

## Rhythmic control of oscillatory sequential dynamics in heteroclinic motifs



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### ABSTRACT

Cognitive/behavioral brain functions are implemented through temporary correlated sequential activity of many brain elements that form universal anatomical and functional motifs, i.e., characteristic functional interactions among brain nodes, at different levels of the neural hierarchy. Such motif dynamics is determined by both the interconnections among nodes and their intrinsic oscillations. This paper focuses on heteroclinic motifs, i.e., those built in networks of oscillatory nodes that interact through asymmetric inhibitory coupling in a winnerless competitive way. We introduce a basic rate-phase motif model – based on a generalization of the well-known ecological Lotka–Volterra model – for the analysis and prediction of control processes that emerge in interacting heteroclinic motifs under periodic stimulation. This approach describes both intensity and phase in each node. We study how a rhythmic signal, which can be linked to internal or external sources, can functionally change the heteroclinic network and produce a rich gallery of motifs in the form of coordinated sequential activations. In computer simulations of the model in a “master-slave” approximation, we report phenomena such as dynamical filtering, encoding enhancement and transition to chaos. Our results are relevant in the context of several experimental protocols related to the role of brain rhythms and/or the use of external rhythmic stimulation, in particular in the context of transcranial control and evoked potentials, to assess cognitive functions and their associated pathologies.

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### 1. Introduction

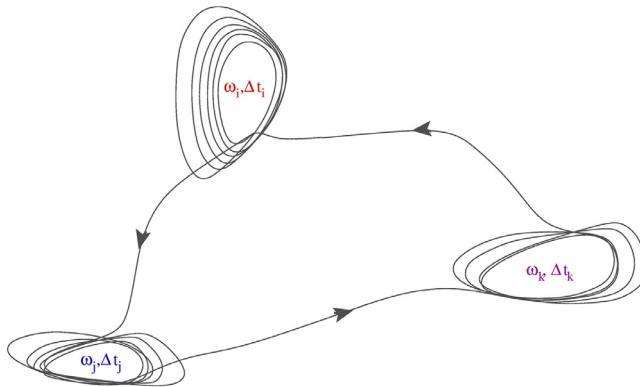
The human brain is composed of a vast number of elements that form hierarchical networks that cooperate and compete in wide spatial and temporal scales [1–5]. The dynamical features of brain networks, from microcircuits to global systems, provide the performance of diverse important cognitive functions, which involves robust transient sequential activity among different coordinated brain regions [6–10]. Key mechanisms of robust brain sequential dynamics are: (i) winnerless competition (WLC) [11], (ii) entrainment of oscillatory activity at different levels of the hierarchy [12,13], and (iii) binding of different cognitive/perception modalities [10,14]. Modern nonlinear dynamical theory can suggest several tools for the analysis of multiscale transient brain activities (e.g., see [9,15,16]). However, keeping in mind that theoretical and computational complexity exponentially increases with the number of degrees of freedom, investigators require construc-

tive network analysis tools and reduced approaches based on key dynamical principles [17–21]. Approximations in this context can profit from the consideration of: (i) the topological reduction of the structural organization of complex networks through the representation of the corresponding graphs as sets of connected functional networks; and (ii) the low-dimensionality of oscillatory dynamics, which in many cases arises from asymmetric inhibitory interactions [9,22,23].

The term “network” is used in this paper in a general sense to denote a set of interconnected neural groups in the brain (a physical space), while the term “heteroclinic network” denotes a set of invariant objects/structures produced in the phase space by the dynamics of the physical network constituents. In this phase space, nodes in the network are metastable states connected through separatrices. We call motifs the recurrent patterns of interactions in such modular heteroclinic hierarchical networks. The modern theory of dynamical systems considers both robust (i.e., structurally stable) and non-robust heteroclinic networks. Robust heteroclinic structures are mathematical objects that often appear as attractors in the phase space of dissipative dynamical systems with invariant subspaces or manifolds. Investigating the link between

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**Fig. 1.** Schematic representation of a heteroclinic chain that consists of a sequence of saddle limit cycles, which gives rise to sequential activity among different nodes. In the example,  $\omega_i$  represents the different metastable states and  $\Delta t_i$  corresponds to the timing of the node activity.

physical brain networks and the presence of robust heteroclinic structures in the phase space has been a hot topic in the last years both in dynamical system theory and neuroscience [11,24–28]. Here, we focus on transient sequential dynamics phenomena in global network oscillatory activity controlled by an endogenous rhythm or by an external rhythmic stimulus. Rhythmic stimulation is widely used both in cognitive studies as well as in clinical or rehabilitation procedures (e.g., see [29–31]). Recent modeling efforts have pointed out the importance of taking into account ongoing rhythms in brain stimulation protocols [32]. However, the effect of rhythmic stimulation on sequential brain dynamics based on oscillatory motifs has not been addressed yet. To motivate experimental research in this direction, the basic model proposed in this paper allows studying the effect of periodic input on the switching dynamics of metastable network oscillatory activity. Such activity is the result of temporal entrainment of different oscillatory nodes. The heteroclinic dynamics of the metastable state sequential switching (see Fig. 1) builds up the phases of the node oscillations resulting in coordinated motif dynamics.

Brain rhythms are considered to be involved in higher cognitive activities ranging from functional coordination and integration to attentional control [1,33–36]. The corresponding information processing phenomena are thought to be implemented mainly through neural synchronization mechanisms (e.g., see [37–39]), not necessarily involving synaptic transmission [40], and include transient coordination processes between hemispheres [41]. Microelectrode recordings and modern brain imaging, in particular fMRI, have unveiled the transient functional reorganization of large scale brain networks during the performance of different cognitive tasks (e.g., see [42,43]). The dynamical mechanisms underlying the fast functional restructuring of flexible cognitive networks are still unclear. Departing from observed metastable informational patterns in the nervous system [21,44,45], our basic dynamical model helps to understand different dynamical phenomena that can be related to behavioral/cognitive programs in the framework of the same structural heteroclinic network. In particular, our results suggest that by changing the frequency of an input field that models a brain rhythm band or an external rhythmic input, it is possible to alter the level of coherence between different oscillating competitive patterns in the heteroclinic motif network and dynamically control their sequential interactions while preserving the coordination.

We assume that the human cognitive control system employs multiple strategies that include brain rhythms as a mechanism for the robustness and functional changing of circuits in specialized

networks like those that build up working memory, information binding and attention processes. Brain functional networks require having a dependence on the phase, as this is probably the only way to be sensitive to entrainment and perform frequency control. However, it is not clear that neural sequential activity can keep its stability when modulated by extrinsic rhythms, e.g., by ephaptic interactions [40,46]. Inhibition plays a key role in shaping cognitive network architectures [23] and can be responsible for stable dynamics and sequential behavior, as a key factor for suppressing noise, but at the same time can prevent the interaction with excitation that depends on extrinsic rhythms. We also proceed from the hypothesis that brain networks display WLC, a competitive process through inhibitory interactive nodes that are only transient winners during a finite time [10,47,48]. Thus, the network generates sequential dynamics through node switching activity [49,50]. From this view, top-down approaches, although far from a biophysical detailed description, provide the required ingredients to model cognitive dynamics, being also suitable for the interpretation of activation sequences in regions of interest in EEG and fMRI (see also [16,51,52]).

External rhythmic stimulation has been suggested as a control paradigm to manipulate the brain's intrinsic oscillatory properties of networks driven via a variety of input-driven mechanisms [31]. Noninvasive protocols such as steady state visually evoked potentials (SSVEPs) [53,54] and transcranial alternating current stimulation are examples where an external rhythm drives brain dynamics [29–31,55]. Rhythmic light stimulation evoking SSVEPs is used in cognitive studies dealing with visual attention [56,57]. Transcranial periodic stimulation allows modulating brain oscillations and, in turn, influence cognitive processes to assess their causal link. In particular, transcranial rhythmic protocols have been used to modulate basic motor and sensory processes as well as higher cognitive processes like memory, ambiguous perception, and decision making [58–60].

