W19 PHYS 178/278 Final Project Logistics

- **Team up**
  You are going to forming a team, ideally of two, for working on a project together. We will have a short project team-up mixer on Tuesday, Feb 19th.

- **Topics**
  You may choose the topic from the suggested topics lists or bring up a topic that interest you or is relevant to your ongoing research. The project sign-up sheet will be emailed to you.

- **Presentation**
  Each group will give a short presentation of their project during the final, on March 21st, 8am -11am. It will be about 8 mins long plus 2 mins Q&A.

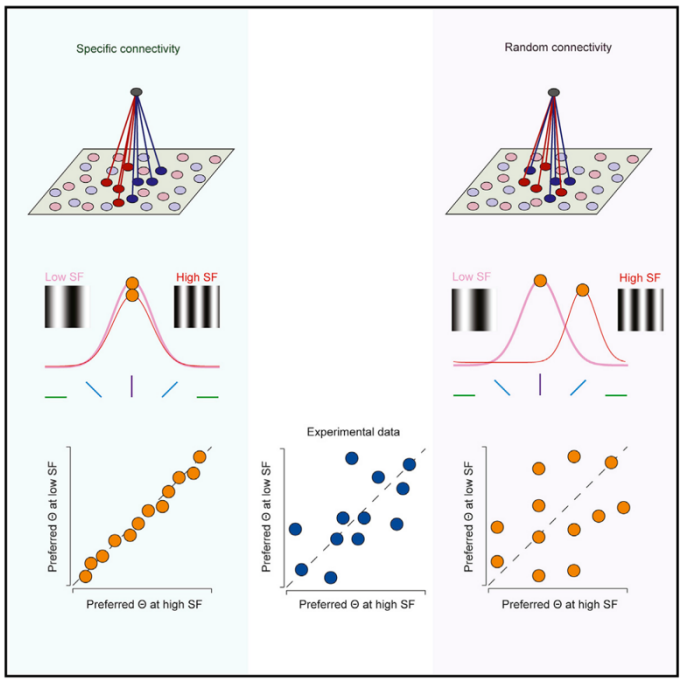
- **Final report**
  Each group need to submit a single report on the project by March 28th, 11:59 pm. Ideally, the report should not exceed 5 pages, including figures (the lists of references are not counted). Please email your final report and the relevant source code to Prof. Kleinfeld (dk@physics.ucsd.edu). Remember to have your name and PID typed in the report.

W19 PHYS 178/278 Final Project Topics

1. Emergent orientation selectivity from random networks

Emergent Orientation Selectivity from Random Networks in Mouse Visual Cortex
Emergent Orientation Selectivity, Pattadkal J. J., Mato G., van Vreeswijk C, Priebe N. J., Hansel D., *CellReports*, *24*(8):2042–2050.e6. https://doi.org/10.1016/j.celrep.2018.07.054

Pattadkal et al. show that orientation selectivity in primary visual cortex (V1) can emerge from random connectivity and offer a distinct perspective for how computations occur in the neocortex. They propose that a random convergence of inputs can provide signals for orientation preference in contrast with the dominant model that requires a precise arrangement.



The figure illustrates two types of V1 neuron models. A V1 neuron receive ON and OFF inputs from the thalamus, and the inputs that are sampled on the basis of a Gabor filter:

1) **Hubel & Wiesel Connectivity** - ON and OFF inputs have spatial preferences elongated along the preferred orientation axis and are spatially segregated.

2) **<u>Random Connectivity</u>** - V1 neuron that receives ON and OFF inputs with nearby spatial preferences, which are randomly intermixed

Considering the model with **random connectivity**:

- Whether the random connectivity could give rise to orientation selectivity?
- How is the emergent orientation selectivity sensitive to the number of inputs? What will happen if excitatory and inhibitory inputs are ***balanced***?
- Explore the dependencies between preferred orientation and spatial frequency in the model.

2. Emergent orientation selectivity from a ring network model

Theory of orientation tuning in visual cortex, BEN-YISHAI, R., LEV BAR-OR, R., Sompolinsky, H., *PNAS 92*:3844–3848 (1995). https://doi.org/10.1073/pnas.92.9.3844

The role of intrinsic cortical connections in processing sensory input and in generating behavioral output is poorly understood. This study examined this issue in the context of the tuning of neuronal responses in cortex to the orientation of a visual stimulus. They proposed a **ring network model** that incorporates both orientation-selective input from the lateral geniculate nucleus and orientation-specific cortical interactions. Depending on the model parameters, the network exhibits **orientation selectivity** that originates from within the cortex, by a symmetry-breaking mechanism. Based on the ring model, several experimental consequences of this cortical mechanism of orientation tuning are derived:

- The tuning width is relatively independent of the contrast and angular anisotropy of the visual stimulus.
- The transient population response to changing of the stimulus orientation exhibits a slow "virtual rotation."
- Neuronal cross-correlations exhibit long time tails, the sign of which depends on the preferred orientations of the cells and the stimulus orientation.

