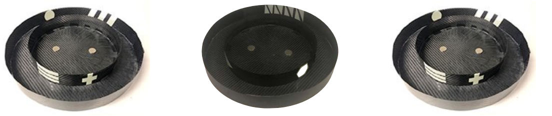
Multi-scale neural dynamics underlying memory encoding and recall in hippocampal area CA1

MRes Neurotechnology Name: Shengyuan Cai CID: 02468309
Supervisors: Meghdad Saeedian, Mary Ann Go, Mauricio Barahona, Simon Schultz

THE DEPARTMENT OF BIOENGINEERING
IMPERIAL

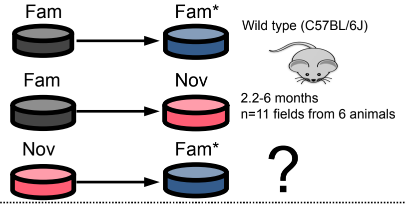
Motivation & Experiment design

Question: How does learning a new memory reorganize the functional network topology of an old memory in hippocampal area CA1?



Change the order and shape of the 4 cues

Familiar environment (Fam) one week → Novel environment (Nov) 20 mins → Return to familiar environment (Fam*) 20 mins



Old memory recall:

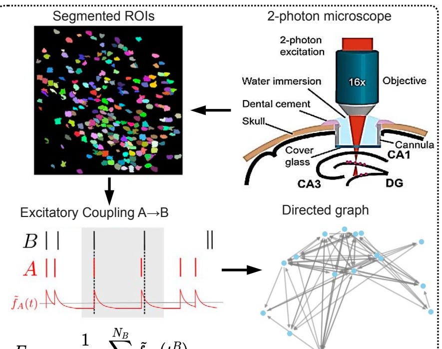
New memory Perturb:

Reorganization:

Wild type (C57BL/6J)

2.2-6 months
n=11 fields from 6 animals

Approach of dynamic functional connection



$$F_{AB} = \frac{1}{N_{AB}} \sum_{i=1}^{N_B} \tilde{f}_A(t_i^B)$$

$$f_A(t_i^B) = \xi_{\mathrm{exc}}\left(t_i^B - t_{\mathrm{last}}^A\right) = e^{-\left(t_i^B - t_{\mathrm{last}}^A\right)/\tau}$$

Perturbation (encoding) results at the network level

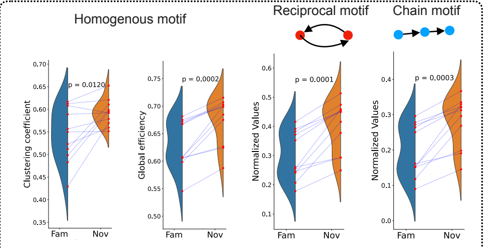
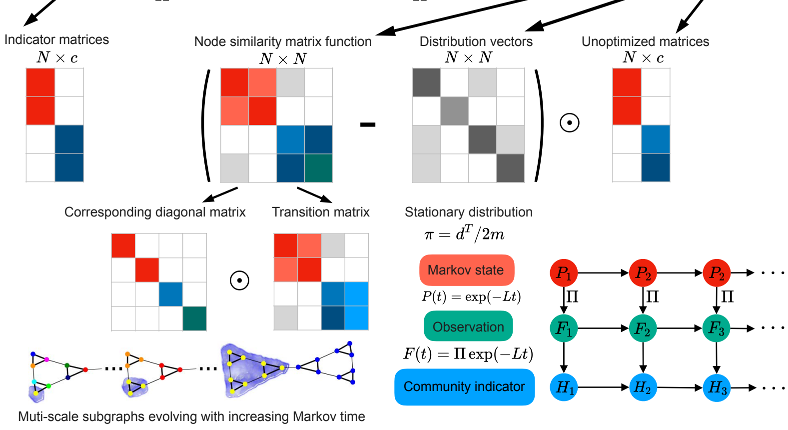


Figure.1 At the network level, a higher average clustering coefficient and global efficiency with exploring the novel environment. In fam*, these returned to the level of fam.

In the novel environment, both the Chain motif and Reciprocal motif exhibited an increase, resulting in the emergence of homogeneous structures.

Multi-scale subgraph detection with generalized Markov Stability

$$\boxed{H^*(t)} = \underset{H}{\operatorname{argmax}}\, Q_{gen}(t,H) := \underset{H}{\operatorname{argmax}}\, \operatorname{Tr}\left[H^T\left(\boxed{F(t)} - \boxed{\pi^T\pi}\right)\boxed{H}\right]$$

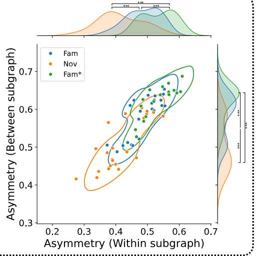


Muti-scale subgraphs evolving with increasing Markov time

Asymmetry of connections between subgraphs & within subgraph

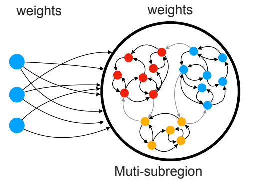
Figure.5 As the scale of the subgraphs transitioned from coarse to fine granularity, both the intra-subgraph and inter-subgraph asymmetry exhibited an increase. Furthermore, the perturbation introduced by new memories led to a decrease in the asymmetry of connections within and between subgraphs, indicating a higher degree of homogenization in the functional networks.

During the subsequent reorganization process, the asymmetry of connections within and between subgraphs was elevated in the fam* condition compared to the fam condition.



