

Qualitative changes in spike-based neural coding and synchronization at the saddle-node loop bifurcation

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(Dated: November 14, 2016)

Information processing in the brain crucially depends on encoding properties of single neurons, with particular relevance of the spike-generation mechanism. The latter hinges upon the bifurcation type at the transition point between resting state and limit cycle spiking. Prominent qualitative changes in encoding have previously been attributed to a specific switch of such a bifurcation at the Bogdanov-Takens (BT) point. This study unveils another, highly relevant and so far underestimated transition point: the saddle-node loop bifurcation. As we show, this bifurcation turns out to induce even more drastic changes in spike-based coding than the BT transition. This result arises from a direct effect of the saddle-node loop bifurcation on the limit cycle and hence spike dynamics, in contrast to the BT bifurcation, whose immediate influence is exerted upon the subthreshold dynamics and hence only indirectly relates to spiking. We specifically demonstrate that the saddle-node loop bifurcation (*i*) ubiquitously occurs in planar neuron models with a saddle-node on invariant cycle onset bifurcation, and (*ii*) results in a symmetry breaking of the system's phase-response curve. The latter entails close to optimal coding and synchronization properties in event-based information processing units, such as neurons. The saddle-node loop bifurcation leads to a peak in synchronization range and provides an attractive mechanism for the so far unresolved facilitation of high frequencies in neuronal processing. The derived bifurcation structure is of interest in any system for which a relaxation limit is admissible, such as Josephson junctions and chemical oscillators. On the experimental side, our theory applies to optical stimulation of nerve cells, and reveals that these techniques could manipulate a variety of information processing characteristics in nerve cells beyond pure activation.

Keywords: phase-response curve, saddle-node homoclinic orbit, saddle-node noncentral homoclinic, saddle-node separatrix-loop, homoclinic orbit, saddle separatrix loop, membrane capacitance, infrared neural stimulation

I. INTRODUCTION

Survival in a complex environment often demands nervous systems to provide acute senses, intricate computations and speedy reactions [1], carried out in an economical fashion [2]. Efficient neuronal information processing is hence considered an evolutionary favorable trait [3]. Information processing can be optimized on the level of neuronal networks [4], but also on the level of single cells [5–7]. For the latter, tuning the cell's voltage dynamics into a regime that flexibly supports computational needs is decisive.

In this study, we describe a point of drastic transition in neuronal single-cell dynamics with consequences for information processing and network synchronization. While the underlying bifurcation is not unknown [8], its consequences for neural processing are severely underestimated. This article shows that the transition in question turns out to be a ubiquitous feature in (planar) type-I neuron models, known to describe various neurons, ranging from isolated gastropod somata (Conner-

Stevens model as stated in Ref. [9]) to hippocampal neurons [10, 11].

Nerve cells are thought to encode information in the sequence of spikes produced in response to their input. *What* is encoded, crucially depends on the specific mechanism of spike generation [12–16]. Different types of spike generation were first classified by Hodgkin [17] and later linked to particular bifurcations ruling the transition from rest to spiking [18, 19]. The detailed analysis of bifurcations in single neurons has so far explained many of the complex responses that neurons show, *e.g.*, bursting or rebound spiking [19–21]. The mechanisms of other response properties, such as the sharp voltage increase at spike onset, are still a highly debated topic [12, 22, 23].

Recently, the ability of neurons to change the mechanism of spike generation under physiological conditions has attracted the interest of both theoreticians and experimentalists [24–27]. Attention was mostly directed at the transition between the two traditional excitability types, which involve either a *fold* (saddle-node) or a *Hopf* bifurcation [Fig. 1(a)], along with their differential subthreshold filtering properties [28–31]. Here, we investigate an alternative transition, which switches the spike onset from a *saddle-node on an invariant cycle* (SNIC) bifurcation to a *saddle homoclinic orbit* (HOM) bifurcation [Fig. 1(b)]. This transition is organized by a

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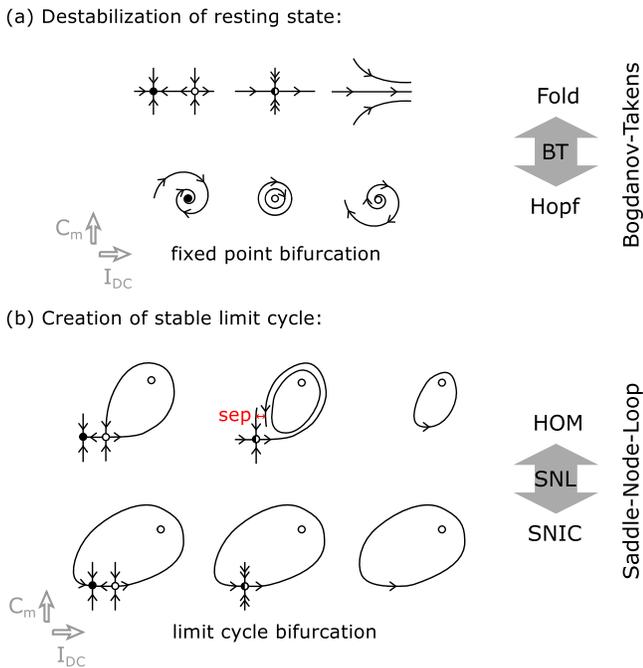


Figure 1. Color) The transition from rest to spiking in response to an increase in input current I_{DC} requires (a) that the resting state loses stability (illustrated are fold and subcritical Hopf bifurcations) and (b) the creation of a limit cycle (illustrated are saddle homoclinic orbit (HOM) and SNIC bifurcations). The membrane capacitance C_m allows to switch between these bifurcations. The separation function, sep , marked in red, measures the distance between the stable and unstable manifold of the saddle. The overlap of both, *i.e.*, $sep = 0$, results in a homoclinic orbit.

codimension-two bifurcation: the *saddle-node loop* (SNL) bifurcation [32] [33]. As we demonstrate, the SNL bifurcation causes an abrupt change in phase-response curve, with far-reaching functional consequences for spike-based coding. Moreover, the increase in synchronization ability of individual cells observed at an SNL bifurcation affects network synchronization [Fig. 2], with potential relevance for various pathological conditions ranging from epilepsy to Parkinson’s disease [34, 35].

SNL bifurcations can occur with several bifurcation parameters, for example the time constant of the gating kinetics [21]. In this study, we identify the separation of time scales between voltage and gating dynamics as the decisive bifurcation parameter, underlying the effect of other parameters, such as capacitance or temperature. Starting at a SNIC bifurcation in planar general neuron models, we demonstrate that a variation in the separation of time scales provokes a generic sequence of firing onset bifurcations. Compared to other bifurcation studies, which rely on a *local* unfolding of a codimension-three bifurcation [36, 37], our approach proves the generic bifurcation structure including appearance and ordering of codimension-two bifurcations on a *global* scale not restricted to local analysis. The composed bifurcation

diagram hence predicts the behavior of a class of neurons over the whole range of time-scale parameters, and thereby warrants a direct comparison with biological neurons.

The organization of the paper reflects the intricate relation between the dynamical and computational aspects of the SNL bifurcation. Formally, this relation is established via the phase-response curve (PRC) [38]. While Sec. II introduces the phase-response curve as spike-based stimulus encoder, Sec. III describes how it can be identified from the limit cycle of a dynamical system. With the relation established, Sec. IV proves that a symmetry breaking of the phase-response curve occurs at SNL bifurcations. The functional consequences for coding and synchronization in spiking systems are discussed in Sec. V. The significance of these consequences are perpetuated by the results in Sec. VI, where we prove that SNL bifurcations generically occur in planar neuron models.

II. SPIKE-BASED INFORMATION ENCODER

The following two sections introduce phase oscillator models and conductance-based neuron models, which we use to describe neuronal dynamics on two different levels, the spike times, and the underlying membrane voltage, respectively. In many nervous systems, the integration of sensory stimuli from multiple modalities into an appropriate behavioral response is achieved by translating the impinging information into a series of spike times, $\{t_k^{sp}\}$, a universal code for computation [39]. A single neuron can be surmised as a *spike time encoder* that maps input signals, $I(t)$, to a spike train, $y(t) = \sum_k \delta(t - t_k^{sp})$. One way to formally identify a spike encoder from a biophysical model of membrane voltage dynamics is the reduction to a phase equation producing the same input-output mapping (*i.e.*, an *input-output (I/O) equivalent* phase oscillator [40]). The I/O equivalent phase equation is used throughout the paper to derive characteristics of neuronal information processing, such as the maximal rate at which information is transmitted, or the ability of neurons to synchronize their activity. Similar settings apply to many system ranging from chronobiology [41] to pulsars [42], where the only observations of the complex dynamical system are pulse-like threshold crossings resulting in an event time series.

