

### **3. Assembly structure expands the dimension of shared variability in cortical networks**

#### **3.1 Abstract**

Cortical circuits often receive multiple inputs from upstream populations with non-overlapping stimulus tuning preferences. Both the feedforward and recurrent architectures of the receiving cortical layer will reflect this diverse input tuning. We study how population-wide neuronal variability propagates through a hierarchical cortical network receiving multiple, independent, tuned inputs. We present new analysis of *in vivo* neural data from the primate visual system showing that the number of latent variables (dimension) needed to describe population shared variability is smaller in V4 populations compared to those of its downstream visual area PFC. We successfully reproduce this *dimensionality expansion* from our V4 to PFC neural data using a multi-layer spiking network with structured, feedforward projections and recurrent assemblies of multiple, tuned neuron populations. We show that tuning-structured connectivity generates attractor dynamics within the recurrent PFC current, where attractor competition is reflected in the high dimensional shared variability across the population. Indeed, restricting the dimensionality analysis to activity from one attractor state recovers the low-dimensional structure inherited from each of our tuned inputs. Our model thus introduces a framework where high-dimensional cortical variability is understood as “time-sharing” between distinct low-dimensional, tuning-specific circuit dynamics.

## 3.2 Introduction

Contemporary recording technologies have enabled us to simultaneously monitor the single unit activities of large populations of neurons within and across cortical areas [7]. Neuroscientists have since sought to understand the patterns of activity across many neurons in a cortical circuit, as this provides insight into the population dynamics underlying sensory and motor computations. The trial-to-trial fluctuations of neural responses are one important measure of neural population dynamics that help characterize and differentiate private sources of neural variability from shared fluctuations in activity due to common afferent projections or recurrent network architectures [16, 17].

Network models offer a means to control the wiring rules governing network architecture and then observe the resulting structure and propagation of trial-to-trial variability in model neuron responses. As such, these models are a tool uniquely suited for the difficult challenge of relating network connectivity to network dynamics. Early spiking network models commonly employed uniform, random recurrent connections with balanced excitation and inhibition to internally generate the large variability observed in single neuron responses *in vivo* [111, 63, 112]. However, balanced network models with uniform connectivity produce asynchronous spiking dynamics with mean zero co-variability between the trial-to-trial responses of pairs of neurons [64]. These classical balanced models are thus inadequate to describe several datasets in which neurons have positive noise correlations, or shared variability [113, 114, 115, 54, 22]. More recent recurrent network models have used non-uniform connectivity to produce neural activity with positive, structured noise correlations. Recurrent networks with spatially-dependent coupling profiles can produce spatially-dependent noise correlations [71, 72, 116, 117]. Other wiring architectures that give rise to structured shared variability include local connectivity motifs [118, 119, 120, 121, 122], coupling described by connectivity matrices of constrained form [123, 124], and assembly structures [60].

A handful of studies have explicitly investigated how non-uniform recurrent connectivity architectures determine the dimension of shared variability. Huang et al. [24] internally generated low-dimensional shared variability in spiking networks with slow inhibitory kinetics and spatially-dependent coupling profiles. Recanatesi et al. [125] demonstrated that the rank of

shared variance in recurrent networks depends on the local connectivity motifs, like chains and loops, that make up the network’s full architecture. Mastrogiuseppe & Ostojic [123] were able to predict the minimum rank of a connectivity matrix required to implement a computation of specified complexity. Williamson et al. [59] discovered that the dimension of a spiking network’s shared variance scaled linearly with the number of excitatory cell assemblies in Litwin-Kumar & Doiron [60]’s clustered spiking network framework. All of the above models provide mechanisms by which shared variability of determinate rank is internally generated through recurrent network interactions in one layer of a cortical circuit. However, this class of “internally-generated variability” models does not consider variability inherited from outside sources. Conversely, there are models that accurately capture the structure of neural data with low-dimensional shared variance by assuming that structure is inherited from fluctuations in an external brain area [16, 126, 127, 128, 129]. This class of “externally-inherited variability” models has historically not considered how recurrent network interactions might affect the rank of inherited co-variability.

Our study’s central goal is to create a unifying theory of how structured recurrent connectivity can transform the dimension of the shared variability inherited from external brain regions. We are motivated by our finding that the dimension of shared variance expands between multiple, simultaneously recorded regions of a visual circuit. We first present novel data analysis of neural activity recorded *in vivo* showing that the dimension of shared variance in prefrontal cortex (PFC) is significantly greater than that of upstream visual area V4. We note that the significant dimensionality expansion between V4 and PFC activity either precludes linear dynamics in PFC or necessitates that PFC receives many additional, unobserved cortical inputs. While it is well known that PFC receives information from several sensory cortices to implement integrative brain functions [130, 131, 132, 133], we believe that appealing to unobserved data in order to explain our PFC activity “punts” the responsibility of developing a mechanistic theory of the cortical region’s dynamics. We instead choose to develop a parsimonious model in which PFC can expand the dimensionality of shared variance inherited from V4 through non-linear recurrent interactions alone. We note that our parsimonious modeling choice still self-consistently allows for additional PFC inputs not observed in this study.

Our model accounts for PFC’s laterally-tuned projections carrying visual inputs from both hemispheres of the brain. We show that a strongly coupled, balanced recurrent network exhibits

multi-stable, non-linear dynamics when receiving disjoint projections from multiple independent, tuned upstream neuron populations. When the activity from each of these tuned upstream neuron populations is highly self-correlated, as is the neural activity in a single V4 hemisphere [32, 23], each attractor state of dynamics is marked by pathological anti-correlations between the activity of recurrent cells receiving opposing projections. Motivated by studies showing that cortical neurons have clustered recurrent architecture reflecting tuning preferences, we investigate the consequences of adding clustered excitatory ( $E$ ) and inhibitory ( $I$ ) connections to our model PFC network. We find that tuning-specific recurrent assemblies of  $E$  and  $I$  cells diffuse the pathological anti-correlations induced by lateralized input projections and temper winner-take-all recurrent dynamics. We identify a degree of clustering at which our recurrent network model successfully predicts the dimension of shared variance observed in our PFC neural data recorded *in vivo*. Finally, we show that the high-dimensional shared variance generated by our recurrent network model is the result of “time-sharing” between multiple states of activity, each of which independently has low-dimensional, linear dynamics reflective of our tuned inputs. Together, our results provide a new circuit-based model by which recurrent networks with structured connectivity can internally amplify the shared variability they inherit from upstream brain areas. Furthermore, our results provide a framework in which the high-dimensional dynamics commonly observed in sensory integration areas of the brain can be decomposed into multiple states of interpretable linear dynamics representing discretely tuned neural populations.

### 3.3 Methods

#### 3.3.1 Experimental methods

All neural data were collected by the students and staff of the Smith Laboratory (formerly University of Pittsburgh Department of Ophthalmology, currently Carnegie Mellon University Department of Biomedical Engineering.) All procedures were approved by the University of Pittsburgh Institutional Animal Care and Use Committee and complied with the National Institute of Health’s *Guide for the Care and Use of Laboratory Animals*.

A 96-electrode “Utah” Array (Blackrock Microsystems, Salt Lake City, UT) was implanted in right 8Ar of the dorsolateral prefrontal cortex (PFC) of a male rhesus macaque (*Macaca*

*mulatta*). The PFC array was positioned on the pre-arcuate gyrus, medial to the principal sulcus and anterior to the arcuate sulcus. A second 96-electrode Utah Array was implanted in right V4.

The implanted monkey performed a memory guided saccade (MSG) task as follows. The monkey watched a 21" monitor with 1024x768 pixel resolution and 100 Hz refresh rate from 36 cm viewing distance. A 0.5 diameter dot appeared at the center of the screen. After fixation was established for 200 ms, a target appeared for 50 ms at one of forty 2D screen locations, defined by its coordinates at one of eight angular location ( $0^\circ$  to  $315^\circ$  in increments of  $45^\circ$ ) and one of five radial distances (5 degrees visual acuity (dva), 7.5 dva, 9.9 dva, 12.3 dva, 14.7 dva). When the target disappeared, the monkey was required to maintain fixation at the center of the screen for 500 ms. The disappearance of the central fixation point would then signal the monkey to make a saccade to the remembered target location. Each recording session consisted of blocks of 40 trials, in which a random 1 of the 40 possible target locations was presented on each trial. At least 40 blocks, or presentations of a given target condition, were collected during a single recording session. Further details about the array implantation, task, and neural data collection procedures can be found in Khanna et al. [134] and Cowley et al. [61].

### 3.3.2 Spike train statistics

Spike train statistics for both recorded neural data and the spiking network model realizations were computed as follows. A neuron  $i$  spikes at times  $\{t_{i1}, t_{i2}, t_{i3}, \dots\}$ . Neuron  $i$ 's spike train is then defined as  $y_i(t) = \sum_k \delta(t - t_{ik})$ , where  $\delta(t - s)$  is a Dirac delta function centered at time point  $s$ . The number of spikes emitted by the neuron between times  $t$  and  $t + \Delta t$  is

$$N_i(t, t + \Delta t) = \int_t^{t+\Delta t} y_i(t') dt'. \quad (3.1)$$

The firing rate of neuron  $i$  over interval  $(t, t + \Delta t)$  is defined as:

$$f_i(t, t + \Delta t) = \frac{1}{\Delta t} \langle N_i(t, t + \Delta t) \rangle, \quad (3.2)$$

where  $\langle \cdot \rangle$  denotes an expectation over trials. Finally, the Fano factor of neuron  $i$  is defined as

$$F_i(t, t + \Delta t) = \frac{\text{Var}(N_i(t, t + \Delta t))}{\langle N_i(t, t + \Delta t) \rangle}. \quad (3.3)$$

The spike count correlation coefficient between neurons  $i$  and  $j$  is their covariance normalized by the geometric mean of their variances:

$$\rho_{ij}(t, t + \Delta t) = \frac{\text{Cov}(N_i(t, t + \Delta t), N_j(t, t + \Delta t))}{\sqrt{\text{Var}(N_i(t, t + \Delta t)) \text{Var}(N_j(t, t + \Delta t))}}. \quad (3.4)$$

Unless otherwise specified, spike count covariance and spike count correlation analyses of both the neural data recorded *in vivo* and the simulated data were performed on populations of excitatory neurons, and all spike train statistics were averaged across trials.

### 3.3.3 Neural data preparation

The neural data recorded were sorted into single unit activity. Units without at least a 2.5 signal-to-noise ratio (SNR), defined as the ratio of the average waveform amplitude to the standard deviation of the waveform noise, were disregarded. Remaining units were included in our analyses and taken to represent single neuron activity. Only neurons with a mean firing rates of at least 1 Hz ( $\Delta t = 500$  ms, (3.2)) for all target locations relevant to a given analysis were used in that analysis. The analyzed neural population was further filtered to include only neurons showing evidence of spatial tuning. To test tuning specificity, PFC neural responses were calculated from 10 ms to 260 ms after the presentation of the target. These peak delay period responses were baseline-corrected by subtracting a neuron's average activity across all conditions in the 30 ms to 180 ms epoch after fixation. A Kruskal-Wallis one-way analysis of variance on a neuron's average firing activity across locations was then used to determine whether a neuron had significant ( $p < .05$ ) spatial tuning.

Each neuron's full spatial response field was obtained by averaging its baseline-corrected response across multiple presentations of the same target condition. The resulting response portrait over target space was linearly interpolated to obtain 0.25 dva x 0.25 dva resolution response map, which was then convolved with a 2D gaussian filter of 1 dva variance for smoothing. A neuron's preferred spatial location was defined as the center of mass (COM) of all map points where the magnitude of the neural response was at least 75% that of the maximum response on the map. Responses that were suppressed below baseline were not considered in the COM calculation. Response fields presented are oriented such that the contralateral visual hemifield encodes the left half of the image displayed to the monkey.

### 3.3.4 Noise correlation analyses of neural data

Spike counts of PFC neurons were summed over the delay period of the task ( $\Delta t = 500$  ms, (3.2)) for each trial. Neural responses for trials of the same target condition were then normalized such that each target condition had mean a spike count of zero and variance of one. The residual spiking activity around the baseline response of each target condition represents a neuron's response to "noise", or sources of fluctuation other than the stimulus tuning. Pearson correlation coefficients were computed between these noise responses of all pairs of neurons (3.4). Pairs of neurons were then organized according to the Euclidean distance between the COMs of the two neurons' spatial response fields, in bin increments of 2.25 dva.

### 3.3.5 Factor Analysis of neural data

To understand the dimensionality of the noise fluctuations in both layers of our network, we performed Factor Analysis (FA) [135, 136] on the simultaneously recorded PFC and V4 neural data. Target conditions on the right half of the visual field do not evoke meaningfully tuned responses in the recorded V4 hemisphere. All FA results (in both V4 and PFC neural populations) were therefore calculated using only the 25 stimulus conditions on the left visual hemifield, in which the target orientation was between 90 and 180 dva, inclusive of those boundaries.

PFC neural responses were analyzed over the task delay period, while V4 neural responses were analyzed during the period of target presentation. PFC spike counts were computed over a 0 to 540 ms interval following the target presentation, binned in windows of 180 ms. V4 spike counts were computed over a 0 to 90 ms interval beginning with the target presentation, binned in windows of 30 ms. Note that by binning spike counts with different window sizes for V4 and PFC data, we were able to instead hold constant the number of observations used in FA for each brain area. FA is sensitive to the number of data observations it receives [59]. Our bin width choices result in the same number of observations of PFC and V4 neural data, despite the fact that PFC data was measured surrounding a 500 ms delay period and V4 data could only be meaningfully measured surrounding the considerably shorter 50 ms target presentation period. In making this choice, we assume that the firing activity of PFC neurons is stationary over 180 ms periods, which is reasonable given the average firing rate of a neuron in the PFC population was  $< 5$  Hz.

Neural data from both brain areas were normalized for each target condition such that the mean firing rate per target condition was zero. Spike count observations from all trial repetitions of all left hemifield target conditions were then concatenated into a single matrix of data observations per brain region in preparation for FA. Each matrix of data observations used in FA represented sorted single unit activity during a single recording session. We assume that data collected throughout a single recording session were from consistent V4 and PFC neuronal populations. FA was never performed on data pooled across multiple recording sessions, as we did not attempt to track single unit activity across days of recording.

Appendix A provides a detailed description of the computations underlying FA. In brief, FA finds a latent basis set that describes the shared variance of the analyzed neural data. We order the latent dimensions of this basis set by their percentage of shared variance explained. We define  $d_{\text{shared}}$  as the number of (ordered) latent dimensions required to cumulatively explain 95% of the neural data's shared variance. We calculated  $d_{\text{shared}}$  of the V4 and PFC neural data over each recording session. The FA loading matrix  $\mathbb{L}$  describes how the activity of individual neurons loads onto each latent dimension. We computed the loadings of each PFC neuron onto the top 3 latent dimensions  $\mathbb{L}_{1:3}$  to determine whether PFC neurons that preferred the ipsilateral versus contralateral visual hemifield were separable in the latent space.

### 3.3.6 Spiking network simulations

Layer 1 of our spiking network model represents two inputs from V4, encoding both the left ( $L$ ) and right ( $R$ ) visual hemifield. The neural activity of each model V4 hemifield was simulated as a doubly-stochastic process. V4 neurons with a given hemifield preference  $h \in L, R$  shared a rank 1 fluctuation generated by the Ornstein-Uhlenbeck (OU) process

$$\tau \frac{d\lambda_h}{dt} = \bar{\lambda} - \lambda_h + \sqrt{\sigma^2 \tau} \xi_h(t), \quad (3.5)$$

where  $\lambda_h$  is the shared firing rate of hemifield  $h$ ,  $\bar{\lambda}$  is the baseline firing rate of that hemifield,  $\xi_h(t)$  is the hemifield's shared white noise process, and  $\tau$  and  $\sigma$  are the timescale and amplitude of the shared fluctuations, respectively. Each neuron  $i$  in hemifield  $h$  then emitted spikes according to the Poisson process

$$v_{i_h}(t) \sim \text{Pois}(\lambda_h) \quad (3.6)$$

Each V4 hemifield consisted of  $N_L^{\text{FF}} = 2000$  excitatory neurons preferring the left visual hemifield and  $N_R^{\text{FF}} = 2000$  excitatory neurons preferring the right visual hemifield, where the superscript FF denotes that these neurons make only feedforward projections.

Layer 2 of our model represents PFC and consists of excitatory ( $E$ ) and inhibitory ( $I$ ) populations of  $N_E^{\text{Rec}} = 4000$  and  $N_I^{\text{Rec}} = 1000$  neurons, respectively, where the superscript Rec denotes that these neurons make recurrent connections. Each Layer 2 neuron was modeled as a leaky integrate-and-fire unit obeying membrane potential dynamics given by:

$$\dot{V} = \frac{1}{\tau_{\text{mem}}} (\mu - V) + I_{\text{syn}}(t). \quad (3.7)$$

Neurons emit spikes when they reach the voltage threshold  $V_{th} = 1$  in our non-dimensionalized units, at which time they are reset to  $V_{re} = 0$  for an absolute refractory period of 5 ms. All other parameter values are specified in Table 3.1.

Synaptic currents were modeled as differences of exponentials according to the equation:

$$F^\beta(t) = \frac{H(t)}{\tau_2 - \tau_1} \left( e^{-t/\tau_1} - e^{-t/\tau_2} \right), \quad (3.8)$$

where synaptic timescale parameters are provided in Table 3.1. Here  $H(t)$  is a Heaviside function and a pre-synaptic spike occurred at time  $t = 0$ .

The uncoupled network analyzed in Figure 3.3 consisted exclusively of feedforward projections from Layer 1 to Layer 2. The total synaptic input to Layer 2 neuron  $i$  of cell type  $\alpha \in \{E, I\}$  was then:

$$I_{i,\text{syn}}^\alpha(t) = \sum_j J_{ij}^{\text{FF}} F^{\text{FF}} * v_j^{\text{FF}}(t), \quad (3.9)$$

$J_{ij}^{\text{FF}}$  is the strength of the synaptic projections from neuron  $j$  in the feedforward population to neuron  $i$  in population  $\alpha$ ,  $F^{\text{FF}}$  is the synaptic filter for projections from neurons in the feedforward population,  $*$  denotes convolution, and  $v_j^{\text{FF}}(t) = \sum_k \delta(t - t_{jk})$  is the spike train of neuron  $j$  in population the feedforward population ( $t_{jk}$  is the  $k^{\text{th}}$  spike time from neuron  $j$ ).

