

Department of Biology Course Outline

**Biol 4310, Physiology of Circadian Timing
W, 2016**

Course Description

This course examines the mechanism by which cells generate 24h (circadian) rhythms, how the numerous sites of these cells are coordinated by nerves and hormones and the critical roles of human circadian clocks in health and diseases. Three lecture hours per week. One term. Three credits.

Prerequisites

SC/BIOL 2020 4.00 or SC/BIOL 2020 3.0; SC/BIOL 2021 4.00 or SC/BIOL 2021 3.0; SC/BIOL 3060 4.0.

Course Instructors and Contact Information

Course Director: Dr. Michael Cardinal-Aucoin
Email: mdca@yorku.ca
Office: 108A Farq
Office hours: Fridays 13:30-15:30

Schedule

MWF 12:30-13:30

Evaluation

Mid Term Test, February 12 th (on basic concepts, subcellular mechanisms, key model systems)	=	30%
Student in-class presentation of recent research paper, c. March 7-14 th (details will be given at a later date)	=	20%
Final Exam (3 hours), during exam period, April 6-20 th (on whole course)	=	50%

Important Dates

Mid Term Test, February 12th
Student in-class presentation of recent research paper, c. March 7-14th
Final Exam (3 hours), during exam period, April 6-20th

NOTE: for additional important dates such as holidays, refer to the "Important Dates" section of the Registrar's Website at <http://www.yorku.ca/yorkweb/cs.htm>

Resources

No required text. Readings will be assigned from books and recent review articles, all of which will be available on line as e-journals which I will make available via the course Moodle page or will be kept on reserve for this course in the Steacie Library.

Learning Outcomes

Upon successful completion of this course, students should be able to:

- understand the nature and characteristic properties of circadian rhythms,
- compare the circadian organization of diverse organisms at the molecular, cellular, and physiological levels, and
- appreciate the integral regulatory role played by the circadian timing system in the physiology of organisms and its important contribution to human health and disease.

Course Content

EXPANDED COURSE DESCRIPTION:

Life evolved in a cyclical environment alternating between the freezing darkness of night and the searing radiation of day. Early nucleated cells evolved the ability to time their various activities to occur in the most appropriate portion of daily and seasonal cycles. These cellular biological "clocks" are retained in modern organisms where they coordinate both cellular and physiological activities which are expressed in the whole organism as overt rhythms ranging from hormone secretion rhythms to sleep-wake (activity) rhythms. Interactions between the component "clocks" of an organism, mediated primarily by nerves and hormones, lead to internal temporal organization of events within it. The fundamental cellular and physiological mechanisms of biological clocks were developed in key animal model systems such as bacteria, mollusks, and insects and later applied to mammals and humans. Molecular clocks are now known in nearly all human tissues; new research reveals their importance in synchronizing the functions of various tissues with each other, to produce coordinated functioning of the various body parts. Clocks are master coordinators of physiology.

The analysis of human biological clocks has made extraordinarily rapid advances in recent years at the levels of physiology and cell and molecular biology. Human clocks are critical factors in the development of cancers, heart attacks, diabetes, and a host of other diseases. This knowledge is creating profound changes in numerous medical practices. The subject has acquired a prominence in public awareness (rhythms in human performance, shift-work, jet-lag, etc.). In medicine, treatment of many diseases has been revolutionized by precise timing of administration of medications. Numerous disorders are now recognized as due to malfunctions of human biological "clocks" and are treated by the new techniques of "chronotherapy". Others are simply natural variants of timekeeping genes in humans (e.g. 'larks' and 'owls'). We will discuss the need for education of society in general regarding the serious dangers to human health of requiring people to adopt work schedules or lifestyles that defy their biological clockwork.

The course will emphasize the physiological mechanisms underlying biological clocks but will also discuss the subject at the level of its cellular and molecular mechanisms and its human and medical implications. Therefore, the course crosses a number of the conventional disciplinary boundaries within biology.

