



### Conflownet 2025

Flow networks are fundamental to the transport of information and matter, ubiquitous in systems ranging from blood vasculature and societal networks to porous media. These complex systems dynamically self-organize, leading to fascinating features like optimal nutrient transport and opinion polarization.

Despite the growing number of applications of flow networks, there is a pressing need for generic foundational principles that bring together the advancements made in the different areas. This interdisciplinary conference aims to coalesce recent theoretical and experimental advancements made in the field of flow networks from the various perspectives of biology, city networks, and porous media. It is designed to be accessible to master/PhD students, thus providing exposure to current research and offering a platform to engage with the leading experts in the field. There is a poster session for networking and exchange of ideas, enabling the participants to foster collaborations and contribute to the emergence of new perspectives in the field.

Join us in Raitenhaslach on 25th and 26th of September 2025 for an exciting and enriching experience that promises to advance our understanding of flow networks and their myriad of applications.

### Conference schedule

Time		25.09.2025		26.09.2025
7:00 - 8:30		Breakfast		Breakfast
08:30		Bus transfer		Bus transfer
9:00 - 9:15		Opening Words		
9:15 - 10:15		Karen Alim		Eleni Katifori
10:15 - 10:30		Coffee break		Coffee break
10:30 - 11:30	Session 1	Ariel Amir	Session 3	Franca Schmid
11:30 - 11:50		Tomasz Szawełło		Fatemeh Mirzapour
11:50 - 12:10		Jan Smink		Thomas Fai
12:10 - 12:30		Ludovic Jami		Ivan Lobaskin
12:30 - 14:00		LUNCH + Coffee		LUNCH + Coffee
14:00 - 14:20	Session 2	Ignacio Bordeu	Session 4	Joseph Knight
14:20 - 14:40		Miguel Ruiz Garcia		Laureline Julien
14:40 - 15:00				
15:00 - 15:20		Carl Modes		Tom Shimizu
15:20 - 15:40				
15:40 - 16:00		Coffee break		Coffee break
16:00 - 18:00		Poster Presentation		
18:00 - 19:00		Networking and Aperitiv		

NB: Talks should be 45min+15min questions or 15min+5min questions.

#### Session 1 : Flow, Form, and Optimization

- Karen Alim\*: Lesson from smart slime: How active flow networks process information for complex behaviour
- Ariel Amir\*: Travelling waves in our immune system
- Tomasz Szawełło: Self-limiting flow networks in rocks: lessons for CO2 storage
- Jan Siemen Smink: Optimizing branched fluidic networks: A unifying theory
- Ludovic Jami: Elasto-Active Fluidic Networks

#### Session 2 : Growth and Collective Dynamics

- Ignacio Bordeu: On the Growth of Branching Networks in Developing Organs
- Miguel Ruiz Garcia: Collective phenomena in nonlinear flow networks
- Carl Modes\*: Complex Spatial Networks through a Different Lens

#### Session 3: Vascular Networks in Health and Disease

- Eleni Katifori\*: Broken symmetries and power generation in living flow networks
- Franca Schmid\*: Computational models to study the perfusion of the brain under healthy conditions and investigate its role in neurological disorders
- Fatemeh Mirzapour: Flow-Induced Vascular Remodeling On-Chip: Insights into Anti-VEGF Therapy Optimization
- Thomas Fai: Multiscale model of red blood cell clogging in microfluidic devices
- Ivan Lobaskin: Statistical theory of human bronchial airway development from organ-scale imaging

#### Session 4: Biological Transport Strategies Beyond Vessels

- Joseph Knight: An underwater microbial railway network
- Laureline Julien: Drivers for transport in the gastrovascular network of Aurelia Aurita jellyfish: cilia vs. peristaltism
- Tom Shimizu\*: How mycorrhizal fungi build fluid-flow networks for underground nutrient trade

### Important information

#### Accommodation

We have booked rooms for all participants at the <u>hotel Glöcklhofer</u>, which is located in Burghausen (1 km away from the Burghausen train station). This includes breakfasts and two dinners (24.09 & 25.09) at the hotel. Lunch and coffee breaks will be provided by Altstadt Hotel directly at the Raitenhaslach monastery.

### Reaching Burghausen

The nearest airports are in Salzburg and Munich. Most of you will likely arrive via Munich. Unfortunately, the train connection to reach Burghausen from Munich <u>has been modified</u> by Deutsche Bahn (DB) due to construction work. Here is an example of the new connection from Munich main train station (München Hbf) to Burghausen, from the <u>DB website</u>:



#### Directions to reach Munich main train station from Munich airport:

The Franz-Josef-Strauß Munich airport is located north of the city center. To reach Munich main train station, an S-Bahn train service departs every 20 minutes. The lines are S1 and S8, and they directly connect the airport to the main train station, München Hbf. The price of a ticket is 13.60€.

#### Conference venue

The conference will be held at Raitenhaslach, a monastery near the town of Burghausen. The transfer from Burghausen to Raitenhaslach (and back) will be ensured by a shuttle service we booked for the conference duration.

