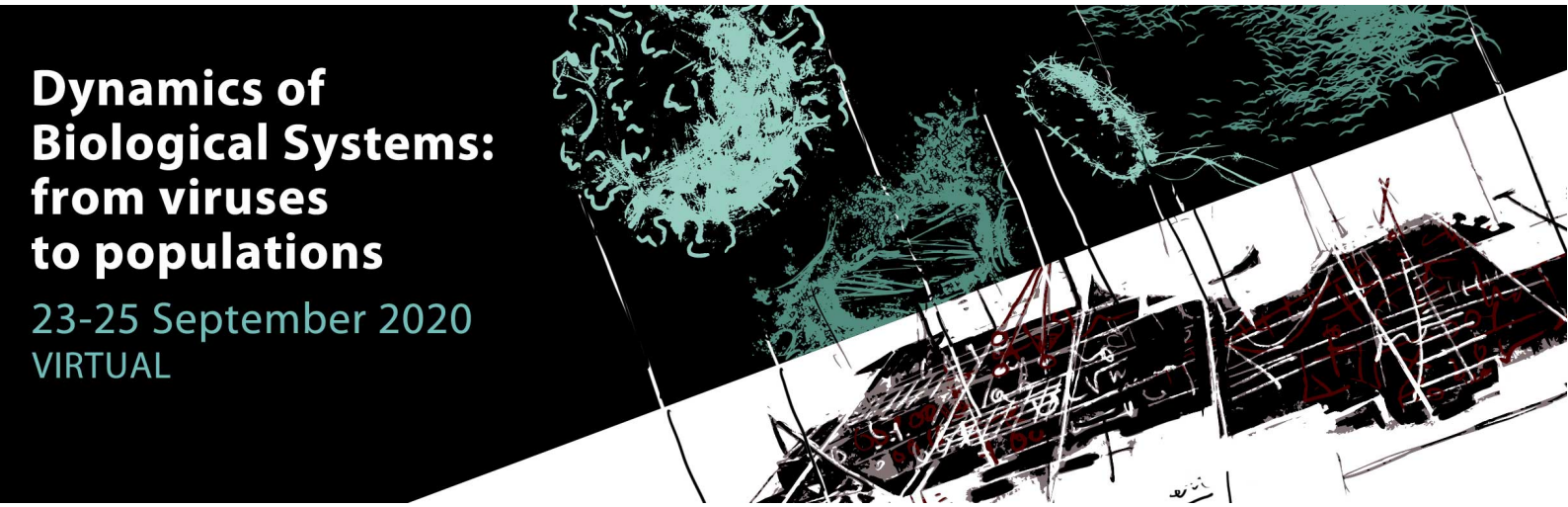
Jagiellonian University, Kraków, 2020



Book of Abstracts

DBS 2020: Final timetable

Wednesday, the 23rd of September

	VIRUSES
10:00-10:10	Opening remarks
10:10 – 10:50	Janusz Kocik
10:50 – 11:20	Ardigen R&D talk Piotr Skoczylas
11:20 – 11:40	Coffee break
11:40 – 12:10	Fakhteh Ghanbarnejad
12:10 – 12:40	Marek Kochańczyk
12:40 – 13:00	Sina Sajjadi & Alireza Hashemi
13:00 – 14:00	Lunch break
	BACTERIA
14:00 – 14:40	Tobias Bollenbach
14:40 – 15:00	Bor Kavčič
15:00 – 15:15	Marcin Rubin
15:15 – 15:30	Łukasz Szydłowski
15:30 – 15:35	Coffee break
15:35 – 15:55	Gerrit Ansmann
15:55 – 16:25	Marjon de Vos
16:25 – 16:55	Rafał Mostowy
16:55 – 17:00	Coffee break
17:00 – 17:30	Mindfulness for academics

Thursday, the 24th of September

	CELLS I
10:00 – 10:40	Alex Fletcher
10:40 – 11:00	Laura Bocanegra-Moreno
11:00 – 11:20	Felix Jonathan Meigel
11:20 – 11:40	Coffee break
11:40 – 12:00	Tim Liebisch
12:00 – 12:30	Steffen Rulands
12:30 – 13:00	Edouard Hannezo
13:00 – 14:00	Lunch break
	CELLS II
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14:40 – 14:55	Camile Fraga Delfino Kunz
14:55 – 15:25	Anna Ochab-Marcinek
15:25 – 15:55	Thomas Sokołowski
15:55 – 16:00	Coffee break
16:00 – 17:00	**Jazz Concert**

Friday, the 25th of September

	POPULATIONS
10:00 – 10:40	Szymon Drobniak
10:40 – 11:00	Adolfo Alsina
11:00 – 11:20	Javier Suárez
11:20 – 11:40	Coffee break
11:40 – 12:00	Purnedu Mishra
12:00 – 12:30	Bartłomiej Dybiec
12:30 – 13:00	Dominika Włoch-Salamon
13:00 – 14:00	Lunch break
	MEDICAL BIOLOGY
14:00 – 14:40	Bartłomiej Wacław
14:40 – 15:00	Debasmita Mukherjee
15:00 – 15:20	Michał Silarski
15:20 – 15:30	Coffee break
15:30 – 15:45	Jan Jędryszek
15:45 – 16:15	Tomasz Kościółek
16:15 – 16:55	Ewa Stępień
16:55 – 17:00	Closing remarks

