May 1996

Classification of Rhythmic Patterns in the Stomatogastric Ganglion

Patrick D. Roberts
R.S. Dow Neurological Sciences Institute
1120 N.W. 20th Ave.
Portland, OR 97209
e-mail: proberts@reed.edu

Abbreviations: AB, anterior burster; AM, anterior median; DG, dorsal gastric; GM, gastric mill; IC, inferior cardiac; Int1, interneuron 1; LG, lateral gastric; LP, lateral pyloric; LPG lateral posterior gastric; MG, medial gastric; PD, pyloric dilator; PIR, postinhibitory rebound; PY, pyloric; STG, stomatogastric ganglion; STNS, stomatogastric nervous system; VD, ventricular dilator.

Running title: Stomatogastric Rhythms

Abstract--There is a large class of central pattern generators that may change their rhythmic output under the influence of neuromodulators. The generation of patterns by neural networks is dependent on mechanisms that operate on different time scales. We present a classification scheme for the rhythmic patterns that may be generated by small neural networks, as a method for investigating the biological mechanisms responsible for pattern generation and pattern switching. Discrete methods based on transition graphs are applied to dynamic biological networks to map out the set of possible rhythmic behaviors. There is a restriction in the number of patterns that may arise due to specific mechanisms and it is possible to identify the routes that are available for switching between different patterns. A measure is introduced onto the set of rhythms to quantify their differences and organize the set according to clusters of similar rhythms. Each cluster represents a different operational mode of the network. Examples are drawn from the stomatogastric ganglion, a well studied network that controls the muscles of the foregut in crustaceans. Classes of rhythms are found that correspond to experimentally observed patterns. In addition, other classes of rhythms are found that have not yet been observed. The method presented here proves to be an efficient means to scan the space of possible rhythms that can be generated by a small neural network.

Key words: Stomatogastric, network, rhythm, discrete, dynamic, modulation.

The development of theoretical tools is essential for a thorough understanding of complex biological systems. At the present time, there are many powerful computational methods available to simulate biological systems, and powerful hardware on which to implement these methods. However, there is little in the way of theoretical techniques that can be used to ferret out the underlying principles of complex biological systems. When simulating a complicated interaction of many elements, it is seldom clear how much fine detail of the interactive mechanisms is necessary to reproduce behavior that has been observed in the natural world. In some instances the precise time course of a synaptic response may be essential for the firing pattern of a biological neural network, and in other cases there may be enough other reinforcing mechanisms available that many details may be overlooked[23].

Complex systems can be characterized by the need for many conceptual schemes to elucidate their operation[24]. Dynamic biological networks are complex neural systems that can reconfigure their functional circuitry to generate multiple patterns[13]. The study of these networks can benefit from the application of various mathematical techniques to understand their principles of operation. The principles that one may uncover depend upon the questions asked of the system, and different questions require different mathematical techniques. In the following we address the question concerning what patterns a given network can generate.

The purpose of this article is to present a formalism that predict the rhythmic repertoire of dynamic biological networks exhibiting complicated behavior[21]. Discrete methods are chosen rather than the continuous approach taken by dynamical systems studies so that a classification theorem for rhythmic networks begins to emerge. This will help to fill a gap between simulation studies of biological networks and a global understanding of the systems. The result uncovers some interesting mathematical questions as well as opens the door to useful biological applications.

Our focus will be on networks containing cells with bursting properties so that the membrane has two quasi-stable resting potentials: quiescence and firing a burst of action potentials. The general method is to classify the rhythmic behavior of neural networks by constraining the set of all possible rhythms by the synaptic connections and cellular properties of the neurons in the network. A relationship between different temporal patterns is used to cluster the patterns into groups, thus dividing the generated patterns into distinct classes.

At each point in time the neurons in a network will be either quiescent of firing a burst of action potentials. There are often competing mechanisms that determine the evolution of the network in time, so all discrete changes in the neurons' membrane potential will be identified in order to capture the full dynamics of the system. There will be many possible paths that the system can take through this dynamical labyrinth, but we will be interested only in the paths that return on themselves to enumerate the rhythmic behavior. Finally, time courses for the various cellular and synaptic properties are introduced in order to simulate the phasic relationship of burst patterns of neurons in networks. This

method is applied to the stomatogastric ganglion (STG), and predictions will be made about the phasic output under certain conditions.

The Stomatogastric Ganglion

The foregut of decapod crustaceans is a complicated system that is responsible for the storage, chewing, and filtering of food for digestion[13]. The motor neurons that control the musculature of the foregut reside in the stomatogastric ganglion (Fig. 1)[19]. This neural network consists of fewer than thirty cells, yet can generate several distinct rhythms required for the chewing and filtering of food in the crustacean foregut. The STG is a distinctive example of a complex biological system and there is a large body of literature detailing its the anatomy[20], modulation[8], and electrophysiology[19].

[Fig. 1 near here]

A striking aspect of this network is the abundance of inhibitory synaptic connections. Because of the dampening effect of these connections, the neurons of the network require other forms of driving currents to maintain rhythmic excitations. The most important source of driving currents come from the membrane properties of the neurons themselves. Many of the neurons of the STG fire action potential spikes in bursts lasting up to a second in duration. The bursting behavior is due to the presence of plateau potentials[9] that hold the membrane beyond the threshold for action potentials for extended periods. The root cause of this behavior arises from a bistability of the membrane potential. When enough current enters the cell to push the voltage over the threshold to the bursting potential, the restoration of the voltage after each action potential returns to this second level until long-term currents pull the potential down to the resting level.

The bistability of the membrane lends itself to important behaviors. The currents involved may interact so that oscillations occur and the neuron sends out repetitive bursts[7] separated by short periods of silence. Such oscillations can drive a network at a frequency that is phase locked to the frequency of the oscillation[22]. Of course, in biological systems the behavior is not always so simple. The interaction between the oscillating neuron and others in the network may modify the frequency of the circuit as a whole so that the endogenous frequency of one cell is not enough to predict the frequency of the whole pattern. In fact, it can often be difficult to distinguish the “driving” neurons from the “follower” neurons as feedback from a supposed follower interferes with the activity of the driver.

Another important property that can occur in neurons with plateau potentials is postinhibitory rebound (PIR)[1]. If a neuron experiences a sustained inhibition, it is likely to adapt to the conditions to restore a preferred resting potential. After the neuron is released from inhibition, there may be enough added inward current to drive the potential over the threshold yielding a burst on a plateau potential. In a highly inhibitory network like the STG, where many of the neurons fire in bursts, PIR can be a major driving mechanism to maintain a rhythmic output.

The importance of membrane properties in a neural network make it quite susceptible to modulation by diffuse application of peptides and neurotransmitters[8]. In the STG, modulatory influences come from both hormonal infusion and activity of neurons that project to the network from other ganglia of the crustacean nervous system. There is a wide variety of identified modulators that have an influence on the frequency and rhythmic pattern of STG's output. In some cases specific target cells have been identified[10] that change their membrane properties and response to synaptic input and alter the behavior of the network as a whole.

The STG has traditionally been divided into two subnetworks with some interconnections between them: the pyloric and the gastric networks[20]. These networks can generate distinct rhythmic patterns simultaneously and innervate functionally different regions of the foregut. This division has proven to be somewhat artificial since it turns out that some neurons can switch roles and participate in the pattern generation of either network depending on the influence of neuromodulators or external synaptic input [2,11].

In the following, the *rhythm space method*[21] will be used to predict the phasic relations of neuronal activity based upon the connectivity and cellular properties reported in the literature, and correspondences with published data will be noted. The next section we will introduce the mathematical (rhythm space) method that is useful in classifying the output of dynamic biological networks. The following section reports the results of applying the technique to two subcircuits of the STG. In addition, a simulation of an experimental cell removal paradigm is presented to show how the behavior of smaller networks can be contained in the behavior of a larger network. We conclude with a discussion about what this method can teach us about the STG and other small biological networks.

Mathematical Methods

The technique will be demonstrated with a simple example designed by Warshaw and Hartline[27] based on the pyloric network of the STG. The simplified network contains three cells: **a**, **b**, and **c**. All three cells exhibit post inhibitory rebound and there are only inhibitory synapses throughout the network connected as shown in (Fig. 2A) The correspondence to the pyloric neurons is, {**a**: AB, PD}, {**b**: LP, IC}, {**c**: VD, PY}. The precise (perhaps unknown) ionic mechanisms responsible for the plateaus, oscillations, and PIR of the cells need not be explicitly stated, but can be compared in terms of the strengths of the ionic currents and their time courses.

