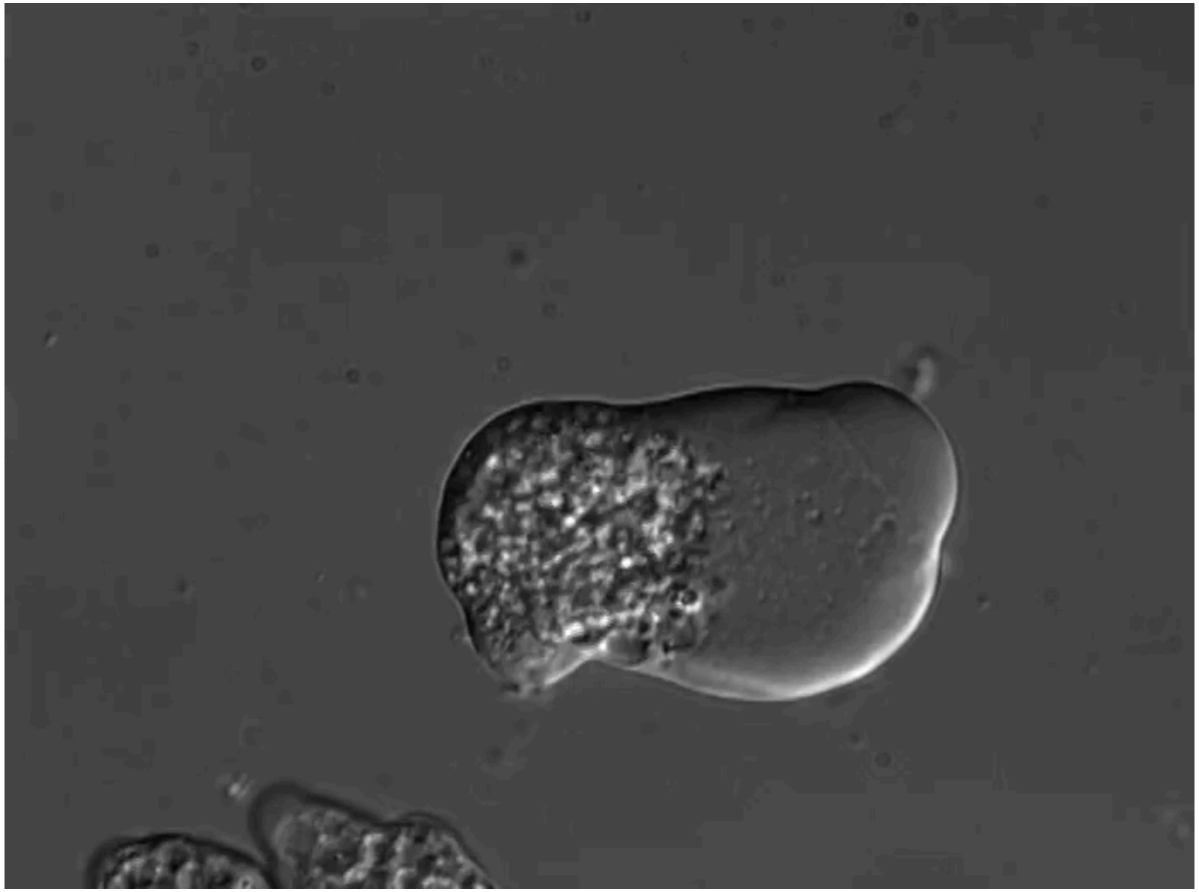
This course is about life, although it might not look like it at first — *there's a lot of equations*



