

**2025 Croucher Summer Course on
Computational Neuroscience**

Mathematical Minds: Modeling Neural Phenomena with Equations and Insight

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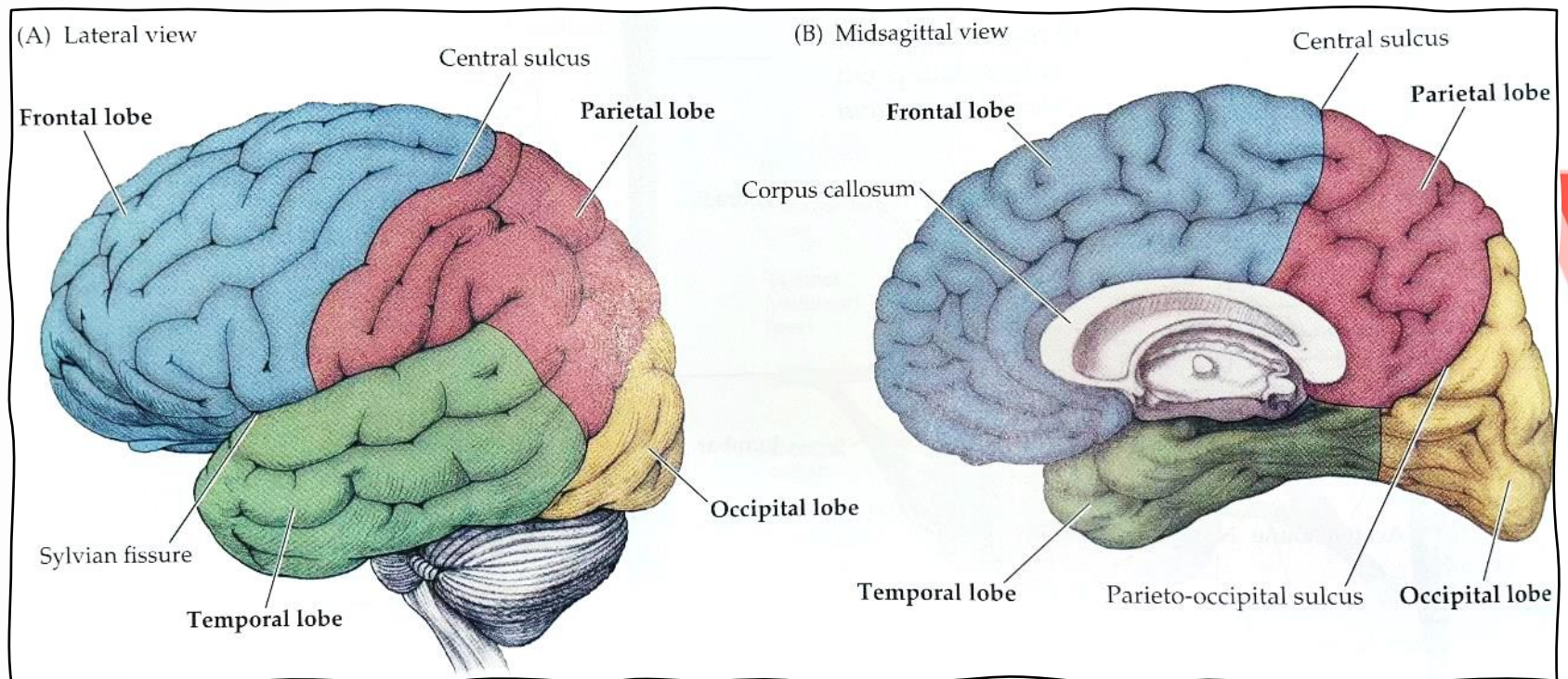


Agenda

- Neural Systems
- Mathematical Models
- Models for Phenomena
- Implications of Models

Big Picture of Our Brains

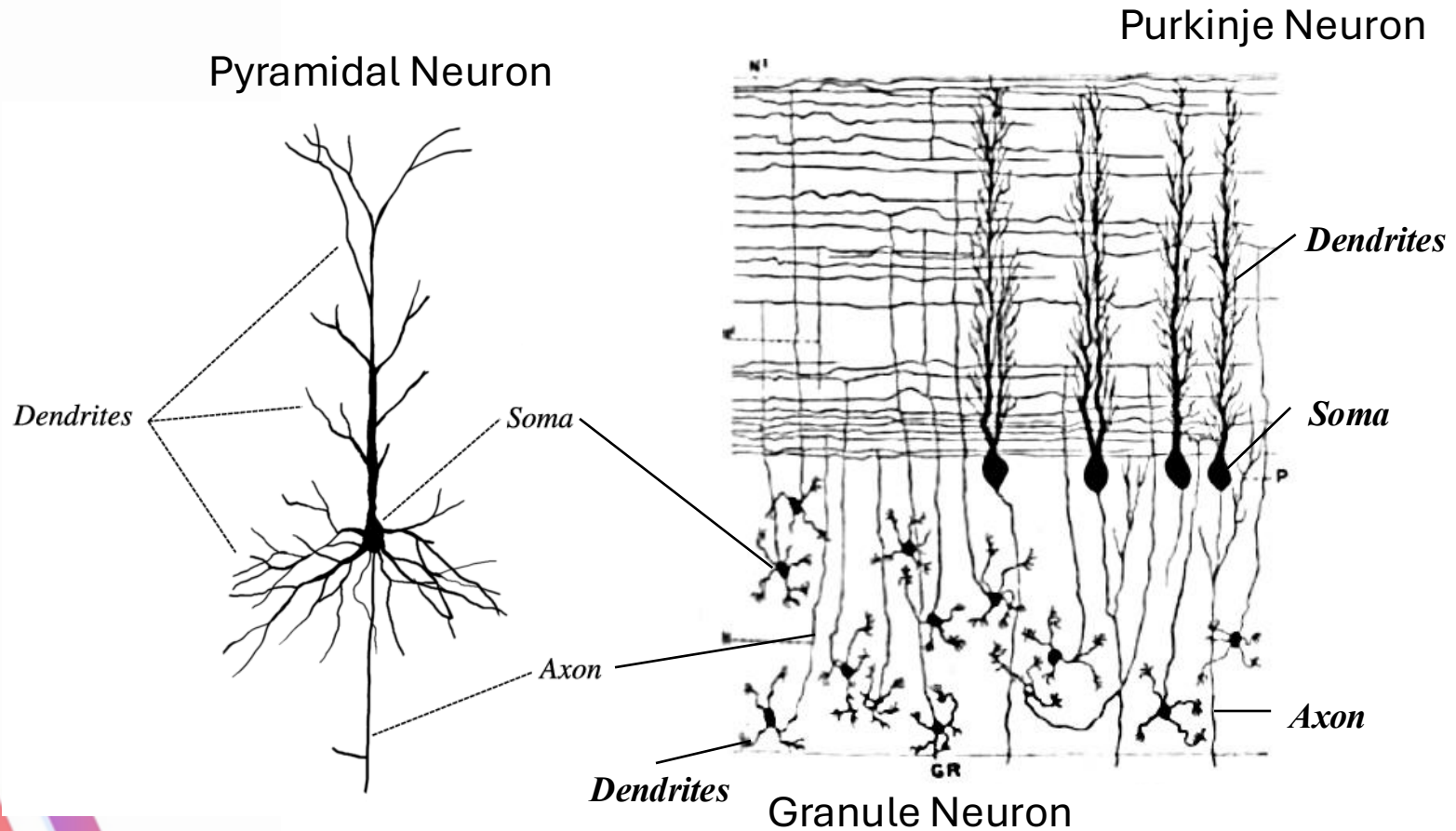
Cortical Areas



P.24, Neuroanatomy through Clinical Cases by Hal Blumenfeld (2022)

Building Blocks

Neurons



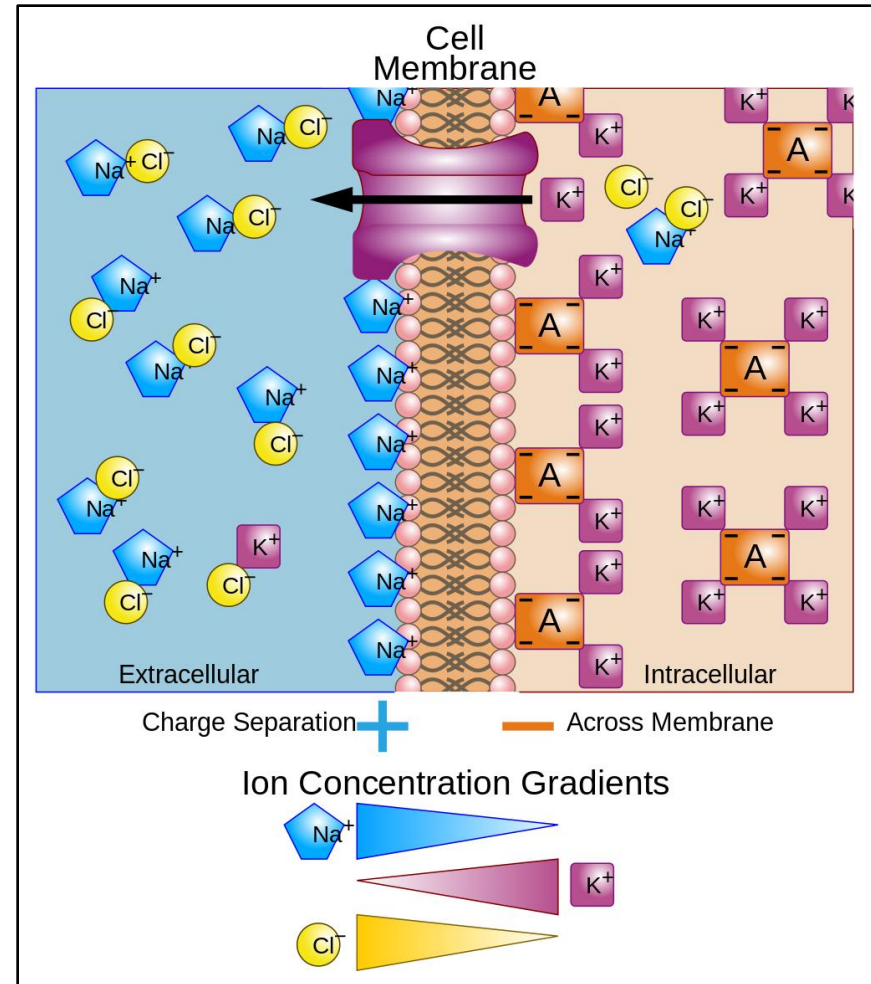
Walter, Röhrbein & Knoll (2016)

Looie496, Wikimedia (2009)

Building Blocks

Cell Membrane

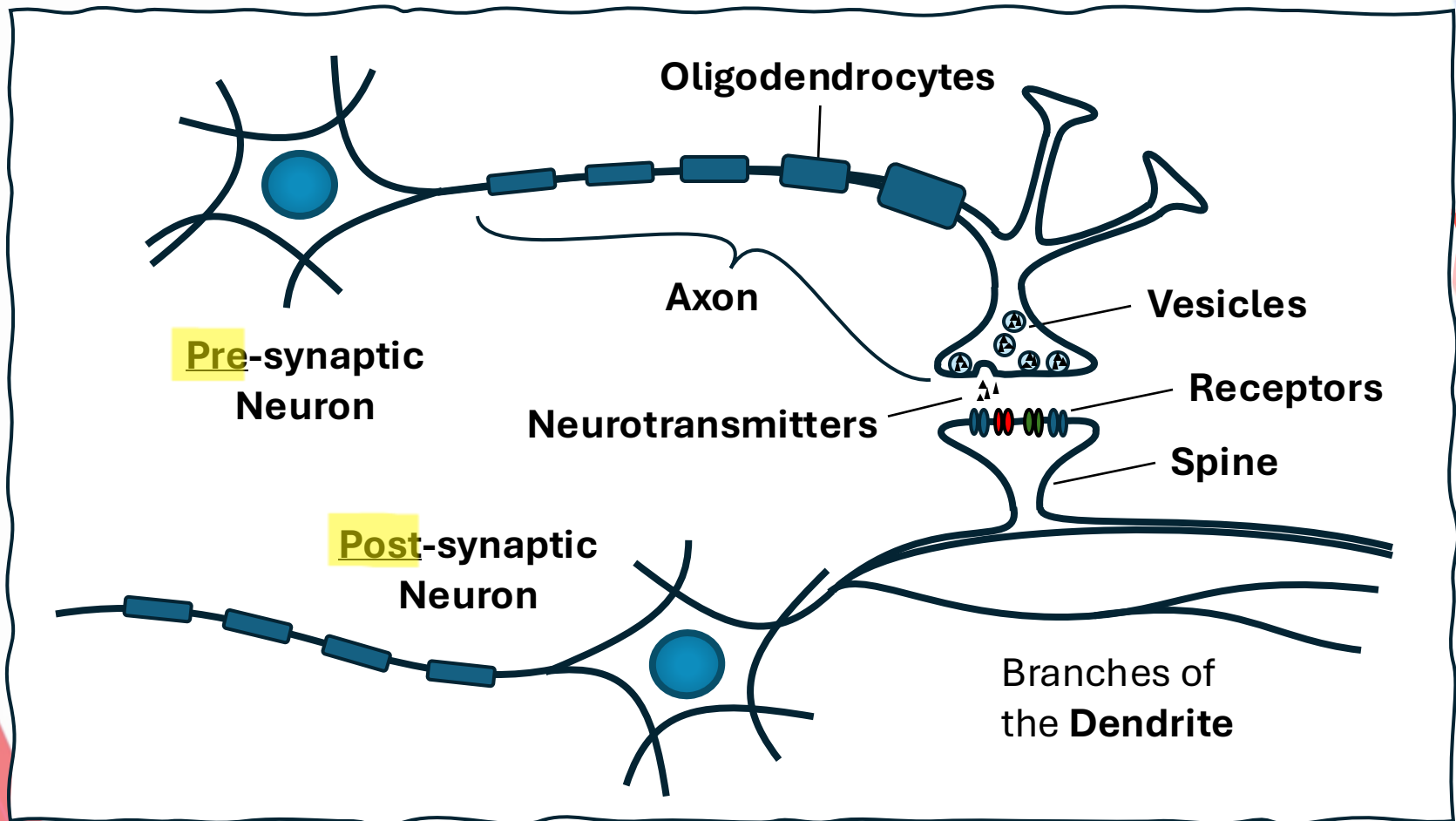
- Outside the neuron, there are more positive charges
- In contrast, inside the neuron, there are more negative charges
- **Insulating Dielectric:** In an electrical capacitor, the dielectric material serves as an insulator between the two conductive plates
- **Separation of Charge:** In a capacitor, the accumulation of opposite charges on the two plates creates an electric field between them



