CPB | Cambridge Centre for Physical Biology

Annual Meeting 2022

29th April | Old Divinity School

POSTER

Blurbs

The mechanical control of differential growth in plants

Ross Carter, Ankit Walia, Alexander Jones, Henrik Jönsson
Sainsbury Laboratory, Cambridge University, UK

Morphogenesis in plants is driven wholly by growth and cell division. To efficiently grow into the diverse forms seen in plant organs the careful control of differential growth must be achieved. In this work we use the Arabidopsis apical hook as a model system the understand the mechanical control of differential growth.
With the use of analytics and dynamic, anisotropic, hyper-elastic mechanical models we can account for several surprising observations and make estimates on biologically relevant parameters. We show that the careful control of material anisotropy, through the differential alignment of cellulose, is key for achieving predictable and efficient differential growth. We also highlight the importance of differential force gradients in enabling robust morphogenesis.

The mechanical regulation of Eph/ephrin signalling in the developing frog brain

Jana Sipkova, Sudipta Mukherjee, Kristian Franze
PDN, Cambridge University, UK

Eph receptors and their membrane-bound ligands, ephrins, are key in many developmental processes including neuronal guidance. As axon pathfinding is regulated by chemical and mechanical signals, and discrepancies between *in vivo* and *in vitro* work on Eph/ephrin signalling remain, we investigated the role of mechanical cues in this signalling pathway. We found that Eph/ephrin signalling in cultured frog retinal neurons is affected by substrate stiffness, and a stiffness gradient develops across the visual area of the brain at the time of innervation. Our data suggests mechanical cues could be important in tuning neuronal guidance through the regulation of chemical signalling.

Mechanical and long-range signalling interactions in the developing *Xenopus* brain

Rachel Mckeown
PDN, Cambridge University, UK

Many studies have shown that embryonic axons can be guided to their targets by chemical guidance cues, but more recently local tissue stiffness has been found to contribute. Preliminary data suggest that the strength of chemical guidance cue responses is regulated by substrate stiffness through changes to resting biochemical state. To further explore interactions between chemical and mechanical signalling pathways, we have developed a novel microfluidics-based turning assay to assess *Xenopus* retinal ganglion cell axon

responses to chemical guidance cues on hydrogels of tunable stiffness. Ultimately, such interactions may enable high-fidelity axon pathfinding despite shallow and noisy *in vivo* gradients.

Evolution of genome fragility enables microbial division of labour

Enrico Sandro Colizzi
Sainsbury Laboratory, Cambridge University, UK

The genome architecture of multicellular organisms has evolved to enable cell differentiation into distinct phenotypes. Cell differentiation may be coordinated through gene regulation, as occurs during embryonic development. Alternatively, when mutation rates are high, mutations themselves can guide cell and functional differentiation: however, how this evolves and is organized at the genome level remains unclear.
Using a model of antibiotic-producing bacteria based on multicellular Streptomyces, we show that if antibiotic production trades off with replication, genomic organization co-evolves with genomic instabilities to enable reproductive division of labor. These results are consistent with recent experimental observations and may underlie division of labor in many bacterial groups.

Hollow-core photonic crystal fibres for label-free protein analysis

Jan Heck
Department of Physics, Cambridge University, UK

We report on our latest advances in using hollow-core photonic crystal fibres for label-free protein analysis. These optofluidic waveguides surround a microfluidic 30 µm channel with a glass microstructure that guides and confines light by anti-resonant interference. The microfluidic waveguiding channel collects light along its entire length, allowing us to analyse sub-µL quantities of label-free proteins under flow by exciting their weak intrinsic fluorescence at 280 nm deep-UV over a 10 cm pathlength. Our vision is to develop this system into a versatile, low sample volume, preparation-free biosensing platform easily integrated with microfluidic technology.

Development and preliminary testing of an optical, wearable, neuroimaging system

Georgina Leadley
Department of Paediatrics, Cambridge University, UK

Recently, optical technology has emerged as an exciting alternative to conventional functional brain imaging, such as fMRI. Infrared light can be used to create imaging caps which are cheap, non-invasive, portable and capable of obtaining maps of brain activity. An array of hexagonal imaging tiles with 5-wavelength LEDs and photodetectors are used to reconstruct 3D images of brain oxygenation and metabolism. These caps have the potential to be used on newborn babies with brain injuries where there is a critical treatment window or with Alzheimer's patients. Where in both cases an early diagnosis could improve their outcome.

