

Neurons ReUnited

Second Periodic Report
22.03.2022



FLAG-ERA

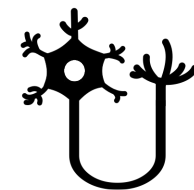


AGENCIA
ESTATAL DE
INVESTIGACIÓN



Human Brain Project

Consortium NeuronsReunited



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Nestor Timonidis



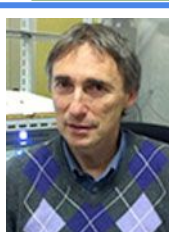
Francisco Clasca
María García-Amado
Mario Rubio



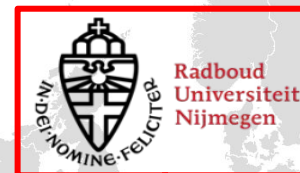
Sacha
van Albada



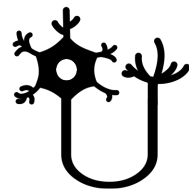
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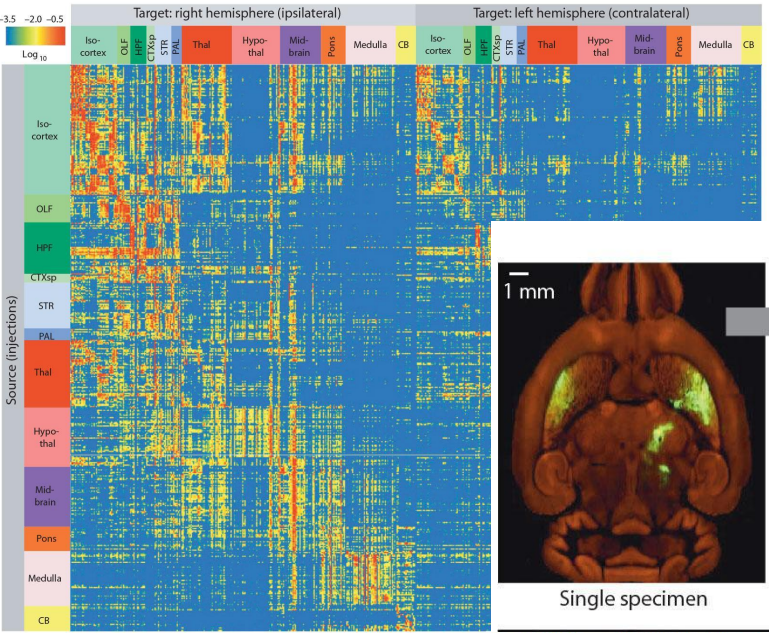


Recently published mesoconnectome is of tremendous importance for experimental and computational neuroscientists alike, but it needs augmentation

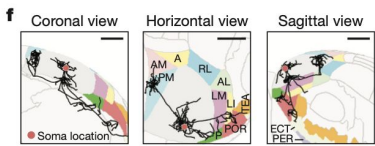
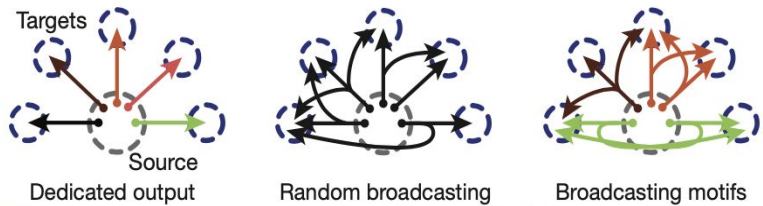


A mesoscale connectome of the mouse brain

Seung Wook Oh^{1*}, Julie A. Harris^{1*}, Lydia Ng^{1*}, Brent Winslow¹, Nicholas Cain¹, Stefan Mihalas¹, Quanxin Wang¹, Chris Lau¹, Leonard Kuan¹, Alex M. Henry¹, Marty T. Mortrud¹, Benjamin Ouellette¹, Thuc Nghi Nguyen¹, Staci A. Sorensen¹, Clifford R. Slaughterbeck¹, Wayne Wakeman¹, Yang Li¹, David Feng¹, Anh Ho¹, Eric Nicholas¹, Karla E. Hirokawa¹, Phillip Bohn¹, Kevin M. Jones¹, Hanchuan Peng¹, Michael J. Hawrylycz², John W. Phillips¹, John G. Hohmann¹, Paul Wahnoutka¹, Charles R. Gerfen², Christof Koch¹, Amy Bernard¹, Chinh Dang¹, Allan R. Jones¹ & Hongkui Zeng¹



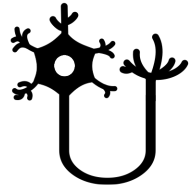
The logic of single-cell projections from visual cortex



Oh et al 2014; Han et al 2018; Tiesinga & Timonidis 2021

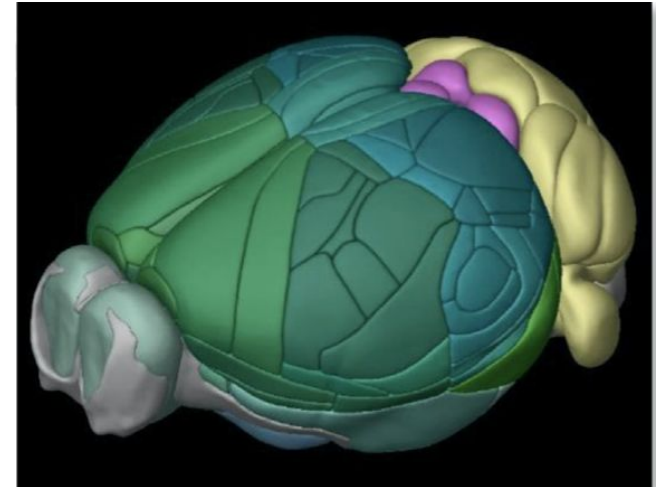
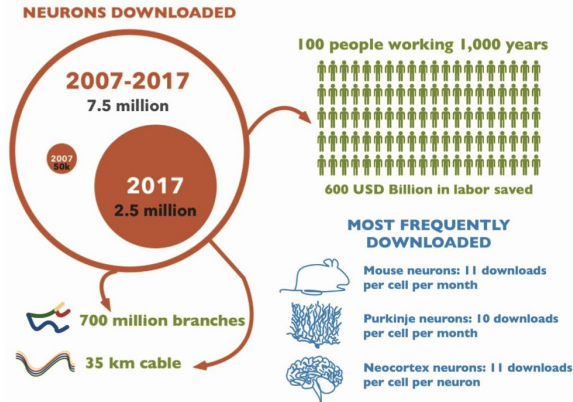
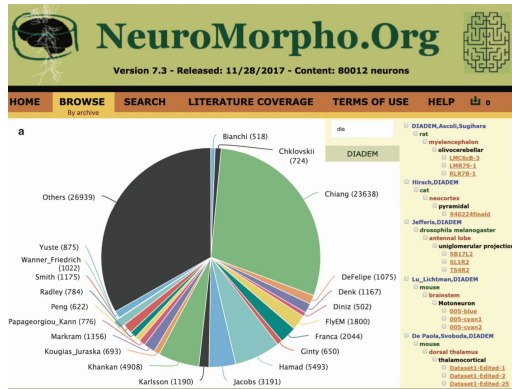
Orphans: Neurons that need a home

