About the course

language: 中文/English。

When you first learned about action potentials and resting potentials in the senior high school, have you ever thought that these two things could be precisely predicted by a set of mathematical equations?

When you first learned about ASCII and Unicode in your freshman year, have you ever considered about how the human brain encodes information?

When you heard about AlphaGo defeating Lee Sedol, DALL-E 2 complementing Mona Lisa, or ChatGPT assisting Terence Tao, have you ever pondered the similarities and differences between biological neural networks and artificial neural networks?

You've heard the saying, 'The eyes are the windows to the soul.' But when you gaze into his/her eyes, do you truly believe that you can see his/her soul through them?

When you complete this course, you will know the answers to the first three questions, and you will have a deeper understanding of the fourth question.

If you choose to continue reading, then we are friends.

Course Objective: Let students have a general idea of theoretical neuroscience/computational neuroscience.

Duration: Weeks 1-18, 4 (3,4)

Location: Room 2603

Instructor: Wen Quan

Credits: 2

Course Introduction:

First, we will begin with an interesting mathematical problem as a prologue. Then, we will start with a single neuron and gradually transition to multiple neurons. This is a method of progressing from simple to complex, much appreciated by physicists.

Part 0, Part 1, Part 2, Part 3 will approximately take 2, 6, 6, and 4 class sessions, respectively (detailed descriptions of the four parts are provided below).

Assignments and Exams:

There will be approximately 5 assignments in total, with two types of questions: either deriving formulas or writing code.

The final exam for this course will take the form of the last assignment and will be entirely open-book, identical to the regular assignments. (This is the correct way to conduct an exam.)

Programming Assignments:

Programming languages are not restricted, with recommendations for MATLAB or Python or Julia.

Once, the programming assignments in this course caused much pain for students from the Mathematics and Physics schools, but now, times have changed! **Strongly recommend using ChatGPT, New Bing, Bard, and other Large Language Models**, as the small code snippets covered in this course are effortless for them. As long as you understand the logic of an assignment, programming will not be a barrier for you. Even if you currently only know how to `print("Hello World!")`, you'll be able to complete any programming assignment within a few days (with their assistance). (P.S.: If you want to improve your programming skills alongside studying computational neuroscience, such as elegant naming, thoughtful commenting, modular programming, vectorized programming, structured programming and Object Oriented Programming, you can also have more conversations with them. They are good teachers)

Please let me know if there are any other modifications or additions you need!

Prerequisites: Calculus, Linear Algebra, Probability Theory and Mathematical Statistics

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GitHub repository of this course:

Switch branches to view different semesters of the course!

Every fall semester, we create a new branch that contains all the materials for that term, including lectures, slides, assignments, textbooks, recommended papers, etc.

Some Notes:

- This course was once a required course for the Biophysics Department in the School of Physics and has been reformed into a recommended elective for that department.
- The course is challenging, recommended for students of the 20 grade and 21 grade students who **have available time and at least one opportunity to drop a course**.
- The difficulty of this course lies not in its depth but its breadth (in principle, if you have studied calculus, linear algebra, and statistics, you can take this course). For example, students from the Physics school will need to learn a lot about statistics.
- This course requires you to have a strong ability to acquire information. For instance, concepts from other disciplines, highly challenging assignment questions, answers found in a book, paper, or Wikipedia page, can be sought rather than reinventing the wheel. (Of course, thinking on your own is also vital, but most of the time in this course, you won't have time to reinvent the wheel for every subject.)
- In this course, the instructor will teach in English, but the teaching assistants' tutorial classes will be conducted in Chinese.

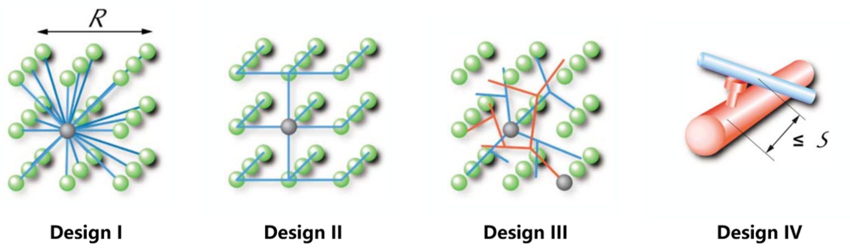
Part 0 neuromorphology

reference:

- PhD thesis of Quan Wen
- Chklovskii, 2004

The question we study in this part is - why do neurons need axons, dendrites, and dendritic spines?