The following analysis assumes tonic responses of a mean-driven neuron [29], *i.e.*, spikes are emitted with a mean spike rate, f_0 , in response to a constant mean stimulus intensity, I_{DC} , and their occurrence is modulated by a time dependent, zero-mean signal, $I(t)$, sufficiently weak to only shift spike times. In this case, the mapping of input to spike times is given by the *phase-response curve* (PRC) of the neuron [43]. The PRC, Z , relates the timing of occurrence of a weak perturbation to the resulting temporal advance or delay of the following spike, $Z : \phi \mapsto \Delta\phi$. The spike times $\{t_k^{sp}\}$ correspond

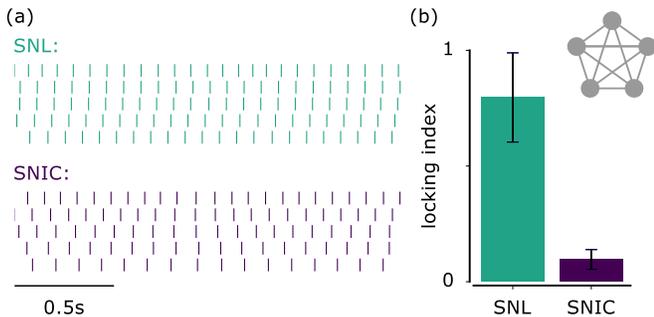


Figure 2. Color) (a) Spike raster plot of two small globally coupled network of 5 Wang-Buzsaki models, one close to the SNL bifurcation with $C_m = 1.47 \mu\text{F}/\text{cm}^2$, the other at a SNIC bifurcation with $C_m = 1 \mu\text{F}/\text{cm}^2$. Synaptic connections are modeled as δ -perturbations of 0.35 mV. The frequency detuning of the neuron is approximately equally spaced between 5 and 11 Hz. (b) The phase locking index was calculated between pairwise neurons i and j with phase $\phi_{i,j}$ as $\langle e^{i2\pi(\phi_i - \phi_j)} \rangle$, where the brackets denote temporal averaging. Error bars denote standard deviations.

to the level crossings of the phase, $\phi(t_k^{\text{sp}}) = k$ for $k \in \mathbb{Z}$, and their occurrence is governed by the phase equation

$$\dot{\phi} = f_0 + Z(\phi)I(t) + \xi(t). \quad (1)$$

The intrinsic noise $\xi(t)$ and the input $I(t)$ are assumed to be zero-mean stochastic processes of different time scales: $\xi(t)$ is white noise, $\langle \xi(0)\xi(\Delta t) \rangle = \sigma^2\delta(\Delta t)$ and $I(t)$ is wide-sense stationary with correlations $\langle I(0)I(\Delta t) \rangle = \varepsilon^2 C(\Delta t)$.

To linear order, the I/O equivalent spike train is $y(t) = \sum_k \delta(k - \phi(t))$. In the following, the mean spike rate f_0 in response to the mean drive I_{DC} and the PRC $Z(\phi)$ are implicitly taken to be functions of the parameters of the detailed neuron model introduced below.

III. CONDUCTANCE-BASED NEURON MODEL

To investigate the mapping of input to spikes, our model neurons are stimulated by a constant DC current and a zero-mean, time-varying stimulus, $I_{\text{in}} = I_{\text{DC}} + I(t)$. The dynamics of the membrane voltage v follows a current balance equation, $I_{\text{in}} = I_{\text{cap}} + I_{\text{ion}}$. The input causes a capacitive current, $I_{\text{cap}} = \frac{dC_m v}{dt}$ (with membrane capacitance C_m) and an ionic current, $I_{\text{ion}} = I_{\text{ion}}(v, m_i, \dots)$, which is a function of v itself and the open probability of ion channels given by their *gating variables* m_i .

Combined, this so-called *conductance-based neuron model* entails a dynamical system, $\dot{X} = F(X) + G(X, t)$, with the following structure:

$$\begin{pmatrix} \dot{v} \\ \dot{m} \\ \dots \end{pmatrix} = \begin{pmatrix} \frac{1}{C_m}(I_{\text{DC}} - I_{\text{ion}}(v, m, \dots) + I(t)) \\ \frac{m_{\infty}(v) - m}{\tau_m(v)} \\ \dots \end{pmatrix}, \quad (2)$$

where the dot $\dot{}$ denotes the derivative by time, F determines the dynamics of the unperturbed system, and $G = C_m^{-1}I(t)e_v$ is some time-dependent voltage perturbation (e_v represents the basis vector in voltage direction). The dynamical variables consist of the voltage and the gating variables such as m . The gating is typically modeled by first-order kinetics (for details see Appendix A).

The input I_{DC} acts as bifurcation parameter for the bifurcations of both fixed point destabilization and limit cycle creation [Fig. 1]. For our analysis, we focus on neuron models in which the fixed point loses stability at a fold bifurcation. To identify the I/O equivalent phase model in Eq. (1), the PRC needs to be calculated for the conductance-based model in Eq. (2). From a dynamical systems perspective, the PRC Z is the periodic solution to the adjoint of the first variational equation of the unperturbed dynamics in Eq. (2), $\dot{X} = F(X)$,

$$\frac{dZ}{d\phi}(\phi) = -J^{\top}(\phi)Z(\phi), \quad (3)$$

where \top denotes the matrix-transpose and $J = \frac{\partial F}{\partial X}$ is the *Jacobian* evaluated on the limit cycle. To comply with Eq. (1), the PRC associated with input current perturbations needs to be normalized as $Z(\phi) \cdot F(\phi) = f_0/C_m, \forall \phi$. The resulting relation between PRC and parameters of the conductance-based neuron model allows us to consider coding properties at different firing onset bifurcations. In the following, we use the dynamics on the homoclinic orbit to infer PRC properties of the limit cycle that arises from the homoclinic orbit, and, for convenience, we refer to the limit cycle PRC as the PRC at the limit cycle bifurcation (SNIC or SNL), *i.e.*, Z_{SNIC} or Z_{SNL} .

IV. A FLIP IN THE DYNAMICS ALTERS THE PRC SYMMETRY AT AN SNL BIFURCATION

In a first step, we infer coding properties from the dynamics at firing onset bifurcations, in particular around the SNL bifurcation. As bifurcations imply in general qualitatively different dynamics [44], limit cycle dynamics are expected to change at the switch in firing onset dynamics at the SNL bifurcation. But what are the specific consequences for the way neurons encode stimuli and synchronize in networks? To answer this question, we start by discussing changes in limit cycle dynamics at the SNL bifurcation. We then show that this also alters the PRC in such a profound way that it has, in turn, drastic implications for the resulting coding properties discussed in Sec. V. To this end, we use the tight relation between spike coding and PRC [Eq. (1)], as well as PRC and dynamics [Eq. (3)].

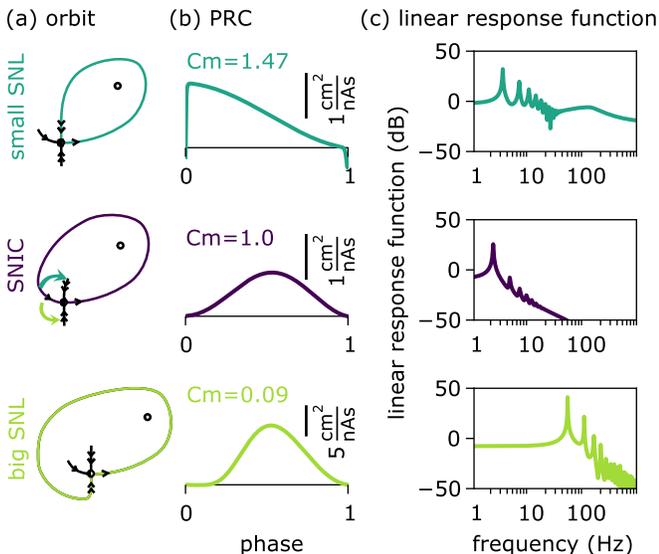


Figure 3. Color) Top to bottom: (a) Schematic illustration of the orbits at small SNL bifurcation, non-degenerated SNIC bifurcation, and big SNL bifurcation, with semi-stable (small single arrow) and strongly-stable manifold (double arrows). These bifurcations occur in the Wang-Buzsaki model for $I_{DC} \approx 0.16 \mu\text{A}/\text{cm}^2$, $C_m \approx [1.47, 1, 0.09] \mu\text{F}/\text{cm}^2$. (b) and (c) show the associated phase-response curves and transfer functions, for I_{DC} 2% above the fold bifurcation.