The Roberto Stock group at IBt-UNAM

Entamoeba histolytica

- anaerobic protozoan,
- no mitochondria
- produces ATP by glycolysis

hyaline - clear cytosol
vesicle-filled - granular cytosol
leading edge - lobopod

Differential interference microscopy, 5x speedup

We're not looking at biology like this, as in a microscope …

Example of a model system
Circadian oscillator

$$\frac{dM}{dt} = v_s \frac{K_I^n}{K_I^n + P_N^n} - v_m \frac{M}{K_m + M},$$

$$\frac{dP_C}{dt} = k_s M - v_d \frac{P_C}{K_d + P_C} - k_1 P_C + k_2 P_N,$$

$$\frac{dP_N}{dt} = k_1 P_C - k_2 P_N.$$

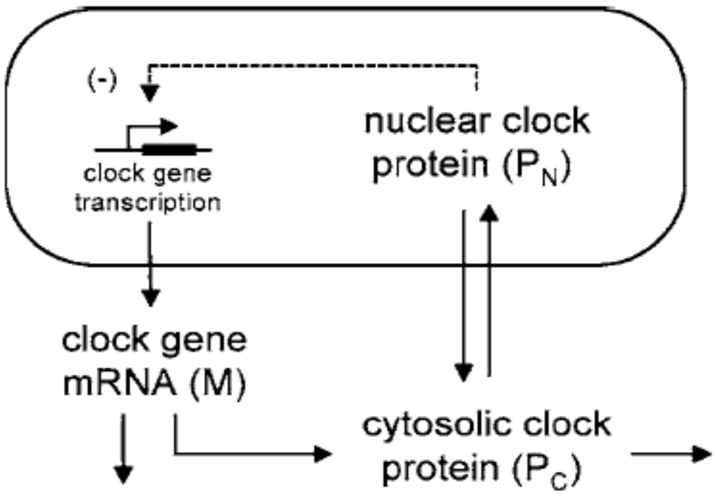
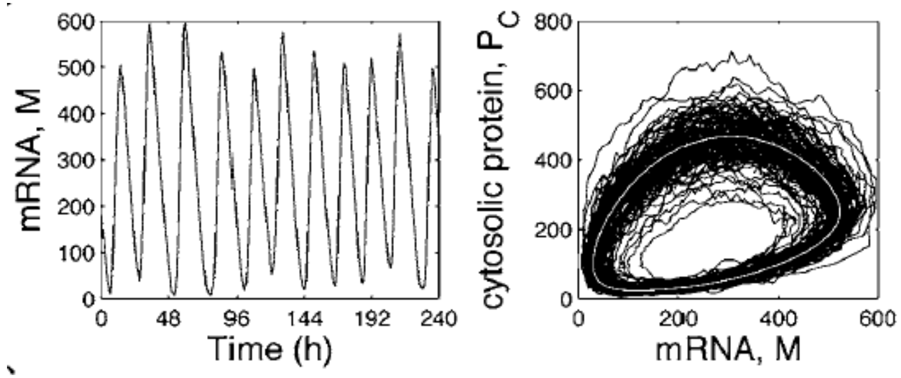
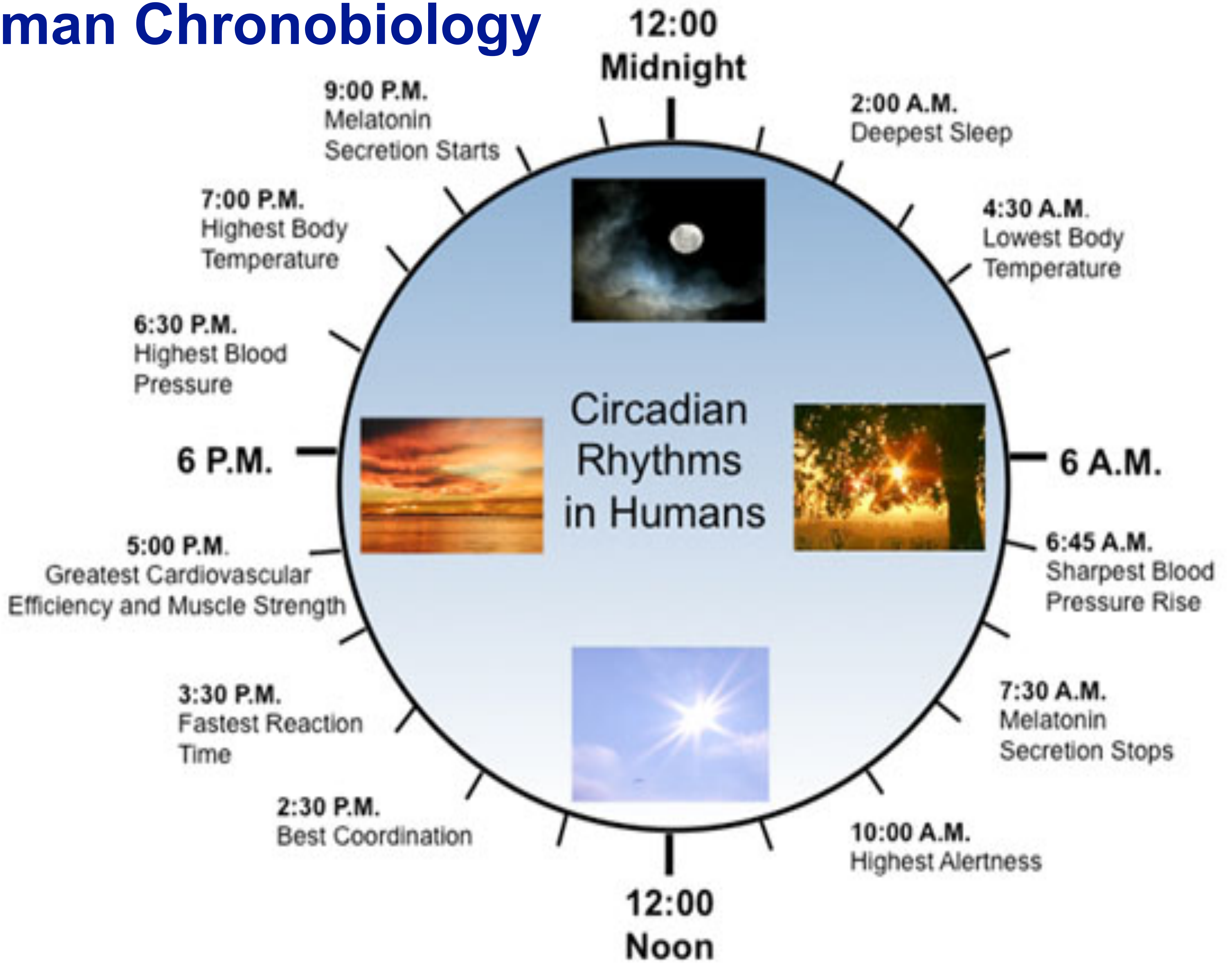


