# Effect of Adult-Born Immature Granule Cells on Pattern Separation in The Hippocampal Dentate Gyrus

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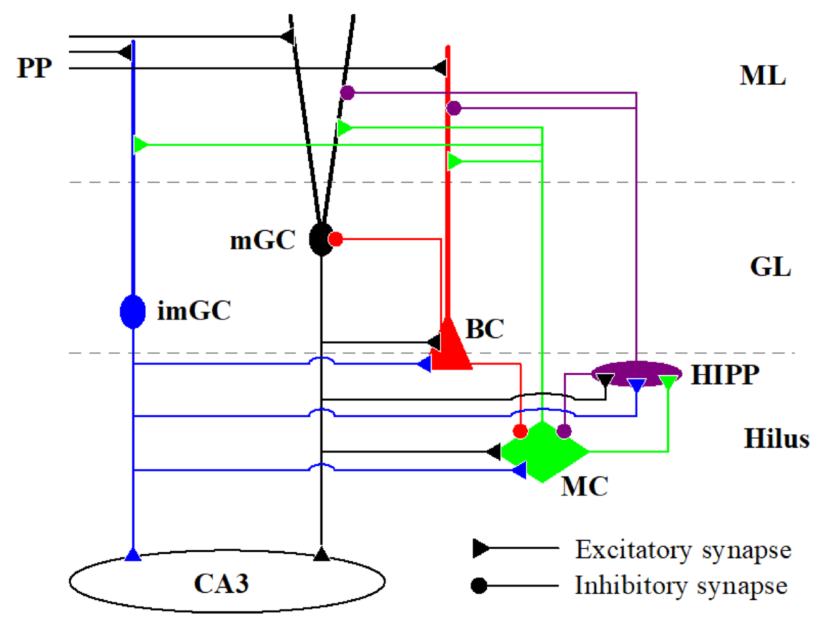
## Introduction

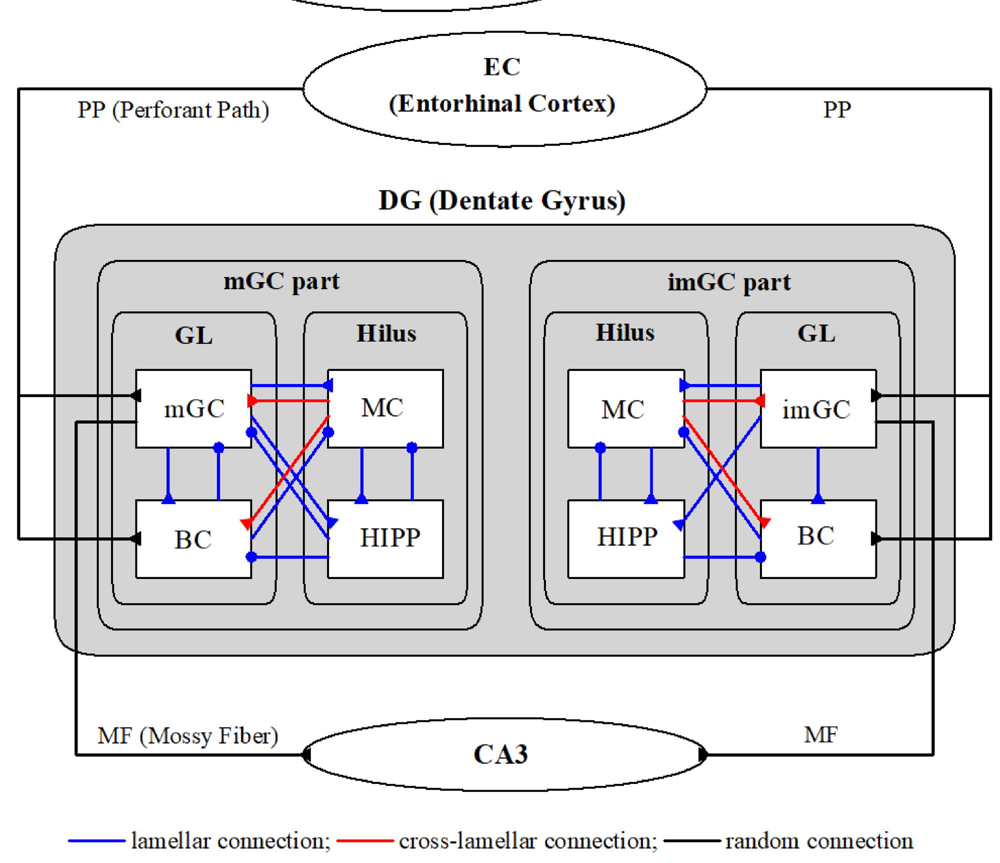
- **Hippocampus**
  - Consisting of the dentate gyrus (DG) and the areas CA3 and CA1
  - Play a key role in memory formation, storage, and retrieval
- **Pattern Separation**
  - Pattern Separation: Transforming input patterns into sparser and orthogonalized patterns
  - DG: Pre-processor for the CA3: Granule cells (GCs) in the DG performs pattern separation, facilitating pattern storage and retrieval in the CA3
  - Sparsity → Enhancing the pattern separation
- **Young Adult-Born Immature Granule Cells (imGCs)**
  - Young adult-born imGCs: High excitability (causing high activation) and low excitatory innervation (reducing activation)
- **Purpose of Our Study**
  Investigation of Adult-Born Immature Granule Cells on Pattern Separation in The Hippocampal Dentate Gyrus