Here, we propose a complementary view on brain rhythms from the perspective of their interaction with neural sequential dynamics involved in a wide variety of information processing tasks [50,61–63]. Thus, the network that we consider has a general function, the generation of input rhythm-specific coordinated sequential activity, which can be adapted to many specific neural systems. In the next sections, we show that a multifunctional network with sequential activations entrained by external rhythms, described by a simple frequency and amplitude, can evolve through distinct dynamical states. These states can be related to different brain functions and characterized by the broadness of their frequency spectrum, their level of regularity and the specific features of the sequential activations generated in a heteroclinic network.

## 2. Canonic model of heteroclinic motif interaction

To test our hypothesis, we need a model able to describe both components of cognitive dynamics – i.e., sequential transient behavior and oscillatory activities of elements (nodes, motifs and complex networks as a whole). Robust heteroclinic dynamics emerges in neural networks with prevailing inhibitory connections. Experimental studies support that most brain temporal activities are inhibitory-based interactions [22]. Thus, a convenient top-down paradigm to represent sequential activity is the generalized Lotka–Volterra model (GLV) with asymmetric inhibitory interactions [17,64]. Such dissipative models are extensively used approximations to a wide class of kinetic and ecological equations. GLV models exhibit WLC dynamics, i.e., sequential activations in temporally active units. This sequential activity arises from a heteroclinic chain, i.e., a sequence of saddle limit cycles on the axes that form the corresponding phase space (see Fig. 1). GLV models are also suitable to study heteroclinic synchronization, coordina-

tion and binding/chunking of sequential patterns [65–67]. Our approach here is to model transient cognitive network dynamics in a novel GLV approximation that contains oscillatory nodes. For the sake of simplicity, we introduce in this paper a rate-phase model in the case of a “master-slave” interaction, in which the rhythmic input does not depend on the network dynamics. In this approximation, we analyze the phenomena of dynamic entrainment under the action of external forcing.

Assuming that the difference between the phase of intrinsic oscillations and the phase of an external rhythmic field is a relevant information for the control of sequential dynamics, the model used in this study is given by the following equations:

$$\frac{dA_i}{dt} = A_i \left( \sigma_i + \eta_i + \frac{Q_i}{a_0 \varepsilon} \int_{t-\varepsilon}^t \cos \xi_i d\xi - \sum_{j=1}^N \rho_{ij}^0 A_j \right) \quad (1)$$

$$\xi_i = \psi_i - \phi_i \quad (2)$$

$$\frac{d\psi_i}{dt} = \omega_i + A_i \frac{Q_i}{b_0^2} \omega_0 \sin(\psi_i - \phi_i) \quad (3)$$

$$\frac{d\phi_i}{dt} = \Omega_i \quad (4)$$

where  $A_i$  is the level of activity of each interacting node (with  $i = 1, \dots, N$ ). Such oscillatory activity can correspond to different description levels: from single neurons to large neural ensembles with coherent activity [10,17]. For each oscillatory node,  $\omega_i$ ,  $\sigma_i$ ,  $\psi_i$  and  $\eta_i$  represent the intrinsic frequency, the level of self-excitation of the intrinsic oscillatory activity, the phase of the oscillations and the noise, respectively. To test the robustness of the discussed phenomena, we have chosen to add noise in the same way we describe the self-excitation and the rhythmic stimulation terms. Hereafter, we call “mode” the oscillatory pattern characterized by the joint action of variables  $A_i$  and  $\psi_i$ . The oscillator phase in this model scales with the level of activity, so that it is insensitive to input when the node is silent. The third term in the parenthesis in Eq. (1) represents the effect of an input rhythmic field through its phase difference ( $\xi_i$ ) with the corresponding intrinsic oscillations, and  $\varepsilon$  is the time interval for the integration of the past history of the oscillatory input. This rhythmic field, which can correspond to an endogenous rhythm (such as a brain rhythm) or an external rhythmic stimulus, is characterized by parameters  $Q_i$ ,  $\Omega_i$  and  $\varphi_i$  that represent its strength, frequency and phase, respectively. Finally, the intrinsic inhibitory interaction is given by the fourth term in the parenthesis in Eq. (1), where  $\rho_{ij}^0$  is an element of the inhibitory connection matrix.

Note that in this approach the rhythmic field can represent a direct or an ephaptic coupling. When  $Q_i = 0$  the proposed model is equivalent to the GLV model, whose autonomous dynamics can be complex and its understanding is an important departing point for the analysis of external forcing dynamics. In particular, even the simplest GLV autonomous system, i.e., a 3-dimensional competitive network, demonstrates the coexistence of several limit cycles including the heteroclinic cycle [68,69]. If the network is more complex, in particular consisting of two coupled motifs, one of them can demonstrate chaotic behavior but the other one, in spite of the interaction, can keep a regular switching [70].

Our hypothesis is that an endogenous or external periodic frequency  $\Omega_i$  can control the switching among different cognitive subprocesses that rely on the coherence and coordination of the sequential activity of the network. Throughout this paper, we will use attention focusing in the context of sensory perception as an illustrative example to discuss the proposed frequency-driven dynamics in functional cognitive networks. In this context, specific

rhythms can change key aspects of the sequential dynamics involving the different sensory modalities (visual, auditory, etc.) and be responsible for moving the attention focus from one modality to another (e.g., see [71]).

Following this idea, let us consider an illustrative example consisting of a two coupled network dynamics,  $A_{1-3}$  (first modality) and  $A_{4-6}$  (second modality) with parameters  $\omega_1 = \omega_2 = \omega_3 = 1.177$  a.u. and  $\omega_4 = \omega_5 = \omega_6 = 0.333$  a.u., i.e., we consider two functional motifs with different characteristic intrinsic frequencies. For simplicity, first we will focus on the analysis of the dynamics of two modalities. In our example, these two modalities could be linked, for instance, to the joint perception of auditory and visual sensory information, and the input rhythm be responsible for focusing attention in one of them. As in the experimental rhythmic stimulation protocols described above, in this example we assume that all nodes in the network receive the same stimulus and thus the parameters related to the external field ( $Q_i$ ,  $\Omega_i$  and  $\varphi_i$ ) have the same values. To assess the stability of the model dynamics, Gaussian noise with zero correlation is introduced in the system as  $\eta_i(t)$ ,  $\eta_i(t') = \mathcal{A} \cdot \delta(t - t')$ , being  $\mathcal{A}$  a scale factor for the amplitude noise. In the simulations discussed in this paper, unless specified otherwise, we fix the maximum noise amplitude to 0.160 (around 10% of the maximum activity in the isolated network). Self-excitation is given by the vector:

$$\sigma_i = (0.301 \ 0.474 \ 0.585 \ 0.601 \ 0.203 \ 0.114)$$

Unless specified otherwise, we set  $a_0 = 1.00$ ,  $b_0 = 1.28$ ,  $\varepsilon = 24.78$ ,  $Q_i = 7.81$  and we consider the following connection matrix:

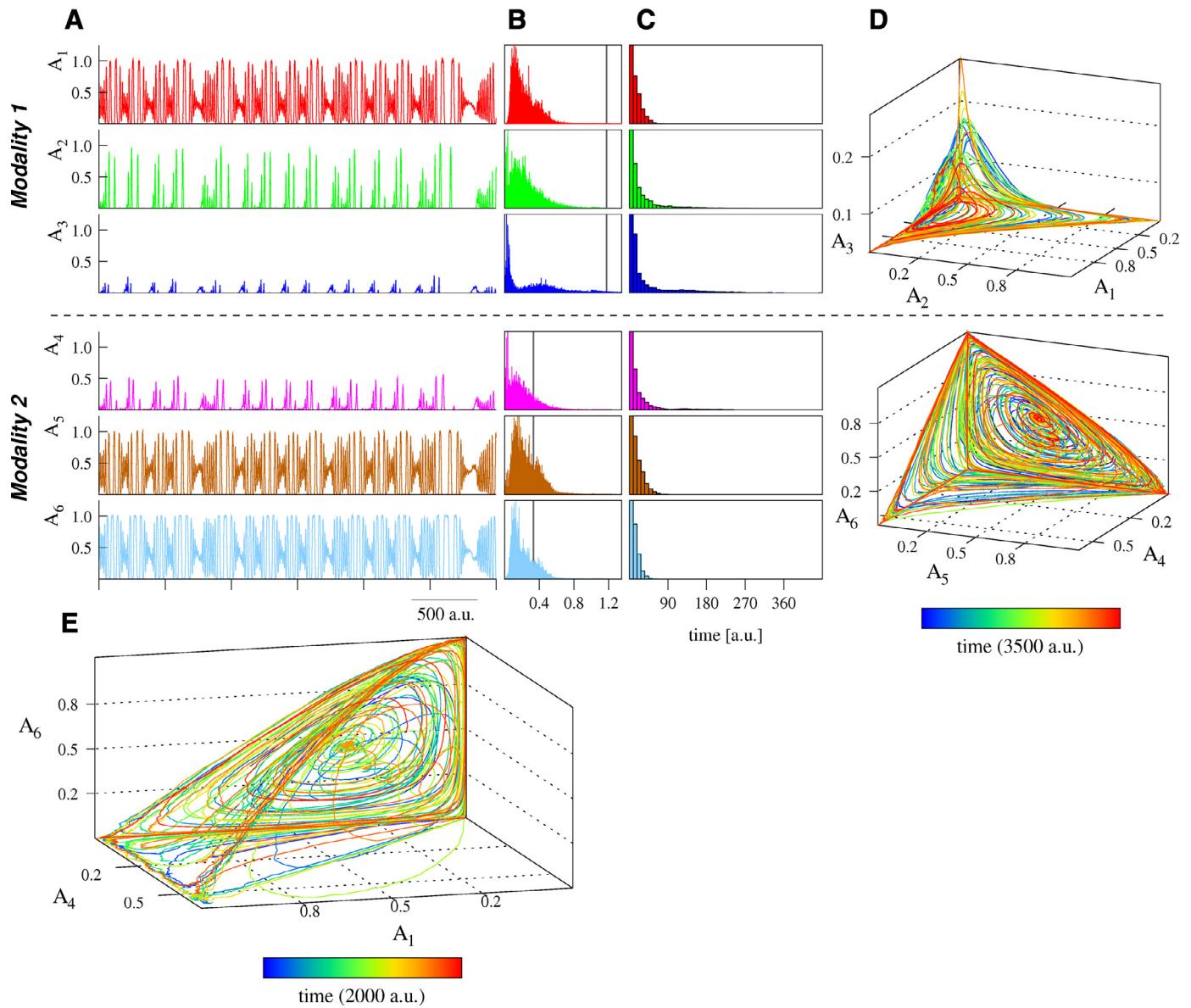
$$\rho_{ij}^0 = \begin{pmatrix} 1.00 & 0.00 & 3.98 & 0.00 & 0.00 & 1.50 \\ 2.97 & 1.00 & 0.00 & 0.69 & 0.00 & 0.00 \\ 0.00 & 4.88 & 1.00 & 0.00 & 2.03 & 0.00 \\ 0.45 & 0.00 & 1.69 & 1.00 & 0.00 & 1.84 \\ 1.93 & 0.00 & 0.00 & 2.21 & 1.00 & 0.00 \\ 0.00 & 1.21 & 0.00 & 0.00 & 1.55 & 1.00 \end{pmatrix}$$

This matrix has the level of asymmetry required to generate WLC – saddles have one dimensional unstable separatrix and are dissipative, see [50,72,73]. The set of parameters specified above corresponds to a moderate value of the stimulus amplitude, previous history integration and self-excitation, which help to illustrate the effect of rhythmic input in the sequential dynamics. Later in this paper, we test the generality of the observed phenomena in other network configurations that also satisfy the conditions for WLC. In general, the knowledge regarding inhibition of specific brain areas [22] and in particular the asymmetry level can be used to build  $\rho_{ij}^0$ . For all examples discussed in this work, simulations were run for 500,000 arbitrary time units.

### 3. Results

#### 3.1. Motif sequential heteroclinic dynamics in the absence of periodic stimulation

In the absence of external stimulation, i.e., when  $Q_i = 0$  in Eqs. (1) and (3), the different nodes generate oscillatory activity covering a broad range of frequencies. Fig. 2 illustrates the network sequential dynamics in this autonomous regime. Inhibitory interactions among the oscillatory nodes produce activity with a wide variety of amplitude and frequency profiles. In spite of the overall broad power spectra for all nodes, WLC among them induces the generation of coordinated transient sequential activations, which can be partially characterized by the silent period histograms displayed in panel C. The interaction is such that the main frequency peaks in the power spectra characterizing the oscillatory activity of each node do not correspond to the intrinsic frequencies



**Fig. 2.** Characterization of a two modality interaction: network autonomous sequential dynamics,  $Q_i=0$  in Eqs. (1) and (3). Panel A shows fragments of the time series corresponding to the interaction of two coupled network dynamics ( $A_{1-3}$ ) and ( $A_{4-6}$ ). Panel B depicts the corresponding normalized power spectra (scale 0–1) identified by the same color code for each individual interacting mode ( $A_{1-6}$ ). Gray vertical lines denote the intrinsic frequency of the corresponding node ( $\omega_{1-3}=1.177$  a.u. and  $\omega_{4-6}=0.333$  a.u.). Panel C shows the normalized histograms of the silent periods (time intervals between consecutive activations). Panel D shows the phase portraits for the first (top) and second modality (bottom). Panel E depicts a projection involving the activity of nodes in the first ( $A_1$ ) and second ( $A_4$  and  $A_6$ ) modality.

