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Applications of the Poincaré mapping technique to analysis of neuronal dynamics

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Abstract

A single neuron can demonstrate different spiking and bursting patterns which can be elicited naturally depending on modulation status or artificially due to disturbances caused by distinct recording techniques. For example, when pharmacologically isolated with bicuculline a leech oscillatory heart interneuron can show an endogenous bursting activity while recorded extracellularly, or the periodic tonic spiking activity while recorded intracellularly. Transitions between these oscillatory patterns are in general non-local and could not be understood using only the local analysis of the neuron's rest states, but the global theory tools such as the Poincaré return mapping analysis. The mappings constructed then predict the temporal characteristics of the spiking and bursting patterns and allow one to study transitions between them. The technique is directly applicable to neuronal models of various types, as well as is aimed to be employed in neurophysiological experiments.

Keywords: Tonic spiking; Bursting neuron; Active transitions; Poincaré mapping

1. Introduction

Exploration of generic mechanisms of transitions between distinct types of neuronal activity is a fundamental task for determining the basic principles of a neuron's functioning. Commonly, neuronal networks controlling rhythmic movements (central pattern generators) produce bursting patterns of activity [4]. In systems like the leech, the central pattern generator controlling heartbeat, invariability of the pattern is important for survival. The ability of an endogenous bursting of single oscillatory interneurons brings robustness to the system versus variations of the strength of the intra-network coupling [3]. Thus, keeping the system away from the transitions could be vital for this system. Previously, we have developed a powerful averaging technique for the analysis of oscillatory spiking and bursting modes in neuronal models without their slow–fast decomposing. It allowed us to discover two new scenarios of generic transitions between bursting and tonic spiking activities [7,6].

Here, we present a computationally more efficient technique, which is based on the measurements of the minimum values of voltage in spiking cycles and does not involve the averaging, which gives a number of advantages especially for experimental implementations.

2. Model

In this paper we employ a three-dimensional model of a pharmacologically reduced oscillatory heart interneuron [1,7,6]. It is given by

$$\begin{aligned}\dot{V} &= -2[30\,m_{K2}^2(V+0.07)+8(V+0.046)\\ &\quad +200 f_\infty^3(-150,0.0305,V)h_{Na}(V-0.045)],\\ \dot{m}_{K2} &= 4[f_\infty(-83,V_{1/2}\,V_{K2}^{shift},V)-m_{K2}],\\ \dot{h}_{Na} &= 24.69[f_\infty(500,0.0333,V)-h_{Na}],\end{aligned} \quad (1)$$

where V, m_{K2}, and h_{Na} are the membrane potential, activation of the persistent potassium current, I_{K2}, and inactivation of the fast sodium current, I_{Na}, respectively; $f_\infty(k,V_{1/2},V)=1/(1+e^{k(V_{1/2}+V)})$ is a Boltzmann function describing dependence of kinetics of activation/

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inactivation of an ionic current. The state variables m_{K2} and h_{Na} assume values between 0 and 1. If the voltage is clamped to some value V, then each state variable (i.e. m_{K2} and h_{Na}) approaches the corresponding value determined by the Boltzmann function. Thus defined, $V_{1/2}$ determines the voltage at which the Boltzmann function equals 1/2. Following up our previous studies we use V_{K2}^{shift} as the bifurcation parameter which is a shift off $V_{1/2}$ for I_{K2} relative to its canonical value $0.018V$. It ranges within $[-0.026; 0.0018]V$; its upper boundary value corresponds to the hyperpolarized rest state of the neuron, whereas the neuron fires tonically at the lower bound of V_{K2}^{shift}. Dynamically, in the model (1) its variations move vertically, along V, the slow nullcline $\dot{m}_{K2} = 0$ thereby delaying the activation of m_{K2} if shifted towards more negative values. Its shifts cause the model to exhibit multiple transitions between the activities at intermediate values of V_{K2}^{shift}.

3. Central manifolds of slow motion

One may notice from (1) that the time constant of the potassium current in the model is several times slower than those of the other variables in the system. Hence, due to this disparity of time scales, Eqs. (1) could be considered within a framework of fast–slow systems. The feature of such a system is that its dynamics is centered around the manifolds of slow motions. In other words, no matter how system is perturbed for a short time, it will be found again near the stable manifolds of slow motions. Also, while demonstrating any pattern of activity the system's solutions spend almost all the time close to these manifolds thus forming the skeleton of possible activity patterns in the system. This is the reason for these manifolds to be called *central*. A Hodgkin–Huxley-type model has two such manifolds: tonic spiking and quiescent.

The corresponding manifolds of the model under consideration are shown in Fig. 1: the spiking manifold, M_{lc}, consisting of the periodic solutions of the system, and the quiescent one M_{eq} comprised of its equilibrium states. The lower branch of M_{eq} is correlated with the hyperpolarized state of the neuron. A solution of the model, switching repeatedly between these manifolds, is associated with bursting activity of a neuron. The lower knee of M_{eq} indicates the beginning of a burst. A solution of the system, periodic or aperiodic, coiling permanently around M_{lc} without entering a quiescent phase, is associated with the continuous spiking.

One may wonder about the conditions under which the neuron starts to burst, and how this bursting activity evolves into tonic spiking activity as the control parameter is varied. An evident observation that both tonic spiking and bursting activities have the oscillatory character, lets one take the full advantage of the technique of Poincaré return mappings to reveal the hidden mechanisms governing transitions between activities.

4. Poincaré mapping toolkit

A straightforward approach for constructing a Poincaré mapping is the following: one needs a relatively long recoding of the membrane potential where pairs (V_i, V_{i+1}) of successive minima (or maxima) in V are singled out; these points comprise the graph of a one-dimensional Poincaré mapping: $T : V_i \to V_{i+1}$. A drawback of this approach is obvious: if the number of distinct pairs is relatively small, the graph is sparse, and gives limited information about the prevailing type of neuronal activity

