NGG 584: Neurobiology of Sleep

COURSE DESCRIPTION AND SYLLABUS

Course Director: Dr. David Raizen 215-476-4809; raizen@mail.med.upenn.edu, Department of Neurology

Other Faculty: Various
Time: Once weekly on Wed 2:30-4:00 PM (tentative time)

Room: Zoom

Textbook: None. Readings will all be from the primary literature.
Website: Penn+Box (https://upenn.app.box.com/login)

Course Description: This is a 15-session seminar course where literature involving the neurobiology of sleep and arousal will be discussed. The format will consist of a journal club styled discussion of 2-3 primary papers, distributed to students the previous week. Three students will be assigned to present in each session. One student will begin with a brief (10 min) introductory lecture to the topic of the day. Then, two students will each present a paper for that session. The students need not present every single figure in the paper, if irrelevant to the key conclusions (but should have all the figures ready as power-point slides in case questions arise). After summarizing the key results from the paper presented and supplementary papers (including more recently published papers), the student will propose future directions for this line of work. Students that are not assigned to present on a given week are expected to read the assigned papers and will get called on randomly to explain figures in the papers. They should prepare to ask questions and comment on the conclusions drawn from particular data.

Dr Raizen or another member of the faculty with relevant expertise will be available to help the student understand the methodology of the papers and key concepts. We encourage students to contact the faculty with questions well in advance of the session when they are to present.
The goals of this course are:

1. To teach students some of the outstanding questions in the field of sleep and arousal including comparison to other quiescent behavioral states.
2. To introduce students to the model systems used to study sleep as well as to the phylogeny of sleep.
3. To guide students through the reading of influential papers in the sleep research field.
4. To introduce students to some of the methodological approaches in sleep science
5. To improve critical thinking and analysis when approaching scientific literature.

While the course is designed for neuroscience graduate students, the course will be opened to post docs, fellows and advanced undergraduate students on a case-by-case basis. Students or post-docs who audit the course with the instructors' permission are required to read all the papers and to participate in all the discussions. Tardiness and absences are eschewed and may result in grade penalty unless the reason for the absence is a good one (e.g. going to a scientific conference).

Prerequisites: The students should have a basic understanding of nervous system structure (neuroanatomy) and function including electrical properties of neurons and synaptic transmission. We would expect a basic understanding of wet lab techniques including molecular biology, staining, Western blots, etc. Experience in reading and evaluating scientific journal articles is strongly encouraged.

Faculty: Along with Raizen, other faculty with expertise relevant to the topic under discussion will be invited to specific classes.

Requirements and grading: Students will be graded on attendance (30%), participation in the discussion (20%), presentation of papers (40%), and completion of study guide questions (10%). Each student will be expected to read the required assigned papers (usually two papers) each week and be prepared to explain any figure in those papers. Additional bibliography will be provided to the students but reading these additional papers will be optional. The additional papers will fall into 2 categories: those that are directly relevant to the discussed papers and those that are not directly relevant but are for your library.

Papers should be read critically and should be approached as one approaches a journal club paper. Supplementary data when relevant should be read as critically as the main body of the paper. While in general, papers under discussion will be scientifically sound and will carry important conclusions, one should critically read all aspects of the papers including methods, results, the writing, and the conclusions. Instructors will be available to help if questions arise while reading the papers during the week before class. A series of study guide questions will be handed out with the papers. The students should turn in their typed answers at the start of the session, preferably by emailing the answers to the instructors. Answers should be typed. They will be graded as pass/fail. A PASS would consist of answers that show that the student had thought about the question and read the papers (even if the instructors disagree with the answer) and a FAIL would be a lack of answers or clear evidence that the student did not read the papers. Class auditors are expected to complete all assignments.

