Animal behavior is a wondrous thing
Understanding neural computations underlying behavior
Data: Simon Peron and Karel Svoboda

Visualization: Jonathan Amazon
Towards a detailed understanding of the relation between dynamics and computation

Central notion:
Principles of how the brain computes lie embedded in the complexity of neuronal circuit responses

Structure (of dynamics) to function

OK. But how?
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Short term memory

persistent, selective representation from transient stimuli
Short term memory is a basic, yet important computation.

Persistent activity supports persistent network representation.
Problem: cortical time-invariant activity is rare

Brody, alii, et Romo, 2003
Intuitively, changes in firing rate cause changes in encoding.

Representing points on a plane:

Stimulus dimension: 2

Number of neurons (activity dimension): 2
Intuitively, changes in firing rate cause changes in encoding.

Representing points on a plane:

Stimulus dimension: 2

Number of neurons (activity dimension): 2
Many neural circuits have divergent architectures

Input structure to Cortex is the Thalamus

Number of cortical neurons much greater than the number of thalamic input neurons
Divergent architectures can complicate relating activity to encoding

Stimulus dimension: 2

Number of neurons (activity dimension): 3
In divergent representations not all changes in activity change the encoded stimulus

More neurons than stimulus dimensions results in freedom of representation

Non-coding (null)
Freedom in network representation can explain variable single neuron activity.

Even a computation as simple as keeping track of a presented stimulus can have diverse, dynamic neural responses.
In divergent representations not all changes in activity change the encoded stimulus.
How can we know that non-coding spaces are relevant for the brain?
How can we know that non-coding spaces are relevant for the brain?
The experimental work was done as part of a collaboration with the Svoboda lab

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Simons Foundation
Data: delayed response tactile discrimination task in mice

Note, this is different from a pure working memory task

(Guo et al., Neuron, 2014)
Anterior lateral motor cortex (ALM) is necessary for motor planning and movement.
Neurons exhibit time variable task related activity
Directly testing dynamics by perturbation: inhibition of ~1 mm square of cortex

- Not activity-space specific perturbation
- Perturb dynamics and correlate perturbation with behavior
Neural recordings during photo inhibition

Lick right
Lick left

Spikes /s
0 50

Time (s)
-2 0 2

Sample  Delay
Perturbation is very effective

Lick right perturbed
Lick left perturbed

Spikes /s

Sample
Delay

Time (s)
Perturbation is very effective

Lick right perturbed
Lick left perturbed
Perturbation is very effective, yet selectivity and behavior recover.
Perturbation is very effective, yet neuron recovers to where it should have been.
Recovery is not just rebound effect
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Though some neurons don’t properly recover...
Return to trajectory is very different from the predictions of most models.
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Possible trivial explanation of “catch-up”: this area is just a readout
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Possible trivial explanation of “catch-up”: this area is just a readout
What of the activity needs to recover for behavior?
In pursuit of the activity related to the computation (finding the coding-space)
Normalized firing rate neuron 1

Normalized firing rate neuron 2

Mode:

$0.75 \times \text{rate neuron 1} - 0.25 \times \text{neuron 2}$
PCA

Mode:

0.75 * rate neuron 1 - 0.25 * neuron 2
PCA

Mode:
0.75* rate neuron 1 - 0.25 * neuron 2
PCA

Mode:

0.25* rate neuron 1 - 0.75 * neuron 2
Normalized firing rate neuron 1

Normalized firing rate neuron 2

PCA
PCA

Normalized firing rate neuron 1 vs. Normalized firing rate neuron 2.
PCA

Normalized firing rate neuron 1

Normalized firing rate neuron 2
PCA

Normalized firing rate neuron 1 vs.Normalized firing rate neuron 2
Linear discriminant analysis (LDA)

Normalized firing rate neuron 1

Normalized firing rate neuron 2
LDA

Normalized firing rate neuron 1

Normalized firing rate neuron 2
LDA

Normalized firing rate neuron 1 vs. Normalized firing rate neuron 2
LDA

Normalized firing rate neuron 1

Normalized firing rate neuron 2
LDA may differ from PCA

First PC

First DC
LDA may (not) differ from PCA
Intuition for decomposition into modes: readout neurons
Intuition for decomposition into modes: readout neurons

\[ 0.8 \times \text{rate neuron 1} + 0.1 \times \text{neuron 2} \]

\[ 0.1 \times \text{rate neuron 1} + 0.8 \times \text{neuron 2} \]
Intuition for decomposition into modes

Neural activity

Mode activity

Neural weights per mode

Mode 1

Mode 2
Decomposition of activity space: Finding the coding space
Decomposition of activity space: Finding the coding space

Activity neuron 1

Activity neuron 3

Mode 1
Discriminating direction (LDA)
LDA discriminant direction shows strong single trial selectivity.
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LDA discriminant direction shows strong single trial selectivity
Discriminating direction in activity space is affected by perturbation, but can recover.
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Can behavior be predicted from perturbation size on trial-by-trial basis?
Effect of perturbation predicts behavior on trial-by-trial level, even when errors are common

![Graph showing effect of perturbation on behavior performance.](image)

**Behavior performance (%)**

After bilateral photoinhibition

**Discriminating direction distance from decision boundary (a.u.)**

Lick left
Effect of perturbation predicts behavior on trial-by-trial level, even when errors are common.
Mode that carries decodable information is made robust by the circuit.
Decomposition of activity space

Activity neuron 1

Activity neuron 3

Persistently perturbed

Discriminating direction
Modes that carry decodable information return, rest do not.

Persistently perturbed direction distance from decision boundary (a.u.)

Proj. on persistently perturbed direction

mode # 2

Frac. total variance

Behavior performance (%)

Persistently perturbed direction distance from decision boundary (a.u.)
Evidence for null spaces: modes that carry decodable information return, rest do not.
Coding and persistently perturbed modes are mixed across population.
Schematic of non-mixed results
Interim summary

We find a surprising robustness of the detailed trajectory

“Not all population activity modes are created equal”, Similar to theoretical ideas of null-space dynamics

Activity we see is a mix of both modes, perturbation allowed us to dissect them
What is the fundamental unit of meaning?
Modes or ensembles?
What is the fundamental unit of meaning? Modes or ensembles?

- Selective
- Non-selective

Modes

- Selective
- Non-selective

- Selective
- Non-selective

- Selective
- Non-selective
How does one obtain such robustness?
Return to trajectory is very different from the predictions of most models.
Any single module circuit we tried isn’t robust as the experimental findings.
Two principles result in networks that have the needed robustness.

Modular

Stabilized by feedback
Three principles result in networks that have the needed robustness.
Feedback

Direct coupling
Three simple principles result in networks that have the needed robustness.
Three simple principles result in networks that have the needed robustness.
Three simple principles result in networks that have the needed robustness.
Three simple principles result in networks that have the needed robustness.
Strong asymmetry between ipsilateral and contralateral perturbation
Gating can explain weak effect of contralateral inhibition, modularity

Gated coupling
Any single-module implementation can be made robust by these principles.
Summary

We find a surprising robustness of the detailed trajectory

“Not all population activity modes were created equal”, Similar to theoretical ideas of null-space dynamics

Initial evidence for a distributed, error-correcting multi-regional segregation of circuit computation

Li, Daie, Svoboda, Druckmann; Nature, (2016)
Open questions

Experimental
What in these dynamics is working memory and what is motor preparation?
How does robustness develop over learning?
Can we directly perturb directions in activity space?

Theoretical
Why is this robustness present in the first place?
How general are these ideas of modularity?
What exactly are non-coding spaces and why are they there???