SC/BIOL 4310 3.0 | WINTER TERM 2009/10

DEPARTMENT OF BIOLOGY | YORK UNIVERSITY

BIOLOGICAL TIMEKEEPING

Calendar Description:

An examination of the biological rhythms of cells, tissues and whole animals, the mechanisms of biological timekeeping and how these 'clocks' interact with each other to coordinate physiological events within an animal and with the environment. Prerequisites: SC/BIOL 2020 4.0; SC/BIOL 2021 4.0; one of SC/BIOL 2030 4.0 or SC/BIOL 2031 3.0.

Course Director:

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Scheduling:

Lectures : M, W, F, 12:30 - 13:30.
Room 020, Farquharson Building.

Text:

No required text.
Reading will be assigned from books and review articles all of which will be available on line as e-journals, or kept on Reserve for this course in Steacie.

Suggested Grading and Dates:

Term Test #1, January 29 (on concepts and basic properties)	=	20%
Term Test #2, March 5 (on mechanisms and systems)	=	30%
Final Exam (3 hours), in exam period, April 7 - 23 (on whole course)	=	50%
TOTAL	=	100%

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 sleep-wake activity rhythms to seasonal reproductive cycles. Interactions between the component "clocks" of an organism, mediated primarily by nerves and hormones, lead to internal temporal organisation of events within it. The cellular and physiological principles of biological timekeeping will be illustrated by examples from unicellular algae, molluscs, insects, birds and mammals. Species have divided the modern world between themselves not only on the basis of space but also on the basis of time.

The subject of biological timekeeping has made very rapid strides in recent years and has also acquired a prominence in public awareness (rhythms in human performance, shift-work, jet-lag, etc.). In medicine, treatment of many diseases has been revolutionised by precise timing of administration of medications. Numerous disorders are now recognised 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 (eg ‘larks’ and ‘owls’). We will discuss the need for education of society in general regarding the dangers to human health of requiring people to adopt work schedules or lifestyles that defy their biological clockwork.

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

Short Course Lecture Outline

General concepts and properties of biological clocks
How cells keep time; cellular basis of 24h rhythms
Term Test #1
Physiology of circadian clocks in invertebrates, birds, mammals
Human implications
Term Test #2
Seasonal timing, or photoperiodism
Orientation by the sun and stars: birds and bees
Lunar, tidal, annual rhythms

LECTURE SCHEDULE

The initial part of the course will be based on the book **"An Introduction to Biological Rhythms"(1977)** by D.S. Saunders (3 copies on Reserve in Steacie). The basic concepts of the field have not changed since this book was published. A slightly more detailed treatment of the same topics 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 the latter book covers all the same topics. Use it when you find the little book inadequate.

"Chronobiology: Biological Timekeeping" (2004) eds. J.C. Dunlap, J.J. Loros, P.J. DeCoursey, will be referred to at points during the course that I will specify. Also on Reserve in Steacie. For the bulk of the course, I will refer you to selected recent reviews and articles that are available as e-Journals on line via York Libraries.

I. Basic Concepts and Properties of Biological Clocks

Origin and nature of periodicities in the environment. Parallel periodicities in organisms: daily, lunar, tidal, annual rhythms. Contrast rhythmic phenomena not under control of 'clocks'.
Evolutionary origin and adaptive significance of biological clocks.

Circadian rhythms in whole organisms.
- Properties and evidence of endogenous nature.
- What is a circadian clock?
- Physiology of activity rhythm as example of circadian clock that controls behaviour.

Circadian rhythms in populations.
- Circadian gating: *Drosophila* eclosion rhythm.
- Genetic control of circadian properties: `clock mutants'.

Mechanism of synchronisation of clocks with environmental signals ie Entrainment.
- The phase response curve. Pacemakers and slaves.
- Use of 'skeleton' photoperiods.
- Stopping the clock with light: Damping and singularity points.
- Entrainment to temperature cycles.
- Conflict between Zeitgebers.

Term Test #1: January 29th (on basic concepts and properties of circadian clocks)

(From this point on, recent reviews will be used as reading material, available as e-journals or provided on Reserve in Steacie.)

II. How Does a Cell Function as a Clock?
- How many clocks in a cell? Unicellular clocks of algae and bacteria.
- Clock genes in bacteria (*kai* genes).
- The molecular oscillators of *Drosophila*, *Neurospora* and mammals.
- Clock gene products and transcription regulators: the transcription/translation oscillator.
- From the TTO to cellular clock: roles of cytosolic factors eg Ca^{++}, K^{+} fluxes, membranes.

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 a timekeeping system. Discussion of key animal systems:

Invertebrates:

- Molluscan eye clock: a simple neuronal oscillator.
- Insect neuroendocrine clocks: a model multioscillator system of mammals.
- Neuroarchitecture of the clockwork in the brain and how it controls rhythms in behaviour and release of hormones.
- Hormones as ‘messengers of time’.

Birds:

- Pineal as pacemaker and roles of melatonin.

Mammals:

- The suprachiasmatic nucleus (SCN) in the brain of man and other mammals.
- Mechanisms of rhythm generation by SCN cells.
- Circadian photoreceptors in the eye; melanopsin.
- Melatonin and circadian timing.
- Interaction of SCN with melatonin rhythms; the multioscillator timing system
- How the SCN controls rhythms in hormone release and behaviour.

Term Test #2: March 5th (on mechanisms of timekeeping and circadian systems)

IV. Human Implications.

Jet-lag, shift-work, depression, ‘SAD’, consequences of bright lights at night.
Health problems resulting from ignoring your clocks.
‘Night owls’, ‘larks’ and natural clock mutations in humans.
Self help techniques in the 24/7 world: Use of melatonin and phototherapy.
Timing medications for effectiveness; ‘chronopharmacology’.
Circadian rhythms and cancer; role in both cause and treatment.

V. Photoperiodism, or Seasonal Timing:

Photoperiodic response curves, critical day length.
Is the circadian system used to measure photoperiodic time?
Physiology of photoperiodism:

- Diapause and polymorphism in insects.
- Melatonin and bird migration.
- Mammalian breeding cycles; pineal melatonin rhythms and reproduction.

VI. If Time Permits…

Time-compensated orientation by the sun and stars: birds and bees.
Lunar, tidal and annual rhythms: Bird migration, and rhythms at the equator.
Derivation of ‘long period’ (annual) rhythms from circadian oscillators.

Final exam in period April 7 – 23, 2010 (on whole course)