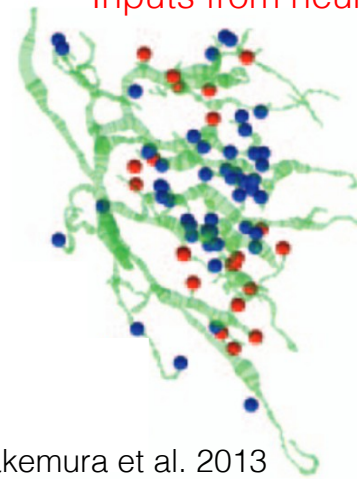
Introduction to fly connectomics

Some details about the data format

Potential directions

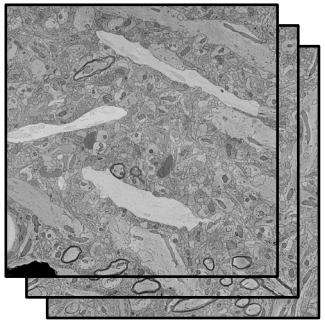
Inputs from neuron j

Inputs from neuron k

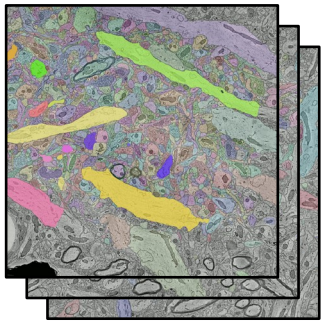


Takemura et al. 2013

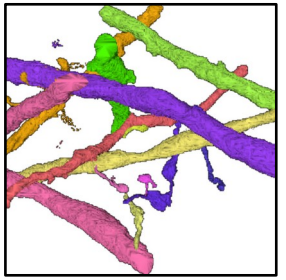
Electron microscopy images



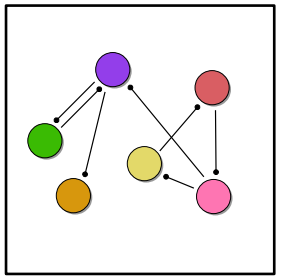
Segmentation



3D reconstruction



Graph



Cell types
"Names"
Neurotransmitter types
Size/number of synaptic connections
Recordings/effects of activation/inactivation
Transcriptomic

C. elegans

~300 neurons

1986

wormwiring.org

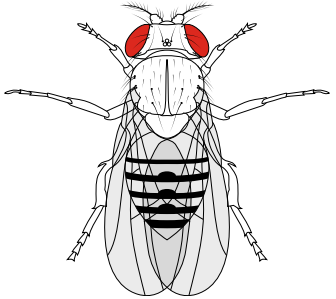
Drosophila larva

~2,000 neurons

~2010-2023

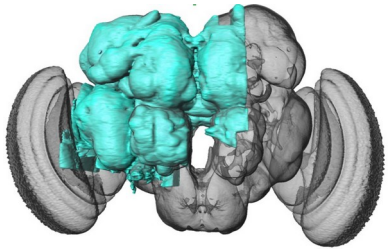
l1em.catmaid.
virtualflybrain.org

Drosophila adult



~20,000 neurons

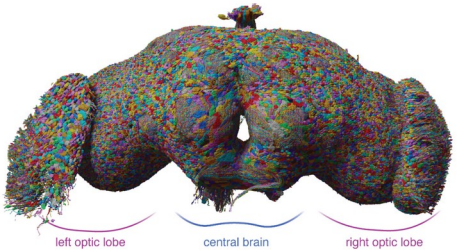
2020



neuprint.janelia.org

~120,000 neurons

2023



codex.flywire.ai

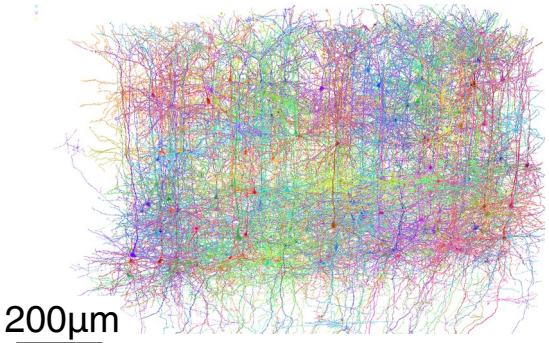
?

Mouse

~75,000,000 neurons

~200,000 neurons

2021

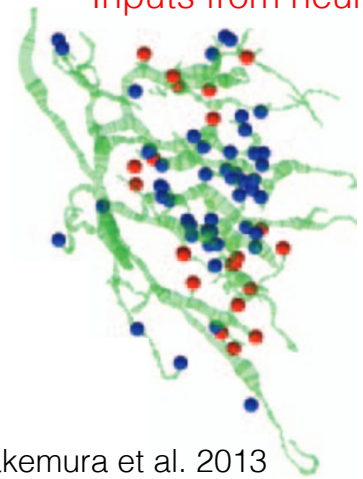


microns-explorer.org

Upcoming: complete male fly brain, ventral nerve cord

Inputs from neuron j

Inputs from neuron k



Takemura et al. 2013

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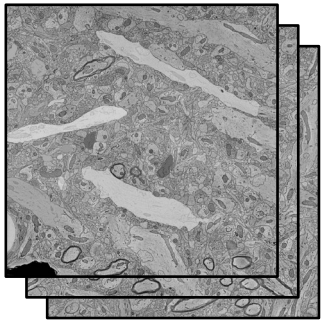

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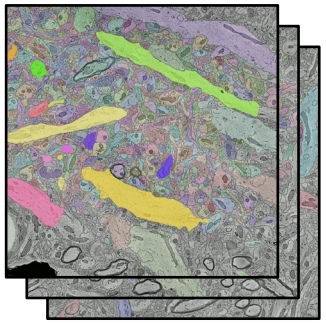
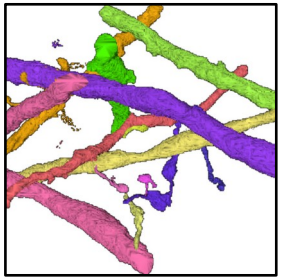
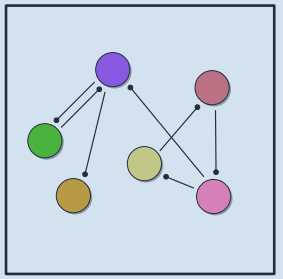


