

Cellular functional networks dynamically encode novelty in the mouse visual cortex

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Abstract:

Novelty detection is critical for survival in a dynamic environment. It has been proposed that novelty detection involves cell-type specific neural circuits and top-down modulation. However, whether and how novelty is encoded by the dynamic interactions of a neuronal network is still unclear. With the large-scale electrophysiology dataset from Allen Institute, we studied the dynamic representation of novelty in the networks constituted by single neurons while the mouse is performing a visual change detection task. Based on functional networks constructed with Granger causality, we applied an unsupervised consensus clustering method and uncovered distinct modular structures between familiar and novel stimuli, which indicated stronger feedforward and recurrent processes induced by novelty. We further investigated the dynamics of network structure by building snapshots of the network. Obtaining network embeddings through graph decomposition, we revealed a time-varying difference between the representations of neuronal networks induced by familiar and novel images, which is also reflected by the network decoding analysis. Altogether, our work suggested novelty induced systematic changes in the information flow and the novelty signal is dynamically encoded in the topology of the cellular-resolution functional networks.

Keywords: dynamic network; network decoding; novelty; information flow

Introduction

Salient response to novelty (Ranganath & Rainer, 2003; Schomaker & Meeter, 2015) are crucial for organisms to survive in a dynamic environment (Homann et al. 2022; Rust & Cohen, 2022). Different cell types are involved differently in novelty detection, forming specific neural circuits and dynamics (Aitken et al. 2023; Garrett et al. 2023). It has been suggested that top-down modulation from higher areas is necessary for novelty detection (Bastos et al., 2023; Sikkens, Bosman & Olcese, 2019), but more evidence is needed to elucidate the network mechanism underlying novelty detection.

It has been shown that synchronization of a population can enhance signal propagation efficacy (Diesmann, Gewaltig & Aertsen, 1999; Jia, Tanabe & Kohn, 2013; Ratté et al. 2013), E/I balanced network possesses high representational capability (Denève & Machens, 2016), and decision making is more effectively encoded in small networks (Francis et al. 2018). All these evidence suggested an additional dimension of neural coding lay in the topology of cellular networks. Meanwhile, topological information of networks has been demonstrated effective in node and graph classification tasks (Kipf & Welling, 2016; Xu et al. 2019). However, it remains unclear whether and how novel signals are encoded in the cellular-resolution

networks, especially in the dynamical changes of topological structure.

In this work, we investigated the novelty coding in the dynamic network of neurons in mouse visual cortex. With the electrophysiology dataset of mouse performing image-change detection task (Figure 1A), we adopted Granger causality in the frequency domain with a sliding window approach to construct dynamic networks from spike trains recorded from 40 mice (sessions) while they are performing the visual change-detection tasks.

Results

We constructed fully connected functional networks by calculating Granger causality (GC) of the spike train between neural pairs within the 0-30 Hz frequency range. Directed asymmetry index, defined as $DAI_{x \rightarrow y} = \frac{GC_{x \rightarrow y} - GC_{y \rightarrow x}}{GC_{x \rightarrow y} + GC_{y \rightarrow x}}$, serves as an indicator of the directionality of information flow between neurons. Building upon previous research by Jia et al. (2022), which identified multi-region modules mediating feedforward and recurrent processes, we applied the same method here to detect the modular structure in the networks. Our findings demonstrate that this modular structure is present in both familiar and novel networks (Figure 1C). Strikingly, novel stimuli tend to evoke significantly more driver and driven neurons (Figure 1D, bottom), facilitating enhanced information flow. The excess of driver neurons in novel networks can originate from any neuron, while driven neurons are mainly replenished by the silencing neuron in response to familiar images.

To investigate how neuronal interactions dynamically encode novelty, we employed a sliding window approach with a duration of 200 ms and a step of 10 ms, ranging from [-200 ms, 0 ms] to [550 ms, 750 ms] anchored to stimulus onset. Our analysis revealed heightened information flow between driver and driven neurons during stimulus presentation which markedly diminished during the gray screen interval (Figure 2A, bottom). Generalized singular value decomposition (GSVD) exhibits great potential for embedding directed networks (Abdi, 2007). Through GSVD, we embedded DAI networks in a low-dimensional space. Network embeddings were then obtained using mean pooling and subsequently aligned across sessions through mean subtraction (Figure 2B). This approach allows direct comparisons of familiar and novel networks across different sessions with varying network size (Figure 2B, right). Notably, both familiar and novel network trajectories exhibit two distinct 'cycles', with one corresponding to the networks' response to stimulus onset and the other to stimulus offset. (Figure 2C, top). The networks' responses to stimulus onset display differences between familiar and novel stimuli, whereas the offset networks remain similar. Decoding analysis

based on network embedding showed the capacity of novelty encoding in the dynamic networks (Figure 2D).

