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On the origin of reproducible sequential activity in neural circuits

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Robustness and reproducibility of sequential spatio-temporal responses is an essential feature of many neural circuits in sensory and motor systems of animals. The most common mathematical images of dynamical regimes in neural systems are fixed points, limit cycles, chaotic attractors, and continuous attractors (attractive manifolds of neutrally stable fixed points). These are not suitable for the description of reproducible transient sequential neural dynamics. In this paper we present the concept of a stable heteroclinic sequence (SHS), which is not an attractor. SHS opens the way for understanding and modeling of transient sequential activity in neural circuits. We show that this new mathematical object can be used to describe robust and reproducible sequential neural dynamics. Using the framework of a generalized high-dimensional Lotka–Volterra model, that describes the dynamics of firing rates in an inhibitory network, we present analytical results on the existence of the SHS in the phase space of the network. With the help of numerical simulations we confirm its robustness in presence of noise in spite of the transient nature of the corresponding trajectories. Finally, by referring to several recent neurobiological experiments, we discuss possible applications of this new concept to several problems in neuroscience. © *2004 American Institute of Physics*. [DOI: 10.1063/1.1819625]

Generation of sequential activity is one of the most important functions of neural circuits. For example, the high vocal center of songbirds produces a sequence of bursts that controls generation of unique and reproducible songs by the vocal system. The predator marine mollusk Clione produces a sequential hunting motion to find its prey and, in spite of the irregularity of this motion, the sequence of Clione's tail positions is also reproducible. Reproducible sequential neural activity is involved in sequential memory processes, fast recognition of stimuli by olfactory and auditory sensory systems and many other dynamical functions of the nervous system. What is the dynamical origin of such reproducibility? Which conditions do the synaptic connections of the neural circuits have to satisfy to generate reproducible transient sequences? In this paper we answer these questions using a generalized Lotka–Volterra model. We present a new mathematical construction—a stable heteroclinic sequence (SHS)—that describes reproducible sequence generation in the phase space of the dynamical model of a neural circuit. This construction keeps the trajectories in the vicinity of the heteroclinic skeleton due to the existence of a stable manifold on which the saddle points lie. These saddle points and the one-dimensional separatrices that connect them organize the SHS. We present rigorous results about the existence of the SHS that are supported by computer simulations of the dynamics along the SHS in presence of noise. We also discuss how the concept of

SHS may help to understand observations of sequential dynamics in various neurobiological experiments.

I. INTRODUCTION

The principles of organization of neural circuits that are responsible for the formation of reproducible animal behavior are not completely known. The best understanding of such principles has been obtained for rhythmic motor functions like heart beating, breathing or walking. Such rhythmic functions are controlled by neural circuits that produce motor commands in the form of periodic spatio-temporal patterns of neural activity. The repetitive dynamics in these circuits is usually reproducible and can be described by a regular attractor, i.e., a limit cycle. However, many sensory, motor, and other neural systems demonstrate transient, nonperiodic activity, which, nevertheless, is reproducible from trial to trial. In these neural systems similar stimuli lead to the execution of similar sequential behaviors. The dynamics in neural circuits that control these finite-time nonperiodic behaviors is transient and, hence, cannot be implemented by a dynamical system with a limit cycle attractor.

In this paper we propose a new object in nonlinear dynamics of dissipative systems—a stable heteroclinic sequence (SHS), which represents a reproducible sequential pattern in the phase space of the system. We assume that the motor systems do not respond to all the detailed features of

the output of sensory systems but just to the sequence of key events. Therefore, the reproducibility of spatio-temporal patterns that are generated by sensory neural circuits does not have to be perfect, but can be imperfect, i.e., the sequence of neuronal activations has to be reproducible, but their timing may not be. Such spatio-temporal sequential activity in neural ensembles is similar to the sequence of snapshots in a movie. It has been observed in the insect olfactory system,[1,2] mollusk sensory-motor system,[3] vocal tract of songbirds[4] and other neural systems. In those observations the time intervals between the "snapshots" were found to vary slightly from trial to trial but sequences of neuronal activations were found to be the same for the same stimulus and were changing with the stimulus. From the point of view of dynamical systems the observed reproducibility of sequential activity looks very intriguing because such transient dynamics is expected to depend strongly on initial conditions and fluctuations.

To explain this phenomenon we use as an example a Lotka–Volterra-type model of a neural network with inhibitory connections. Based on the results of computational experiments with this model we hypothesize that winnerless competition (WLC)[5] among the neurons in the network with dense inhibitory connections may explain the reproducibility of sequential neural activity. A WLC network of n neurons is a network which has a sequence of heteroclinic connections of saddle fixed points in its n-dimensional phase space. Each of these fixed points lies on a $(n-1)$-dimensional stable manifold and these fixed points are connected along unstable directions by one-dimensional separatrices that induce transitions from one fixed point to the next. In this paper we formulate the necessary conditions on the connectivity of the WLC network that have to be satisfied in order for the network to exhibit reproducible sequential dynamics along the heteroclinic orbit.