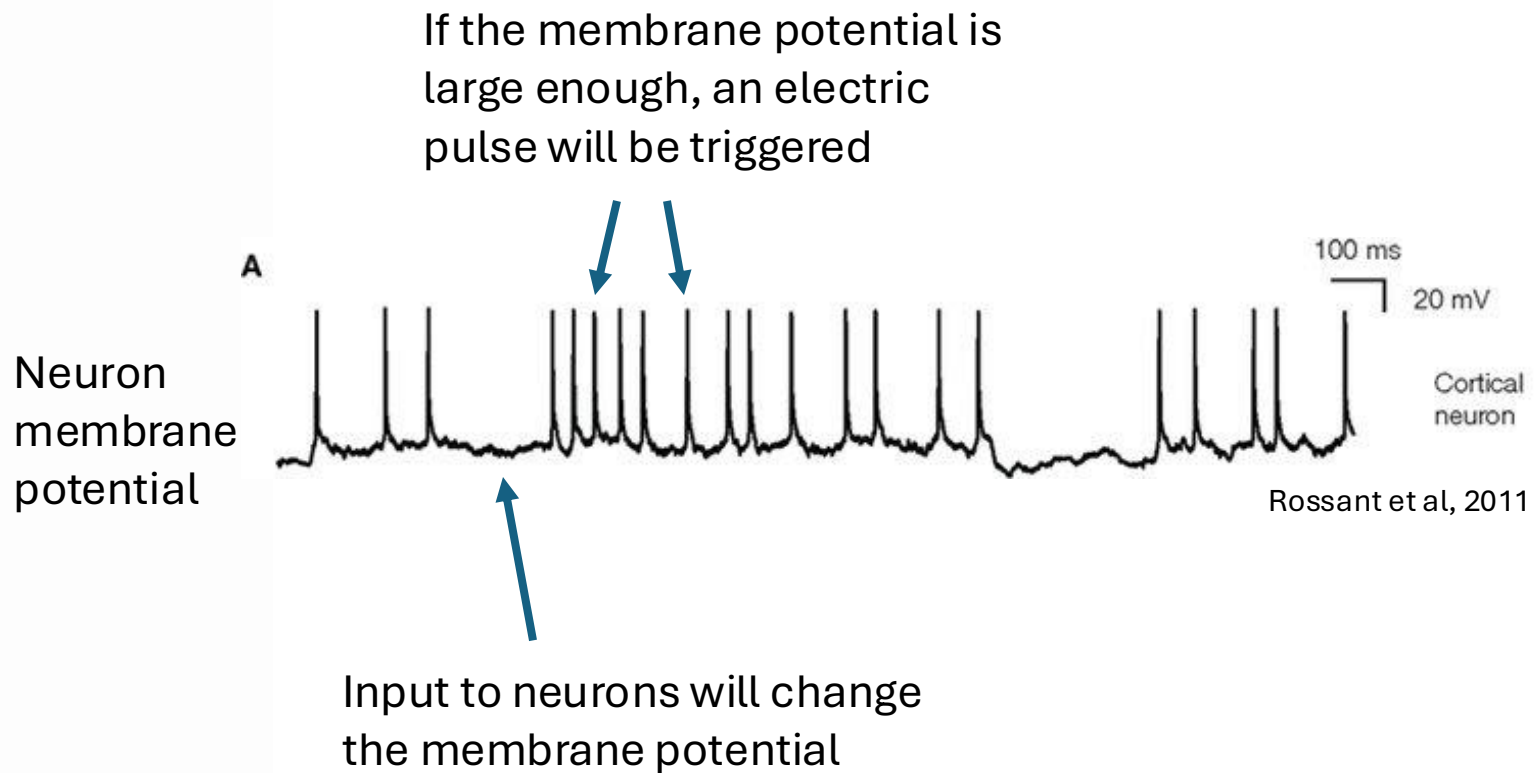
Д.Ильин (2021) Wikimedia

Building Blocks

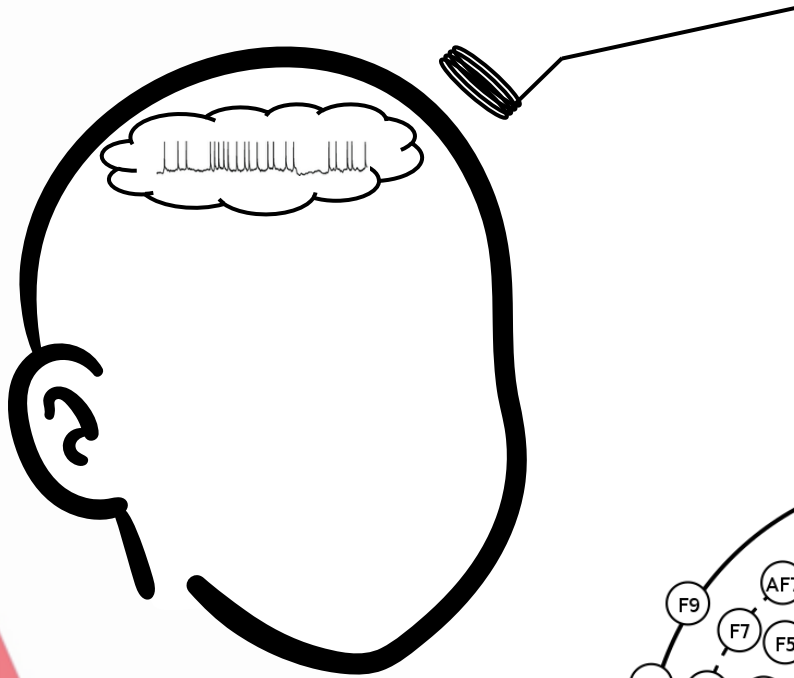
Synaptic Connections



What do Nerve Cell Electrical Signals Look Like?

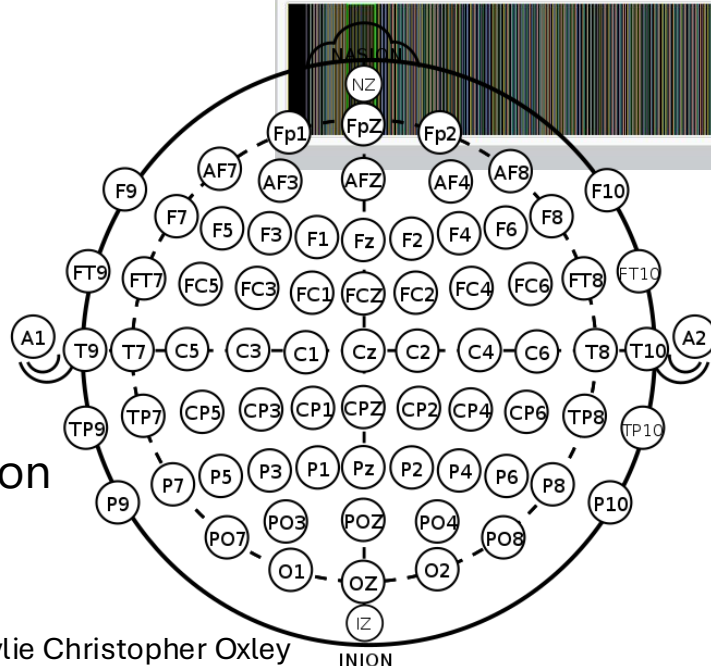


Neuronal Activities Generate Electric Signals



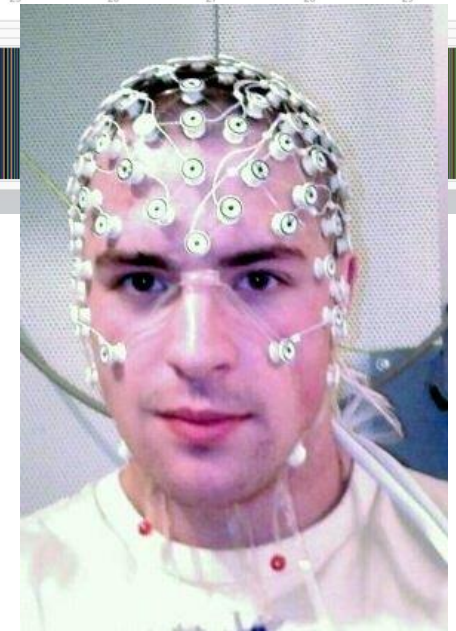
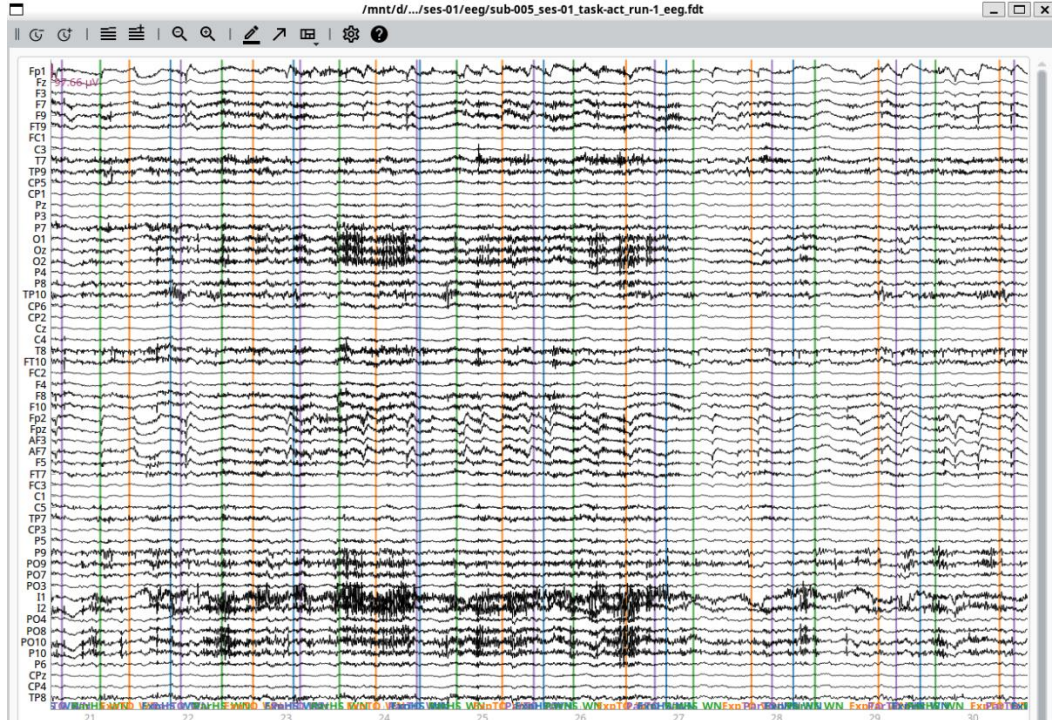
電極位置圖

Electrode position map



Brylie Christopher Oxley

INION



From Thuglas at English Wikipedia 8

Neuronal Coding

Tuning Curves in V1

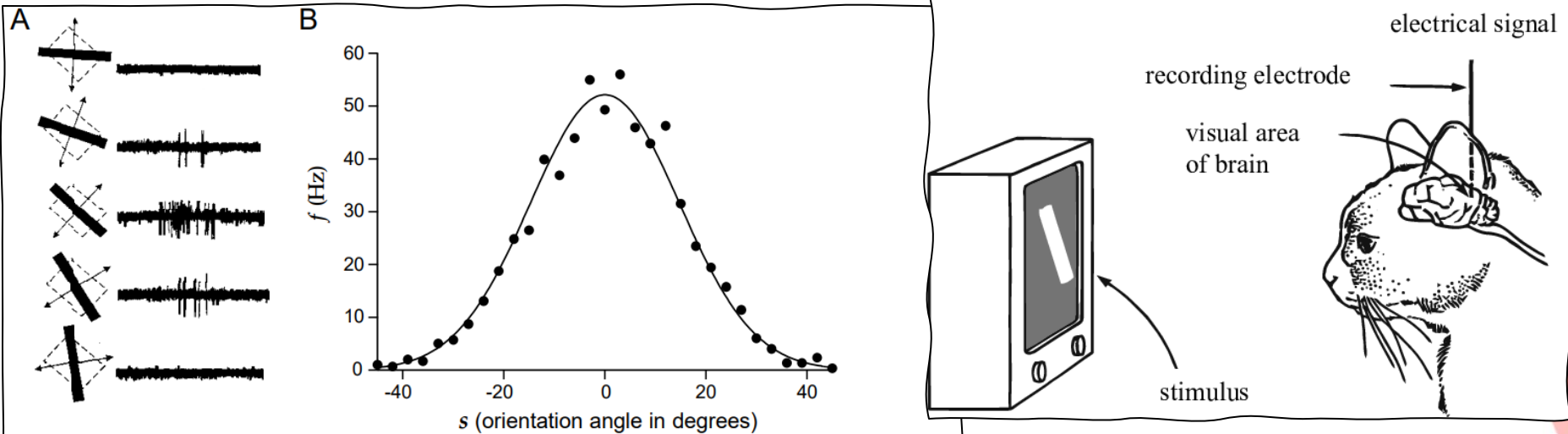
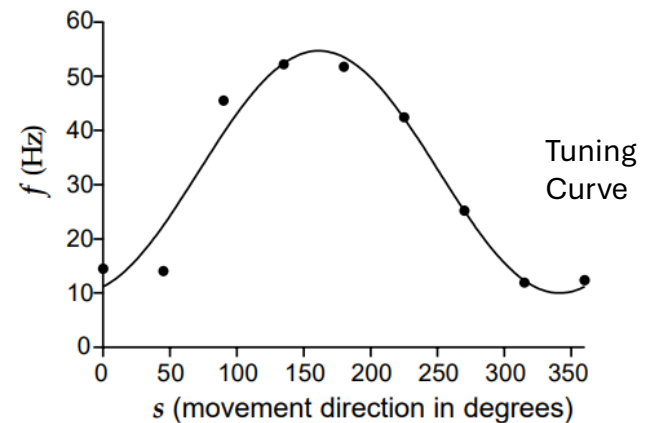
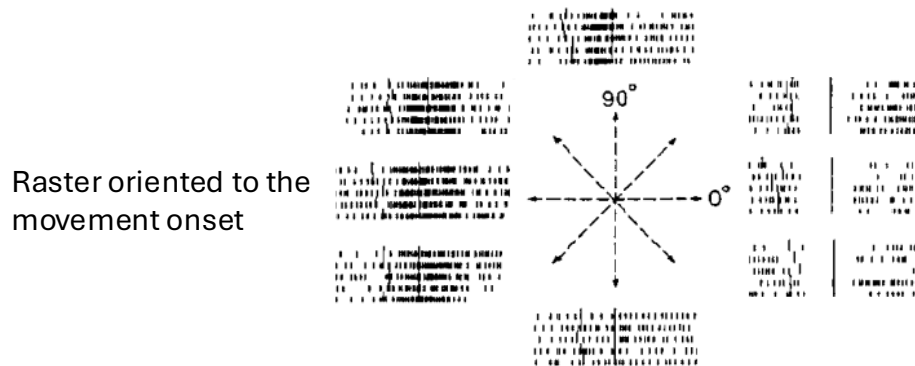
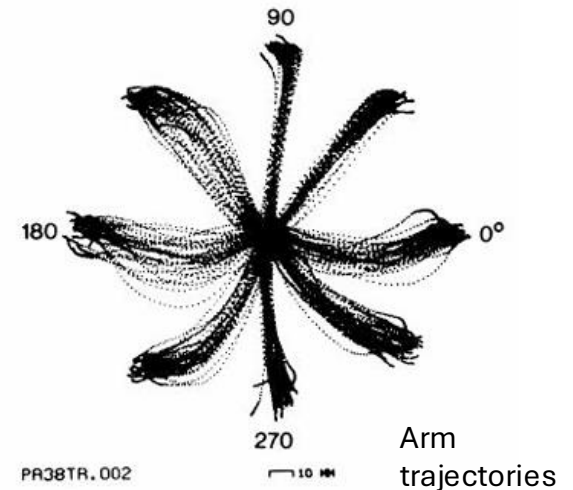
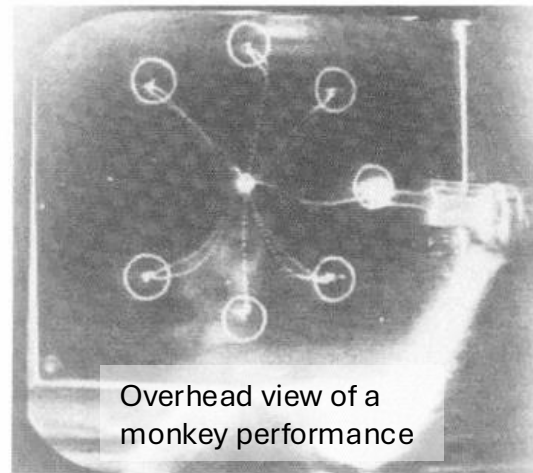
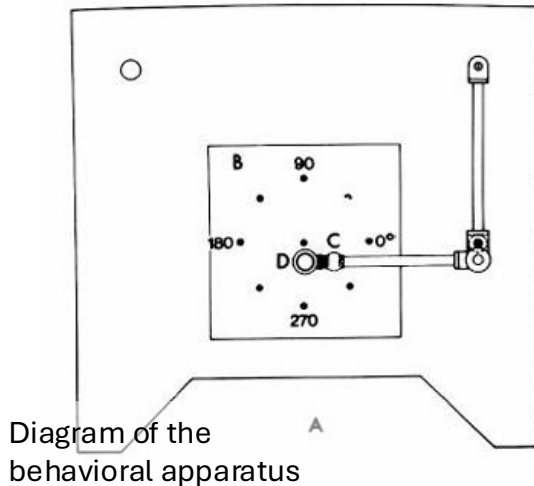


Figure 1.5: A) Recordings from a neuron in the primary visual cortex of a monkey. A bar of light was moved across the receptive field of the cell at different angles. The diagrams to the left of each trace show the receptive field as a dashed square and the light source as a black bar. The bidirectional motion of the light bar is indicated by the arrows. The angle of the bar indicates the orientation of the light bar for the corresponding trace. B) Average firing rate of a cat V1 neuron plotted as a function of the orientation angle of the light bar stimulus. The curve is a fit using the function 1.14 with parameters $r_{\max} = 52.14$ Hz, $s_{\max} = 0^\circ$, and $\sigma_f = 14.73^\circ$. (A from Hubel and Wiesel, 1968; adapted from Wandell, 1995. B data points from Henry et al., 1974.)