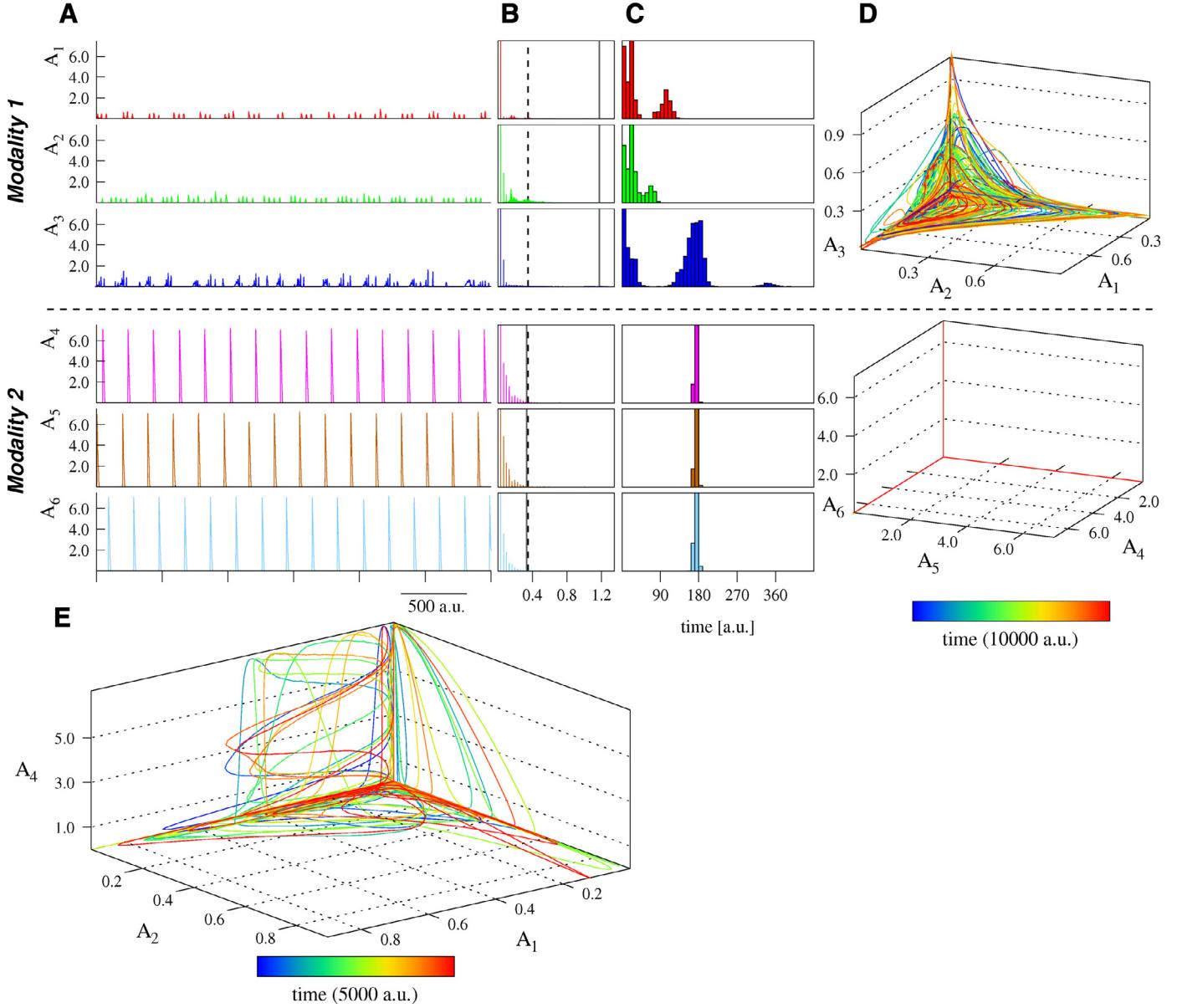
$\omega_{1,2,3}=1.177$  and  $\omega_{4,5,6}=0.333$ . Phase portraits in this figure characterize the heteroclinic dynamics in the network, both between nodes belonging to the same (panel D) and different perception modalities (panel E). Below we will compare this autonomous sequential dynamics with the dynamics generated under the effect of rhythmic stimulation.

### 3.2. Heteroclinic sequential dynamics under periodic stimulation

When the network receives the influence of an external rhythmic field, the individual node and the collective dynamics in the network change as a function of the frequency of the external field. In the following analyses, we will characterize the network sequential dynamics in relation to the external field applied covering frequencies related and unrelated to the intrinsic oscillatory activity of each modality. A strong external rhythmic field causes a full entrainment of the network. Thus, for our study, we chose a mod-

erate amplitude of the external rhythmic stimulus. In general, if the frequency is close to the intrinsic frequency of a node ( $\omega_i$ ), its oscillation amplitude increases, while its oscillation frequency is reduced and regularized (i.e., the power spectrum is focused) as compared to the network activity in the absence of the external field (see Figs. 3 and 4). The regularization of the oscillations is produced because of a multiple-fold period entrainment with the corresponding motif's intrinsic frequency. Modality 2 components in Fig. 3 have a mean period of  $193 \pm 3$  (A<sub>4</sub>),  $192 \pm 3$  (A<sub>5</sub>) and  $193 \pm 4$  a.u. (A<sub>6</sub>), respectively. Similarly, mean periods within each activation sequence in modality 1 components in Fig. 4 are  $69.3 \pm 4$ ,  $69.5 \pm 3$  and  $68.6 \pm 3$  a.u. for A<sub>1</sub>, A<sub>2</sub> and A<sub>3</sub>, respectively (cf. the period for  $\Omega=1.10$  a.u.).

Because of the entrainment, the collective behavior is coordinated to an also more regularized regime. The resulting dynamic frequency filter produces a spectrum focusing (cf. broad power spectra in the absence of external stimulation – Fig. 2 – and sharper

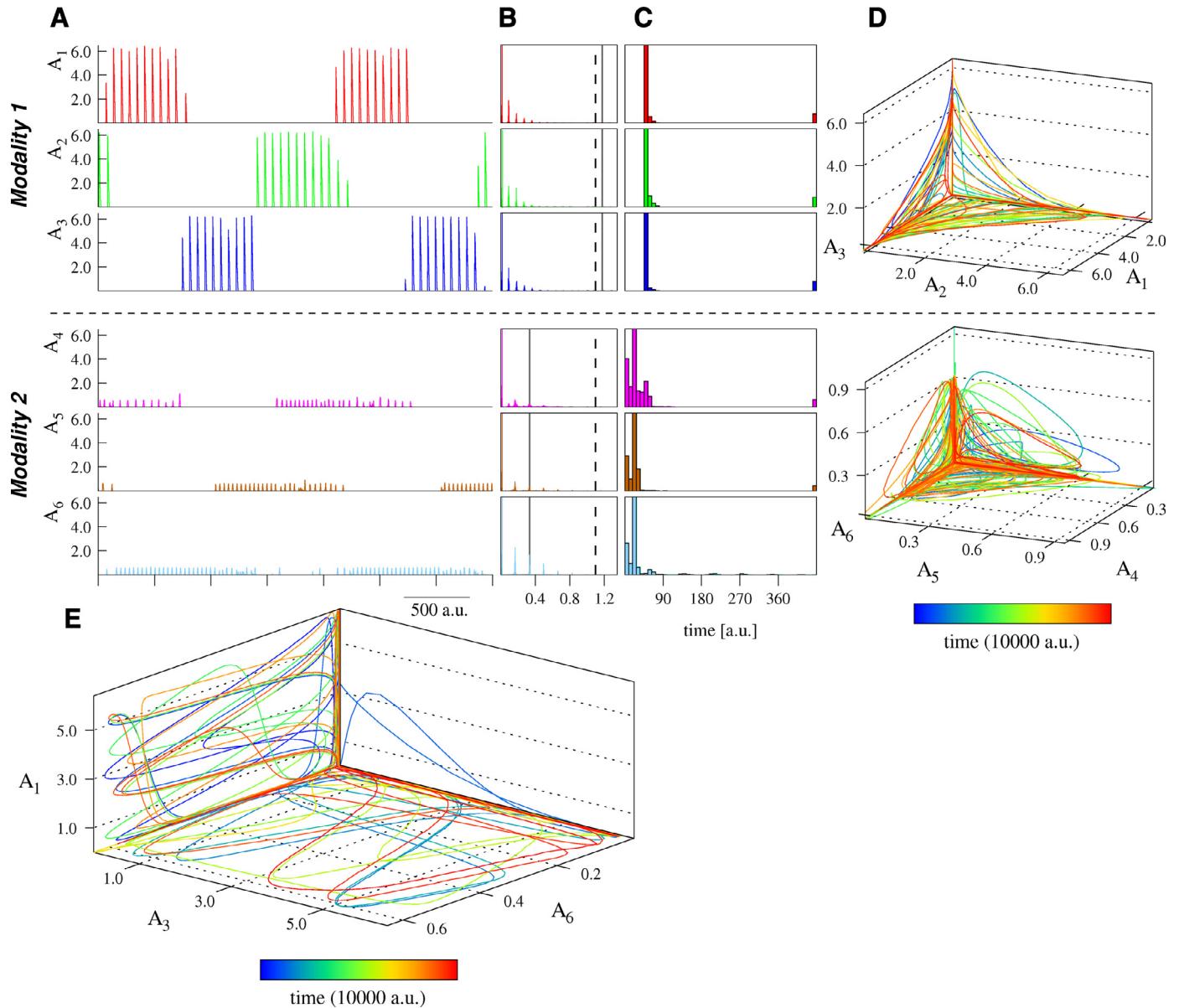


**Fig. 3.** Modality 2 prevails over modality 1 under an external rhythmic input with  $\Omega = 0.35$  a.u., i.e., the external field frequency is close to  $\omega_4$ ,  $\omega_5$  and  $\omega_6$ .  $Q_i = 7.81$ . Panels show time series, power spectra, silent period histograms and phase portraits of the network dynamics. Solid and dashed vertical lines in the power spectra denote the intrinsic frequency of the corresponding node ( $\omega_i$ ) and the frequency of the external field, respectively. One can see a higher regularization (as characterized by a reduced Kolmogorov-Sinai entropy, see below) due to a ten-fold period entrainment with the characteristic intrinsic frequency associated to the second perception modality. For example, the upper panel can represent an auditory modality and the lower one a visual modality. Note the effect of the rhythmic input in the heteroclinic dynamics (cf. Fig. 2D-E).

