Abstract in English

While axon fasciculation plays a key role in the development of neural networks, very little is known about its dynamics and the underlying biophysical mechanisms. In a model system composed of neurons grown *ex vivo* from explants of embryonic mouse olfactory epithelia, we observed that axons dynamically interact with each other through their shafts, leading to zippering and unzippering behaviour that regulates their fasciculation. Taking advantage of this new preparation suitable for studying such interactions, we carried out a detailed biophysical analysis of zippering, occurring either spontaneously or induced by micromanipulations and pharmacological treatments.

We show that zippering arises from the competition of axon-axon adhesion and mechanical tension in the axons. This is upheld on quantitative level by conforming change of network global structure in response to various pharmacological treatments, without active involvement of growth cones. The calibrated manipulations of interacting shafts provide qualitative support for the hypothesis, and also allow us to quantify the mechanical tension of axons in our system. Furthermore, we introduce a biophysical model of the zippering dynamics, which efficiently serves the purpose of estimating the magnitude of remaining involved biophysical quantities. We provide several independent and consistent quantifications of the force of axon-axon adhesion, which is to our knowledge first such estimate. The framework of our model allows us to carefully examine dissipative forces related to local shaft dynamics, determine dominating dissipative mechanism for a particular type of observed process, and estimate the value of corresponding friction coefficient.

We perform segmentation of the developing axonal network from the time lapse recording, and extract statistical and shape descriptors of its graph representation. We show that the network global statistics and local geometry changes are correlated and their time course consistent with qualitative predictions of our zipper model. We then quantitatively relate the individual zipper properties to global characteristics of the developing axon network *ex vivo*, and apply the model framework to reconcile *in vivo* data of population-wide distribution of axon incidence angles with data of probability of particular axon crossing in that population, reported by Roberts and Taylor in 1982. We compare the topological evolution of our *ex vivo* system to two-dimensional froths; the unique character of axonal network evokes many analogies with liquid foams, while it demonstrates many unique features, notably more robust stability of topological configurations and reversibility of some processes which change topology.

We show that there is a consistent mechanism which governs local interactions between axon shafts, supported by broad experimental evidence. This mechanism can be reconciled with changes in global structure of axonal network developing on slower time scale, analogically to well-studied relation between local relaxations, and topological changes and coarsening in two-dimensional liquid foams. We assess our observations and analysis in light of possible *in vivo* functional significance and propose a new role of mechanical tension in neural development: the regulation of axon fasciculation and consequently formation of neuronal topographic maps.