Contents

1 Wednesday

1.1 Morning session: Viruses

Morning Session / 79

Emergence of COVID-19 – ground for its evolutionary success

Author: Janusz Kocik[1]

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To prevent the spread of SARS-CoV-2, many countries adopted strict non-pharmacological interventions such as non-essential businesses or complete lockdowns. All these measures seem to be of little effectiveness. This is unlike its predecessors, SARS – CoV and MERS-CoV, that affected limited populations and disappeared shortly after they had emerged. High virulence of these viruses, severity of disease and death toll reduced transmissibility since the hosts had been too sick to expose others. COVID-19 found its intermittent evolutionary niche due to its high transmissibility by vast majority of non-symptomatic cases and lack of pre-existing immunity.
Social media are flooded with arousing trepidation speculations on 'dangerous mutations' in the new virus. Looking into the history of epidemiology, we shouldn't worry when a virus mutates during disease outbreaks.
Most RNA virus populations are complex mixtures of genetic variants, resulting from the high RNA polymerase error rate. Usually multiple genes are likely involved in the primary evolution of an emerging virus. Mutations are requisite for 'spill over' from an animal reservoir or use a new vector for transmission. The continuous pandemic may enable accumulation of immunologically relevant mutations. Immunological response durability to SARS-CoV2 is doubted and the genetic drift may influence the future vaccines utility.
Favored mutations constitute the backbone for further genetic variants but the latent usually are not 'game-changers' in a current epidemic. It is unusual to find viruses that have changed or expanded their mode of transmission over short time-scales despite high rates of mutation. Unfortunately, the role of natural selection in virus evolution is not easily predicted. This opens the field for speculation around the evolutionary trajectory of a virus during a newest COVID-19 outbreak.

Morning Session / **78**

SARS-CoV-2 Vaccine Development: Incorporating AI into epitope-based vaccine design

Author: Piotr Skoczylas[1]

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After the initial outbreak in China, the spread of infectious disease caused by novel coronavirus has rapidly transformed to a global pandemic. The rapid speed of modern DNA sequencing technology has enabled the quick determination of COVID-19 genetic sequence, which has triggered multiple efforts worldwide for the development of a vaccine against the novel coronavirus.
During the talk, I will present the results from our recent work [1], including viral pathogenesis of SARS-CoV-2, the description of the defensive machinery existing within the human body, and how the immune system can be boosted by a T-cell epitope vaccine. Starting with the Machine Learning 101, I will outline the three consecutive biological events essential for the recognition of virus-infected cells by the immune system, and discuss how to model them using AI algorithms. The population coverage of a COVID-19 vaccine will also be discussed through the analysis of HLA sharedness among the selected epitopes.

[1] AI aided design of epitope-based vaccine for the induction of cellular immune responses against SARS-CoV-2, G. Mazzocco, I. Niemiec, A. Myronov, P. Skoczylas, J. Kaczmarczyk, A. Sanecka-Duin, K. Gruba, P. Król, M. Drwal, M. Szczepanik, K. Pyrć, P. Stępniak, bioRxiv 2020.08.26.267997

Morning Session / **7**

Modelling disease ecology

Author: Fakhteh Ghanbarnejad[1]

[1] *Sharif University of Technology*

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Here I will review my recent works [1] on modeling interacting contagious dynamics, for example coupled SIR or SIS dynamics, in mean field approximations and also on different random generated or empirical complex networks. I show and discuss how our recent results have been improving our understanding and prediction of epidemic dynamics and disease ecology while raising new questions and challenges in Dynamics of Biological Systems like diversity and population of viruses.

[1] Nature Physics 11, 936–940 (2015)
[2] Europhys. Lett. 104, 50001 (2013), PRE 93, 042316 (2016)
[3] New J. Phys. 19, 103041 (2017)
[4] Frontiers in Physics, V 5, P 46 (2017)
[5] Sci Rep. 9: 6463 (2019)
[6] Physica A, 518, Pages 50-70 (2019)
[7] PRE 100, 012307 (2019)
[8] PRE 100, 062308 (2019)
[9] Royal Society Open Science 7(1), 2054-5703 (2020)
[10] arXiv:2003.01268 (2020).

Morning Session / 15

Super-spreading events initiated the exponential growth phase of COVID-19 with R0 higher than initially estimated

Author: Marek Kochańczyk[1]

Co-authors: Frederic Grabowski [2]; Tomasz Lipniacki [1]

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The basic reproduction number R_0 of the coronavirus disease 2019 has been often estimated to range between 2 and 4. We used a SEIR model that properly accounts for the distribution of the latent period and, based on empirical estimates of the doubling time in the near-exponential phases of epidemic progression in China, Italy, Spain, France, United Kingdom, Germany, Switzerland, and New York State, we estimated that R_0 lies in the range 4.7–11.4. We explained this discrepancy by performing stochastic simulations of model dynamics in a population with a small proportion of super-spreaders. The simulations revealed two-phase dynamics, in which an initial phase of relatively slow epidemic progression diverts to a faster phase upon appearance of infectious super-spreaders. Early estimates obtained for this initial phase may suggest lower R_0.

