Canonical Models in Mathematical Neuroscience

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Abstract. Our approach to mathematical neuroscience is not to consider a single model but to consider a large family of neural models. We study the family by converting every member to a simpler model, which is referred to as being canonical. There are many examples of canonical models [7]. Most of them are derived for families of neural systems near thresholds; that is, near transitions between the rest state and the state of repetitive spiking. The canonical model approach enables us to study frequency and timing aspects of networks of neurons using frequency domain methods [6]. We use canonical (phase) models to demonstrate our theory of FM interactions in the brain: Populations of cortical oscillators self-organize by frequencies [6]; same-frequency sub-population of oscillators can interact in the sense that a change in phase deviation in one will be felt by the others in the sub-population [7]; and oscillators operating at different frequencies do not interact in this way. In our theory, sub-networks are identified by the firing frequency of their constituents. Network elements can change their sub-population membership by changing their frequency, much like tuning to a new station on an FM radio. Also discussed here are mechanisms for changing frequencies obtained in our recent work using similar models to study spatial patterns of theta and gamma rhythm phase locking in the hippocampus.

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A promising approach to mathematical neuroscience is to consider not a single neural model but a large family of such models. A reasonable way to study such a family is to convert every member to a simpler model by a continuous (possibly non-invertible) change of variables. We refer to such a simple model as being canonical for the family [7]. We present here a few examples of such families and their canonical models.

1 Neural Excitability

Most neurons are at rest, but they can fire repeatedly when stimulated. If the emerging firing pattern has very low frequency, then the neuron is said to exhibit

Class 1 neural excitability [5]. If it starts with a high frequency, it is said to exhibit Class 2 excitability.

The transition from rest to oscillatory firing as the stimulus is increased is a bifurcation. A typical bifurcation corresponding to Class 1 excitability is the *saddle-node on limit cycle* (SNLC) bifurcation. The family of all neural systems having this bifurcation has the canonical model

$$\theta' = (1+\cos\theta) + (1-\cos\theta)\lambda\ , \qquad \theta \in S^1\ , \tag{1}$$

where λ is the bifurcation parameter that characterizes the stimulus [4, 7].

A typical bifurcation corresponding to Class 2 excitability is the *supercritical Andronov-Hopf* (AH) bifurcation. The family of all neural systems having this bifurcation has the canonical model

$$z' = (\lambda + i)z - z|z|^2\ , \qquad z \in C\ , \tag{2}$$

which is a topological normal form for the bifurcation. Notice that (2) is local in the sense that a continuous change of variables that converts a dynamical system into (2) is defined is some small neighborhood of equilibrium. The canonical model (1) is not local in this sense. Many other canonical models for neuroscience applications are derived in [7].

2 FM INTERACTIONS IN PHASE MODELS

Rhythmic behavior is ubiquitous in nature and especially in the brain. Since we do not know (and probably will never know) the exact equations describing any neural system we consider a family of brain models of the following general form

$$x_i' = f_i(x_i) + \varepsilon g_i(x_1, \dots, x_n, \varepsilon)\ , \qquad x_i \in R^m\ , \tag{3}$$

where each x_i describes activity of the ith neural element (neurons, cortical columns, etc.), and the dimensionless parameter $\varepsilon \geq 0$ measures the strength of connections. Many neuro-physiological experiments suggest that ε is small; see discussion in [7].

When each neural element exhibits oscillatory activity; that is, when each subsystem $x_i' = f_i(x_i)$ in (3) has a limit cycle attractor, then the weakly connected system (3) can be transformed into the canonical (phase) model

$$\theta_i' = \Omega_i + \varepsilon h_i(\theta_1, \dots, \theta_n, \varepsilon)\ , \qquad \theta_i \in S^1\ , \tag{4}$$

by a continuous change of variables. Here $\Omega_i > 0$ is the frequency, and θ_i is the phase of the ith oscillating element.

The phase model (4) can be simplified further depending on the presence of resonances between the frequencies $\Omega_1, \dots, \Omega_n$. For example, when the frequencies are non-resonant and some other technical conditions are satisfied, each connection function h_i can be transformed into a constant. This implies that such oscillators do not interact even though there are synaptic connections between them; i.e., even though the functions g_i are non-constant in (3). A detailed analysis [7, 8] shows that the interaction between oscillators is most effective when their frequencies are nearly identical, less effective when the frequencies are nearly low-order resonant, and practically non-effective otherwise.

Since this result was obtained for the canonical model (4), it can be applied to an arbitrary neural system of the form (3) regardless of the details of the mathematical equations. This universality suggests a far-reaching biological principle: The existence of synaptic connections between two neurons or two cortical columns does not guarantee that the they interact. To interact they must establish a certain low-order resonant relation between their frequencies. We say that interactions are frequency modulated (FM) in this case.

We see that an entire network can be partitioned into relatively independent ensembles of neurons processing information on different frequencies (channels). Each neuron can change its membership simply be changing its frequency. Thus, the entire brain can reconfigure itself by changing the frequency of oscillations of its units without changing the efficacy of synaptic connections (the wiring).

