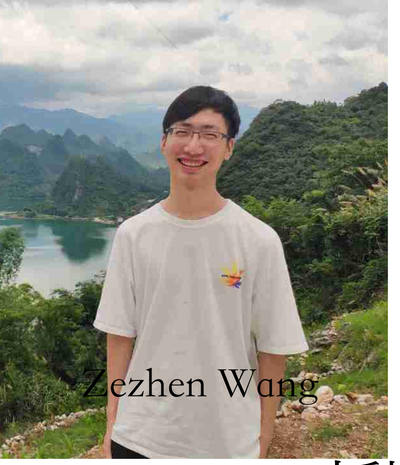


Zezhen Wang

中科大



Yuming Chai



Weihao Mai & Yu Hu

港科大

The Geometry and Dimensionality of Brain-wide Activity

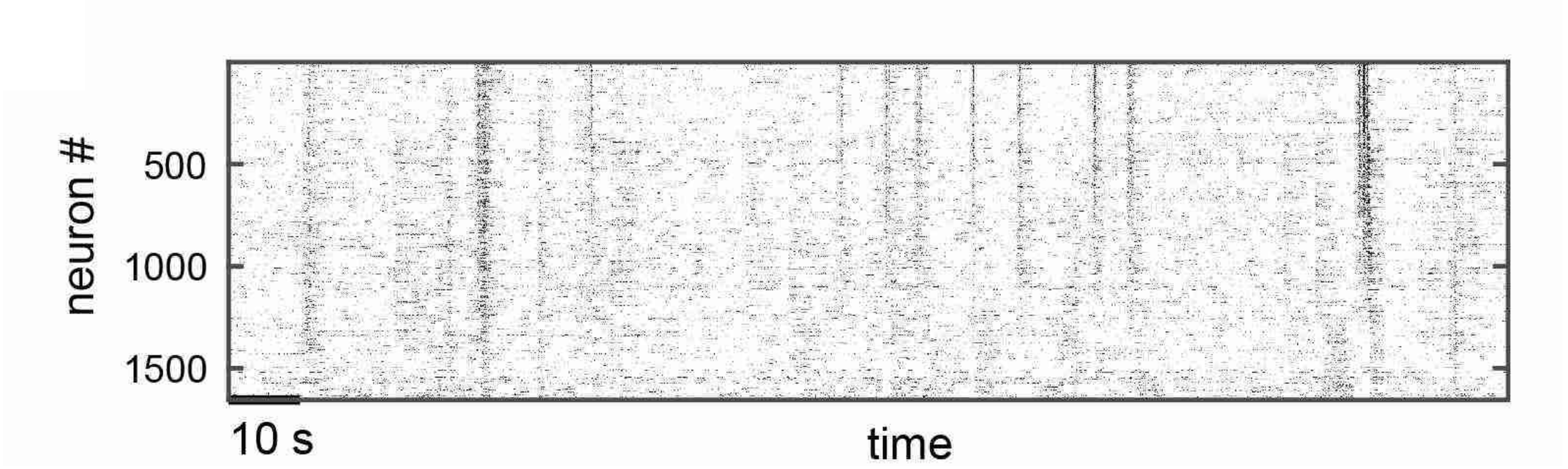
June 27, 2025

Quan Wen

Division of Life Sciences and Medicine

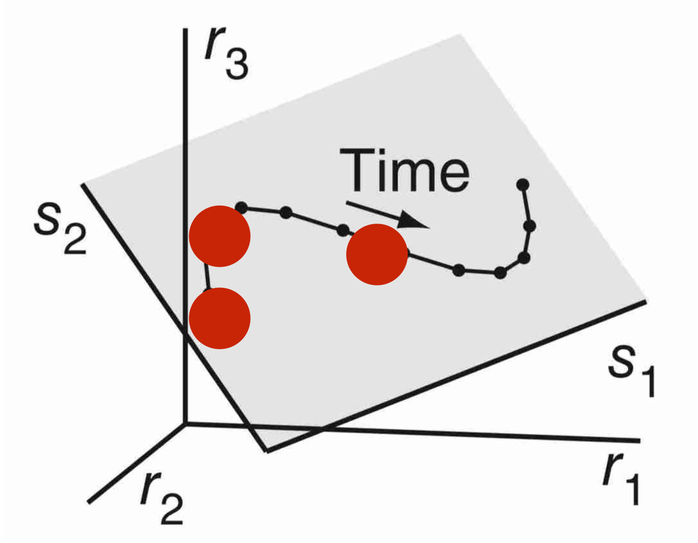
School of Data Sciences

University of Science and Technology of China


neuron #
500
1000
1500
10 s
time

- generalization from fewer examples

The geometry of the neural activity space



Review by Cunningham & Yu, 2014

Review:
Cunningham and Yu ’14

Reviews:
Fusi, Miller, R
Bengio ’09 “L
Deep Architec
DiCarlo and F
Anselmi and

How many dimensions does neural activity fill up?

How many dimensions does neural activity really fill up?

$$Cov(r_i(t), r_j(t)) = \mathbb{E}\left[(r_i(t) - \mathbb{E}(r_i(t)))(r_j(t) - \mathbb{E}(r_j(t)))\right]$$

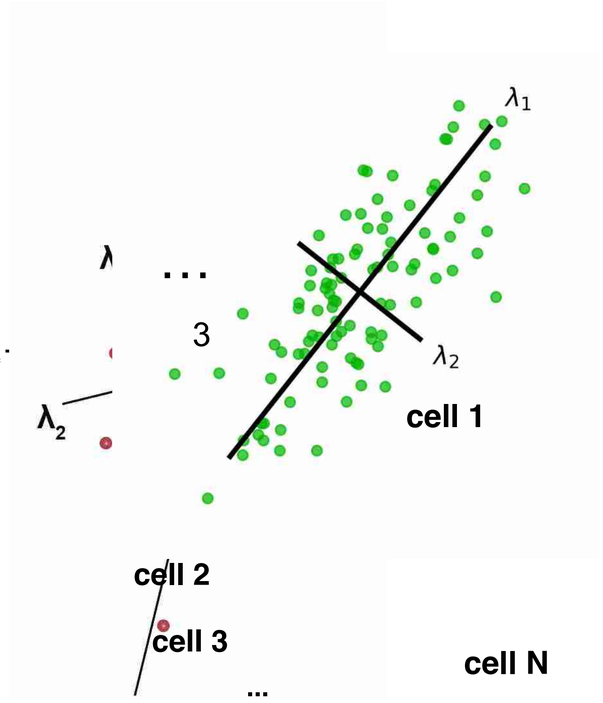
$$= C_{ij}$$

Abbott et al, ’11
Mazzucato et al. ’15
Gao and Ganguli ’17
Cayco-Gajic et al ’17
Litwin-Kumar et al ‘17

$$C\vec{v}_i = \lambda_i \vec{v}_i$$

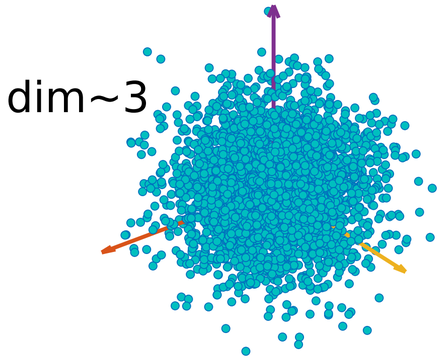
eigenvectors: v_i

eigenvalues: λ_i

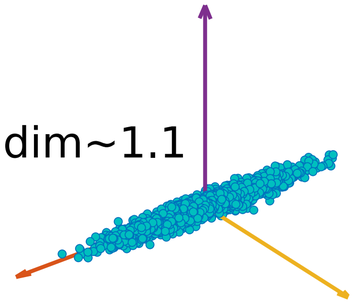


Abbott et al, ’11
Mazzucato et al. ’15
Gao and Ganguli ’17
Cayco-Gajic et al ’17
Litwin-Kumar et al ’17
Dahmen et al ’20
Recanatesi et al ‘22

$$\tilde{\lambda}_i = \frac{\lambda_i}{\sum_j \lambda_j} \qquad D = \frac{(\sum_i \lambda_i)^2}{\sum_i \lambda_i^2} = \frac{1}{\sum_i \tilde{\lambda}_i^2}$$

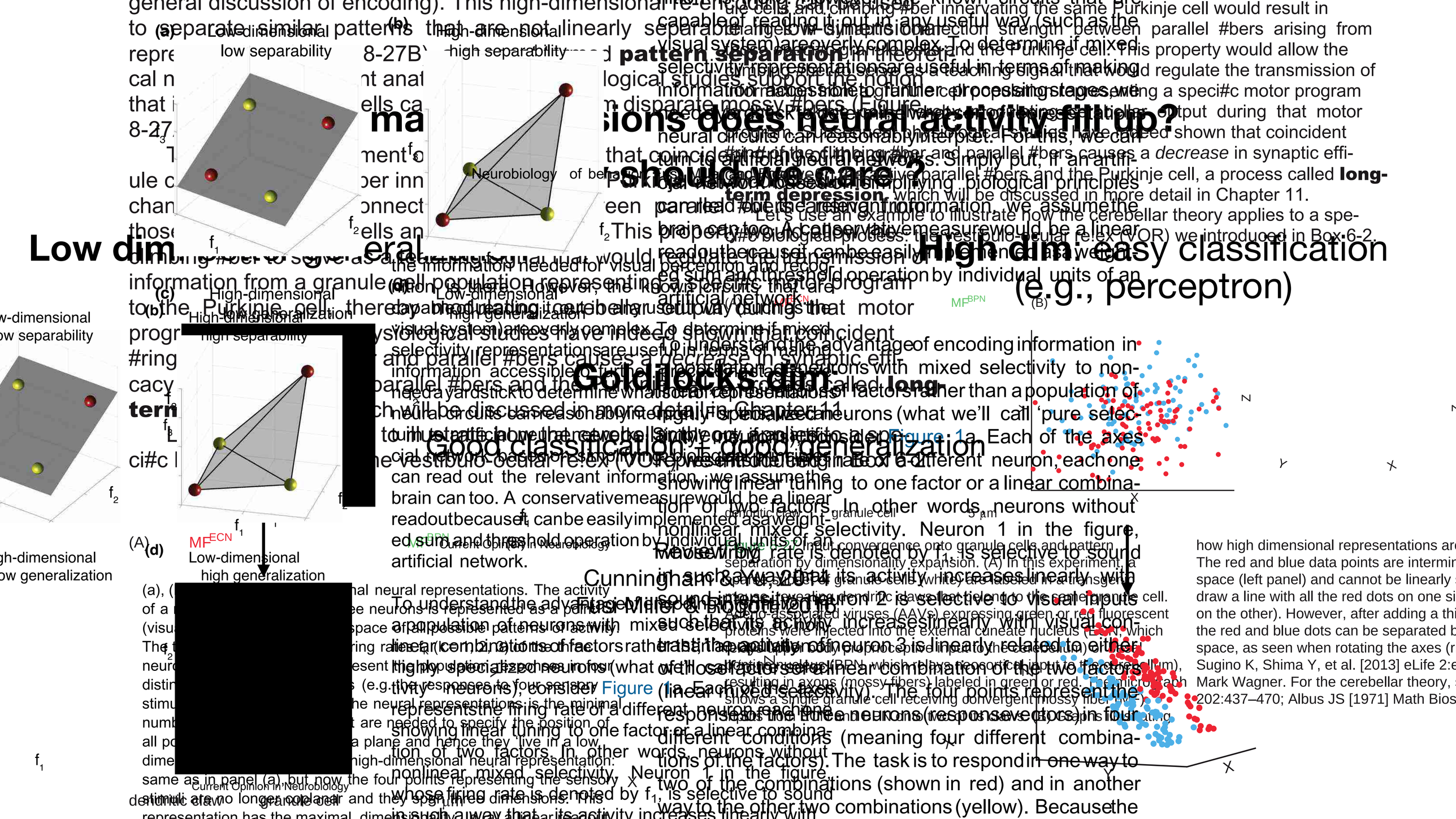


$\tilde{\lambda}_1 = 1/3$
$\tilde{\lambda}_2 = 1/3$
$\tilde{\lambda}_3 = 1/3$
$\tilde{\lambda}_4 = 0$
$\tilde{\lambda}_N = 0$



$\tilde{\lambda}_1 = 0.95$
$\tilde{\lambda}_2 = 0.025$
$\tilde{\lambda}_3 = 0.025$
$\tilde{\lambda}_4 = 0$
$\tilde{\lambda}_N = 0$

Modified from Eric Shea-Brown



Neurobiology of behavior

should we care?

sions does neural activity fill up?

ma

pattern separation

Low dim

High dim: easy classification (e.g., perceptron)

Goldilocks dim:

Good classification + good generalization

(a), (b), (c), (d) nal neural representations. The activity of a ee neurons is represented as a point in (visu space of all possible patterns of activity. The f ring rates (r1, r2, r3) of three neurons neur esent the activity pattern in four distin s (e.g. the responses to four sensory stimu he neural representations is the minimal numb t are needed to specify the position of all po a plane and hence they 'live' in a low dime high-dimensional neural representation: same as in panel (a) but now the four points representing the sensory stimuli are no longer coplanar and they span three dimensions. This representation has the maximal dimensionality that can be achieved with four neurons and four conditions.

Current Opinion in Neurobiology

granule cell

dendritic claw

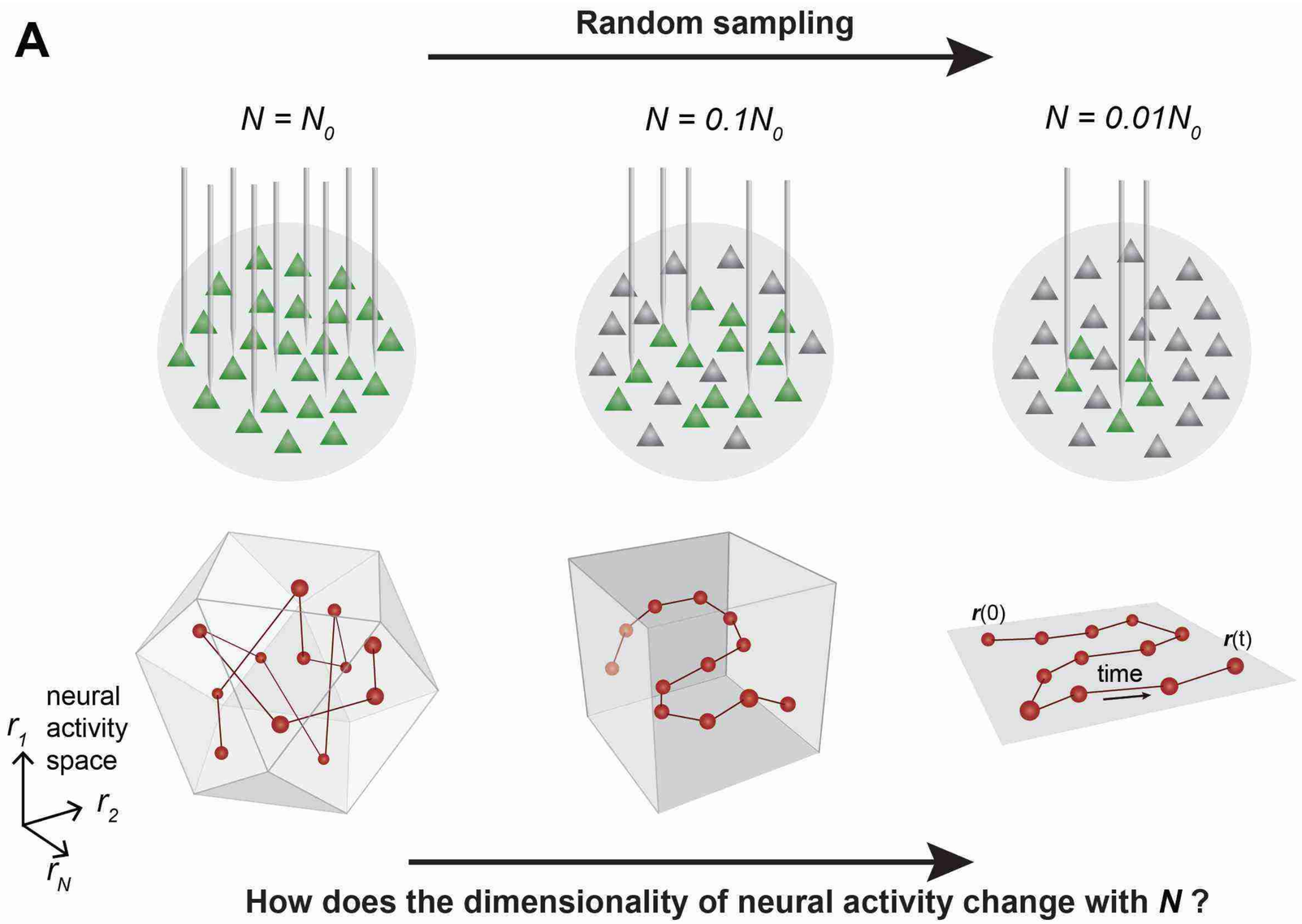
how high dimensional representations are
The red and blue data points are intermin
space (left panel) and cannot be linearly
draw a line with all the red dots on one si
on the other). However, after adding a thi
the red and blue dots can be separated b
space, as seen when rotating the axes (r
Sugino K, Shima Y, et al. [2013] eLife 2:e
Mark Wagner. For the cerebellar theory,
202:437–470; Albus JS [1971] Math Bios

Neuron
Viewpoint

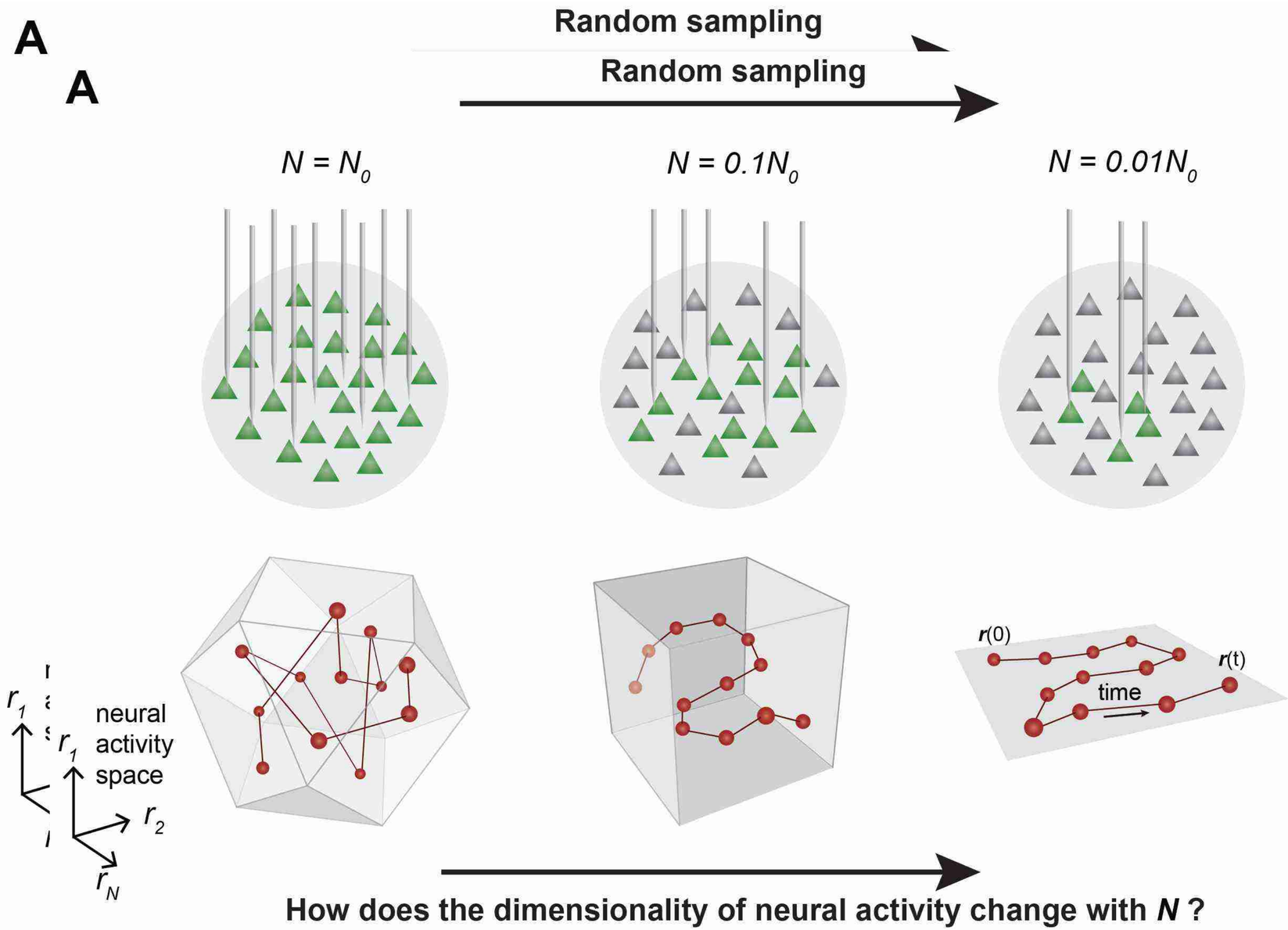
Can One Concurrently Record Electrical Spikes from Every Neuron in a Mammalian Brain?

