



Integrative Frameworks in Single-cell Connectomics

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HBP Partnering Projects Meeting: Status quo & outlook

5-7 September 2022 | Nijmegen, The Netherlands



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the European Union



Beyond bulk injections, towards single-cell reconstructions

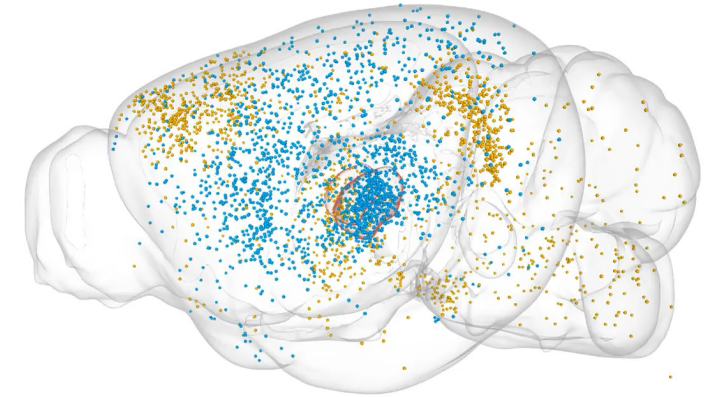
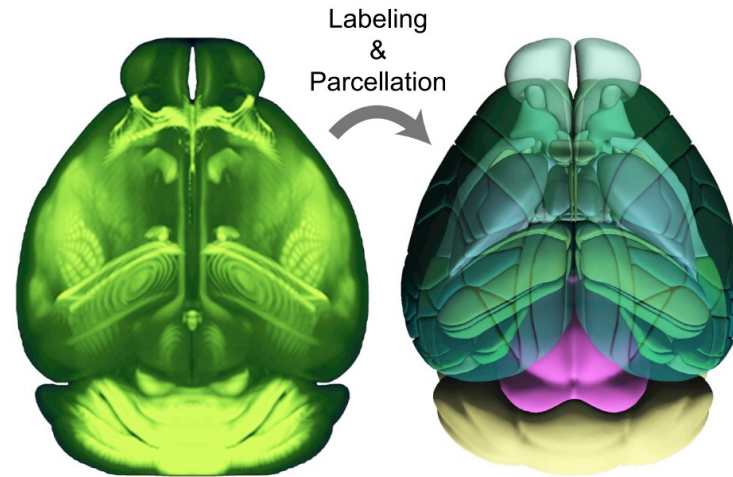
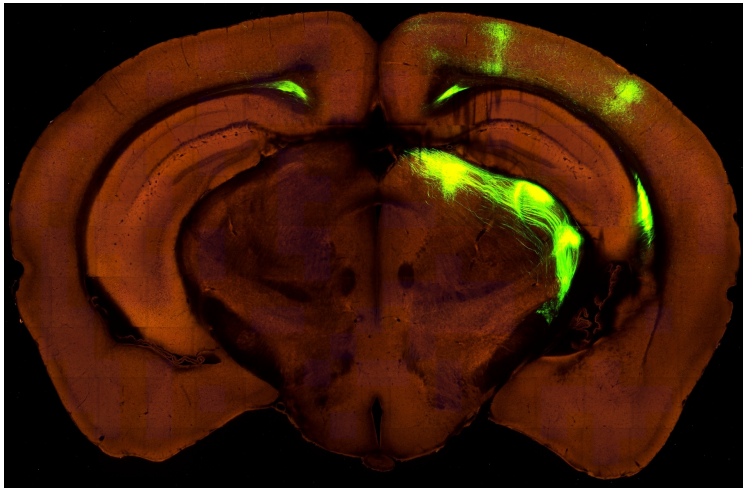
Tract-tracing experiments



3D Brain Atlases



Neuronal Reconstructions



Oh et al. 2014 Nature
Harris et al. 2019 Nature

Wang et al. 2020 Cell

Mouselight (Janelia Farms): 1544 neurons
Braitell (Southeast Univ./Allen Institute):
1741 neurons

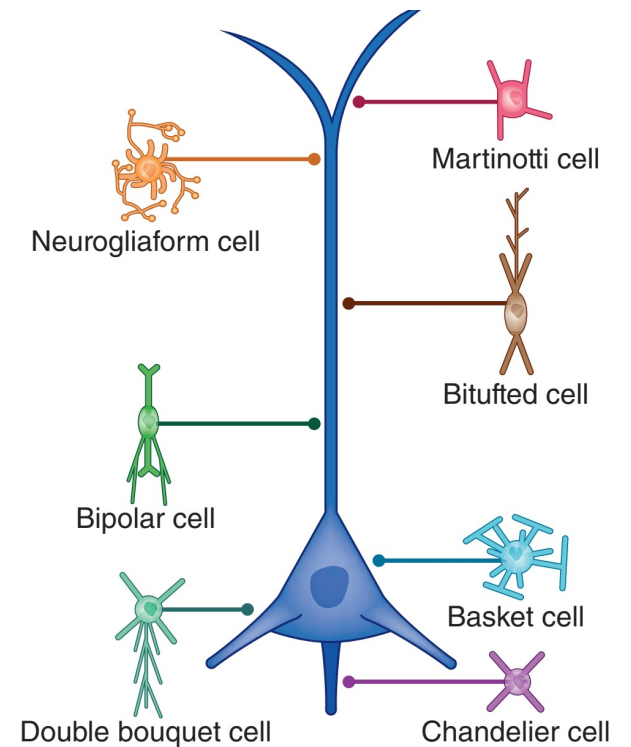
Winnubst et al. 2019 Cell
Peng et al. 2020 Nature

How can we transition from cell-to-area to cell-to-cell connectivity statistics?

How do different types of cells project to each other across the brain?