Objective goals: investigate different mechanisms for orientation selectivity in visual cortex by using a **ring network model.**

- Steady-state:
  - Derive the steady-state solution $M(\theta)$
  - Study the orientation tuning properties $M(\theta)$. How does **tuning width** θ_c of $M(\theta)$ depend on the **stimulus contrast** (c), and **anisotropy** ($\mathcal{E}$) for different ranges of values of the connectivity parameters?
- Time-dependent response:
  - Study the time-dependent response $m(\theta, t)$ to a change in the orientation of the external stimulus, and the cross-correlations (CCs) between the neurons in the network.

3. Ring attractor dynamics

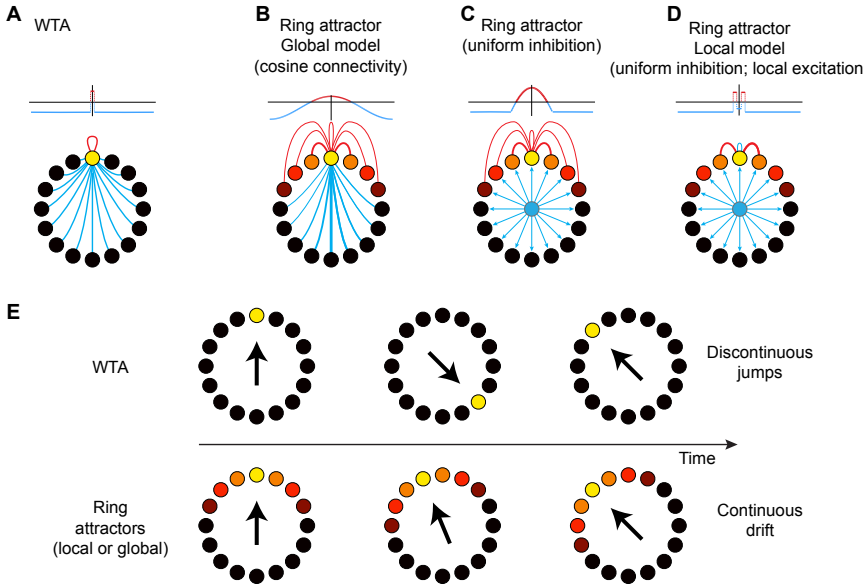
Ring attractor dynamics in the *Drosophila* central brain, Kim, S. S., Rouault, H., Druckmann, S., Jayaraman, V., *Science*, *356*(6340): 849-853 (2017).
https://doi.org/10.1126/science.aal4835

A population of cells called compass neurons represents a fruitfly's heading direction. Kim et al. used imaging and optogenetics in behaving flies to elucidate the functional architecture of the underlying neuronal network. They observed **local excitation** and **global inhibition** between the compass neurons. The features of the network were best explained by a **ring attractor network model**. Until now, this hypothesized network structure has been difficult to demonstrate in a real brain.

Objective goals:
Explore the response dynamics of two extreme ring network architectures, and one intermediate case:

- A "global model" based on **global** cosine-shaped interactions (fig. S3B).
- A "local model" based on relatively **local** excitatory interactions (fig. S3D).
- A "intermediate model" that lie between the extremes of the local and global models.

Compared the model predictions to experimentally observed *activity bump* dynamics. Which model does explain the experimental observation better?



4. Rhythmically neural control of breathing

Computational models of the neural control of breathing, Molkov, Y. I., Rubin, J. E., Rybak, I. A., Smith, J. C., *Rev Syst Biol Med. 9*:1–22 (2017). https://doi.org/10.1002/wsbm.1371

The ongoing process of breathing underlies the gas exchange essential for mammalian life. Each respiratory cycle ensues from the activity of rhythmic neural circuits in the brainstem, shaped by various modulatory signals, including mechanoreceptor feedback sensitive to lung inflation and chemoreceptor feedback dependent on gas composition in blood and tissues. This paper reviews a variety of computational models designed to reproduce experimental findings related to the neural control of breathing and generate predictions for future experimental testing. The review starts from the description of the core respiratory network in the brainstem, representing the central pattern generator (CPG) responsible for producing rhythmic respiratory activity, and progresses to encompass additional complexities needed to simulate different metabolic challenges, closed-loop feed- back control including the lungs, and interactions between the respiratory and autonomic nervous systems. The integrated models considered in this review share a common framework including a distributed CPG core network responsible for generating the baseline three-phase pattern of rhythmic neural activity underlying normal breathing.