### Participants & Abstracts

#### **Talks**

# <u>Lesson from smart slime: How active flow networks process information for complex behaviour</u>

Karen Alim, Technical University of Munich, Germany

Propagating, storing and processing information is key to take smart decisions – for organisms as well as for autonomous devices. In search for the minimal units that allow for complex behaviour, the slime mould Physarum polycephalum stands out by solving complex optimization problems despite its simple make-up. Physarum's body is an interlaced network of fluid-filled tubes lacking any nervous system, in fact being a single gigantic cell. Yet, Physarum finds the shortest path through a maze. We unravel that Physarum's complex behaviour emerges from the physics of active flows shuffling through its tubular networks. Flows transport information, information that is stored in the architecture of the network. Thus, tubular adaptation drives processing of information into complex behaviour. Taking inspiration from the mechanisms in Physarum we outline how to embed complex behaviour in active microfluidic devices and how to program human vasculature.

#### <u>Travelling waves in our immune system</u>

Ariel Amir, Weizmann Institute, Israel

In various biological scenarios, cells rely on the diffusion of signaling molecules to communicate, yet information needs to be communicated quickly and over large distances. How can the limitations of diffusion be surpassed? One solution Nature utilizes relies on "diffusive relays": upon sensing the signal, cells release more of it, thus creating an outgoing information wave. Mathematically, this mechanism manifests itself as an additional, non-linear, term in the diffusion equation, allowing for propagating wave solutions. The properties of these waves strongly depend on system dimensionality, and manifest intriguing phenomena, including regimes where wave velocity is independent of the diffusion constant. We recently proposed that such waves arise in the immune system, where upon sensing a signal, white blood cells known as neutrophils release a signaling molecule. However, in this case the waves must be self-extinguishing, since the range of cell recruitment must be limited. After introducing diffusive relays, I will discuss new mathematical models of self-extinguishing relays, and compare them to recent experiments on neutrophils.

### <u>Self-limiting flow networks in rocks: lessons for CO2 storage</u>

Tomasz Szawełło, University of Warsaw, Poland

When the processes that reshape a transport network are self-limiting, the network need not settle into dominant flow pathways; instead, it can keep opening and closing channels throughout the domain. River deltas display this behaviour on kilometre scales, and the same feedback can occur inside rocks when one mineral dissolves while another precipitates in the pore space. Harnessing such self-organisation could aid geological CO<sub>2</sub>

storage, as the continual creation of new flow pathways helps distribute reactants and products more evenly, maximising the trapped volume.

We investigate these dissolution–precipitation dynamics with a pore network model that solves coupled flow and transport, updates pore geometry, and allows topological changes such as pore merging. We apply it to explore how different flow rates and reactant concentrations affect mineral replacement dynamics. The simulations reveal distinct regimes—including self-sustained reactions through dynamic blockage and reopening—which we validate against experimental data for limestone dissolution and gypsum precipitation. These results offer insight into how injection strategies can be optimized to enhance efficiency of reactant distribution in a transport network.

### Optimizing branched fluidic networks: A unifying theory

Jan Siemen Smink, University of Twente, Netherlands

Network optimization for fluid transport in branched fluidic networks has gained significant attention in biology and engineering applications, such as transport systems, reactors, additive manufacturing and microfluidics. In an optimal network, optimal channel radii are found by minimizing the total viscous dissipation and the energetic costs per volume for the whole network. However, a unifying theory in which both laminar and turbulent flows, Newtonian and non-Newtonian fluid models and wall roughness can be incorporated is lacking. Therefore, we introduce an unifying optimization approach that is applicable to any Darcy friction factor, and we apply this approach to networks with turbulent flows, shear-thinning, shear-thickening and yield-stress fluid models and arbitrary wall roughness. The intermediate Reynolds number turbulent regime is accessed for the first time using this network optimization approach. In addition, the limitations of broadly-used limit cases in network optimization, such as complete turbulence and smooth channels approximations, such as Blasius' formula, are discussed. The approach also opens up optimization of networks with bubbly flows, porous media and slip flow.

#### Elasto-Active Fluidic Networks

Ludovic Jami, IRPHE Marseille CNRS, France

Biological vascular systems—such as those of the slime molds, the lymphatic system, or the intestine—can autonomously drive internal flows through spontaneous contractions of their channels. These flows emerge from local interactions involving fluid–structure coupling, mechanosensory feedback, and inter-channel fluid exchange. Inspired by these principles, we designed a controllable poroelastic network that incorporates pressure-based mechanosensory feedback. Such feedback emulates the core mechanisms of biological self-contracting networks. Varying the dynamics of the pressure feedback, we explore how flow patterns self-organize and further how active networks dynamically interact with external fields. These poroelastic, self-contracting networks provide both a model system for uncovering the design principles underlying biological transport networks and a basis for developing novel fluidic systems in soft robotics.