Connection probabilities  $p^{\alpha\text{FF}}$  from neurons in the feedforward layer to neurons in the recurrent population were  $p^{E\text{FF}} = 0.2$  and  $p^{I\text{FF}} = 0.5$ , respectively. Importantly, every neuron in Layer 2 was assigned a preference for the left or right visual hemifield, and Layer 1 neurons projected

exclusively to Layer 2 neurons preferring their same visual hemifield. That is,  $p^{\alpha_{h^{\text{Rec}}} \text{FF}_h} = p^{\alpha \text{FF}}$  when  $h^{\text{Rec}} = h$  for  $\{h^{\text{Rec}}, h\} \in \{L, R\}$  and  $p^{\alpha_{h^{\text{Rec}}} \text{FF}_h} = 0$  when  $h^{\text{Rec}} \neq h$ . If a connection from neuron  $j$  in the feedforward population to neuron  $i$  in population  $\alpha$  existed,  $J_{ij}^{\alpha \text{FF}} = J^{\alpha \text{FF}}$ ; otherwise  $J_{ij}^{\alpha \text{FF}} = 0$ . Synaptic strengths  $J_{ij}^{\alpha \text{FF}}$  for a strongly coupled network are provided in Table 3.1. These synaptic strengths are proportional to  $1/\sqrt{K}$  where  $K = p^{\alpha \text{FF}} N_\alpha^{\text{Rec}}$ . Linear response theory for the weakly coupled network (Methods 3.3.9.2) assumes synaptic strengths proportional to  $1/K$ . Synaptic strengths describe the postsynaptic target's membrane potential deflection, neglecting leak, in the non-dimensional units of Eq. (3.7).

In Figures 3.4-3.6, we model Layer 2 of our network with recurrent connections. With the inclusion of these recurrent interactions, the total synaptic input to Layer 2 neuron  $i$  in population  $\alpha$  is:

$$I_{i,syn}^\alpha(t) = \sum_j J_{ij}^{\text{FF}} F^{\text{FF}} * v_j^{\text{FF}}(t) + \sum_{k\beta} J_{ik}^{\alpha\beta} F^\beta * s_k^\beta(t), \quad (3.10)$$

where  $\alpha, \beta \in \{E, I\}$ ,  $J_{ik}^{\alpha\beta}$  is the strength of the synaptic projections from recurrent layer neuron  $k$  in population  $\beta$  to recurrent layer neuron  $i$  in population  $\alpha$ ,  $F^\beta$  is the synaptic filter for projections from neurons in recurrent population  $\beta$ , and  $s_k^\beta(t)$  is the spike train of neuron  $k$  in recurrent population  $\beta$ , consisting of  $\delta$  functions at each spike emission time.

Connection probabilities  $p^{\alpha\beta}$  from neurons in the recurrent population  $\beta$  to neurons in the recurrent population  $\alpha$  were  $p^{EE} = 0.2$  and  $p^{EI} = p^{IE} = p^{II} = 0.5$ . If a connection from neuron  $k$  in population  $\beta$  to neuron  $i$  in population  $\alpha$  existed,  $J_{ik}^{\alpha\beta} = J^{\alpha\beta}$  in the uniformly connected recurrent network. In networks with clustered architecture, each recurrent layer neuron  $i, j$  was assigned membership to an assembly based on hemifield preference  $h^{\text{Rec}}$ . The ratio  $R$  dictated the gain on synaptic strengths of two neurons in the same assembly. See the Results section for further information on tuned assemblies.  $J_{ik}^{\alpha\beta} = 0$  when there was no connection from neuron  $k$  to neuron  $i$ . All synaptic strengths  $J_{ik}^{\alpha\beta}$  for a strongly coupled network are provided in Table 3.1. These synaptic strengths are proportional to  $1/\sqrt{K}$  where  $K = p^{\alpha\beta} N_\alpha^{\text{Rec}}$ . Linear response theory for the weakly coupled network (Methods 3.3.9.2) assumes synaptic strengths proportional to  $1/K$ . Synaptic strengths describe the postsynaptic target's membrane potential deflection, neglecting leak, in the non-dimensional units of Eq. (3.7). All spiking network simulations were performed using Euler integration with a 0.1 ms timestep.

Symbol	Description	Value
$N^{\text{FF}}$	Number of feedforward (E) neurons	4,000
$N_E^{\text{Rec}}$	Number of E neurons, recurrent layer	4,000
$N_I^{\text{Rec}}$	Number of I neurons, recurrent layer	1,000
$p^{\text{EFF}}$	Connection probability, feedforward to E	0.2
$p^{\text{IFF}}$	Connection probability, feedforward to I	0.5
$p^{EE}$	Recurrent connection probability, E to E	0.2
$p^{IE}$	Recurrent connection probability, E to I	0.5
$p^{EI}$	Recurrent connection probability, I to E	0.5
$p^{II}$	Recurrent connection probability, I to I	0.5
$\bar{\lambda}$	baseline firing rate of feedforward neurons	4 Hz
$\tau_\lambda$	timescale of input fluctuations	60 ms
$\sigma$	amplitude of input fluctuations	0-2.4 Hz
$\mu_{\text{Rec}}^E$	membrane potential bias, E neurons, recurrent coupling	1.1-1.2
$\mu_{\text{Rec}}^I$	membrane potential bias, I neurons, recurrent coupling	1.0-1.05
$\mu_{\text{Uncoupled}}^E$	membrane potential bias, E neurons, uncoupled network	-1.1
$\mu_{\text{Uncoupled}}^I$	membrane potential bias, I neurons, uncoupled network	-1.0
$\tau_{\text{mem}}^E$	membrane time constant, E neurons	15 ms
$\tau_{\text{mem}}^I$	membrane time constant, E neurons	10 ms
$\tau_1^E$	Rise time for E synapses	1 ms
$\tau_2^E$	Decay time for E synapses	3 ms
$\tau_1^I$	Rise time for I synapses	1 ms
$\tau_2^I$	Decay time for I synapses	2 ms
$J^{\text{EFF}}$	feedforward to E synaptic weight	0.0707
$J^{\text{IFF}}$	feedforward to I synaptic weight	0.0354
$J^{EE}$	E to E synaptic weight, recurrent layer, unclustered	0.0236
$J^{IE}$	E to I synaptic weight, recurrent layer, unclustered	0.0141
$J^{EI}$	I to E synaptic weight, recurrent layer, unclustered	-0.0453
$J^{II}$	I to I synaptic weight, recurrent layer, unclustered	-0.0566
$R$	recurrent clustering strength	1-2.5

Table 3.1: Spiking network parameters

### 3.3.7 Visualizing clustering

Visualizations of each network architecture in Figure 3.4 were performed on subsets of 250 neurons, sampled uniformly across all populations, using network visualization software Gephi [137]. Network nodes were visually distributed according to the strength of synaptic connections between neurons using Gephi’s implementation of the Fruchterman-Reingold force-directed algorithm [138].

### 3.3.8 Variance of model V4 activity

Model V4 neurons in each hemifield were correlated through a common OU process as described by Eq. (3.5). The covariance of V4 activity across both hemifields is then

$$V = \begin{bmatrix} & & \\ & V_L & 0 \\ \hline & & \\ 0 & & V_R \end{bmatrix}, \quad (3.11)$$

where the matrix has block structure because spiking activity between the left and right V4 hemifields is uncorrelated.

The covariance of each visual hemifield  $V_h$  for  $h \in \{L, R\}$  is:

$$\begin{aligned} V_h &= \text{Cov}(v_h^{\text{FF}}, v_h^{\text{FF}}) \\ &= \begin{bmatrix} \bar{\lambda} + \frac{\sigma^2}{2} & \frac{\sigma^2}{2} \\ \ddots & \ddots \\ \frac{\sigma^2}{2} & \bar{\lambda} + \frac{\sigma^2}{2} \end{bmatrix}, \end{aligned} \quad (3.12)$$

which is the variance of the stationary solution to the OU process described by Eq. (3.5).

### 3.3.9 Linear response approximations of model PFC shared variance

Linear approximations of our network dynamics assume that a recurrent neuron  $i$  linearly transforms its synaptic inputs to emit spiking response  $y_i(t)$ . See Appendix B for a more detailed review of the assumptions underlying this ansatz.

#### 3.3.9.1 Uncoupled Network

When Layer 2 is uncoupled, the firing response of each neuron  $i$  has the linear approximation:

$$y_i^\alpha(t) \approx G_i^\alpha \left( \sum_j J_{ij}^{\text{FF}} F^{\text{FF}}(t) * v_j^{\text{FF}}(t) \right), \quad (3.13)$$

where  $v_j^{\text{FF}}(t)$  is the firing response of a feedforward neuron that projects to  $y_i^\alpha(t)$ ,  $J_{ij}^{\alpha\text{FF}}$  is the strength of synaptic connection from neuron  $j$  in population FF to neuron  $i$  in population  $\alpha$  (see Eq. (3.9)),  $F^{\text{FF}}(t)$  is the synaptic filter (see Eq. (3.8)), and  $G_i^\alpha$  is the gain of neuron  $i$  in population  $\alpha$ , which quantifies its sensitivity to its inputs. We remark that Eq. (3.13) is only valid under an expectation, and when the system is observed at sufficient long time windows [120, 139] (See Appendix B). Under the second stated assumption, we need only consider the effects of the synaptic filter  $F^{\text{FF}}(t)$  integrated over all time:

$$\begin{aligned} y_i^\alpha(t) &\approx G_i^\alpha \int_0^\infty F^{\text{FF}}(t) dt \left( \sum_j J_{ij}^{\text{FF}} v_j^{\text{FF}}(t) \right) \\ &\approx G_i^\alpha \left( \sum_j J_{ij}^{\text{FF}} v_j^{\text{FF}}(t) \right) \end{aligned} \quad (3.14)$$

We chose the form of  $F^{\text{FF}}(t)$  such that synaptic filter effects integrated to 1 (see Eq. (3.8)).

Using this linear approximation, the covariance of Layer 2 activity due to feedforward inputs is:

$$\begin{aligned} C_y &\approx \text{Cov}(\vec{y}, \vec{y}) \\ &\approx G J^{\text{FF}} V (G J^{\text{FF}})^\top, \end{aligned} \quad (3.15)$$

where  $\vec{y}$  is the firing responses of all Layer 2 neurons,  $V$  is the shared variance of V4 activity (3.11),  $J^{\text{FF}}$  is the full feedforward connectivity matrix, and  $G$  is a diagonal matrix of all Layer 2 neuron gains. When we apply this linear response theory to our simulated data, we observe our network and compute spike count covariance statistics over a 50 ms time window. Though this breaks the previously stated condition that we observe our system over infinitely long time windows, we make the assumption that 50 ms is a sufficiently long observation period such that our network's trial averaged responses resemble those to static inputs and not to time-varying signals (see Appendix B).

Each entry of matrix  $C_y$  represents the covariance of a pair of Layer 2  $E$  neurons,  $i$  and  $k$ , which inherit correlations from two feedforward mechanisms according to

$$C_{y_{ik}} = (J^{\text{EFF}})^2 \left( N p^2 \left( \bar{\lambda} + \frac{\sigma^2}{2} \right) + N^2 p \left( \frac{\sigma^2}{2} \right) \right), \quad (3.16)$$

where  $J^{\text{EFF}}$  is the connection strength of projections from V4 neurons to Layer 2  $E$  neurons,  $p$  is the probability of connection for projections from V4 neurons to Layer 2  $E$  neurons,  $N$  is the total number of Layer 2  $E$  neurons, and  $\bar{\lambda}$  and  $\sigma^2/2$  are the mean rate and fluctuation amplitude of the OU process underlying V4 spiking activity, respectively (3.5). The first term on the right hand side of Eq. (3.16) represents common projections that the Layer 2 neuron pair receives from the same V4 neuron. The second term of Eq. (3.16) represents projections that the Layer 2 neuron pair receives from two (or more) different V4 neurons preferring the same visual hemifield, whose spiking activity is correlated through the underlying OU process (3.5). Recalling that synaptic connectivity strengths  $J^{\text{FF}}$  scale according to the balanced network condition such that  $J^{\text{FF}} \propto 1/\sqrt{N}$  [62], it becomes evident that each of the two feedforward mechanisms of correlation scales as

$$C_{y_{ik}} \propto \underbrace{p^2 \left( \bar{\lambda} + \frac{\sigma^2}{2} \right)}_{\mathcal{O}(1)} + \underbrace{N p \left( \frac{\sigma^2}{2} \right)}_{\mathcal{O}(N)}. \quad (3.17)$$

In the large  $N$  limit of neurons, correlations due to common projections (term 1) are negligible as compared to correlations arising from the spike count covariance of V4 activity (term 2). It is thus the shared variance, or off-diagonal terms of  $V$  (3.12) that predominantly contribute to

$C_y$  in Equation (3.15). Defining the shared variance of  $V$  as

$$V_h^{\text{shared}} = \begin{bmatrix} 0 & \frac{\sigma^2}{2} \\ & \ddots \\ \frac{\sigma^2}{2} & 0 \end{bmatrix}$$

$$V^{\text{shared}} = \begin{bmatrix} V_L^{\text{shared}} & 0 \\ \hline 0 & V_R^{\text{shared}} \end{bmatrix}, \quad (3.18)$$

the shared variance of Layer 2 activity is approximately

$$C_y \approx G J^{\text{FF}} V^{\text{shared}} (G J^{\text{FF}})^\top, \quad (3.19)$$

in the large  $N$  limit.

Notably, the rank of  $V^{\text{shared}}$  is 2. (Each block  $V_h^{\text{shared}}$  for  $h \in \{L, R\}$  is rank 1.) The rank of Layer 2 shared variance  $C_y$  is thus restricted by the rank of  $V^{\text{shared}}$  through the Frobenius Inequality:

$$\begin{aligned} \text{rank}(C_y) &\leq \min \left( \text{rank}(G), \text{rank}(J^{\text{FF}}), \text{rank}(V^{\text{shared}}) \right) \\ &\leq \text{rank}(V^{\text{shared}}) \\ &\leq 2. \end{aligned} \quad (3.20)$$

### 3.3.9.2 Recurrent Network

Linear response theory can be applied to recurrent networks so long as a single neuron's spiking response still scales linearly with sum of its synaptic inputs. This implies that neurons in the recurrent network are weakly coupled, such that it takes many inputs to one neuron to produce

spiking activity in that neuron. Under these conditions, the linear approximation of Layer 2 neuron  $i$ 's firing response is the scaled sum of its inputs from both feedforward projections and recurrent interactions:

$$y_i^\alpha(t) \approx G_i^\alpha \left( \sum_j J_{ij}^{\alpha\text{FF}} F^{\text{FF}}(t) * v_j^{\text{FF}}(t) + \sum_{k\beta} J_{ik}^{\alpha\beta} F^\beta(t) * y_k^\beta(t) \right), \quad (3.21)$$

where  $y_k^\beta(t)$  is the firing response of a neuron  $k$  from recurrent population  $\beta$  that projects to neuron  $i$  from recurrent population  $\alpha$ ,  $J_{ik}^{\alpha\beta}$  is the strength of synaptic connection from neuron  $k$  in recurrent population  $\beta$  to neuron  $i$  in recurrent population  $\alpha$ ,  $F^\beta(t)$  is the synaptic filter of that connection (see Eq. (3.10)), and all other terms were included in our uncoupled linear approximation in Eq. (3.13). We showed previously that we need only consider the effect of our synaptic filter integrated over all time, and that our synaptic filter integrates to 1 (Eq. (3.14)). Eq. (3.21) therefore reduces to

$$y_i^\alpha(t) \approx G_i^\alpha \left( \sum_j J_{ij}^{\alpha\text{FF}} v_j^{\text{FF}}(t) + \sum_{k\beta} J_{ik}^{\alpha\beta} y_k^\beta(t) \right). \quad (3.22)$$

The shared variance of Layer 2 activity is then the shared variance of our network in the absence of coupling (3.19) filtered through our recurrent interactions such that:

$$\begin{aligned} C_y &\approx \text{Cov}(\vec{y}, \vec{y}) \\ &\approx (\mathbb{I} - GJ^{\text{Rec}})^{-1} GJ^{\text{FF}} V^{\text{shared}} (GJ^{\text{FF}})^\top (\mathbb{I} - (GJ^{\text{Rec}})^\top)^{-1}, \end{aligned} \quad (3.23)$$

where  $J^{\text{Rec}}$  is the full recurrent connectivity matrix in which each element is  $J_{ik}^{\alpha\beta}$  and all other terms are taken from the definition of Layer 2 shared variance in the absence of coupling (3.19).

Notably, the rank of Layer 2 shared variance  $C_y$  is still bound by the rank of  $V^{\text{shared}}$  through the Frobenius Inequality:

$$\begin{aligned} \text{rank}(C_y) &\leq \min \left( \text{rank}(G), \text{rank}(J^{\text{FF}}), \text{rank}(J^{\text{Rec}}), \text{rank}(V^{\text{shared}}) \right) \\ &\leq \text{rank}(V^{\text{shared}}) \\ &\leq 2. \end{aligned} \quad (3.24)$$

### 3.3.10 Mathematical analysis of correlated and asynchronous states in recurrent networks

This section aims to provide a theory linking our recurrent network's degree of clustering to shifts between strongly correlated/anti-correlated, multi-stable dynamics and balanced network dynamics. We now outline derivations from Rosenbaum et al. [72] and Baker et al. [140] and explain their novel relevance to our own, clustered network architectures.