Objective goals:
Refer to the models discussed in this review, construct a mathematical model of **the respiratory central pattern generator (CPG)** that captures three neural activity 'phases' presence in the rhythmic motor pattern during normal breathing,

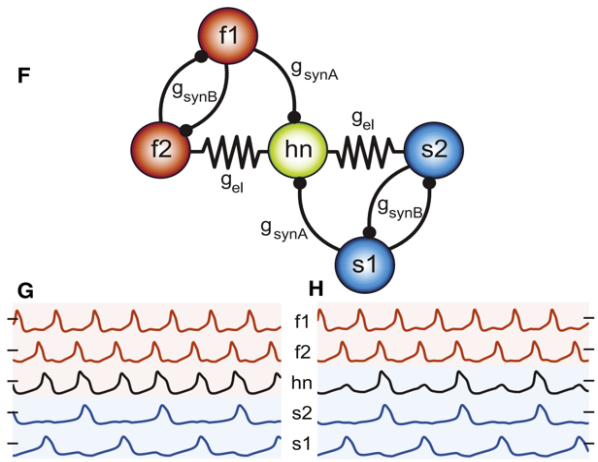
- inspiration (I),
- post-inspiration (post-I or P-I) or the first stage of expiration, and
- the later or second stage of expiration (called E-2),

Compare the simulations of your model with the existing experimental findings.

5. Competing rhythmic oscillators

Multiple mechanisms switch an electrically coupled, synaptically inhibited neuron between competing rhythmic oscillators, Gutierrez GJ, O'Leary T, Marder E, *Neuron* 77.5 (2013) https://doi.org/10.1016/j.neuron.2013.01.016

Rhythmic oscillations are common features of nervous systems. One of the fundamental questions posed by these rhythms is how individual neurons or groups of neurons are recruited into different network oscillations. More specifically, how are individual neurons or groups of neurons switched between, or recruited into, different oscillatory networks as a function of the strength of the electrical and chemical synapses in the network?



Objective goals:
Model a five-neuron circuit in which a hub neuron is connected to two different oscillatory subnetworks.

- Firstly, investigate the dynamics of each subunit of the five-neuron circuit (see Fig.1 B, C, D and E of the paper).

- Explore the patterns of coordination shown in the network as a function of the **electrical coupling** (g_{el}) and **inhibitory synapse** (g_{synA}, g_{synB}) strengths, and how the hub neuron can be switched between the fast and slow oscillators.

  Three-dimensional parametrical space:
  - The role of **electrical coupling** (g_{el}).
  - The **inhibitory synaptic conductance** (g_{synA}) connecting to the hob neuron.
  - The inhibitory synaptic conductance (g_{synB}) of half-center oscillators.

  Quantify the activities of five neurons in terms of
  - Spiking frequencies
  - Phase relations

6. Coupled oscillators, modeling fish locomotion

The Nature of the Coupling Between Segmental Oscillators of the Lamprey Spinal Generator for Locomotion: A Mathematical Model, Cohen, A. H., Holmes, P. J., and Rand, R. H., *J. Math. Biology 13*:345–369 (1982). https://doi.org/10.1007/BF00276069

This study introduced a theoretical model which is used to explain the intersegmental coordination of the neural networks responsible for generating locomotion, i.e., swimming, in the isolated spinal cord of *lamprey*.

The electromyographic activity of the myotomal muscle of a fish exhibits a stereotyped temporal pattern. In spinal cord the ventral root (VR) output pattern underlying the muscle activity is believed to have three important features: (1) The activity of the two ventral roots of a single segment strictly alternates in time; (2) the duration of the activity of a VR is a constant proportion of the period of the cycle; (3) there is a delay between the bursts of any two ipsilateral ventral roots and that delay is proportional to the period (Fig 1.2).

Here, the model assumes that each segment of the cord consists of a pair of neural networks which can generate oscillatory activity. Pairs of oscillators (in ventral root) are assumed to be coupled together to form the central pattern generators (CPG) which then generates the complete stable pattern.

