Ne rons Re nited

First Periodic Report
18.03.2021

FLAG-ERA

AGENCIA ESTATAL DE INVESTIGACIÓN

NWO
Netherlands Organisation for Scientific Research

Human Brain Project

Consortium NeuronsReunited

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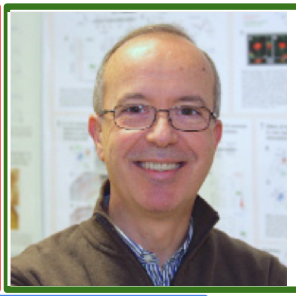

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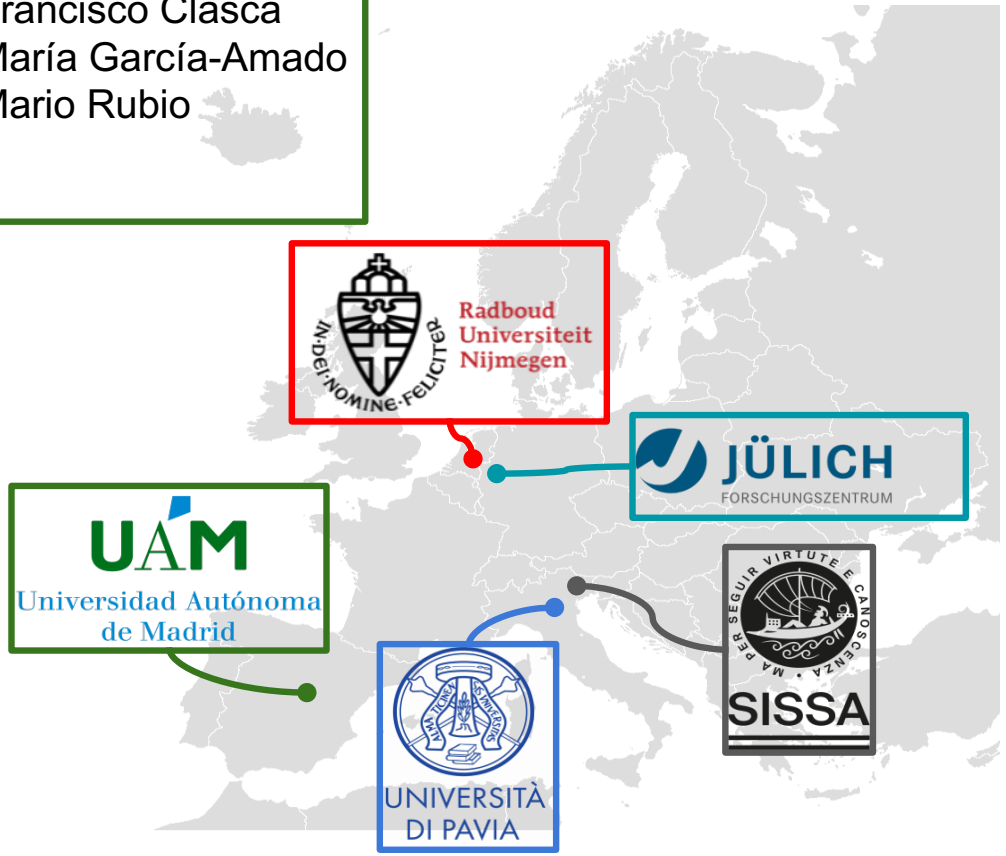
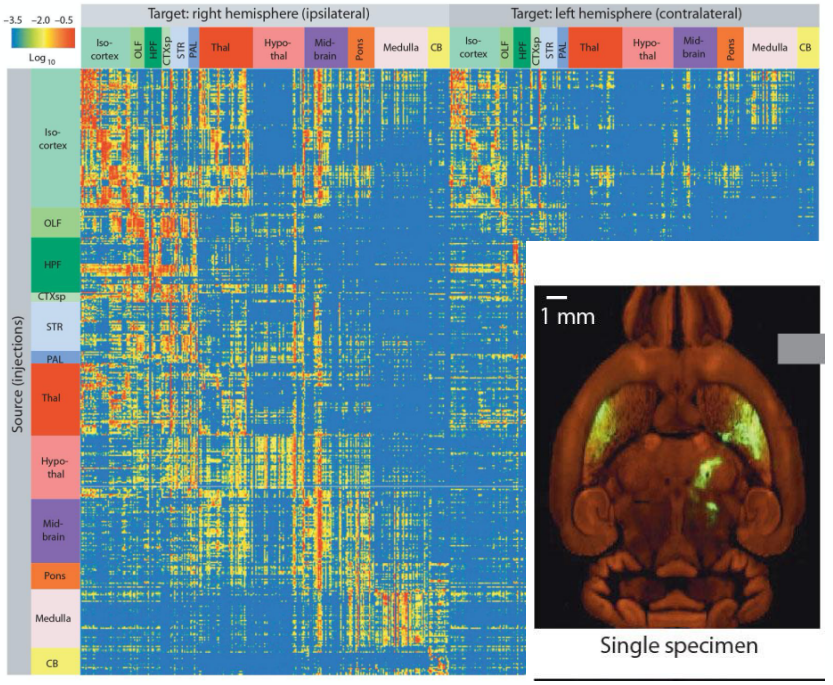