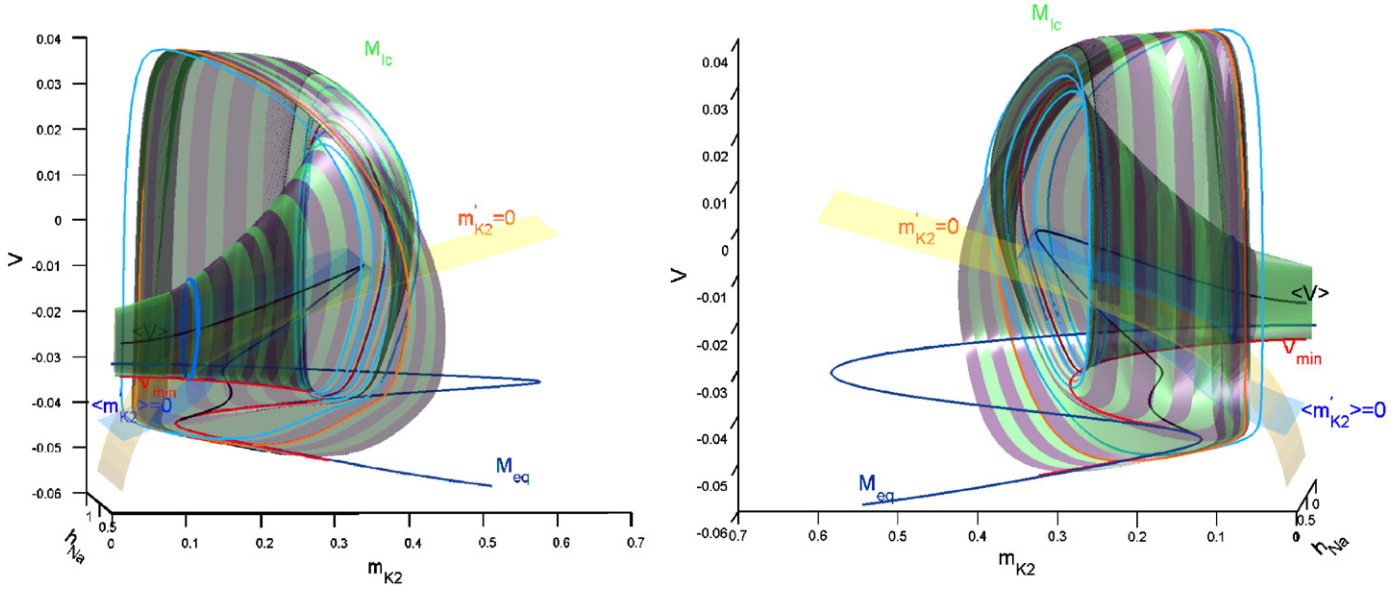

Fig. 1. Central manifolds of slow motions: 2D spiking surface M_{lc} is foliated by the periodic orbits of (1) as V_{K2}^{shift} increased from −0.026 to 0.0018 V. At the later value, the spiking manifold glues to the quiescent manifold, M_{eq}, at its lower knee. An intersection point of M_{eq} with the slow nullcline $\dot{m}_{K2} = 0$ yields an equilibrium state of the model at given V_{K2}^{shift}.

corresponding to an attractor of the mapping. Besides, unstable solutions cannot be detected with this procedure.

The approach applied in this study allows for the creation of the complete family of the onto Poincaré return mappings. First, we single out the spiking manifold in the phase space of the full model. It should be emphasized that we find the manifolds of the slow motion without engaging the standard slow–fast decomposition. Instead, we apply a parameter continuation technique yielding the manifold itself, not its approximation. To apply the continuation technique a stable periodic orbit is detected in the phase space of (1) at a low value of the bifurcation parameter V_{K2}^{shift}. Here we observe that the small amplitude orbit is the edge of the manifold M_{lc} in Fig. 1. Next, the branch of the periodic orbits is continued numerically using the package Content/Matcont [2] as V_{K2}^{shift} is increased. Approaching to $V_{K2}^{shift} = 0.002\,V$, the stable manifold M_{lc} folds back, wraps around the quiescent manifold M_{eq} and terminates at the homoclinic saddle-node equilibrium state on the low knee point on M_{eq}. Thus, by its construction the aforementioned center manifold M_{lc} is a parametrically sought surface foliated by a large number of the spiking periodic orbits of model (1).

At the second stage, we determine the minimum voltage value (V_0) on each periodic orbit. The corresponding phase point is then used as an initial one for integration of the solution of (1). Then we determine the following minimum of the voltage in the thus generated voltage trace. This procedure is repeated for all periodic orbits composing the center spiking manifold M_{lc}. All found pairs (V_0, V_1) comprise the graph of the mapping for the selected bifurcation parameter value.

Four Poincaré mappings are shown in Fig. 2 in insets (B)'s for different V_{K2}^{shift} along with the corresponding attractors (A)'s of model (1) and the traces (C)'s of the membrane potentials.

The top-left portrait represents the (m_{K2}, V)-phase portrait of the tonic spiking attractor in (A) of the model at $V_{K2}^{shift} = -0.012\,V$. Its single V-minimum corresponds to the only stable fixed point of the Poincaré mapping (B) at