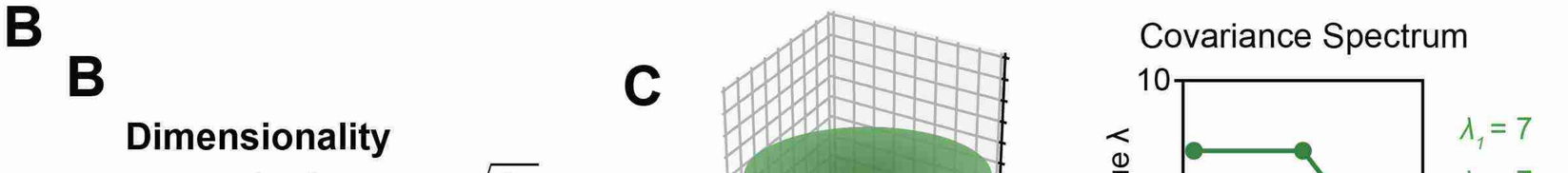
David Kleinfeld, [1,2,13,*] Lan Luan,[3] Partha P. Mitra, [4] Jacob T. Robinson, [5] Rahul Sarpeshkar, [6,7,8,9] Kenneth Shepard, [10] Chong Xie,[3] and Timothy D. Harris [11,12,*]
[1]Section of Neurobiology, University of California, San Diego, CA, USA
[2]Department of Physics, University of California, San Diego, CA, USA
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[4]Cold Spring Harbor Laboratory, Cold Spring Harbor, NY, USA
[5]Department of Electrical and Computer Engineering, Rice University, Houston, TX, USA
[6]Department of Engineering, Dartmouth, Hanover, NH, USA
[7]Department of Microbiology and Immunology, Dartmouth, Hanover, NH, USA
[8]Department of Molecular and Systems Biology, Dartmouth, Hanover, NH, USA
[9]Department of Physics, Dartmouth, Hanover, NH, USA
[10]Department of Electrical Engineering, Columbia University, New York, NY, USA
[11]Howard Hughes Medical Institutes, Janelia Research Campus, Ashburn, VA, USA
[12]Department of Bioengineering, Johns Hopkins University, Baltimore, MD, USA
[13]Lead Contact
*Correspondence: dk@physics.ucsd.edu (D.K.), harrist@janelia.hhmi.org (T.D.H.)
https://doi.org/10.1016/j.neuron.2019.08.011

Kleinfeld et al ‘19


A
Random sampling
N = N0
N = 0.1N0
N = 0.01N0
neural activity space
r1
r2
rN
r(0)
r(t)
time
How does the dimensionality of neural activity change with N ?
B
Dimensionality
C
Covariance Spectrum
10
5
λ1 = 7
λ2 = 7

and unambiguously show its organizing principles, with unexplored consequences for neural computation.





How does the dimensionality D change with N?

$$D = \frac{N^2 \mathbb{E}(\sigma_i^2)^2}{N\mathbb{E}(\sigma_i^4) + N(N-1)\mathbb{E}_{i \neq j}(C_{ij}^2)}$$

$$\lim_{N \to \infty} D = \frac{\mathbb{E}(\sigma_i^2)^2}{\mathbb{E}_{i \neq j}(C_{ij}^2)}$$

σ_i^2 : **variance of neural activity of a single neuron**

C_{ij} : **covariance between two neurons**

N : **the number of neurons in the population**

The dimensionality D is invariant under random subsampling for large N

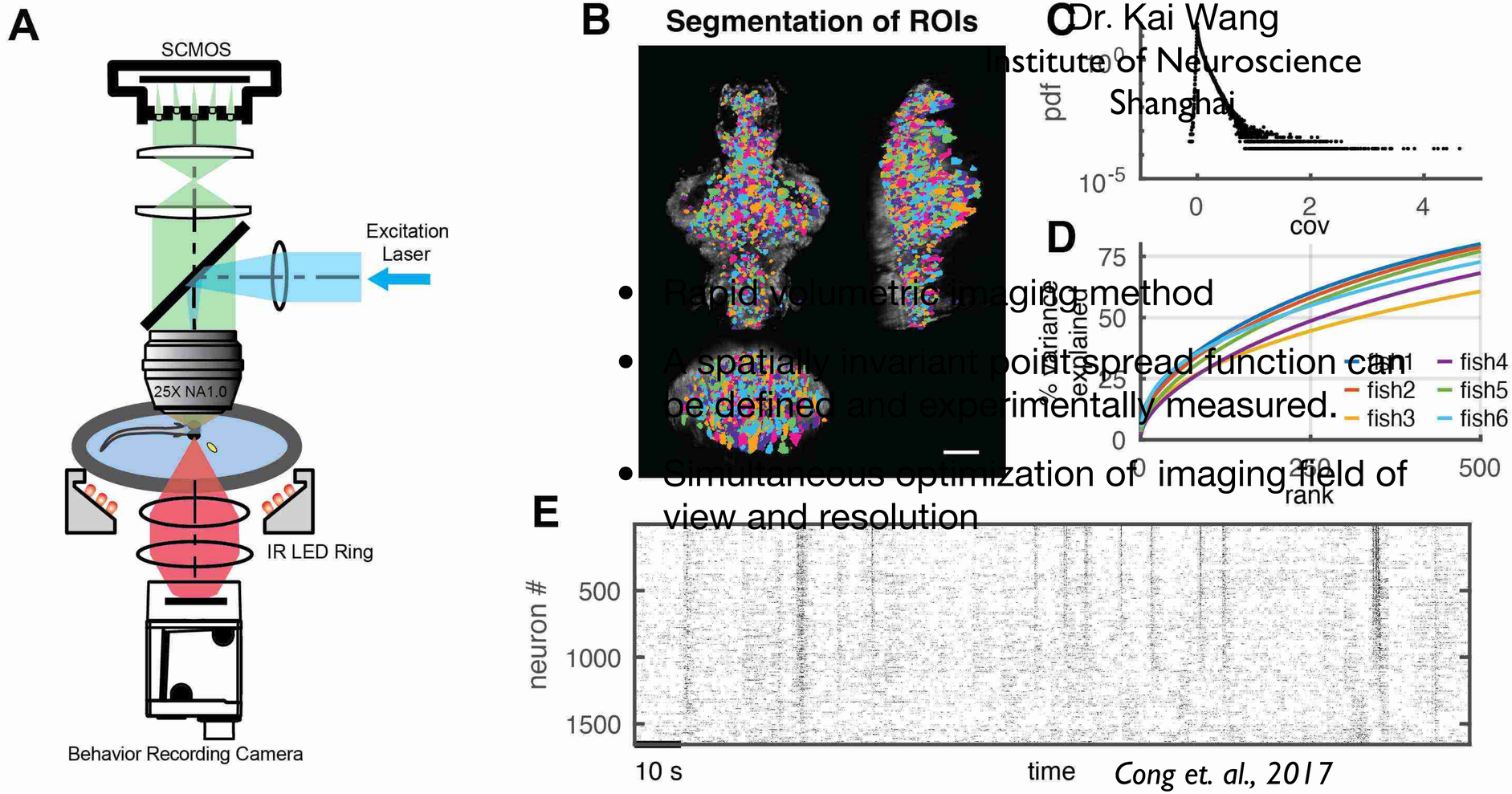
Also See Dahmen et al ’19 & ’20 for a relevant discussion, but Renart et al ’10 for a completely different scenario!

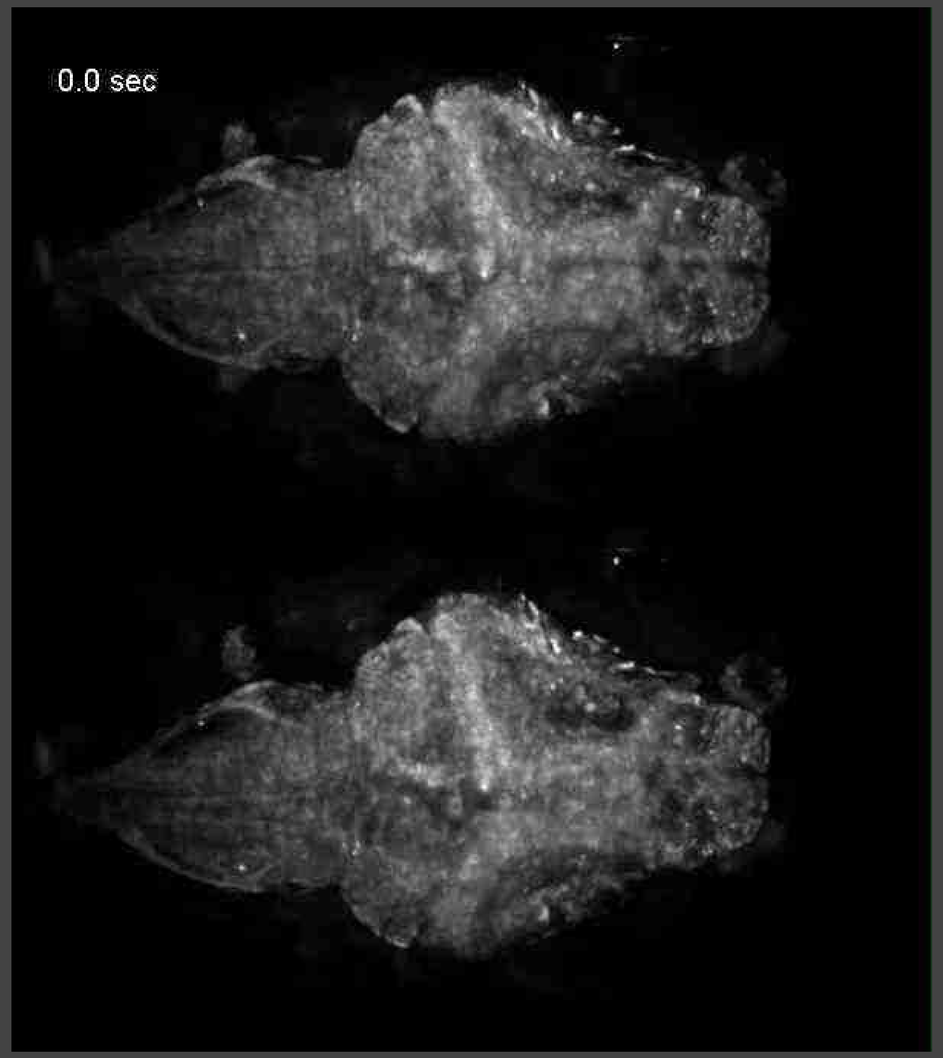
Fourier Light Field Microscopy (XLFM)



Dr. Kai Wang
Institute of Neuroscience
Shanghai

- Rapid volumetric imaging method
- A spatially invariant point spread function can be defined and experimentally measured.
- Simultaneous optimization of imaging field of view and resolution





800 um x 800 um x 200 um FOV

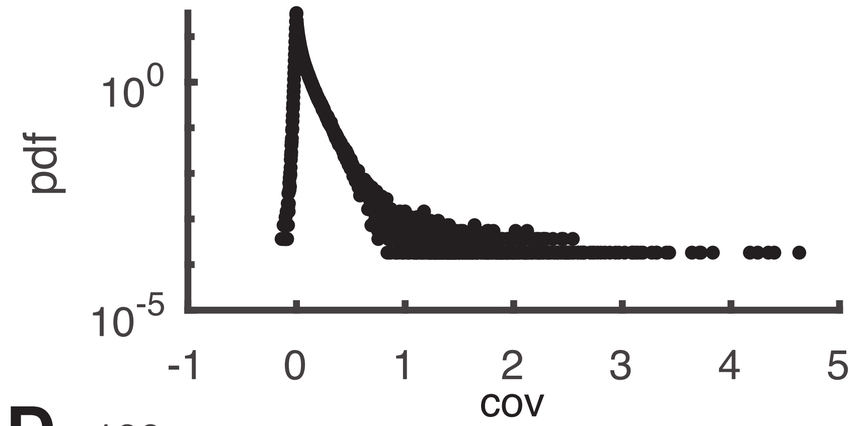
3.4 um x 3.4 um x 5 um spatial resolution for sparsely labelled sample

100 Hz volume rate

Cong et. al., 2017

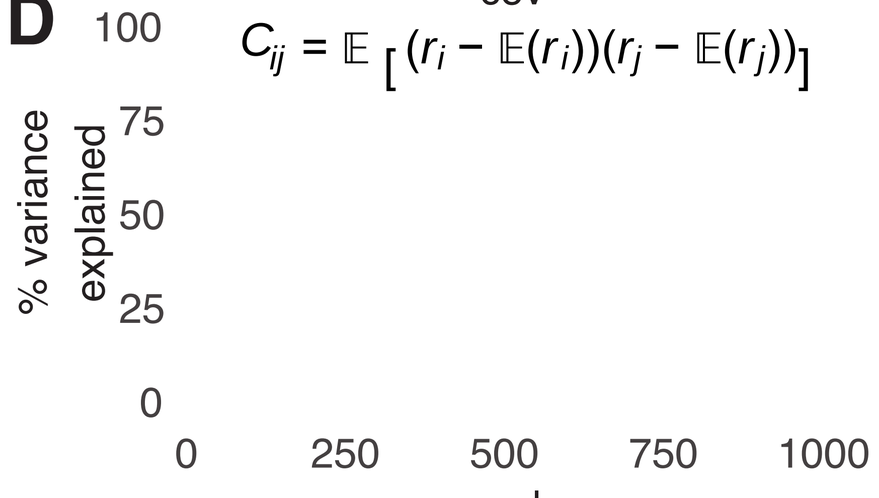
The bounded dimensionality of brain-wide activity in larval zebrafish

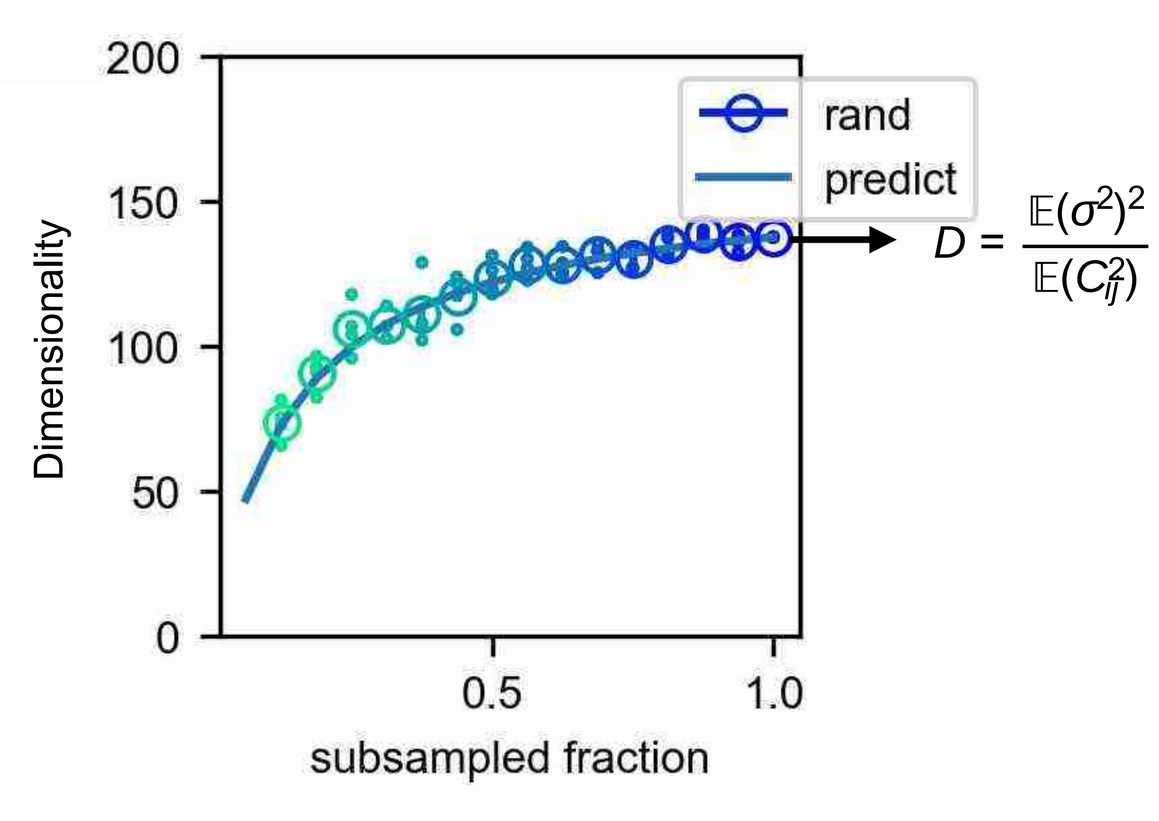




D

$$C_{ij} = \mathbb{E}\left[(r_i - \mathbb{E}(r_i))(r_j - \mathbb{E}(r_j))\right]$$