## Hippocampal Dentate Gyrus (DG) Network

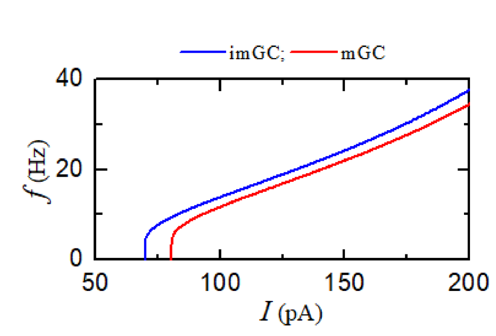
- **Cells in The DG Network**
  - DG receives inputs from the entorhinal cortex (EC) via the perforant paths (PPs)
  - Granular Layer:
    Excitatory granule cells (GCs): providing the output to the CA3 via the mossy fibers (MFs)
    Inhibitory basket cells (BCs)
  - Hilus:
    Excitatory mossy cells (MCs)
    Inhibitory hilar perforant path-associated (HIPP) cells




- **Architecture of The DG Network**
  - EC Network $N_{EC}$ (=400) EC cells
  - Granular-layer Network
    $N_C$ (=20) GC clusters
    $N_{GC}$ (=100) GCs & one BC in each GC cluster
    → Total No. of GCs = 2000
    No. of BCs $N_{BC}$ = 20
    Fraction of imGCs = 10 %
    10 imGCs in each GC cluster
    → Total No. of imGCs (mGCs) = 200 (1800)
  - Hilus Ring Network
    $N_{MC}$ (=60) MCs
    $N_{HIPP}$ (=20) HIPP cells
    MCs & HIPP cells are also grouped into 20 GC clusters