We offer a theoretical explanation: if all neurons must communicate with each other pairwise, then having these three structures would minimize the overall volume of the brain.



(figure adapted from Chklovskii, 2004)

Part 1 single neuron

reference:

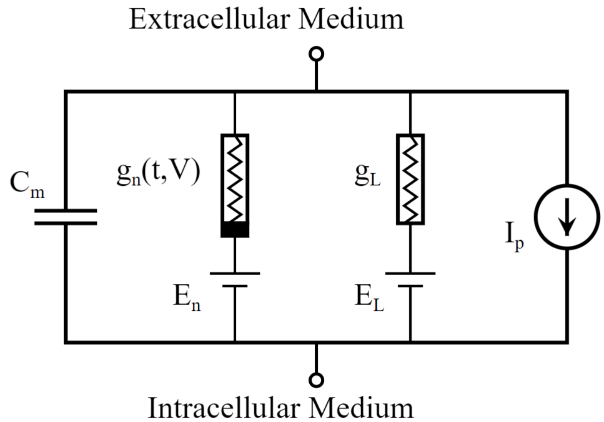
- CH5-CH6 of ***Theoretical Neuroscience***
- CH4 of ***Dynamical System in Neuroscience***
- Biological neuron model in Wikipedia

The study of a single neuron is quite thorough, so Part 1 has a clear main thread. In the end, what we get is a **biologically plausible model**, which is a very rare thing.

We first introduce the Nernst Equation (partly for which Walther Nernst won the Nobel Prize in Chemistry in 1920).

Then we present the integrate-and-fire model (the first theoretical model in neuroscience, proposed by Louis Lapicque and his wife Marcelle Lapicque in 1907).

Finally, we introduce the Hodgkin-Huxley model (for which Alan Hodgkin and Andrew Huxley won the Nobel Prize in Physiology or Medicine in 1963).



(electrical circuit diagram of HH model, figure from the Internet)

Part 2 from single neuron to multi neurons

reference:

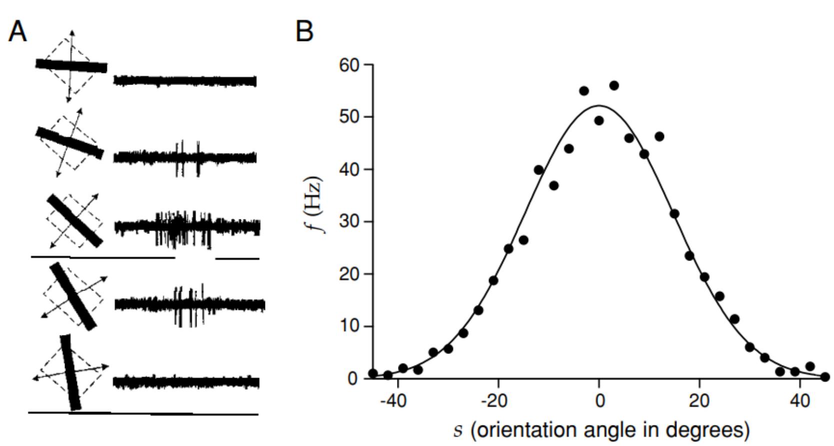
- CH1-CH4 of ***Theoretical Neuroscience***
- CH5 of ***Introduction to Probability Models***

"In order to study multiple neurons, we must introduce some necessary concepts and mathematical tools. Here, we only introduce two concepts—encoding and decoding.

encoding

Encoding is the process from stimulus s to action potential frequency r.

Traditional neuroscience believes that neurons use a simple (Gauss or Sigmoid or cos) function $r = r(s)$ to encode information. The figure below is the electrophysiological recording of a cat's V1 area neurons for rectangles of different orientations. (David Hubel and Torsten Wiesel won the Nobel Prize in Physiology or Medicine in 1981 for this work)".