A. Orbit flip

We consider models with classical type-I excitability where the transition from rest to repetitive firing is marked by (i) the elimination of the resting state in a fold bifurcation, and (ii) the existence of a limit cycle to which the dynamics relax instead. This limit cycle is born at a *limit cycle bifurcation*, which is in type-I neurons typically a SNIC bifurcation. At a codimension-two SNL bifurcation, the limit cycle bifurcation switches between a SNIC and a HOM bifurcation [Fig. 1(b)]. The following, model-independent analysis focuses on the *small* SNL bifurcation that transitions from a SNIC orbit to a small HOM orbit [Fig. 3(a)], because it entails more drastic changes in PRC shape, as discussed later. The *big* SNL bifurcation (transitioning to a big HOM orbit) will be studied with numerical continuation [Sec. V].

The limit cycle created at a HOM, SNIC or SNL bifurcation arises from a homoclinic orbit to a saddle (HOM) or saddle-node (SNIC, and also SNL). Under the assumption of sufficiently large limit cycle periods, the slow velocity in the vicinity of these fixed points contracts the dynamics such that limit cycle properties, *e.g.*, period or PRC, can be extracted from a linear approximation around the fixed point.

The linearized dynamics around the saddle-node fixed point is given by its Jacobian. Assuming non-degeneracy, the Jacobian has a single zero eigenvalue, associated with the *semi-stable* manifold, while the other eigenvalues are

strictly negative (*strongly-stable* manifolds). Trajectories always leave the saddle-node along the semi-stable manifold. When a trajectory loops around in a homoclinic orbit, it can either re-approach the saddle-node along the same manifold (SNIC bifurcation), or along the much faster, strongly-stable manifold (SNL bifurcation). The approach of the saddle-node at an SNL bifurcation flips from the semi-stable manifold to one of the strongly-stable manifolds (hence *orbit flip* bifurcation [45]) [Fig. 3(a)]. For neuron models, this flip can be induced by a scaling of the relative speed in the voltage and gating kinetics [Fig. 4]. When the saddle-node disappears after the fold bifurcation, its remaining *ghost* still dominates the resulting limit cycle dynamics. The limit cycle period drastically decreases around the SNL bifurcation [Fig. 5(a), see also [8]], mainly because of the separation of time scales between strongly-stable and semi-stable manifold, which renders the approach along the strongly-stable manifold much faster than the approach along the semi-stable manifold.

B. PRC symmetry and Fourier modes

Numerical continuation of several neuron models shows that the PRC is drastically altered at the SNL bifurcation. Exemplified in Fig. 3(b) for the Wang-Buzsaki model [Sec. A], the symmetric PRC at a (non-degenerated) SNIC bifurcation becomes increasingly asymmetric when an increase in membrane capacitance tunes the model towards the SNL bifurcation. The strong asymmetry at the SNL bifurcation directly affects the synchronization ability of the neuron [see Sec. V].

The sudden occurrence of PRC asymmetry at an SNL bifurcation can be directly inferred from the orbit flip in the dynamics described in the last section [Sec. IV A]. The PRC peaks when the phase reaches the ghost of the saddle-node, where the slow dynamics allow infinitesimal perturbations to maximally advance phase. In the case of the SNIC bifurcation, the same velocity governs approach and exit of the ghost, both aligned with the semi-stable manifold [Fig. 4, for details see Appendix B]. The orbit flip to the strongly stable manifold at the SNL bifurcation either decreases or increases the time spent on the approach compared to exit for the small or big SNL, respectively. This in turn breaks the symmetry of the PRC at the SNIC bifurcation by advancing or delaying the phase at which the maximum of the PRC resides.

Neglecting the fast approach at the small SNL bifurcation, it seems as if the flow of the limit cycle trajectory is directly injected at the ghost. Because the exit dynamics at SNL and SNIC bifurcations are similar, the PRC at the small SNL bifurcation appears as a rescaled version of the second half of the PRC at the SNIC bifurcation, $Z_{\text{small SNL}}(\phi) \propto Z_{\text{SNIC}}(0.5\phi + 0.5)$. This reasoning is supported by numerical continuation [Fig. 3(b), Fig. 4], and explains the observation that the limit cycle period is approximately halved at the SNL bifurcation [Fig. 5(a)].

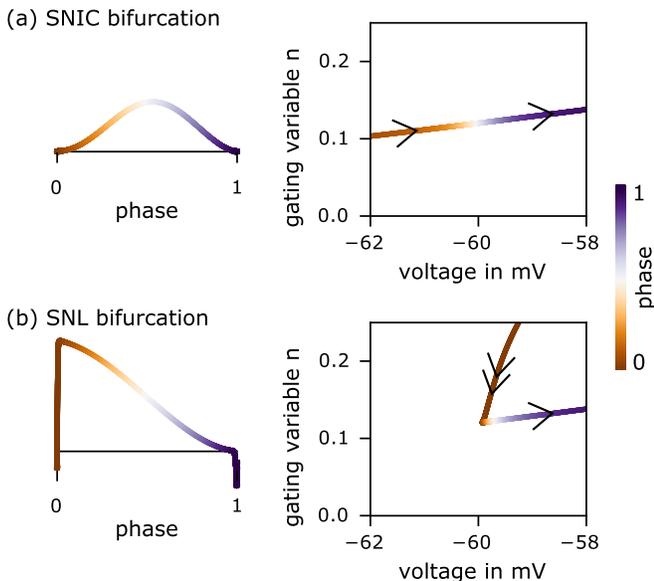


Figure 4. Color) Phase-response curve (left) and phase plot around the saddle-node (right) for (a) a non-degenerated SNIC bifurcation with $C_m = 1 \mu\text{F}/\text{cm}^2$ and (b) a small SNL bifurcation with $C_m \approx 1.47 \mu\text{F}/\text{cm}^2$ in the Wang-Buzsaki model with the limit cycle period fixed in both cases to 2 Hz.

The necessity of the PRC symmetry breaking at the SNL bifurcation can also be seen from normal form theory. For the SNIC bifurcation (and the supercritical Hopf bifurcation), the PRC is a simple trigonometric function, $Z_{\text{SNIC}}(\phi) \propto 1 - \cos(2\pi\phi)$ ($Z_{\text{Hopf}}(\phi) \propto \sin(2\pi\phi)$) [46]. Approached from the SNIC, the small SNL bifurcation, however, registers a sudden emergence of higher Fourier modes in the PRC. On the other side of the small SNL bifurcation, the canonical PRC at a small HOM bifurcation is an exponential with some decay constant τ , $Z_{\text{HOM}}(\phi) \propto \exp(-\phi/\tau)$ [46, 47]. Hence, in contrast to the trigonometric PRCs with a single Fourier mode at the SNIC or supercritical Hopf bifurcations, the PRCs at HOM and small SNL bifurcations have an infinite amount of Fourier modes. This results in Gibb's phenomenon if finite approximations are used.

The significant increase in PRC Fourier modes, as well as the breaking in PRC symmetry, are generic properties of SNL bifurcations. The consequences for coding are detailed in the next section [Sec. V].

V. SPIKE-BASED CODING AND SYNCHRONIZATION AROUND SNL BIFURCATIONS

While the previous section established changes in PRC properties at SNL bifurcations using dynamical system's theory, this section takes up the computational perspective again, with the PRC as a spike-time encoder. From the PRC, the following paragraphs derive various measures to probe the performance of an information encod-

ing system. The pertinence of these measures for spike-based coding is discussed at the end of this section. We start by interpreting the spike-time encoder as an information filter, which allows for the derivation of the stimulus characteristics to which the neurons are particularly sensitive [Sec. V A]. The transmission of information through such a filter is quantified in Sec. V B. The remaining paragraphs consider the ability of the neuron to align its activity to an entraining stimulus, either in the context of stochastic synchronization due to a common input [Sec. V C], or by classical synchronization, for example with the population activity [Sec. V D]. All four measures peak around the SNL bifurcation. Two factors are decisive: The reduced limit cycle period at the SNL bifurcation and the PRC symmetry breaking with the emergence of high frequency Fourier modes. Both occur generically at SNL bifurcations [Sec. IV], such that the consequences derived in this section generalize to other information-processing systems beyond neuroscience. In particular, neurons close to an SNL bifurcation behave radically differently from what is expected for SNIC neurons that show traditional type-I excitability.

A. High-frequency transmission peaks around SNL points

The natural environment is brimming with dispensable information from which sensory systems filter out behaviorally relevant information [49–51]. From a computational perspective, frequency band selectivity is given by the first-order relationship between input and output, the *linear response function* (first-order Volterra expansion of the full non-linear relationship). In biological systems, this can be probed by a broad-band noise stimulus. The Laplace transform of the linear response function is known as the *transfer function*, $H(s)$. It can be derived from the noisy phase oscillator [Eq. (1)], with PRC $Z(\phi) = \sum_k c_k e^{i2\pi k\phi}$, as [16]

$$H(s) = \sum_{k=-\infty}^{\infty} \frac{sc_k}{s - \nu_k}, \quad (4)$$

with $s \in \mathbb{C}$ and poles at $\nu_k = -i2\pi k f_0 - (\sigma k)^2/2$ for $k \in \mathbb{Z}$. The transfer function $H(s)$ in Eq. (4) establishes a link between PRC coefficients and filter characteristics. The low frequency limit of the transfer spectrum, $|H(i2\pi f)|$, is given by the mean for the PRC, $\lim_{f \rightarrow 0} |H(i2\pi f)| = c_0 = \overline{Z(\phi)}$, and informs us whether the system can track slow signals. On the other hand, the higher the frequencies present in $|H(i2\pi f)|$, the faster the signals a neuron can follow. Each non-zero Fourier mode of $Z(\phi)$ results in a spectral peak. The peaks of the spectrum are given by the poles ν_k , located at multiples of the neuron's mean spike rate, f_0 .