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

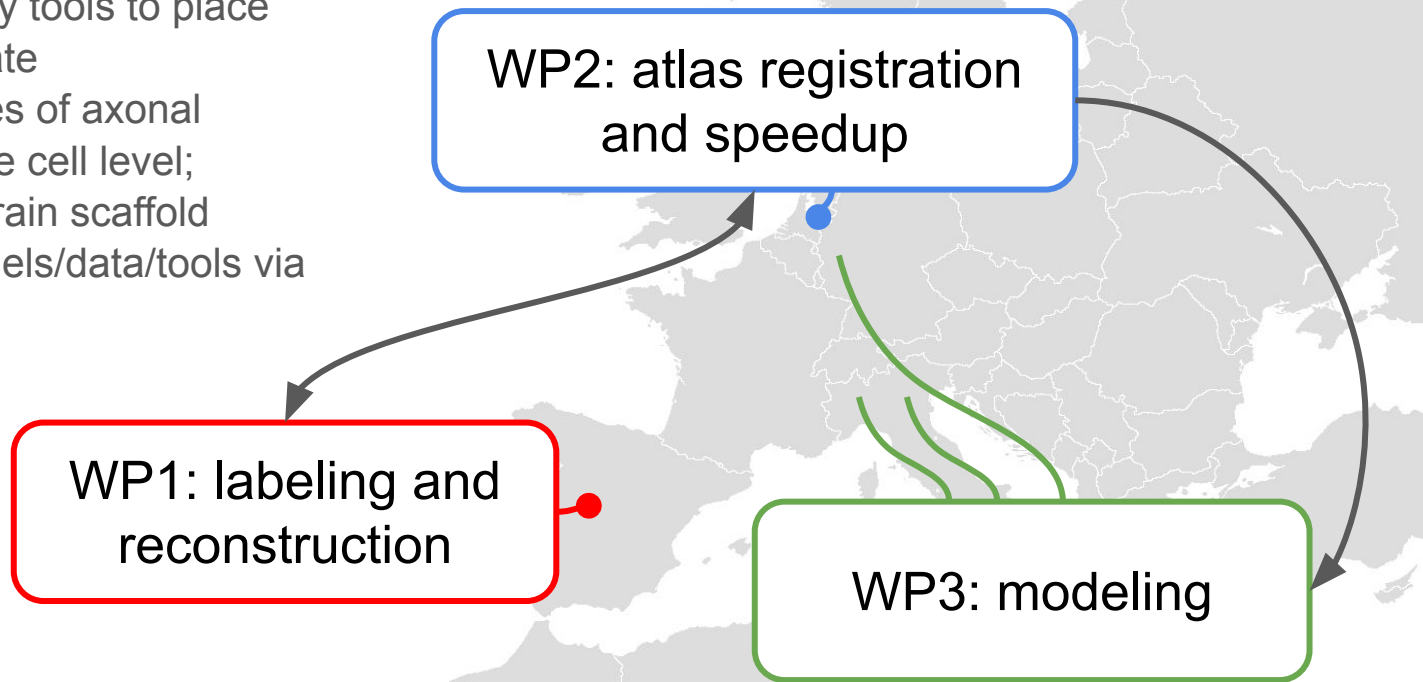


NeuronsReunited

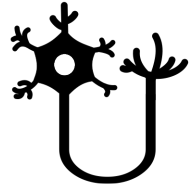
- Reconstruct long-range thalamocortical synaptic connections
- Implement and apply tools to place them in atlas template
- Model consequences of axonal morphology at single cell level; network level and brain scaffold
- Make available models/data/tools via EBRAINS



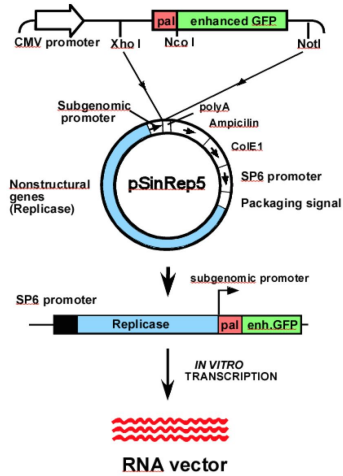
Human Brain Project



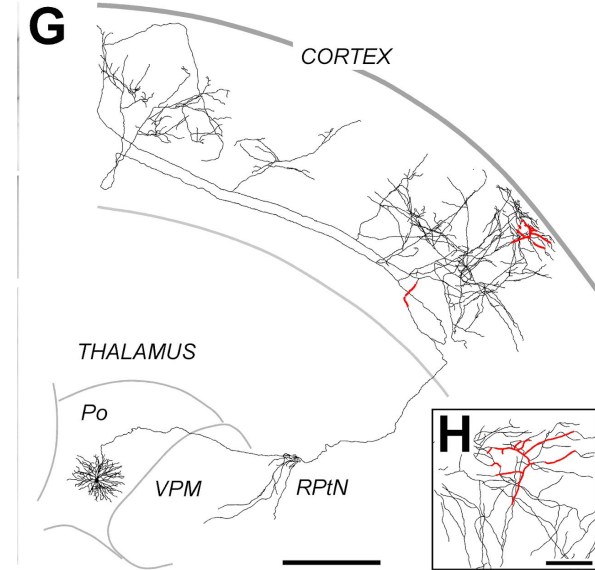
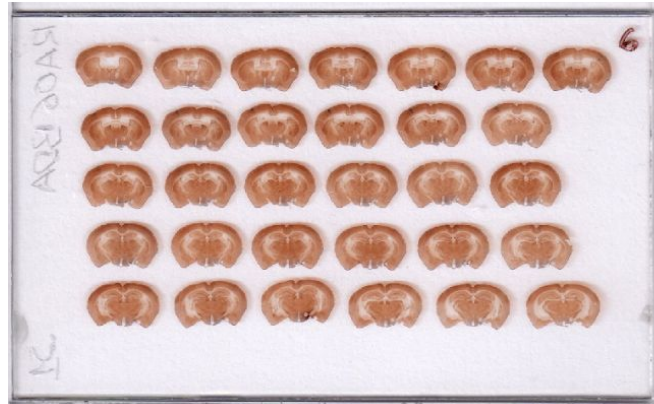
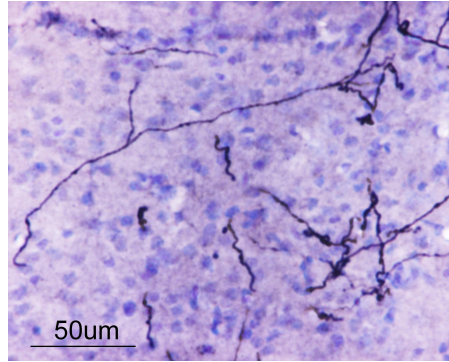
WP1: Single-cell labeling in adult brains