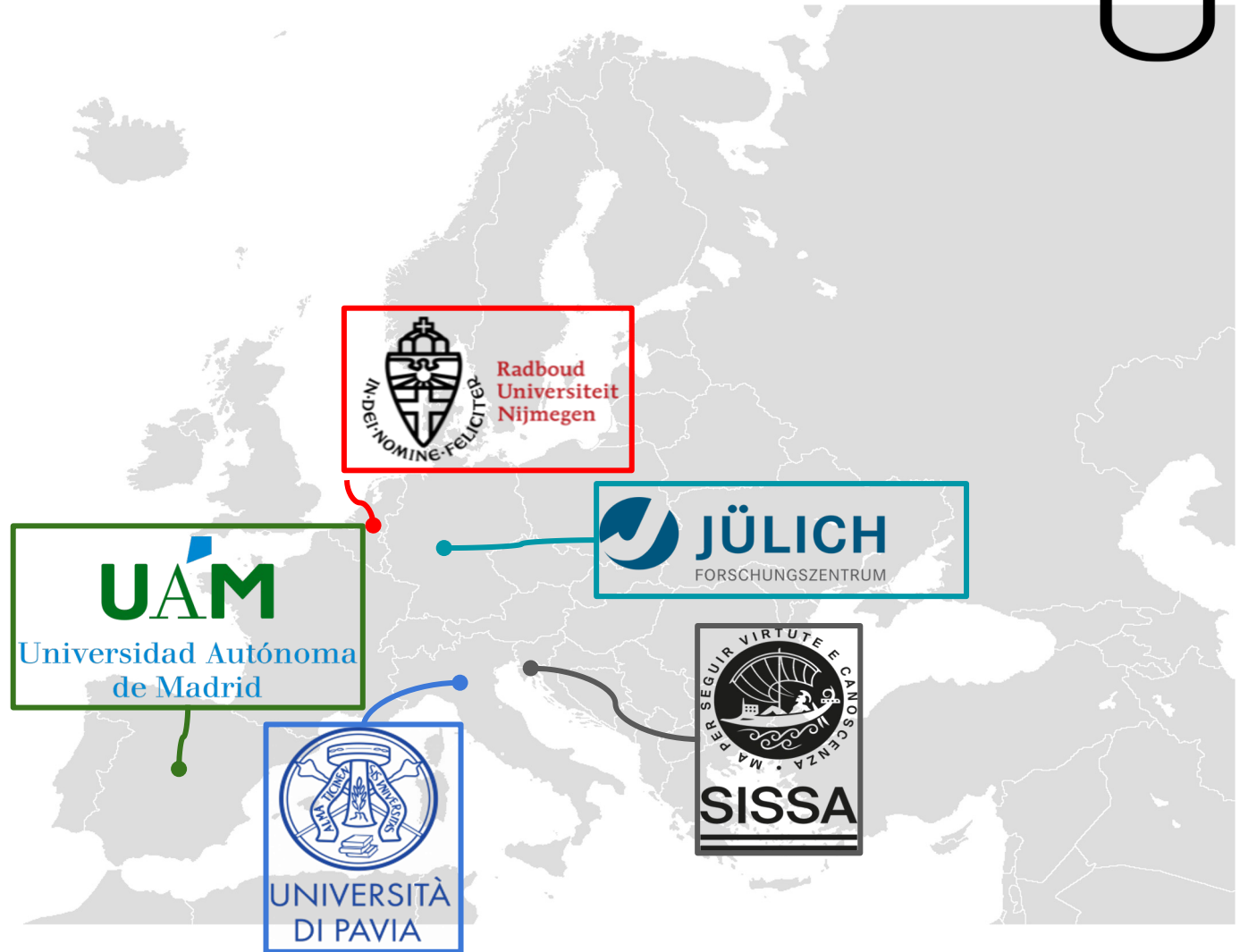
www.alleninstitute.org



Larkum, M. 2013. Nat. Neuro.

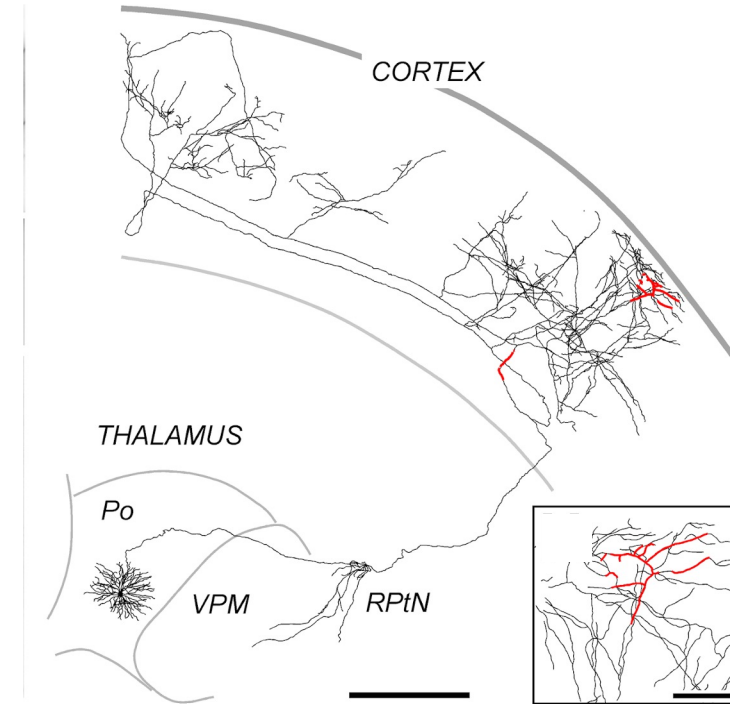
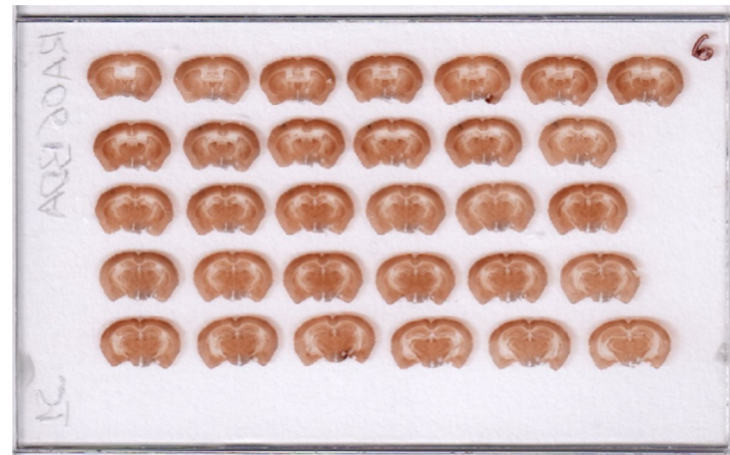
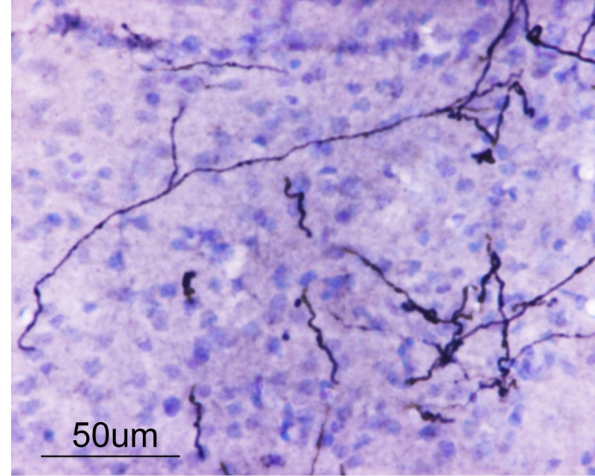
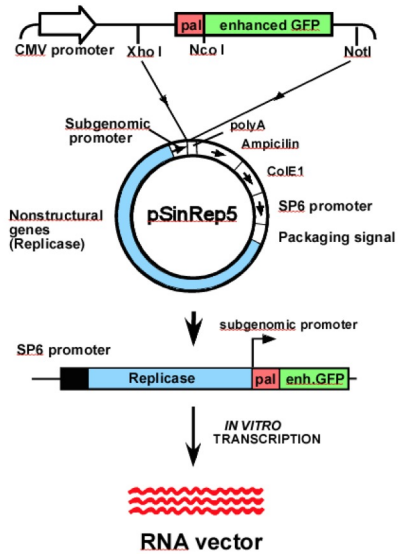
NeuronsReunited Project

