The dynamical and structural properties of a random neural network are affected by its directed assortativity profiles

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One of the topological parameters of greatest interest when studying complex networks is the degree-degree correlation or degree assortativity because it gives information about the structure of the network [1]. This parameter can be obtained by using either the Pearson correlation coefficient or the Spearman’s rho [2]. The degree correlations between nodes were first defined for undirected networks and later extended to directed networks [3], therefore giving place to a set of four assortativities (labeled in-in, in-out, out-in and out-out) known as the assortativity profile (AsP). However, most of the methods used to characterize a network were developed for undirected networks and there is little literature focused on the study of structural properties of directed networks.

In this work, we first numerically address the effects of the AsP over network-structure related quantities as the average path length and algebraic connectivity. We show that there are interdependecies between the four assortativities of the AsP and obtain network realizations exhibiting the highest correlation values that can be reached for each profile. Secondly, in order to explore the impact of directed assortativity on neural networks, we took a model of stochastic binary neurons interacting with fixed coupling strength under background noise [4]. Finally, we calculate the AsP of networks as taken from real brain networks available at several scales: at neuroanatomical from the rat BAMS connectome project and at cell scale from mouse retina, and compare their dynamics under the same model.

To reach our first goal, we generated random graphs with sparse connectivity from gaussian degree distributions and exhibiting none-degree correlations, which we used as null models. Then, we evolved the network by degree preserving rewiring schemes of higher order [1, 5] as the key feature to expand the graph-space and obtain profiles that can not be reached by a standard 2-swap methods. Therefore, the network realizations were tuned to exhibit any possible assortativity profile with increased or decreased values of pearson coefficients and Spearman’s rho.

We remark that important experiments in barrel cortex in rodents [6] have unravel notable properties of real neural networks, namely their ability to detect very small stimuli while maintaining stable stochastic activity under normal conditions. Moreover, recent findings on clustered neuronal cultures have shown the presence of assortativity giving shape to a connectivity backbone which constitutes an intrinsic survival mechanism for the cultures [7]. Our results shed light on how these functional properties (stability and sensitivity) can be accomplished with different assortativity profiles in real neural networks.

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References
Extending Spectral Sparsification of Graphs

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The brain is a large, complex system with an enormous range of scales and unknown variables. To make progress in understanding its behavior, mathematical models must make simplifying assumptions. A common theme of several classes of models is representing neural activity as dynamics on some graph, with nodes representing neural ensembles, and edges communication between them. More generally, a common theme of many biological systems is the appearance of complicated pathways that produce a relatively simple result (e.g. protein activation pathways), and semantic understanding comes from the reduction of these subsystems to their resulting behavior (e.g. this protein activates a chain that eventually inhibits X), a sort of “coarse-graining” of the system that preserves the relevant structure. Here, we consider how a generalization of graph sparsification might be used to reduce the complexity and computational cost of graphical models.

How might one “compress” a graph? That is, given a graph $G$, how might one generate a reduced graph $\tilde{G}$ that approximately preserves the structure of the original graph $G$? A prototypical example of such an approximation are the Ramanujan graphs, which effectively mimic the connectedness of the corresponding (same vertex set) complete graph. In fact, the spectrum of the graph Laplacian $L(G) = D - A$ is frequently used to characterize graph connectedness (e.g. Cheeger’s inequality), and the Ramanujan graphs are optimal, in the sense that they have a spectral gap almost as large as possible. This inspired Spielman & Srivastava [2] to consider whether such sparsification could be done (and efficiently) for arbitrary graphs. They constructed a fast algorithm for reducing the number of edges of any graph while approximately preserving the Laplacian quadratic form $x^T L x$. Their algorithm involves calculating the “effective resistance” to obtain a measure of the relative importance of an edge. This suppresses the deletion of spectrally important edges, encouraging instead the downsampling of more redundant edges.

This algorithm is similar in spirit to that of parameter reduction of sloppy models by Transtrum et al. [1]. Sloppy models are those in which the behavior is insensitive to perturbations along many directions in parameter space, and only a much reduced subset of parameter space is actually relevant to the output of the model. Parameter reduction can be performed by moving along these sloppy directions until one reaches a boundary in parameter space. Indeed, this algorithmic reduction is a powerful tool for making sense of complex systems. E.g. Transtrum et al. [1] distilled a tangled web of protein interactions into a comprehensible reduced diagram, removing unimportant components, summarizing relevant pathways, and preserving feedback loops important for fitting the data. The connection to graph sparsification is as follows: the parameters are the weights of the edges, the outputs are the Laplacian spectral properties of the resulting graph, sloppy directions correspond to perturbations on the weight of spectrally unimportant edges, and edge deletion is a case of parameter reduction.

The primary motivations of Spielman & Srivastava [2] proposed graph sparsification were computational: reducing memory requirements and accelerating numerical methods. Indeed, edge deletion assists in these endeavors. However, the capabilities of parameter reduction may not be fully realized with edge deletion alone; an alternative boundary in parameter space is the limit of infinite edge weight. In the case of the graph Laplacian, this has the clear physical meaning of edge contraction: as the connection between a pair of nodes becomes infinitely strong, they behave as though they were effectively the same. As edge deletion and edge contraction are dual operations with respect to the associated graphical matroid, this suggests the search for a dual analogue of the importance of an edge. In this work, we propose to generalize the concept of “effective resistance” and its use in sparsifying graphs. In particular, we show that this quantity can be neatly expressed in terms of differential geometry, specifically, the importance of an edge is give by the operation $d(\delta d)^\dagger \delta$, where $d$ is the differential, $\delta$ is the codifferential, and $\dagger$ is the pseudoinverse. We propose that generalizations of this expression can be used to obtain the importance of an edge with respect to its dual operation (edge contraction), or with respect to other relevant matrices, such as the adjacency matrix, Bethe Hessian[3], and nonbacktracking operator.

References
Spatiotemporal dynamics and computations in spiking neural networks

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Randomly connected networks of spiking neurons provide a parsimonious model of neural variability [5, 2], but are unreliable for performing computations. We show that this difficulty is overcome by incorporating the well-documented dependence of connection probability on distance. Spatially extended spiking networks exhibit symmetry-breaking Turing-Hopf bifurcations to generate spatiotemporal patterns. We show that standard integro-differential firing rate equations cannot capture the history-dependence of rate dynamics in spiking networks and therefore do not predict the bifurcations we observed. We instead derive an integral equation that more accurately represents rate dynamics in spiking networks and predicts the emergence of Turing-Hopf bifurcations observed in simulations. The resulting spatiotemporal dynamics impart spiking neural networks with the ability to perform dynamical computations while maintaining the ability to track network input [4].

Biological neuronal networks exhibit irregular and asynchronous activity that is often modeled using spiking networks with approximate excitatory-inhibitory balance, but these models have limited utility for performing computations. On a local level, spikes are too irregular, making computations unreliable. On a larger scale, the activity of the network is reliable, but merely tracks input. How do neural circuits produce intricate yet still reliable dynamics useful for computation? One possible solution is to use spatially-extended networks with a distance dependent connection probability, as is widely reported in neural recordings. In such networks, local inhibition produces spatially uniform, Poisson-like spiking while broad inhibition produces intricate, asymmetric spatiotemporal activity patterns. A common approach to modeling dynamics in spatially extended networks is through equations of the form

\[ \tau \frac{d\bar{r}}{dt} = -\bar{r} + \phi \left( \int_{\Gamma} W(y)\bar{r}(x-y,t)dy, \int_{\Gamma} U(y)\bar{r}(x-y,t)dy \right) \]  

or similar forms [1]. While this approach captured the steady-state firing rates in spiking networks with local inhibition, it did not capture the patterns that emerge with broader inhibition. A generalization that accounts for the history-dependence of firing rates in spiking neurons produces an integral equation of the form

\[ \bar{r}(x,t) = \int_{\Gamma} \int_{0}^{\infty} A(\tau)W(y)\bar{r}(x-y,t-\tau)d\tau dy + \int_{0}^{\infty} B(\tau)U(y)\bar{r}(x-y,t-\tau)d\tau dy. \]  

Transitioning to the temporal Laplace and spatial Fourier domains gives

\[ \text{det}[\hat{A}(\lambda)\hat{W}(n) + \hat{B}(\lambda)\hat{U}(n) - \text{Id}] = 0 \]  

where \( \text{Id} \) is the 2 by 2 identity matrix, \( \hat{W}(n) \) and \( \hat{U}(n) \) are Fourier coefficients of \( W(u) \) and \( U(u) \), and \( \hat{A}(\lambda) \) and \( \hat{B}(\lambda) \) are matrices of susceptibility functions, which can be computed under a diffusion approximation using a Fokker-Planck formalism [3]. Solutions, \( \lambda \), to Eq. (3) are eigenvalues of the rate dynamics and the associated Fourier modes, \( n \), are eigenmodes. Broad inhibition introduces complex eigenvalues with positive real part at non-zero spatial modes, indicating a Turing-Hopf bifurcation. This bifurcation produces intricate firing rate dynamics that implement high-dimensional transformations on external input to the network. Due to the symmetry-breaking properties of the bifurcation, these transformations are only reliable across trials when external input is spatially heterogeneous. In this case, the network can be trained to implement non-trivial dynamical computations using a reservoir computing framework.

References

Consequences of different network topologies for the dynamical stability of the network and its correlations

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Structural changes in a recurrent neural network may cause the system to change its dynamical properties or even get unstable. The influence of several parameters contributes and to control the stability it is important to understand the various effects. For that reason, analytic expressions for stability conditions are investigated in order to make quantitative predictions based on network parameters. Dynamical stability of a recurrent network model can, for example, be studied in terms of the eigenvalue spectrum of the coefficient matrix of an associated linearized firing rate equation. Since a network is stable if, and only if all eigenvalues have a negative real part, sets of critical parameters can be deduced from explicit expressions for limiting eigenvalue distributions. Therefore, methods from random matrix theory are applied to describe explicitly the density of the spectrum. Aside from the limiting distributions of the eigenvalue spectra, the quantitative dependence of correlations on the network structure is studied. For this purpose, a method based on functional integrals is used. The results for the linear stability prediction demonstrate the dependence of the limiting distribution on different network structures and it remains to resolve the open question whether these distributions can be related to the functionality of the network. The functional integral approach for the correlations end up with having an explicit expression for the network-averaged covariance in terms of structure parameters.

Both parts aim for necessary or even sufficient quantitative conditions on the parameter set of a neural network to become dynamically unstable or highly/weakly correlated and try to relate this dynamical behaviour to certain brain diseases. So far, statements about linearized models can be made, but a natural next step would be to investigate the systematic generalization of the functional integral approach to non-linear interactions.
Structural and dynamic properties of neural networks with robust associative memory recall in the presence of fluctuations in neuron firing

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Neural networks in the brain have the ability to function reliably despite various sources of noise in synaptic transmission. Therefore, each neuron in the network must be robust to (i) presynaptic noise, such as failure in generation or propagation of action potentials and spontaneous firing, (ii) synaptic noise, such as fluctuations in synaptic strength, and (iii) postsynaptic noise, which includes fluctuations in postsynaptic potential and threshold of firing. In this study, we investigate memory storage in the presence of presynaptic noise and examine the effects of robustness in memory recall on structural and dynamic properties of the network.

Specifically, we train recurrent networks of McCulloch and Pitts neurons on predefined temporal sequences of network states. The probability of successful learning decreases with sequence length, and at the probability of 0.5 the network is said to be at a critical state. Since, memory recall must be robust with respect to fluctuations in neuron firing, each neuron in the network must learn to correctly associate noisy input patterns, within some Hamming distance $h$ of the original inputs, with the desired outputs. Parameter $h$ in this model characterizes the degree of robustness of neurons to input fluctuations. We use the replica theory from statistical physics [1,2], as well as numerical simulations to determine the memory storage capacity of robust, critical networks and examine structural and dynamic properties of such networks as function of $h$.


Inferring Latent Variability in Neural Populations from Calcium Imaging

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Note: Not to be considered for oral presentation.

Calcium imaging is a modern experimental method capable of observing the activity of hundreds of neurons in vivo. Much work currently focuses on using this data to infer the network connectivity of biological neural circuitry [5]. However, many of these approaches are affected by the common input problem under which direct connectivity is difficult to distinguish from latent variability (common input from unobserved neurons). We examine the extent to which the common input problem can be resolved by combining calcium recordings with electrophysiological data to untangle the effects of connectivity and latent variability on the covariance structure of neural populations.

By reviewing three common models of neural activity with biased latent variability (common input from unobserved neurons), we show that the mathematical results for the cross-covariance functions share a similar algebraic structure [2] [4]. Unfortunately, this similar structure does not allow exact connectivity to be recovered from the covariance alone. While very little can easily be said about fully recovering functional connectivity in these paradigms [1], we can make statements by averaging the covariance matrix over cell types. This yields simple expressions for the relationship between latent covariability, connectivity and spike train correlations in the mean-field. [6]

By assuming the network to have an approximate Erdős - Rényi structure, our problem reduces to inferring the parameters of high-dimensional stochastic processes. Using electrophysiologically determined values for connection probabilities and strengths [3] to constrain the degrees of freedom, we present an equation to infer the average amount of latent variability projecting to each sub-population according to cell-type (determined by parvalbumin expression). We further apply the theory to real calcium imaging data from mouse L23 visual grating experiments. The results imply that PV neurons in these areas receive much more latent input over large distances.

References
Determination of the spike-train second-order power spectrum statistics in heterogeneous spiking networks

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Spike-trains produced in recurrent neural networks are in general of non-Poissonian nature as revealed by their non-white (colored) power spectrum. Nevertheless, most theoretical studies are based on the assumption that the stimulus delivered to a single-neuron has a Poisson nature, consequently missing temporal correlations. For instance, the standard Fokker-Planck approach in its simplest version assumes that single neurons are stimulated by white Gaussian noise.

If we assume that the major source of noise received by any neuron in the network comes from the quasi-random input from other cells, we encounter the following problem of self-consistency for a heterogeneous network: for neurons arbitrarily picked in every population of the network, the input spike-trains should have the same second-order statistics of the output spike-train per population. By self-consistency, temporal correlations should be preserved.

We investigate this self-consistency by using an extended version of an iterative scheme proposed by Lerchner et al. [1] and extended by Dummer et al. [2]: instead of simulating a network, we simulate one single neuron for each population over several generations injecting surrogate noise input with the same second-order statistics of the output of the previous generation. We show that the power spectrum statistics converge to a self-consistent result when the mean input is close to balance. The neurons were modeled as leaky integrate-and-fire neurons [3]. We compare our results with a large random sparsely connected network of leaky integrate-and-fire neurons [4].

References


Fractional order excitable neural system with bidirectional coupling

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Fractional-order dynamics are applicable to biological excitable systems with strong interactions or systems with long-term memory effect. The activity of neural membrane voltage depends on the long-range correlations of conductance. Such a behavior of the membrane voltage with long-range correlation can be better described with a fractional-order dynamics. A fractional-order coupled modified three dimensional (3D) Morris-Lecar (M-L) neural system has been presented to show the variations in the firing patterns from resting state → oscillatory pattern → bursting and the synchronous behavior by designing a bidirectional coupling mechanism. The fractional exponents are lying between 0 and 1. The predominant controller of the changes of firing behavior is the fractional exponent. The stability of synchronization and nature of the fractional system dynamics have been analyzed. To make the investigations more convincing and biologically plausible, we consider a network of M-L oscillators with bidirectional synaptic coupling functions using global type connections and present the effectiveness of the coupling scheme.

