

NEUROSCIENCE IN THE DATABASE

MAPPING THE MORPHOLOGY
OF NEURONS AND SYNAPSES
WITH CATMAID AND POSTGIS

Tom Kazimiers | kazmos GmbH


PostGIS Day 2021, November 18

WHO?



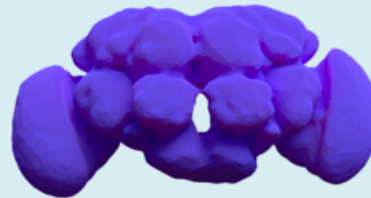
- Tom Kazimiers, Main developer of CATMAID, MSc CS (Dipl.Inf.) TU Dresden
- 3+ years at MPI CBG (Dresden, DE)
- 6+ years at HHMI Janelia Research Campus (Ashburn, Virginia, USA)
- Since 2020: Open Source Research Software Engineer and founder of consultancy kazmos GmbH (DE)

TOPICS

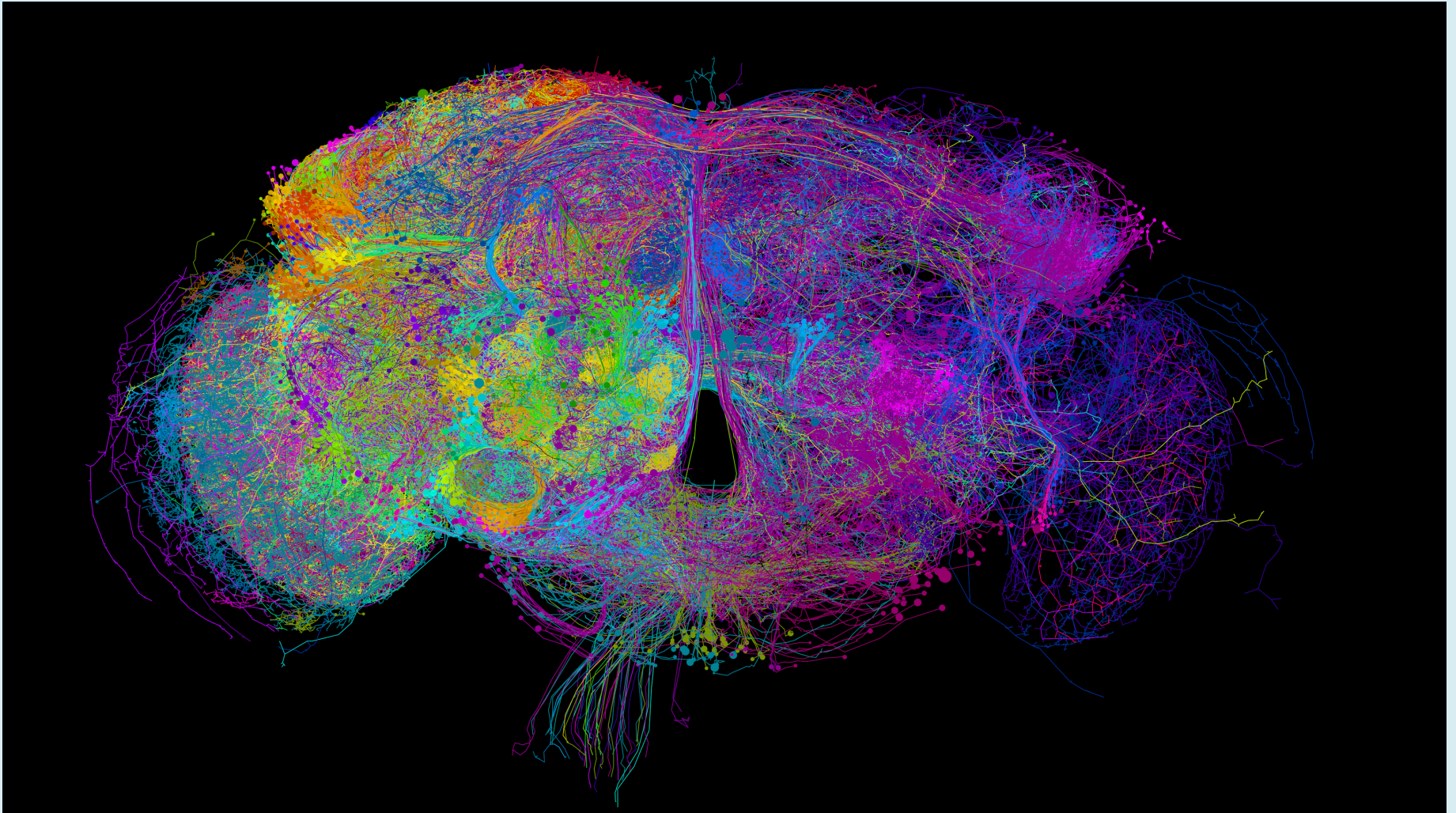
- Motivation and data
-  Overview
- Data representation
- Neuron graph queries
- PostGIS queries

MOTIVATION: CONNECTOMICS

- Structure/development of central nervous system
- Function of specific neurons and neuron classes
- Synapses and resulting networks
- How is behavior controlled?
- Fundamental research

