KTH ROYAL INSTITUTE OF TECHNOLOGY

Modelling and Topological Analysis of the striatal microcircuitry in health and Parkinson's disease

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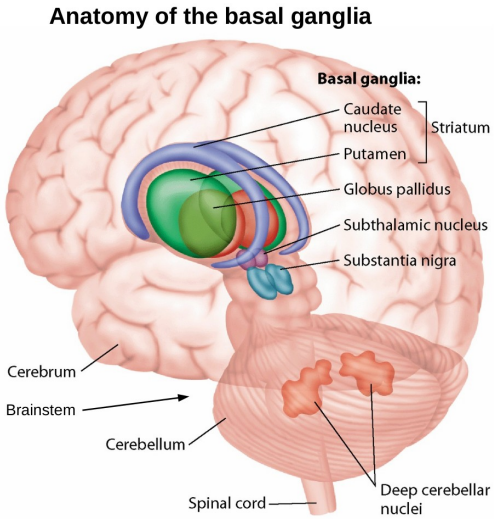
Carannante et al., 2023: https://www.biorxiv.org/content/10.1101/2023.09.15.557977v1

digital futures

dBrain

EBRAINS

What and where is the striatum?



From W. W. Norton

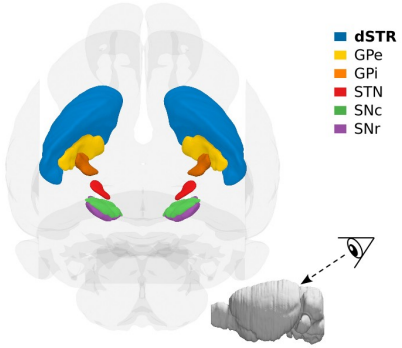
Striatum is the largest nucleus and main input stage of the basal ganglia.

Basal ganglia are involved in motor learning, action-selection and reinforcement learning.

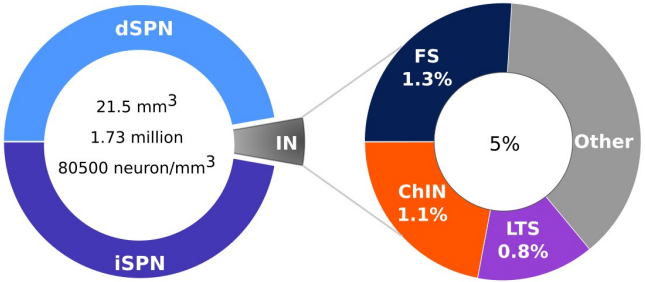
Their dysfunction leads to a variety of brain disorders like Huntington's and **Parkinson's diseases**.

Rodent striatum

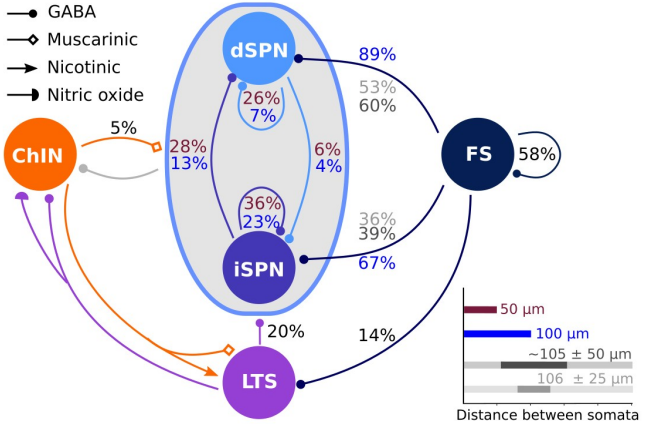
A Basal ganglia



B Cell type distribution in striatum



C Striatal microcircuit



Principal cells, about 95%

dSPN - direct striatal projection neurons (targets directly the output nuclei GPi/Snr).

iSPN - indirect striatal projection neurons (targets GPe).