Near the SNL bifurcations, $H(s)$ passes considerably higher frequencies than at the SNIC bifurcation

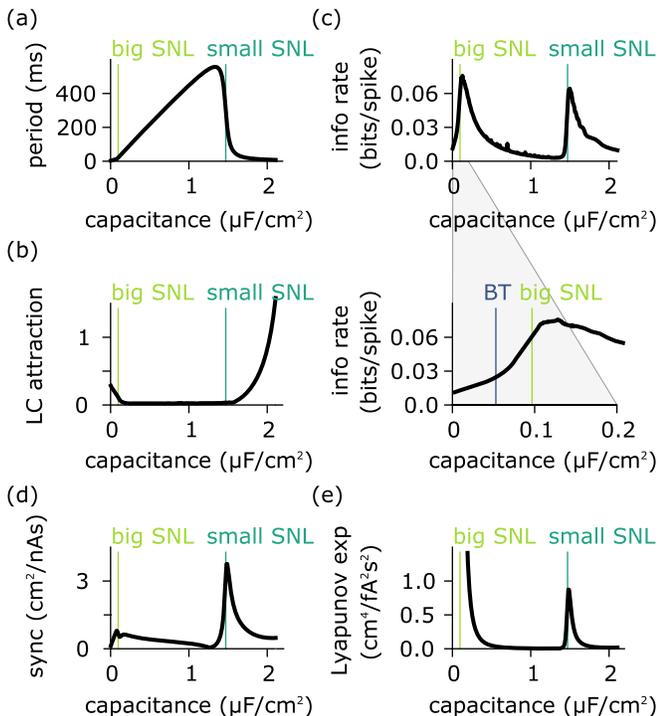


Figure 5. Color) Coding properties against the capacitance C_m for the Wang-Buzsaki model with input fixed at 2% above limit cycle onset at $I_{DC} \approx 0.16 \mu\text{A}/\text{cm}^2$. (a) Limit cycle period. (b) Relative limit cycle (LC) attraction given by the ratio of the limit cycle attraction time (inverse of the Floque exponent) and the period. A small LC attraction supports the validity of the phase description [48]. (c) Information rate as defined in [16], see Sec. V B, with zoom below. Note the maxima in proximity of both SNL bifurcations. (d) Maximal amplitude of the odd part of the PRC (entrainment range normalized by the coupling strength assuming δ -coupling; abbreviated sync). (e) Magnitude of the Lyapunov exponent, $|\lambda|$, of the locking state to a time-varying white noise stimulus.

[Fig. 3(c)], because the number of spectral peaks is directly determined by the higher number of Fourier modes in Z_{SNL} (which is infinite in the case of the small SNL bifurcation).

Note that Z_{Hopf} implies that the transfer spectrum of a neuron near a supercritical Hopf bifurcation has a single peak and suppresses low frequencies, $|H(0)| = 0$. This is in contrast to the SNL, SNIC and HOM bifurcations, which all pass arbitrarily slow signals. Although the spectrum of the Hopf bifurcation has more power beyond its peak compared to the SNIC neuron, it is only at the SNL and HOM bifurcations that individual mean-driven neurons can truly follow frequencies much higher than their own firing rate.

B. Mutual information peaks around SNL points

According to the data processing inequality [52], the output of a neuron is an incomplete representation of

the information it receives as input. How much a certain ensemble of input patterns, $I(t)$, is able to change a neuron's output ensemble, $y(t)$, is quantified by the mutual information rate, $M(y, I)$. A lower bound to the mutual information rate, $M_{\text{lb}} \leq M$, results from the transfer function [16, 53]

$$M_{\text{lb}} = \int_0^{f_c} df \ln \left(1 + \frac{|H(i2\pi f)|^2 P_{II}(f)}{P_{y_0 y_0}(f)} \right), \quad (5)$$

where H is defined in Eq. (4), and P is the power spectrum of input $I(t)$, respectively unperturbed output y_0 . The input spectrum P_{II} is taken to be band-limited white noise with cutoff frequency f_c , $P_{II} = \varepsilon^2/f_c$, $\forall 0 \leq f \leq f_c$ and $P_{II} = 0$ else. According to Eq. (5), the information at a particular frequency is high if the power of the output spectrum, $|H(i2\pi f)|^2 P_{II}(f)$, is high compared to the power of spike trains without input, $P_{y_0 y_0}$. M_{lb} sums up information in all frequency bands. The increase of information transmission around the SNL point [Fig. 5(c)] is a result of the facilitation of high frequency transmission, cf. Sec. V A.

C. Spike-time reliability and locking to stimuli peak around SNL points

The information transmission of a neuron also depends on how reliable it encodes a time-varying stimulus into a sequence of spike times [54]. This can be quantified by observing how fast an uncoupled population of identical neurons gets synchronized by a common time-varying input (*stochastic synchronization* [55, 56]). Assuming a set of identical phase oscillators from Eq. (1) with random initial conditions and white noise input, the relaxation time constant is given as the reciprocal of the Lyapunov exponent of the phase fixed points [57]

$$\lambda = -\varepsilon^2 \int_0^1 \left(\frac{dZ(\phi)}{d\phi} \right)^2 d\phi. \quad (6)$$

For neural computations, λ^{-1} sets for example the integration time scale a neuron requires to detect new transient stimuli (*evoked responses*). The interaction time scale is minimized at the SNL bifurcations [Fig. 5(e)]. The peaks of the Lyapunov exponent λ furthermore imply efficient locking to a common input. High Fourier modes, responsible for the peaks around the SNL points, are emphasized by the derivative in Eq. (6), which amounts to a multiplication of the k^{th} -mode by k . This results in an even stronger stochastic synchronization than in the bi-phasic PRCs emerging from some type-II excitable neurons [56].

D. Synchronization peaks around SNL points

The asymmetry of the PRC scales the frequency detuning over which a neuron entrains to its input (the width

of the Arnold tongue [48, 55]). The input can either be a periodic signal or the recurrent input from other neurons in a network. Here, we use synchronization in the sense of a constant phase relation between oscillators, compare Fig. 2. The relation between PRC and synchronization can be illustrated by two delta-coupled phase oscillators, $\phi_{1,2}$, as defined in Eq. (1),

$$\dot{\phi}_{1,2} = f_{1,2} + Q(\phi_{1,2} - \phi_{2,1}) + \sigma \xi_{1,2}, \quad (7)$$

where the coupling function Q results from an averaging step if the interaction between both oscillators are assumed to be weak [58], $Q(\Delta) = \int_0^\infty Z(\varphi)G(\varphi + \Delta)d\varphi$, where $G(\phi)$ is the time-varying synaptic input evaluated on the limit cycle. The phase difference, $\psi = \phi_1 - \phi_2$, evolves as $\dot{\psi} = \Delta f + Q_{\text{odd}}(\psi)$, where $Q_{\text{odd}}(\psi) = Q(\psi) - Q(-\psi)$ is twice the odd part of the coupling function. Synchronization (*i.e.*, a constant phase lag ψ) requires $\dot{\psi} = 0$, and the maximal admissible frequency detuning Δf is given by the image of Q_{odd} . In the case of δ -coupling, Q_{odd} is equal to twice the odd part of the PRC, Z_{odd} , so that phase locking only occurs if $\Delta f \in [\min Z_{\text{odd}}, \max Z_{\text{odd}}]$. In Fig. 5(d), the synchronization range $\max Z_{\text{odd}} - \min Z_{\text{odd}}$ is plotted. The increased synchronization range will also manifest itself in globally coupled networks of the type studied in Refs. [59, 60].

The synchronization boost around the SNL points [Fig. 5(d)] arises from period scaling and PRC asymmetry, alongside a significant odd part in Z_{SNL} compared to Z_{SNIC} . For two coupled oscillators, a small SNL bifurcation favors alternated spiking, which is sometimes called *anti-synchronization*. This is in contrast to the stable in-phase locking that is observed for PRCs shaped like a negative sine [36, see appendix].