Heteroclinic phenomena such as heteroclinic cycles and networks of several heteroclinic cycles have attracted the attention of many authors in the last 30 years (see, for example, Ref. 6). It has recently been proposed that the complex neural dynamics may be associated with these phenomena.[1] Although there are some results on the dynamics arising from the existence of heteroclinic contours and the behavior of the system in their vicinity, to the best of our knowledge results concerning dynamic behavior induced by an open heteroclinic sequence are absent. In our opinion, the SHS is the most suitable mathematical object for the description and analysis of reproducible sequential dynamics in biological and artificial neural networks and in complex systems in general.

The paper is organized as follows: In the second section we consider general features of the model, find conditions for the existence of a heteroclinic sequence, and formulate and prove a theorem about the reproducibility of sequential dynamics; in the third section we present results of numerical simulations that confirm our theoretical analysis and illustrate its generality; finally, we discuss the applicability of the results to several interesting problems of neuroscience.

II. ANALYTICAL RESULTS

A. The model

Our goal is to understand the reproducibility of sequential neural activity regardless of the exact timing of spikes. Hence, let us describe each neuron by one dynamical variable, $a_i(t)$, which corresponds to its average firing rate. Neurons in our model form a network with inhibitory synaptic connections. This model can also be extended to the case of excitatory-inhibitory networks, where excitatory principal neurons are connected through inhibitory interneurons like, for example, in the olfactory system of insects.[1]

The dynamics of an inhibitory network of $n=N+M$ neurons can be described by the following system of ordinary differential equations (ODEs):

$$\frac{da_i(t)}{dt} = a_i(t)\left[\sigma_i(S) - \sum_{j=1}^{N+M} \rho_{ij}(S)a_j(t)\right] + \xi_i(t), \qquad (1)$$

where N will be defined below [see inequality (32)], each $a_i(t) > 0$ represents an instantaneous firing rate of ith neuron, σ_i represents strength of stimulation of ith neuron, ρ_{ij} represents strength of inhibition of neuron i by neuron j and $\xi_i(t)$ represents external noise.[5,7,8] In this model it is assumed that the stimulus S forms the matrix ρ_{ij} and increments σ_i. Each increment σ_i controls the time constant of an initial exponential growth from $a_i(t)=0$.

Let us use a simplified model,[5] in which $\sigma_i > 0$ when the stimulus S has a component at element i and $\sigma_i = 0$ otherwise. If we single out only indices i for which $\sigma_i > 0$ we obtain a system that could contain less than n equations, say $N+M_1$, so (may be after relabeling of the indices) the system will have the form

$$\frac{da_i(t)}{dt} = a_i(t)\left[\sigma_i - \left(a_i(t) + \sum_{j \neq i}^{N+M_1} \rho_{ij}a_j(t)\right)\right], \qquad (2)$$

where $\sigma_i > 0$, $i=1,\ldots,N+M_1$ and the external noise is assumed to be absent. Equation (2) implies, first of all, that the equilibrium at the origin $\mathbf{O}(a_i=0)$ is an unstable node.

B. Behavior of orbits around the origin

From now on we assume that

$$0 < \sigma_{i_1} < \sigma_i, \quad i=1,\ldots,N+M_1, \quad i \neq i_1. \qquad (3)$$

It means that the strongly unstable manifold W_O^{uu} at $\mathbf{O}$ is the hyper plane $a_{i_1}=0$ and the leading direction is the a_{i_1}-axis. In other words, all orbits go to $\mathbf{O}$ as $t \to -\infty$ being tangent to the a_{i_1}-axis except for those belonging to W_O^{uu}. If one chooses randomly an initial point in a small neighborhood of O than almost surely the point will not belong to W_O^{uu}, and will leave the neighborhood following a_{i_1} direction.

C. The first saddle

Denote by A_1 the equilibrium point $(0,\ldots,0,\sigma_{i_1},0,\ldots,0)$ on the a_{i_1}-axis. By direct verification

one can find the increments of the point A_1; they are $-\sigma_{i_1}$ and $(\sigma_i - \rho_{ii_1}\sigma_{i_1})$, $i = 1, \ldots, N+M_1$, $i \neq i_1$. We assume that there exists a number i_2, $1 \leq i_2 \leq N+M_1$ such that

$$\sigma_{i_2} - \rho_{i_2 i_1}\sigma_{i_1} > 0 \tag{4}$$

and, in addition,

$$\sigma_i - \rho_{ii_1}\sigma_{i_1} < 0, \quad 1 \leq i \leq N+M_1, \quad i \neq \{i_1, i_2\}. \tag{5}$$

It follows from these assumptions that the point A_1 is a saddle with one-dimensional unstable manifold. Moreover, the index i_2 indicates a direction in which the unstable separatrix of A_1 will go—see below.