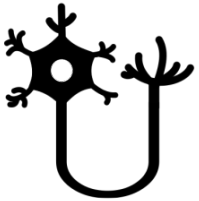
Recently published mesoconnectome is of tremendous importance for experimental and computational neuroscientists alike

A mesoscale connectome of the mouse brain

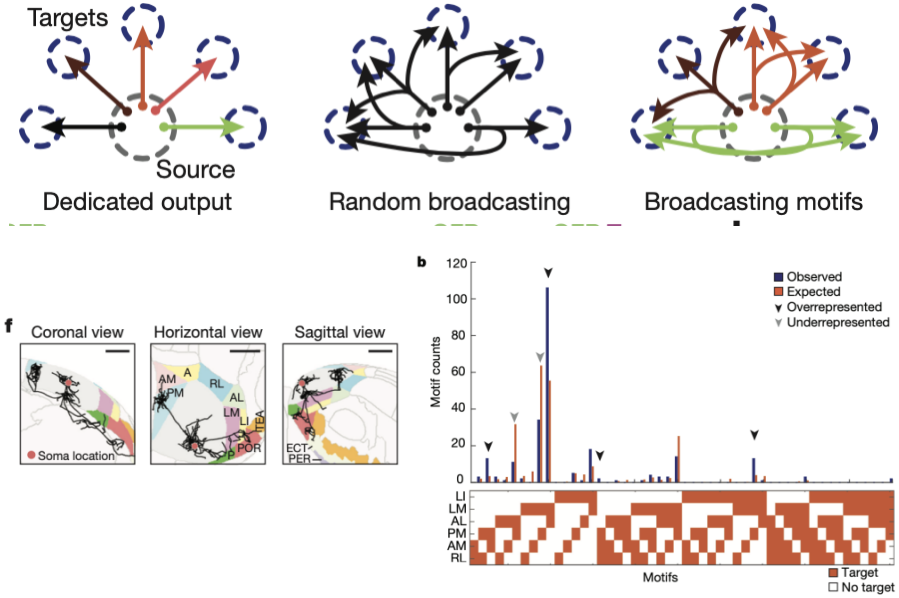
Seung Wook Oh[1]*, Julie A. Harris[1]*, Lydia Ng[1]*, Brent Winslow[1], Nicholas Cain[1], Stefan Mihalas[1], Quanxin Wang[1], Chris Lau[1], Leonard Kuan[1], Alex M. Henry[1], Marty T. Mortrud[1], Benjamin Ouellette[1], Thuc Nghi Nguyen[1], Staci A. Sorensen[1], Clifford R. Slaughterbeck[1], Wayne Wakeman[1], Yang Li[1], David Feng[1], Anh Ho[1], Eric Nicholas[1], Karla E. Hirokawa[1], Phillip Bohn[1], Kevin M. Joines[1], Hanchuan Peng[1], Michael J. Hawrylycz[1], John W. Phillips[1], John G. Hohmann[1], Paul Wohnoutka[1], Charles R. Gerfen[2], Christof Koch[1], Amy Bernard[1], Chinh Dang[1], Allan R. Jones[1] & Hongkui Zeng[1]



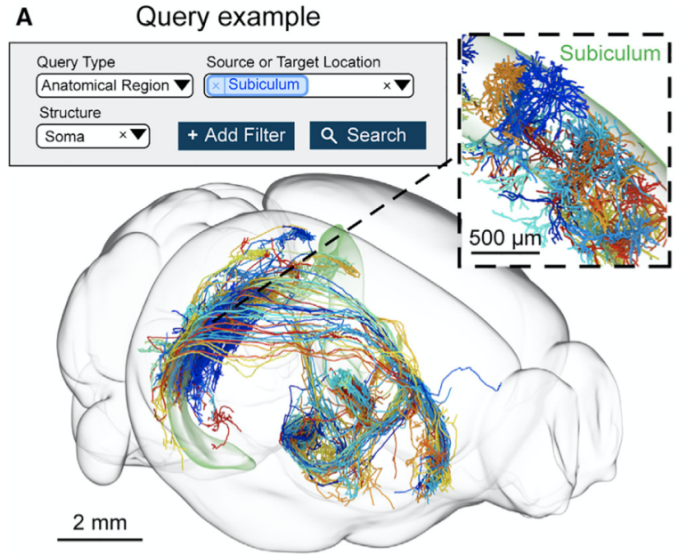
Bulk injection is not enough: need single cell resolution