3D reconstruction



Graph



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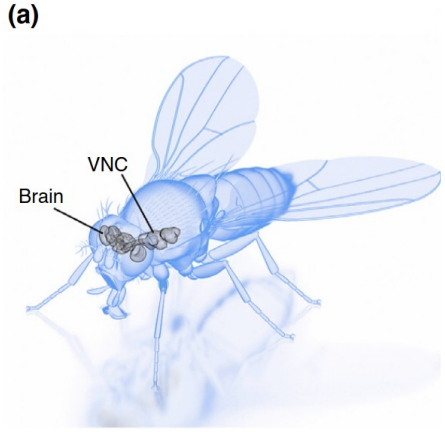
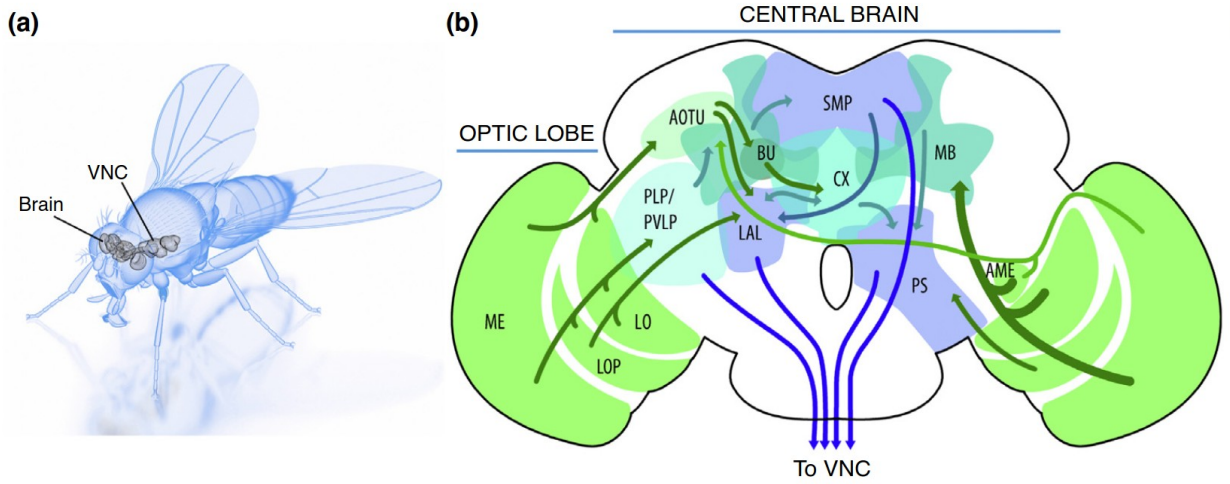
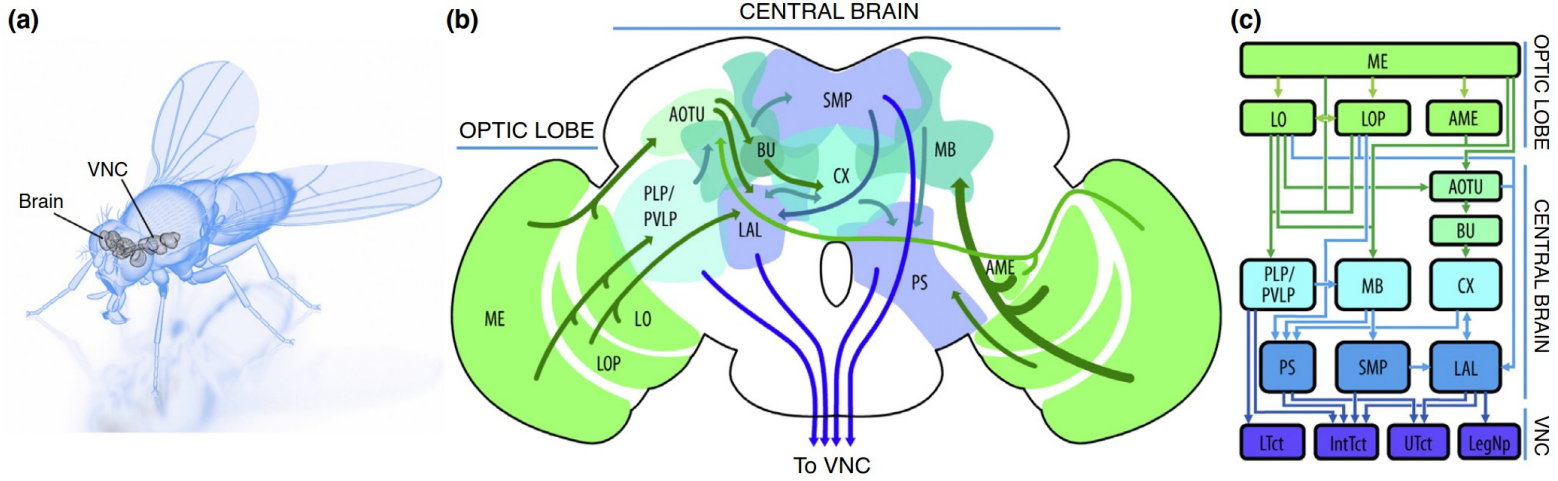
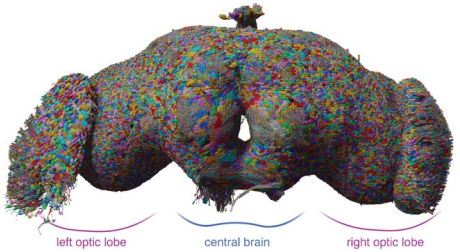


Chiang, Siwanowicz, Card 2020



Chiang, Siwanowicz, Card 2020





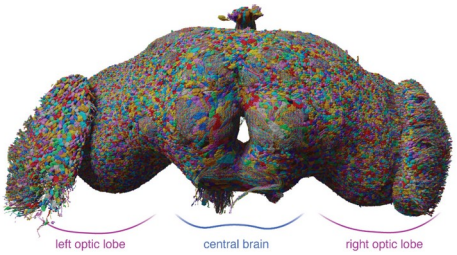
codex.flywire.ai

Chiang, Siwanowicz, Card 2020

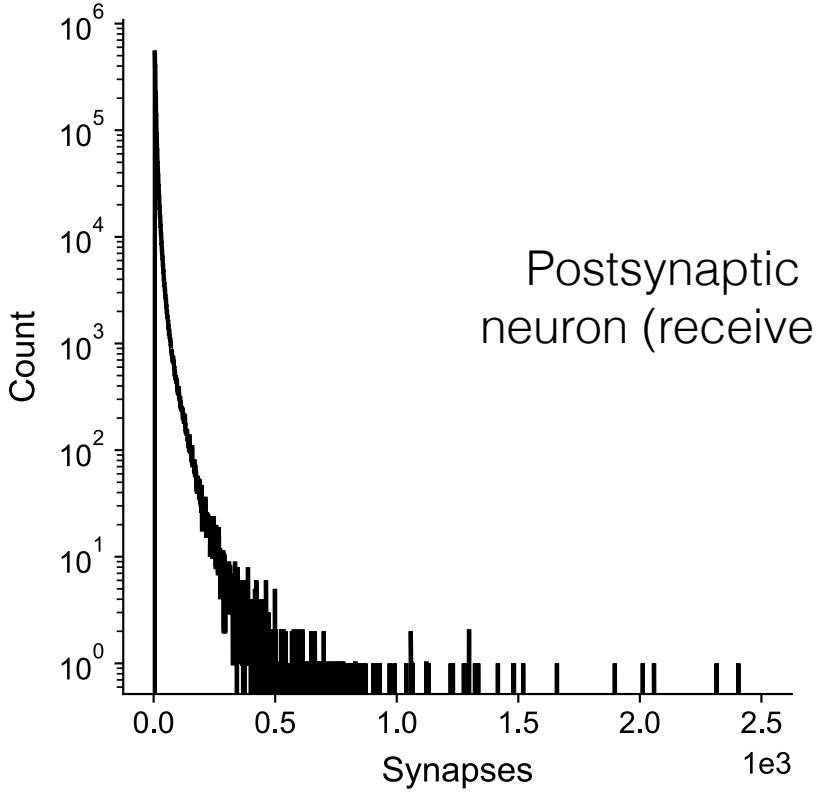
$N = 139255$

$p(\geq 5) = 0.00014$

$p(\geq 10) = 0.000055$



codex.flywire.ai

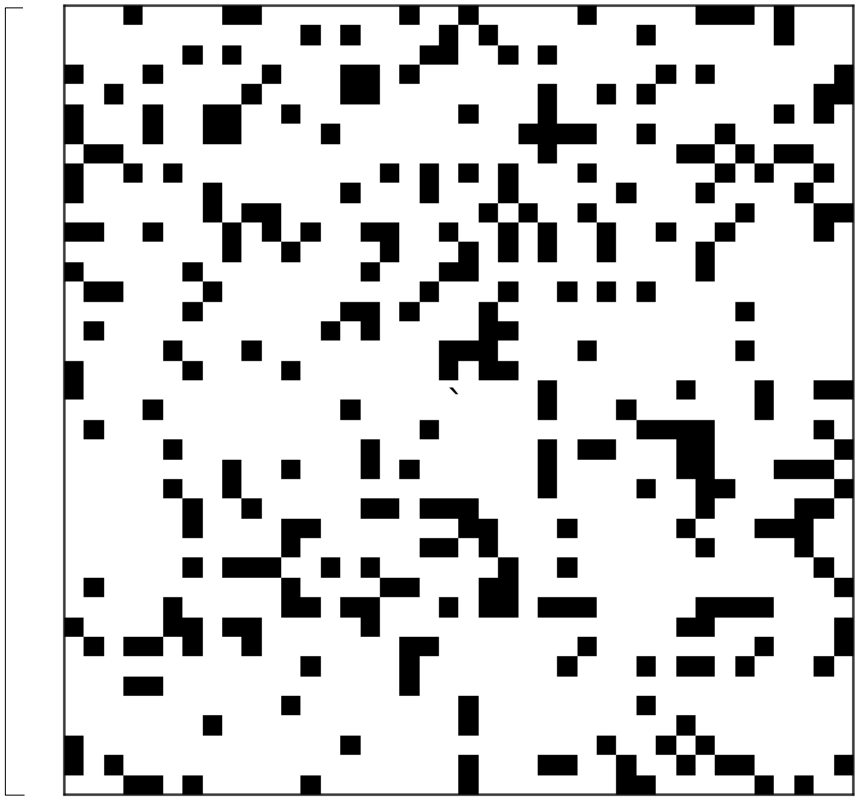


Postsynaptic neuron (receiver)