For the sake of simplicity of the proof of further results, we assume that a_{i_1}-axis is a leading direction for the node A_1 on the hyperplane $a_{i_2} = 0$, i.e., we assume that

$$\sigma_i - \rho_{ii_1}\sigma_{i_1} < -\sigma_{i_1}, \quad 1 \leq i \leq N+M_1, \quad i \neq \{i_1, i_2\}. \tag{6}$$

There is an important quantity, the so-called saddle value, that measures the evolution of a deviation from the stable and unstable manifolds along the orbits going through the neighborhood of A_1.[9,10] A restriction of such a map to the plane $P_{i_1 i_2}$ has the form

$$\xi = c\,\eta^{\nu_{i_1}}, \tag{7}$$

where c is a constant, η is a deviation from the stable manifold, ξ is a deviation from the unstable one and the saddle value is

$$\nu_{i_1} = \frac{\sigma_{i_1}}{\sigma_{i_2} - \rho_{i_2 i_1}\sigma_{i_1}}. \tag{8}$$

If $\nu_{i_1} > 1$ then the saddle A_1 is called dissipative: There is a contraction of a deviation after passing through a neighborhood A_1.

D. The second saddle

The unstable direction of a point A_1 has a positive projection on the vector $\mathbf{e}_{i_2} = (0, \ldots, 0, 1, 0, \ldots, 0)$, where 1 corresponds to the i_2th coordinate. Let us consider now the equilibrium point $A_2 = (0, \ldots, 0, \sigma_{i_2}, 0, \ldots, 0)$. The increments at A_2 are $-\sigma_{i_2}$ in the direction $\mathbf{e}_{i_2}$ and $\sigma_i - \rho_{ii_2}\sigma_{i_2}$ in the ith direction, $i = 1, \ldots, N+M_2$, $i \neq i_2$.

We assume that there exists $i_3 \neq \{i_1, i_2\}$, $1 \leq i_3 \leq N+M_1$ such that

$$\sigma_{i_3} - \rho_{i_3 i_2}\sigma_{i_2} > 0 \tag{9}$$

and

$$\sigma_i - \rho_{ii_2}\sigma_{i_2} < 0, \tag{10}$$

for $1 \leq i \leq N+M_1$, $i \neq \{i_2, i_3\}$. Under these assumptions the point A_2 is a saddle with one-dimensional unstable manifold. Moreover, the index i_3 shows the next point to be visited.

The intersection of hyperplanes $P_{i_1 i_2} = \cap_{j \neq i_1, i_2}^{N+M_1}\{a_j = 0\}$ is the plane containing points A_1, A_2 such that A_1 is a saddle point on $P_{i_1 i_2}$ and A_2 is a stable node on it. The restriction of the system (2) on $P_{i_1 i_2}$ has the form

$$\dot{a}_{i_1}(t) = a_{i_1}(t)[\sigma_{i_1} - (a_{i_1}(t) + \rho_{i_1 i_2}a_{i_2}(t))], \tag{11}$$

$$\dot{a}_{i_2}(t) = a_{i_2}(t)[\sigma_{i_2} - (a_{i_2}(t) + \rho_{i_2 i_1}a_{i_1}(t))], \tag{12}$$

and it follows from (4) and (10) that

$$\sigma_{i_2} - \rho_{i_2 i_1}\sigma_{i_1} > 0 \quad \text{and} \quad \sigma_{i_1} - \rho_{i_1 i_2}\sigma_{i_2} < 0. \tag{13}$$

This implies that if

$$1 - \rho_{i_1 i_2}\rho_{i_2 i_1} \neq 0 \tag{14}$$

then there are no equilibrium points in the region $a_{i_1} > 0$, $a_{i_2} > 0$. It is not difficult to show that the separatrix of the point A_1 belonging to the positive quadrant on $P_{i_1 i_2}$ must go to attractor A_2 on the plane $P_{i_1 i_2}$, i.e., there is a heteroclinic connection $\Gamma_{i_1 i_2}$ between points A_1 and A_2. The increments of A_2 on $P_{i_1 i_2}$ are $-\sigma_{i_2}$ and $(\sigma_{i_1} - \rho_{i_1 i_2}\sigma_{i_2})$, which is less than 0 because of (13). We assume that

$$-\sigma_{i_2} < \sigma_{i_1} - \rho_{i_1 i_2}\sigma_{i_2} \tag{15}$$

or

$$\rho_{i_1 i_2} < \frac{\sigma_{i_1} + \sigma_{i_2}}{\sigma_{i_2}}.$$

Thus, the leading direction at A_2 is transversal to the a_{i_2}-axis on the plane $P_{i_1 i_2}$. It is natural to ask if this direction is the leading one on the hyperplane $\{a_{i_3} = 0\}$ (on which A_2 is a stable node). It will be so if all negative increments at A_2 will be less than $\sigma_{i_1} - \rho_{i_1 i_2}\sigma_{i_2}$, in other words if

$$\sigma_i - \rho_{ii_2}\sigma_{i_2} < \sigma_{i_1} - \rho_{i_1 i_2}\sigma_{i_2} \tag{16}$$

for $i = 1, \ldots, N+M_1$, $i \neq \{i_1, i_2, i_3\}$. We assume that (15) and (16) are satisfied.