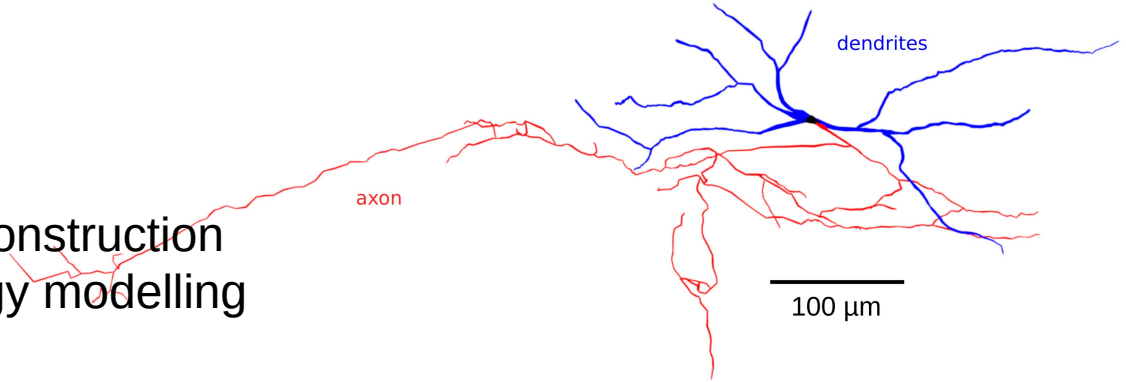
Interneurons, about 5%

FS – PV+, fast-spiking cells, 1.3%

LTS – NPY/SOM+, low-threshold spiking, 0.8%

ChIN – cholinergic interneurons, 1.1%

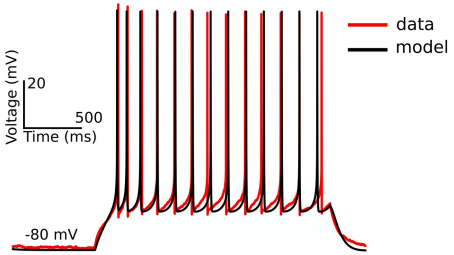
Digital microcircuit reconstruction



- Single-cell morphology reconstruction
- Single-cell electrophysiology modelling

- Cell placement reproducing realistic neuron densities
- Touch detection of putative synapses and synaptic pruning to reproduce realistic connectivities

- Input setting
- Network simulation



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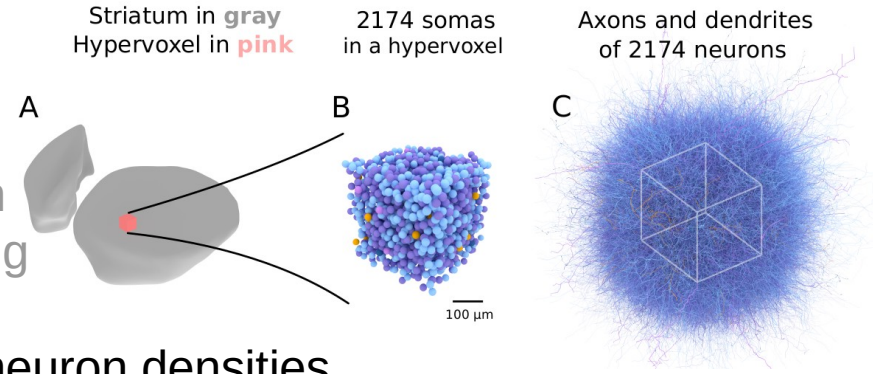

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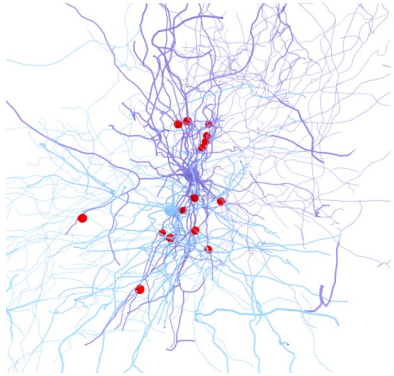