Finally, we notice that when the frequencies are chosen appropriately, the neural elements interact through modulation of the timing of their spikes. Therefore, the brain might employ FM radio principles: The frequency of neural rhythmic activity does not encode any information other than identifying the channel of communication; the information is carried by phases.

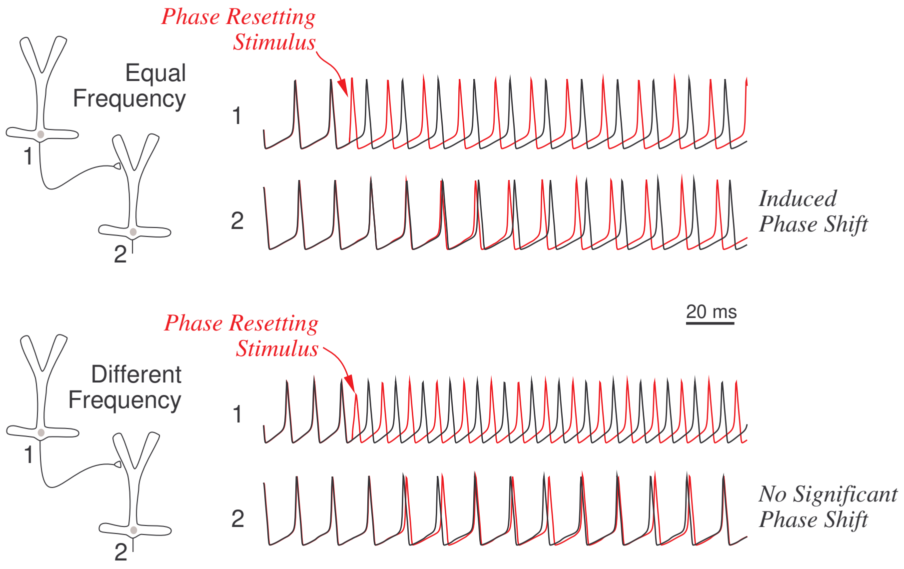

Figure 1: Temporal integration of a periodic input depends on the frequency of the input. *Upper part:* Neurons have identical frequencies. If a brief strong stimulus is applied to neuron 1 to change its phase, then neuron 2 can "feel" the change by acquiring a phase shift. *Lower part:* Neurons have different frequencies (close to the resonance 4 : 5.) The post-synaptic neuron is relatively insensitive to

the phase of the pre-synaptic one. (These simulations are based on space-clamped Hodgkin-Huxley equations.)

3 THE HIPPOCAMPUS

Similar methods are used to study the hippocampus and its role in information processing [1, 2]. In this, the three dimensional structure of the CA1, CA3 and DG regions of the hippocampus and their inputs from the medial septum and the entorhinal cortex are modeled by lumping the continuum model into discrete segments. These segments do not necessarily correspond to anatomical features of the hippocampus; they result from standard mathematical analysis. The model is

$$\dot{x}_j = \gamma + \cos x_j + (1 - \cos x_j)(\cos\phi_j(t) + \cos\psi_j(t) + \sum_{i=1}^{N} C_{i,j}V(x_i))$$

where

- γ is the gamma-rhythm frequency ($\approx 40Hz$).
- x_j is the phase of the j^{th} segment.
- ψ_j is the phase deviation of the input to the j^{th} segment from the entorhinal cortex. This is taken to be a theta-rhythm ($\approx 5Hz$) having phase deviations increasing along the array of sites from the right, so $\psi_j(t) = \omega t + j\Delta + \Phi$ where Δ is the propagation time of stimulation from one segment to the next.
- ϕ_j is the phase deviation of the input from the medial septum to segment j: $\phi_j(t) = \omega t + (N - j)\Delta$
- Φ indicates the difference in timing between the two inputs.

This system is depicted in Figure 2.

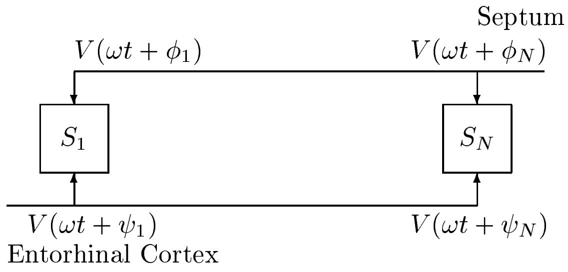

FIGURE 2: A segment model comprising N identical segments that have inputs from the Septum and from the Entorhinal Cortex, that have a fixed wave form (V), a fixed frequency (ω) and a phase deviation (ϕ_j or ψ_j). The phase differences along the line are $\phi_j - \psi_j$ for $j = 1, \cdots, N$.

