IST Austria Graduate School

Biology Track Core Course 2018

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1. Important dates

Lectures:
Start: Mon, 26-Feb-2018 (08:45 - 10:00), Mondi 3
End: Wed, 20-Jun-2018 (08:45 - 10:00), Mondi 3

Recitations:
Start: Mon, 05-Mar-2018, (10:15-11:00), Mondi 3

Proposal deadline:
June 29th

Final grade:
July 16th

2. Course description
Every big biological problem has a structural, mechanical, evolutionary, genetic and population side to it. The goal of the biology core course is to illustrate that fundamental biological problems and phenomena can be approached from vastly different angles.

In this course we will bridge different areas in biology to show students how fundamental biological problems and phenomena can be approached from different perspectives.

This year we will discuss one broad topic: Spatiotemporal organization. The instructors will provide a list of papers to be studied, typically in the form of a review paper or something equivalent.

3. Grades

The final grade is given based on participation in class (50 %, presentation + discussions) and the written proposal (50%).

The presentation is given by two students who should present the paper in about 60 min. The presentation should be an interactive presentation and include a discussion: focus on critical reading, formulating questions/hypotheses and follow up experiments.

The written proposal should be about 3-4 pages long on any topic regarding spatiotemporal organization in biology within the expertise of the teaching faculty. It should include, background, aims, methods and significance.

Deadline for the written proposal is June 29th, final grade is given on July 16th. Grade and proposal can be discussed with the instructors personally until end of July.

4. Course instructors & TAs

<table>
<thead>
<tr>
<th>Instructor</th>
<th>TA</th>
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<tbody>
<tr>
<td>1 Nick Barton</td>
<td>Daria Shipilina</td>
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<tr>
<td>2 Eva Benkova</td>
<td>Juan Carlos Montesinos</td>
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<td>3 Johann Danzl</td>
<td>Sven Truckenbrodt</td>
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5. Students

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<tr>
<th>Number</th>
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<tbody>
<tr>
<td>1</td>
<td>Bettina Zens</td>
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<td>Jakub Hajny</td>
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<td>Louise Arathoon</td>
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<td>Kristina Lukic</td>
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<td>Lukas Hörmayer</td>
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<td>Michael Riepl</td>
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<td>Michaela Misova</td>
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<td>8</td>
<td>Nikola Canigova</td>
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<td>Vladyslav Kravchuk</td>
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<td>10</td>
<td>XiXi Zhang</td>
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6. Schedule

<table>
<thead>
<tr>
<th>Lecture</th>
<th>Date</th>
<th>Instructor</th>
<th>Topic</th>
<th>Students presenting</th>
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<tr>
<td>1</td>
<td>26.2.</td>
<td>All</td>
<td>Welcome</td>
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<td>2</td>
<td>28.2.</td>
<td>Nick Barton</td>
<td>Spatial patterns in populations: adaptation and speciation</td>
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<td>3</td>
<td>5.3.</td>
<td>Nick Barton</td>
<td>Student presentations/Problems class</td>
<td>Jakub &amp; Louise</td>
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<td>Week</td>
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<td>Nick Barton</td>
<td>Spatial patterns in populations: Invasions</td>
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<td>5</td>
<td>12.3</td>
<td>Nick Barton</td>
<td>Student presentations/Problems class</td>
<td>Bettina &amp; Lukas</td>
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<td>6</td>
<td>14.3</td>
<td>Eva Benkova</td>
<td>Principles of plant body architecture establishment</td>
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<td>7</td>
<td>19.3</td>
<td>Eva Benkova</td>
<td>Student presentations/Problems class</td>
<td>Kristina &amp; Vladyslav</td>
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<td>8</td>
<td>21.3</td>
<td>Edouard Hannezo</td>
<td>Design principles of genetic and biochemical oscillators</td>
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<td>9</td>
<td>26.3</td>
<td>Edouard Hannezo</td>
<td>Student presentations</td>
<td>Michael &amp; Nika</td>
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<td>10</td>
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<td>Edouard Hannezo</td>
<td>Models of wave propagation and pattern formation</td>
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<td>Edouard Hannezo</td>
<td>Student presentations</td>
<td>Xixi &amp; Michaela</td>
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<td>18.4</td>
<td>Carl-Philipp Heisenberg</td>
<td>Force generation and transduction in cell and tissue morphogenesis</td>
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<td>Carl-Philipp Heisenberg</td>
<td>Student presentations</td>
<td>Lukas &amp; Jakub</td>
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<td>Carl-Philipp Heisenberg</td>
<td>Mechanosensation in cell division, extrusion and specification</td>
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<td>Carl-Philipp Heisenberg</td>
<td>Student presentations</td>
<td>Vladyslav &amp; Michaela</td>
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<td>16</td>
<td>2.5</td>
<td>Eva Benkova</td>
<td>Interpretation of auxin morphogen gradients</td>
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<td>17</td>
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<td>Eva Benkova</td>
<td>Student presentations/Problems class</td>
<td>Louise &amp; Nika</td>
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<td>18</td>
<td>9.5</td>
<td>Johann Danzl</td>
<td>Introduction: spatial organization of cells and tools</td>
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<td>19</td>
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<td>Johann Danzl</td>
<td>Student presentations</td>
<td>Louise &amp; Kristina</td>
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<td>16.5</td>
<td>Johann Danzl</td>
<td>Introduction: the synapse as model for nanoarchitecture</td>
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<td>Johann Danzl</td>
<td>Student presentations</td>
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<td>22</td>
<td>28.5</td>
<td>Martin</td>
<td>Intro: Mechanisms of intracellular organization</td>
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### 7. Lecture content