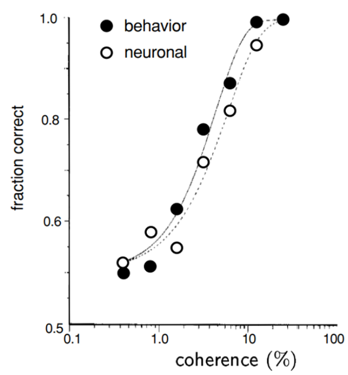


(***Theoretical Neuroscience***, figure 1.5)

decoding

Decoding is the process from action potential frequency r to stimulus s.

Neuroscientists believe that the Bayesian formula $P(s|r) = \frac{P(r|s)P(s)}{P(r)}$ can be used to decode information from neural activity. The figure below shows the decoding results of the neurons in a monkey's MT area. In this experiment, the results of neural activity decoding are very similar to the behavioral results."



(***Theoretical Neuroscience***, figure 3.2)

Note: In neuroscience research, behavioral data refers to the recording of an animal's behavior (for example, training your pet dog to retrieve a frisbee that you throw), and neural activity data refers to the direct or indirect recording of whether neurons are firing action potentials through means such as electrophysiology, calcium imaging, fMRI, etc. (for example, Wilder Penfield, a skilled neuroscientist and physician, casually recorded many electrophysiological data while performing surgery on epilepsy patients, with their consent). **Furthermore, you can think of the brain as a black box, where the stimulus is the input, behavior is the output, and recording neural activity is humanity's effort to open the black box.** In the past, neural activity data was often hard to obtain, and only behavioral data was available for analysis. Now, with the development of technology, more and more neural activity data is available.

Note: **All neural activity in vivo is a stochastic process, not a deterministic process.** This is why starting from Part 2, there will be a lot of involvement with statistical knowledge, and it's also why neuroscience greatly needs statistics.

Part 3 multi neurons/neural network

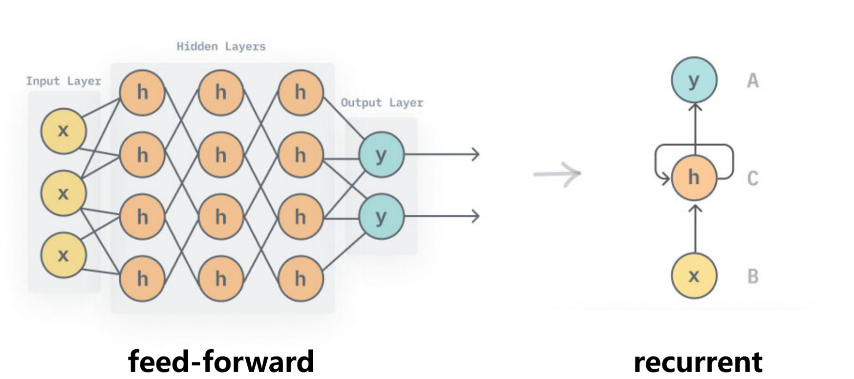
reference:

- CH7-CH10 of ***Theoretical Neuroscience***
- CH5 of **《机器学习》 周志华**
- [deep learning video of 3Blue1Brown]
- [deep learning video of StatQuest]

Finally, we come to the section on multiple neurons.

In Part 2, we characterized a neuron using a whole curve $r = r(s)$ or $r = r(t)$. But in Part 3, we represent a neuron using only a real number r. Whether this simplification is excessive is a matter of debate. Regardless, we adopt this simplification for most of Part 3.

We will sequentially introduce feedforward neural networks and recurrent neural networks. These are the two most basic types of neural networks.



(figure adapted from the Internet)

Lastly, we will move beyond this simplification and introduce some content related to spiking neural networks.