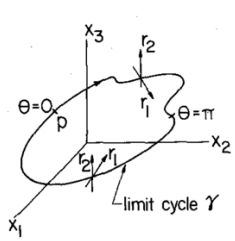
Objective goals:
Each segmental oscillator of spinal cord is approximated as a limit cycle oscillator which consists of only a single dependent variable, the phase θ(t). By considering set of N coupled limit cycle oscillators, demonstrate that,

- how stable phase locked motions which correspond to traveling waves in the spinal cord can be generated, thus simulating "fictive swimming";

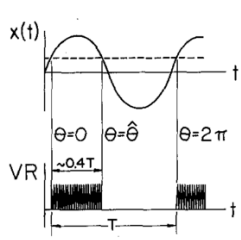
- bidirectional coupling between the oscillators can generate a stable **traveling wave**.

Fig. 1.2. Ventral root recordings from an isolated piece of spinal cord. Recordings are from the right and left roots of segments 7 and 19 (from Cohen and Wallén, 1980)

There is a delay between the bursts of any two ipsilateral ventral roots and that delay is proportional to the period. The third feature implies that the delay occupies a constant phase of the cycle, i.e. there is a constant phase coupling between the two segments.



2.1



2.2

Fig. 2.1. The phase space of Eq. (2.1) in the special case $n = 3$, for which $\mathbf{r}$ is a 2-vector, $\mathbf{r} = (r_1, r_2)$

Fig. 2.2. The oscillator output $x(t)$ and its relation to the ventral root output VR. The threshold level is shown as a *dashed line*

7. Oscillators with time-delayed coupling

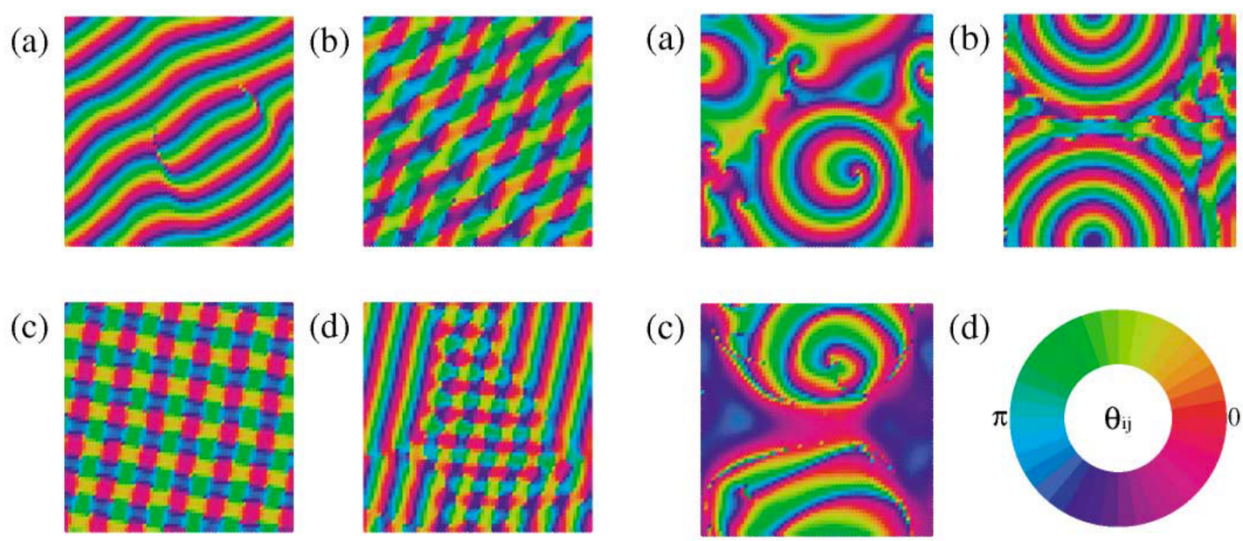
Time-Delayed Spatial Patterns in a Two-Dimensional Array of Coupled Oscillators, Jeong, S., Ko, T., Moon, H., *Phys. Rev. Lett. 89* (15) (2002).
https://doi.org/10.1103/PhysRevLett.89.154104

Spatiotemporal patterns arise in numerous physical, chemical, and biological systems. The brain, one of the most complex systems, is now also known to generate spatiotemporal patterns such as plane waves and spirals. This study investigated the effects of **time-delayed** interactions in an ensemble of **two-dimensional coupled phase oscillators**. Each oscillator is allowed to interact with its neighbors located within a finite radius r_0, and the coupling signal propagates at speed v.

Objective goals:

- Demonstrate that distance-dependent time delays induce various patterns including traveling rolls, square like and rhombus like patterns, spirals, and targets.