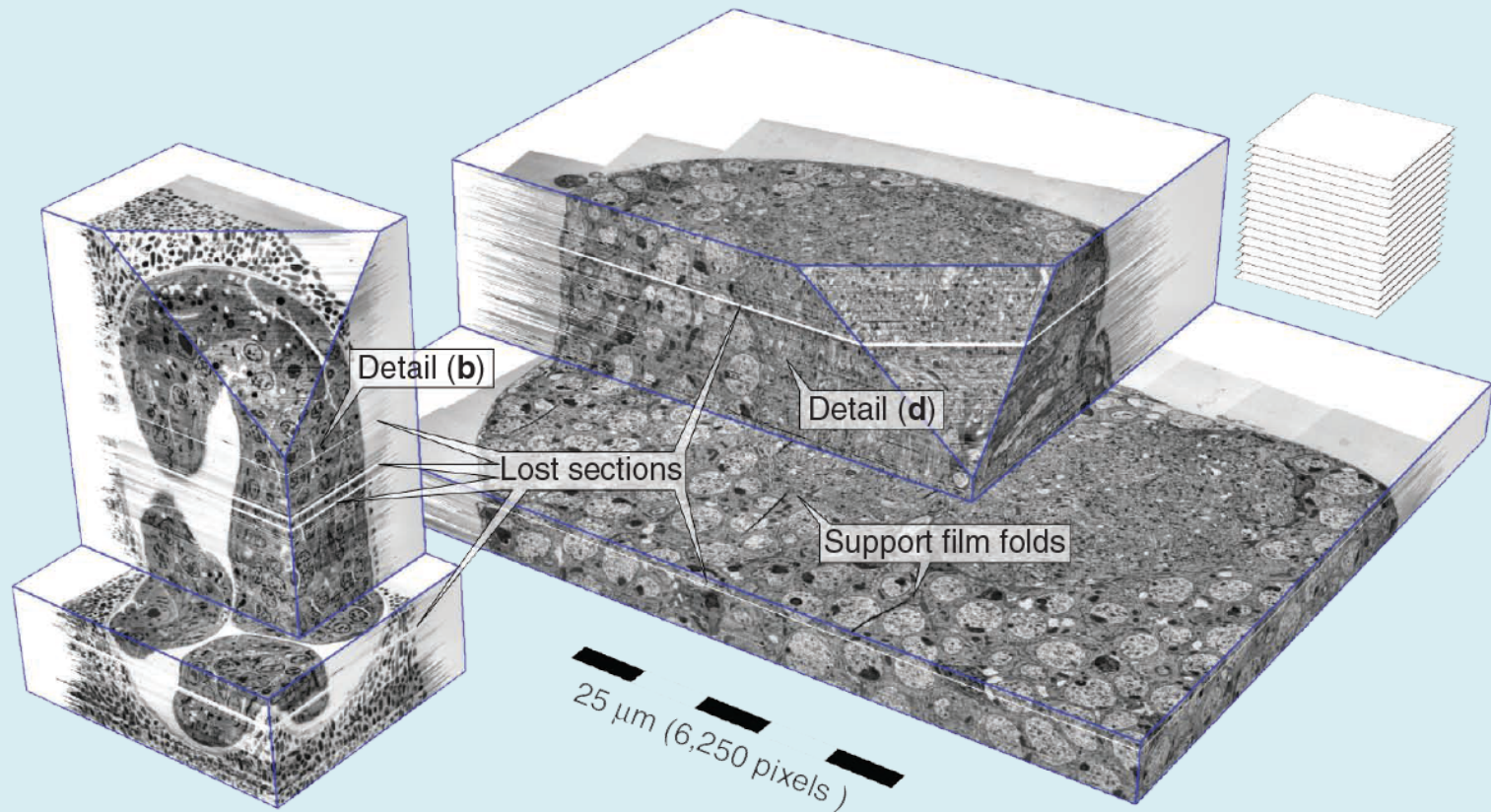


Model organism *Drosophila Melanogaster* ("fruit fly")
Images: Wikimedia, CC-BY-SA 2.5 (left) and CC-BY-SA 4.0 (right)



~7 meters of neurons in brain of fruit fly, 20 labs, 186 users
created and reviewed 33 million nodes in more than 60 person years
Image by Philipp Schlegel, Jefferis lab

IMAGE DATA: ELECTRON MICROSCOPY



ssTEM: Elastic volume reconstruction from series of ultra-thin microscopy sections
S. Saalfeld, R. Fetter, A. Cardona, *et al.*, *Nature Methods*, 2012

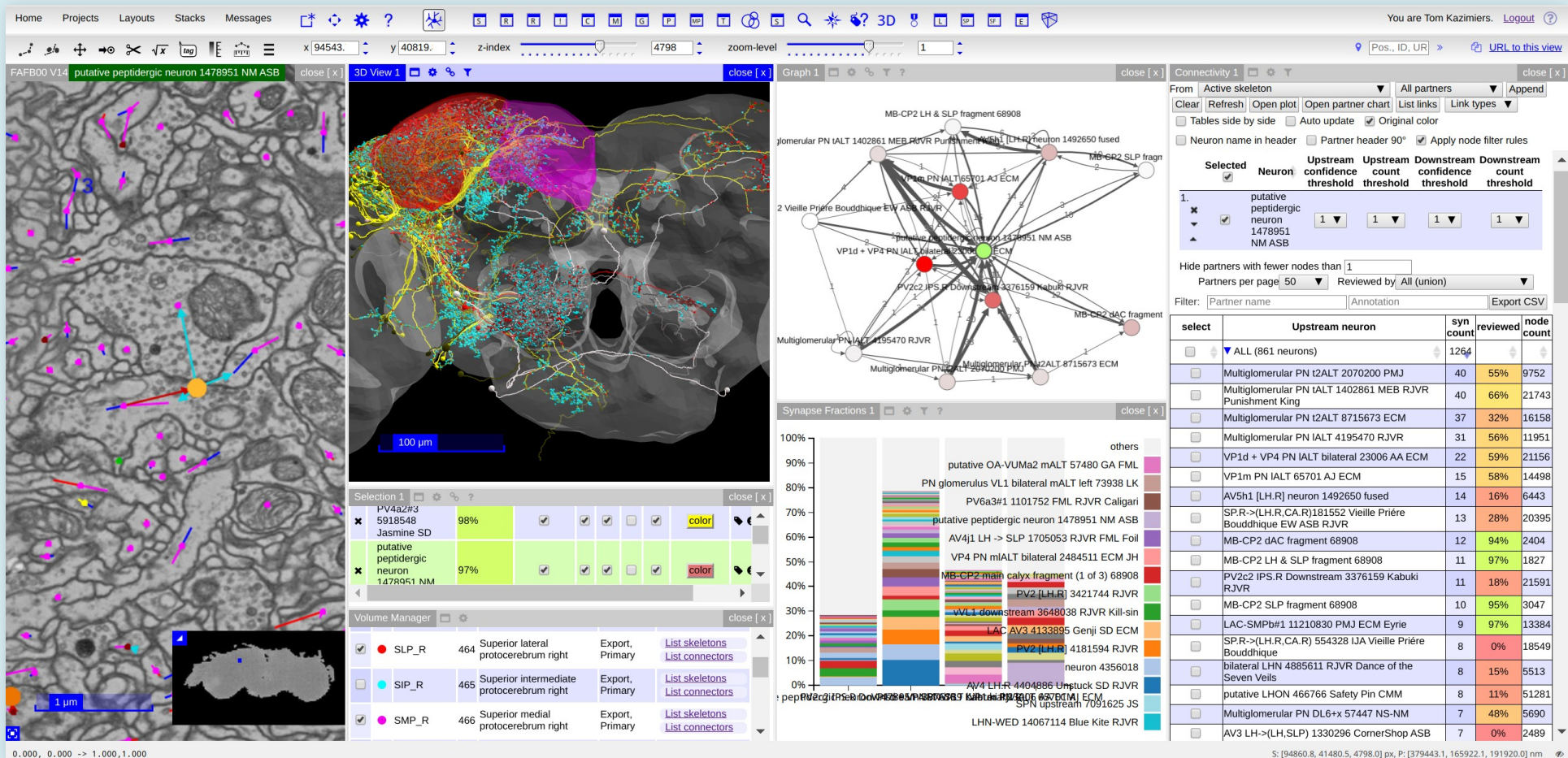
REPRESENTATIVE DATA SETS

- **Drosophila Larva L1 Dataset (ssTEM):**
28,128 x 31,840 x 4,841 px @ 3.8 x 3.8 x 50 nm/px
0.9TB as JPEG tiles (512 x 512)
- **Drosophila FAFB Dataset (ssTEM):**
253,952 x 155,648 x 7,063 px @ 4 x 4 x 40 nm/px
10.9TB as JPEG tiles (1024 x 1024)
- **Drosophila Hemibrain Dataset (FIBSEM):**
40,959 x 34,815 x 43,007 px @ 8 x 8 x 8 nm/px
5.3TB as Neuroglancer Precomputed (64 x 64 x 64)
- **Compare: OpenStreetMap tiles (z18):**
Scandinavian countries: 1TB (Geofabrik)
North + South America: 11TB (Geofabrik)
North America: 5.4TB (Geofabrik)