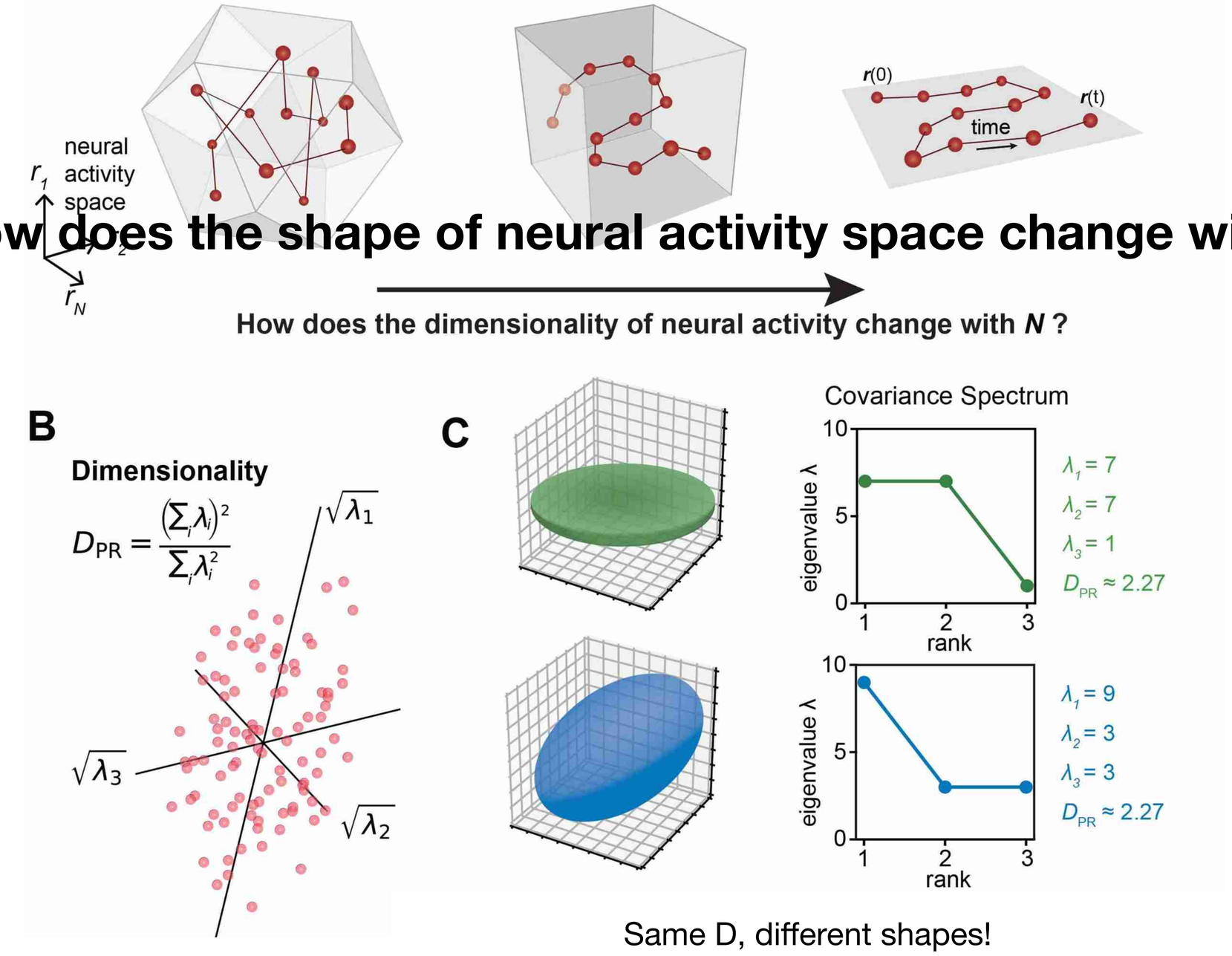
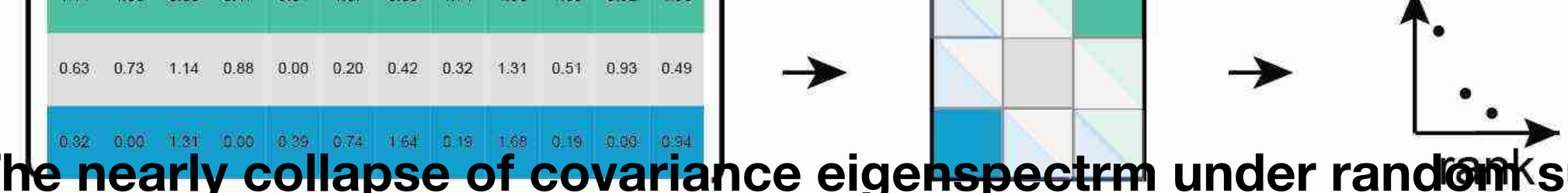
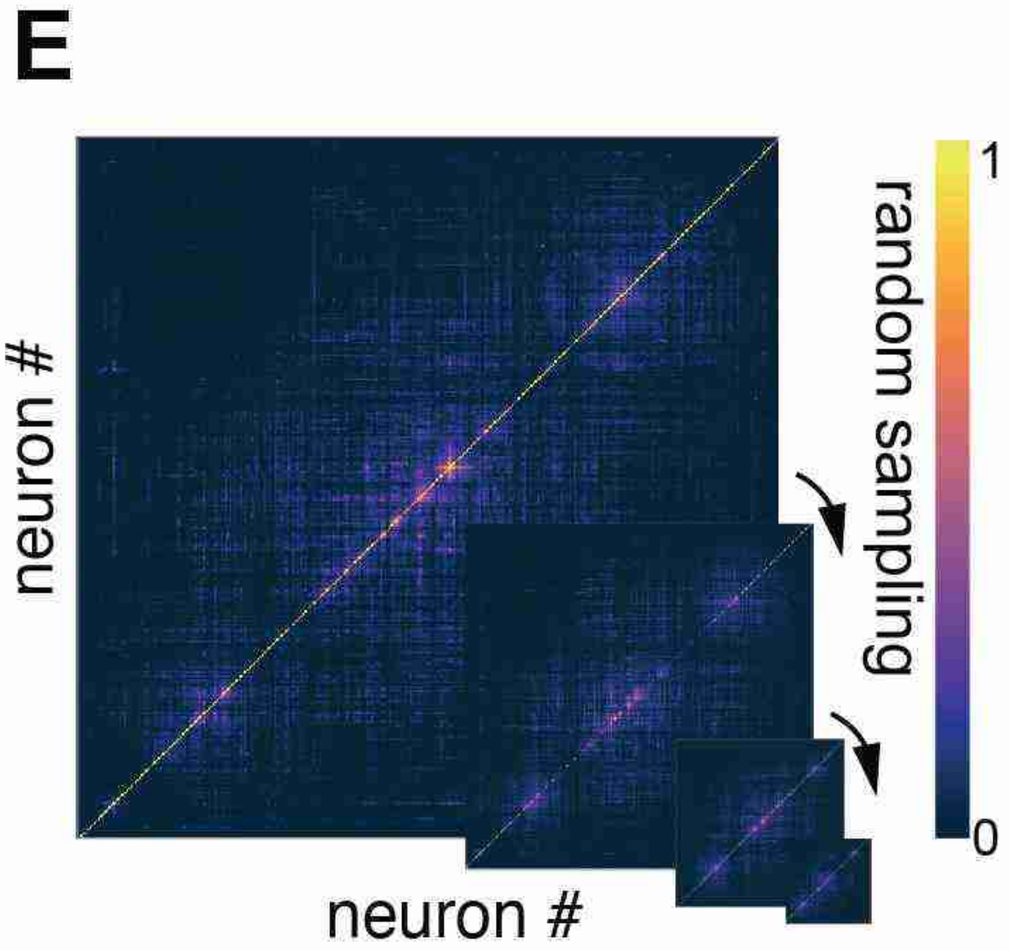
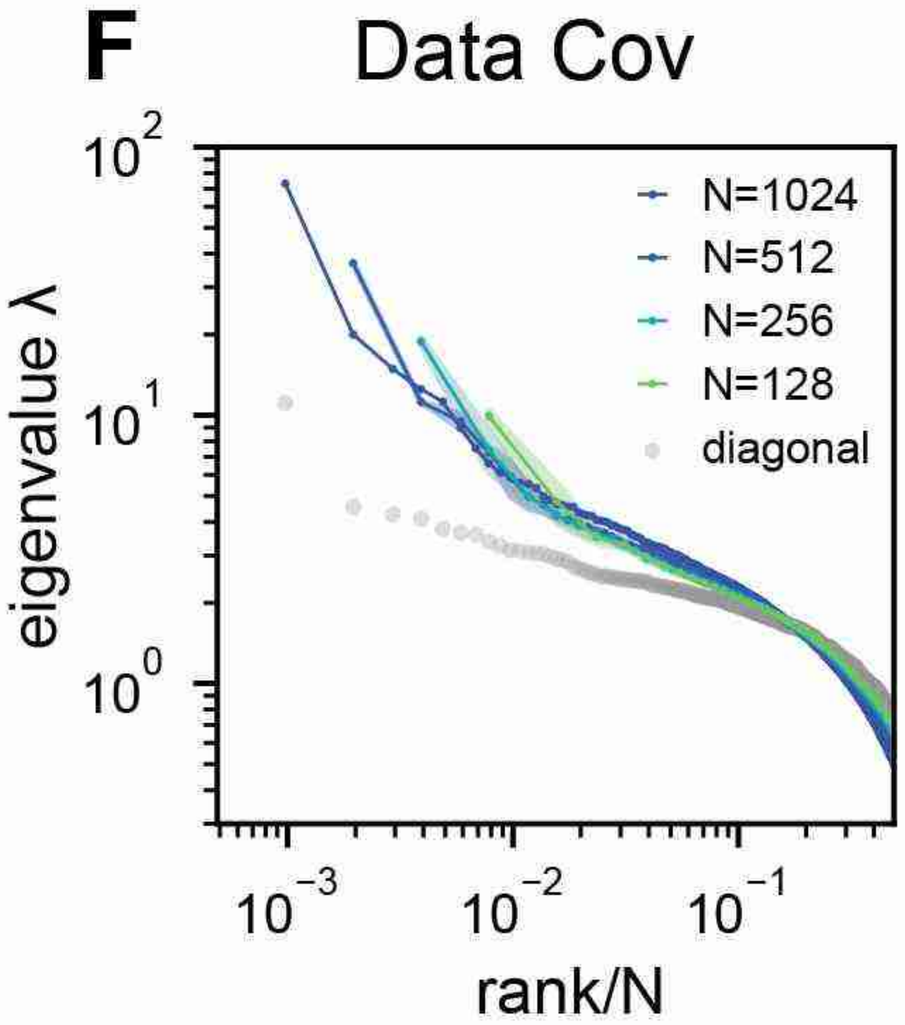


Figure 1. The relationship between the geometric properties of the neural activity space and the size of neural assemblies. A. Illustration of how dimensionality of neural activity (D_{PR}) changes with the number of recorded neurons. **B.** The eigenvalues of the neural covariance matrix dictate the geometrical configuration of the neural activity space with $\sqrt{\lambda_i}$ being the

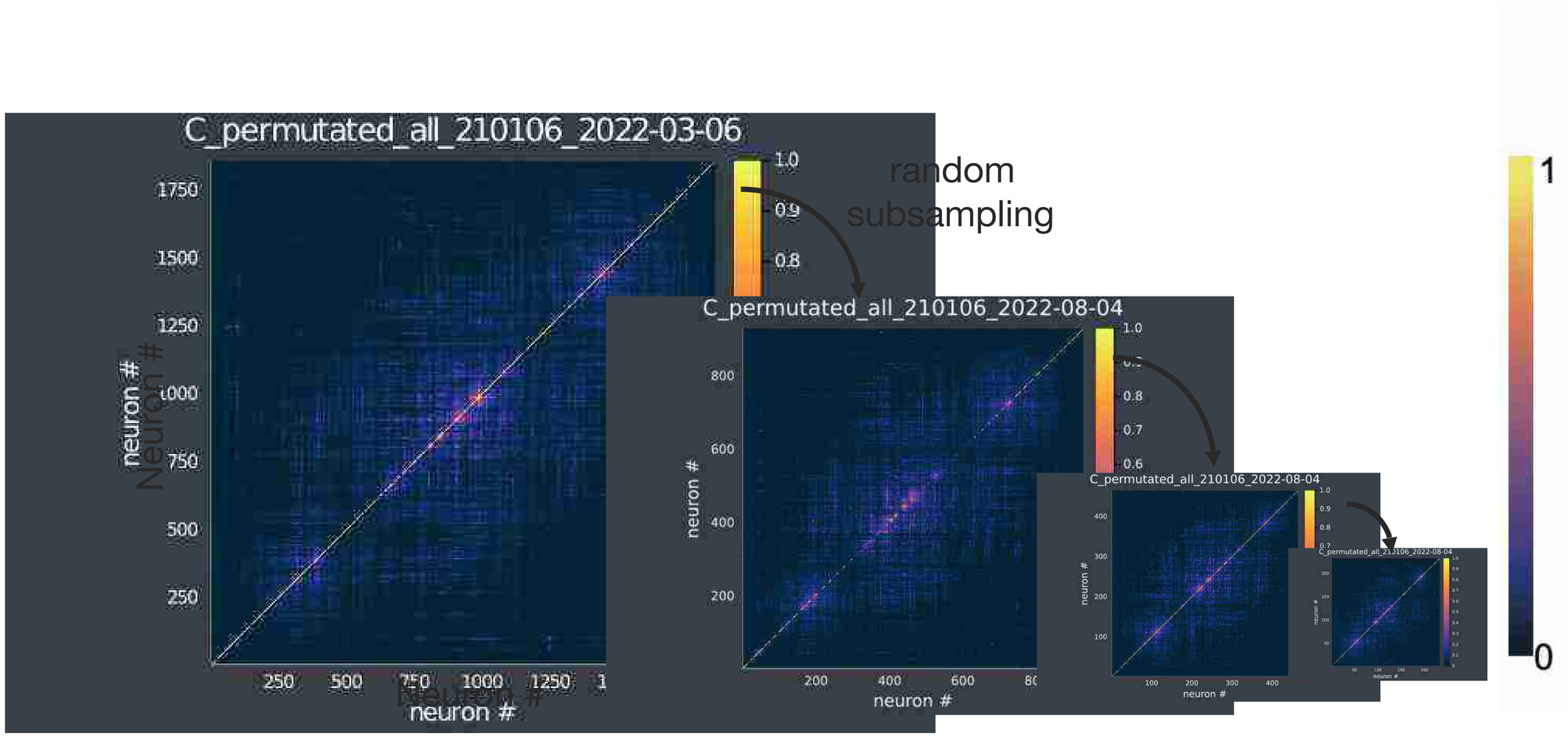


The nearly collapse of covariance eigenspectrm under random subsampling

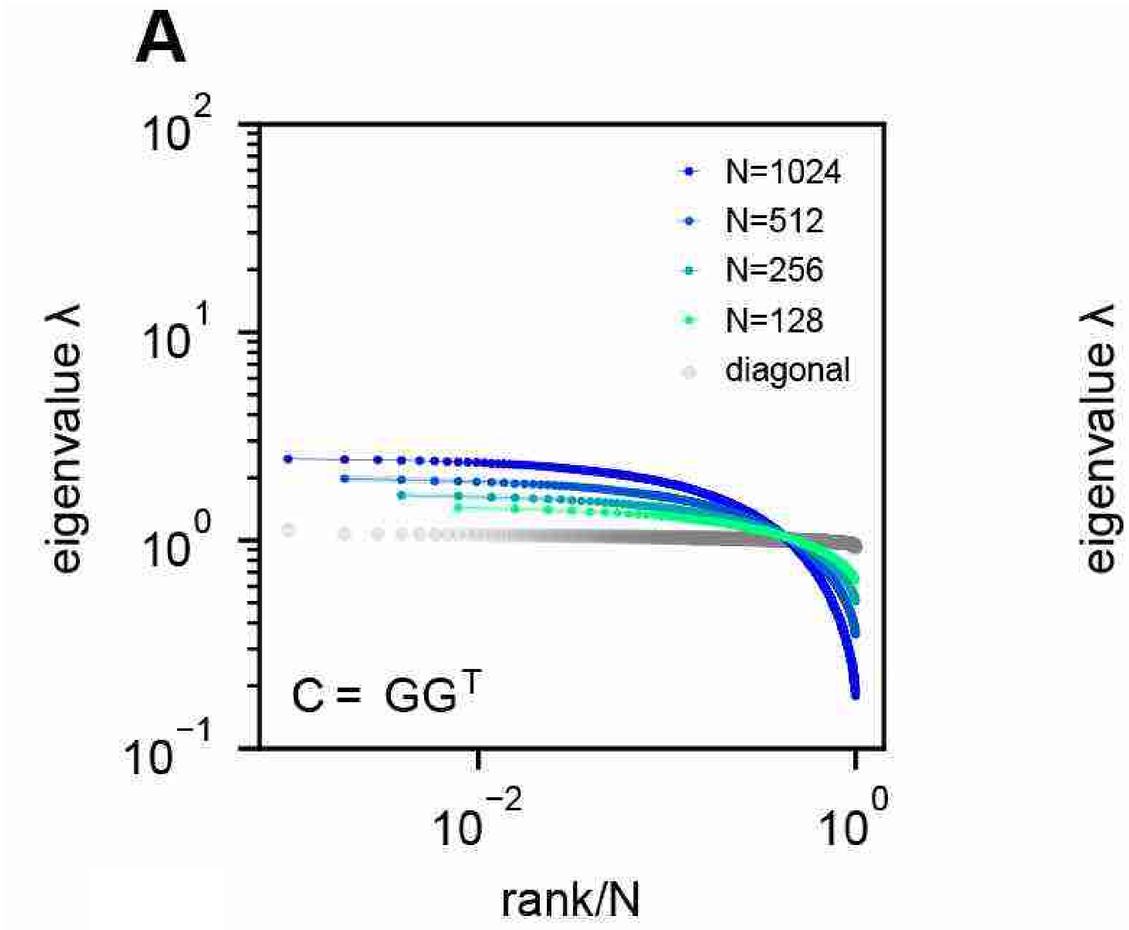


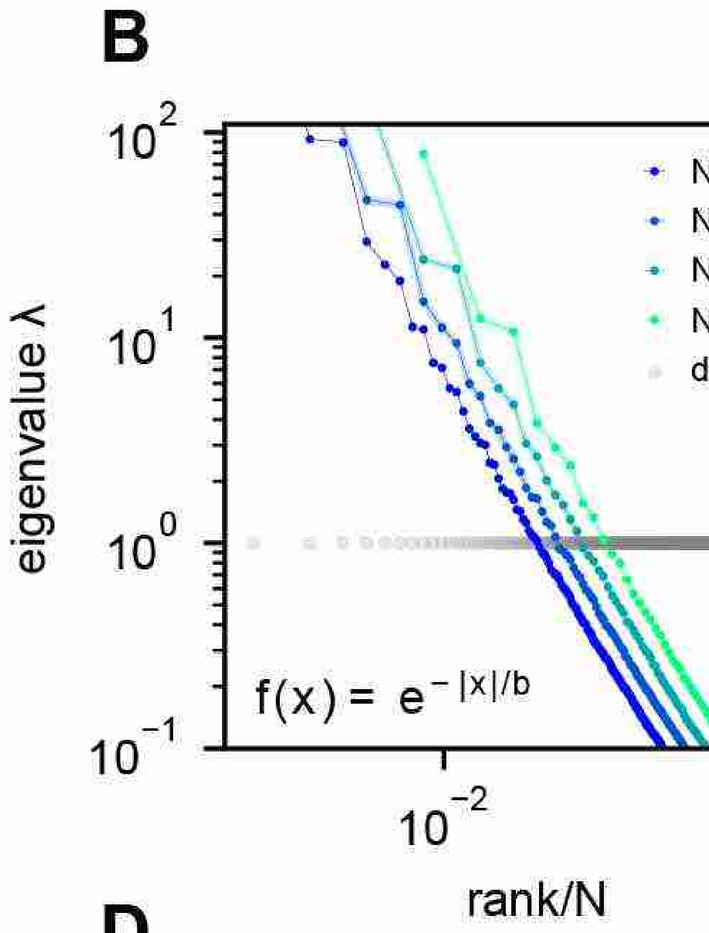


The scale-invariance of covariance matrix

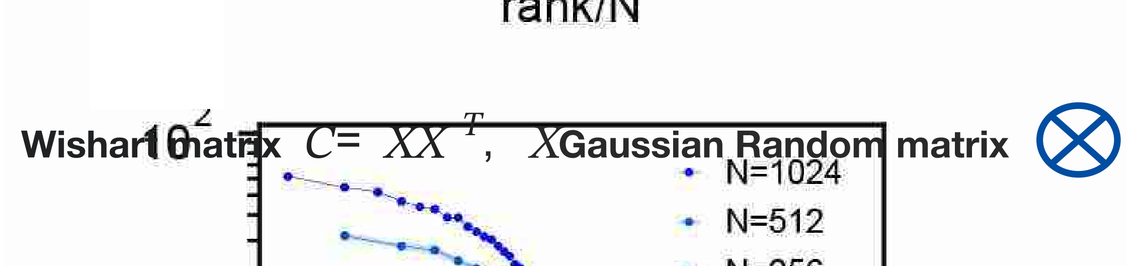


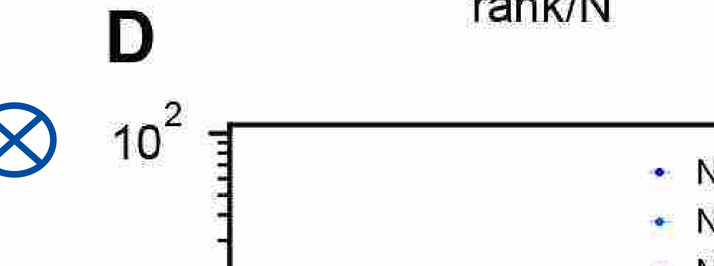
What statistical properties across brain-wide activity are essential for the observed self-similarity?