- Explore the parametrical space of **coupling length r_0**, **coupling coefficients K**, and **signal propagation speed v**. and analyze the stability boundaries between the synchronized planar solutions (when all oscillators are in the same phase) and the emerging patterns.



8. Propagating Neuronal Discharges in Neocortical Slices

Propagating Neuronal Discharges in Neocortical Slices: Computational and Experimental Study, Golomb D, Amitai Y., *J Neurophysiol. 78*(3):1199-211 (1997).
https://doi.org/10.1152/jn.1997.78.3.1199

When synaptic γ-aminobutyric acid-A ($GABA_A$) inhibition is pharmacologically suppressed in neocortical slices, neuronal population discharges[1] appear as responses to electrical stimulation above a certain strength. In extracellular recording, they are found to be abrupt, all-or-none field potentials (FPs). In intracellular recordings, they correspond to depolarizing shifts (DSs) in membrane potentials, above which rides a high-frequency train of action potentials. These discharges are referred to as "synchronous" or "epileptiform," implying that adjacent cells tend to fire together.

Objective goals:

Based on the model of neocortical cells present in this study, construct a one-dimensional network with spatially decaying synaptic efficacies, and investigate the dynamic mechanisms that lead to the creation, propagation, and cessation of discharges. Specifically, seek the answers to the following questions:

1) What are the spatiotemporal properties of the discharge propagation, and how are they related to the network architecture?

2) How do the velocity and shape of the discharge depend on the synaptic parameters, such as the strength of AMPA and NMDA synaptic efficacies, and the level of synaptic depression?

3) What is the relationship between the propagation velocity and the synaptic kinetics?

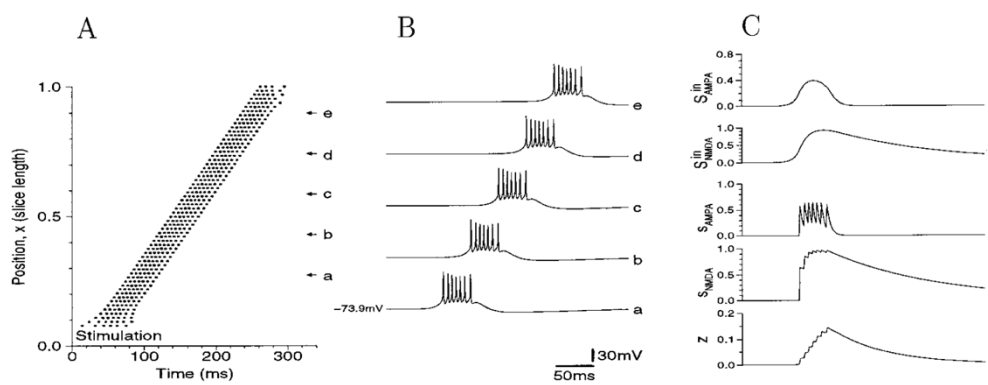


FIG. 3. Propagation of discharges in cortical slice model. There is no synaptic depression ($k_t = 0$), $g_{AMPA} = 0.31$ mS/cm^2, $g_{NMDA} = 0.25$ mS/cm^2. *A*: rastergram of excitatory cells. Only firing times from every 4th cell are shown. Arrows at *right*: position of 5 cells along slice whose voltage time courses are plotted in *B*. Initially cells at left ($x \leq 0.06$) are depolarized ($V = 10$ mV) and all others are at rest. Discharge propagates to *right* and far from edges maintains its shape; every neuron fires 7 spikes during discharge. *C*: time courses of internal variables of neuron denoted by *a*. From *top*: total AMPA and NMDA synaptic conductance, S^{in}_{AMPA} and S^{in}_{NMDA}, that this neuron receives (the neuron's ''input''); AMPA and NMDA auxiliary variables, s_{AMPA} and s_{NMDA}, of postsynaptic synapses connecting this neuron to others (the neuron's ''output''); slow potassium activation variable *z*. Auxiliary variables are normalized such that 1 means that all corresponding channels are open.