The logic of single-cell projections from visual cortex



Reconstruction of 1,000 Projection Neurons Reveals New Cell Types and Organization of Long-Range Connectivity in the Mouse Brain

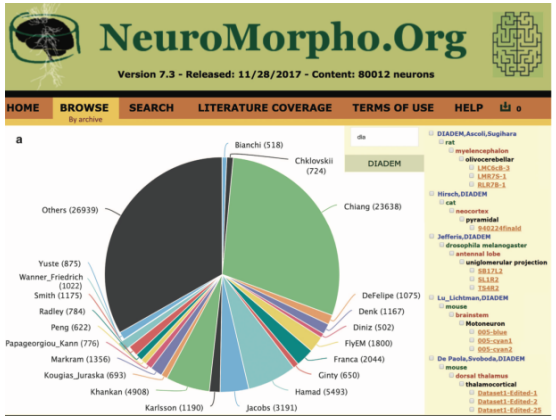


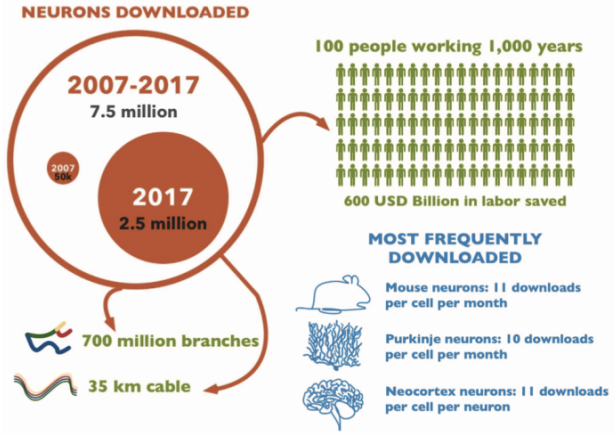
Winnubst et al 2019; Han et al 2018;

Orphans: Neurons that need a home

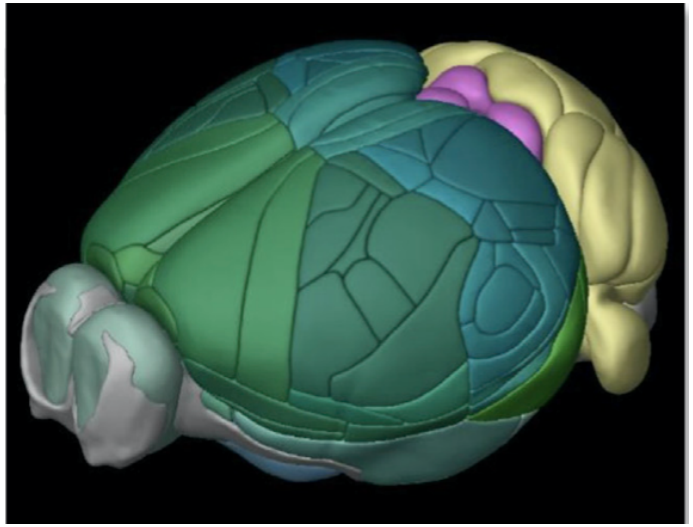
Generate gold standard reconstruction, properly register them, to facilitate "crowd sourcing" neurons and computational studies