Morning Session / 12

Social distancing in pedestrian dynamics and its effect on disease spreading

Authors: Sina Sajjadi[1]; Alireza Hashemi[1]; Fakhteh Ghanbarnejad[1]

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The ongoing Covid-19 pandemic has had severe consequences on nations worldwide. With about 26 million cases and nearly 1 million deaths to date (05.09.2020). It has imposed so many costs to the local, regional and global markets including hundreds of billions to the global insurance industry, tourism and other businesses. It has been considered as one of the costliest disasters after WWII.
Facing these difficulties without any approved vaccine so far, governments have turned to non-pharmaceutical measures such as social distancing to limit the transmission of the disease and flattening the growth of the spreading dynamics. Thus, we study the effectiveness of social distancing, using a mathematical epidemic modeling. In this work, for combining human mobility and disease spreading, we design an agent based model consisting of pedestrian dynamics with a novel type of social distancing and spreading phenomena. We also consider indirect transmission with the footprints of the infectious pedestrians. We show that the increase in the intensity of social distancing has a significant effect on the exposure risk. By classifying the population into social distancing abiders and non-abiders, we conclude that the practice of social distancing even by a minority of potentially infectious agents not only results in a drastic change on the population exposure risk, but also boosts the effectiveness of the protocols when practiced by the rest of the population.

1.2 Afternoon session: Bacteria

Afternoon Session / 6

Drug interactions between translation-inhibiting antibiotics

Author: Tobias Bollenbach[1]

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Antibiotics that interfere with translation, when combined, interact in diverse and difficult-to-predict ways. We explain these interactions by "translation bottlenecks": points in the translation cycle where antibiotics block ribosomal progression. To elucidate the underlying mechanisms of drug interactions between translation inhibitors, we generate translation bottlenecks genetically using inducible control of translation factors that regulate well-defined translation cycle steps. These perturbations accurately mimic antibiotic action and drug interactions, supporting that the interplay of different translation bottlenecks causes these interactions. We further show that growth laws, combined with drug uptake and binding kinetics, enable the direct prediction of a large fraction of observed interactions, yet fail to predict suppression. However, varying two translation bottlenecks simultaneously supports that dense traffic of ribosomes and competition for translation factors account for the previously unexplained suppression. These results highlight the importance of "continuous epistasis" in bacterial physiology.

Afternoon Session / 74

Ribosome traffic jams underlie suppressive drug interactions

Authors: Bor Kavčič[1]; Gašper Tkačik[1]; Tobias Bollenbach[2]

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[2] *University of Cologne*

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The effects of antibiotics targeting protein synthesis are poorly understood when applied in combination. The combined antibiotic effect determines the type of drug interaction, which ranges from synergy to antagonism and suppression. In suppression, at least one of the drugs loses its potency in the presence of the second drug. We hypothesize that suppressive drug interactions result from the interplay between ribosomes halted in different stages of translation. We mimic this interplay by creating translation bottlenecks genetically by titration of translation factors. We rationalize the effects of translation bottlenecks by modeling dense traffic of ribosomes that move on transcripts in a translation factor-mediated manner. We base this model on the growth laws and quantitative relationships between different translation and growth parameters. This model predicts a dissolution of traffic jams caused by inhibited translocation when the density of ribosome traffic is reduced by lowered initiation, thus explaining suppression.

Afternoon Session / **67**

To make things simpler: classical Powell's ideas for describing bacterial population revisited.

Author: Marcin Rubin[1]

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In 1956, E. O. Powell introduced a novel approach that allowed one to understand the relations between various types of probability distributions used for description of a bacterial population such as interdivision-time probability distribution or age structure. Since then, numerous other authors extended Powell's ideas by introducing additional complications within the model, e.g., taking into consideration bacterial cell volume, protein concentrations, or more complex metabolic pathways. Recently, an increasing interest in these types of models can be observed because of newly developed methods that allow for observation of a single bacterial cell growth. In my talk, I want to return to the roots and to briefly present a slightly different approach to the Powell's results, which, as I believe, has a didactic value. It turns out that a single probability distribution, easily obtainable using a simple argumentation, is enough to retrieve most of the results that were initially presented in Powell's original work.

Afternoon Session / **77**

High-throughput screening and selection of electrogenic microbial communities using single chamber microbial fuel cells based on 96-well plate array

Author: Lukasz Szydlowski[1]

Co-authors: J Ehlich ; I Goryanin

[1] *Jagiellonian University*

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We demonstrate a single chamber, 96-well plated based Microbial Fuel Cell (MFC) with printed electronic components. This invention is aimed at robust selection of electrogenic microbial community under specific conditions, e.g. electrode potential, pH, nutrient concentration, salt concentration that can be altered within the 96 well plate array. This invention enables robust selection of electrogenic microbial community under homogeneous reactor, with multiple conditions that can be altered to allow comparative analysis. It can be used as a standalone technique or in conjunction with other selective processes, e.g. flow cytometry, microfluidic-based dielectrophoretic trapping. Mobile conductive elements, like carbon paper, carbon sponge, activated charcoal granules, metal mesh, can be inserted inside to increase the anode surface area in order to collect electrogenic microorganisms and to transfer them into new reactors or for other analytical works. This 96-well plate enables robust selection for electrogenic microorganisms under homogeneous reactors, with multiple conditions that can be altered to allow comparative analysis. An array of 96-well plate allows this device to be operated by automated pipetting stations. Well plate MFC can be also used as a multicompound biosensor system, especially in conjunction with genetically engineered strains that can indicate and quantify single molecule. Electric signal can be used as a direct output, reducing the post-production quality control steps.