Neural Coding

Neuronal Tuning in Motor Cortex



Georgopoulos (1982)

Then...

- There are phenomena in different scenarios
- How are these phenomena generated?
 - ◆ What are the factors affecting the phenomena?
- How can these phenomena support brain functions?

Mathematical Models

■ What Are Mathematical Models?

A mathematical model is a description of a system using mathematical concepts and language. Models help us understand, analyze, and make predictions about real-world phenomena.

Mathematical Models

■ Common Types of Models

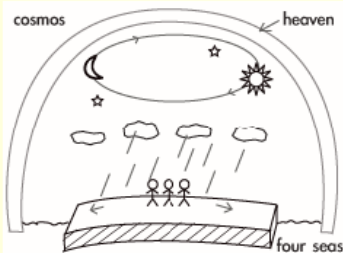
- ◆ Deterministic vs. Stochastic
- ◆ Linear vs. Nonlinear
- ◆ Continuous vs. Discrete
- ◆ Static vs. Dynamic

■ Real-World Applications

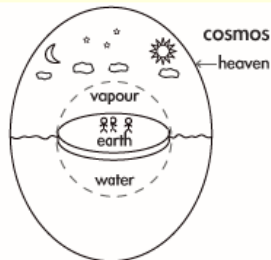
- ◆ Mathematical models are used in physics, engineering, economics, biology, climate science, and many other fields to simulate complex systems and guide decision-making.

Example: How did Our Ancestors Describe Our World

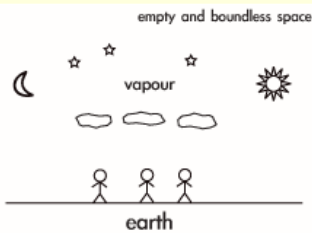
Ancient China



The Gai Tian Model (Hemispherical Dome)



The Hun Tian Model (Celestial Sphere)



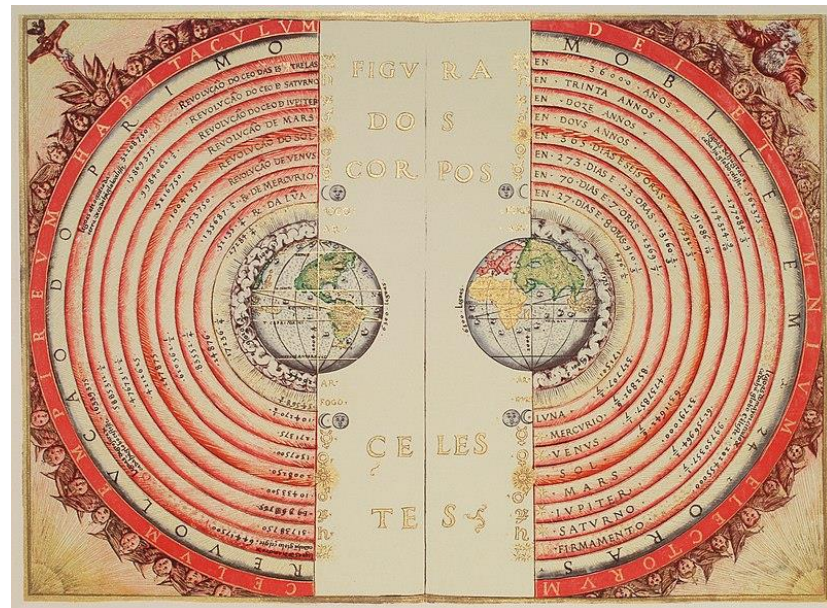
The Shuen Ye Model (Infinity)

Ancient Egypt



British Museum, Object # = 92687

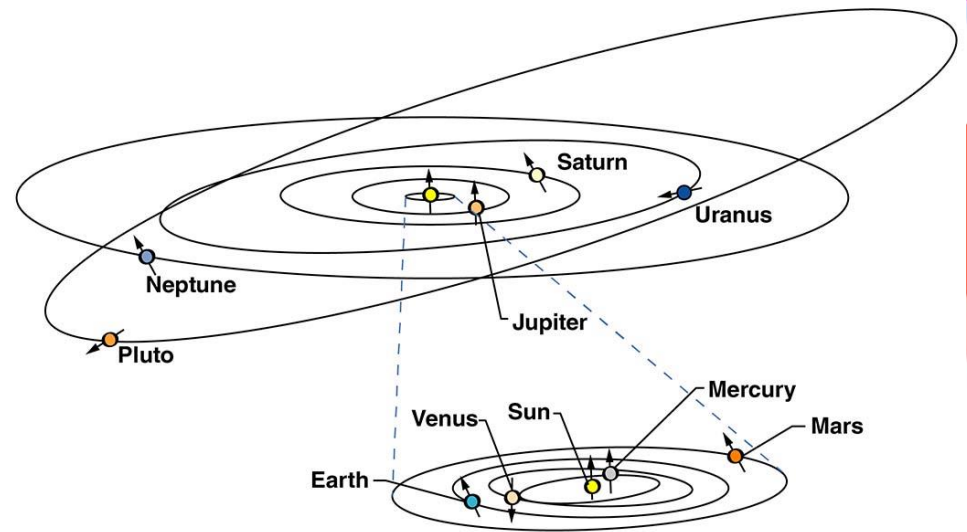
Ancient Europe



Bartolomeu Velho (1568)

Mathematical Model: Newtonian Gravity

- The Newtonian mechanics with the gravity theory can explain most of the observed phenomena
- Of course, now we can predict eclipses accurately
- The Newtonian gravity is a successful model of the phenomena
- It was good at prediction and explanation

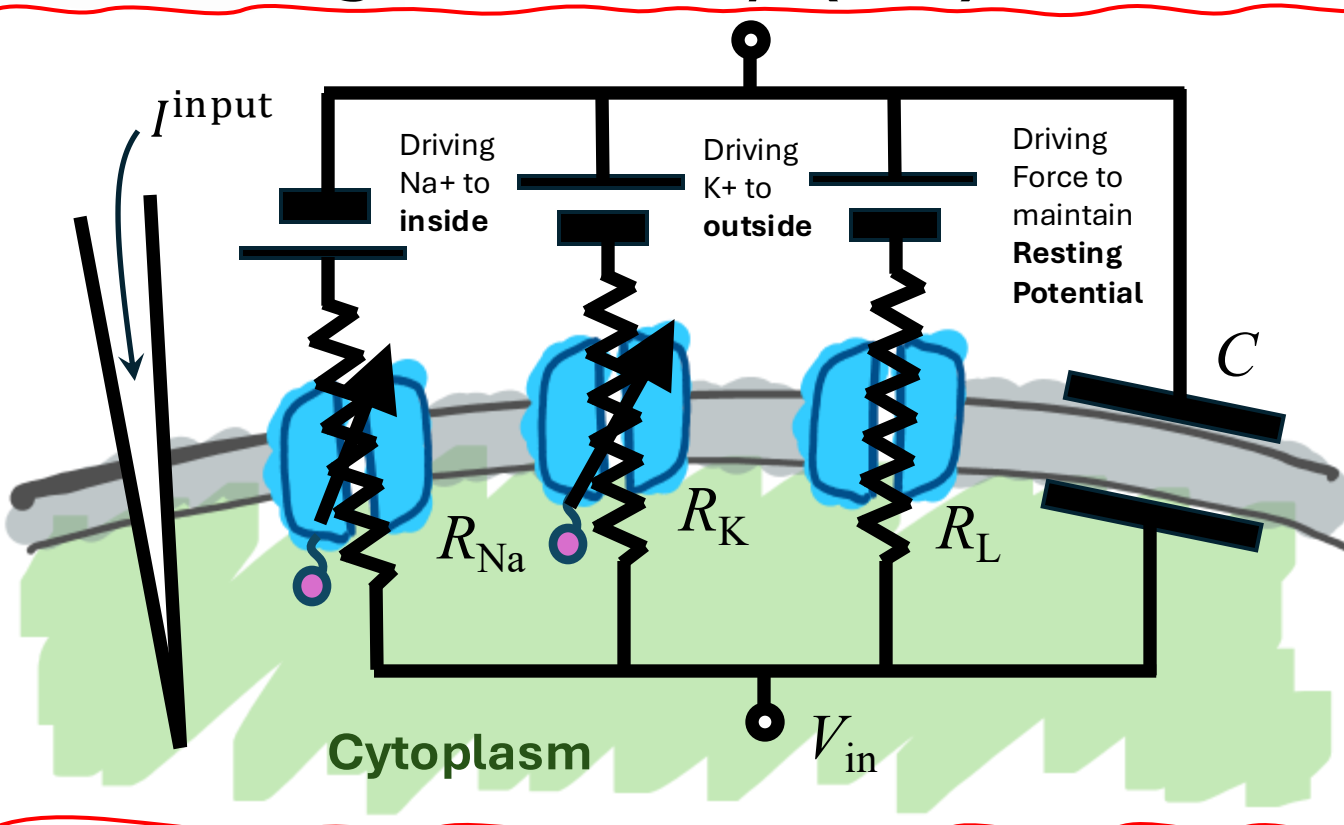


<https://www.nasa.gov/learning-resources/for-kids-and-students/what-is-pluto-grades-k-4/>

Neuronal Model

Neuron

■ Hodgkin-Huxley (HH) Model



Oligodendrocytes

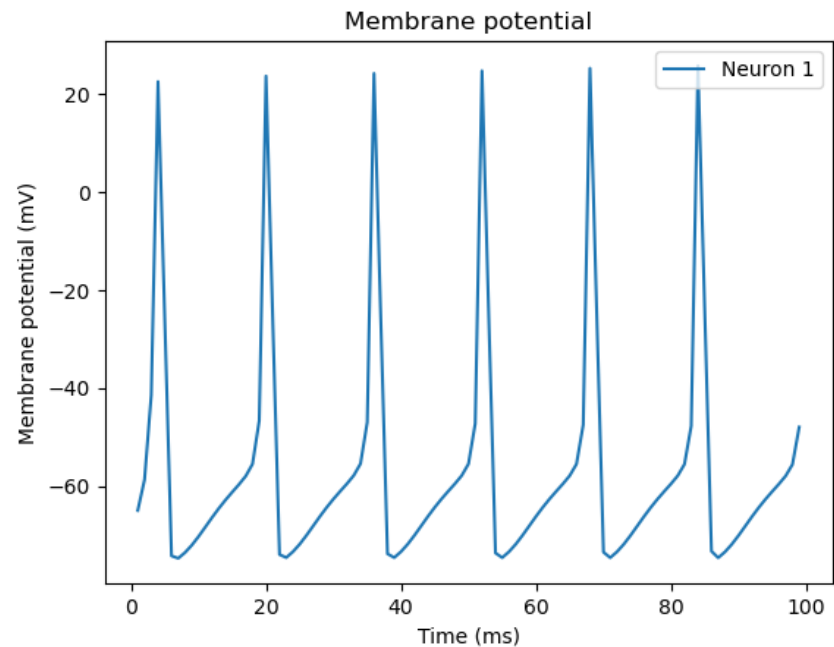
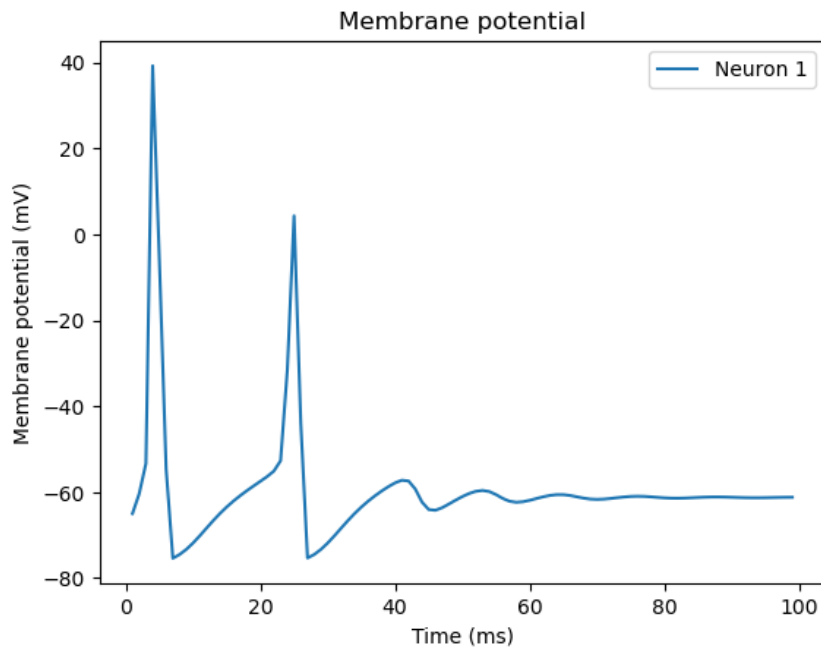
Axon

Soma

Dendrite

Behaviour of HH Model

- The membrane potential generated by HH model is more realistic than the LIF model



Implementation in Python

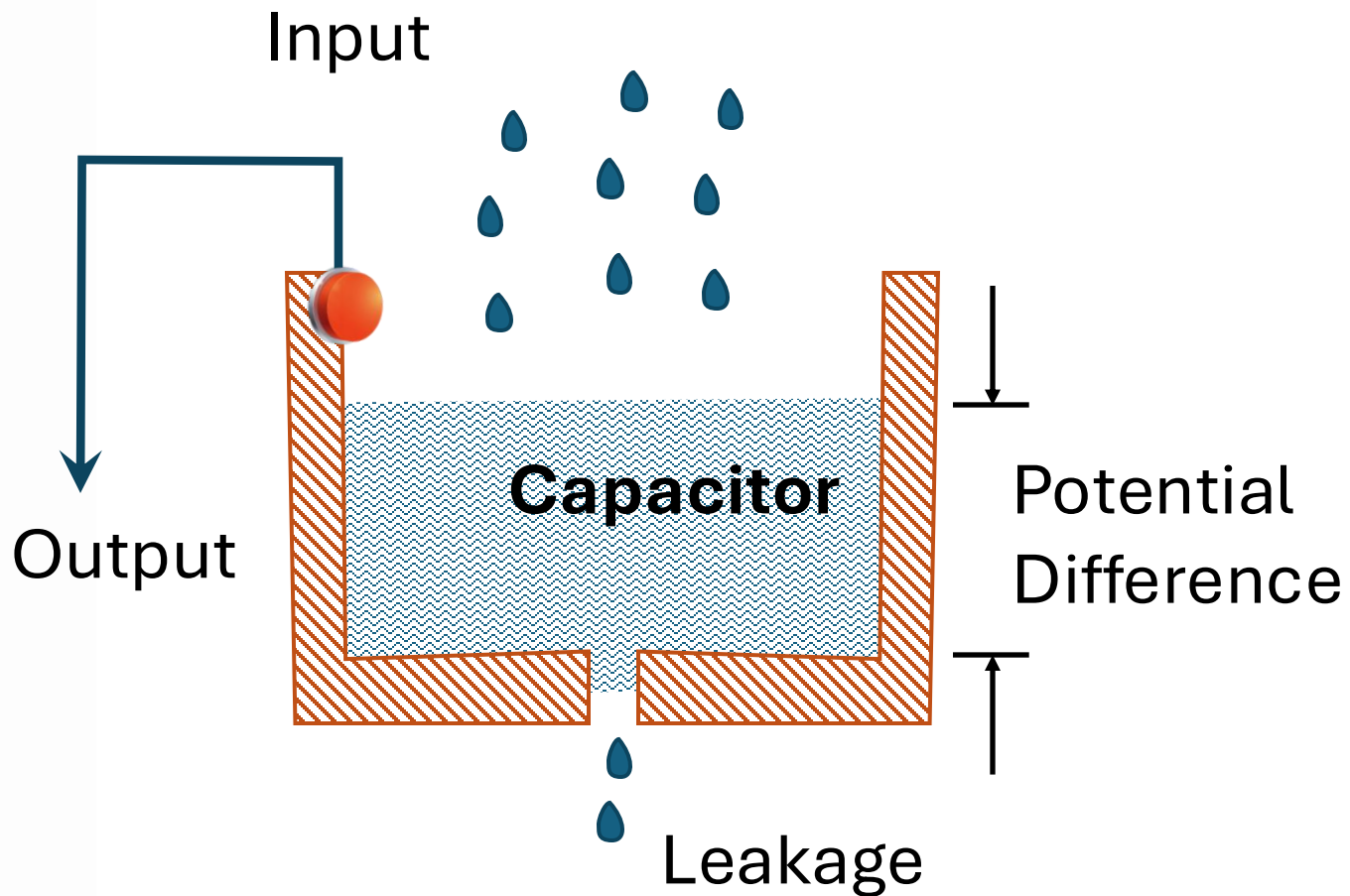
- Here is my implementation of the HH model in Python

https://colab.research.google.com/drive/1DFU22JZq6df_Ty-VPtbXpWFOKx7XKsQB?usp=sharing