An open repository for single-cell reconstructions of the brain forest





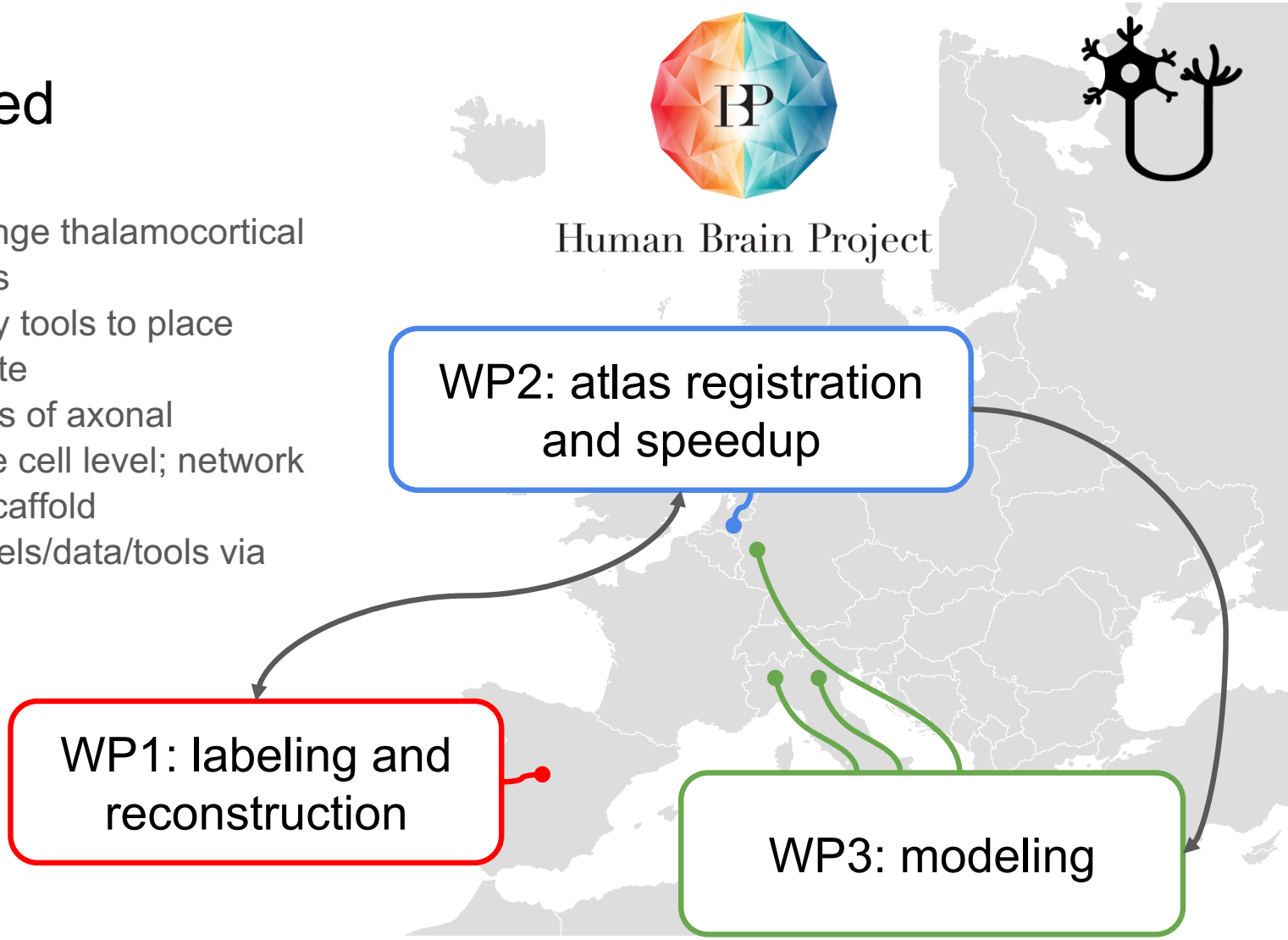
The Allen Mouse Brain Common Coordinate Framework: A 3D Reference Atlas



Wang et al 2020; Akram et al 2018

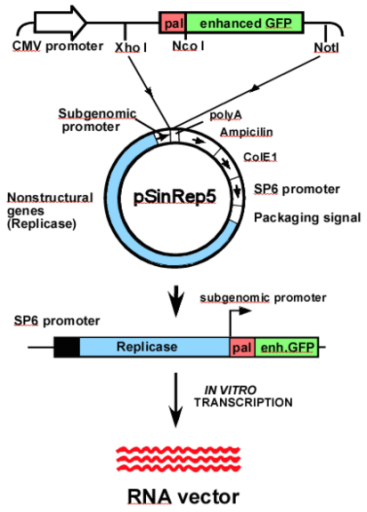
NeuronsReunited

- Reconstruct long-range thalamocortical synaptic connections
- Implement and apply tools to place them in atlas template
- Model consequences of axonal morphology at single cell level; network level and for brain scaffold
- Make available models/data/tools via EBRAINS

