Effect of Adult-Born Immature Granule Cells on Sparsely Synchronized Rhythms in The Hippocampal Dentate Gyrus

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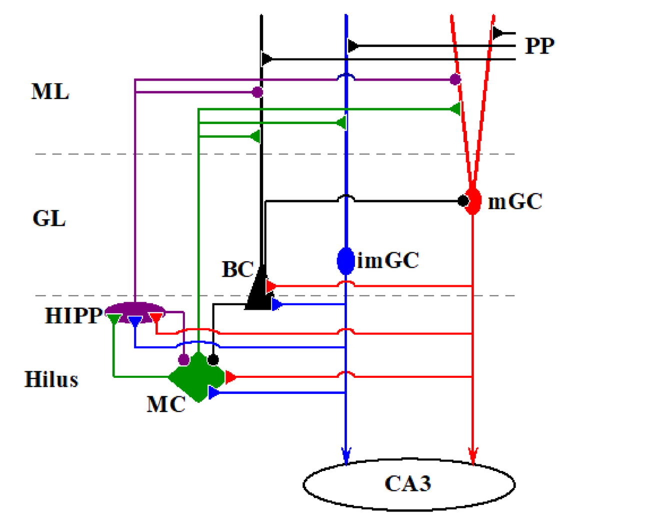
Introduction

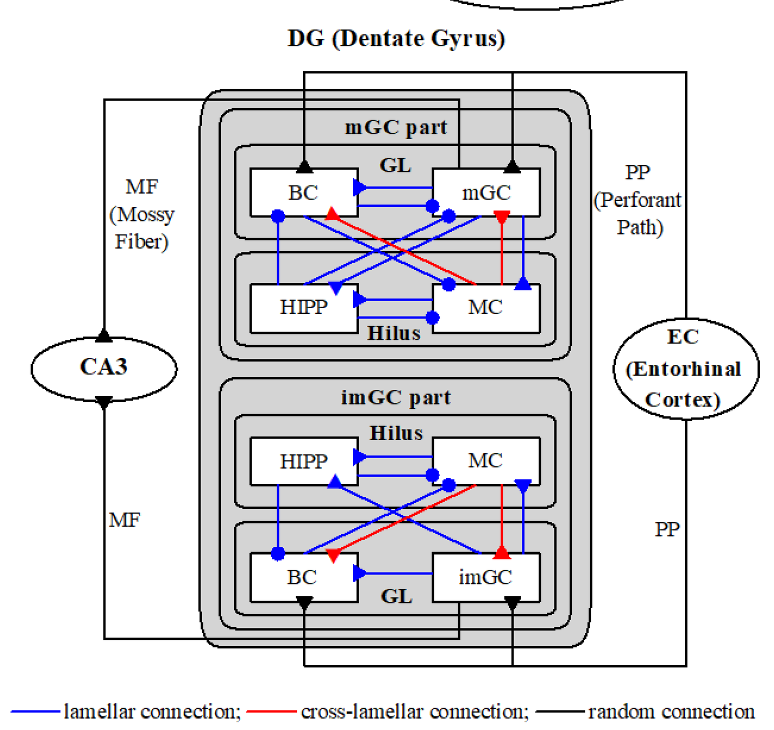
- **Hippocampus**
  - Consisting of the dentate gyrus (DG) and the areas CA3 and CA1
  - Play a key role in memory formation, storage, and retrieval
- **Pattern Separation**
  - Pattern Separation: Transforming input patterns into sparser and orthogonalized patterns
  - DG: Pre-processor for the CA3: 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 Sparsely Synchronized Rhythms (SSR) in The Hippocampal Dentate Gyrus