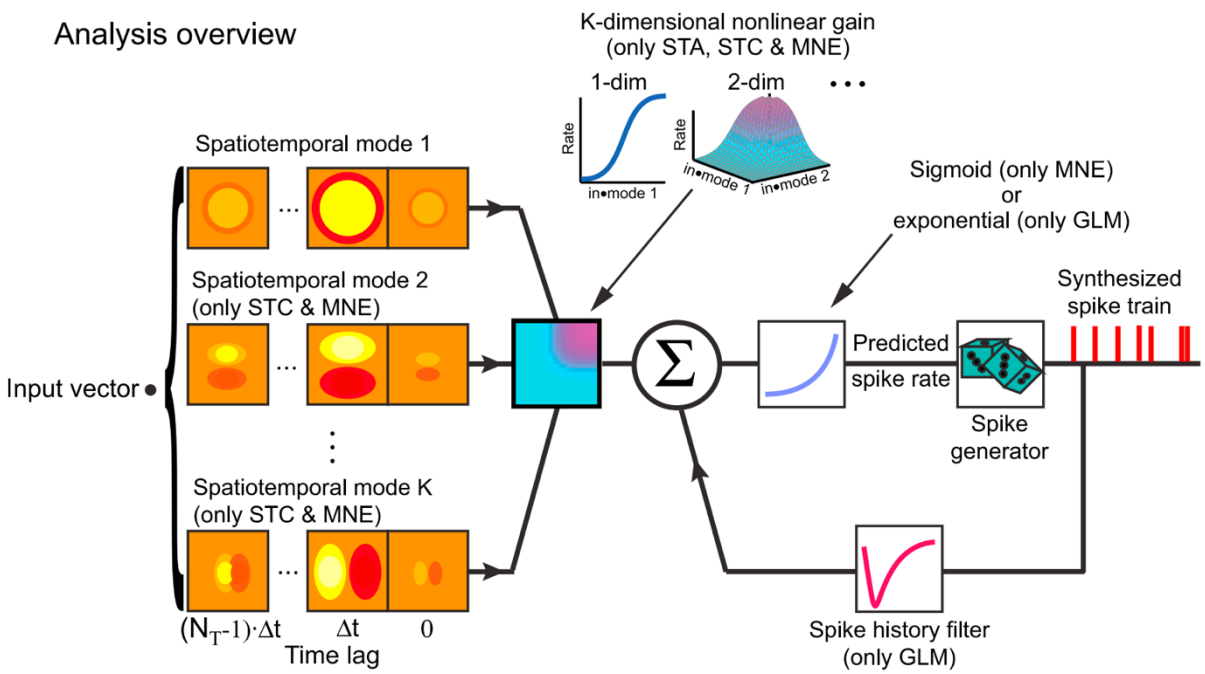
9. Neuronal spike trains data analysis

Analysis of Neuronal Spike Trains, Deconstructed, Aljadeff, J., Lansdell, B. J., Fairhall, A. L., & Kleinfeld, D., *Neuron*, *91*(2), 221–259 (2016).
https://doi.org/10.1016/j.neuron.2016.05.039

As information flows through the brain, neuronal firing progresses from encoding the world as sensed by the animal to driving the motor output of subsequent behavior. One of the more tractable goals of quantitative neuroscience is to develop predictive models that relate the sensory or motor streams with neuronal firing.

Objective goals:
Based on the statistics of applied stimuli (uncorrelated or correlated), select the proper analysis approaches to analyze the spike trains and extracting the relevant stimuli features.
- Spike-triggered average (STA)
- Spike-Triggered Covariance (STC)
- Maximum Noise Entropy Method (MNE)
- Generalized Linear Models (GLM)

The group can use the dataset acquired from their research project or search the available dataset online. Dataset and accompanying code presented in the paper is also available (https://github.com/NeuroInfoPrimer/primer).



10. Recurrent neural integrator network model for horizontal eye position (line attractor)

Stability of the Memory of Eye Position in a Recurrent Network of Conductance-Based Model Neurons, Seung, H. Sebastian, et al., *Neuron 26*.1: 259-271 (2000).
https://doi.org/10.1016/S0896-6273(00)81155-1

Develop an oculomotor integrator model as a network of conductance-based neurons which interact with each other by recurring excitatory synapses. The integrator neurons receive feedforward inputs from three neurons. The vestibular neuron which is tonically active at a constant rate, simulating the background activity present in vestibular afferents when the head is stationary. The excitatory and Inhibitory burst neurons that are normally silent, except for occasional brief burst of action potentials that cause saccadic eye movements. These bursts change the firing rates of neurons in the network which is maintained by recurrent excitation after the feedforward input is over. Signals from the integrator neurons lead to the oculomotor plant so that persistent changes in these signals cause persistent changes in the angular position of the eyes.

Objective goals:
This model should reproduce the following properties of biological integrator -

- Each integrator neuron in the model should exhibit a linear relationship between firing rate and eye position when it is active. However, there is also a threshold eye position below which it is silent. The linear slope and the threshold vary from neuron to neuron.

