# Neurons reunited: data and software to reconstruct long-range projection neurons, place them in a digital reference brain with high precision, and model their interactions

**Main area:** Reconstruction of neuronal morphology from microscopic image data
**Keywords:** axonal reconstruction, EBRAINS, morphology registration,
**Duration:** 36 months
**Total project funding:** € 786.772

## Abstract

Cognitive processes emerge from the properties of individual neurons and their synaptic cell-to-cell interactions, which may be local or long-range. While the first are relatively well understood, long-range synaptic connections remain mostly known at a gross region-to-region "mesoconnectome" level. Lacking cellular resolution, such data are not adequate to model the computations carried out by the brain; this presents the field with a major challenge for understanding at a mechanistic level both the normal and the diseased brain functioning.

The mesoconnectome describes the statistics of projections between brain regions based on the labeling, usually incomplete, of the axons from a large number of cells of different types. A growing number of single-cell labeling studies show that the projections of individual neurons in these projections are remarkably diverse and precise. Most regions can be reached in about two steps rather than one, which means that the overlap between projections and postsynaptic neurons in the intermediate area is critical. In this project we consider the projections from basal ganglia and cerebellum that project to cortex via thalamus. It is extremely difficult to get a grasp on long-range projections, but we believe that labeling and gold-standard reconstruction of axons of individual neurons is one of the most promising approaches.

Current reconstruction and measurement tools face the challenge of combining the brain-wide scale of a long-range projection axon with the cellular scale at which its tens of thousands of boutons are distributed within the target regions. During the histological processing required for precise histological delineation of postsynaptic cells and neuropils, the tissue sections become subtly deformed, hence the different axonal branches will not automatically line up with the areas they targeted when the sections are registered to a template brain.

We have assembled five partners to address this challenge. The two experimental partners (Clasca, d'Angelo) will produce and reconstruct projecting axons innervating cortex or converging in deep nuclei, the neuroinformatics partner (Tiesinga, Bakker), with help of a consultant (Meijering) will build pipelines to process the raw data and create tools for the precise placement of axonal arbors in a digital reference brain and generate statistics for the two stage connectivity. One computational group (Giugliano) will translate these axonal arbors in multicompartmental neuron models in order to explore the physiological effectiveness of this two-stage feedforward projection, whereas the other (Van Albada) will translate the connection statistics to single-compartment neuron network models to assess the effect on population activity.

This project will directly use and contribute tools to the EBRAINS infrastructure produced by the HBP, the data and models produced are also to be published via EBRAINS.

## Consortium

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Sacha van Albada – Forschungszentrum Jülich – Germany – Funded by: With own funds
Michele Giugliano – Universiteit Antwerpen – Belgium – Funded by: FWO
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Egidio D'Angelo – University of Pavia – Italy – Funded by: MIUR