLC}}, 0)\). The solution of the full system appears to pass close to the cusp and approach the saddle-point, where it spirals away. Summarizing, the averaged system has the same (local) structure as the FHN system studied above, and we expect a singular Hopf bifurcation to be responsible for the SAOs seen in Fig. 1.

#### B. Geometric analysis

To proceed as for the FHN system, we would like to describe the critical averaged manifold with \(z = (z_\perp, z_\perp)\) defined as a function of \(\bar{u} = (\bar{u}_l, \bar{u}_\perp)\) near \((\bar{u}_{\text{PFLC}}, 0)\). Let \(\bar{u}\) be given. From Fig. 5E, we note that, for fixed \(z_\perp\), we can write \(z_\perp\) as a smooth function of \(\bar{u}_\perp\), say \(z_\perp = \Phi(\bar{u}_\perp; z_\perp)\). Note that \(\bar{u}_\perp\) defines which of three branches we consider in case there are more solutions for fixed \(z_\perp\). Consider now the function that, for fixed \(u_\perp\), associates \(z_\perp\) to the average of \(u_l\) via \(\phi\), i.e., \(z_\perp \mapsto \psi(z_\perp; u_\perp) := \bar{u}_l(\bar{u}_l, \Phi(\bar{u}_\perp; z_\perp))\). This function is well defined by the comment above. Moreover, it is smooth and strictly decreasing (Fig. 5C), hence invertible. Thus, the function \(z = \Phi(\bar{u}) = \psi^{-1}(\bar{u}_l; u_\perp)\) gives the relation we are looking for. We have that \(\Phi\) is differentiable, and we can write the critical averaged manifold as
\[
z_\perp = \Phi_l(\bar{u}), \quad z_\perp = \Phi_\perp(\bar{u}),
\]
and thus the slow dynamics on \(S\) is given by
\[
z' = \begin{pmatrix}
\frac{\partial}{\partial u_l} \Phi_l(\bar{u}) \\
\frac{\partial}{\partial u_\perp} \Phi_\perp(\bar{u})
\end{pmatrix} \bar{u}' := A(\bar{u})\bar{u}'.
\] (26)
FIG. 4. The small-amplitude oscillations in the FHN system are due to passage through a folded singularity near a saddle point. A: Bifurcation diagram with c as parameter and γ = -0.2. The x||-coordinate of the full-system equilibrium (c, 0) of the desingularized system (15) is given by the blue line, whereas the black curve indicates the location of the symmetric folded singularities (\sqrt{1 - 2γ/3}, 0) ≈ (1.06458, 0). Full (respectively, dashed) lines indicate stable (respectively, saddle) equilibria. At c = \sqrt{1 - 2γ/3} the equilibria meet in a transcritical bifurcation (TC; red dot). The vertical red dotted line indicates the value c = 1.06 used in panels B and C. B: Simulation of system (6)-(9) projected onto the (x||,x⊥)-plane (green). The magenta curves show the projected fold curves. Folded singularities are shown by black crosses. The blue triangle indicates the original full-system saddle equilibrium. C: A zoom onto the small-amplitude oscillations occurring after the passage near the folded node close to the saddle-point.

This system has a fold where the matrix A(\bar{u}) becomes singular, for example at the pitchfork-of-limit-cycles, similar to the FHN system studied above. At points where z⊥ = 0, we have \frac{\partial^2}{\partial u⊥^2} \Phi || (\bar{u}) = 0 = \frac{\partial^2}{\partial u⊥^2} \Phi ⊥ (\bar{u}) because of symmetry, and thus detA(\bar{u}) = \frac{\partial}{\partial u⊥} \Phi || (\bar{u}) \frac{\partial}{\partial u⊥} \Phi ⊥ (\bar{u}). Note that here \frac{\partial}{\partial u⊥} \Phi || (\bar{u}) < 0 and symmetric fold points are given by \frac{\partial}{\partial u⊥} \Phi ⊥ (\bar{u}) = 0.