A More Intuitive Description of Neurons

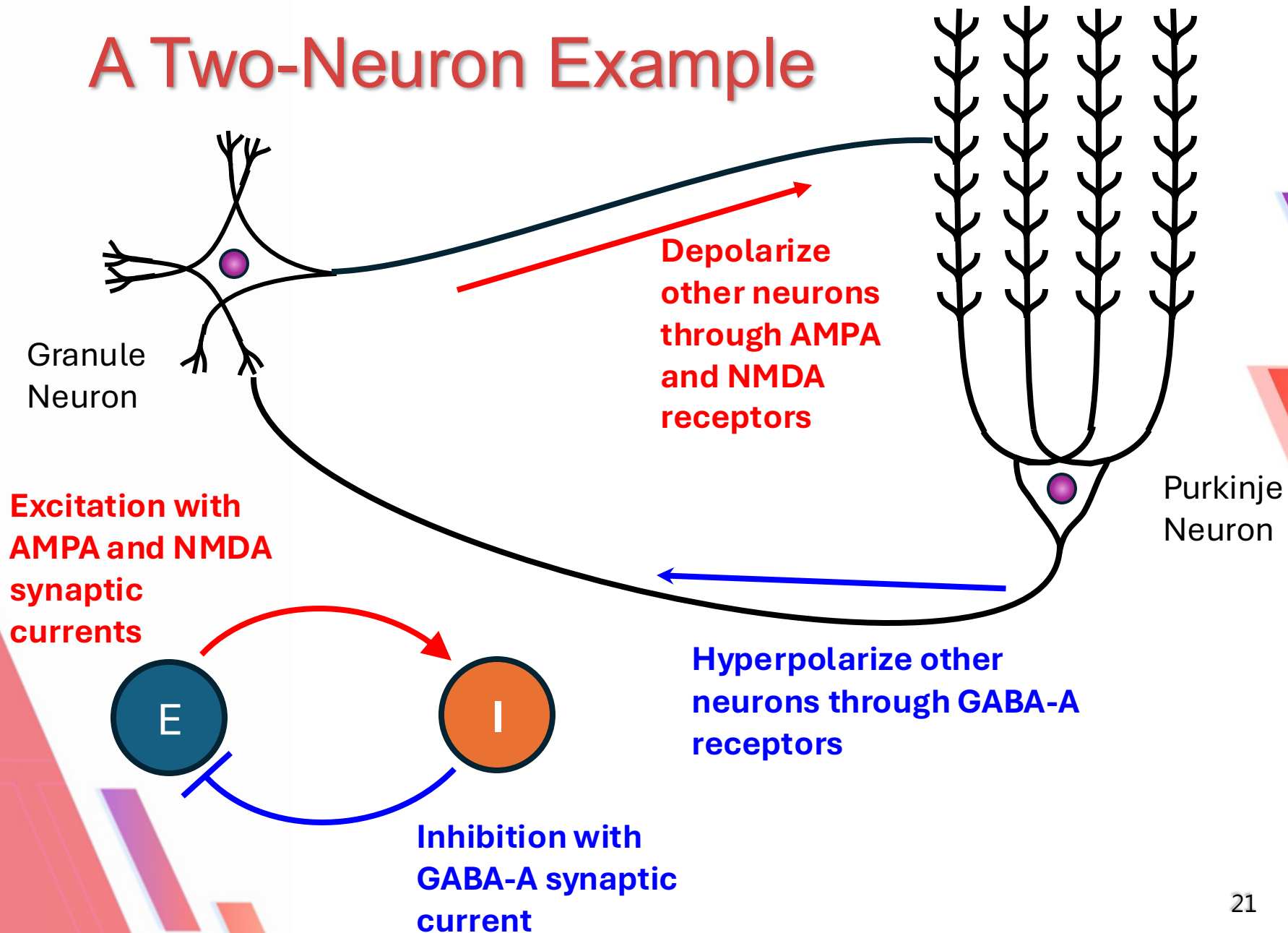
Analogy: Leaky Bucket



Networks of Neurons

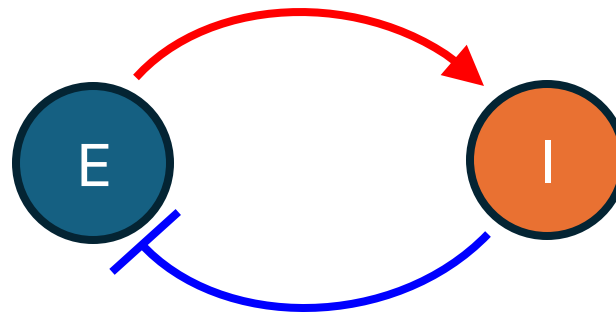
- Neurons do not work alone – they work in networks
- Neurons send (receive) signals to (from) its neighbours
- Loss of neuronal connections will cause dysfunctions
- Looking into neuronal networks will be essential for our understanding of our brain

A Two-Neuron Example



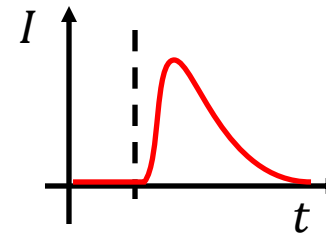
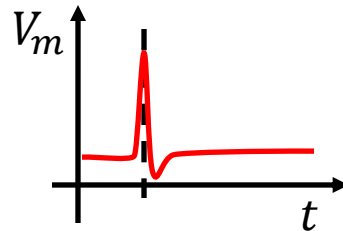
How this Two-Neuron System Works?

Inhibited by
GABA-A synaptic
current



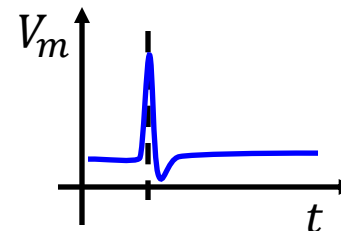
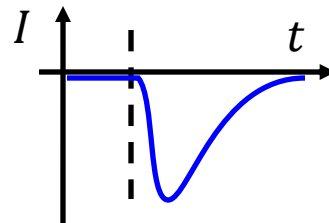
Excited by AMPA
and NMDA
synaptic
currents

The excitatory
neuron has a
spike



An excitatory
post-synaptic
current will be
triggered on the
targeted neuron

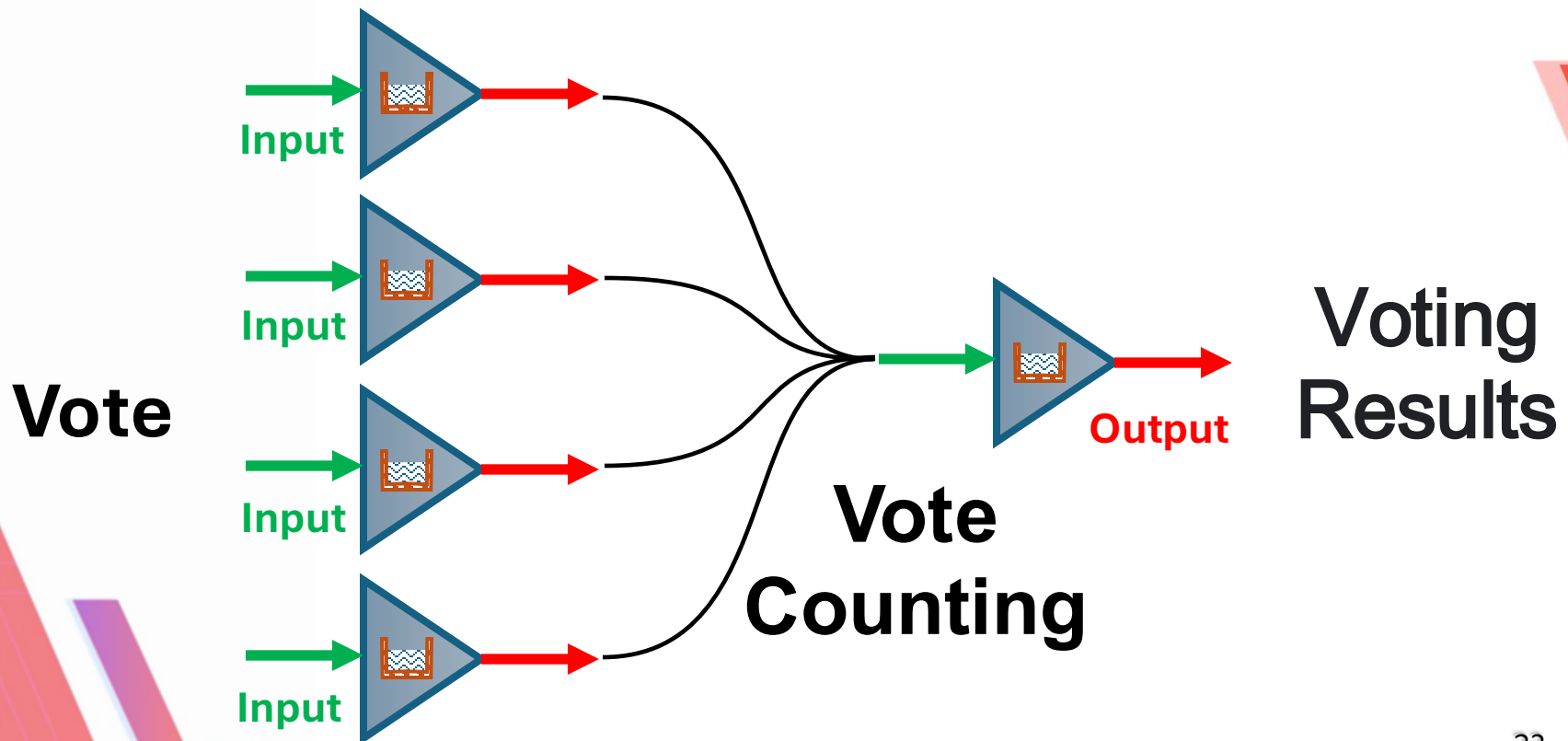
An inhibitory
post-synaptic
current will be
triggered on the
targeted neuron



The inhibitory
neuron has a
spike

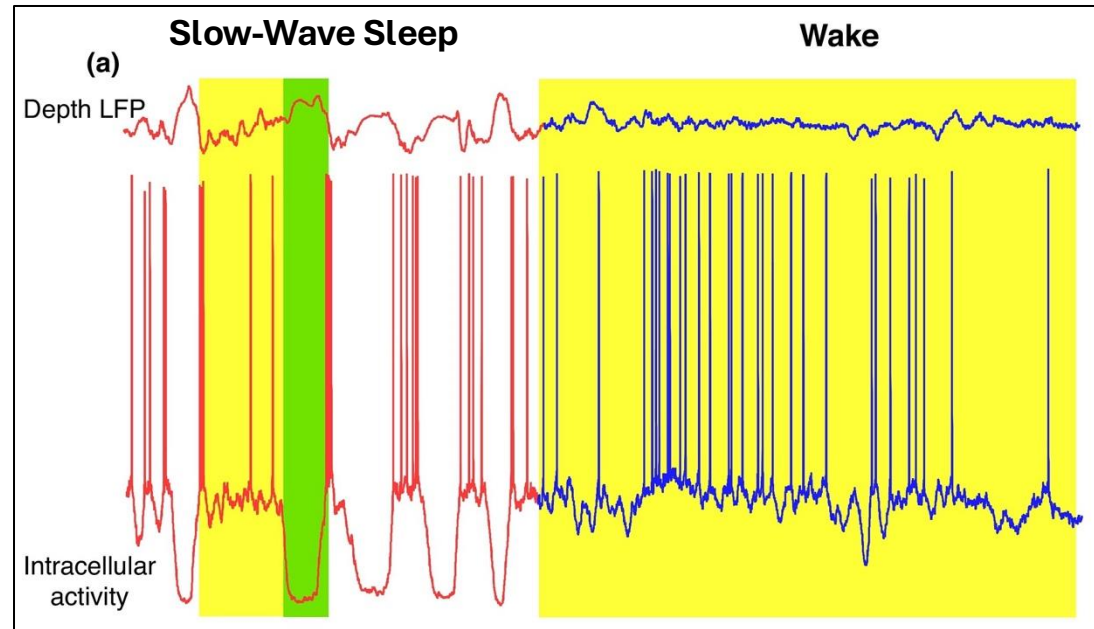
Can Neurons Compute?

- What can this composition of neurons do?