In this article, the behavior of the coupled fractional-order M-L model have been investigated using the bidirectional coupling method: nonlinear open loop controller. The relationship between the integer order and fractional-order systems are analyzed. First, the stability and coupling mechanism of the fractional order neural system are presented. To observe the synchronization effect, we also consider a network of fractional order M-L system with bidirectional synaptic coupling functions using global type connections. Our results show that the fractional order coupled neural systems can better synchronize at certain fractional exponents. It can be extended to show the targeted synchronous state for a large network of such type oscillatory M-L neurons as well as other types of excitable neural systems with bidirectional coupling mechanism.

We investigate the dynamical behavior of the two types of planar burster using fractional exponents. The integer and corresponding fractional order M-L system are analyzed using the dissipativity condition and LEs (Lyapunov Exponents). The associated fractional order system is examined based on FRH (Fractional Routh Hurwitz) stability criterion. The dynamical characteristic of the neural system depicts the changes in the firing behavior from resting state → simple oscillatory behavior → bursting patterns at various fractional exponents which has been increased from 0.8 to 1.

The driver-response coupled fractional order M-L system are investigated by designing a bidirectional mutual coupling technique based on nonlinear open loop controller scheme to achieve the synchronization state. Synchronization analysis has potential applications in fractional order neural systems as the fractional order systems preserve the long term memory effect. The significance of this work is that the bidirectional coupling mechanism is applied in bursting M-L neurons and the targeted synchronized behavior is achieved for certain values of fractional exponents. The neuronal network with chemical type coupling can be made bidirectional by considering the electrical coupling functions in the network. It can be extended to show synchronous behavior for a network of such type fractional order commensurate as well as incommensurate M-L neurons with bidirectional coupling and other type interesting network connections with suitable coupling strengths which presents synchronous behavior at certain fractional exponents.

References
Period doubling bifurcation transitions in synchronous model neurons

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Period-doubling bifurcation cascades are known to mediate transitions between periodic and chaotic states in nonlinear dynamical systems. This goes back to the primordia of chaos theory, including Feigenbaum’s seminal work demonstrating that the constant ratio between consecutive windows of periodicity in the bifurcation diagrams, before the onset of chaos, occurs in a wide class of mathematical functions [1].

In this presentation I will discuss the transition between states of periodicity and of chaos in the context of synchronous model neurons. An intrinsic feature of a modified Hodgkin-Huxley neuronal model equations, associated with the tonic (rhythmic single spiking) to bursting (repeating sequences of multiple spiking) regimes transition in the single neuron, seems to be carried over to coupled synchronized neurons when they undergo an equivalent tonic-to-bursting transition. The neuronal mathematical model we use incorporates physiologically relevant properties of excitable lipid bilayer cell membranes embedded with proteins functioning as ion channels, receptors and transporters [2]. The equations incorporate mechanisms for neuronal fast spiking and slow subthreshold oscillations, both directly related to sodium and potassium ion channels. In particular, the potassium calcium-dependent current $I_{\text{sr}}$, associated with slow repolarization of the cell’s membrane potential, plays a major role in the dynamical state of the neuron. The corresponding conductance $g_{\text{sr}}$ is here used as a control parameter to set the neuron’s firing regime, depicted in Fig. 1, where in the $g_{\text{sr}}$ range $[0.2 : 0.305]$ the neuron displays tonic behavior whereas in the range $[0.305 : 0.5]$ the behavior is bursting. The corresponding firing rates in Hz are shown along the $y$-axis.

Two gap-junction coupled neurons, one tonic ($g_{\text{sr}} = 0.26 \text{ mS/cm}^2$) and the other bursting ($g_{\text{sr}} = 0.38 \text{ mS/cm}^2$), exhibit a variety of dynamical states for increasing values of their reciprocal coupling strength $g_c$, as illustrated in the bifurcation diagram of Fig. 2. Initially, with weak coupling, the two neurons remain non-synchronous up to $g_c = 0.046 \text{ mS/cm}^2$, at which point they synchronize in a period-one tonic state. At $g_c = 0.071 \text{ mS/cm}^2$ the first period doubling bifurcation takes place, followed by the typical period doubling cascade into chaos at $g_c = 0.081 \text{ mS/cm}^2$, and then in a bursting regime at $g_c = 0.119 \text{ mS/cm}^2$. The insets show voltage traces of (a) tonic neuron ($g_{\text{sr}} = 0$, red), (b) bursting neuron ($g_{\text{sr}} = 0.66 \text{ mS/cm}^2$), (c) both neurons at $g_{\text{sr}} = 0.06 \text{ mS/cm}^2$, (d) both neurons at $g_{\text{sr}} = 0.09 \text{ mS/cm}^2$, and (e) both neurons at $g_{\text{sr}} = 0.119 \text{ mS/cm}^2$. The tonic-to-bursting transition observed in this bifurcation diagram happens with the synchronous neurons exhibiting the critical firing rate $f^{\text{critical}} = 1.25 \text{ Hz}$ shown in Fig. 1 for the single neuron. This is further illustrated in the color map of Fig. 3, where the $x$ and $y$ axes represent, respectively, the conductances $g_{\text{sr}0}$ for a tonic neuron and $g_{\text{sr}1}$ for a bursting neuron, gap-junction coupled to each other. The color code indicates their common firing rate when they first synchronize, quantified in Hz on the color palette on the right-hand-side. The negative-slope dark stripe on the color map separates parameter space regions for synchronized neurons in the tonic regimes (on the left) and in the bursting regime (on the right). The firing rate for the pairs of synchronous neurons with $g_{\text{sr}}$ values along this stripe happens to be the same as the $f^{\text{critical}}$ depicted in Fig. 1.

Concluding, I will show that the critical firing rate observed in single as well as in pairs of coupled neurons is also found in the case of triads of neurons, suggesting that this common feature could be more general, extended into larger number of networked neurons.

![Fig. 1](image1.png)  ![Fig. 2](image2.png)  ![Fig. 3](image3.png)

References
Breaking the Vicious Limit Cycle: Addiction Relapse-Recovery as a Fast-Slow Dynamical System

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Abstract

Symptoms of addictive disorders often manifest as periodic episodes of sudden relapse followed by relatively long periods of recovery. For certain types of addiction, a relapse is precipitated by a state of elevated well-being (hyperthymia) wherein cravings supersede cessation efforts. A relapse satiates cravings temporarily, but is usually followed by a state of depression, which slowly improves as cravings reintensify. All addictive substances mimic natural neurotransmitter molecules and indulgence in these substances triggers a deluge of dopamine and norepinephrine. To counteract this surplus, the brain increases production of enzymes that break down these chemicals and nerve cells develop more receptor sites to handle the increased number of norepinephrine molecules. When an addict ceases to indulge in the addictive substance, the mass of enzymes and greatly increased number of receptor sites cause severe depletion of dopamine and norepinephrine which leads to a state of depression and fuels craving.

To better understand the underlying mechanisms driving relapse-recovery cycles, we examine the macroscopic effects of this highly complex chemical process by constructing a fast-slow dynamical system model of the relationship between an addict’s propensity to relapse and their current disposition, i.e., craving and mood. The model (parameterized by data on alcohol addiction) captures the dynamics of addiction relapse and recovery by admitting relaxation oscillations, which we prove exist by exploiting time-scale separation. We derive predictions of cycle period and amplitude to measure relapse frequency and intensity, respectively. As a parameter identified as being responsive to treatment is varied, the system transitions from a state of periodic relapse-recovery to a relapse-free state through reverse Hopf bifurcation. We calculate the threshold value of the treatment parameter, which corresponds to the equilibrium point passing through the fold of the critical manifold. Our predictions agree well with relapse data taken from a sample of alcoholism sufferers.
An impedance profile represents the interaction between a neuron and periodic forcing. The interplay of frequency preference and amplitude give us insight into the preferred input for a given neuron. However, this idea becomes much more complex when applied to a network. Although resonance has been observed in several neuron types, the resonant properties of neuronal networks and the functionality of the impedance profile are still not well understood. The interactions of multiple frequency preferences can open up behaviors that no individual cell would be capable of alone. The frequency preference of a network is unable to be determined given the intrinsic frequency preference of its cells. We aim to develop a tool that allows us to predict and analyze the resonant properties of a coupled network from the resonant properties of the participating neurons. Diffusive coupling, intuitively, should pull the network behavior towards the average. However, this is often not the case. We test these ideas in a minimal network model of two electrically coupled neurons. We measure the network response in terms of impedances of the two coupled cells. We consider the idea of viewing the electrical coupling as a second external forcing to each individual cell, and examine the validity of this analysis.
Survival requires adaptation mechanisms to produce appropriate responses to environmental stimuli, such as light, that constantly reset the endogenous rhythms of organisms and generate the circadian clock. Stimuli-induced resetting in neuronal oscillators has important biological functions in visual perception [5], memory [1], representation of temporal durations [4], sleep and arousal [3], and learning [2]. An important class of biologically-relevant applications of phase resetting in neural oscillators is the prediction of phase-locked modes in central pattern generators (CPGs), which are autonomous neural networks capable of producing multi-phase rhythms underlying motor behaviors, such as those responsible for heartbeat, respiratory functions and locomotion [8] and sensory processing. Motivated by experimental studies of swim CPGs of the sea slugs Melibe leonina and Dendronotus iris [6], extensive numerical studies using three-neuron motifs of were developed for the purpose of modeling different rhythmic patterns. Another extensively studied three-neuron motif contained generic and identical FitzHugh-Nagumo relaxation oscillators with all-to-all coupling [7]. By phase reduction, bifurcation and perturbation analysis, and stochastic dynamics they mapped a wide range of parameter space and identified relevant network multistable phase-locked modes [7].

Conceptually, unidirectional coupling between neural oscillators, i.e. a driving-driven system, is the simplest possible synchronization mechanism that uses phase resetting to drive a neural population to a desired phase-locked firing pattern. Phase resetting methodology has been successfully used for predicting one-to-one entrainment in networks where the receiving population always follows the driving population. It was recently shown that unidirectional coupling also allows for “anticipated synchronization” [9] in which the receiving population anticipates the states of the driving population.

We used a generalized phase resetting method to predict the existence and the stability of phase-locked modes in a driving-driven networks with a dynamic feedback loop. This study brings two novel solutions to phase-locked mode prediction in neural networks. First, we generalized the phase response curve definition to include the more realistic case when neural oscillators receive more than one input per cycle. Secondly, we applied the generalized phase resetting definition to a biologically relevant neural network that has been shown to produce both delayed and anticipated synchronization. Our PRC generalization to multiple inputs per cycle is a significant advance in phase resetting theory that allows investigation of large networks in which individual neurons receive multiple inputs per cycle without assuming special network connectivity. Furthermore, our generalization of phase resetting curve and the detailed procedure we presented for predicting the existence and the stability of phase-locked modes in a biologically relevant three-neuron network with a dynamic feedback loop is not limited to weak coupling nor to only one-to-one firing patterns. We carried out a detailed numerical analysis of the stability domain for the predicted phase-locked modes.

References
Entrainment implies that an endogenous oscillator has matched its period to that of an external periodic forcing and has established a stable phase relationship with the forcing signal. The process of circadian entrainment has been studied extensively using tools from oscillator theory, in particular phase response curves (PRCs) that measure the change in the phase of an endogenous limit cycle oscillation (typically in constant darkness or DD) induced by a perturbation (typically a light pulse) as a function of the phase at which the perturbation is applied. Such PRCs can be constructed for light pulses of arbitrary strength and duration. However, for a PRC to accurately predict properties of entrainment to periodic light pulses, the perturbations must be weak or brief enough that the oscillator would relax back to the DD limit cycle attractor before the next pulse arrives. We show that PRCs do not accurately predict the phase of entrainment in a model of the *Drosophila* circadian clock subjected to photoperiods with substantial amounts of both light and dark, such as 12:12 light:dark (LD) cycles. In this talk, we introduce entrainment maps, which are one-dimensional maps that are not based on perturbing the DD oscillator and thus are able to accurately predict the phase of entrainment for any photoperiod.
A map-based approach to understanding bifurcations in a model of sleep-wake behavior

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A homeostatic need for sleep increases with time awake and decreases during sleep [1]. Typically, for adult humans, this homeostatic sleep drive produces one nighttime sleep episode per day. However, when the timing of the growth and recovery of sleepiness varies, different patterns of sleep are produced. Such differences in timing may reflect changes associated with development and, specifically, the transition that occurs in early childhood as children move from a pattern of two sleep cycles per day, a nap as well as nighttime sleep, to a single period of nighttime sleep [2]. To investigate this transition between one and two sleep cycles per day, we analyzed bifurcations in a physiologically-based model for human sleep/wake dynamics [3] as the time constants related to the build up and recovery of sleepiness were decreased. Our model describes states of wake, rapid eye movement (REM) sleep, and non-REM (NREM) sleep based on the activity of neuronal populations in a sleep/wake regulatory network. We found that the system exhibits an incremental increase in the number of sleep cycles per day as homeostatic time constants are decreased. In previous work, we developed an algorithm to numerically construct a one-dimensional map to represent the dynamics of the full system [3]. Here, we use this map to relate the increase in the number of sleep cycles per day to a border collision bifurcation in the piecewise continuous one-dimensional system, and we provide numerical evidence for period-adding behavior. The progression in the number of sleep cycles per day is summarized in the Devil’s staircase diagram in Figure 1. Similar period adding behavior has been observed in two-state models of sleep/wake behavior [4]. However, in our model, the transition in the number of sleep cycles per day interacts with transitions in the number of bouts of REM sleep per sleep cycle to produce more complicated dynamics within the greater period adding structure. This analysis has implications for understanding the dynamics of the transition from napping to non-napping behavior in early childhood.

**Figure 1.** Devil’s staircase structure in number of sleep cycles per day. Multiplication by the scaling factor, $\chi$, decreases the time constants of the homeostatic sleep drive so sleep need grows and decays more quickly. As these time constants decrease, the average number of sleep cycles per day increases according to a period-adding bifurcation as seen in this bifurcation diagram with a characteristic Devil’s staircase structure: a continuous monotonic function which is constant locally almost everywhere.

**References**


Estimation of Hidden Dynamics in Non-Linear Systems for Predicting Sleep-Wake States

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There is extensive clinical and experimental evidence that links state of vigilance to seizure generation [1, 3]. Sleep-wake regulation is also altered in epileptic brain [2]. In order to understand this bi-directional coupling we need to further investigate the underlying neurophysiological interactions of brainstem sleep-wake regulatory system in normal and epileptic brain. Towards this end, we have been using physiologically-based mathematical models of sleep-wake regulatory network [4] synchronized with experimental measurements to reconstruct and predict the state of sleep-wake regulatory system in chronically implanted animals. We have implemented these models in an Unscented Kalman Filter (UKF) framework to serve as source and observer models and to show that the UKF-based data assimilation algorithm we have implemented is extremely robust and can reconstruct hidden dynamics even when the observer model is intentionally made inadequate [5].

Critical to applying this technique to real biological systems is the need to estimate the underlying model parameters. We have developed an estimation method capable of simultaneously fitting and tracking multiple model parameters to optimize the reconstructed system state. Performance is gauged by reconstruction and forecasting of state from noisy observations of model-generated data, and compared to other conventional parameter tracking methods [6].

In parallel with these computational efforts, we have obtained a feature set of experimental data from our continuously cabled rodents and used these features to classify state of vigilance; Wake, Rapid-Eye Movement (REM), and Non-Rapid-Eye Movement (NREM). These indirect, discretized observations are then used as the ‘noisy observables’ in the implemented UKF framework to first estimate model parameters and then to track and reconstruct the inaccessible variables of the sleep-wake model. This will allow for further forecasting of state transitions.