- Generate gold standard reconstructions
- Provide spatial registration tools
- Provide visualization tools
- Search for similar neurons in other databases
- Utilize axonal morphologies as a structural scaffolding for more realistic
 - Multi-compartmental single-neuron models
 - Brain network level models
- Use-case: modelling connectivity loops between the **Cortex**, **Thalamus** and **Cerebellum**



Generating gold standard reconstructions

Sindbis Pal-eGFP & RNA electroporation



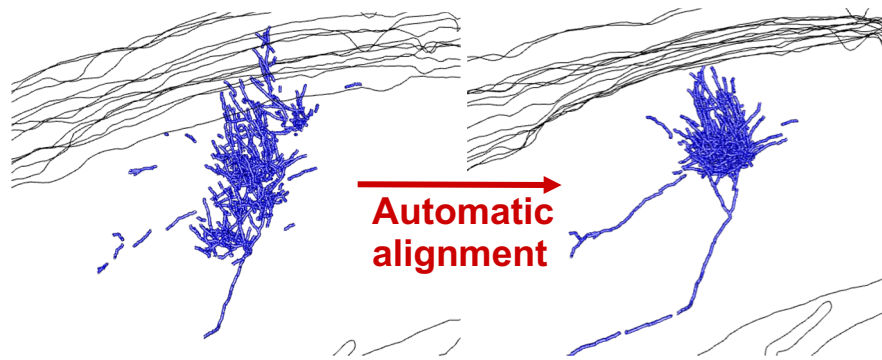
Porrero et al. 2016 *Front. Neurosci.*

Furuta et al. 2001 *Neuroscience*

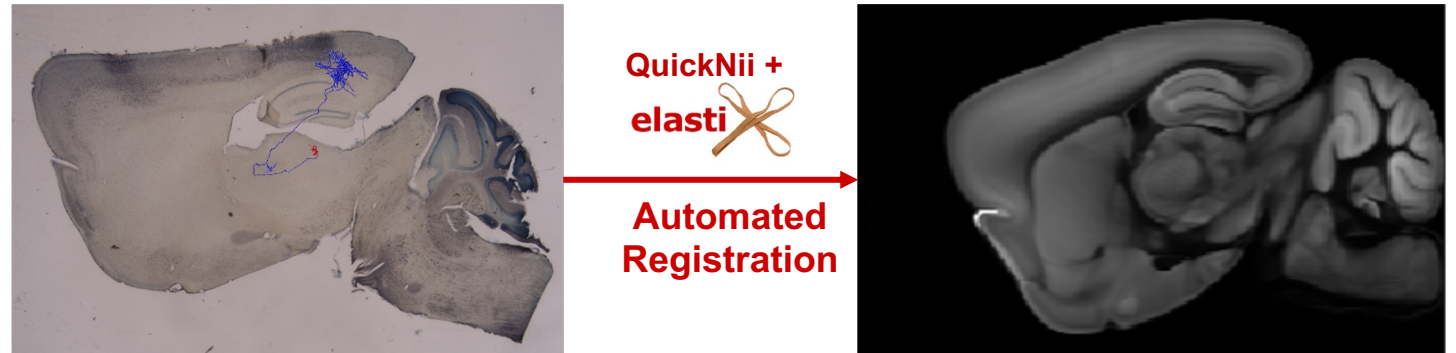
Providing spatial registration tools

1) Speeding up single-neuron tracing and improving registration to an anatomical template

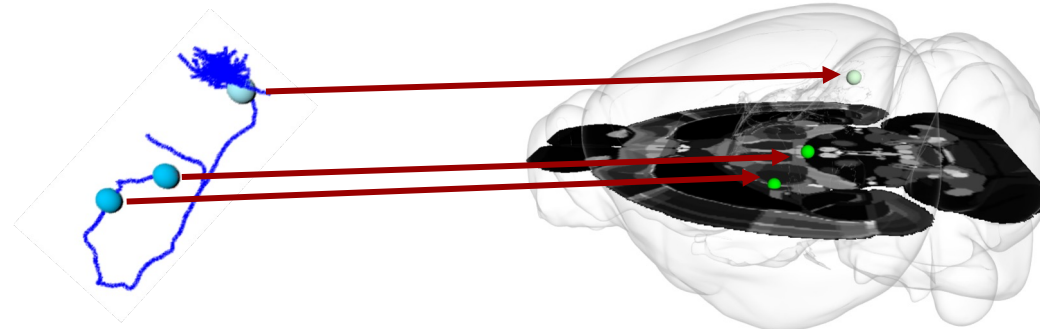
1. Align and stitch axonal fragments together



2. Registration of experimental slices to the Allen Reference Atlas (CCF v3.0)



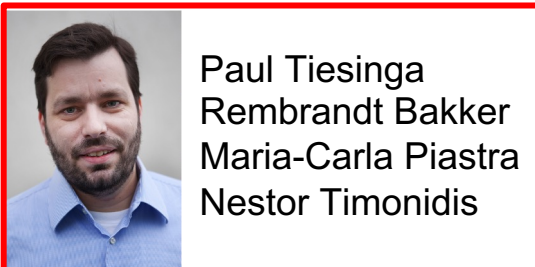
3. Morphology re-alignment based on corresponding points



Links:

<https://neuroinformatics.nl/HBP/morphology-stitcher-dev>

<https://neuroinformatics.nl/HBP/morphology-viewer>

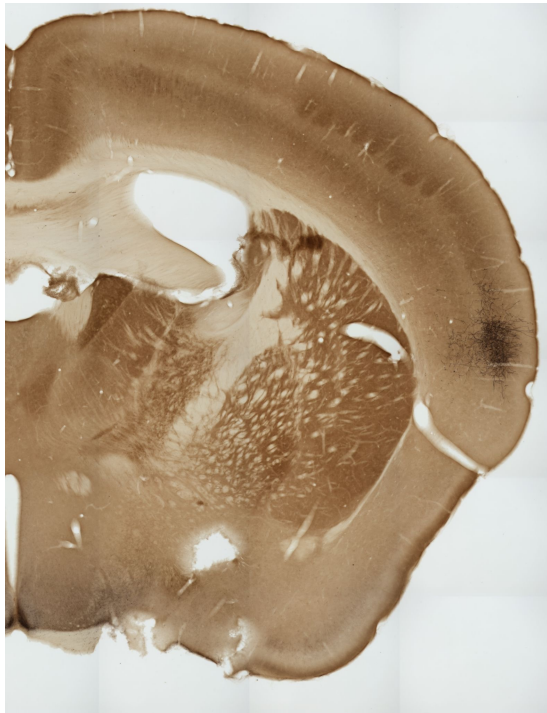


Providing spatial registration tools

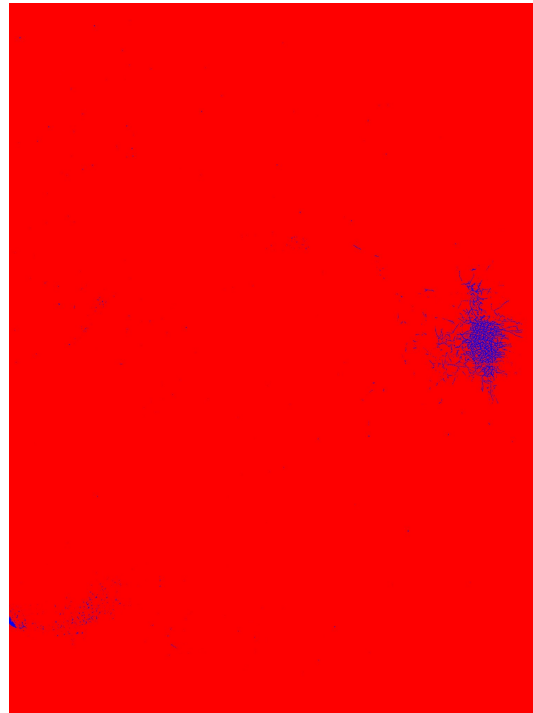
2) Providing 3D registration of population-level tracing experiments to an anatomical template



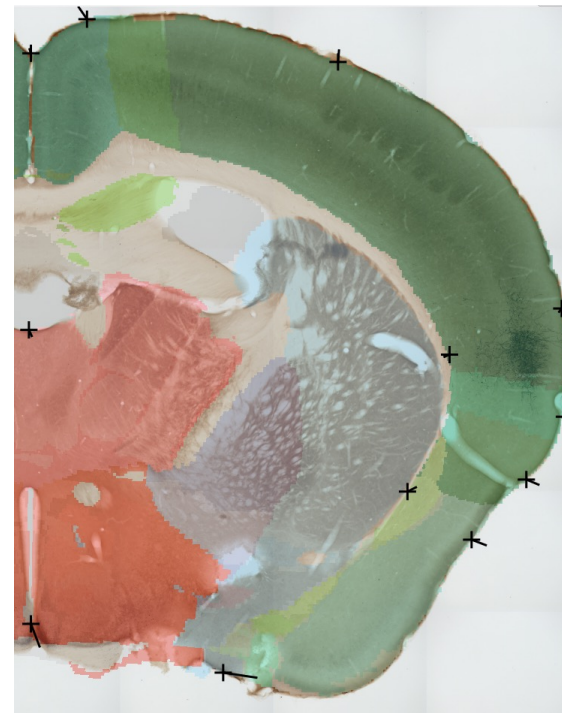
Anterograde population tracing experiment images