Sindbis Pal-eGFP & RNA electroporation

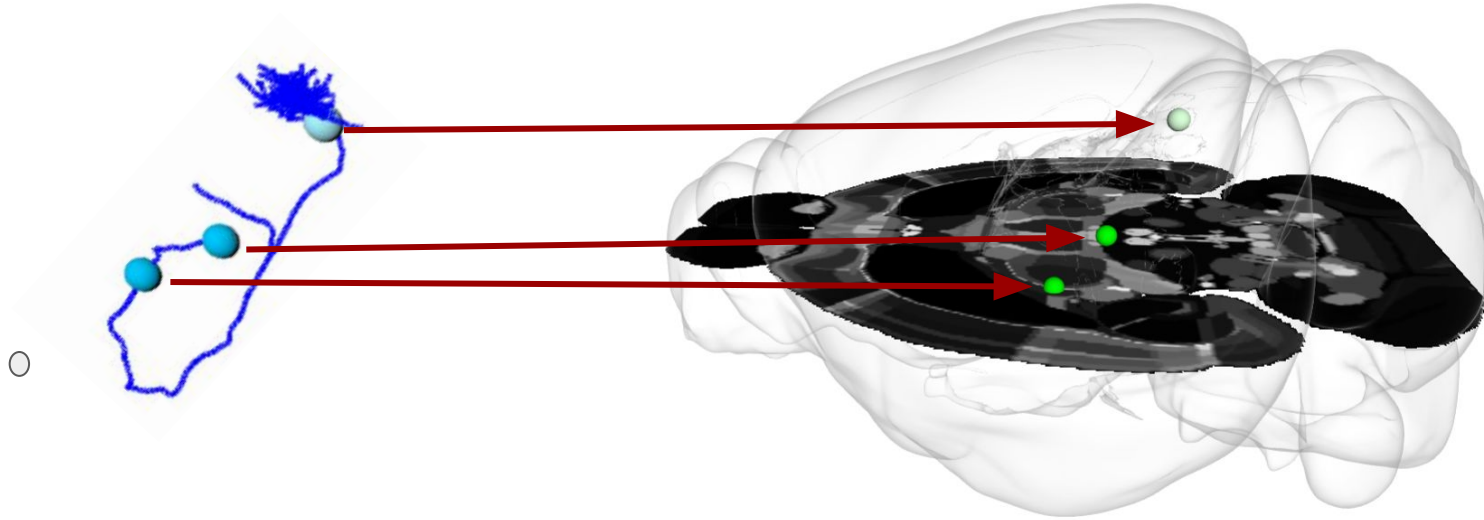
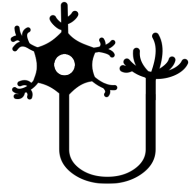


Furuta et al. *Neuroscience* (2001)



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

WP2: Neuron alignment based on corresponding points



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

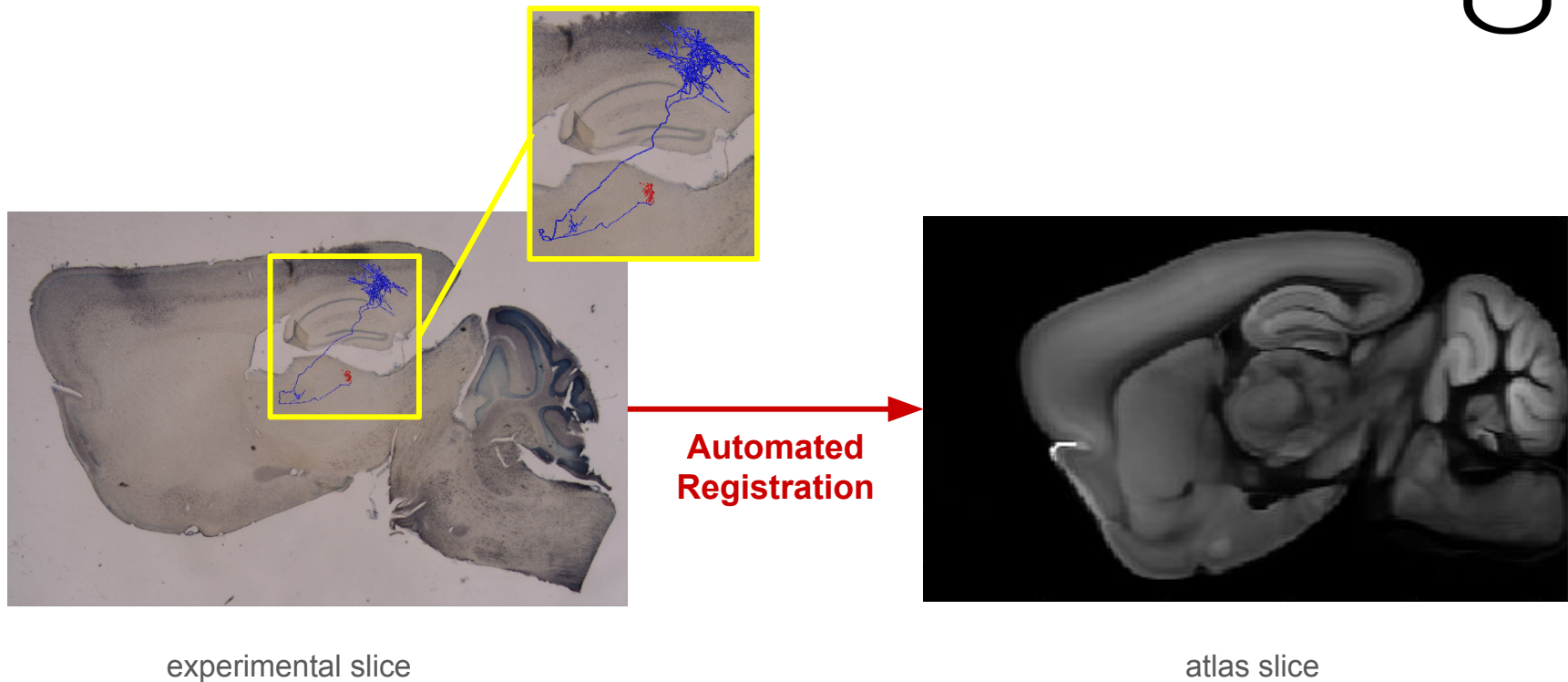
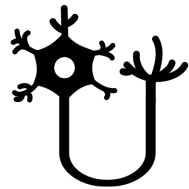
Placing the points requires expert anatomical knowledge.

