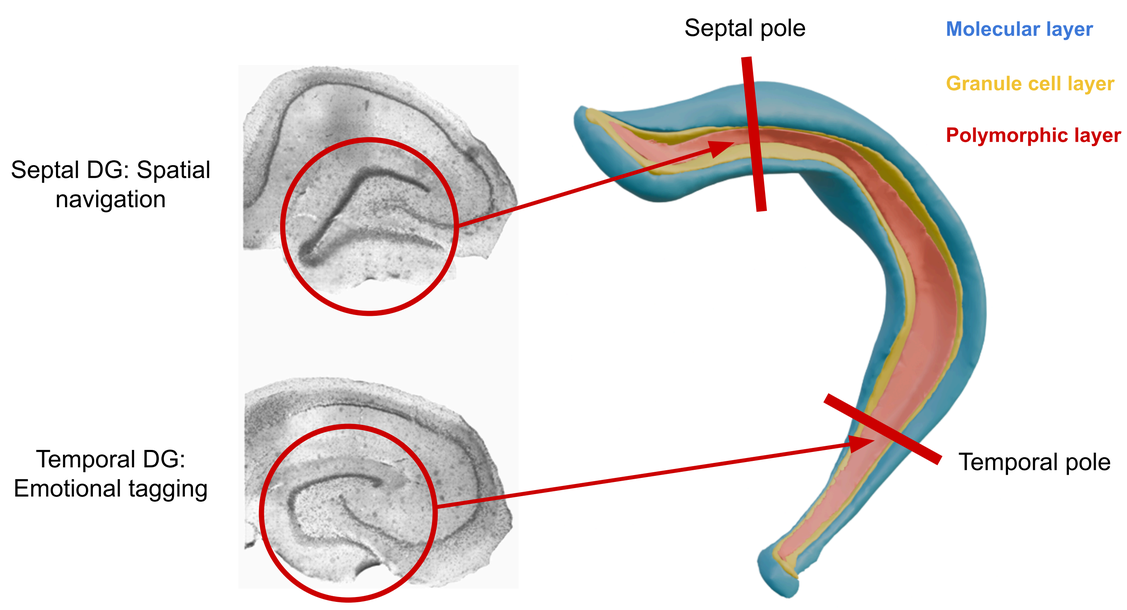
Structural basis of functional specialization in the dentate gyrus

Khashayar Baghizadeh, Centre for Genomic Regulation, khashayar.baghizadeh@crg.eu
Pau Clusella, Universitat Politècnica de Catalunya
Mara Dierssen, Centre for Genomic Regulation

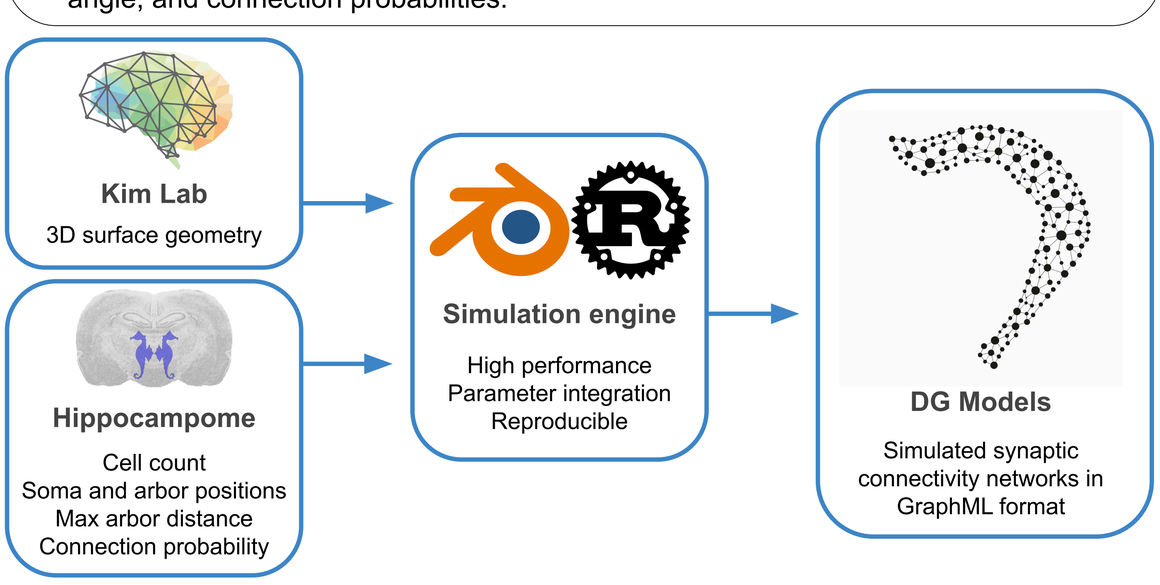
Background

- The dentate gyrus (DG) is the gateway to the hippocampus, critical for memory, and is functionally specialized along its septo-temporal axis.
- Septal (dorsal) DG is responsible for spatial navigation, but temporal (ventral) DG is responsible for emotional regulation.
- These functional differences imply distinct local circuit organization, but the underlying laminar structure and cell composition is the same.
- **Hypothesis:** Changes in DG geometry along the septo-temporal axis may explain the reorganization of neuronal connectivity.

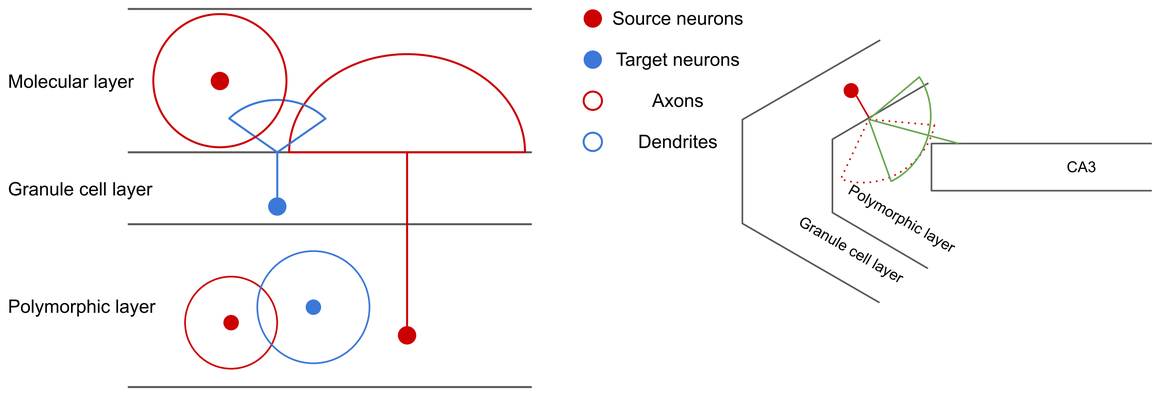


Methods

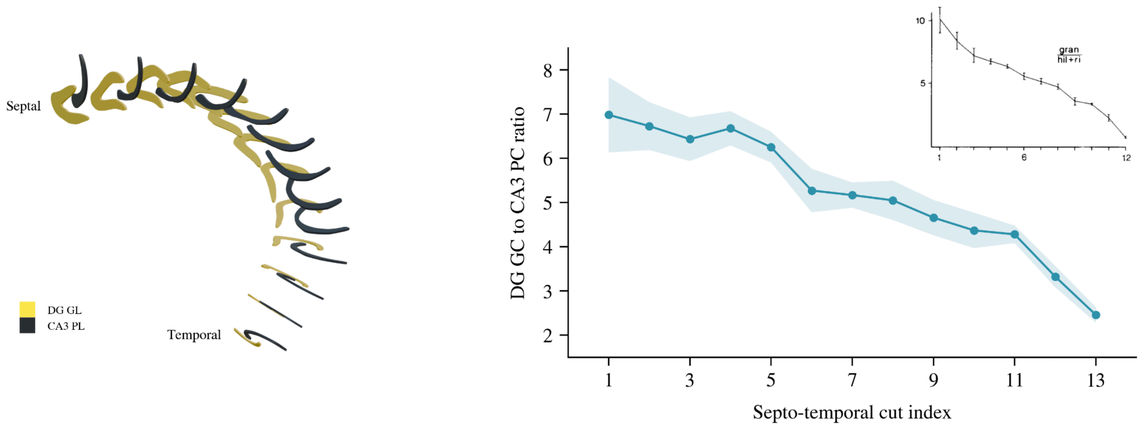
- We developed a data-driven simulator that generates large-scale network models of the DG.
- Kim brain atlas was used to define 3D surface geometry of the DG layers.
- Poisson disc distribution allowed random, non-overlapping neuron placement.
- We built a custom Rust program to automatically generate connectivity using Hippocampome neuroanatomical data.
- Used anatomical constraints are the DG layer topology, arbor size and dispersion angle, and connection probabilities.



A data-driven simulator that generates large-scale network models of the DG



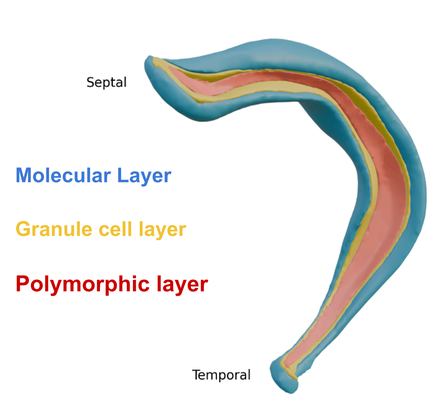
Connectivity rules for automating the connectivity generation

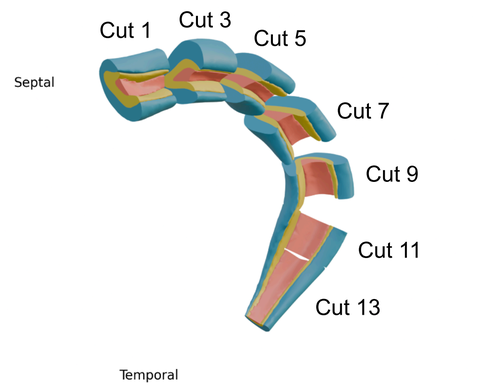


Reproducing the decreasing septo-temporal granule cell to pyramidal cell ratio, matching experimental data (Gaarskjaer, 1978)