when the external rhythm is close to the intrinsic frequency of one of the perception modalities – Figs. 3 and 4). Note that the entrainment does not directly correspond to the external field frequency (cf. peaks in the power spectra). Sequential activations can only be built from a reduced number of allowed oscillation frequencies. For example, the second perception modality in Fig. 3 (A<sub>4</sub>, A<sub>5</sub> and A<sub>6</sub>), a motif formed by nodes with an intrinsic frequency commensurable with the external rhythm, generates a sequential rhythm with sharp peaks in the power spectra (note also the sharper silent period histograms, cf. Fig. 2). Nodes A<sub>1</sub>, A<sub>2</sub> and A<sub>3</sub> can transiently be coordinated with the rhythm produced by motif A<sub>4</sub>-A<sub>5</sub>-A<sub>6</sub> and also participate in the generation of joint sequential activations involving the two perception modalities. The sharper power spectra are due to the dynamical filtering induced by the external rhythm, i.e. many frequencies that build up the sequential activity of the autonomous network are filtered out when the rhythmic stimulus

is applied. Panel E shows a representative phase portrait among nodes belonging to different modalities where changes in the heteroclinic interactions due to the external rhythm can be observed (cf. Fig. 2E).

Fig. 4 illustrates the same entrainment phenomena but when the external rhythm is commensurable with the intrinsic frequency of motif A<sub>1</sub>-A<sub>2</sub>-A<sub>3</sub>. Note the distinct sequential activations and specific rhythms following the change of nodes with intrinsic frequencies similar to the external stimulus. The analysis of the balance between self-excitation and inhibition, provided by the positive and negative terms inside the parenthesis in Eq. (1), respectively, points out that activation sequences in a given oscillatory mode arise after intervals of prolonged self-excitation, while silent periods occur after strong inhibition. The duration of the silent periods is related to the inhibition amplitude. To illustrate these phenomena, panel A of Fig. 5 displays representative exam-

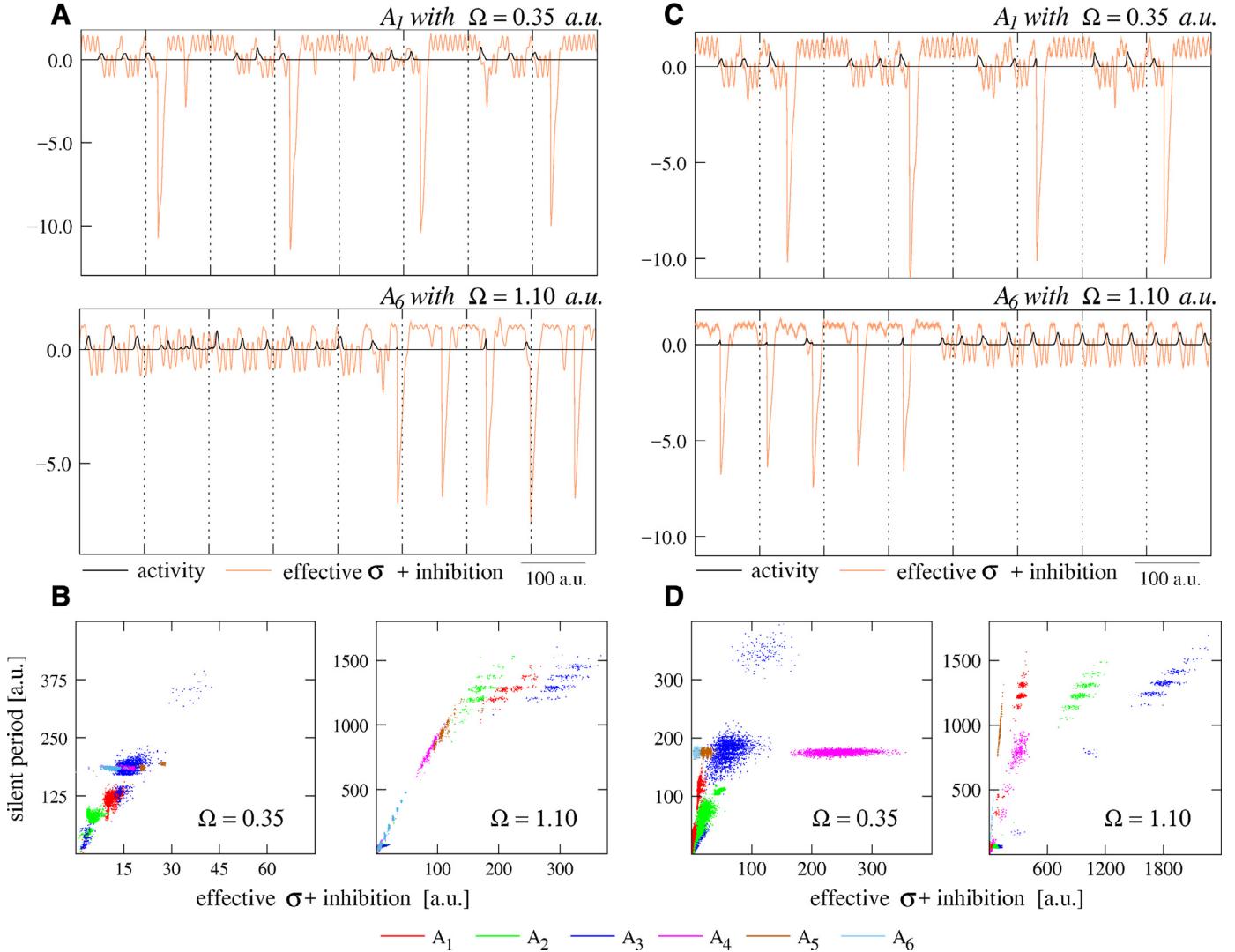


**Fig. 4.** The grouping/chunking dynamics of modality 1 prevails over modality 2 when the external input is  $\Omega = 1.10$  a.u., i.e., the external field frequency is close to  $\omega_1$ ,  $\omega_2$  and  $\omega_3$ ,  $Q_i = 7.81$ . Panels show time series, power spectra, silent period histograms and phase portraits of the network dynamics. In this case, the autonomous chaotic dynamics turns to a nearly regular regime due to a ten-fold period entrainment with this motif. Like the entrainment in Fig. 3, this activity is characterized by a small value of the Kolmogorov-Sinai entropy, see Fig. 7.

ples of sequential activations (black traces) together with the corresponding effective self-excitation and inhibition (orange traces) as given by the terms inside the parenthesis in Eq. (1) in networks without and with noise (panels A and B; and C and D, respectively). Note how small inhibitions after a prolonged period of self-excitation induce oscillations sequences compatible with the combination of the intrinsic and the external field frequencies. On the other hand, a strong inhibition produces a silent interval. The duration of these silent periods depends on the level on inhibition. Panel D in Fig. 5 shows for the simulations described in Figs. 3 (left plot) and 4 (right plot) the relationship between the effective inhibition (defined as the sum of self-excitation and inhibition) and the duration of the subsequent silent periods in the different nodes. In all cases, there is a stair step relationship between these values whose slope depends on the specific node and its level of coherence with the external field.