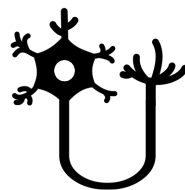
Next step:

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

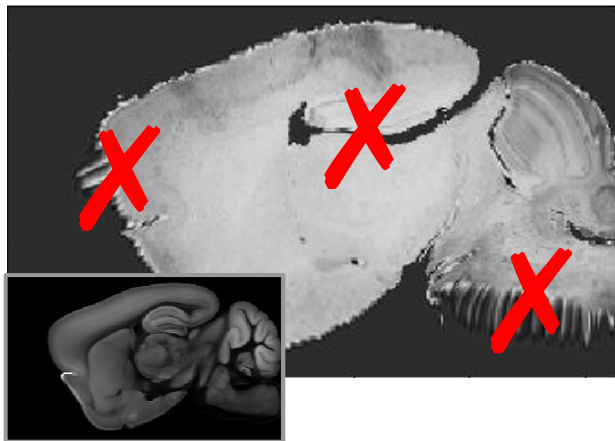
*<https://neuroinformatics.nl/HBP/morphology-viewer> and <https://sba-dev.incf.org/composer>

WP2: Improved alignment with tissue images

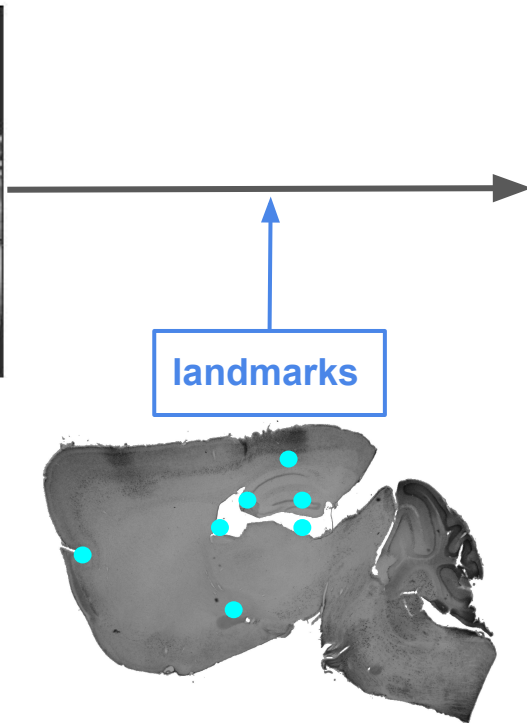




Challenge: dealing with large deformations

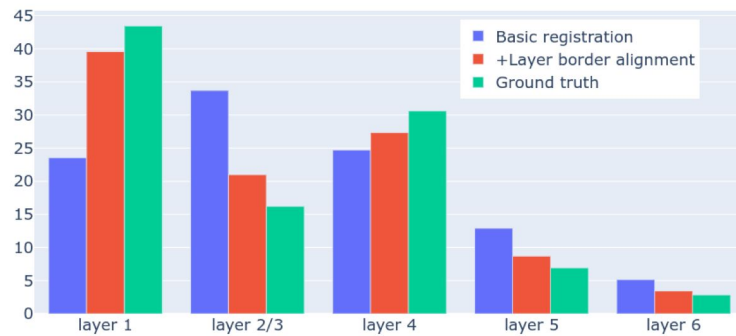
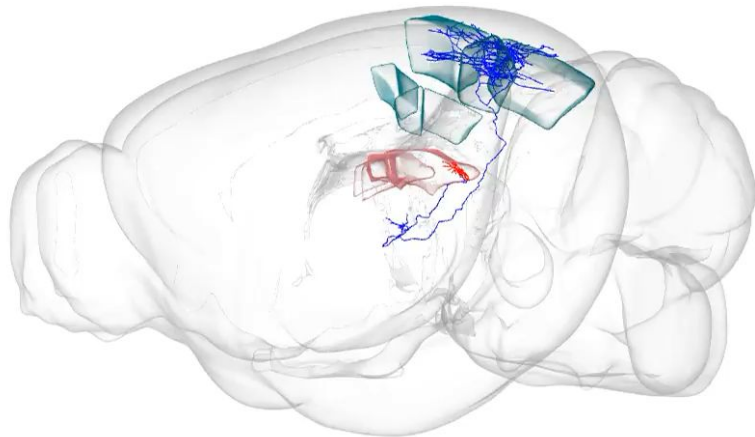
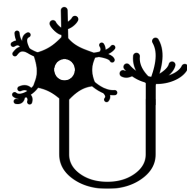


Test 1: Deformable registration, comes with huge artifacts.



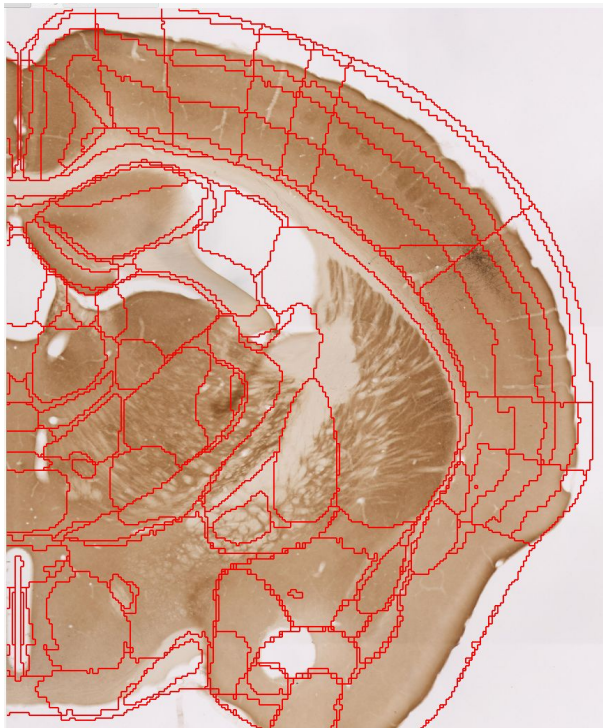
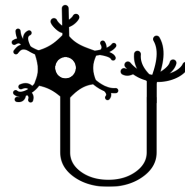
Test 2: Deformable registration, including a set of manually inserted landmarks.

End result of the procedure:

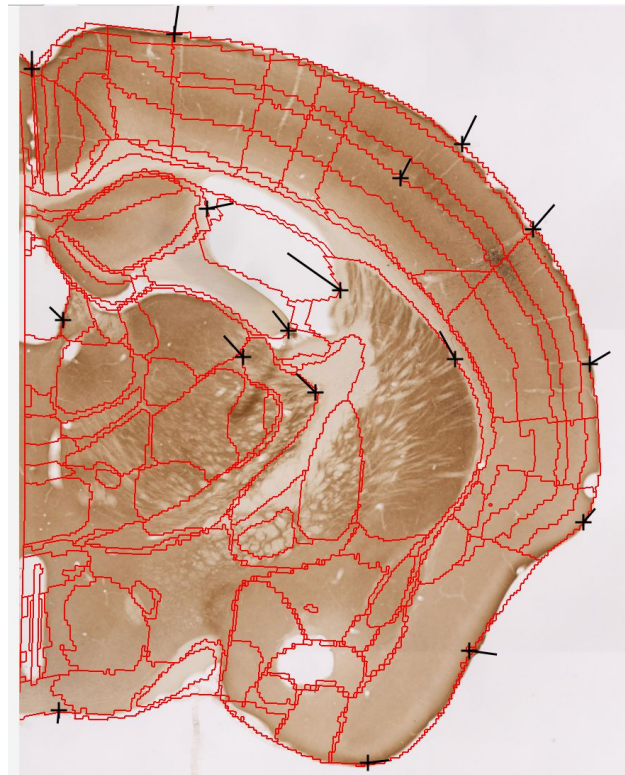


VisuAlign (HBP) presents a user friendly alternative

(after we managed to invert the transformations)