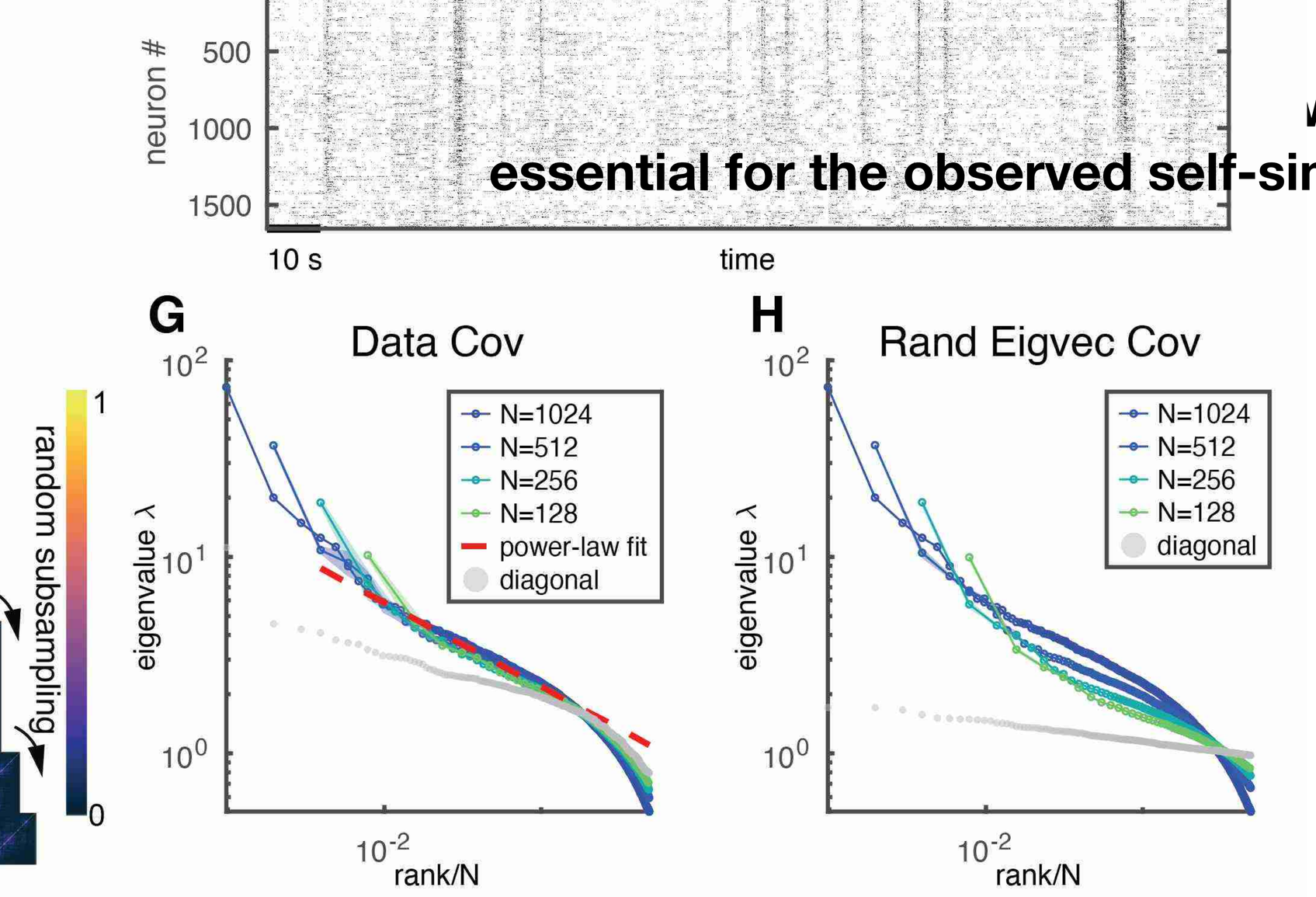
Wishart matrix $C = XX^T$, X Gaussian Random matrix ⊗





wide activity are

essential for the observed self-similarity?

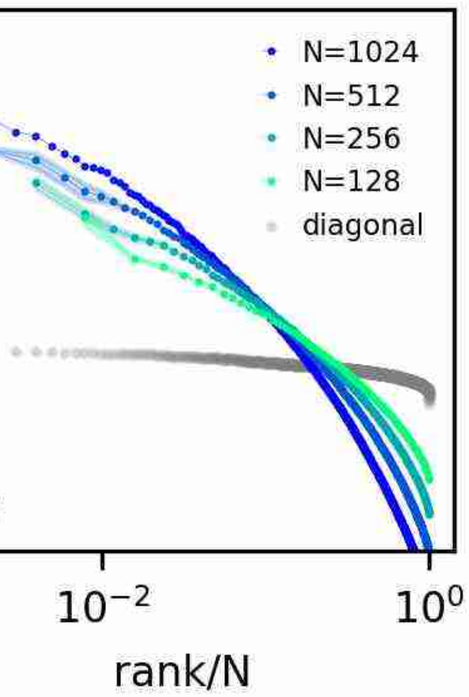


$C = U^T \Lambda U$ U: Gaussian orthogonal matrix

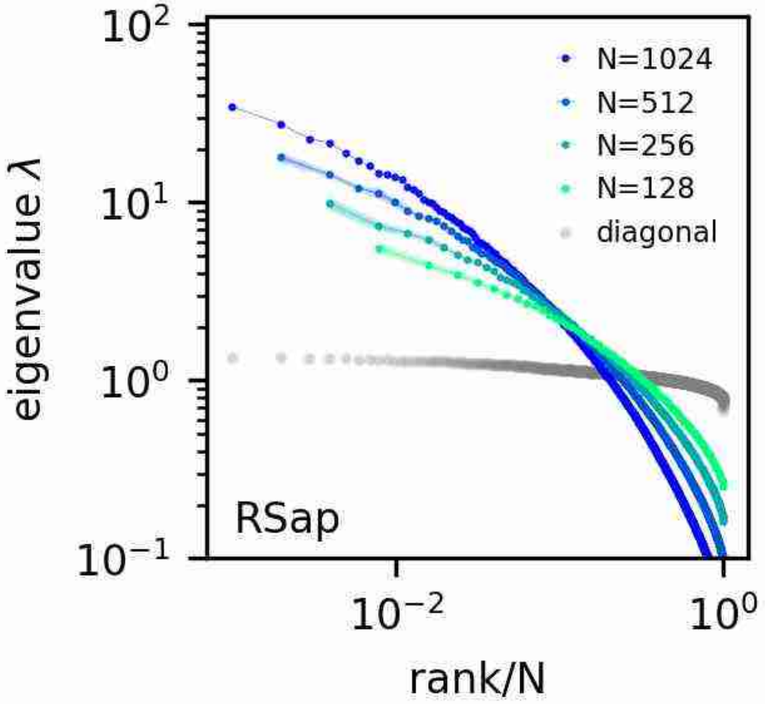
zebrafish neural activity and the phenomenon of its scale-invariant eigenspectrum.

$^+$ imaging of whole brain neural activity. **B.** Spatial distribution of segmented ROIs (shown to 3086 ROIs in each animal. Scale bar, 100 μm. **C.** Distribution of normalized pairwise The mean of the diagonal entries of the covariance matrix is normalized to be 1. **D.** Explained

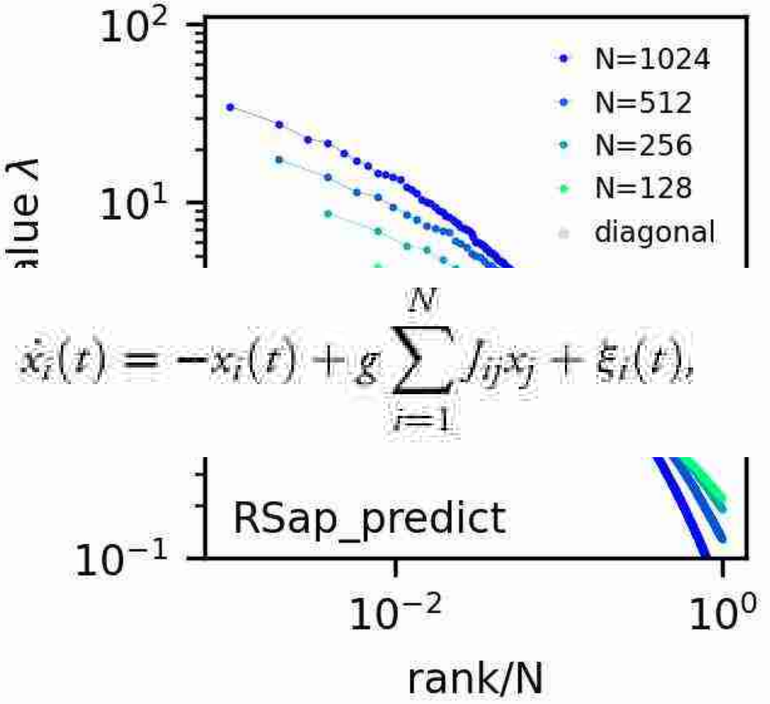
What statistical properties across brain-wide activity are essential for the observed self-similarity?



B

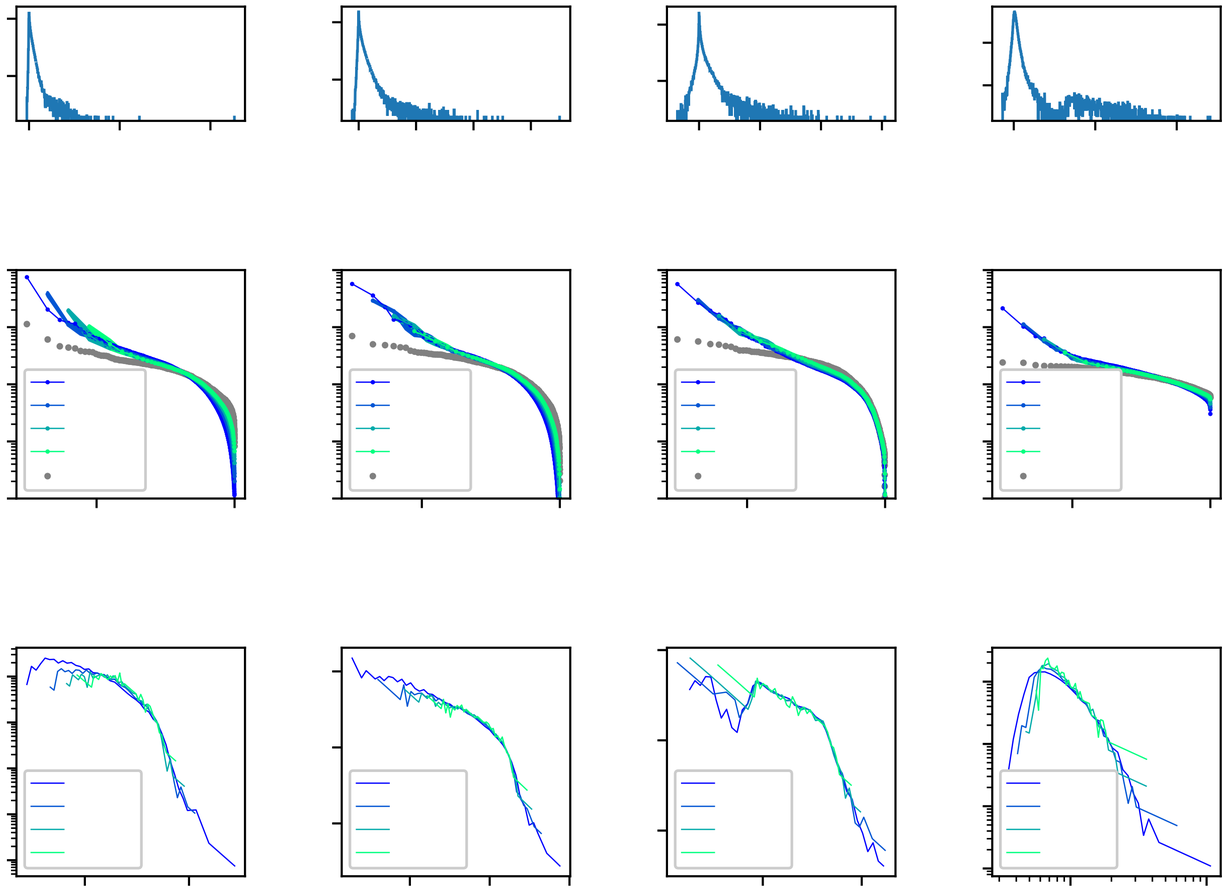


C



Recurrent neural network with random connectivity ⊗

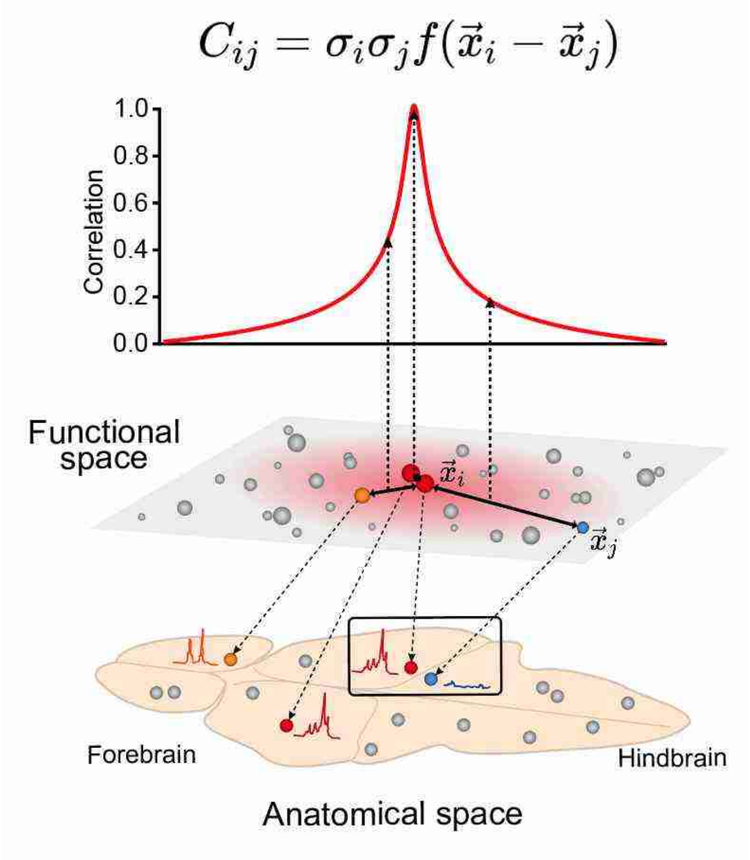
Large-scale brain-wide activity in fish and mice



Light field | **Light sheet** | **Two-photon Mouse** | **Neuropixels Mouse**

Chen et. al., 2018
Stringer et. al., 2019A
Stringer et. al., 2019B

Reorganizing neurons from the anatomical to the functional space



C_{ij} : **covariance between two neurons**

σ_i^2 : **variance of neural activity**

x_i : **neural coordinates in the functional space**

$f(x)$: **distance-dependent correlation function**

The physical picture of the functional space:

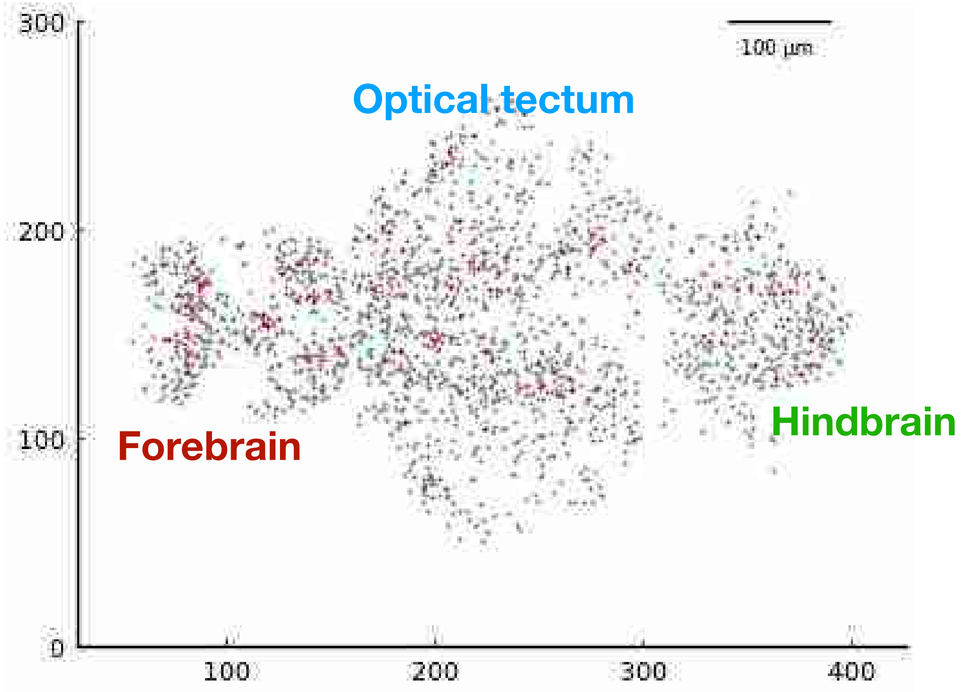
- The closer the two neurons, the higher their correlation
- The bigger the neuron, the larger its neural activity fluctuation (neural activity heterogeneity)

What is the biological meaning of the functional space?

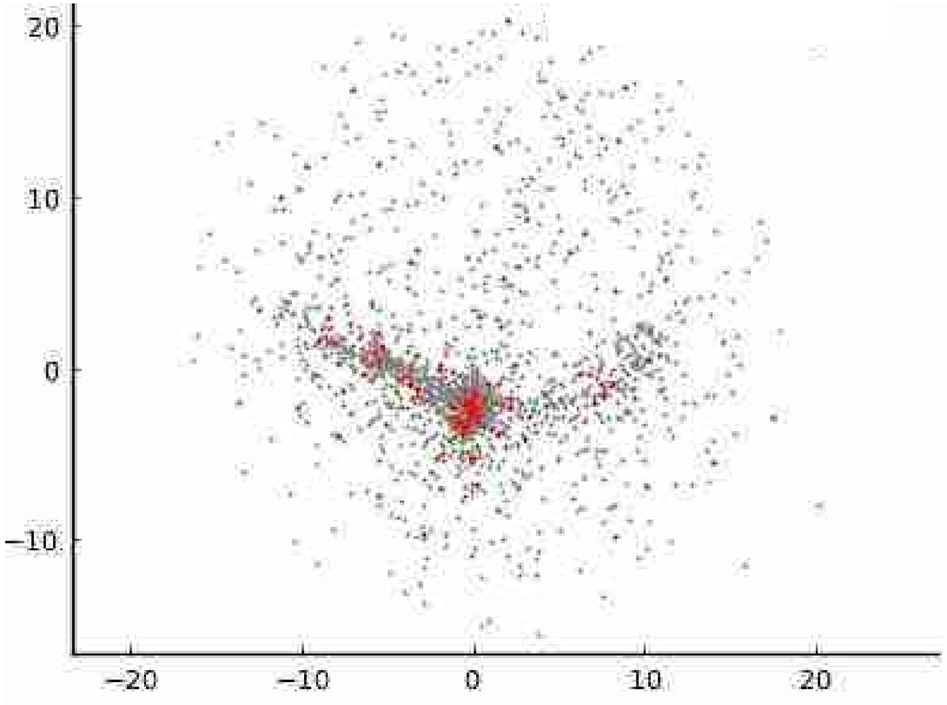
- Feature map in the sensory or motor system
- Place field in the hippocampus
- Latent variables that represent cognitive factors

25 simultaneously recorded place cells

Reorganizing neurons from anatomical to functional space, an example



Anatomical space



Functional space

The slow-decay distance correlation function

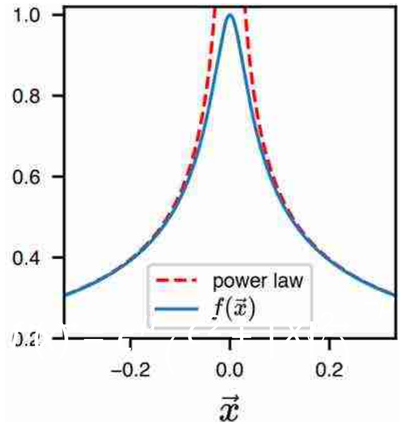
$$f(x) \cong \epsilon^{\mu} \left(\epsilon^2 + \|x\|^2\right)^{-\mu/2}$$