When the frequency of the external field is not close to the intrinsic frequency of any node, the oscillatory activity in the network becomes irregular both in frequency and in amplitude (e.g., see Fig. 6). The associated power spectra are also broader. The network dynamics in this case is qualitatively similar to the autonomous dynamics. However, changes in the heteroclinic interactions due to the lack of coherence between the intrinsic and the input rhythm frequencies produce a larger interplay among nodes as compared to the case without external rhythmic stimulation (cf. phase portraits in Figs. 2 and 6).

We have quantitatively characterized the network dynamics with Kolmogorov-Sinai (KS) entropy, as the sum of time-dependent positive Lyapunov exponents calculated from the vector field. KS entropy is used as a measure of information creation [47,74]. The top panel in Fig. 7 shows this analysis for networks built up by motifs with different intrinsic oscillation frequencies ( $\omega_i$ ) as a



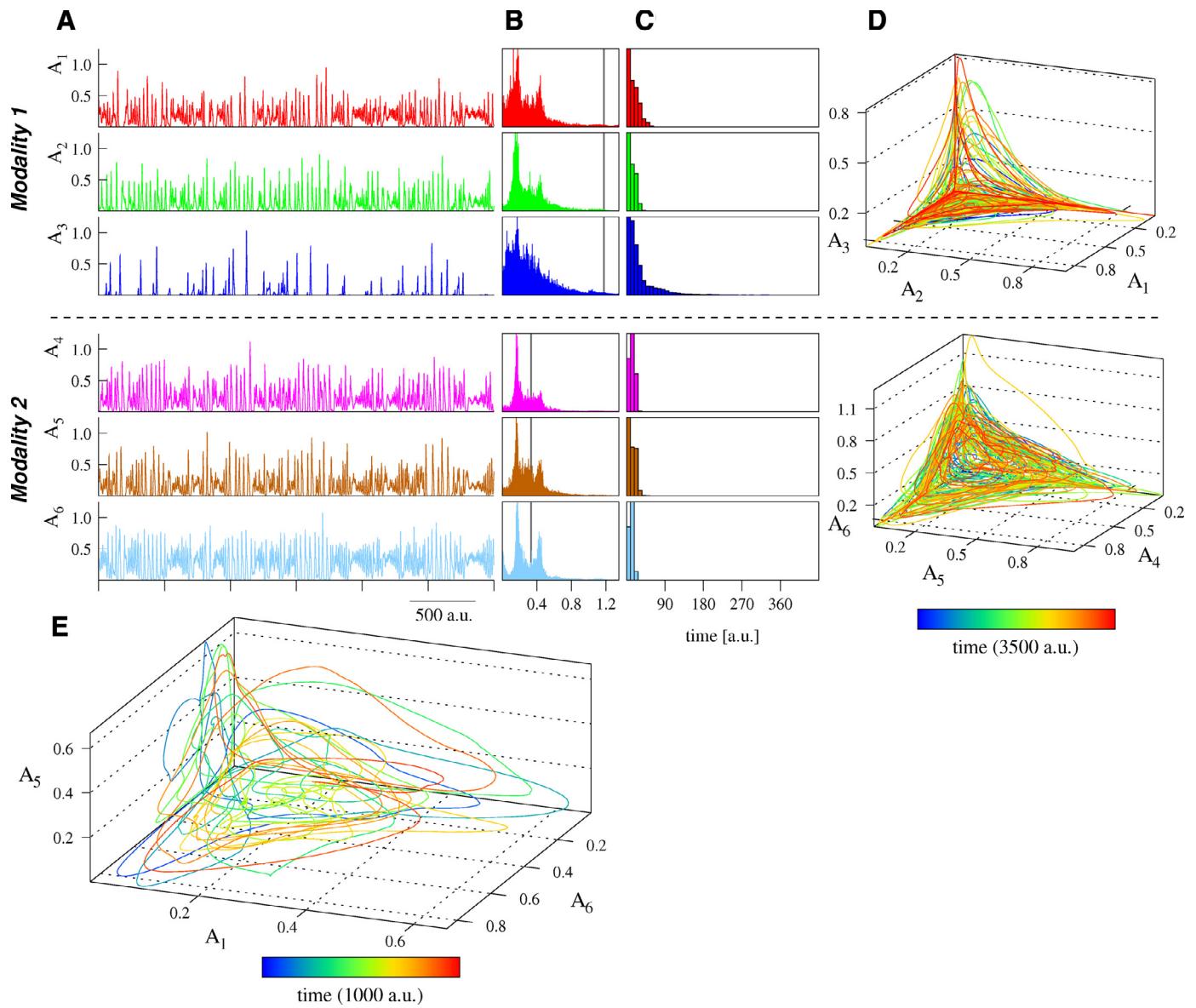
**Fig. 5.** Stair-step relationship between effective inhibition and evoked silent intervals. Analysis of the relation between silent periods and inhibition in the network without noise (panels A,B) and in the presence of Gaussian noise (panels C,D). Panels A, C show representative examples of node activations (black) together with the effective self-excitation and inhibition (orange, overall contribution of the terms inside the parenthesis in Eq. (1)). Top time series corresponds to activity of  $A_1$  when  $\Omega = 0.35$  (cf. Fig. 3) and bottom ones correspond to  $A_6$  when  $\Omega = 1.10$ ,  $Q_i = 7.81$ . (cf. Fig. 4). Note that the intrinsic frequency in both cases is different from  $\Omega$ . Robust activation sequences arise after intervals of prolonged self-excitation. Silent periods occur after strong inhibition. Panels B, D depict the relationship between effective inhibition in a node (calculated as the overall inhibition between consecutive activations, x-axis) and the duration of the subsequent evoked silent period (y-axis). Panel D corresponds to simulations shown in Figs. 3 (left) and 4 (right). The different oscillatory modes are identified by the same color code as in the previous figures.

function of the external field frequency ( $\Omega$ ). The cases discussed in Figs. 2–6 correspond to specific values of  $\Omega$  in the gray trace. We observe that the network always has chaotic behavior as measured by a positive KS entropy. The minimal values of the KS entropy are obtained for values of  $\Omega$  that are related to one of the subnetwork's intrinsic frequencies. These regimes are close to entrainment. See for instance the two minimal KS entropy peaks for  $\Omega$  around 0.333 and 1.177 a.u. in the network depicted with a gray trace, and around 1.971 and 0.333 in the network depicted with a red trace. As the different intrinsic frequencies become closer, low values of the KS entropy are observed for wider intervals of the external field frequency (see network depicted with a cyan trace around  $\Omega = 0.500$  a.u.). This is in agreement with the analysis of the time series, power spectra, silent periods, and phase portraits presented above. Those oscillatory modes coherent with the external field tend to focus their oscillations and coordinate their activity within the network competitive sequential dynamics. Consequently, the power spectra of other nodes in the network are

also focused (e.g., see panel B in Fig. 3), and thus the KS entropy reaches lower values.

We also simulated system given by Eqs. (1–4) with different levels of noise computed modifying the value of  $\mathcal{A}$  from 0 to 2. All discussed phenomena occur in the presence or absence of noise (cf. dashed lines in the top panel of Fig. 7 which indicate simulations without noise). Simulations with a maximum noise level below 35% of the maximum activity in the isolated network produced equivalent results, which points out the robustness of the discussed sequential dynamics.