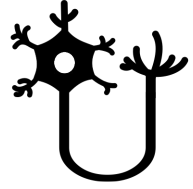


Before

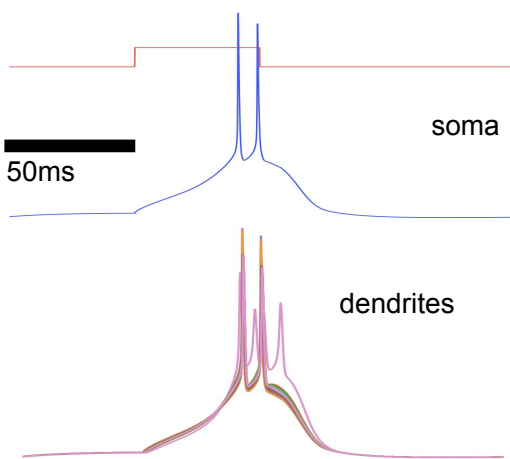


After multiple manual, local deformations *of the atlas*

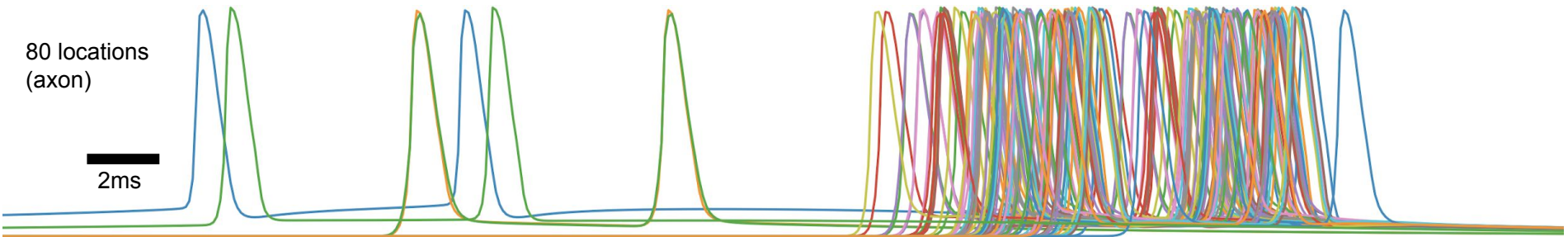
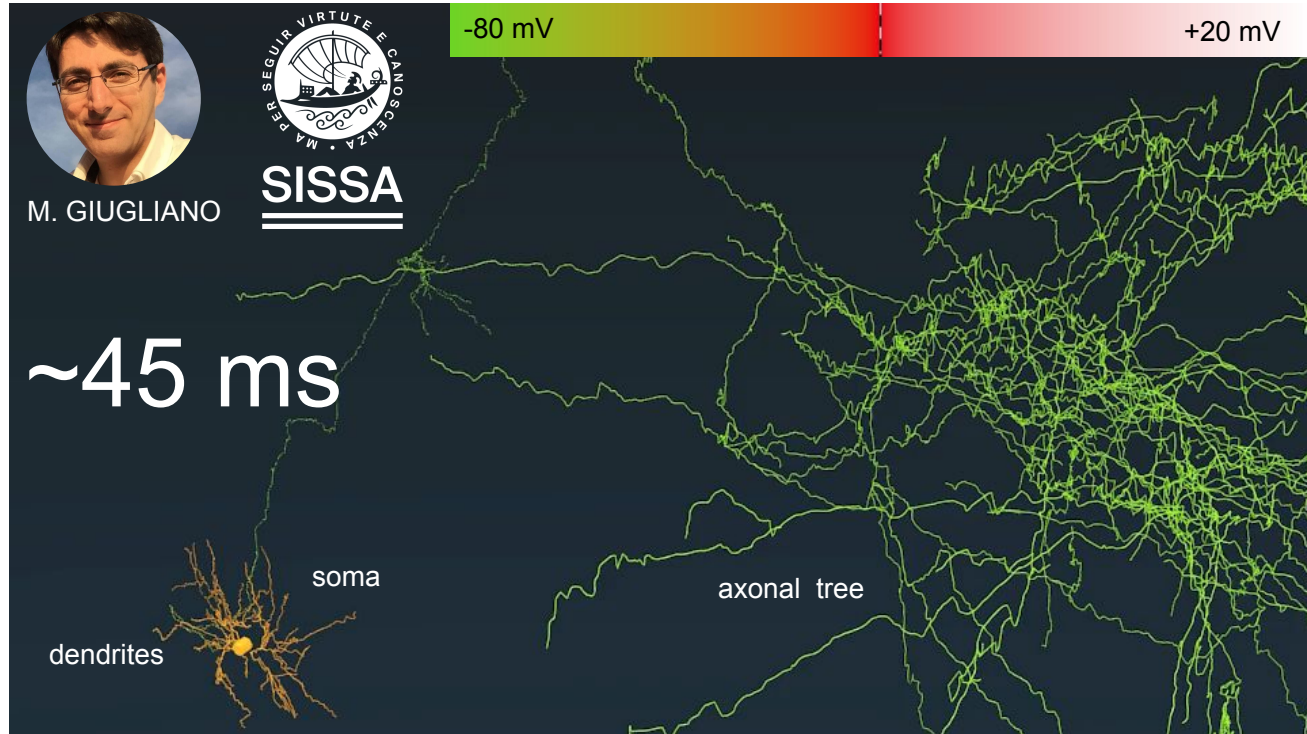
WP3: Modeling



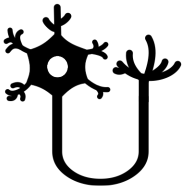
- Part 1: Consequences of realistic axons in multicompartmental models (SISSA)
- Part 2: Adding proper thalamocortical projections to cortex model (Juelich) □ extract necessary statistics from databases



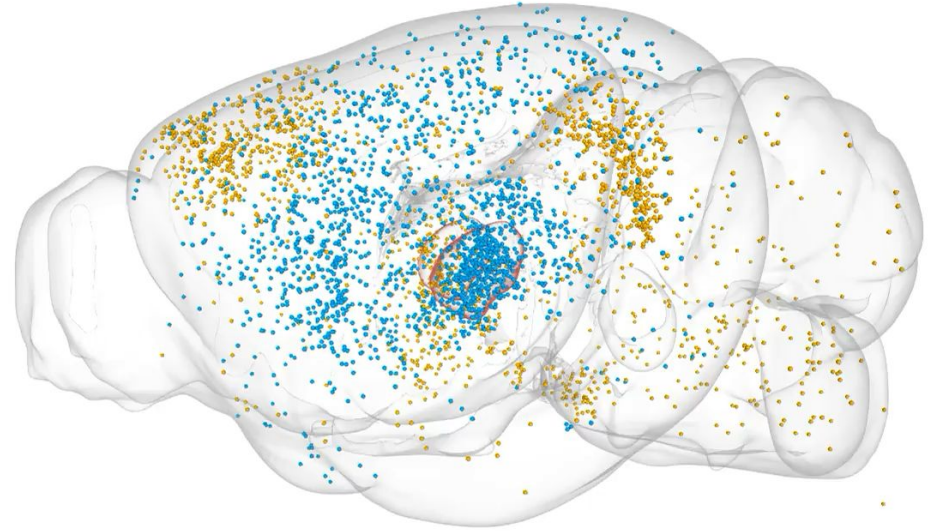
- SK-type Ca-activated K⁺ current
- Fast Na⁺ and K⁺ currents
- Fast Transient K⁺ Current I_A
- L-current, (high-thr.) Ca⁺⁺ current
- I_h current