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Digital microcircuit reconstruction

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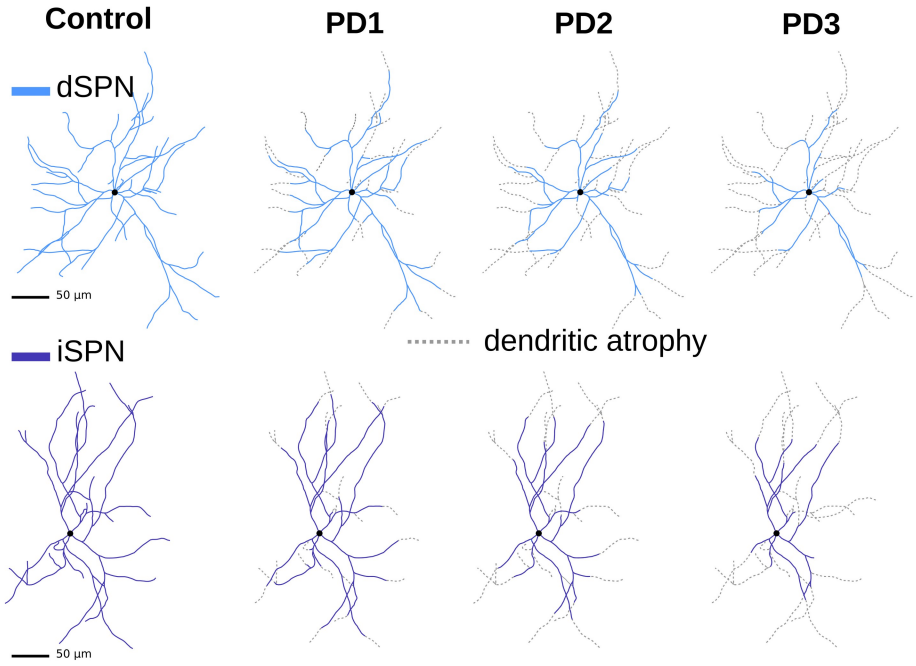
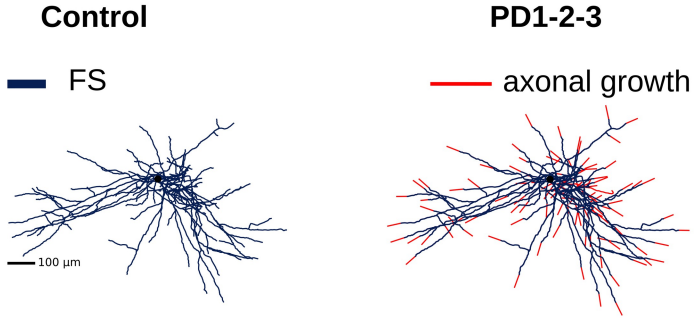
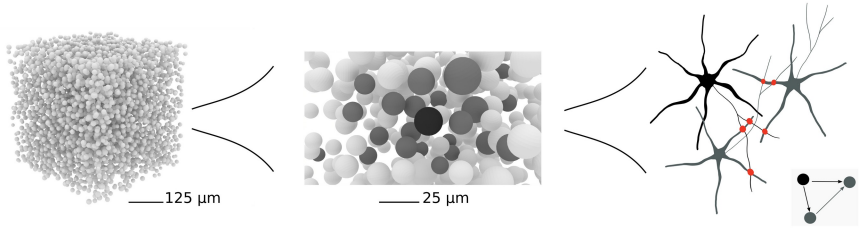
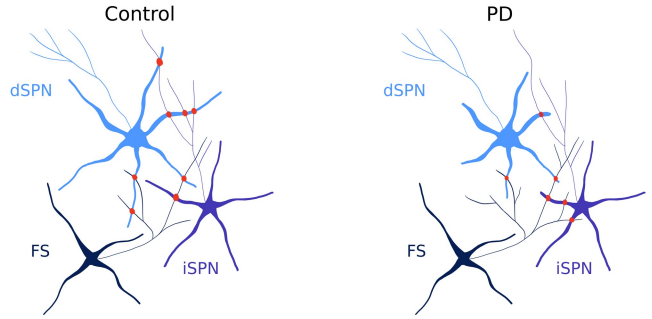
Morphological changes in Parkinson's disease