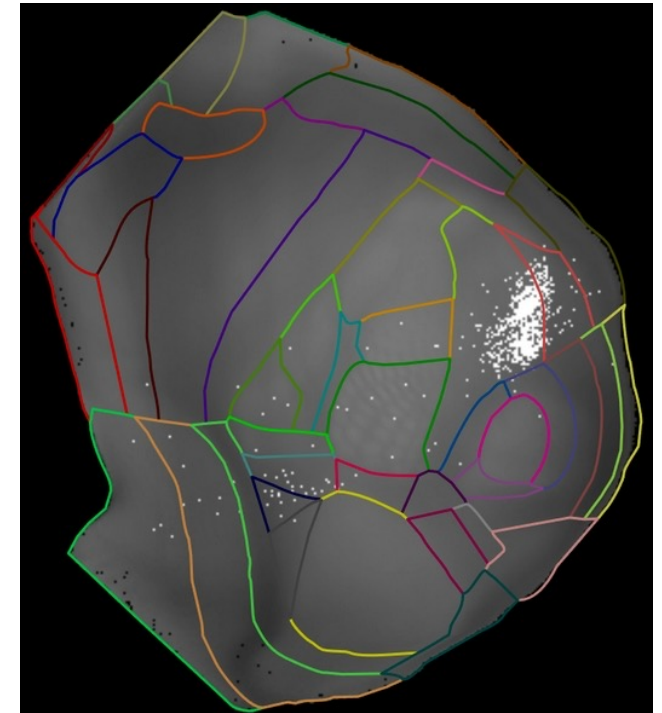
Ilastik segmentation



QuickNii+DeepSlice+VisuAlign registration to Allen CCF v3.0

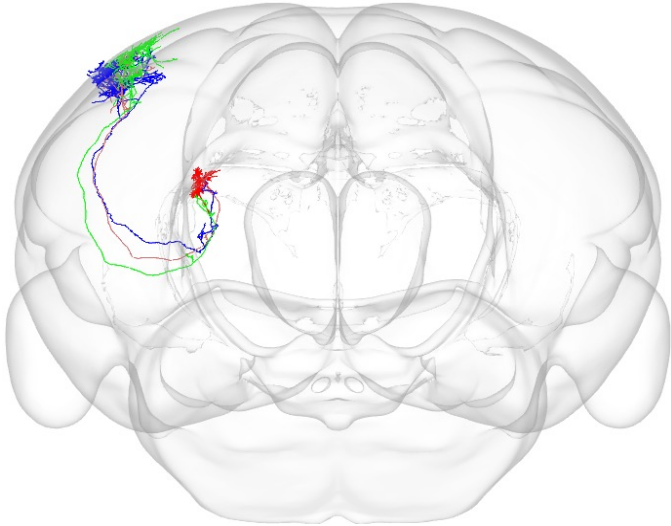
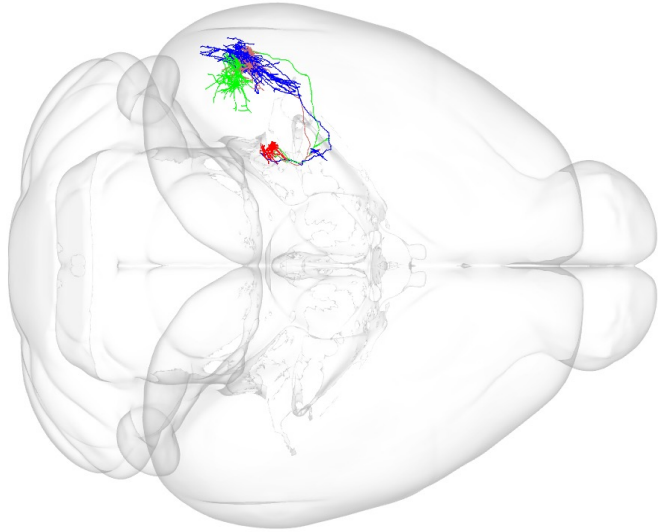
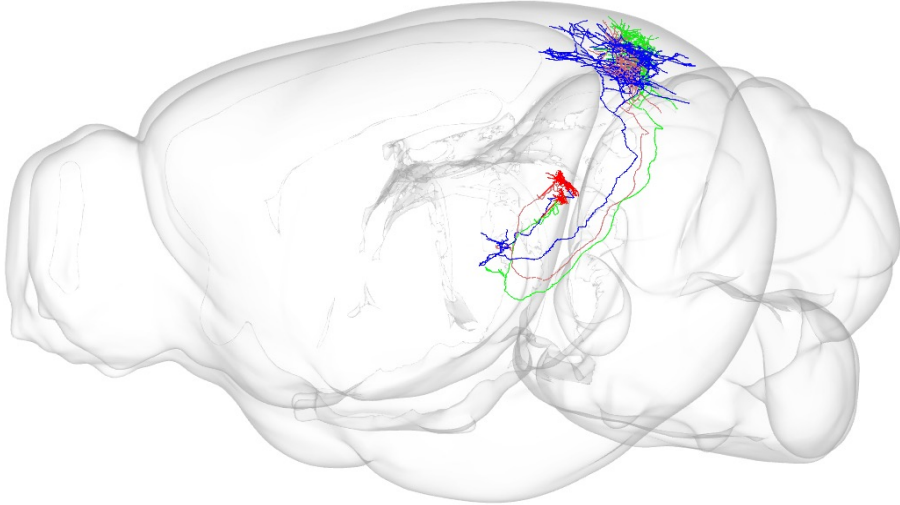
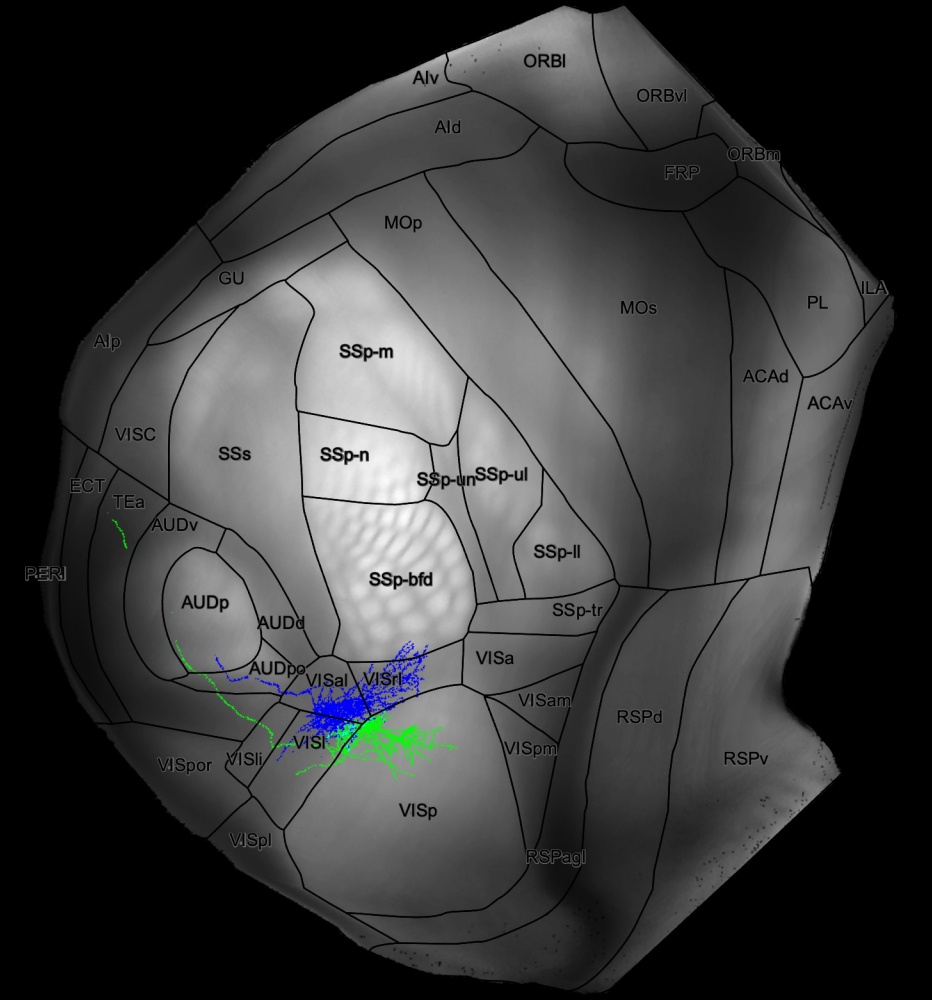