A restriction of the local map in the neighborhood of A_2 on the plane $P_{i_2 i_3}$ has the form

$$\xi = c\,\eta^{\nu_{i_2}}, \tag{17}$$

where c is a constant, η is a deviation from the stable manifold, ξ is a deviation from the unstable one and the saddle value is

$$\nu_{i_2} = -\frac{\sigma_{i_1} - \rho_{i_1 i_2}\sigma_{i_2}}{\sigma_{i_3} - \rho_{i_3 i_2}\sigma_{i_2}} = \frac{\rho_{i_1 i_2}\sigma_{i_2} - \sigma_{i_1}}{\sigma_{i_3} - \rho_{i_3 i_2}\sigma_{i_2}}. \tag{18}$$

If $\nu_{i_2} > 1$ then the saddle A_2 will be dissipative and an orbit comes closer to the unstable manifold of A_2 after going through a neighborhood of this point.

E. The mth saddle

Continuing inductively the procedure described above for the selection of saddle points and heteroclinic connections between them, we arrive at the mth level of the procedure. We suppose that the following assumptions were satisfied until now:
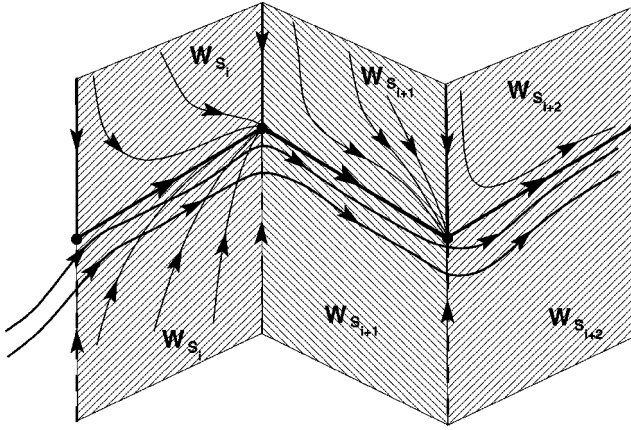
FIG. 1. A stable open heteroclinic sequence in a neural circuit with WLC. This is a mathematical image of reproducible nonrhythmic sequential activity. W_i is a stable manifold of the ith saddle fixed point (heavy dots). The trajectories in the vicinity of the SHS represent sequences with different timings; the time intervals between switches are proportional to the square root of the distance from the SHS.

(1) **Selection of saddles.** The saddles $A_k = (0, \ldots, 0, \sigma_{i_k}, 0, \ldots, 0)$, $k = 2, \ldots, m$ were selected in such a way that

$$\sigma_{i_{k+1}} - \rho_{i_{k+1} i_k} \sigma_{i_k} > 0, \tag{19}$$

$$\sigma_i - \rho_{i i_k} \sigma_{i_k} < 0, \tag{20}$$

for $1 \le i \le N + M_1$, $i \ne \{i_{k+1}, i_k\}$. Thus, all points $A_k, 2 \le k \le m$ are saddles with one-dimensional unstable manifolds (see Fig. 1). Moreover, the index i_{m+1} gives a way to proceed to the next step of induction.

(2) **Heteroclinic connections.** Under the condition (which is supposed to be satisfied)

$$1 - \rho_{i_{k-1} i_k} \rho_{i_k i_{k-1}} \ne 0, \tag{21}$$

there is a heteroclinic orbit $\Gamma_{i_{k-1} i_k}$ joining A_{k-1} and A_k. This orbit belongs to the plane $P_{i_{k-1} i_k} = \cap_{j \ne i_{k-1}, i_k}^{N+M_1} \{a_j = 0\}$. This is easy to show taking into account the facts that there are no other equilibria on $P_{i_{k-1} i_k}$ except for A_{k-1} and A_k, the point A_k is an attractor on $P_{i_{k-1} i_k}$, and there are no limit cycles on this plane.

(3) **Leading directions.** Under the conditions (which are supposed to be satisfied)

$$-\sigma_{i_k} < \sigma_{i_{k-1}} - \rho_{i_{k-1} i_k} \sigma_{i_k}, \tag{22}$$

$$\sigma_i - \rho_{i i_k} \sigma_{i_k} < \sigma_{i_{k-1}} - \rho_{i_{k-1} i_k} \sigma_{i_k}, \tag{23}$$

for $1 \le i \le N + M_1$, $i \ne \{i_{k-1}, i_k, i_{k+1}\}$, the separatrix $\Gamma_{i_{k-1} i_k}$ comes to A_k following a leading direction, transversal to the a_{i_k}-axis on the plane $P_{i_{k-1} i_k}$. Let us remark that the saddle value

$$\nu_{i_k} = \frac{\rho_{i_{k-1} i_k} \sigma_{i_k} - \sigma_{i_{k-1}}}{\sigma_{i_{k+1}} - \rho_{i_{k+1} i_k} \sigma_{i_k}}, \tag{24}$$

is defined for every saddle A_k.