N

Presynaptic neuron (sender)

N



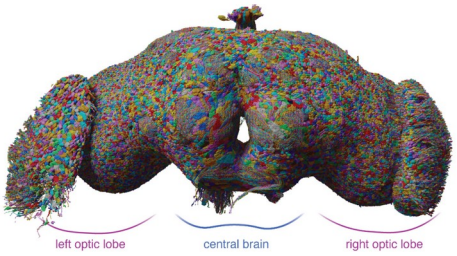
Connected

Disconnected

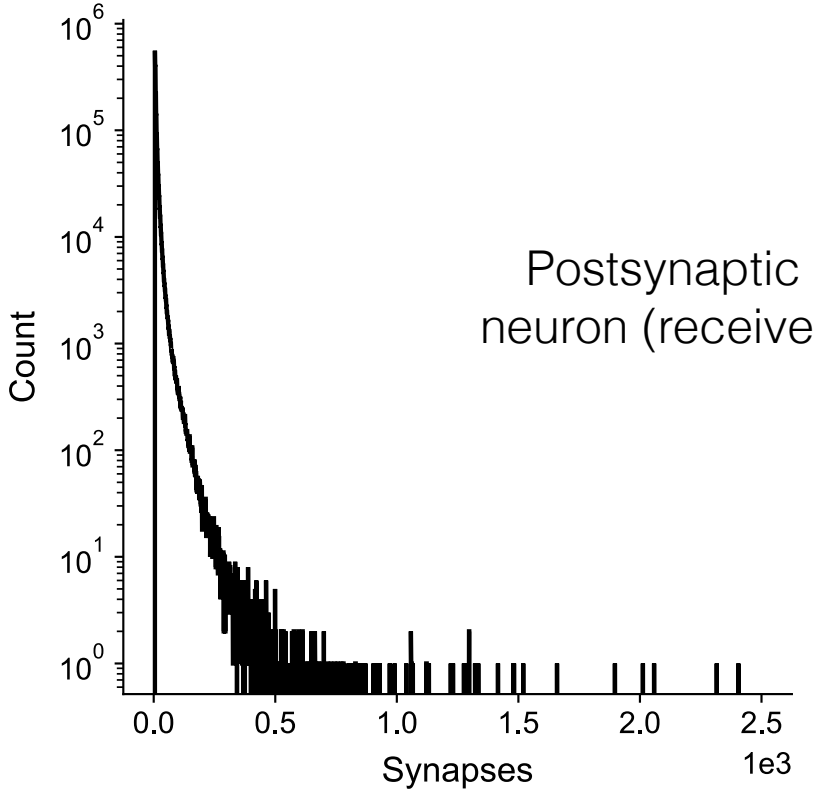
$N = 139255$

$p(\geq 5) = 0.00014$

$p(\geq 10) = 0.000055$



codex.flywire.ai

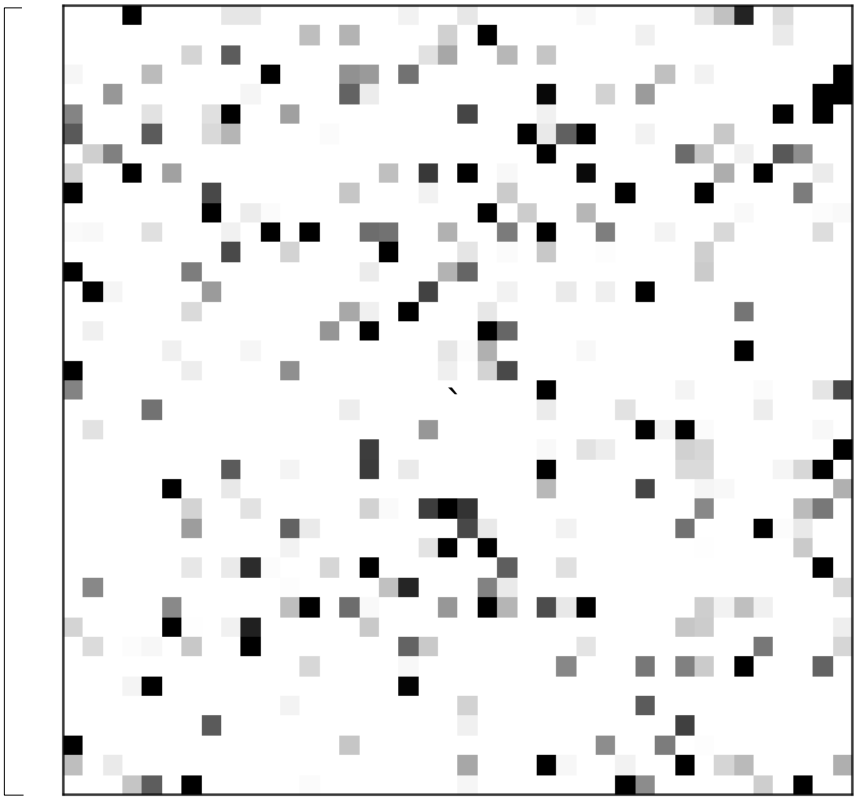


Postsynaptic neuron (receiver)

Presynaptic neuron (sender)