As for the FitzHugh-Nagumo system, we multiply by the cofactor co (A(\bar{u})) to get

\[ \text{det}(A(\bar{u})) \bar{u}' = \text{co}(A(\bar{u})) z' = \text{co}(A(\bar{u})) \left( \bar{u}|| - c \over \bar{u}⊥ \right). \]

Finally, we rescale time to remove \text{det}(A(\bar{u})) and obtain the desingularized system

\[ \bar{u}' = \left( \begin{array}{c} \frac{\partial}{\partial u⊥} \Phi || (\bar{u}) - \frac{\partial}{\partial u⊥} \Phi ⊥ (\bar{u}) \\frac{\partial}{\partial \bar{u}||} \Phi || (\bar{u}) \end{array} \right) \left( \bar{u}|| - c \over \bar{u}⊥ \right) \]

\[ = \left( \begin{array}{c} \left[ \frac{\partial}{\partial u⊥} \Phi || (\bar{u}) \right] (\bar{u}|| - c) - \left[ \frac{\partial}{\partial \bar{u}||} \Phi || (\bar{u}) \right] \bar{u}⊥ \\left[ \frac{\partial}{\partial u⊥} \Phi ⊥ (\bar{u}) \right] (\bar{u}|| - c) + \left[ \frac{\partial}{\partial \bar{u}||} \Phi ⊥ (\bar{u}) \right] \bar{u}⊥ \end{array} \right) \]

\[ J = \left( \begin{array}{c} \frac{\partial^2}{\partial u⊥^2} \Phi || (\bar{u}|| - c) + \frac{\partial}{\partial \bar{u}||} \frac{\partial}{\partial \bar{u}⊥} \Phi || (\bar{u}|| - c) - \frac{\partial^2}{\partial u⊥^2} \Phi ⊥ (\bar{u}|| - c) - \frac{\partial}{\partial \bar{u}||} \frac{\partial}{\partial \bar{u}⊥} \Phi ⊥ (\bar{u}|| - c) \\frac{\partial^2}{\partial u⊥^2} \Phi || (\bar{u}|| - c) - \frac{\partial}{\partial \bar{u}||} \frac{\partial}{\partial \bar{u}⊥} \Phi || (\bar{u}|| - c) - \frac{\partial^2}{\partial u⊥^2} \Phi ⊥ (\bar{u}|| - c) - \frac{\partial}{\partial \bar{u}||} \frac{\partial}{\partial \bar{u}⊥} \Phi ⊥ (\bar{u}|| - c) \end{array} \right), \]

which has trace \(Tr(J) = \frac{\partial \Phi ||}{\partial \bar{u}||} + \frac{\partial \Phi ⊥}{\partial \bar{u}⊥} = Tr(A)\). Near the fold,

\[ Tr(J) \approx \frac{\partial \Phi ||}{\partial \bar{u}||} < 0. \]

Symmetric equilibria of this system solve

\[ \left( \frac{\partial}{\partial \bar{u}⊥} \Phi ⊥ (\bar{u}) \right) (\bar{u}|| - c) = 0. \]

Here, \(\bar{u}|| = c\) is a solution to the original system (26), and the solutions to \(\frac{\partial}{\partial \bar{u}⊥} \Phi ⊥ (\bar{u}) = 0\) lie on the fold and are thus folded singularities. The Jacobian of (27) is

For the symmetric equilibrium of the original system, \(\bar{u} = (c,0)\), \(Tr(J) = Tr(A)\) and \(\text{det}(J) = \text{det}(A)\). Thus, the ordinary symmetric equilibrium has the same character as the corre-
sponding fast-subsystem equilibrium: it is a stable node for $c < \bar{u}_{\text{PFLC}}$, the value where the pitchfork bifurcation of limit cycles occurs, and a saddle point for $c > \bar{u}_{\text{PFLC}}$.