Cortical flatmap visualization



Visualizing morphologies in 3D space

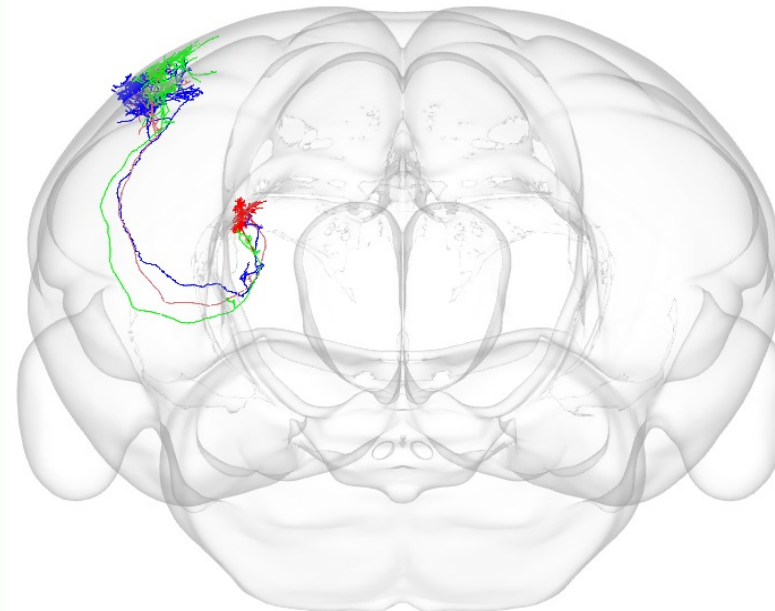
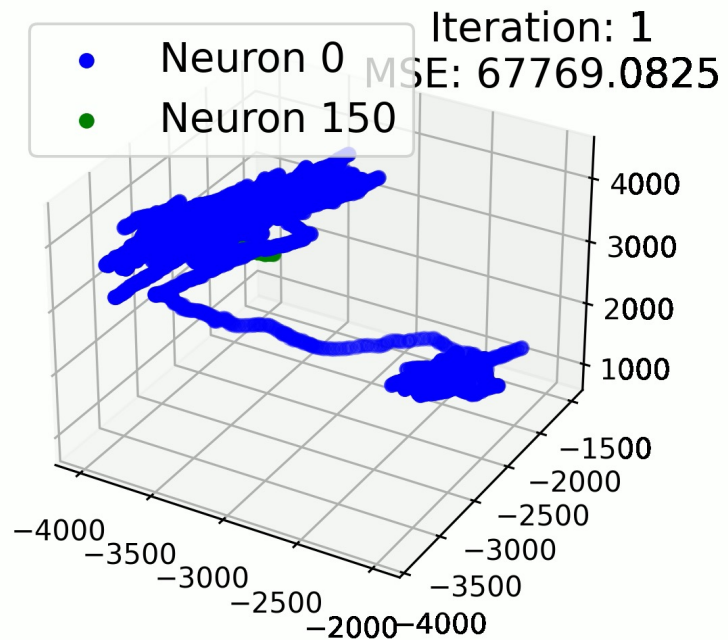
Rembrandt Bakker



<https://neuroinformatics.nl/HBP/neuronsreunited-viewer/>
<https://sba-dev.incf.org/>

Bakker et al. 2016 *Neuroinformatics*

Searching for similar neurons in other databases



Apply the *Coherent Point Drift* method for registering b to a

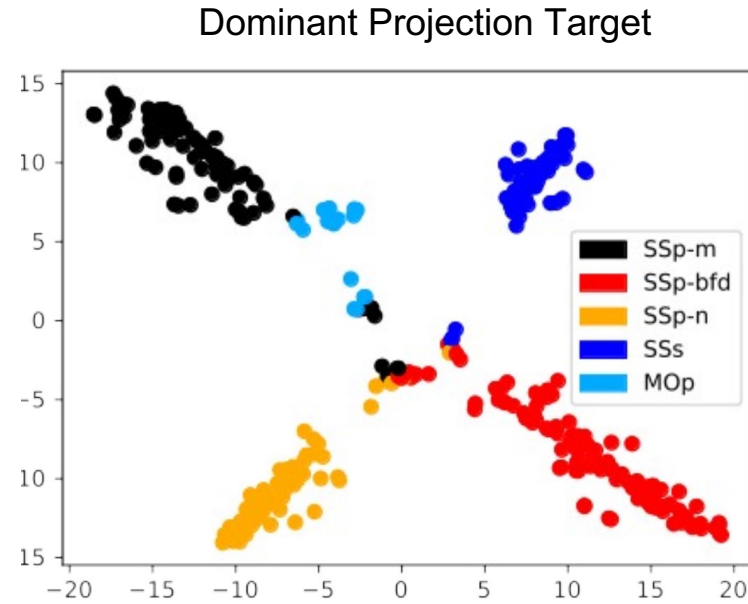
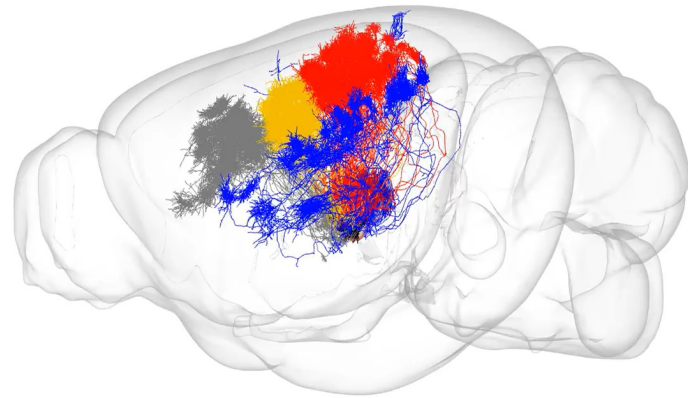
Repeat until convergence

- Expectation Step: compute probability matrix P of correspondence between points of a and b
- Maximization Step: solve the rigid registration of b to a for the optimal rotation matrix, scale and translation vectors

