Maturing neurons and dual structural plasticity enable flexibility and stability of olfactory memory

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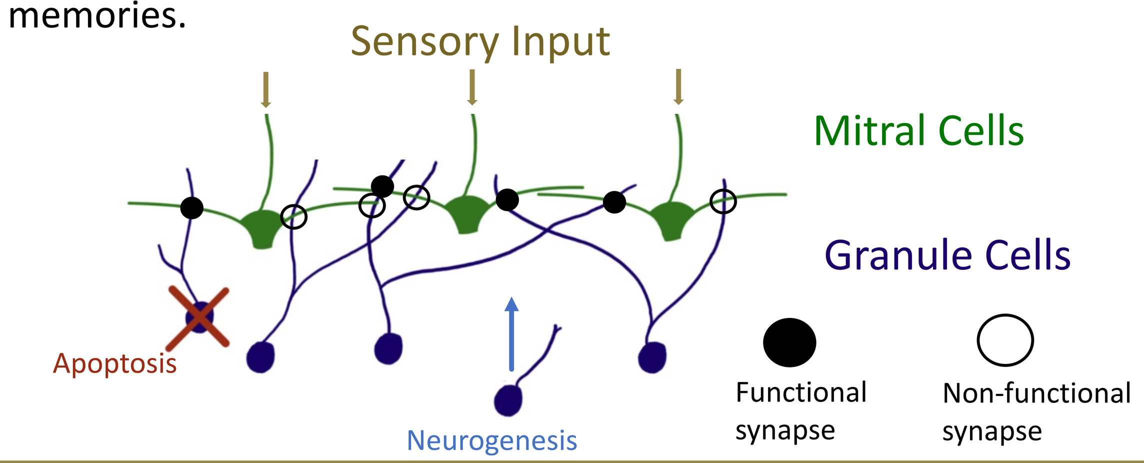
Overview: Computational model shows adult neurogenesis leads to birthdate-dependent, odor-specific subnetworks in the OB, enabling stable encoding of memories, while apoptosis maintains the flexibility of the network over time.

Introduction

The olfactory system allows organisms to detect and discriminate a vast array of odors in their environment. The olfactory bulb (OB) is the primary site of processing for olfactory information and is responsible for the initial encoding and processing of odors before they are transmitted to higher brain regions. One remarkable feature of the OB is its high degree of structural plasticity, most notably through the birth and death of inhibitory granule cells (GCs) that occur even throughout adulthood. Adult neurogenesis in particular has been shown to be essential in perceptual learning tasks, but why the OB uses this form of plasticity over metabolically cheaper mechanisms remains unclear.

A general concern in learning systems is the flexibility-stability tradeoff: the system must be flexible enough to encode new memories without overwriting old ones.

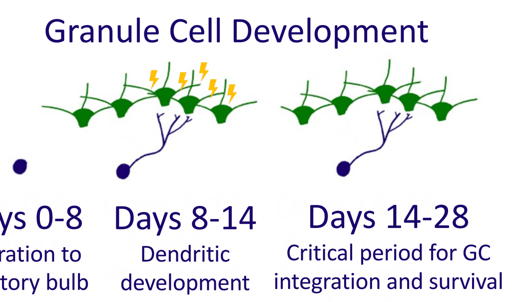
Using a computational model informed by bulbar anatomy and properties of adult neurogenesis and synaptic plasticity, we show that adult neurogenesis and apoptosis provide a mechanism for reconciling this tradeoff, enabling flexible and stable encoding of memories.



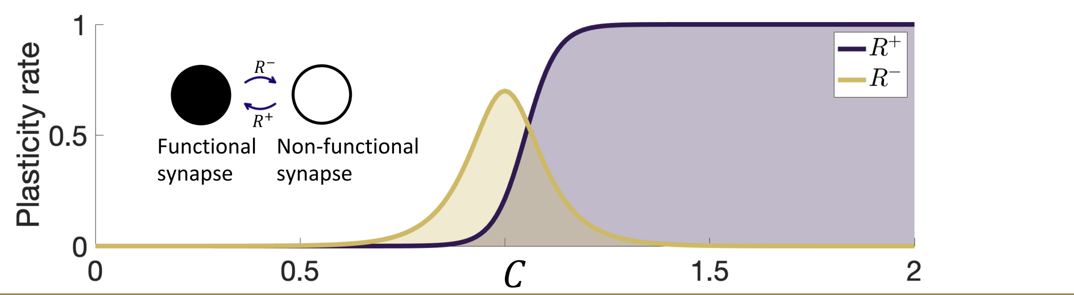
Model

- Firing rate equations for MC and GC activity :