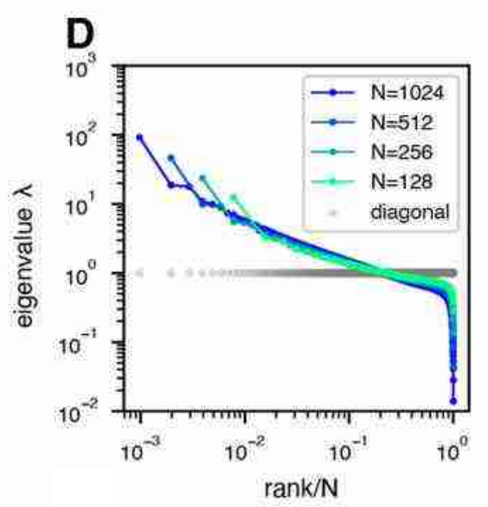
when $\|x\| \ll \epsilon$

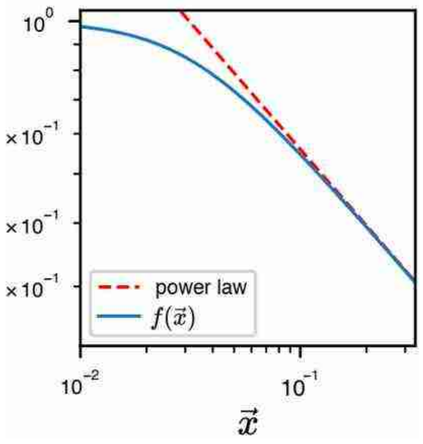
$$f(x) \approx 1$$

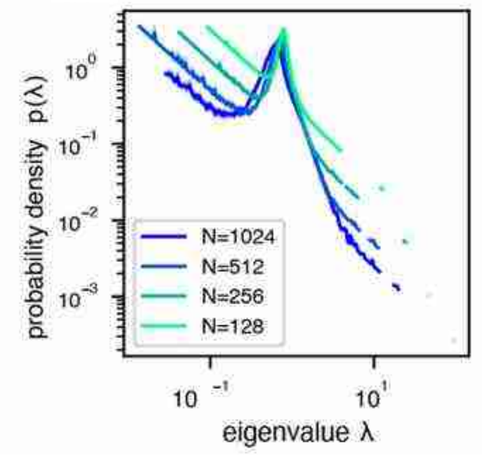
when $\|x\| \gg \epsilon$

$$f(x) \approx \epsilon^{\mu} \|x\|^{-\mu}$$



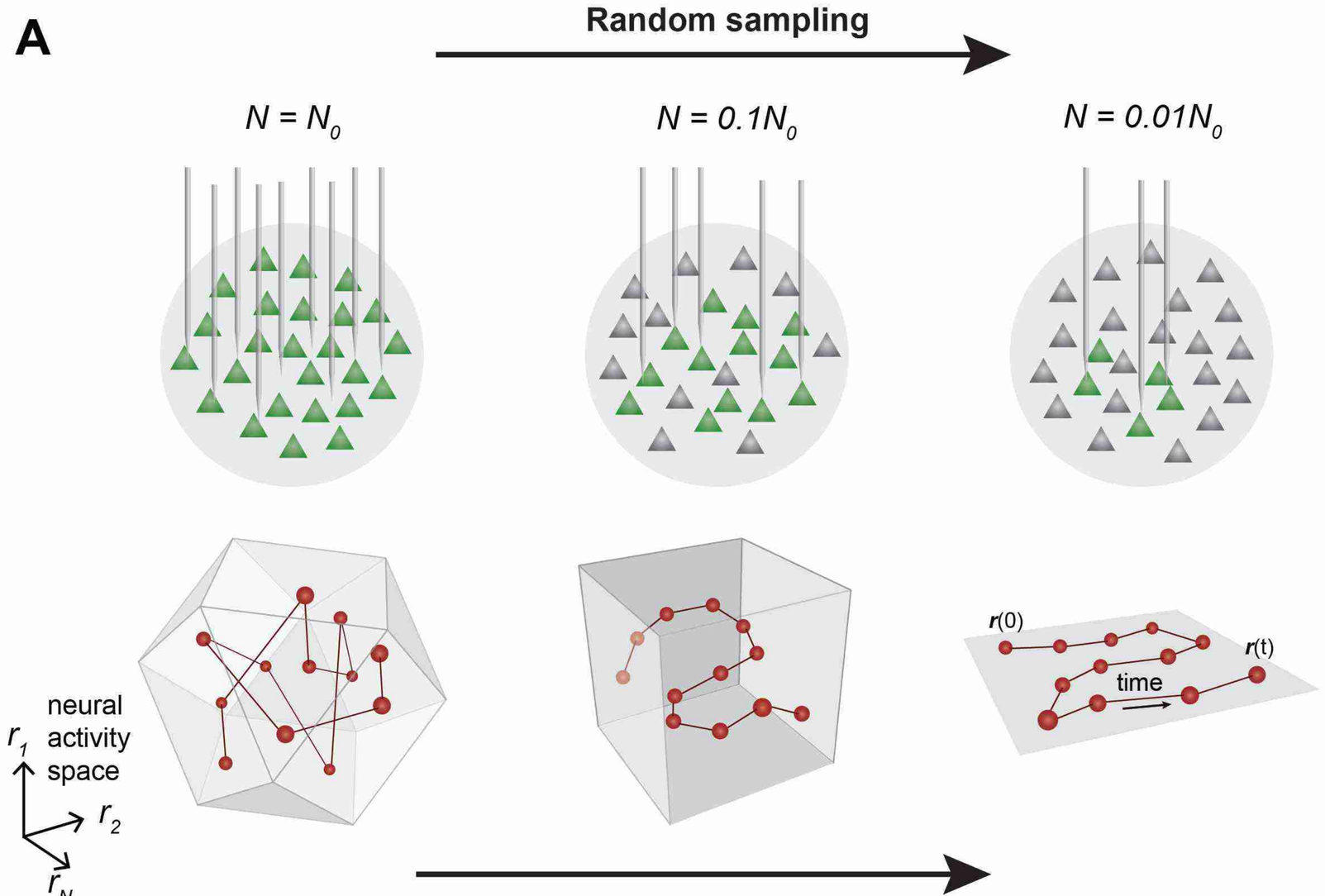






random sampling, "anatomical" sampling (akin to optical "recording of" all neurons within a specific region of the brain) and functional sampling (20). Our ERM theory makes distinct predictions regarding the scaling relationship between dimensionality and the size of cell assembly, as well as the shape of covariance eigenspetrum under various sampling methods. Taken together, our results offer a new perspective for interpreting brain-wide activity and unambiguously show its organizing principles, with unexplored consequences for neural computation.

Under what conditions would the eigenspectra collapse?



Euclidean Random Matrix Theory (ERM)

pioneered by Freeman Dyson

Eigendensity: $p(\lambda) = \frac{1}{N} \left\langle \sum_{n=1}^{N} \delta(\lambda - \lambda_n) \right\rangle$ $\langle \ldots \rangle$ **average all possible matricies**

Resolvent: $g(z) = \frac{1}{N} \left\langle \mathrm{Tr} \frac{1}{z - C} \right\rangle = \frac{1}{N} \left\langle \sum_{n=1}^{N} \frac{1}{z - \lambda_n} \right\rangle$

$$p(\lambda) = \frac{1}{\pi} \lim_{\epsilon \to 0^+} \mathbf{Im}\, g(\lambda - i\epsilon)$$

See also Mezard, Parisi and Zee, Nuclear Physics B, 1999

Under what conditions would the eigenspectra collapse?

1. The kernel function $f(\vec{x})$ decays slowly in the d-dimensional functional space. e.g., $f(\vec{x}) \approxeq \epsilon^{\mu} \|x\|^{-\mu}$, $\|x\| \gg \epsilon$. The collapse is exact as $\mu/d \to 0$.

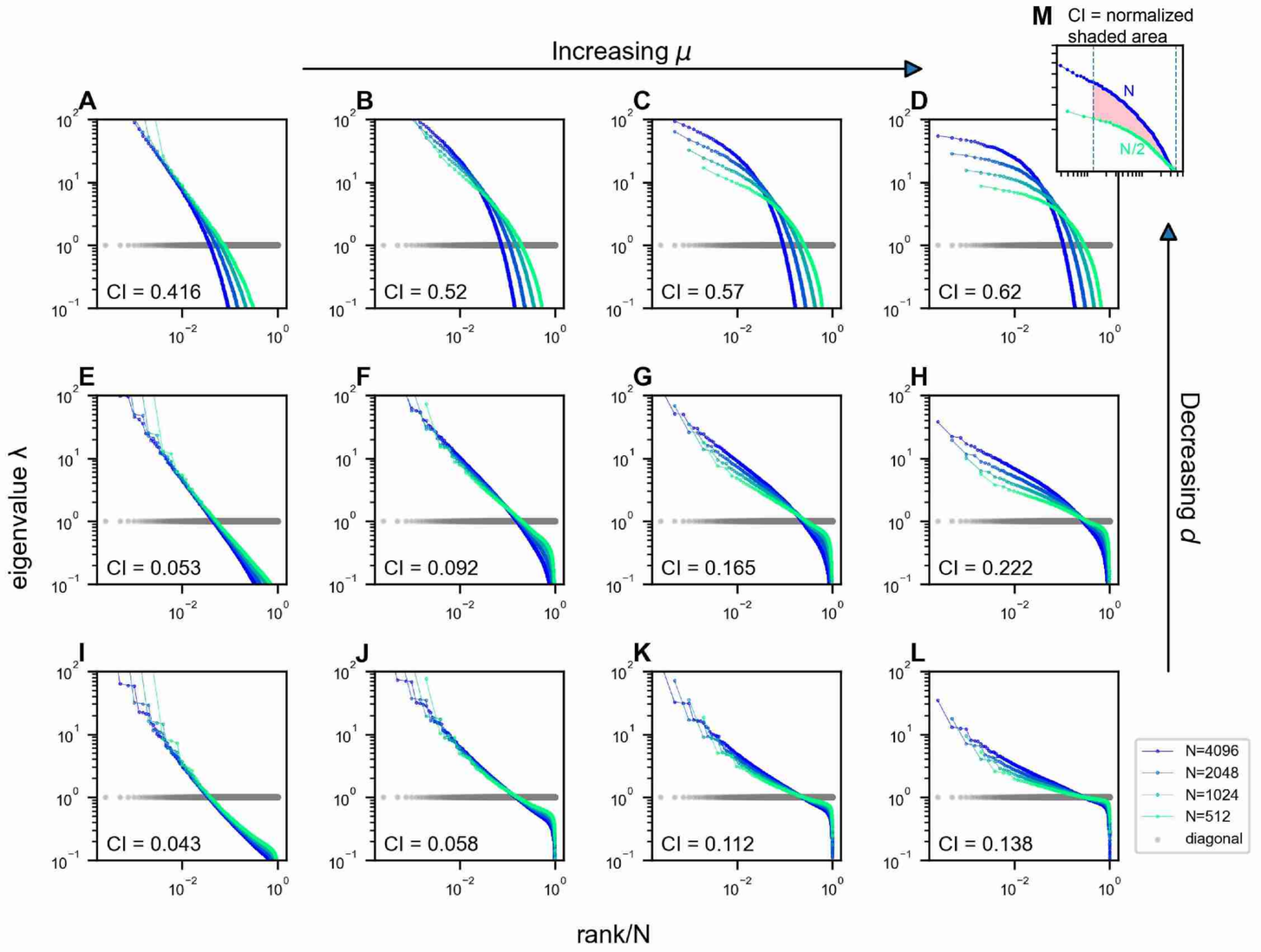
μ dictates how slow the decay of the correlation with functional distance

d dictates the dimensions of the functional space

In the high density limit: $\lambda_r \sim (r/N)^{-1+\frac{\mu}{d}} \rho^{\frac{\mu}{d}}; \ \lambda_r > 1$

Wang and Mai et. al., 2025

Quantifying the scale-invariance: collapse index (CI)



$$\mathrm{CI} := \frac{1}{\log(q_0/q_1)} \int_{\log q_1}^{\log q_0} \left| \frac{\partial \log \lambda(q)}{\partial \log \rho} \right| \mathrm{d} \log q$$

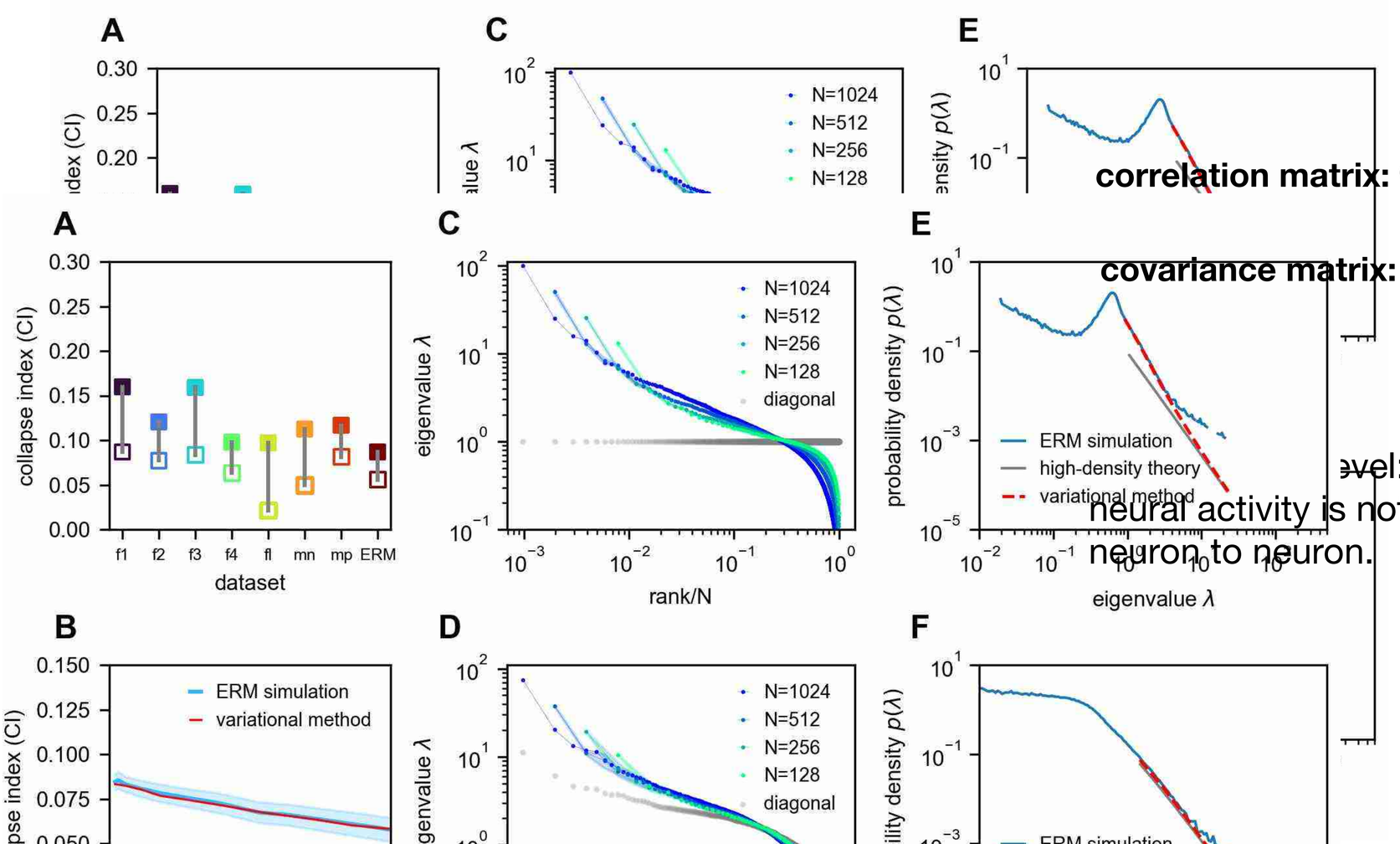
$$q = \mathrm{rank}/N$$

- The smaller the CI, the better the scale-invariance

Figure 4. Impact of μ and d on the scale invariance of covariance eigenspectra in the ERM with slow-decaying $f(x) =$

Under what conditions would the eigenspectra collapse?

2. The heterogeneity of population neural activity improves the collapse



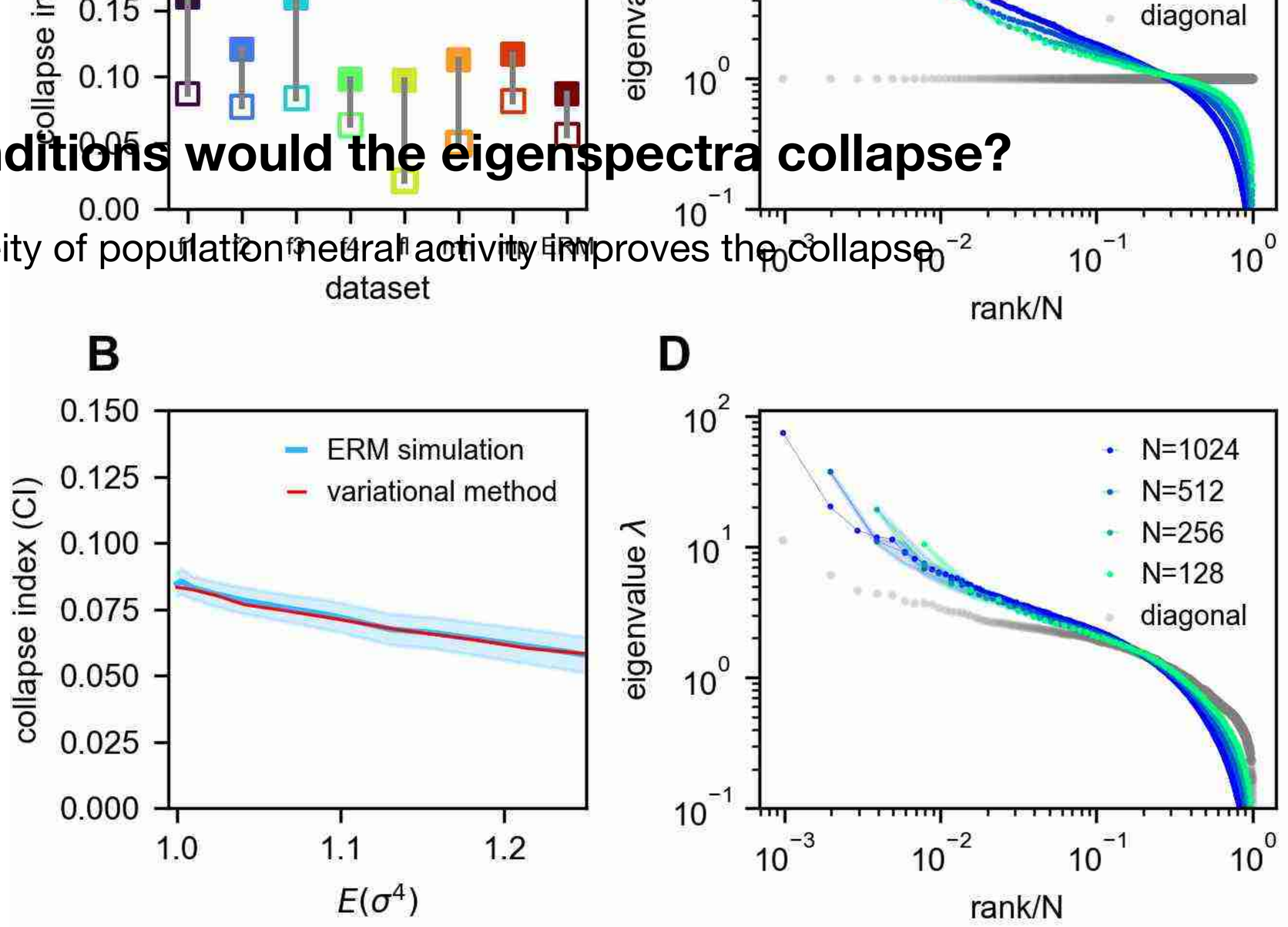
correlation matrix: $\sigma_1^2 = \sigma_2^2 = . . = \sigma_N^2 = 1$

covariance matrix: A distribution of $\{\sigma_i\}$

…evel: the fluctuation of neural activity is not fixed! It varies from neuron to neuron.

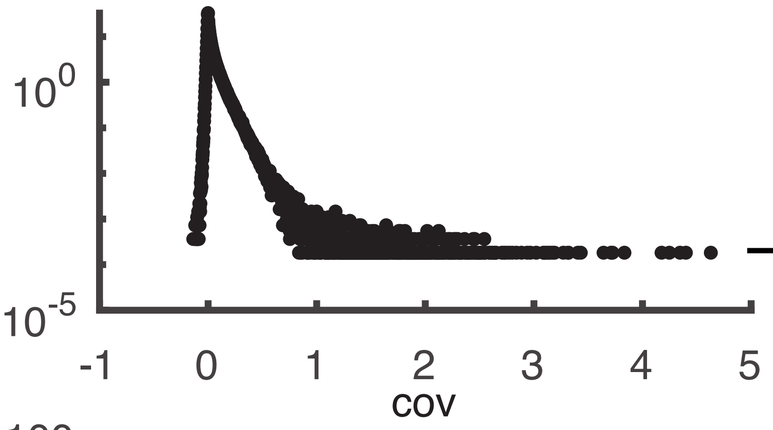
Under what conditions would the eigenspectra collapse?

