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Continuum mechanical modeling of axonal growth

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Abstract

Axonal growth is a complex phenomenon in which many intra- and extra-cellular signals collaborate simultaneously. Two different compartments can be identified in the growing axon: the growth cone, the leading tip that guides and steers the axon, and the axonal shaft, connecting the soma to the growth cone. The complex relations between both compartments and how their interaction leads the axon to its final synaptic target remain a topic of intense scrutiny. Here, we present a continuum and computational model for the development of the axonal shaft. Two different regions are considered: the axoplasm, filled with microtubules, and the surrounding cortical membrane, consisting mainly of F-actin, Myosin II motor proteins and the membrane. Based on the theory of morphoelasticity, the deformation gradient is decomposed into anelastic and viscoelastic parts. The former corresponds to either a growth tensor for the axoplasm, or a composition of growth and contractile tensors for the cortical membrane. The biophysical evolution for the anelastic parts is obtained at the constitutive level, in which the polymerization and depolymerization of microtubules and F-actin drive the growth, while the contractility is due to the pulling exerted by the Myosin II on the F-actin and depends on the stress. The coupling between cytoskeletal dynamics and mechanics is naturally derived from the equilibrium equations. The framework is exploited in two representative scenarios in which an external force is applied to the axonal shaft either along the axis or off the axis. In the first case three states are found: growth, collapse and stall. In the second case, axonal turning is observed. This framework is suitable to investigate the complex relationship between the local mechanical state, the cytoskeletal polymerization/depolymerization rates, and the contractility of the cortical membrane in axonal guidance.

Keywords: axonal guidance, axonal turning, continuum modeling, axonal elongation

Las neuronas son células de formas delicadas y elegantes, las misteriosas mariposas del alma, cuyo batir de alas quién sabe si esclarecerá algún día el secreto de la vida mental.
Santiago Ramón y Cajal

1. Introduction

The pioneering work of Santiago Ramón y Cajal taught us that cognitive functions are carried out in the brain by neurons through synaptic connections (Cajal, 1909; DeFelipe and Jones, 1988; Pasik and Pasik, 1999). Neurons are electrical excitable cells that are morphologically divided into two different compartments: *the cell body* or *soma*, where the cell nucleus and other organelles are situated; and *the neurites*, which are thin tube-like processes extending from the soma and aimed at establishing synaptic connections with other processes of other neurons to create the neuronal network. The neurites can be classified into dendrites and axons: The electrical signal travels from the synapses to the soma for the former, and the signal is transmitted away from the soma to the synapses for the latter.

Neuronal growth is the key process necessary to establish the neuronal network during neurogenesis. Besides its vital role, neuronal growth also fulfills crucial functions in human brain plasticity (Pascual-Leone et al., 2005) and neuronal regeneration (Silver and Miller, 2004; Case and Tessier-Lavigne, 2005; Bradke et al.,