

Sensory perception is a complex process that allows organisms to realise their environment and to respond accordingly. Therefore, sensory dysfunction can be a major handicap that dramatically decreases the quality of life of the affected individual. Because sensory systems consist of sensory receptors connected to higher brain areas with cognitive functions *via* neural pathways, the establishment of sensory organ **innervation** is crucial for behaviour, social interaction and survival. Vertebrate sensory organs represent an excellent model for studies that converge at the interface between intrinsic and activity-dependent processes controlling the establishment and maintenance of organ innervation.

A major obstacle in studies of sensory systems is that direct observation of the sensory organs in their native context at spatial and temporal high resolution is very challenging. For example, mechanosensory hair cells in birds and mammals can only be found in the inner ear, which is very difficult to access, even in new-born animals. By contrast, the zebrafish senses fluctuations in water pressure *via* a functionally sophisticated but anatomically simple mechanosensory organ called **the lateral line**, whose structure and physiology are homologous to those of the mammalian inner ear. The lateral line is formed by a collection of isolated functional units called **neuromasts** composed of a core of mechanosensory hair cells innervated by at least two **afferent neurons** (*figure 1A-C*). After the neuromasts have fully developed, their constituent hair cells are continually renewed and can be efficiently replaced after injury. New hair cells become functional within a few hours after birth, which indicates that they re-innervate quickly and with exquisite precision.

Some aquatic vertebrates such as the zebrafish have neuromasts consisting of two subpopulations of hair cells, equal in number, whose **hair bundles are oriented at 180° relative to each other** (*figure 1D*). How hair cells of opposite planar polarities are innervated remains controversial. It is also not known how sensory neurons behave during the regeneration of hair cells.

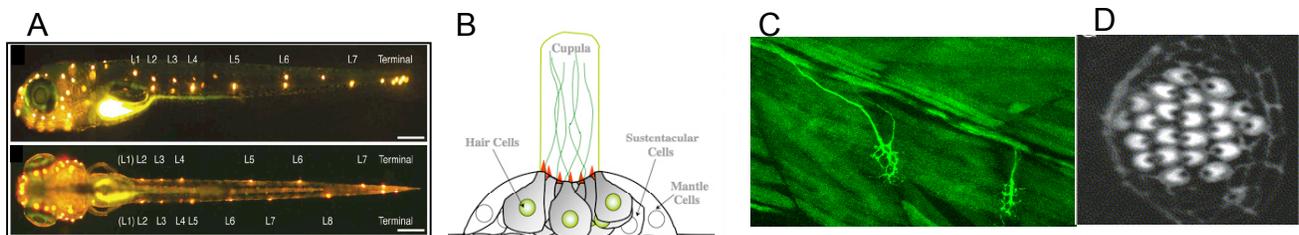


Figure 1 : Zebrafish lateral line. (A): The zebrafish lateral line comprises 2 parts : the anterior lateral line (ALL) which is localised anterior to the ear and the posterior lateral line (PLL) which extends along the body and tail of the fish (L1 to Terminal; 4-Di-2-Asp in 6dpf larva). (B): Scheme of a neuromast with all its constituent cells. Neurons innervate hair cells from the base of the organ. (C) : Dendritic arbour of two afferent neurons branching off the lateralis nerve. (D) : The polarization of hair cells is evident in this neuromast whose actin-rich stereocilia were stained with rhodamine-phalloidin.

To investigate the mechanisms that govern the appropriate innervation of hair cells, we conducted a systematic and comprehensive study of the processes that underlie the elaboration and remodeling of sensory-neuronal architecture in the lateral-line organ. We showed that afferent neurons are **strict selectors** of polarity that can re-establish synapses with identically oriented targets during hair-cell regeneration. To gain insight into the mechanism that underlies this selection, we devised a simple method to gather dynamic morphometric information of axonal terminals in toto by four-dimensional imaging. Applying this strategy to the zebrafish allowed us to correlate hair-cell orientation to single afferent neurons at sub-cellular resolution. We show that in zebrafish with absent hair-cell mechanoreception (deaf fish mutants), lateralis afferents arborize profusely in the periphery, display less stability, and make improper target selections (*figure 2*). We propose that **the hardwired developmental mechanisms that underlie peripheral arborization and target recognition are modulated by evoked hair-cell activity**. This interplay between intrinsic and extrinsic cues is essential for plane-polarized target selection by lateralis afferent neurons.

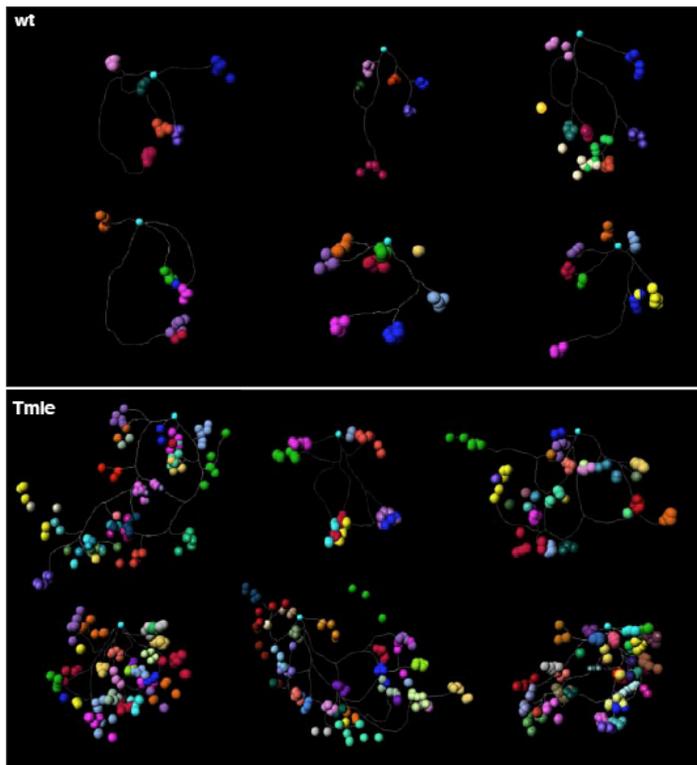


Figure 2: Four-dimensional representations of single labeled afferent neuron.

Upper panel : Four dimensional representation of single labeled afferent neuron in the six wild-type fish. Lower panel : Four dimensional representation of single labeled afferent neuron in the six deaf mutant fish (Tmie mutant). Each neuron terminal point has been plotted with a different color. For each terminal point (ie, for each color) positions have been spotted over time, every 10 min during one hour.

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