Consider now the point $A_{m+1} = (0, \ldots, 0, \sigma_{i_{m+1}}, 0, \ldots, 0)$. We assume that the following conditions are satisfied:

(1) $A_{m+1} \ne A_k$, $1 \le k \le m$. If $A_{m+1} = A_k$ then we have a heteroclinic contour. Such a situation has been studied in Ref. 11.

(2) There exists $1 \le i_{m+2} \le N + M_1$ such that the following inequalities are satisfied

$$\sigma_{i_{m+2}} - \rho_{i_{m+2} i_{m+1}} \sigma_{i_{m+1}} > 0, \tag{25}$$

$$\sigma_i - \rho_{i i_{m+1}} \sigma_{i_{m+1}} < 0, \tag{26}$$

for $1 \le i \le N + M_1$, $i \ne \{i_{m+1}, i_{m+2}\}$. Thus A_{m+1} is a saddle with one-dimensional unstable manifold.

(3) Condition for heteroclinic connections is satisfied:

$$1 - \rho_{i_m i_{m+1}} \rho_{i_{m+1} i_m} \ne 0. \tag{27}$$

It implies that there is a heteroclinic orbit $\Gamma_{i_m i_{m+1}}$ joining A_m and A_{m+1}.

(4) Conditions for following the leading direction

$$-\sigma_{i_{m+1}} < \sigma_{i_m} - \rho_{i_m i_{m+1}} \sigma_{i_{m+1}}, \tag{28}$$

$$\sigma_i - \rho_{i i_{m+1}} \sigma_{i_{m+1}} < \sigma_{i_m} - \rho_{i_m i_{m+1}} \sigma_{i_{m+1}}, \tag{29}$$

for $1 \le i \le N + M_1$, $i \ne \{i_m, i_{m+1}, i_{m+2}\}$ are supposed to be satisfied.

Now, under formulated conditions, there is a sequence of separatrices

$$\Gamma_{m+1} := \bigcup_{k=1}^{m+1} A_{i_k} \bigcup_{k=1}^{m} \Gamma_{i_k i_{k+1}}, \tag{30}$$

joining A_{i_1} and $A_{i_{m+1}}$. Let us assume that we can follow this inductive procedure until $k = N$, i.e., the conditions (19)–(23) are satisfied for $k = 2, \ldots, N$. Thus, there exists a heteroclinic sequence Γ_N consisting of saddle points A_k and separatrices $\Gamma_{i_k i_{k+1}}$ that join them. This sequence can be attracting in a sense.

Let

$$\lambda_1 := \nu_{i_1}, \lambda_2 := \nu_{i_1} \cdot \nu_{i_2}, \ldots, \lambda_N := \prod_{k=1}^{N} \nu_{i_k}$$

$$= \frac{\sigma_{i_1}}{\sigma_{i_2} - \rho_{i_2 i_1} \sigma_{i_1}} \cdot \prod_{k=2}^{N} \frac{\rho_{i_{k-1} i_k} \sigma_{i_k} - \sigma_{i_{k-1}}}{\sigma_{i_{k+1}} - \rho_{i_{k+1} i_k} \sigma_{i_k}}. \tag{31}$$

Then the following statement holds.

Theorem: Assume that the conditions (19), (20), (22), and (23) are satisfied for $k = 1, \ldots, N$ and the conditions (21) are satisfied for $k = 2, \ldots, N$. Assume also that

$$\lambda_k > 1, \quad k = 1, \ldots, N. \tag{32}$$

Then for any sufficiently small neighborhood U of the sequence Γ_N there exists $\epsilon_0 = \epsilon_0(U) > 0$ such that for every initial condition $a^0 = (a_1^0, \ldots, a_{N+M_1}^0)$ in a small neighborhood of A_1 with $0 < a_{i_2}^0 = \epsilon \le \epsilon_0$, one has $a(t) \in U$ for $0 \le t \le T(\epsilon)$, where $a(t)$ is a solution of (2) going through a^0 and $T(\epsilon) = -K \log \epsilon + C$ where C is a constant independent of ϵ and

$$K = \frac{1}{\sigma_{i_2} - \rho_{i_2 i_1}\sigma_{i_1}} + \sum_{k=2}^{N} \frac{\nu_{i_{k-1}}}{\sigma_{i_{k+1}} - \rho_{i_{k+1} i_k}\sigma_{i_k}}. \tag{33}$$

Moreover, $a(t)\backslash V(\cup_{k=1}^{N} A_{i_k})$ (where V is the ϵ_0- neighborhood of equilibria A_{i_k}) consists of N segments, and

$$\text{dist}(a(t),\Gamma_{i_k i_{k+1}}) \leqslant C_1 \epsilon^{\lambda_k}, \tag{34}$$

for values of t for which $a(t)$ belongs to the kth segment, where C_1 is a constant independent of ϵ.