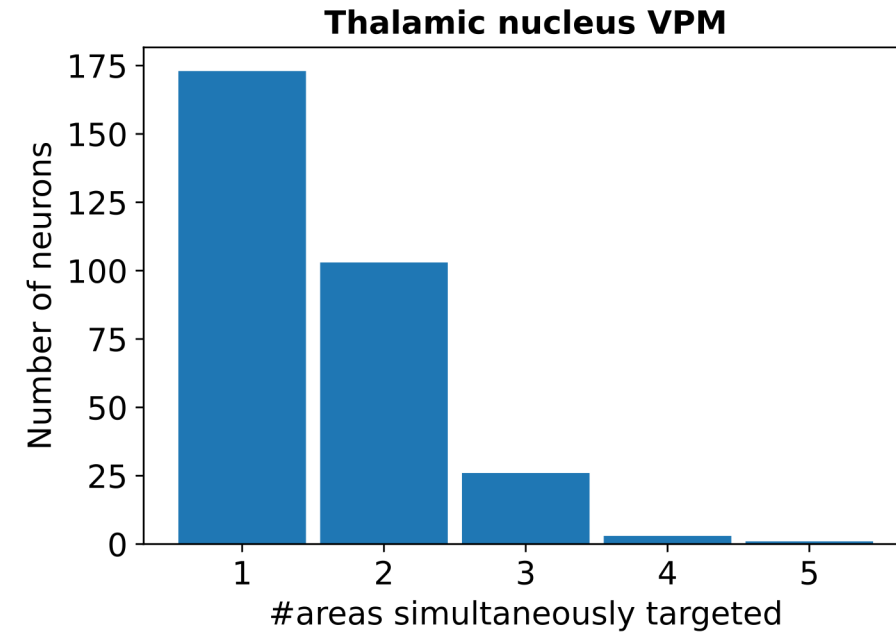
Myronenko and Song 2009 IEEE

Translating morphologies into brain-wide projection motifs

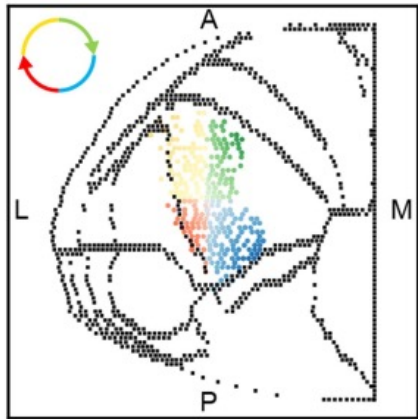
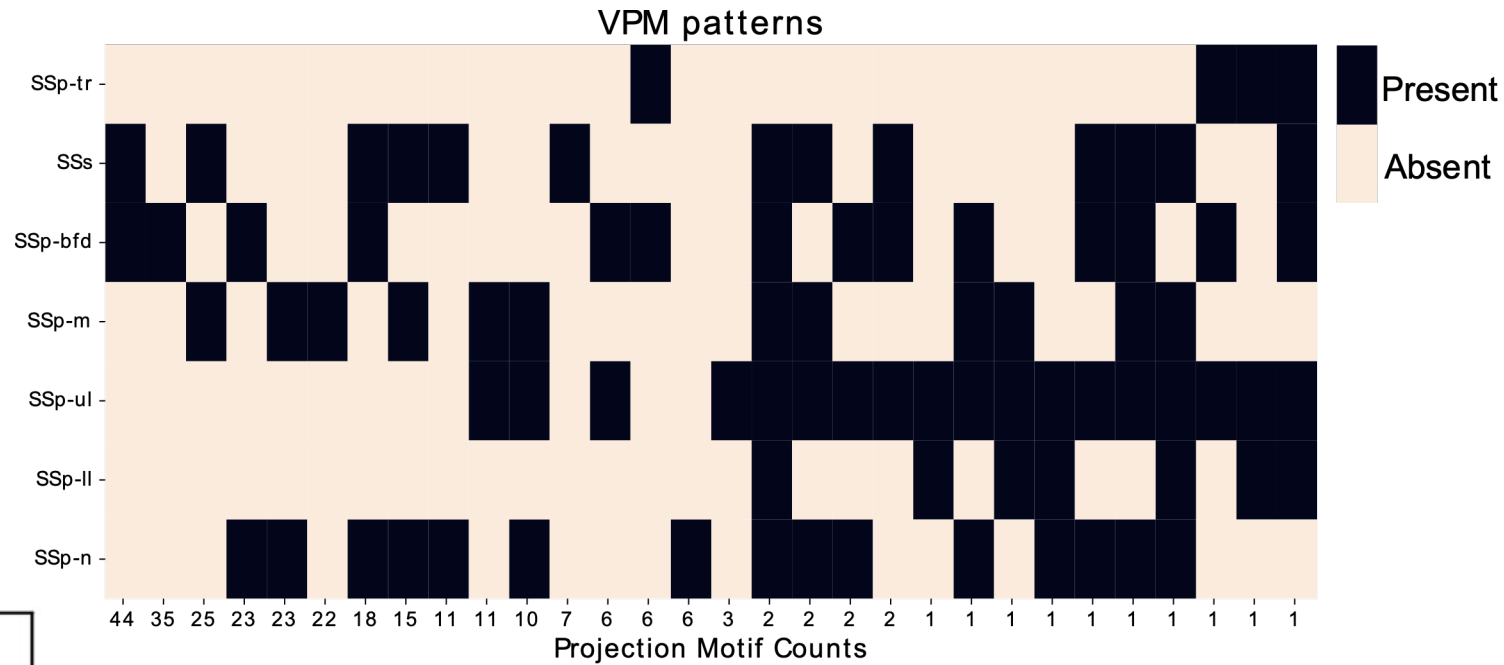
Case-study for simple projection motifs: Ventral Posteromedial Nucleus (VPM)



Even within VPM,
not all neurons
predominantly
target the same
area

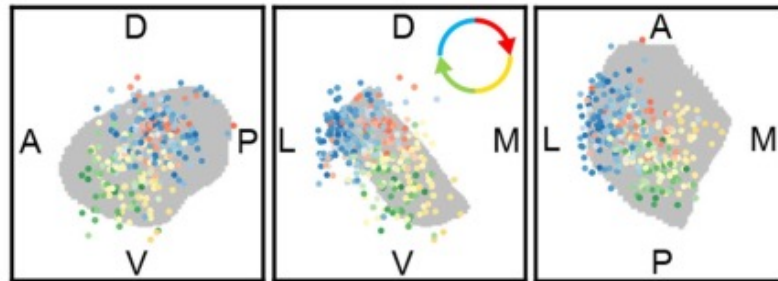


Under development: Unravelling higher order connectivity statistics and topography mapping of Thalamocortical neurons

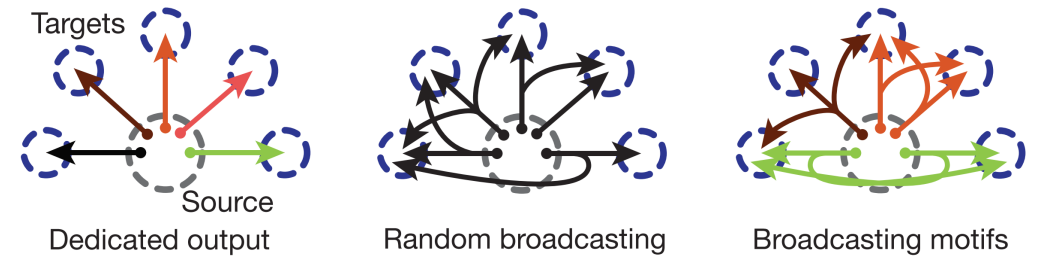


Peng et al. 2020 Nature

Topographical Organization



Higher order connectivity



Han et al. 2018 Nature

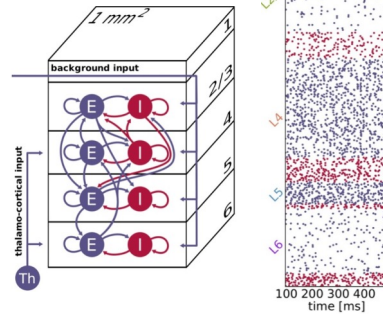
Under development: Somatosensory thalamocortical model

- Cortical microcircuit adapted from Potjans & Diesmann (2014)