#### 3.3.10.1 Cross-spectral density as a measure of co-variability

In the derivations that follow, we will use the cross-spectral density (CSD) to measure co-variability, defined as:

$$\langle U, Z \rangle(f) = \int_{-\infty}^{\infty} C_{UZ}(\tau) e^{-2\pi i f \tau} d\tau, \quad (3.25)$$

where

$$C_{UZ}(\tau) = \text{Cov}(U(t), Z(t + \tau)) \quad (3.26)$$

is the cross-covariance of  $U$  and  $Z$ . The CSD will simplify our co-variability calculations because many commonly used co-variability measures can be expressed as functions of the CSD. Note that cross-covariance (3.26) is the inverse Fourier transform of the CSD. Additionally, when we express spike count as the integral of a spike train over interval  $[t, \Delta t]$  as in (3.1), we note that spike count covariances over long windows ( $\Delta t \rightarrow \infty$ ) can be expressed as the zero-frequency CSD:

$$\lim_{\Delta t \rightarrow \infty} \frac{1}{\Delta t} \text{Cov} \left( \int_t^{\Delta t} U(t') dt' \int_t^{\Delta t} Z(t') dt' \right) = \langle U, Z \rangle(f = 0). \quad (3.27)$$

The spike count covariance between neurons  $i$  and  $j$  can then be approximated (for large  $\Delta t$ ) as:

$$\text{Cov}(N_i(t, t + \Delta t), N_j(t, t + \Delta t)) \approx \Delta t \langle y_i(t'), y_j(t') \rangle(f = 0) \quad (3.28)$$

### 3.3.10.2 Balance conditions for strongly coupled recurrent networks with disjoint inputs

We define the population averaged cross-spectral matrix of input currents  $I_{\text{syn}}$ :

$$\langle I_{\text{syn}}, I_{\text{syn}} \rangle = \begin{bmatrix} \langle I_{\text{syn}}^E, I_{\text{syn}}^E \rangle & \langle I_{\text{syn}}^E, I_{\text{syn}}^I \rangle \\ \langle I_{\text{syn}}^I, I_{\text{syn}}^E \rangle & \langle I_{\text{syn}}^I, I_{\text{syn}}^I \rangle \end{bmatrix}, \quad (3.29)$$

where

$$\langle I_{\text{syn}}^\alpha, I_{\text{syn}}^\beta \rangle = \mathbb{E}_{i,k} \left( \langle I_{\text{syn}_i}^\alpha, I_{\text{syn}_k}^\beta \rangle \right) \quad (3.30)$$

is the expectation over pairwise CSDs between the total input current to recurrent layer neuron  $i$  from population  $\alpha$  and recurrent layer neuron  $k$  from population  $\beta$  where  $\{\alpha, \beta\} \in \{E, I\}$ . Pairwise CSDs where  $i = k$  and  $\alpha = \beta$  are excluded from this expectation. We similarly define  $\langle \text{FF}, \text{FF} \rangle$  and  $\langle \vec{y}, \vec{y} \rangle$  as the 2 x 2 population averaged cross-spectral matrices of feedforward inputs FF and recurrent layer spiking activity  $\vec{y}$ , respectively. The asynchronous state, in which excitatory activity is balanced by inhibitory activity in the recurrent layer, is defined by the scaling laws:

$$\langle I_{\text{syn}}, I_{\text{syn}} \rangle, \langle \vec{y}, \vec{y} \rangle \propto \mathcal{O}(1/N) \quad (3.31)$$

$$\langle I_{\text{syn}}, \text{FF} \rangle, \langle \vec{y}, \text{FF} \rangle \propto \mathcal{O}(1/\sqrt{N}) \quad (3.32)$$

The population averaged cross-spectral matrix of input currents  $I_{\text{syn}}$  can then be restated in terms of FF and  $\vec{y}$  such that

$$\langle I_{\text{syn}}, I_{\text{syn}} \rangle = \langle \text{FF}, \text{FF} \rangle + \sqrt{N} (J_{\text{Rec}} \langle \vec{y}, \text{FF} \rangle + \langle \text{FF}, \vec{y} \rangle J_{\text{Rec}}^*) + N J_{\text{Rec}} \langle \vec{y}, \vec{y} \rangle J_{\text{Rec}}^* + J_{\text{Rec}} A J_{\text{Rec}}^* + \mathcal{O}(1/\sqrt{N}), \quad (3.33)$$

where  $J^{\text{Rec}}$  is the recurrent connectivity matrix first defined in ,  $*$  denotes a conjugate transpose, and  $A$  is defined as

$$A(f) = \begin{bmatrix} A^E(f)/q^E & 0 \\ 0 & A^I(f)/q^I \end{bmatrix}, \quad (3.34)$$

where

$$A^\alpha(f) = \mathbb{E}_k \langle y_k^\alpha(t), y_k^\alpha(t) \rangle \quad (3.35)$$

is the expectation over the power spectral densities of recurrent spiking activity from each neuron  $k$  from population  $\alpha = \{E, I\}$  and  $q^\alpha$  is the proportion of neurons that belong to population  $\alpha$ . The  $\mathcal{O}(1/\sqrt{N})$  term in (3.33) represents the diagonal elements omitted from  $\langle \vec{y}, \text{FF} \rangle$ .

The asynchronous state condition (3.32) necessitates

$$\sqrt{N} J_{\text{Rec}} \langle \vec{y}, \text{FF} \rangle = \sqrt{N} \langle \text{FF}, \vec{y} \rangle J_{\text{Rec}}^* = -\langle \text{FF}, \text{FF} \rangle + \mathcal{O}(1/\sqrt{N}). \quad (3.36)$$

Equation (3.33) can then be simplified to

$$\langle I_{\text{syn}}, I_{\text{syn}} \rangle \propto -\langle \text{FF}, \text{FF} \rangle + N J_{\text{Rec}} \langle \vec{y}, \vec{y} \rangle J_{\text{Rec}}^* + J_{\text{Rec}} A J_{\text{Rec}}^*. \quad (3.37)$$

We invoke the assumption that each neuron  $i$ 's conversion of synaptic input  $I_{\text{syn}_i}$  to spiking activity  $y_i(t)$  is  $\mathcal{O}(1)$  such that

$$\langle I_{\text{syn}}, I_{\text{syn}} \rangle \propto \langle \vec{y}, \vec{y} \rangle. \quad (3.38)$$

Combining (3.37) and (3.38):

$$\langle \vec{y}, \vec{y} \rangle \propto -\langle \text{FF}, \text{FF} \rangle + N J_{\text{Rec}} \langle \vec{y}, \vec{y} \rangle J_{\text{Rec}}^* + J_{\text{Rec}} A J_{\text{Rec}}^*. \quad (3.39)$$

This apparent inconsistency can be resolved using the asynchronous state requirement  $\langle \vec{y}, \vec{y} \rangle \propto \mathcal{O}(1/N)$  (3.31). The right hand side of (3.39) then cancels such that:

$$\lim_{N \rightarrow \infty} N J_{\text{Rec}} \langle \vec{y}, \vec{y} \rangle J_{\text{Rec}}^* = \langle \text{FF}, \text{FF} \rangle - J_{\text{Rec}} A J_{\text{Rec}}^*. \quad (3.40)$$

The asymptotic scaling of spike count correlations in the asynchronous state is then

$$\lim_{N \rightarrow \infty} N \langle \vec{y}, \vec{y} \rangle = (J_{\text{Rec}})^{-1} \langle \text{FF}, \text{FF} \rangle (J_{\text{Rec}}^*)^{-1} - A. \quad (3.41)$$

Notably one of two conditions must be satisfied to obey these asynchronous state requirements. For (3.41) to be satisfied,  $J_{\text{Rec}}$  must be invertible. Alternatively (if  $J_{\text{Rec}}$  is singular), (3.40) can be satisfied if  $\langle \text{FF}, \text{FF} \rangle$  is in the column space of  $A \mapsto J_{\text{Rec}} A J_{\text{Rec}}^*$ .

In our network, every recurrent layer cell is assigned a preference for the left ( $L$ ) or right ( $R$ ) visual hemifield, corresponding to whether that neuron receives feedforward inputs from

left or right V4. The full recurrent connectivity matrix is then

$$J_{\text{Rec}} = \begin{bmatrix} J^{E_L E_L} & J^{E_L E_R} & J^{E_L I_L} & J^{E_L I_R} \\ J^{E_R E_L} & J^{E_R E_R} & J^{E_R I_L} & J^{E_R I_R} \\ J^{I_L E_L} & J^{I_L E_R} & J^{I_L I_L} & J^{I_L I_R} \\ J^{I_R E_L} & J^{I_R E_R} & J^{I_R I_L} & J^{I_R I_R} \end{bmatrix} \quad (3.42)$$

In the network with uniform recurrent connectivity,  $J^{E_h E_{h'}} = J^{EE}$ ,  $J^{I_h I_{h'}} = J^{II}$ ,  $J^{I_h E_{h'}} = J^{IE}$ , and  $J^{E_h I_{h'}} = J^{EI}$  for  $\{h, h'\} \in \{L, R\}$ . Thus,  $J_{\text{Rec}}$  is singular.

Moreover, the symmetry of our network with uniform recurrent connectivity implies that the average power spectral density is the same for populations  $E_L$  and  $E_R$ , as well as for populations  $I_L$  and  $I_R$ . Therefore,

$$A(f) = \begin{bmatrix} A^{E_L}(f)/q^{E_L} & 0 & 0 & 0 \\ 0 & A^{E_R}(f)/q^{E_R} & 0 & 0 \\ 0 & 0 & A^{I_L}(f)/q^{I_L} & 0 \\ 0 & 0 & 0 & A^{I_R}(f)/q^{I_R} \end{bmatrix} \quad (3.43)$$

where  $A^{\alpha_h}$  is the average CSD of neurons in population  $\alpha_h$  and  $q^{\alpha_h}$  is the proportion of neurons in population  $\alpha_h$  for  $\alpha \in \{E, I\}$  and  $h \in \{L, R\}$ .

To determine whether  $\langle \text{FF}, \text{FF} \rangle$  is in the column space of  $A \mapsto J_{\text{Rec}} A J_{\text{Rec}}^*$ , and subsequently, whether the asynchronous state is possible, we need to more closely examine the structure of  $\langle \text{FF}, \text{FF} \rangle$ . The average CSD from feedforward inputs  $\langle \text{FF}, \text{FF} \rangle$  will be due to both spike count correlations between neurons in the V4 afferent populations and correlations owing to common projections from V4 to PFC. We reference the derivations in Baker et al. [140] and define the CSD due to feedforward inputs between recurrent neuron  $i$  and recurrent neuron  $k$  as

$$\langle \text{FF}_i^\alpha, \text{FF}_k^\beta \rangle = \left\langle \sum_j J_{ij}^{\alpha \text{FF}} (F^{\text{FF}} * v_j^{\text{FF}}(t)), \sum_{j'} J_{kj'}^{\beta \text{FF}} (F^{\text{FF}} * v_{j'}^{\text{FF}}(t)) \right\rangle \quad (3.44)$$

where  $v_j^{\text{FF}}(t)$  is the spike train of feedforward neuron  $j$ ,  $v_{j'}^{\text{FF}}(t)$  is the spike train of feedforward neuron  $j'$ ,  $J_{ij}^{\alpha \text{FF}}$  is the strength of projection from neuron  $j$  to recurrent neuron  $i$  of cell type

$\alpha \in \{E, I\}$ ,  $J_{kj'}^{\beta FF}$  is the strength of projection from neuron  $j'$  to recurrent neuron  $k$  of cell type  $\beta \in \{E, I\}$ , and  $F^{FF}$  is the post-synaptic current waveform. The mean-field CSD due to feedforward inputs is then

$$\langle FF, FF \rangle = \underbrace{N J_{FF} \langle \vec{v}_{FF}, \vec{v}_{FF} \rangle J_{FF}^*}_{\mathcal{O}(N)} + \underbrace{q_{FF}^{-1} J_{FF} r_{FF} J_{FF}^* - q_{FF}^{-1} J_{FF} \langle \vec{v}_{FF}, \vec{v}_{FF} \rangle J_{FF}^*}_{\mathcal{O}(1)}, \quad (3.45)$$

where  $\langle \vec{v}_{FF}, \vec{v}_{FF} \rangle$  describes spike count correlations between neurons in the feedforward layer,  $J_{FF}$  is the full feedforward connectivity matrix,  $q_{FF}$  is the proportion of neurons belonging to the feedforward layer, and  $U^*$  denotes the conjugate transpose of  $U$ . Note that the first term on the right hand side of Eq. (3.45), which scales according to  $\mathcal{O}(N)$ , represents feedforward correlations inherited through the spike count correlations in V4 activity. The second term of Eq. (3.45), which scales according to  $\mathcal{O}(1)$ , represents feedforward correlations inherited through common projections from the same V4 neuron to a Layer 2 neuron pair. These two mechanisms of feedforward correlation correspond exactly to those expressed in Eq. (3.16), our time-domain expression of the Layer 2 covariance owing to feedforward input.

For a network with feedforward correlations owing exclusively to shared projections from V4,  $\langle \vec{v}_{FF}, \vec{v}_{FF} \rangle = 0$ . This corresponds to  $\sigma = 0$  from Figure 3.4. The mean-field CSD due to feedforward inputs is then reduced to

$$\langle FF, FF \rangle = q_{FF}^{-1} J_{FF} r_{FF} J_{FF}^*. \quad (3.46)$$

Notably,  $\langle FF, FF \rangle$  will inherit all of its structure from connectivity matrix  $J_{FF}$ . Because V4 neurons make disjoint projections to PFC neurons with their same visual hemifield preference,  $J_{FF}$  has the block structure

$$J_{FF} = \begin{bmatrix} J^{E_L FF_L} & 0 \\ J^{I_L FF_L} & 0 \\ 0 & J^{E_R FF_R} \\ 0 & J^{I_R FF_R} \end{bmatrix} \quad (3.47)$$

$\langle FF, FF \rangle$  will also have block structure, and cannot be in the column space of  $A \mapsto J_{\text{Rec}} A$ . By extension,  $\langle FF, FF \rangle$  cannot be in the column space of  $A \mapsto J_{\text{Rec}} A J_{\text{Rec}}^*$ . We therefore conclude that our network with disjoint V4 projections and uniform recurrent connectivity cannot achieve

the asynchronous state.

In the network with clustered recurrent connectivity reflecting hemifield tuning, our recurrent connectivity matrix  $J_{\text{Rec}}$  (3.42) changes such that  $J^{\alpha_h \beta_h} = R J^{\alpha_h \beta_{h'}}$  for  $\{\alpha, \beta\} \in \{E, I\}$  and  $\{h, h'\} \in \{L, R\}$ . Clustering therefore restores the asymmetry to  $J^{\text{Rec}}$  necessary to make it invertible, and the network with hemifield tuned assemblies can achieve the asynchronous state, even in the presence of disjoint inputs from V4 (Figure 3.4b, top left). Note that all our derivations in this section assume the large neuron limit ( $N^{\text{Rec}} \rightarrow \infty$ ). According to these derivations,  $J^{\text{Rec}}$  is either invertible and asynchrony is possible, or  $J^{\text{Rec}}$  is singular and asynchrony is impossible. In our neural activity simulated from a network with uncorrelated V4 activity ( $\sigma = 0$ ), the smooth transition from correlated recurrent activity to asynchrony that we observe as we increase  $R$  results from the finite size of our network simulations.

### 3.3.10.3 The correlated state

Our V4 neurons with a given visual hemifield preference  $h$  receive common fluctuations from the OU process described by Eq. (3.5). When  $\sigma > 0$  (Figure 3.4),  $\langle \vec{v}_{\text{FF}}, \vec{v}_{\text{FF}} \rangle > 0$ . In the large  $N$  limit of this *correlated state*, only the  $\mathcal{O}(N)$  correlations due to V4 spiking co-variability will have significant effect on  $\langle \text{FF}, \text{FF} \rangle$  (3.45), which in turn reduces to

$$\langle \text{FF}, \text{FF} \rangle \approx N J_{\text{FF}} \langle \vec{v}_{\text{FF}}, \vec{v}_{\text{FF}} \rangle J_{\text{FF}}^*. \quad (3.48)$$

Balance is achieved in the correlated state when  $\mathcal{O}(N)$  input correlations are reduced to  $\mathcal{O}(1)$  spike count correlations in Layer 2 activity such that

$$\langle \text{FF}, \text{FF} \rangle \propto \mathcal{O}(N) \quad (3.49)$$

$$\langle \vec{y}, \vec{y} \rangle \propto \mathcal{O}(1). \quad (3.50)$$

Using Equation (3.48), Equation (3.39) can then be restated as

$$\underbrace{\langle \vec{y}, \vec{y} \rangle}_{\mathcal{O}(1)} \propto N \left( \underbrace{J_{\text{Rec}} \langle \vec{y}, \vec{y} \rangle J_{\text{Rec}}^* - J_{\text{FF}} \langle \vec{v}_{\text{FF}}, \vec{v}_{\text{FF}} \rangle J_{\text{FF}}^*}_{\mathcal{O}(1/N)} \right) + \underbrace{J_{\text{Rec}} A J_{\text{Rec}}^*}_{\mathcal{O}(1)}, \quad (3.51)$$

where the parenthetical terms must scale according to  $\mathcal{O}(1/N)$  for self-consistency. Solving the parenthetical terms for  $\langle \vec{y}, \vec{y} \rangle$ , we find that Equation (3.51) is self-consistent if and only if  $J_{\text{Rec}}$  is invertible:

$$\langle \vec{y}, \vec{y} \rangle = (J_{\text{Rec}})^{-1} J_{\text{FF}} \langle \vec{v}_{\text{FF}}, \vec{v}_{\text{FF}} \rangle J_{\text{FF}}^* (J_{\text{Rec}}^*)^{-1} \quad (3.52)$$

Analogously to the previous section, uniform recurrent connectivity makes  $J_{\text{Rec}}$  singular, while clustered recurrent connectivity makes  $J_{\text{Rec}}$  invertible (3.42).

In conclusion, the asynchronous state can be restored in a network with uncorrelated, disjoint inputs by adding hemifield specific recurrent clustering. This makes the spatial scale of the inhibitory recurrent architecture commensurate to the spatial scale of each input, and allows the network to reduce  $\langle \text{FF}, \text{FF} \rangle \propto \mathcal{O}(1)$  correlations due to feedforward inputs to  $\langle \vec{y}, \vec{y} \rangle \propto \mathcal{O}(1/N)$  correlations in the recurrent layer. By analogous mechanisms, hemifield specific recurrent clustering is able to reduce  $\langle \text{FF}, \text{FF} \rangle \propto \mathcal{O}(N)$  feedforward correlations from correlated, disjoint inputs to  $\langle \vec{y}, \vec{y} \rangle \propto \mathcal{O}(1)$  correlations in the recurrent layer.