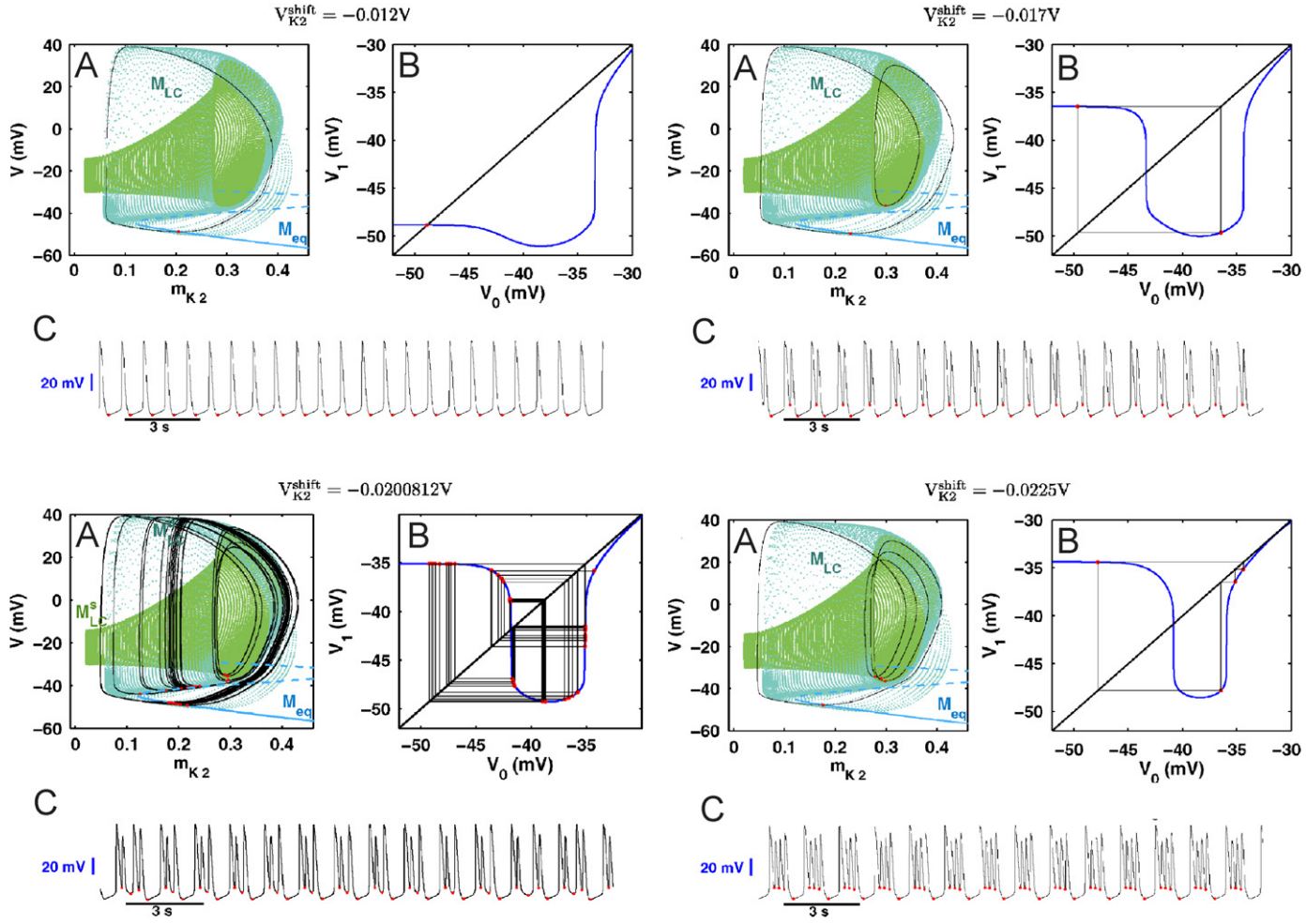

Fig. 2. Types of activity in the model at $V_{K2}^{shift} = -0.012, -0.0170, -0.0200812$ and $-0.0225\,V$, as the neuron becomes more depolarized: the tonic activity evolves into bursting with the increasing number of intra-spikes. Insets (A) show the corresponding attractors of the neuron model in the (m_{k2}, V)-phase space projection: tonic spiking with a single revolution around the manifold M_{lc}, and bursting ones with two and more turns around M_{lc} followed by the quiescence period. Insets (B) show the evolution of the Poincaré mapping and its attractors: the number of the points in the attractor is that of spikes per burst in traces (C).