Identifying Piezo1-dependent chemical signals in the developing *Xenopus laevis* neuroepithelium

Sudipta Mukherjee
PDN, Cambridge University, UK

During development, neurons extend axons across large distances to predefined targets, ensuring proper development of functional neural circuits. Axon pathfinding is regulated by both chemical and mechanical signals. However, how chemical and mechanical signals interact is currently unclear. Here, we conducted a candidate-based screen of chemical signalling molecules regulating axon pathfinding in embryonic *Xenopus* brains with downregulated expression of the mechanosensitive ion channel, Piezo1, using *in situ* hybridisation chain reaction. Our results suggest that the availability of key signalling molecules in the brain depends on mechanical signalling through Piezo1, which will likely be highly relevant to many other biological systems.

Invagination of the mesoderm mechanically impacts the adjacent elongating ectoderm during Drosophila gastrulation: what are the consequences for morphogenesis?

Lye CM, Blanchard GB, Nestor-Bergmann A, Evans J, Sanson B.
PDN, Cambridge University, UK

As tissues grow and change shape during animal development they physically pull and push on each other. Are these mechanical interactions important for the morphogenesis of tissues? And, if so, by what mechanisms? During *Drosophila* axis extension it has been shown that an axial pull from the posterior endoderm mechanically drives cell shape

changes and helps orient cell rearrangements in the extending ectodermal germband[1-2]. We now address the impact on the elongating germband of a perpendicular pull from the mesoderm, which has been proposed to increase the rate of cell rearrangements in the germband through mechanical augmentation of MyoII polarity.

Self-assembled RNA origami-based codes for exploring RNA diversity

Filip Boskovic
Department of Physics, Cambridge University, UK

RNA is a key player in the transfer of information and regulation of biological processes underlined by the immense potential for RNA-based therapeutics. Identifying RNA requires intricate protocols that suffer from various enzymatic biases and lead to irreversible loss of native RNA information. Here we design three-dimensional molecular constructs that enable identification of native RNA at the single-molecule level using nanopore microscopy. We identified multiple RNA variants of messenger RNA and long non-coding RNA in human cervical adenocarcinoma. Our approach has the potential to discriminate up to 10 billion unique RNAs in a one-step, enzyme-free reaction in a human transcriptome.

In-vivo reconstruction of the main evolutionary transitions during vertebrate gastrulation

Guillermo Serrano Najera
Department of Genetics, Cambridge University, UK

The morphology of gastrulation driving the internalisation of the mesoderm and endoderm differs dramatically among vertebrate species. It ranges from involution of epithelial sheets of cells through a circular blastopore in amphibians to ingression of mesenchymal cells through a primitive streak in amniotes. How these different morphologies arise during evolution remains unresolved. We generated crescent- and ring-shaped mesendoderm territories in which cells can or cannot ingress by targeting key signalling pathways controlling critical cell behaviours in the chick embryo. We found that these alterations subvert the formation of the chick primitive streak into the gastrulation modes seen in amphibians, reptiles, and fish.

Synonymous mutations reveal genome-wide driver mutation rates in healthy tissues

Gladys Y. P. Poon, Caroline J. Watson1, Daniel S. Fisher, Jamie R. Blundell
Department of Oncology, Cambridge University, UK

Genetic alterations under positive selection in healthy tissues have implications for cancer risk. However, total levels of positive selection across the genome remain unknown. Passenger mutations are influenced by all driver mutations, regardless of type or location in the genome. Therefore, the total number of passengers can be used to estimate the total number of drivers—including unidentified drivers outside of cancer genes that are traditionally missed. Here we analyze the variant allele frequency spectrum of synonymous mutations from healthy blood and esophagus to quantify levels of missing positive selection.

Diverse multiscale mathematical approaches can reveal the secrets behind plant morphogenesis

Euan Smithers
Sainsbury Lab, Cambridge University, UK

We apply various mathematical modelling and analysis techniques to understand how plants grow complicated shapes across multiple scales. By examining the microscale, we can provide insights into how the cell wall is structured and loosened to permit growth. At the cell scale, by simulating dynamic intertwining signalling pathways we can answer how cells form elaborate shapes. Finally, by modelling inflated plant cells at the tissue scale, how plant tissues form complex morphologies can be understood. All of these processes feedback on one another, making it vital to examine multiscale dynamics.

The nanoscale architecture of filopodia tips

Thomas Blake
Department of Biochemistry, Cambridge University, UK

Filopodia are narrow plasma membrane protrusions used for cell motility, formed of an F-actin bundle, and controlled by a “tip complex” of actin binding proteins. The composition of the tip complex is heterogeneous, and the nanoscale architecture of actin bundle, tip complex and surrounding membrane remains to be determined. I am studying *Xenopus* retinal ganglion cells – where filopodia contribute to neuronal development – with nanoscopy techniques such as STORM and PALM, to compare the arrangement of actin with tip complex proteins Ena/VASP, Myosin X and SNX9. These proteins show distinct localisation patterns, revealing that the architecture of filopodia tips is complex.