### 3.3.11 Partitioning model PFC activity into states

Our model networks with strong recurrent coupling and correlated, disjoint inputs exhibit multi-stable dynamics with alternating states of high firing activity from model PFC neurons preferring the left (State L) or right (State R) visual hemifield. To partition model PFC activity into State L or State R over time, we first projected each hemifield's population activity onto its mean activity and variance of activity over time. Let  $Y_h = \{y_{1_h}^E(t), \dots, y_{N_h}^E(t)\}$ , where  $y_{i_h}^E(t)$  is the vector of spike counts over time, binned in non-overlapping windows of  $\Delta t = 50$  ms, of excitatory neuron  $i$  in model PFC with visual hemifield preference  $h \in \{L, R\}$ .  $\mathcal{Y} = \{\langle Y_L \rangle, \text{Var}(Y_L), \langle Y_R \rangle, \text{Var}(Y_R)\}$  was then used as the feature matrix for State L versus State R classification by a Gaussian Mixture Model (GMM) [141], where angle brackets denote an expectation over PFC model neurons preferring hemifield  $h \in \{L, R\}$ . Note that a single observation of the feature matrix, which we will denote  $\mathcal{Y}_t$ , represents one timepoint of the original hemifield population activity. In brief, the GMM uses an Expectation-Maximization algorithm to learn without supervision  $p(z_{tS} = 1 | \mathcal{Y}_t)$ , or the probability that timepoint  $\mathcal{Y}_t$  belongs to the cluster of activity of representing  $S \in \{\text{State L, State R}\}$ , where that cluster of activity is modeled as multivariate Gaussian  $\mathcal{N}(\mu_S, \Sigma_S)$  in the feature space of  $\mathcal{Y}$ .  $\Sigma_S$  was constrained to be diagonal.

Each timepoint of neural activity  $\mathcal{Y}_t$  in which  $p(z_{\text{State L}} = 1 | \mathcal{Y}_t) > 0.97$  was assigned to State L. Each timepoint of neural activity  $\mathcal{Y}_t$  in which  $p(z_{\text{State R}} = 1 | \mathcal{Y}_t) > 0.97$  was assigned to State R. Remaining timepoints were considered to represent dynamics in which the neural activity was transitioning between the two states, and these timepoints were excluded from analyses on state partitions. State transitions never exceeded 20% of the total time over which we analyzed simulated network activity.

### 3.3.12 Factor Analysis of model PFC activity

We performed Factor Analysis (FA) (Appendix A) on the spike count activity of random subsets of 100 excitatory neurons from our PFC model simulations, sampled uniformly across hemifield preferences. Neurons whose firing rates were smaller than 1 Hz were excluded from analysis. Spike trains were binned in non-overlapping intervals of  $\Delta t = 50$  ms.

For factor analysis of state partitioned data (Figure 3.8), we began our state partitioning procedure described in Methods 3.3.11 with 220 network simulations per connectivity matrices realization of length 10 s per simulation. Population activity was in a single state  $S \in \{\text{State L}, \text{State R}\}$  for an average of 4.2 s per simulation. There were 20 non-overlapping sampling of neurons (10 sampling per realization of connectivity matrices, for 2 realizations of connectivity matrices). We applied FA on each sampling of neuron spike counts in state  $S \in \{\text{State L}, \text{State R}\}$ . FA was performed on non-state-partitioned activity by uniformly sampling network activity over both states  $S \in \{\text{State L}, \text{State R}\}$  and transition timepoints for the same total duration as the average time spent in a single state  $S$ .

### 3.3.13 Linear response fits to simulated PFC activity

We fit our linear response theory from Methods 3.3.9 to our simulated Layer 2 data. We recall that a neuron's gain  $G$  is simply the derivative of the neuron's frequency-current ( $f$ - $I$ ) curve evaluated at its steady-state firing rate. We computed the mean input current  $I_{syn_i}^{\alpha_h} = \mathbb{E}_t[I_{syn_i}^{\alpha_h}(t)]$  (3.9) and firing rate  $f_i^{\alpha_h} = \mathbb{E}_t[f_i^{\alpha_h}(t)]$  of each neuron  $i$  in a population  $\alpha_h$ , where  $\alpha \in \{E, I\}$  denotes cell type and  $h \in \{L, R\}$  denotes visual hemifield preference.

An  $f$ - $I$  curve for the mean activity of all neurons in population  $\alpha_h$  was then fit according to the piecewise regression model:

$$f_{\alpha_h} = \begin{cases} \beta_0 + \beta_1 I_{syn}^{\alpha_h} + \beta_2 (I_{syn}^{\alpha_h})^2, & I_{syn}^{\alpha_h} \leq \mathcal{I} \\ \beta_0 + \beta_1 I_{syn}^{\alpha_h}, & I_{syn}^{\alpha_h} > \mathcal{I} \end{cases} \quad (3.53)$$

Knot location  $\mathcal{I}$  was selected by comparing the cross-validated likelihood functions of models of the form (3.53) for varying values of  $\mathcal{I}$ . Once a mean-field  $f$ - $I$  curve was fitted for population  $\alpha_h$ , the gain of each neuron in the population was approximated by the derivative

$$\begin{aligned} G_{\alpha_h} &= \frac{df_{\alpha_h}}{dI_{syn}^{\alpha_h}} \\ &= \begin{cases} \beta_1 + 2\beta_2 (I_{syn}^{\alpha_h}), & I_{syn}^{\alpha_h} \leq \mathcal{I} \\ \beta_1, & I_{syn}^{\alpha_h} > \mathcal{I} \end{cases} \end{aligned} \quad (3.54)$$

evaluated at each neuron's mean firing rate.

These gains could then be used to compute a theoretical approximation of the full, pairwise covariance matrix of the network activity defined as  $C_y$ . We define the theoretical estimate of pairwise co-variability in the uncoupled network as  $C_y^{\text{Uncoupled}}$ , which was computed using Eq. (3.15). In the multi-stable network with strong recurrent coupling,  $C_y$  was computed according to Eq. (3.23) separately for State L and State R, where network activity was partitioned into states using the process described in Subsection 3.3.11. Linear response techniques provide accurate estimates of the pairwise co-variability of neural activity, but do not provide accurate estimates of each neuron's private variability [120]. We can re-write our state-partitioned linear response estimates of the network with strong recurrent coupling (3.23) as

$$\begin{aligned} C_y &= (\mathbb{I} - GJ^{\text{Rec}})^{-1} GJ^{\text{FF}} V(GJ^{\text{FF}})^\top (\mathbb{I} - (GJ^{\text{Rec}})^\top)^{-1} \\ &= (\mathbb{I} - GJ^{\text{Rec}})^{-1} C_y^0 (\mathbb{I} - (GJ^{\text{Rec}})^\top)^{-1}, \end{aligned} \quad (3.55)$$

where  $C_y^0$  is the theoretical estimate of the network's pairwise co-variability in the absence of recurrent coupling. While we could replace the entirety of  $C_y^0$  in this computation with the linear response estimate from our uncoupled network simulations  $C_y^{\text{Uncoupled}}$ , this would break

a key linear response assumption that each neuron has one, stationary gain  $G_i$  at the fixed point of our linearization. Instead, we make only the substitution

$$\text{diag}(C_y^0) = \text{diag}\left(C_y^{\text{Uncoupled}}\right) \quad (3.56)$$

to correct for linear response theory's flawed estimates of private neuronal variability.

## 3.4 Results

### 3.4.1 Characterizing variability in V4 and PFC

A non-human primate engaged in a memory-guided saccade (MSG) task in which a target was presented at one of forty locations in 2D screen space (Figure 3.1a). The primate had to make a saccade to the remembered location after a delay period. We analyzed simultaneous micro-electrode array recordings from visual area V4 and visually-responsive [142] integration area PFC during this distributed visual task. Single neuron responses in PFC during the task's delay period were spatially tuned, demonstrating specificity for both the angular location and radial eccentricity of our dense mapping of target space (Figure 3.1b). We distilled each PFC neuron's 2D spatial response profile to a single preferred location, computed as the center of mass (COM) of the neuron's receptive field (black Xes, Figure 3.1b,d). PFC neurons recorded across all sessions ( $N = 784$  total neurons, 19 recording sessions) exhibited preferences for a wide range of spatial eccentricities and radial locations that spanned the entire visual scene (Figure 3.1c-d). This is consistent with previous findings that PFC neurons show spatial tuning both contralateral and ipsilateral to the recorded hemisphere[143, 144, 142], owing to the converging projections that one PFC hemisphere receives from both hemispheres of upstream visual brain areas[145, 146, 147]. By contrast, V4 has retinotopic organization and only encodes visual information contralateral to the recorded hemisphere (Figure 3.1d)[148].

Having mapped V4 and PFC receptive fields, we sought to understand the coordinated population dynamics of both brain areas. We examined the structure of pairwise spike count co-variability that was not due to stimulus tuning. These shared fluctuations underlying trial-to-trial variability are commonly referred to as noise correlations (see [Methods](#)). Consistent with previous studies demonstrating spatially-dependent correlations [72], noise correlations

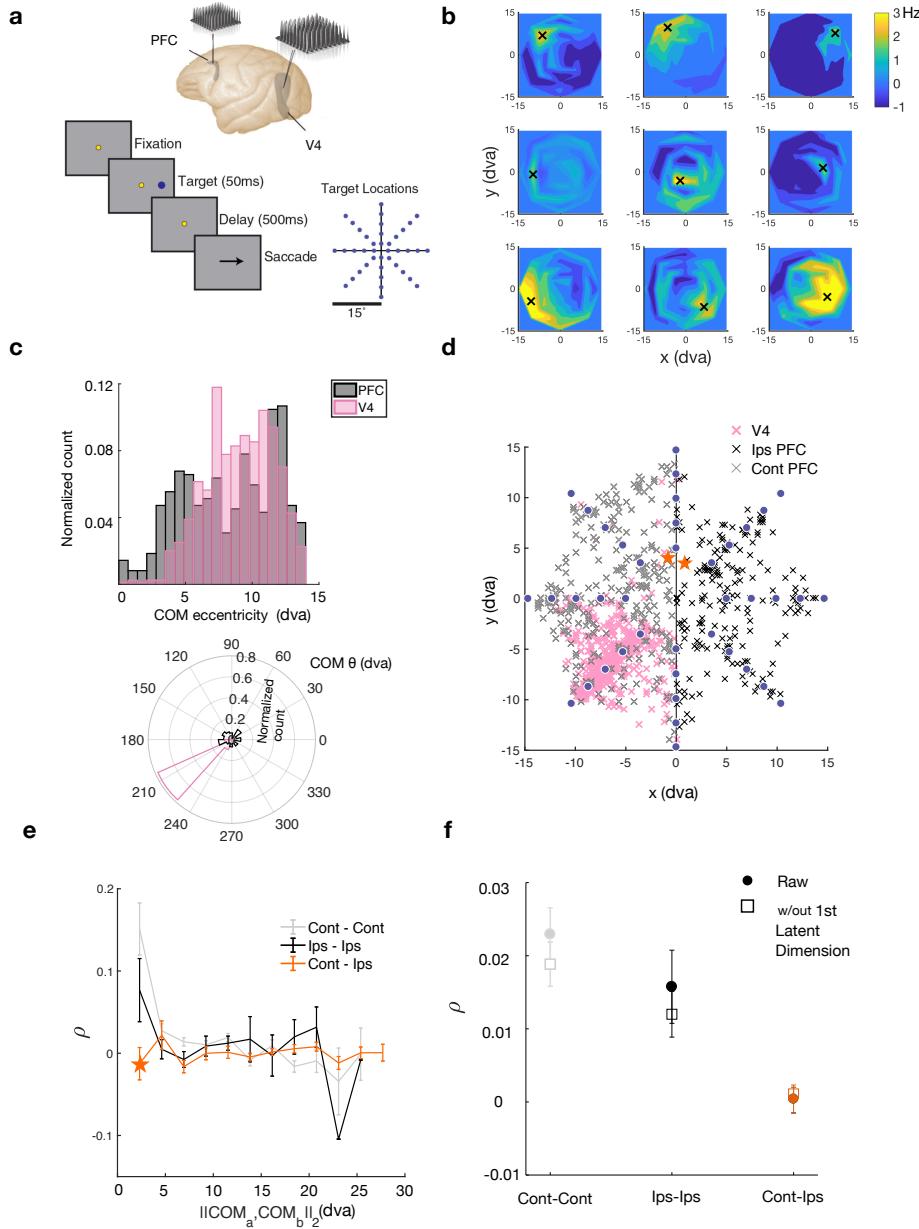


Figure 3.1: **(a)** Illustration of the visual task, in which a non-human primate made a saccade to a remembered target location in 2D space. Neural data were simultaneously recorded in V4 and PFC. **(b-d)**: Analysis of V4 and PFC tuning. **(b)** 2D spatial receptive fields of 9 example PFC neurons. A neuron's preferred location, calculated as the center of mass (COM) of its receptive field, is shown with a black X. Visual space is represented in units of degrees of visual acuity (dva). **(c)** Distribution of preferred eccentricity (top) and preferred angular location (bottom) of recorded V4 and PFC populations. Data from 747 V4 neurons and 487 PFC neurons shown, pooled across 19 recording sessions. **(d)** Preferred locations of all recorded neurons (see c) plotted in the 2D visual space. Targets shown in blue. **e-f**: Analysis of PFC noise correlations. Analyses were conducted on the responses of 487 PFC neurons across 19 recording sessions,  $56 \pm 3$  trials per matched target condition in each session. Error bars are SEM. **(e)** Pairwise spike count correlation  $\rho$  as a function of the Euclidean distance between neurons' preferred spatial locations. Spike counts were summed over the 500 ms delay period. Pairs are organized by visual hemifield preference. Neurons preferring opposite visual hemifields are shown in orange. The orange star denotes pairs of neurons preferring similar spatial locations that still span the visual midline (example pair shown in d). **(f)** Pairwise spike count correlation by hemifield preference, averaged over all space. Raw correlations denoted by solid dots. Open squares denote residual correlations after subtracting the effects of the FA-identified top latent dimension of shared variance (Methods 3.3.5). Spike counts were binned in 180 ms windows.

between pairs of PFC neurons preferring the same visual hemifield were positive and decreased as a function of the Euclidean distance between the COMs of the neurons' spatial receptive fields (Figure 3.1e). However, pairs of neurons preferring opposite visual hemifields exhibited near-zero correlations, even when the distance between their COMs was very small. We sought to understand whether nearby neurons preferring opposite hemifields were truly uncorrelated or alternatively, exhibited competitive anti-correlations that were masked by shared common fluctuations inherited from outside sources. Using factor analysis, we tested whether we could recover anti-correlation structure between PFC neurons with opposite hemifield preferences after removing the dominate latent dimension of globally shared variability (see Methods 3.3.5). Residual correlations with the dominate latent dimension removed were still near-zero across all recorded pairs of PFC preferring opposite visual hemifields (Figure 3.1f). Thus, we concluded that PFC neurons with opposite hemifield preferences were not exhibiting strongly competitive dynamics.

We sought to further characterize the coordinated fluctuations underlying the noise correlations of our neuronal populations. We again used factor analysis (FA), which partitions the spike count co-variability of neuronal activity into a private variance component, representing the independent, Poisson-like firing variability of individual neurons, and a shared variance component, which represents the coordinated fluctuations of interest (Methods 3.3.5 and Appendix A). FA finds a latent basis set of dimensions that describe the neuronal population's shared variance. To assess the dimensionality of the coordinated fluctuations in both brain areas, we adopted metric  $d_{\text{shared}}$  from Williamson et al. [59], defined as the number of ordered latent dimensions required to explain 95% of the neuronal population's shared variance. Consistent with prior findings of low dimensional dynamics in V4 [24, 23], the average  $d_{\text{shared}}$  of V4 activity across recording sessions was one (Figure 3.2a). PFC exhibited much higher dimensional dynamics, with an average  $d_{\text{shared}}$  of five across recording sessions (Figure 3.2a). Possessing simultaneous recordings of our two brain areas, we were able to do a more direct comparison of the dimensionality expansion between V4 and PFC. Even when assessing the FA results of V4 and PFC activity from matched recording sessions, we found  $d_{\text{shared}}$  in PFC was typically  $\geq 4$  despite it consistently inheriting only one-dimensional shared variance from a single hemisphere of V4 (Figure 3.2b). We note once again that our recorded PFC hemisphere would have received information from both the left and right visual cortices. Assuming symmetric transmission of

V4 activity from both cortices, we would expect PFC to have at most two dimensions of shared variability if it directly reflected its V4 inputs. We thus concluded that PFC activity contained additional dimensions of shared variance from those possibly inherited from V4.

We pause now to consider whether it comes as a surprise that PFC has much higher dimensional shared variance than V4. PFC integrates information from multiple senses and is complicit in working memory and other executive functions [130, 131, 132, 133]. These high-level functions are made possible through the myriad of afferent projections that PFC receives from cortical areas other than V4. The most naive hypothesis of our dimensionality results would state that our observed high-dimensional, shared fluctuations in PFC reflect inputs from other brain regions unrecorded in this study. However, the logistics of confirming or refuting this hypothesis would be intractable with contemporary neural recording technologies [7]. Analyzing spike count co-variability with dimensionality reduction techniques like FA requires simultaneous recordings of single unit activity from many neurons. It is currently infeasible to collect single unit recordings of this scale across several brain areas simultaneously in an awake, behaving animal [7]. We instead chose to adopt a parsimonious modeling approach, in which we set out to determine whether PFC could expand the dimensionality of shared variance inherited from V4 through recurrent interactions alone. We note that our parsimonious model does not preclude the existence or influence of inputs to PFC from unobserved brain areas.