[Fig. 2 near here]

In order to study the activity of the pattern generator we need to introduce two concepts: the *neural state* and a mathematical object called an *operator*. The neural states represent the neural activity of the network at any given time[4]. A coarse-grained approach is taken here so that the neurons are treated as either resting state firing a burst of action potentials[15]. In this context, an operator is a

mathematical object that contains the information of the synaptic connections in the network or the cellular properties of the neurons. An operator acts on a neural state to transform it into other neural states in a manner consistant with the properties of the network. Following Getting[4] who defines a neuron as a current detector that fires when the inward current exceeds the outward current, then an operator formalizes the membrane currents into a single mathematical object. Once the ionic mechanisms are defined, the set of all possible transitions between neural states can be determined. The set of all transitions makes a directed graph that includes all accessible states of the network[14]. The *state transition diagram* (or *transition graph*) for our demonstration network is shown in Fig. 2B. The boxes correspond to the neural states where the cells are in the order given in the upper left. The neurons are in the depolarized state when the boxes are shaded and are considered to be firing a burst of action potentials, otherwise they are silent.

The complete transition graph in Fig. 2B contains spurious transitions that would either be out-paced by faster mechanisms or suppressed by combined actions of countering mechanisms. In the example there are three active mechanisms: PIR, inhibition, and plateau termination (given in order of speed). For instance, inhibitory synapses are faster than the recovery mechanism that terminates a plateau potential, so in the event that both compete, the transition that the network experiences will be due to inhibition. The *temporally reduced* transition graph of the network is in Fig. 3 (where all states without parents are removed). A further reduction is made by competing ionic strengths such as two inhibitions suppressing the oscillatory behavior of a cell, or making it unlikely for a cell to rebound if actively inhibited. The completely reduced transition graph, which is a combination of both reductions, is also in Fig. 3.

[Fig. 3 near here]

A *rhythm* is a cycle through the graph where each neuron changes state exactly twice. Each distinct rhythm gives a sequence of state changes that can repeat itself indefinitely. This definition is the simplification that makes our analysis possible, and there are several plausible reasons for why it is not too restrictive. Double bursts within a cycle of central pattern generators appear to be quite uncommon. The only case observed in the STG is in the pyloric network and there is room for argument about whether it a double burst or a long plateau that has its spikes suppressed by inhibitory input during the middle of the plateau[16]. A good reason for allowing only one burst for each neuron per cycle is that the plateau mechanisms are slow enough that in small neural networks the full cycle is complete before any neuron has been in a recovered state for very long after its last burst. Larger networks may have a tendency to break-up into smaller *functional* subnetworks as seems to be the case in the STG, but this question would have to be proven. Fortunately, this issue is probably accessible using the formalism presented here.

From the ionically reduced transition graph one can count the number of unique rhythms that

follow from the network. There are only three cycles on the graph that involve all three neurons (Fig. 4). Choices between these rhythms are determined by the relative strengths and time courses of the mechanisms. Although some rhythms were previously eliminated by gross violations of temporal and ionic selection principles, more subtle changes in membrane properties can lead the network to switch from one rhythm to another. In addition, if cell **a** is driven to fast oscillations that out-pace the plateau termination of **c**, then the network can switch to a 4-cycle involving only **a** and **c**, and effectively cut **b** out of the circuit. Here the network breaks into either of two half-center oscillators, one driven by an endogenous oscillator and the other driven by rebound currents, while the third neuron effectively drops out of the network. Thus, from this simple network, the mechanisms required for switching rhythmic output and reconfiguration of the functional network can be examined.

[Fig. 4 near here]

Most networks will generate a large number of rhythms so it is useful to have a means of comparing different rhythms of a given length. By comparing similar rhythms we will then be able to classify the patterns generated by a given network into groups that reflect a similar property. This can be accomplished by introducing a distance function onto the set of rhythms to quantify the differences between them.We define a distance between two rhythms to be the minimum number of adjacent transpositions of transitions that change one rhythm into another (Fig. 5).

[Fig. 5 near here]

The distance function defines contiguous regions in the set of rhythms generated by the network. Shown in Fig. 6B are the relations between rhythms arranged so that each line represents a distance of one between adjacent rhythms. The surrounding box corresponds to the subset generated by the reduced graphs, grey representing temporal reduction and a broken line denoting ionic reduction. The rhythms of both reduced graphs fall into two clusters, while the full set of rhythms forms one large cluster. The clusters are displayed above by superimposing the rhythms and shading the depth of how many cell states are coincident on each square. One can clearly see here that the two classes of rhythms from the reduced graphs are characterized by **a**-**b**-**c** and **a**-**c**-**b** sequences.

[Fig. 6 near here]

To compare clusters of rhythms to spike train data available in the laboratory, it is useful to convert rhythms to *phase diagrams* that show the relative fraction of each cycle when neurons are in a depolarized state. In order to make this conversion we must make estimates of the time courses of the various mechanisms responsible for transitions. The length of plateaus involve many variables and are individual to each neuron, but we will use a rough estimate for STG neurons in the pyloric network of 1/3 sec[20]. In addition, we assume that this is symmetric with the endogenous mechanisms for spontaneous activity so that the time courses of plateau termination, tonic activity, and endogenous oscillation are 300 msec.

The chemical synapses have a shorter time course of about 30 msec (300 msec without spike activity) according to various sources[5,6]. We will use this number for inhibitory synapses of our network. Post inhibitory rebound follows the dispersal of neurotransmitters from the synaptic cleft of inhibitory synapses. This dispersion takes place a little faster than the onset of inhibition, but since there is a slight lag before the membrane potential reaches threshold we will use 30 msec as the time course for the PIR transitions. Applying these time courses to the first three rhythms, normalizing to the period, and using the onset of the burst of neuron **a** to mark to beginning of the cycle, one obtains the phase diagrams shown in Fig. 6. In these clusters, the heavier regions represent a phase of the cycle where there are more supportive mechanisms reinforcing neuronal activity.

Results

Pyloric Patterns

The pyloric subcircuit of the STG typically generates a triphasic pattern with the AB-PD neurons acting as pacemakers, followed by the LP and IC neurons, and finally the VD and PY neurons. The twelve phase clusters shown in Fig. 7 are the result of applying the rhythm space method with the following assumptions:

- The synaptic connectivity is as shown above.
- The rhythms are derived from a reduced transition graph (both temporal and ionic).
- All synaptic strengths are equal.
- The time course ratio (electrical synapses : chemical synapses : plateau properties) is 1:3:20.
- AB and VD neurons are endogenous oscillators.

The identifiable patterns found in the literature correspond to; cluster 1, Flamm and Harris-Warrick[3], cluster 7, Selverston, *et al.*[26], cluster 11: Hooper, *et al.*[12] (?). The correspondence between cluster 11 and the observed phase pattern[12] is somewhat questionable because only three of the neurons are given in the reference. The correspondence is given because the simulated pattern is dominated by the AB-PD and LP-IC bursts, while the burst of VD-PY is short enough to escape detection.

[Fig. 7 near here]

It is encouraging that with such rough assumptions previously observed patterns are predicted by the method, and with the deepest occurrence of rhythms. The appearance of unobserved clusters indicated either limitations of the assumptions, or an as yet uncovered potential of the circuit. The question that these clusters raises is what mechanisms exist in the pyloric network that normally forbid them.

We should emphasize here that conclusions should not be drawn from the number of clusters that have been computed. Due to the lack of efficient algorithms to compute distances between rhythms

so that clusters are only formed by nearest neighbors, there may be cases of clusters that are very similar yet are separated by more that a distance of one. In Fig. 7, this appears to be the case, for instance, upon comparing clusters 1 and 2. The phasic relationship between these two clusters are very similar so one would expect that they differ by a short distance in rhythm space.

Cell Removal

The cell removal paradigm[17] can be easily simulated using this method. Neurons could be selectively removed from the biological network by filling the soma with dye and then focusing a laser onto the cells. The results lend insight into the dependency of certain patterns on the presence of individual cells and subnetworks. The patterns that are generated by the remaining neurons indicate what subrhythms contribute to the patterns of the whole. The rhythms are not necessarily the same functional patterns that would be generated by the subnetwork if the removed neurons were still present. These killed neurons could contribute to the patterns even if they did not participate in the particular functional network. This procedure actually changes the anatomical network so any transitions with reference to the killed neuron are removed from the analysis.

