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News & views

Neuroscience

Volatile neurons unite to stabilize visual experience

Tatiana A. Engel

It has been unclear how the brain creates stable visual experiences from the highly variable activity of individual neurons. Imaging from thousands of neurons across the entire mouse visual cortex provides an explanation.

Our senses provide us with a stable experience of the surrounding world. Whether you look at the family photo on your desk now, in an hour or next week, you'll still see the same image. This perceptual stability is astonishing, given how variable neural activity is in the brain's visual cortex. Single neurons respond with different strengths every time we look at the same image. Moreover, neurons change their sensitivity across days – so a neuron that reliably responds to an image today might be unresponsive tomorrow. Writing in *Nature*, Ebrahimi *et al.*[1] provide an explanation for this apparent contradiction.

The authors performed a first-of-a-kind experiment, simultaneously recording the activity from thousands of neurons scattered across the entire visual cortex, in mice performing an active visual task. They obtained recordings on this extraordinary scale by using advanced microscopy techniques and proteins called genetically encoded calcium indicators (GECIs). GECIs provide a pulse of fluorescence when a neuron is active and – under the right microscope – reveal the activity of thousands of individual neurons at once. The researchers tracked the activity of the same neurons as the mice performed the task multiple times over five to seven days.

The animals had to discriminate between two visual stimuli on a screen. One cued them to lick a spout for a water reward; the other indicated that they should not lick. Ebrahimi and colleagues measured how reliably the activity of cortical neurons differentiated between the two stimuli and how stable this activity was over time. They also linked neural activity patterns to the animals' perception of the stimuli – assessed by whether the mice licked or did not lick in response to the stimulus they were presented with.

As has been observed[2–4] in other areas of the mouse cortex, the sensitivity of single neurons to visual stimuli changed within recording sessions (in which animals repeated the task several times), and across days. Some cells became better at discriminating between the stimuli; others became worse (Fig. 1a).

How, then, can a mouse reliably distinguish between visual stimuli, given that neural responses are so volatile? The authors used an algorithm called an optimal linear decoder to separate the neural-activity patterns triggered by the two stimuli. Such decoders analyse neural activity and find the linear 'boundary' that best separates patterns triggered by one stimulus from those triggered by the other. Remarkably, the optimal decoding boundary was invariant across days (Fig. 1b). Thus, the same activity patterns differentiated the stimuli on different days, even though individual neurons were constantly in flux.

How can these two apparently contradictory properties of neural activity be aligned? Ebrahimi *et al.* found that the solution involved fast fluctuations in neural activity, from one task iteration (trial) to the next. These trial-to-trial activity fluctuations are known to be correlated across cortical populations (that is, the responses of nearby neurons tend to wax and wane together)[5]. The correlated