Thus, an orbit starting in an ϵ-vicinity of the stable manifold of A_1 spends a long time in a neighborhood of the chain Γ_N following heteroclinic connections $\Gamma_{i_k i_{k+1}}$. In other words, one may observe the same sequence of switching from one equilibrium to another for a large number of orbits. This qualitative statement is true even without conditions (22) and (23), but constants K, C, and C_1 might be different.

The proof of Theorem is obtained in the same way as the proof of Theorem 1 in Ref. 11.

Remark: One can see that the inequalities in the conditions of Theorem are the same as the ones in Theorem 1 in Ref. 11. The difference is that in Theorem 1 of Ref. 11 these conditions guarantee the stability of the heteroclinic contour as an attractor while here they only imply stability of the SHS during finite interval of time. Such kind of statements while being standard in, say, the theory of averaging is not so familiar in the dynamical systems theory. In other words, we construct the sequence of mappings of transversal to heteroclinic orbits sections along orbits close to these heteroclinic orbits absolutely in the same way as we did in Ref. 11. The conditions of Theorem imply that all these mappings are contractions. Thus, any orbit going through a point close to the first heteroclinic orbit will remain close to the SHS until it intersects the last transversal section to the unstable separatrix of the nth saddle point. In Theorem 1 of Ref. 11 the first and the last sections were the same—the heteroclinic orbits formed a closed heteroclinic contour—therefore, the corresponding Poincare mapping was a contraction. Here the first and the last sections are different, and one can guarantee the closeness of the SHS and an orbit only during a finite interval of time $T(\epsilon)$.

Corollary: Under the conditions of Theorem and provided that (3) is satisfied and given a neighborhood U as in Theorem, there exists an open set V^+ in the positive octant in a small neighborhood V of the origin such that every orbit going through V^+ comes to U at a point $a^0 = (a_1^0, \ldots, a_{N+M_1}^0)$ with $0 < a_{i_2}^0 = \epsilon \leqslant \epsilon_0$, and then follows the heteroclinic sequence Γ_N staying in U for the time $T(\epsilon)$.

The proof of Corollary directly follows from the fact [assumption (3)] that most orbits leave V following the a_{i_1}-axis.

Remark: In reality V^+ can be very large, it can contain, say, 90% of all positive initial points in V. It explains reproducibility of sequences of switching $\{A_{i_k}\}$ while one repeats choosing points in the small neighborhood V of the origin and looks at the resulting orbits.

Summarizing the results of this section one can say that:

(1) Among saddle-type equilibria of the system (4) there are the ones with one-dimensional unstable separatrices and they can be found by using the inequalities (19) and (20).

(2) Such saddle points can be connected by heteroclinic orbits that form ordered collections of saddles, so-called heteroclinic sequences.

(3) A heteroclinic sequence can be stable and sufficient conditions for its stability are given in inequalities (32).

(4) If these conditions are satisfied then an orbit through a point in a neighborhood of the first saddle of the heteroclinic sequence will stay in a vicinity of this sequence until its last saddle point.

(5) The last statement holds for any choice of an initial point belonging to an open set in the phase space, hence reproducibility of spatio-temporal responses to similar stimuli is guaranteed.

III. NUMERICAL RESULTS

A. Simulation procedure

Let us represent conditions of Theorem in a more convenient form. First, the inequalities (20) and (22) are equivalent to

$$\frac{\sigma_{i_{k-1}}}{\sigma_{i_k}} < \rho_{i_{k-1} i_k} < \frac{\sigma_{i_{k-1}}}{\sigma_{i_k}} + 1. \tag{35}$$

Furthermore, we assume that $\nu_{i_k} > 1$, $k = 1, \ldots, N$. Then the conditions $\lambda_k > 1$ will be automatically satisfied. Thus, the inequality

$$\nu_{i_k} = \frac{\rho_{i_{k-1} i_k}\sigma_{i_k} - \sigma_{i_{k-1}}}{\sigma_{i_{k+1}} - \rho_{i_{k+1} i_k}\sigma_{i_k}} > 1, \tag{36}$$

implies that

$$\rho_{i_{k+1} i_k} > -\rho_{i_{k-1} i_k} + \frac{\sigma_{i_{k-1}}}{\sigma_{i_k}} + \frac{\sigma_{i_{k+1}}}{\sigma_{i_k}}, \tag{37}$$

and, together with (35), it implies the inequality

$$\rho_{i_{k+1} i_k} > \frac{\sigma_{i_{k+1}}}{\sigma_{i_k}} - 1. \tag{38}$$

Combining the last result with (19) we obtain

$$\frac{\sigma_{i_{k+1}}}{\sigma_{i_k}} - 1 < \rho_{i_{k+1} i_k} < \frac{\sigma_{i_{k+1}}}{\sigma_{i_k}}. \tag{39}$$