Afternoon Session / 10

Building clone-consistent ecosystem models

Authors: Gerrit Ansmann[1]; Tobias Bollenbach[1]

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Many ecological studies employ general models that can feature an arbitrary number of populations. A common requirement imposed on such models is what we call *clone consistency:* If the individuals from two populations are indistinguishable, joining these populations into one shall not affect the outcome of the model. Otherwise a model produces different outcomes for the same scenario. Using functional analysis, we comprehensively characterize all clone-consistent models: We prove that they are necessarily composed from basic building blocks, namely linear combinations of parameters and abundances. These strong constraints enable a straightforward validation of model consistency or reveal implicit assumptions required to achieve it. Moreover, our insights facilitate building new clone-consistent models, which we illustrate for a data-driven model of microbial communities.

Afternoon Session / 57

Eco-evolutionary interactions in polymicrobial infections

Author: Marjon de Vos[1]

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Communities of bacteria derived from polymicrobial urinary tract infections (UTIs) together with commensal residents can be viewed as small ecosystems. By measuring pair-wise interactions we obtained a unique insight in the ecological interactions of these microbiome members. We find that many of these bacterial interactions affect the immediate tolerance to antibiotics, as well as their ability to evolve antibiotic resistance.

2 Thursday

2.1 Morning session: Cells I

Afternoon Session / **8**

Genomic epidemiology, sex & evolution of bacterial sugars

Author: Rafał Mostowy[None]

Horizontal gene transfer, or HGT, is a fundamental mechanism of genetic innovation and phenotypic change in bacterial evolution. In the last twenty years, by sequencing and comparing a large number of bacterial genomes, we have learned that HGT is much more pervasive and important than some have thought. However, research studies have also highlighted that different HGT processes are under different selective forces, that bacterial populations vary in their propensity to undergo HGT, and that more HGT is not always better. Hence understanding how HGT drives bacterial evolution requires knowing the precise evolutionary and ecological context in which it occurs and the phenotypes is generates. One interesting system to study the impact of HGT on bacterial evolution are genetic loci that synthesise the production of bacterial surface polysaccharides, like polysaccharide capsules and lipopolysaccharides. In this talk, I will show that such loci can be thought of as diversity generating machines that are evolutionary optimised to rapidly generate novel bacterial antigens via HGT under diversifying selection. Then, using a dataset of over 27,000 genomes of bacterial isolates from the order Enterobacteriales, I will demonstrate the importance of between-species and between-genus horizontal exchanges in evolution of bacterial surface polysaccharides. Finally, I will discuss one hypothesis that could potentially explain the elevated HGT rates in surface polysaccharide loci, namely co-evolution with bacteriophages.

Morning Session / **65**

Modelling planar polarised cell behaviours in epithelial tissues

Author: Alexander Fletcher[1]

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Polarisation is one of the most basic levels of cell and tissue organisation. In developing epithelial tissues, planar polarisation is vital for coordinated cell behaviours during morphogenesis. Alongside experimental approaches, mathematical modelling offers a useful tool with which to unravel the underlying mechanisms. I will describe our recent efforts to model the planar polarised behaviours of cells in developing epithelial tissues, how these models have given new mechanistic insights into various aspects of Drosophila development, and the mathematical and computational challenges associated with this work.

Morning Session / 16

Epithelial dynamics during mouse neural tube development

Author: Laura Bocanegra-Moreno[1]

Co-authors: Marcin Zagórski [2]; Edouard Hannezo [1]; Anna Kicheva [1]

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[2] *Institute of Theoretical Physics, Jagiellonian University Lojasiewicza*

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Spinal cord formation is achieved through dynamic changes of the cellular and tissue properties over time. In amniotes, its formation starts from a flat epithelial sheet which extends and folds at the embryo midline to form a closed neural tube. This morphogenetic transition involves changes in the epithelial organization as well as in the rates of cell proliferation and differentiation. However, how tissue growth is coupled to epithelial dynamics is unknown. Here, we investigate how the temporal dynamics of epithelial rearrangements in the neuroepithelium is controlled. To this end, we performed high resolution mosaic analysis at different developmental stages. We observed that clones of related cells are spatially fragmented when generated at early but not at late stages of development. This indicates that cell rearrangements occur frequently at early developmental stages and subsequently decline. To understand how cellular properties such as proliferation, differentiation and mechanical forces affect cell rearrangements, we are developing a computational vertex model of the mouse neural epithelium. To parameterize the model, we measured the cell shapes at different developmental stages. Interestingly, the model predicts that the rate of proliferation determines the degree of clonal fragmentation. We are currently designing assays that will allow us to test this prediction. Overall, the quantitative understanding of epithelial dynamics that we obtain in this study will provide insight into how cell rearrangements may affect pattern formation in the neural tube.