References
Inter-Ictal Seizure Onset Zone Localization Using Unsupervised Clustering and Bayesian Filtering

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Background: Epilepsy is a neurological disease characterized by recurrent seizures. Epilepsy surgery, which can reduce and often eliminate seizures[2], is considered as an option for those epilepsy patients who do not respond to drug treatment. The success of resective surgery depends on accurately localizing the Seizure Onset Zone (SOZ). Typically, the SOZ is identified based on visual inspection of the intracranial EEG (iEEG) captured at the time of seizures. However, this process is time-consuming, costly, and associated with potential morbidity. Hence, localizing the SOZ based on inter-ictal (non-seizure) iEEG recordings is considered as an alternative, or a complementary, procedure [2]. Here we report an unsupervised technique for automatic inter-ictal SOZ localization. Existing approaches focus on identifying abnormal electrophysiologic events using features extracted from iEEG data. Additionally, we also utilize the temporal and spatial behaviors of those events to enhance the accuracy of localization. Power in Bands (PIB), [1]), a feature extracted from iEEG, is used to capture the abnormal events. A Bayesian filter and a grouping strategy based on K-means clustering, respectively, are used to capture the temporal and spatial patterns of such events.

Methods: The analyzed dataset consists of iEEG recordings collected from 34 epilepsy patients via a Mayo Clinic IRB approved study. Two-hour inter-ictal recordings were selected per patient and divided into non-overlapping 3-second epochs. PIB features, derived as spectral powers in standard clinical Berger Bands (0-3 Hz = Delta, 3-8 Hz = Theta, 8-13 Hz = Alpha, 13-25Hz = Beta) as well as higher oscillations frequencies (25-55Hz = Low Gamma, 55-100Hz = High Gamma, 100-150Hz = epsilon Gamma, >150Hz taken as ripple) were extracted in the 3-second epochs to capture abnormal electrophysiologic events. Based on the features extracted in a 3-second recording of a channel, a binary observation (normal or abnormal) was assigned to that channel. This was achieved through grouping the features of all the channels using a K-means clustering algorithm. These observations were used in the Bayesian filter to infer whether a channel belonged to SOZ. The likelihoods resulted from the filtering process were compared against Gold standard SOZ channels that were determined by a trained epileptologist, to generate ROC curves for each patient.

Results: Our technique with PIB feature provides an average AUC (Area under ROC curve) of 0.72 on the dataset consisting of 34 patients. Same technique when used with standard features such as high-frequency oscillations and inter-ictal spikes, provides average AUCs of 0.71 and 0.69 respectively. PIB feature, when used alone without the grouping strategy and the Bayesian filtering technique, provides an average AUC of 0.63.

Conclusions: We developed an unsupervised technique for inter-ictal SOZ localization and validated on clinically collected iEEG data from 34 epilepsy patients. Our results indicate that using a Bayesian filter for capturing temporal properties of the iEEGs recorded from epileptic brains remarkably improves localization accuracy (AUC: 0.63 → 0.72). Our study also shows that the feature PIB, which could be implemented with relatively low computational burden, performs as well as the standard bio-markers (high-frequency oscillations and inter-ictal spikes) when used in this setting (AUC: HFO - 0.71, Spike - 0.69, PIB - 0.72). These promising results suggest further investigation of this approach in making the technique robust for clinical use.

References

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Confusing one environmental state for another can be costly due to a subsequent suboptimal choice of action. For example, mistaking a lion for a domesticated cat might lead to death, while mistaking a domesticated cat for a lion might lead to unnecessary energy spent running. However, correctly identifying a greater number of objects requires more mental effort, whether that be measured by a larger number of neurons devoted to object recognition or a correspondingly larger number of ATP molecules consumed in their function.

Previous work suggests that resource constraints such as these are critical in shaping the neural code. We describe the tradeoff between energetic costs and information transmission. Our approach differs from most previous efforts in two major ways. First, we use rate-distortion theory (a branch of information theory) and recent advances in nonequilibrium statistical mechanics to place lower bounds on material, timing, and energy costs without specifying a particular neural code. Second, we use a distortion measure (e.g., loss function) to quantify the quality of sensory information processing; confusing sensory input $x$ for $\tilde{x}$ costs the organism $d(x, \tilde{x})$.

The rate-distortion function $R(D)$ is the smallest rate for which expected distortion $D$ is still achievable. The rate-distortion functional also has a physical interpretation as a total energetic cost.

Numerical experiments, e.g. as shown in Fig. 1, and analytic arguments not shown here suggest that, when there are many possible environmental inputs ($N \gg 1$), the rate-distortion function $R(D)$ does not depend on the specific distortion measure or environmental input probabilities, but only on the distribution from which distortions were drawn, $\rho(d)$, and the distribution from which the input probabilities were drawn, characterized by concentration parameter $\alpha$. A combination of analytical and numerical evidence suggests that the rate-distortion function converges in probability to a curve which depends only on $\rho$ and $\alpha$.

Our results suggest that the necessary size of sensory brain regions, the minimum possible timing delays in sensory perception, and the minimal power required to maintain sensory brain regions all depend only on coarse environmental statistics, even though optimal neural wiring fluctuates wildly from environment to environment. In the examples above, these coarse environmental statistics are $\rho(d)$ and $\alpha$.

In apparent agreement with these findings, environmental cues are scarce during development, and seem to have limited effect on neuron number (2), and there are few reports of neurogenesis in mammalian sensory brain regions (1). Number may be fixed, but wiring is not, and there are many reports of synaptic plasticity in sensory brain regions; the particular wiring of neurons in sensory brain regions does depend on the details of environmental cues.

References

Figure 1: In both figures, $\rho(d) = e^{-d}$ and $\alpha = 2$. At left, rate-distortion functions of 10 different worlds with $N = 20$. At right, rate-distortion functions of 100 different worlds with $N = 800$. 

Deep Brain Stimulation Driven Synaptic Depletion is a Robust Phenomenon Independent of Synapse Type

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One hypothesis that can help explain the mechanism of deep brain stimulation (DBS) is the exhaustion of synaptic transmitter release in directly stimulated pathways. Synapses typically have a readily releasable pool of neurotransmitters packaged in vesicles and machinery to replenish that pool once they are released. However, high frequency (~100 Hz) driving of a synapse quickly exhausts the readily releasable pool and overwhelms the recycling machinery. In turn, postsynaptic currents (PSC) during DBS can be dramatically reduced, effectively eliminating the ability of the synapse to modulate the post-synaptic neuron. This basic phenomenon can be most easily studied at glutamatergic synapses; however, multiple synapse types are known to exist, including Depressing (D), Facilitating (F), and Pseudo-linear (P). Therefore, we set out to explore how different synapse types would response to DBS. We simulated the response of classical Tsodyks and Markram (TM) synapse models to high frequency driving [Tsodyks and Markram, 1997 PNAS]. TM models provide a phenomenological description of short term synaptic plasticity, including both depression and facilitation. Well established TM models exist for D, F, and P synapses [Markram et al., 2015 Cell], so we used them to evaluate their response to driving at frequencies that ranged from 1-150 Hz. We then used a leaky integrate and fire (LIF) neuron model to integrate the synaptic input and estimate post-synaptic responses to stimulation. Fig. 1 illustrates the gain diagram of D, F, and P synapses. Independent of the synapse type, high frequency driving of the synapse generated substantially reduced excitatory post-synaptic currents (EPSCs) via synaptic depletion. The reduced EPSCs generated by high frequency DBS driven inputs, effectively eliminated the role of those synaptic connections on modulating post-synaptic firing.

Fig. 1

Most DBS models focus on stimulation induced action potential initiation and propagation in the brain. While the fundamental effect of action potential invasion into a synapse is transmitter release, little attention is typically paid to quantifying the actual synaptic effect of the DBS activated pathways on their post-synaptic targets. Our theoretical results suggest that the synaptic effect of DBS activated pathways are substantially limited by transmitter depletion, and effectively create a “synaptic lesion”.

[Graph showing EPSC amplitude vs. Frequency (Hz) for D, F, and P synapses.]
Correlations Induced by Depressing Synapses in Quenched Critically Self-Organized Networks

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In a recent work, mean-field analysis and computer simulations were employed to analyze critical self-organization in networks of excitable cellular automata where randomly chosen synapses in the network were depressed after each spike (the so called annealed dynamics). Calculations agree with simulations of the annealed version, showing that the nominal branching ratio $\sigma$ converges to unity in the thermodynamic limit, as expected of a self-organized critical system. However, the question remains whether the same results apply to the biological case where only the synapses of firing neurons are depressed (the so called quenched dynamics). We show that simulations of the quenched model yield significant deviations from $\sigma = 1$, due to spatial correlations. However, the model is shown to be critical, as the largest eigenvalue of the synaptic matrix is shown to approach unity in the thermodynamic limit, that is, $\lambda_c = 1$. We also study the finite size effects near the critical state as a function of the parameters of the synaptic dynamics.

References

A simple spiking neuron model based on stochastic STDP

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It is commonly accepted that neurons mostly communicate by spikes. A neuron receives spikes from thousands other neurons which affect the neuron’s morphology, sensitivity and reactivity. In particular, they can induce changes of the synapses. This evolution in time is called synaptic plasticity. Such a plastic behaviour is thought to be at the basis of our memory formation which makes it particularly interesting. Over the last few decades, this phenomenon has been widely studied. These studies gave rise to new research fields in artificial intelligence and allowed much progress in our understanding of the brain.

Nowadays, popular plasticity models are based on Spike-Timing-Dependent-Plasticity (STDP) rules. The later have been developed on the idea of Hebb’s law: “When an axon of cell A is near enough to excite a cell B and repeatedly or persistently takes part in firing it, some growth process or metabolic change takes place in one or both cells such that A’s efficiency, as one of the cells firing B, is increased” [1]. In STDP models spiking times are central, but current works showed that firing rate, membrane potential [2], neuromodulators and many other factors are responsible for synaptic plasticity. These numerous factors partially explain the stochastic behaviour of neurons and plasticity. Chemical reactions and ions flows at synapses are also highly stochastic. Finally, the widely used curve of STDP from Bi & Poo has been obtained after averaging experiment results [3]. Experimentally, the same pairings can give different changes of synaptic weights. Another important remark about plasticity is the presence of different time scales [4]. Indeed, long term plasticity time scale ranges from minutes to more than one hour. On the other hand, a spike lasts for 1 millisecond.

Thus, there is a need to understand how to bridge this time scale gap at the synapse level and how it interplays with noise. Common models of networks with plasticity are computationally expensive because of their complexity. Here, we would like to present a new model of stochastic plasticity in networks of spiking neurons described by 2 states Markov chains. The non-plastic network is rich enough to be realistic: it reproduces phenomena which have been widely observed by biologists. For example, spontaneous oscillations, bi-stability and different time scales. In addition, it is simple enough to be mathematically analysed and numerically simulated with thousands of neurons. The most original point of our study concerns the introduction of a new STDP rule which we implement in the well-known stochastic Wilson-Cowan model of spiking neurons presented in [5]. More precisely, because of the plasticity rule, our model is a piecewise deterministic Markov process when it is a pure point process in [5].

There exist only few mathematical studies of plasticity [6, 7]. In our case we can produce such an analysis studying the Markov process composed of three components: the synaptic weight matrix, the inter-spiking times and the neuron states. In the context of long term plasticity, synaptic weights dynamic is much slower than the network one. A time scale analysis enables us to remove the neurons dynamics from the equations. Indeed, this allows us to derive an equation, for the slow weight dynamic alone, in which neurons dynamics are replaced by their stationary distributions. Thereby, we don’t need to simulate the dynamics of thousands fast neurons any more and we get an equation much simpler to analyse. We then discuss the implications of such derivation for learning and adaptation in neural networks.

References

Synaptic Deficiencies and Robustness of Excitatory Neuronal Networks

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Synaptic deficiencies are known to be a hallmark of neurodegenerative diseases [1] but the diagnosis of impaired synapses on the cellular level is not an easy task. Nevertheless, the collective behavior of neurons on the network level and changes in the dynamics of networks can reveal impairments in smaller resolution elements of the network [2]. This study investigates how the persistent activity of excitatory neuronal networks is affected as a result of synaptic deficiencies. The link between persistent activity and working memory is one of the reasons why we are interested in persistent activity especially because working memory is known to be adversely affected in patients with Alzheimer’s disease. Through numerical simulations of biophysical neuronal networks, we show that the persistent activity of neuronal networks depends on the topology of the studied network when the synaptic connections between the neurons are weakened. We consider different network structures that are generated by specifying their degree distribution. The degree distribution of purely random networks follows a unimodal Poisson distribution [3]. However, more complex random networks can be constructed by using degree distributions with more than one mode. For example, networks with bimodal degree distribution are shown to have features of small-world networks as well as consisting of rich clubs. We investigate the generation of persistent activity in networks consisting of 200 Hodgkin-Huxley type model neurons coupled through excitatory synaptic currents. Synaptic impairment is modeled by decreasing the maximum conductance of synapses. Our results demonstrate that the self-sustained activity of networks with bimodal degree distributions is more robust to synaptic impairment than random networks. Rich clubs of networks with distinct modes increase the overall robustness by keeping the network active during synaptic loss. Interestingly, our results show that the percentage of neurons which participate in the persistent activity of the network is lower for highly robust networks. We also propose three different scenarios of synaptic impairment, which may correspond to different biological conditions. In the first impairment scenario, synapses are randomly selected and then weakened or removed. Implementation of random impairments is considered as the control scenario to determine if other impairment scenarios lead to different results. In the second impairment scenario, neurons that have a higher number of synapses are more likely to be weakened or removed. The rational for this type of defect is based on the significance of intracellular transport since we propose that the synapses of neurons with large number of out-going synapses are more likely to be weakened in case of inefficient axonal transport [4]. In the third impairment scenario, synapses of neurons that are highly active are more likely to be weakened or removed [5], taking into account the level of individual neuronal activity, not just the network topology. In the third method, if a neuron is not firing frequently, then even under impaired axonal transport, it might be capable of keeping synapses functional. Our results show that for all network topologies that we studied, the nonrandom impairment scenarios of synaptic loss have more destructive effect on the activity of networks with the third scenario having the most impact. Therefore, we speculate that pathological or other conditions in which synaptic loss is correlated with neuronal activity can be timely detected by monitoring the activity of the network. Moreover, our results suggest that the transition in the network structure can be used as an early disease indicator as the robustness of a neuronal network decreases when it loses its structured topology. Such transition of the brain network towards randomness has already been shown even in normal aging in several studies [6]. Therefore, monitoring alteration in the brain network structure has the potential to be used as an early diagnostic method in neurodegenerative diseases.

References

Humans learn to classify images in at least two distinct ways. One way uses procedural memory to form stimulus-response associations via trial and error. The resulting learning yields gradual improvements in classification accuracy that is not flexibly altered. An instance of this rigidity is that categories learned through this system cannot quickly compensate for category label permutations. On the other hand, declarative memory is used to test explicit hypotheses about category membership. This yields sudden increases in classification accuracy that can be applied flexibly, easily adapting to label permutations.

Theoretical models of the procedural system are typically grounded in simple connectionist architectures in which synapses are strengthened via reinforcement learning. Theoretical models of the declarative system, on the other hand, are grounded in if-then-else symbolic programs. However, if the brain is inherently connectionist, then this latter point reveals a highly significant and unanswered question: How is rule-based behavior — explicit hypothesis testing — of category membership implemented in the connectionist architecture of the human brain?