$$\tau_M \frac{dM_i}{dt} = -M_i + [S_i - \gamma \sum_j w_{ij} G_j]_+$$
$$\tau_G \frac{dG_i}{dt} = -G_i + \alpha \sum_j w_{ji} M_j.$$

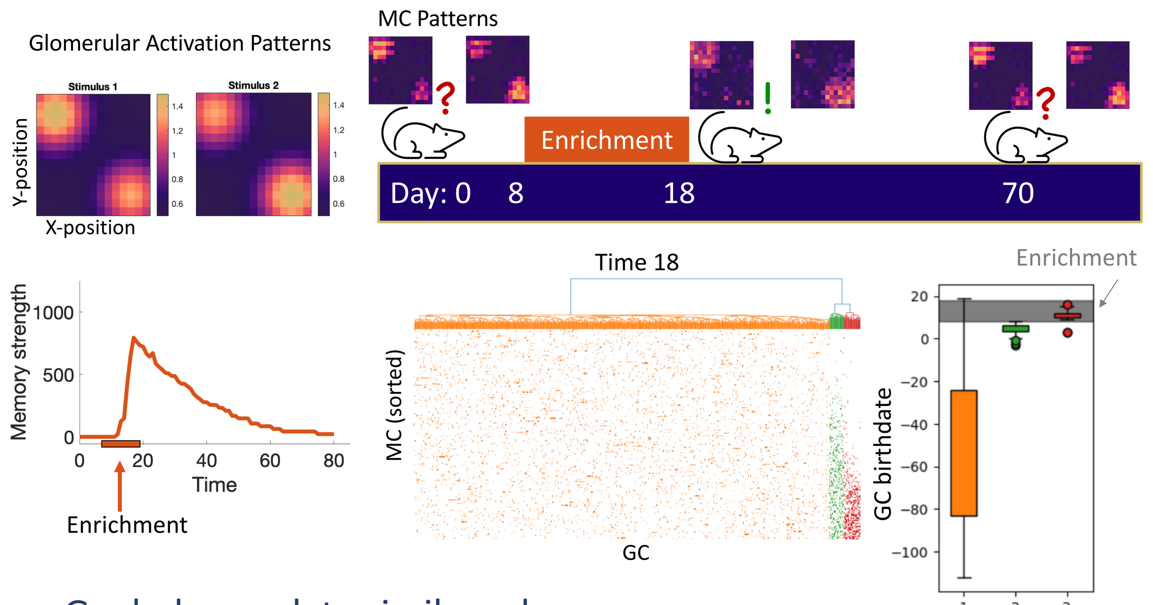


- Apoptosis:
  - Activity-dependent GC removal
  - No significant apoptosis is observed in a control environment[6] thus we assume that apoptosis only occurs when an enrichment odor is present.
- Neurogenesis:
  - Continually add new abGCs that have transiently increased excitability, plasticity rate, and survival activity threshold as observed experimentally
- Dendritic development:
  - AbGCs can only form synapses with a randomly chosen subset of MCs that is biased by the activity of the MCs during dendritic growth.
- Synaptic plasticity:
  - Driven by calcium-like variable[3] C at each spine