- Because of some imperfection in persistence, there is some drift of neural activity with time, which leads to drift in the eye position during fixation. The drift velocity depends systematically on eye position, generally in a nonlinear manner.

- The persistence of neural activity degrades when synaptic strengths are mistuned, neurons are destroyed, or the strength of feedback is otherwise perturbed.

11. Decision making

A Recurrent Network Mechanism of Time Integration in Perceptual Decisions

Wong, K.-F., Wang, X.-J., *J. Neurosci. 26*(4):1314-1328 (2006).

https://doi.org/10.1523/JNEUROSCI.3733-05.2006

Recent physiological studies using behaving monkeys revealed that, in a two-alternative forced-choice visual motion discrimination task, reaction time was correlated with ramping of spike activity of lateral intraparietal cortical neurons. The ramping activity appears to *reflect temporal accumulation*, on a timescale of hundreds of milliseconds, of sensory evidence before a decision is reached. In this paper, they adopt this reduced a biophysically based cortical microcircuit network model for decision making (Wang, 2002), to an **eleven-variable or two-variable version model** through mean-field approach.

Objective goals:
Understand the cortical circuit for decision making (Fig 1), and the re-derive the reduced version decision making model. With stability analysis and numerical simulation, try to investigate the following questions (you may use either **eleven-variable or two-variable** model for simulation depending on the questions):

- How does the recurrent dynamics give rise to a much longer integration time? Is this slow linear ramping a consequence of a network with slow recurrent excitation?
- Can the model still work when recurrent excitation is solely mediated by the much faster AMPA receptors (AMPARs)?
- Is it necessary that neurons subserving integration during stimulation also show persistent activity during working memory?

12. Dynamic gain control

Adaptation without parameter change: Dynamic gain control in motion detection, Borst, A., Flanagin, V. L., and Sompolinsky, H., *PNAS* 102(17): 6172-6176 (2005).
https://doi.org/10.1073/pnas.0500491102

Motion detection sensitive neuron of the fly visual system (H1) adapts its input-output relationship to changes in the statistics of the ambient stimulus. The rapid adaptation of the velocity response gain has been interpreted as evidence of optimal matching of the H1 response to the dynamic range of the stimulus, thereby maximizing its information transmission. Develop a motion detection model using Reichardt detectors, which extract the direction of motion by multiplying the brightness signals from neighboring image locations after asymmetric temporal filtering.

Objective goals:
The model should illustrate the following properties,

- Increasing the amplitude of the velocity fluctuations (variance) suppresses the contribution of the stimulus past, which leads to a marked reduction in the response gain.

- Increasing the stimulus variance shortens the time scale of the motion detection response thereby reducing it to the correlation time of the stimulus fluctuations.

As we know that nervous system is inherently nonlinear and multidimensional, develop a simple neuron model which shows that changing the form of nonlinearity may have significant effects on the magnitude of the resultant adaptive response.

13. Hebbian learning rule

Spike-Timing-Dependent Hebbian Plasticity as Temporal Difference Learning
Competitive Hebbian learning through spike-timing-dependent synaptic plasticity (STDP), Song, S., Miller, K. D., Abbott, L. F., *Nat. Neurosci. 3* (9): 919-926 (2000).
https://doi.org/10.1038/78829

A spike-timing-dependent Hebbian mechanism governs the plasticity of recurrent excitatory synapses in the neocortex: synapses that are activated a few milliseconds before a postsynaptic spike are potentiated, while those that are activated a few milliseconds after are depressed. We show that such a mechanism can implement a form of **temporal difference learning for prediction of input sequences**. Using a biophysical model of a cortical neuron, this paper show that a temporal difference rule used in conjunction with dendritic backpropagating action potentials reproduces the temporally asymmetric window of Hebbian plasticity observed physiologically. Furthermore, the size and shape of the window vary with the distance of the synapse from the soma. This work show how a spike-timing-based temporal difference learning rule can allow a network of neocortical neurons to predict an input a few milliseconds before the input's expected arrival.

Objective goals:
Reproduce the paper's simulation: model the balanced excitation network with LIF neurons (n = 1000). The (excitation) synapses are updated by STDP modification rule.

1) Given different mean presynaptic input rates (stochastic presynaptic spike trains), what is the
   (a) equilibrium distribution of synaptic strengths arising from STDP;
   (b) the spiking variability, i.e., coefficient of variation (CV) of the postsynaptic spike train.

2) **Latency reduction**: given the presynaptic inputs are correlated in various ways, how does the latency between post- and presynaptic spikes change, before and after the synaptic strengths are learned (and stable) through the STDP rule.