Collaborative Annotation Toolkit
for
Massive Amounts of Image Data

USER INTERFACE I



Typical CATMAID workspace with 2D and 3D views plus some connectivity tools
Example circuit from Dolan et al. 2019, FAFBv14 dataset

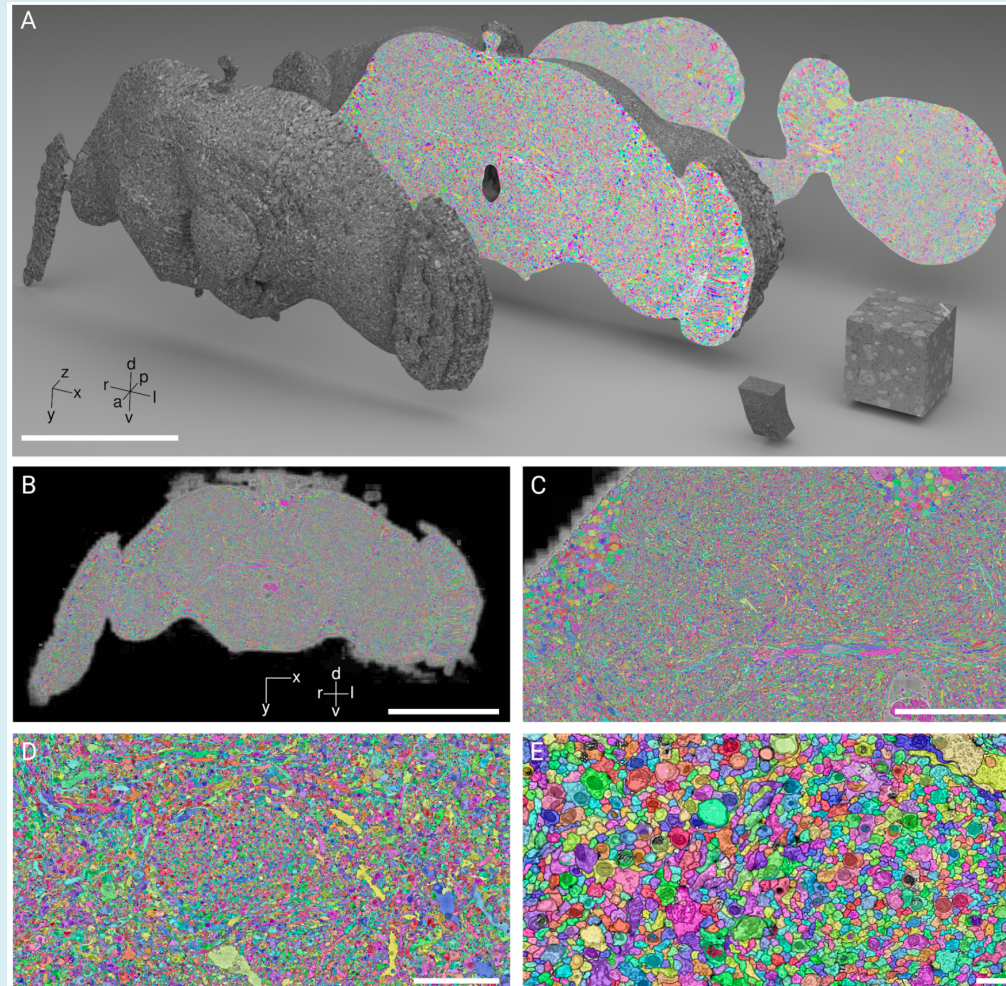
USER INTERFACE II

The screenshot displays the CATMAID software interface, which is used for managing and analyzing neuron data. The interface is divided into several panels:

- Top Panel:** Contains navigation tabs (Home, Projects, Layouts, Messages) and a toolbar with various icons for file operations, viewing, and analysis.
- Left Panel:** Shows a 3D view of a neuron point cloud (neuron 10860.3157) with a color-coded skeleton. Below it, a table lists similarity results for various neuron pairs, including columns for ID, Name, User, Status, Config, Created on (UTC), Alpha, Normalized, Query objects, Target objects, Scoring, and Action.
- Center Panel:** Displays a 3D view of a neuron point cloud (neuron 10860.3157) with a color-coded skeleton. Below it, a table lists similarity results for various neuron pairs, including columns for ID, Name, User, Status, Config, Created on (UTC), Alpha, Normalized, Query objects, Target objects, Scoring, and Action.
- Right Panel:** Shows a 3D view of a neuron point cloud (neuron 10860.3157) with a color-coded skeleton. Below it, a table lists similarity results for various neuron pairs, including columns for ID, Name, User, Status, Config, Created on (UTC), Alpha, Normalized, Query objects, Target objects, Scoring, and Action.
- Bottom Panel:** Contains a similarity configuration window with a heatmap showing the similarity matrix for selected skeletons and random skeletons. The heatmap is color-coded from blue (low similarity) to red (high similarity). Below the heatmap, a table lists the source and target landmark groups for the similarity analysis.