Assessing the registration accuracy of neurons from two large repositories-1



- 1) Mouselight (Janelia Farms)
contains 1544 neurons (yellow)
- 2) Braintell (Southeast Univ. / Allen Inst.)
contains 1741 neurons (blue)
- 3) The most densely sampled area
is the VPM thalamic nucleus.
It projects primarily to layer IV of
somatosensory cortex



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

Johan Winnubst,¹ Erhan Bas,^{1,2} Tiago A. Ferreira,¹ Zhuohao Wu,² Michael N. Economo,¹ Patrick Edson,³ Ben J. Arthur,¹ Christopher Bruns,^{1,2} Konrad Rokicki,¹ David Schauder,¹ Donald J. Olbris,¹ Sean D. Murphy,¹ David G. Ackerman,¹ Cameron Arshadi,¹ Perry Baldwin,¹ Regina Blasko,¹ Ahmad Elsayed,¹ Mashura Hasan,¹ Daniel Ramirez,¹ Bruno Dos Santos,¹ Monet Weldon,¹ Amina Zafar,¹ Joshua T. Dudman,¹ Charles R. Gerfen,¹ Adam W. Hartman,¹ Wyatt Korf,¹ Scott M. Stenson,¹ Nelson Spruston,¹ Karel Svoboda,¹ and Jayaram Chandrasekar^{1,2,4}

Morphological diversity of single neurons in molecularly defined cell types

<https://doi.org/10.1038/s41586-021-03941-1>

Received: 27 September 2020

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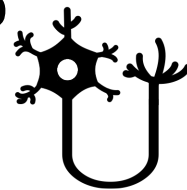
Published online: 6 October 2021

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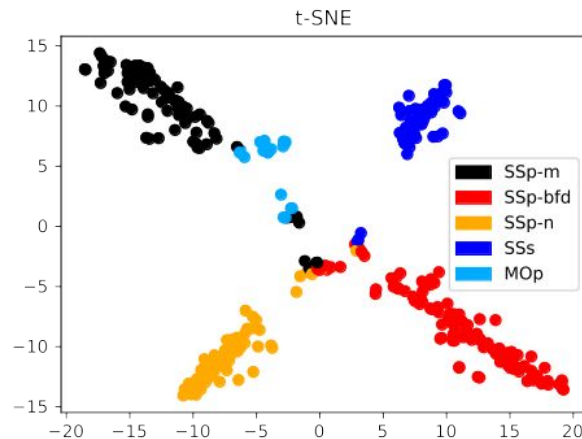
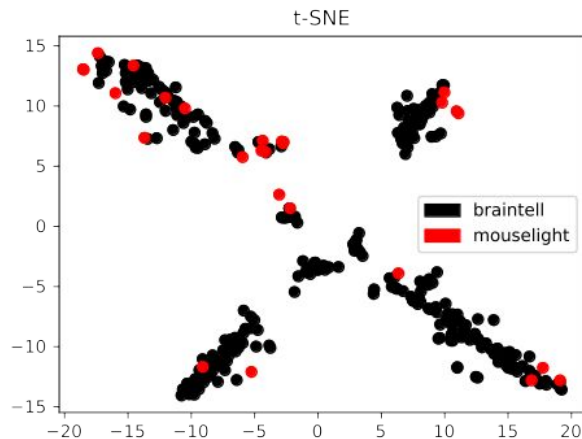
Check for updates

Henchuan Peng^{1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20,21,22,23,24,25,26,27,28,29,30,31,32,33,34,35,36,37,38,39,40,41,42,43,44,45,46,47,48,49,50,51,52,53,54,55,56,57,58,59,60,61,62,63,64,65,66,67,68,69,70,71,72,73,74,75,76,77,78,79,80,81,82,83,84,85,86,87,88,89,90,91,92,93,94,95,96,97,98,99,100,101,102,103,104,105,106,107,108,109,110,111,112,113,114,115,116,117,118,119,120,121,122,123,124,125,126,127,128,129,130,131,132,133,134,135,136,137,138,139,140,141,142,143,144,145,146,147,148,149,150,151,152,153,154,155,156,157,158,159,160,161,162,163,164,165,166,167,168,169,170,171,172,173,174,175,176,177,178,179,180,181,182,183,184,185,186,187,188,189,190,191,192,193,194,195,196,197,198,199,200,201,202,203,204,205,206,207,208,209,210,211,212,213,214,215,216,217,218,219,220,221,222,223,224,225,226,227,228,229,230,231,232,233,234,235,236,237,238,239,240,241,242,243,244,245,246,247,248,249,250,251,252,253,254,255,256,257,258,259,260,261,262,263,264,265,266,267,268,269,270,271,272,273,274,275,276,277,278,279,280,281,282,283,284,285,286,287,288,289,290,291,292,293,294,295,296,297,298,299,300,301,302,303,304,305,306,307,308,309,310,311,312,313,314,315,316,317,318,319,320,321,322,323,324,325,326,327,328,329,330,331,332,333,334,335,336,337,338,339,340,341,342,343,344,345,346,347,348,349,350,351,352,353,354,355,356,357,358,359,360,361,362,363,364,365,366,367,368,369,370,371,372,373,374,375,376,377,378,379,380,381,382,383,384,385,386,387,388,389,390,391,392,393,394,395,396,397,398,399,400,401,402,403,404,405,406,407,408,409,410,411,412,413,414,415,416,417,418,419,420,421,422,423,424,425,426,427,428,429,430,431,432,433,434,435,436,437,438,439,440,441,442,443,444,445,446,447,448,449,450,451,452,453,454,455,456,457,458,459,460,461,462,463,464,465,466,467,468,469,470,471,472,473,474,475,476,477,478,479,480,481,482,483,484,485,486,487,488,489,490,491,492,493,494,495,496,497,498,499,500,501,502,503,504,505,506,507,508,509,510,511,512,513,514,515,516,517,518,519,520,521,522,523,524,525,526,527,528,529,530,531,532,533,534,535,536,537,538,539,540,541,542,543,544,545,546,547,548,549,550,551,552,553,554,555,556,557,558,559,560,561,562,563,564,565,566,567,568,569,570,571,572,573,574,575,576,577,578,579,580,581,582,583,584,585,586,587,588,589,590,591,592,593,594,595,596,597,598,599,600,601,602,603,604,605,606,607,608,609,610,611,612,613,614,615,616,617,618,619,620,621,622,623,624,625,626,627,628,629,630,631,632,633,634,635,636,637,638,639,640,641,642,643,644,645,646,647,648,649,650,651,652,653,654,655,656,657,658,659,660,661,662,663,664,665,666,667,668,669,670,671,672,673,674,675,676,677,678,679,680,681,682,683,684,685,686,687,688,689,690,691,692,693,694,695,696,697,698,699,700,701,702,703,704,705,706,707,708,709,710,711,712,713,714,715,716,717,718,719,720,721,722,723,724,725,726,727,728,729,730,731,732,733,734,735,736,737,738,739,740,741,742,743,744,745,746,747,748,749,750,751,752,753,754,755,756,757,758,759,760,761,762,763,764,765,766,767,768,769,770,771,772,773,774,775,776,777,778,779,780,781,782,783,784,785,786,787,788,789,790,791,792,793,794,795,796,797,798,799,800,801,802,803,804,805,806,807,808,809,810,811,812,813,814,815,816,817,818,819,820,821,822,823,824,825,826,827,828,829,830,831,832,833,834,835,836,837,838,839,840,841,842,843,844,845,846,847,848,849,850,851,852,853,854,855,856,857,858,859,860,861,862,863,864,865,866,867,868,869,870,871,872,873,874,875,876,877,878,879,880,881,882,883,884,885,886,887,888,889,890,891,892,893,894,895,896,897,898,899,900,901,902,903,904,905,906,907,908,909,910,911,912,913,914,915,916,917,918,919,920,921,922,923,924,925,926,927,928,929,930,931,932,933,934,935,936,937,938,939,940,941,942,943,944,945,946,947,948,949,950,951,952,953,954,955,956,957,958,959,960,961,962,963,964,965,966,967,968,969,970,971,972,973,974,975,976,977,978,979,980,981,982,983,984,985,986,987,988,989,990,991,992,993,994,995,996,997,998,999,1000}