Hippocampal Dentate Gyrus (DG) Network

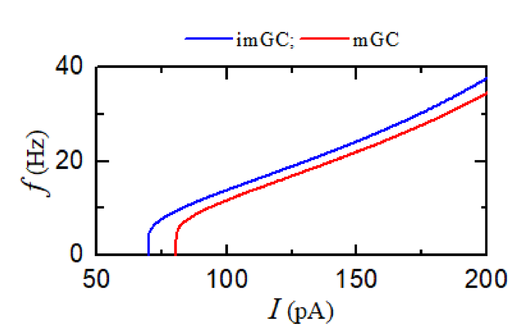
- **Cells in The DG Network**
  - DG receives inputs from the entorhinal cortex (EC) via the perforant paths (PPs)
  - Granular Layer:
    Excitatory granule cells (GCs): providing the output to the CA3 via the mossy fibers (MFs)
    Inhibitory basket cells (BCs)
  - Hilus:
    Excitatory mossy cells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

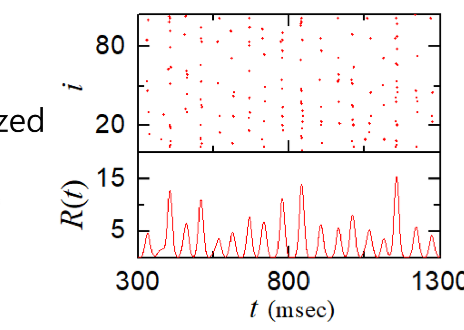


- **Firing Transitions of mGCs and Adult-Born imGCs**
  - Each BG cells are modeled by leaky integrate-and-fire neuron models with additional afterhyperpolarization currents
  - mGC with leakage reversal potential V_L=−75 mV
    → Threshold for the firing transition: I^*=80 pA
  - imGC with V_L=−72 mV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

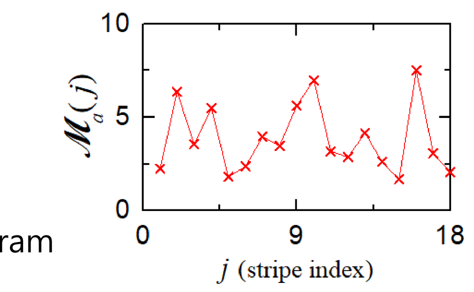


Characterization of The Sparsely Synchronized Rhythm (SSR) in The Presence of Only The mGCs

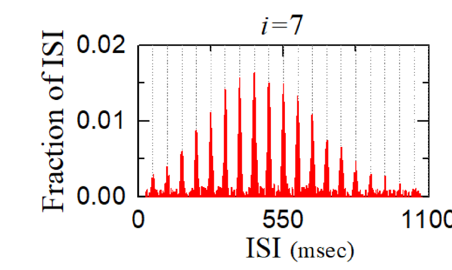
- **Emergence of SSR and Population Behavior of The Active mGCs**
  - No. of active mGCs: 120 → Activation degree = 6 %
  - Raster plot of spikes of active mGCs: Appearance of sparsely synchronized stripes with the population frequency f_p (≃ 18.2 Hz)
  - Emergence of sparsely synchronized rhythms in the GC-BC loop due to the feedback inhibition from the BCs



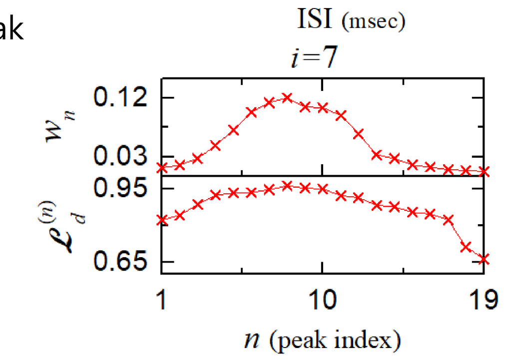
- **Characterization of Population Behavior**
  - Amplitude Measure $\mathcal{M}_a$: Synchronization degree of the SSR
    $\mathcal{M}_a = \overline{\mathcal{M}_a(j)}$; $\mathcal{M}_a(j) = \frac{R_{max}^{(j)}(t) - R_{min}^{(j)}(t)}{2}$ → $\mathcal{M}_a$=3.83



- **Individual Firing Behavior of The Active mGCs**
  - Stochastic spike skipping
    → Distinct multiple peaks at the integer multiples of global period T_G (≃ 54.9 msec) of the population rhythm in interspike (ISI) histogram
    → Standard sparse synchronization