[Fig. 8 near here]

Using the same assumptions of cellular properties as in the last sections for the pyloric network, Fig. 8 was constructed by finding the sequence of transitions of the lower rhythms in clusters of the upper rhythms. All of the rhythms were then converted to phase diagrams as shown. This reveals which clusters are destroyed by cell removal and which patterns were not dependent upon the presence of the removed cell. The breakdown of the triphasic pattern shown here is consistent with the results of Selverston and Miller[18,25].

Gastric Modulation

The gastric subcircuit of the STG drives the musculature of the gastric mill. It is capable of changing its output to produce different chewing modes depending on the presence of modulatory substances. The phase clusters in Fig. 9 show how the output changes as particular neurons change their properties. The following assumptions are used:

- The synaptic connectivity is as shown above.
- The rhythms are derived from a reduced transition graph (both temporal and ionic).
- All synaptic strengths are equal.
- The time course ratio (electrical synapses : chemical synapses : plateau properties) is 1:3:50.
- The Int1 neuron is tonically active and others are as shown.

The figure is presented in tabular form to make clear that the patterns can drastically change by changing the cellular properties of individual neurons. We have been unable to locate in the literature patterns that correspond to clusters 1-4 and 7-10. On the other hand, when the LPG and GM neurons are tonically active, the network generates clusters that are found in the literature. Cluster 5 and cluster 13 correspond to patterns that were reported by Miller and Selverston[17]. These patterns have behavioral correlates as the squeeze and the cut-and-grind chewing modes respectively. The observed clusters suggest that the gastric circuit requires a certain amount of endogenous activity to maintain normal activity.

[Fig. 9 near here]

The arrow in the right hand column denotes an observation of Heinzel and Selverston[10] that the chewing mode changes when the DG neuron begins endogenous oscillations. The incidence of the clusters in the top right quadrant is overwhelmed by the new rhythm that appears in the bottom. This does not mean that the other rhythms have disappeared, but there are more mechanisms reinforcing the new rhythm that correspond to a potential change in behavior.

Discussion

Mechanisms that distinguish rhythmic clusters

Having classified the rhythmic behavior of networks in the STG, it is now possible to investigate the mechanisms responsible for differences in the rhythmic output. Each rhythm can be related to a specific functional network, but clusters of rhythms can include several functional networks. Thus, the combination of several functional networks can reinforce a behavior. Many of the rhythmic clusters that arise from a given anatomical network will share common phasic relations of the neuronal bursts. An important aspect to notice when comparing rhythms is the point in the phase when two clusters diverge in their phasic relations. These juncture points localize the mechanisms responsible for the differences between the behaviors.

In the list of rhythmic clusters generated by the pyloric network (Fig. 7), we will compare the most prominent examples; cluster 1, 7, 9, and 11. The first two, 1 and 7 differ in the relative plateau termination sequence of the LP and IC neurons. From a point about half way through the cycle, the two clusters diverge. In cluster 7, the VD and PY neurons begin their burst nearly simultaneously when the IC neuron terminates. On the other hand, when the LP neuron terminates its plateau in cluster 1, the VD neuron's burst is delayed. This is due to the inhibitory synapse from the IC to the VD neuron, but no inhibition of the PY neuron allowing it to begin its burst early. Thus, the main difference between these two patterns is dependent on the relative burst lengths of LP and IC, while the rest of the differences follow as a result. By adjusting the membrane properties in these neurons, the organism can switch between the two patterns.

Cluster 11 is very similar to 7 except for the shorter bursts of the VD and PY neurons. This pattern would be the result of a reduced strength of the VD neuron's plateau potential so that it could not plateau until after the LP neuron completes its burst. This applies even though there should be a rebound current after the release of inhibition by the IC neuron. Another possibility for the differences between these patterns is to implicate the relative differences of synaptic strengths. For instance, cluster 7 would be favored over cluster 11 if the inhibitory synapse from LP to VD were weaker. This example shows that *even though the synaptic strengths are set to be equal, knowledge about the relative synaptic strengths in the biological network can be recovered* by comparing the resulting rhythmic clusters.

Although we have been unable to find a rhythm in the published literature corresponding to cluster 9, this cluster is prominent in our analysis. Cluster 9 differs from the observed prominent clusters by the burst of the PY neuron following the AB and PD neurons' bursts. This pattern implicates strong rebound properties of the PY neuron and strong inhibitory synapses that suppress the activity of the LP and IC neurons. Again, we have a case that by classifying the *possible* rhythmic outputs we can deduce properties of the *actual* biological network even though these properties are given the same weight in the model. Since this pattern is not found in recordings of the STG, one is led to the conclusion that the LP and IC neurons have stronger rebound properties than the PY neuron or there are differences in synaptic strengths between these neurons.

Turning now to the behavior of the gastric network, we find an interesting result of changing cellular properties. In the two left quadrants of Fig. 9 there is little change in the patterns when the DG neuron changes behavior from quiescent to oscillating. The main difference is that the burst length of the DG neuron extends a little and that of the interneuron is diminished. These clusters represent quite stable patterns that are generated under the given conditions because they are not eliminated when one of the neurons in the network changes behavior, nor are any new patterns created. In contrast, the clusters of the two right quadrants reflect an instability with respect to the changes in the DG neuron. A new and prominent cluster is created when the DG neuron begins to oscillate. The new cluster represents a different behavior mode of the system that requires oscillations of the DG neuron to be expressed.

The lack of published experimantal evidence for clusters 1-4 and 7-10 may be due to the focus of our analysis on the neurons of the STG. There are neurons outside of the STG that make excitatory contacts onto the LPG and GM neurons that may keep these neurons tonically active to induce the gastric rhythms found in the literature. In the case of the STG, these external neurons are known, but this method could suggest the existence of external influences on a biological network when the predictions do not match observations of rhythmic behavior. The patterns that remain unobserved are intriguing, but we leave this as an open question about what mechanisms forbid these rhythms in the

isolated stomatogastric ganglion.

Rhythm Space as a Tool

The formalism presented here proves quite useful in studying neural networks with cyclic outputs. The restriction to cyclical outputs is in contrast to much of the theoretical work done in artificial neural networks where the most useful restriction is to symmetric synaptic connectivity. The rhythmic formalism contains much depth mathematically, connecting fields such as combinatorics, group theory, and topology[21]. It would be interesting to know in general what rhythms are created and destroyed by changes in synaptic connectivity or changing cellular properties.

An important aspect of the approach presented here is that clusters in rhythm space designate the behaviors that are latent in the network. The particular output depends upon specific values of parameters relating to the relative strengths of membrane currents. Thus, the formalism can be used to tease out the behavior that is inherent in the network from the properties that depend on the details of the ionic currents. This is useful to let the experimenter know what details are necessary to quantify in the lab for a thorough understanding of the system.

Perhaps general statements may be made about the regions of rhythm space to which specific networks are restricted, and whether the regions are simply connected and where clusters of rhythms appear. In addition, this formalism appears to be directly applicable to precisely those biological questions that are theoretically intractable using standard neural network theory such as sparse, asymetrically connected neural networks. There may yet be general statements that can be made about the modular structure of larger nervous systems of vertebrates. Larger anatomical networks may naturally break up into smaller functional networks that interact, exchange member neurons and fuse into larger networks depending upon the presence of neuromodulators and the outputs of subunits.

Conclusions

The main objective of this work is to fashion a tool useful in the study of biological neural networks. Simple assumptions were made in the modelling effort in hopes of capturing the broadest collection of phase patterns. The fact that a large numbers of rhythms fall into a relatively small number of clusters implies that there are few restricted modes of operations for these networks. A refinement of the assumptions, such as inclusion of parameters for individual cells and synapses, promises to yield an efficient modelling technique. In addition, the general method can be used to predict and classify the rhythmic output of dynamic biological networks.

Acknowledgements The author would like to thank Gin McCollum and Jan Holly for discussions and many helpful suggestions regarding the mathematical details. In addition, several ideas presented

here were inspired by the author's participation in the 1994 Santa Fe Institute's Summer School on Complex Systems. This research was supported by National Institutes of Health grant R01-DC02482.

References

1. Calabrese R.L., Angstadt J.D. and Arbas A.E. (1989) A neural oscillator based on reciprocal inhibition. In *Perspectives in Neural Systems and Behavior*, T.J. Carew and D.B. Kelly (eds.) Liss, New York, pp. 35-50.

2. Dickinson P.S. and Moulins M. (1992) Interactions and combinations between different networks in the stomatogastric nervous system. In *Dynamic Biological Networks* (eds. Harris-Warrick R.M., Marder E., Selverston A.I. and Moulins M.) pp. 139-160. The MIT Press, Cambridge.