Morning Session / 11

Active organelle dynamics facilitates precise sensing of fluctuating signals

Authors: Felix Jonathan Meigel[1]; Philipp Mergenthaler[2]; Steffen Rulands[1]

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[2] *Charite - Universitätsmedizin Berlin, Department of Experimental Neurology*

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Tissue development and homeostasis rely on cellular decision-making in response to fluctuating environmental signals. The process of cellular decision-making integrates dynamics on different spatial scales ranging from the molecular to the tissue scale, where all spatial scales are subject to fluctuations and consume chemical energy to fuel interactions. How are information and fluctuations propagated in a dynamic multi-scale organisation of non-equilibrium dynamics and how can biological systems exploit this to process environmental information? Here, we show how the dynamics of active organelles suppresses cellular responses to fast fluctuating environmental signals, but facilitates the response to slow biological relevant signals. We demonstrate that active organelle dynamics gives rise to a kinetic low pass filter. Starting from a full stochastic treatment, we derive a generalized Fokker Planck equation in which a localized mode gives rise to a collective degree of freedom. We identify the localization mode in full stochastic simulations, demonstrate how the dynamics of the localization mode builds a kinetic low pass filter, and show how this gives rise to strongly increased sensitivity of selectivity of cellular decisions. We demonstrate our findings in the specific context of the metabolic regulation of cell death focusing on the interplay of Bax protein dynamics with rapid mitochondrial fusion and fission. Our work shows paradigmatically how biological function relies on the integration of non-equilibrium processes on different spatial scales in order to control and respond to fluctuations.

Morning Session / 75

Cell Fate Clusters in ICM Organoids Arise from Cell Fate Heredity & Division – a Modelling Approach

Authors: Tim Liebisch[1]; Armin Drusko[2]; Biena Mathew[3]; Ernst Stelzer[3]; Sabine Fischer[4]; Franziska Matthäus[5]

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[2] *Goehte University*

[3] *Goethe University*

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During the mammalian preimplantation phase, cells undergo two subsequent cell fate decisions. Within the second decision, the inner cell mass (ICM) segregates into the epiblast and the primitive endoderm. Recently, ICM organoids have been published as an in vitro model system towards preimplantational development. ICM organoids mimic the cell fate decision taking place in the in vivo mouse embryos. In a previous study, the spatial pattern of the different cell types was investigated. The study revealed that cells of the same fate tend to cluster stronger than expected for the currently hypothesised purely random cell fate distribution. Three major processes contribute to the final cell fate arrangements at the mid and late blastocysts or 24 h old and 48 h old ICM organoids, respectively: 1) intra- and intercellular chemical signalling; 2) a cell sorting process; 3) cell proliferation.

To quantify the influence of cell proliferation on the emergence of the cell type clustering behaviour, a computational model was developed. The model accounts for mechanical cell-cell interactions, cell growth and cell division and was applied to compare several assumptions of how ICM neighbourhood structures are generated. The model supports the hypothesis that initial cell fate acquisition is a stochastically driven process. The model further shows that the observed neighbourhood structures can emerge due to cell fate heredity during cell division and allows the inference of a time point for the cell fate decision.

Simulations show that cell divisions involving cell fate heredity seem sufficient to lead to the local clustering observed in 24 h old ICM organoids, and that the initial cell differentiation process takes place only during a small time window. Our results leave little room for extracellular signalling believed to be important in cell fate decision, therefore we are discussing an alternative role of chemical signalling in this process.

Morning Session / **14**

Setting up the epigenome: a collective phenomenon

Authors: Steffen Rulands[None]; Fabrizio Olmeda[None]; Stephen Clark[None]; Tim Lohoff[None]; Felix Krüger[None]; Wolf Reik[None]

Corresponding Author: srulands@gmail.com

Recent breakthroughs in single-cell genomics allow probing molecular states of cells with unprecedented detail along the one-dimensional sequence of the DNA. Biological function relies, however, on emergent processes in the three-dimensional space of the nucleus, such as droplet formation through phase separation. Here, we combine single-cell multi-model sequencing with a theoretical approach to rigorously map measurements along the DNA sequence to a description of the emergent spatial dynamics in the nucleus. Drawing on scNMT-seq experiments in vitro and in vivo we demonstrate our approach in the context of early development. We show how epigenetic modifications of the DNA, DNA methylation, are established through the interplay between chemical and topological modifications of the DNA, leading to the formation of condensates of methylated DNA in the nucleus. Using this theoretical framework, we identify epigenetic processes that precede lineage decisions in the early embryo. Our work sheds new light on epigenetic mechanisms involved in cellular decision making. It also provides a general framework of how mechanistic insights into the spatio-temporal processes governing cell-fate decisions can be gained by the combination of methods from single-cell multi-omics and theoretical physics.

Morning Session / **66**

Stochasticity and mechanics of stem cell fate in intestinal crypts

Author: Edouard Hannezo[1]

[1] *IST Austria*

Corresponding Author: edouard.hannezo@ist.ac.at

Understanding to what extent stem cell potential is a cell-intrinsic property or an emergent behavior coming from global tissue dynamics and geometry is a key outstanding question of systems and stem cell biology. Here, we propose a theory of stem cell dynamics as a stochastic competition for access to a spatially localized niche, giving rise to a stochastic conveyor-belt model. Cell divisions produce a steady cellular stream which advects cells away from the niche, while random rearrangements enable cells away from the niche to be favorably repositioned. Importantly, even when assuming that all cells in a tissue are molecularly equivalent, we predict a universal functional dependence of the long-term clonal survival probability on distance from the niche, as well as the emergence of a well-defined number of functional stem cells, dependent only on the rate of random movements vs. mitosis-driven advection. We verify the predictions of this theory in multiple organs. This argues for a key role of positional fluctuations in dictating stem cell number and dynamics.
Moreover, in a second study, we investigate the mechanics of how intestinal crypt geometry arises itself, using intestinal organoids as a model system. We find through a combination of experiments and biophysical modelling that cell fate-specific changes in osmotic and actomyosin forces coordinate robust organoid morphogenesis.