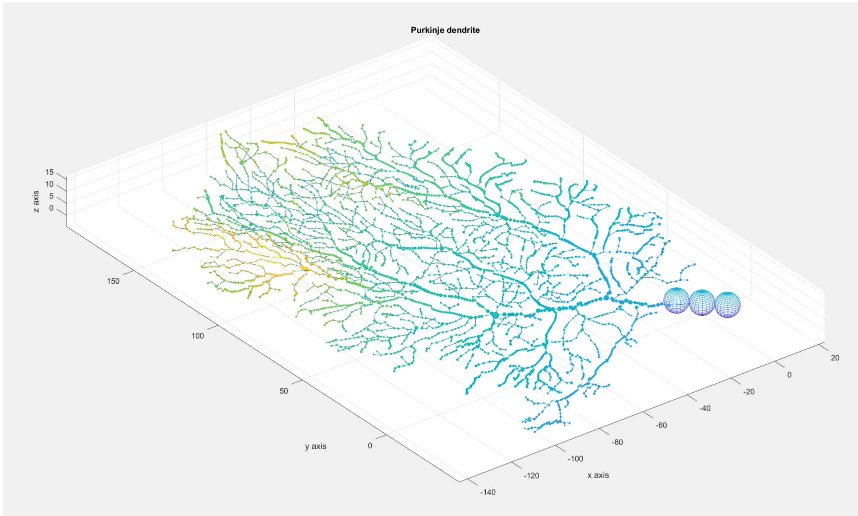
Note: In Part 1, you will feel a clear main thread, from the Nernst equation, to the integrate-and-fire model, and then to the Hodgkin-Huxley model. However, in Parts 2 and 3, the main thread of the course no longer seems so clear. This is because everyone who has studied the HH model knows how a single neuron works, but no one in the world knows **how biological neural networks (attention! not artificial neural networks) actually function, no one knows how they truly implement learning and memory, no one knows why they are efficient and versatile, and no one knows why they need sleep**. At the same time, some content in Parts 2 and 3 is controversial, and different scholars have different views. This leaves an opportunity for you to make some noise. Perhaps you will be the Alan Hodgkin and Andrew Huxley of the neural network field, and then Parts 2 and 3 of this course will become clear. With the development of electrophysiology (Neuropixel) and calcium imaging (whole brain imaging), this goal is not out of reach.

Note: This course **will not** cover recent popular deep learning models like LSTM, transformers, diffusion models, etc. We are not experts in the AI field, so it would not be appropriate for us to discuss these topics. We do frequently talk about them in the lab, though, as one of our long-term goals is to accurately track the neurons of small animals (such as nematodes, fruit flies, zebrafish). Since neurons can deform, this is an extremely challenging computer vision task. Although it is difficult, the potential results are highly enticing. 为有牺牲多壮志，敢教日月换新天。

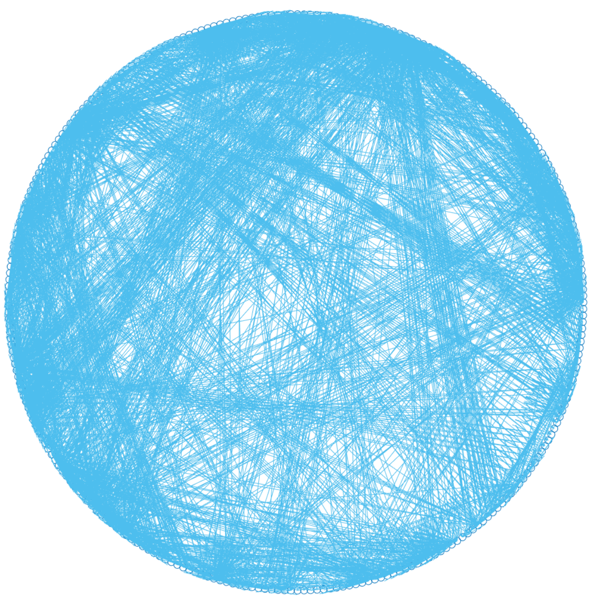
Homework paragon

Here are some homework paragons in the previous seasons. However, each season Prof. Quan will assign some brand new homework...