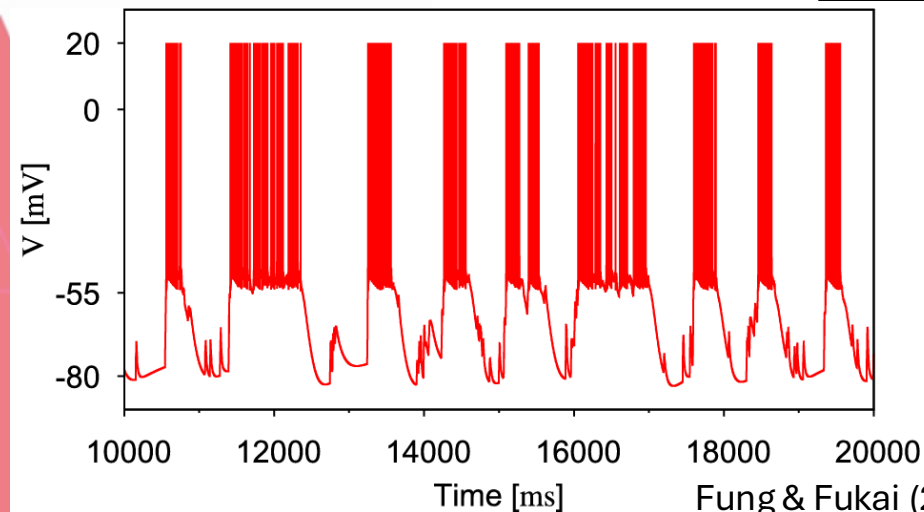
Model for Slow Oscillation

**Experimental
Observation**



Steriade, Timofeev & Grenier (2001)

Simulation



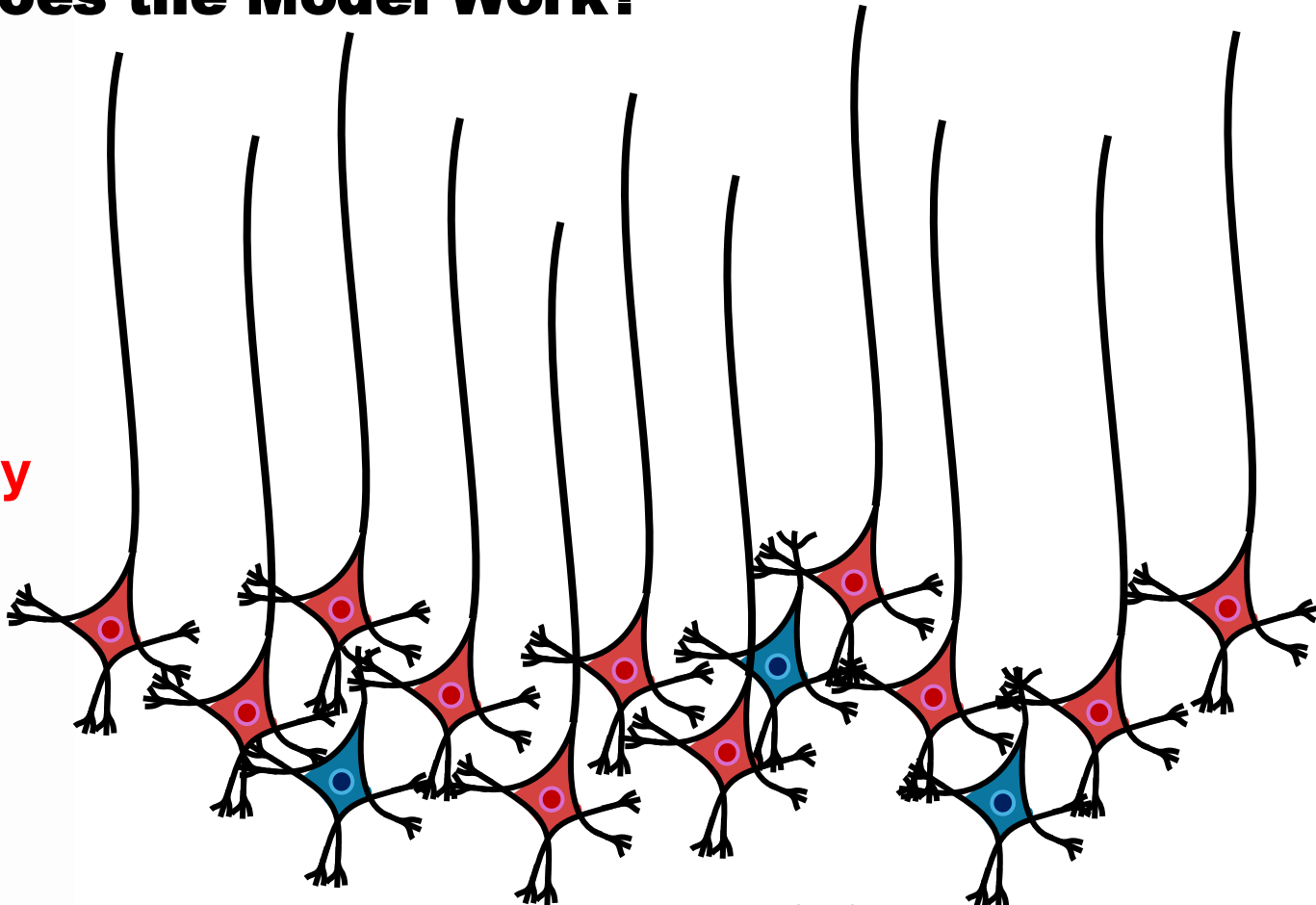
Fung & Fukai (2018)

- ❖ Mathematical models provide explanations to observations
- ❖ Here, the slow oscillations are explained by the balance between excitatory and inhibitory connections

Model for Slow Oscillation

How does the Model Work?

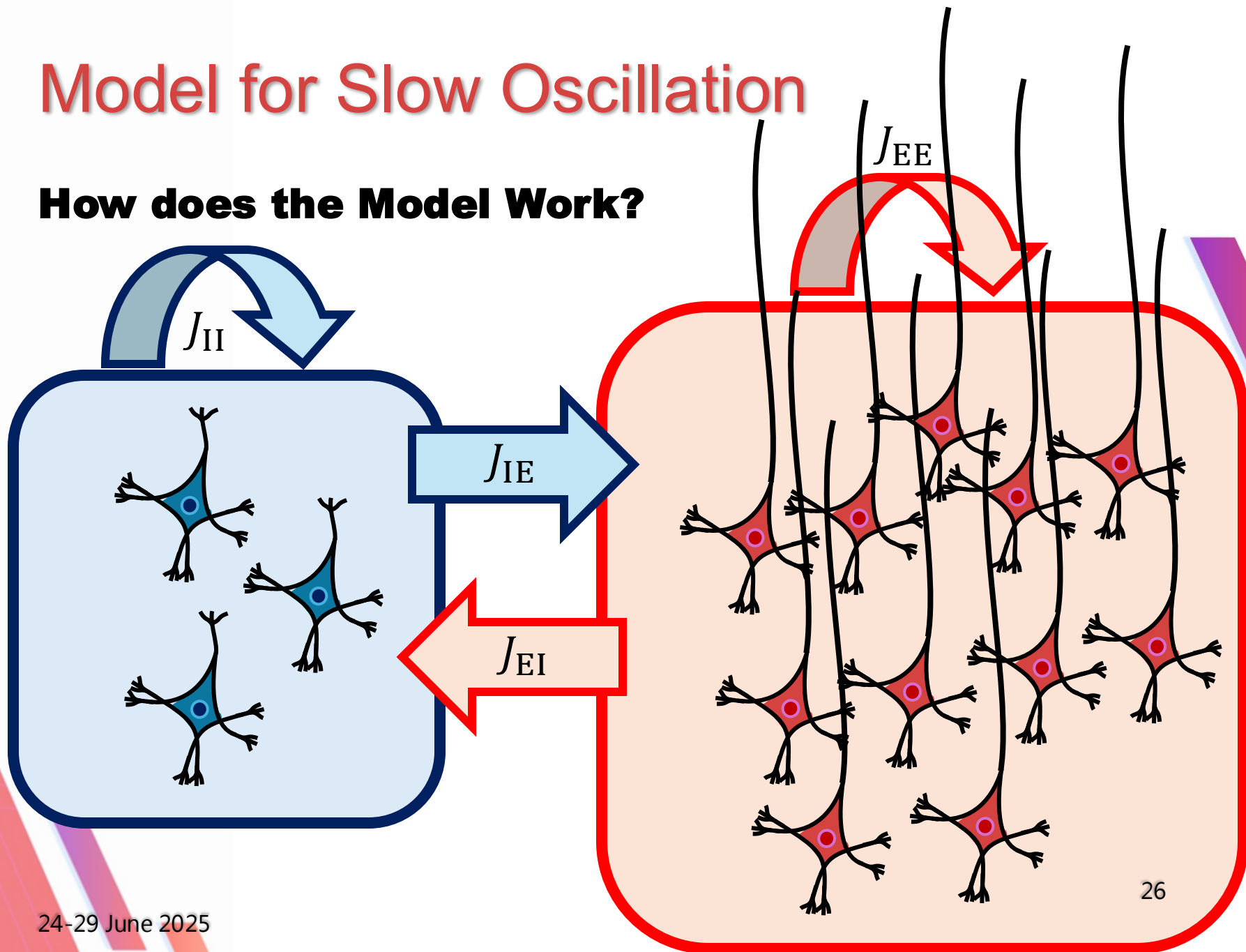
**Excitatory
Neurons**



**Inhibitory
Neurons**

Model for Slow Oscillation

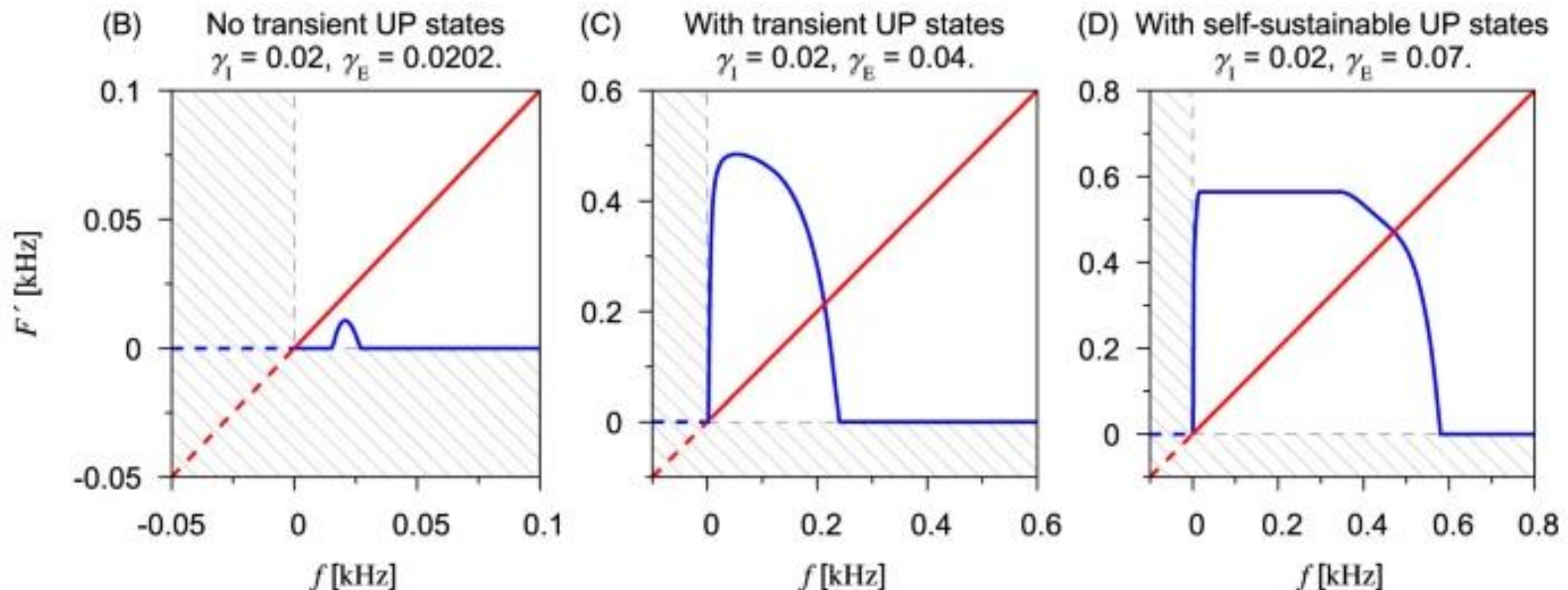
How does the Model Work?



Model for Slow Oscillation

How does the Model Work?

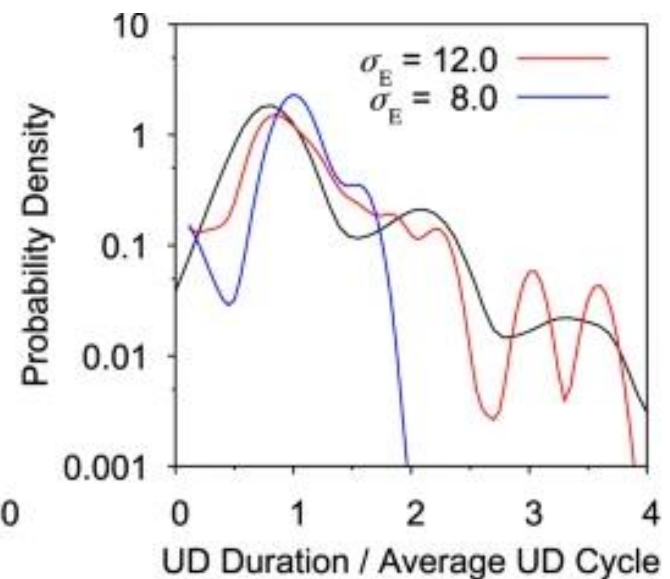
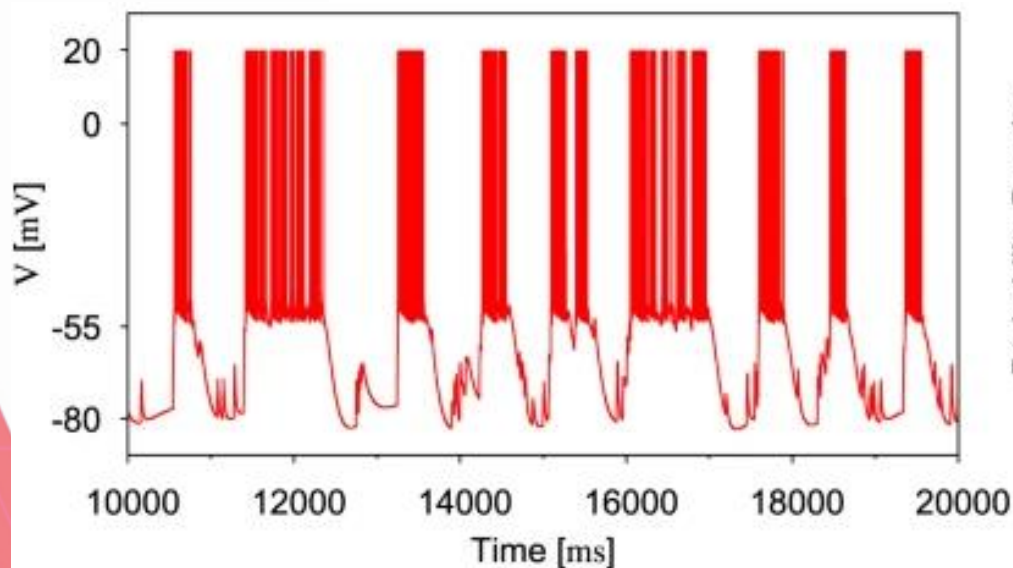
- There is a range of the ratio between excitatory and inhibitory connections to support slow oscillation



Model for Slow Oscillation

Duration of UP States

- The spreading of UP state duration depends on the variation of E connections
- It could explain the wide spreading of the durations

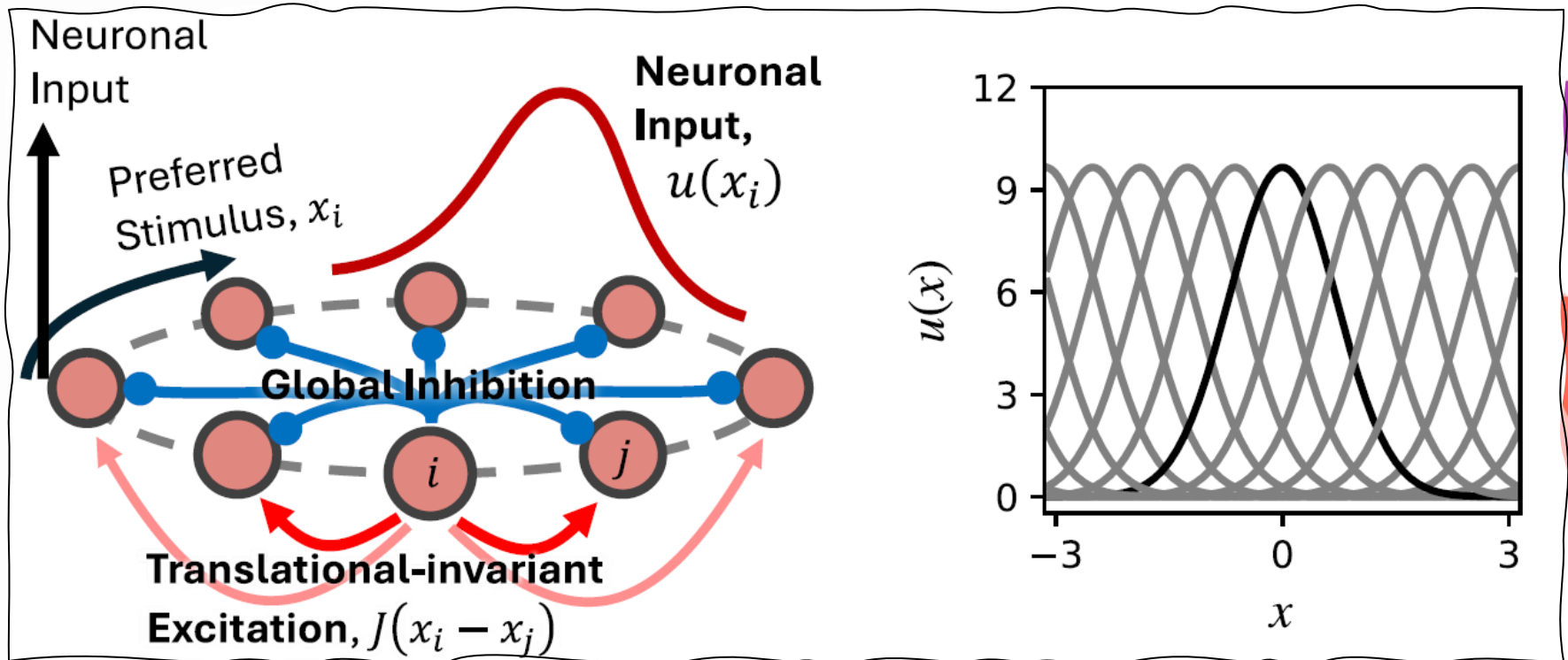


Model for Slow Oscillation

Implications and Limitation

- Slow oscillations can be supported by local connections
 - ◆ Supported by the experiment that slow oscillation can take place even if the thalamic input was suppressed
- The wide-distributed UP-state durations can be reproduced by locally connected networks
- Limitations:
 - ◆ Homogeneous network, network size, no plasticity considered, etc...