E. Coding at an SNL bifurcation

In summary, Secs. VA to VD suggest that passing the SNL point affects a variety of neural coding schemes. Regarding spike-timing codes, the shape of the PRC at the SNL bifurcation is similar to the optimal PRC for synchronization by common Poisson input [61]. Furthermore, the lower bound of the information rate is increased, because higher frequencies emerge in the linear response function. Regarding phase codes [62], a consequence of the PRC at the SNL bifurcation is a temporally more precise locking of spikes to a reference signal. This prevents spurious spikes, *i.e.*, fewer phase slips occur, reducing the decoding error. Regarding rate codes, the lower bound of the decoding error (Cramer-Rao bound) is connected to the slope of the firing rate as a function of the input I_{DC} [9]. At firing onset, this slope is known to be larger for a HOM bifurcation compared to a SNIC bifurcation [21], and hence rises around the SNL point, potentially minimizing the decoding error.

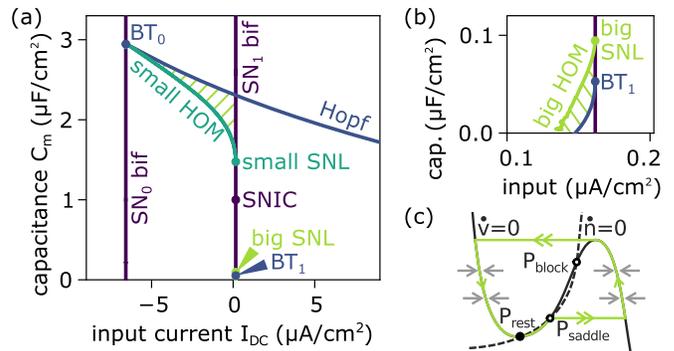


Figure 6. Color (a) Bifurcation diagram of the Wang-Buzsaki model under variation of membrane capacitance C_m and input current I_{DC} . With $C_m = 1 \mu\text{F}/\text{cm}^2$, the limit cycle arises from a SNIC bifurcation. Increasing C_m leads to the small SNL at $C_m \approx 1.47 \mu\text{F}/\text{cm}^2$. Dashed areas mark bistability. (b) Decreasing C_m leads to the big SNL, and then to a Bogdanov-Takens (BT) bifurcation. Note that a change of stability in the big HOM branch, not shown here, follows from Ref. [64]. (c) Schematic illustration for the limit $C_m \rightarrow 0$, in which the system corresponds to a relaxation oscillator: Drawn in the state space of gating variable n versus voltage v , the solid line with inverted N-shape represents the voltage nullcline, and the dashed line represents the gating nullcline. At some I_{DC} , the resting state loses stability and a big HOM orbit around all fixed points (green) is created.

VI. GENERIC OCCURRENCE OF SNL BIFURCATIONS

The multifarious consequences of the SNL bifurcation discussed in Sec. V will be of particular relevance for neuronal processing if the SNL bifurcation generally occurs in realistic neuron models. Next, we demonstrate that indeed any two-dimensional, type-I conductance-based neuron model can always be tuned to SNL bifurcations. More precisely, we show that the SNL bifurcation is an essential element in the bifurcation diagram that uses input current and membrane capacitance as control parameters. This bifurcation diagram also allows us to relate the SNL bifurcation to other bifurcations such as the Bogdanov-Takens (BT) bifurcation, classical termed the switch of type-I/II excitability [58, 63].

Concentrating on bifurcations relevant for neuronal spiking (*i.e.*, bifurcations affecting a stable limit cycle), Fig. 6 shows a bifurcation diagram of the Wang-Buzsaki model [Sec. A] with input current and membrane capacitance as control parameters. Along the dimension spanned by the capacitance, two SNL bifurcations enclose the SNIC bifurcation. The lower SNL bifurcation corresponds to a big SNL bifurcation for which the arising limit cycle encircles the ghost of the saddle-node, and the upper SNL bifurcation corresponds to a small SNL bifurcation for which the ghost of the saddle-node lies outside of the limit cycle [Fig. 3(a)]. In particular, decreasing the capacitance, an SNL point is passed *before* the BT bifurcation is reached.

We show in Appendix C that this bifurcation structure generalizes (under mild assumptions) to planar neuron models. The membrane capacitance C_m is used as bifurcation parameter in the general bifurcation diagram that we construe, because it simply changes the time scale of the voltage dynamics [Eq. (2)]. The proof separately considers the lower and the upper part of the bifurcation diagram. The lower part is based on the so-called *relaxation limit* with infinitely fast voltage dynamics that arises from the limit $C_m \rightarrow 0$ [Fig. 6(c)], where the bifurcation structure is known [64]. Non-zero capacitance values are deduced from several observations that restrict the path of limit cycle bifurcation branches in planar systems. The upper part of the bifurcation diagram is extracted from the unfolding of a BT point.

Our derivation may be an interesting starting point for similar results in other dynamical systems in which the time scale of a single dynamical variable is used as bifurcation parameter. For our planar neuron models, we find that the SNIC bifurcation branch is generically enclosed by two SNL bifurcations that are reached by an adaptation of the voltage time scale. In particular, our results show that a continuous variation of the voltage time scale reaches the BT point only *after* passing one of the SNL bifurcations.

VII. DISCUSSION

This article explores the intricate relation between SNL bifurcations and neuronal processing. SNL bifurcations entail optimal synchronization and coding properties, with several measures of information and synchronization peaking in the vicinity of SNL bifurcations [Fig. 5]. Moreover, the approach to the SNL point could be a mechanism to unify recent explanations of how neurons transmit frequencies far above the cutoff given by their membrane time constant [12, 23, 65, 66]. Indeed, homoclinic neurons at the small SNL point seem to resemble the idealized *perfect integrate-and-fire* neuron [67], as both are transmitting arbitrarily high frequencies.

Drastic changes in spike-based coding can be expected at a bifurcation that affects not only the fixed points, but also the stable limit cycle. This is the case for the SNL bifurcation, in distinction to the BT point classically referred to as the transition between type-I to type-II excitability: In neuron models, the BT-associated Hopf bifurcation is typically subcritical. The limit cycle arising at the subcritical Hopf bifurcation is unstable and has only indirect implications for spiking dynamics. The subcritical Hopf bifurcation affects the resting state, changing subthreshold dynamics and filtering [28, 30, 36, 58]. Spike-based coding is in this case only affected if the system behaves like a fluctuation-driven escape problem [13, 68], while we focus on mean-driven limit cycle dynamics.

Note that models in vicinity of a BT point have a different bifurcation structure than models such as the

original Hodgkin-Huxley (HH) model [69]. While in the latter, the unstable limit cycle that terminates in the subcritical Hopf bifurcation is born at a fold of limit cycles bifurcation, the normal form of the BT bifurcation shows that the unstable limit cycle is in the former case born at a HOM bifurcation [70]. This difference will probably affect the PRC of the stable limit cycle, for which the canonical shape is still unresolved [71]. Moreover, the identified generic bifurcation sequence shows that a smooth change in time-scale parameters does not justify the previously used heuristic formula that exploits a single Fourier mode to interpolate between Z_{SNIC} and Z_{Hopf} [16, 72, 73].

As codimension-two bifurcation, the SNL bifurcation is reached in neuron models by an appropriate tuning of both the input current and one additional model parameter. Examples for the second control parameter are the membrane capacitance, maximal gating conductances, tonic inhibition [36], neuromodulators [74], or gating time constants [21]. With the membrane capacitance as bifurcation parameter, we demonstrate for planar conductance-based models with a SNIC bifurcation that, ubiquitously, an SNL bifurcation is the first bifurcation reached for lowered or increased capacitance, respectively. With the three bifurcation parameters capacitance, input, and leak conductance, the identified sequence of bifurcations collapses into a codimension-three cusp BT point [36, 37]. This potentially generalizes the described bifurcation structure beyond the planar case.

Focusing on neuron models that spike at low firing rates, where the dynamics are dominated by the bifurcation that creates the limit cycle, allows us to draw model-independent conclusions. Furthermore, the used phase description demands for small inputs compared to the limit cycle stability. The strong stability of the limit cycle around the SNL point, shown by the Floquet exponent [Fig. 5(b)], validates the phase reduction even for reasonably sized inputs. Our setting with low firing rates and relatively weak synaptic connections is typical for cortical neurons [75, 76].

