Investigating the role of dendrites in pattern separation: A computational approach

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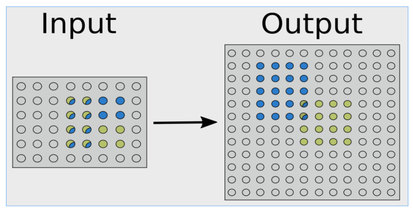
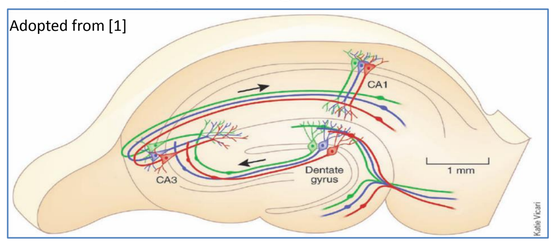
FENS KAVLI NETWORK OF EXCELLENCE

Introduction

- Pattern separation: computational task which transforms overlapping (similar) input to non-overlapping representations



- Dentate Gyrus: hippocampal subregion that accomplishes this task



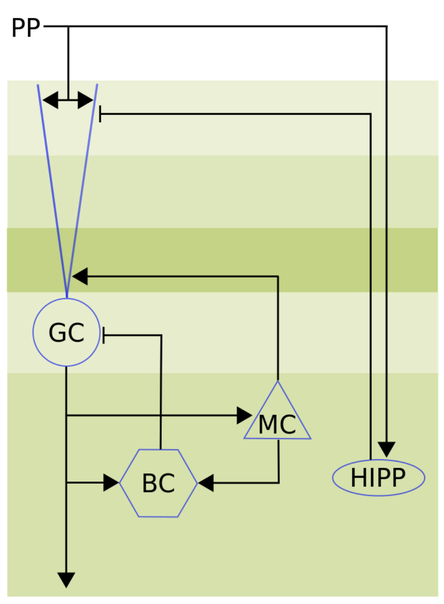
- Dentate principal neurons, Granule Cells, fire sparsely (2-5%) [2] . This sparse coding of GCs via inhibition enhances pattern separation [3]
- DG dysfunction is associated with Alzheimer's Disease (AD) and Temporal Lobe Epilepsy (TLE) [4]

AIM: To understand the role of indirect inhibition and dendrites in pattern separation

Materials and Methods

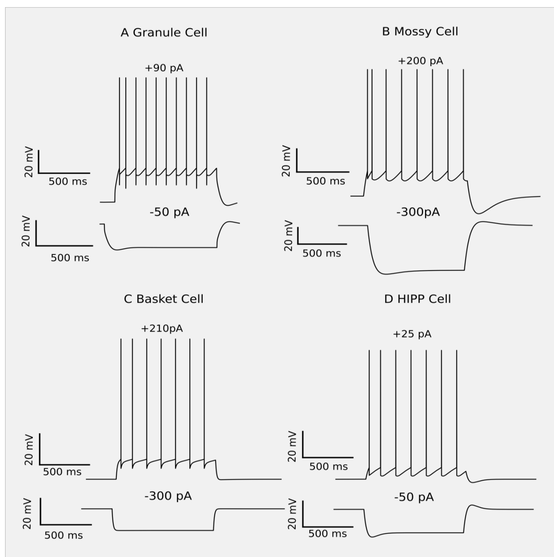
Dentate Gyrus network model

- A model of DG is implemented containing the four major neuronal cells; granule cells, mossy cells, basket cells and HIPP cells
- 2,000 GCs, 40 MCs, 100 BCs, 40 HIPP cells, 400 EC Layer II cells (input)



- Synaptic mechanisms: AMPA, NMDA, $GABA_A$
- Neurons are simulated as simple point neurons without internal geometry using the adaptive exponential Integrate-and-Fire model [5]
- Granule cells are simulated with a leaky Integrate-and-Fire somatic compartment and 12 dendrites

Validation of the model



Input protocol

- 10% of input cells are active
- 4 groups of input patterns with different degrees of similarity