Continuous Attractor Neural Network

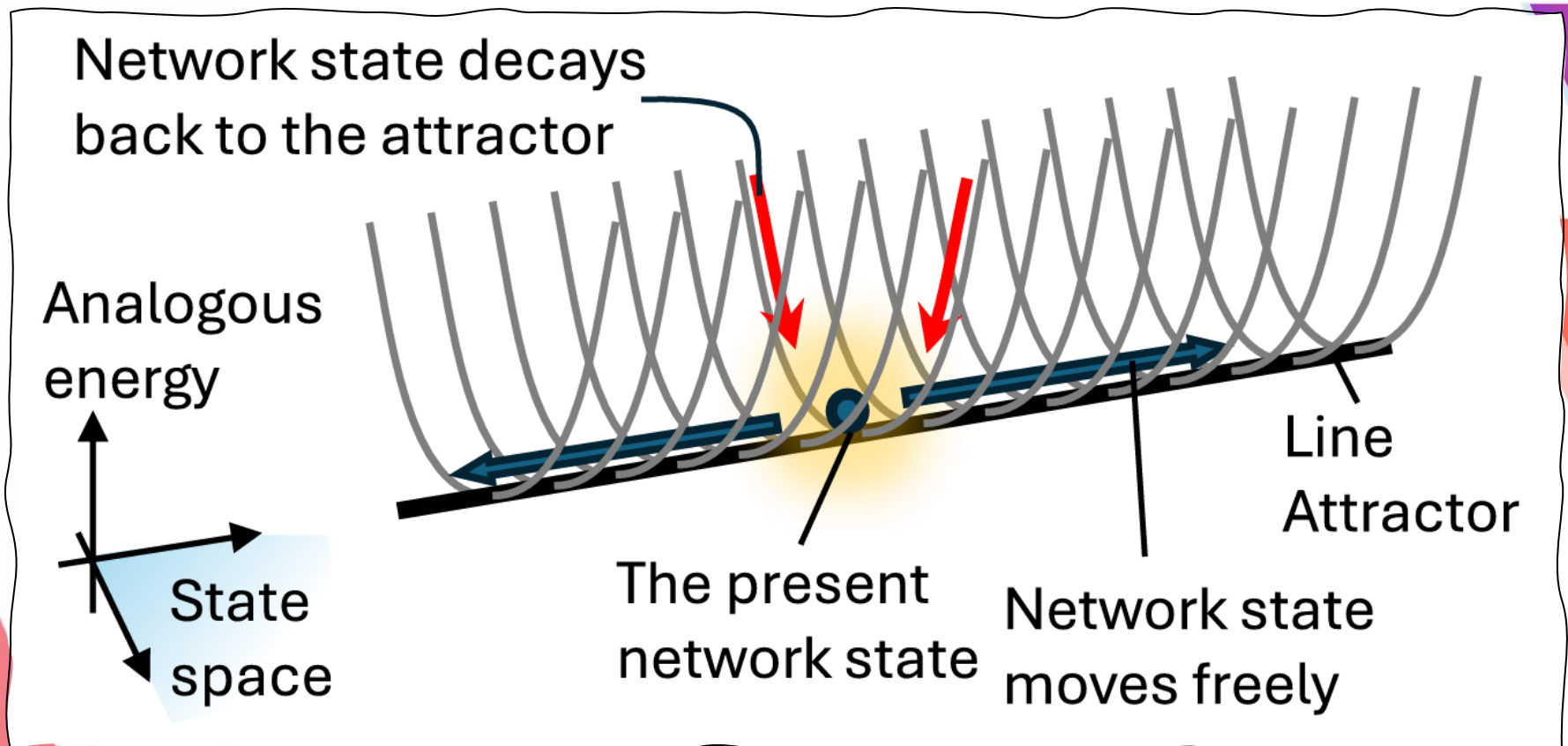


Synaptic Input $u(x, t)$ evolves as

$$\tau_s \frac{\partial u}{\partial t} = -u(x, t) + \int dx' J(x - x') r(x', t) + I^{\text{ext}}(x, t)$$

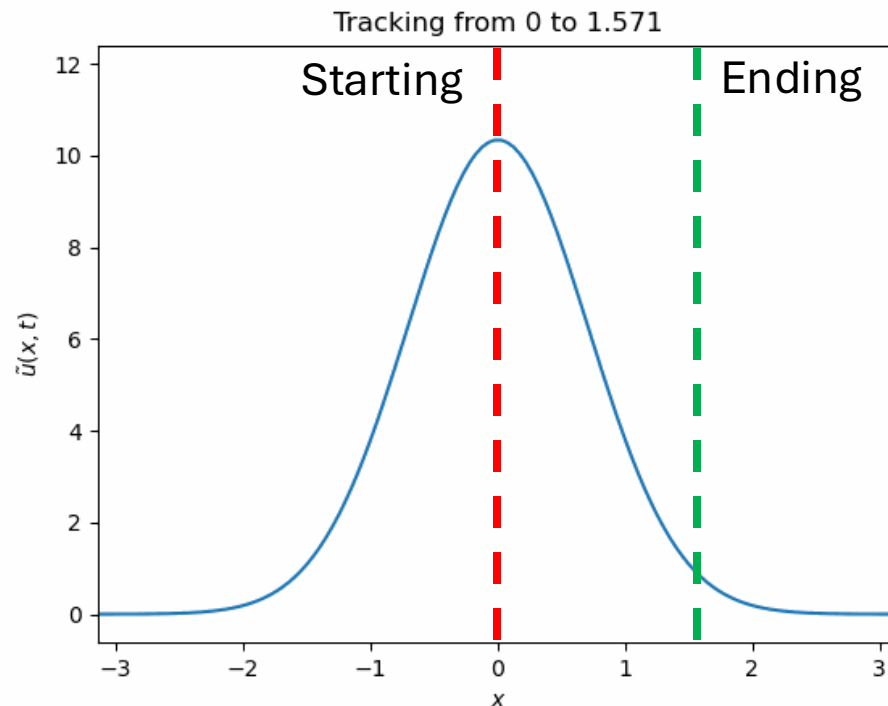
Wu and Amari (2008)

Continuous Attractor



Tracking Dynamics

- The attractor state can shift smoothly upon **the change of external stimulus**
 I_{ext}

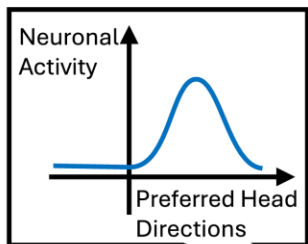


CANN as Models

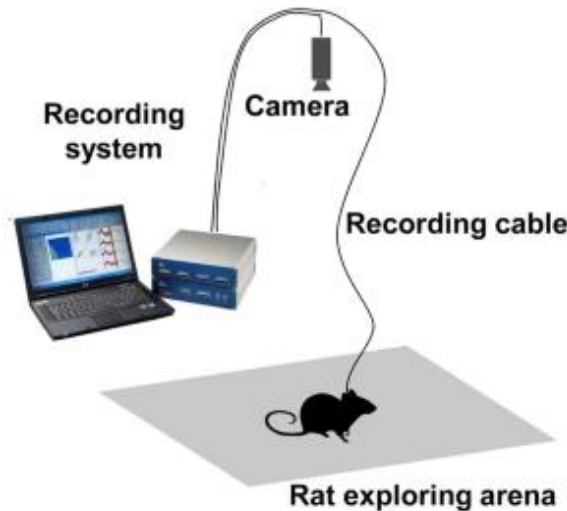
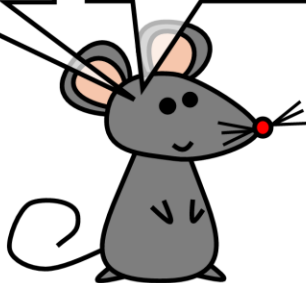
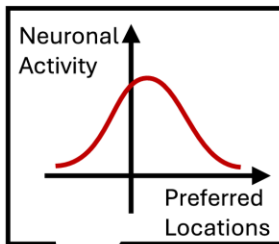
Place Cells

- Cells in the hippocampus tuned to a particular self location in a particular context

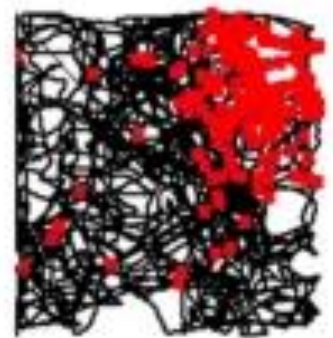
Head-Direction Cells



Place Cells



Place cell



 = Spikes

 = Path of rat

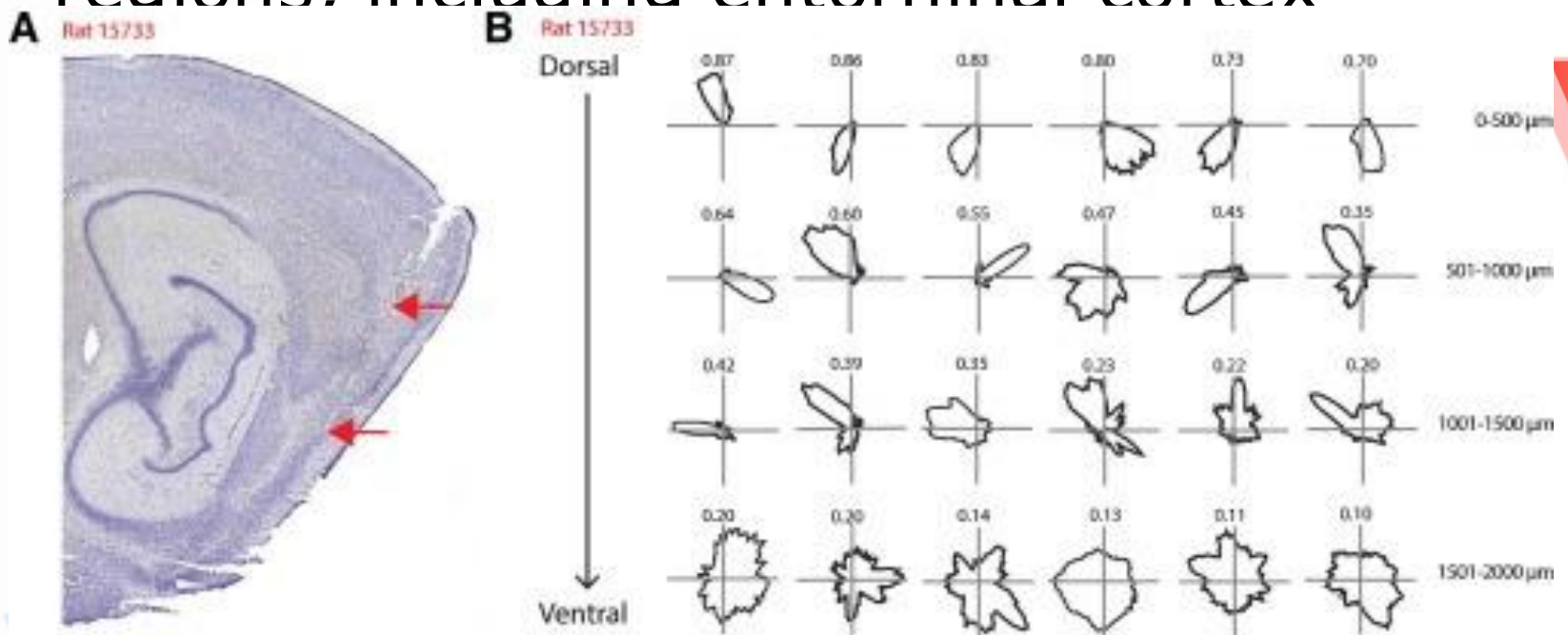


 Hippocampus
 Entorhinal cortex

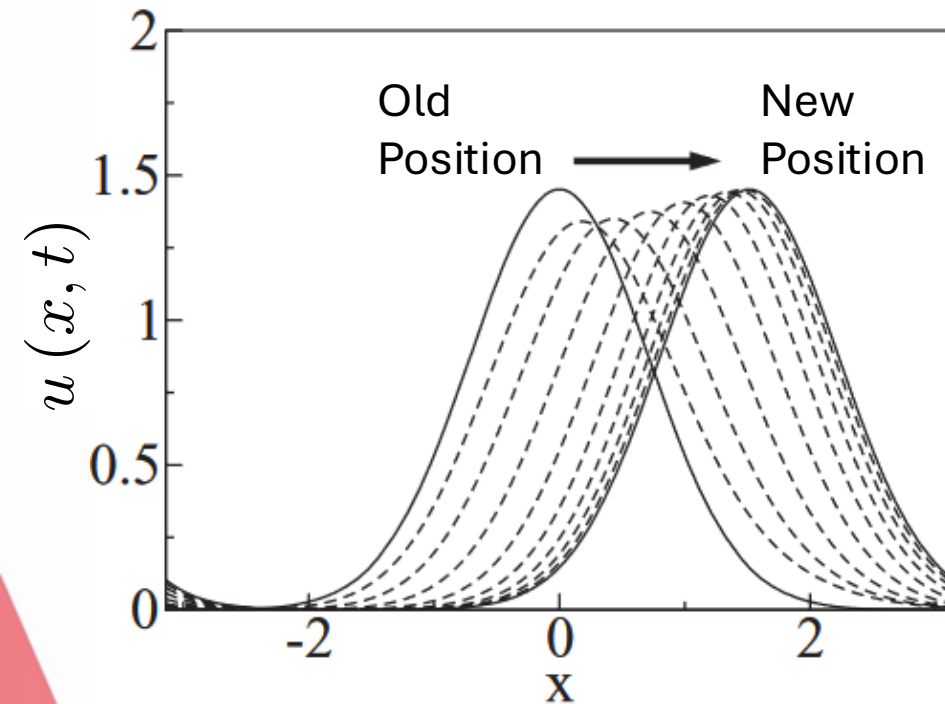
CANN as Models

Head-direction Cells

- Head-direction cells are found in many regions, including entorhinal cortex



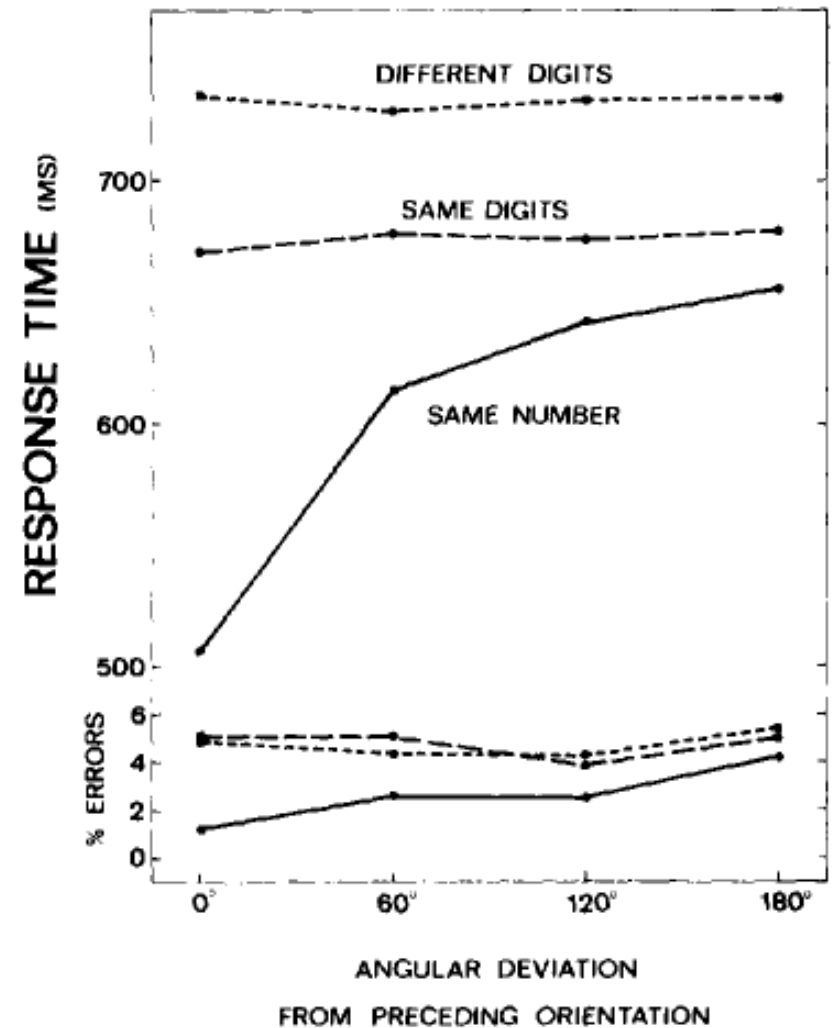
Tracking Changes of Stimulus



Fung, Wong & Wu (2010)

