NeuroForceSensor - Does inter-tissue mechanical coupling coordinate neural tube closure?

Failure of neural tube closure causes neural tube defects (NTDs), which continue to affect 1:1,000 births in Europe. Successful closure requires poorly understood coordination of cellular force-generating mechanisms in different embryonic tissues. By adopting a novel bio-engineering approach, I aim to generate the first spatiotemporal map of mechanical forces in neural tube closure. This unified biomechanical understanding of morphogenesis will provide a step-change in our interpretation of genetic/teratogenic insults underlying NTDs.

In this project, I will identify the physical forces mediating neural tube closure and describe their inter-tissue coordination during development. This will be based on intravital 3D (i3D) bioprinting, a novel method established by the Elvassore group at UniPd (host).

This method allows 3D printing of biocompatible force sensors directly inside the neural tube of living chick embryos, a wellestablished vertebrate model. Combined with cutting edge chemical engineering and computational modelling, I will investigate the spatiotemporal coordination of mechanical forces and assess whether connected epithelial tissues are mechanically coupled. The high positional accuracy of i3D enables previously unfeasible perturbations of morphogenesis to test mechanical coupling between connected epithelia. These physical interventions will be paralleled by microfluidic regional delivery of pharmacological inhibitors to biochemically perturb the same morphogenetic processes. Together these studies will pave the way for the identification of novel preventative and therapeutic strategies to enhance cellular force-generating mechanisms during neural tube closure.

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