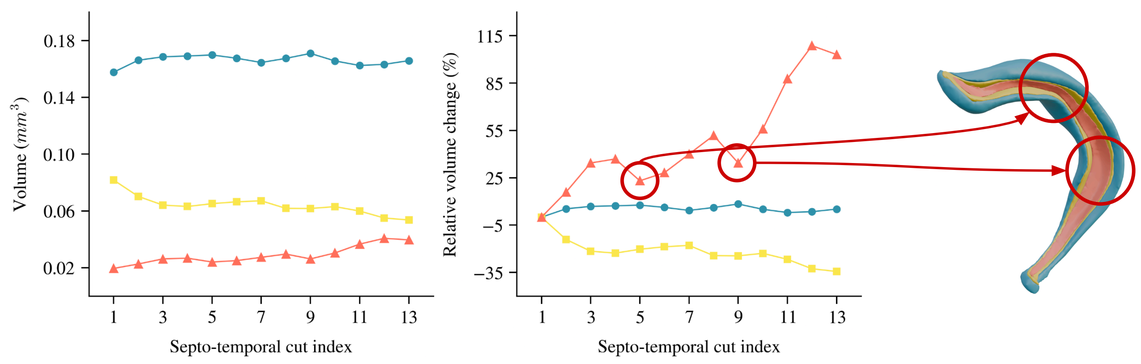
Results

- Along the septo-temporal axis, the volume of the molecular layer is relatively stable, while granule cell layer volume decreases by 40% and polymorphic layer volume expands by 100%. As density is considered to be homogeneous, this will affect the number of cells.
- Regarding connectivity, molecular layer total out-degree follows the volume of granule cell layer, polymorphic layer total out-degree follows its volume and drives the granule cell layer total out-degree.
- Single granule cell out-degree to hilar cells increases. Instead single hilar cell out-degree to granule cells decreases as opposed to their total out-degree. This apparent discrepancy is explained by the increase in the number of hilar cells along the axis.
- Interestingly, along the septo-temporal axis, granule cells receive more inhibition from hilar cells, but hilar cells receive less excitation from granule cells.

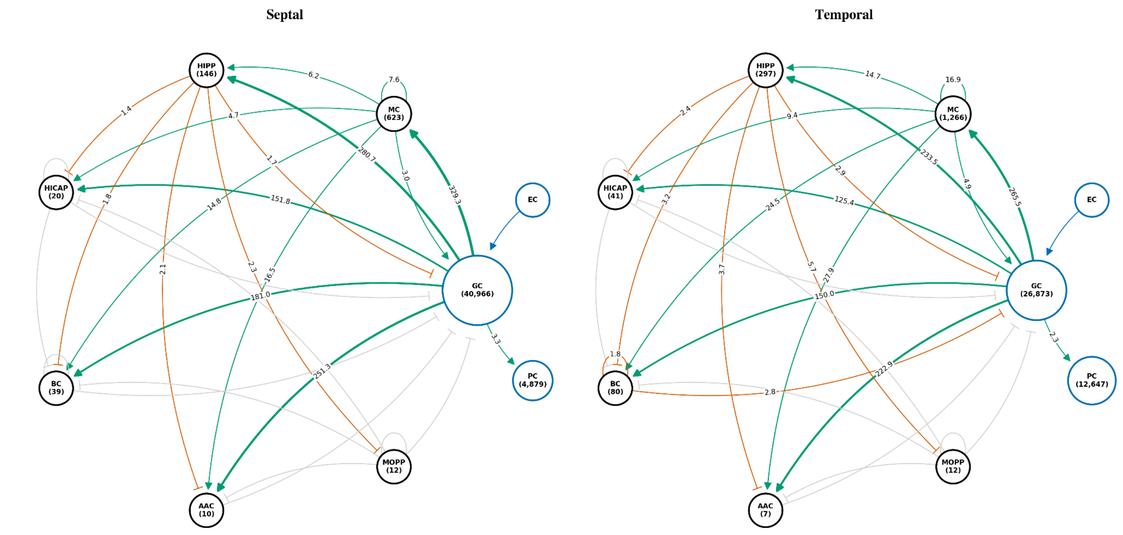




Isovolumetric and perpendicular cuts to the septo-temporal axis



The local minima corresponding to DG inflection points with maximum curvature



Single cell in-degree among different cell types

Conclusions

- **We constructed a highly adaptable, data-driven simulation framework** bridging meso-scale anatomy with micro-scale circuitry and enabling the exploration of evolutionary changes and disease conditions.
- **Geometry can drive circuit architecture:** Volumetric changes alone can drive cell population shifts and connectivity reorganization.
- **Connectivity reorganization:** Network topology transitions from high convergence at the septal pole to a low-convergence architecture at the temporal pole.

References

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