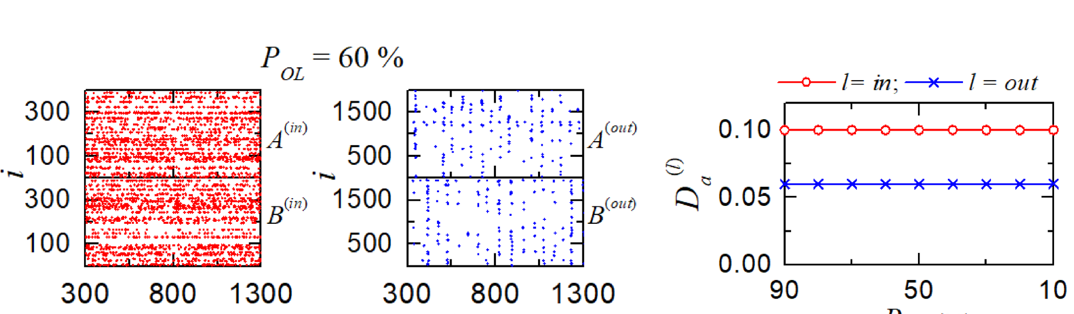



- **Firing Transitions of mGCs and Adult-Born imGCs**
  - Each BG cells are modeled by leaky integrate-and-fire neuron models with additional afterhyperpolarization currents
  - mGC with leakage reversal potential $V_L = -75$ mV
    → Threshold for the firing transition: $I^* = 80$ pA
  - imGC with $V_L = -72$ mV → $I^* = 69.7$ pA → Lower firing threshold
    → High excitability

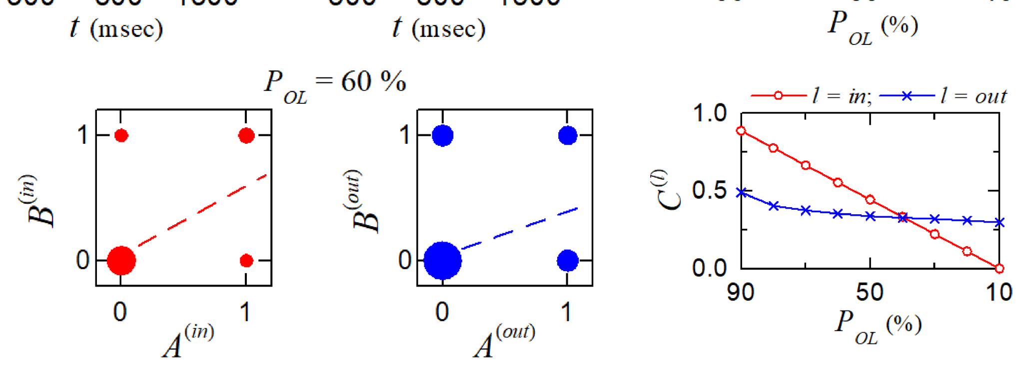



## Pattern Separation in The Presence Only The mGCs without imGCs

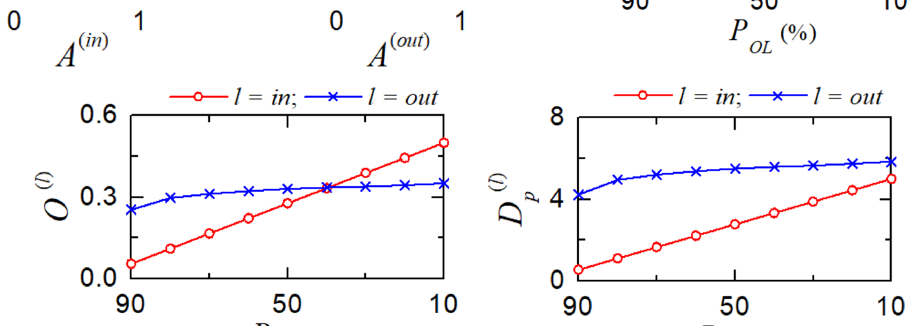
- **Binary Representation of Spiking Activity of EC Cells**
  - Direct Excitatory EC Inputs via PP
    Input density = 10 % → 40 active EC cells & Remaining ones: silent
    Active EC cells: at least one spike during the stimulus stage (1) otherwise, silent EC cells (0)
  - $A^{(in)}$ : Randomly-chosen input pattern
    Construct another input patterns $B_i^{(in)}$ from the with the overlap percentage $P_{OL}$
- **Binary Representation of Spiking Activity of GCs**
  - Active GCs: at least one spike during the stimulus stage (1) otherwise, silent GCs (0)
- **Characterization of Pattern Separation**
  - Activation Degrees
    GCs: More sparse firings than EC cells
    Average activation degree:
    $D_a^{(in)}(=0.1) > D_a^{(out)}(=0.06)$