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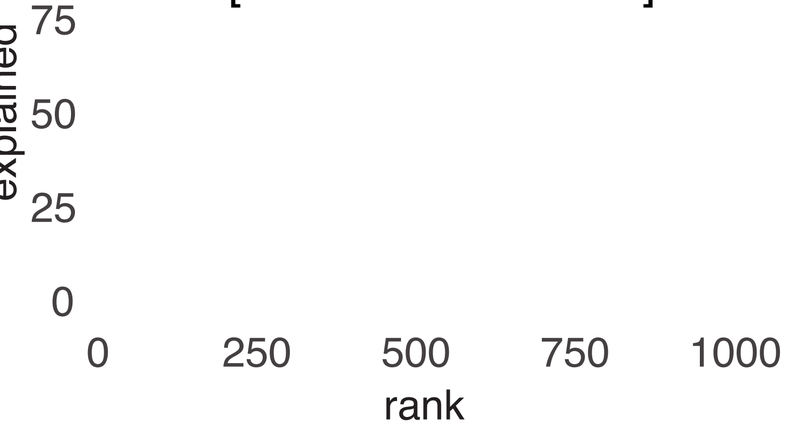


Wang Mai et. al., 2025

Recapitulate data covariance matrix and its eigenspectrum



$$C_{ij} = \mathbb{E}\left[(r_i - \mathbb{E}(r_i))(r_j - \mathbb{E}(r_j))\right]$$



$$f(x) \cong \epsilon^{\mu} \left(\epsilon^2 + \|x\|^2\right)^{-\mu/2}$$

fit μ, ρ for given d

Pairwise distance
In functional space

MDS

x_i ; $i = 1 \ldots N$

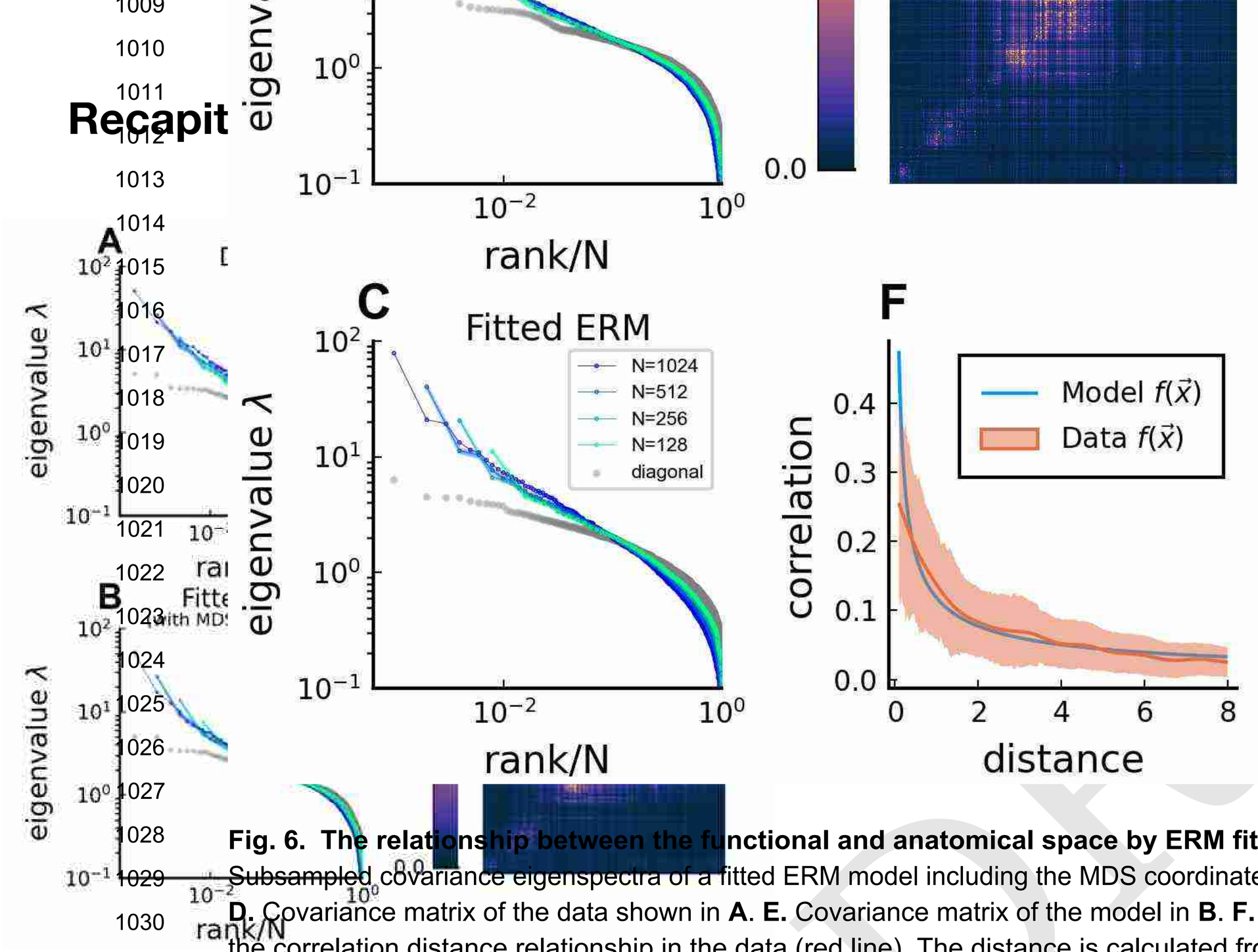
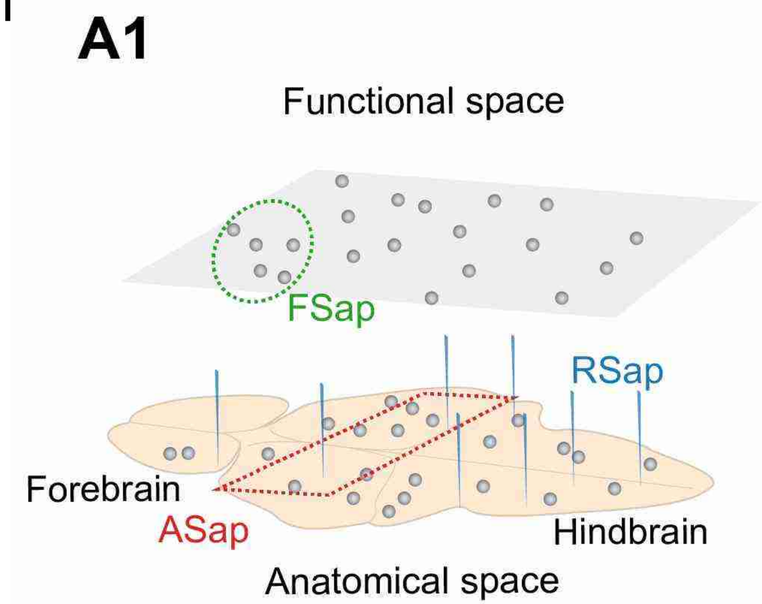
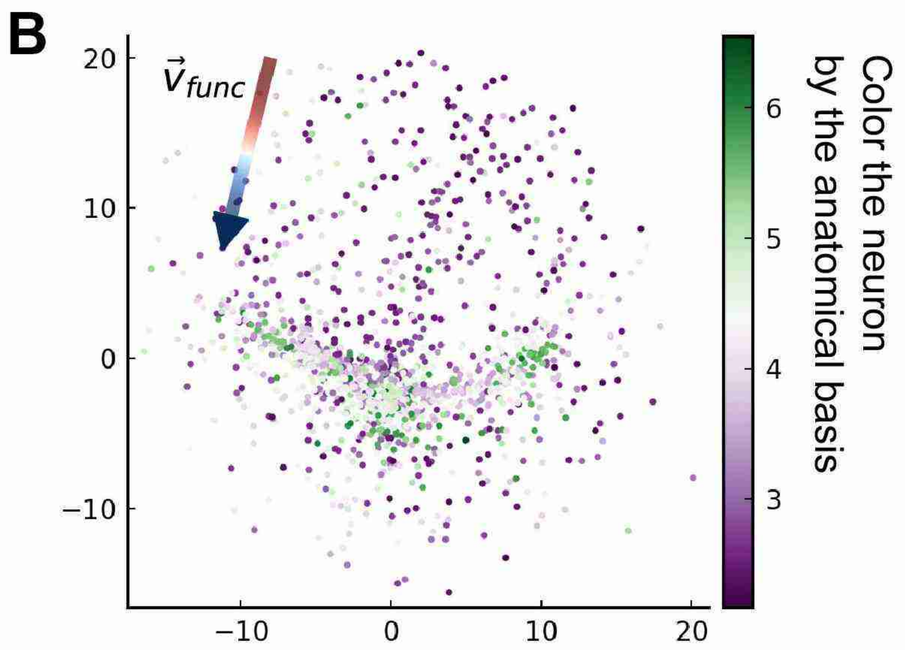


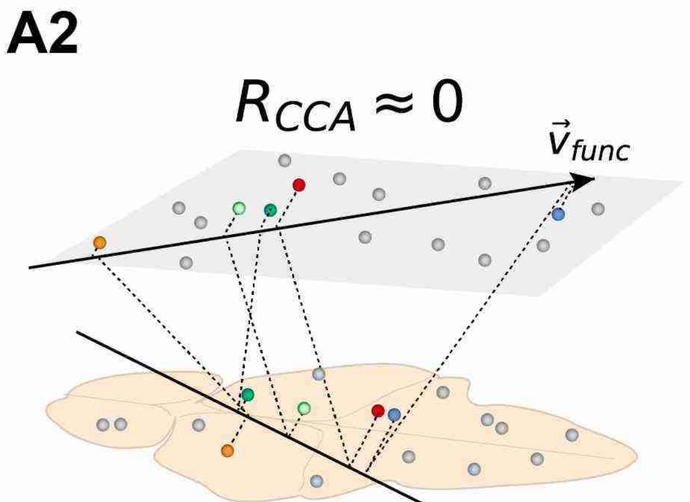
Fig. 6. The relationship between the functional and anatomical space by ERM fitting to data. **A.** Subs
Subsampled covariance eigenspectra of a fitted ERM model including the MDS coordinates (see text). **C.** Subsam
D. Covariance matrix of the data shown in **A**. **E.** Covariance matrix of the model in **B**. **F.** Comparison of the pow
the correlation distance relationship in the data (red line). The distance is calculated from the inferred coordina

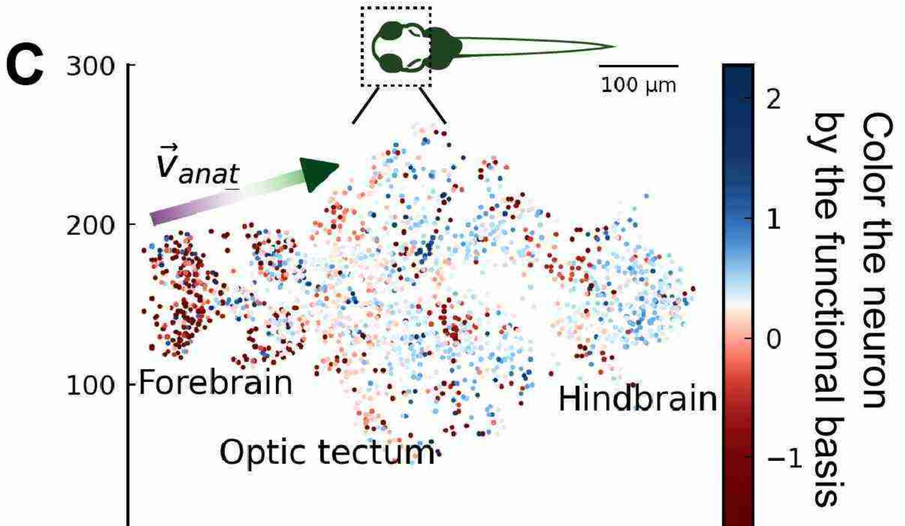
Different sampling methods

- **Anatomical Samp**
- **Random Samplin**
- **Functional Samp**

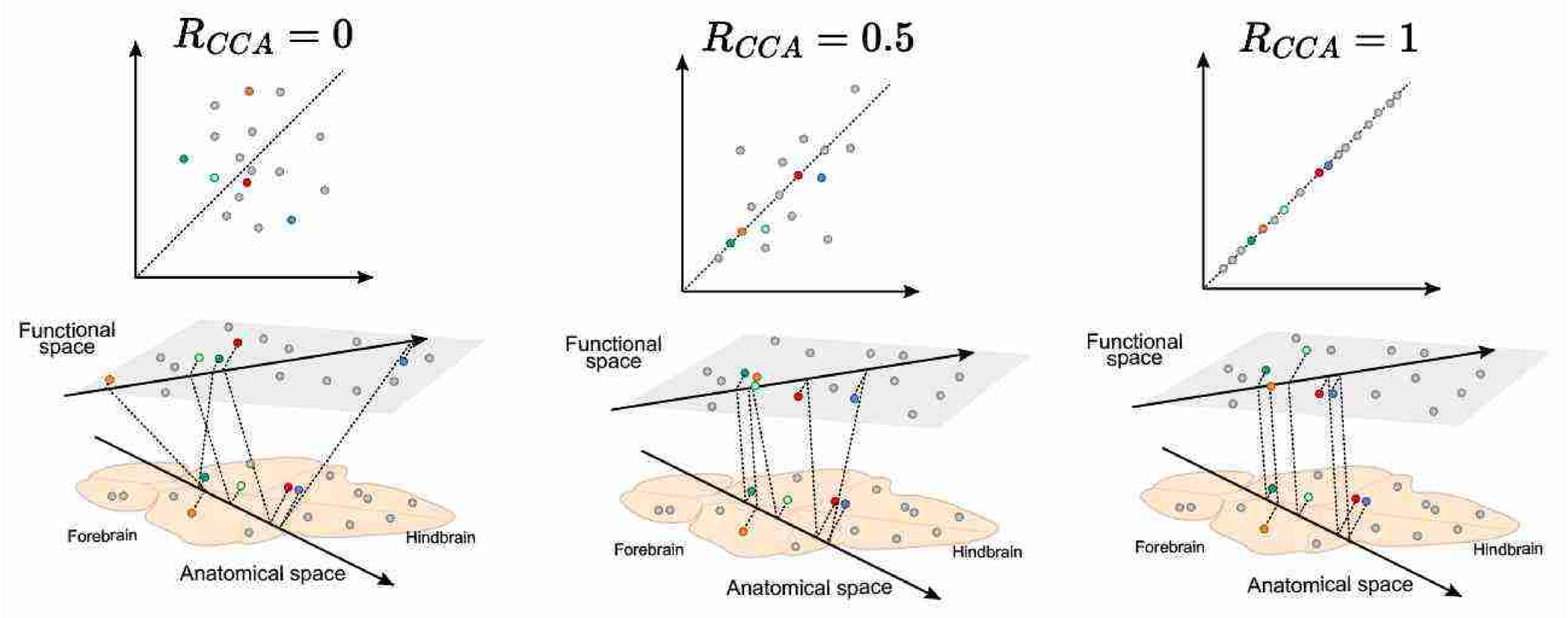








The relationship between the neuron distribution in functional and anatomical space: Canonical Correlation Analysis (CCA)



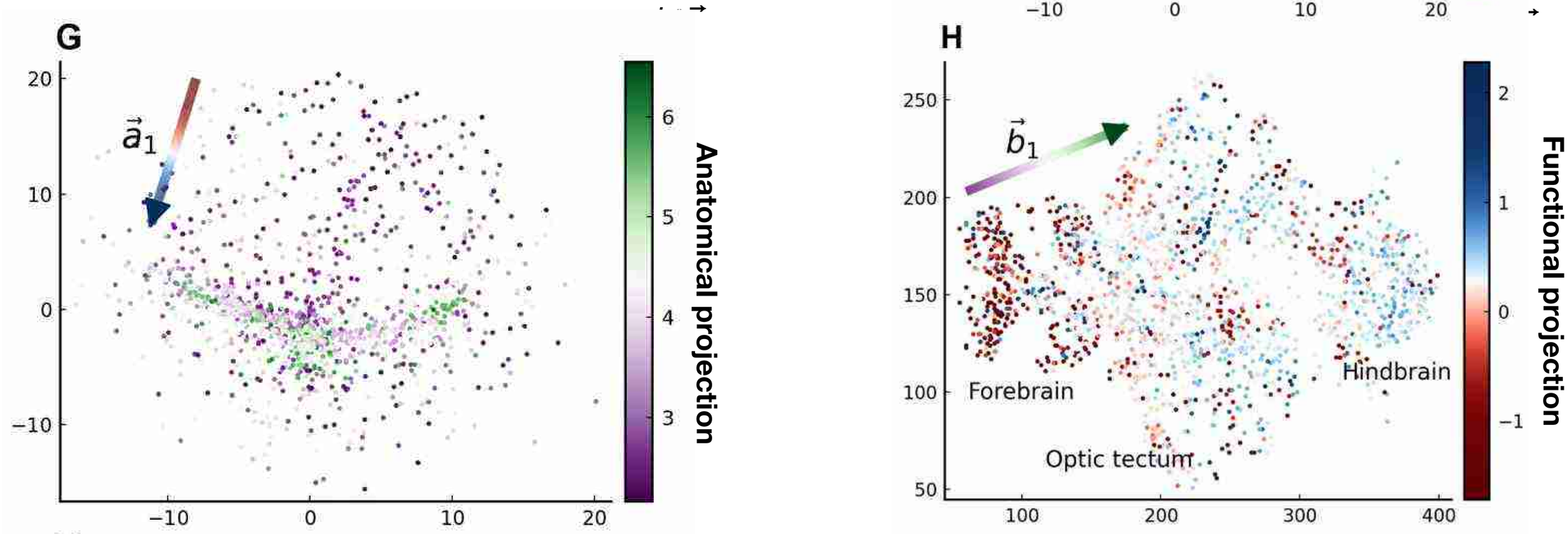
ASap = RSap

ASap = FSap

The relationship between the functional a ta

x_i : neuronal functional coordinates

: neuronal anatomical coordinates



$R_{CCA} = Corr(a_1 \cdot \vec{x}_i, b_1 \cdot \vec{y}_i) \approx 0.3$

The Dimensionality under different sampling methods

$$D_{ASap} \approx (1 - R^2_{CCA} + k^2 R^2_{CCA})^{\mu/d} D_{RSap}$$

k : **the fraction of neurons being sampled**

μ : **power law exponent in the distance correlation function**

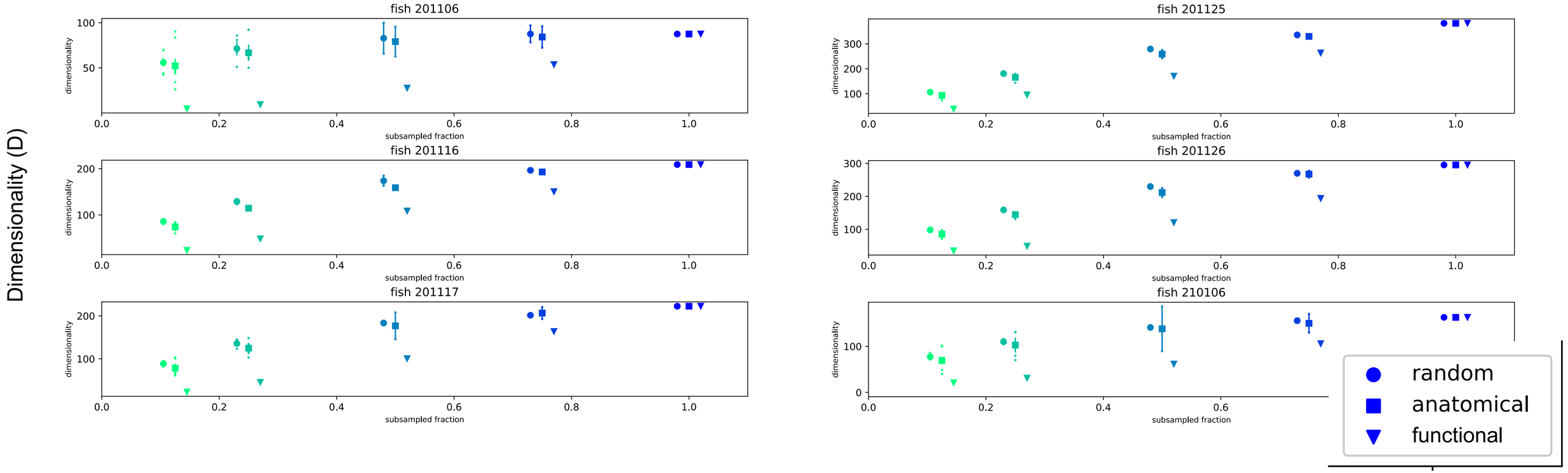
d : **functional space dimensions**

$$R_{CCA} = 1;\ D_{ASap} = D_{FSap} = k^{2\mu/d} D$$

$$R_{CCA} = 0;\ D_{ASap} = D_{RSap}$$

$$D_{FSap} \leq D_{ASap} \leq D_{RSap}$$

The dimensionality of population neural activity under different sampling methods