Overall, the network demonstrates a wide variety of dynamical regimes, including WLC chaotic dynamics generating new information. The specific features of the sequential activations, the broadness of their frequency spectrum, and their level of regularity can characterize the different dynamical regimes. The network behavior and particularly the coordination arising from the WLC are controlled by the extrinsic rhythmic field. When the frequency of this field is close to the intrinsic frequency of some nodes, their coord-

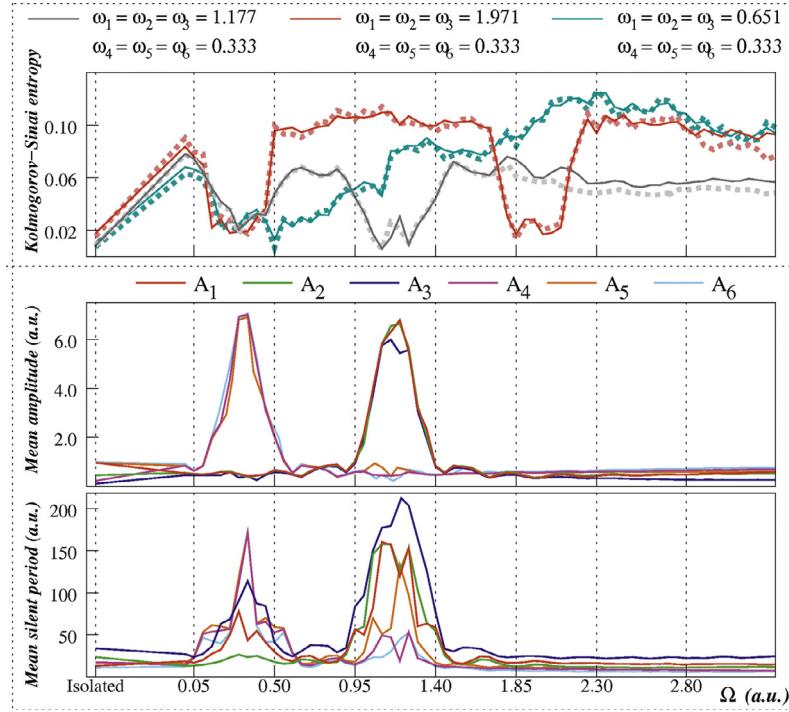


**Fig. 6.** Loose of coherence when the external field is very slow. Time series, power spectra, silent period histograms and phase portraits of the network dynamics when  $\Omega=2.95$  a.u., i.e., the external field frequency is far of the intrinsic frequency of all nodes (cf. Fig. 2),  $Q_i=7.81$ . Since the external field in this case is very slow, it is not indicated with the corresponding dashed vertical line.

dininating role for the global sequential behavior becomes stronger. Because of the rhythmic entrainment to particular frequencies, the distinct modes in the network dynamics can be related to different information processing tasks. Thus, this input rhythm dependence of the sequential dynamics could be a mechanism to implement multifunctionality in brain networks. For example, in attention control, the choosing of a sensory modality may be represented by the entrainment of different motifs to an input field. Attention signals in the form of specific brain rhythms can produce more coherent sequential dynamics involving the different modalities. This can switch the attention focus from one modality to another one. In this regard, we would like to emphasize the variability of amplitude, frequency, duration of the silent intervals and phase relationships in the characteristic sequential activations of the different oscillatory modes. The variability of these measurable quantities within the global coordinated activity endows the system with a high encoding capacity, as information can be conveyed in any of these different domains.

In our analysis, we observe that the presence of sharp spectra, i.e., the dynamical filtering, is not linked to the absence of positive Lyapunov exponents, nor the presence of these exponents is directly linked to the presence of broad spectrum. The chaotic dynamics of the individual nodes serves to flexibly negotiate the overall coordination of their sequential activity and to produce new information. Interestingly, when the power spectra of the network are focused by the external rhythm, the resulting specific frequencies in the network can be unrelated to the external frequency.

It is worth noting the coexistence of broad and sharp spectra in motifs that are nevertheless coordinated. The external rhythm distinctly induces dynamical filtering and frequency cut-offs or blow-ups in the network. The different levels of information creation as quantified by the KS entropy can be explored in terms of sequential activations, silent periods and amplitude variations. The effect of the external rhythm amplitude on the dynamics of multifunctional brain networks could also be analyzed using this model.



**Fig. 7.** Information creation measured with the Kolmogorov-Sinai entropy as a function of the external field in three different networks with distinct intrinsic frequencies depicted in three different colors ( $\Omega_i = 7.81$ ). Dashed lines correspond to simulations without noise while solid lines correspond to the noise level described in the main text. Note that all phenomena discussed occur for a significant level of noise. Middle and bottom panels show the mean amplitude and the mean silent interval, respectively, as a function of the external field frequency applied to the network corresponding to the gray trace in the top panel.

### 3.3. Generalization of the observed phenomena in larger motif networks

For the sake of simplicity, in the presentation of the phenomena derived from our model, we have constrained our analysis to a heteroclinic network built by two functional motifs with three nodes each. Nevertheless, the phenomena illustrated in this investigation occur for large regions of the parameter space as long as the asymmetry of the connections is kept to meet the requirement of the WLC dynamics [50,72,73].

Fig. 8 shows an example of sequential dynamics in a larger network with five perception modalities. The spectrum focusing, entrainment and the coordination of the sequential activity holds for this network, with a richer dynamics arising from the combination of a larger number of modalities (see phase portraits built with nodes belonging to different modalities in panel D). Equivalent results were obtained for networks of different sizes and connection matrices resulting in heteroclinic dynamics for a wide range of stimulus amplitudes, previous history integration and self-excitation parameters. All observed phenomena in the simulations described above highlight the distinct function-related node recruitment modes in the competitive sequential dynamics as a function of the external oscillation frequency  $\Omega$ . This suggests the relevance of a simple external field as a binding mechanism for sequential activity between different brain areas that do not need to be directly connected.