Our mathematical arguments rely on the relative time scale between state variables as the bifurcation parameter that takes us to the relaxation limit used in Appendix C. The membrane capacitance is one such parameter. From a biological perspective, the membrane capacitance is in several aspects an interesting bifurcation parameter. The effective membrane capacitance depends on cell parameters such as the morphology of the neuron or the myelination of its axon [7], and it may hence be adapted on developmental or evolutionary time scales. Furthermore, the experimental method of infrared neural stimulation uses a change in membrane capacitance to depolarize neurons [77]. The neurons are stimulated by infrared laser pulses [78], and the deposition of energy leads to an increase in the membrane capacitance, changing the capacitive current $I_{\text{cap}} = \frac{dC_m v}{dt} = \dot{C}_m v + C_m \dot{v}$. The transient capacitance increase leads to a non-zero capacitive term $\dot{C}_m v$, which can be sufficient to excite the neuron

[77]. Our study concentrates on neuronal properties beyond this transient dynamics. We have demonstrated a rich impact on neuronal dynamics of the specific value of C_m , even in its steady state with $\dot{C}_m = 0$. For infrared neural stimulation, this implies that the observed changes in capacitance, in addition to a short-term excitation, could also push the neurons closer to an SNL bifurcation, with potentially drastic implications for coding properties. Moreover, passing the SNL point causes a region of bistability between limit cycle and resting state P_{rest} [Fig. 6(a-b)]. The consequential hysteresis results in spiking that persists beyond the duration of the transient current stimulation. The respective switching statistics (*i.e.*, between silent periods and periodic firing) and their dependence on the timing of excitation and inhibition may hence be characteristic of the different SNL types and allow for a distinction between these dynamical regimes, see also [21]. Overall, our results demand for a careful interpretation of infrared neural stimulation experiments because of our prediction that infrared neuronal stimulation may drive neurons into a significantly different dynamical regime.

Last but not least, our results suggest that also under natural conditions, neurons may favor a position close to an SNL point in order to profit from its unique coding flexibility. On the other hand, SNL bifurcations may also be relevant in pathology (*e.g.*, epilepsy). Experimentally, the measurement of phase-response curves is technically involved, even more so if multiple dynamical regimes are probed in the same neuron. Experimental reports exist for the transition between type-I and type-II excitability [36, 74]. While several studies report PRCs that are compatible with a spike onset either at a SNIC bifurcation or at a HOM bifurcation [79–82], the observation of an SNL bifurcation in an experimental setting remains an open challenge.

In summary, our study consists of two parts: We have first extracted from the dynamics at an SNL bifurcation the phase-response curve, and used this knowledge to infer the associated coding properties. Both the PRC asymmetry and its high Fourier modes are generic properties at SNL bifurcations. Thereby, our results are not only independent of the particular neuron model, but are equally applicable to any system that allows for a phase reduction. Moreover, we have demonstrated that SNL bifurcations ubiquitously occur in a set of planar neuron models. With the time scale of one dynamical variable as bifurcation parameter, the structure of our proof is likely to generalize to other systems with a subcritical Hopf bifurcation in the relaxation limit, such as lasers [83, 84], Josephson junctions [85–88], and chemical reactions [89, 90]. Together, both parts highlight the SNL bifurcation as a hitherto underestimated bifurcation with prominent importance for neuronal dynamics.

ACKNOWLEDGMENTS

We thank Dr. Martin Wechselberger for inspiring discussions and pointing out the connection to his work on the relaxation limit and Grigory Bordyugov for advice on numerical continuation and homoclinic bifurcations. Funded by the German Federal Ministry of Education and Research (01GQ0901, 01GQ1403).

Appendix A: Generic definition of conductance-based neuron models

We consider a generic class of conductance-based neuron models [36]:

$$\dot{v} = \frac{I_{\text{cap}}(v, \dots)}{C_m} = \frac{1}{C_m} (I_{\text{in}} - g_L(v - v_L) - I_{\text{gating}}) \quad (\text{A1})$$

$$I_{\text{gating}} = \sum_{i=0}^n g_i(v - v_i) \prod_{k=0}^K m_{ik}^{p_{ik}} \quad (\text{A2})$$

where ion channel i has maximal conductance g_i and reversal potential v_i and its open probability is given by a product of gating variables (potentially to some power of p_{ik}). Each gating variable m_{ik} of ion channel i is either a function of the voltage, $m_{ik} = m_{ik\infty}(v)$, or relaxes exponentially to its steady state value $m_{ik\infty}(v)$, with gating kinetics given by

$$\dot{m}_{ik} = \frac{m_{ik\infty}(v) - m_{ik}}{\tau_{ik}(v)} \quad (\text{A3})$$

For numerical continuation, we use a single-compartmental version of the Wang-Buzsaki model for hippocampal pyramidal cells [11] with the following dynamics:

$$\begin{aligned} \dot{v} &= (I + g_L(E_L - v) + I_{\text{gate}})/C_m, \\ \dot{h} &= 5(\alpha_h(v)(1 - h) - \beta_h(v)h), \\ \dot{n} &= 5(\alpha_n(v)(1 - n) - \beta_n(v)n), \end{aligned}$$

with membrane capacitance $C_m = 1\mu\text{F}/\text{cm}^2$, maximal conductances $g_L = 0.1\mu\text{S}/\text{cm}^2$, $g_{\text{Na}} = 35\mu\text{S}/\text{cm}^2$, $g_K = 9\mu\text{S}/\text{cm}^2$, reversal potentials $E_L = -65\text{mV}$, $E_{\text{Na}} = 55\text{mV}$, $E_K = -90\text{mV}$, and the following functions:

$$\begin{aligned} I_{\text{gate}} &= g_{\text{Na}} m_{\infty}(v)^3 h (E_{\text{Na}} - v) + g_K n^4 (E_K - v), \\ m_{\infty} &= \frac{\frac{v+35}{\exp(-0.1(v+35))-1}}{\frac{v+35}{\exp(-0.1(v+35))-1} - 40 e^{-(v+60)/18}}, \\ \alpha_h(v) &= 0.07 \exp(-(v+58)/20), \\ \beta_h(v) &= 1/(1 + \exp(-0.1(v+28))), \\ \alpha_n(v) &= -0.01 \frac{v+34}{\exp(-0.1(v+34))-1}, \\ \beta_n(v) &= 0.125 \exp(-(v+44)/80). \end{aligned}$$

Appendix B: PRC symmetry

The PRC asymmetry at the SNL bifurcation is a direct consequence of the broken symmetry in the dynamics at the SNL bifurcation. This section gives more detail on the relationship between dynamics and PRC, both intuitively and with a mathematical argument. We will describe first how the dynamics at the SNIC bifurcation leads to a symmetric PRC and then show that these conditions are not met at the SNL bifurcation, predicting an asymmetric PRC at an SNL bifurcation. While the arguments are presented with a small SNL bifurcation in mind, they hold in a similar way for a big SNL bifurcation.

As introduced in the main text, the orbit at a SNIC bifurcation follows the semi-stable manifold of the saddle-node fixed point, which corresponds to the central manifold of a fold bifurcation. The zero eigenvalue of the Jacobian J at the saddle-node on the semi-stable manifold eliminates the linear term. The leading second order term results in a parabolic normal form. For dynamics centered around $x = 0$, stimulated with input s , the dynamics is

$$\dot{x} = s + x^2, \quad (\text{B1})$$

where all variables are chosen unitless for convenience.

The dynamics is symmetric around the saddle-node fixed point, i.e., the orbit has corresponding velocities at approach and exit of the saddle-node. The orbit flip at the SNL bifurcation breaks this symmetry in the dynamics, and, as we will show, also in the PRC.

From a mathematical perspective, the normal form allows for a calculation of the PRC. We, however, will use the normal form to directly analyze PRC symmetry. For the SNIC bifurcation, the reflection symmetry of the PRC can be inferred from the symmetry of the dynamics: If $x(t)$ is a solution of the dynamical system given by Eq. (B1), then the same holds for $-x(-t)$, $x(t)$ is hence point symmetric in time, $x(t) = -x(-t)$. Derivation of the right-hand side of Eq. (B1) by x results in a Jacobian linear in x , that is hence point symmetric in x , $J(x) = -J(-x)$. Inserting both into the adjoint equation, Eq. (3), directly leads to a PRC reflection symmetric in time, $Z_{\text{SNIC}}(t) = Z_{\text{SNIC}}(-t)$. In contrast, the asymmetric dynamics at the SNL bifurcation lead to an asymmetric PRC.

Intuitively, on an orbit that connects to a saddle-node fixed point, the dynamics becomes arbitrary slow at the fixed point. The limit cycle shows the slowest dynamics in the same region in state space, in proximity to the ghost of the former saddle-node. A perturbation that propels the dynamics over the ghost of the saddle-node will therefore maximally advance the next spike. The maximum of the PRC is at the phase value that corresponds to the saddle-node. For a SNIC bifurcation, the PRC maximum lies at $\phi = 0.5$ because the symmetric dynamics of a SNIC take equal time for the approach

(from $\phi = 0$ to $\phi = 0.5$) and the exit (from $\phi = 0.5$ to $\phi = 1$) of the saddle-node. In comparison, the PRC maximum is shifted towards the left at the SNL bifurcation, because the accelerated entry along the strongly-stable manifold advances the saddle-node to earlier phases. The shift of the maximum away from the center destroys the symmetric shape of the PRC.