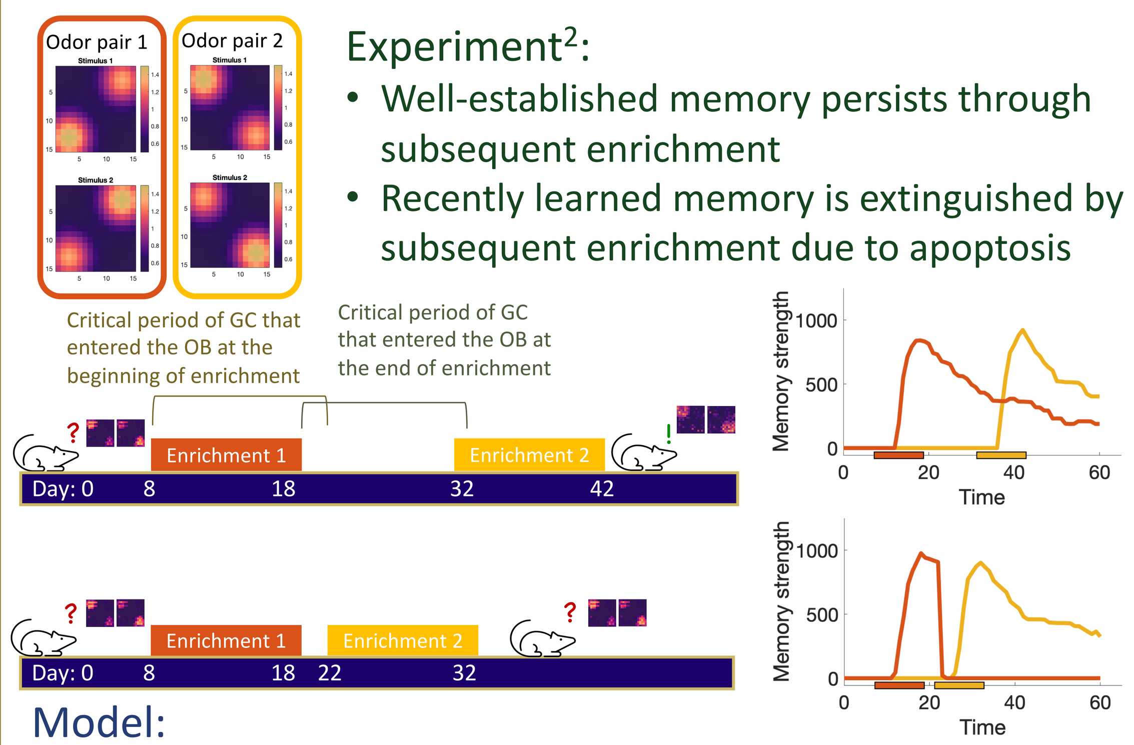
Results

Enrichment Enhances Discriminability



- Goal: decorrelate similar odors
- Two clusters of GCs develop an odor specific connectivity
- Clusters differ in age: GCs born during enrichment make more specific connections

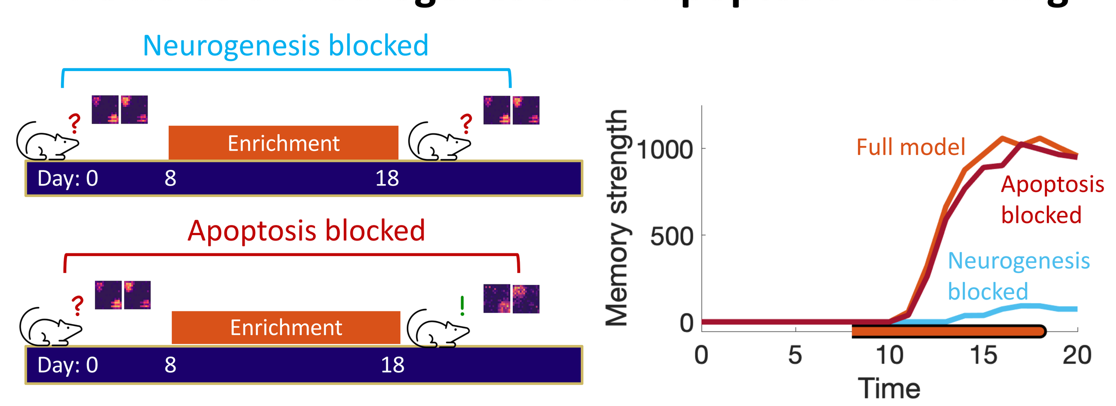
Dual Enrichment and Cell Death



Experiment[2]:
- Well-established memory persists through subsequent enrichment
- Recently learned memory is extinguished by subsequent enrichment due to apoptosis