FIG. 1. Scheme of the core model for circadian oscillations. The model is based on the effect exerted by a clock protein (P_C) which can enter the nucleus (P_N) to repress the transcription of its gene into mRNA (M).



- How to mathematically describe biological properties that change with time? e.g., size of a population, biochemical reactions, gene expression …
- New phenomena appear in 1D, 2D (oscillations), 3D (chaos)
- What equation represents oscillations? robustness? hysteresis?
- Non-linear equations are very sensitive to tiny changes in parameters and initial conditions (how is this compatible with robustness?)

Human Chronobiology



There are two ways of seeing this course …

a lot of equations to be memorised / solutions

or

look for patterns in the equations that are the mathematical equivalent of time-dependent processes in living organisms

or

What is the *shape* of an equation?

BIO-341 Dynamical systems in biology 2024

Julian Shillcock, julian.shillcock@epfl.ch
School of Life Sciences, LBM@EPFL

Felix Naef
School of Life Sciences, IBI@EPFL

Computational biology, modelling, bioinformatics,
gene regulation, biological oscillators, circadian rhythm, chronobiology

responsible assistant: eliane.duperrex@epfl.ch

14 lectures (2 hour lecture + 2 hours exercises per week, 4 credits)

Organisation Autumn 2024

- **Lectures**
  - Tuesday 15.15-17h, Room **CM14**
  - Course notes (PDF, etc) on Moodle
- **Exercises**
  - Friday 10-12h **CO 021, CO 023**
  - **Ed** (cf. Moodle Forum)
    - Asynchronous discussion channel
  - Exercises/Jupyter notebook/python tutorials on moodle

PDF notes (moodle)

http://moodle.epfl.ch (ModelBio, enrollment key: modelbio99, but you should already be added)