The value Φ is the key control variable, and we show in [1] that as Φ increases through 2π various patterns of phase locking to the theta rhythm occur in the model; the other segments oscillate at near the gamma rhythm. Thus, Φ is encoded in a spatial pattern of theta-rhythm activity. Figure 3 shows typical power-spectrum densities resulting from a simulation of 64 segments. Note that there is for the choice of Φ used here an interval of segments that are locked at the theta rhythm while the remaining segments oscillate at or near the gamma rhythm. Changing Φ changes the pattern of theta-rhythm oscillations. So, the firing frequency of individual cells can be changed by external forcing (here Φ) that is applied uniformly to the entire network.

Each of these phase variables has an asymptotic limit of the form $x_j \to \rho_j t + \phi_j(t)$ where ρ_j is the asymptotic frequency (rotation number) and $\phi_j(t)$ is the asymptotic phase deviation. This result is the basis of the rotation vector method which is discussed later.

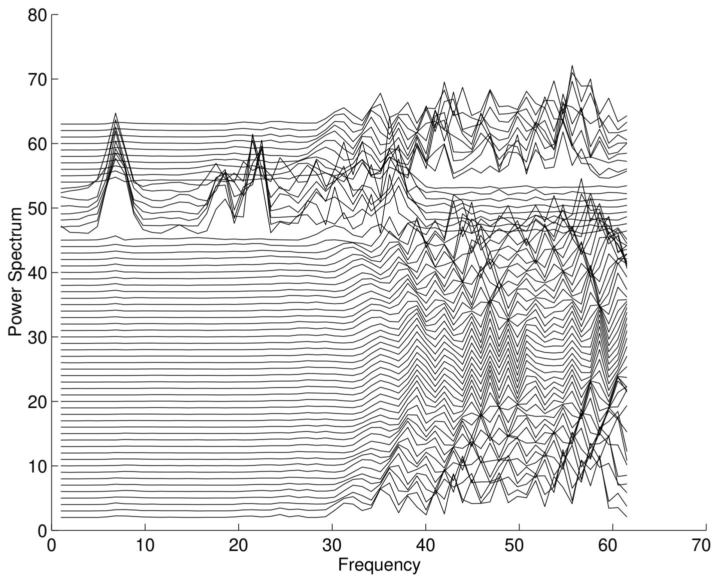

Figure 3: Power spectrum of 64 segments. There is an interval of segments having frequency $\approx 5Hz$, and the rest are near $40Hz$.

A sequence of input phases Φ_k can be memorized by adaptive connections within the structure. Lateral connections along the longitudinal axis of the hippocampus are modeled as before (Equation (??)), but now the connection strengths C change in response to correlation between pre- and post- synaptic activities:

$$\Omega \dot{C}_{i,j} + C_{i,j} = K \sin x_i \sin x_j$$

where K is a mixer gain and Ω is a time constant for a synapse. The matrix C accumulates memory traces, and it forms a slowly changing record of memorized states and transitions between them. In particular, this matrix can learn a sequence of input control variables $\Phi_1, \Phi_2, \cdots, \Phi_M$, and the resulting matrix has a left to right structure that can be used to recall this sequence. This is short term memory in the circuit.

In addition, this matrix C serves as the basis for studying recall of information in the presence of random noise. Its structure reflects the connections that correspond to memorized stimuli and to the transition from one memory to the next. This form can be abstracted into a Markov chain, and it can be studied by methods for Markov chains in random environments [1, 9].

4 Discussion

We will never know a complete model of any brain structure, no matter how small. However, a powerful aspect of mathematics is that (usually) quite simple models can accurately describe aspects of broad ranges of physical and biological systems. In particular, the approach we have developed for mathematical neuroscience is based on canonical models [7]. Care must be taken in interpreting and applying results obtained using canonical models, but a principal goal of this work is to suggest experiments and alternate ways of interpreting experimental data. Some outcomes of this approach are the use of VCONs to process voltage recordings from electrodes in behaving animals and the use of Markov chains to describe navigation by behaving rats.

Patterns of phase locking in networks of VCONs can be determined using the rotation vector method [6]: The vector $\vec{x}$ describes the phases in an entire network. If this population is in synchrony, then the phases have the form $\vec{x} \to \omega \mathbf{1} t + \vec{\phi}(t)$ where ω is the common frequency, $\mathbf{1}$ is the vector of all ones, and the phase deviations $\vec{\phi}$ are less significant in the sense that $\vec{\phi}(t)/t \to 0$ as $t \to \infty$. In FM radio, ω identifies the sending station and $\vec{\phi}$ carries the signal. We have shown here how two cells that are in synchrony can interact by demonstrating that a change in the timing of one will induce a change in the timing of the receiver. We propose that this is a fundamental mechanism for propagating and processing information in the brain. Using this approach, we can derive a system of equations for the phase deviations $\vec{\phi}$, and results of Liapunov and Malkin can be combined with singular perturbation methods to determine energy surfaces that govern the dynamics of $\vec{\phi}$ [6].

The illustrations from our hippocampus model suggest that there are many possible mechanisms for cells to change their firing frequency; for example, as described here through external oscillatory inputs or through chemical modification by hormones, neurotransmitters, etc.

The systems approach described here is based on canonical models, and it brings out possibilities for FM interactions and communications in brain structures by describing how a network can process such complex data in parallel.

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