The role of ongoing spatio-temporal activity on shaping responses to inputs in biological networks

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Abstract

Biological systems such as networks of neurons are able to produce a wide range of intrinsic patterns such as waves and synchronous oscillations. On the other hand, these systems must constantly respond to external stimuli. The goal of this project is to find conditions generating complex spatio-temporal activity in these networks networks and then use various mathematical tools to examine how these dynamics affect responses to extrinsic activity such as noise or patterned inputs.

Biological systems are built in order that they can respond rapidly to external signals on time scales ranging from milliseconds to months. (Here I am not talking about evolutionary time scales, but those that occur in the ordinary lifetime of an organism.) In the most general setting, we can regard the response as obeying some (non-autonomous) differential equation where the external inputs are either independent of the response or perhaps, themselves, depend on the response. The "internal" state of the organism plays an important role in shaping the response to the external signal and thus, I am, first interested in what unperturbed internal responses can be. I will present two examples from previous work that I have done and then discuss nwe research that I want to pursue.

Flicker phosphenes. When exposed to diffuse flickering light, the human subjects will often perceive complex geometric patterns called *flicker phosphenes.* Similar patterns are produced by pressure on the eyes and in the early stages of drug-induced hallucinations. In [3] we showed that a network of spatially distributed excitatory and inhibitory neurons of the form:

$$\begin{aligned}\tau_e\frac{\partial u}{\partial t}+u &= F(K_{ee}(x)*u-K_{ie}(x)*v+I_e(x,t)) \qquad (1)\\ \tau_i\frac{\partial v}{\partial t}+v &= F(K_{ei}(x)*u-K_{ii}(x)*v+I_i(x,t))\end{aligned}$$

was able to produce this type of pattern only when various internal dynamics occurred in the system. Here u, v are the excitatory and inhibitory neuron populations and $K(x)*u$ means the spatial convolution of K with u. In the

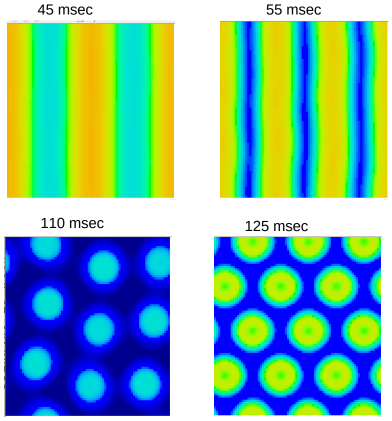

Figure 1: Patterns in a square domain with low frequency and high frequency flicker

case of flicker phosphenes, I is a uniform periodic input. Figure 1 shows sample simulations of the network on a square domain. We showed that when there was a stable spatially homogeneous rest state, $(\bar{u}, \bar{v})$, such that it was in the so-called "inhibitory-stabilized" state [6], then we could obtain spatially complex patterns from uniform inputs. Key to this response to the external stimulus was the fact that the internal dynamics without inputs had damped oscillatory responses and had certain kinds of spatial coupling.

Flocking with predators. In the second example, I consider the effect of a predator on the flocking behavior of prey. A simple model for flocking of animals involves rules in which each individual wants to maintain a certain distance between itself and others yet not be too far away. If x_i is the spatial position of the organism (x could be in any space dimension, although, typically, 2 dimensions), then a standard model [5] for flocking has the form

$$\frac{dx_i}{dt} = \sum_{j \neq i} K(|x_i - x_j|) \frac{x_j - x_i}{|x_j - x_i|}$$

where $K(r)$ is negative for small r and positive for large r. Thus, if the distance between organisms is too small, then they repel each other, otherwise, they attract. In general, this model forms a compact swarm where all the individuals group together but maintain a finite distance between them. The internal dynamics is completely determined by the function $K(r)$. We have recently explored what happens when a predator is introduced. It's position is y and we assume that the predator repels the flock and is itself attracted to the flock. In one spatial dimension, we have found that there are multiple stable states such as the predator in the middle or the predtor on the outside chasing the flock.

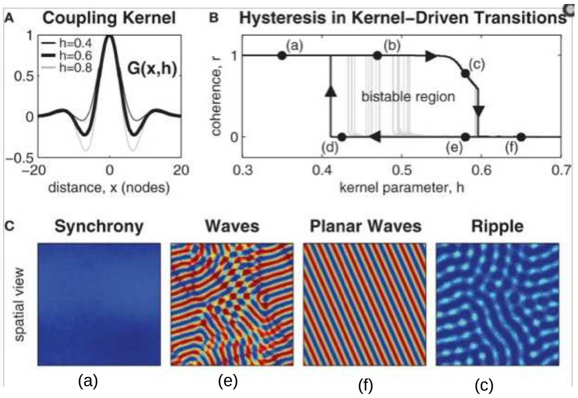

Figure 2: Modulation of the surround inhibition (h) shon in (A) results in different bifurcations of waves and synchrony. (B) shows the global coherence as h varies and (C) some representative spatial patterns.