If it were true that PFC filtered our V4 input through complex recurrent dynamics rather than inheriting the structure of its activity directly, it would perhaps mean we would see no obvious hallmark of the V4 latent dimension in the shared fluctuations of our PFC activity. We set out to investigate this premise. Knowing that the visual system is lateralized and our recorded V4 activity was likely transmitted preferentially to PFC neurons encoding the same (contralateral) visual hemifield, we investigated whether PFC shared variability was dominated by any latent dimension that loaded differentially onto PFC neurons with opposite visual hemifield preferences (Figure 3.2c). A differentially-loaded latent would be quantified by a difference in the sign or polarity of that latent's loadings onto PFC neurons preferring the contralateral versus ipsilateral visual hemifield. Such a result would be evidence that the contralaterally-tuned PFC population directly inherits and trivially transforms the single latent dimension of shared variance observed in our V4 activity. To the contrary, we found that none of the latent dimensions describing PFC's shared variance cleanly exhibited differential loadings onto PFC neurons with

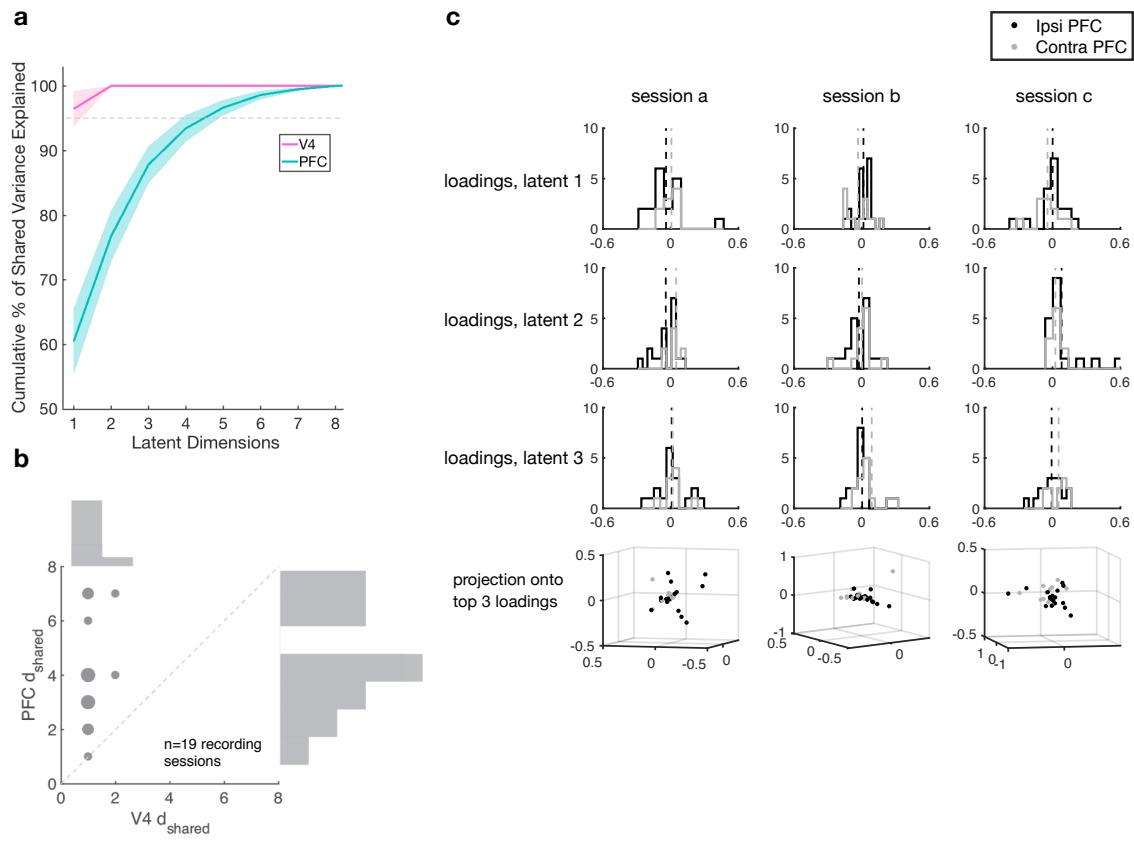


Figure 3.2: Factor analysis (FA) of residual activity (trial-to-trial variability) in V4 and PFC. Analyses performed on each of 19 recording sessions, where there were  $39 \pm 9$  V4 neurons,  $25 \pm 4$  PFC neurons, and  $56 \pm 3$  trials per matched target condition in each session. **(a)** Cumulative percentage of shared variance explained by each ordered FA latent dimension. Results are pooled across sessions. Error bars are SEM. **(b)** Session by session comparison of  $d_{\text{shared}}$  (number of latent FA dimensions required to explain 95% of population shared variance) for simultaneously recorded V4 and PFC data. Marker size proportional to number of sessions represented at that datapoint (marginal data distributions shown). **(c)** Distribution of FA loadings onto the top 3 latent dimensions (Methods 3.3.5) for ipsilateral-preferring (black) and contralateral-preferring (grey) PFC neurons. 3 representative recording sessions are shown out of the 19 total sessions.

ipsilateral versus contralateral tuning. Figure 3.2c visualizes the distribution of loadings from the top three latent dimensions of shared variance onto ipsilateral and contralateral preferring PFC cells for 3 example recording sessions of the 19 analyzed in total. The polarity of these loadings did not cleanly decompose onto PFC neurons with opposite visual hemifield preferences. Moreover, ipsilateral and contralateral preferring PFC cells were not obviously separable in the multi-dimensional space of the loadings from all three top latents. It appeared that the strong, one-dimensional latent that would have been selectively-inherited by a PFC subpopulation had been transformed non-linearly across PFC's network and could no longer be extracted from the

activity of its target subpopulation.

### 3.4.2 Linear network dynamics cannot expand dimensionality

Our findings in the previous section suggested that PFC expands the dimensionality of shared variance inherited from its inputs through recurrent interactions. The remainder of this chapter will use spiking network models to gain a mechanistic understanding of the recurrent connectivity architectures that are capable of dimensionality expansion.

We begin by modeling the laterally-tuned V4 inputs to PFC. In the previous section, we confirmed findings that the shared variance of activity in a single V4 hemisphere is approximately one-dimensional [24, 23]. We thus modeled our recorded V4 hemisphere as the activity of 2000 excitatory ( $E$ ) neurons generated from a doubly-stochastic process, in which individual neurons had Poisson spiking statistics but were correlated through a common, one-dimensional fluctuation induced by an Ornstein-Uhlenbeck (OU) process (Methods, Equation 3.5). Previous studies indicate that noise correlations within a V4 hemisphere are positive, while spiking activity across V4 hemispheres is uncorrelated [32, 114]. We captured this effect by simulating two V4 populations, representing the two visual hemifields, each of which consisted of 2000  $E$  cells correlated through two different realizations of the OU process ( $\lambda_L$  and  $\lambda_R$ , respectively, Figure 3.3a). The pairwise spike count covariance of our simulated V4 activity converged to the covariance of our underlying OU processes computed in Equation 3.12 (Figure 3.3a).

To first understand how PFC activity would reflect V4 inputs in the absence of recurrent interactions, we begin with the simplest PFC model architecture consisting of 4000 uncoupled  $E$  cells with leaky-integrate-and-fire (LIF) dynamics (Figure 3.3b). Noise correlation analyses of our PFC neural data showed that PFC cells preferring opposite visual hemifields lacked shared fluctuations (Figure 3.1e). This indicates that PFC neurons preferring opposite visual hemifields did not receive the same global fluctuations from a common afferent pool. Accordingly, we chose to model our feedforward connections from V4 to PFC (expressed by connectivity matrix  $J^{\text{FF}}$ ) as disjoint projections reflective of hemifield tuning, where V4 model neurons preferring the left visual hemifield projected exclusively to PFC model neurons preferring the left visual hemifield (Figure 3.3b).

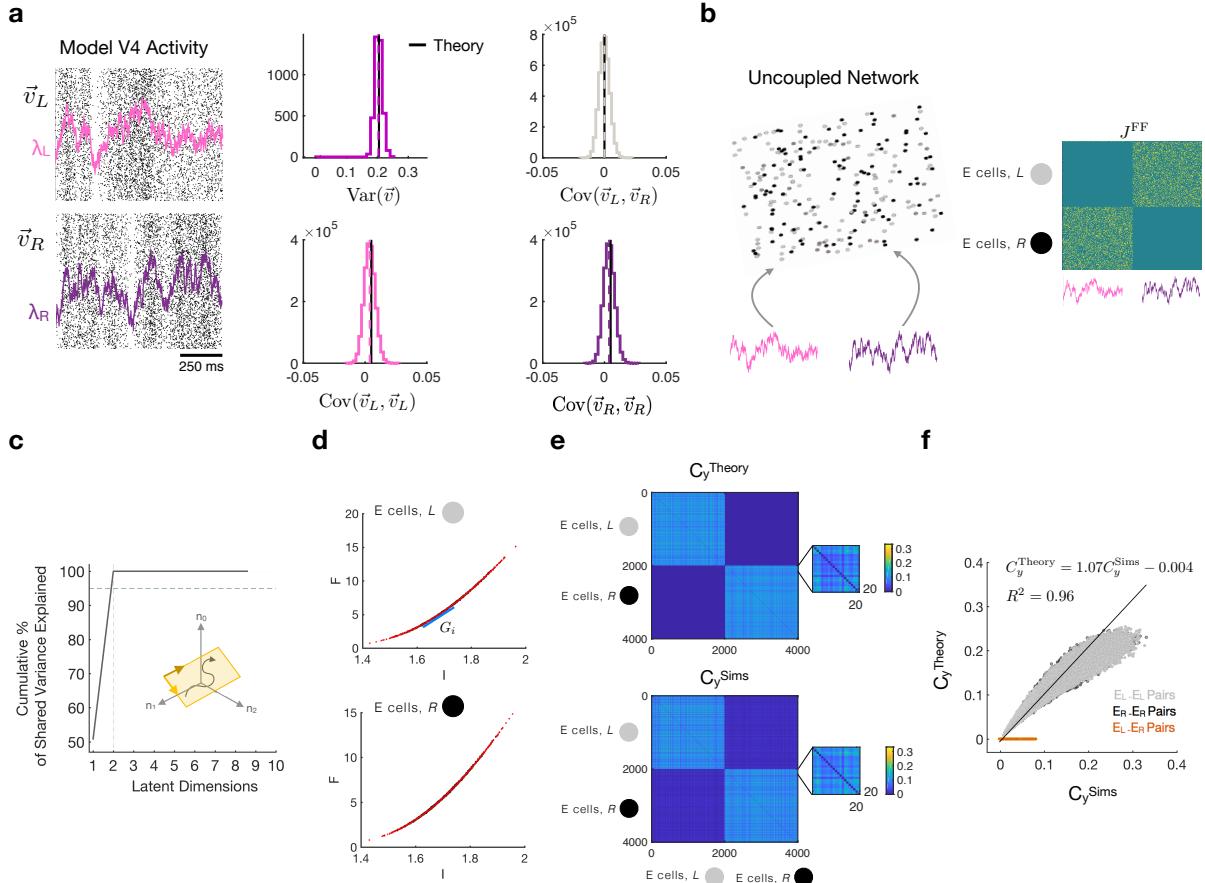


Figure 3.3: Propagation of shared variability through an uncoupled network with linear dynamics. **(a)** Left: Model network input consisting of two V4 hemifield populations of spiking neurons,  $\vec{v}_L$  and  $\vec{v}_R$ . Spiking activity in each hemifield is correlated through a common, 1 dimensional fluctuation (OU process) specific to that hemifield ( $\lambda_L$  or  $\lambda_R$ ). Right: Spike count variance and marginal spike count covariance of simulated V4 activity (colored distributions, mean denoted by dotted line) compared to the theoretical estimate of the underlying OU process (black line). Spike counts binned in 50 ms windows. **(b)** Schematic of a 2-layer network model in which the V4 inputs (a) project disjointly (weight matrix  $J^{FF}$  shown) to an uncoupled, downstream population of spiking neurons. **(c)** Factor analysis (FA) of the population activity from the output layer of the uncoupled network. Two FA latent dimensions capture 100% of the population shared variance because the network behaves with linear dynamics and directly inherits the variability structure of the inputs. (FA was performed on 1000 s of simulated activity, binned in 50 ms windows, from 10 samples of 100 excitatory neurons per network graph realization, for 2 realizations.) **d-f:** Linear response theory of the uncoupled network (activity from the full output layer population of 4000  $E$  neurons, simulated over 1000 s, for 1 graph realization). Spike counts binned over 50 ms windows. **(d)** F-I curve for excitatory ( $E$ ) neurons preferring the left ( $L$ ) or right ( $R$ ) visual hemifield (simulated data, black; subpopulation fits, red). The gain  $G_i$  of each neuron in the subpopulation was fit according to the slope of the F-I curve (blue). **(e)** Full pairwise covariance structure  $C_y$  of the network for the simulated data (bottom, Sims) and as predicted by linear response theory (Theory, top). Insets show that theory captures the microstructure of pairwise statistics. **(f)** Pairwise comparison of linear response predicted covariance  $C_y^{\text{Theory}}$  and covariance of simulated data  $C_y^{\text{Sims}}$ . Each datapoint is 1 matrix entry from **e** ( $E_L-E_L$  pairs, grey;  $E_R-E_R$  pairs, black;  $E_L-E_R$  pairs, orange).

Neurons in our uncoupled model directly inherit the spiking activity of their V4 inputs, with the exception of minor variability generated through each neuron's LIF dynamics. The spiking activity of each PFC neuron in the uncoupled model, defined here as  $y_i(t)$ , can thus trivially be approximated through a linear combination of its V4 inputs (Methods 3.3.9):

$$y_i(t) = G_i \left( \sum_j J_{ij}^{\text{FF}} v_j^{\text{FF}}(t) \right), \quad (3.57)$$

where  $v_j^{\text{FF}}(t)$  is the spiking activity of a V4 neuron  $j$  that projects to PFC neuron  $i$  with connection strength  $J_{ij}^{\text{FF}}$ .  $G_i$  is simply the gain by which each PFC neuron  $i$  scales its inputs, often denoted as the neuron's *linear response* [139, 120, 149]. When the network receives sufficiently slow perturbations and is observed over sufficiently long time windows such that its trial averaged response is static rather than locked to fast-timescale signal,  $G_i$  is well approximated by the slope of a neuron's frequency-current (F-I) curve, or average firing response to fixed input current. Given the linear response approximation in (3.57), the shared variance of PFC activity is:

$$\begin{aligned} C_y &= \text{Cov}(\vec{y}, \vec{y}) \\ &= G J^{\text{FF}} V^{\text{shared}} (G J^{\text{FF}})^{\top}, \end{aligned} \quad (3.58)$$

where  $\vec{y}$  contains the firing responses of all model PFC neurons. See Methods (3.19) for details. Importantly, the dimension of model PFC's shared variance  $C_y$  will be bounded by the two-dimensional spiking co-variability of V4 activity ( $V^{\text{shared}}$ ) through the linear algebra Frobenius Inequality:

$$\begin{aligned} \text{rank}(C_y) &\leq \min(\text{rank}(G), \text{rank}(J^{\text{FF}}), \text{rank}(V^{\text{shared}})) \\ &\leq \text{rank}(V^{\text{shared}}) \\ &\leq 2. \end{aligned} \quad (3.59)$$

Factor analysis of the activity simulated from the uncoupled model reveals a  $d_{\text{shared}}$  of 2 (Figure 3.3c), confirming the bounded rank of share variance predicted by our linear response theory (3.59). Together, this exercise reveals that a network with linear dynamics cannot amplify

dimensions; a linear network’s shared variance will instead always be constrained by the minimum dimensionality of its input co-variability. So long as our PFC model network has linear dynamics and receives two-dimensional fluctuations from V4, its coordinated fluctuations will be confined to a two-dimensional subspace of neuronal activity (Figure 3.3c). We used our linear response theory for shared variance (3.58) to successfully predict the covariance structure, at the level of neuron pairs, of our simulated uncoupled network activity (Figure 3.3e-f). This involved first computing each neuron’s gain  $G_i$  (3.57), which quantified the neuron’s sensitivity to its inputs (Figure 3.3d). Individual neuron gains are well approximated by the slope of their population’s frequency-current ( $f$ - $I$ ) curve. (See Methods Section 3.3.13 for details.)

A network with uniform recurrent coupling is also linearizable when that coupling is sufficiently weak such that a single neuron’s spiking response is still linearly related to the sum of its synaptic inputs (in this case, of both the feedforward and recurrent variety). Linear response theory has been commonly applied to such weakly coupled recurrent networks [149, 139, 120]. Derivations of the linear response theory for the weakly coupled recurrent version of our model are contained in Methods Section 3.3.9.2. However, so long as linear response approximations are appropriate, the dimensionality constraint placed on the shared variance of our network by Equation (3.59) will still hold, and our population activity will still be confined to two-dimensional subspace (schematic, Figure 3.3c). This implies that even a PFC model network with weak recurrent coupling cannot generate dimensionality or expand the dimension of shared variance that it inherits from V4.

### 3.4.3 Metastable dynamics of recurrent networks with multiple, tuned inputs

The previous section demonstrated that linear dynamics are insufficient to explain the dimensionality expansion that we observe between the shared variance of V4 activity and PFC activity. We now move to studying strongly coupled networks, with the intuition that strong recurrent interactions are likely necessary to generate non-linear dynamics.