N

N

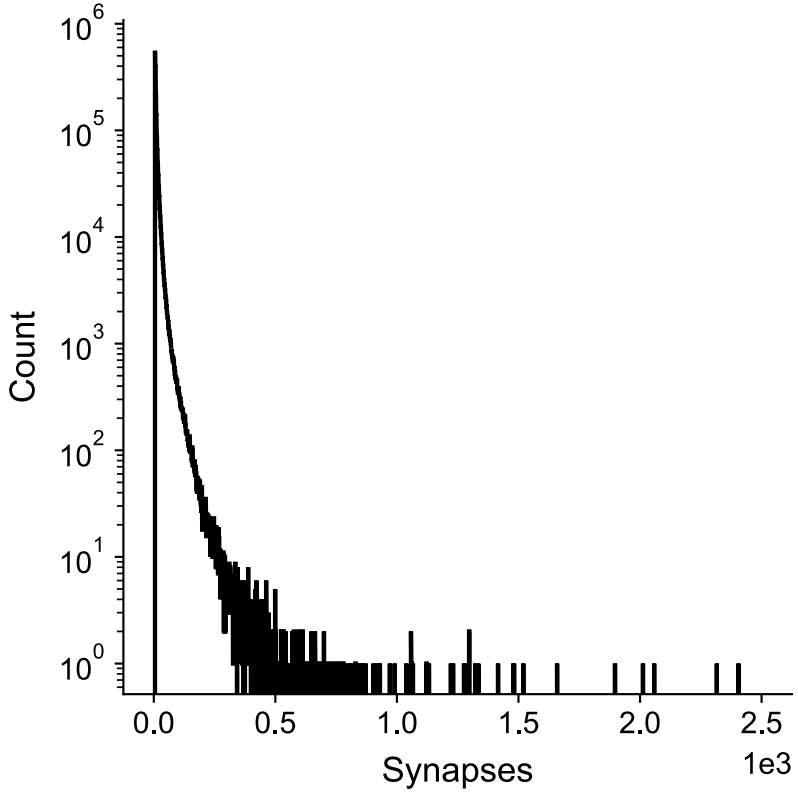


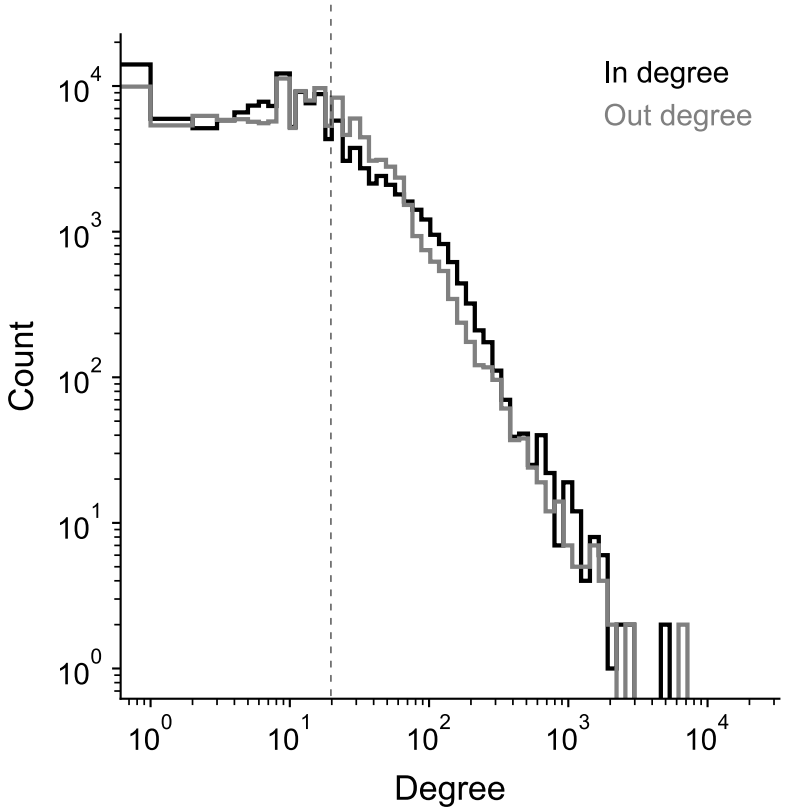
Number/size of connections

$N = 139255$

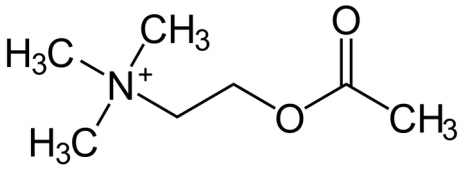
$p(\geq 5) = 0.00014$

$p(\geq 10) = 0.000055$

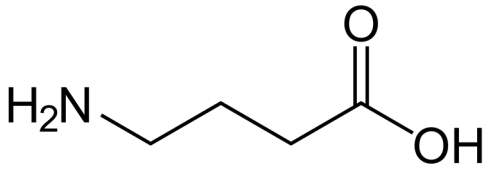




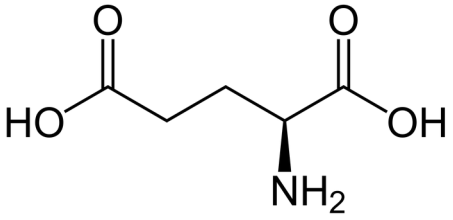
Acetylcholine (excitatory)



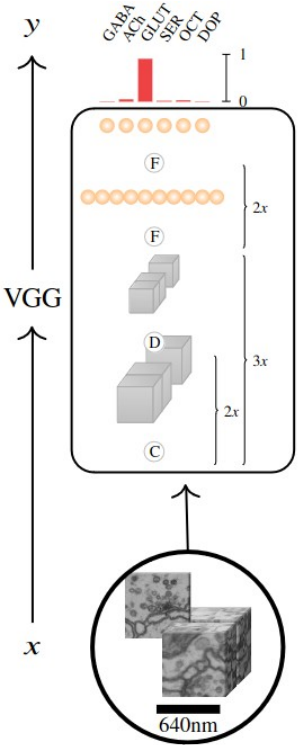
GABA (inhibitory)

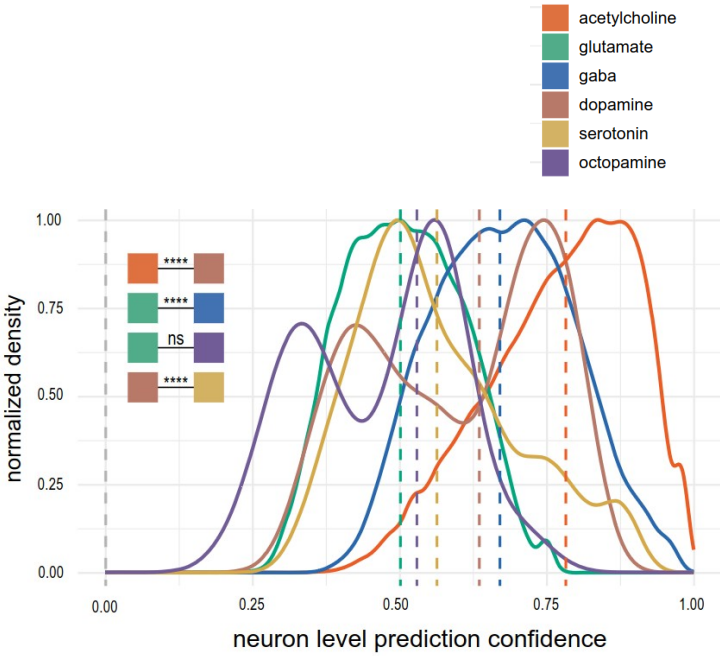


Glutamate (probably inhibitory)