**Course Material**

Course material such as large data files and documents can be found using [this link](#).

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**February 26: Welcome (all instructors)**

Instructors will give an introduce the content and scope of the course.

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**February 28: Nick Barton: Spatial patterns in adaptation and speciation**

Populations often show striking spatial and temporal patterns: cicadas with prime-numbered life cycles, or sharp boundaries between areas where butterflies share different wing patterns. These are interesting in themselves, but also practically important, for understanding epidemics and invasive species, and important for evolution, in relation to local adaptation and speciation.
In these sessions, we will focus on the interplay between selection and gene flow, and how this can be modelled by diffusion. The same processes will recur later, in modelling development and intracellular organisation.

**General background:**

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**March 5: Nick Barton**

**Student presentations:**


**Problems class:** Simulating clines and hybrid zones

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**March 7: Nick Barton: Invasions of genes and species**

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**March 12: Nick Barton**

**Student presentations:**


**Background review**


**Problems class:** Simulating the spread of a favourable allele

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**March 14: Eva Benkova: Principles of plant body architecture establishment**

Plants are sessile organisms permanently attached to one location. Throughout evolution, this lack of mobility has been compensated by a unique survival strategy – an exceptional developmental flexibility of the plant body. Plants are able to rapidly modulate their growth and whole body architecture in order to efficiently use local resources and to adapt to fluctuating
environmental conditions. In this session, we will focus on the basic principles of plant body architecture establishment.

March 19: Eva Benkova

**Students presentation:**
von Wangenheim D, Fangerau J, Schmitz A, Smith RS, Leitte H, Stelzer EH, Maizel A.

[Local, efflux-dependent auxin gradients as a common module for plant organ formation.](https://doi.org/10.1016/j.cub.2015.12.047)
Benková E, Michniewicz M, Sauer M, Teichmann T, Seifertová D, Jürgens G, Friml J.

**Background review:**
[As above, so below: Auxin’s role in lateral organ development.](https://doi.org/10.1016/j.cub.2015.12.047)
Taylor-Teeples M, Lanctot A, Nemhauser JL.

March 21: Edouard Hannezo: Design principles of biochemical and genetic oscillators

**Introduction:** How do cells regulate complex temporal oscillations?

Are there generic models to understand genetic and biochemical oscillations?
- Cell cycle regulation
- Circadian rhythm
- Segmentation clock

March 26: Edouard Hannezo

**Students presentation:**
[Analysis of a generic model of eukaryotic cell-cycle regulation.](https://doi.org/10.1016/j.bpj.2006.06.044)

[Modeling the cell cycle: why do certain circuits oscillate?](https://doi.org/10.1016/j.cell.2011.02.016)

**Background review:**
[Design principles of biochemical oscillators.](https://doi.org/10.1038/nrmb.2008.223)

March 28: Edouard Hannezo: Models of wave propagation and pattern formation
**Introduction:** Precise spatio-temporal patterning must occur at every stage of morphogenesis.

Are there generic models to understand these patterns in tissues?

- Action potential propagation
- Turing patterns
- Sequential patterning

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**April 16: Edouard Hannezo**

**Students presentation:**

Notch-mediated lateral inhibition regulates proneural wave propagation when combined with EGF-mediated reaction diffusion.


Interactions between zebrafish pigment cells responsible for the generation of Turing patterns.


**Background review:**

Positional information and reaction-diffusion: two big ideas in developmental biology combine.