#### On the Growth of Branching Networks in Developing Organs

Ignacio Bordeu, Universidad de Chile, Chile

Branching architectures are a hallmark of many biological tissues and organs, enabling efficient transport and exchange of fluids in systems such as the salivary and mammary

glands, bile ducts, and lungs. These intricate networks emerge from simple local rules—cell division, branching, and tissue expansion—yet give rise to highly organized global structures. In this talk, I will present recent and ongoing work that combines biological data and physical modeling to understand how such structures develop. I will first share some of our results on the mouse salivary gland and bile organoids, where spatially embedded stochastic models reveal how ductal growth is shaped by both local dynamics and global tissue constraints. If time allows, I will then discuss current work on human lung development, where time-resolved imaging suggests that internal fluid flows may contribute to remodeling and stabilizing the growing network. Together, these studies illustrate how physics-based models can uncover universal principles behind the organization of biological flow networks.

### Collective phenomena in nonlinear flow networks

Miguel Ruiz Garcia, Complutense University of Madrid, Spain

In this talk, we will explore systems that combe soft materials and fluids. Drawing inspiration from plant and animal vasculature, our research focuses on flow networks that incorporate valves with negative differential resistance [1]. These valves are coupled through the fluid and act as internal degrees of freedom. When the external pressure is controlled, the system exhibits emerging collective phenomena. We will discuss the fluidic memristor, a system whose global resistance can be tuned through the applied protocol [1]. Finally, as we increase the complexity of the system, other collective phenomena can emerge, such as soliton-like waves, excitability and self-sustained oscillations [2].

#### References

[1] Martínez-Calvo, A., Biviano, M. D., Christensen, A. H., Katifori, E., Jensen, K. H., & Ruiz-García, M. (2024). The fluidic memristor as a collective phenomenon in elastohydrodynamic networks. Nature Communications, 15(1), 3121.

[2] Ruiz-García, M., & Katifori, E. (2021). Emergent dynamics in excitable flow systems. Physical Review E, 103(6), 062301.

#### Complex Spatial Networks through a Different Lens

Carl Modes, MPI CBG, Germany

The nodes of many real-world networks, flow networks among them, exist in physical space, which strongly constrains their possible connectivity patterns: only nearby nodes are or can be connected. At the same time reduced-dimensional models or even characteristics for spatial networks that respect both the topology and geometry of the spatially embedded network would be of great utility, but have been notoriously difficult to come by. This is in part because much of the effort in network science more broadly has concentrated on non-spatial, purely relational networks, but also because of the inherent difficulty of combining the geometric and topological properties. Here, we will discuss the possibility of leveraging the so-called  $\beta$ -skeletons, which are a family of excluded volume proximity graphs that naturally capture the shape of

spatial point sets, to create one parameter families of spatial networks whose scaling properties reflect information of the real network.

#### Broken symmetries and power generation in living flow networks

Eleni Katifori, University of Pennsylvania, USA

Circulatory systems in animals require active mechanisms to sustain fluid flow. Typically, this is achieved through a centralized pump, such as the heart in the cardiovascular system. But what happens when a centralized pump is absent?

In this talk, we explore decentralized mechanisms of fluid transport in biological flow networks, and the mathematical inevitabilities that govern power generation in cases where forcing from the heart is absent or insufficient. We first examine the lymphatic system, which relies on peristalsis and a series of one way valves. We begin with the lymphatic system, which relies on peristalsis and a series of one-way valves. We show how non-reciprocity leads to experimentally observable, counterintuitive behaviors—such as retrograde (backward) peristalsis improving forward flow—and present an engineering analogue.

We then move to another peristaltically driven flow network, the gastrovascular canal system of jellyfish, where large body deformations drive flow. Using a theoretical model, we describe fluid transport driven by radial and longitudinal peristalsis on a single tube and develop a coarse-grained framework applicable to the jellyfish circulatory system and other large networked systems. We discuss how time reversal symmetry constrains which jellyfish swimming motions can productively propel flow, and present some unsolved mysteries.

# Computational models to study the perfusion of the brain under healthy conditions and investigate its role in neurological disorders

Franca Schmid, University of Bern, Switzerland

As the energy storage capacity of the brain is limited, a robust blood and oxygen supply is indispensable for its well-functioning. This aspect is further underlined because microvascular alterations play an important role during pathologies. However, experimentally quantifying the isolated impact of specific vascular alterations is challenging but well-suited for in silico modeling. In this context, we will present three exemplary projects, including the underlying numerical models, that show how in silico modeling goes beyond what is accessible to in vivo experiments.

The basis for these projects is a 1D blood flow model applicable to realistic microvascular networks. Within the first project, this model is employed to quantify the impact of vascular alterations as observed during aging, e.g., locally reduced capillary densities. In the second project, our blood flow model is combined with an inverse model, which enables us to directly align our simulations to in vivo measurements. The 1D blood flow model has additionally been extended to describe vessel diameter changes in response to changes in inflow pressure (cerebral autoregulation). This framework is employed in the context of ischemic stroke to quantify the role of vascular anastomoses, i.e., vascular loops, and to study the loss of autoregulatory capacity. Lastly, I present a mixed-dimensional modeling approach to simulate oxygen transport in the vasculature and the brain tissue. With this model we assess the contribution of different types of capillaries to the overall oxygen supply and study the severity of capillary occlusions on local oxygen availability.