[1] Corominas-Murtra et al, PNAS, 2020, Yang et al, bioRxiv, 2020

2.2 Afternoon session: Cells II

Afternoon Session / **69**

Dynamics of cell migration process

Author: Zenon Rajfur[1]

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Cell migration is one of the fundamental cellular phenomenon connected to several important biological processes like embryonic development, wound healing, tissue engineering or neural development. Impaired regulation of cell migration can be the cause of many diseases like osteoporosis, arthritis or cancer metastasis. For these reasons, studies of cell migration are of particular interest for life sciences. Cell migration is inherently dynamic process where the local, transient signaling events cooperate with global changes in cellular architecture and behavior. Here, the dynamic aspects of these interactions will be discussed in the light of recent advances in the studies of cell migration.

Afternoon Session / **72**

Chemotaxis impact on a Turing reaction-diffusion system

Author: Camile Fraga Delfino Kunz[1]

Co-author: Franziska Matthäus [1]

[1] *Goethe University Frankfurt*

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During embryo development there is a rapid growth in cell numbers that forms complex structures. Skin pattern formation is an early process during the embryogenesis and happens before the cells fully differentiate. In the present project we consider skin patterning in mouse embryos, where cell aggregates form based on a hierarchical process, involving interactions between the epidermal cell populations. The reaction-diffusion pre-pattern is driven by fibroblast growth factor (FGF20), bone morphogenic protein (BMP) and WNT. Considering mathematical models, there are two main processes involved in the pattern formation: Turing reaction-diffusion systems and chemotaxis. The Turing system models the concentration of two interacting chemicals, and the patterns arises from an instability driven by a difference between their diffusion coefficients. Some previous studies show that this behavior is essential for self-organization in the mouse hair follicle and chicken feather pre-pattern formation. Another key mechanism is chemotaxis, where the cells move in the direction of a chemical attractant, where patterns can also be observed. Experimental data indicates a hierarchical system, where cell chemotaxis is guided by a Turing system. We aim at developing mathematical models to describe the underlying biological processes leading to skin patterning, especially the interaction of chemotaxis with reaction-diffusion (Turing) systems. A mathematical model using partial differential equations is solved numerically, and some results are presented and compared to the experimental data. We study the parameter-dependence of the model and different model structures, and their impact on the pattern forming process. According to the experimental data the Turing system and the chemotaxis seems to be intrinsically related on the mouse skin patterning. Using a numerical approach for the PDE system, we develop a framework to study quantitatively how chemotaxis and Turing systems are related and their impact on the patterning process.

Afternoon Session / 68

How cell growth, division, and stochastic gene expression contribute to the protein noise floor

Authors: Jakub Jędrak[1]; Anna Ochab-Marcinek[1]

[1] *Institute of Physical Chemistry, Polish Academy of Sciences*

Corresponding Author: ochab@ichf.edu.pl

The origins of the protein noise floor – a lower bound for noise in gene expression, experimentally observed in highly expressed genes – are still debated. We propose a minimal model of gene expression in bacteria, which combines several contributions to the stochastic noise in protein levels: Variation in mean protein concentration during cell cycle, translational bursts, protein partitioning at cell division, and cell-cycle age distribution within the population. Our model is capable of predicting the existence of the noise floor and to semi-quantitatively reproduce the shapes of the experimental noise vs. protein concentration plots. Thus, it allows one to disentangle the contributions to the noise floor coming from the specific sources.

[1] J. Jędrak, A. Ochab-Marcinek, Contributions to the 'noise floor' in gene expression in a population of dividing cells, Scientific Reports, 10, 13533 (2020)

Afternoon Session / 64

The many ends of a never-ending story: Deriving the Drosophila gap gene system by ab-initio optimization

Author: Thomas Sokolowski[1]

Co-authors: Thomas Gregor [2]; William Bialek [3]; Gašper Tkačik [4]

[1] *Frankfurt Institute for Advanced Studies (FIAS)*

[2] *Institut Pasteur & Princeton University*

[3] *Princeton University & CUNY*

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Early embryogenesis is driven by complex spatio-temporal patterns that specify distinct cell identities according to their locations in the embryo. This process is remarkably reproducible, even though it results from regulatory interactions that are individually noisy. Despite intense study, we still lack a comprehensive, biophysically realistic model for at least one biological system that could simultaneously reproduce quantitative data and rigorously explain the emergence of developmental precision. Moreover, traditional approaches fail to provide any insight as to why certain patterning mechanisms (and not others) evolved, and why they favor particular sets of parameter values. We address both questions during early fly embryo development. Previous work has shown that the gap gene expression patterns in Drosophila optimally encode positional information. We therefore asked whether one can mathematically derive the gap gene network—without any fitting to data—by maximizing the encoded positional information. To this end we constructed a generic, biophysically accurate spatial-stochastic model of gene expression dynamics, where genes respond to morphogen input signals and mutually interact in an arbitrary fashion, and optimized its parameters for positional information. Firstly, our results show how the experimentally observed precision can be achieved with basic biochemical processes and within known resource and time constraints. Secondly, we show that multiple optimal solutions exist and systematically explore their characteristics. Finally, we show that some of the optimal solutions closely correspond to the real Drosophila gap gene expression pattern. To our knowledge this is the first successful ab-initio derivation of any biological network in a biophysically realistic setting. Our results suggest that even though real biological networks are hard to intuit, they may represent optimal solutions to optimization problems which evolution can find.