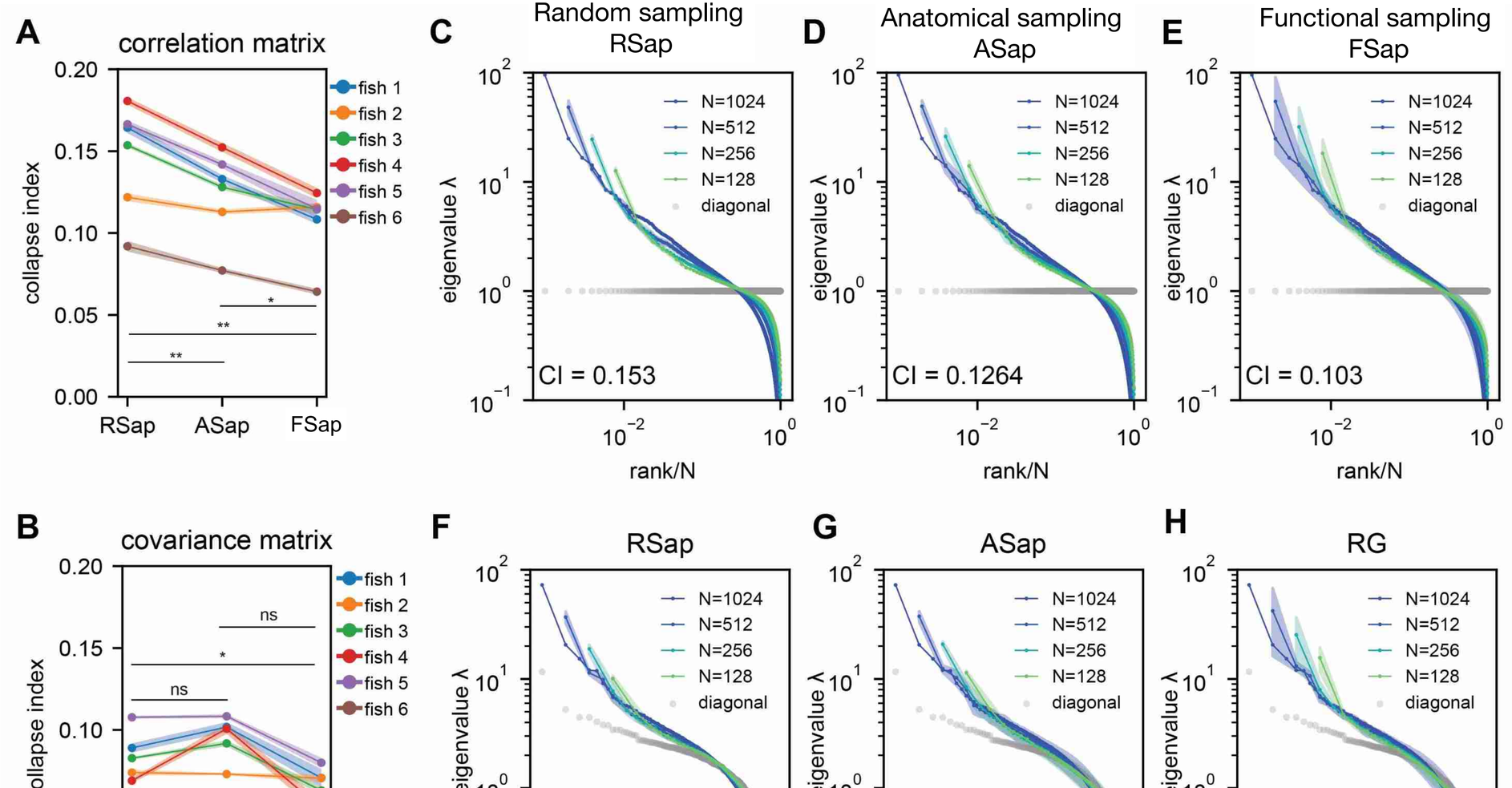


The Dimensionality under different sampling methods

$$D_{ASap} \approx (1 - R^2_{CCA} + k^2 R^2_{CCA})^{\mu/d} D_{RSap}$$

They become equivalent under the condition of scale-invariance, namely $\mu/d \to 0$!

The data eigenspectrum under different sampling methods

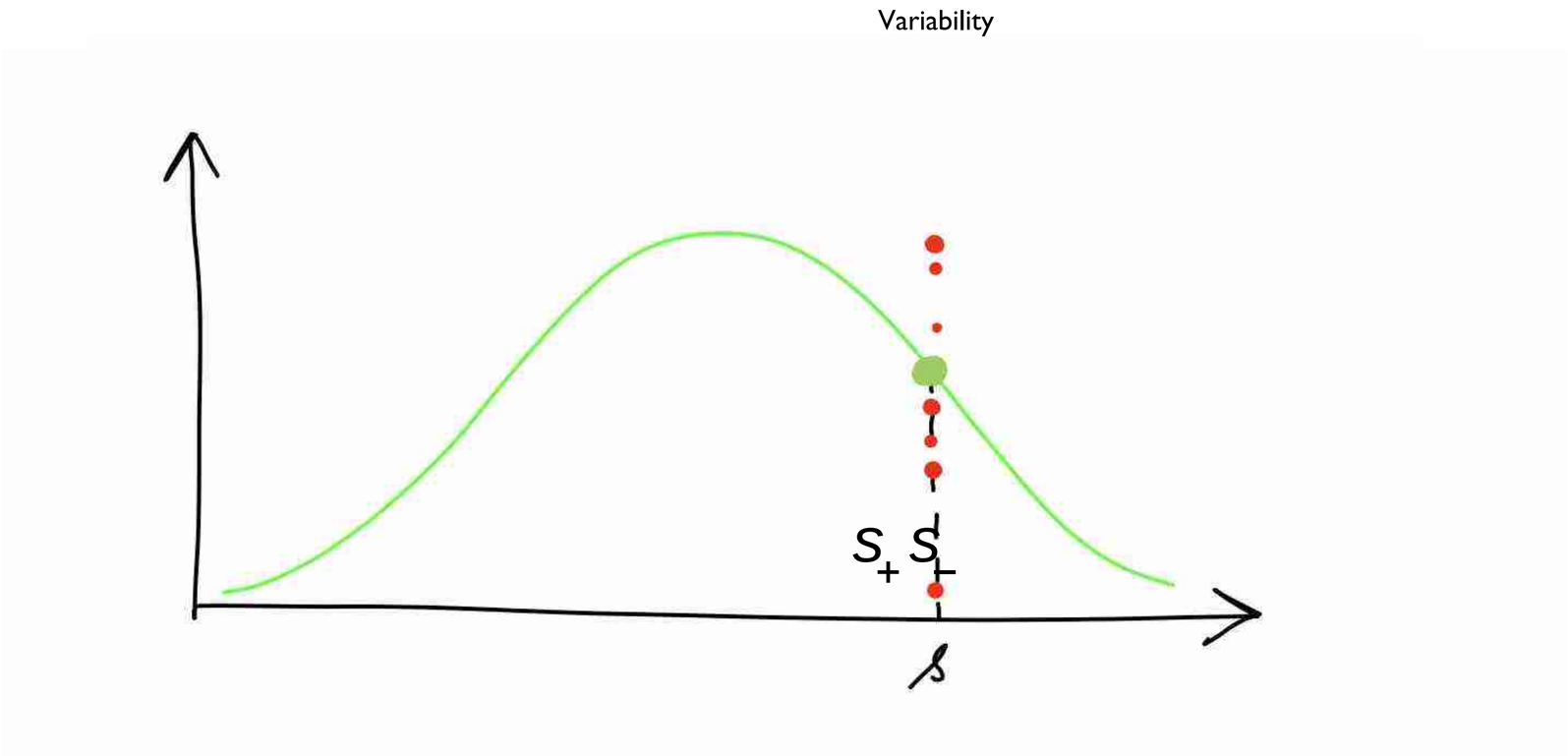


What are the neurobiological implications of the theory?

- Is scale-invariance beneficial for downstream computation?
- What is the task-dependent dimensionality and geometry?
- What biological mechanisms give rise to scale-invariant geometry?

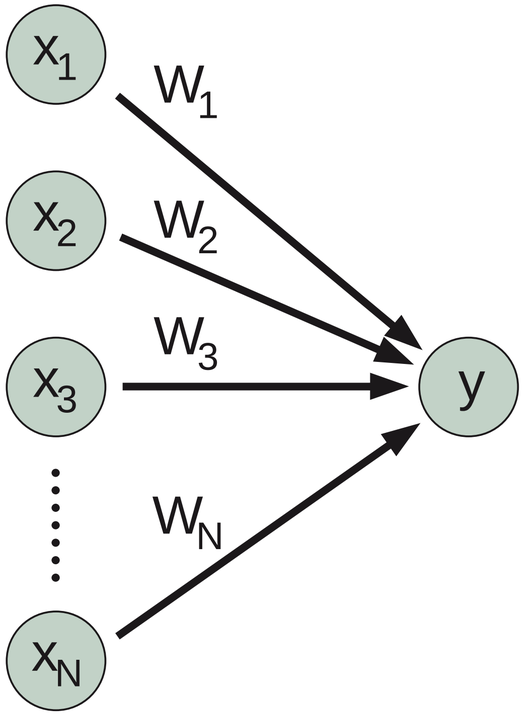
Wang, Mai et. al., eLife 2025

Linear decoding population neural activity



The optimal linear decoder

(A) input



output

(B) input

$$y^+ = \sum_{i=1}^{N} w_i x_i^+ \qquad y^- = \sum_{i=1}^{N} w_i x_i^-$$

association response

$$SNR = \frac{(\langle y^+ \rangle - \langle y^- \rangle)^2}{\frac{1}{2}(\delta y^{+2} + \delta y^{-2})}$$

$$w_{opt} \propto \mathbf{C}^{-1}(\langle \mathbf{x}^+ \rangle - \langle \mathbf{x}^- \rangle) \equiv \mathbf{C}^{-1}\mathbf{\Delta}\mu$$

$\mathbf{C}$: noise covariance matrix of $\mathbf{x}$

$\mathbf{\Delta}\mu$: population activity vector difference encoding two stimuli

random connectivity initially

$$SNR = \Delta\mu^T \mathbf{C}^{-1} \Delta\mu$$

This is also called linear Fisher Information **I**

where y is the activity of a neuron receiving N inputs, w_i (each of which can b

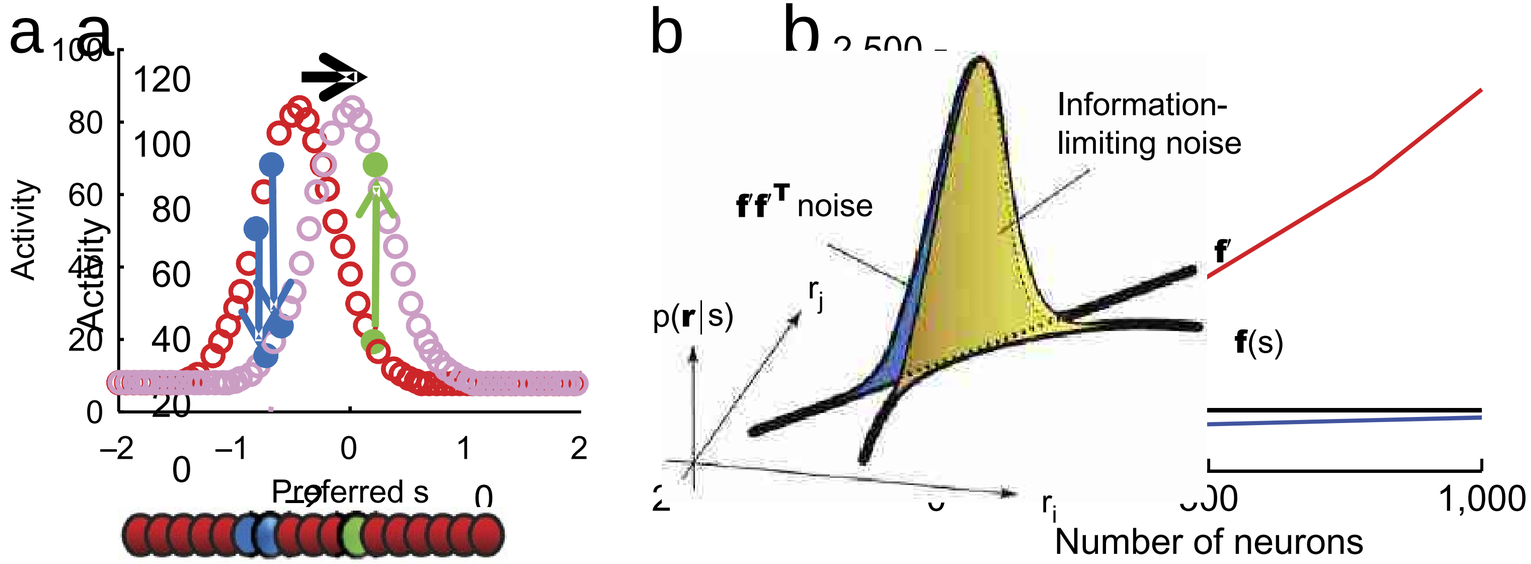
Linear Fisher Information I

$I \sim O(N)$ indepedent neurons

$I \sim O(1)$ differential correlation $\mathbf{C} = \mathbf{C}' + \epsilon \Delta\mu \Delta\mu^T$

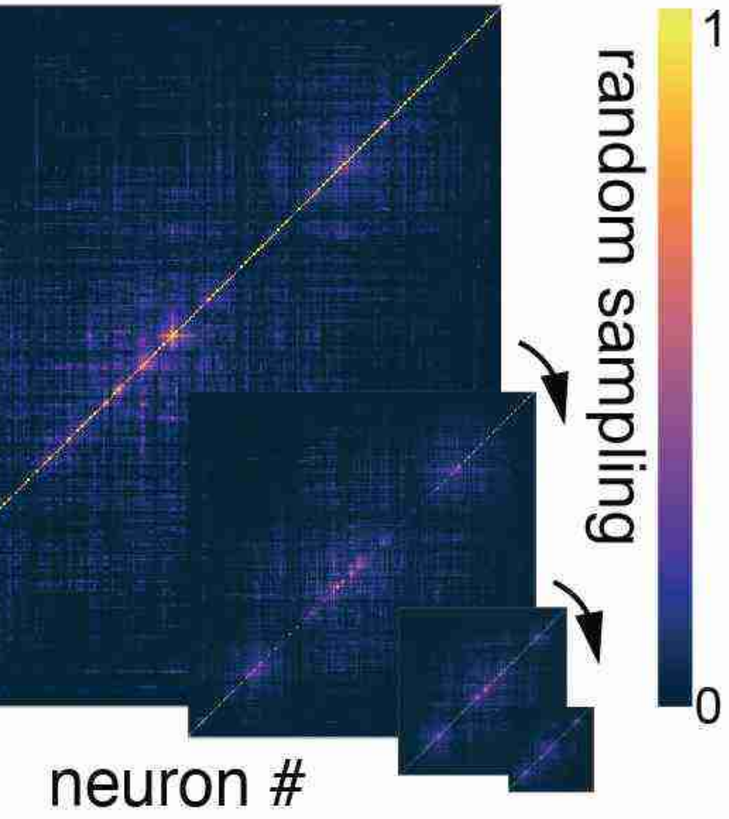
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indistinguishable

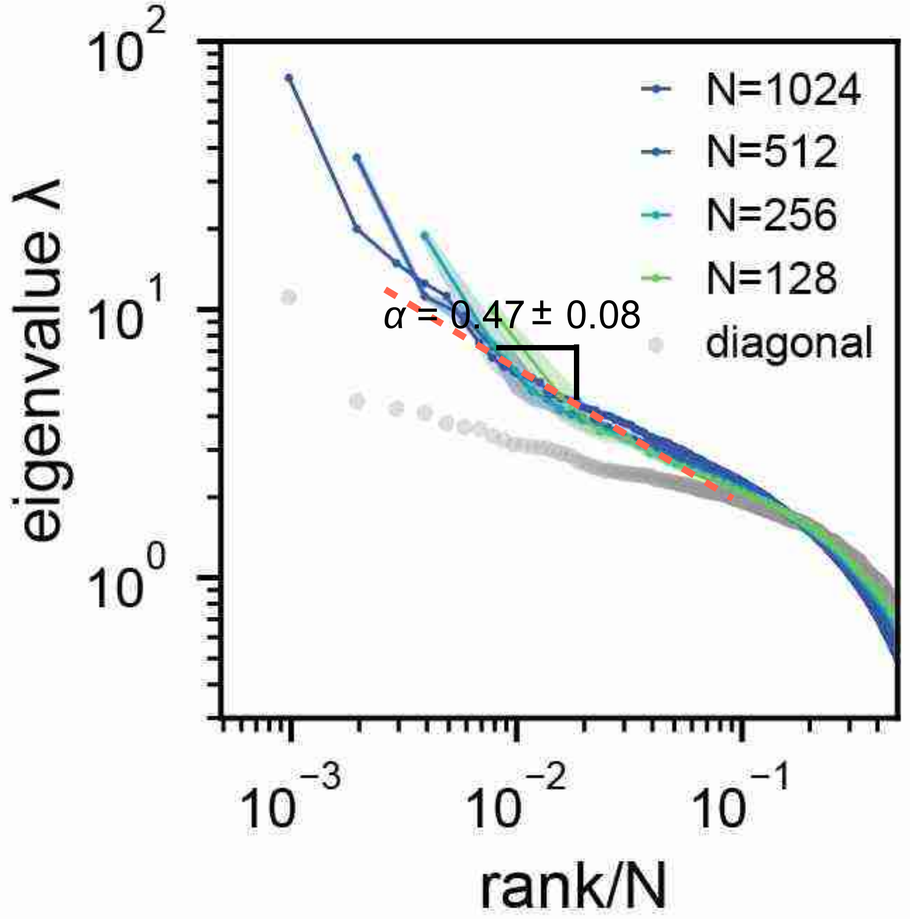


ought of as points in an N-dimensional space, in which each axis corresponds to the activity of one

Ruben Moreno-Bote et al 2014



F Data Cov

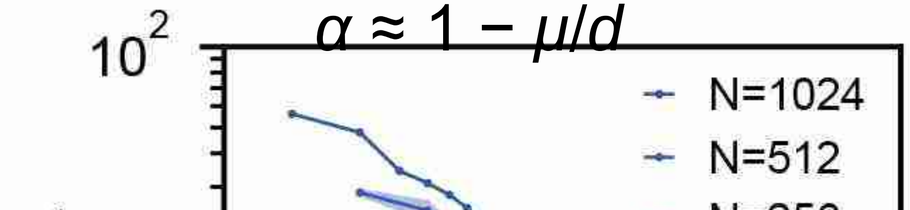


and Eigvec Cov



I Random RNN $\gg 1$

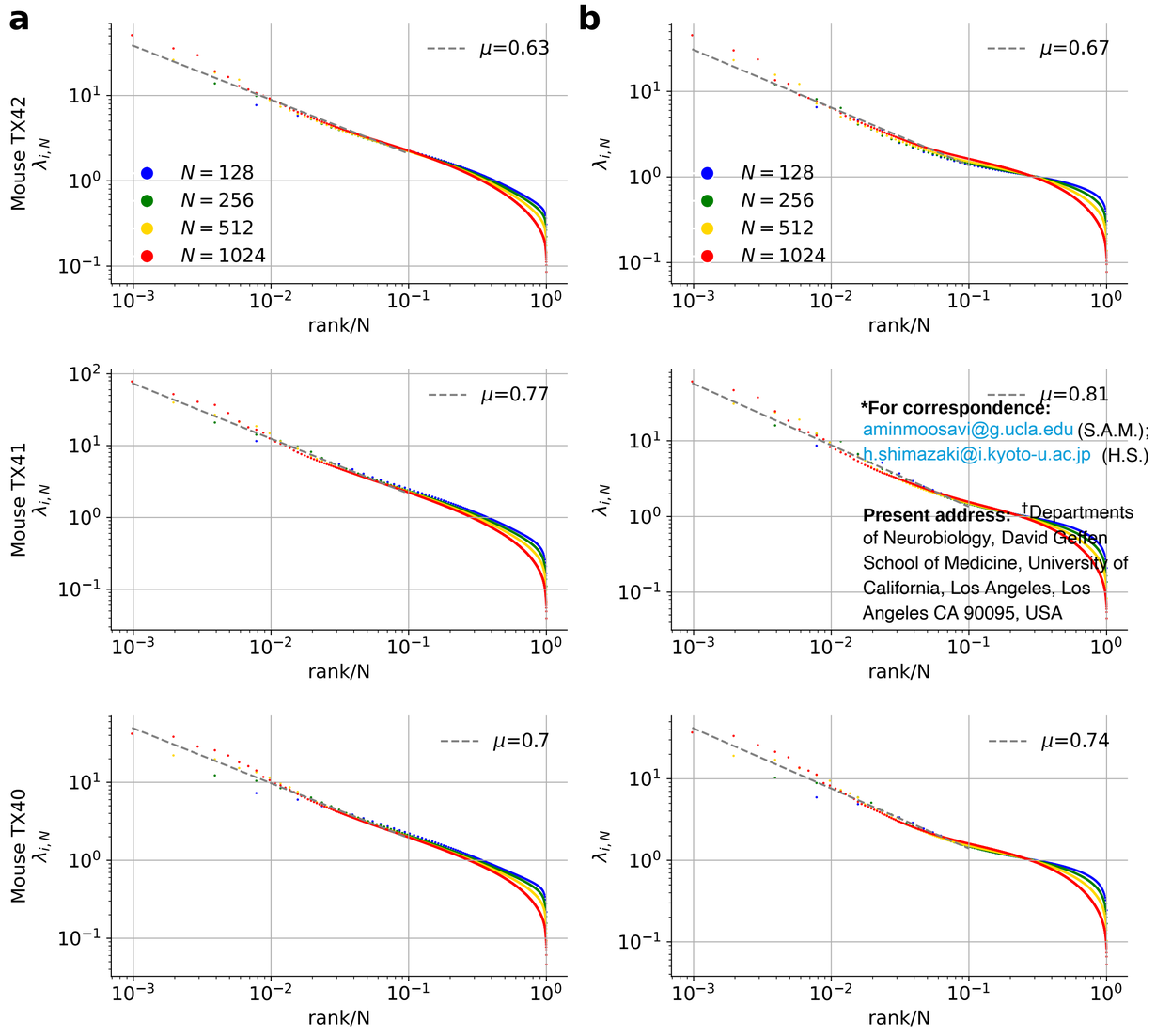
$\alpha \approx 1 - \mu/d$



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α is μ in this figure

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Population coding under the scale-invariance of high-dimensional noise

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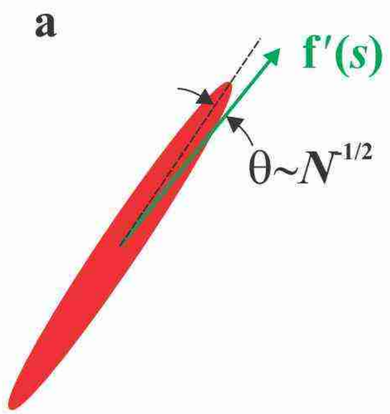
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h.shimazaki@i.kyoto-u.ac.jp (H.S.)

