

**BIPN194 Advanced Topics in Modern Biology: Synapse and Autism**

Class time and location: Wednesdays 10:00am-11:20am, YORK 3010

Professor Yishi Jin

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[*please include BIPN194 in subject line of any emails concerning the class*]

Office Hours: Mon 9-10:00am at 2418 Bonner Hall, and by appointment.

*(group presentation meetings: first one generally Wed or Thursday afternoon; second one Mon, or latest Tues, morning)*

**Short outline of the course:**

Jan 9: Introduction lecture on synapses, class organization and assignment of discussion groups.

Jan 16: pre-synaptic terminal/group 1

Jan 23: post-synaptic terminal/group 2

Jan 30: synaptic adhesion/group 3

Feb 6: autism genetics/group 4

Feb 13: autism genetics/group 5

Feb 20 autism genetics/group 6

Feb 27: autism genetics /group 7

Mar 6: autism genetics /group 8

Mar 13 11am: *course final reports due by email with subject title “BIPN194 final report\_ last name”*

Prerequisites: *This course will assume upper division knowledge of genetics, cell biology, molecular biology and neurobiology. BICD 100 (Genetics), BIPN 100 (Mammalian Physiology), BICD 110 (Cell Biology), and BIPN140 (cellular neurobiology) are strongly recommended.*

**Course Description**

Synapses are where the actions in the nervous system take place! Many neurological diseases are associated with synapse dysfunction. Recent genetic studies of Autism or Autism spectral disorders (ASD) have implicated many mutations affecting genes that function in synapses. The goals of the course are to provide basic knowledge on how

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synapses are formed and regulated, and to discuss cutting-edge research on understanding the causative associations of genes in Autism. Specifically, we will first focus on the key studies that reveal the tripartite components of the synapse. We will then discuss representative research on understanding autism-associated genetic mutations on synapses and behaviors using animal models.

With the exception of the first introductory lecture, the meetings in this course will be student-led discussions of primary research literature. The course is highly interactive, and everyone must speak and give feedback to each other!

Evaluation. There is NO final exam. Your grade will be based on four equal components:

- (1) Your performance in your group’s presentation of the paper.
- (2) Your attendance and audible participation in class discussions.
- (3) Your summaries of the papers when you are not presenting. These are due in class at the beginning of the meeting. Late hand-in or email will not be accepted.
- (4) Your final report (2 pages, single-space) on class readings, due on **Wed 3/13, 11am.**

### Readings

All reading materials are primary research papers and reviews, which are freely available online. We will go over how to find the papers via Pubmed (<https://www.ncbi.nlm.nih.gov/pubmed/>) or Google Scholar ([scholar.google.com](https://scholar.google.com)) in the first meeting. In some cases you will need to use a UCSD IP address to access the research papers. PDFs are convenient ways to read the papers; hard copies will not be provided. For your presentations of figures, the html files are more useful for downloading individual panels of figures.

There is no textbook for this course. Use your textbooks from other classes (such as BIPN140) for general knowledge on neuroscience. Scholar review articles are recommended to help understanding the general background.

Expect to spend at least 4 hours a week on the reading, 8-10 hours if you are presenting a paper.

### Group presentations

#### *PRESENTERS:*

Each of you is a member of a group that will make a 45-minute presentation on one of the assigned research papers. This includes approximately 35 minutes for the presentation and 10 minutes for questions and discussion. Each member of the group should be prepared to answer questions and engage class discussion of their portion of the presentation.

#### *NONPRESENTERS:*

You are expected to read EVERY discussion paper before coming to class and to be prepared to discuss it. At the beginning of the class you will turn in a one-page single-space summary on the discussion paper. During the class presentation you are expected to actively participate in discussion. After each presentation (except your own), you will write a short and constructive evaluation of the presentation.

### PRESENTATION FORMAT

Each member of a group should prepare between 3-5 slides (in ppt or a format agreeable by the entire group); handouts and chalkboard drawings are helpful to facilitate long-term memory. The entire presentation (made as powerpoint or keynote or other format) should be on one computer and uploaded to class website after presentation. Presenting group should arrive 10 minutes early to set up.

### PRESENTATION CONTENT

1. *Background/Introduction*: What is the *biological problem*? What are the authors attempting to show? How does this work fit into the overall findings of the field? What tools or methodologies are going to be used to approach the problem?
2. *Results /data*: recommend that each group member present one or two Figures/Tables each. For each Figure or experiment, address (a) what is being shown, and (b) why and how was this experiment done, in the context of the paper. Discuss reservations or questions you have about the data. It is required that you read and understand all the data, including those in “supplemental information”, which is often in a separate file from the pdf of the article.
3. *Conclusions*: What are the conclusions? How strong does the data support the model or hypothesis? What are the ‘next steps’ or remaining questions?