Model:
- Confirms GCs retain memory if second enrichment occurs after their critical period

The Roles of Neurogenesis and Apoptosis in Learning

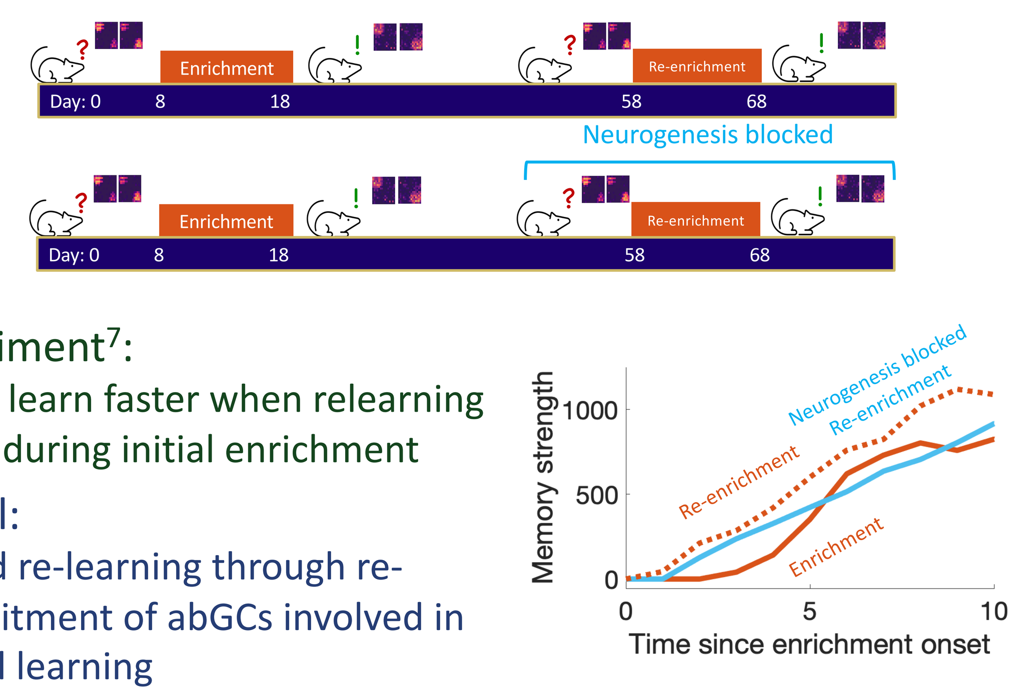


Experiments:
- Without neurogenesis, mice fail to learn during enrichment[4]
- Suppressing apoptosis makes no difference in initial learning[5]

Model:
- Confirms neurogenesis but not apoptosis is required for this task
  - What is the role of apoptosis? See **Neurogenesis and Apoptosis Increase the Flexibility and Stability of the OB**