Ongoing directions - Simulate neural dynamics of memory recall with perturbation

$$\tau_r \frac{dr_i}{dt} + r_i = \mathrm{ReLU}\left(\boxed{\sum_{j=1}^{N^m} W_{ij}^{FF} r_j^{\mathrm{in}}} + \boxed{\sum_{j=1}^{N} W_{ij}^{IN} r_j} - I + \epsilon_i(t)\right)$$



$$\tau_W \frac{dW_{ij}}{dt} = (1 + \mathrm{S}(t)) * \tanh\left(r_i * (r_j - r_j^0(t))\right)$$

Figure.6 By conducting rest simulations at different time scales, we aim to observe the impact of the consolidation process duration following perturbation on the reorganization during recall.

Initial result.

Modeling networks of different environments by self-organizing processes.

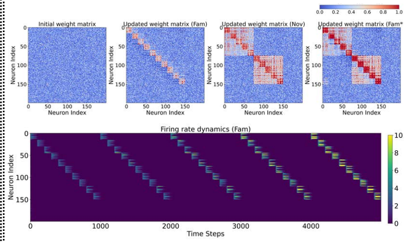


Figure.7 To simulate perturbation, we designed receptive fields based on the graph structure we inferred . Initial findings suggest that when returning to the initial environment, greater inhibitory neuron weights are required to maintain stable neural dynamics.

Reorganization (recall) results at the subgraph level

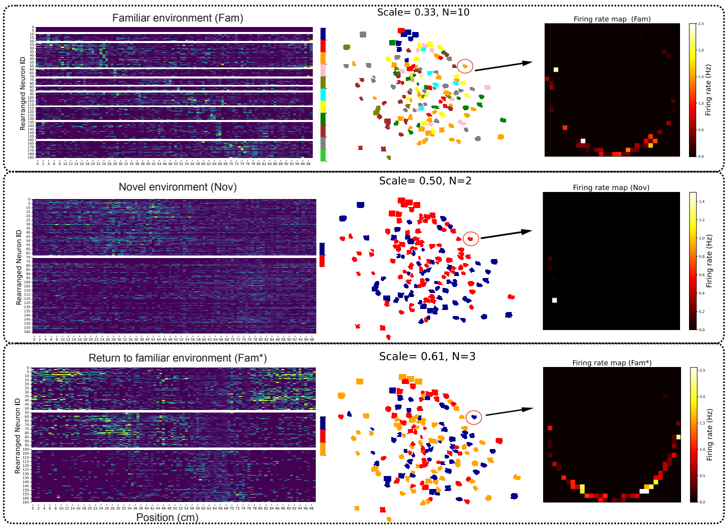


Figure.2 At certain time scales that exhibit considerable stability, our method demonstrates the capability to detect highly reliable subgraphs. These subgraphs effectively capture neurons that possess similar firing fields.

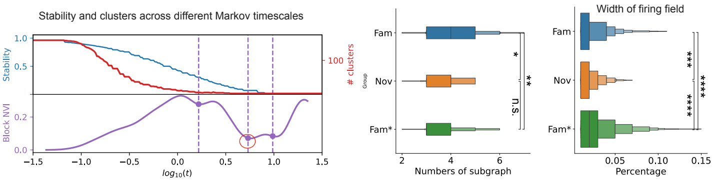


Figure.3 During the reorganization process, we observe that the stable subgraph scales become coarser, indicating a reduction in the number of stable subgraphs in the Fam*. This effect appears to be a consequence of the previous perturbation. Furthermore, among ~1761 cells analyzed, a significant broadening of the firing rate map was discovered.

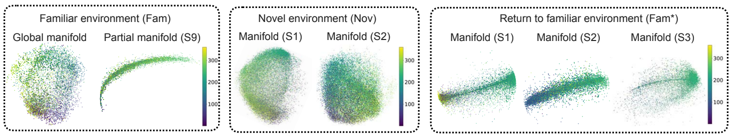


Figure.4 The perturbation process initially disrupted the previously stable global manifold. Further analysis of the manifolds corresponding to each neural sub-population revealed that, compared to the Fam, the sub-population manifold spanned broader local field during the reorganization process in Fam*.

Conclusion and discussion

- The perturbation (new memory encoding) initially led to the homogenization of the CA1 network.
- Population structure exhibits differences across spatial scales.
- During the reorganization (recall) process, neurons extended their firing fields, resulting in a reduction in the number of functionally distinct subpopulations.
- However, the asymmetry of the existing subpopulations was enhanced.

[1] Go, Mary Ann, et al. "Place cells in head-fixed mice navigating a floating real-world environment." Frontiers in cellular neuroscience 15 (2021): 618658.
[2] Arnaudon, Alexis, et al. "Algorithm xxx: PyGenStability, a multiscale community detection with generalized Markov Stability." *ACM TMS* (2024).
[3] Billeh, Yazan N., et al. "Revealing cell assemblies at multiple levels of granularity." Journal of neuroscience methods 236 (2014): 92-106
[4] Delamare, G., Tomé, D. F., & Clopath, C. (2024). Intrinsic neural excitability biases allocation and overlap of memory engrams. *Journal of Neuroscience, 44*(21).
[5] Delvenne, J. C., Yaliraki, S. N., & Barahona, M. (2010). Stability of graph communities across time scales. *PNAS, 107*(29), 12755-12760.
[6] Schneider, S., Lee, J. H., & Mathis, M. W. (2023). Learnable latent embeddings for joint behavioural and neural analysis. *Nature, 617*(7960), 360-368.