	Date	Topic	Topic in papers	Papers
1	9/10	Sleep Regulation 1: Phenomenology	Two process model and other quantitative EEG.	Franken, J. Neurosci . // Forced desychrony paper
2	9/17	Sensory Gating	Sensory gating in worms and mammals	Cho and Sternberg Cell '13 // Hallasa Cell '14
3	9/24	Arousal mechanisms: Neuropeptides	Hypocretin in mice and fish	Adamantidis et al Delecea, Nature // Yokogawa, Hyp rece in fish PLoS Biol 07
4	10/1	Arousal mechanisms: Neuropeptides	PDF in flies and worms	Choi and Kaplan, Neuron '13 //. Parisky et al Griffith , Neuron 08
5	10/8	Sleep Circuitry	Sleep-promoting circuitry in flies and mice	Szymusiak, VLPO Brain Res '98 // Ancalet PFZ, Nat Neurosci '14
6	10/15	Sleep Circuitry	Wake promoting circuitry in mice: LC	Carter et al Delecea LC Nature Neurosci '10 // Vazey& Aston-Jones, LC and anesthesia PNAS '14
7	10/22	Sleep Circuitry	Role of dopamine	Kume paper on fly dopamine; saper paper on vPAG
8	10/29	Sleep deprivation	Physiological consequences	Rechtschaffen paper // Shaw Nature 02 Drosophila paper
9	11/5	Sleep function 1	Relationship to metabolism	Nedergaard Science '13 // Alex Keene feeding and sleep JEB '14 // maybe Holtzman paper in Science in beta Amyloid?
10	11/12*	Sleep function 2	Relationship to brain plasticity (bird song, Cirelli/Tononi)	Aton et al Frank Neuron '09 // Bushey, Cirelli, Tononi, Science '11
11	11/19*	Sleep function 3	Relationship to brain plasticity (Walker, Born)	
12	11/26	OFF for THANKGIVING		
13	12/3	Anesthesia and sleep	Mechanisms of anesthesia	Kottler et al Van Swinderwin Curr. Biol '13 // Moore et al, CB 13
14	12/10	Sleep Phylogeny: a potpourri	FORMAT TO BE DETERMINED	
15	12/17	Sleep Phylogeny: a potpourri	FORMAT TO BE DETERMINED	

#SFN meeting
*Max away

Conferences/Seminars with relevance to class:

Schedule and topics of classes:

1. **Week 1: Sleep regulation phenomenology**. Instructor: Anafi. Introduction and presenter:.
   a. Franken P, Chollet D, Tafti M., The homeostatic regulation of sleep need is under genetic control. J Neurosci. 2001 Apr 15;21(8):2610-21.
   b. Dijk DJ[1], Duffy JF, Czeisler CA. Circadian and sleep/wake dependent aspects of subjective alertness and cognitive performance. J Sleep Res. 1992 Jun;1(2):112-7.

2. **Week 2: Sensory gating during sleep**. Instructors: Raizen and Contreras (guest instructor). Introduction:

a. Halassa MM, Chen Z, Wimmer RD, Brunetti PM, Zhao S, Zikopoulos B, Wang F, Brown EN, Wilson MA., State-dependent architecture of thalamic reticular subnetworks., Cell. 2014 Aug 14;158(4):808-21. Presenter **Rich**
b. Cho JY, Sternberg PW. Multilevel modulation of a sensory motor circuit during C. elegans sleep and arousal., Cell. 2014 Jan 16;156(1-2):249-60. Presenter

3. **Week 3: Arousal Mechanisms—Neuropeptides** I. Instructor: Kelz. Introduction:
   a. Adamantidis AR[1], Zhang F, Aravanis AM, Deisseroth K, de Lecea L., Neural substrates of awakening probed with optogenetic control of hypocretin neurons. Nature. 2007 Nov 15;450(7168):420-4. Presenter **Connie Ji**
   b. Yokogawa T, Marin W, Faraco J, Pézeron G, Appelbaum L, Zhang J, Rosa F, Mourrain P, Mignot E., Characterization of sleep in zebrafish and insomnia in hypocretin receptor mutants, PLoS Biol. 2007 Oct 16;5(10):e277. Presenter

4. **Week 4**: **Arousal mechanisms—Neuropeptides** II. Instructor: Raizen. Introduction:
   a. Parisky KM, Agosto J, Pulver SR, Shang Y, Kuklin E, Hodge JJ, Kang K, Liu X, Garrity PA, Rosbash M, Griffith LC. PDF cells are a GABA-responsive wake-promoting component of the Drosophila sleep circuit., Neuron. 2008 Nov 26;60(4):672-82. Presenter
   b. Choi S, Chatzigeorgiou M, Taylor KP, Schafer WR, Kaplan JM., Analysis of NPR-1 reveals a circuit mechanism for behavioral quiescence in C. elegans., Neuron. 2013 Jun 5;78(5):869-80. Presenter

5. **Week 5**: **Sleep circuitry—sleep promoting circuitry**. Instructors: Raizen. Introduction:
   a. Szymusiak R, Alam N, Steininger TL, McGinty D., Sleep-waking discharge patterns of ventrolateral preoptic/anterior hypothalamic neurons in rats., Brain Res. 1998 Aug 24;803(1-2):178-88. Presenter
   b. Anaclet C, Ferrari L, Arrigoni E, Bass CE, Saper CB, Lu J, Fuller PM. The GABAergic parafacial zone is a medullary slow wave sleep-promoting center. Nat Neurosci. 2014 Sep;17(9):1217-24. Presenter