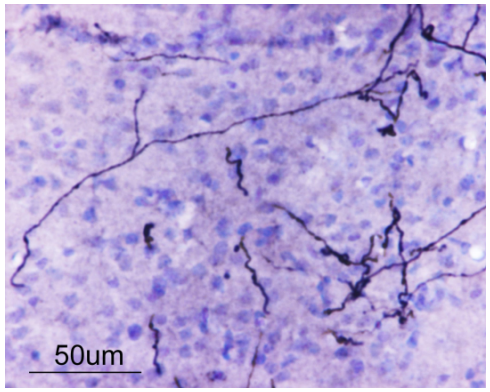


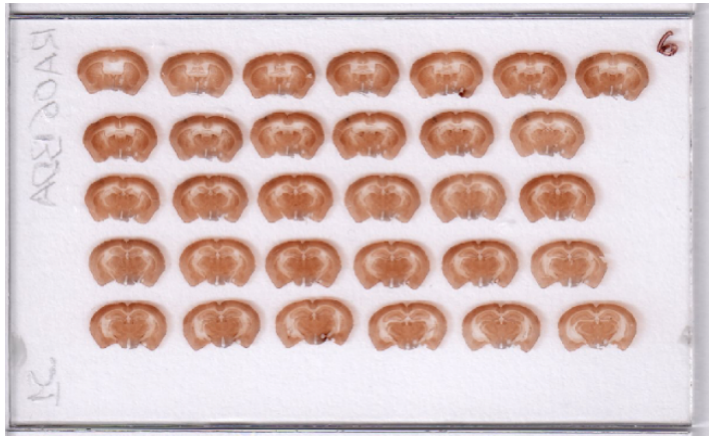
WP1: Single-cell labeling in adult brains

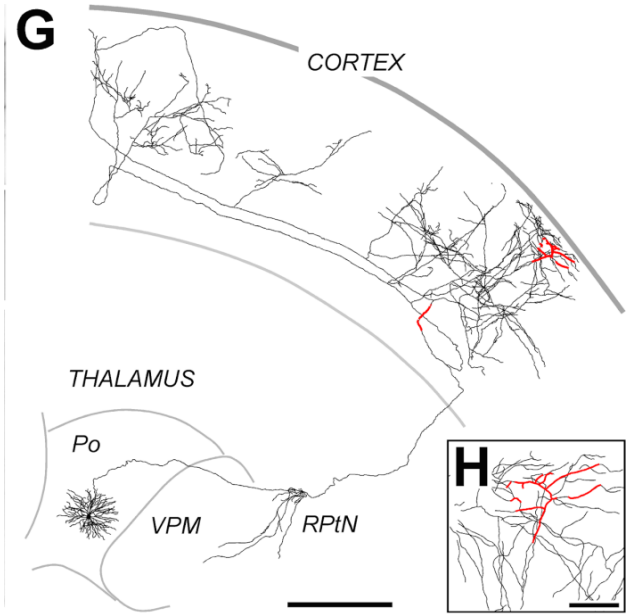
Sindbis Pal-eGFP & RNA electroporation



Furuta et al. *Neuroscience* (2001)







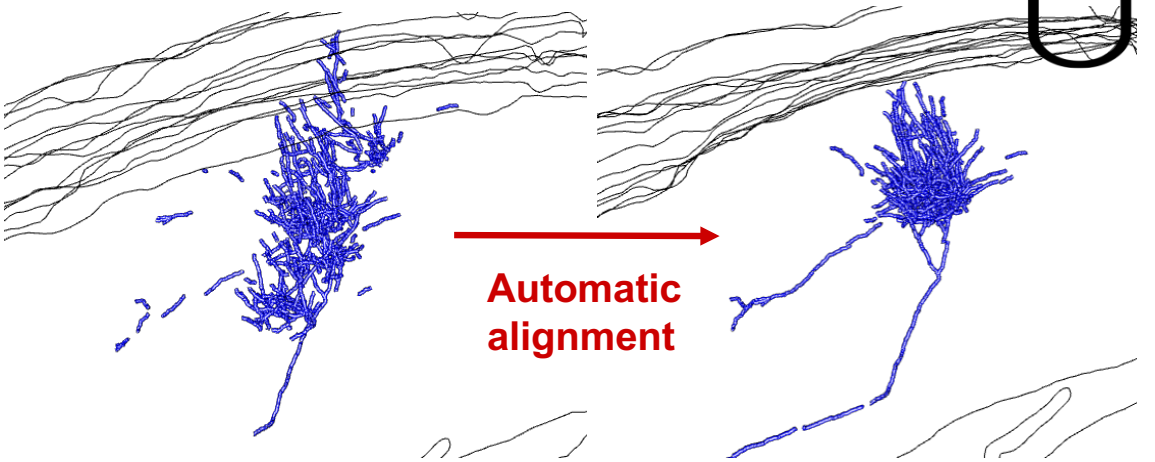
Porrrero et al. *Front. Neurosci.* (2016)