Also, condition (23) may be rewritten as

$$\rho_{ii_k} > \rho_{i_{k-1} i_k} + \frac{\sigma_i - \sigma_{i_{k-1}}}{\sigma_{i_k}}. \tag{40}$$

In order to check predictions of Corollary, we performed numerical simulations of the dynamics in a network of $N = 50$ neurons described by Eq. (2) with Gaussian white noise with $mean = 0.02$ and $\sigma = 0.015$ added to its right hand side.[12] Increments $\sigma_i (i = 1, \ldots, N)$ were set to random numbers that were taken uniformly from the interval (5;10). Elements of the connectivity matrix ρ_{ij} were then chosen according to the following rules:
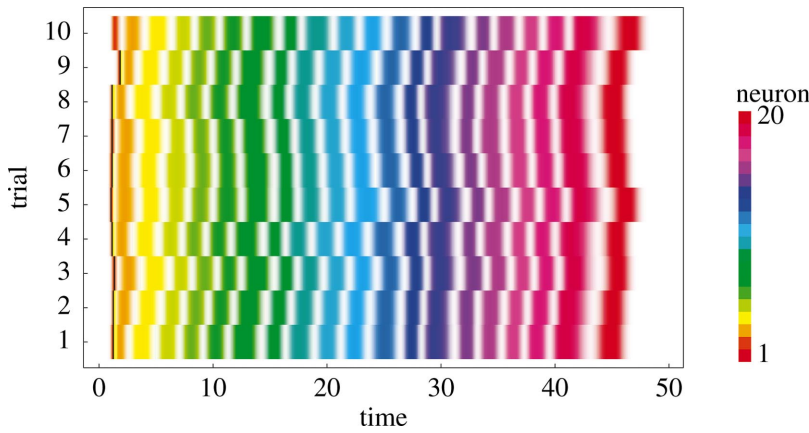
FIG. 2. (Color). Time series of ten trials, simulations of each trial were started from a different random initial condition. Only one neuron is active at any given time, except for very short initial transient time (see Fig. 3).

$$\rho_{i_{k-1}i_k} = \frac{\sigma_{i_{k-1}}}{\sigma_{i_k}} + 0.5, \tag{41}$$

$$\rho_{i_{k+1}i_k} = \frac{\sigma_{i_{k+1}}}{\sigma_{i_k}} - 0.5, \tag{42}$$

$$\rho_{ii_k} = \rho_{i_{k-1}i_k} + \frac{\sigma_i - \sigma_{i_{k-1}}}{\sigma_{i_k}} + 2, \tag{43}$$

that satisfy the conditions (35), (39), and (40).

The resulting system of equations was simulated 10 times, each time starting from a random initial condition within the hypercube $R_{(0;0.2)}^{50}$. In each simulation the sequence of crossings of the threshold $a=4$ by a_i was recorded. Ten such networks with random sets of σ_i were simulated and, as a result, 100 sequences were obtained, 10 for each network.

B. Results

Equations (41)–(43) satisfy the conditions of the Corollary. However, these conditions are not sufficient to observe reproducibility for arbitrary initial points. Hence, one cannot expect that all the networks with random σ_i and strengths of connections which satisfy (41)–(43) will exhibit reproducible sequential dynamics. Nevertheless, most of the networks produced identical sequences in all 10 trials. In Fig. 2 we show an example of 10 color-coded time series for a network with a particular realization of σ_i. Simulations of each trial were started from a different random initial condition. In this plot each neuron is represented by a different color and its level of activity is represented by the saturation of the color. This figure illustrates that the sequence of neuronal activations in the network is reproducible and the time intervals between switchings of neuronal activity are roughly the same.

In Fig. 3 we plot an example of the time series $a_i(t)$ during the initial stage of switching dynamics in the network. This plot illustrates the fact that the system "forgets" the initial conditions very quickly and from the very beginning starts to follow the heteroclinic sequence.

IV. DISCUSSION

The processing of sequential discrete events is important on every level of organization of neural systems: From one neuron to neural ensembles and microcircuits. One of the general dynamical principles that can be responsible for sequence generation in neural systems is the winnerless competition (WLC) among neurons.[1,5,8,11] The mathematical image of the WLC dynamics is a trajectory in the vicinity of a stable heteroclinic sequence (SHS) in the phase space of the system. Such a sequence (see Fig. 1) is a chain of saddle-node fixed points connected by one-dimensional separatrices which retains nearby trajectories in its vicinity. In neural systems the WLC dynamics is realized by inhibitory connections between different neural clusters: Inhibitory neurons sequentially inhibit (turn off) or stop to inhibit (turn on) excitatory neurons. Flexibility of WLC dynamics may be provided by the dependence of the identity of participating neural clusters on the stimuli.

