PhD THESIS DEFENSE:Bridging Fast Volumetric Imaging and Mechanical Stimulation: A Platform for Studying Mechanosensitive Neurons Functionality Onset in C. elegans Embryos

COSTANZA AGAZZI

June 27, 2025

14:15

ICFO Auditorium

In Caenorhabditis elegans, the embryo develops within the protective confines of an eggshell, shielded from direct interactions with the outside world. In this isolated environment, neuronal mechanosensory circuits, responsible for translating physical forces into biochemical signals, are among the first to emerge during development. While their primary function is to mediate interactions with the external mechanical world, they also play a significant role in broader physiological and behavioral processes, including synaptic plasticity and social bonding.

c. elegans neurons responsible for the sense of touch arise very early during embryogenesis, long before any physical interaction, raising the question: when does the nervous system first awaken to the mechanical world it has yet to experience?

Unraveling the onsets of mechanosensation has critical implications for neuroscience and human health, as its dysregulation is linked to various diseases and neurodevelopmental disorders. For example, studies on mouse models of autism spectrum disorder (ASD) have demonstrated that the timing of mechanosensory disruptions during embryogenesis plays a pivotal role in determining the severity of the condition. Despite its importance, our understanding of when mechanosensitivity first emerges remains limited, also due to the practical and ethical challenges of studying the application of mechanical forces to developing neural systems.

To address these challenges, the goal of this project was to develop a multifunctional experimental platform that combines precision mechanical stimulation with live volumetric imaging, enabling the investigation of induced calcium signals in the developing neural

system of C. elegans embryos. Central to this platform is a custom open-top light sheet fluorescence microscope, optimized for fast, 3D imaging of calcium dynamics.

The imaging unit is integrated with a fiber-optic-based nanoindenter, which provides precise force application and quantitative characterization of the mechanical properties of the sample. This setup allows for controlled mechanical stimulation while capturing real-time neuronal activity, facilitating the analysis of how and when external forces influence mechanosensory circuits during critical developmental stages.

Using this platform, we conducted proof-of-concept experiments to explore mechanosensory responses in C. elegans embryos. These studies validated the system's ability to trigger and record precise neuronal activity, demonstrating its experimental effectiveness. Preliminary findings suggest that mechanosensory functionality might begin to emerge during the late stages of embryogenesis of C. elegans embryos, offering a glimpse into the elusive timing of sensory circuits development. Overall, this work sets the stage fo future investigations into how these circuits awaken and their vital role in early neura development.

Friday June 27, 14:15 h. ICFO Auditorium
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