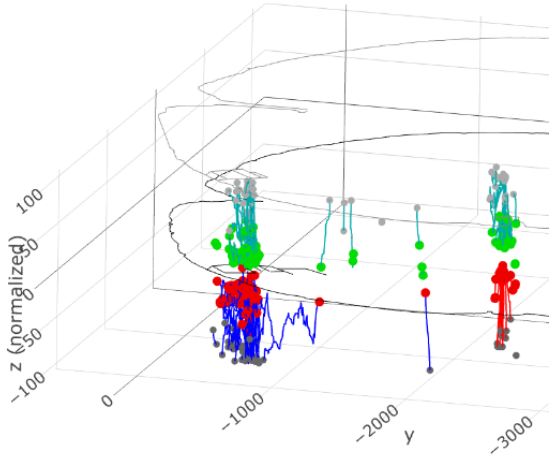
WP2: Speeding up tracing by automated stitching

Manual tracing in Neurolucida takes **a week** per neuron:

1. 1-2 days: trace all pieces of axon in every section.
2. 3-4 days: align and stitch pieces together.

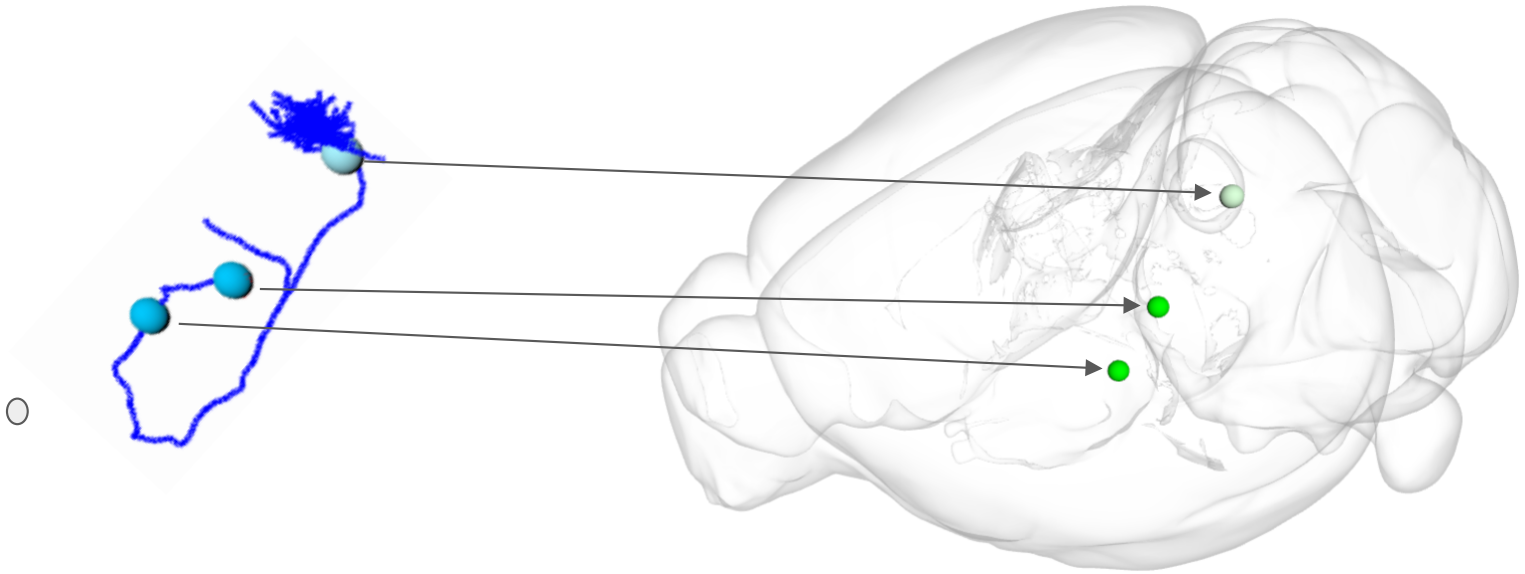
We implemented a workflow that speeds up part 2, it matches the locations of axon-fragments in successive sections.





After alignment, suggested stitches are manually inserted using an online tool.

WP2: Neuron alignment based on corresponding points



Basic corresponding points registration implemented as **online workflow***.

