Experimental evaluation of biophysical neurite growth models
ZACHARY WISSNER-GROSS, Harvard University, MARK SCOTT, DAVID KU, PRIYA RAMASWAMY, MEHMET YANIK, Massachusetts Institute of Technology — During nervous system development, neurons exhibit complex growth dynamics, as several neurites compete to become each neuron’s axon. Numerous mathematical and biophysical models have been proposed to explain this competition, but these models remain experimentally unverified. Large-scale and repeatable measurements of neurite dynamics are difficult to perform, since neurons have varying numbers of neurites, which themselves have complex morphologies. To overcome these challenges using a minimal number of primary neurons, we generated repeatable neuronal morphologies by laser-patterning micron-wide stripes of adhesive proteins on an otherwise highly non-adherent substrate. Upon analyzing thousands of time-lapse measurements, we observed three key neuronal behaviors: total neurite growth accelerated until neurons polarized, immature neurites competed even at very short lengths, and neuronal polarity underwent an apparent phase transition as the neurites grew beyond a critical length. Proposed biophysical neurite growth models agreed only partially with our experimental observations, and simple yet specific modifications significantly improved these models. The protein patterning and high-content analyses presented here could also be employed for studying other structural or biomechanical cellular phenomena.

Zachary Wissner-Gross
Harvard University

Date submitted: 19 Nov 2010

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