In this work, we show that simple rule-based learning can be obtained from standard connectionist artificial neural networks (ANN). We accomplish this by coercing the ANN weights matrix during learning with an information entropy based regularization penalty in conjunction with a dual stage optimization strategy. The optimizer first uses standard regularization penalties, commonly used in machine learning tasks, to initialize a search direction. In the next stage, the optimizer then pursues the solution aggressively using the information entropy regularization. Jointly, these cause the connectivity between input and output neurons to be sparser, with fewer connections being made strongly. This results in a weights matrix distribution with lower information entropy.

We evaluated this approach by generating 30x30 sine-wave gratings that varied in spatial frequency and orientation. These were passed to a convolutional neural network that was trained to regress the cycles per degree and orientation given input grating images. This perceptual network was not updated during subsequent categorical training. We then attached a softmax classification layer on top of this perceptual network, which we trained using the dual stage information entropy approach.

As a litmus test of rule-based behavior, we take three key findings from the human classification literature: (1) rule-based classification learning is fast [MA93]. (2) rule-based classification is easily generalized to novel stimuli [CRA12]. (3) rule-based classification adapts to label swaps quickly and effectively [AEW03]. We were able to replicate these findings using the ANN learning paradigm described above.

Finally, we tested the ability of this method to train ANNs to provide simple explanations in novel task domains, since providing simple explanations that accurately describe response strategy is another important aspect of rule-based behavior [Lom07]. We developed a machine tutoring task, and evaluated how well explanations generated by several ANN learning methods performed on this task. We found that explanations derived from our rule-based ANN method performed best. We also found that our method was able to generate explanations with the greatest diversity in the range of inputs.

References


Neurogenesis as a natural substrate for backpropagation

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The creation of new neurons, or neurogenesis, in the adult mammalian brain was first discovered in the early 1960s. Though initially controversial, it has been commonly accepted since the late 1990s [1]. It has been observed in two brain areas: the dentate gyrus and the olfactory bulb. The properties of the newly generated neurons as a function of their maturation stage are well studied, and their implication in learning and memory has been proposed. However it is still unclear how the new neurons are integrated into the preexisting network, and what their functional role is (the main alternative viewpoints are reviewed in [2] and [3]).

The dentate gyrus is the entry point of the hippocampus, which is commonly believed to be the substrate of learning and memory. It thus seems intuitive that the neurogenesis of its main excitatory cell type, the granule cells, could increase the capacity of the network to learn new memories. Indeed, behavioral experiments have shown that enhanced dentate granule cells neurogenesis promotes discrimination of similar - yet different - spatial stimuli, while a decrease of neurogenesis is responsible for a lower discrimination ability (reviewed in [4]). However, it is not trivial how neurogenesis would increase network performance, because it has been shown experimentally that, except for animals living in a highly enriched environment, the population of dentate granule cells does not increase over a rodent life time [5]. Thus the newly created neurons are not simply added, but should replace other neurons.

We use a three layer, fully connected, feedforward network and a normalized (between 0 and 1) MNIST handwritten digit dataset to assess classification performance. Firstly, we want to determine if at all neurogenesis enhances the classification capability of the network. Secondly, we are interested to determine how the newly generated dentate granule cells should be integrated into the hippocampal network to maximize classification performance. The whole network comprises several hundreds of rectified linear units. The input layer corresponds to the entorhinal cortex, the major input to the hippocampus; the hidden layer corresponds to the dentate gyrus; the output layer corresponds to area CA3.

We learn the readout weights and incorporate neurogenesis in our network through a replacement model. In the implementation, it is reflected by the fact that the total number of neurons in the hidden layer is kept fixed, but some neurons (and indirectly their connections) are replaced by other neurons. It helps us to be more conservative: indeed, if an addition model would have been used (where neurons are continuously added to the hidden layer), it would not be surprising that classification performance increases. Interestingly, when silent hidden neurons were replaced by new neurons, classification performance was significantly increased compared to the identical network without neurogenesis. As expected, classification performance in the reference case, where all network weights and biases are learnt using the standard backpropagation algorithm, is higher than when only the readout weights are learnt. However, our network with neurogenesis has the advantage to be more biologically plausible, because its learning rule is local. Furthermore, neurogenesis increases classification performance significantly, to levels close to the ones achieved with backpropagation.

To conclude, the functional role of neurogenesis is mainly believed to be the enhancement of pattern discrimination. Here, we investigate a seemingly different aspect: classification performance. Nevertheless, these two tasks are similar, because if newly created neurons help classification performance, they probably do so by analyzing a different feature, and thus by discriminating better different facets of an input. Our results show that replacement of silent neurons through neurogenesis is sufficient to enhance classification performance.

References
Nervous systems constantly receive and process input from various sensory modalities. Sensory information converges at many neural centers, including those that directly control motor output and behavioral plasticity. Little is known about how sensory information affects processing in premotor circuits and the functional connectivity within them. Using the crustacean stomatogastric nervous system, we investigate the effects of distinct sensory modalities on the population activity and functional connectivity of premotor neurons, and describe a mathematical methodology to achieve this goal. The stomatogastric motor circuits are under continuous modulatory control by descending projection neurons located in a premotor region that receives various sensory inputs [1]. Using statistical analysis, we have previously characterized the 3D structure of this premotor region, and the location of descending neurons involved in motor control [2].

To assess the neuronal population activity and the effects of sensory inputs on functional connectivity, we use voltage-sensitive dye imaging (imaged region shown in Fig. (a)). Two sensory modalities, a chemosensory and a mechanosensory, known to produce distinct motor outputs were stimulated. Changes in spike activity were used as a measure to correlate neuronal responses to each sensory modality stimulation. Experimental data processing consisted of a drift removal function in combination with a nonlinear energy function, and a spike threshold based on the variance of the signal. Neurons responded (i) to both sensory modalities (multimodal), or (ii) to only one (unimodal), or (iii) were unaffected by sensory stimulation. The majority of neurons in the premotor region analyzed were multimodal neurons (Figs. (b), (c)), and the mechanosensory modality consistently elicited stronger changes in neuronal activity than the chemosensory. To characterize the functional connectivity between neurons, we used pairwise correlations between activity responses. Distinct connectivity configurations were observed for processing chemosensory (Fig. (d)) and mechanosensory (Fig. (e)) stimuli, but when combined (Fig. (f)), sensory stimuli were processed by a network distinct from both individual networks. This reconfiguration of the network connectivity in response to both sensory stimuli is not a simple union of the individual configurations. It is a more complex reorganization of functional connectivity, suggesting that a neuronal network may not exist as a predefined entity within the nervous system. Rather, it may be dynamically built according to changes in sensory conditions.

References

A computational account of the development of a preferred retinal locus
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We constantly make rapid eye movements (saccades) to project objects of interest to the center of our retina, the fovea. The fovea is densely populated with Cone receptors and provides the highest visual acuity. Some diseases of the visual system, such as age-related macular degeneration, render the fovea dysfunctional and cause central field loss (CFL).

CFL is an irreversible impairments and currently about 1.75 million Americans suffer from it. This number is expected to raise to almost 3 million by 2020 [1]. To adjust to CFL, patients of macular degeneration adopt a consistent extra-foveal location called Preferred Retinal Locus (PRL) for fixations and saccades re-referenced to it [2]. PRL development is a lengthy process and takes at least 6 months [3]. While studies have improved our understanding of PRL development, many aspects of this development remain unclear. What factors derive the PRL formation? What accounts for the slow development of PRL? What makes a retinal locus advantageous over other loci to become a PRL? Studying these question on patient population is challenging due to confounding factors such as the differences in the pathology of individuals, the slow process of PRL development, and the progress of the diseases with time. Having a model of PRL development can help to control for the confounding factors while examining the key factors. Here we show that a conceptually simple computational model can account for the formation of a PRL and its idiosyncrasies.

We assume that the visual system always intends to aim the retinal locus with the highest expected post-saccade acuity at the saccade target. The expected post-saccade acuity of a retinal locus is a function of the physiological acuity at and around the locus and the expected saccade error. The expected saccade error is a combination of motor error that is proportional to the saccade amplitude (vector error) and the spatial uncertainties associated with the retinal locus and the saccade target (endpoint errors). We assume that the motor error does not improve, but the spatial uncertainties associated with the neural representation of the endpoints are optimally re-estimated after each saccade from the observed saccade error. A generic forgetting function is assumed to prevent spatial uncertainty from vanishing.

Simulations showed that immediately after CFL, the utilized retinal loci are close to the edge of the scotoma on the side nearest to saccade targets. After each saccade, spatial uncertainties associated with the pre-saccade target and utilized retinal locus decrease. Decrease in spatial uncertainty increases the expected post-saccade acuity of the retinal locus. The net effect is that a previously selected retinal locus is more likely to be selected for a future saccade, further reducing its spatial uncertainty, and forming the PRL. Idiosyncrasies at the early stages of CFL strongly influence PRL formation.

Our computational model of PRL formation can account for PRL development and its idiosyncrasies. In addition, it can be used as a framework to study the development of PRL under different settings of an impaired visual system. Ultimately this model can assist in designing better rehabilitation regimens and adaptive tools to elevate impairments in patients of CFL.

References
Developing a predictive model for compulsivity in individuals with OCD

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For the past 30 years, the most often used method of diagnosing Obsessive-Compulsive Disorder (OCD) has been the Yale-Brown scale, however the scale only considers the quantifiable time and energy lost to compulsions, while also relying purely on self-reporting which may be fallacious. In previous studies, it has been determined that clinical subjects will often report more symptoms than they would in a traditional interview format. Furthermore, OCD differs significantly from other anxiety disorders by the existence of compulsive behavior to nullify pervasive anxiety. In light of this, current means of diagnosing and treating OCD cannot be measured by their efficacy in treating other anxiety disorders. This research is focused on developing a predictive model of compulsive behavior based upon Minsky’s Society of Mind. The objective is to develop a model which would predict, given a set of environmental parameters, the probability and prevalence of an individual performing compulsive behavior. Each neurological agent, as an automaton, has a certain probability of reacting to an environmental stimulus and moving into an excited state. Thus, the agent will send a signal to the next agent, either of being excited or not excited and the resulting agent will have a certain probability of also changing states. Thereby, if each agent within the ensuing chain shifts into an excited state, the subject will perform a compulsion. By applying this concept continually, with agents given by the sectors of the worry circuit, a computer algorithm was designed which implied that the number of compulsions performed could be predicted by an exponential distribution. Later revisions of the model may potentially take into consideration probabilistic determination of playing order, as well as utilizing a function of the number of compulsions already performed to determine the probability of each agent reacting to a stimulus. Given the lack of understanding of how to effectively treat anxiety disorders, the research has applications both in understanding pervasive anxiety, and in treating the physical manifestations of anxiety. A successful method must be capable of empirically quantifying compulsivity, however it has the potential to improve the therapeutic treatment of OCD. In addition, by including within the model a variant for the subject’s average number of compulsions, the model may be customized to each party and thus provide a more personal means of treatment. Finally, the proposed research has implications for brain mapping; by detailing the nature of compulsivity, scientists may be able to isolate the direct functions of the worry circuit which could give us clues into brain cell function.

References


An algorithmic question concerning the experimental interrogation of neural circuits

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Neuroscience continues to witness remarkable advances in experimental techniques. At the neuronal and network level, we have both the ability to image activity in, as well as to activate/silence neurons in-vivo, in awake behaving animals. Recent progress has included the ability to perform simultaneous all-optical readout and manipulation of neural activity [1] and the capability to independently control subsets of neurons within the genetically targeted population via two-photon optogenetics [2]. The recent report of a “crystal skull” preparation in awake behaving mice [3] that allows long-term two-photon access to an estimated million neurons and the efforts under the umbrella of the U.S. BRAIN initiative to scale up technology to reach the ability to simultaneously access a million cells are remarkable developments as well. As a result of these ongoing advances, the prospect of understanding how networks of neurons mechanistically perform computations that lead to specific behaviors, seems increasingly within reach.

However, given the dauntingly large numbers of neurons (and synapses) involved, asking and answering specific questions about aspects of networks that mediate these computations will require efficient algorithms for neural circuit interrogation. The algorithms will seek to prescribe the smallest number of experiments\(^1\) necessary (say as a function of the number of neurons in the network) in order to determine answers to the said questions. Also, of fundamental interest, are questions about the network, for which one would need a prohibitively large (e.g. exponential in the number of neurons) number of experiments to determine answers; the answers to such questions are therefore de facto unknowable.

Here, I consider the question of which subset of neurons participate in producing a behavior and how we can determine this subset efficiently in a hypothetical experimental setting. I start by observing that the question of what participation means is not straightforward and discuss the subtleties in making this notion precise. I then consider a much simpler case – namely one of deterministic feedforward networks – where I define this notion precisely and argue that this is the most natural definition in light of the aforementioned subtleties. I assume that one has the experimental capability to silence arbitrary subsets of neurons in the animal and ascertain if the behavior is evoked in each such instance. Manipulation of neural activity seems to be essential in this setting, since I seeks to establish causality, not merely correlations. I also assume that the connectome of the animal is unavailable; indeed, current connectomic approaches obtain the data by destroying the tissue. One is then faced with the algorithmic question – namely of prescribing the smallest number of such experiments in order to ascertain which subset of neurons participate in the said behavior. I prove, mathematically, that the decision version of this question is \(NP\)-complete. This strongly suggests that this problem will require exponentially-many experiments in the number of neurons involved in order to determine the answer and is therefore out of our reach, in practice. In Theoretical Computer Science, the set of \(NP\)-complete problems is one with the characteristic that a polynomial-time algorithm for one \(NP\)-complete problem implies a polynomial-time algorithm for all \(NP\)-complete problems. Given hundreds of known \(NP\)-complete problems, and no known polynomial-time algorithm for any of them\(^2\), it is generally assumed that no sub-exponential algorithms exist for \(NP\)-complete problems.

If the above result holds up for recurrent networks with stochasticity as well, it would imply a strong (and hitherto unexpected) computational barrier to understanding mechanistic computation in neuronal networks. This is because determining which subset of neurons are involved in a behavior appears to be a prerequisite to understanding how they mechanistically perform computations that lead to the behavior in question.

References


\(^1\)Here, by an experiment, we will mean a single trial – possibly involving optogenetic manipulation – where one might attempt to evoke the behavior in question.

\(^2\)In spite of this question being open for over 4 decades and having a $1 million bounty on a solution.
Energy Landscapes of the Brain During Wakefulness and General Anesthesia

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Summary: The Ising model and variants are widely used to capture emergent brain dynamics in terms of binary activation states. The free-energy principle postulates that within this state space, the brain tends to move toward low energy (more organized) states [1]. These low-energy states may play an important role in maintaining consciousness. To test this hypothesis, we analyzed resting-state BOLD fMRI time series data for nine subjects in awake resting and pharmacologically sedated states. By thresholding the BOLD time series and using an energy function based on the Hamiltonian for the Ising model, we find that the awake resting brain spends significantly more time in lower-energy states than the brain on exposure to sedative doses of general anesthesia. Although Ising energy landscapes have been studied previously in the context of neuronal populations [2], this work extends some of these ideas to the context of higher-level functional brain network dynamics.

Data and Methods: We used resting-state BOLD fMRI data, acquired from 9 subjects before and after being rendered unresponsive by the anesthetic drug sevoflurane (1.2%). Network weights were identified by performing Pearson correlations between all voxel pairs, generating the connection weighting matrix $J$. Let $\tilde{x}_i(t)$ denote the BOLD contrast at a given voxel $i$ and time $t$, and $x_i(t) \in \{+1, -1\}$ the quantized activation state generated according to $x_i(t) = \text{sign}(\tilde{x}_i(t) - \bar{x}_i)$, where $\bar{x}_i$ denotes the mean of $\tilde{x}_i$ over the recorded time. The dynamic energy is computed according to the Ising Hamiltonian $H(x(t)) = -\sum_{i,j} J_{ij} x_i(t) x_j(t)$.

