Welcome to PSY397H Biological Rhythms, Fall, 2023.
Tuesdays 10 am-1 pm.

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DATE	TOPIC	READINGS
Sept. 12	Biological and psychological representations of time; Temporal programs; Temporal biology and the organization of living things; Adaptive significance; "hierarchy" of circadian clocks.	**A**
Sept. 19	Properties and synchronization of biological clocks. Resetting by light and nonphotic mechanisms including *social zeitgebers* and metabolism.	**B**
Sept. 26	Molecular mechanisms of rhythm production and regulation – Molecular clocks throughout the living world. Discovery of clock genes.	**C**
Oct. 3	The structure of circadian systems. Comparative anatomy and physiology across the 5 taxonomic groups.	**D**
Oct. 10	**TEST 1** (25%) covers everything including Oct 3. Followed by: Sleep, and circadian rhythms in human beings and other organisms. *Chronotype*, jet lag, temporal isolation.	**E**
Oct. 17	The "other" circadian systems? Food entrainable oscillators; amphetamine sensitive oscillators; metabolic clocks, circadian disorganization in chronic mental disorders.	**F**
Oct. 24	Non-circadian biological clocks: tidal, lunar, annual, ultradian rhythms. Time memory, time-place learning and the perception of time.	**G**
Oct. 31	Seasonality. Photoperiodic time measurement	**H**
Nov. 7	**Reading week (Nov. 6-10)**	
Nov. 14	**TEST 2** (30%), Covers up to and including Oct. 31. Followed by lecture on Sleep, hibernation and memory consolidation.	**I**
Nov. 21	Migration orientation and the sun compasses	**J**
Nov. 28	Circadian disorganization, chronic disease, and longevity	**K**
Dec. 5	New models and conceptualizations of Time in biology; Daylight Saving Time and life on the Moon.	**L**

PSY397 Biological Rhythms

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Course description

Biological rhythmicity is found throughout Nature, from bacteria to humans. While all living systems display various cycles, specific types of rhythms have evolved which provide temporal organization to the physiology and behavior of organisms and the ability to anticipate regular, cyclic changes in their environments. These are what we call "biological clocks". Some mechanisms have become adapted for use in complex behaviors such as migration, seasonality, and coordinated reproduction. In addition, organisms gain an adaptive advantage from being able to predict the possible recurrence of conditioned that they have experienced. This is time memory, an aspect of circadian biology that is used in concert with the biological clock to predict the likelihood that significant events are going to recur at the same time as the initial experience. In this course, we will examine both mechanisms, the highly conserved systems that predict the regular changes in the environment, as well as the systems that underlie the memory of events that are not regular, nor linked to specific times of day. We will review current findings at all levels of organization from molecular genetic, to anatomical, to behavioral, always coming back to the question of how these rhythmic systems are able to function to predict demand, thereby operating as biological clocks, and we will examine the consequences of disordered timing systems.

Marking scheme

Term test 1: 25%; Term test 2: 30%; Final 2 hour exam: 45%

Tests will be a combination of multiple choice, short answer, matching, and fill-in-the-blanks. Some minor arithmetic calculations are required for some questions. No aids are allowed on tests.

Missed tests may be made up only with University of Toronto approved documentation.

If you become ill and it affects your ability to do your academic work, consult me right away. Normally, I will ask you for documentation in support of your specific medical circumstances. This documentation can be an Absence Declaration (via ACORN) or the University's Verification of Student Illness or Injury (VOI) form. The VOI indicates the impact and severity of the illness, while protecting your privacy about the details of the nature of the illness. If you cannot submit a VOI due to limits on terms of use, you can submit a different form (like a letter from a doctor), as long as it is an original document, and it contains the same information as the VOI (including dates, academic impact, practitioner's signature, phone and registration number). For more information on the VOI, please see http://www.illnessverification.utoronto.ca. For information on Absence Declaration Tool for A&S students, please see https://www.artsci.utoronto.ca/absence. If you get a concussion, break your hand, or suffer some other acute injury, you should register with Accessibility Services as soon as possible. Please note that students can only use the Absence Declaration on ACORN ***once per***

semester. Documentation must be given to me within one week of missing a term test, in any of the forms mentioned above.