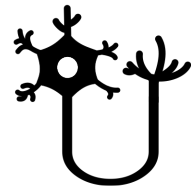
Assessing the registration accuracy of neurons from two large repositories-2



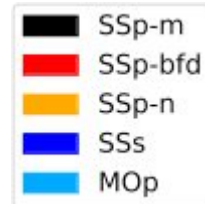
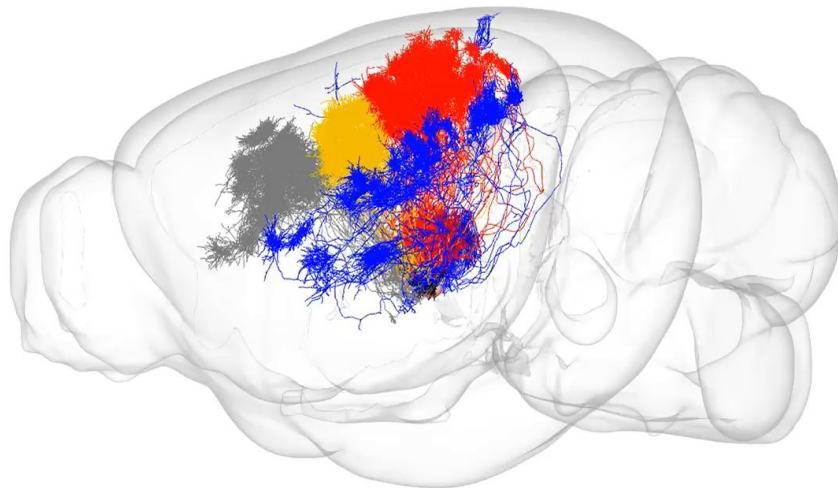
- 1) For each neuron, the axonal length in 8 pre-defined cortical areas is calculated
- 2) The 8x300 'feature matrix' is compressed to two dimensions with t-SNE.
- 3) There are 5 clusters based on the **dominant projection target**.



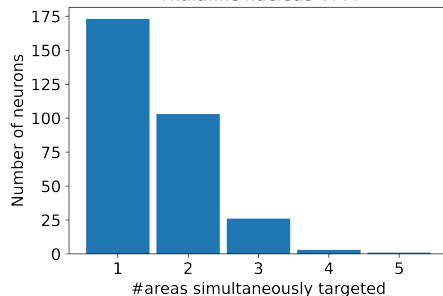
Visualizing the neurons that target a single cortical region



The various somatosensory targets (barrel field, mouth, nose) can be seen to originate in spatially distinct subareas of VPM.

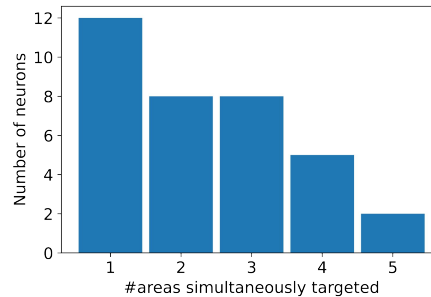


Thalamic nucleus VPM



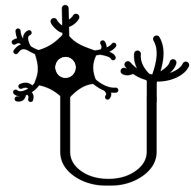
Most VPM neurons have 90% of axonal length in a single cortical region (primary projection neurons that target layer 4).

Thalamic nucleus PO

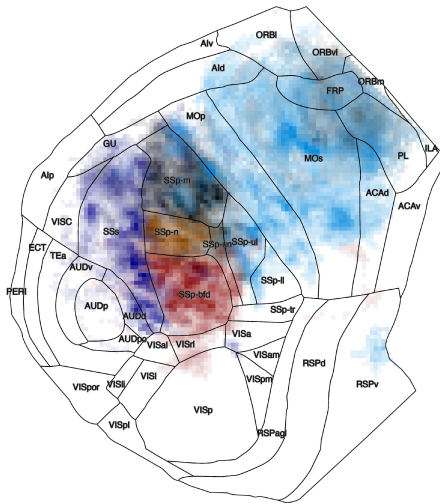


Adjacent nucleus PO typically targets multiple cortical areas.