6. **Week 6**: **Sleep circuitry—wake promoting circuitry (Locus Coeruleus)**. Instructor**.**
   a. Carter ME, Yizhar O, Chikahisa S, Nguyen H, Adamantidis A, Nishino S, Deisseroth K, de Lecea L., Tuning arousal with optogenetic modulation of locus coeruleus neurons., Nat Neurosci. 2010 Dec;13(12):1526-33. Presenter
   b. Vazey EM[1], Aston-Jones G. Designer receptor manipulations reveal a role of the locus coeruleus noradrenergic system in isoflurane general anesthesia, Proc Natl Acad Sci U S A. 2014 Mar 11;111(10):3859-64. Presenter

7. **Week 7: Sleep circuitry—wake promoting circuitry (Dopamine)**. Instructors: Raizen and Kelz. Introduction:
   a. Ueno T, Tomita J, Tanimoto H, Endo K, Ito K, Kume S, Kume K., Identification of a dopamine pathway that regulates sleep and arousal in Drosophila., Nat Neurosci. 2012 Nov;15(11):1516-23. Presenter
   b. Lu J[1], Jhou TC, Saper CB., Identification of wake-active dopaminergic neurons in the ventral periaqueductal gray matter., J Neurosci. 2006 Jan 4;26(1):193-202. Presenter

8. **Week 8**: **Sleep deprivation**. Instructor: Anafi. Introduction:
   a. Rechtschaffen A, Gilliland MA, Bergmann BM, Winter JB., Physiological correlates of prolonged sleep deprivation in rats., Science. 1983 Jul 8;221(4606):182-4. Presenter

b. Shaw PJ, Tononi G, Greenspan RJ, Robinson DF., Stress response genes protect against lethal effects of sleep deprivation in Drosophila, Nature. 2002 May 16;417(6886):287-91. Presenter

9. **Week 9**: **Sleep Function I**—relationship to metabolism and waste generation and clearance. Instructor: Anafi. Introduction:
   a. Xie L, Kang H, Xu Q, Chen MJ, Liao Y, Thiyagarajan M, O'Donnell J, Christensen DJ, Nicholson C, Iliff JJ, Takano T, Deane R, Nedergaard M., Sleep drives metabolite clearance from the adult brain., Science. 2013 Oct 18;342(6156):373-7. Presenter
   b. Masek P, Reynolds LA, Bollinger WL, Moody C, Mehta A, Murakami K, Yoshizawa M, Gibbs AG, Keene AC., Altered regulation of **sleep** and feeding contributes to starvation resistance in **Drosophila** melanogaster., J Exp Biol. 2014 Sep 1;217(Pt 17):3122-32. Presenter

10. **Week 10**: **Sleep function II—relationship to brain plasticity**. Instructor: Raizen. Introduction:
   a. Bushey D, Tononi G, Cirelli C., Sleep and synaptic homeostasis: structural evidence in Drosophila. Science. 2011 Jun 24;332(6037):1576-81. Presenter
   b. Aton SJ, Seibt J, Dumoulin M, Jha SK, Steinmetz N, Coleman T, Naidoo N, Frank MG., Mechanisms of sleep-dependent consolidation of cortical plasticity., Neuron. 2009 Feb 12;61(3):454-66. Presenter

11. **Week 11**: **Sleep function III—relationship to brain plasticity (cont)**. Instructor: Anafi. Introduction: No intro (continue last week's theme)
   a. Derégnaucourt S, Mitra PP, Fehér O, Pytte C, Tchernichovski O.,How **sleep** affects the developmental learning of **bird song**, Nature. 2005 Feb 17;433(7027):710-6. Presenter
   b. Hauner KK, Howard JD, Zelano C, Gottfried JA., Stimulus-specific enhancement of fear extinction during slow-wave **sleep**, Nat Neurosci. 2013 Nov;16(11):1553-5 Presenter
12. **Week 12. Local Sleep**. SKIP for THANKGIVING
   a. Vyazovskiy VV[1], Olcese U, Hanlon EC, Nir Y, Cirelli C, Tononi G., Local sleep in awake rats, Nature. 2011 Apr 28;472(7344):443-7. Presenter
   b. Hinard V, Mikhail C, Pradervand S, Curie T, Houtkooper RH, Auwerx J, Franken P, Tafti M., , Key electrophysiological, molecular, and metabolic signatures of sleep and wakefulness revealed in primary cortical cultures, J Neurosci. 2012 Sep 5;32(36):12506-17. Presenter
13. **Week 13: Anesthesia and Sleep**. Instructor: Kelz. Introduction:
   a. Moore JT[1], Chen J, Han B, Meng QC, Veasey SC, Beck SG, Kelz MB., Direct activation of sleep-promoting VLPO neurons by volatile anesthetics contributes to anesthetic hypnosis, Curr Biol. 2012 Nov 6;22(21):2008-16. Presenter
   b. Kottler B[1], Bao H, Zalucki O, Imlach W, Troup M, van Alphen B, Paulk A, Zhang B, van Swinderen B., A sleep/wake circuit controls isoflurane sensitivity in Drosophila., Curr Biol. 2013 Apr 8;23(7):594-8. Presenter

14. **Week 14-15: Phylogeny of sleep I**, a potpourri. Instructor: Raizen.