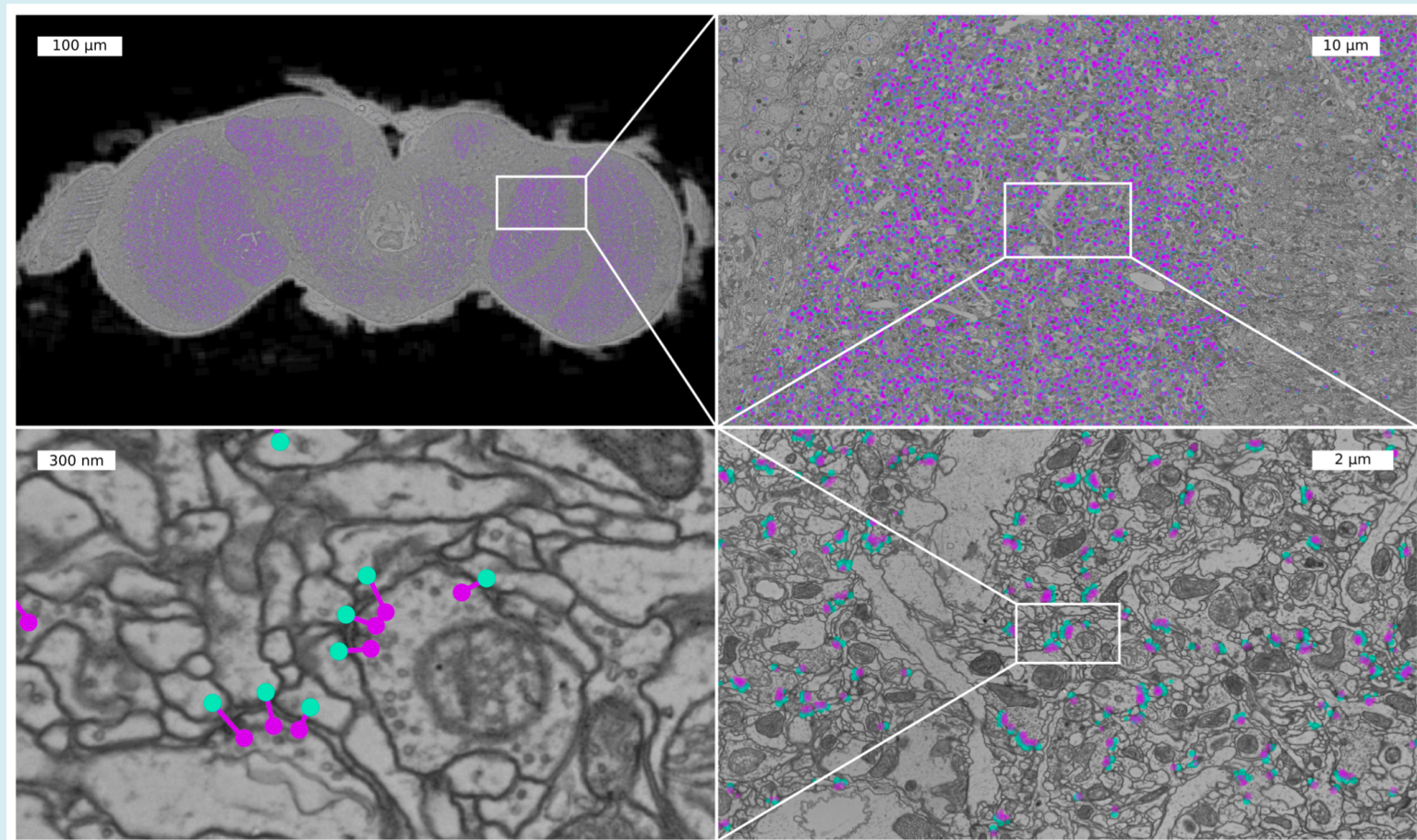
CATMAID with neuron similarity tools and point-clouds from light data
Screenshots from Albert Cardona's Drosophila L1 dataset

NEURON SEGMENTATION



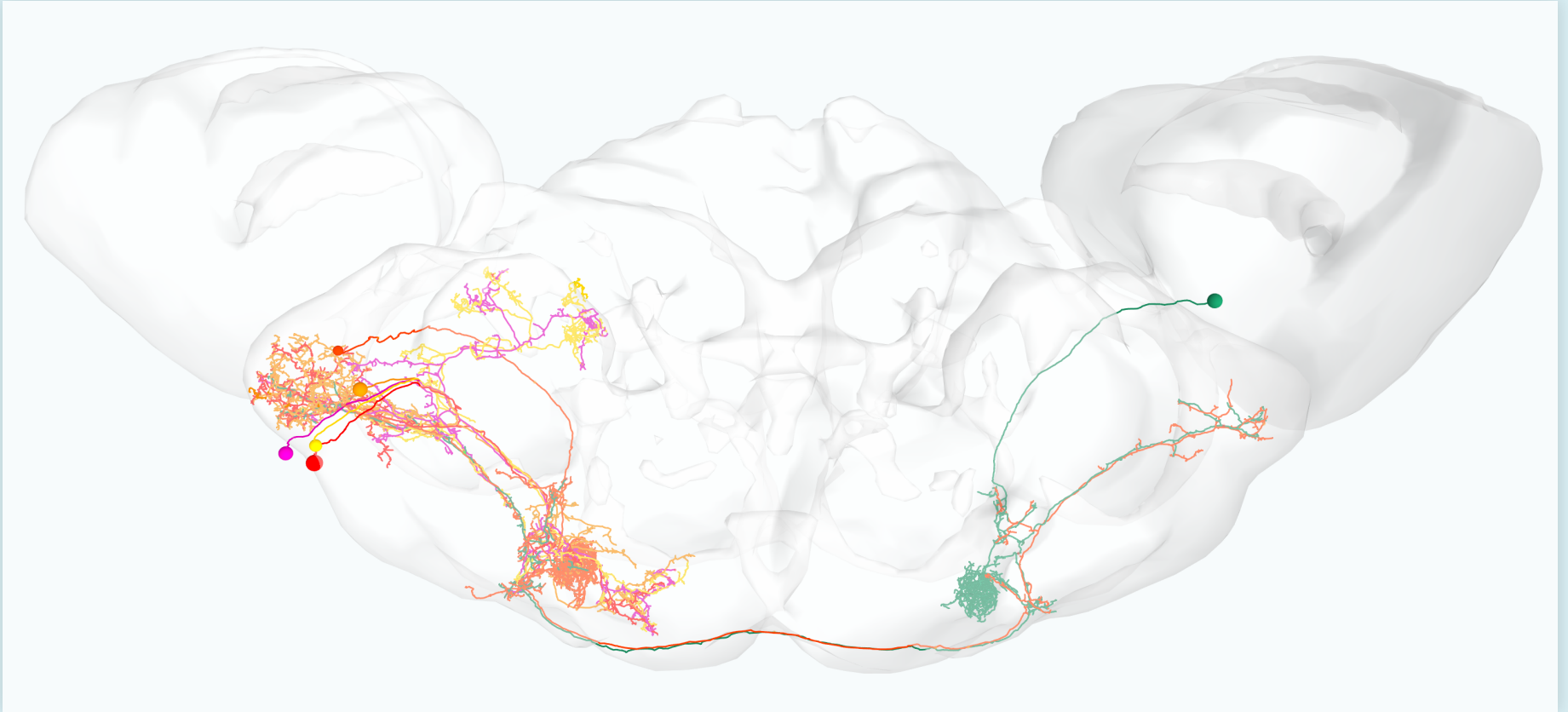
Segmentation of FAFB dataset: used also for skeletonization; Similar in FlyWire project
Li, Jain et al, bioRxiv 2020