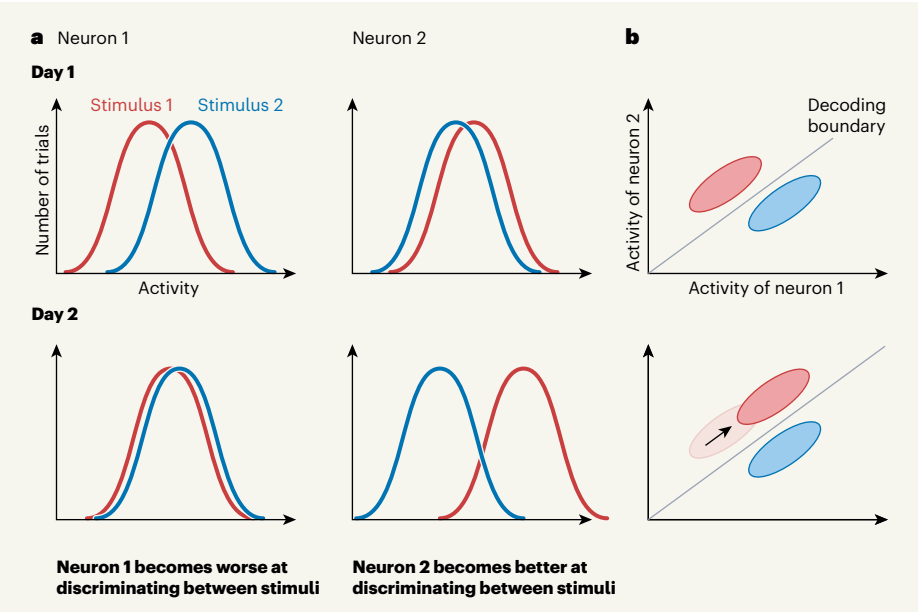

Figure 1 | Decoding neural activity in the brain's visual cortex. Ebrahimi *et al.*[1] analysed the activity of thousands of neurons across the entire visual cortex as mice performed a visual task, in which they had to discriminate between two stimuli on a screen. Here, activities for only two neurons are shown, for simplicity. **a**, Each of these graphs depicts the distribution of activity triggered in an individual neuron as an animal performs the task many times on a given day. The more similar the distributions triggered by the two stimuli, the less well a neuron discriminates between stimuli on that day. The authors found that the ability of individual neurons to discriminate between stimuli varied as animals repeated the task on different days – some neurons became worse at discriminating, others better. **b**, The authors used an algorithm called an optimal linear decoder to separate the neural activity patterns triggered by the two stimuli (the activity of the two neurons in each iteration of the task was used to generate coordinates; here, the area within which these coordinates fell is represented by an ellipse). The decoder delineated a boundary that separated patterns triggered by one stimulus from those triggered by the other. On day 2, although the activity of individual neurons had changed, the coordinates still fell on either side of the same boundary.

fluctuations distort activity patterns triggered by different stimuli, making them 'noisy' and harder to distinguish. The optimal decoder mitigates this problem by adjusting the decoding boundary to minimize the number of patterns misclassified owing to noise[6]. The authors showed that the way in which collective activity fluctuated from trial to trial aligned with the slower changes in neural responses across days, making it possible for the optimal decoder to robustly respond to both types of change. This provides a simple and elegant explanation for how long-term, invariant stimulus decoding is possible in a population of volatile neurons.

Ebrahimi and colleagues next probed the relationship between correlated fluctuations and the stimulus information conveyed across the entire visual cortex. Correlated fluctuations mean that a subset of cells can reliably transmit the same information as a whole population. The authors found that, shortly after a stimulus appeared on the screen, the magnitude of correlated fluctuations rose sharply, both within and across visual cortical areas. Thus, different areas shared much of the same information about the stimulus: if, in one trial, the stimulus signalling was weaker or stronger in one area, this was usually also the case in other areas. Yet different cortical areas signalled synergistically, and collectively conveyed more stimulus information than any area alone.

The authors analysed patterns of inter-area signalling to reveal more about how cortical processing strategies support stable visual perception. They found that activity patterns in different areas co-fluctuated. A primary co-fluctuation pattern across the entire visual cortex signalled an animal's decision to lick. Several other patterns, specific for pairs of areas, carried visual stimulus information. The co-fluctuation patterns for stimulus and decision were separate. Thus, cortical areas shared information about stimulus and decision through non-interfering communication streams.

Ebrahimi and colleagues' work has revealed unexpected connections between correlated cortical fluctuations, volatile neural responses and the stability of visual perception. But these discoveries lead to more questions. What mechanisms result in the alignment of fluctuations across disparate temporal scales? What is the source and function of the decision signal broadcast to all visual areas? Why is cortical activity so volatile in the first place? Although visual perception might be stable, our holistic experience is not. The same picture triggers different thoughts, memories and emotions every time you look at it, and all these factors are themselves in constant flux. Large-scale neural recordings during complex behaviours will continue to uncover the brain mechanisms that allow us to cope with the competing demands of behavioural stability and flexibility.

Tatiana Engel is at Cold Spring Harbor Laboratory, Cold Spring Harbor, New York 11724, USA.
e-mail: engel@cshl.edu

1. Ebrahimi, S. *et al. Nature* https://doi.org/10.1038/s41586-022-04724-y (2022).
2. Deitch, D., Rubin, A. & Ziv, Y. *Curr. Biol.* **31**, 4327–4339 (2021).
3. Driscoll, L. N., Pettit, N. L., Minderer, M., Chettih, S. N. & Harvey, C. D. *Cell* **170**, 986–999 (2017).
4. Schoonover, C. E., Ohashi, S. N., Axel, R. & Fink, A. J. P. *Nature* **594**, 541–546 (2021).
5. Cohen, M. R. & Kohn, A. *Nature Neurosci.* **14**, 811–819 (2011).
6. Averbeck, B. B., Latham, P. E. & Pouget, A. *Nature Rev. Neurosci.* **7**, 358–366 (2006).

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