Network coding has not received the attention commensurate with its importance. The complex, time-varying and high-dimensional nature of network topology harbors abundant information that may not be readily apparent through a straightforward analysis of neural responses alone. Hence, there is an escalating demand for research focused on uncovering the crucial stimulus information encoded within these dynamic networks.

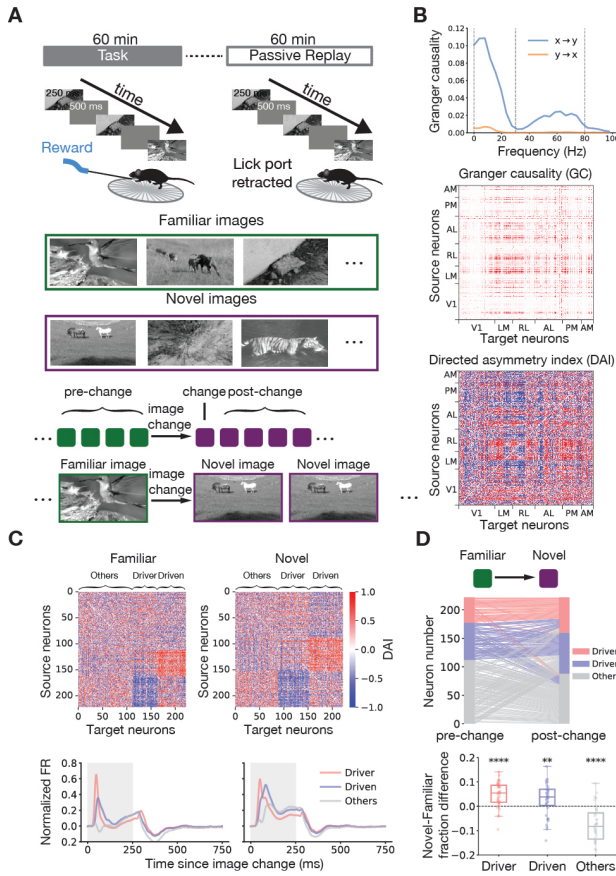


Figure 1: Stronger information flow induced by novelty. (A) Illustration of the experimental setting (Adapted from Garrett et al. 2023 & Siegle & Jia et al. 2021). Each mouse is trained on a set of images (familiar images) and tested on both familiar and novel images. (B) Granger causality (GC) in the frequency domain is used to define the functional connections between neurons. Directed asymmetry index (DAI) reflects the directionality of information flow. (C) The modular structure of the DAI matrices (top) and normalized firing rates for different modules (bottom). Gray bands indicate stimulus presentation while the rest are gray screen. (D) Change of neuron's role in the information flow between familiar and novel networks. ** p < 0.01, **** p < 0.0001, n=40, paired t-test.