LECTURE SCHEDULE

I. Basic Concepts and Properties of Circadian Clocks

Origin and nature of periodicities in the environment.
The solar day cycle as a formative factor in the origin of life.
Evolutionary origin and adaptive significance of circadian clocks.

Circadian rhythms in whole organisms.
Properties and evidence of endogenous nature.

Definitions: 'circadian clock' and related terminology.

Circadian rhythms in populations. Circadian gating: *Drosophila* eclosion rhythm.

Mechanism of synchronisation of clocks with environmental signals ie Entrainment.

The phase response curve. Pacemakers and slaves.

Importance of both 'dawn' and 'dusk': use of 'skeleton' photoperiods.

Entrainment to temperature cycles.

Conflict between Zeitgebers.

Reading for the above topics:

1) Chapters 1, 2 and 3 in **Saunders, D.S. (1977) "An Introduction to biological rhythms"** (3 copies on Steacie Reserves). Basic concepts have not changed despite the age of this book.

2) Slightly more detailed version of the above is in Chapters 1, 2, and 3 of **"Insect Clocks" (2002)** by D.S. Saunders, C.G.H. Steel, X. Vafopoulou, R.D. Lewis (also on Reserve). All the basic concepts were developed in insects, so this book covers all the same topics. Use it if you find the little book inadequate, otherwise not required reading.

3) Pages 1063-1071 of Golombek, D.A. and Rosenstein, R.E. (2010). Physiology of circadian entrainment, *Physiol. Rev.* 90, 1063-1102. The remaining pages of this review are not very well presented, do not read the rest!

From this point on, recent reviews will be used as reading material, available as e-journals that I will make available via the course Moodle page as they are needed. Some reviews may be published during the course, so I cannot specify ahead of time what these will be.

II. How Does a Cell Function as a Clock?

Circadian clocks of bacteria and their mechanism. *kai* genes. Antibiotic targets.

Circadian clocks in single celled eukaryotes: one or more clocks in a cell?

The molecular mechanism of circadian timing in *Drosophila* and mammals.

Clock gene products and transcription regulators: the transcription/translation oscillator (TTO).

A complete cellular clock needs many post-translational factors: circadian cycling of K^+ , Ca^{2+} , phosphorylases, phosphatases.

III. Neurobiology and Endocrinology of Circadian Timing Systems.

Structure and function of clocks in the brain and other tissues. Multiple clocks are connected together into timekeeping systems. Concepts discovered in insects are applied to mammals.

Invertebrates:

Molluscan eye clock: the simple neuronal clock that foreshadowed the SCN.

Insect neuroendocrine clocks: a model multioscillator system of mammals.

Neuroarchitecture of the clockwork in the brain and how it controls rhythms in behaviour and rhythmic release of hormones.

Hormones as 'messengers of time'.

Discovery of oscillator cells in various tissues (peripheral oscillators) of insect models: evidence of hormones and nerves in driving these oscillators and their role in the broader circadian system.

Mid Term Test: Friday February 12th

Birds: Pineal gland as pacemaker and roles of melatonin.

Mammals (including humans):

The suprachiasmatic nucleus (SCN) in the brain of humans and other mammals.

Mechanisms of rhythm generation by SCN cells.

Circadian photoreceptors in the eye; melanopsin.

Melatonin and circadian timing.

Interaction of SCN with clocks in the retina and the pineal gland (melatonin).

Student Presentations of Recent Research Articles c.March 7-14th

Peripheral oscillators in diverse mammalian tissues including:
Adrenal gland clock and corticosteroid rhythms as 'messengers of time'.
Clock in the heart (cardiomyocyte clock): relation to heart diseases.
Food entrainable oscillator: relation to diabetes, heart attacks etc.
Why clocks are everywhere and how they are coordinated together.
The emerging concept that networks of circadian clocks coordinate the timing of activities in diverse tissues by timing nervous activity and release of hormones.