14. Resistance of stored memory to the ongoing noise

Fundamental limits on persistent activity in networks of noisy neurons,
Burak, Y., Fiete I. R., *PNAS 23*;109(43):17645-50 (2012) https://doi.org/10.1073/pnas.1117386109

Neural noise limits the fidelity of representations in the brain. This limitation has been extensively analyzed for sensory coding. However, **in short-term memory and integrator networks**, where noise accumulates and can play an even more prominent role, much less is known about how neural noise interacts with neural and network parameters to determine the accuracy of the computation.

This paper analytically derives how the stored memory in continuous attractor networks of probabilistically spiking neurons will degrade over time through diffusion.

Suppose that a memory network's initial state was set to Θ on the attractor by a stimulus that was then removed at t=0. At a later time T, a cue is presented signaling that the stimulus variable has to be recalled. Over what interval ΔT following the cue should a decoder collect spikes from the memory network to obtain an accurate estimate of Θ?

Objective goals:
Go through the derivation of how the stored memory in continuous attractor networks of probabilistically spiking neurons (noisy neural spiking) will degrade over time through diffusion and compare the analytical result with the numerical simulation using the ring structure neural network presented in the paper.

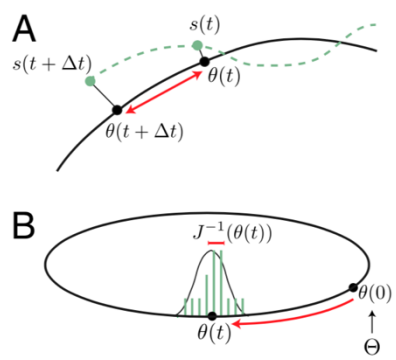


Fig. 1. Internal FI and derivation of diffusivity in attractor networks. (*A*) The network's instantaneous attractor state (black point, right) is defined as the point on the attractor (black line) to which the instantaneous state (green point, right) would flow if evolved without noise. To derive the diffusivity (details in *SI Appendix*), we evolve the network dynamics over a small time interval Δt using Eq. **10**. We project the new state (green point, left) back to the attractor (black point, left). The variance between the two attractor states, divided by Δt, is $2\mathscr{D}$. (*B*) An illustration of internal FI and diffusivity in an example network: A ring network with a single activity bump is initialized to the attractor state $\theta(0) = \Theta$ by an external input that is taken away at $t = 0$. After time t, the activity bump has moved to some location $\theta(t)$, due to probabilistic neural spikes that contribute noise to the network dynamics. The typical displacement at relatively short times t is $\sqrt{2\mathscr{D}t}$. At t, an ideal estimator trying to decode the network's instantaneous state on the attractor from a finite sample of spikes will have a variance bounded below by the inverse of the internal FI, $J^{-1}(\theta(t))$.

15. Coincidence detection – a building block model for sound localization

Simple models show the general advantages of dendrites in coincidence detection, Dasika, V. K., White, J. A. & Colburn, H. S., *J. Neurophysiol. 98*(5): 3449 (2007). https://doi.org/10.1152/jn.00669.2005

Simple models are used to elucidate mechanisms underlying the dendritic enhancement of coincidence detection. This paper focus on coincidence-detecting cells in the auditory system, which have bipolar dendrites and show acute sensitivity to ***interaural time difference (ITD)***, a critical cue for spatial hearing.

Builds a model cell that consists of a single-compartment soma with two identical passive dendritic sections attached to the soma, where each dendritic section is composed of a single dendritic-compartment or either a finite number or an infinite number (i.e., a cable) of compartments.

Objective goals:
Based on the model neuron, identify the fundamental mechanisms that underlie the dendritic improvement of **coincidence detection**.

1) Constant-conductance inputs
   How does the soma response change with different dendritic conductance for the two dendritic sections, each of which has either single-, multiple-, or infinite- dendritic compartments?

2) Dynamic inputs (Paired-pulse inputs)
   The precision/accuracy to detect coincidence depends on **a) the timing** and **b) the width of action potential** that triggers the presynaptic neuron to release neurotransmitters (let the waveform of potential is a pulse with a finite width), **c) the difference between two dendritic lengths** of postsynaptic neuron. Investigate how the three factors affect the coincidence sensitivity.

   *The synaptic transmission can be model with the opening-closing dynamics of Ca^{2+} channels.

Other refs: http://gureckislab.org/courses/spring13/robots/SoundLocalization-5.html

16. Bring up the topic that interest you

You are welcome to find a topic that you are interested in or relevant to your on-going research.