We begin by studying a network model with strong, uniform recurrent connectivity. Strongly coupled networks require inhibition to prevent mass, pathological recurrent excitation and stabilize network dynamics [62, 64]. We therefore introduce 1000 inhibitory ( $I$ ) cells to our recurrent network and make our network connections respect the relative synaptic strengths required

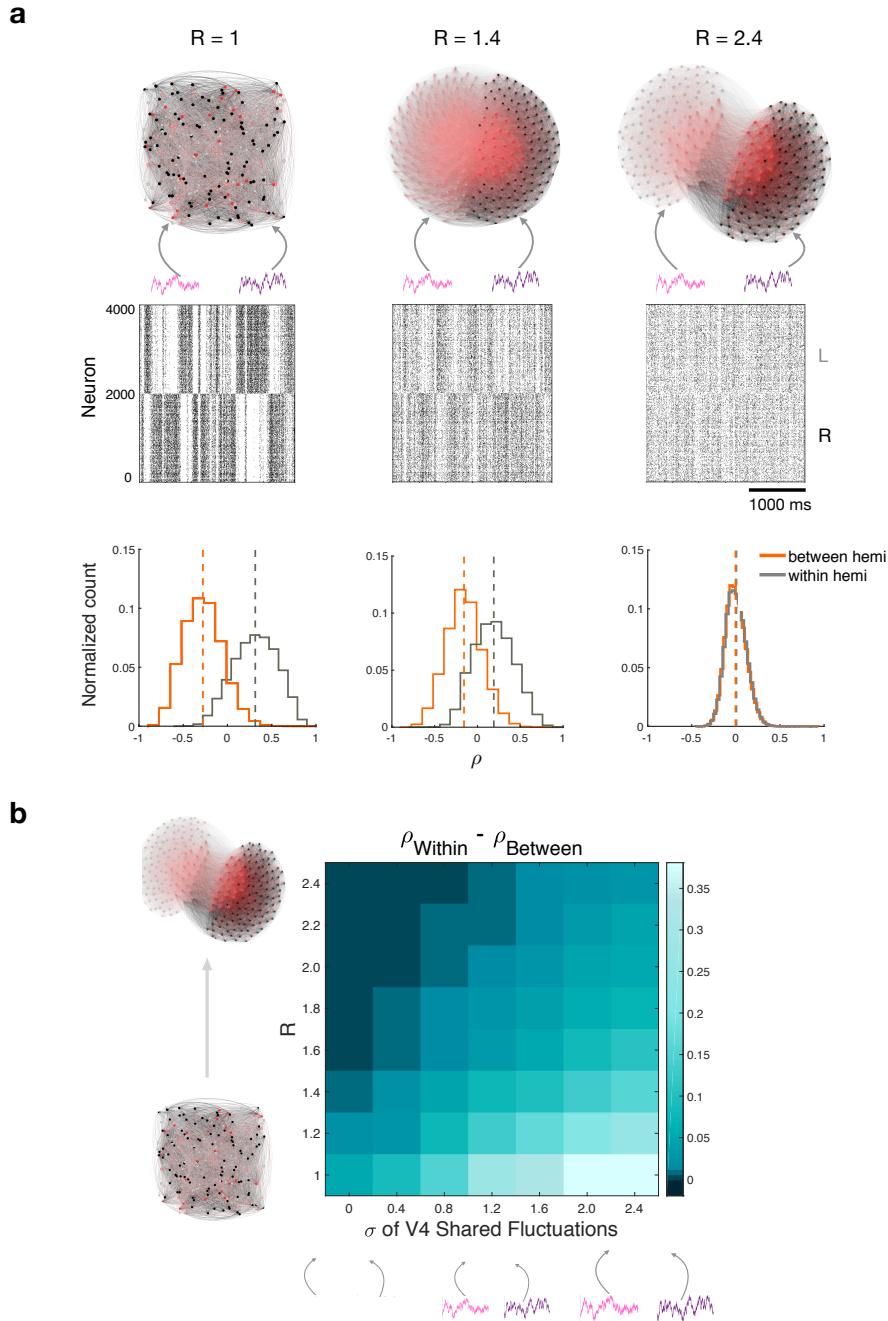


Figure 3.4: Dynamics of networks with assembly structure that inherit shared variability. **(a)** Top: Visualization of connectivity in recurrent networks, with increasing degrees of clustering ( $R$ ), that inherit shared fluctuations from tuned, disjoint inputs (pink and purple). The  $R = 1$  network has uniform, random recurrent connectivity.  $E$  cells are shown in grey (left hemifield preference) and black (right hemifield preference).  $I$  cells are shown in pink (left hemifield preference) and red (right hemifield preference). Networks of 250 neurons are visualized. Our simulated network contained 4000  $E$  and 1000  $I$  neurons. Middle: Spike rasters showing the spike times of all  $E$  neurons. Bottom: Distribution of spike count correlation  $\rho$  for pairs of  $E$  neurons within a hemifield (grey) or between hemifields (orange).  $\rho$  was computed over 150 ms windows. Dotted lines denote distribution means. **(b)** Heatmap of the difference between the mean within hemifield pairwise spike count correlation  $\rho_{\text{Within}}$  and the mean between hemifield pairwise spike count correlations  $\rho_{\text{Between}}$ , as a function of clustering strength  $R$  and amplitude of shared fluctuations  $\sigma$ .  $\rho$  was computed over 150 ms windows. Statistics for each network architecture were computed over 30 s of simulated data for 3 realizations of the network graph.

for  $E/I$  balance [62]. Our two V4 populations reflecting visual hemifield tuning still project disjointly to PFC layer cells preferring their same visual hemifield. Under this model architecture, pairs of neurons in PFC receiving inputs from the same V4 population now exhibit strong spike count correlations, while neuron pairs receiving inputs from opposing V4 populations exhibit strong anti-correlations ( $R = 1$ , Figure 3.4a). In fact, the anti-correlation mode of population activity with this model architecture is so strong that the network exhibits winner-take-all dynamics to the point of pathology – when PFC neurons tuned to one visual hemifield are active, neurons tuned to the opposite visual hemifield are nearly silent.

Networks in which multiple inputs disjointly project to a layer of neurons with strong, uniform, recurrent coupling cannot avoid this mass anti-correlation mode of activity [72, 117]. The intuition for this known result requires us to consider the relative spatial scales of our feedforward projections and recurrent interactions. Asynchronous dynamics are achieved in balanced networks when correlations due to feedforward inputs and recurrent inputs cancel [64]. A single, broad recurrent architecture cannot, however, dynamically balance multiple, spatially-localized pockets of correlated activity from tuned inputs with disjoint projections. (See Methods Section 3.3.10 for a formal derivation of this claim.) What results is multi-stable dynamics in our PFC network model, with alternating states of highly-correlated activity and silence from PFC neurons tuned for each visual hemifield.

#### 3.4.4 Tuned recurrent assemblies counterbalance tuned inputs

Our pathological anti-correlations in the previous section resulted from a spatial imbalance of feedforward projections and recurrent interactions. To reduce these anti-correlations, we would need recurrent architecture with spatial structure similar to the hemifield-specific projections from our V4 populations [72]. We considered that clustered synaptic connections between neurons with similar functional tunings are commonly observed in cortex [150, 151, 152]. PFC neurons that we recorded *in vivo* preferring the same visual hemifield also showed strong evidence of increased covariability as compared to PFC neurons with opposite hemifield preferences (Figure 3.1e). We thus introduce recurrent assemblies that reinforce visual hemifield tuning. Similar to Litwin-Kumar & Doiron [60], we define a clustering parameter  $R$  used to control the degree of increased connectivity between two PFC neurons preferring the same visual

hemifield:

$$R^{\alpha\beta} = \frac{J_{\text{in}}^{\alpha\beta}}{J_{\text{out}}^{\alpha\beta}}. \quad (3.60)$$

Here, subscript “in” denotes two PFC neurons in the same assembly, preferring the same visual hemifield. Subscript “out” denotes two PFC neurons in opposite assemblies.  $J^{\alpha\beta}$  describes the synaptic strength of connections from neurons of cell type  $\beta$  to neurons of cell type  $\alpha$ , where  $\{\alpha, \beta\} \in E, I$ . Note that, unlike the study by Litwin-Kumar & Doiron [60], this means both  $E$  and  $I$  connections in our network are clustered. Recent experimental studies support the existence and maintenance of clustered inhibition that is related to functional tuning [153, 154]. Moreover, inhibitory assemblies were shown to moderate firing rates of active excitatory assemblies in Litwin-Kumar & Doiron [60]’s model framework, tempering winner-take-all dynamics. We employ them for a related but different purpose – to provide recurrent connections with spatial scale commensurate to our input projections and help dynamically counterbalance the feedforward correlations arising from our disjoint V4 inputs.

For computational simplicity, we will induce a symmetric clustering constraint in all the work that follows such that  $R = R^{EE} = R^{EI} = R^{IE} = R^{II}$ . Note that  $R = 1$  describes the uniform recurrent connectivity explored in the previous section. Competitive dynamics between PFC neurons preferring the left and right visual hemifield diluted when we introduced tuned assemblies to the recurrent architecture of our network model, corresponding to clustering coefficients of  $R > 1$  (Figure 3.4a). This was measurable through shifts in the distributions of spike count correlations, both within and between assemblies. As the clustering coefficient  $R$  increased, PFC neurons within assemblies became less correlated, and PFC neurons in opposite assemblies became less anti-correlated. At  $R = 2.5$  we see convergence of our two distributions such that there are near-zero mean correlations both within and between hemifields. Critically, the  $R = 2.5$  network’s ability to counterbalance input correlations arises exclusively from increased communication within assembly; there is no decrease in interactions between neurons in opposite assemblies as compared to recurrent network with uniform connections ( $R = 1$ ), and we are not trivially restoring balance with two, independent networks.

We observed that our network now contained competing co-mechanisms of variability; strongly correlated, lateralized projections introduced competitive spiking dynamics with a

strong anti-correlation mode, and strong recurrent assemblies ( $R > 1$ ) appeared to dynamically re-balanced the anti-correlation mode. To better understand the interplay of these two mechanisms, we traversed the 2D model parameter space defined by ranging over the clustering coefficient  $R$  and the magnitude of our shared fluctuations inherited from V4 (Figure 3.4b). These V4 fluctuations are defined by the variance  $\sigma^2$  of the OU process underlying our V4 spiking activity (Equation (3.5)). For each value of  $R$  and  $\sigma$ , we measured  $\rho_{\text{within}} - \rho_{\text{between}}$ , where  $\rho$  is the mean spike count correlation across neuron pairs, trials, and graph realizations ( $N^E = 4000$  neurons, 30s of data per graph realization, 3 graph realizations) and the subscripts “within” and “between” denote pairwise correlations within the same hemifield assembly and between opposing hemifield assemblies, respectively.

The bottom left of the Figure 3.4b heatmap represents a uniformly connected recurrent network ( $R = 1$ ) inheriting V4 correlations due exclusively to common projections; at  $\sigma = 0$  spiking activity from our model V4 neurons is uncorrelated. This exact case is covered by Rosenbaum et al. [72], and correlations within hemifield are  $\mathcal{O}(1)$  [140]. The top left of Figure 3.4b represents a network with the same input structure but strong recurrent assemblies. We have already presented the intuition for how assemblies restore the spatial scale of feedforward and recurrent connectivity and dynamically restore balance to the network. Derivations in Methods Section 3.3.10.2 show that the balance condition is dependent on the invertibility of our recurrent connectivity matrix. Assemblies restore the asymmetry to our recurrent connectivity matrix needed to make it invertible. When  $\sigma = 0$ , in the large  $N$  limit of neurons, recurrent assemblies can perfectly balance the feedforward correlations arising from our disjoint inputs and to produce asynchronous network dynamics.

As we move along the  $\sigma$  axis of Figure 3.4b, we increase the amplitude of the shared fluctuations induced by our OU process, and subsequently, the magnitude of spike count correlations in our V4 activity. Baker et al. [140] refer to this as the “correlated state”, because the activity of the feedforward neuronal population has  $\mathcal{O}(1)$  correlations. These correlations compound with correlations due to our common input projections, which are also  $\mathcal{O}(1)$ . The total feedforward correlations received by PFC model neurons are in turn  $\mathcal{O}(N)$  (Methods, Equation (??)). Uniform recurrent connectivity ( $R = 1$ ) cannot dynamically balance these spatially-localized feedforward correlations, producing model PFC spike count correlations also of  $\mathcal{O}(N)$  (Bottom

right, Figure 3.4b, and Methods 3.3.10.2). In this “correlated” state, strong recurrent assemblies still significantly dilute both within hemifield correlations  $\rho_{\text{within}}$  and between hemifield anti-correlations  $\rho_{\text{between}}$  (Top right, Figure 3.4b). In fact, in the large  $N$  limit of neurons, hemifield-tuned assemblies of sufficient clustering strength are able to dynamically restore balance (Methods 3.3.10.3). Assemblies cannot, however, restore truly asynchronous dynamics in the “correlated state”, as model PFC spike count correlations/anti-correlations are then still at minimum  $\mathcal{O}(1)$  (Methods 3.3.10.3).

### 3.4.5 Assembly networks expand the dimension of inherited shared variability

We established that a network model with correlated, disjoint V4 inputs and strong, uniform ( $R = 1$ ) recurrent connectivity was sufficient to produce non-linear dynamics in the form of multi-stability. Identifying a network architecture that gave rise to non-linear recurrent interactions was our original goal, as non-linear dynamics are required for any system to intrinsically generate dimensionality; we specifically aimed to replicate a dimensionality expansion of shared variability observed between V4 and PFC. Though our  $R = 1$  network had non-linear recurrent interactions, it also had pathological levels of anti-correlations that were not representative of the PFC neural activity we observed *in vivo*. We solved this problem in Results 3.4.4 by introducing hemifield-tuned recurrent assemblies, which could successfully dilute the pathological anti-correlations of the  $R = 1$  model. We showed that in the large  $N$  limit of neurons and as  $\sigma \rightarrow 0$ , strongly clustered assemblies can even restore the balanced, asynchronous state of network activity.

Armed now with a model architecture exhibiting both non-linear recurrent dynamics and a biologically-plausible range of correlation outputs, we sought to test whether this architecture could indeed expand the two-dimensional shared variability of our model V4 activity. We performed dimensionality analyses on activity simulated from a network with a relatively strong clustering coefficient ( $R = 2.3$ ) and relatively weak V4 input correlation parameter ( $\sigma = 0.71$ ) (Figure 3.5). Working in this approximate parameter regime produced recurrent layer spiking activity that looked nearly asynchronous but contained subtle correlations, qualitatively similar to our PFC neural data recorded *in vivo*. Factor analysis (FA) confirmed that our chosen model architecture could successfully expand the two-dimensional shared variance inherited from V4

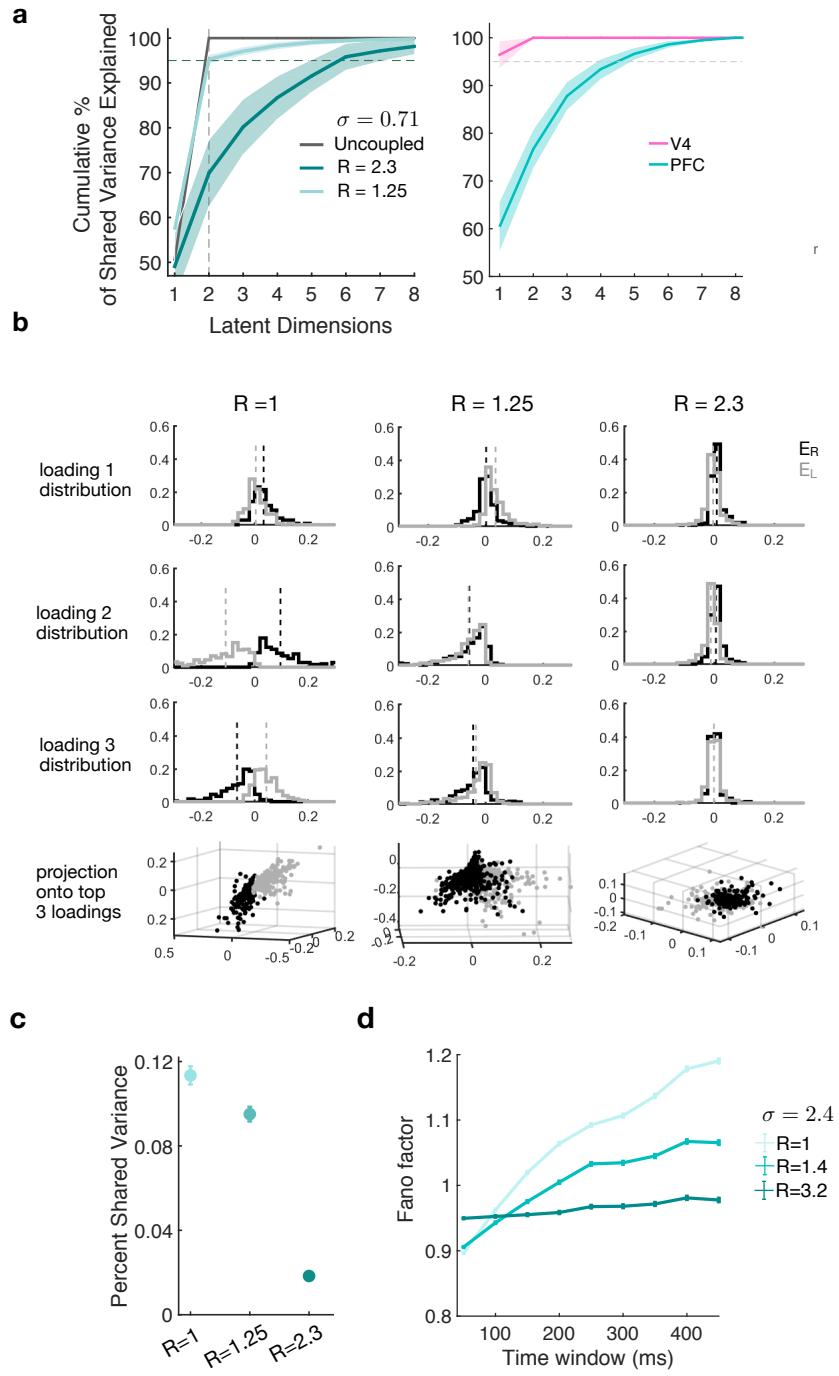


Figure 3.5: The dimension of shared variability in networks with assembly structure. **a-c** Factor analysis (FA) of population activity for networks with various strengths of recurrent clustering  $R$ , inheriting common fluctuations of amplitude  $\sigma = 0.71$ . Analyses of each network architecture were computed over 1000 s of simulated activity from 10 samples of 100 neurons each per network graph realization, for 2 realizations. Spike counts were binned in 50 ms windows. Error bars are SEM. **(a)** Cumulative percentage of shared variance explained by each FA-identified, ordered latent dimension in simulated data (left) and PFC neural data (right, see Fig. 3.2). Error bars are SEM across FA samples. **(b)** Distribution of FA loadings onto the top 3 latent dimensions (Methods 3.3.12) for model neurons of left (grey) or right (black) hemifield preference. **(c)** Percentage of each neuron's total variance that is shared amongst the population, averaged across all analyzed neurons. **(d)** Fano factor of simulated neural activity as a function of the time window over which spike counts are binned, for networks of varying  $R$ ,  $\sigma = 2.4$ . Analyses of each network architecture were computed over 300 s of simulated activity for 2 realizations of the network graph.

(uncoupled network, control) to  $d_{\text{shared}} = 6$  dimensions of shared variability in model PFC (Figure 3.5a). These results qualitatively replicated the shared variance that we observed from PFC activity recorded *in vivo*. Networks with smaller clustering parameters ( $R = 1.25$  shown,  $\sigma = 0.71$ , Figure 3.5a) still showed slightly expanded shared variance from the uncoupled control. (Indeed, even our  $R = 1$  network has multi-stable dynamics, albeit with a highly anti-correlated population mode that swamps factor analyses.) Networks with weak clustering were not able to reproduce the magnitude of dimensionality expansion seen in the PFC data recorded in *in vivo*.