Results: Fig. 1 (left) shows awake vs. sedated energy distributions for the DMN network across all subjects during awake and anesthetized conditions. At right we have compiled the results by energy quartile for seven different resting state networks (RSNs, determined through winner-take-all voxel sampling). We observe that the human brain during wakefulness spends significantly more time in lower-energy states than the brain during anesthesia-induced sedation, across all subjects and across all RSNs. The difference is less pronounced in the vision (VIS) and language (LAN) networks, suggesting resilience of this network to sevoflurane. It remains uncertain what mechanisms may be driving the brain toward more organized states, but we have preliminary findings that suggest this behavior may result from a distributed computation in which each region is endowed with asynchronous, locally optimal activation dynamics.

Figure 1: Ising energy distributions of the DMN network for wakeful and anesthetized conditions (left) and compiled by quartile for seven different resting state networks over all subjects (right).

References
Nonlinear dynamics analysis of optogenetic data

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Memory consolidation, decision-making, and many other cognitive processes involve large-scale synchronization of neural oscillators [3]. Gamma oscillations showed strong coherence across different areas of the brain during associative learning [2] and during successful recollection [1]. Additionally, organization and consolidation of working memory seems to involve cross-frequency coupling between brain rhythms. Such a cross-frequency coupling between gamma and theta oscillations is believed to code multiple items in an ordered way in hippocampus where spatial information is represented in different gamma subcycles of a theta cycle. It is believed that gamma rhythm is generated by the reciprocal interaction between interneurons, mainly parvalbumin (PV+) fast spiking interneurons (FS PV+) and principal cells [8]. The predominant mechanism for neuronal synchronization is the synergistic excitation of glutamatergic pyramidal cells and GABAergic interneurons [6].

Although each neuron is described by a relatively large number of parameters, using nonlinear dynamics it is possible to capture some essential features of the system in a low-dimensional space [4]. One possible approach to low-dimensional modeling is by using the method of phase resetting, which reduces the complexity of a neural oscillator to a lookup table that relates the phase of the presynaptic stimulus with a reset in the firing phase of the postsynaptic neuron. Extracting quantitative features from recorded brain electrical activity, such as local field potentials (LFPs), uses nonlinear time series analysis tools to detect epileptic seizures [5] and to reset the phase of the underlying synchronous activity to disrupt the synchrony and re-establish normal activity [7].

We used nonlinear time series analysis of LFP recordings from PV+ neurons to determine (1) if nonlinearity is present using time reversal asymmetry and false nearest neighbor (FNN) statistics between the original signal and surrogate data, (2) to measure the phase shift (resetting) induced by brief light stimuli, and (3) to compute the delay (lag) time and embedding dimension of LFP data. We showed that the recorded LFPs from mPFC of ChR2 expressing PV+ interneurons could be successfully embedded in a three dimensional space. The embedding dimension estimation based on the false nearest neighbor method was stable for a broad range of lag times around the optimally predicted values. We also considered a wide range of values both for the ratio of the distances between neighbors in successively larger phase spaces and different Thieler window. We found the same “8”-shaped attractor, or its topologically equivalent counterparts after appropriate phase shifting, in all six animals, which covers over 80% of recorded data.

References
A Signal Processing Approach to Detect Spindles Automatically

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The functional role of sleep plays in memory consolidation remains a mystery. The current study includes 20 sleep session recordings consisting of 30-minute naps between 2 cognitive tasks (https://osf.io/chav7/) during electroencephalogram (EEG) recordings. Neural events are labeled manually based on multiple channels and this project implements signal processing and machine learning algorithms to automatically classify spindles, K-complexes, and sleeping stages in multiple channels, which are important biomarkers for measuring sleep quality. We will investigate the relationship of these neural events with learning and memory performance before and after sleep in order to understand how sleep influences individual’s cognitive performance. The proposed algorithms are expected to make more efficient analysis of large neural dataset and complex behavioral patterns.

The data is under-analyzed, but due to its diverse and complexity with many measurements across brain space and time, it is time-consuming with standard data analysis pipeline. Manual classification of neural events takes lots of time and is low in inter-rater agreement. This study classifies the most consistent neural events, namely spindles, K-complexes, and sleeping stages. By consistent, we expect to classify neural events that occur in multiple EEG channels representing different brain regions at the same time points. A gap in the current literature is that most studies focus on just a single or a few EEG channels to count these neural events, and implementing signal processing to automated detection pipeline is hard to optimize due to the dimensionality of the parameter space. Our preliminary data adapts an application of the algorithms to count neural events on 6 channels of the EEG, where it captures signals frontal to occipital area of the brain. With more information of the sleep stages adding to the pipeline, better performance is observed during the optimizing process.

Analyzing different neural events provides insights into how sleep facilitates remembering and forgetting, as well as diagnostic measurements for various sleep disorders (e.g. REM sleep behavior disorder, apnea, restless leg syndrome). Our automated detection pipeline aims to process sleep recordings and classify neural events with limited human input to it, including pre-processing, post-processing, and parameter optimization.

References

Recently there has been interest in the application of data assimilation tools to the improvement of neuronal models. Often, the only data one has access to is the measured voltage from a current-clamp experiment with a prescribed injected current. Our work aims to improve understanding of the impact that injected current stimuli has on the identifiability of parameters in a neuronal model. Parameter estimation results will be shown from 4D-variational data assimilation (4D-var) and an Unscented Kalman Filter (UKF). We will test the performance of characteristic currents, including steps and ramps, as well as chaotic currents and currents optimized to uncover the full dynamic range of the gating variables. The ability of these various stimulus protocols to enable state and parameter estimation will be assessed using simulated data from the Morris-Lecar model and a biophysical model of mammalian circadian clock neurons in the suprachiasmatic nucleus.
Decoding 2D environment from dCA1 while learning a spatial memory task

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The hippocampus is known to play a role in spatial representation and memory, but how 2D spatial representations are encoded and potentially changed by learning a memory task is still unclear. Here we use a variety of quantitative methods to analyze dCA1 electrophysiology data in rats with respect to both population coding and single cell behavior as they learn the structure and content of a spatial memory task. We expect spatial representations to become more defined and representative of the animal's location throughout a session. We further expect to see changes due to reward locations and increasing behavioral stereotypy across sessions.

**Experimental setup:** Animals were trained on a cheeseboard task (Dupret et al., 2010) over several sessions. Each session had a distinct set of 3 water reward locations and consisted of 30-40 trials concurrent with bilateral extracellular recordings from the pyramidal cell layer of dCA1 (N = 4 rats with ~100 cells per session). Each rat learned a new reward configuration across trials within each session. They also gained experience performing this foraging task over sessions.

**Data analysis and preliminary results:** To understand the dynamics of learning we use several analytic approaches. At the level of single cell activity, we use the KL-divergence to test how spatial firing distributions shift with learning. Further we explore the role that bursting plays in the emergence of stable firing rate maps. We also analyze how theta phase specific firing changes with learning to determine changes in temporal input patterns from EC and CA3. To study assembly dynamics, we use a population vector correlation to track stability of the ensemble activity throughout trials and across sessions. This metric reveals how stability corresponds with spatial learning as well as higher-order task structure learning. We use a Bayesian decoder based on a Poisson firing model to predict the animal’s physical position from the population activity (Zhang et al. 1998). Thereby we obtain a population measure for decoding accuracy, which we hypothesize, will increase with learning. We compare these measures with simulations in which firing of cells is entirely dependent on space. Finally, we use the population vector and Bayesian decoder analyses while systematically excluding subsets of cells to quantify the impact that individual cell properties have on the ensemble activity and predictability.

In order to find cellular correlates of learning, we evaluate performance within a trial using the time and distance taken to complete the trial (*i.e.* shorter time spent or distance travelled corresponds to higher performance). As expected, performance improves within a session. On a single cell level we observe an increase of ripples within the first half of the trials and on a behavioral level a decrease in the KL divergence measure of trial-trajectories. These results remain to be further explored regarding content of ripples and KL divergence of firing maps.

Preliminary results also indicate that the decoding accuracy of the Bayesian decoder increases with performance. However, accuracy of the Bayesian decoder still varies strongly within a trial, showing unexpected fluctuations in error. Identifying the cause of this variability may reveal additional information about the activity of the network that we are recording from. For a simulated grid of Poisson-firing place cells with model place fields, the error is low and consistent across space, eliminating the possibility of a general failure of the Bayesian decoder. Poisson firing of the cells is also tested using the distribution of Fano Factor values over space. The distribution centers around 1 indicating that Poisson firing is a fair assumption. Further sources of error include under sampling from the cells encoding space or from the environment (as the animal does not travel over each possible location). Still, the relative uniformity of the expected error from the decoder suggests that the issue is not under-sampling, as this would likely lead to a heterogeneous distribution over space. At this point, understanding the error of the Bayesian decoder could elucidate the dynamics of the neural population that are not captured in its assumptions, providing valuable insight to how the system changes throughout learning. These results can then be compared with the results of the other analytic methods described above to work towards a more complete picture of population dynamics over learning.

In all, this work draws from a variety of analysis paradigms to provide a more nuanced perspective on changing neural dynamics during learning on both a single cell and population level.

**Reference**


E. Kelemen, A. Fenton, Key Features of Human Episodic Recollection in the Cross-Episode Retrieval of Rat Hippocampus Representations of Space, PLOS Biology (11, 7) pp. 1-11, 2013
Computational modeling of hippocampus lesions during time perception

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The perception and use of durations in the supra-second range (interval timing) is essential for survival and adaptation, and is critical for fundamental cognitive processes like decision making, rate calculation, and planning of action [2]. In the vast majority of species, protocols, and manipulations to date, interval timing is time-scale invariant: time-estimation errors increase linearly with the estimated duration [1]. Time-scale invariance is ubiquitous in many species from invertebrates to fish, birds, and mammals, such as rats [3], mice and humans. Scale invariance is the fundamental property of interval timing, as it is extremely stable over behavioral, lesion, pharmacological, and neurophysiological manipulations.

Hippocampal lesions have been suggested to affect peak times in the peak-interval procedure and the subjective equivalence points in the temporal bisection procedure [4]. Rats with hippocampal damage responded earlier than the scheduled time of reinforcement in a variety of peak-interval procedures [4]. Both pre-training and post-training dorsal hippocampal (DH) lesions produced leftward shifts in peak times, confirming previous investigations and suggesting a possible role for the DH in the cortical striatal-based timing mechanisms [4]. In contrast, ventral hippocampal (VH) lesions produced a temporary rightward shift of peak times. Moreover, when peak times and peak rates were modulated by reversal learning, pre-DH lesions appear to have dramatic effects on the adaptability of temporal associations, whereas VH lesions only have effects on response levels. Given the spatially localized effect of interval timing observed in DH and VH, we may ask if there are any other evidences for a spatial localization of possible oscillatory activity, i.e. a topological organization for neural oscillators.

In our numerical simulations we used the Striatal Beat Frequency (SBF) in which timing is coded by the coincidental activation of neurons, which produces firing beats with periods spanning a much wider range of durations than single neurons [5]. SBF model [1] assumes that time is coded by the coincidental activation of a large number of cortical (input) neurons projecting onto spiny (output) neurons in the striatum that selectively respond to particular reinforced patterns. To mimic the variability in memorized criterion time $T$, we randomly generated a wide range of values around the desired criterion time using a specified distribution. As with any numerical implementation, the number of memory cells must be finite and, therefore, the continuous, smooth, distribution from is replaced by a discrete counterpart. Based on the selected memory distribution, different memory cells hold slightly different values of criterion time in a topologically ordered manner. We assumed that the randomly generated criterion times are first ordered, e.g. from low to high, and then stored in successive memory locations (topological map). In our implementation, memory lesions are implemented by selectively removing memory cells post-training. As a result, the memory of criterion time becomes non-symmetric, which is reflected in a corresponding shift of the output of the model - according to observed experimental data [4].

References

Calibrated nonparametric analysis of monosynaptic interactions from extracellular spike trains

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Jitter-type spike resampling methods are applied in neurophysiology for detecting temporal structure in spike trains (point processes). The concern has been raised, based on numerical experiments involving Poisson spike processes, that such procedures can be conservative. We study the issue and find that it can be resolved by re-emphasizing the distinction between spike-centered (basic) jitter and interval jitter. Focusing on spiking processes with no temporal structure, interval jitter generates an exact hypothesis test, guaranteeing valid conclusions. In contrast, such a guarantee is not available for spike-centered jitter. We construct explicit examples in which spike-centered jitter hallucinates temporal structure, in the sense of inflated false positive rates. The effect of the hallucination can be arbitrarily large. The theoretical results highlight the value of classical statistical frameworks for guiding the design and interpretation of spike resampling methods.

As an application of these distinctions, we demonstrate their relevance to the problem of using in vivo spike train interactions, in behavioral conditions, to identify neuron pairs that are monosynaptically-connected. The identification draws upon fine distinctions in temporal structure. Simultaneous large-scale juxtacellular-extracellular recordings enable precise evaluation of the statistical assumptions.

This is collaborative work with Gyorgy Buzsaki, Daniel English, Samuel Mackenzie, and Eran Stark.

References
The characterization of hippocampal interneurons --- a time delayed mutual information approach

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Interneurons are important for computation in the brain, in particular, in the information processing involving the generation of oscillations in the hippocampus. Yet the functional role of interneurons in the generation of hippocampal oscillations remains to be elucidated. In general, nonlinearity in interactions in neuronal systems presents a methodological challenge to analyze their behaviors. To circumvent this difficulty, here we use time-delayed mutual information to investigate information flow related to various types of interneurons to characterize the interactions between interneurons and hippocampal oscillations. For freely behaving mice, we identify two classes of interneurons whose firing activities share high mutual information with the slow theta-band (4-12 Hz) and the fast ripple-band (100-250 Hz) of local field potential, respectively. Information flow direction further suggests their distinct contribution to theta and ripple oscillations. In contrast, Granger Causality analysis fails here to infer the causality between activities of interneurons and hippocampal oscillations.
Comparing dynamical models for brain-wide cortical activity

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An exciting new type of data on cortical dynamics is wide-field calcium imaging data, which is both spatially extensive and temporally well-resolved. Consisting of images of the entire brain surface at a ten millisecond timescale, this enables the analysis of large scale data at a temporal resolution not available from other techniques such as fMRI. Similarly well-resolved data sets have already yielded interesting insights, particularly patterns in spontaneous activity as compared with response to a stimulus [1]. Moving beyond this, we report on work towards creating a dynamical model for brain-wide activity.

We use recently collected data from the Allen Institute for Brain Science, collected while mice perform a visual detection task. These data contain activity from tens of anatomically defined brain regions. We fit a dynamical model to activity of these brain regions of the following general form, similar to that used in [2]:

\[ \dot{x}(t) = Ax(t) + Bu(t) + \sum_{i=1}^{K} u_i(t)D_i x(t) \]

where \( x(t) \in \mathbb{R}^D \) is a vector of the regional activity and \( u(t) \in \mathbb{R}^K \) is a vector of input variables. Importantly, the input \( u \) includes both variables related to the task and behavioral variables: stimulus contrast, reward information, licking, and running speed. In this model, \( A \in \mathbb{R}^{D \times D} \) describes region-region interactions and \( B \in \mathbb{R}^{D \times K} \) describes the effect each input variable has on the regional activity. The bilinear terms, with each \( D_i \in \mathbb{R}^{D \times D} \), tell us how each input variable modulates the region-region interactions. This allows for more complex interactions than the basic linear model, as the input variables can affect the regional activity both directly through \( B \) and indirectly through \( D \) by modifying the effective region-region interactions. The parameters \( A, B, D \) can be fit using linear regression.