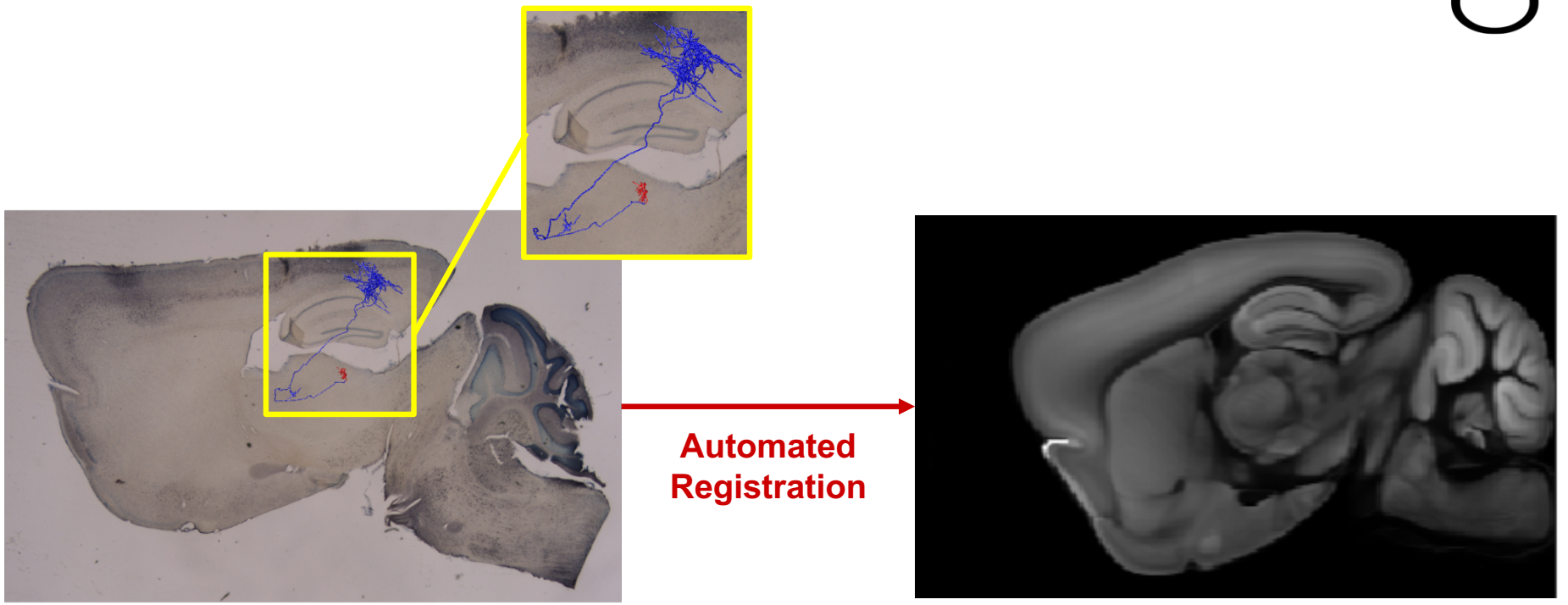
Placing the points requires expert anatomical knowledge.

Next step:

- Add digital tissue images to the neuron and develop semi-automatic registration pipeline.

*https://neuroinformatics.nl/HBP/morphology-viewer and https://sba-dev.incf.org/composer

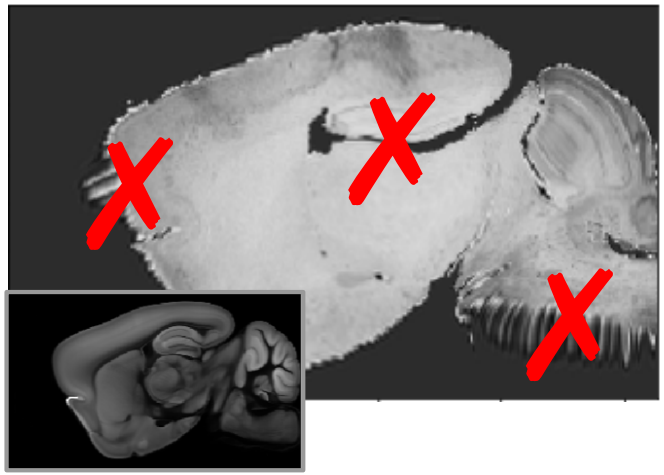
WP2: Improved alignment with tissue images