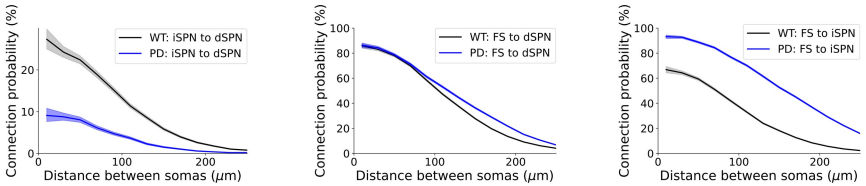




From morphologies to connectivity

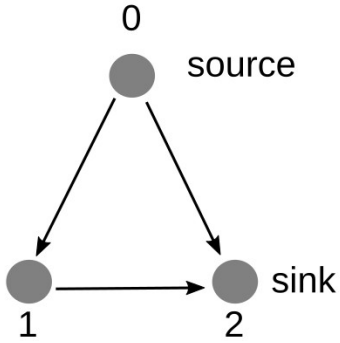


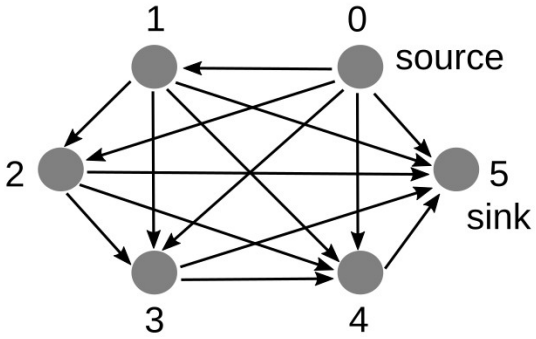


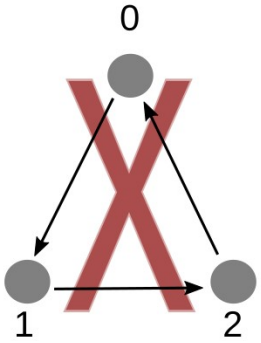


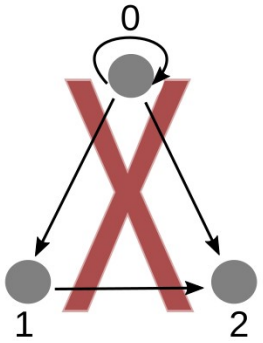
Directed cliques

- A **directed graph** *G* is a pair *(V,E)* where *V* is a finite set of vertices (corresponding to neurons) and *E* is a set of ordered pairs of distinct vertices *(v,w)* called edges (corresponding to synaptic connections).
- A vertex *v* is a **source** (or a **sink**) if all edges including *v* are from (or to) *v*.
- A set $\{v_0,..,v_n\}$ of vertices is a **n-directed clique** if it contains a source and a sink. We refer to directed cliques as **simplices**.