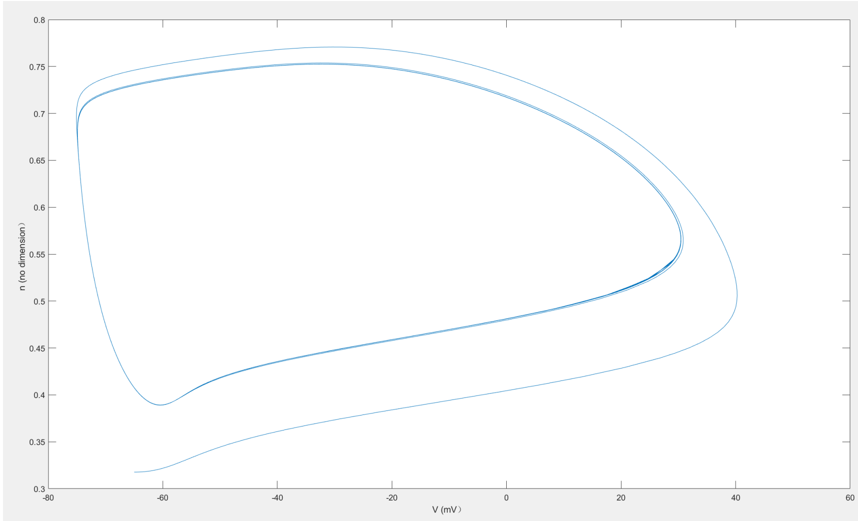
- Visualization of the Beautiful Purkinje.
  - Purkinje has the largest convergence in the human brain~
  - You will then be asked to do some analysis based on this graph.



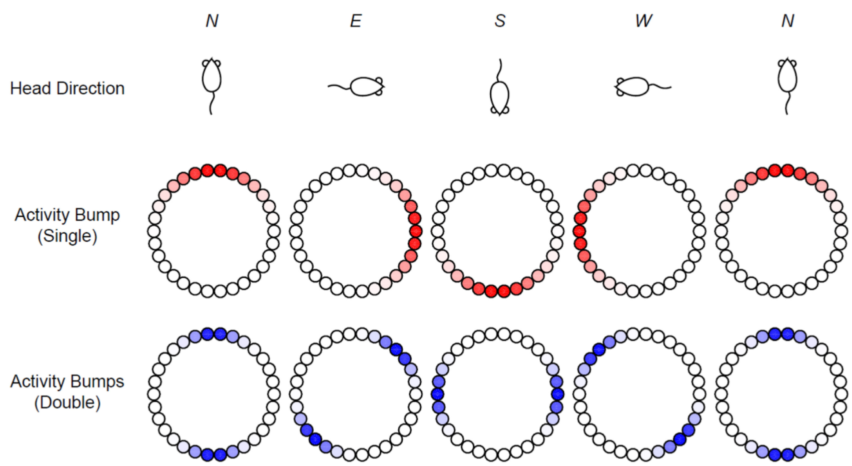
- Visualization of the Connectome of C.elegans.
  - Below is just a sketch map, each dot is a neuron and each line is a synapse.
  - You will then be asked to do some analysis based on this graph.



- Simulation of the HH model.
  - Below is a **limit cycle** of V and n.
  - You will be asked to do many many analysis on this problem.

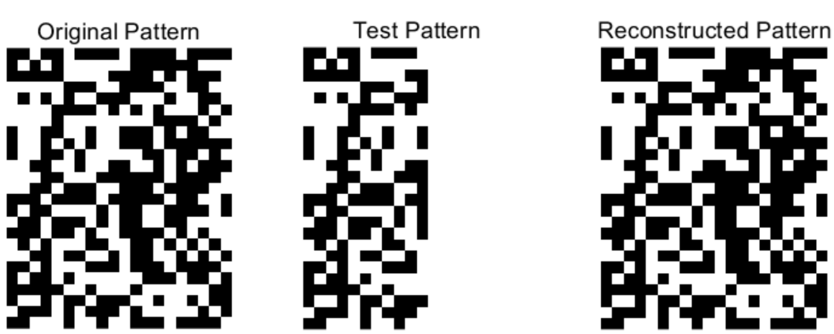


- Ring network.
  - The story of the ring network is a legend: it is firstly raised in theory (Ben-Yishai, 1995) (Kechen Zhang, 1996), and then is proofed in experiment (Kim, 2017).
  - You will be asked to reproduce some of the theory work.



(figure from Caixia Wang, 2020)

- Hopfield network.
  - You will be asked to use the Hopfield network to realize "memory", like the graph below.
  - You can also try to use this to solve the Travelling Salesman Problem, if you like.



(figure from Rong Wei, a student of 2022FA class)

Recommend reading

Strongly recommend

Theoretical Neuroscience: The classic textbook co-authored by Peter Dayan and L. F. Abbott. Reading this book will save you time.

