# The Effect of Neuronal Interactions with Nano-Topographical Cues on the Morphology and Network Formation

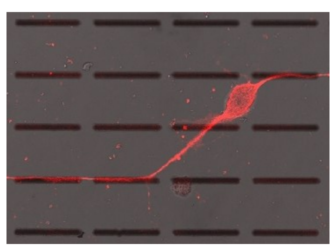
Koby Baranes, Erez Zion, Amos Sharoni and Orit Shefi, *Member, IEEE*

THE neurons are the fundamental building blocks of the nervous system. Understanding the influence of the neuronal chemical and physical environment on the neuronal growth has great implications for both neuronal repair and for neuro-engineering. Previous studies have identified processes that take place along neuronal growth and influence the geometry of the neuronal dendrites and axons, which show extremely diverse complex structures. A key mechanism is the ability of the motile growth cones at the tips of growing processes to measure environmental cues including mechanical cues. Thus, the substrate topography has an important role in neuronal growth. We study the effect of topographical cues at the nano-scale on the neuronal growth and morphology and on network formation.

We use photolithography to fabricate substrates with repeatable pattern ridges of nano-scale heights between 10nm and 150nm. We plate primary leech neurons atop of the patterned substrates and follow their growth for several days, from single isolated neurons to elaborated networks. We compare the growth process to neurons atop non-patterned substrates. We use high resolution microscopy and immunostaining to examine the effects on the morphology and the interactions with the nano-ridges. We analyze the response of single branches as well as the entire neuronal branching tree to the patterned substrates.

We show that nano-scale topographical cues substantially modify the neuronal growth pattern that can be altered even by cues as low as 10nm [1]. We demonstrate that the attachment of the neuronal processes to the nano-cues significantly promotes neuronal growth. The effect on the neuronal growth is measured by the change of the process direction, meaning when the process reaches the topographical ridges whether it continues in its original direction or changes it. According to our findings, there is a correlation between the interaction strength and the ridges' height (between 10nm to 100nm heights). Lower ridges provide less support and less anchoring possibilities for turning neurites where the higher ridges are more effective and deflect most of the crossing processes. Thus, we underline the adhesion as a key mechanism in the neuron-ridges interaction. Moreover, we find that the interactions with the nano-cues trigger a growth strategy similar to growth after the formation of contact with other neuronal cells [2]. The number of branches and the number of neurites originating from the soma decrease following the interaction, demonstrating a tendency to a more simplified neuronal branching tree.

Our results raise the question whether neurons identify the interactions with the nano-ridges as functional. Further investigation will strengthen our understanding of the interplay between neuronal function and form and will enable us to develop and design neural networks for neuronal-based devices.



## References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K. B. Author is with the Faculty of Engineering and Bar Ilan Institute of Nanotechnologies and Advanced Materials (BINA), Bar Ilan University, Ramat Gan, 5290002 Israel (Phone: 972-3-7384646; fax: 972-3-7384646; e-mail: baranesk@gmail.com).

E. Z. Author is with the Department of Physics and BINA, Bar Ilan University, Ramat Gan, 5290002, Israel (e-mail: zion.erez@gmail.com).

A. S. Author is with the Department of Physics and BINA, Bar Ilan University, Ramat Gan, 5290002, Israel (e-mail: amos.sharoni@biu.ac.il).

O. S. Author is with the Faculty of Engineering and BINA, Bar Ilan University, Ramat Gan, 5290002, Israel (e-mail: orit.shefi@biu.ac.il).