Results

Neurogenesis Not Needed for Rapid Re-learning

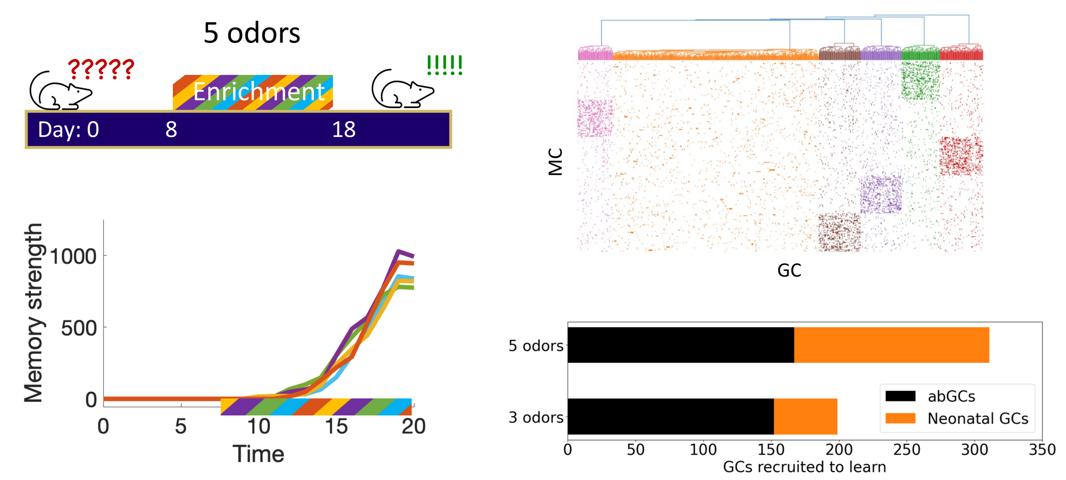


Experiment[7]:
- Mice learn faster when relearning than during initial enrichment

Model:
- Rapid re-learning through re-recruitment of abGCs involved in initial learning
- Despite slower plasticity rate, these cells have the advantage of having dendrites near enriched MCs

Prediction:
- Rapid re-learning will occur even if neurogenesis is blocked during re-enrichment
  - Why is this surprising? See **The Roles of Neurogenesis and Apoptosis in Learning** where there is no substantial initial learning without neurogenesis

Complex Enrichment Involves also Neonatal GCs



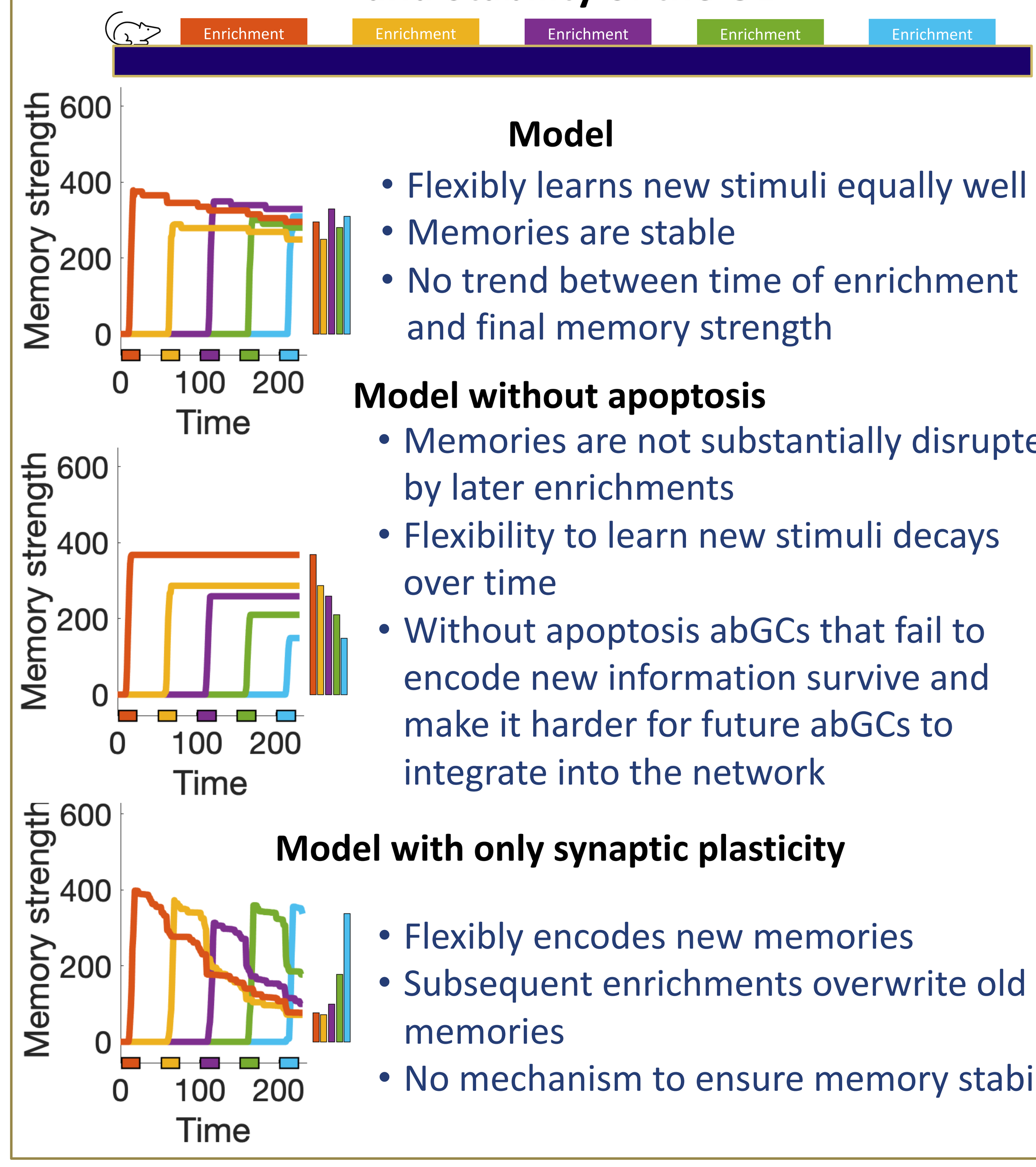
Experiment[1]:
- Simple enrichment (single odor pair): only abGCs are required for learning
- Complex enrichment (multiple odor pairs): both adult-born and neonatal cells are required for learning