# Flow-Induced Vascular Remodeling On-Chip: Insights into Anti-VEGF Therapy Optimization

Fatemeh Mirzapour, TU Darmstadt, Germany

The interplay between vascular endothelial growth factor (VEGF) signaling and blood flow is critical for vascular remodeling, particularly in pathological contexts such as tumor

progression. Tumor vasculature often exhibits excessive VEGF-driven growth, resulting in disorganized, dysfunctional networks that impede drug delivery. Anti-VEGF therapies aim to normalize these networks, but have shown inconsistent clinical results, in part due to a limited understanding of how VEGF and flow dynamics interact to influence remodeling. We present a human vasculature-on-chip platform optimized for long-term perfusion and live imaging that allows controlled study of vascular remodeling under physiological low and tumor mimicking high VEGF conditions. At low VEGF levels, flow-induced remodeling improved network hierarchy and flow velocities, similar to animal models. In static networks without flow, vessels showed gradual uncontrolled growth, loss of hierarchy and reduced flow velocities. Under tumor mimicking high VEGF conditions, flow-conditioned networks showed rapid, aberrant overgrowth that disrupted remodeling, while the anti-VEGF agent bevacizumab restored remodeling and network hierarchy, highlighting its role in vascular normalization. Static networks exposed to high VEGF showed slower growth than those exposed to low VEGF, but bevacizumab treatment restored gradual continuous growth. These findings highlight the context-dependent efficacy of anti-VEGF therapies and the critical influence of the local VEGF levels and tumor vascularity on treatment outcomes. Our vasculature-on-chip platform enables precise control of flow and VEGF conditions, providing a robust tool for investigating vascular remodeling mechanisms and developing personalized treatment strategies for cancer and vascular disease.

#### Multiscale model of red blood cell clogging in microfluidic devices

Thomas Fai, Brandeis University, USA

Microfluidic devices that sort cells by their deformability hold significant promise for medical applications including low-cost diagnostics. However, clogging in these microfluidic systems may cause them to change behavior over time, potentially limiting their reliability. Here, we propose a coarse-grained theoretical model to capture the aging of microfluidic devices under different conditions including constant flow and constant pressure. We compare the predictions of the coarse-grained model to those of stochastic simulations and previous studies. Lastly, we apply the model to experimental data on the clogging of sickle red blood cells in a microfluidic cell-sorter and discuss its wider applicability.

### <u>Statistical theory of human bronchial airway development from organ-scale imaging</u> Ivan Lobaskin, University of Cambridge, United Kingdom

The human bronchial airway presents one of the canonical examples of flow networks in biological systems. It develops though a process of branching morphogenesis, during which branches undergo many rounds of bifurcations to generate a highly ramified structure. While much progress has been made in uncovering the molecular mechanisms involved in the regulation of individual branching events, there is yet little understanding of how thousands of growing branches organize on a large scale. Recently, advances in tissue clearing and image processing techniques have made it possible to generate high fidelity 3D images of complex organs, including human lungs. Using a new dataset of human foetal lung images throughout the key developmental stages, we are able to reconstruct its full network structure during development and map its organization in 3D. Leveraging computational tools, we carry out extensive network and morphological analysis. We show that—despite the complexity of the regulatory mechanisms involved—the growth dynamics can be described at a statistical level in terms of a few collective variables. We propose a minimal model of network growth based on a small set of simple, conserved rules, which reproduces key topological and morphological features. Our findings highlight the

importance of heterogeneity in the population of growing tips, the asymmetry in the branching dynamics, and the interplay between surface and bulk growth.

#### An underwater microbial railway network

Joseph Knight, University of Edinburgh, United Kingdom

Labyrinthula species are protist organisms found predominantly in coastal marine environments, notably as residents on seagrass leaves. A fascinating characteristic of this order, observed over a century ago but little studied since, is the ability for cells to secrete an extracellular ectoplasmic net. This allows colonies to form a spatial network of interconnected extracellular filaments across a substrate. Individual Labyrinthula cells are confined within these filaments and move independently about this network, akin to a microbial railway system. The collective and interconnected behaviour amongst moving cells and the expanding network invites a physics-based description to this biological system. In this developing project, we describe and classify the behaviour of growing network colonies and further show that the network morphology requires colony submersion beneath a seawater layer.