3. Flamm R.E. and Harris-Warrick R.M. (1986) Aminergic modulation in lobster stomatogastric ganglion. I. Effects on motor pattern and activity of neurons within the pyloric circuit. *J. Neurophysiol.* **55** 847-881.

4. Getting P. (1989) Emerging principles governing the operation of neural networks. *Ann. Rev. Neurosci.* **12** 185-204.

5. Graubard K., Raper J.A., and Hartline D.K. (1980) Graded synaptic transmission between spiking neurons. *Proc. Natl. Acad. Sci. U.S.A.* **77** 3733-3735.

6. Graubard K., Raper J.A., and Hartline D.K. (1983) Graded synaptic transmission between identified spiking neurons. *J. Neurophysiol.* **50** 508-521.

7. Harris-Warrick R.M. and Flamm R.E. (1987) Multiple mechanisms of bursting in a conditional bursting neuron. *J. Neurosci.* **7**: 2113-2128.

8. Harris-Warrick R.M., Nagy F., Nusbaum M.P. (1992) Neuromodulation of the stomatogastric networks by identified neurons and transmitters. In *Dynamic Biological Networks* (eds. Harris-Warrick R.M., Marder E., Selverston A.I. and Moulins M.) pp. 87-137. The MIT Press, Cambridge.

9. Hartline D.K. (1987) Plateau potential. In: *Encyclopedia of Neuroscience*, G. Adelman (ed.) Boston: Birkhauser, pp. 955-956.

10. Heinzel H.-G. and Selverston A.I. (1988) Gastric mill activity in the lobster. III. *J. Neurophysiol.* **59** 566-585.

11. Hooper S.L. and Moulins M. (1989) Switching of a neuron from one network to another by sensory-induced changes in membrane properties. *Science* **244** 1587-1589.

12. Hooper S.L., Moulins M., and Nonnotte L. (1989) Sensory input induces long lasting changes in the output of the lobster pyloric network. *J. Neurophysiol.* **64** 1555-1573.

13. Johnson B.R. and Hooper S.L. (1992) Overview of the stomatogastric nervous system. In *Dynamic Biological Networks* (eds. Harris-Warrick R.M., Marder E., Selverston A.I. and Moulins M.) pp. 1-30. The MIT Press, Cambridge.

14. Lewis J.E. and Glass L. (1992) Nonlinear dynamics and symbolic dynamics of neural networks. *Neural Comp.* **4** 621-642.

15. McCulloch W.S. and Pitts W. (1942) A logical calculus of the ideas immanent in nervous activity. *Bull. Math. Biophys.* **5** 115-133.

16. Miller J.P. (1987) Pyloric mechanisms. In: *The Crustacean Stomatogastric System*, A.I. Selverston and M. Moulins (eds.) Berlin, Springer-Verlag, pp. 109-136.

17. Miller J.P. and Selverston A.I. (1979) Rapid killing of single neurons by irradiation of intracellularly injected dye. *Science* **206** 702-704.

18. Miller J.P. and Selverston A.I. (1982) Mechanisms underlying pattern generation in lobster stomatogastric ganglion as determined by selective inactivation of identified neurons IV. *J. Neurophysiol.* **48** 1416-1432.

19. Mulloney B. (1987) Neural circuits, In *The Crustacean Stomatogastric System* (ed. Selverston A.I. and Moulins M.) pp. 110-145. Springer-Verlag, Berlin.

20. Mulloney B. and Selverston A.I. (1974) Organization of the stomatogastric ganglion of the spiny lobster I, II, III. *J. Comp. Physiol.***91** 1-74.

21. Roberts P. (1996) Classification of temporal patterns in dynamical biological networks, *Phys. Rev. E* (accepted).

22. Robertson R.M. and Moulins M. (1981) Oscillatory command input to the motor pattern generators of the crustacean stomatogastric ganglion: I. The pyloric rhythm. *J. Comp. Physiol.* **154** 473-491.

23. Rowat, P.F., and A.I. Selverston. (1993) Modeling the gastric mill central pattern generator of the lobster with a relaxation-oscillator network. *J. Neurophys.* **70** 1030-1053.

24.Segel L.A. (1995) Grappling with complexity. *Complexity* **1** 18-25.

25. Selverston A.I. and Miller J.P. (1980) Mechanisms underlying pattern generation in the lobster stomatogastric ganglion as determined by selective inactivation of identified neurons. I. Pyloric system. *J. Neurophysiol.* **44** 1102-1121.

26. Selverston A.I., Russel D.F., Miller J.P. and King D.G. (1976) The stomatogastric nervous system: Structure and function of a small neural network. *Prog. Neurobiol.* **7** 215-290.

27. Warshaw H.S. and Hartline D.K. (1976) Simulation of network activity in stomatogastric ganglion of the spiny lobster, *Panulirus*. *Brain Res.* **110**: 259-272.

Figure captions

Figure 1. *The stomatogastric ganglion.* The pyloric network consists of 14 neurons divided into six groups as follows: The anterior burster neuron (AB), two pyloric dilator neurons (PD), eight pyloric neurons (PY), the lateral pyloric neuron (LP), the inferior cardiac neuron (IC), and the ventricular dilator neuron (VD). The gastric network consists of 11 neurons divided into seven cell groups as follows: The lateral gastric neuron (LG), the medial gastric neuron (MG), the dorsal gastric neuron (DG), the anterior median neuron (AM), the interneuron 1 (Int1), two lateral posterior gastric neurons (LPG), and four gastric mill neurons (GM). There is synaptic communication between these two subcircuits that can influence the interaction of different regions of the foregut. Figure from Mulloney ('87).

Figure 2. *The network and the transition graph.* **A**) The model network contains 3 bistable neurons that exhibit postinhibitory rebound[17]. All synapses are inhibitory. **B**) The transition graph captures the dynamics of the network. From any neural state there is one or more mechanisms that can bring about a change of state. Arrows represent the responsible mechanisms and the transitions induced by them.

Figure 3. *Reduced transition graphs.* Competition between transitions eliminates some transitions through either the time course of each transition or the summation of ionic currents. The full transition graph is thus reduced to smaller graphs by eliminating the spurious transitions.

Figure 4. *Rhythms of the 3 cell circuit.* **A**) A cycle through the transition graph where each neuron changes state twice defines a *rhythm*. **B**) Rhythms are depicted as a sequence of neural states where we use the convention that the left-most state is the final state of a transition in which neuron **a** begins a burst. The vertical line between each state denotes that transition(s) responsible for the change in state. **C**) The 14 rhythms that can be generated by the 3 neuron network of Fig. 2A. The rhythms surrounded by a grey line are from the temporally reduced graph and those surrounded by a broken line are from the ionically reduced graph.

Figure 5. *Distance between rhythms.* The nearest neighbor of any rhythm in rhythm space can by found by transposing two adjacent transitions. **A**) The cycle on the transition graph is deformed by exchanging a transition where neuron **b** changes state with a transition where neuron **c** changes state. **B**) The exchange of transitions in a rhythm generates a functionally similar rhythm.

Figure 6. *Models from rhythms.* **A**) Rhythms may be converted into a phase diagram by including a

time course for each transition and then normalizing to the phase. **B**) The rhythms form clusters in rhythm space. A line between each rhythm denotes a distance of one. The full transition graph generates one large cluster. The temporal reduction breaks the set into two clusters denoted by a grey box surrounding the included rhythms and grey lines connecting them. Broken boxes surround the two clusters of rhythms that result from an ionic reduction. **C**) Clusters are displayed by superimposing the rhythms in each cluster and darkening the regions on a scale that depends on the number of rhythms that align phasically.

Figure 7. *Pyloric patterns.* The set of rhythmic clusters that are generated from the pyloric network using the assumptions in the text. Three of the clusters (1, 7, and 11) correspond to patterns that have been reported in the literature[3,26,12].

Figure 8. *Cell removal.* Selective cell removal experiments can be simulated using the rhythm space method. The remaining network after removal of neurons from the pyloric network is given in each panel along with the associated rhythm clusters. The arrows show which clusters are preserved in the removal process.

Figure 9. *Gastric modulation.*The four quadrants show the rhythmic clusters generated under different conditions for the DG, LPG, and GM neurons. Two clusters (5 and 13) have been reported in the literature[17]. The transition between patterns associated with chewing modes of the gastric mill is given by the arrow on the right and has also been reported in the literature[10].