### GROUP MEETINGS PRIOR TO PRESENTATION

It is essential that all members of the group meet prior to the presentation.

Group members should exchange phone numbers and e-mail addresses and arrange to meet at least twice to prepare for the presentation. The papers are complicated, and the level of background within the class varies. By working as a team you can give an effective presentation.

***I will meet with the entire group on Wednesday to discuss presentation.***

### SUMMARY/EVALUATIONS OF PAPERS

At the beginning of class, the non-presenters will turn in a one-page summary of the paper to be discussed. This should be both a brief *summary* of the paper and also an *evaluation* of how well the authors support their claims. There is no need for statements about how hard or confusing the papers are.

*I DO NOT accept weekly summaries by email.*

### PEER EVALUATIONS

After each presentation, non-presenters will fill out a short evaluation of the presentation. Did the presentation and discussion clarify the work? Were your questions answered? Do you have suggestions for improving the quality of the presentations? Comments should be constructive. This is a very important factor in your course participation.

### ATTENDANCE

You are expected to attend ALL class meetings. Late arrival (i.e. > 15 minutes) will likely cause grade reduction. Acceptable excuses for missing a class are: documented medical emergency and family emergency; university sponsored events. Vacation, missing the bus, oversleeping, or deadlines or demands from other

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courses/exams are not acceptable excuses for missing this class.

READING LIST (please download pdf from PubMed:  
<http://www.ncbi.nlm.nih.gov/sites/entrez?cmd=search&db=pubmed>)

**General readings for the entire course**

[The autism sequencing consortium: large-scale, high-throughput sequencing in autism spectrum disorders.](#) Buxbaum JD, Daly MJ, Devlin B, Lehner T, Roeder K, State MW; Autism Sequencing Consortium. *Neuron*. 2012 Dec 20;76(6):1052-6.

[Behavioral profiles of mouse models for autism spectrum disorders.](#) Ey E, Leblond CS, Bourgeron T. *Autism Res*. 2011 Feb;4(1):5-16.

[Current knowledge on the genetics of autism and propositions for future research.](#) Bourgeron T. *C R Biol*. 2016 Jul-Aug;339(7-8):300-7.

**Weekly topic and discussion papers**

**Jan 9: Introduction and organization of the course**

**Presenter: Jin**

**Jan 16: presynaptic terminal/group 1**

**Presenters: Beheshta Amiri, Mary Belaya, Raul Curiel, Sarah Stumpf**

**Background reading:**

[A molecular machine for neurotransmitter release: synaptotagmin and beyond.](#)

Südhof TC. *Nat Med*. 2013 Oct;19(10):1227-31.

**Discussion paper:**

[Synaptotagmin I: a major Ca<sup>2+</sup> sensor for transmitter release at a central synapse.](#)

Geppert M, Goda Y, Hammer RE, Li C, Rosahl TW, Stevens CF, Südhof TC. *Cell*. 1994 Nov 18;79(4):717-27.

**Jan 23: postsynaptic terminal/group 2**

**Presenters: Alex Cerda, Gavina Kahlon, Isabelle Velloze**

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**Background reading:**

[The Shank family of scaffold proteins.](#)

Sheng M, Kim E. *J Cell Sci.* (2000) v113:1851-6.

**Discussion paper:**

[A preformed complex of postsynaptic proteins is involved in excitatory synapse development.](#)

Gerrow K, Romorini S, Nabi SM, Colicos MA, Sala C, El-Husseini A. *Neuron.* 2006 Feb 16;49(4):547-62.

**Jan 30: synaptic adhesion/group 3**

**Presenters: Robin Fong, Marsha Liem, Zong Li**

**Background reading:**

[Neuroligins and neuroligins link synaptic function to cognitive disease.](#)

Südhof TC. *Nature.* 2008 Oct 16;455(7215):903-11.

**Discussion paper:**

[Neurexin mediates the assembly of presynaptic terminals.](#)

Dean C, Scholl FG, Choih J, DeMaria S, Berger J, Isacoff E, Scheiffele P. *Nat Neurosci.* 2003 Jul;6(7):708-16.

**Feb 6: autism genetics/group 4**

**Presenters: Emerald Liu, Idally Reyes, Naguiba Williams, Yan Zhao**

**Background reading:**

[The autism sequencing consortium: large-scale, high-throughput sequencing in autism spectrum disorders.](#)

Buxbaum JD, Daly MJ, Devlin B, Lehner T, Roeder K, State MW; Autism Sequencing Consortium. *Neuron.* 2012 Dec 20;76(6):1052-6.