## <u>Drivers for transport in the gastrovascular network of Aurelia Aurita jellyfish : cilia vs. peristaltism</u>

Laureline Julien, University Paris-Cité, France

The jellyfish Aurelia aurita possesses a gastrovascular network responsible for digestion and nutrient transport throughout the organism. In the absence of a heart, with an open circulatory system and no smooth muscles lining the canals, the question arises: how is internal fluid flow maintained? Two main hypotheses have been proposed—ciliary-driven transport and peristaltic movements. Initial observations by Southward pointed to ciliary currents, a finding confirmed by our in vivo imaging of active cilia within the jellyfish's canals. The beating of the cilia generates directed flow and leads to measurable particle displacement, suggesting an active transport mechanism. To further characterize ciliary-driven flow, we combine analyses of ciliary beating patterns with rheological measurements of the canal fluid. As in many biological systems, transport likely results from a cooperative interaction between cilia and mucus. In addition, during swimming, the canals undergo rhythmic longitudinal compression and elongation, indicating that a length imposed peristaltic motion may also contribute. Our results show that in one canal two flow directions are visible, with or without contractions, but such contractions significantly increase mean flow velocity compared to anesthetised organisms. Moreover, this peristaltism is not purely local—it propagates as a network-wide effect, with spatially and temporally heterogeneous deformations impacting different regions of the canal system in distinct ways. Finally, we address the coexistence of these two transport mechanisms. Our observations suggest a complex interplay that may reflect an adaptive strategy for efficient internal transport in the absence of centralized pumping.

#### How mycorrhizal fungi build fluid-flow networks for underground nutrient trade Tom Shimizu, AMOLF

The exchange of nutrients between arbuscular mycorrhizal (AM) fungi and their plant hosts underlies growth of terrestrial vegetation that makes up ~85% of the Earth's biomass, and funnels several Gt of carbon into soil environments each year. Yet despite their importance for ecosystem function and carbon cycling at the planetary scale, little is known about the mechanisms that enable these fungal trade and transport behaviors. The hyphal tubes that

make up AM fungal networks are open conduits where carbon and other nutrients flow dynamically both toward and away from host roots. At AMOLF, we have been building new robotic imaging systems to map the full network topology of growing fungal networks, as well as internal flow dynamics. In this talk I will describe some of the insights gained from our efforts so far, about how an organism whose entire anatomy is a fluid-flow network functions as a 'connective tissue' for soil ecosystems, by efficiently exploring and moving resources to support an underground market of resource exchange evolved over ~450 million years.

#### **Posters**

Material for hanging posters and panels will be provided by Raitenhaslach.

#### Fluid Transport in Networks Inspired by the Lymphatic Vascular System

Omar Abukabsha, Aix-Marseille University, France

Vascular networks are essential for transporting resources and information in biological systems, from unicellular organisms[1] to humans[2]. In contrast to the cardiovascular system which is driven by a central pump (the heart), many biological networks rely on local driving mechanisms, leading to emergent[3] dynamics at the network scale. We investigate (1) how local nonlinear flow–pressure relationships promoted by simple valve geometries can generate flow directionality, and (2) how these local nonlinearities control global transport in connected networks.

We use numerical simulations[4] (lattice Boltzmann & immersed boundary) on a 2D channel containing two thin, flexible leaflets that deflect under oscillatory pressure gradients. Each leaflet is modeled as a rigid plate connected to a torsional spring and we solve the coupled fluid–structure interaction problem. Two nondimensional parameters govern the fluid-structure dynamics: the Womersley number, controlling flow inertia - which can play a role even in millimetric channels depending on the forcing frequency, and the visco-elasto number, controlling leaflet stiffness. Our results show that, at low Womersley numbers, the average flow rate is controlled by the visco-elasto number. At higher Womersley numbers, the averaged flow decreases due to fluid inertia. Extending this framework, we study how collective effects in densely packed multi-leaflet channels may reinforce pumping efficiency in bio-inspired systems, where we observe an optimum visco-elasto number for which the flow is maximized and we investigate how leaflet density affects this optimum and overall transport efficiency.

Insights from these local simulations provide a basis for developing phenomenological models to predict network scale dynamics. Building on these single- and multi-leaflet insights, we construct minimal flow network topologies by connecting flexible leaflet channels at junctions via Kirchhoff type conservation laws. This approach allows us to probe how network connectivity influences nonlinearity and flow directionality

This two-scale study will allow us to understand how microscopic leaflet mechanics drive macroscopic transport behaviors and give inspiration of bio-inspired pumping network designs.

- [1] Alim et al., Proceedings of the National Academy of Sciences 110 (2013)
- [2] Moore & Bertram, Annual Review of Fluid Mechanics 50, 459-482 (2018).
- [3] Ruiz-Garc´ıa & Katifori, Phys. Rev. E 103 (2021).
- [4] Gsell et al., J. Comput. Phys. 429, 109943 (2021).

#### Flow Imaging in Bi-directional Fungal Hyphae

Simon van Staalduine, VU Amsterdam / AMOLF, Netherlands

Arbuscular Mycorrhizal Fungi (AMF) have had a symbiotic relationship with land flora for millions of years, exchanging nutrients it finds in the soil for fixated carbon from its plant host. For this exchange to happen, nutrients need to move from the edge of the fungal network to the plant root, and carbon has to go the opposite direction. This macro bi-directionality in transport can also be seen in the micro, as bidirectional flows can be observed in almost all hyphae in a network, simply through videos made in brightfield. Analysing this transport can be challenging, as opposite flows frequently obstruct each other. Progress has been made in trying to find the flow velocity in both directions by treating it as a line finding problem in 3D space (x, y, and time). This analysis will aid in monitoring the decisions in transport that the fungus makes over the course of its network growth.