SYNAPTIC PARTNER DETECTION



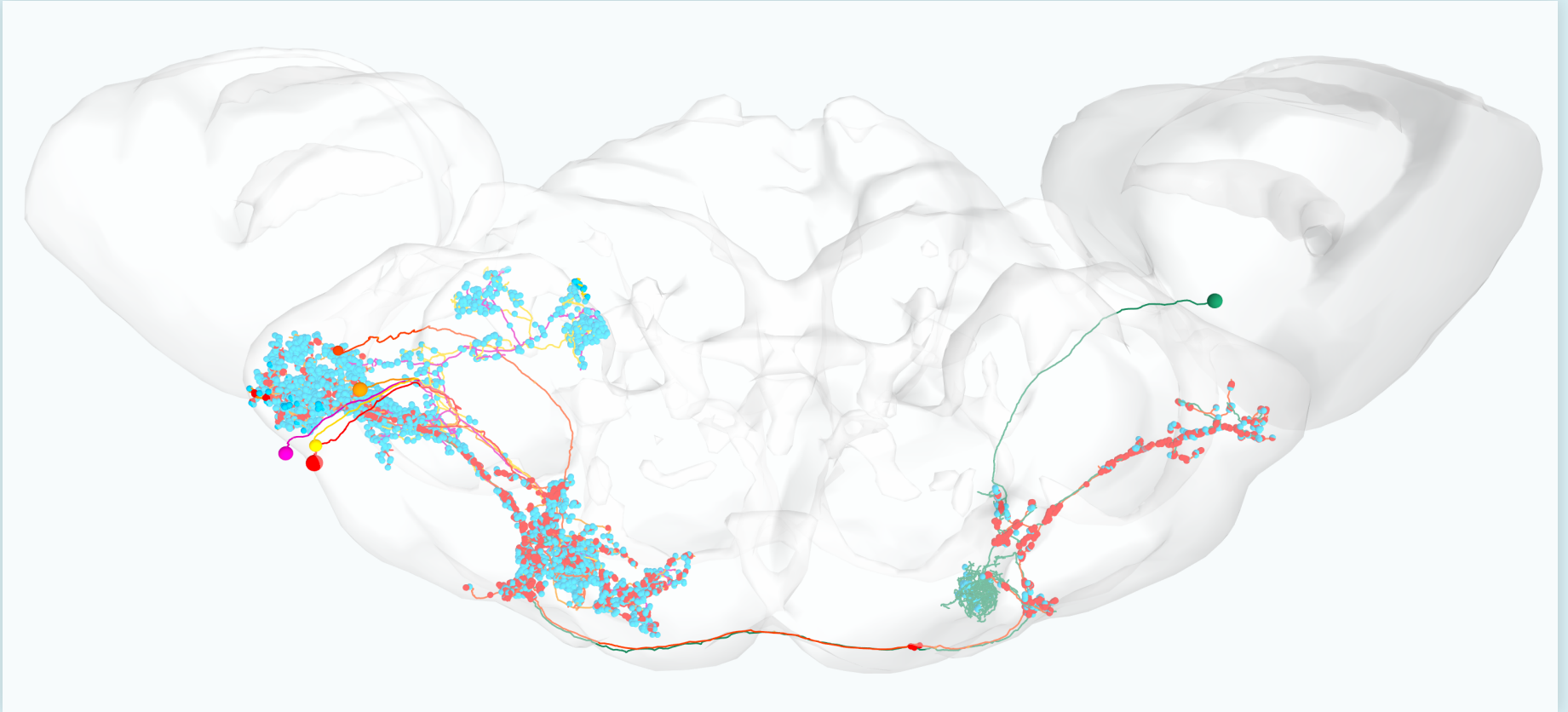
Automatic detection of synaptic partners (CircuitMap tool in CATMAID)
Buhman et al, Nature Methods, 2021

MODELLING NEURONS



First order (downstream) partners (orange/red) to MBON a2sc Left ASB (green)
From Dolan and Belliart-Guérin et al. 2018

MODELLING NEURONS

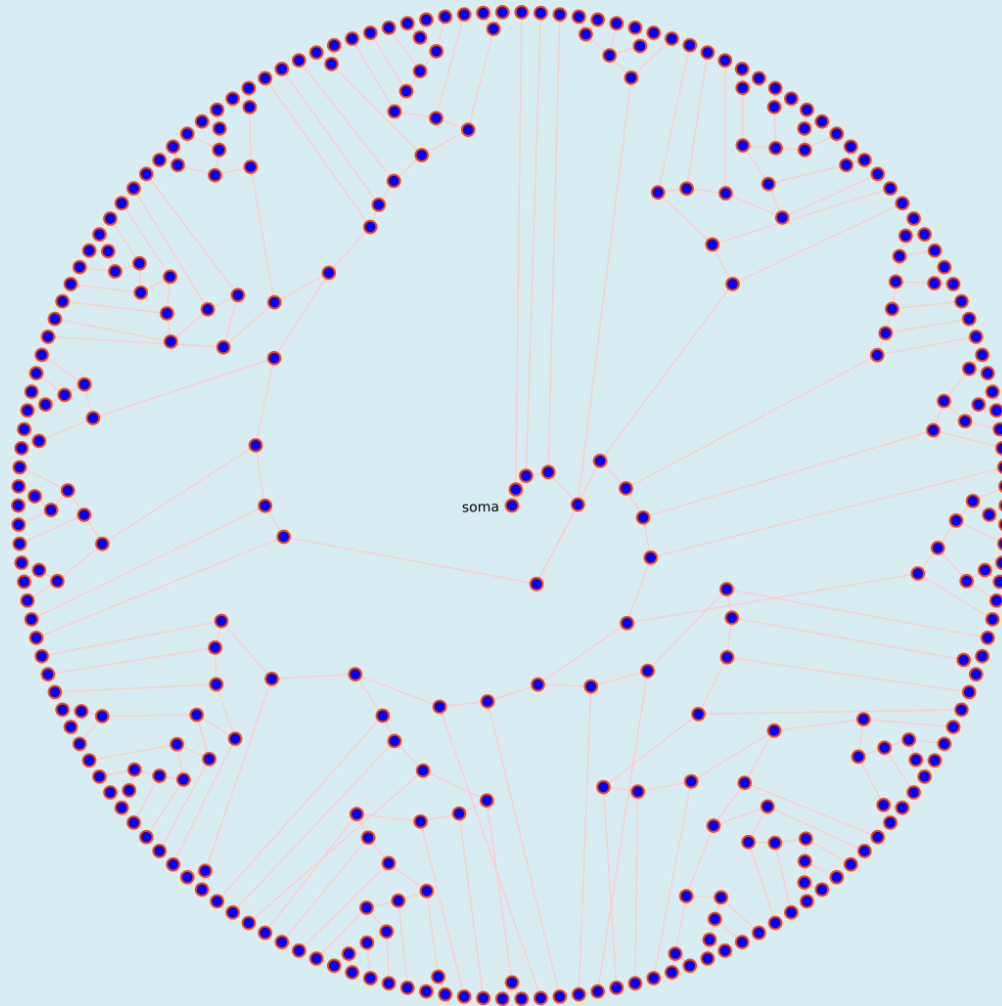


MBON and PD neurons with synapses highlighted (pre: red, post: cyan)
From Dolan and Belliart-Guérin et al. 2018

MORPHOLOGY OF A NEURON



TOPOLOGY OF A NEURON



REPRESENTING NEURONS IN A DATABASE

- Relational data, explicit schema: PostgreSQL
- Nodes of all skeletons in single table
- Every element knows parent or is root (trees)

```
# \d treenode
      Column      |      Type      | Nullable | Default
-----+-----+-----+-----
id                 | bigint          | not null |
parent_id          | bigint          |          |
skeleton_id        | bigint          | not null |
project_id         | integer         | not null |
location_x         | real            | not null |
...                | ...             | ...      |
```

Foreign-key constraints:

```
"treenode_parent_id_fkey" FOREIGN KEY (parent_id)
                           REFERENCES treenode(id)
```

QUERY NODES OF A SKELETON

- Query ignores any structure/relation between nodes

```
1 SELECT id, parent_id, location_x, location_y, location_z
2 FROM treenode
3 WHERE skeleton_id = {skeleton_id}
```