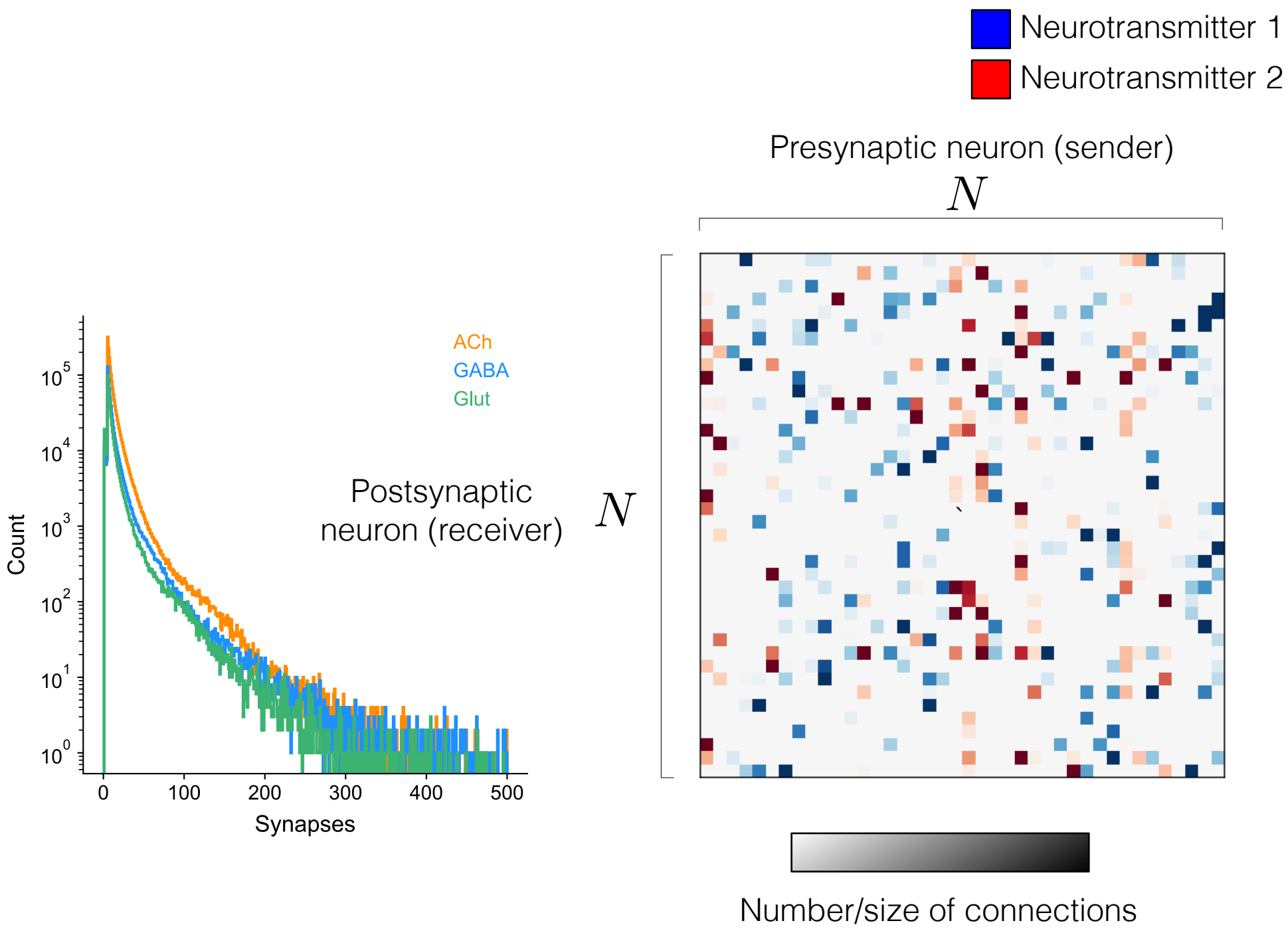


Predicted neurotransmitter





Eckstein et al. 2024


Neurotransmitter 1
Neurotransmitter 2
Presynaptic neuron (sender)
N
ACh
GABA
Glut
Count
10^5
10^4
10^3
10^2
10^1
10^0
0
100
200
300
400
500
Synapses
Postsynaptic
neuron (receiver)
N
Number/size of connections

$$\tau_i \frac{dx_i(t)}{dt} = -x_i(t) + \sum_j W_{ij} f_j(x_j(t)) + I_i(t)$$

$$W_{ij} \propto g_{ij} A_{ij}$$

$g_{ij} = g$	Global scale factor
$g_{ij} = \pm g$	Excitatory/inhibitory
$g_{ij} = \pm g / \sum_j A_{ij}$	Normalized by incoming weights
$g_{ij} = \pm g_{(\mathrm{NT})} / \sum_j A_{ij}$	Neurotransmitter-specific gain

Introduction to fly connectomics

Some details about the data format

Potential directions

Inspecting neurons

In [5]:
```
print(neurons.columns)
neurons
```

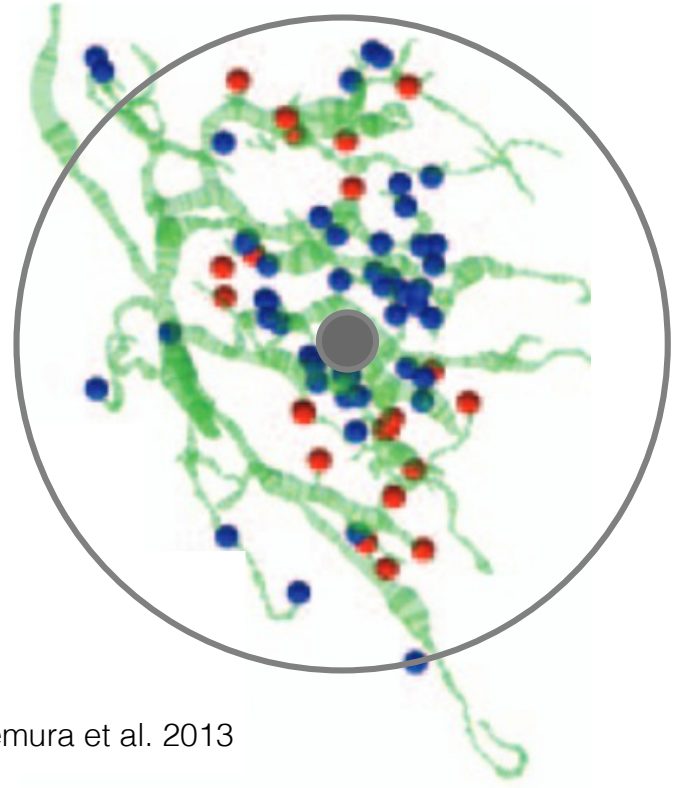
```
Index(['root_id', 'group', 'nt_type', 'nt_type_score', 'da_avg', 'ser_avg',
       'gaba_avg', 'glut_avg', 'ach_avg', 'oct_avg', 'flow', 'super_class',
       'class', 'sub_class', 'cell_type', 'hemibrain_type', 'hemilineage',
       'side', 'nerve', 'x', 'y', 'z', 'x_presyn', 'y_presyn', 'z_presyn',
       'rho_presyn', 'x_postsyn', 'y_postsyn', 'z_postsyn', 'rho_postsyn',
       'J_idx', 'J_idx_post', 'J_idx_pre'],
      dtype='object')
```

Out[5]:

	root_id	group	nt_type	nt_type_score	da_avg	ser_avg	gaba_avg	glut_avg	ach_avg	oct_avg	...	y_pr
0	720575940596125868	LO.LOP	ACH	0.57	0.03	0.00	0.05	0.28	0.57	0.07	...	272101.65
1	720575940597856265	ME	ACH	0.85	0.01	0.00	0.03	0.04	0.85	0.07	...	332566.47
2	720575940597944841	ME.LO	ACH	0.82	0.02	0.00	0.01	0.05	0.82	0.09	...	315764.23
3	720575940598267657	ME	GABA	0.74	0.01	0.01	0.74	0.19	0.03	0.02	...	291869.89
4	720575940599333574	ME	ACH	0.61	0.02	0.00	0.13	0.13	0.61	0.11	...	301811.97
...	...	...	...	...	...	...	...	...	...	...	...	
139250	720575940661335681	GNG	GABA	0.71	0.00	0.00	0.71	0.17	0.11	0.00	...	332268.83
139251	720575940661336193	ME.LO	ACH	0.62	0.02	0.00	0.18	0.16	0.62	0.03	...	187984.46
139252	720575940661337217	SCL.MB_ML	ACH	1.00	0.00	0.00	0.00	0.00	1.00	0.00	...	163719.61
139253	720575940661338497	GNG	NaN	0.00	0.00	0.00	0.00	0.00	0.00	0.00	...	
139254	720575940661339777	NO_CONS	NaN	0.00	0.00	0.00	0.00	0.00	0.00	0.00	...	