#### Neuromorphic Computing with Microfluidic Memristors

Nex Stuhlmüller, Utrecht University, Netherlands

Conical microfluidic channels filled with electrolytes exhibit volatile memristive behavior, offering a promising platform for energy-efficient, neuromorphic computing. Here, we integrate these iontronic channels as additional nonlinear elements in nonlinear Shinriki-inspired oscillators and demonstrate that they exhibit alternating chaotic and non-chaotic dynamics across a broad frequency range. Exploiting this behavior, we construct XOR and NAND gates by coupling three Memriki oscillators (Shinriki-like oscillators with memristors), and we further realize the full set of standard logic gates through combinations of NAND gates. Our results establish a new paradigm for iontronic computing and open avenues for scalable, low-power logical operations in microfluidic and bio-inspired systems.

#### The development of the jellyfish transport network

Stanisław Żukowski, University of Warsaw / Université Paris Cité, Poland/France

The jellyfish gastrovascular system is an example of a biological transport network providing nutrients to the tissues of the animal. As the jellyfish grows, new canals appear at the circular canal at the rim and grow towards the stomachs in the center. We study the morphogenesis of this canal network both in experiments in vivo and in numerical models. The growth of the canals occurs only at their tips. We investigate how the direction of their propagation is related to the physical mechanisms at play in the jellyfish - pressure inside the canals and tension in the tissue. The cells at the tip of a growing canal may sense the pressure or tension gradients, and similarly to the pattern formation processes in physics, be guided by the gradients of these physical fields. The changing geometry of the developing canal network affects the distribution of pressure in the canals and stress in the tissue. We study the feedback loop between changing geometry of the network and the physical fields around. We show how the canal network develops in time and what parameters are at play in morphogenesis of this network.

#### The role of cilia in pancreatic network morphogenesis

Yasmin Abdelghaffar, Technische Universität Dresden, Germany

During the course of development, the mammalian pancreatic ductal network remodels from a fully connected plexus to a tree-like branched network optimized for fluid transport. Previous in silico modeling suggested that this remodeling could be guided by flow through the network [1]. Yet the question of the mechanism of flow sensing within the pancreas remains open.

We quantitatively analyze duct network morphology at subsequent developmental time-points, including a spatial zonation of statistical network properties, to reverse-engineer putative physical mechanisms of network remodeling. We put forward theoretical descriptions e.g. of cilia-based flow sensing, which reproduce different variants of Murray's law, which should be distinguishable by future experiments.

[1] Dahl-Jesen et al., PLOS Biology, 2018.

# Nonlinear air invasion in compliant microfluidic networks: from one-dimensional series to reticulate models

Ludovic Keiser, Univ. Côte d'Azur, CNRS, France

Air invasion in vascular networks, or embolism, is a critical phenomenon in plant xylem, where sap flows under intense evaporative suction. In this work, we investigate the dynamics of embolism propagation using biomimetic microfluidic systems composed of compliant channels. Combining theory and experiments, we show how the coupling between capillarity, viscous dissipation, elastic deformation, and pervaporation leads to nonlinear front dynamics in simple one-dimensional series of constricted microchannels. By tuning geometric and material parameters, we map transitions between quasi-static and diffusion-limited regimes.

Building on these results, we extend our analysis to reticulate two-dimensional networks inspired by natural leaf venation. Beyond embolism propagation, our platform provides a versatile testbed for exploring other plant-related phenomena such as embolism repair.

# Numerical investigation of the effect of disease-induced red blood cell stiffness on red blood cell distribution in the microvasculature

Claire Denham, University of Edinburgh, United Kingdom

Several diseases and conditions, such as iron deficiency anaemia (IDA) and spherocytosis, may lead to red blood cells (RBCs) becoming stiffer. The distribution of the RBCs in microvasculature with the presence of these stiffer cells remains unclear. The stiffer cells may change the wall shear stress (WSS) detected by the endothelial cells (ECs) leading to vascular remodelling within the network. We hypothesise that these stiffer RBCs change the distribution across the network, in turn changing the WSS and morphology of the microvasculature. Using immersed-boundary-lattice-Boltzmann simulations, we explore the effect of presence of IDA and spherocytes on the haemodynamics of a honeycomb network with two generations of bifurcations. We investigate the change in distribution of RBCs as a result of the stiffer cells and the vessel constrictions. Our simulations show that the presence of stiffer cells changes the distribution of RBCs and in turn the WSS in networks. The

average WSS was found to be higher in the presence of stiffer cells for all vessel segments. For most vessel segments the stiffer RBCs lead to higher WSS peaks and variation. These differences in WSS patterns may lead to changes in the network morphology as a result of the conditions.