The symmetry breaking generalizes beyond the SNL bifurcation: A saddle homoclinic orbit shows an asymmetric PRC [46], if the saddle has different stabilities along stable and unstable manifold, and hence non-symmetric dynamics. In summary, we showed that the symmetry breaking in the PRC is an immediate consequence of the symmetry breaking in the dynamics that occurs as orbit flip at the SNL bifurcation. Hence, the observed symmetry breaking in the PRC is a general property of the SNL bifurcation.

Appendix C: Mathematical argument for the generic occurrence of the SNL bifurcation in planar models

We show in the following that, with a variation of the time-scale parameter, such capacitance, in a broad set of planar conductance-based models, a SNIC bifurcation is always enclosed by two SNL bifurcations, and that a decrease in capacitance passes the big SNL bifurcation, and only afterwards reaches the BT point. Beyond the BT point, a Hopf bifurcation destabilizes the resting state before the fold bifurcation occurs.

To this aim, we prove that the general structure of the bifurcation diagram [Fig. 6] holds for any planar neuron model that conforms with our assumptions [Sec. C 1].

1. Model definition

We consider a generic class of type-I planar conductance-based neuron models. The single gating variable, n , commonly models the opening and closing of a restorative current originating, say, from the potassium ion channel. The dynamics is given by

$$\begin{pmatrix} \dot{v} \\ \dot{n} \end{pmatrix} = F(v, n) = \begin{pmatrix} \frac{1}{C_m}(I_{\text{DC}} - I_{\text{ion}}) \\ \frac{n_{\infty}(v) - n}{\tau_n(v)} \end{pmatrix}. \quad (\text{C1})$$

with $I_{\text{ion}}(v, n) = g_{\text{L}}(v - v_{\text{L}}) + g_{\text{K}}n(v - v_{\text{K}})$, compare Eq. A1.

We chose the model such that it fulfills the following assumptions:

(A1) The firing onset of the model occurs, for some capacitance value C_{SNIC} and a specific input current $I_{\text{DC}} = I_{\text{SN1}}$ (the *threshold* current), at a non-degenerated SNIC bifurcation.

(A2) We demand that at the capacitance C_{SNIC} , the subthreshold dynamics for $I_{\text{DC}} < I_{\text{SN1}}$ relax to a single stable fixed point, the *resting state*. We furthermore

assume that with an increase in input current, the limit cycle dynamics eventually terminates in a bifurcation denoted *excitation block*, after which the dynamics relaxes again to a stable fixed point. This assumption prevents diverging dynamics.

(A3) The nullcline of the voltage has an inverted N-shape.

(A4) We require that $n_\infty(v)$ from Eq. C1 is an increasing, positive, bounded, twice differentiable function that becomes sufficiently flat in the limit $v \rightarrow \pm\infty$, $\lim_{v \rightarrow \pm\infty} v \partial_v n_\infty(v) = 0$. This assumption allows us to use results from Ref. [36].

All of these assumptions are fulfilled in common neuron models with type-I excitability.

2. Construction of the bifurcation diagram

The following proof establishes an ordering in a sequence of limit cycle bifurcations, whereby a SNIC is enclosed by two SNL bifurcations. The ordering is established by analyzing the relaxation limit as an anchoring point. We thereby capitalize on recent results from the relaxation limit, $C_m \rightarrow 0$. As we will show, the ordering that arises in this limit along I_{DC} implies the same ordering along C_m , mainly because limit cycle bifurcation branches cannot cross in planar systems.

The limit cycle bifurcation branches that we consider lie in the region with $I_{DC} \leq I_{SN1}$, because, for neuronal firing, the limit cycle creation has to happen before (*i.e.*, at lower I_{DC}) or at the fold bifurcation at which the resting state is eliminated. C_{SNIC} separates the region $I_{DC} \leq I_{SN1}$ in a lower and upper subregion. Since the occurrence of limit cycle bifurcations at C_{SNIC} is prevented by the requirement (A2) that stable dynamics are given by a unique fixed point, all limit cycle bifurcation branches lie either in one or the other subregion. In the proof, we start with the lower subregion, and then consider the upper one.

3. The lower part of the bifurcation diagram, $C_m < C_{SNIC}$

Observation 0 *Vertical fold bifurcation branches: Fixed point location depends on I_{DC} , but not on C_m .* The nullclines of Eq. C1 are given by $I_{DC} - I_{ion}(v, n) = 0$ and $n = n_\infty(v)$. The nullclines are independent of C_m , and therefore also the location of the fixed points, because the fixed points sit at intersections of the nullclines. Hence the location of the fold bifurcations is also independent of C_m , which ensures that the fold branches [marked with SN in Fig. 6(a)] are vertical in a bifurcation diagram of C_m versus I_{DC} .

Based on the inverted-N shape of the voltage nullcline and the monotonous shape of the gating nullcline, we can infer the existence of one to three fixed points. For the following discussion, we name these fixed points, a

visualization of our nomenclature is shown in Fig. 6(c). The number and location of the fixed points is set by the input current I_{DC} , which shifts the voltage nullcline up or down in the state space. For low, *i.e.*, subthreshold I_{DC} , the model has a single, stable fixed point, P_{rest} . With an increase in I_{DC} , the knee of the voltage nullcline approaches the gating nullcline from below, and results in a fold bifurcation at some $I_{DC} = I_{SN0}$. The fold bifurcation creates a saddle, P_{saddle} , and a node, P_{block} . Our assumptions ensure that P_{block} is unstable because (A2) requires that P_{rest} is the only stable fixed point at $C_m = C_{SNIC}$. Increasing the input current further leads to a second fold bifurcation at some $I_{DC} = I_{SN1}$. This fold bifurcation annihilates P_{rest} and P_{saddle} . Beyond the bifurcation, P_{block} remains as the only surviving fixed point.

The saddle fixed point P_{saddle} only exists between I_{SN0} and I_{SN1} . The association of HOM bifurcations with saddles directly constrains their bifurcation branches to the region $I_{SN0} \leq I_{DC} \leq I_{SN1}$. In an analogue way, Hopf bifurcation branches are constrained by the existence of the associated focus fixed point: The Hopf branch that destabilize the resting state P_{rest} is restricted to input currents below I_{SN1} , and the other Hopf branch that changes the stability of P_{block} is restricted input currents above I_{SN0} . Further constraints will be developed throughout the following arguments.

Observation 1 *Starting points for the branches of big HOM and neighboring Hopf bifurcation: Anchoring the bifurcation diagram in the limit $C_m \rightarrow 0$ yields $I_{big\,HOM} < I_{Hopf}$.* In the limit $C_m \rightarrow 0$, the conductance-based model is transformed into a relaxation oscillator with voltage as fast variable, as sketched in Fig. 6(c) [91]. For this limit, de Maesschalck and Wechselberger have identified the full bifurcation structure for generic planar neuron models [64]. Their *Theorem 2* demonstrates for sufficiently small C_m that an increase in I_{DC} results for model neurons such as ours in a generic sequence of bifurcations. Relevant for our consideration is the occurrence of a big HOM bifurcation at input $I_{big\,HOM}$, and a subcritical Hopf bifurcation that destabilizes P_{rest} at I_{Hopf} . Their full bifurcation structure ensures furthermore that neither the big HOM branch nor the Hopf branch returns to the limit $C_m \rightarrow 0$, which is important to ensure the existence of a codimension-two bifurcation at the other end. They state an ordering of the bifurcation currents, $I_{big\,HOM} < I_{Hopf} < I_{SN1}$, which will be used in the following to infer the same ordering at finite values of C_m .

Lemma 1 *HOM branches cannot "bend backwards": A variation in C_m generically breaks homoclinic orbits to hyperbolic fixed points.* In order to constrain the location of HOM bifurcations in subsequent paragraphs, we want to show that the tracing of a HOM branch leads us always in one direction along the input current (increasing or decreasing input). Equivalently, we can show that a HOM branch cannot "bend backwards" along the input current dimension. This is the case if we show that HOM

branches cannot have "vertical parts": A HOM branch cannot align with a parameter variation exclusively in C_m , because, as we show with this lemma, a variation in C_m generically breaks the homoclinic orbit.

Homoclinic orbits arise when the trajectory of the unstable direction of a fixed point connects to its stable direction, i.e., stable and unstable manifold overlap. A parameter variation can separate stable and unstable manifold from each other, allowing for the definition of a distance. This distance is measured by the so-called separation function, sep [Fig. 1(b)]. For parameter values that lie on the HOM branch, the separation function is zero, $\text{sep}(C_{\text{HOM}}) = 0$, and it increases to some finite value, $\text{sep}(C_m) > 0$, if a variation in the parameter breaks the homoclinic orbit, i.e., leaves the HOM branch. This is analogue to a non-zero value of the partial derivative of the separation function, which is known as the *Melnikov integral*, M [for a derivation in planar systems see for example Ref. [92], leading to Equation (6.12) that we use in Eq. C3].