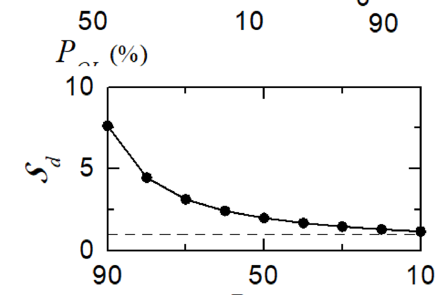

  - Pattern Correlation Degree $C^{(l)}$
    $C^{(l)} = \rho^{(l)}$ ($l$ = in or out)
    Pearson's correlation coefficient $\rho^{(l)}$ : denoting similarity degree between two patterns




  - Orthogonalization degree
    $O^{(x)}=(1-\rho^{(x)})/2$;  $x$ = in, out
    representing dissimilarity degree between two patterns
    $P_{OL}$≥40% → $O^{(out)}>O^{(in)}$, $P_{OL}$<40% → $O^{(in)}>O^{(out)}$
  - Pattern Distance: $\mathcal{D}_p^{(x)} = O^{(x)}/D_a^{(x)}$

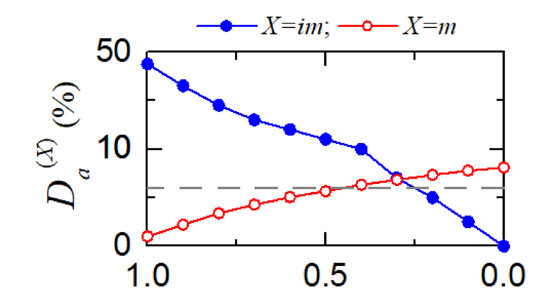



  - Pattern Separation Degree
    $\mathcal{S}_d = \mathcal{D}_p^{(out)}/\mathcal{D}_p^{(in)}$
    $\mathcal{S}_d$>1 for all values of $P_{OL}$ → Pattern separation occurs