## <u>Microvascular structures and hypoxia in an animal model of glioblastoma</u> multiforme

Romain Enjalbert, University of Edinburgh, United Kingdom

Tumours have an abnormal microvasculature, which leads to impaired transport of oxygen to tumour tissue. A consequence of tumour hypoxia is that tumours are more aggressive and difficult to treat. The aim of this work is to compare microvascular phenotypes in an animal model of glioblastoma multiforme (GBM) compared to control brain tissue, and correlate tumour vascular phenotypes with hypoxia to further our understanding the structure-function relationship of the microvasculature in GBM.

We quantify the phenotypes in control and tumour-bearing mice, both expressing the fluorescent Cdh5-tdTomato vascular marker in endothelial cells. To generate tumours, mice were intracranially injected with GFP labelled GBM cells derived from a syngeneic mouse model of GBM (005). After tumour development the mice were injected with the hypoxia marker pimonidazole, prior to cull. Tissue sections of 508.94 µm x 508.94 µm x 150 µm had the vascular marker imaged with multiphoton microscopy to obtain three-dimensional images of sub-sections of the tumour microvasculature, which were then reconstructed in three-dimensional microvascular networks. The hypoxia and vascular markers were then imaged across the entire tumour slices in two-dimensions. The measured phenotypes in three-dimensions were vessel inter-bifurcation distance, vessel diameter, vessel aspect ratio, and mean tissue-vessel distance. While in two-dimensions, the tissue-vessel distance and hypoxic fraction of the tissue were quantified. The two-dimensional hypoxia images were registered to the three-dimensional vascular images to assess correlations of vascular phenotypes with hypoxia.

Our results show that in the two-dimensional tumour slices, the hypoxic fraction is heterogeneous throughout the tumour and does not correlate strongly with the tissue-vessel distance, nor the distance to the tumour core. In three dimensions, our results show that, in the tumours, the vessel interbifurcation distance and the mean tissue-vessel distance were significantly lower than in the control mice. The other quantified phenotypes did not show a statistically significant difference from the control. In addition, we see a significant difference between vascular metrics between the core and the edge of the tumour, with the core having larger vessels, higher tissue-vessel distance, and lower vessel interbifurcation distance. Next, we investigated the correlation of hypoxic fraction with the three-dimensional vascular metrics, with the vessel radius, aspect ratio and tissue-vessel distance correlating with the fraction of hypoxic tissue, and the interbifurcation distance having a strong negative correlation with the hypoxic fraction. Finally, we observe areas of hypoxic fraction superposed with the presence of vessels, suggesting the presence of acute hypoxia from poorly perfused blood vessels.

In this work we characterised the microvascular landscape and its correlation to hypoxia in an animal model of GBM. Our work shows that tissue-vessel distance does not always predict hypoxia, with extreme cases showing overlap of hypoxia and vascular markers, while other abnormal phenotypes, such as reduced interbifurcation distance, predict hypoxia. Given the importance of the microvasculature in the tumour microenvironment, the relationship between vascular phenotypes and hypoxia can lead to better tumour treatment

and diagnosis. Future work will quantify how vasculature, drug delivery and hypoxia are interrelated to further investigate the structure and function of microvascular networks in GBM.

#### Morphogenetic dynamics of endothelial cells on microparticle arrays

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Endothelial cells, which form the inner lining of blood vessels, can self-organize into capillary-like networks, a key process in vascular morphogenesis. We investigated how the spatial arrangement of microparticles affects endothelial network formation. Using time-lapse confocal microscopy and a custom Python-based image analysis pipeline, we quantified the influence of inter-particle spacing on network morphology, including e.g. area or connectivity, providing insight into the dynamics of capillary growth under geometric constraints. We also examined the effects of cytostatic drugs and tumor cells on network development. To support the experimental findings, we applied Cellular Potts Model iterated via the Metropolis Monte Carlo algorithm, and including diffusive transport of angiogenic factors and endothelial cells proliferation. Currently, the model captures some fundamental cellular behaviors in simplified single-microparticle systems. The ongoing integration of experimental and modeling approaches offers a versatile tool to investigate the principles of vascular network formation, including the impact of system geometry on endothelial cells behavior.

# Morphogenesis of the gastrovascular canal network in discomedusae: Variability and possible mechanisms

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Discomedusae are free-swimming medusae which are part of the phylum Cnidaria, the sister group to all animals with bilateral symmetry. Discomedusae possess a gastrovascular system with a canal network distributing nutrients and oxygen to tissues in the subumbrella. A large diversity of canal networks exists, from highly reticulated networks in Rhizostoma pulmo to purely branching networks in Cyanea capillata. The canal network of Aurelia jellyfish has a sparse reticulated network. By day-to-day macroscopic observations, we study the dynamics of the network formation in juvenile Aurelia jellyfish and model it numerically.

During the network development, at the circular canal at the rim of the jellyfish umbrella, an instability emerges in form of sprouts. They then grow toward the center of the jellyfish and reconnect to already existing radial canals. These reconnections have a bias to reconnect to the younger side radial canal. However, even in clones, there exists a variability towards which canal the reconnections occur. Similar to the revolutionary idea of Turing on morphogenic instabilities (1952), the canal network pattern is not strictly regulated, but rather grows from an instability, keeping trace of noise, and then self-organizes, guided by physical rules. We show that in Aurelia both the hydrodynamic effects, such as pressure in the canals, and elastic effects, such as deformation of the jellyfish body during swimming, govern the direction toward which the canal sprouts grow. We suggest that these morphogenic instabilities also play a role in the diverse patterns of canal networks in Rhizostoma pulmo and Cyanea capillata.