3 Friday

3.1 Morning session: Populations

Morning Session / 62

Intermediate social bonds and the evolution of reproductive cooperation

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Reproductive cooperation represents one of the most surprising behaviours. Individuals forego their reproductive output (partially or entirely) and instead cooperate with other members of their social group in raising their offspring. Theoretical basis of reproductive cooperation in kin groups was laid out in the form of kin-selection theory. However, we still have little knowledge of the exact evolutionary paths that led to its evolution, and many existing results are conflicting and ambiguous. Here, I show how family groups may have constituted an important intermediate step in the evolution of social cooperation. More broadly, I show how social groups of intermediate strength may have acted as a trigger in the evolution of highly integrated assemblages of individual entities from simple, loose ones.

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Specialization and plasticity in a primitively social insect

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Biological systems not only have the remarkable capacity to build and maintain complex spatio-temporal structures in noisy environments, they can also rapidly break up and rebuild such structures. How such systems can simultaneously achieve both robust specialisation and plasticity is poorly understood. Here we use primitive societies of Polistes wasps as a model system where we experimentally perturb the social structure by removing the queen and follow the re-establishment of the social steady state over time. We use a unique experimental strategy correlating time-resolved measurements across vastly different scales of biological organisation at the level of individual insects, from video recordings to multi-modal sequencing of brain gene expression and DNA methylation profiles. In combination with a theoretical approach, here we show that Polistes integrates antagonistic processes on multiple scales of biological organisation to distinguish between intrinsic perturbations of molecular states and extrinsic cues affecting the society as a whole, and thereby achieves both robust specialisation and rapid plasticity. Furthermore, we show that the long-term stability of the social structure relies on dynamic DNA methylation which controls transcriptional noise. Such dynamics provide a general principle of how both specialization and plasticity can be achieved in biological systems.

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A part-dependent account of biological individuality: why holobionts are individuals and ecosystems simultaneously

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Given one conception of biological individuality (evolutionary, physiological, etc.), can a holobiont – that is the host + its symbiotic (mutualistic, commensalist and parasitic) microbiome – be simultaneously a biological individual and an ecological community? Herein, we support this possibility by arguing that the notion of biological individuality is part-dependent. In our account, the individuality of a biological ensemble should not only be determined by the conception of biological individuality in use, but also by the biological characteristics of the part of the ensemble under investigation. In the specific case of holobionts, evaluations of their individuality should be made either host-relative or microbe-relative. We support the claim that biological individuality is part-dependent by drawing upon recent empirical evidence regarding the physiology of hosts and microbes, and the recent characterization of the 'demibiont'. Our account shows that contemporary disagreements about the individuality of the holobiont derive from an incorrect understanding of the ontology of biological individuality. We show that collaboration between philosophers and biologists can be very fruitful in attempts to solve some contemporary biological debates.

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Pattern formation in a predator-prey model with defense in fearful prey

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This paper deals with mathematical modeling and analysis of a predator-prey interaction model with fear-induced anti-predator defense. The main goal of this non-linear study is to investigate the drivers that are responsible for pattern formation in the predator-prey system. To my knowledge, this study is the first systematic study showing the simultaneous effects of fear and group defense mechanisms in the complex predator-prey relationship. Conditions for instability have been discussed and numerically obtained patterns give us an understanding of such complex ecological interaction.

Morning Session / 60

Uncertainties and epidemics spread

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Epidemic is a complicated process which spreads onto a complex not fully known topology. It affects not only properties of the population itself but also the network on which it spreads. The effective control measure should stop the epidemic at the lowest possible costs, therefore the problem of disease eradication cannot be separated from the economic layer, which includes, among others, costs of treatment and contact tracking. The lack of knowledge about full epidemiological status of individuals, delay in detection and presence of long-range links are the most important factors determining the overall costs. We demonstrate that despite uncertainties it is still possible to design the most effective treatment strategy. Furthermore, we identify key elements responsible for epidemics severity.

Morning Session / **13**

How unicellular yeast form a community for the benefit of long-term survival.

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Living organisms have been traditionally classified into two main categories: unicellular and multicellular. However, the boundary between these two groups are less strict and clear than was previously presumed. Studies on the unicellular communities have revealed that various properties, processes and behaviour so far mainly associated with metazoa are also important for the development and survival of facultatively multicellular microbial populations. I will discuss these phenomena using example baker yeast Saccharomyces cerevisiae, of one of the most popular model microorganism. Unicellular S. cerevisiae form communities by staying together or coming together scenarios that greatly influence genetic composition and properties of the emerging group. Cells within the structured colony, grow, age and experience differences in its microenvironment that leads to phenotypic heterogeneity. This leads to multiple social interactions within colony including cooperation, division of labour but also competition and cheating. Such cell strategies differentiation within a colony can be evolutionary beneficial for the long-term survival of a community in the unpredictable environment.

3.2 Afternoon session: Medical Biology

Afternoon Session / **59**

Predictive models of bacterial response and the evolution of resistance to antibiotics

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The emergence of antibiotic-resistant microorganisms is a global problem. Despite significant advances in our understanding of molecular mechanisms of resistance, quantitative models that could predict the response of bacterial populations to antibiotic treatment are rare.
I will present our attempts at constructing such predictive models. I will first discuss experimental approaches that we use to understand short- and long-time bacterial response to antibiotics. I will then discuss how experimental results can be understood using physics-inspired models. Finally, I will show how these models can be used to predict some aspects of the emergence of antibiotic resistance.

