Subcellular Force Dynamics of Outgrowing Axons Measured by Free-standing Nanowires.

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The mechanical interactions between living cells (e.g nerve cells) and their environment are tremendously dynamic at the sub-micrometer scale. Together with bio-chemical signaling, those interactions play an important role for cell functions as well as for cell/substrate and cell/cell communication. Therefore, suitable methods for studying such subtle mechanical systems are required. This is especially important when trying to measure the minute forces exerted by sub-cellular structures of outgrowing nerve fibers (axons). The leading edge of a nerve fiber – the growth cone, continuously sends out and withdraws very fine processes. Those processes, called lamellipodia and filipodia have dimensions in the 100 nm regime or below. The avail of dedicated nano-structures to study them is obvious.

Here we show that free-standing monolithic GaP nanowires grown by MOCVD can be used as a substrate to measure forces of axonal growth cones with excellent resolution in time, space and force magnitude.
Nanowires were grown in regular arrays defined by ebl with a wire-separation of 1 µm. The wires were fluorescently labeled and nerve cell solution was added. The nerve cells were allowed to grow on top of the nanowires, adhering to their tips [1]. The movements of the wire tips were monitored and recorded by confocal microscopy (fig 1). From analysis of the tip movements (i.e the nanowire deflections) values on magnitudes and directions of the cell-generated forces could be extracted at each wire position at each time point (fig 2 and 3).

Knowledge of the growth cone force dynamics in outgrowing nerve fibers improves the understanding of the developing or regenerating nervous system, and provides a stronger platform for controlling axonal outgrowth in artificial systems.

[1] W. Hällström, T. Mårtensson, C. Prinz, P. Gustavsson, L. Montelius, L. Samuelson, M. Kanje : *Gallium phosphide nanowires as a substrate for cultured neurons*. Nano Letters 7 (10) : 2960-2965 Oct 2007.

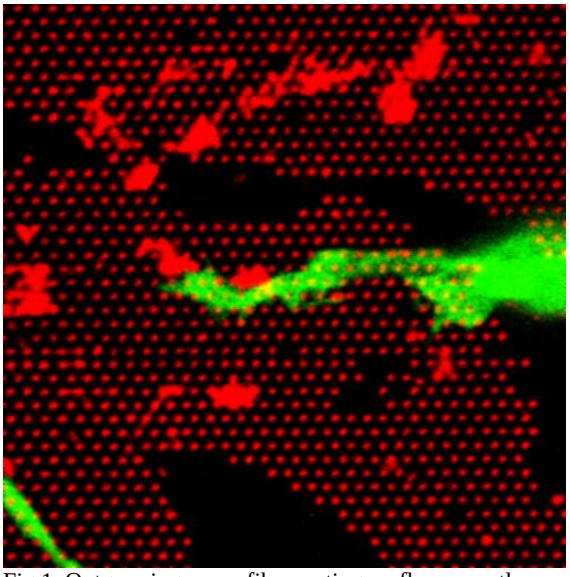

Fig 1. Outgrowing nerve fiber resting on fluorescently labeled nanowires. The force dynamics of the nerve-process are obtained from the motions of the wire tips (red dots). The distance between wires (horizontally) is 1 μm.

Fig 2. Force field from an axonal growth cone. The magnitudes and directions of the forces generated by the evolving structure are illustrated. The distance between wires (horizontally) is 1 μm.

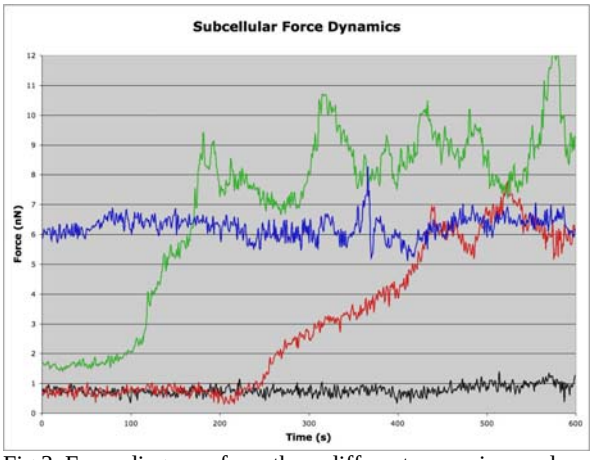

Fig 3. Force diagrams from three different nanowires under an outgrowing neural growth cone. The black curve illustrates a nanowire not in contact with the growth cone.