A Multiscale-Multiphysics Model for Axon Pathfinding Simulation, the Example of the Olfactory System

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Abstract

In the developing embryo, neurons form connections by projecting axons to appropriate target areas. The projection process includes neurite elongation, resulting from the assembly of new cytoskeletal material at the free end of the axon [1], a complex cascade of steering decisions, driven by signals in the surrounding environment [2,3], and the biomechanical properties of the extracellular matrix [4]. In the olfactory system, individual axons of olfactory receptor neurons (ORNs) located in the epithelium lining the nasal cavity project to the olfactory bulb where they synapse on the dendrites of second-order neurons within globular structures of neuropil - glomeruli [5]. It was recently discovered that all of the axons from ORNs expressing the same odorant receptor gene converge onto two (or a few) glomeruli in the bulb. The location of these glomeruli is bilaterally symmetrical and invariant across animals. However, little is understood about the mechanisms in the olfactory bulb governing such precise topographical targeting by ORN axons. Continual neurogenesis in the subventricular zone of postnatal and adult forebrain has been well documented, but the mechanisms underlying cell migration/differentiation from this region are poorly understood [6]. In this work we focus on the early development of the olfactory nerve. In particular, we discuss a mathematical and numerical multiscale framework aimed at obtaining a description of the morphological organization of the axons at the first steps of the olfactory system formation. In Figure 1. we briefly described the main factors involves in migration, guidance and organization of axon projection. We represent each axon as a 1D elastic body immersed in the extracellular matrix, modeled in turn as a 2D continuum deformable body. The axon is supposed to be clamped at a boundary of the matrix and to grow away from this position with an intrinsic growth rate. Unless otherwise in by virtue of the inherent rigidity of their internal microtubular structure Axon motion can be deviated by the presence of chemical signals [7,8] and by the deformations imposed by the surrounding matrix. Then we have to couple biochemical models, biomechanical properties, diffusion of suitable cues in a moving domain in a multiphysics framework. In Figure 2. we report an example of a 2D simulation of axon fasciculation. Here we also discuss possible applications and generalizations with the numerical difficulties in the computational approach.

Reference

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Figures used in the abstract

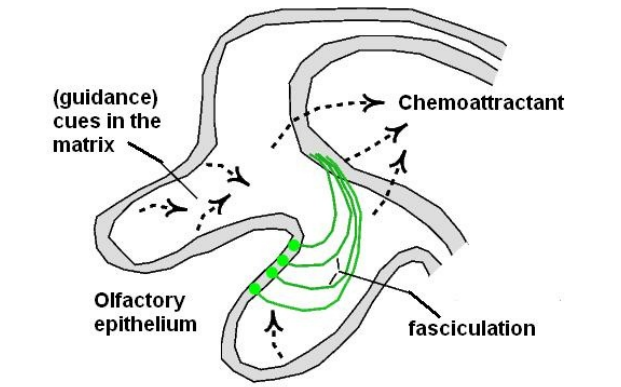

Figure 1: Schematic representation of main factors in axon projection for the olfactory system.

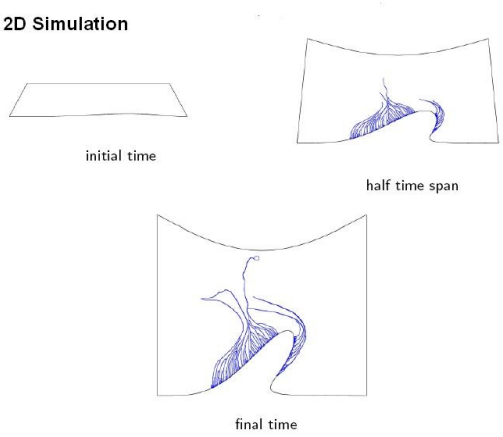

Figure 2: Numerical simulation of 2D axon fasciculation in a deformable region.