Input pattern A

1	1	1	1	0	1	0	0	0	0	0	0

Input pattern B

0	1	1	1	1	1	0	0	0	0	0	0

- Similarity metric

$$f_{in,out} = 1 - \frac{HD_{in,out}}{2(1 - s_{in,out})N_{in,out}}$$

When $f_{in} > f_{out}$

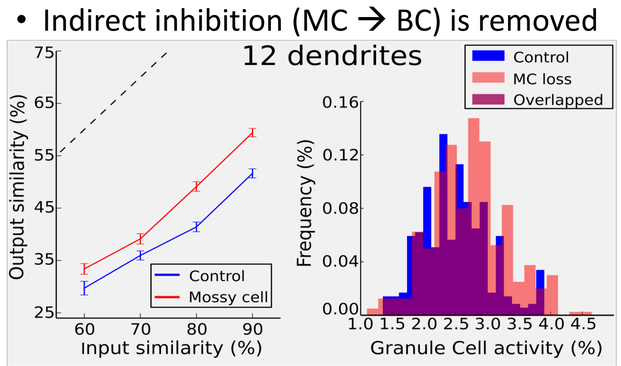
⇓

pattern separation

Results

Ablation of Mossy Cells

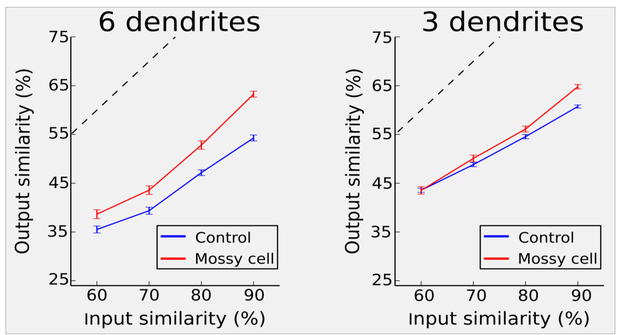
- Feed-back loop (GC → MC → GC) is removed
- Indirect inhibition (MC → BC) is removed



Mossy cells enhance pattern separation using healthy granule cells

MC ablation + dendrite ablation

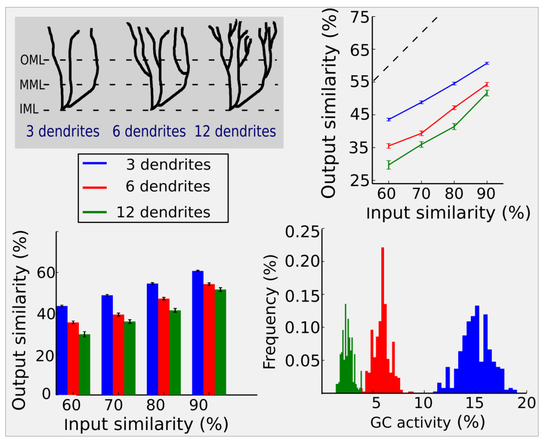
- Ablating mossy cells in granule cell models with different numbers of dendrites



Mossy cells enhance pattern separation in healthy aging, but their effect is decreased in AD

Dendrites in pattern separation

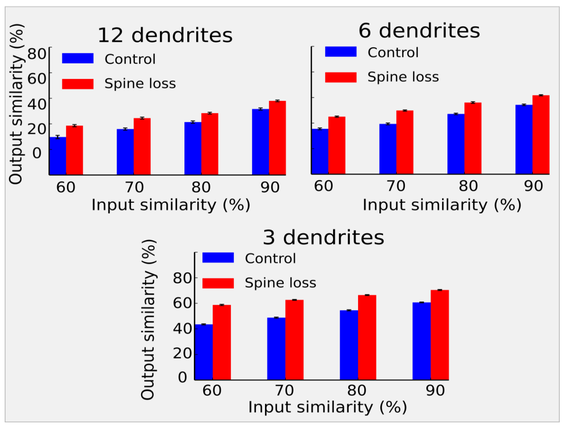
- GC models with 12, 6, 3 dendrites
- Control model → 12 dendritic model



Positive correlation between dendritic number and pattern separation efficiency; the more dendrites the better

Spine loss

- Dendritic capacitance is reduced to simulate the spine loss condition



Spine loss condition associated with Alzheimer's Disease leads in pattern separation deficits

Conclusions

We have implemented a simple, yet biophysically relevant, computational model of Dentate Gyrus network to study the mechanisms that govern pattern separation.

1. Inhibition provided via mossy cells enhances pattern separation
2. Dendrites enhance pattern separation
3. Spine loss leads to pattern separation deficits

References

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Acknowledgements

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