139255 rows × 33 columns

Inputs from neuron j
Inputs from neuron k



Takemura et al. 2013

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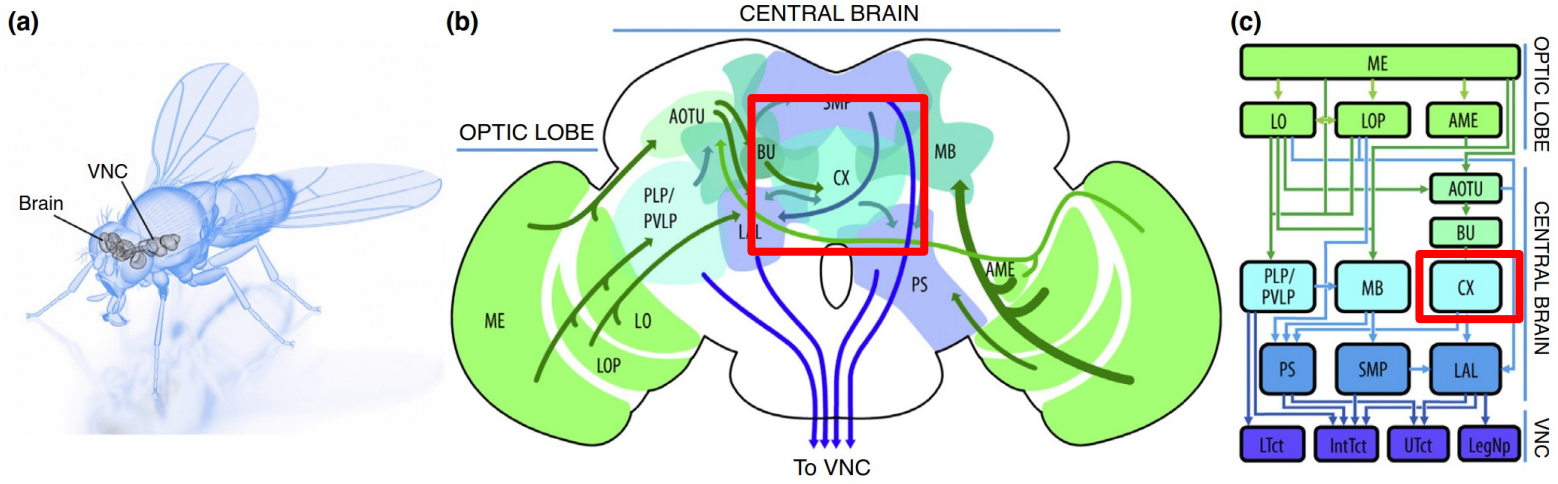
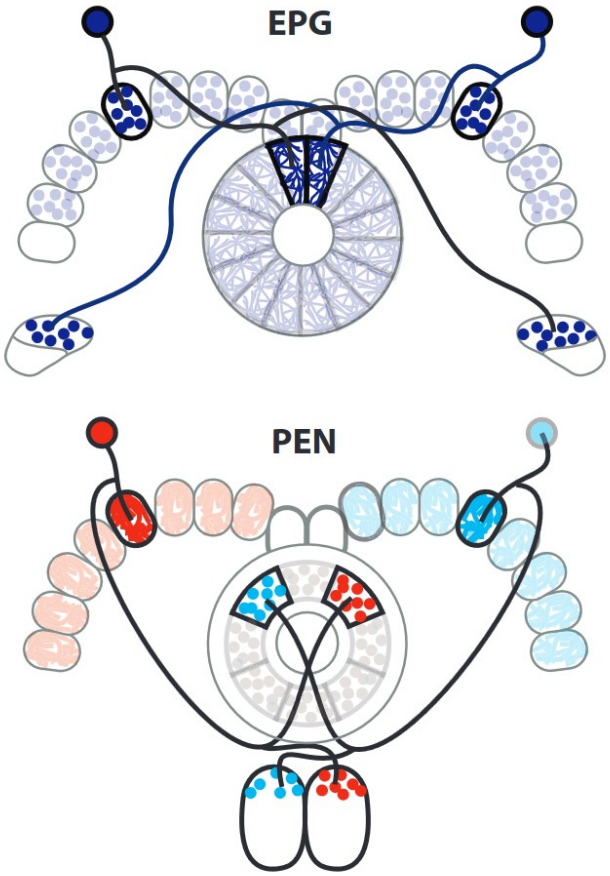
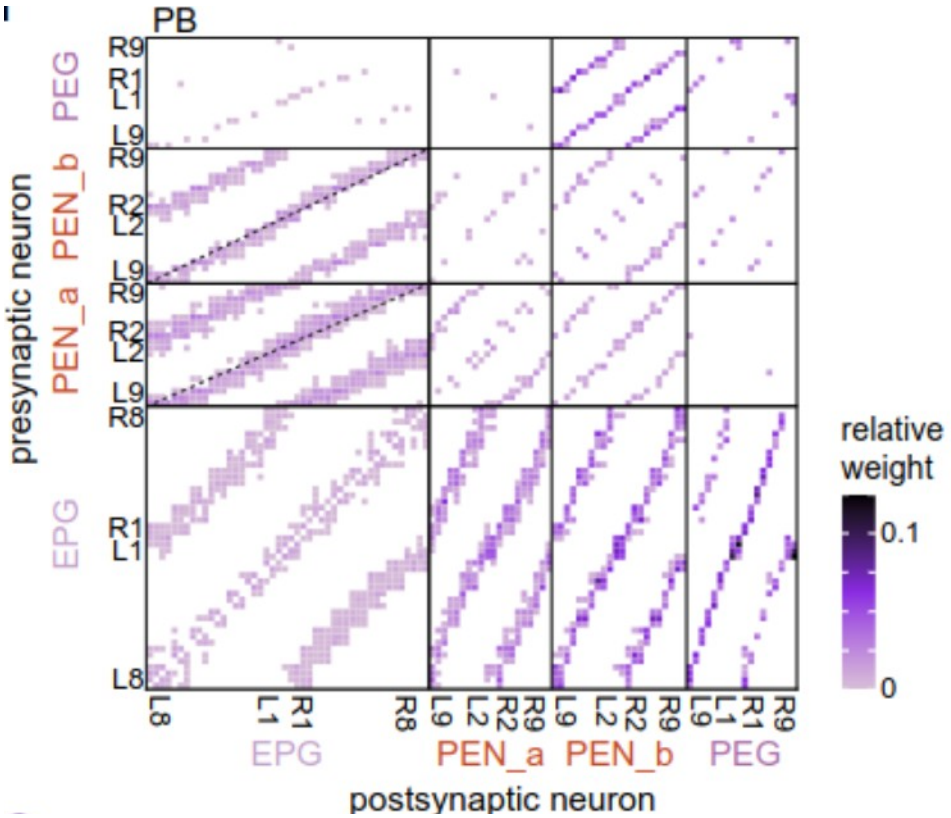