A symmetric folded singularity has Jacobian with trace

$$
\text{Tr}(J) = \frac{\partial^2 \Phi}{\partial u_1 \partial u_2} < 0 \quad \text{and determinant}
$$

$$
\det J = \left( \frac{\partial^2 \Phi}{\partial u_1 \partial u_2} - (\bar{u}_1 - c) \frac{\partial^2 \Phi}{\partial u_1 \partial u_1} \right) (\bar{u}_2 - c) \frac{\partial^2 \Phi}{\partial u_2 \partial u_2},
$$

which, for $\bar{u}_1 \approx c$, is negative for $\bar{u}_1 < c$ and positive for $\bar{u}_1 > c$, since $\frac{\partial^2 \Phi}{\partial u_1 \partial u_1} < 0$. Thus, the symmetric folded singularity is a folded saddle for $\bar{u}_{\text{PFLC}} > c$ and a folded node for $\bar{u}_{\text{PFLC}} < c$. At $\bar{u}_{\text{PFLC}} = c$ the folded singularity and the ordinary one meet in a transcritical bifurcation, as seen for the FHN system studied above. Thus, we expect a singular Hopf bifurcation at or near this value, which makes $(\bar{u}_1, \bar{u}_2)$ oscillate, giving rise to SAOs in amplitude of the original limit cycles $(u_1, y_1, u_2, y_2)$, i.e., a singular torus bifurcation occurs.

V. CONCLUSIONS

Summarizing, we have shown that symmetry breaking in a system of two coupled cells can induce MMOs. In the simpler case of two coupled FHN oscillators, which are stable when uncoupled, MMOs are caused by a singular Hopf bifurcation related to passage through a cusp point. Similarly, coupling of two spiking cells can cause amplitude-modulated spiking and transition to bursting due to a singular torus bifurcation. The averaged system has the same structure as the coupled FHN oscillators, with a cusp-related folded singularity and a singular Hopf bifurcation causing SAO. We note that the dynamics near the cusp is different from the scenario studied previously due to the inverted stability of the sheets of the critical manifold and the presence of a full-system saddle-equilibrium located near the cusp point. Future work should study unfolding of cusp-related folded singularities, singular Hopf bifurcations and mixed-mode oscillations.

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DATA AVAILABILITY

Data sharing is not applicable to this article as no new data were created or analyzed in this study.


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FIG. 5. Fast subsystem bifurcation analysis of (20)-(23). 

A: Fast subsystem bifurcation diagram for $z_\perp = 0$ with $z_\parallel$ as parameter. Black (respectively red) curves indicate stable (unstable) equilibria, green (blue) curves indicate stable (unstable) limit cycles. For the limit cycles, the maximum and minimum values of $u_\parallel$ is shown. The equilibrium loses stability in a Hopf bifurcation (HB) where in-phase (IP) limit cycles are born. These lose stability in an upper pitchfork-of-limit-cycles (PFLC) bifurcation, where a stable branch of anti-phase oscillations is born. The stability of the IP branch is regained at another lower PFLC at $z_{PFLC} \approx 0.7095$. The horizontal dashed line $\bar{u}_\parallel = 0.115$ corresponds to the $z_\parallel$ nullcline $c = 0.115$ used for the simulation in Fig. 1, which is projected (for $12310 < t < 14750$) onto the $(z_\parallel, u_\parallel)$ plane (gray).

B: As in panel A, but with the average of $u_\parallel$ over a cycle, $\bar{u}_\parallel$ shown. The projection of the rolling average of the numerical solution over three action potentials is plotted in gray. 

C: A zoom on the lower PFLC in panel B. Note the SAO around the $z_\parallel$ nullcline, which are highlighted in the inset. 

D: As in panel C, but with $\bar{u}_\perp$ shown. The blue and light green curves correspond to $z_\perp = 0$ as in panel D, whereas the lightblue (unstable) and dark green (stable) curves are for $z_\perp = 0.0002$ where a saddle-node of limit cycles (SNLC) is present, i.e., we have an imperfect PFLC. 

E: Bifurcation diagram with $\bar{u}_\perp$ and $z_\perp$ as parameter for $z_\parallel = 0.720$ (full curve) and $z_\parallel = 0.712$ (dashed curve). 

F: Two-parameter bifurcation diagram following the PFLC/SNLC bifurcations (black). The critical manifold is attracting inside the triangular area on the right. The gray curve shows $(z_\parallel, z_\perp)$ at the times when $u_\parallel$ is minimum between action potentials in the simulation from Fig. 1. Note the small-amplitude oscillations emerging after the passage over the fold, which are highlighted in the inset.