Our work so far identifies two primary constraints for fitting these types of models. The first is that in the form written above, the model cannot properly capture meaningful effects from the input variables. This is because many of the input variables (stimulus contrast, reward, licking) are usually zero, with nonzero values at very few time points. To address this, we modify the model slightly to allow \( B \in \mathbb{R}^{D \times K \tau} \), \( D_i \in \mathbb{R}^{D \tau \times D} \) to be a set of filters of length \( \tau \) which are convolved with the input variables. This form can still be fit using linear regression, but allows the input variables to have an effect over longer than a single time step. The second observation we make when fitting this type of model is that what we expect to be downstream effects show up as direct input-region effects in \( B \). For instance, looking at the filters in \( B \), the stimulus contrast shows the strongest effects on the visual areas but also has effects on non-visual areas. We would expect the stimulus response in the non-visual areas to come from region-region interactions from the visual areas, rather than directly from the stimulus input. Thus in order to fit an interpretable model, we conclude that we need to limit the stimulus-region interactions to include only anatomically motivated pairings.

To evaluate the models, we look at the \( R^2 \) value of computing \( \dot{x}_i \approx x_i - x_{i-1} \). The linear model with no inputs has an \( R^2 \) value of about 6% on trial-locked data (we note that these are not trial averaged and contain significant unexplainable variance). Looking at the parameter \( A \), we see that the strongest components are effects going from the left visual areas to other areas across the brain, consistent with the fact that the mice are performing a visual task with the stimulus visible in only the right eye. The model with inputs, where \( B \) consists of filters, admits an \( R^2 \) value of about 10%. We find that the bilinear model overfits the training data, and ongoing work seeks to regularize the form of these terms. We note that the above results come from the Emx1-Cre mice, which have been discovered to produce pathological activity [3, 4]. In the future, work will be done using data from other Cre lines.

Next steps are to fit nonlinear models, particularly a regularized form of the bilinear model described above, and to determine if this offers an improved description of the regional activity. The bilinear model in particular may give insight into how input variables such as the stimulus affect region-region interactions.

References
Summary. In daily life, the auditory system sorts the mixture of sounds from different sources into specific acoustic information, a process called auditory scene analysis. Sequential integration is one important component of the auditory scene analysis characterized by grouping of acoustic events over time and forming internal mental representations of sound streams. A particular set of stimuli that have been used intensively in behavioral experiments of sequential integration consists of sequences of alternating high (A) and low (B) pure tones presented as repeated triplets, ABA ABA ..... Depending on the frequency separation (df) between the two tones, subjects report either of two percepts: “integration” (a single, coherent stream of high and low tones, like a galloping rhythm) and “segregation” (two parallel distinct streams). After the stimulus onset, it takes several seconds for the probability of stream segregation to build up, and this probability depends on df. Furthermore, at intermediate values of df, subjects report spontaneous alternations between the two percepts. Multi-unit recordings from monkeys’ primary auditory cortex (area A1) show similarities between build-up functions of stream segregation obtained from psychophysical experiments (the *psychometric* functions) and those inferred from neural data (the *neurometric* functions) [1]. In this presentation, we demonstrate that a signal-detection model introduced in [1] to compute neurometric functions, generates neither realistic mean durations nor percept durations of gamma/lognormal distribution as reported in [2-3]. We then propose a new model that implements evidence accumulation over time at the readout of the signal-detection component. Our proposed model fits well the psychophysics data from various df conditions; it captures desired statistical attributes of percept durations, and it provides insights into the dynamical mechanisms of perceptual switching.

**Psychophysical experiment.** 15 human subjects of normal hearing were prompted to listen to repeating sequences of ABA triplets at df=3, 5, 7 semitones, with a total of 675 trials per df condition. Each sequence was comprised of sixty 500 ms-long triplets, resulting in a 30 s-long presentation. Subjects were asked to press and hold different buttons on a keypad when they perceive integration and segregation, respectively.

The evidence accumulation model. First, we simulated the signal-detection model from [1] and tested the statistical properties of the resulting percept durations. Neuronal responses to tone B (spike counts) were generated using mean spike counts extracted from cortical spiking neural data [1]. We showed numerically and theoretically that the signal-detection model produces percept durations whose distribution is exponential and whose means are significantly smaller than those reported experimentally. We then propose an extension to this model in the form of a multi-stage feedforward auditory network with components: i) area “A1” whose local outputs (mean spike counts) are subject to threshold-based binary classifiers (binary neurons); ii) An ensemble of binary neurons receiving local input from “A1”; and iii) Two competing units (“the accumulators”) whose activities depend on accumulated evidence from neuronal ensemble (ii) for each of the two percepts, integration and segregation. The suppressed neuronal unit accumulates evidence against the current percept while the dominant unit gradually reduces its activity. Both are racing towards their given thresholds. Escape and release type of dynamic mechanisms control the switches from one percept to another, depending on df conditions.

Results. The proposed evidence accumulation model was able to reproduce qualitatively and quantitatively switching behavior between integration and segregation in auditory streaming of triplets. In particular, the model produced percept durations whose distribution is gamma-like and whose means are comparable to those obtained in our psychophysical experiment, at each df. Moreover, consecutive percept durations yielded positive linear correlation as reported in [2] and as found in our own experimental data. The positive correlation is a direct consequence of the accumulation of evidence against the current percept as implemented in the model.

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References


Phasic response motifs are optimal for persistent detections

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Recent evidence suggests that the stimulus-evoked responses of early olfactory neurons dichotomize into phasic and tonic temporal motifs. Presumably, such responses mediate the eventual decoding of the stimulus identity. However, the precise mechanisms of such decoding and, in particular, the advantages of having these different sets of temporal dynamics is not well understood. Here, we perform a computational study to disentangle these different sensory-evoked responses. We consider a Two Alternative Detection (TAD) paradigm in which sensory ‘evidence’ towards each of two stimulus compositions is integrated within a drift-diffusion model (DDM) framework [1] and a detection is made in favor of one of the compositions. Representing the neural response to sensory inputs as the evidence driving the latent state of the DDM, we investigate the optimality of these neural motifs with regards to different drift dynamics.

We examined stimulus evoked responses of projection neurons in the locust antennal lobe circuit that receive direct sensory input from the olfactory receptor neurons. We observed that evoked responses contain two major, mutually exclusive motifs: spiking activity during stimulus presentation followed by inhibition (‘ON’ type) or inhibition during the stimulus presentation followed by pronounced phasic activation after stimulus termination (‘OFF’ type). The ON, OFF clusters observed in our data (Figure 1a). It should be noted that additive Gaussian noise would not change the stimulus persistence, and a phasic response on stimulus withdrawal. These motifs are consistent with the ON and OFF clusters can be further sub-classified according to the magnitude of their phasic parts, as shown in Figure 1a.

We then asked whether such motifs might be optimal conveyors of sensory ‘evidence’ within a DDM decoding scheme in a proposed Persistent response paradigm, where the objective of the neural response is to retain the sensory percept until the stimulus is withdrawn. For this, we considered a quadratic cost function of the form

\[
\begin{align*}
\text{minimize} & \quad J(y) = \int_0^\infty \frac{1}{2} (\nu(t) - z)^T \nu(t) + x(t)^T R_1(t) x(t) + y(t)^T R_2(t) y(t) \, dt \\
\text{subject to} & \quad \dot{\nu}(t) = f(\nu, x), \quad \dot{x}(t) = y, \quad \nu(0) = \nu_0, \ x(0) = x_0
\end{align*}
\]

where \(\nu \in \mathbb{R}^2\) is the latent state, \(x \in \mathbb{R}^M\) is the neural response from \(M\) neurons. Here, \(f(\nu, x)\) is the drift function and \(z\) represents the target representation, within which is embedded the detection threshold as well as the suppression of competing processes. The cost over an indefinite horizon penalizes: (i) the latent state’s departure from the desired threshold (thus yielding a persistent detection); (ii) the energy and velocity \(y\) of the neural response (via \(Q(t) \geq 0, R_1(t) \geq 0, R_2(t) > 0\) respectively). This framework allows for explicit penalization of ambiguity, so that all competing latent states must also be sufficiently away from their own thresholds (Figure 1b).

In Figure 1c we plot the optimal motif for the equilibrium model \((f(\nu, x) = A\nu + bx, \ \sigma(A) \in \mathbb{R}^n_{<0}\) without noise. The first motif (red) displays a phasic response following stimulus onset, followed by a tonic component during stimulus persistence. The second motif (blue) displays a relatively tonic inhibition during stimulus persistence, and a phasic response on stimulus withdrawal. These motifs are consistent with the ON and OFF clusters observed in our data (Figure 1a). It should be noted that additive Gaussian noise would not change the optimality of these motifs.

Our results indicate how neural responses in early sensory networks may enable time-optimal formation and maintenance of representations of a persistent stimulus.

References


Figure 1: (a) Neural responses in olfactory projection neurons dichotomize into two response classes: Phase/Tonic ON (left) and OFF (right). (b) We consider a DDM framework with an objective function designed to allow thresholds to be hit and held with minimal ambiguity due to competing latent variables. (c) Optimizing persistent detection according to the cost (1) in an equilibrium DDM results in production of similar response motifs.
Utilizing local discrete structure for perceptual distortion in natural images

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Summary. A major challenge in image processing is quantifying the perceptual quality of distorted images. Solutions to this problem allow new lossy compression algorithms to be more easily and accurately evaluated. Motivated by failings of mean-squared error (MSE / PSNR), Bovik and others proposed a perceptual image measure called “Mean Structural Similarity” (MSSIM), which decomposes the distortion of image patches into three components: a difference in mean luminance; a difference in luminance variance; and a structural component, the cosine of the angle between the original and distorted image patch. We present a new distortion measure that replaces the structural component of MSSIM by the Hamming distance between suitably discretized distorted and original image patches. We demonstrate that this new image measure is highly correlated with human scoring using standard human psychophysics dataset, the UT Austin LIVE Image Quality Assessment Database (Release 2). Its success suggests, consistent with experiment and theorems about lossy compression, that the human visual system is fundamentally concerned with underlying discrete structure in natural images.

Background. A major goal in image processing research is to find accurate and easily calculated measures of perceptual image quality. Mean-squared error (MSE / PSNR) is ubiquitous, but unlike the human visual system (HVS), MSE is very sensitive to luminance shifts and contrast increases. Researchers have been searching for a perceptual distortion measure that can replace MSE and its relative, peak signal-to-noise ratio (PSNR). Previously, workers looking to replace MSE have used computational models of the HVS to develop perceptual distortion measures. However, computational models of the HVS can be quite complicated and are still the subject of active research [1]. In 2004, Wang and colleagues developed a new full-reference perceptual distortion measure by assuming that the HVS utilizes “structure” in natural images [2] to discern differences. The “structural similarity index” (SSIM) decomposes the distortion of image patches into three components: a difference in mean luminance; a difference in luminance variance; and a structural component, the cosine of the angle between the original and distorted image patch. These components are evaluated and multiplied together for each patch in a larger image, and local patch-wise SSIM scores are pooled to calculate the mean SSIM (MSSIM) of the image. MSSIM and variants thereof have been used widely, in some cases replacing MSE / PSNR. We propose a new measure of the “structural distortion” component for an image patch: the Hamming distance between suitable binarizations of the distorted and reference patch [3]. Our efforts stem from theorems in rate-distortion theory that identify discrete codings as optimal compressors, suggesting that perceptual structure even in continuous-valued natural images is fundamentally a discrete object, a departure from typical models of natural images. Using this definition of structure, we can calculate a mean discrete structural similarity index MDSSIM.

Results. We demonstrate that MDSSIM is a good candidate for image quality assessment by assessing its high correlation with mean opinion scores (MOS) scores from the LIVE image quality assessment dataset, Release 2. The surprisingly good performance of MDSSIM suggests a new understanding of part of the transformation performed by the HVS. In particular, the HVS may be far more responsive to local discrete structure in natural images than previously expected [1], pointing the way towards novel experiments in vision science, e.g. by extending visual psychophysics to the model of [3].

Fig. 1: Mean Opinion Scores MOS against MDSSIM in the LIVE dataset (779 images); Pearson, Spearman, and Kendall's correlation (PSNR: .80, .82, .62; MSSIM: .74, .85, .66).

References

Deep brain stimulation (DBS) is an effective treatment to reduce motor symptoms in both advanced Parkinson’s Disease (PD) and essential tremor. However, how the therapy works is poorly understood and it is believed there is room for improvement in terms of efficacy, reduction of side effects, and decrease in power usage [1]. In PD, motor symptoms correlate with increased power in beta oscillations [2] and complex models have been used to suggest stimulation protocols reducing beta power better than conventional DBS (for instance [3]).

To get analytic insights on the effects of DBS, we are studying stimulation in the simpler Wilson-Cowan model describing the firing rates of an excitatory and an inhibitory population (Fig. 1A). This model can be fully analysed in the phase plane, and yet still produces complex behaviour. Oscillations can be obtained for a range of parameters (limit cycle in Fig. 1B). The model has been shown to produce beta oscillations relevant to PD in the STN [4]. To further investigate the relevance of our model, we show that a stochastic version of this model can fit to both human tremor data and beta oscillations in rat Subthalamic Nucleus (STN) Local Field Potential (LFP).

We model stimulation as an increase in the firing rate of the excitatory population. As shown in Fig. 1B, the effect of stimulation on the system phase can then be visualized by looking at the isochrons of the system in the phase plane (obtained as in [5]): We compute Amplitude Response Curves (ARC, Fig. 1C) and Phase Response Curves (PRC, Fig. 1D) for weak and strong stimulations.

![Figure 1 A: Wilson Cowan model phase plane. B: Phase plane with isochrones (level sets of the color map). Red lines are stimulation pulses. C: ARC. D: PRC.](image)

The goal of stimulation is to reduce pathological oscillations. We find that only certain phases are conducive to amplitude reduction through stimulation, and even then, only when the stimulation magnitude is below a certain threshold. Indeed, a reduction in amplitude is achieved only when the system is brought inside the limit cycle of Fig. 1B. We further observe that the maximum decrease in the model oscillation amplitude is obtained when bringing the system to the fixed point at the centre of the limit cycle in Fig. 1B. This corresponds to stimulating at the PRC phase which has maximum slope (dashed line in Fig. 1C and 1D).

Some of the model predictions can be contrasted with other models. In particular, the concomitance of the maximum effect of the stimulation on amplitude and the maximum slope of the PRC has been suggested in [6]. It is noteworthy that the Kuramoto model makes a different prediction. The dataset behaviour in that regard may inform us as to what type of model is more appropriate.

From the results of the fit to different patients (for tremor) and rats (for LFP), we compare the topology of the corresponding phase planes, PRC and ARC, and discuss how the model predictions are modulated. This may yields predictions that will help to bridge the gap between stimulation experiments and theory.

References

Brain images are the data for modeling and verifying neurodevelopment. The significant geometric structure in the mouse images\(^1\) of Fig. 1(a) was the visual stimulus to create the discrete dynamics of cell differentiation visualized in Figs. 1(b) - 1(d).