- Root node of skeleton

```
1 SELECT id, parent_id, location_x, location_y, location_z
2 FROM treenode
3 WHERE skeleton_id = {skeleton_id} AND parent_id IS NULL
```

QUERY NEIGHBOR NODES

```
1 SELECT c.id, c.location_x, c.location_y, c.location_z
2 FROM treenode c
3 WHERE parent_id = {node_id}
4
5 UNION ALL
6
7 SELECT p.id, p.location_x, p.location_y, p.location_z
8 FROM treenode t
9 JOIN treenode p
10   ON p.id = t.parent_id
11 WHERE t.id = {node_id}
```

TRAVERSE SKELETONS

- Walk treenode DAG from root to leaves breadth-first, e.g. to find nodes *not* connected to root

```
1 WITH RECURSIVE nodes (id, depth) AS (  
2     SELECT t.id, 1  
3     FROM treenode t  
4     WHERE t.parent_id IS NULL  
5         AND t.skeleton_id = {skeleton_id}  
6     UNION ALL  
7     SELECT t.id, p.depth + 1  
8     FROM treenode t  
9     JOIN nodes p ON t.parent_id = p.id  
10 )  
11 SELECT t.id, t.parent_id  
12 FROM treenode t  
13 WHERE t.skeleton_id = {skeleton_id}  
14     AND NOT EXISTS (SELECT n.id FROM nodes n WHERE n.id = t.id);
```


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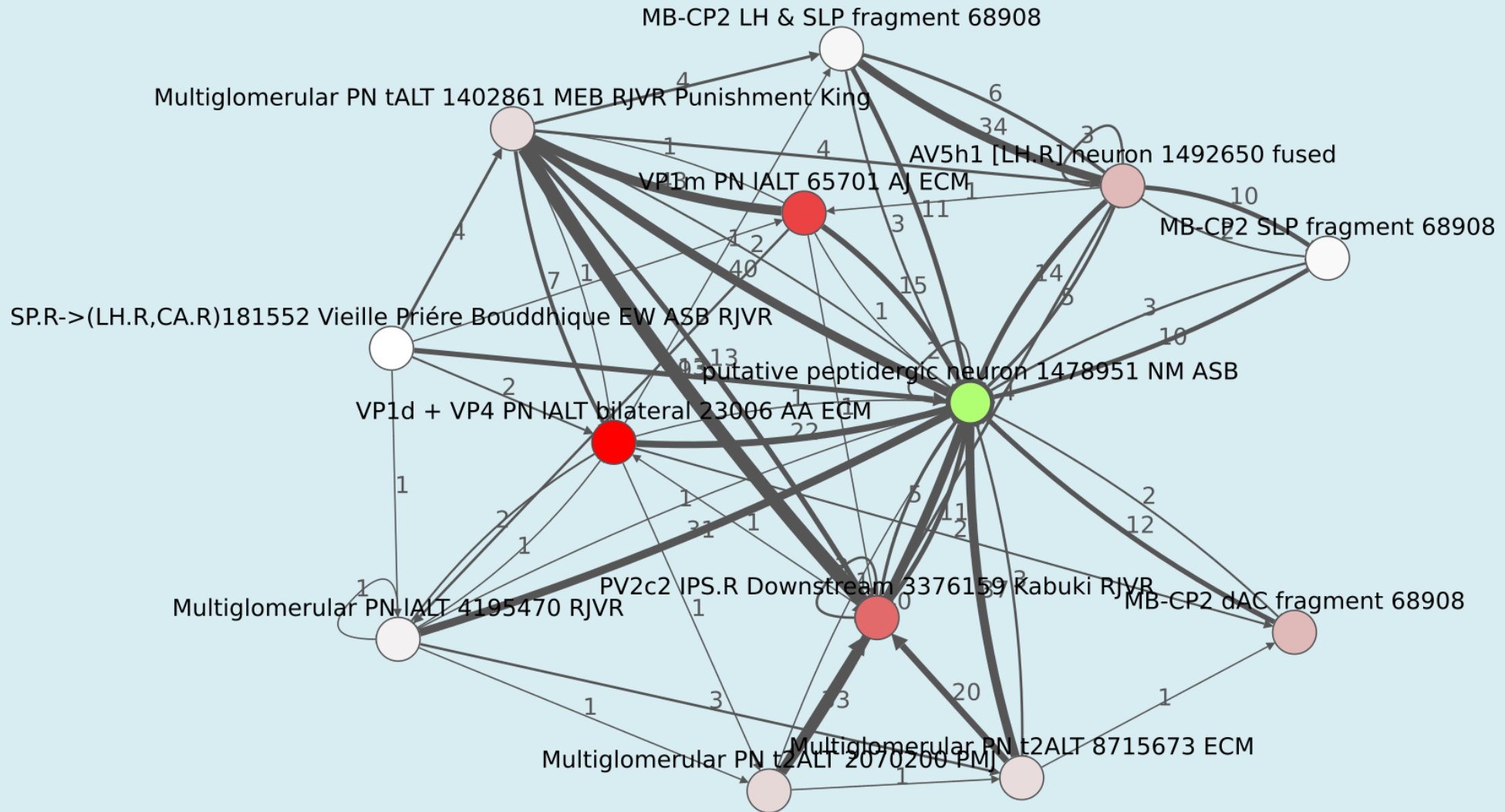
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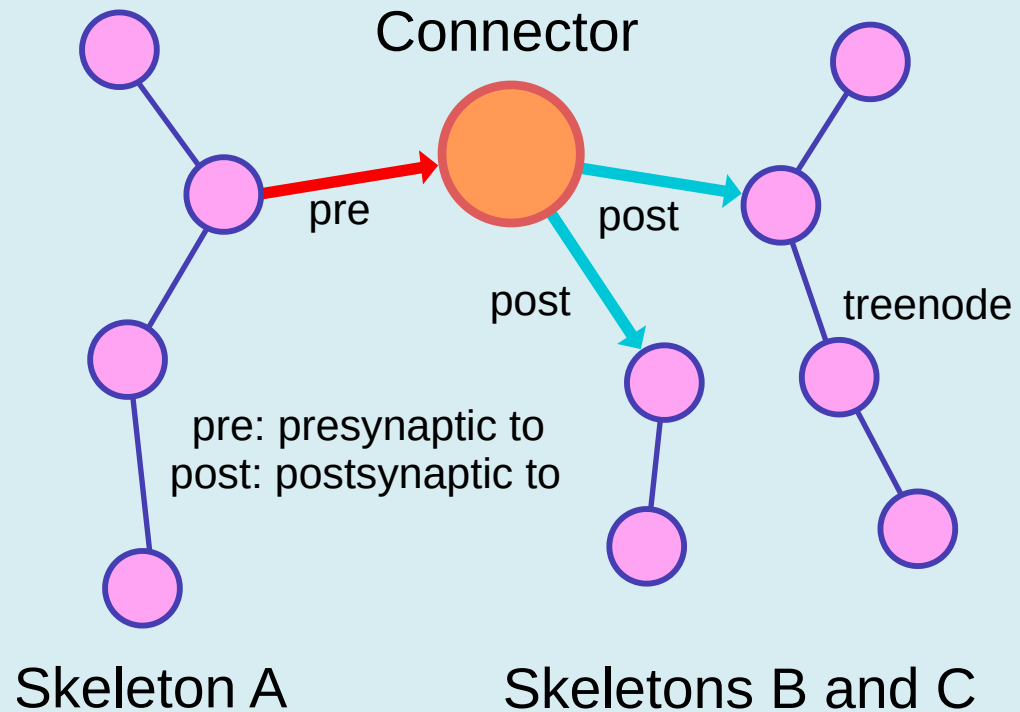
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14     AND NOT EXISTS (SELECT n.id FROM nodes n WHERE n.id = t.id);
```

CONNECTED NEURONS



NEURON GRAPHS IN CATMAID



NEURON GRAPHS IN SQL