Model:
- Both newborn and mature GCs are recruited for complex stimuli
  - Why is this surprising? See **Enrichment Enhances Discriminability** where only abGCs are involved in learning
- With increasing complexity, more mature GCs are recruited

Prediction:
- Even in complex environments GC connectivity becomes highly selective with GCs tuned to individual odorants

Results

Neurogenesis and Apoptosis Increase the Flexibility and Stability of the OB



Model
- Flexibly learns new stimuli equally well
- Memories are stable
- No trend between time of enrichment and final memory strength

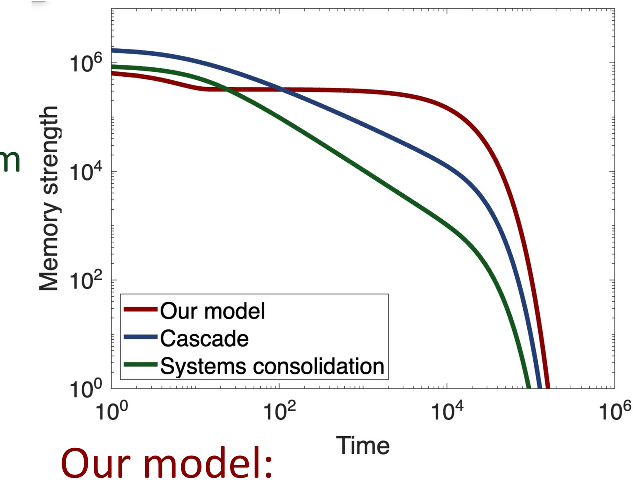
Model without apoptosis
- Memories are not substantially disrupted by later enrichments
- Flexibility to learn new stimuli decays over time
- Without apoptosis abGCs that fail to encode new information survive and make it harder for future abGCs to integrate into the network

Model with only synaptic plasticity
- Flexibly encodes new memories
- Subsequent enrichments overwrite old memories
- No mechanism to ensure memory stability

Conclusions & Future Work

Comparison with Other Methods

Systems consolidation model[8]:
- Memory is transferred from highly plastic subnetworks to weakly plastic subnetworks
- Memory decay $\sim 1/t$



Cascade model[9]:
- Plasticity rates are activity-dependent
- Memory decay $\sim 1/t$

Our model:
- Plasticity rates are age-dependent
- Memory decay $\sim e^{-q_1 t} + e^{-q_2 t}$

Mean field abstraction of our model performs similarly to other models designed to solve the flexibility-stability problem

Conclusions

- Adult neurogenesis leads to the development of birthdate-dependent, odor-specific subnetworks
  - Enables flexible and stable encoding of memories
  - Young highly plastic abGCs form new memories that become stable as the neurons age
- Flexibility of learning relies on apoptosis and the enhanced excitability of young abGCs
- Dendritic elaboration develops preconfigured subnetworks
  - Leads to "hidden memories" that are quickly retrievable
  - Decreases exposure to interfering stimuli

References & Acknowledgements

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