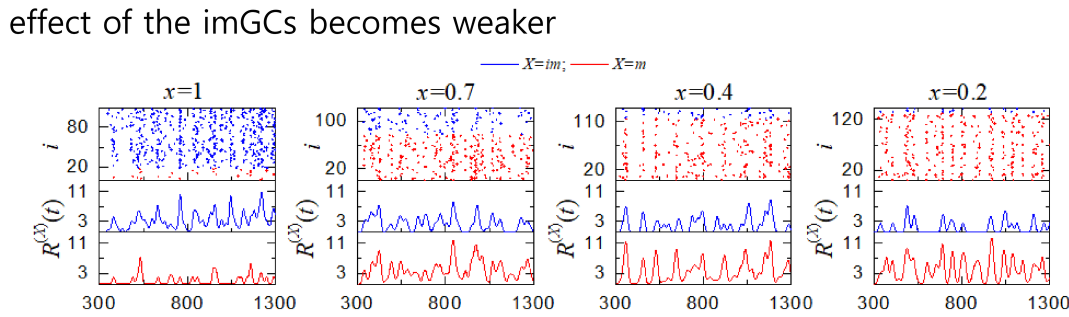


- **Characterization of Individual Firing Behavior**
  - Random phase locking degree : Given by the product of the normalized weights w_n and matching contributions $\mathcal{L}_d^{(n)}$ of ISI
  - Normalized weight w_n of the nth peak:
    $w_n = \frac{N_{\rm ISI}^{(n)}}{N_{\rm ISI}^{(tot)}}$; $N_{\rm ISI}^{(tot)}$: Total No. of ISIs, $N_{\rm ISI}^{(n)}$: No. of ISIs in the nth peak
  - Matching contribution $\mathcal{L}_d^{(n)}$: Representing the average contribution to the locking degree in the nth peak
    $\mathcal{L}_d^{(n)} = \frac{1}{N_{\rm ISI}^{(n)}} \sum_{j=1}^{N_{\rm ISI}^{(n)}} \cos\psi_j^{(n)}$
  - Random phase-locking degree $\mathcal{L}_d(i)$ of the ith mGC
    $\mathcal{L}_d(i) = \sum_{n=1}^{N_p(i)} w_n(i) \cdot \mathcal{L}_d^{(n)}(i) = \frac{1}{N_{\rm ISI}^{(tot)}(i)} \sum_{n=1}^{N_p(i)} \sum_{j=1}^{N_{\rm ISI}^{(n)}(i)} \cos\psi_j^{(n)}(i)$
  - Random phase-locking degree $\mathcal{L}_d$: $\mathcal{L}_d = \frac{1}{N_a}\sum_{i=1}^{N_a} \mathcal{L}_d(i)$ → $\mathcal{L}_d$=0.92

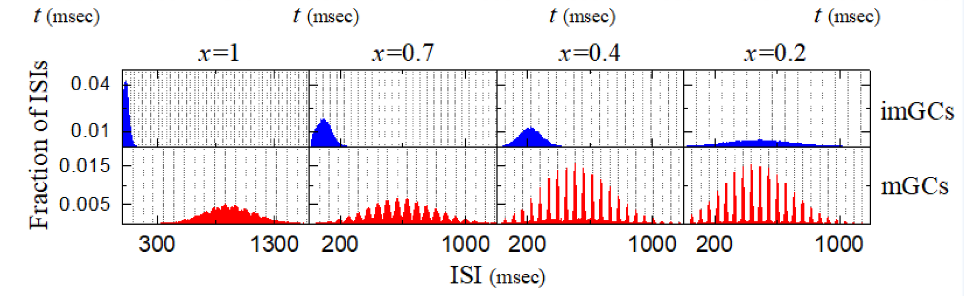


Effect of The imGCs on SSRs

- **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 on Population Behaviors**
  - With decreasing x from 1, the effect of the imGCs becomes weaker
    mGCs: Spiking stripes become clearer and Amplitude of $R^{(m)}(t)$ increases
    imGCs: Spiking tripes become more smeared and Amplitude of $R^{(im)}(t)$ decreases