## 4. Discussion

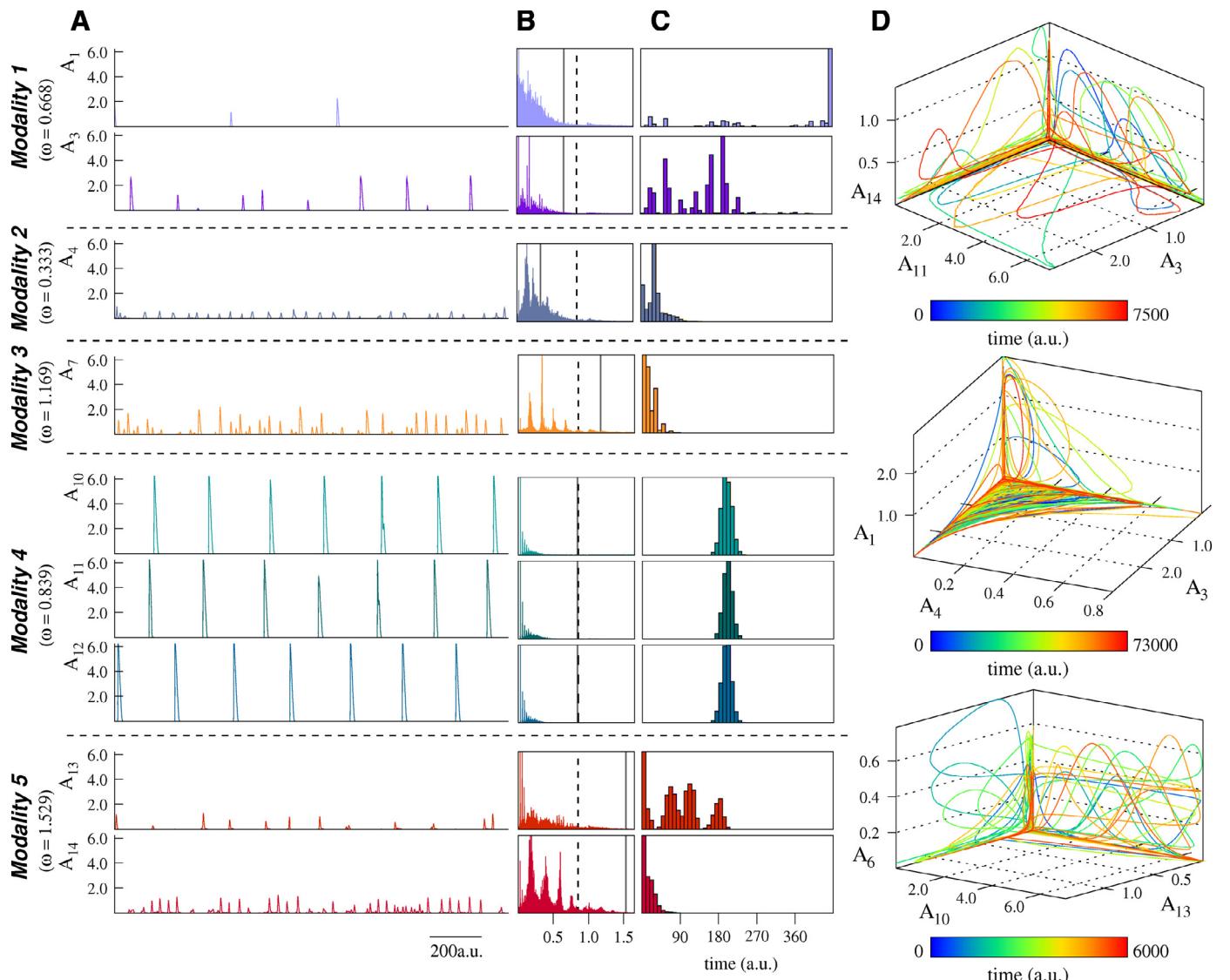
### 4.1. Rhythm control and cognitive functions

Brain rhythm control of sequential dynamics is linked to important cognitive functions: improving attentional mechanisms

[75,76] and working memory capacity [77]; providing novel mechanisms for information binding and integration [10,78,79]; modulating multifunctional networks into different kinds of encodings and information execution, and making sequential dynamics act as dynamical filters. Rhythmic entrainment has been found in the brain of several animal species [80], and its study contributes to the understanding of the cognitive architectures and dynamics related to key neural functions [60].

In this paper, we have presented a heteroclinic network model of brain activity coordination, which illustrates how sequential dynamics can be controlled as a function of a rhythmic input. The model expresses a range of key properties including self-organization, input rhythm dependent switching dynamics, and metastability. Our results motivate the analysis of sequential relationships among brain oscillations in neurophysiological data. Although there is not a real technical limitation, the analysis of sequential activity is typically not addressed in fMRI or EEG studies (see [6]).

The GLV type models do not provide quantitative predictions, but the phenomena found in our analysis can be qualitatively compared with experimental studies addressing the effect of rhythmic input in cognitive networks (see also [51]). Our model predictions could also be assessed with other types of models, such as mean-field approaches [16,51] and conductance-based models [81]. In this regard, the hierarchical dynamics described by rate-phase models can serve to study heteroclinic network activity giving rise to phenomena such as chunking, working memory, attention and decision making [14,48,79,82]. Here, we have illustrated the ability of a motif network model displaying sequential pattern activations to distinctly respond to different input rhythms while sustaining coherence among network members. This can result in (i) an encoding capacity enhancement of multifunctional brain networks built with competitive dynamics; (ii) transient synchroniza-



**Fig. 8.** Robustness of the sequential entrainment illustrated throughout this paper in a larger network with five modalities (3 nodes per modality). The characteristic intrinsic frequency ( $\omega_i$ ) of each perception modality is 0.668, 0.333, 1.169, 0.839 and 1.529 a.u., respectively. Panels A–C show time series, power spectra and silent period histograms, respectively, of nine representative nodes of the whole ensemble when the external input is  $\Omega = 0.85$  a.u., i.e., the external field frequency is close to the frequency of modality 4,  $Q_i = 7.81$ . Note the higher oscillation amplitude and the sharp structure for the silent period histograms for nodes A<sub>10</sub>–A<sub>11</sub>–A<sub>12</sub>. Panel D displays the phase portraits built with nodes corresponding to different modalities. Phase portraits for nodes belonging to the same modality are similar to those shown in the previous figures.

tion/entrainment and coherence involving distinct types of sequential activations and a different number of participants as a function of the input rhythm; (iii) dynamical filtering and spectrum control; and (iv) enhancement of the encoding space that can include specific sequential activations, silent periods and amplitudes (see also [70,83]). Along this paper, attention between different sensory modalities was used as an illustrative domain to explain and apply the results of our model. The reported phenomena is also relevant in the context of perception disambiguation within a single sensory modality, as rhythmic stimuli have been proved to contribute to the disambiguation process [84]. The proposed model can also be easily generalized to multiple inputs with different amplitude and frequency properties.

#### 4.2. Rhythmic transcranial stimulation and sequential brain dynamics

The origin of the controlling rhythmic field represented in our motif network model can be related to intrinsic brain rhythms or

an external rhythmic stimulation such as a transcranial signal used in research and rehabilitation procedures [32]. Non-invasive stimulation with direct or alternating currents can contribute to the understanding of specific processes, and might provide future protocols to deal with pathological dynamics [59,85,86]. This type of stimulation is able to bias brain dynamics by affecting the competitive interplay of functional subnetworks [87]. In particular, recent studies have shown the sensitivity of working memory performance and global neocortical connectivity to the phase and rhythm of externally driven theta-gamma cross-frequency synchronization [88] (cf. Fig 5B). Modulation of cortical oscillations by rhythmic transcranial stimulation has been shown to be state dependent [55], which points out the putative multifunctional nature of these oscillations. The rich variety of sequential responses hypothesized in this work could be tested and related to specific cognitive functions using this kind of stimulation. Note that the characterization of sequential activations arising from rhythmic stimulation is typically not addressed in these experimental protocols.

Our results can be related to studies in the context of the default mode network and in the context of memory processes [89]. Variation of brain oscillation frequency is one of the key factors in the control of autobiographic memory. Autobiographic and especially episodic memory are responsible for the human ability to remember the past and to predict the future, and thus play an important role in decision making and consciousness [90]. The dynamical mechanisms of such control are still unclear. Episodic memory is primary based on the activity of the hippocampus and the prefrontal cortex, which are interconnected [90,91] and receive/produce characteristic oscillatory rhythms in different frequency bands. An extension of the dynamical system (1–4) that we have suggested here can be useful for modeling this coupled network. The function of the interaction – binding – between the two subnetworks is governed in our model by the effective excitation/inhibition and the degree of asymmetry, see Eq. (1). These parameters are very sensitive to the oscillatory perturbations and depend on their frequencies. The different sequential modes can be associated to those observed in cognitive experiments. For example, prefrontal cortex and hippocampus are differently activated by music auditory input [92]. However, during working memory they work in synchrony [93,94].

Abnormal functional interactions between the hippocampus and prefrontal cortex have been reported in several psychiatric disorders, in particular, schizophrenia [95]. The modeling of hippocampal-prefrontal circuit interaction under the action of rhythmic input will be essential for developing novel therapeutic interventions for such disorders. Similarly, the proposed model can be used in the context of bilateral brain function to address hemisphere coordination by external/internal frequencies while keeping their own intrinsic dynamics. Finally, the results discussed in this paper also suggest the analysis of sequential activity in novel protocols that use rhythmic input for transcranial stimulation to relate neural activity to cognitive functions, and their associated pathologies. The use of specific stimulation frequencies for each protocol and patient as a function of this study can lead to novel personalized treatments.

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