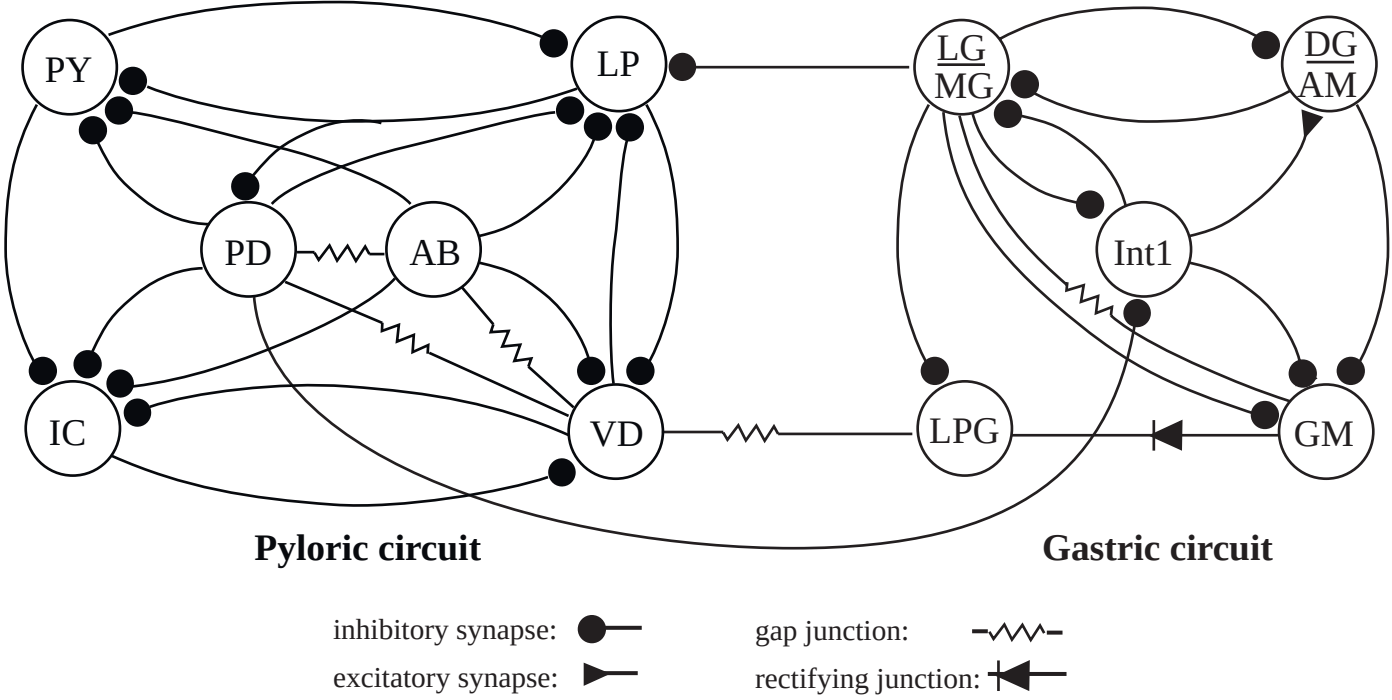

PY
LP
PD
AB
IC
VD
LG
MG
DG
AM
Int1
LPG
GM
Pyloric circuit
Gastric circuit
inhibitory synapse:
excitatory synapse:
gap junction:
rectifying junction:

Fig. 1

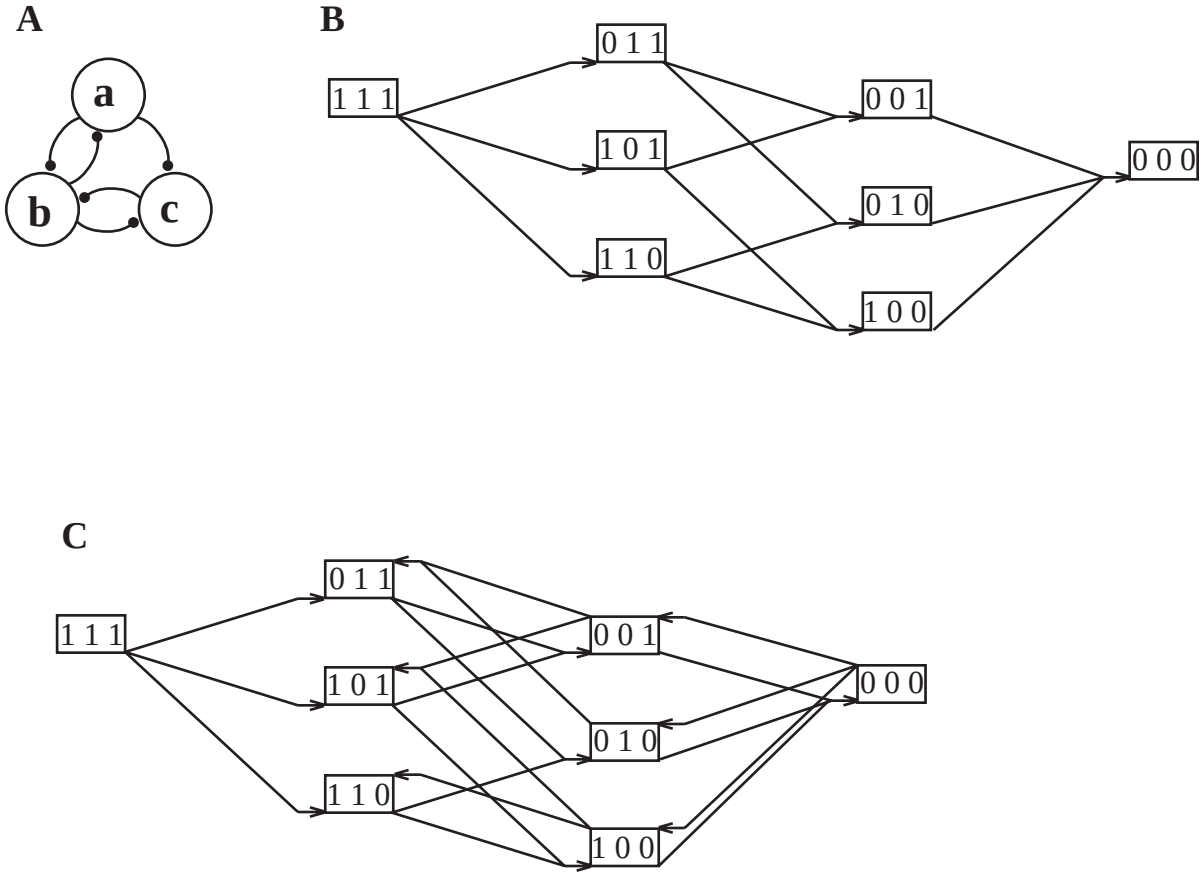

A
a
b
c
B
1 1 1
0 1 1
1 0 1
1 1 0
0 0 1
0 1 0
1 0 0
0 0 0
C
1 1 1
0 1 1
1 0 1
1 1 0
0 0 1
0 1 0
1 0 0
0 0 0