Sequence generation in the chain- or layer-like networks of neurons may result from feedforward wave-like propagation of spikes (like the waves in synfire chains[13]). In contrast, WLC dynamics does not need a specific spatial organization of the network. However, the image of a wave is a useful
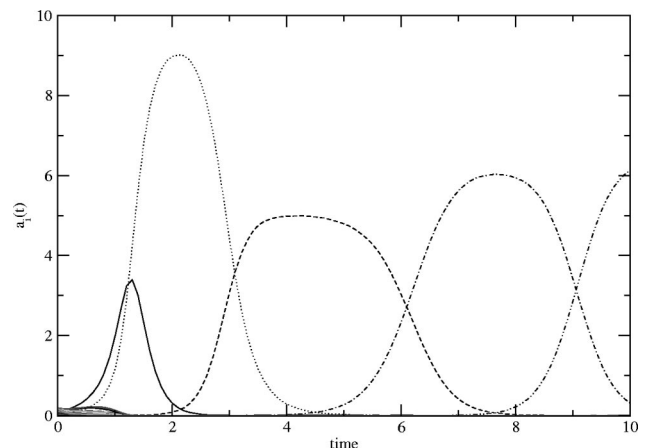

FIG. 3. Example of the time series of average firing rates $a_i(t)$ during the initial stage of switching dynamics in the network. System forgets initial conditions very quickly as all but two firing rates decay to zero at the beginning of the response.

one, because in the case of WLC a "wave" of neural activity propagates in the network along the SHS. Such a wave is initiated by a stimulus. The speed of the sequential switching depends on the noise level.[11] The noise controls the distance between the realized trajectories of the system and the SHS. For trajectories that get closer to the SHS the time that the system spends near semi-stable states (saddle-nodes), i.e., the interval between switchings, becomes longer.

The mechanism of reproducibility of transient sequential neural activity that we have analyzed above is quite general and, as our preliminary results indicate, does not depend on the details of the neuronal model. We conjecture that saddle points in the phase space of the neural network can be replaced by saddle limit cycles[14] or even chaotic sets that would describe neural activity in more detail, as in typical spiking or spiking-bursting models. This is extremely important for neurobiological applications because it may help to build a bridge between the concepts of neural competition and of neural synchronization. Formulation and proof of theorems like those presented in this paper for the more detailed neural models is a very interesting mathematical problem in itself. As our recent results indicate,[15] reproducible nonperiodic sequences can be generated even in neural networks with random inhibitory and excitatory connections given that the networks are far from the excitatory-inhibitory balance. Deep mathematical understanding of the spatio-temporal dynamics in random networks is also lacking.

Olfactory system may serve as one example of a neural system that generates transient, but reproducible from trial to trial sequences of neuronal activations. Complex intrinsic dynamics in the antennal lobe (AL) of insects transform static sensory stimuli into spatio-temporal patterns of neural activity.[1,2] Recently, new experimental results about the reproducibility of the transient spatio-temporal AL dynamics have been published.[2] In their experiments the authors presented bees with different odors and recorded neural activity in the ALs using calcium imaging. They have analyzed transient trajectories in the projection neuron activity space and found that the trajectories representing different trials of stimulation with the same odor were very similar. It was shown that after a time interval of about 800 ms different odors are represented in the phase space by different static attractors, i.e., after sufficiently long odor presentations the transient spatio-temporal patterns converge to different spatial patterns of activity. However, the authors emphasize that due to the reproducibility of the transient dynamics some odors were recognized in the early transient stage as soon as 300 ms after the onset of the odor presentation. It is highly likely that the transient trajectories observed in these experiments represent realizations of a SHS.

We would like to add here two more possible biological applications of the proposed mechanism of reproducible sequence generation. The first one is related to the observations of sequential dynamics exhibited by the place cells in hippocampus.[16] The dynamical principle for the sequential memory based on WLC has been suggested in Ref. 17. The essence of the idea is that the sequential memory is encoded in a multidimensional dynamical system with a heteroclinic sequence, where each saddle point represents an event of a sequence that is to be remembered. Once the state of the system approaches one fixed point representing a certain event, it is drawn along an unstable separatrix toward the next fixed point (event) and so on. Using the biologically motivated model of the sequential spatial memory it has been shown that, after learning, the system with WLC dynamics is capable of associative retrieval of pre-recorded sequence of patterns.[17]

The second application is related to the dynamics of the high vocal center (HVC) in the brain of songbirds. It was observed that HVC dynamics is strictly sequential, with each projection neuron generating just one burst per sequence.[4] The sequence of bursts is highly reproducible because adult male birds produce precisely the same song in each performance. Taking into account the fact that the HVC neural circuit contains a lot of inhibitory interneurons, it is reasonable to hypothesize that its inhibitory connections are non-symmetric and are organized in a way that is similar to the one described above.

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