![Image & Art](a) Image & Art  
![Start](b) Start  
![Disjoint](c) Disjoint  
![Collision](d) Collision

**Figure 1: Pinwheel Image, Art & Dynamics.**

Our algorithms first focus on geometric combinatorics that arise during the discrete dynamics. In Fig. 1(b), the start of the differentiation process is shown, with the central black triangles modeling the stem cells that are dividing to produce the surrounding hexagonal ‘petals’, shown sequentially by the two shades of red. The next depicted frame of Fig. 1(c) shows the trivial case where another stem cell spawns structures that are totally disjoint, as shown by the completed red and green petal configurations, each with a central black ‘hub’. Note the introduction of a purple quadrilateral. In Fig. 1(d), the purple visualizes the geometric combinatoric of intersection as a formal model of the biophysical phenomena of the right half of Fig. 1(a), which shows similar geometry and color changes.

Extending the 2D images of Fig. 1 to a 4D spatiotemporal visualization depends upon modeling 3D geometric changes over time, subject to biophysical assumptions that volumes and topology are preserved for stem cells. The hexagonal grids shown in Figs. 1(b) - 1(d) are similar to the pixelated screens of digital topology [KKM91]. Similar to the digital screen, consider a point to be an hexagon with its location designated by an integer-valued ordered pair, with a digital neighborhood around a point defined by the six adjacent hexagons. The obvious supremum metric, denoted by \(D_{sup}\), leads to the criterion between points \(p, q\):

\[
\text{If } D_{sup}(p, q) \leq 2, \text{ then the geometric combinatorics should be investigated for biophysical significance.}
\]

This formal criterion will support investigation into proximity as a factor in inhibition of cell division.

Clearly, biological cells do not follow the precise geometric boundaries imposed by the hexagons, initially chosen to simplify algorithmic development. Building from this promising ‘proof of concept’ [PCM\(^*\)17], the software is being extended to free-form shapes, with initial sketches shown in magenta in Fig. 2. The objects are modeled by swept volumes on spline curves, chosen for facile volumetric control by an integral equation. Additionally, the metric constraint, above, is being integrated with these morphs to preserve volume while avoiding pairwise intersections, as appropriate for the biophysics.

These mathematical models will be verified by statistical studies on MRI images for hydrocephalus. Hydrocephalus is a common birth defect in premature babies. Its prominence for treatment by pediatric neurosurgeons provides a rich store of sequential MRI images to correlate with the images generated by the visualization software.

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**References**


\(^1\)Image used with permission of author & publisher.
Ratio of slow and fast synaptic currents regulates the synchrony of population rate activity in a spiking layered cortical network model

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Slow synaptic currents conveyed by NMDA have been shown to increase or decrease the synchrony of biological neural networks at γ frequency [1,2]. Here, we extend a layered spiking cortical network model describing a microcircuit in the primary visual cortex [3] by slowly decaying postsynaptic currents. The model is composed of four layers (L2/3, L4, L5 and L6), where each layer contains an excitatory and an inhibitory population of leaky-integrate-and-fire (LIF) neurons. The model exhibits population rate oscillations around 64 Hz and 250 Hz [5], referred to as the low- and high-γ peak. The number of neurons in each population, as well as the number of connections between and within populations was extracted from biological data sets [4]. Potjans et al. [3] showed that the population firing rates generated within the model reproduce those observed in experiments. The original model has exclusively fast currents with time constants of 0.5 ms. Substituting a variable percentage of the excitatory and inhibitory fast currents by slowly decaying postsynaptic currents, with synaptic time constants of 100 ms, we show that the firing rates of the populations are approximately preserved, when assuming that the total current conveyed by single synapses is conserved over time.

The response properties of LIF neurons receiving slow as well as fast currents have been investigated by Moreno-Bote and Parga [8], who apply an adiabatic approach to solve the Fokker Planck equation which describes the probability densities of the membrane potentials and synaptic currents. Building this formalism into the recently introduced theoretical framework [5], which builds on linear response theory [6] and the mapping of the dynamics of coupled populations of LIF neurons to coupled rate models [7], allows us to predict the population rate spectra of the microcircuit model for various ratios of slow and fast synapses. Increasing the amount of slow synaptic currents for all, excitatory and inhibitory, connections homogeneously desynchronizes the population activity in the low- as well as high-γ range. In [5], we introduced a sensitivity measure, which identifies dynamically relevant connections at each frequency. Reformulating this sensitivity measure, with respect to the connection specific ratio of slow and fast currents, we locate connections where changes in the receptor ratio are most efficient in regulating population rate synchrony.

This abstract applies for poster presentation only.

References

Macroscopic Phase-Resetting Curve of Spiking Neural Networks: Theory and Application.

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The study of brain rhythms is one of the most challenging subject of interest in neuroscience. An understanding of their functional implications and computational roles could be facilitated by the use of phase resetting curve (PRC); a powerful analytical tool in use to study rhythms [2,9]. However, the topic of PRC for global oscillations observed at the macroscopic scale in neural circuits has received little attention so far. The reason is that macroscopic rhythms emerge from the synaptic interaction of thousands of spiking cells. Although we look at the network as an oscillator and define its phase cycle in term of ongoing self-sustained rhythmic activity, it is made up of individual units which are not oscillators.

In this study, we take advantage of a thermodynamic approach combined with the Ott-Antonsen theory. The thermodynamic framework produces an analytically tractable population models written in term of a partial differential equation (PDE), from which we extract the firing rate of the spiking network [5]. The Ott-Antonsen theory, see [10], allows further reduction and breaks down the PDE into a low dimensional system [6,8]. Bifurcation analysis of the reduced system enables us to reveal how synaptic interactions and inhibitory feedback permit the emergence of macroscopic rhythms. The usual adjoint method can then be applied and a semi-analytical expression of the macroscopic infinitesimal PRC is derived [3].

Our analytical computations allow to make key predictions. First we observed that only stimulus targeting the inhibitory cells can generate a biphasic PRC. Such PRCs are known to facilitate entrainment to periodic inputs at both higher and lower frequencies than the natural frequency of the network. Then we investigate the effect of coupling strength and transmission delay on the dynamical emergence of phase locking mode within two bidirectionally delayed-coupled spiking networks. Within the framework of weakly coupled oscillators, we clarify why macroscopic oscillations show phase relations that are persistent across time, and provide reasons for the reported diversity of phase lags between cortical regions [7]. For the first time we bring theoretical support regarding the strong implication of inhibitory cells not only in the emergence of macroscopic rhythms, but also on phase locking modes between different neural circuits engaged in rhythmic oscillatory patterns. Our predictions are supported by extensive numerical simulations and are consistent with empirical data [1,4].

References
Thalamic modulation of cortical dynamics permits a massive reduction in neural resources for motor sequence generation

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Complex behaviors may be decomposed into sequences of motifs. In this view, sequence generation relies on the brain’s ability to select the current motif and then produce the neural activity needed to execute it. Here, we explore these phenomena with a model respecting anatomical constraints, and consisting of cortex (a recurrent structure), thalamus (a non-recurrent structure), and the reciprocal connections between them (Fig. 1a). During motor sequences, external thalamic inputs such as those from basal ganglia can show sustained activity that switches at the boundaries between motifs [1]. Assuming that these inputs can clamp the activity of their target thalamic units, we study the effect of thalamic activity switching on cortical dynamics. We analyze the simple case where all thalamic units but one are clamped by their inputs during a given motif. Hence, a single thalamic unit is freely interacting with cortex (Fig. 1b right), but the main conclusions would still hold if there were several such units during a motif. We show that thalamic activity switching effectively acts as a rank-one perturbation of the corticocortical connectivity matrix. Further, we show that half of the parameters of this perturbation (corresponding to thalamocortical weights) can be easily adjusted to set the eigenvalues governing the effective cortical dynamics at will (Fig. 1b). In addition, we show that robustness to noise in the neuronal activities can be improved by using the corticothalamic weights to control how much each eigenvector aligns with the readout vector $\mathbf{W}$ on which the cortical activities are projected to form the motor command. We can also write equations to examine the sensitivity to noise in the synaptic weights. Note that in agreement with experiments [2], and to robustly prevent the development of chaotic activity, we effectively model neuronal dynamics as a switching multilinear system. Finally, our analysis reveals the efficiency of the thalamocortical architecture for motor sequences generation. In the thalamocortical circuit, the number of cortical units has to scale linearly with the number of eigenvalues necessary to shape the motor command for an individual motif ($N_{eigs}$), while the number of thalamic units has to scale linearly with the number of motifs that the circuit needs to encode ($N_{motifs}$), for a total of $N_{eigs} + N_{motifs}$ units. In contrast, an unstructured recurrent cortical network similarly respecting the experimental constraint of linearizable dynamics [2], requires a number of units that scales with $N_{eigs} \times N_{motifs}$. Hence, the motor thalamocortical loop architecture may have evolved because of this tremendous improvement in efficiency.

Figure 1: (a) Left: The modeled motor thalamocortical architecture. Cortex produces a motor command by a linear readout (with weights $\mathbf{W}$). During a specific motif, some thalamic units (here, the left one) are released from clamping basal ganglia inputs. Right: The dynamics. Cortical units have a linear Input-Output function [2]. Thalamic units have a piecewise linear I-O function, parameterized such that corticothalamalic inputs operate within the linear regime, while the strong basal ganglia inputs can push thalamic units to saturation. (b) Left: The uncontrolled cortical network follows an arbitrary linear dynamical system, characterized by an arbitrary set of eigenvalues $\lambda$ which shape the function produced through its readout $\mathbf{W}$. Hence, this function cannot be reshaped for each motif. Right: When the basal ganglia input leaves one (or several) thalamic unit(s) unclamped during a given motif, the cortical dynamics effectively obeys a different linear system whose eigenvalues can be set (here, to approximate the sinc function) by adjusting the thalamocortical weights with noise robustness assured by setting the corticothalamic weights.

References


A lateral inhibition model of the Hermann grid illusion beyond Baumgartner’s theory

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Visual perception is constructed in the brain by processing luminous stimuli detected by the retina and transmitted through the visual pathway. Visual illusions provide important insights on the way brains process luminous stimuli, because they uncover the mechanisms through which the visual pathway distorts the original signal to extract salient information, in other words, to help creating the illusion of the sensed world. The Hermann grid illusion [3] is perceived by gazing around intersections of white lines presented on a black background forming a grid of evenly spaced black squares. Dark smudges appear at the intersections to which the subject is not directly looking at. Understanding the mechanisms underlying this illusion is important, because it uncovers the way in which the brain partially filters out visual signals not coming directly from the focal point of the visual field. The classical explanation of the Hermann grid illusion was firstly proposed by Baumgartner [6]. The series of visual experiments proposed in [3] reveal that this classical explanation is untenable and that a new theory involving cortical processing is necessary. In this work, we present preliminary exploration of an abstract model that might capture the qualitative features of the Hermann grid illusion beyond Baumgartner’s theory.

The model is a reaction-diffusion realization of lateral inhibition. This consists in a local autocatalytic excitation in parallel with a longer range recurrent inhibition. Lateral inhibition is wide spread in the brain both in the retina and beyond. In the retina it is mediated by horizontal cells [4]. In the thalamus, the principal hub of sensory information processing, it is mediated by reticular nucleus neurons [7]. Beyond neuronal processing, lateral inhibition underlies general morfonegenesis in biological systems [5]. In the brain, it might similarly underlies the genesis of perceived forms.

The main difference between the proposed model and Baumgartner’s model is in the footprint size of excitation. Whereas in Baumgartner’s model it is of the order of the bar width, in our model it is of the order of the square width. As a preliminary exploration, we test our model on a one-dimensional cartoon of the Hermann grid illusion. Although many properties are lost in the reduction from two dimensions to one, we show that the proposed model explains why the illusory effect is largely reduced when the ratio of square width to line width is reduced, a property that is already not captured by Baumgartner’s theory. We geometrically discuss the obtained results based on the theory in [1, 2]. Future directions include the generalization of our results to the full two-dimensional illusion to explore whether the proposed model is able to explain all the salient properties not captured in Baumgartner’s theory. We will also test the proposed mechanism in neuronal field models [8], more physiologically sound in the neuronal context than reaction diffusion models. Finally, we will rely on the recent paper [9] to explore multiscale generalizations of the Hermann grid illusion.

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References

A Theoretical Framework for Analyzing Coupled Neuronal Networks: Application to the Olfactory System

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Sensory processing is known to span multiple regions of the nervous system. However, electrophysiological recordings during sensory processing have traditionally been limited to a single region or brain layer. Recent advances in experimental techniques [1]–[2] have enabled simultaneous recordings of multiple populations and across different regions. This new data allow us to pose the following question: what are the crucial neural network connections that enable sensory processing across different regions? Furthermore, how are these these connections interrelated?

Here, we develop a novel theoretical framework that relies on efficiently calculating the first and second order statistics in a multi-population firing rate (non-spiking) model [3]. We apply this method to determine qualitative relationships between important yet hard to measure network connections in the rat olfactory system, when the model is constrained by data from simultaneous dual micro-electrode array in vivo recordings from two distinct regions, the olfactory bulb (OB) and anterior piriform cortex (PC), Fig 1A. In particular, the model makes predictions which we subsequently validate in a full spiking (leaky integrate-and-fire) neural network model of the OB–PC pathway (Fig 1B) that satisfies the many constraints from our experimental data. We find when the derived relationships (e.g. Fig 1C) are violated, the spiking statistics no longer satisfy the constraints from the data. In principle this modeling framework can be adapted to other systems and be used to investigate relationships between other neural attributes besides network connection strengths.

References

Figure 1: A) In vivo dual array experiments inspire theoretical framework. B) Schematic of neural network model: in spiking model, all connections are considered; in the firing rate model, the gray connections are omitted. C) One example of a prediction from the firing rate model that is verified in the full spiking model. The theory enables characterizing how the important connections are all related to each other.
Firing probability for a noisy leaky integrate-and-fire neuron receiving arbitrary external currents

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(I don’t want this work to be considered for oral presentation)

In many applications, it is important to understand how quickly and reliably a neuron receiving noisy background input would respond to a stimulus in the form of post-synaptic currents or post-synaptic potentials (PSPs). In this work, we consider a leaky integrate-and-fire neuron receiving Gaussian white noise and obtain analytically the probability of the neuron firing at least one action potential when an additional PSP is applied. In particular, we derive a correction, in terms of the time derivative of the additional PSP, to the solution in the adiabatic limit [1] such that our analytic approximation is drastically improved for cases in which the dynamical time scale of the PSP is comparable to that of membrane integration. With the correction, our analytical approximations match well with the results obtained from numerical simulations for a wide range of PSP sizes and shapes, and for both, strong or weak background noise (see Figure 1). Our method can be used to estimate the response latency of sensory neurons and to study the reliability of neural responses to temporally filtered and jittered synchronous input.

Figure 1. The approximation of \( t=25\,\text{ms} \) with PSP which shape is shown in the inset. Black (red) lines show the simulation (approximation) results. Solid/dashed line corresponds to different background noise amplitude \( \sigma \). The approximation remains excellent even with PSPs of complex shapes for both values of \( \sigma \).