**Discussion papers:**

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[Mutations of the X-linked genes encoding neuroligins NLGN3 and NLGN4 are associated with autism.](#)

Jamain S, Quach H, Betancur C, Råstam M, Colineaux C, Gillberg IC, Soderstrom H, Giros B, Leboyer M, Gillberg C, Bourgeron T; Paris Autism Research International Sibpair Study. *Nat Genet.* 2003 May;34(1):27-9.

[Autism-related neuroligin-3 mutation alters social behavior and spatial learning.](#)

Jaramillo TC, Liu S, Pettersen A, Birnbaum SG, Powell CM. *Autism Res.* 2014 Apr;7(2):264-72.

### **Feb 13: Shank autism genetics/group 5**

**Presenters: Korie Almanza, Eishlee Jasa, Eleanor Kim**

#### **Background reading:**

[The emerging role of SHANK genes in neuropsychiatric disorders.](#) Guilmatre A, Huguet G, Delorme R, Bourgeron T. *Dev Neurobiol.* 2014 Feb;74(2):113-22.

#### **Discussion paper:**

[Mice with Shank3 Mutations Associated with ASD and Schizophrenia Display Both Shared and Distinct Defects.](#)

Zhou Y, Kaiser T, Monteiro P, Zhang X, Van der Goes MS, Wang D, Barak B, Zeng M, Li C, Lu C, Wells M, Amaya A, Nguyen S, Lewis M, Sanjana N, Zhou Y, Zhang M, Zhang F, Fu Z, Feng G. *Neuron.* 2016 Jan 6;89(1):147-62.

### **Feb 20: Cntnap 2 in autism /group 6**

**Presenters: Elisabeth McCallum, Mathew Orozco, Diana Wong**

#### **Background reading:**

[Recessive symptomatic focal epilepsy and mutant contactin-associated protein-like 2.](#)

Strauss KA, Puffenberger EG, Huentelman MJ, Gottlieb S, Dobrin SE, Parod JM, Stephan DA, Morton DH. *N Engl J Med.* 2006 Mar 30;354(13):1370-7.

#### **Discussion paper:**

[Exogenous and evoked oxytocin restores social behavior in the Cntnap2 mouse model of autism.](#)

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Peñagarikano O, Lázaro MT, Lu XH, Gordon A, Dong H, Lam HA, Peles E, Maidment NT, Murphy NP, Yang XW, Golshani P, Geschwind DH. *Sci Transl Med.* 2015 Jan 21;7(271):271ra8.

**Feb 27: autism genetics/group 7**

**Presenters: Nanea Dominguez, Alan Faulks, Lauren Hui**

**Background reading:**

[Cutting Edge: Critical Roles for Microbiota-Mediated Regulation of the Immune System in a Prenatal Immune Activation Model of Autism.](#)

Lammert CR, Frost EL, Bolte AC, Paysour MJ, Shaw ME, Bellinger CE, Weigel TK, Zunder ER, Lukens JR. *J Immunol.* 2018 Aug 1;201(3):845-850.

**Discussion paper:**

[Microbial Reconstitution Reverses Maternal Diet-Induced Social and Synaptic Deficits in Offspring.](#)

Buffington SA, Di Prisco GV, Auchtung TA, Ajami NJ, Petrosino JF, Costa-Mattioli M. *Cell.* 2016 Jun 16;165(7):1762-1775. doi: 10.1016/j.cell.2016.06.001.

**Mar 6: autism genetics/group 8**

**Presenters: Vivian Lin, Teresa Chou, Jennifer, Truong**

**Discussion paper:**

[TSHZ3 deletion causes an autism syndrome and defects in cortical projection neurons.](#)

Caubit X, Gubellini P, Andrieux J, Roubertoux PL, Metwaly M, Jacq B, Fatmi A, Had-Aissouni L, Kwan KY, Salin P, Carlier M, Liedén A, Rudd E, Shinawi M, Vincent-Delorme C, Cuisset JM, Lemaitre MP, Abderrehamane F, Duban B, Lemaitre JF, Woolf AS, Bockenhauer D, Severac D, Dubois E, Zhu Y, Sestan N, Garratt AN, Kerkerian-Le Goff L, Fasano L.

*Nat Genet.* 2016 Nov;48(11):1359-1369.

**Mar 13 no class meeting**

**Final paper due 11am by email, using subject title “BIPN194\_final report\_ last name”**