Reaction Time

$$T \approx \frac{\tau}{\alpha} \ln \left(\frac{|z_0|}{\theta} \right)$$



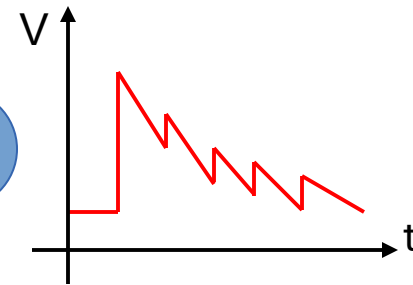
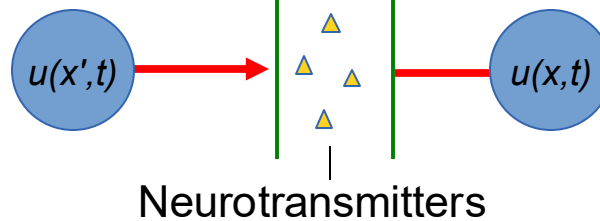
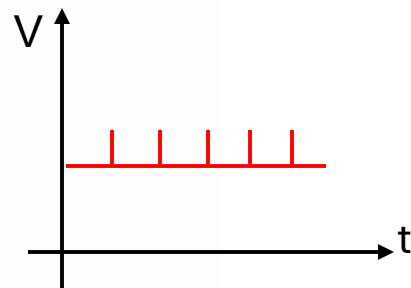
Koriat, Norman (1989)

CANN + Short-term Synaptic Depression (STD)

Dynamics of $u(x,t)$

$$\tau_s \frac{du}{dt}(x, t) = -u(x, t) + \sum_{x'} J(x, x') \boxed{p(x', t)} r(x', t) + I^{\text{ext}}(x, t)$$

Short-term Synaptic Depression



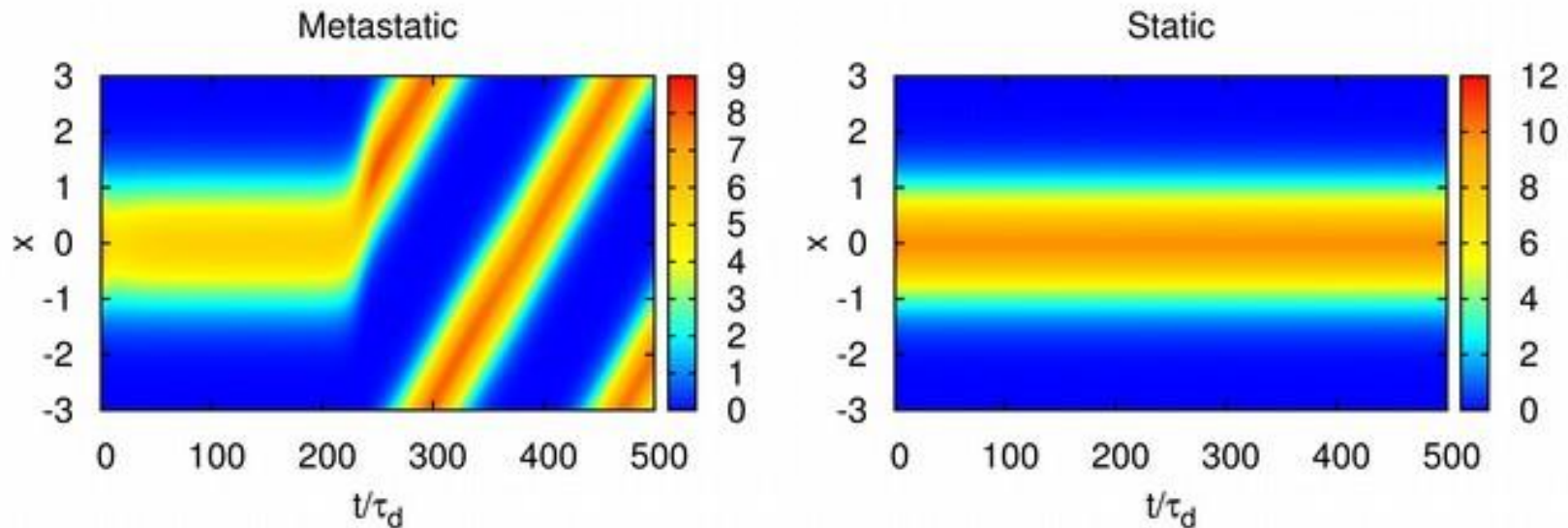
Dynamics of $p(x,t)$

$$\frac{dp}{dt}(x, t) = \frac{1 - p(x, t)}{\tau_d} - \beta p(x, t) r(x, t)$$

- $p(x,t)$ is the portion of usable neurotransmitters
- β is the consumption rate of neurotransmitters
- τ_d is the timescale of neurotransmitter recovery (of the order of 100 ms)

Intrinsic Motion

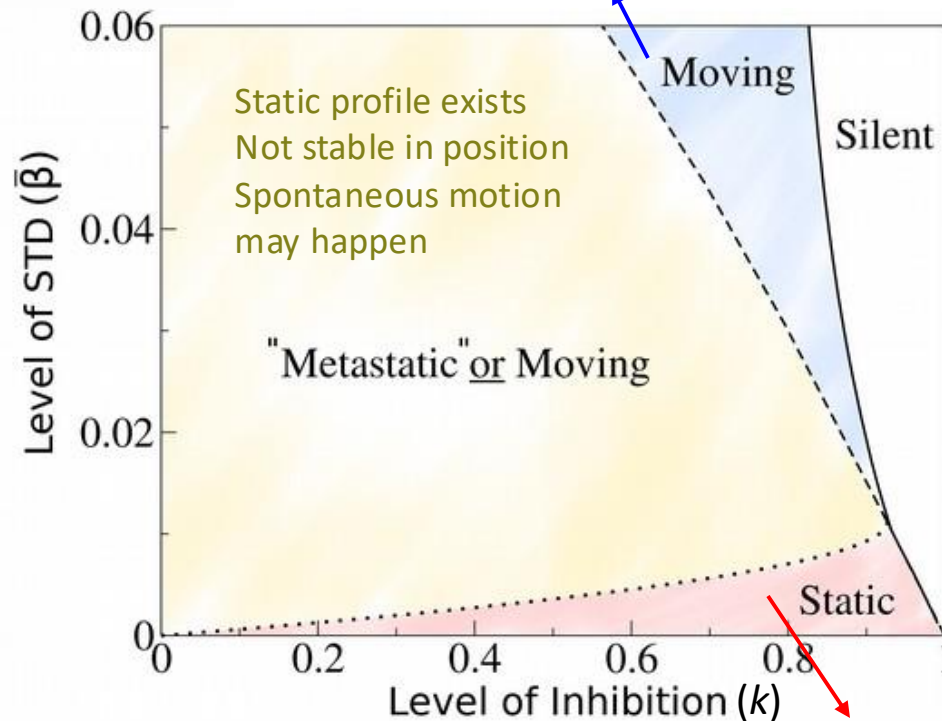
- Short-term depression (STD) can destabilize attractor states
- If STD is too strong, it may drive the attractor to follow its intrinsic dynamics."



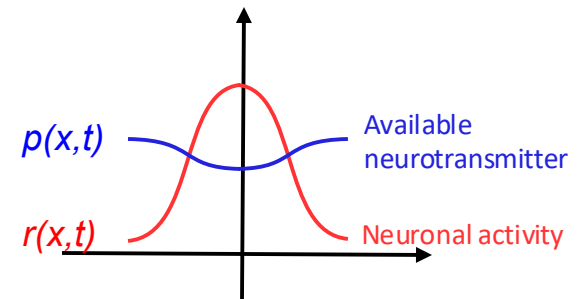
The Dynamics of CANN+STD

$$\bar{\beta} \equiv \frac{\tau_d \beta}{\rho^2 J_0^2} \quad \bar{k} \equiv k \frac{8 \sqrt{\pi} a}{\rho J_0^2}$$

No static profile
Only spontaneous motion
can happen

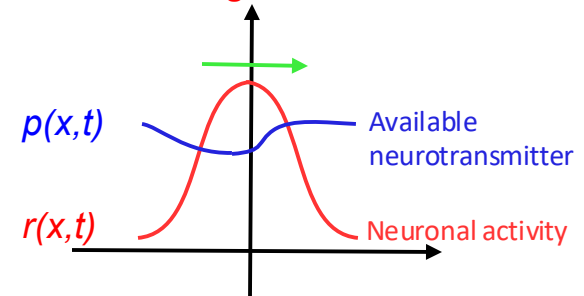


Static Profile



- Symmetric
- Not moving in any directions

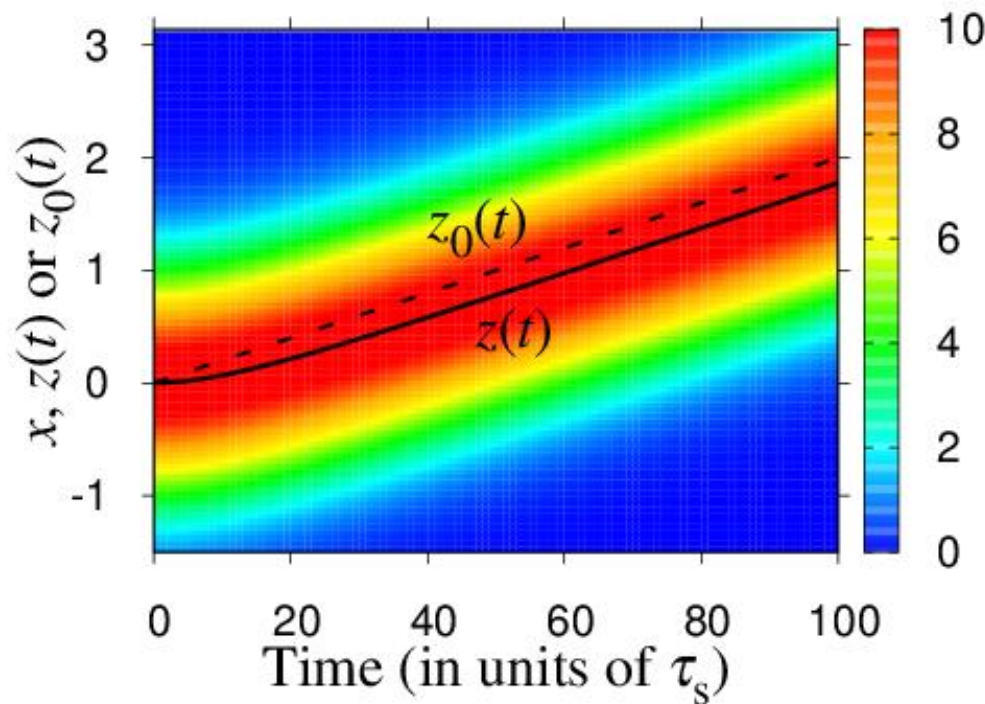
Moving Profile



- Asymmetric
- Moving in any direction

Tracking a Moving Stimulus ($A > 0$ and no STD)

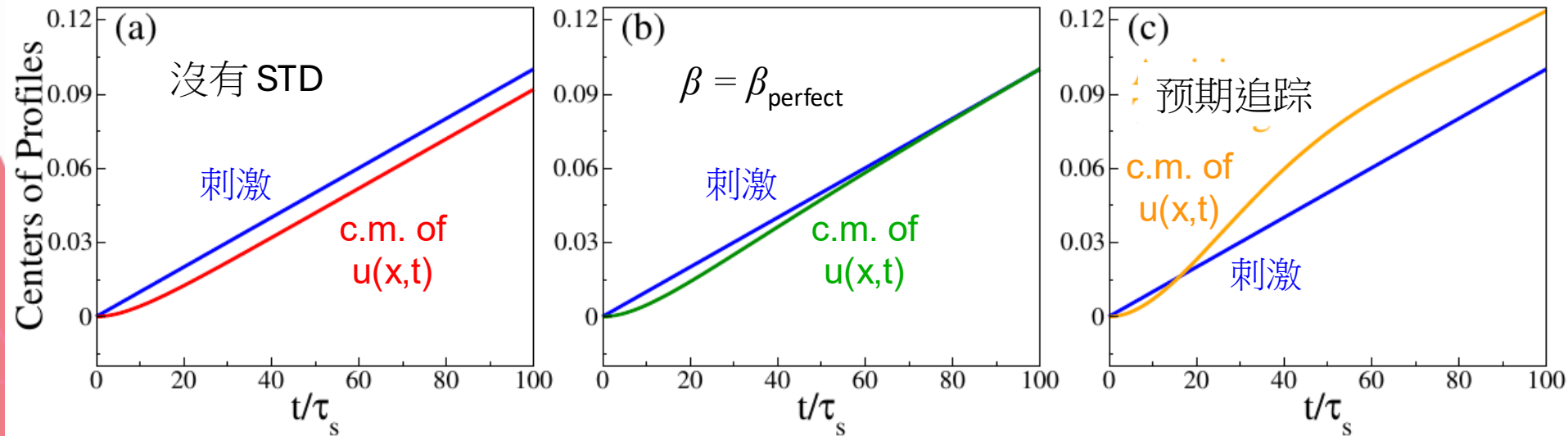
$z_0(t)$: stimulus, $z(t)$: center of $u(x,t)$



Tracking with STD

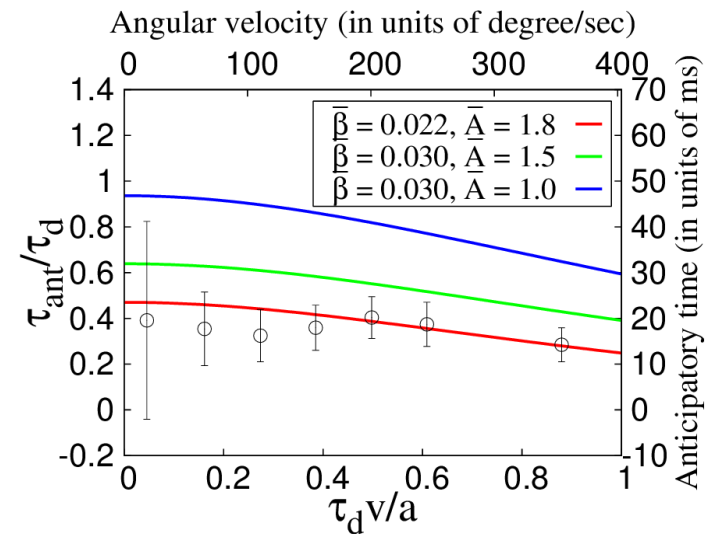
- How STD affects the tracking dynamics ?
- For each k , there is a particular β_{perfect} such that, the terminal lag is zero
- $\beta < \beta_{\text{perfect}}$: Lagging behind
- $\beta \sim \beta_{\text{perfect}}$: Lag ~ 0
- $\beta > \beta_{\text{perfect}}$: Overtake the stimulus