What Mad Pursuit: An autobiography written by Francis Crick in 1988, translated into Chinese as **《狂热的追求》**. This book is quite thin, and if there is no language barrier, it can be read in just a few hours. The early chapters tell the story of his life before college, his research in physics, participation in World War II, and his work in molecular biology (including the discovery of the DNA double helix, the genetic code, mRNA, and tRNA, all related to Crick). The final chapter discusses his transition into neurobiology. He was friends with Alan Hodgkin, Andrew Huxley, David Marr, and Terry Sejnowski. Crick compares the current state of research in molecular biology and neurobiology and offers his criticism of the field of theoretical neuroscience, providing much food for thought.

> They are existence proofs that units somewhat like neurons can indeed do surprising things, but there is hardly anything to suggest that the brain actually performs in exactly the way they suggest.

Crick applied the principles of physics, such as the pursuit of simplicity, universality, and a progression from simplicity to complexity, to both molecular biology and neurobiology (for example, his own explanation of the central dogma is far clearer than any textbook). At the same time, he conducted numerous biological experiments himself, paying attention to the experimental details of biology, and understanding what can be discarded and what must be retained when building models. This is something that many scholars in theoretical neuroscience lack.

Crick was a charismatic and unrestrained individual: flipping a coin with James Watson to decide who would be the first and second authors on the paper describing the DNA double helix; writing to his subordinates that only the two of them knew the genetic code was a triplet; and even declaring his intention to create 'molecular psychology' (though this grand statement eventually became a joke).

When you get a chance

This section's book is optional; reading it is better, but not reading it will not affect your study of this course.

Dynamical System in Neuroscience: A book about the application of dynamical systems in neuroscience. If time is limited, Chapter 4 is the most worthwhile to read, covering related concepts of 2D dynamical systems: fixed point, limit cycle, bifurcation. (P.S.: Reading this book will also save you time, as answers to several questions from previous years' homework can be found in Chapter 4.)

《常微分方程》丁同仁、李承治：If you want to delve deeper into dynamical systems, Chapter 8 of this book is a good start.

Introduction to Probability Models: A classic textbook on stochastic processes written by Ross. This course will embrace Poisson processes, Markov processes, and stationary processes, all of which are included in this book. If time is limited, Chapter 5 is the most worthwhile to read.

《机器学习》 周志华: A book that introduces machine learning in a comprehensive yet straightforward way. Chapter 5 discusses deep learning, helping readers understand the differences between how machine learning practitioners and computational neuroscientists perceive neural networks. Chapter 10 covers dimensionality reduction, talks about methods such as Principal Component Analysis and Multi-Dimensional Scaling, which are commonly used in neuroscience and the entire biology.

Principles of Neural Design: A book that discusses the advantages of how the neural system is designed. If time is limited, Chapter 2 is the most worthwhile to read. In this chapter, the author adopts a bottom-up approach, just like in this course, starting with **E. coli (you read that right; E. coli, although a prokaryote and lacking neurons, can still implement memory)**, moving on to paramecia, and then to nematodes. The writing style of this book is quite witty, much like that of Crick and Ross.

Vision: David Marr's (1945-1980) posthumous work. In this book, Marr first proposed three levels that he believed should be present in theoretical neuroscience research (computational theory, algorithms, hardware implementation), and then put forth an algorithm that could implement human vision (image -> Primal sketch -> 2.5D sketch -> 3D representation). The last chapter of this book features scientists, led by Francis Crick, questioning and criticizing Marr's method, with Marr individually answering these questions and defending his approach. The Chinese version of the book was published in 2022, with prefaces by 朱松纯, 汤晓鸥, 李飞飞, who all read this book when they were around your age.

In 1979, knowing that his days were numbered due to leukemia, David Marr chose to meet Francis Crick at The Salk Institute and then devoted himself to writing this book upon his return. Marr passed away in 1980, and the book was published in 1982. Marr has since been considered one of the founding figures of computer vision due to his work and this book.

This book carries a flavor reminiscent of **《九阴真经》** and **《武穆遗书》**, but acquiring it does not require 华山论剑 or 倚天屠龙. The USTC library has this book, although there's only one copy each in the east and west libraries."