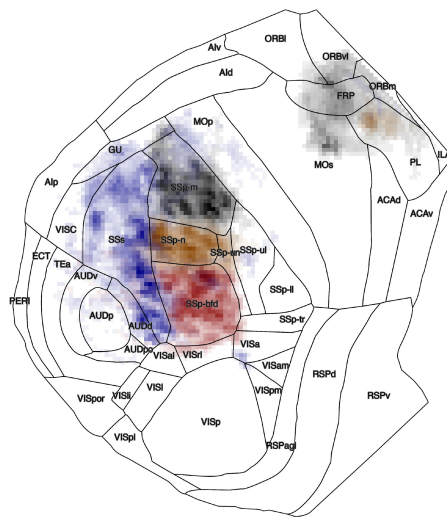
Some 'VPM neurons' that target multiple areas might belong to adjacent nuclei: imprecise registration



All neurons



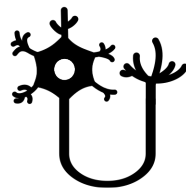
Targeting a single cortical area



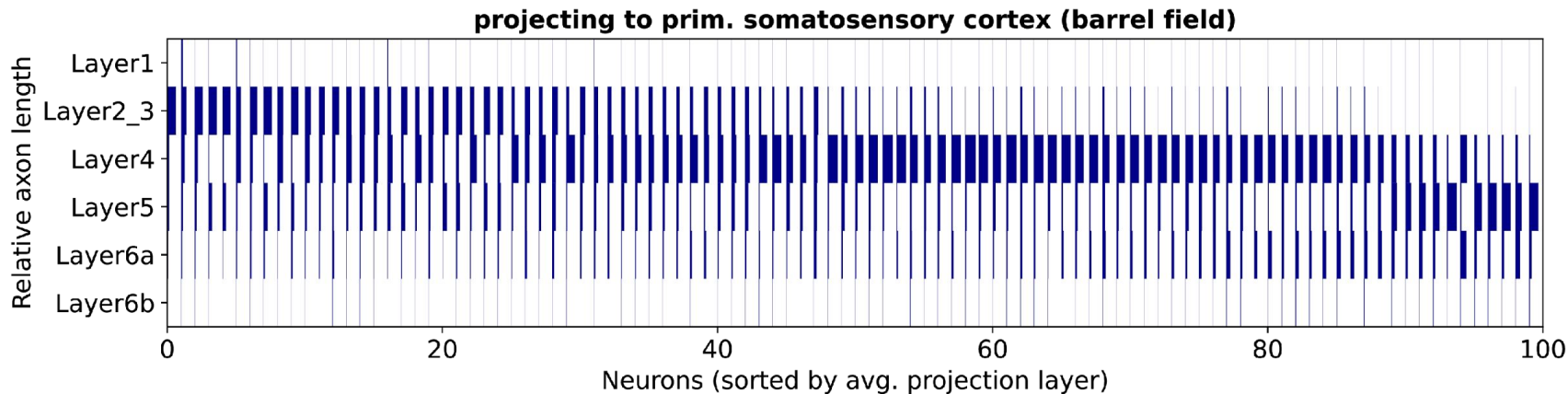
Neurons colored according to dominant target (see legend).

Made with the NeuronsReunited online flatmap service, <https://neuroinformatics.nl/HBP/allen-flatmap/>.

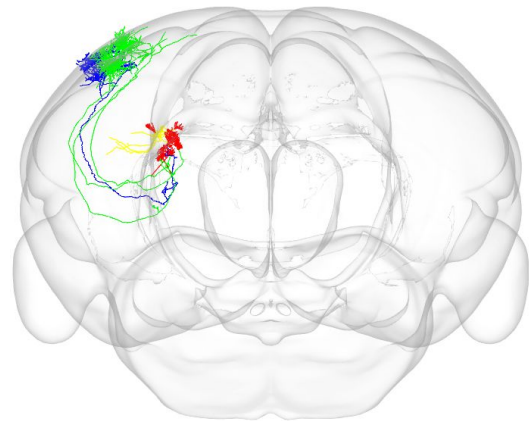
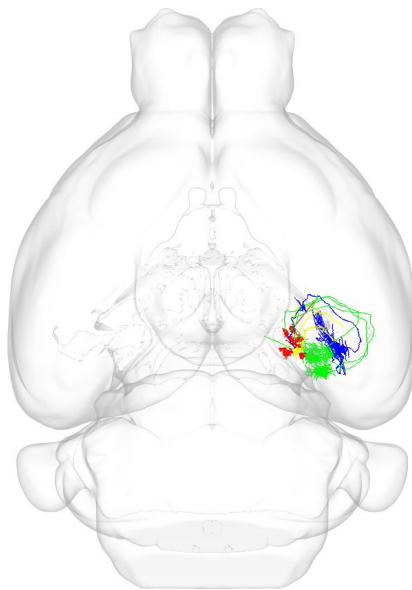
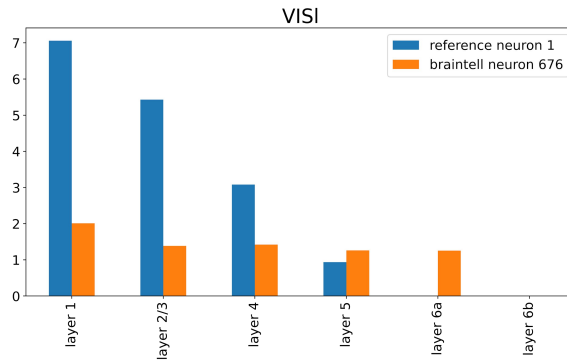
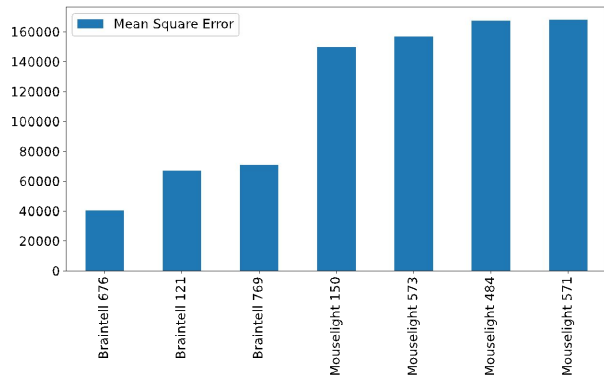
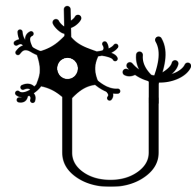
Layer distribution of VPM neurons targeting barrel cortex

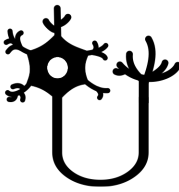


- A clear majority of neurons targets layers 2/3 and 4.



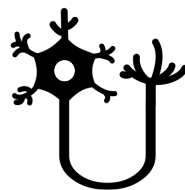
Finding friends with Coherent Point Drift (CPD) and comparing statistics





Future steps

- Automatic registration pipeline for high quality/undamaged slices based on volume reconstruction
- Thalamocortical model of integration/gain modulation
- Impact of timing variation due axonal branching (oscillations)



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).

The screenshot shows the EBRAINS website interface. At the top, there is a logo and the text 'EBRAINS'. To the right are links for 'Share data' and 'About'. Below this is a yellow banner with the text 'DATASET' and icons for a folder and an envelope. The main title of the dataset is '3D reconstruction and measurement of individual thalamocortical projection neuron axons of somatosensory and visual thalamic nuclei'. Below the title, the authors are listed: 'García-Amado, M.; Porrero, C.; Rubio, M.; Evangelio, M.; Clascá, F.'. At the bottom of the banner are two buttons: 'Cite dataset' and 'Data-descriptor'. Below the banner, the DOI is '10.25493/AWS5-MZG'. The license is 'Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International'. The project is '3D reconstruction of thalamocortical projection neurons'. The custodians are 'Clascá, Francisco'.

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

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Project: 3D reconstruction of thalamocortical projection neurons

Custodians: Clascá, Francisco