NEUROSCIENCE AND PHYSIOLOGY SEMINAR SERIES

MECHANOSENSING IN NEURONAL GROWTH AND GUIDANCE

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NEUROSCIENCE &
PHYSIOLOGY

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Neuronal growth cones are highly dynamic structures at the end of neurite tips, that explore the environment and establish new connections during neuronal development. It is well known that growth cones respond to diverse types of environmental cues such as a topography, stiffness, electrical fields, and molecular cues. Moreover, several studies had found that during axonal growth, the growth cone produces traction forces on the underlying substrate and pull the axon forward. However, the biophysics and molecular mechanism behind the growth cone's response to extracellular stiffness is unknown. To answer this problem, we fabricated polyacrylamide (PAA) hydrogels with different stiffnesses to characterize the growth of Aplysia bag cell neurons during mechanosensing. We found that in a stiff range between 0.3 and 30 kPa, the neurite outgrowth exhibits a biphasic behavior with respect to the stiffness and is optimal at 3 kPa. Moreover, when neurons were grown on PAA gels with a stiffness gradient between 0.3 and 3 kPa or between 3 and 30 kPa, the neurite outgrowth was higher towards the 3 kPa side, which supports the findings from uniform stiffness PAA gels. Additionally, we used experimental data of substrate-mediated growth cone advance to adapt an existing computational model of the substrate-cytoskeleton coupling to understand the cytoskeletal dynamics during growth cone mechanosensing. We found that adhesion reinforcement and the increase of myosin force explain the fastest growth cone's response at a substrate stiffness of 4 pN/nm and the higher substrate deformation on soft substrates. Together, these results suggest that the neuronal outgrowth is optimal on softer substrates, which is relevant for the design of compliant materials and promote neuronal regeneration.

TUESDAY, APRIL 15TH, 2025
12:00 PM, LILY 1-117

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