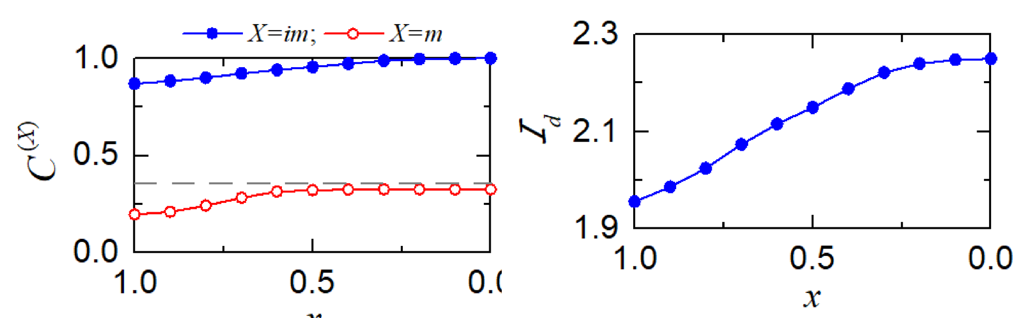



## Effect of Adult-born Immature GCs (imGCs) on the Pattern Separation

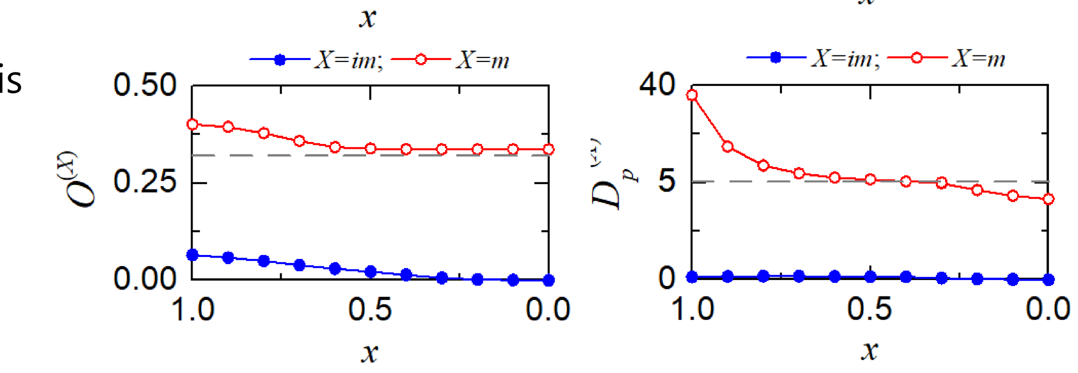
- **Double Averaging over 30 Realizations and 9 Pairs**
  9 pairs of input patterns with $P_{OL}$ =90 % ~ 10 %
  → 9 realization-averaged Pearson's correlation coefficients for each $P_{OL}$ via 30 realizations
  → Average Pearson's correlation coefficient over all the 9 pairs
  → Average pattern correlation degree and the average orthogonalization degree
- **Low Excitatory Innervation of imGCs**
  - Connection probability $p_c$ from the EC cells and the MCs to the mGCs = 20 %
  - imGCs: $p_c$ is decreased to 20 $x$ % [$x$ (synaptic connectivity fraction); 0 ≤ $x$ ≤ 1]
- **Effect of Low Excitatory Innervation for The imGCs**
  - Pattern Integration by imGCs
    With decreasing $x$ from 1, the imGCs receive low excitatory drive from the EC cells and the MCs
    → $D_a^{(im)}$ of the imGCs decreases so rapidly.
    → Effect of imGCs becomes weaker



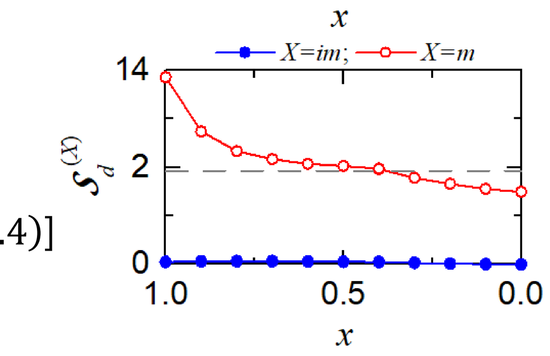

    $C^{(im)}$ of the imGCs are very high
    → imGCs: good pattern integrators with the pattern integration degree $\mathcal{I}_d$ [= $C^{(im)}/C^{(in)}$] >1




  - Pattern Separation by mGCs
    With decreasing $x$ from 1, the feedback inhibition to the mGCs is decreased due to decrease $D_a^{(im)}$
    → Increase in $D_a^{(m)}$
    → Decrease in pattern separation efficacy $\mathcal{S}_d^{(m)}$ of the mGCs