FORMAT: Each person will have ~10 minutes to present. They should (1) Introduce the species in context of the phylogenetic tree. (2) Show 1-2 figures from the paper, and (3) Explain the implications of this work to

understanding sleep function and/or regulation (4) Propose a future direction for this research. Each person will be responsible for reading just their own assigned paper in detail; others' papers are optional.

WEEK 14 (Dec 10)

a. **WHALES (Max): "oy, this baby just never sleeps…."** Lyamin O, Pryaslova J, Lance V, Siegel J. (2005) Animal behavior: continuous activity of cetaceans after birth, Nature 435, p 1177.
    i. Also read commentaries by Gnone et al and by Sekiguchi et al same year in Nature.
b. **EGG-LAYING MAMMALS (Mike): "REM sleep is profound in these critters…".** Siegel, J.M., Manger, P. R., Nienhuis1, R., Fahringer, H. M., and Pettigre, J. D. (1998) Monotremes and the evolution of rapid eye movement sleep, Phil. Trans. Roy. Soc. Lond. B 353, pp. 1147-1157.
c. **REPTILES (Ron): "Cold-blooded dreaming?"** F. Ayala-Guerrero, G. Mexicano (2008) Sleep and wakefulness in the green iguanid lizard (Iguana iguana), Comparative Biochemistry and Physiology, Part A 151, pp. 305-312.
d. **MIGRATING BIRDS (Greg): "Are we there yet?"** Rattenborg, N.C., Mandt, B. H., Obermeyer, Winsauer, Huber, Wikelski, Benca, R. M. (2008) Migratory Sleeplessness in the White-Crowned Sparrow (Zonotrichia leucophrys gambelii), PLOS Biology 2(7) pp. 924-936.
e. **BIRDS AND MATING (Walter): "Sleepless in Alaska"** Lesku JA, Rattenborg NC, Valcu M, Vyssotski AL, Kuhn S, Kuemmeth F, Heidrich W, Kempenaers B. (2012) Adaptive sleep loss in polygynous pectoral sandpipers., Science 337, pp1654-8.
f. **CAVE FISH (Salika)**: **"My fat cousins who live at the surface are lazy and sleep too much"** Duboue, Keane and Borowski (2011) Evolutionary convergence on sleep loss in cavefish populations, Current Biology 21, pp 671-676.

WEEK 15 (Dec 17)

g. **OSTRICHES (Nick) "Every one loves Big Bird (except Romney)"** Lesku JA, Meyer LC, Fuller A, Maloney SK, Dell'Omo G, Vyssotski AL, Rattenborg NC. "Ostriches sleep like platypuses. PLoS One 2011.
h. **BARN OWLS (Nick):** Scriba MF[1], Rattenborg NC, Dreiss AN, Vyssotski AL, Roulin A. **"pigmented sleep"**. J Evol Biol. 2014 Oct;27(10):2057-68.
i. **HONEY BEES (Mi Shi): "…floats like a butterfly and [sleeps] like a bee"** Barrett A. Klein, Kathryn M. Olzsowy, Arno Klein, Katharine M. Saunders, and Thomas D. Seeley (2008) Caste-dependent sleep of worker honey bees, J. of Experimental Biology 211, pp. 3028-3040.
j. **MOLLUSCS (Connie): "…coat of many colors"** Frank et al (2012) A preliminary analysis of **sleep**-like states in the **cuttlefish** Sepia officinalis. PLoS One 7(6) e38125.
    a. See also Vorster AP, Krishnan HC, Cirelli C, Lyons LC. (2014) Characterization of **sleep** in **Aplysia** californica. Sleep 37(9), 1453-1463.
k. **JELLY FISH (David): "don't get stung"** Seymour, Carrette, and Sutherland (2004) Do box jellyfish sleep at night? The Medical Journal of Australia 181, p 707. http://www.mja.com.au/public/issues/181_11_061204/sey10757_fm.html
l. **ARCHAE and BACTERIA** "sleep" (**Hilary**): **"we are the world, we are (most) of the species"** Rachel S. Edgar et al (2012) Peroxiredoxins are conserved markers of circadian rhythms., Nature 485, p 459.

m. **ANNELID** “sleep” (**Rich**): **“Process C in the sea”** Tosches MA, Bucher D, Vopalensky P, Arendt D. (2014) Melatonin signaling controls circadian swimming behavior in marine zooplankton. Cell. 159(1):46-57.