Fung, Wong and Wu (2012)



Anticipatory Tracking

- In 1998, the Anticipatory effect was observed in the brain
- Our work provides an explanation for this phenomenon



HIPPOCAMPUS 8:87-108 (1998)

Comparisons of Head Direction Cell Activity in the Postsubiculum and Anterior Thalamus of Freely Moving Rats

Jeffrey S. Taube^{1*} and Robert U. Muller²

¹Department of Psychology, Dartmouth College, Hanover, New Hampshire

²Department of Physiology, SUNY Health Science Center Brooklyn, New York

ABSTRACT: Single cells in the rat anterior thalamic nucleus (ATN) and postsubiculum (PoS) discharge as a function of the rat's directional

INTRODUCTION

Theory: CCA Fung, KYM Wong & S Wu 2012

Experiment: JP Goodridge & DS Touretzky 2000

CANN with STD also explains the memory playback phenomenon in the hippocampus

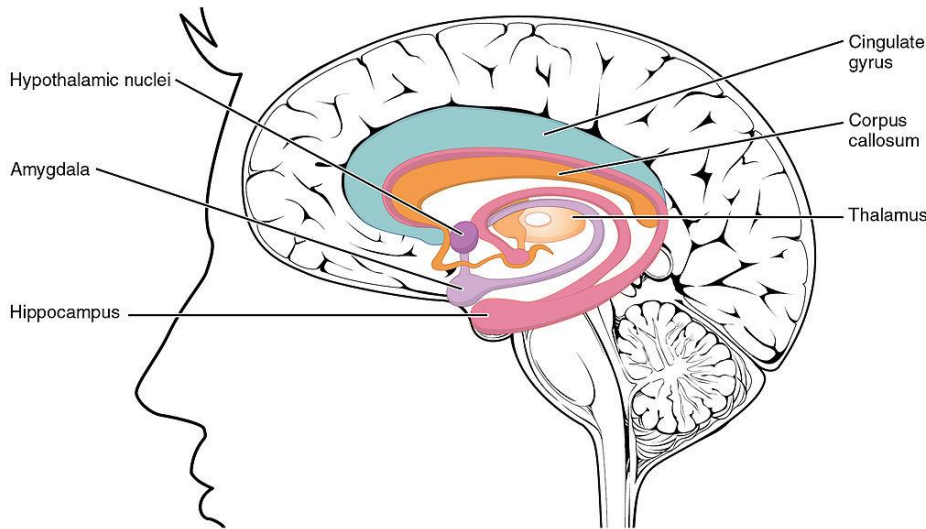
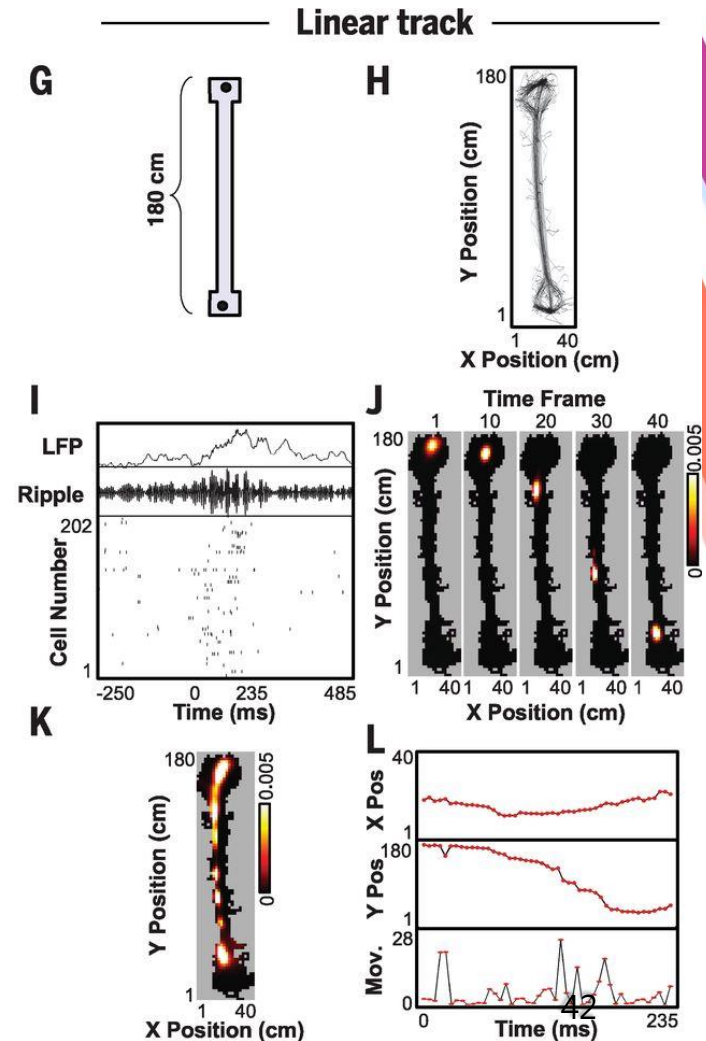


Illustration from Anatomy & Physiology, Connexions Web site. Jun 19, 2013.

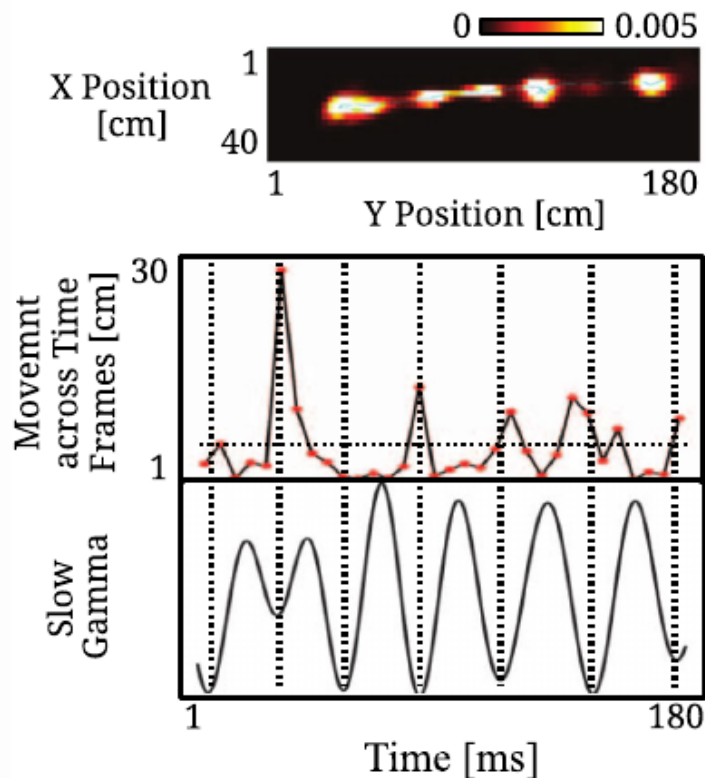
Pfeiffer and Foster (2015)



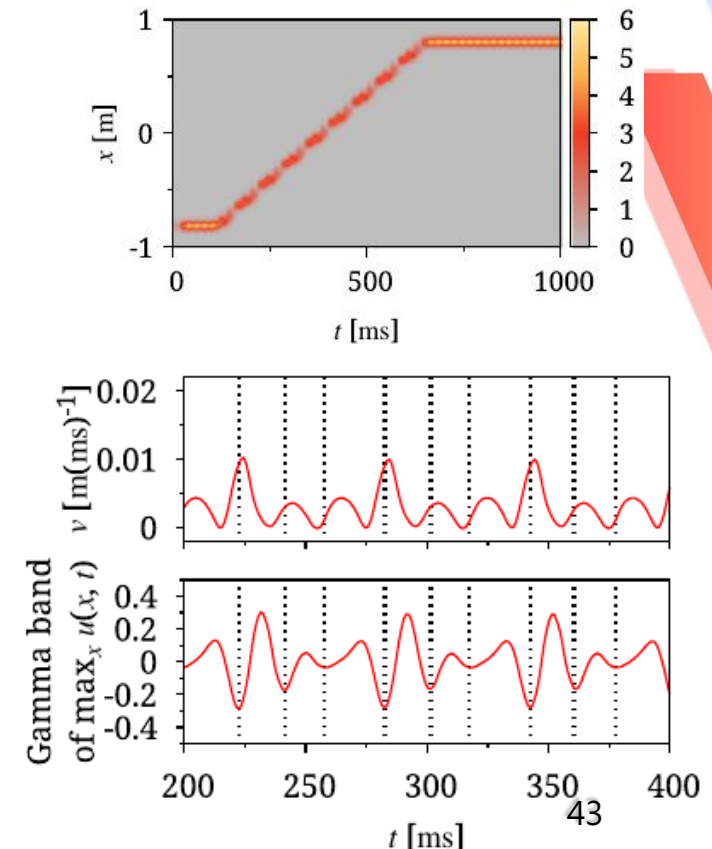
Strong inhibition makes the continuous attractor appear discrete

- Pfeiffer and Foster (2015) state in the report that the replay of continuous memories during NREM sleep is discrete

Experiment (Pfeiffer and Foster, 2015)



Simulation (Fung and Fukai, 2019)



Implementation in Python

- Here is my implementation of the CANN in Python

<https://colab.research.google.com/drive/1rLN3McoD5T5Ulv9u7lhpPiwd-HWxafKr?usp=sharing>



Models We have Covered So Far..

Spiking Neuronal Network

- Network of spiking neurons
- More biological realistic
- Reproduced some phenomena
- Can't explain memory replay (for example)

Continuous Attractor Neural Network

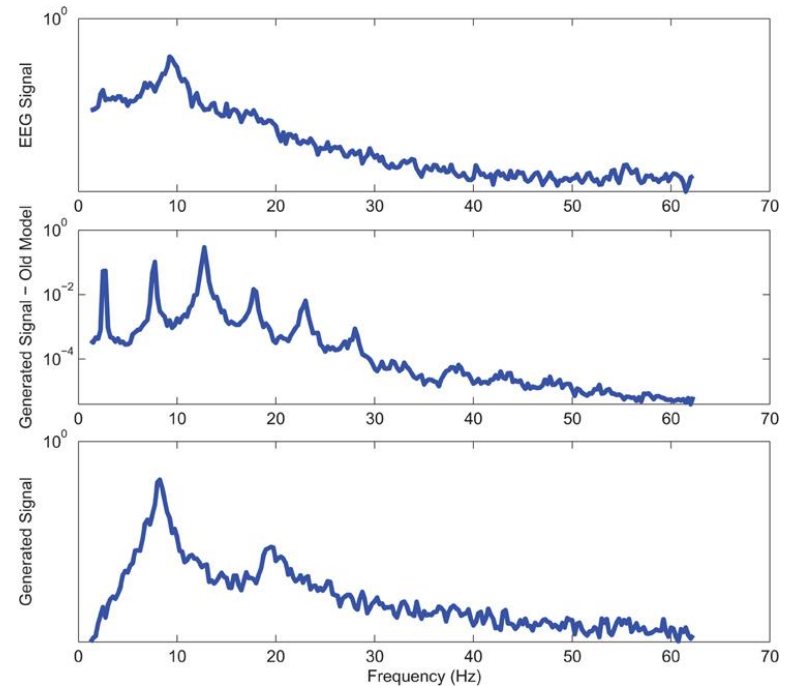
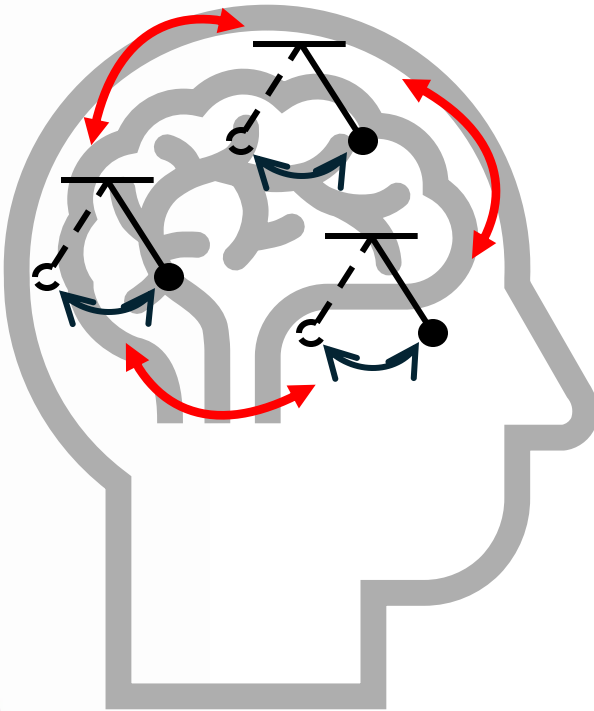
- Network of abstract neurons
- Less biological realistic
- Also reproduced some phenomena
- Can't reproduce detailed neuronal activity

Different Models

- Which one is more correct?
 - ◆ They all both work well in their domains
- Models and theories have their limitations
 - ◆ Because of the detail/assumption of the model
- Can abstract theories be “correct”?
 - ◆ For example, CANNs was made of artificial units, can it be valid?

More Abstract Model...

Coupled Oscillator Model for EEG



Ghorbanian, Ramakrishnan & Ashrafiuon (2015)

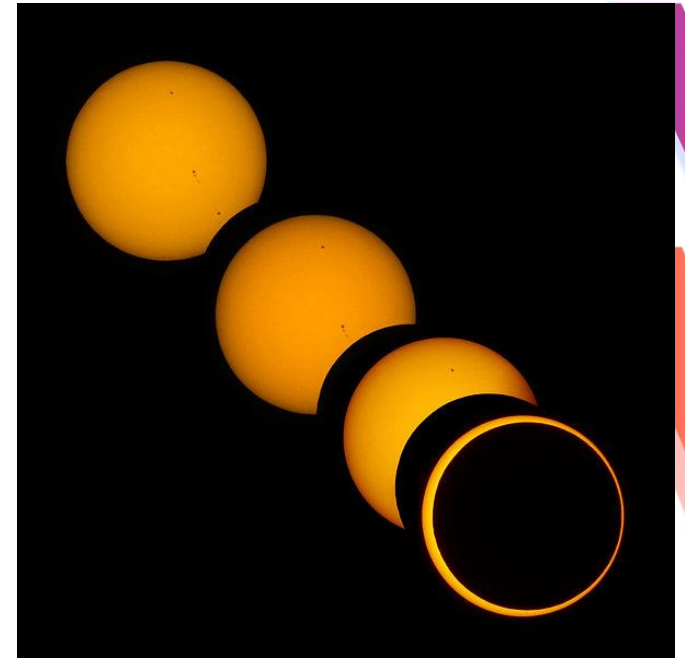
Theory vs Philosophy

The Sun Eaten by a Heavenly Dog, 天狗食日

- In the story, the heavenly dog ate up the sun. That's why people on the ground observed an incomplete sun.
- The heavenly dog story aimed to address the phenomenon, but why is it not accepted?

✓ Can “tell” why the sun was incomplete

✗ No prediction
✗ Cannot be validated



Wikimedia: Brocken Inaglory (2012)



How Models are Being Made?

Steps in Developing a Mathematical Model

- General steps involved in developing a mathematical model:
 1. Identify the problem or question to be addressed.
 2. Collect relevant data and information.
 3. Formulate assumptions and simplifications.
 4. Choose appropriate mathematical equations or functions to represent the problem.
 5. Solve the equations or use computational methods to analyse the model.
 6. Validate the model by comparing its predictions with real-world observations.
 7. Refine and improve the model based on feedback and further analysis.

In Short