- exercises + solutions (PDFs, jupyter notebooks)
- course notes in PDF + supplementary material
- Ed discussion forum on moodle
- tricky concept(s) for each lecture (not the *only* important point, just the one(s) that seem difficult)

Books

- A.W. Murray, Mathematical Biology (Springer)
- **S. Strogatz, Nonlinear Dynamics and Chaos (Perseus)**
  (Copies are available in the section — use them! it has many good examples)

Exercises

- 12 sets
  - Theory (pencil and paper)
  - Programming (jupyter-notebooks)
  - Appear on moodle each week after lecture, solutions posted after Friday's exercise

- The exercises are **crucial** in order to pass the written exam (which is pencil and paper only!)

Assistants (2 PhD students + 4 SA):

Responsible person:

Eliane.duperrex@epfl.ch

#	Date	Content	Exercise
1	Sep 10	Dynamical systems in 1D, fixed points; linear stability analysis; **Graphs 1 and 2, Recipe in 1D**	Growth models in 1D, Gompertz model
2	Sep 17	Population models; logistic equation; 2 alleles problem	Allee effect, dimers
3	Sep 24	Autocat. 1D genetic switch; hysteresis; Newton's method for finding zeroes of a function	Insect outbreaks
4	Oct 1	Linear 2D systems; phase portraits; classification of fixed points; **Recipe for linear systems in 2D;**	Linear 2D systems, gene networks
5	Oct 8	Non-linear 2D systems; Jacobian at a fixed point; Euler and Runge-Kutta numerical integration schemes	First graded exercise (1 week allowed)
6	Oct 15	Non-linear 2D systems; populations, spirals; **Recipe for non-linear systems in 2D**	Population dynamics with a limit cycle
	Oct 22	Semester break - no lecture / exercise period	
7	Oct 29	Limit cycles in 2D; Poincaré-Bendixson theorem; Biological oscillators (Selkow model)	Biochemical circuit with feedback
8	Nov 5	Bifurcations in 1D and 2D; saddlenode, transcritical, pitchfork; simple 2D model	Bifurcations
9	Nov 12	Genetic control system in 2D	van der Pol oscillator
10	Nov 19	Forced oscillators, entrainment (Felix Naef)	Second graded exercise (1 week allowed)
11	Nov 26	Kuramoto model (Felix Naef)	Model exam question
12	Dec 3	Hopf bifurcation in 2D; Super- and sub-critical Hopf bifurcation, hard/dangerous transitions	Felix question
13	Dec 10	Chaos; Discrete logistic/sine map; period doubling	Model exam question
14	Dec 17	Recap of course	

Learning objectives

- Understand the basics of dynamical systems in 1D and 2D, in particular the *qualitative* analysis of ordinary differential equations (ODE): why? because different physical systems map to the same model
- Introduction to modelling in biology
  $\Rightarrow$ systems biology:
  How do you apply mathematical, physical, and computational tools in biology?
- Interdisciplinarity, the course combines elements of mathematics, physics, biology, and numerical analysis (in the exercises)
- Learn how to construct dynamical models of simple biological processes, identify their dynamics and dependence on parameters;
- This course lays the foundation for learning quantitative biology, and synthetic biology (BIOENG-320, project iGEM)

Prerequisites

- analysis, linear algebra
- biology, programming, physics

Methods and techniques developed

- 1st order ordinary differential equations (ODE)
- qualitative (graphical) analysis of ODEs
- numerical simulations (cf. Numerical Analysis)
- programming in python, jupyter-notebooks

Evaluation

- Final written exam in January 2025 (80% of grade)
- Graded exercises
    - 2 graded exercises (20% of the grade)
    - weeks 5-6 and 10-11, to be confirmed

Background quiz

Background quiz: go.epfl.ch/turningpoint

Session Id: julian23

All input is anonymous; data are stored outside CH

Break

Difficulties? Silly mistakes? Tricky points?

These are NOT the only important points in the lecture, but experience has shown that some people forget them.

- Be able to relate Graph 1 to Graph 2, i.e., go from the vector field to trajectories
- Trajectories never cross (but do meet at nodes)
- Adjacent fixed points are always of opposite stability
- What about adjacent semi-stable fixed points?