the crossing point of the graph with the 45° line. A decrease of V_{K2}^{shift} depolarizes the neuron and counterintuitively the tonic spiking turns into bursting shown at $V_{K2}^{shift} = -0.017$ V. The bursting attractor makes now two complete revolutions around the spiking manifold M_{lc}. The trace in (C) shows two action potentials separated by a period of quiescence. One sees from the Poincaré mapping (B) that the transition into bursting occurs when the fixed point attractor becomes unstable, thereby giving rise to a period-two attractor. Two bottom insets in Fig. 2 depict the chaotic transition from the bursting with two to three intra-spikes, and the robust four-spike-burster at −0.0225 V.

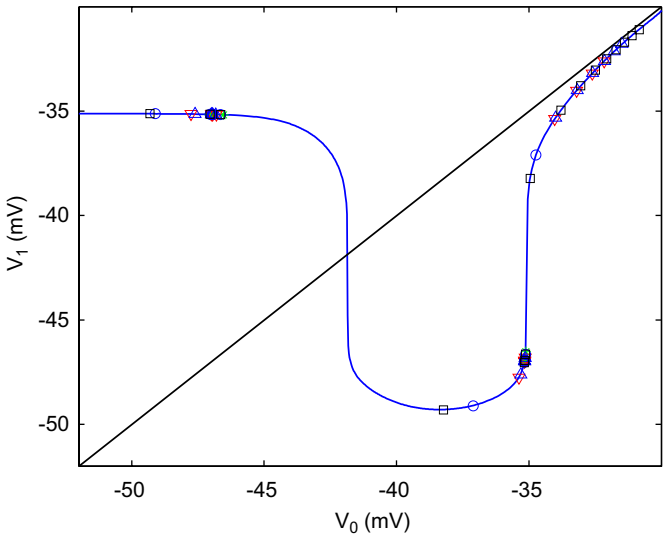

Fig. 3. Poincaré return mapping at $V_{K2}^{shift} = -0.02$ V and the local minima pairs on it generated by five distinct voltage traces introduced through the voltage clamp. The initial voltages for the traces are: 0.015, −0.015, −0.042, −0.030, and −0.025 V. The initial values for h_{Na} and m_{K2} are found by plugging the initial voltage values into the Boltzmann function. The corresponding pairs localized in the voltage traces are marked by ▽, △, □, ○ and ⋆.

In addition to this precise correspondence of the stable activity patterns observed in the model to those in the mapping, we can demonstrate the applicability of the mapping technique to studies of the transient activity too. Essentially, the advantage of the technique is that it can predict activity of the neuron after any biophysically plausible perturbations of the initial conditions. Let us apply a voltage clamp technique to the model. By doing so, we set the membrane voltage to any biophysically meaningful value. If we keep the voltage clamped for a sufficiently long time, the activation and inactivation state variables, determining the conductances of the ionic currents, will reach their stationary values. Then, we release the neuron from the clamp and analyze the voltage trace generated for the given initial conditions. The corresponding V-minima pairs (V_i, V_{i+1}) are detected and the trace are mapped. As the system transiently approaches the stable activity pattern, it illuminates different points on the mapping, that are labeled with different markers in Fig. 3 for five distinct initial