Fig. 2

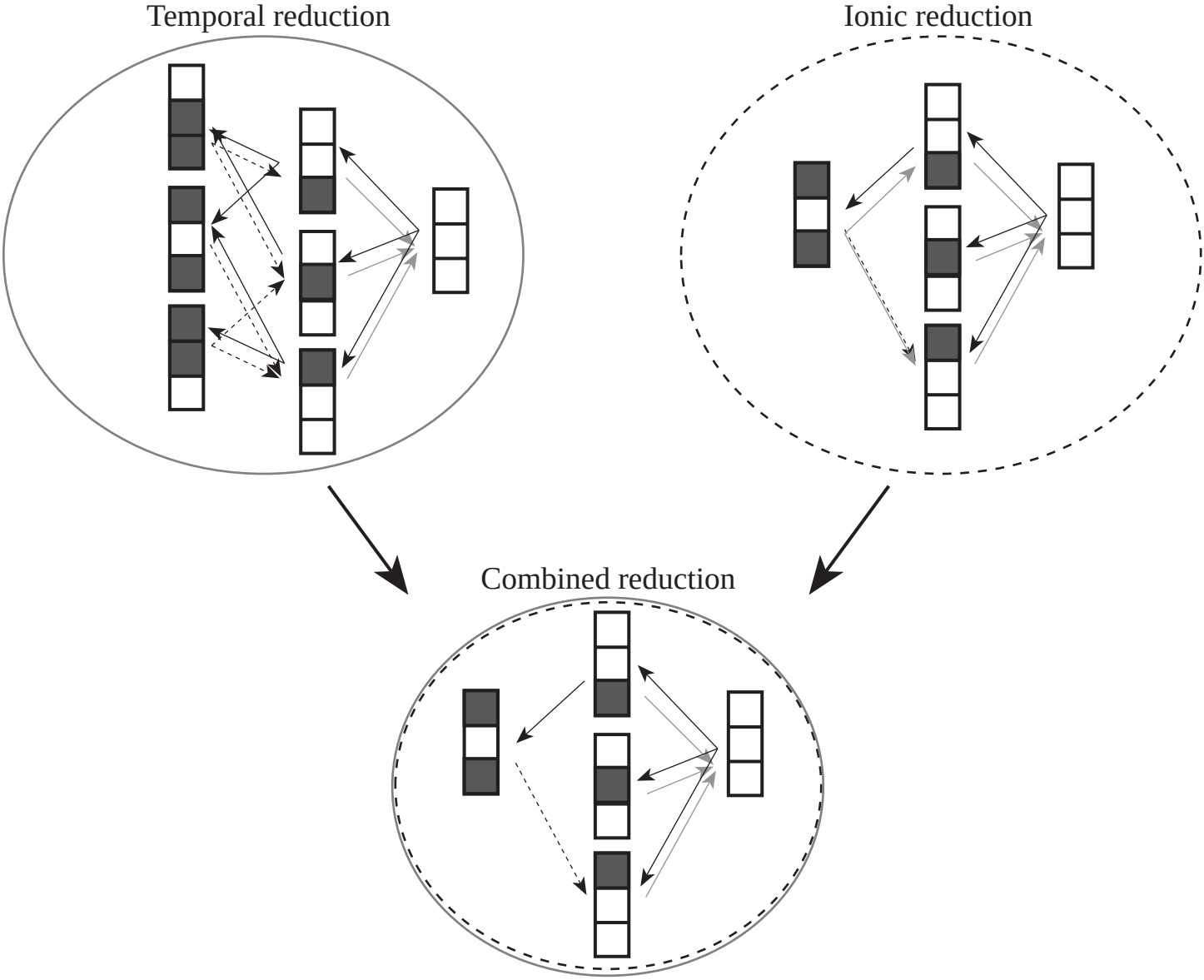
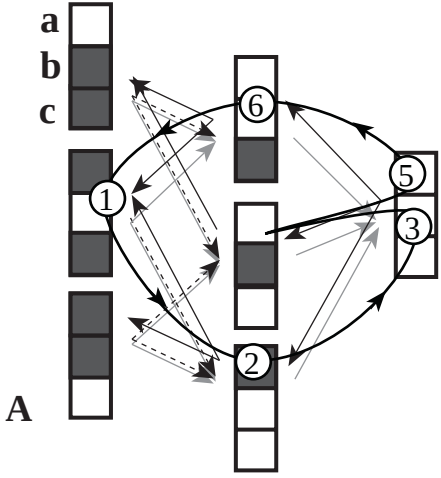
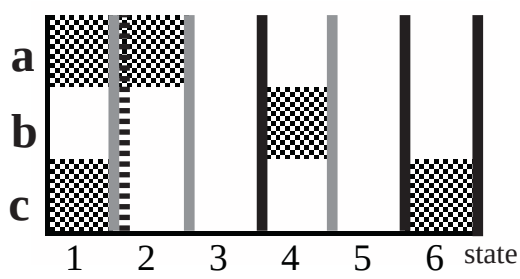


Fig. 3



A



B

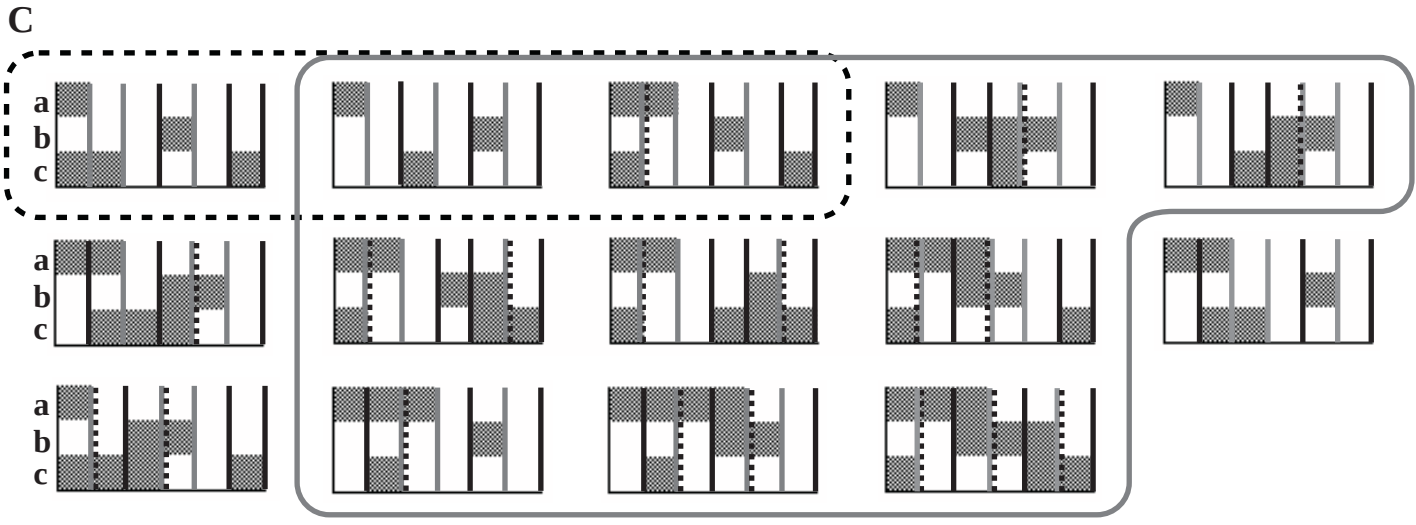


Fig. 4

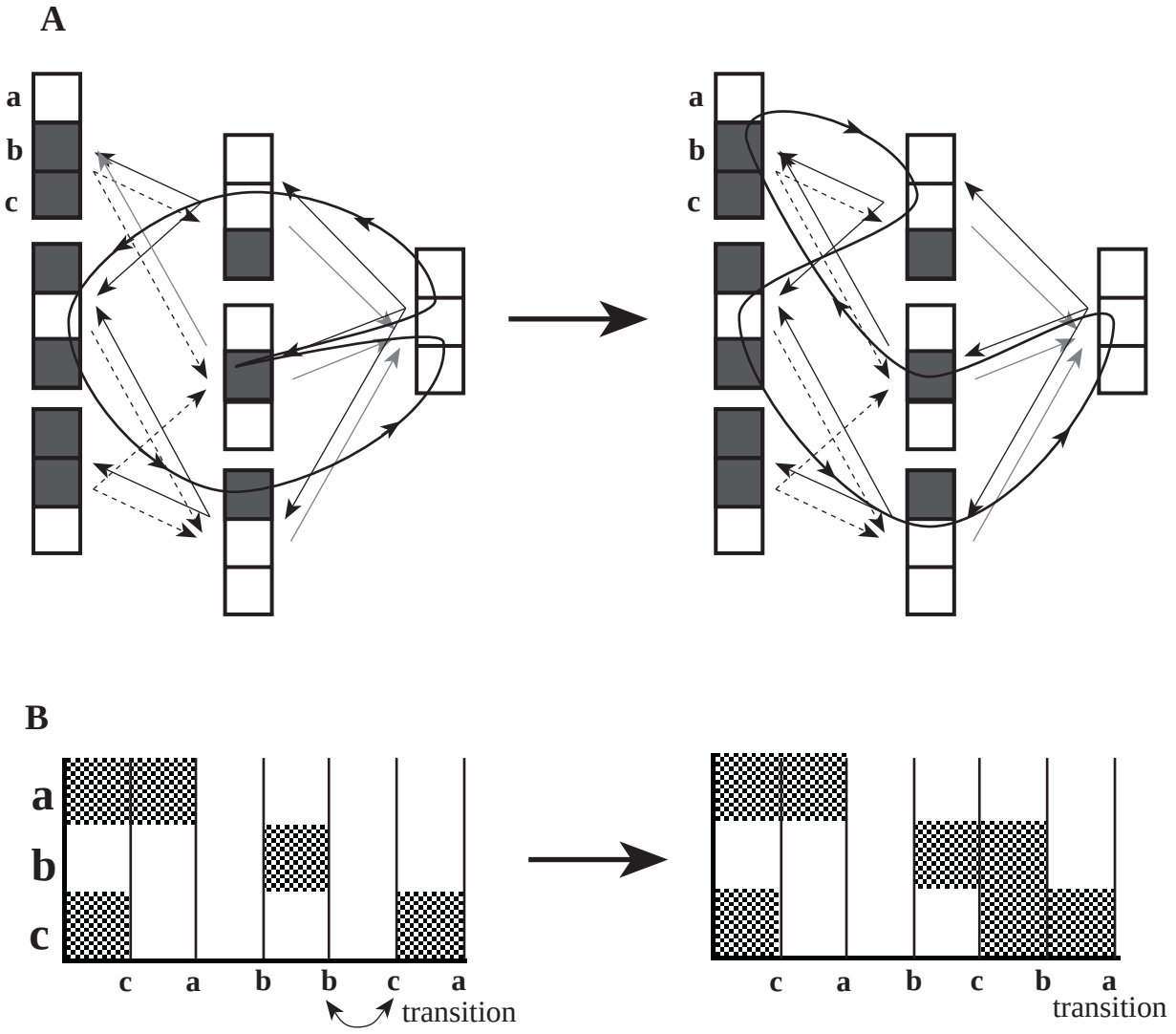


Fig. 5

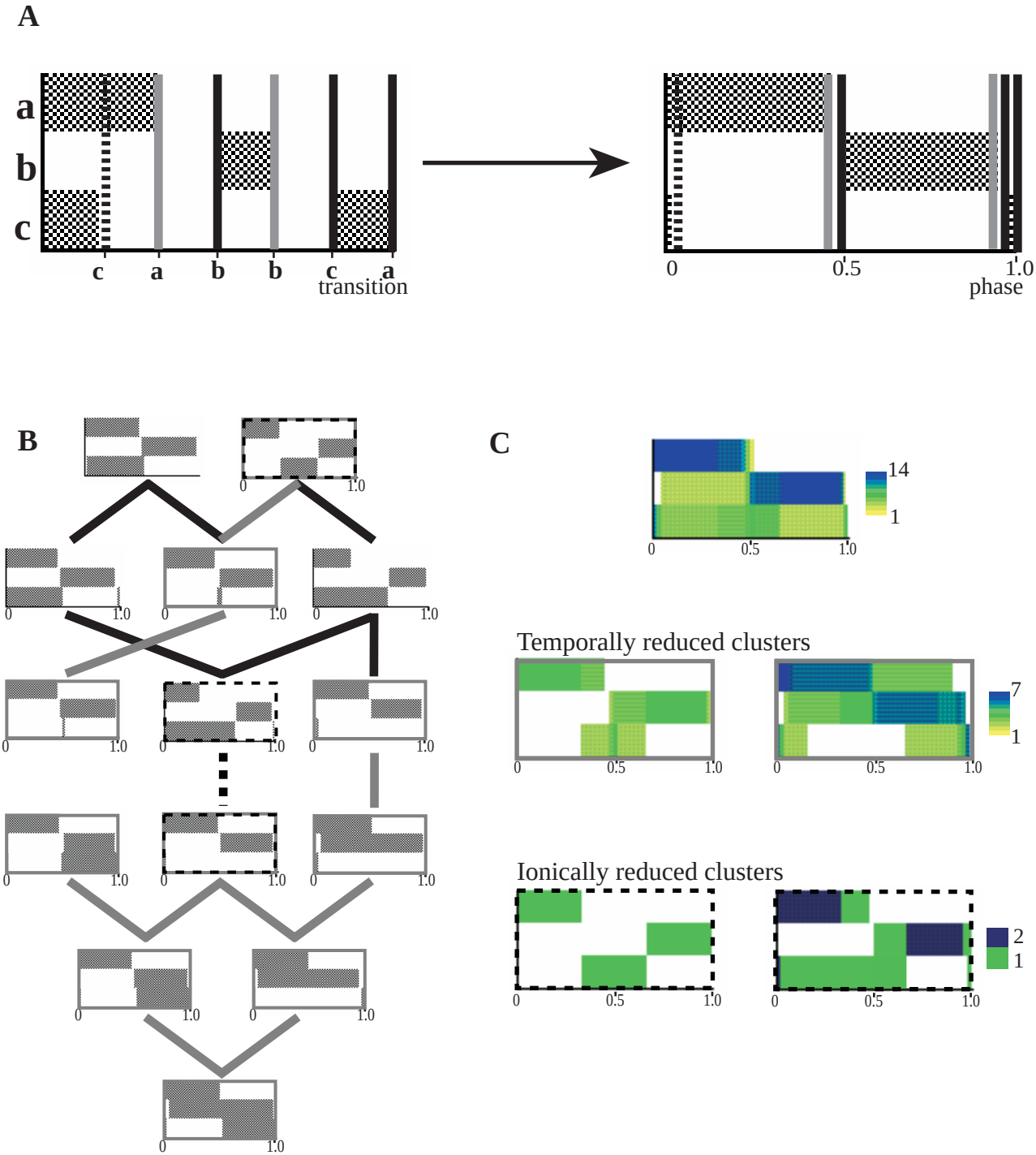

A
a
b
c
c a b b c a
transition
0
0.5
1.0
phase
B
0
1.0
C
14
1
0
0.5
1.0
Temporally reduced clusters
7
1
Ionically reduced clusters
2
1

Fig. 6

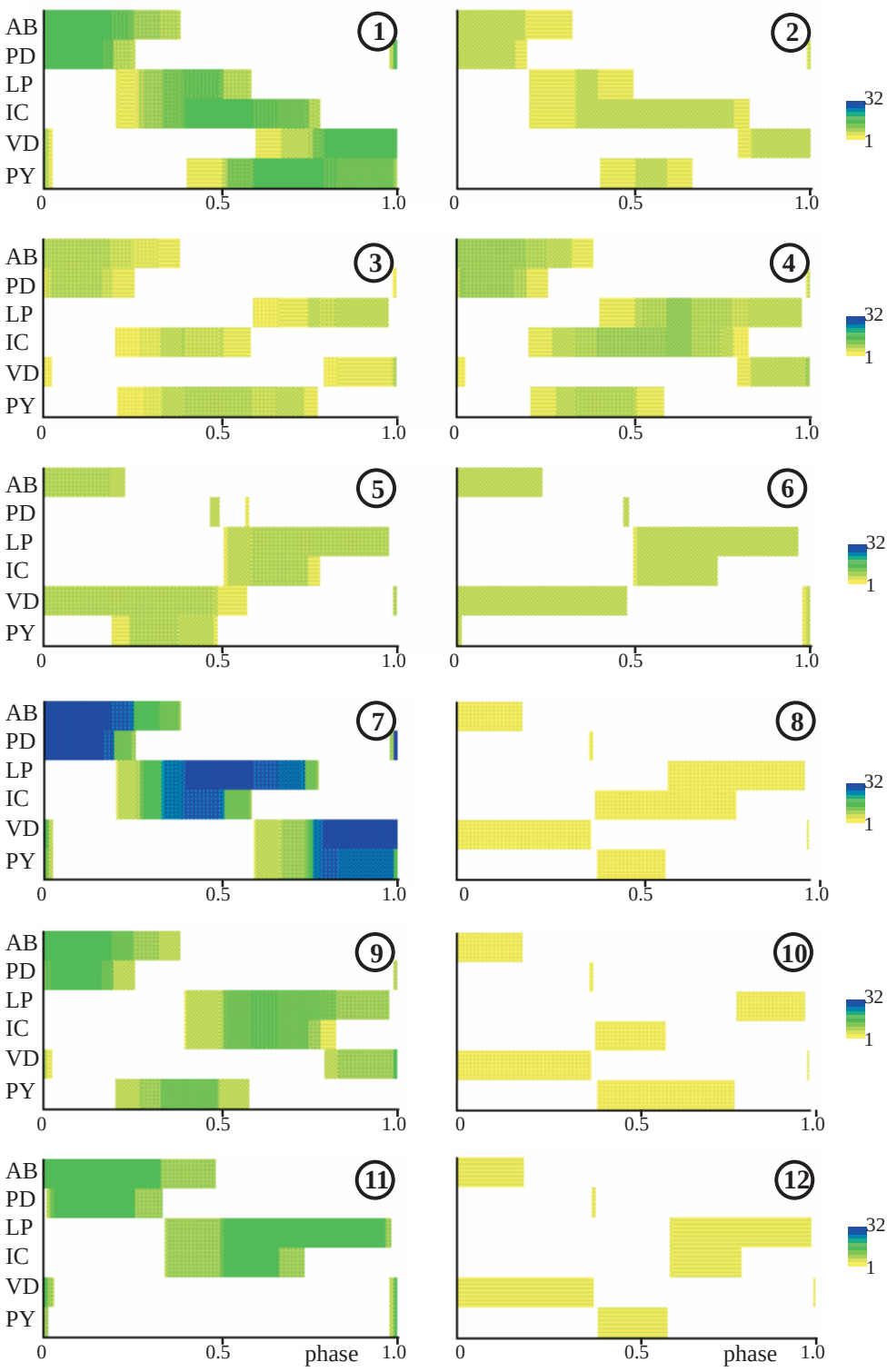


Fig. 7

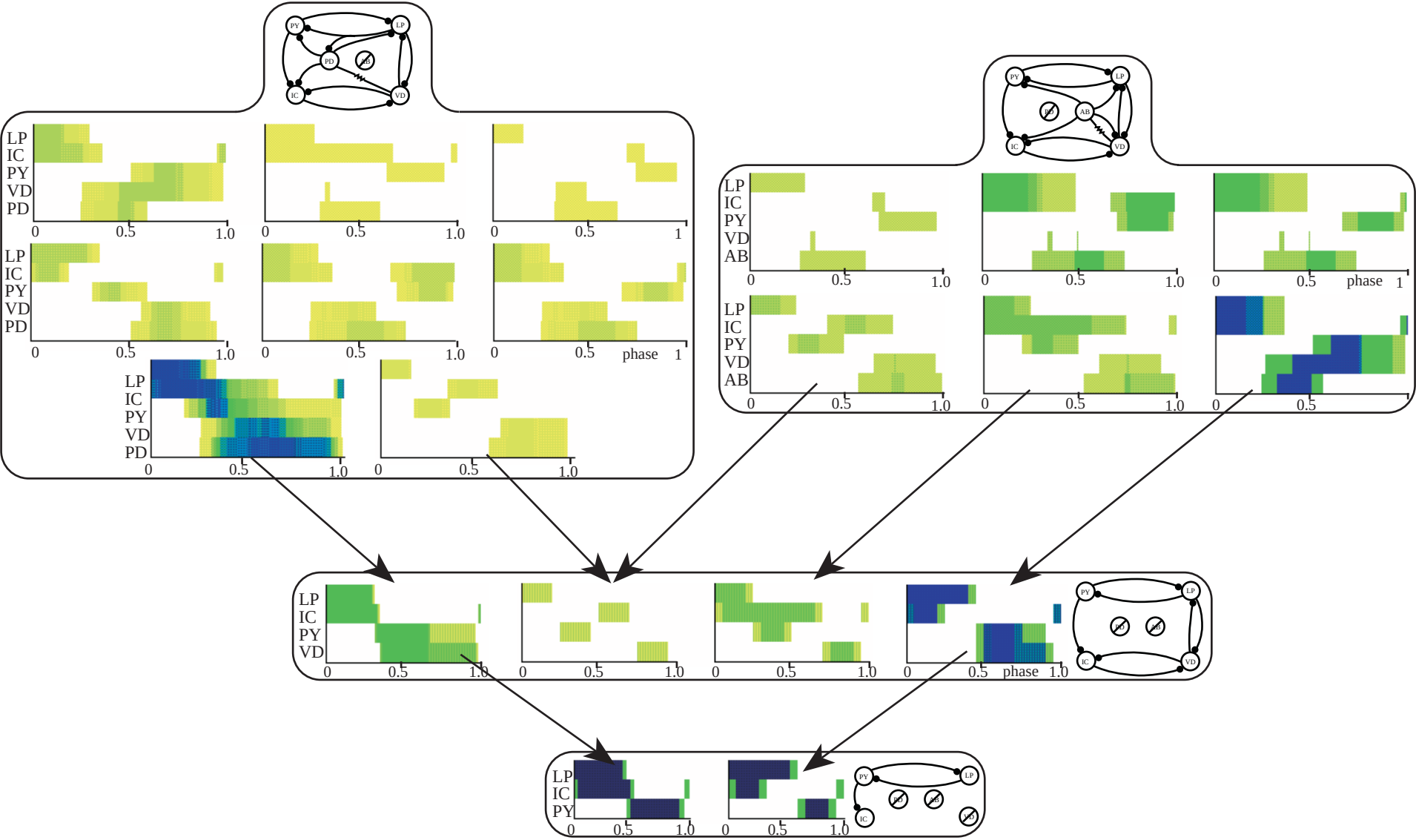


Fig. 8

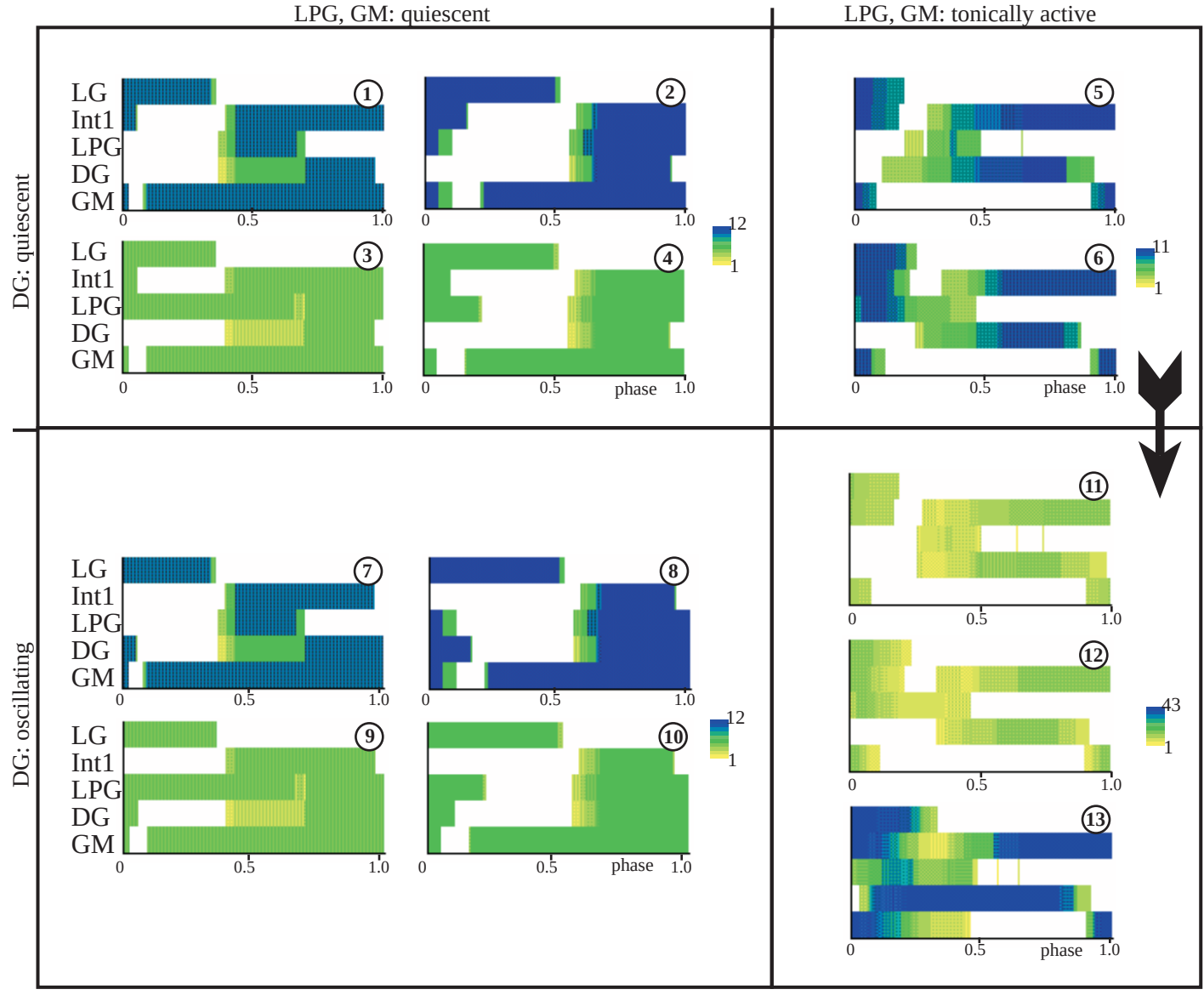

LPG, GM: quiescent
LPG, GM: tonically active
DG: quiescent
DG: oscillating
LG
Int1
LPG
DG
GM
1
2
3
4
5
6
7
8
9
10
11
12
13
0
0.5
1.0
phase
12
1
11
43

Fig. 9