```
# \d treenode_connector
```

Column	Type	Nullable	Default
relation_id	bigint	not null	
treenode_id	bigint	not null	
connector_id	bigint	not null	
skeleton_id	bigint	not null	
project_id	integer	not null	
confidence	smallint	not null	5
...	

Foreign-key constraints:

...

FINDING PARTNER NEURONS

- Useful for direct connections between skeletons, e.g. find partner skeleton IDs and synapse counts
- Gets more complex with additional levels

```
1 SELECT tc2.skeleton_id AS partner, COUNT(*) AS n_post_sites
2 FROM treenode_connector tc1
3 JOIN treenode_connector tc2
4   ON tc1.connector_id = tc2.connector_id
5   AND tc1.treenode_id != tc2.treenode_id
6 WHERE tc1.relation_id = {presynaptic_to_id}
7   AND tc2.relation_id = {postsynaptic_to_id}
8   AND tc1.project_id = {project_id}
9   AND tc2.project_id = {project_id}
10  AND tc1.skeleton_id = {skeleton_id}
11 GROUP BY tc2.skeleton_id
```


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7   AND tc2.relation_id = {postsynaptic_to_id}
8   AND tc1.project_id = {project_id}
9   AND tc2.project_id = {project_id}
10  AND tc1.skeleton_id = {skeleton_id}
11 GROUP BY tc2.skeleton_id
```

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6 WHERE tc1.relation_id = {presynaptic_to_id}
7   AND tc2.relation_id = {postsynaptic_to_id}
8   AND tc1.project_id = {project_id}
9   AND tc2.project_id = {project_id}
10  AND tc1.skeleton_id = {skeleton_id}
11 GROUP BY tc2.skeleton_id
```

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5   AND tc1.treenode_id != tc2.treenode_id
6 WHERE tc1.relation_id = {presynaptic_to_id}
7   AND tc2.relation_id = {postsynaptic_to_id}
8   AND tc1.project_id = {project_id}
9   AND tc2.project_id = {project_id}
10  AND tc1.skeleton_id = {skeleton_id}
11 GROUP BY tc2.skeleton_id
```

FINDING PARTNER NEURONS

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- Gets more complex with additional levels

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5   AND tc1.treenode_id != tc2.treenode_id
6 WHERE tc1.relation_id = {presynaptic_to_id}
7   AND tc2.relation_id = {postsynaptic_to_id}
8   AND tc1.project_id = {project_id}
9   AND tc2.project_id = {project_id}
10  AND tc1.skeleton_id = {skeleton_id}
11 GROUP BY tc2.skeleton_id
```

POSTGIS DATA

- In 2D view: *intersections* of skeletons with 2D plane and store *edges* between nodes
- Main planar access in a single direction (usually Z)

```
# \d treenode_edge
```

Column	Type	Collation	Nullable	Default
id	bigint		not null	
parent_id	bigint			
project_id	integer		not null	
edge	geometry(LineStringZ)		not null	

Indexes:

```
"treenode_edge_pkey" PRIMARY KEY, btree (id)
"treenode_edge_project_id_index" btree (project_id)
"treenode_edge_2d_gist" gist (edge)
"treenode_edge_3d_gist" gist (edge gist_geometry_ops_nd)
"treenode_edge_z_range_gist" gist (floatrange(
    st_zmin(edge::box3d), st_zmax(edge::box3d), '[]'::text))
```

BOUNDING BOX QUERIES

- 2D view: cross section of all neurons in a field of view at a particular depth
- Different FoV BBs can benefit from different indexes, so CATMAID tries to use fitting query, e.g.:
 - Whole slice is visible
 - Medium-sized rectangle
 - Small FoV with BB closer to a cube
- For analysis/filters: intersect with 3D meshes (e.g. compartments)

LARGE FIELD OF VIEW

```
1 SELECT *
2 FROM (
3   SELECT DISTINCT ON (id) UNNEST(ARRAY[te.id, te.parent_id]) AS id
4   FROM treenode_edge te
5   WHERE te.project_id = {project_id}
6   AND floatrange(ST_ZMin(te.edge), ST_ZMax(te.edge), '[]')
7     && floatrange({z1}, {z2}, '[]')
8   AND te.edge && ST_MakeEnvelope({left}, {top}, {right}, {bottom})
9   AND ST_3DDWithin(te.edge, ST_MakePolygon(ST_MakeLine(ARRAY[
10     ST_MakePoint({left}, {top}, {halfz}),
11     ST_MakePoint({right}, {top}, {halfz}),
12     ST_MakePoint({right}, {bottom}, {halfz}),
13     ST_MakePoint({left}, {bottom}, {halfz}),
14     ST_MakePoint({left}, {top}, {halfz}]]::geometry[])),
15     {halfzdiff}))
16 ) bb_treenode
17 JOIN treenode t1
18   ON t1.id = bb_treenode.id
```

Get all child and parent nodes of edges in a 3D bounding box

LARGE FIELD OF VIEW

```
1 SELECT *
2 FROM (
3     SELECT DISTINCT ON (id) UNNEST(ARRAY[te.id, te.parent_id]) AS id
4     FROM treenode_edge te
5     WHERE te.project_id = {project_id}
6     AND floatrange(ST_ZMin(te.edge), ST_ZMax(te.edge), '[]')
7         && floatrange({z1}, {z2}, '[]')
8     AND te.edge && ST_MakeEnvelope({left}, {top}, {right}, {bottom})
9     AND ST_3DDWithin(te.edge, ST_MakePolygon(ST_MakeLine(ARRAY[
10         ST_MakePoint({left}, {top}, {halfz}),
11         ST_MakePoint({right}, {top}, {halfz}),
12         ST_MakePoint({right}, {bottom}, {halfz}),
13         ST_MakePoint({left}, {bottom}, {halfz}),
14         ST_MakePoint({left}, {top}, {halfz}]]::geometry[])),
15         {halfzdiff})
16 ) bb_treenode
17 JOIN treenode t1
18 ON t1.id = bb_treenode.id
```

Constrain result edges to those in a user-defined Z range and allow use of index
"treenode_edge_z_range_gist" gist (floatrange(
ST_ZMin(edge::box3d), ST_ZMax(edge::box3d), '[]'::text))

LARGE FIELD OF VIEW

