How to make an eye – Mechanics of optic cup formation across species

Supervisory team:
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Project description:
Morphogenesis is a mechanical process whereby forces exert stress, causing cell and tissue deformation and leading to the formation of 3D tissue and organ shapes. During organ development, epithelial tissues - the key building blocks - undergo morphogenetic remodelling through complex interactions with the basement membrane (BM), a specialized extracellular matrix. The BM, primarily composed of a Collagen network, provides rigidity essential for tissue shape and resistance to mechanical stress. Notably, defects in BM formation, structure or turnover are hallmarks of various human diseases and developmental anomalies, including eye malformations. Despite their importance in development and disease, the role of BMs in shaping tissues remains poorly understood.

This PhD project will explore how BM structure and growth generate stresses that mechanically guide early vertebrate eye morphogenesis. In early eye development, the optic vesicle epithelium bends inward to form the optic cup (OC). Epithelial bending and OC formation depend on the BM: Mutations in the major BM proteins lead to strongly reduced OC invagination in zebrafish and chicken embryos. Interestingly, OC invagination is fast (few hours) and linked to cell migration in zebrafish but slow (few days) and likely migration-independent in chickens. Collectively, these results highlight an essential role for the BM in early eye morphogenesis, though the precise mechanistic logic of OC invagination remains elusive.

Recent work by the Harmansa group shows that differences in BM growth lead to stress accumulation, elastic deformation and tissue bending. This PhD project aims to investigate whether such differences in BM growth and structure explain the distinct dynamics and mechanisms of OC invagination between fish versus chickens. Specifically, the project will examine how BM remodelling and structure influence the stress patterns driving this process.

This interdisciplinary PhD offers a unique opportunity to work at the intersection of developmental biology, biophysics and computational modelling. The successful candidate will use a combination of genetics (transgenesis in zebrafish), advanced high-resolution imaging, quantitative biophysical methods (AFM, laser ablation), and genetic perturbations in fish and chicken, while collaborating with theorists to develop data-informed simulation frameworks. This cross-species analysis will provide novel insights into the role of BM's in OC morphogenesis and offer an excellent training opportunity in a wide range of techniques bridging biology, physics, and mechanics.

Our aim as the SWBio DTP is to support students from a range of backgrounds and circumstances. Where needed, we will work with you to take into consideration reasonable project adaptations (for example to support caring responsibilities, disabilities, other significant personal circumstances) as well as flexible working and part-time study requests, to enable greater access to a PhD. All our supervisors support us with this aim, so please feel comfortable in discussing further with the listed PhD project supervisor to see what is feasible.