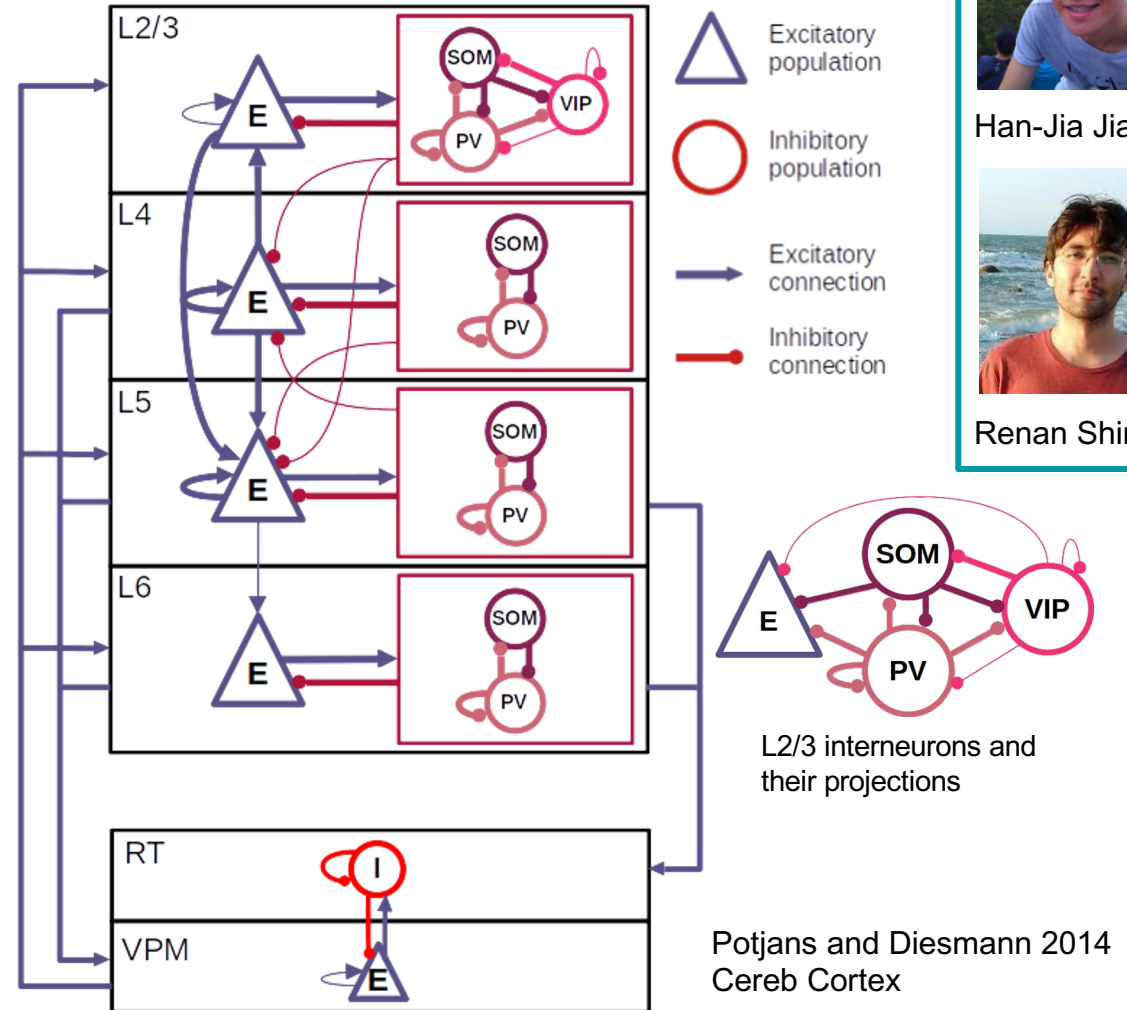
Integrate-and-fire neuron model with exponential current-based synapses:

$$C_m \frac{dV(t)}{dt} = -g_l(V(t) - E_l) + I_{syn}(t) + I_{inj}(t)$$

$$\tau_{syn} \frac{dI_{syn}(t)}{dt} = -I_{syn}(t) + \sum_{j,k} J_{j,k} \delta(t - t_{j,k}^*)$$



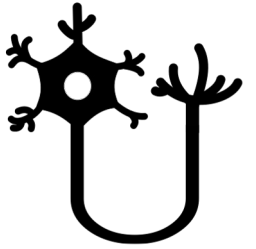
- Model dimensions:
 - cylinder with a surface radius of 138.2 μm
- Barrel column:
 - N = 6448
 - 4 subtypes:
 - E: excitatory neuron
 - SOM: somatostatin-expressing interneuron
 - PV: parvalbumin-expressing interneuron
 - VIP: vasoactive intestinal peptide-expressing interneuron
- Thalamus:
 - Composed by 200 RT and 200 VPM neurons
- Layer- and type-specific connection probability based on experimental data
- Non-simulated areas as Poisson drive



Han-Jia Jiang



Renan Shimoura



EBRAINS accessibility

Data, tools, models and related documentation/tutorials will be available via EBRAINS and other public repositories: Scalable Brain Atlas, GitHub, Donders Repository

EBRAINS Collaboratory

Collabs Documentation Support Forum Q 🔔 👤 🚪 Log-out

🏠 / Collabs / Atlas registration of neuronal morphologies obtained from mouse brain sections

Atlas registration of neuronal morphologies obtained from mouse brain sections

♥️ 0 ⋮

Last modified by Rembrandt Bakker on 2022/05/23 22:23

Use case:

Long-range projection neuron and 33 section images

Pipeline performing coregistration of the neuron and the 2d-sections from which it was traced

EBRAINS

Share data About

DATASET

3D reconstruction and measurement of individual thalamocortical projection neuron axons of somatosensory and visual thalamic nuclei

García-Amado, M.; Porrero, C.; Rubio, M.; Evangelio, M.; Clascá, F.

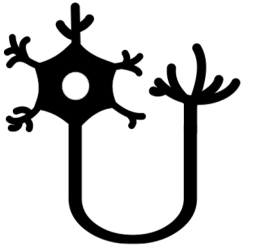
🗨️ Cite dataset 📄 Data-descriptor

DOI: [10.25493/AWS5-MZG](https://doi.org/10.25493/AWS5-MZG)

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Project: 3D reconstruction of thalamocortical projection neurons

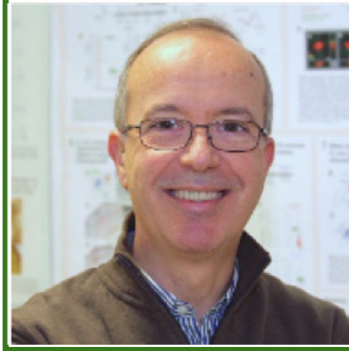
Custodians: [Clascá, Francisco](#)



NeuronsReunited Consortium



Paul Tiesinga
Rembrandt Bakker
Maria-Carla Piastra
Nestor Timonidis



Francisco Clasca
María García-Amado
Mario Rubio
Carmen Alonso Martinez



Sacha van Albada
Renan Shimoura
Han-Jia Jiang



Egidio D'Angelo



Michele Giugliano
Ludovica Liotti



Thank you

www.humanbrainproject.eu

www.ebrains.eu



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