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**April 18: Carl-Philipp Heisenberg: Force generation and transduction in cell and tissue morphogenesis**

**April 23: Carl-Philipp Heisenberg**

**Students presentation:**

Tensile forces govern germ-layer organization in zebrafish

Krieg M, Arboleda-Estudillo Y, Puech PH, Käfer J, Graner F, Müller DJ, Heisenberg CP

Forces for Morphogenesis Investigated with Laser Microsurgery and Quantitative Modeling

M. Shane Hutson, Yoichiro Tokutake, Ming-Shien Chang, James W. Bloor,Stephanos Venakides, Daniel P. Kiehart, Glenn S. Edwards

**Background review:**

Forces in Tissue Morphogenesis and Patterning

Carl-Philipp Heisenberg  and Yohanns Bellar’che
April 25: Carl-Philipp Heisenberg: Mechanosensation in cell division, extrusion and specification

April 30: Carl-Philipp Heisenberg
Students presentation:
**Mechanical stretch triggers rapid epithelial cell division through Piezo1**

S. A. Gudipaty, J. Lindblom, P. D. Loftus, M. J. Redd, K. Edes, C. F. Davey, V. Krishnegowda & J. Rosenblatt

**Role of YAP/TAZ in mechanotransduction**
Sirio Dupont, Leonardo Morsut, Mariacelete Aragona, Elena Enzo, Stefano Giulitti, Michelangelo Cordenonsi, Francesca Zanconato, Jimmy Le Digabel, Mattia Forcato, Silvio Bicciato, Nicola Elvassore & Stefano Piccolo

**Background review:**
*Multiscale force sensing in development*
Petridou NI, Spiró Z, Heisenberg CP

May 2: Eva Benkova: Interpretation of auxin morphogen gradients
Plant hormones represent important endogenous regulators of plant development that allow plants to rapidly adjust their growth to environmental signals. Among them, the hormone auxin is essential to control plant growth and development including early embryogenesis and postembryonic organogenic processes, such as root branching, phyllotaxis, shoot and root apical meristem activity. In this session, we will focus on the common aspects of molecular mechanisms underlying auxin regulation of various plant developmental processes.

May 7: Eva Benkova

Students presentation:
**MONOPTEROS controls embryonic root initiation by regulating a mobile transcription factor.**

**TIR1/AFB-Aux/IAA auxin perception mediates rapid cell wall acidification and growth of Arabidopsis hypocotyls.** Fendrych M, Leung J, Friml J. Elife. 2016 Sep 14;

**Background review:**
May 9: Johann Danzl

Cells are composed of a diverse set of molecules, including proteins, nucleic acids, lipids, and a wide range of small molecule metabolites, that act together to enable the functions that characterize them as living systems.

A cell operates far from thermal equilibrium, such that its constituents are organized in highly elaborate structures. Finding out how the cell is organized spatially and how the interaction with the environment shapes the molecular architecture of the cell is a central requirement for gaining a mechanistic understanding of biological processes.

Our discussion will bridge from the tissue level of cell-cell contacts to the level of macromolecular complexes in subcellular compartments. We will explore chemical synapses as a highly specialized structure and one of the best studied examples of vesicle trafficking and release. We will also put an emphasis on the methodology to unravel spatial organization with molecular specificity, in particular advanced light microscopy methods.

Questions to be addressed:
How can we analyse single cells?
What do analyses on the DNA, RNA, and protein level tell us?
How can we analyse single cells while preserving cellular and tissue spatial context?
How does diffraction-unlimited optical imaging increase spatial resolution into the nanometer range?

Background reading on diffraction-unlimited optical imaging:
Fluorescence nanoscopy in cell biology

Breaking the diffraction barrier: Super-resolution imaging of cells

May 14: Johann Danzl

Students presentation:
A subcellular map of the human proteome
Thul et al., Science 10.1126 (2017)
A rather comprehensive workup of subcellular protein distribution. Raises interesting questions of what type of information one can obtain from such proteomics scale in situ experiments.

Nanoscale architecture of cadherin-based cell adhesions:
Berocchi et al., Nature Cell Biology 19, 28 (2017)
Bridging the scale from cell-cell contacts in the tissue and their architecture to biochemically reduced reconstitution experiments.

May 16: Johann Danzl

Introduction: the synapse as a model system for nanoscale protein architecture and membrane vesicle fusion

Presynaptic boutons contain a well-studied machinery for sensing of a release signal (the action potential), its relay via a second messenger (Ca2+), and vesicle release. Many of the mechanisms are conserved in other vesicle/membrane fusion events, such that the synapse can serve as a valuable didactic example for a much broader class of cellular events beyond neurotransmitter release.

Questions to be addressed:
What are the peculiar organizational principles of neurons?
How are cell-cell contacts arranged here?
What can we learn about the vesicle fusion and release machinery?

May 23: Johann Danzl

Students presentation:
Composition of isolated synaptic boutons reveals the amounts of vesicle trafficking proteins
Molecular composition of a subcellular compartment derived from average data and condensed into a bioinformatics-based model. Gives an impressive account of how one can think of the molecular makeup of cells.