However, as the attraction of the predator increases, oscillations occur. Believing that this was an artifact of using one space dimension, we have explored the effects of the prey in two-dimensions. We find the former behaviors still hold, but, no oscillations. Surprisingly, we found that if there were certain members of the flock that were more or less attractive to the predator, then the flock oscillations returned. Key to determining which of these responses occurs is the internal flock dynamics in absence of the prey.

While these examples come from quite different biological systems and occur on vastly different scales, there is much similarity in the underlying mathematics, namely, spatio-temporal pattern formation. I have several ongoing projects which involve the interactions between intrinsic ongoing dynamics and external stimuli.

Waves and stimuli Wavelike activity is ubiquitous in the cerebral cortex [8] especially in the motor cortex [7]. The waves take several forms including fronts that represent transitions between up and down states and periodic wavetrains. The latter can be modeled by networks of rhythmically firing neurons and form into so-called plane waves whose direction can serve as a code for motor movements. We have recently explored how the direction of these waves can me modulated and controlled via external inputs into different subpopulations of neurons. (see figure 2). These neurons control the inhibition in the network and the depth of that inhibition controls the stability of ongoing synchronous oscillations. Whwn the synchronous state becomes unstable, it produces the desired waves and their direction is controlled by the active excitatory connections. Thus it is possible to turn off and on the waves and produce (through the appropriate decoder network) the desires outputs. Possible feedback from this network to the inputs could be used to sharpen the transition from synchrony

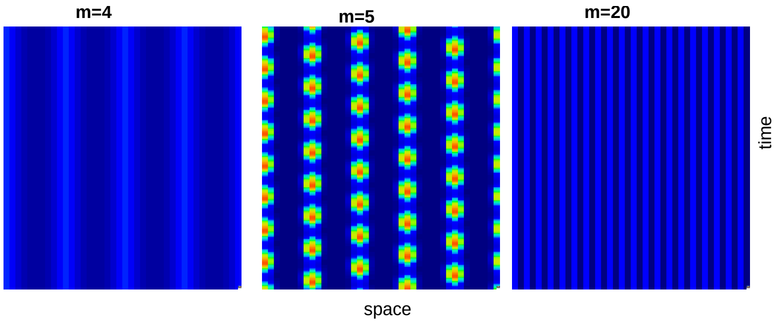

Figure 3: Spatial resonance leading to flicker in a 1-dimensional network. Cosine waves of various spatial frequencies can produce oscillatory instabilities.

and to reduce errors [2].

With my former postdoc, Jonathan Touboul, we have started to look at how external broad-band signals (e.g. noise) interacts with ongoing wave-like activity. We have preliminary results showing that noise acts nonlinearly on the macroscopic activity of large neuronal networks, and as such, modifying noise levels can induce transitions (bifurcations) related to qualitative observable changes in the activity. Since noise is ubiquitous in neural and biological systems, it is important to see how this noise can be harnessed and controlled and to see how it affects these nonlinear spatially extended networks.

Interactions with spatial patterns In previous work, we have examined how temporally patterned stimuli (rhythmic) interact with the ongoing activity in cortical networks to produce spatially structured patterns of activity. The converse of this question is what kinds of activity can be induced by spatially patterned activity. Such questions have been explored in the context of of orientation tuning in the visual cortex [4] but not so much in the case of spatially structured activity. For example, viewing a high contrast striped pattern will produce a sense of flickering in normal subjects and can sometimes produce discomfort in susceptible patients [1]. Thus, we have begun exploring the interactions of networks of the form (1) in the presence of spatial grating in one- and two-dimensions. We have preliminary results that indicate the amplification and instability of certain spatial frequencies. Figure 3 illustrates an example where the network is sensitive to intermediate spatial frequencies ($m = 5$) but not high and low spatial frequencies. In addition to interactions with regular stimuli, we have begun to explore the consequences of locally correlated inputs on networks with disorganized ongoing activity. Feedforward synchronization of activity has been studied in "all-to-all" networks, but there have been few if any studies on the dynamics of spatially distributed networks.

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