We demonstrated in Figure 3.4 that stronger recurrent clustering produced weaker anti-correlations between model PFC hemifield populations. Analogously, FA reveals that activity from the two PFC hemifield populations is more separable in the low-dimensional latent space for smaller network clustering coefficients. We analyzed the distribution of neuronal loadings onto the top three dimensions of the FA-identified latent space (Appendix A), where each PFC model neuron was categorized by its preference for the left or right visual hemifield (Figure 3.5b). In the  $R = 1$  network, PFC neurons with opposite hemifield preferences loaded onto each of the top three latent dimensions with opposite polarity and were linearly separable in a three-dimensional latent space. Weak degrees of recurrent clustering made the hemifield populations load onto the top latent dimension with opposite polarities, but this hemifield separability was not apparent in the second or third latent dimension ( $R = 1.25$ , Figure 3.5b). In the  $R = 2.3$  network chosen to model PFC neural data recorded *in vivo*, model neurons loaded onto the top three latent dimensions nearly indiscriminately, regardless of their hemifield preference. This result reproduces our FA findings from the PFC neural data recorded *in vivo*, in which neurons of opposite hemifield preference were similarly inseparable in the latent space (Figure 3.2c).

The dilution of correlations/anti-correlations with increasing degrees of recurrent clustering is also evident through the proportion of total variability that is shared across the population in networks with different clustering coefficients. We measured the percentage of each neuron's total variability that was explained by the latent space of shared variability. We refer to this measure as a neuron's “percent shared variance” [59]. The disjoint proportion of variance that is not shared across the population constitutes FA's estimate of a neuron's private “noise”, or independent trial-to-trial variability. The  $R = 1$  network had the largest percent shared variance, indicative of the strong, anti-correlating common fluctuations to which the network

activity was entrained (Figure 3.5c). Neurons' percent shared variance decreased as function of recurrent clustering strength, meaning neural activity was less entrained to latent common fluctuations for stronger degrees of clustering.

Finally, we examined the neural population's average Fano factor as a function of recurrent clustering strength, where Fano factor is defined as the ratio between each neuron's trial-to-trial variance and mean spike count over a fixed time window (3.3). Neurons exhibit Poisson-like trial-to-trial variability, and Poisson processes of stationary rate have a Fano factor of 1. Fano factors of greater than 1 can therefore indicate fluctuations in a neuron's underlying firing rate. We measured Fano factor as a function of the window duration over which spike counts were binned to evaluate long-timescale firing rate variability in our model neurons (Figure 3.5d). Fano factors of all evaluated networks were sub-Poisson for time bins less than or equal to 100 ms. These small time bins primarily captured population activity within a single network state, in which the dominant mode of variability is within-hemifield spike count correlations. Unsurprisingly, for very small time bins ( $\Delta t \leq 50$  ms), neurons in the  $R = 1$  network have lower Fano factors than neurons in clustered networks; within state, the  $R = 1$  network activity is most correlated and most entrained to common latent fluctuations. For larger time bins ( $\Delta t \geq 100$  ms), however, neurons in clustered networks exhibit smaller Fano factors than neurons in the uniform network. This discrepancy magnifies as the size of the time bin increases. Large time bins capture fluctuations in firing rate across the two meta-stable states of network activity. Clustered networks exhibit weaker anti-correlations across hemifield populations in a single network state (Figure 3.4). We make the related observation that the spiking activity of a single neuron in a clustered network will then vary less between State R and State L. This observation manifests as lower Fano factors in clustered networks even when the networks are evaluated at timescales that capture state transitions. All Figure 3.5d analyses are performed on networks with larger inherited variability ( $\sigma = 2.4$ ), as larger input correlations will drive firing rate fluctuations over state transitions. The qualitative trend reported in Figure 3.5d is robust across choice  $\sigma$ , but small input noise correlations never give rise to super-Poisson variability.

### 3.4.6 Metastability as time-sharing between states of low-dimensional, linear dynamics

Our networks with strong, recurrent coupling switch between Left and Right metastable states of activity. While this switching behavior clearly does not constitute linear dynamics, we asked whether it was possible to understand the single state dynamics of our network using the linear response frameworks from Results 3.4.2. We hypothesized that each of our two states of network activity exhibited approximately linear dynamics. Since linear systems are incapable of generating dimensionality, this hypothesis would imply that conditioned on each attractor state of activity, our network inherited two dimensions of shared variance from upstream V4 populations in each state of activity. We could then explain PFC’s ability to expand dimensionality through its “time-sharing” between two states of network activity, each of which comprised two-dimensional, linear dynamics (Figure 3.6a). A perfect concatenation of these two linear states of activity (in which hops between states occur instantaneously) would be capable of producing up to four dimensions of shared variance. We proposed that the extra dimensions of shared variance observed in our PFC neural data and  $R = 2.3$  model network ( $d_{\text{shared}}^{\text{PFC}} = 5$ , Figure 3.2a and  $d_{\text{shared}}^{R=2.3} = 6$ , Figure 3.5a, respectively) could arise through non-instantaneous state transitions, during which time the network activity would not behave according to the dynamics of either state.

To begin testing this hypothesis, we collected our model network’s recurrent layer activity in 50 ms time bins. We used a Gaussian Mixture Model [141] to assign each time bin a probability of membership to the Left or Right attractor state of network dynamics. (See Methods 3.3.11 for details and Supplemental C for visualization.) Time bins with less than 0.97 probability of membership to either state were assumed to constitute a state transition and were disregarded from all subsequent analysis. We note from Figures 3.4a and 3.5d that the Left and Right activity states are less differentiable in networks with strong clustering. We therefore conducted all linear response analyses that follow on a model network with clustering coefficient  $R = 1.25$ . In this parameter regime, over 90% of the total analyzed population activity was assigned to the Left or Right state.

Using our state-partitioned population activity, we derived a linear response approximation (Methods 3.3.9) of the full population spike count covariance structure in either the Left and

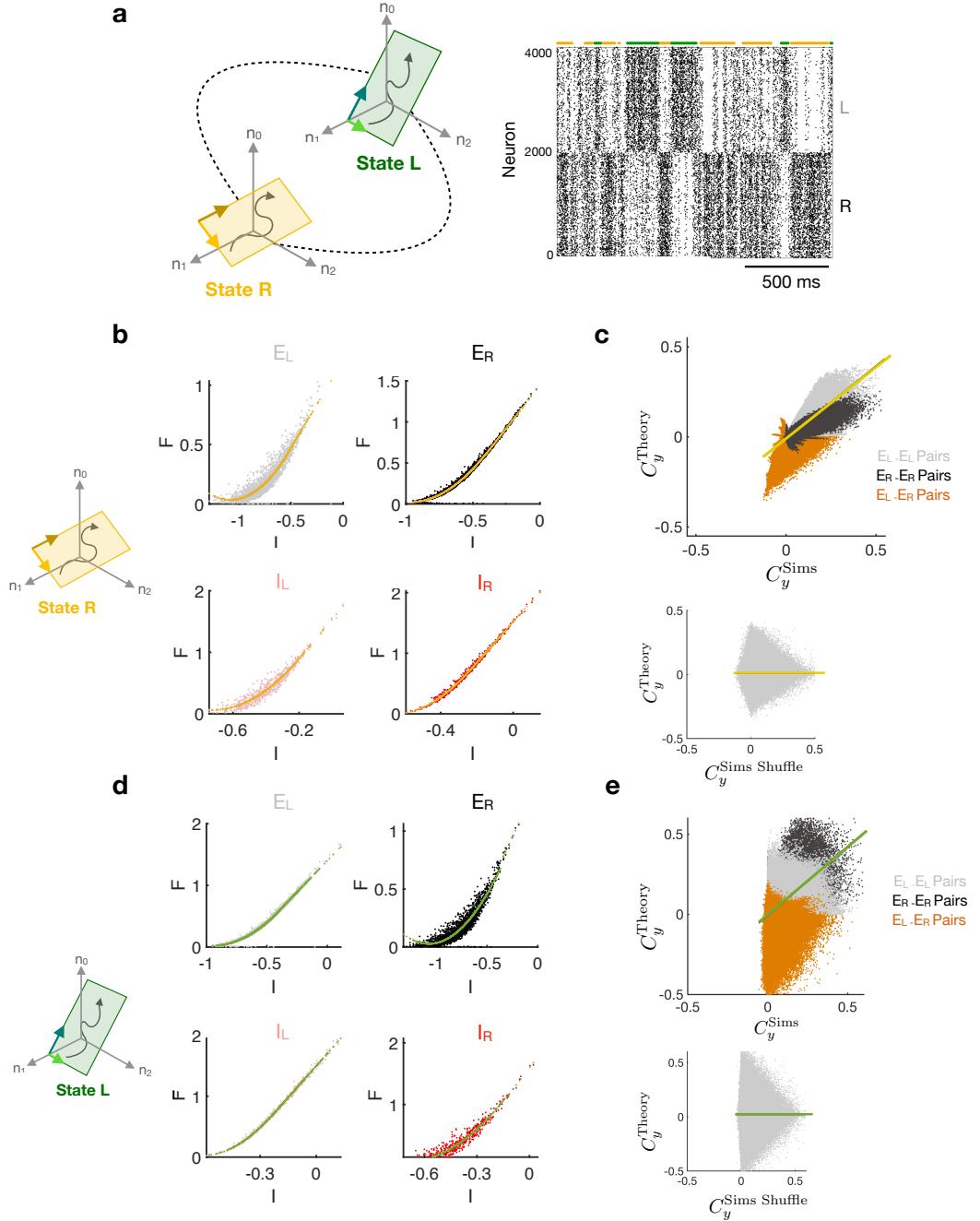


Figure 3.6: Attractor states of linear dynamics in networks with strong recurrent coupling and disjoint inputs. **(a)** Schematic of network activity “time-sharing” between two, low-dimensional attractor states, each of which has linear dynamics. State L (green) corresponds to high activity periods from neurons preferring the left visual hemifield. State R (yellow) corresponds to high activity periods from neurons preferring the right visual hemifield. **b-e:** Linear response theory applied to each attractor state of a network with  $R = 1.25$  recurrent clustering strength that inherits  $\sigma = 0.71$  amplitude shared fluctuations from disjoint inputs. Spike counts were binned in 50 ms windows. See Methods 3.3.11 and 3.3.13 for further details. **(b,d)** F-I curves fitted to each cell type and hemifield-tuned neural subpopulation. Simulated data shown as points with colors corresponding to subpopulation membership (network visualizations, Fig. 3.4). Fits shown in yellow and green for State R and State L, respectively. **(c,e)** Pairwise comparison of linear response predicted covariance  $C_y^{\text{Theory}}$  and covariance of state-partitioned simulated data  $C_y^{\text{Sims}}$  ( $E_L-E_L$  pairs, grey;  $E_R-E_R$  pairs, black;  $E_L-E_R$  pairs, orange). Results are compared against a control in which simulated data is shuffled. Lines represent linear regression summaries of the pairwise relationship between Theory and Sims across all pairs.

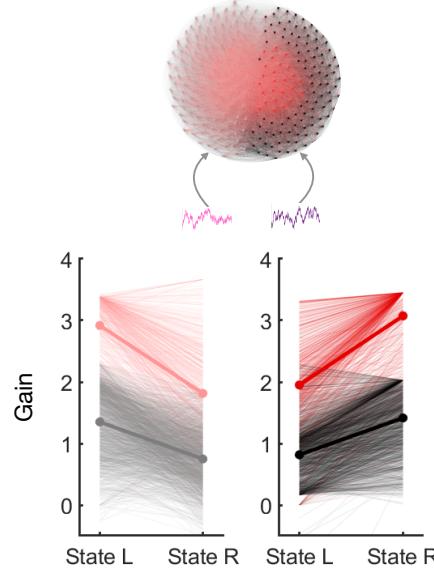


Figure 3.7: Neuronal gain shifts between State L and State R for  $E_L$  (grey),  $I_L$  (pink),  $E_R$  (black), and  $I_R$  (red) neurons, as predicted by the linear response theory in Fig. 3.6. Network schematic is shown above for subpopulation clarity.

Right state of activity. For each state, we computed every neuron’s gain  $G_i$  in that state by differentiating the F-I curves fitted to each population  $\alpha_h$  (Figure 3.6b and d for State R and State L fits, respectively). Here  $\alpha \in \{E, I\}$  denotes cell type and  $h \in \{L, R\}$  denotes visual hemifield preference. (See Methods 3.3.13 for details.)

We used these gains to compute a theoretical approximation of  $C_y$ , the state-conditioned shared variance of all neuron pairs, according to the linear response equations in Methods 3.3.9. In statistical mechanics literature, this is referred to as a linear response theory of the microcanonical ensemble. Theoretical approximations of shared variance in State R were predictive of the spike count covariance of the simulated data in State R at the level of individual neuron pairs (Figure 3.6c,  $C_{yij}^{\text{Theory}} = 0.81C_{yij}^{\text{Sims}} - 0.011$ ,  $R^2 = 0.63$ ; excitatory neuron pairs only). We thus concluded that population activity in our network’s State R behaved according to approximately linear underlying dynamics. Linear response predictions of shared variance were more heteroscedastic in State L, in which the theory tended to overestimate anti-correlations between neurons preferring opposite visual hemifields (Figure 3.6e). However, theory estimates of shared variance were still significantly more related to the shared variance of simulated activity than to the control, in which simulated data were shuffled (Figure 3.6e,  $C_{yij}^{\text{Theory}} = 0.86C_{yij}^{\text{Sims}} - 0.010$ ,  $R^2 = 0.23$ ;  $C_{yij}^{\text{Theory}} = -2.3 \times 10^{-5}C_{yij}^{\text{Shuffle}} + 0.012$ ; excitatory neuron pairs only). Linear response theory assumes that shared variance is shaped by the matrix of

neuronal gains  $G$ . We therefore examined neuronal gains as a function of state to better understand the shift in shared variance structure between State R and State L (Figure 3.7). We remind the reader that all neurons participate in both states, i.e., model neurons preferring the left visual hemifield still participate in State R – they are simply the less active population. Neurons exhibited organized and significant gain shifts between State R and State L. Both model  $E$  and  $I$  neurons preferring the left visual hemifield had larger gains in State L than State R; analogously, model  $E$  and  $I$  neurons preferring the right visual hemifield had larger gains in State R than State L. Symmetries between  $E$  and  $I$  populations preferring the same visual hemifield result from the network activity’s existence in a roughly balanced regime.

Our linear response analyses supported the hypothesis that each state of our metastable network activity obeyed roughly linear dynamics, with interpretable shifts in shared variance structure occurring between State R and State L. We concluded that if this interpretation of our network dynamics was indeed true, FA should uncover at most 2 dimensions of shared variance in state-partitioned population activity. We returned to the  $R = 2.3$  model network used to capture PFC activity recorded *in vivo*, in which we saw significant dimensionality expansion ( $d_{\text{shared}} > 4$ ) in the population activity across all states (Figure 3.5a). As predicted by our hypothesis, FA revealed  $d_{\text{shared}} = 2$  latent dimensions of shared variance in State R of the  $R = 2.3$  network activity. This constituted a highly significantly reduction from the  $d_{\text{shared}} = 6$  latent dimensions of the  $R = 2.3$  network activity across all states.

Factor analysis of State L activity in the same network determined that  $d_{\text{shared}} = 4$  latent dimensions were required to explain 95% of shared variance. While this result is greater than the 2-dimensional shared variance that would be predicted in a system with truly linear dynamics, it still represents a statistically significant reduction from the  $d_{\text{shared}} = 6$  latent dimensionality of the network activity over all time. We note that several sources of variability likely influence our imperfect State L Results. First, in our highly clustered network, the two states of network activity do not have drastically different population spiking statistics (Figure 3.4). Our Gaussian Mixture Model (GMM)’s unsupervised partitioning of activity into states can therefore produce variable results. Lacking a ground truth on network state, we cannot directly quantify the error in the GMM state partition, and all subsequent analyses are dependent upon this partition. This means it is possible that our State L partition of network activity contains instances of transitory dynamics. Second, our factor analyses of state-partitioned activity were performed on a single

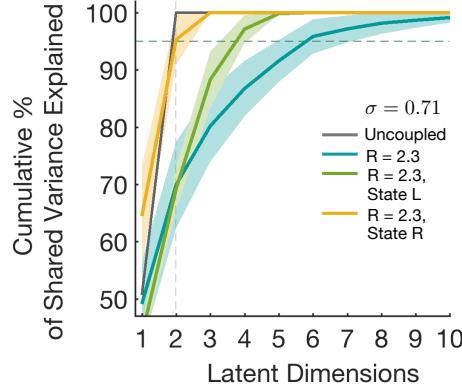


Figure 3.8: Factor Analysis of state-partitioned population activity in the biomimetic model network with  $R = 2.3$  clustering strength and  $\sigma = 0.71$  amplitude shared fluctuations from disjoint inputs (see Fig. 3.5a). Simulated activity was partitioned by a Gaussian Mixture Model (Methods 3.3.11). Spike counts were binned in 50 ms time windows. Analyses were performed over  $\sim 1000$  s of simulated activity from 10 samples of 100 neurons. Error bars are SEM. See Methods 3.3.12 for further details. The dimension of shared variance for state-partitioned activity (yellow and green for State R and L, respectively) is similar to that of the control network without recurrent coupling (grey), which has known linearizable dynamics (Fig. 3.3d-f).

instantiation of the network graph. Because our model network does not contain unlimited neurons, the micro-connectivity structure of our network in each graph instantiation can influence network dynamics. Third, we observe our network over  $\Delta t = 50$  ms time windows, despite the fact that our theory is for time windows of infinite length (Appendix B). Finally, we note that linearization of each state of a network with strong, recurrent coupling and input correlations would be merely an approximation for even a theoretical network of infinite neurons and labeled states of network dynamics that was observed over infinitely long time windows.

## 3.5 Discussion

We have shown that multi-stable attractor dynamics arise in balanced networks receiving structured, feedforward inputs from upstream neural populations with non-overlapping tuning preferences (Figure 3.4). In networks with uniform, random recurrent coupling, this multi-stability is characterized by “winner-take-all” dynamics, in which neurons receiving different feedforward inputs have strongly anti-correlated activity (Figure 3.4). Recurrent assembly structures

reflecting the input tuning help to dilute these pathological, winner-take-all dynamics, giving rise to population activity with smaller, biomimetic degrees of correlation (Figure 3.4). But even with de-correlating assembly architecture, recurrent network dynamics remain subtly metastable. Attractor competition between states of weakly correlated activity produces high-dimensional shared variability across the recurrent population (Figure 3.5). The result is a two-layer network in which low-dimensional shared variance inherited from multiple, tuned inputs is expanded through recurrent interactions. Using a model network with this connectivity architecture, we successfully reproduced *in vivo* neural data from the primate visual system in which V4’s dimension of shared variance was smaller than that of downstream visual area PFC (Figure 3.2a and 3.5a). Finally, we showed that a single attractor state of recurrent activity reflected the low-dimensional structure inherited from our V4 inputs (Figure 3.6-3.8). We thus introduced a new framework in which high-dimensional cortical variability can be understood as “time-sharing” between low-dimensional, tuning-specific circuit dynamics.