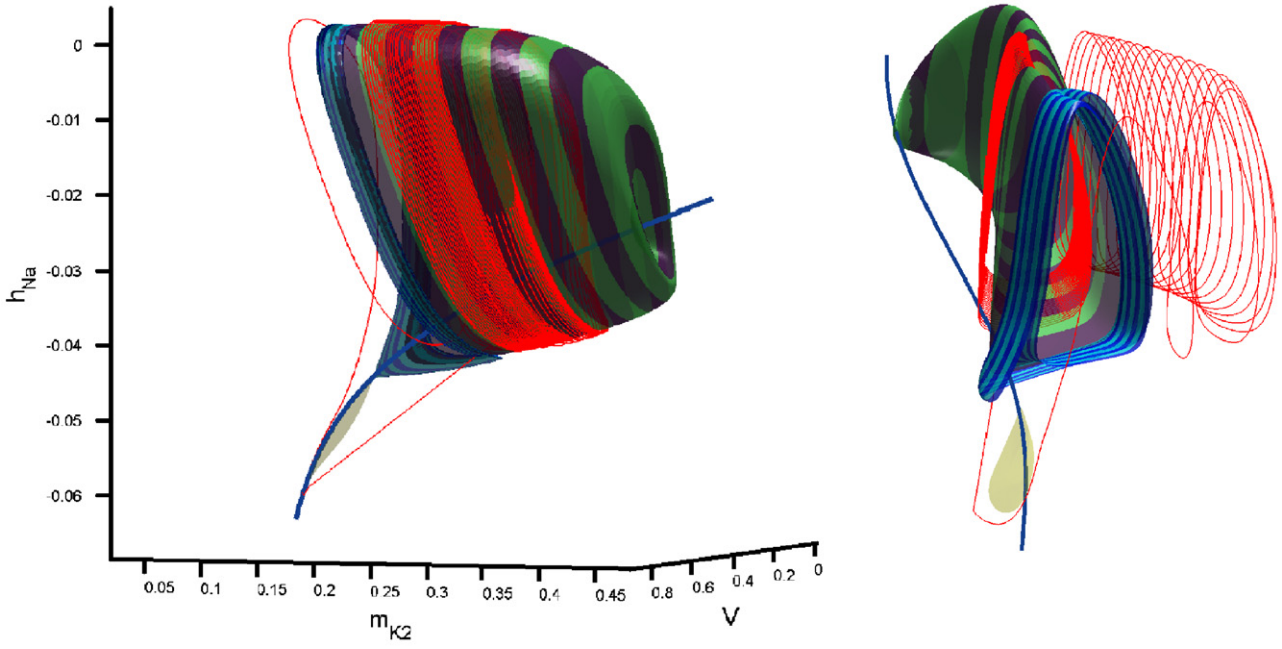

Fig. 4. A bursting solution switching between the central spiking and quiescent manifolds in the original 14D leech heart interneuron model. The manifolds are shown in the projections onto central variables (left) and onto non-principal phase variables (right). In the "non-central" case, the bursting orbit no longer lingers around the spiking manifold. The other evident distinctions between the projections onto the principal and non-principal currents are the way the spiking manifold folds at a saddle-node bifurcation and that it does not encircle the quiescent branch after the Andronov–Hopf bifurcation.

conditions. Thus, by reapplying this approach, we may expect to reveal the entire stable, as well as partly unstable, sections of the mapping.

5. Conclusions

New tools are developed allowing for a reduction to a one-dimensional Poincaré mapping revealing the *hidden* organizing centers of dynamics of the membrane potential in Hodgkin–Huxley-type models. The method is applicable for a broad class of neuronal models with fast–slow dynamics including square-wave type [5]. This assertion is supported in Fig. 4 illustrating two-dimensional projections of the spiking and quiescent central manifolds onto a 3D projection of the phase space of the 14-dimensional model of the leech heart interneuron [3]. We add that the term *cental* bears two meanings here: first, the manifolds, being the Birkhoff centers [8], capture the essential dynamics of the system; second, the manifolds shown in the projection onto the phase variables are directly involved in the bifurcations in a complete analogy with the central manifolds in the bifurcation theory. Thus, we can identify the corresponding currents that determine the dynamics of the model.

The analysis of the mapping lets one describe accurately transitions between various types of neuronal activities and understand their origin. A similar approach can be implemented in experiments through voltage clamp. Finally, let us point out one more advantage: these *exact* onto mappings may be used to replace the ordinal models in time consuming numerical simulations of dynamics of large scale neural networks.

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