```
1 SELECT *
2 FROM (
3     SELECT DISTINCT ON (id) UNNEST(ARRAY[te.id, te.parent_id]) AS id
4     FROM treenode_edge te
5     WHERE te.project_id = {project_id}
6     AND floatrange(ST_ZMin(te.edge), ST_ZMax(te.edge), '[]')
7         && floatrange({z1}, {z2}, '[]')
8     AND te.edge && ST_MakeEnvelope({left}, {top}, {right}, {bottom})
9     AND ST_3DDWithin(te.edge, ST_MakePolygon(ST_MakeLine(ARRAY[
10         ST_MakePoint({left}, {top}, {halfz}),
11         ST_MakePoint({right}, {top}, {halfz}),
12         ST_MakePoint({right}, {bottom}, {halfz}),
13         ST_MakePoint({left}, {bottom}, {halfz}),
14         ST_MakePoint({left}, {top}, {halfz})]::geometry[])),
15         {halfzdiff})
16 ) bb_treenode
17 JOIN treenode t1
18 ON t1.id = bb_treenode.id
```

Constrain result edges to only those in XY user-defined XY area and allow use of index
"treenode_edge_2d_gist" gist (edge);

LARGE FIELD OF VIEW

```
1 SELECT *
2 FROM (
3     SELECT DISTINCT ON (id) UNNEST(ARRAY[te.id, te.parent_id]) AS id
4     FROM treenode_edge te
5     WHERE te.project_id = {project_id}
6     AND floatrange(ST_ZMin(te.edge), ST_ZMax(te.edge), '[]')
7         && floatrange({z1}, {z2}, '[]')
8     AND te.edge && ST_MakeEnvelope({left}, {top}, {right}, {bottom})
9     AND ST_3DDWithin(te.edge, ST_MakePolygon(ST_MakeLine(ARRAY[
10         ST_MakePoint({left}, {top}, {halfz}),
11         ST_MakePoint({right}, {top}, {halfz}),
12         ST_MakePoint({right}, {bottom}, {halfz}),
13         ST_MakePoint({left}, {bottom}, {halfz}),
14         ST_MakePoint({left}, {top}, {halfz}]]::geometry[])),
15         {halfzdiff})
16 ) bb_treenode
17 JOIN treenode t1
18 ON t1.id = bb_treenode.id
```

Test true distance of edge to BB to remove matches where only the BB of the edge is close,
Lowers *false positives* where only query BB and edge BB intersect

SMALL FOV / CUBE-LIKE BB

```
1 SELECT *
2 FROM (
3   SELECT DISTINCT ON (id) UNNEST(ARRAY[te.id, te.parent_id]) AS id
4   FROM treenode_edge te
5   WHERE te.project_id = {project_id}
6   AND te.edge &&& ST_MakeLine(ARRAY[
7     ST_MakePoint({left}, {bottom}, {z2}),
8     ST_MakePoint({right}, {top}, {z1})]::geometry[])
9   AND ST_3DDWithin(te.edge, ST_MakePolygon(ST_MakeLine(ARRAY[
10    ST_MakePoint({left}, {top}, {halfz}),
11    ST_MakePoint({right}, {top}, {halfz}),
12    ST_MakePoint({right}, {bottom}, {halfz}),
13    ST_MakePoint({left}, {bottom}, {halfz}),
14    ST_MakePoint({left}, {top}, {halfz})]::geometry[])),
15    {halfzdiff})
16 ) bb_treenode
17 JOIN treenode t1
18 ON t1.id = bb_treenode.
```

Similar structure like other query, but different index
Small result set, no extra filter conditions are beneficial

SMALL FOV / CUBE-LIKE BB

```
1 SELECT *
2 FROM (
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14    ST_MakePoint({left}, {top}, {halfz})]::geometry[])),
15    {halfzdiff}))
16 ) bb_treenode
17 JOIN treenode t1
18   ON t1.id = bb_treenode.
```

The &&& operator allows the planner to use the index
"treenode_edge_3d_gist" gist (edge gist_geometry_ops_nd)

SMALL FOV / CUBE-LIKE BB

```
1 SELECT *
2 FROM (
3   SELECT DISTINCT ON (id) UNNEST(ARRAY[te.id, te.parent_id]) AS id
4   FROM treenode_edge te
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13     ST_MakePoint({left}, {bottom}, {halfz}),
14     ST_MakePoint({left}, {top}, {halfz})] ::geometry[])),
15     {halfzdiff})
16 ) bb_treenode
17 JOIN treenode t1
18   ON t1.id = bb_treenode.
```

Limit the number of false positive BB-only intersections, just like before

CLOSEST NODE IN 3D

```
1 SELECT treenode.id, skeleton_id, location_x, location_y, location_z
2 FROM treenode
3 JOIN (
4     SELECT id, edge
5     FROM treenode_edge
6     WHERE project_id = {project_id}
7     ORDER BY edge <<->> ST_MakePoint({x}, {y}, {z})
8     LIMIT 100
9 ) closest_node(id, edge)
10 ON closest_node.id = treenode.id
11 ORDER BY ST_StartPoint(edge) <<->> ST_MakePoint({x}, {y}, {z})
12 LIMIT 1
```

Find closest node among the 100 closest edge centroids in order to allow 3D index use.
Assume closest node is among closest edge BB centroids (<<->> operator)

CLOSEST NODE IN 3D

```
1 SELECT treenode.id, skeleton_id, location_x, location_y, location_z
2 FROM treenode
3 JOIN (
4     SELECT id, edge
5     FROM treenode_edge
6     WHERE project_id = {project_id}
7     ORDER BY edge <=> ST_MakePoint({x}, {y}, {z})
8     LIMIT 100
9 ) closest_node(id, edge)
10 ON closest_node.id = treenode.id
11 ORDER BY ST_StartPoint(edge) <=> ST_MakePoint({x}, {y}, {z})
12 LIMIT 1
```

Find 100 closest (euclidean) edges

CLOSEST NODE IN 3D

```
1 SELECT treenode.id, skeleton_id, location_x, location_y, location_z
2 FROM treenode
3 JOIN (
4     SELECT id, edge
5     FROM treenode_edge
6     WHERE project_id = {project_id}
7     ORDER BY edge <-> ST_MakePoint({x}, {y}, {z})
8     LIMIT 100
9 ) closest_node(id, edge)
10 ON closest_node.id = treenode.id
11 ORDER BY ST_StartPoint(edge) <-> ST_MakePoint({x}, {y}, {z})
12 LIMIT 1
```

Get closest edge start node of closest edges

MORE POSTGIS

- More spatial annotations (POIs, bookmarks, text)
- Storing 3D meshes as TIN data
- Store spatial meta data for point clouds (BB, center of mass)

Thank you PostGIS team for making spatial data in the DB easier,
even beyond GIS!

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QUESTIONS?

- catmaid.org
- github.com/catmaid/catmaid
- tom@kazmos.de
- [@tomkazimiers](https://twitter.com/tomkazimiers)
- Docker image:

```
docker run -p 8080:80 catmaid/catmaid
```