Afternoon Session / **61**

Mathematical Investigation of Early Atherosclerosis

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Arteriosclerosis is hardening of arteries. Its one of the variances is atherosclerosis. Atherosclerosis is a chronic inflammatory disease caused by the accumulation of plaque in the intima, the innermost layer of arteries. Atherosclerosis is the leading root cause of many cardiovascular diseases worldwide. The complete biochemical process of atherosclerotic plaque formation in relation to the autonomous system of ten non-linear ODEs is presented here. Concentrations of low-density lipoprotein (LDL), high density lipoprotein (HDL), free radicals, oxidized LDL, chemoattractant, monocytes, macrophages, T cells, smooth muscle cells (SMC), foam cells and collagen are considered as the dependent variables of this non-linear system. To reduce the ten-dimensional nonlinear system into a three-dimensional nonlinear system, quasi steady state approximation theory is applied. Numerical analysis of this reduced system reveals the effects of some important model parameters. This can be carried forward to develop possible clinical strategies in controlling this disease dynamics.

Afternoon Session / **73**

Challenges in the Boron Neutron Capture Therapy

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The use of neutron capture reactions in cancer therapy was proposed already in 1936, four years after the discovery of the neutron. Up to now, this kind of cancer treatment is widely used for tumors with a poor response to traditional therapies (surgery, γ radiotherapy, or chemotherapy). The use of 10B selectively absorbed by the cancer cells provides high dose delivery to the malignancy with substantially smaller irradiation of the healthy surrounding tissues. Despite the rich history feasibility studies and clinical trials of this therapy are still carried out all over the world. In this talk, we present selected open questions in view of the BNCT development in Poland, in particular on the new neutron sources and dose monitoring systems.

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Bio-electric phenomena during growth and regeneration

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The development of new cell imaging techniques has enabled us to investigate spatiotemporal electrical gradients and their influence on cell migration and pattern formation of developing tissues. Membrane voltage changes can trigger biophysical process inside the cell, which in turn can activate genetic signaling pathways regarding processes like cellular differentiation or apoptosis. Because electric signals can travel faster than chemical cues and are more precise than mechanical forces, they have been investigated regarding their potential role as pattern formation regulators. Using targeted manipulation of ion flow and voltage-dependent dyes, it was observed that bioelectric patterns play a vital role in controlling morphogenesis and axial patterning. In this talk, I present the most interesting and promising finding regarding the bio-electrical dynamics of development, outline the techniques used in modern electrophysiology and describe how manipulating bioelectric gradients can alter the target morphology of developing Xenopus frogs and Planarian worms.

Afternoon Session / 9

Structural and Functional Genomics of the Human Gut Microbiome

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The microbiome is a diverse, dynamic, and complex environment important to health. It harbors tens of trillions of microbes represented by more than 2 million unique genes. Through its malleability and links to health - being associated with diseases ranging from obesity, ulcerative colitis, type-1 diabetes, through Parkinson's disease, depression, to modulating cancer therapy response - the microbiome is an attractive target for research and therapeutic interventions. Hindering this is our limited understanding of gene functions and metabolic potential encoded within the microbiome.
Currently, we are able to functionally annotate less than 50% of microbial genes. To address this, we devised a synergistic approach in which through large-scale grid computations we predict *de novo* 3D protein structures of microbial proteins from sequence. Then, using those structures and a combination of LSTM and deep learning Graph Convolutional Networks (GCN), we annotate gene function with higher accuracy and coverage. Finally, those results are used in a custom metagenomic annotation pipeline for high-accuracy and high-coverage annotations of real-world metagenomic datasets.
Thus, we build a gene/protein sequence-structure-function link, which combined with an influx of metagenomic data and the development of machine learning approaches to design individual's microbiome composition opens up new avenues for microbiome-oriented therapies and precision medicine.

Afternoon Session / 63

Coagulation cascade as a dynamic biological system

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Coagulation cascade is one of the best-known physiological systems, which biological role is regulated by 20 coagulation factors, 7 fibrinolytic factors and cell elements (platelets and endothelium). The number of known factors has been incrementally extended within 50-ties of previous century, giving clinicians more understanding about this extremely complicated biological system, to treat patient conditions and decide about a patient outcome.
Traditionally, for the medical purpose, the coagulation cascade is classified into two pathways: an intrinsic and an extrinsic pathway, both of which meet factor X activation. This classical theory of blood coagulation developed by MacFerlane, Davie and Ratnoff is particularly useful for understanding the *in vitro* coagulation. Coagulations factors activity and concentrations easily became to be used as biological indicators (*in vitro* tests) to predict a physiological or pathological state of a patient.
In fact, coagulation process is more complicated, and this simple classification fails to incorporate the central role of cell-based surfaces in in vivo coagulation process. Developing mathematical models of biochemical networks is a significant facet of systems biology. Bottom-up approach assumes specific molecular properties of coagulation and fibrinolytic factors, and quantified interactions as stoichiometry, kinetics, binding properties, inhibition, diffusion, and others. The resulting models then predict the activity of biochemical pathways, platelets, and vascular tissues, either during physiological hemostasis (coagulation and fibrinolysis) or during pathological thrombosis of bleeding.
In this talk I will discuss a traditional model of coagulation (tissue-factor-triggered models) and compare them with a dynamic fibrin polymerization and platelet signaling.