Asking questions, office hours and reviews

Within reason, you are encouraged to ask questions during the lectures. Bear in mind that although the instructor may be responsive in this way, your fellow students may not appreciate too many interruptions. The instructor will reserve some lecture time at the end of each class to answer questions. Official office hours: 11-12 am Fridays. Additional hours will be scheduled prior to term tests (times to determined from class discussions). Other hours by appointment.

Recommended resources

Circadian Rhythms: A Very Short Introduction (Very Short Introductions) 1st Edition, Kindle Edition by Russell Foster and Leon Kreitzman

Rhythms of Life: The Biological Clocks that Control the Daily Lives of Every Living Thing by Russell G. Foster and Leon Kreitzman | Oct 10 2005.
Seasons of Life: The Biological Rhythms That Enable Living Things to Thrive and Survive by Russell G. Foster and Leon Kreitzman | Jun 30 2009

TEXTBOOK (recommended)
Introducing Biological Rhythms: A primer on the Temporal Organization of Life… **(2006)** Willard L. **Koukkari** & Robert B. **Sothern**, authors.

The BioClock Studio, UCSD: https://ccb.ucsd.edu/the-bioclock-studio/index.html

Reading list (articles) and concepts to learn

A. Week 1; September 12 (*Function of clocks and other rhythmic organization in living organisms; discovery of circadian clocks; ubiquity of clocks across species and levels of biological organization*)

1. Pittendrigh, CS (1993) Temporal organization: reflections of a Darwinian clock-watcher. Annu Rev Physiol. 1993;55:16-54.
2. Vitaterna, M. H., Takahashi, J. S., & Turek, F. W. (2001). Overview of circadian rhythms. *Alcohol Research & Health*, *25*(2), 85-93.
3. Roenneberg T, Merrow M. (2005) Circadian clocks - the fall and rise of physiology. Nat Rev Mol Cell Biol. 2005 Dec;6(12):965-71.

B. Week 2; September 19 (*Basic mechanism of biological clocks; synchronization of clocks and other oscillators; environmental synchronizers and mechanisms of entrainment*)

4 Pittendrigh, C. S., & Daan, S. (1976). A Functional Analysis of Circadian Pacemakers in Nocturnal Rodents. IV. Entrainment: Pacemaker as Clock. *Journal of Comparative Physiology A*, *106*(3), 291-331. https://doi.org/10.1007/BF01417856.

5 Golombek, DA and Rosenstein, R (2010) The physiology of entrainment. *Physiol Rev* 90: 1063–1102 doi:10.1152/physrev.00009.2009.

6 Mrosovsky N, Salmon PA, Menaker M, Ralph MR. (1992) Nonphotic phase shifting in hamster clock mutants. *J Biol Rhythms*. 7(1):41-49.

C. Week 3; September 26 (*Comparing and contrasting the physiology and anatomy of circadian clocks across species; methods for identifying pacemakers; applying principles of entrainment*)

7 Lundkvist, GB, Block, GD. (2005) Role of Neuronal Membrane Events in Circadian Rhythm Generation *METHODS IN ENZYMOLOGY,* VOL. 393:623-642.

8 Underwood, H, Steele, CT, Zivkovic, B (2001) Circadian Organization and the Role of the Pineal in Birds. *MICROSCOPY RESEARCH AND TECHNIQUE* 53:48–62.