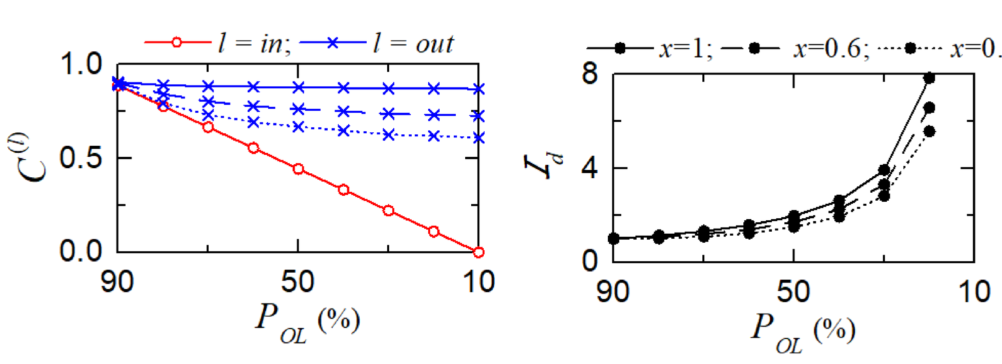



  - Pattern Separation Efficacy of The mGCs
    $\mathcal{S}_d^{(m)}$ varies by competition between high excitability and low excitatory innervation of the imGCs
    Effect of high excitability > Effect of low excitatory [1 ≥ $x$ > $x^*$(≃ 0.4)]
    → Pattern separation efficacy of the mGCs: Enhanced
    Effect of low excitatory innervation > Effect of high excitability ($x$ > $x^*$ ≥ 0)
    → Pattern separation efficacy of the mGCs: Worsened



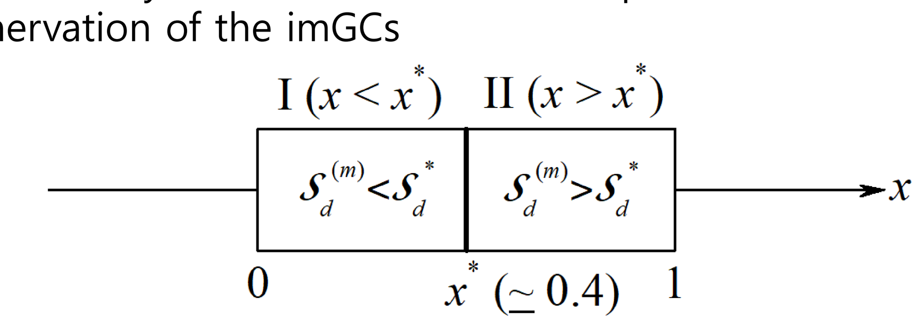

## Pattern Integration in The Presence of Only imGCs

- **Pattern Correlation Degree**
  $C^{(im)} > C^{(in)}$ for all range of $P_{OL}$
- **Pattern Integration Efficacy of The imGCs**
  - Pattern integration efficacy of the imGCs:
    Better for dissimilar input patterns
    Worse for similar input patterns
  - cf. Pattern separation of the mGCs better for similar input patterns




## Summary

- **Investigation of Effect of The Young Adult-Born Immature GCs (imGCs) on The Pattern Separation**
  - In contrast to the mature GCs (mGCs), the imGCs exhibit two competing distinct properties of high excitability (causing high activation) and low excitatory innervation (reducing activation degree)
  - The pattern separation efficacy the mGCs varies via competition between high excitability and low excitatory innervation of the imGCs




State I (0 ≤ $x$ < $x^*$) with lower synaptic maturity:
Effect of the effect of low excitatory innervation to the imGCs > Effect of high excitability
→ Activation degree $D_a^{(im)}$ of the imGCs becomes lower.
→ Reduction of inhibition to the mGCs (imGC → BC/HPP → mGC)
→ Increase in $D_a^{(m)}$ of the mGCs → Pattern separation degree $\mathcal{S}_d^{(m)} < \mathcal{S}^*$
($\mathcal{S}^*$: in the presence of only mGCs without imGCs)
→ Worsened pattern separation efficacy

State II ($x^*$ < $x$ ≤ 1) with higher synaptic maturity:
Effect of high excitability > Effect of the effect of low excitatory innervation
→ Activation degree $D_a^{(im)}$ of the imGCs becomes higher.
→ Strong feedback inhibition to the mGCs
→ Lower $D_a^{(m)}$ of the mGCs → Pattern separation degree $\mathcal{S}_d^{(m)} > \mathcal{S}^*$
→ Enhanced pattern separation efficacy