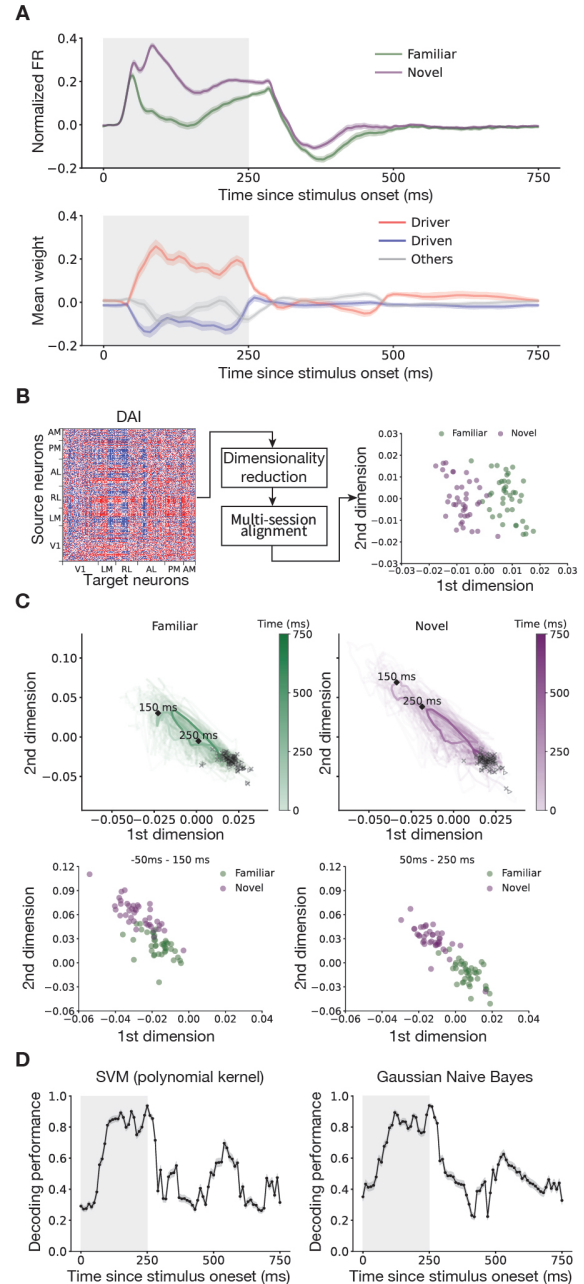


Figure 2: Novelty encoding in the dynamic network. (A) Normalized firing rates for familiar and novel images averaged across 40 mice (top) and the mean weight for each module across time during familiar image presentation (bottom). (B) To obtain the low-dimensional network embeddings across sessions, we reduced the dimension of networks through the generalized SVD and adopted multi-session alignment. (C) The averaged embedding trajectories of familiar and novel networks across time with starting and ending points marked by triangles and crosses, respectively (top) and two example snapshots (bottom). Light trajectories denote individual sessions. (D) Novelty decoding with network embeddings using different decoders.

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References

- Abdi, H. (2007). Singular value decomposition (SVD) and generalized singular value decomposition. *Encyclopedia of measurement and statistics*, 907(912), 44.
- Aitken, K., Campagnola, L., Garrett, M., Olsen, S., & Mihalas, S. (2023). Familiarity modulated synapses model visual cortical circuit novelty responses. *bioRxiv*.
- Bastos, G., Holmes, J. T., Ross, J. M., Rader, A. M., Gallimore, C. G., Wargo, J. A., ... & Hamm, J. P. (2023). Top-down input modulates visual context processing through an interneuron-specific circuit. *Cell reports*, 42(9).
- Denève, S., & Machens, C. K. (2016). Efficient codes and balanced networks. *Nature neuroscience*, 19(3), 375-382.
- Diesmann, M., Gewaltig, M. O., & Aertsen, A. (1999). Stable propagation of synchronous spiking in cortical neural networks. *Nature*, 402(6761), 529-533.
- Francis, N. A., Winkowski, D. E., Sheikhattar, A., Armengol, K., Babadi, B., & Kanold, P. O. (2018). Small networks encode decision-making in primary auditory cortex. *Neuron*, 97(4), 885-897.
- Garrett, M., Groblewski, P., Piet, A., Ollerenshaw, D., Najafi, F., Yavorska, I., ... & Olsen, S. R. (2023). Stimulus novelty uncovers coding diversity in visual cortical circuits. *bioRxiv*, 2023-02.
- Homann, J., Koay, S. A., Chen, K. S., Tank, D. W., & Berry, M. J. (2022). Novel stimuli evoke excess activity in the mouse primary visual cortex. *Proceedings of the National Academy of Sciences*, 119(5), e2108882119.
- Jia, X., Siegle, J. H., Durand, S., Heller, G., Ramirez, T. K., Koch, C., & Olsen, S. R. (2022). Multi-regional module-based signal transmission in mouse visual cortex. *Neuron*, 110(9), 1585-1598.
- Jia, X., Tanabe, S., & Kohn, A. (2013). Gamma and the coordination of spiking activity in early visual cortex. *Neuron*, 77(4), 762-774.
- Kipf, T. N., & Welling, M. (2016). Semi-supervised classification with graph convolutional networks. *arXiv preprint arXiv:1609.02907*.
- Ranganath, C., & Rainer, G. (2003). Neural mechanisms for detecting and remembering novel events. *Nature Reviews Neuroscience*, 4(3), 193-202.
- Ratté, S., Hong, S., De Schutter, E., & Prescott, S. A. (2013). Impact of neuronal properties on network coding: roles of spike initiation dynamics and robust synchrony transfer. *Neuron*, 78(5), 758-772.
- Rust, N. C., & Cohen, M. R. (2022). Priority coding in the visual system. *Nature Reviews Neuroscience*, 23(6), 376-388.
- Schomaker, J., & Meeter, M. (2015). Short-and long-lasting consequences of novelty, deviance and surprise on brain and cognition. *Neuroscience & Biobehavioral Reviews*, 55, 268-279.
- Sikkens, T., Bosman, C. A., & Olcese, U. (2019). The role of top-down modulation in shaping sensory processing across brain states: implications for consciousness. *Frontiers in systems neuroscience*, 13, 31.
- Xu, K., Hu, W., Leskovec, J., & Jegelka, S. (2018). How powerful are graph neural networks?. *arXiv preprint arXiv:1810.00826*.