9 Ralph MR, Foster RG, Davis FC, Menaker M. (1990) Transplanted suprachiasmatic nucleus determines circadian period. Science. 1990 Feb 23;247(4945):975-8. doi: 10.1126/science.2305266.PMID: 2305266
10 Aronson BD, Bell-Pedersen D, Block GD, Bos NP, Dunlap JC, Eskin A, Garceau NY, Geusz ME, Johnson KA, Khalsa SB, et al. Circadian rhythms. Brain Res Brain Res Rev. 1993 Sep-Dec;18(3):315-33. doi: 10.1016/0165-0173(93)90015-r. PMID: 8401597.
11 Antle, MC, Silver, R (2005) Orchestrating time: arrangements of the brain circadian clock *TRENDS IN NEUROSCIENCES* Vol.28.
12 Reppert, SM, Weaver, DR (2002) Coordination of circadian timing in mammals *NATURE* 418:935-941.
13 Page, TL (1982) Transplantation of the Cockroach Circadian Pacemaker. *Science* 216, 73-75.

D. Week 4; October 3 (*Discovery of the molecular circadian systems in representative species across the phylogenetic tree; conservation of circadian mechanisms within taxonomic kingdoms, evidence for separate derivation of clock mechanisms between kingdoms; adaptive significance of circadian mechanisms*)

14 Reppert, SM, Weaver, DR (2001) MOLECULAR ANALYSIS OFMAMMALIAN CIRCADIAN RHYTHMS *Annu. Rev. Physiol*. **63**:647–76.
15 Williams JA, Sehgal A. Molecular components of the circadian system in Drosophila. Annu Rev Physiol. 2001;63:729-55. doi: 10.1146/annurev.physiol.63.1.729. PMID: 11181974.
16 Hardin PE. (2011) Molecular genetic analysis of circadian timekeeping in Drosophila. *Adv Genet.* **74**:141-73. doi: 10.1016/B978-0-12-387690-4.00005-2. PMID: 21924977; PMCID: PMC4108082.
17 Lowrey PL & Takahashi JS (2011) Genetics of Circadian Rhythms in Mammalian Model Organisms. *Adv Genet*. **74**: 175–230. doi:10.1016/B978-0-12-387690-4.00006-4.
18 Tauber, E, Last, KS, Olive, PJW, Kyriacou, CP. (2004) Clock Gene Evolution and Functional Divergence. *J Biol Rhythms*, 19 445-458.
19 OUYANG, Y, ANDERSSON, CR, KONDO, T, GOLDEN, SS, JOHNSON, H (1998) Resonating circadian clocks enhance fitness in cyanobacteria *Proc. Natl. Acad. Sci. USA* **95**, 8660–8664.
20 Green CB, Takahashi JS, Bass J. The meter of metabolism. Cell. 2008 Sep 5;134(5):728-42. doi: 10.1016/j.cell.2008.08.022.

E. Week 5; October 10; Term Test 1
Plus lecture: (*Human chronobiology; ontogeny of circadian rhythms in human beings; clock dysfunction and physical and mental disorder; effects of chronic circadian misalignment or poor entrainment; significance of "chronotype"in health and performance;effects of daylight staving time*)

21. Haraszti RÁ, Ella K, Gyöngyösi N, Roenneberg T, Káldi K. (2014) Social jetlag negatively correlates with academic performance in undergraduates. Chronobiol Int. 2014 Jun;31(5):603-12. doi: 10.3109/07420528.2013.879164.
22. Roenneberg, T. (2015) Having trouble typing? What on earth is chronotype? *J.Biol. Rhythms* Dec;30(6):487-91. doi: 10.1177/0748730415603835.
23. Hahn C1, Cowell JM, Wiprzycka UJ, Goldstein D, Ralph M, Hasher L, Zelazo PD. (2012) Circadian rhythms in executive function during the transition to adolescence: the effect of

synchrony between chronotype and time of day. Dev Sci. 2012 May;15(3):408-16. doi:10.1111/j.1467-7687.2012.01137.x. Epub 2012 Feb 23.
24. Castillo-Ruiz A, Paul MJ, Schwartz WJ (2012) In search of a temporal niche: Social interactions. *In.* A. Kalsbeek, M. Merrow, T. Roenneberg and R. G. Foster (Eds.) *Progress in Brain Research*, Vol. 199 pp 267-280. Elsevier.
25. Chouvet, G et al. (1974) *Periodicite bicircadienne du cycle veille-sommeil dans des conditions hors du temps. Etude polygraphique*. *Electroenceph Clin Neurophysiol* **37**:367-380.