A variation in C_m breaks the homoclinic orbit if the corresponding Melnikov integral evaluated on the homoclinic orbit is non-zero [45]. The Melnikov integral with respect to C_m for a homoclinic orbit with flow $h(t)$ is

$$M = \int_{-\infty}^{\infty} K(t) F(h(t)) \frac{\partial F(h(t))}{\partial C_m} dt \quad (\text{C2})$$

$$= - \int_{-\infty}^{\infty} K(t) \frac{(I_{\text{DC}} - I_{\text{ion}}(h(t)))^2}{C_m^3} dt, \quad (\text{C3})$$

where $K(t) = \exp\left(-\int_0^t \text{div} F(h(s)) ds\right)$. For our system, the Melnikov integral is strictly positive, $0 < M$, because (i) $K(t)$ is, as an exponential function, strictly positive, $\forall t : 0 < K(t)$, and (ii), because we implicitly assume the existence of a homoclinic orbit, the difference of ionic and injected currents cannot be zero at all times, hence $\exists t : (I_{\text{DC}} - I_{\text{ion}}(h(t)))^2 > 0$. With that, the capacitance breaks the homoclinic orbit and thus tracing a HOM branch along one direction results either in continuously increasing or decreasing input current values on the branch. This lemma is used in the following Observation 2 in order to pursue the big HOM branch starting in the limit $C_m \rightarrow 0$ [see Observation 1].

Observation 2 *The big HOM branch eventually approaches the fold bifurcation at I_{SN1} .* Based on the directionality of the big HOM branch derived in the literature, we will show in this observation that the big HOM branch eventually approaches the fold bifurcation branch at which the resting state collides with the saddle. The point of contact corresponds to an SNL bifurcation, as we will show in subsequent paragraphs.

The statement of Theorem 2 by de Maesschalck and Wechselberger states for sufficiently small C_m , in addition to the ordering used in Observation 1, that the big HOM branch departs from its starting point to the right, i.e., in the direction of increasing input current [64]. This directionality of the big HOM branch generalizes to larger values of C_m , because Lemma 1 prevents

"backward bends" of HOM branches. Given that the big HOM branch does not return to the limit $C_m \rightarrow 0$ [Observation 1], the big HOM branch eventually has to approach the fold bifurcation at I_{SN1} . The next lemma ensures that the connection point is an SNL point.

Lemma 2 *A HOM branch and the fold branch at I_{SN1} connect in an SNL bifurcation: A HOM branch is stable when it connects to a non-degenerated fold bifurcation involving a stable node.* An SNL bifurcation involves a stable homoclinic orbit that transitions between a HOM bifurcation and a SNIC bifurcation. The homoclinic orbit of the HOM branch is stable, if the associated saddle-quantity is negative (the sum of the two eigenvalues of the associated fixed point). At the connection point with the fold branch, the homoclinic orbit is associated with a saddle-node fixed point arising from the collision of a stable node and a saddle. It has one zero eigenvalue (prerequisite for the fold bifurcation) and one negative eigenvalue (the former stable node sets the stability of the strongly-stable manifold). The sum evaluates to a negative saddle-quantity, ensuring a stable homoclinic orbit, and hence an SNL bifurcation.

Lemma 3 *The bifurcation sequence in the lower part of the bifurcation diagram: For $I_{\text{DC}} = I_{\text{SN1}}$, increasing C_m from zero passes first a BT point, then an SNL point, before a non-degenerated SNIC bifurcation occurs, $C_{\text{BT1}} < C_{\text{bigSNL}} < C_{\text{SNIC}}$.* Combining Observation 2 and Lemma 2, we conclude that the big HOM branch connects to the fold bifurcation branch at I_{SN1} with a stable homoclinic orbit, i.e., in an SNL bifurcation. This big SNL bifurcation happens at some point $(I_{\text{SN1}}, C_{\text{bigSNL}})$, with $C_{\text{bigSNL}} < C_{\text{SNIC}}$ because the big HOM branch cannot pass the capacitance value of C_{SNIC} as (A2) prohibits stable limit cycle bifurcations for $I_{\text{DC}} < I_{\text{SN1}}$. From Observation 1, we know for $C_m \rightarrow 0$ that a Hopf branch starts at I_{Hopf} , and that this branch does not return to the limit $C_m \rightarrow 0$. Because limit cycle bifurcation branches cannot cross each other in a planar system, the Hopf branch can furthermore not cross the big HOM branch. Instead, it connects to the fold bifurcation branch in a BT bifurcation at some point $(I_{\text{SN1}}, C_{\text{BT1}})$. The ordering $I_{\text{bigHOM}} < I_{\text{Hopf}}$ from Observation 1 immediately implies an ordering in C_m , i.e., $C_{\text{BT1}} < C_{\text{bigSNL}}$. In summary, we have shown in this lemma that $C_{\text{BT1}} < C_{\text{bigSNL}} < C_{\text{SNIC}}$.

These arguments have proven the bifurcation sequence in the lower part of the bifurcation diagram arising from the limit $C_m \rightarrow 0$. In the following, we use the unfolding of a second BT point to show the upper part of the bifurcation diagram.

4. The upper part of the bifurcation diagram, $C_m > C_{\text{SNIC}}$

Observation 3 *The bifurcation diagram contains exactly two BT points.* Kirst et al. identified the BT point for a generic class of conductance-based neuron model

(including our model group) at a capacitance value that can be calculated from the input current at which the fold bifurcation occurs [Ref. [36], Supplemental Material]. With the two fold bifurcation branches occurring in our model group at input currents I_{SN0} and I_{SN1} , we find one unique BT point on each fold branches. Lemma 3 identified one of them at the BT point (I_{SN1}, C_{BT1}) , and the second BT bifurcation occurs at some point (I_{SN0}, C_{BT0}) . From the BT point at (I_{SN0}, C_{BT0}) arises by normal form theory a Hopf bifurcation branch and a branch of a small HOM bifurcation. Both depart in the direction of increasing input I_{DC} , which will be used as before to constrain their location.

Observation 4 *The second BT point lies in the upper part of the bifurcation diagram: The BT point at (I_{SN0}, C_{BT0}) occurs at $C_{BT0} > C_{SNIC}$.* We restrict the region accessible to the Hopf branch that arises from the BT point at (I_{SN0}, C_{BT0}) : A limit cycle bifurcation branch cannot cross other limit cycle bifurcation branches (in a planar system), and hence the Hopf branch cannot pass the SNIC bifurcation line between (I_{SN1}, C_{SNIC}) and (I_{SN1}, C_{bigSNL}) , nor the big HOM branch. Furthermore, (A2) demands that no stable fixed point exists for $I_{DC} < I_{SN1}$ for $C_m = C_{SNIC}$, effectively preventing the Hopf branch to pass this line. The Hopf branch lies hence either entirely within or outside of the region bounded by these lines.

We show that the Hopf branch lies outside of this region by identifying this branch with the excitation block occurring at $C_m = C_{SNIC}$: (A2) demands that the excitation block at some $I_{DC} > I_{SN1}$, i.e., outside of the identified region. Around the excitation block, P_{block} is stabilized by a Hopf bifurcation. This Hopf bifurcation affect

P_{block} and hence belongs to the same branch of Hopf bifurcations that arises at the BT point at (I_{SN0}, C_{BT0}) , because this is where P_{block} is created. With that, the Hopf branch must lie outside the region denoted above, and correspondingly also the BT point at its end. We hence conclude $C_{BT0} > C_{SNIC}$.

Lemma 4 *The small SNL bifurcation: A second SNL bifurcation occurs at some $C_{smallSNL} > C_{SNIC}$.* The branch of the small HOM bifurcation that arises from the BT point at (I_{SN0}, C_{BT0}) [see Observation 3] continues by Lemma 1 in the direction of increasing input I_{DC} . Hence, we find some $C_m = C_{smallSNL}$ for which the small HOM branch connects to the fold bifurcation at I_{SN1} . At the connection point, the HOM branch must be stable by Lemma 2. We identify the point $(I_{SN1}, C_{smallSNL})$ as small SNL bifurcation.

For the overall proof, it remains to show the ordering $C_{smallSNL} > C_{SNIC}$. For that, we observe that a limit cycle exists between the small HOM and the Hopf branch arising from the BT point and contrast this with the limit cycle arising from the SNIC bifurcation. As the Hopf bifurcation has to terminate the limit cycle of the SNIC bifurcation at C_{SNIC} [(A2)], it cannot terminate the limit cycle arising from the small HOM bifurcation at this capacitance value. This only leaves the possibility for the SNL point to occur at some $C_{smallSNL} > C_{SNIC}$.

In summary, we have shown that $C_{BT1} < C_{bigSNL} < C_{SNIC} < C_{smallSNL}$. This generic bifurcation structure occurs with the membrane capacitance C_m as bifurcation parameter at $I_{DC} = I_{SN1}$. For a model starting at a SNIC bifurcation, a variation in the capacitance will thus pass an SNL bifurcation before a BT point is reached.

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