References

Neural responses to repeated presentations of an identical stimulus often show substantial trial-to-trial variability. Although the mean firing rate in response to different stimuli or during different movements (tuning curves) have been extensively modeled, the variability of neural responses can also have clear tuning independent of the tuning in the firing rate. This suggests that the variability carries information regarding the stimulus/movement beyond what is encoded in the mean firing rate [1]. Here we demonstrate how taking variability into account can improve neural decoding. In a typical neural coding model spike counts are assumed to be Poisson with the mean response depending on an external variable, such as a stimulus/movement direction. Bayesian decoding methods then use the probabilities under these Poisson tuning models (the likelihood) to estimate the probability of each stimulus given the spikes on a given trial (the posterior). However, under the Poisson model, spike count variability is always exactly equal to the mean (Fano Factor = 1). Here we use the Conway-Maxwell-Poisson (COM-Poisson) model to more flexibly model how neural variability depends on external stimuli. This model contains the Poisson distribution as a special case, but has an additional parameter that allows both over- and under-dispersed data, where the variance is greater than (Fano Factor >1) or less than (Fano Factor <1) the mean, respectively. We find that neural responses in both primary motor cortex (M1) and primary visual cortex (V1) have diverse tuning in both their mean firing rates and response variability. These tuning patterns can be accurately described by the COM-Poisson model, and, in both cortical areas, we find that a Bayesian decoder using the COM-Poisson models improves stimulus/movement estimation by 4-8% compared to the Poisson model. The additional layer of information in response variability thus appears to be an important part of the neural code.

![Figure 1](image-url)

**Fig. 1:** Diversity in tuning curve dispersion. Left, Fano factors and correlation between Fano factor and mean spike count tuning curve for V1 (top, data from CRCNS pvc-11) and M1 (bottom, data from CRCNS dream-stevenson). Note that the Fano factors are not well described as constant close to 1 (as would be the case for Poisson firing) or even well correlated with the spike count (as would be the case for a fixed mean-variance relationship). Two example neurons from V1 and M1 are shown at middle and correspond to the arrows at left. Curves show fits from COM-Poisson models; dots and error bars denote observed means and 95% confidence intervals (estimated by Bayesian bootstrapping). Decoding accuracy increases as more neurons are modeled for the Bayesian decoders with Poisson and COM-Poisson assumptions as well as for optimal linear estimation (OLE).

**References**
Mathematical modelling of noise-induced escape problems in networks of coupled bi-stable units

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Mathematical models of excitable cells, such as neurones, are often characterized by different dynamic regimes, such as alternating rest and excited states. The transient dynamics responsible for transitions between dynamic states are often discounted or overlooked in favour of the long term asymptotic behaviour. However, analysis of these transitions is instrumental in understanding, for example, the onset and evolution of epileptic seizures. We consider a phenomenological model of seizure initiation represented by a network of coupled bi-stable neurones with noise. Specifically, we consider sequences of noise-included escapes of nodes (assuming that transitions back are very infrequent by comparison) for small motif networks of this model. Using analysis and numerical simulations we investigate how the emergent dynamics are affected by changes in network structure and draw links to transitions observed in experimental and clinical data.
Quasi-synchronization in a stochastic spiking neural network  
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The brain is composed of billions of interacting stochastic neurons of different types. Understanding the behavior of such intricate network is key to answer theoretical questions concerning the way animals learn, adapt, form memories... The large number of parameters necessary to describe these neural networks has led to the study of mathematical models which are more tractable. Yet, the analysis of these mathematical models is still difficult because of the large, but finite, number of neurons.

Hence, their study is often realized by looking at the thermodynamic limit of an infinite number of neurons, e.g a mean field limit whose analysis allows to draw information about the finite network. On the other hand, it has long been observed that the brain activity supports oscillations, as recorded for example by EEG, which are the building blocks of many processes such as attention, memory or communication between brain areas.

As such, the study of the conditions for the appearance of these oscillations in immature networks, composed of excitatory neurons, is key to understanding the first steps in the evolution of the brain dynamics in young animals.

Since the seminal studies [1,2], the dynamics of excitatory pulse-coupled neural network has attracted a lot of attention [3,4] in order to model collective neural oscillations observed in developing hippocampus, as function of synaptic delays, network size, connectivity and noise. More precisely, it has been shown that for slow synapses, the dynamics is asynchronous whereas it shows partial synchronization for fast synapses. The case of noisy network has been much less studied, even when the noise is introduced as an external source [5].

Figure 1 Distribution of membrane potentials as function of time close to the Hopf bifurcation

The main differences of the present work with [5] are 1) the use of very different types of noise (intrinsic spike noise vs. external white noise) and 2) the use of a more basic model of synapse (instantaneous synaptic input vs. a more physiologically accurate synaptic input). We report the same mechanism: destabilization of the asynchronous state though a Hopf bifurcation. The use of a simpler model of chemical synapse is justified by the fact that we also consider electrical synapses.

More precisely, we provide three different numerical evidences for the occurrence of a Hopf bifurcation in a recently derived [6,7,8] mean field limit of a stochastic network of excitatory spiking neurons. The mean field limit is a challenging nonlocal nonlinear transport equation with boundary condition. The first evidence relies on the computation of the spectrum of the linearized equation. The second stems from the simulation of the full mean field. Finally, the last evidence comes from the simulation of the network for a large number of neurons. We provide a “recipe” to find such bifurcation which nicely complements the works in [6,7]. This suggests in return to revisit theoretically these mean field equations from a dynamical point of view.

References
Strange neuronal responses to fluctuated inputs

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Cortical neurons generate irregular spike trains, including highly variable intervals. The irregular spiking has received much attention because it plays functionally important roles in neural information processing. The origins of these irregularities are intrinsic noise, such as synaptic unreliability and ion-channel noise, and highly fluctuating drives that are generated by the balance of the excitatory and inhibitory synaptic inputs to the neurons. Neuronal responses have traditionally been characterized by their frequency-current relationship. However, the frequency-current relationship is not sufficient for understanding the neuronal responses to fluctuated inputs. Several studies have described the responses of neurons to fluctuated inputs, and reactive differences have been reported among neuron models [1].

Regarding the response to the fluctuated inputs, an interesting phenomenon has been reported [2]. “The variability of output spike trains of the Hodgkin-Huxley (HH) neuron model decreases as the input variance increases.” This inverse relationship between input and output variances is seemingly counterintuitive. Thus, we call it a strange response. A schematic representation of an strange response is shown in Fig.1. Sakai et al. suggested that the underlying mechanism of the strange responses of HH neurons may originate from the subthreshold oscillations of the membrane potential. In fact, the input-output (I-O) relationship of a leaky integrate-and-fire (LIF) neuron model, which does not contain subthreshold oscillations, is proportional [Fig.1(b)]. A similar phenomenon has also been observed in an experimental study [3].

Although their findings were important and fundamental, further analyses are required because the comparison was performed with models with dynamics that were very different from each other. The HH and LIF models differ in a number of ways, including the complexity of their dynamics, the number of variables, and the number of parameters. Moreover, the HH model is too complicated to use to determine the origin of the strange responses. Therefore, we have been unable to verify that subthreshold oscillations are the origin of the strange responses as Sakai et al. concluded. In addition, other components may cause or contribute to the strange responses. Thus, the purpose of this study was to reveal the origin of the strange responses.

To examine the origins of the strange responses, a neuron model that can separate the subthreshold oscillations and the bistability should be used. In the current study, we employed the Hindmarsh-Rose (HR) neuron model [4]. The HR model is a neuron model that is described by only two variables, and it has fewer parameters than the HH model. The HR model exhibits both subthreshold oscillations and bistability by controlling only two parameters.

First, we demonstrated that the HR model separated the subthreshold oscillations and bistability and that the origin of the strange responses was the bistability and not the subthreshold oscillations. We then found that the same results were obtained with map-based models. A map-based model that contained bistability reproduced the strange responses, while the map-based model that did not contain bistability did not. These results were further supported by the findings that the strange responses were reproduced by a simple mixture of two interspike interval (ISI) distributions.

References

Cortical circuits exhibit complex activity patterns both spontaneously and evoked by external stimuli. Finding low-dimensional structure in population activity is a challenge. What is the diversity of the collective neural activity and how is it affected by an external stimulus?

Using concepts from ergodic theory, we calculate the attractor dimensionality and dynamical entropy production of these networks. We obtain these two canonical measures of the collective network dynamics from the full set of Lyapunov exponents.

We consider a randomly-wired firing-rate network that exhibits chaotic rate fluctuations for sufficiently strong synaptic weights. We show that dynamical entropy scales logarithmically with synaptic coupling strength, while the attractor dimensionality saturates. Thus, despite the increasing uncertainty, the diversity of collective activity saturates for strong coupling. We find that a time-varying external stimulus drastically reduces both entropy and dimensionality.

Finally, we analytically approximate the full Lyapunov spectrum in several limiting cases by random matrix theory. Our study opens a novel avenue to characterize the complex dynamics of rate networks and the geometric structure of the corresponding high-dimensional chaotic attractor.

**Model** The network dynamics follows [1]: \[ \frac{dh_i}{dt} = -h_i + \sum_{j=1}^{N} J_{ij} \phi(h_j) \], where entries of the coupling matrix \( J_{ij} \) are drawn from a Gaussian \( \mathcal{N}(0, g^2/N) \). The transfer function is \( \phi(h) = \tanh(x) \). Our approach is valid for arbitrary \( \phi \) and \( J_{ij} \).

**Relevance & Applications** Chaotic rate networks recently attracted a lot of attention in studies of network heterogeneity, bistability, external stimuli and the role of single unit transfer function and slow synaptic dynamics for the collective network state (e.g. [2-10]) Also it is increasingly appreciated that chaotic rate dynamics provide a substrate for complex nonlinear computations e.g. learning input-output relations (11-12) and learning temporal sequences (Laje 2013). Intriguingly, transient rate chaos yields exponential expressivity in deep networks (Poole & Ganguli 2016).

Firstly, our approach provides a toolkit from dynamical systems theory to analyze how different factors shape the complex rate dynamics. Secondly, our tools allow to quantify the reorganization of the collective network dynamics during learning and to dissect underlying mechanisms of different reservoir computing strategies.

**References**

Efficient numerical integration and nonlinear filtering of a stochastic Jansen and Rit model

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Neural mass models provide a useful framework for modelling mesoscopic neural dynamics and in this poster we consider the Jansen and Rit Neural Mass Model (JR-NMM). This system of ODEs has been introduced as a model in the context of electroencephalography (EEG) rhythms and evoked potentials and has been proposed as an underlying model in various application settings. We use a stochastic version of the JR-NMM which has the structure of a stochastic Hamiltonian with a nonlinear displacement and has been shown to have a number of structural properties, such as moment bounds and ergodicity. We discuss the quality of simulations based on an efficient numerical integrator developed using a splitting approach. The important feature of this integrator is that it preserves the structural properties of the JR-NMM system. This integrator is then applied in a nonlinear filtering framework and a number of simulation studies imply that it is superior in terms of efficiency (or simply correctness) to using other methods which do not respect the structural properties of the JR-NMM in the filtering setting.
Numerous filigreed protrusions branch off the dendritic trees of many neurons in the cerebral and cerebellar cortex. These dendritic spines harbor excitatory synapses. Spines can shrink and enlarge on time scales as short as seconds, and these size changes correlate with the changes of the synapse strength. Though spines were first described by Ramon y Cajal more than a century ago, their exact purpose is still under debate. Several alternative hypotheses have been put forward over the years but have been difficult to test experimentally due to the small size of dendritic spines. In addition, spines are not simple homogenous structures but contain various nanometer-scale substructures and molecular machinery. All these aspects pose severe challenges to experimental investigation, numerical simulation and mathematical analysis. As a consequence, even estimates of a spine’s electrical resistance are still a matter of controversy.

Dendritic spines are highly plastic and may partake in learning and memory storage processes governed at the ultra-structural level. In order to gain a quantitative understanding of the influence of the spines micro-scale architecture on the electro-chemical signals transferred to dendrites, we are developing a numerical framework to solve an electro-diffusion model described by the Poisson-Nernst-Planck (PNP) equations. Computational complexity is addressed by introducing a novel hybrid-dimensional discretization approach and developing specialized numerical methods based on Finite Volume discretization and geometric multigrid solvers. Ultra-structural reconstructions generated by our collaborators (A. Herz, D. Patirniche, M. Stemmler, LMU Munich, Germany) from 3D electron microscopy images (M. Ellisman, UCSD, USA) can be integrated into the numerical simulation framework in order to investigate the interplay between ultra-structural morphology on electro-chemical signals.

Our approach intends to relate the multi-scale biological organization of dendritic spines to possible functional consequences at the macroscopic and systems level. Deciphering the impact of micro-structural features on spine dynamics is considered a stepping-stone towards understanding neural signal propagation and synaptic plasticity, and can likely reveal novel sub-cellular computational principles.
Cable type model and its application on action potential propagation in a myelinated axon

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The current paper is to construct a mathematical model to describe the transportation of action potential along a myelinated axon and conduct numerical simulations based on this model. Each segment of myelinated axon can be well described by cable model, while the inter-segment node, called node of Ranvier, needs to be described by a reaction-diffusion equation. It is because that on unmyelinated Ranvier’s nodes, the axon membrane is exposed to extracellular environment. Unlike myelinated axon segment, Ranvier’s node can then exchange ions with extracellular domain through gating of ion channels, and therefore generate a transmembrane action potential. The nonlinear part of its governing reaction-diffusion equation is the transmembrane ion currents described by models like the famous Hodgkin-Huxley model. The action potential at a Ranvier’s node is raised by stimulus current, transports through the neighboring myelinated axon segment, and stimulates the next Ranvier’s node to raise another action potential. This pattern is repeated along the axon, and this kind of action potential transportation is called saltatory conduction, which is faster than its counterpart in unmyelinated axons simply governed by reaction-diffusion equation. This is a work of nature evolution to make a faster and more energy-saving action potential transportation along the axon. Besides, a myelinated axon is far less interfered by action potentials of neighboring axon fibers than an unmyelinated one due to the insulation of axon by myelin sheath. Usually the length of Ranvier’s node is far smaller than a myelinated axon segment with the ratio about 1:1000, which means the spatial scale difference of these two governing PDE’s is enormous. We need to simplify the governing PDE on Ranvier’s node to be an ODE coupled with PDE’s on neighboring myelinated segments. Otherwise, resolution of these two scales would request a huge number of spatial discrete points and cause inefficiency of numerical computation even in the currently employed 1D model. Here multi-block Chebyshev pseudospectral method was applied to calculate the resultant equations. This numerical method has the advantage of higher order of accuracy and better numerical stability than tradition finite difference method. Through our numerical experiments, myelin sheath too long or too short, by fixing the radius of axon, would cause conduction failure. There exists a region of aspect ratio, which is the ratio between length and diameter of myelin sheath, for successful conduction. We also found action potential transportation speed is indeed proportional to axon radius with fixed aspect ratio as observed in experiments. By adjusting a few parameters, our model and computation can match experiments on the measurements of axon action potential transportation speed with satisfactory agreement for several species. We also applied this model to study the mechanism of multiple sclerosis, which is a type of neural disease caused by the demyelination of axon via repeated inflammation.

References


Simulated spatial dependence in action potential propagation

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Typically, in analyzing data using the Hodgkin–Huxley model of the axonal membrane [1], qualities of the axon such as membrane capacitance, resistance, and diameter are taken to be constant along the entire length of the axon. However, a more revealing investigation would take into consideration variations in these properties based on location on the axon because these properties will depend on factors such as ion channel density and myelination, which are not constant along an axon length. The nodes of Ranvier, for example, are characterized by a much higher density of ion channels compared to myelinated sections of the axon, which allows for faster action potential propagation speed.

In this study, we explore the impact of such spatially dependent variables on action potential propagation speed and sustainability. We do this using a program that we developed in MATLAB to simulate an action potential based on the Hodgkin–Huxley and telegrapher equations, which allows us to build a multi-compartmental model of the axon. The results from this study may have important implications about certain demyelinating diseases, such as multiple sclerosis.

References