F. Week 6; October 17 (*Non-SCN clocks in mammals; clocks that don't use the canonical clock genes; post-translational oscillators; dopamine-dependent systems*)

26. Stephan FK. (2002) The "other" circadian system: food as a Zeitgeber. *J Biol Rhythms*. Aug;17(4):284-92.
27. Honma K1, Honma S. (2009) The SCN-independent clocks, methamphetamine and food restriction. Eur J Neurosci. Nov;30(9):1707-17. doi: 10.1111/j.1460-9568.2009.06976.x. Epub 2009 Oct 28.
28. Coward, D., Cain, S. and Ralph, M. R. (2001) A circadian rhythm in mice that is unaffected by the period mutation at *clock*. *Biol. Rhythm Res.* **32**: 233-242.
29. Taufique SKT, Ehichioya DE, Pendergast JS and Yamazaki S. Genetics and functional significance of the understudied methamphetamine sensitive circadian oscillator (MASCO) [version 1; peer review: 2 approved] F1000Research 2022, 11:1018 https://doi.org/10.12688/f1000research.125432.1

G. Week 7; October 24 (*time memory; anticipation of significant events*)

30. Mulder CK, Gerkema MP & Van der Zee1 EA. (2013) Circadian clocks and memory: time-place learning. *Front. Mol. Neurosci*. https://doi.org/10.3389/fnmol.2013.00008.
31. Ralph MR, Ko CH, Antoniadis EA, Seco P, Irani F, Presta C, McDonald RJ. (2002) The significance of circadian phase for performance on a reward-based learning task in hamsters. *Behav Brain Res*. Oct 17;136(1):179-84.
32. Cain SW, Yoon J, Shrestha TC, Ralph MR (2014) Retention of a 24-hour time memory in Syrian hamsters carrying the 20-hour short circadian period mutation in casein kinase-1ε (ck1εtau/tau). *Neurobiol Learn Mem*. 114C:171-177. doi: 10.1016/j.nlm.2014.06.004.
33. Cain, SW, Rawashdeh, OA, Siu, M, Kim, SC & Ralph, MR. (2017) Dopamine dependent setting of a circadian oscillator underlying the memory for time of day. *Neurobiol Learn Mem*. 141:78–83.27.
34. Smies CW, Bodinayake KK, Kwapis JL. (2022)Time to learn: The role of the molecular circadian clock in learning and memory. *Neurobiol Learn Mem*. Sep;193:107651. doi: 10.1016/j.nlm.2022.107651. Epub 2022 Jun 10. PMID: 35697314;\

H. Week 8. October 31; TBA (*How organisms determine the time of year; length of day vs. circannual clocks;*

Week 9; November 7 (Reading week)

I. Week 10; November 14 TBA Term test 2. (*Theoretical roles for sleep; role of sleep in memory; remembering over long periods of torpor; circadian rhythms in the old and in the cold*)

J. Week 11; November 21 TBA (*Using the Sun and other celestial objects to determine direction*)

K. Week 12; November 28 TBA (*Circadian dysfunction and chronic, non-communicable disease; circadian disruption and aging; heart disease, diabetes, metabolic syndrome; relationship between circadian rhythms and metabolism*)

L. Week 13; December 5 TBA (*Conceptual and mathematical modelling of circadian patterns over time; potential for diagnostic tools for prevalent disorders; using models to predict disorder over the the lifespan, inform diagnosis, and validated successful treatment; efforts to design sleep and rhythm friendly environments; recognizing temporal restrictions on life in space and other planets*)