Principles of Neurobiology: A textbook written by 骆利群. For the biological aspects, reading this book and Wikipedia will suffice.

What can you benefit from this course?

Neuroscience was born in the early 20th century, with Camillo Golgi and Santiago Ramon y Cajal conducting the first experimental research, and Louis Lapicque and his wife Marcelle Lapicque conducting the first theoretical research.

From its inception to the present, it has always been one of the most interdisciplinary subjects in the world, with its researchers coming from mathematics, physics, statistics, biology, AI, engineering, psychology, and almost every other field. Our laboratory has had students from mathematics, physics, statistics, biology, CS/EE, AI and chemistry backgrounds. Students from various backgrounds can benefit from this course.

In a word, we welcome students from all backgrounds!

If you come from mathematical school, you can learn about how to apply dynamical systems to neuroscience here. Currently, most scholars working on neuroscience and dynamical systems have a background in mathematics, such as Steven H. Strogatz and Eugene Izhikevich. It's worth mentioning that Chapter 8 of ***Theoretical Neuroscience*** has some relation to Alan Turing's later work in mathematical biology.

If you come from physics school, **you can learn how the ideas of physics are applied in neuroscience (and this is not just a grand statement).** Looking across the entire field of biology, besides the HH (Hodgkin-Huxley) model, there are many textbook-level, biologically plausible models that have been proposed by physicists: Archibald Hill's modeling of hemoglobin, Linus Pauling's protein alpha helix, the DNA double helix, and Howard Berg's research on E. coli. **To propose models of this level, one must understand both the ideas of physics and the experimental details of biology.** From the last century to today, there have been many scholars who have transitioned from physics to neuroscience, including those featured in this course: Alan Hodgkin, Andrew Huxley, Francis Crick, J. J. Hopfield, Terry Sejnowski, L. F. Abbott, Haim Sompolinsky, and Mu-ming Poo.

If you come from statistics school, you can learn about how to apply stochastic processes and Bayesian inference to neuroscience from this course. Besides these, many mathematical tools involved in Part 2 are from renowned statisticians such as R. A. Fisher, C. R. Rao, George Box, and David Cox. As the amount of data in neuroscience continues to grow, there are also quite a few scholars who have transitioned from statistics to neuroscience.

If you come from the school of the life science, you will find that this course is entirely different from the biology courses you've taken before. Your biggest concern might be that your mathematical skills are not up to par, but **if you merely want to understand the general ideas of this course, knowing calculus, linear algebra, and probability & statistics is indeed enough**. If you plan to work in theoretical fields in the future, you indeed need to study further. Don't think that having a biology undergraduate degree means you can't work in theory, **never limit yourself**. Here's an example of a world-class scientist who started in biology and psychology and later worked in theory: Geoffrey Hinton.

If you come from the fields of Big Data/AI, you can learn here about the differences in how machine learning researchers and computational neuroscientists perceive neural networks. The mathematical complexity of this course is comparable to that of machine learning, and many mathematical tools used in Parts 2 and 3 are the same as those used in machine learning (e.g., KL divergence, Shannon information, Max Likelihood Estimation, Receiver Operator Characteristic curve, hidden variables). **If you have already studied machine learning and deep learning, you will find Parts 2 and 3 quite easy.** Historically, many figures in the AI field, such as Alan Turing, Marvin Minsky, David Marr, Geoffrey Hinton, were highly interested in biological neural networks, and at that time, AI and theoretical neuroscience were almost synonymous. **Though AI and computational neuroscience have mainly developed independently over the past two or three decades, there is still some cross-fertilization between the two fields (mostly us borrowing from you)**. Your works in VAE, ResNet, NeuroODE have all provided new insights to neuroscience. **Looking forward, many scholars**

believe that the answer to achieving general artificial intelligence may still lie in biological neural networks.

About us

[Home Page of Wen Lab]

[Journal Club Website of Wen Lab]

[GitHub Page of Wen Lab]

Last word

End with Francis Crick's word:

> The brain sciences have still a very long way to go, but the fascination of the subject and the importance of the answers will inevitably carry it forward.
>
> It is essential to understand our brains in some detail if we are to assess correctly our place in this vast and complicated universe we see all around us.