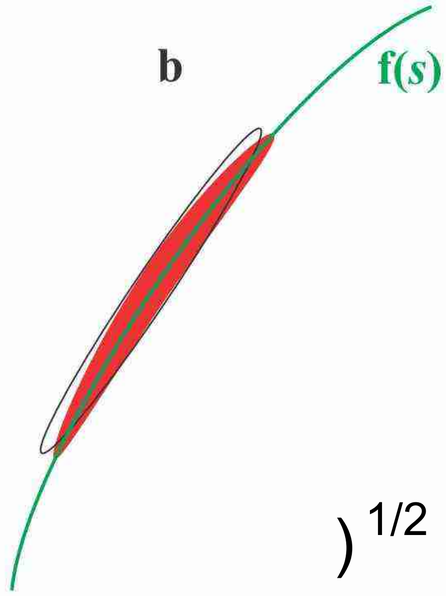
Present address: †Departments of Neurobiology, David Geffen School of Medicine, University of California, Los Angeles, Los Angeles CA 90095, USA

Abstract

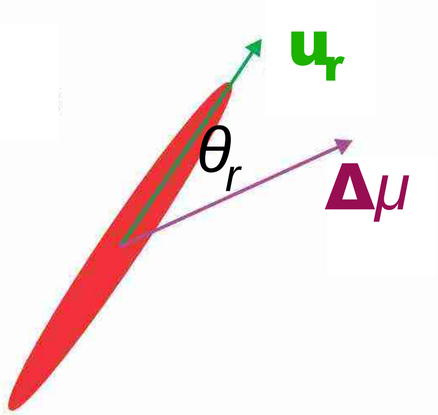
High-dimensional neural activities exhibiting scale-invariant, power-law noise spectra are ubiquitously observed across various brain regions and species. However, their impact on information coding remains unclear. We provide the scaling conditions for noise covariance that clarify the boundedness of information and establish a quantitative relation between information capacity and population size, based on the properties of scale-invariant noise covariance observed in stimulus-evoked activities of mouse V1 neurons. Our analysis reveals that sublinearly scaling small noise components align su ciently with the signal direction, enabling neurons to convey stimulus information unboundedly as population size increases. These ndings demonstrate that the quasi-universal scaling of neural noise covariance lays the foundation for understanding the scaling and boundedness of population codes, highlighting the critical need to consider the full spectrum of high-dimensional noise.

Moosavi, Hindupur, Shimazaki bioRxiv 2024



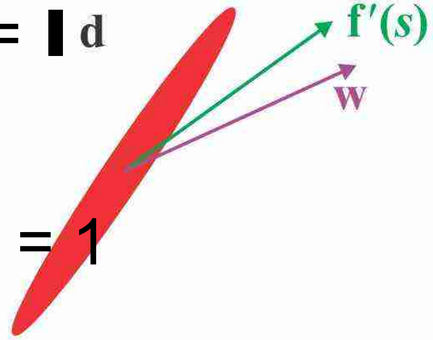


$$)^{1/2}$$



$$\sum_r \mathbf{u}_r\mathbf{u}_r^T = \mathbf{I}_d$$

$$\sum_r \cos^2\theta_r = 1$$



$$\Delta\mu^T\Delta\mu \sim O(N)$$

$$\lambda_r \sim (r/N)^{-\alpha},\ \lambda \gg 1$$

$$I \sim N\sum_r \frac{\cos^2\theta_r}{\lambda_r}$$

$$\geq N\sum_r \frac{\cos^2\theta_r}{\lambda_1}$$

$$N\sum_r \frac{\cos^2\theta_r}{\lambda_1} \sim \frac{N}{N^\alpha}\sum_r \cos^2\theta_r = N^{1-\alpha}$$

$$I \gtrsim N^{1-\alpha}$$

mentary Figure 2

izing information limiting correlations.

Fisher Information will increase at least as $N^{1-\alpha}$!

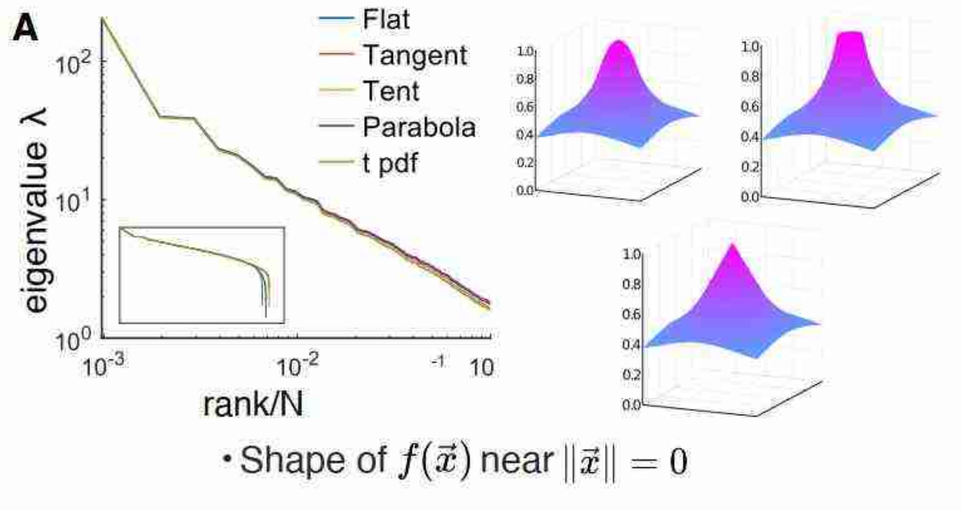
What are the neurobiological implications of the theory?

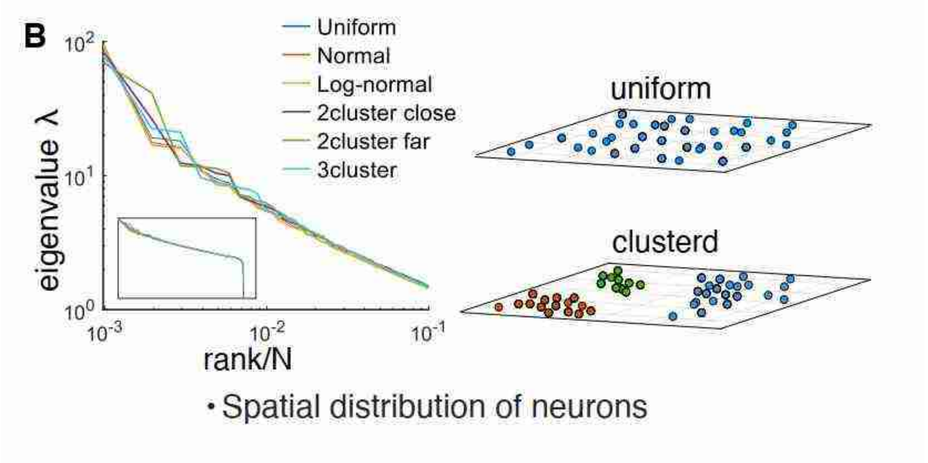
- Is scale-invariance beneficial for downstream computation?

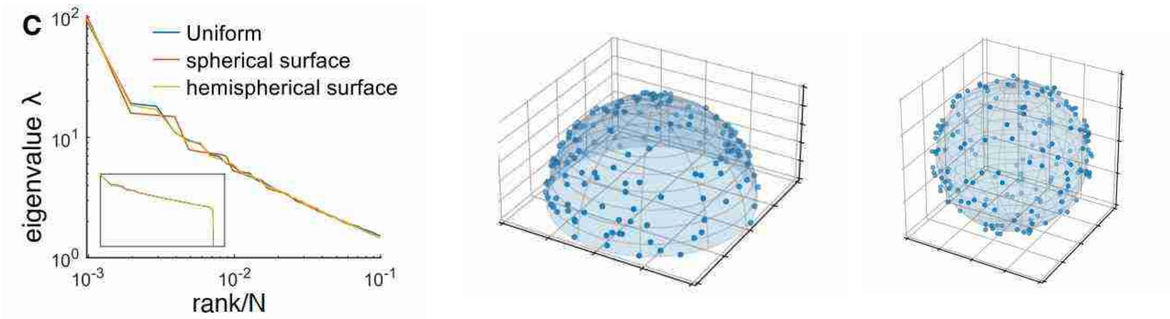
- What is the task-dependent dimensionality and geometry?

- What biological mechanisms give rise to scale-invariant geometry?

Which factors do not affect scale-invariance?







- The topology of the functional space

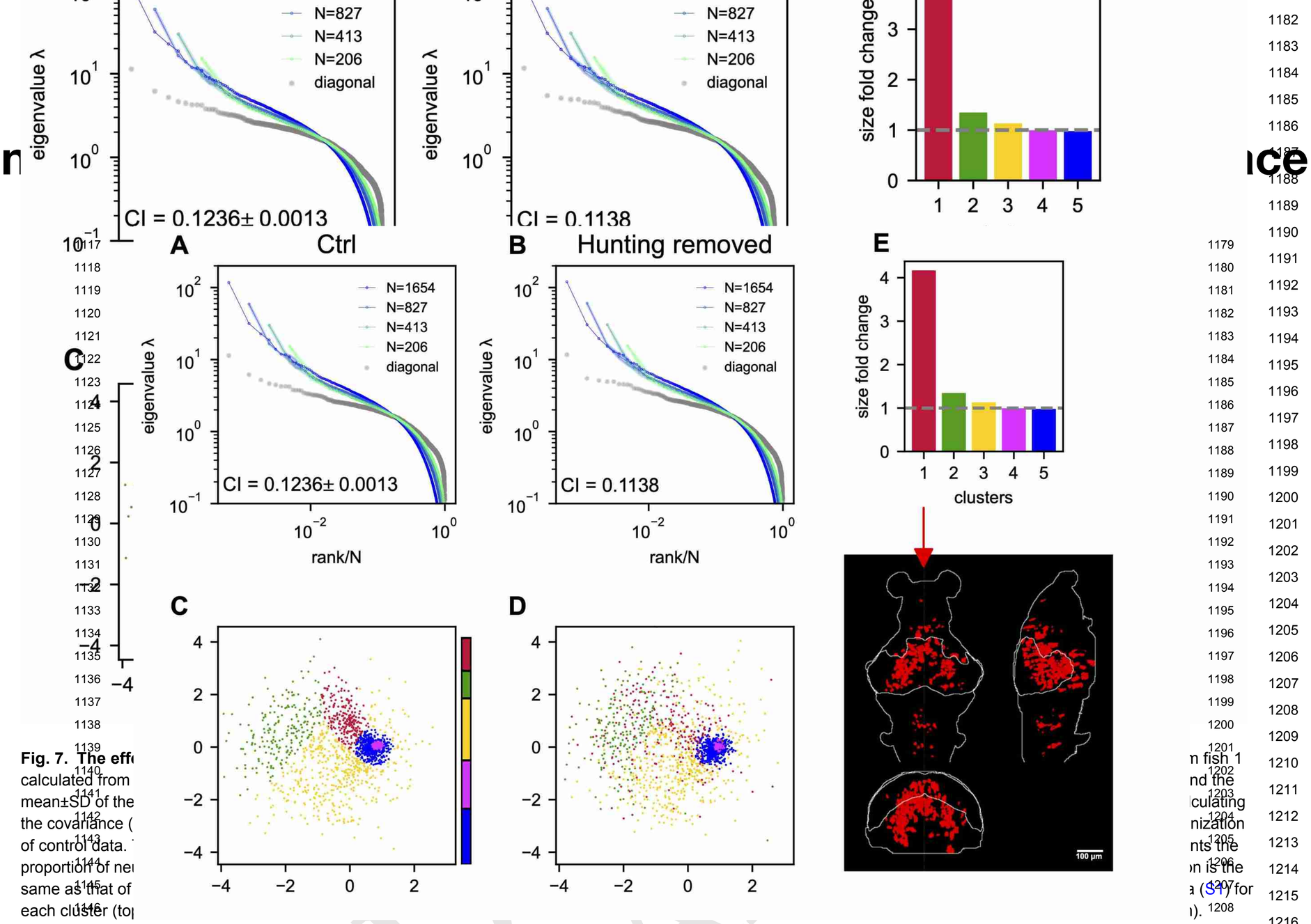


Fig. 7. The effects of hunting behavior on scale invariance and functional space organization. **A,B.** Subsampled covariance eigenspectra of the data from fish 1 calculated from control (**A**) and hunting removed (**B**) data . Ctrl: We randomly remove the same number of non-hunting frames. This process is repeated 10 times, and the mean±SD of the CI is shown in the plot. Hunting removed: The time frames corresponding to the eye converged intervals (putative hunting state) are removed when calculating the covariance (S1). The CI for the hunting removed data appears to be statistically smaller than control (p-value < 0.05, Student's t-test). **C.** Hierarchical organization of control data. The proportion of neurons in each cluster (top) is the same as that of the whole population (S1) for each cluster (top).

space and anatomical space in the brain (fig. 6). In particular, e... over time. Finally, to visualize covariance matrices on a common scale, found that hunting (S1). Therefore, the hunting removed data appears to be statistically smaller than control (p-value < 0.05, Student's t-test). **C.** Hierarchical organization of control data. The proportion of neurons in each cluster (top) is the same as that of the whole population (S1) for each cluster (top).

Hunting behavior reorganizes neurons in the functional space

Fish 1 example trial

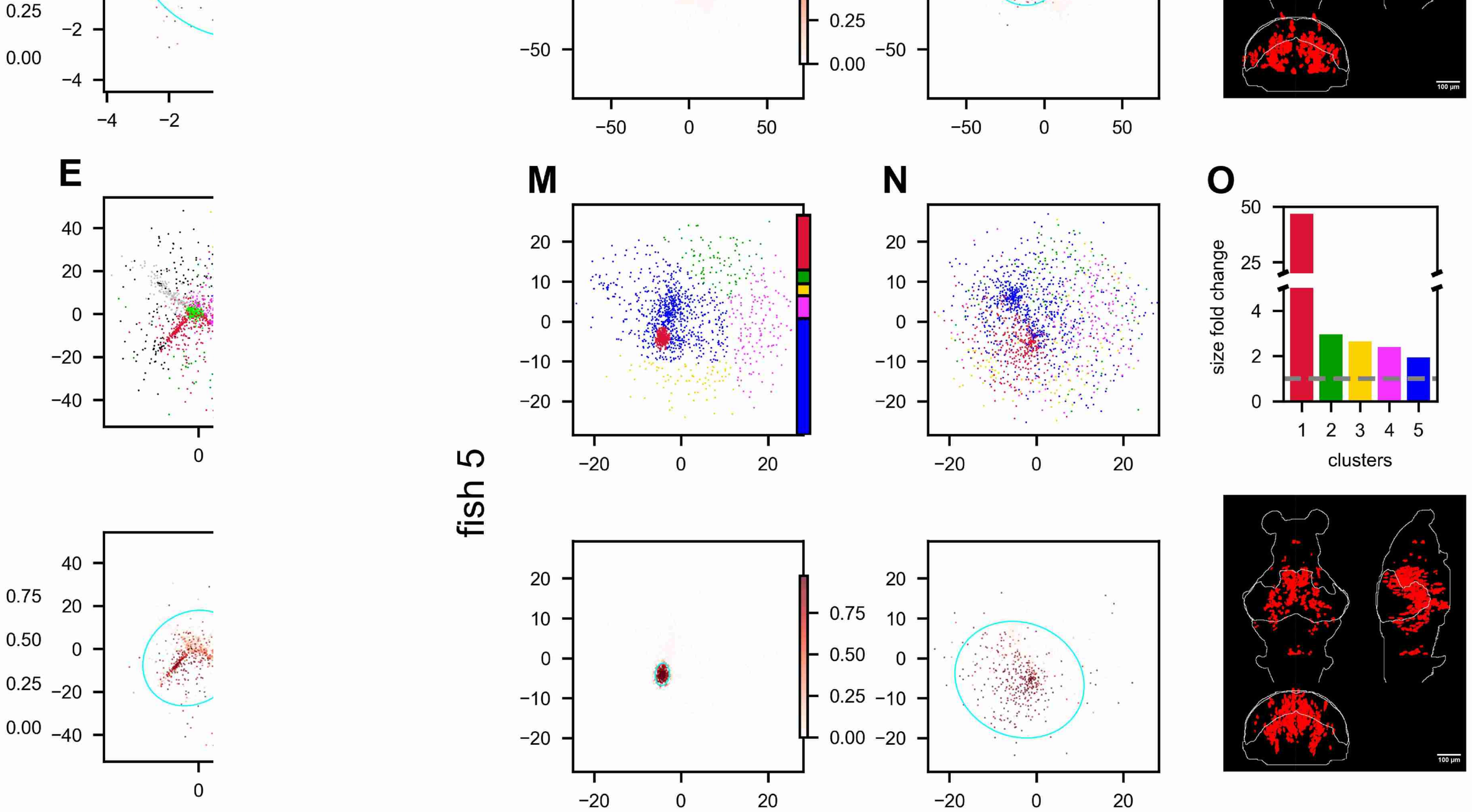


Fig. S13. Hunting behavior reorganizes neurons in the functional space (continued). Rows correspond to 5 light-field recordings of zebrafish engaged in

ar space (continued on next page).

ization. **A,B.** Subsampled covariance

e number of non-hunting frames. This process is repeated 10 times, and the

eye-converged intervals (putative hunting states) are removed when calculating

in the control case (p-value = $1.5 \diamond 10^{-9}$). **C.** Functional space organization

organization of the control data inferred by fitting the ERM and MDS (Methods section F). Neurons are