IV. Human and Medical Implications.

Health problems resulting from ignoring your clocks.
Diseases related/caused by circadian defects: cancers, heart attacks, diabetes etc.
Jet-lag, shift-work.
Psychiatric disorders (depression etc), sleep disorders and 'SAD'.
'Night owls', 'larks' and natural clock mutations in humans.
City light pollution at night and cancers.
Self help techniques for surviving the 24/7 world: Use of melatonin and phototherapy.
Timing medications for effectiveness; 'Chronopharmacology'.
Circadian rhythms and cancer; roles in both cause and treatment.

Final exam during exam period April 6-20th (on whole course)

Experiential Education and E-Learning

N/A

Other Information

N/A

Course Policies

Students who are absent for the midterm or final exam and who wish to write a deferred exam must provide a valid physician's note or other appropriate and legitimate documentation. Students who do not present on their scheduled day will receive a 0% for the presentation unless a valid medical note or other appropriate and legitimate documentation is supplied.

University Policies

Academic Honesty and Integrity

York students are required to maintain the highest standards of academic honesty and they are subject to the Senate Policy on Academic Honesty (<http://secretariat-policies.info.yorku.ca/policies/academic-honesty-senate-policy-on/>). The Policy affirms the responsibility of faculty members to foster acceptable standards of academic conduct and of the student to abide by such standards.

There is also an academic integrity website with comprehensive information about academic honesty and how to find resources at York to help improve students' research and writing skills, and cope with University life. Students are expected to review the materials on the Academic Integrity website at - <http://www.yorku.ca/academicintegrity/>

Access/Disability

York University is committed to principles of respect, inclusion and equality of all persons with disabilities across campus. The University provides services for students with disabilities (including physical, medical, learning and psychiatric disabilities) needing accommodation related to teaching and evaluation methods/materials. These services are made available to students in all Faculties and programs at York University.

Student's in need of these services are asked to register with disability services as early as possible to ensure that appropriate academic accommodation can be provided with advance notice. You are encouraged to schedule a time early in the term to meet with each professor to discuss your

accommodation needs. Please note that registering with disabilities services and discussing your needs with your professors is necessary to avoid any impediment to receiving the necessary academic accommodations to meet your needs.

Additional information is available at the following websites:

Counselling & Disability Services - <http://cds.info.yorku.ca/>

Counselling & Disability Services at Glendon - <http://www.glendon.yorku.ca/counselling/personal.html>

York Accessibility Hub - <http://accessibilityhub.info.yorku.ca/>

Ethics Review Process

York students are subject to the York University *Policy for the Ethics Review Process for Research Involving Human Participants*. In particular, students proposing to undertake research involving human participants (e.g., interviewing the director of a company or government agency, having students complete a questionnaire, etc.) are required to submit an *Application for Ethical Approval of Research Involving Human Participants* at least one month before you plan to begin the research. If you are in doubt as to whether this requirement applies to you, contact your Course Director immediately.

Religious Observance Accommodation

York University is committed to respecting the religious beliefs and practices of all members of the community, and making accommodations for observances of special significance to adherents. Should any of the dates specified in this syllabus for an in-class test or examination pose such a conflict for you, contact the Course Director within the first three weeks of class. Similarly, should an assignment to be completed in a lab, practicum placement, workshop, etc., scheduled later in the term pose such a conflict, contact the Course director immediately. Please note that to arrange an alternative date or time for an examination scheduled in the formal examination periods (December and April/May), students must complete an Examination Accommodation Form, which can be obtained from Student Client Services, Student Services Centre or online at

http://www.registrar.yorku.ca/pdf/exam_accommodation.pdf (PDF)

Student Conduct in Academic Situations

Students and instructors are expected to maintain a professional relationship characterized by courtesy and mutual respect. Moreover, it is the responsibility of the instructor to maintain an appropriate academic atmosphere in the classroom and other academic settings, and the responsibility of the student to cooperate in that endeavour. Further, the instructor is the best person to decide, in the first instance, whether such an atmosphere is present in the class. The policy and procedures governing disruptive and/or harassing behaviour by students in academic situations is available at - <http://secretariat-policies.info.yorku.ca/policies/disruptive-and-or-harassing-behaviour-in-academic-situations-senate-policy/>