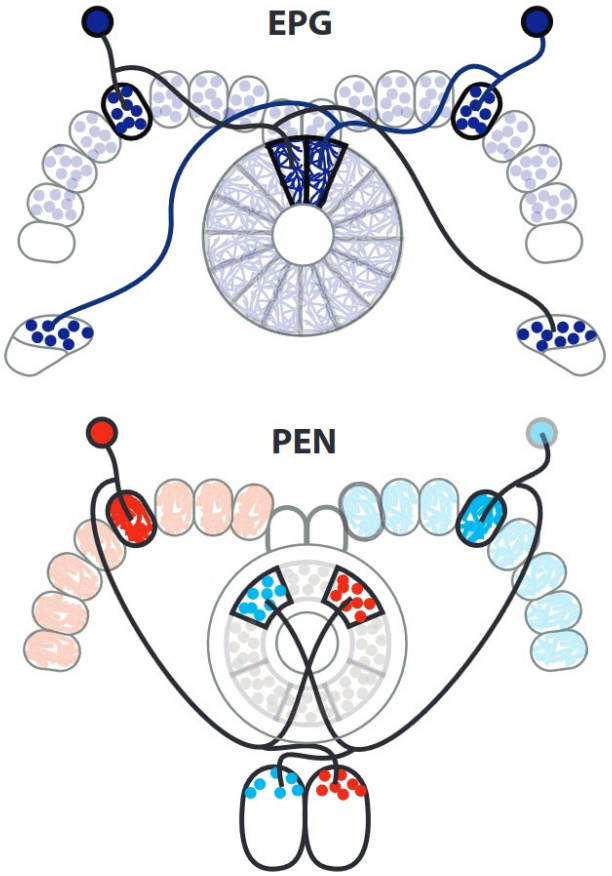
Chiang, Siwanowicz, Card 2020



Hulse & Jayaraman 2020



Hulse et al. 2021

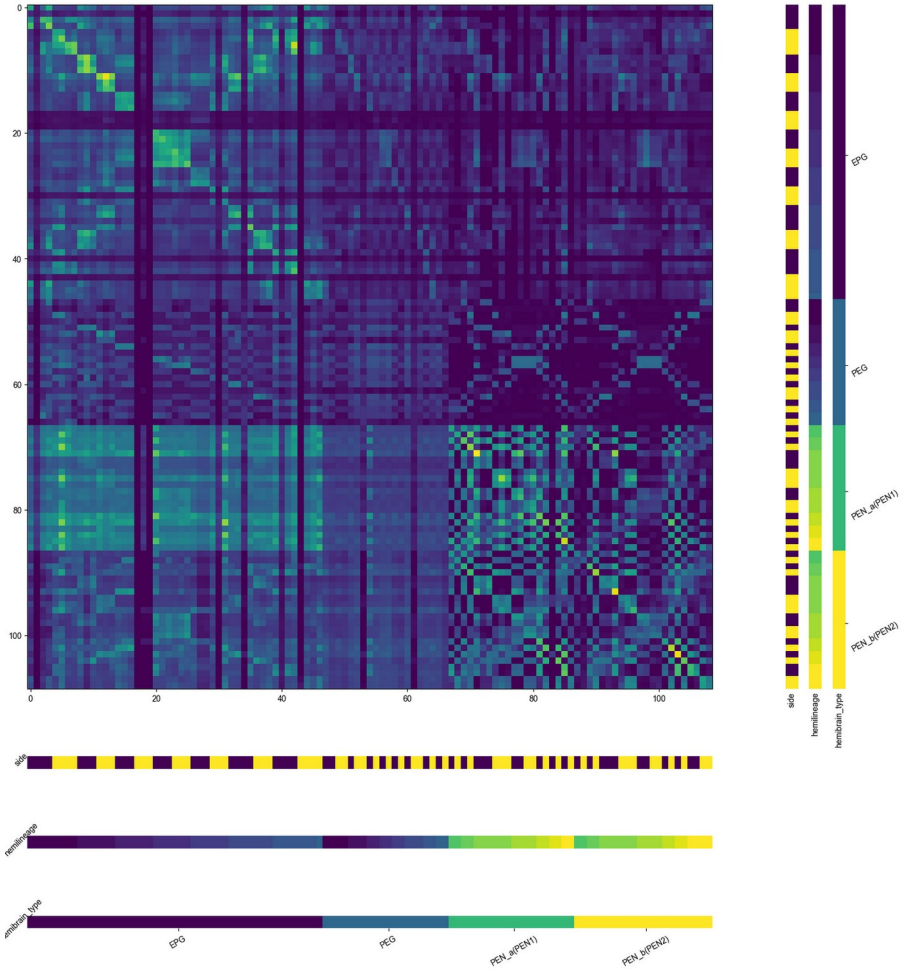


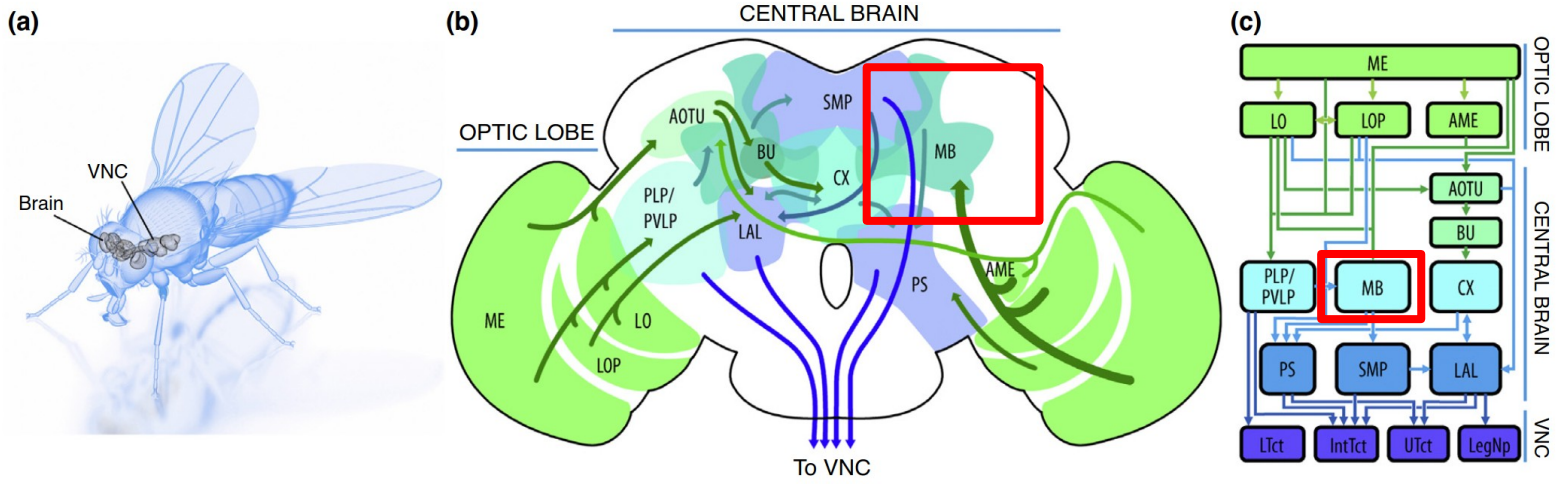
Hulse & Jayaraman 2020

hello_flywire.ipynb

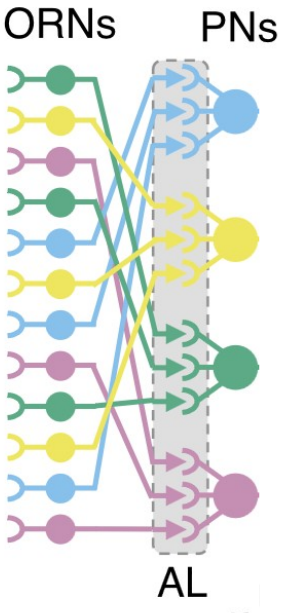
In [20]:

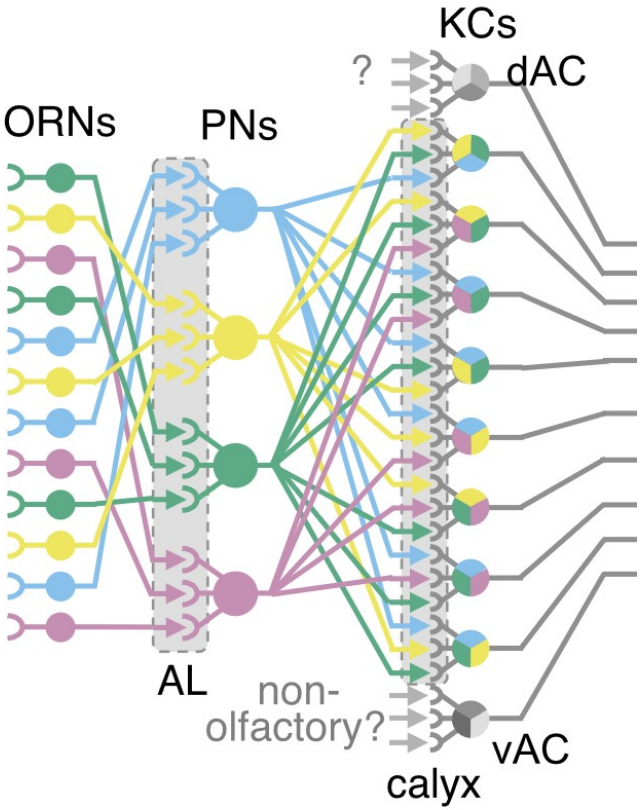
```
hulse_fig17=neurons[(neurons['hemibrain_type']=='EPG') | (neurons['hemibrain_type']=='PEG')| neurons.hemibrain_ty

hulse_fig17_neurons, hulse_fig17_J, hulse_fig17_neurons_pre, hulse_fig17_neurons_post, hulse_fig17_nts_Js = filte
plot_connectivity(hulse_fig17_neurons_pre, hulse_fig17_neurons_post, hulse_fig17_J.todense(), input_tick_labels=1,
```