### 3.5.1 The structure of shared variance across subpopulations

Analyses of our *in vivo* data revealed that PFC neurons preferring the same visual hemifield had positively correlated spiking activity, while PFC neurons preferring opposite visual hemifields had uncorrelated spiking activity (Figure 3.1e-f). This result constitutes an asymmetry in the shared variance of tuning-specific subpopulations. Our network model does not currently capture this feature of the analyzed neural data. For computational simplicity, our model placed a symmetric constraint on the clustering coefficient  $R$  such that in-cluster synaptic strength was scaled uniformly for  $E$ -to- $E$ ,  $E$ -to- $I$ ,  $I$ -to- $E$ , and  $I$ -to- $I$  recurrent connections. As a result, increasing  $R$  symmetrically reduced correlations within hemifield and anti-correlations between hemifields (Figure 3.4a).

We showed in Methods 3.3.10 that the balance condition relies on the invertibility of our recurrent weight matrix. We note that previously studied recurrent architectures of excitatory-only clusters [60] will not restore invertibility to the recurrent weight matrix and will not dynamically balance the correlations inherited from our disjoint inputs. Though some degree of inhibitory cell type clustering is required to prevent our recurrent weight matrix from being singular, the invertibility condition does not require exact weight symmetry between all clustered

subpopulations. We therefore postulate that tuning-specific shared variance structure could be achieved by exploring the full space of recurrent connectivity architectures still satisfying the weight matrix invertibility condition. Characterizing this full connectivity space and relating it to network dynamics is an important topic for future study.

### 3.5.2 Long-timescale variability and co-variability through inheritance

Cortical neurons show firing rate fluctuations over long timescales [155, 156]. Fano factor is used as a measure of these firing rate fluctuations; since neurons are known to exhibit Poisson-like private spiking variability, Fano factors greater than 1 are thought to represent variability in a neuron’s underlying firing rate. In this case, neural activity behaves according to a “doubly stochastic” process [157], in which spike count variability and slow timescale firing rate dynamics are separable. Litwin-Kumar & Doiron [60] reproduced long timescale rate fluctuations by introducing assembly structure to excitatory subpopulations of recurrent layer neurons. In this framework, competing pockets of excitatory activity in the recurrent layer internally gave rise to attractor dynamics. Rate fluctuations, as measured by large Fano factor values, reflect competition between attractor states. Therefore, in Litwin-Kumar & Doiron [60]’s framework, increasing the cluster density lengthened the timescale of rate fluctuations and increased Fano factors.

Our model introduces a completely opposing potential mechanism for firing rate variability, in which tuned, disjoint inputs give rise to attractor dynamics. In our framework, a network with balanced, uniform recurrent coupling can have metastable activity by inheriting structured input correlations from upstream brain areas. Our uniform, balanced recurrent network ( $R = 1$ ) thus produces Fano factors greater than 1 at timescales capturing transitions between attractor states. Moreover, recurrent assemblies in our framework constitute neighborhoods of increased connectivity between all cell types. Our clustering parameter  $R$  strengthens  $E$ -to- $E$ ,  $I$ -to- $I$ ,  $E$ -to- $I$ , and  $I$ -to- $E$  connections. As such, our clusters are mechanisms to make the spatial scale of recurrent connections match the spatial scale of our disjoint inputs. In our framework, increasing the clustering strength  $R$  dilutes the metastable recurrent dynamics that arise through the input structure. Increased degrees of clustering thus result in reduced rate fluctuations and *smaller* Fano factors (Figure 3.5d).

Our framework also demonstrates an inverse relationship between Fano factor and the dimension of shared variability, as stronger clustering is associated with both smaller Fano factors and greater dimensionality expansion (Figure 3.5). Previous network models of internally-generated co-variability have been unable to decouple a direct relationship between the Fano factor magnitude and the rank of population-wide variability [24]. They have thus been unable to explain neural datasets with both low-rank shared variability and long timescale rate fluctuations [32]. Our framework might present a key to understanding such datasets.

These are two of the many ways in which our study highlights major differences in the dynamics of networks with internally generated versus inherited variability. We showed that structured inputs can significantly alter the dynamics of known recurrent architectures previously studied in isolation. We believe that studying the interplay between the mechanisms of inherited and internally-generated variability is an important direction for systems neuroscience, as it is widely acknowledged that integration areas of cortex receive common fluctuations from outside brain areas.



## A. Factor Analysis and the general form of Linear Gaussian Models

This appendix provides an overview of Factor Analysis (FA), a dimensionality reduction technique that has been used extensively on neural data (Introduction 1.2.1),[21] and is applied repeatedly to neural and simulated neural data in Chapter 3 of this thesis.

FA is part of a larger class of Linear Gaussian Models [40], which are discrete time linear dynamical systems of the general form

$$\begin{aligned} \vec{x}_{t+1} &= A\vec{x}_t + \vec{w} & \vec{w} &\sim \mathcal{N}(0, Q) \\ \vec{y}_t &= C\vec{x}_t + \vec{\epsilon} & \vec{\epsilon} &\sim \mathcal{N}(0, R). \end{aligned} \tag{A.1}$$

Here,  $\vec{y}$  is a matrix of observable variables. When Equation A.1 is used to model latent dynamics in neural data,  $\vec{y}$  is the zero-mean population vector of observed spike counts from  $N$  simultaneously recorded neurons.  $\vec{x}$  is the state of the population activity in a  $K$ -dimensional latent subspace, where  $K \ll N$ .  $\vec{x}$  evolves according to first-order Markov dynamics, governed by state transition matrix  $A$ .  $\vec{w}$  is a random variable representing state evolution.  $C$  is the *generative matrix* of model parameters relating the latent space  $\vec{x}$  to the observable data  $\vec{y}$ , and  $\vec{\epsilon}$  is a matrix of observation noise.

If we assume that our neural dataset is i.i.d., the underlying state matrix  $\vec{x}$  has no dynamics. In this case,  $A = 0$ , and the generative model reduces to

$$\begin{aligned} \vec{x} &= \vec{w} & \vec{w} &\sim \mathcal{N}(0, Q) \\ \vec{y} &= C\vec{x} + \vec{\epsilon} & \vec{\epsilon} &\sim \mathcal{N}(0, R). \end{aligned} \tag{A.2}$$

FA is a Linear Gaussian Model with stationary dynamics of form (A.2). FA places a constraint on

the structure of the observation noise  $\vec{\epsilon}$  such that  $R = \text{diag}(R) = \psi$ . In neuroscience, this constraint represents the assumption that the observation noise is uncorrelated between neurons and instead represents private sources of trial-to-trial neuronal variability, such as stochastic vesicle release.

The marginal distribution of  $\vec{y}$  in Equation (A.2) is a Gaussian of form

$$\vec{y} \sim \mathcal{N}(0, CQC^\top + \psi). \quad (\text{A.3})$$

Because there is an arbitrary sharing of scaling between  $Q$  and  $C$ , we can assume  $Q = \mathbb{I}$ . In FA, the generative matrix of model parameters  $C$  are called *loadings* onto latent factors. We will therefore make the variable change  $C = \mathbb{L}$ , where  $\mathbb{L}$  is a loading matrix. Thus, our FA model takes the form

$$\vec{y} \sim \mathcal{N}(0, \mathbb{L}\mathbb{L}^\top + \psi). \quad (\text{A.4})$$

This is equivalent to saying that the spike count covariance of our neural data can be decomposed into a shared variability component  $\mathbb{L}\mathbb{L}^\top$  and a private variability component  $\psi$ . The dimension of shared variability can then be understood as  $\text{rank}(\mathbb{L}\mathbb{L}^\top)$ , which is equivalent to performing an eigendecomposition of the shared variability in the  $K$  dimensional latent space:

$$\text{Cov}(\vec{y}, \vec{y}) = \sum_i^K \lambda_i \nu_i \nu_i^\top + \psi. \quad (\text{A.5})$$

Here,  $\lambda_i$  is the eigenvalue of the  $i$ th latent mode of neural population activity.

We will denote the cumulative percentage of shared variance explained by the top  $J$  latent dimensions  $p_{\text{Cum}}$ ; using (A.5), this is

$$p_{\text{Cum}} = \frac{\sum_i^J \lambda_i}{\sum_i^K \lambda_i} \quad (\text{A.6})$$

for  $J \leq K$  and latent modes of neural activity in descending eigenvalue order.  $p_{\text{Cum}}$  is frequently visualized in Chapter 3. Associated metric  $d_{\text{shared}}$  is the number of latent modes of neural activity  $J$  required to explain 95% of the shared variance, or the number of latent modes  $J$  such that  $p_{\text{Cum}} \geq 0.95$ .

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Chapter 3 also reports the percent of each neuron's total variance that is shared with other neurons in the population [59]. Using Eq. (A.4), we will denote  $p_n^{\text{shared}}$  of neuron  $n$

$$p_n^{\text{shared}} = \frac{\mathbb{L}_n \mathbb{L}_n^\top}{\mathbb{L}_n \mathbb{L}_n^\top + \psi_k}, \quad (\text{A.7})$$

where  $\mathbb{L}_n$  is the  $n$ th row of the loading matrix  $\mathbb{L}$  and  $\psi_k$  is neuron  $k$ 's private trial-to-trial variability, which is the  $k$ th diagonal in diagonal matrix  $\psi$ .

Finally, in Chapter 3, we report the residual spike count covariance without the 1st latent dimension, expressed by

$$Q = \text{Cov}(\vec{y}, \vec{y}) - \mathbb{L}_1 \mathbb{L}_1^\top, \quad (\text{A.8})$$

where  $\mathbb{L}_1$  denotes loadings onto the first latent dimension when FA is only fitted with  $K = 1$  latent dimension.

FA model parameters in Chapter 3 were fitted using an Expectation Maximization (EM) [141] algorithm. Fits were performed using two-fold cross validation, where the dimensionality of the latent space  $K$  was selected according to the cross-validated log-likelihood of the models.



## B. Linear response approximation of covariance

This appendix reviews approximation methods [139, 120] of using network architecture to predict the pairwise spiking covariance of neurons. Consider a neuron with stochastically fluctuating membrane potential dynamics. We begin with a linear ansatz [162] that says the process by which a neuron integrates its inputs and produces a realization of a spike train is linear. This ansatz requires that the input  $X(t)$  to the neuron be weak in relation to the neuron's underlying noise process  $\xi(t)$ , which drive its membrane potential fluctuations. Assuming this is true, a realization of a neuron's spiking output  $y(t)$  can be defined

$$y_i(t) \approx y_{i0}(t) + (G_i * X)(t), \quad (\text{B.1})$$

where  $y_{i0}(t)$  is the unperturbed point process, or realization of the neuron's spiking output due to its unperturbed membrane potential dynamics,  $X(t)$  is a weak input with vanishing temporal average over the window in which we observe the system's behavior, and  $G(t)$  is the neuron's linear response, which measures its sensitivity to its inputs.

When the neuron is part of a larger network, input  $X(t)$  comes from the neuron's recurrent network interactions. So long as those interactions are still sufficiently weak such that the neuron's spike train output is a linear transformation of its inputs, our linear ansatz still applies. In this case, we will replace  $X(t)$  with the expression  $(f_i(t) - \mathbb{E}_t[f_i])$ , where  $E_t[\cdot]$  is an expectation over time and

$$f_i(t) = \sum_j J_{ij} (F_j * y_j)(t). \quad (\text{B.2})$$

Here,  $y_j(t)$  is the spiking response of neuron  $j$  that projects to neuron  $i$  with synaptic strength  $J_{ij}$ , and  $F_j$  is the synaptic filter applied to neuron  $j$ 's output.

The convolution terms of Equations (B.1) and (B.2) become multiplicative relations in the

Fourier domain. We thus consider the Fourier transform of a spike train,  $y_i(\omega) = \int_{-\infty}^{\infty} y_i(t) e^{-2\pi i \omega t} dt$ , where  $\omega$  is frequency. Combining Equations (B.1) and (B.2), the recurrent network formulation of the spike train of neuron  $i$  in the Fourier domain is

$$y_i(\omega) = y_i^0(\omega) + G_i(\omega) \left( \sum_j J_{ij} F_j(\omega) y_j(\omega) \right). \quad (\text{B.3})$$

The linear response  $G_i(\omega)$  now measures the degree to which synaptic currents at frequency  $\omega$  are transferred into modulations about background spike train activity  $y_i^0(\omega)$ .

The cross-spectral density (CSD) of the activity of  $i$  and  $j$  – which is the equivalent to the Fourier transform of the pairwise spike train cross-covariances of  $i$  and  $j$ ,  $C_{ij}(s)$  – is written:

$$C_{ij}(\omega) = \langle y_i(\omega) y_j^*(\omega) \rangle, \quad (\text{B.4})$$

where  $y^*$  is the conjugate transpose of  $y$ . The full pairwise CSD matrix of our network activity is then

$$C(\omega) = (\mathbb{I} - (J \cdot K(\omega)))^{-1} C^0(\omega) (\mathbb{I} - (J \cdot K(\omega))^*)^{-1}, \quad (\text{B.5})$$

where  $\cdot$  denotes element wise multiplication and  $K(\omega)$  is an interaction matrix with entries  $K_{ij}(\omega) = A_i(\omega) F_{ij}(\omega)$ .  $C^0(\omega)$  is the CSD in the absence of recurrent interactions.

We now note that spike count covariances over long windows ( $\Delta t \rightarrow \infty$ ) can be expressed as the zero-frequency CSD:

$$\lim_{\Delta t \rightarrow \infty} \frac{1}{\Delta t} \text{Cov} \left( \int_t^{\Delta t} U(t') dt' \int_t^{\Delta t} Z(t') dt' \right) = \langle U, Z \rangle(\omega = 0). \quad (\text{B.6})$$

For large  $\Delta t$ , the spike count covariance of a pair of neurons  $i$  and  $j$  can then be approximated as:

$$\text{Cov}(N_i(t, t + \Delta t), N_j(t, t + \Delta t)) \approx \Delta t \langle y_i(t'), y_j(t') \rangle(\omega = 0) \quad (\text{B.7})$$

This means the linear response approximation of  $C(\omega = 0)$  can be reduced to

$$C = (\mathbb{I} - (J \cdot K))^{-1} C^0 \left( \mathbb{I} - (J \cdot K)^{\top} \right)^{-1}, \quad (\text{B.8})$$

where  $C$  is the spike count covariance of the network over an infinitely long window (B.7) and

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$C^0$  is the spike count covariance of the network in the absence of recurrent interactions, also over an infinitely long window. Equation (B.8) is known as the zero-frequency linear response approximation. We use the zero-frequency linear response approximation throughout Chapter 3 rather than computing the population CSD over all frequencies  $\omega$  (B.5). The zero-frequency approximation both dramatically simplifies the calculations required to characterize population covariance and makes our predictions of population covariance structure more comparable to the myriad of experimental neuroscience studies that have reported values of spike count covariance and noise correlations (computed using spike count covariance) in the brain [114].

We obviously do not observe our network activity over infinitely long time windows. Why is the approximation of Equation (B.8) then valid? The answer lies in the shape of neuronal linear response functions  $G(\omega)$ , which tend to be approximately constant from  $\omega = 0$  to  $\omega \approx 30$  Hz [65, 163]. This claim is equivalent to saying that neuron  $i$  has the same sensitivity to its inputs for synaptic current modulations of frequency 30 Hz or less.

In Chapter 3, we observe our network activity over windows of  $\Delta t = 50$  ms. This is equivalent of observing our network's response to perturbations at frequency  $\omega = 20$  Hz. While our choice of timescale is probably still within the range  $\omega$  over which  $G(\omega)$  is approximately constant, we do note that we are at the upper boundary of  $\omega$  over which the zero-frequency response (B.8) might provide a good approximation of our second order network statistics. We made a conscious choice to observe our system at  $\Delta t = 50$  ms windows because we needed to capture the spike count covariance of our population activity within one attractor state of our network, and our network tended to transition between attractor states at timescales  $\tau < 300$  ms. However, we acknowledge that the  $\Delta t = 50$  ms windows over which we compute spike count covariance might be another source of error in our reported linear response approximation of  $C$  in network State L (Chapter 3, Figure 3.6d-e).



## C. Chapter 3 Supplemental Figures

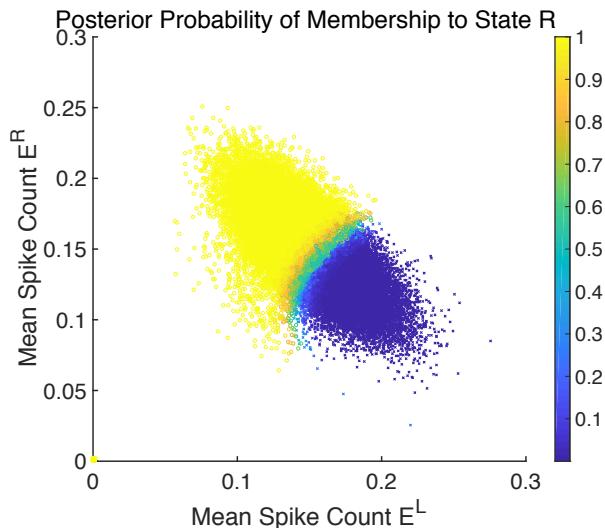


Figure C.1: Gaussian Mixture Model (GMM) state partitions of spiking network activity. Each data point here represents one time bin ( $\Delta t = 50$  ms) of the activity of all  $N^E = 4000$  excitatory cells in the  $R = 2.3, \sigma = 0.71$  network, simulated for a total of  $T = 2000s$ . The  $N^E$  dimensional population activity is projected onto the 4D space described by the mean and variance of the firing activity of each hemifield. (Here we visualize the data in the 2D space described by the hemifield population means.) The GMM computes the posterior probability that each time bin of population activity belongs to State R. (The GMM was constrained to 2 clusters, and the posterior probability of membership to State R and State L sum to 1.) We accepted time bins for which the posterior probability of membership to either state was greater than 0.97. Other time bins (those that are not true yellow or royal blue in this visualization) were considered to represent dynamics in which our network was transitioning between the two attractor states.



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