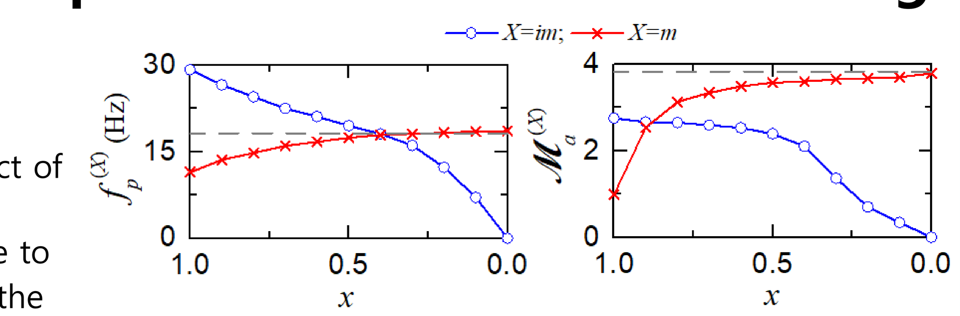


- **Effect of Low Excitatory Innervation on Individual Firing Behaviors**
  - With decreasing x from 1, the effect of the imGCs becomes weaker
    imGCs: More irregular spiking behaviors. Single-peaked ISI histograms become broader → More spike skippings occur
    imGCs: More regular spiking behaviors. ISI histograms become clearer because multiple peaks become sharper and their heights become increased.

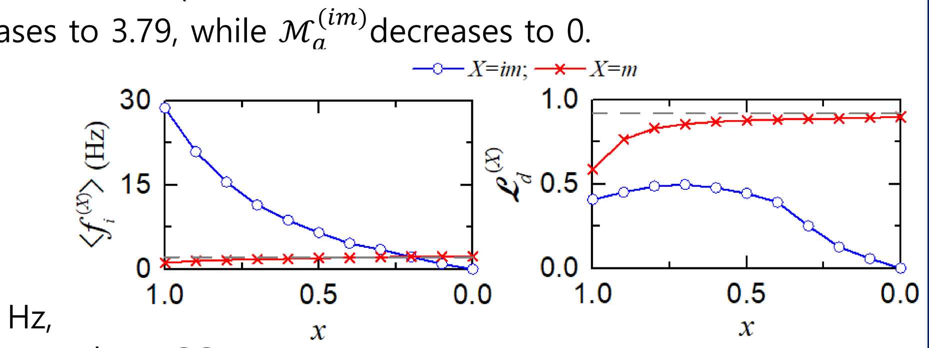


Effect of imGCs on Population and Individual Firing Behaviors of SSRs

- **Effect on Population Frequency**
  As x is decreased from 1 to 0 (the effect of imGCs becomes decreased rapidly),
  imGCs: $f_p^{(im)}$ decreases to 0 rapidly due to rapid decrease in firing activity of the imGCs (resulting from their low excitatory innervation)
  mGCs: $f_p^{(m)}$ increases to 18.6 Hz because of increase in firing activity of the mGCs (resulting from decrease in the feedback inhibition into the mGCs).
  $f_p^{(im)}$ and $f_p^{(m)}$ cross at $x^* \sim 0.4$