Chiang, Siwanowicz, Card 2020


ORNs
PNs
AL

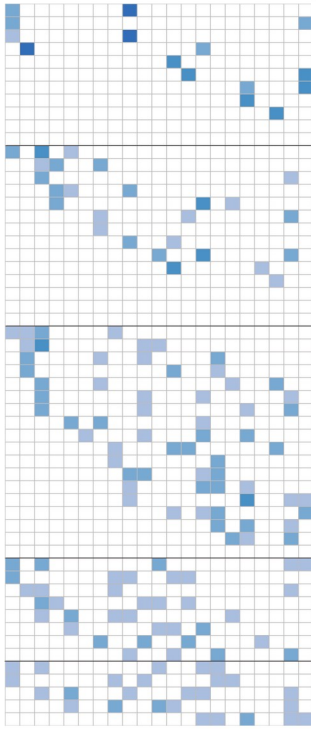


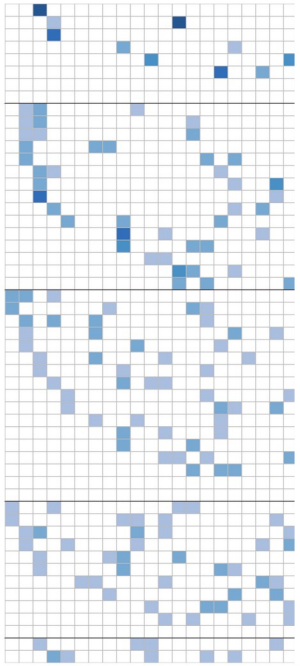
Readout

Left hemisphere

Right hemisphere

Kenyon cells



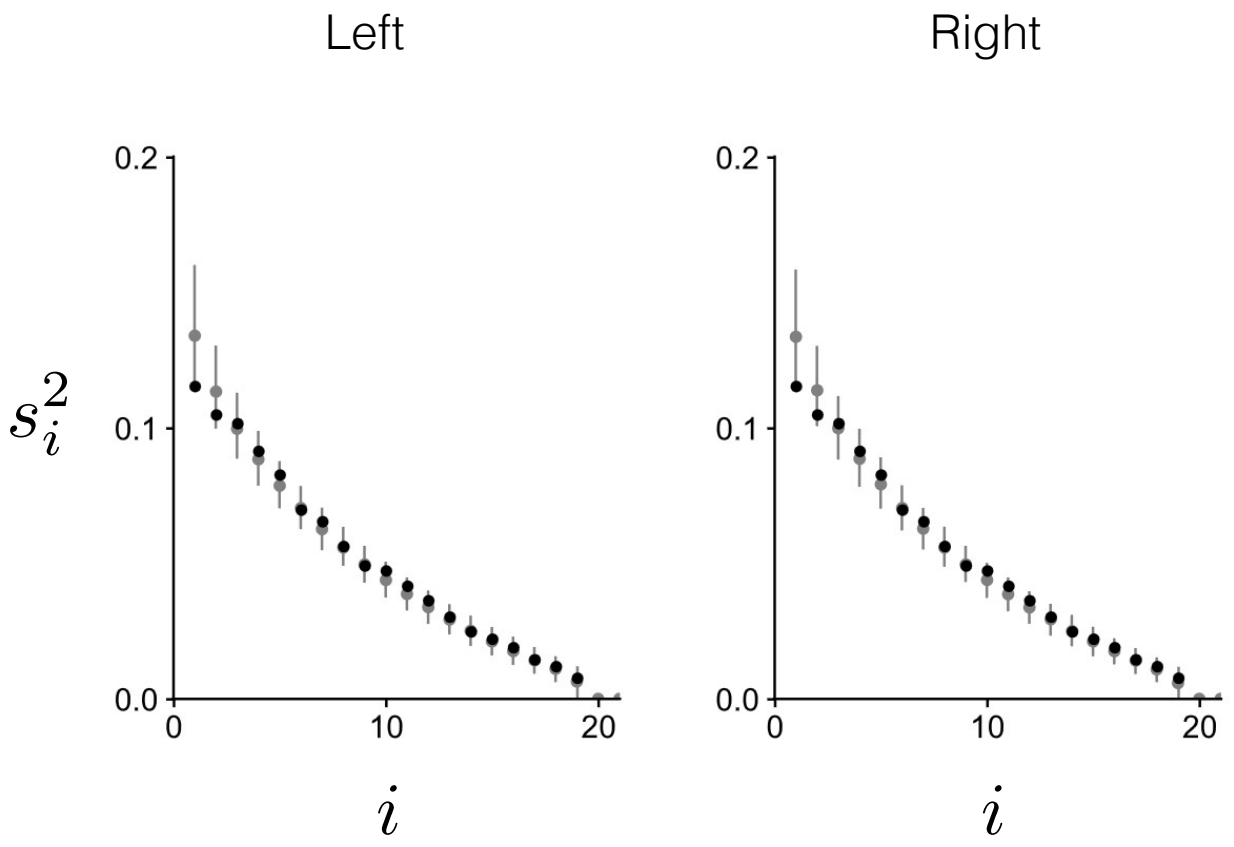


Olfactory projection neurons

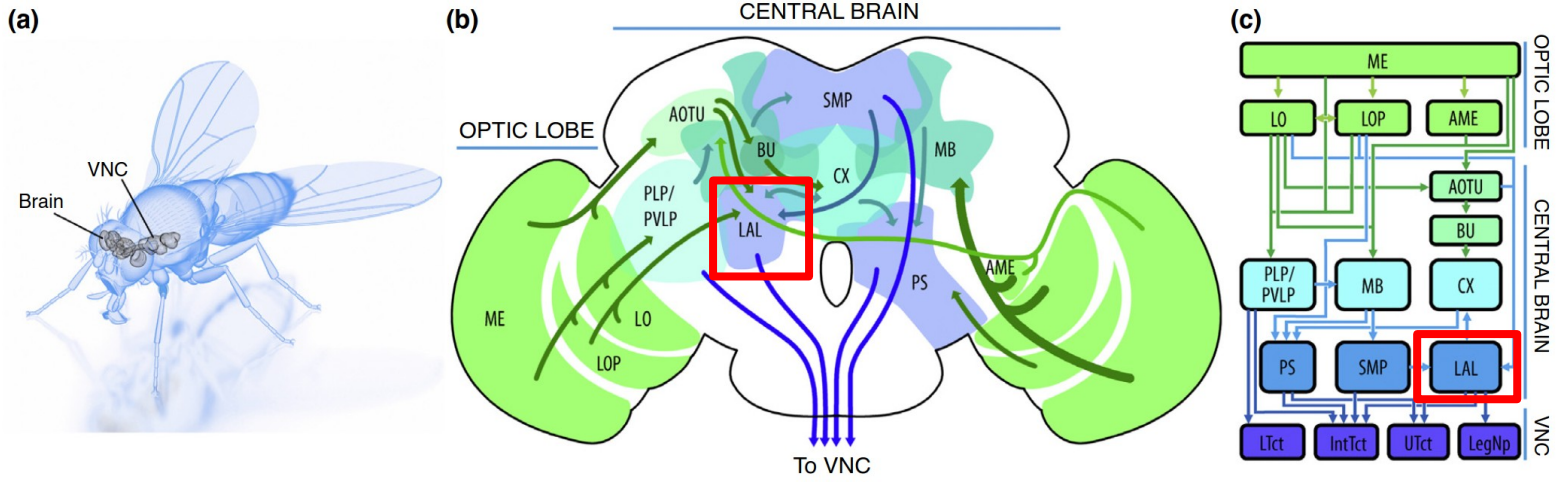
Eichler et al. 2017

Adjacency matrix (unweighted)
Degree-matched random matrices

$$A = USV^T$$



Caron et al. 2013, Eichler et al. 2017, Li et al. 2020, Zheng et al. 2022, Nguyen et al. 2023



Chiang, Siwanowicz, Card 2020

alitwinkumar / **connectome_examples**

`hello_flywire.ipynb`: Loading data, selecting interesting subsets of neurons.

`basic_pandas_tutorial.ipynb`: Pandas tutorial.

`flywire_spatial_analysis.ipynb`: Analyzing synapse locations.

`gnn_tutorial.ipynb`: Using graph neural networks to predict synapses.

$$h_v^{(k)} = f^{(k)}\left(W^{(k)} \cdot \frac{\sum_{u \in \mathcal{N}(v)} h_u^{(k-1)}}{|\mathcal{N}(v)|} + B^{(k)} \cdot h_v^{(k-1)}\right) \quad \text{for all } v \in V.$$

- $h_v^{(k)}$: Node v's embedding at step k.
- $f^{(k)}$: Nonlinearity (ReLU)
- $W^{(k)}$: Learnable weights
- $\frac{\sum_{u \in \mathcal{N}(v)} h_u^{(k-1)}}{|\mathcal{N}(v)|}$: Mean of v's neighbour's embeddings at step $k-1$.
- $B^{(k)}$: Learnable bias
- $h_v^{(k-1)}$: Node v's embedding at step $k-1$.

Adapted from Daigavane, et al., "Understanding Convolutions on Graphs", Distill, 2021