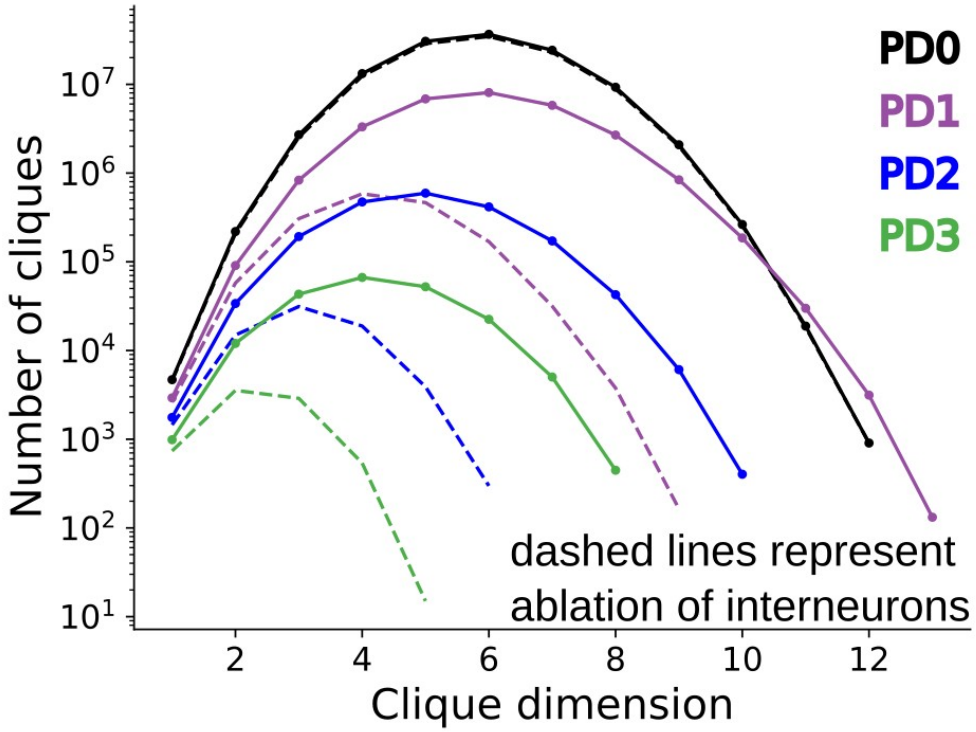


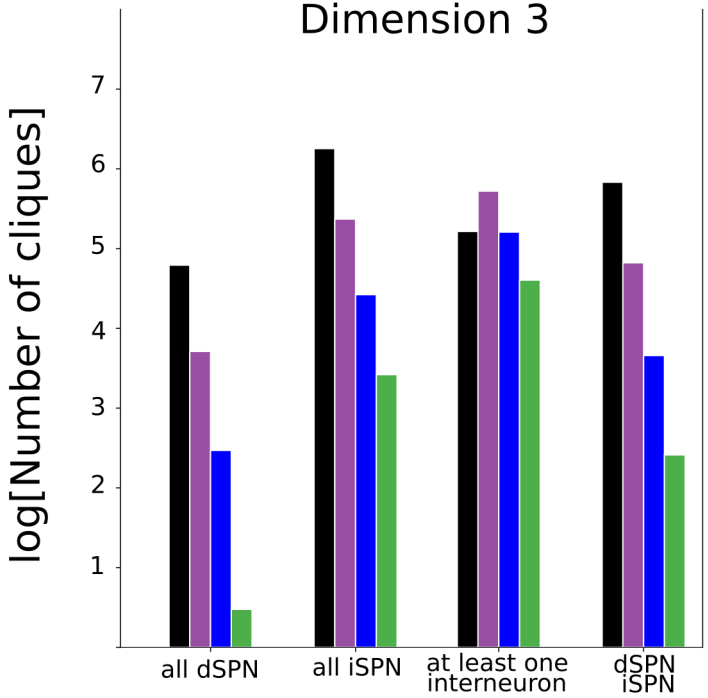




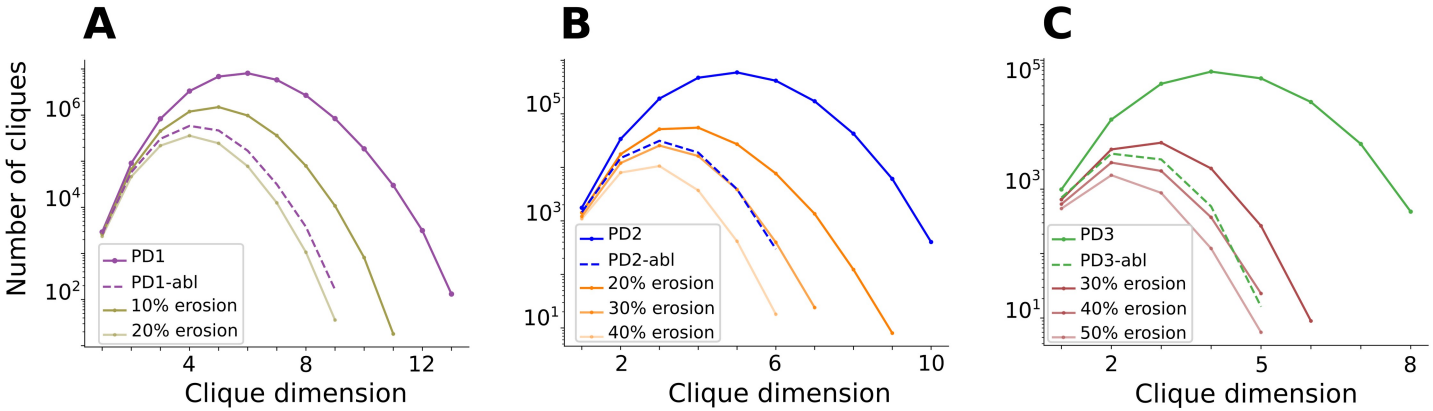


Counting number of directed cliques

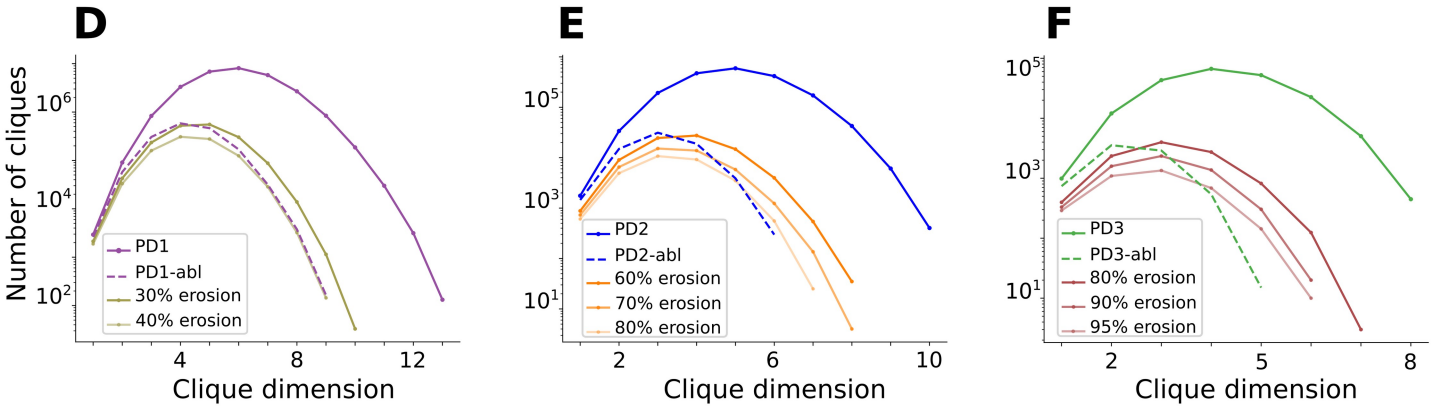




Random erosion of the entire PD network connectivity



Random erosion of only the SPN connectivity



In summary:

- Our work highlighted that just measuring the **pairwise connectivity** between neurons gives an incomplete description of the network connectivity.
- **Directed clique analysis** provided a richer characterization of the network structure with respect to Parkinson’s disease progression.
- **Interneurons** are crucial in both maintaining the network connectivity during PD and in the formation of high dimensional cliques.

Acknowledgements

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