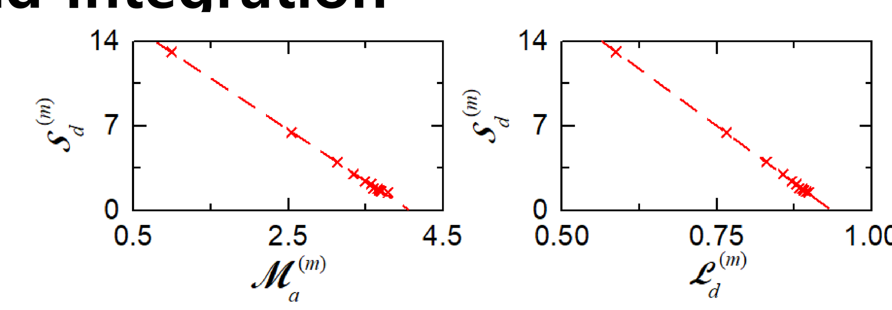


- **Effect on Synchronization Degree**
  As x is decreased from 1 to 0 (the effect of imGCs becomes decreased rapidly),
  More active and coherent firing activity of the mGCs (due to decreased feedback to the mGCs from the BCs and the HIPP cells) → $\mathcal{M}_a^{(m)}$increases to 3.79, while $\mathcal{M}_a^{(im)}$decreases to 0.
- **Effect on Individual Firing Behavior**
  - Mean firing rate
    As x is decreased from 1 to 0, $\langle f_i^{(im)} \rangle$ decreases so rapidly from 28.7 Hz to 0 due to low excitatory innervation.
    $\langle f_i^{(m)} \rangle$ increases slowly from 1.12 to 2.30 Hz, because of decrease in feedback inhibition to the mGCs.
  - Random-phase locking degree
    With decreasing x from 1 to 0, $\mathcal{L}_d^{(m)}$ is found to increase from 0.587 to 0.898, $\mathcal{L}_d^{(im)}$increases a little from 0.408 to 0.497.

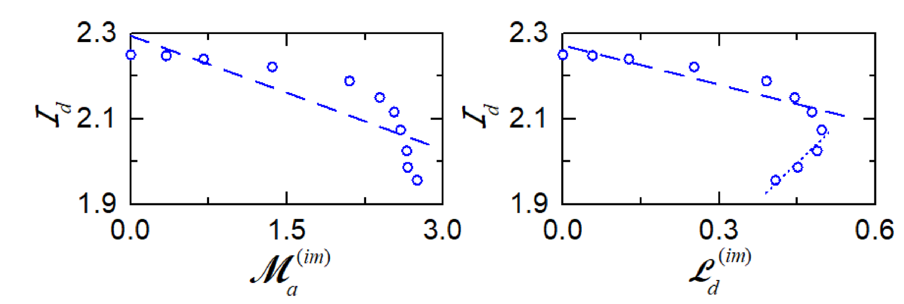


Quantitative Relationship between SSRs and Pattern Separation and Integration

- **Relationship between Pattern Separation Degree and SSRs of mGCs**
  - Negative correlation between pattern separation degree $\mathcal{S}_d^{(m)}$ vs. $\mathcal{M}_a^{(m)}$ (r = −0.9994) & $\mathcal{L}_d^{(m)}$ (r = −0.9998)
    → Better population and individual firing behaviors in their SSR, the worse their pattern separation



- **Relationship between Pattern Integration Degree and SSRs of imGCs**
  - Negative correlation between pattern integration degree $\mathcal{I}_d$ vs. $\mathcal{M}_a^{(im)}$ (r=−0.8483)
    Negative correlation between $\mathcal{I}_d$ vs. $\mathcal{L}_d^{(im)}$ for 0.7 ≤ x ≤ 0 (r = −0.9159)
    → Better population and individual firing behaviors in their SSR, the worse their pattern integration



Summary

- **Investigation of The Effect of Adult Neurogenesis on The Sparsely Synchronized of Granule Cells**
  - In comparison to the mGCs, the imGCs show two competing distinct properties of high excitability (causing high activation) and low excitatory innervation (reducing activation degree).
    → The effect of low excitatory innervation counteracts the effect of high excitability.
  - Decrease in the effect of imGCs → Better population and individual firing behaviors in mGCs' SSR
    → Word population and individual firing behaviors in imGCs' SSR
- **Relationship between Pattern Separation Degree and SSRs of mGCs**
  - Negative correlation between pattern separation degree and $\mathcal{S}_d^{(m)}$ vs. $\mathcal{M}_a^{(m)}$ & $\mathcal{L}_d^{(m)}$
    → Better population and individual firing behaviors in their SSR, the worse their pattern separation
- **Relationship between Pattern Integration Degree and SSRs of imGCs**
  - Negative correlation between pattern integration degree $\mathcal{I}_d$ vs. $\mathcal{M}_a^{(im)}$ & $\mathcal{L}_d^{(im)}$
    → Better population and individual firing behaviors in their SSR, the worse their pattern integration