#### Spectral Properties of Ensnarled Networks

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In the vast realm of complex systems, the interplay between multiple networks is a recurring motif that permeates various domains, from crystal lattices and polymers to vascular systems and coiled DNA structures. Such structures may be represented by a graph theoretic framework, utilizing the Gauss linking numbers to quantify and characterize the interlinked state, which we define as 'ensnarlment'. We explore the spectral properties of the ensnarlment operator in different systems, from highly symmetric to disordered, including the developing liver, with the ultimate goal of understanding the dynamics of organ network architectures and their impact on pathophysiology. Furthermore, we develop a novel bipartite representation for ensnarled states and explore its spectral properties.

#### Structure-function relationship in physical networks via ensnarlment

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Understanding physical networks — whose structure is constrained by the physical properties of their nodes and links — is a growing interdisciplinary challenge, especially in biological systems. Physical constraints such as volume exclusion and non-crossing conditions, along with biological functionality, can drive these networks into non-optimal spatial configurations. One prominent feature is that cycles may go through each other's interior space, which may not be unraveled without removing edges, leading to an ensnarled state. Characterizing the 'ensnarlment' in the space, and its interplay with the functional behaviours of the network, is essential for revealing the structure–function relationship in such systems. In this work, we introduce a graph-theoretic framework based on the linking number operator, obtained by the Gauss linking integral applied to the cycle basis of the network. This approach enables a multiscale analysis of entanglement, spanning local, intermediate, and global structures. Our goal is to reveal how topological complexity shapes, and is shaped by, biological functions, providing new insights into the organizational principles of physical and biological networks.

#### How does an intracellular network generate cellular motion?

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Physarum polycephalum, a unicellular organism, achieves locomotion and maintains homeostasis through an internal porous network composed of actomyosin tubules. At the molecular scale, oscillatory calcium and ATP signals rhythmically trigger actomyosin contractions that propagate as waves through the tubular network, generating peristaltic cytoplasmic flow. Due to the network's porous architecture, the cytoplasm periodically inflates large cellular regions; when this inflation occurs at the cell periphery, it drives directional cell migration. I have developed tracking software capable of detecting the complete tubular network throughout the entire organism and monitoring the spatiotemporal dynamics of inflating and deflating regions. Now and in the future, I plan to employ differential equations to elucidate the causal relationships between tubule contractions and network properties, as well as between network dynamics and whole-cell displacement.

#### Coordination of Migration by Adaptive Mechanics

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The complexity of life emerges from the interactions of fundamental building blocks, whose collective behavior determines the functionality of tissues, organs and entire organisms.

For this reason, specific migration strategies and the associated internal mechano-chemical processes are of central importance in the study of various unicellular organisms, their behavioral adaptation and, ultimately, their role in shaping higher-order structures and interactions. These strategies are not limited to continuous persistent movement but can also involve dynamic regulatory mechanisms that modulate specific migration patterns. One distinct migration 'pattern' observed in unicellular migration are stationary oscillations interrupting persistent locomotion.

In the proposed PhD research, experimentally identified stationary oscillations in unicellular amoebae, particularly the slime mold P. polycephalum will be analyzed and modeled across two scale levels: macroscopic and intermediate. The stationary oscillations are characterized by the formation of protrusions that determine the direction of migration during persistent migration, making them a central measure to be studied on all spatial and temporal scale levels. In the first part, the chemotactic efficiency of larger and smaller plasmodia of the slime mold will be statistically evaluated from experimental data on a macroscopic scale. The second part will focus on the dynamics of the oscillations themselves, tracking and characterizing the oscillation and contraction patterns of individual migrating plasmodia to assess their role in migration phases and energy cost efficiency compared to persistent migration.

By integrating these perspectives, this study aims to provide a more thorough understanding of the mechanisms underlying oscillatory migration phases in the migration strategy of amoeboid organisms.

# <u>Searching for the mechanism of learning-like behavior in the slime mold Physarum polycephalum</u>

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The ability to learn is traditionally attributed to higher organisms and humans. In recent years, the rise of neural networks and an increasing focus on physical learning systems have shifted this paradigm. Physical learning systems, however, are usually passive systems, and their training requires performance feedback from a supervisor. Here we study the unicellular, network-shaped slime mold Physarum polycephalum, which, despite its simplistic makeup, displays a remarkable range of behaviors and problem-solving abilities. Using a combination of live recordings of Physarum networks subjected to stimuli and a reduced mechano-chemical model, we aim to identify the minimal requirements enabling the cell's behavioral repertoire. We hypothesize that a combination of short-timescale contraction patterns and long-term tube radius adaptation in this active system could facilitate processes resembling unsupervised learning in a single cell.