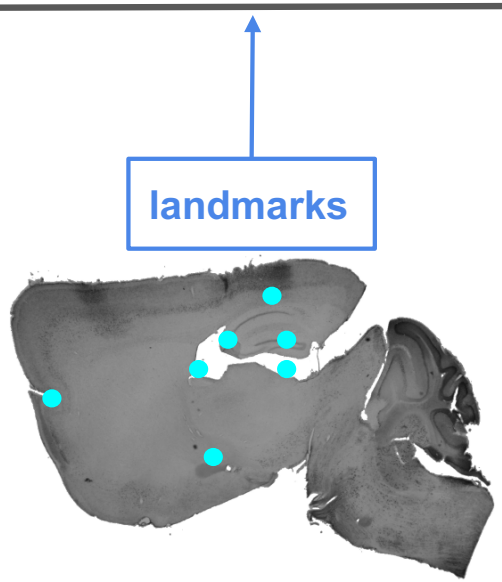
experimental slice

atlas slice

Challenge: dealing with large deformations



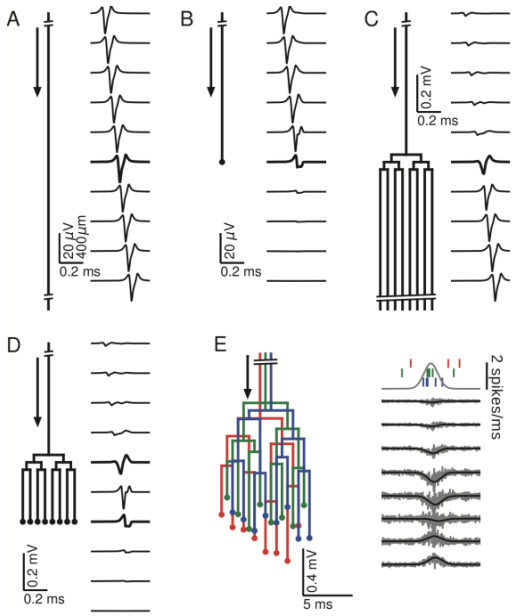
Test 1: Deformable registration, comes with huge artifacts.



Test 2: Deformable registration, including a set of manually inserted landmarks.

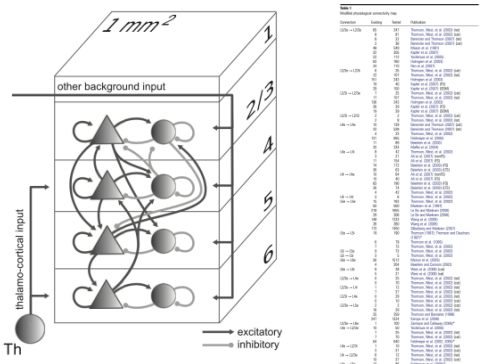
WP3: Modeling

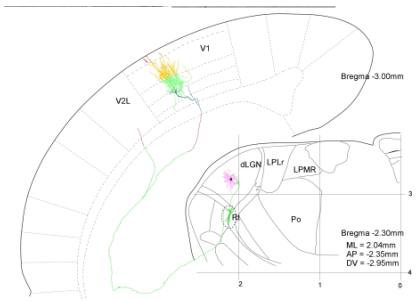
Consequences of realistic axons in multicompartmental models



McColgan et al 2017

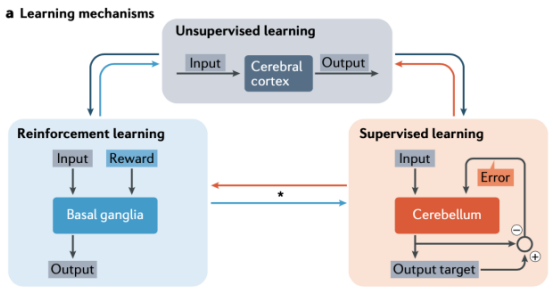
Adding proper thalamocortical projections to cortex model

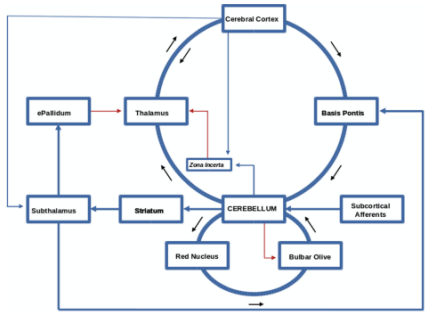




Potjans & Diesmann (2014)

Put the TC projection in the BG-CB-CTX scaffold model





Bostan & Strick (2016);
Habas et al (2019)

Responsible Research and Innovation

- Make available gold-standard, properly registered reconstruction
- Make available tools for other neuroscientists to do the same
- Contribute standards (Brain Addressing System, BIDS)
- Exemplify how to use new data in models

All data, tools & models will be available via EBRAINS as well as other public repositories (Scalable Brain Atlas, GitHub, Donders).