A trans-synaptic nanocolumn aligns neurotransmitter release to receptors
Tang et al., Nature 536, 210 (2016)
Imaging-based analysis of how molecules are organized across the cell-cell contact at synapses with very interesting functional implications for the nanoscale relative spatial arrangement of release sites (signal generation) and receptors (signal detection) in view of fast diffusion and signal deactivation.

Background reading on diffraction-unlimited optical imaging:
Seeing the forest tree by tree: super-resolution light microscopy meets the neurosciences

Superresolution imaging of chemical synapses in the brain.
Dani et al., Neuron 68(5), 843 (2010).

May 28: Martin Loose - Mechanisms of intracellular organization
Introduction: What are the molecular mechanisms of intracellular organization?

In general, biological structures can emerge due to two fundamentally different processes, first via self-assembly, which describes equilibrium structures and second, via self-organization, which corresponds to self-organized structures that exist in a dynamic steady state. In this introductory lecture, we will discuss the differences between these two concepts using two highly complex biological structures as example: the bacteriophage T4 and the mitotic spindle. Furthermore, we will introduce the mechanisms available to cells to organize intracellular space, namely reaction-diffusion processes, biopolymers and phase separation. Using these concepts, we will discuss the following questions: What are advantages and disadvantages of self-assembled versus self-organized structures? Why do cells use self-assembly? Why self-organization?

Reviews for general background:


May 30: Martin Loose - Mechanics of the cytoskeleton - cytokinesis

E. coli and S. pombe both have rod-shaped cells that divide by symmetric division. The aim of this lecture is to get to know the different biological structures these organisms employ to perform cytokinesis. Furthermore, we will discuss advantages, disadvantages, gains and tradeoffs of two different experimental approaches to understand intracellular assemblies: fluorescence versus electron microscopy. The aim of this lecture is also to discuss the current challenges in biology to visualize the architecture and dynamics of the intracellular space.

Questions to address:
1. What is the differences and similarities between cytokinesis in E. coli and S. pombe?
2. What do we learn from in vitro and in vivo experiments?
3. What do we learn from Cryo-ET and SMLM?

Students presentation:

I. Cytokinesis by the actin ring


II. Cytokinesis by the FtsZ ring

Review:

June 4: Martin Loose - Reaction-diffusion mechanisms to organize cells

The unicellular organism S. cerevisae is able to polarize in the absence of any external spatial cue. In this lecture, we will discuss two different mechanisms giving rise to cellular polarization: first, directed transport and second, a reaction-diffusion based process. We will elaborate on the properties of these fundamentally different mechanisms and how they contribute to polarization of the cell. We will also address the general requirements for biochemical circuits to locally amplify biological signals, how to, break intracellular symmetry and how to this spatial information can be maintained over long times.

Students presentation:


Review:

June 6: Martin Loose - Phase-separation in the cytoplasm

In the last couple of years it has become clear that the cytoplasm not necessarily represents one continuous phase, but that the cytoplasm is organized by biomolecular condensates that give rise to liquid-liquid phase separation in the cell. In this lecture, we will discuss the principle of principle liquid-liquid phase separation, the molecular requirements, the regulation of phase separation as well as the function of those condensates. Finally, we will also address the negative consequences of a misregulation of phase separation for the cell.

Research papers:
June 11: Florian Schur - Spatio-temporal regulation of intra/extracellular transport

Introduction: Coated Vesicles and enveloped Viruses
Coated vesicles and enveloped viruses can be considered to perform homologous but opposite processes. Both are higher-order structures, assembled to transport their selectively recruited cargo to distinct target locations. Hence, vesicles and viruses are required for the spatial organization and distribution of components within and across cells. In order to do so efficiently, this requires another level of complexity on the temporal level, where vesicles and viruses need to at one point prime themselves for fusion with their target membranes (e.g. a organelle or cell).

In two sessions we will first focus on how coated vesicles are formed. In the second part we will take a look at a specific example of virus maturation. These two examples are well suited to exemplify the time scales that one can face in experimental biology and what kind of experimental tools one has to study these or similar events.

General concepts & mechanisms
- Higher-order protein assemblies: coated vesicles and enveloped viruses
- General concepts of intracellular vesicular transport
- Virus assembly, budding and maturation
- Protein cages

June 13: Florian Schur - Time scales of coated vesicle formation

Questions to address:
- How does clathrin-mediated endocytosis proceed?
- What direct and indirect measures do we have to observe short-lived dynamic events?
- What do we learn from studies that allow us to decompose such short-lived events?
Student presentations:


Background reviews:


June 18: Florian Schur - Dynamics in virus assembly and maturation

Questions to address:
- How does retroviral assembly and maturation proceed?
- How can a virus regulate the temporal sequence of assembly and maturation?
- Why do retroviruses require a maturation step?

Student presentations:


Background reviews: