Supplementary Materials for

Single-Neuron Network Topology Governs Neural Computation and Learning in Primate Cortex

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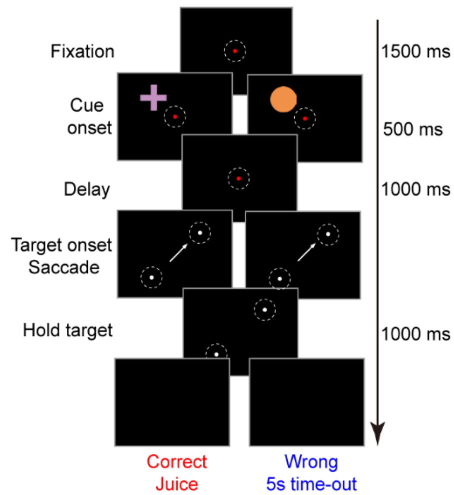

Fig. S1. Behavioral task. In this task, monkeys were required to learn associations between different visual images and two saccade directions. On each trial, monkeys had to saccade to one of two targets based on the presented visual image. Each trial began with the monkey acquiring central fixation, which was maintained for 1500 ms. A visual image then appeared on the screen for 500 ms. After a 1-second delay, the fixation point disappeared, and two saccade targets appeared simultaneously on the left and right sides of the screen. Monkeys were required to saccade to the target associated with the presented visual image within a 400 ms time window and maintain fixation on the chosen target for 1 second to receive a juice reward. If the monkey failed to respond correctly, it received a 5-second timeout as a punishment.

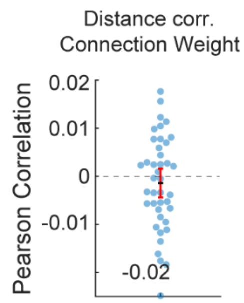

Fig. S2. Lack of significant correlation between connection weights and spatial distance between neurons. Pearson correlation was calculated between the connection weight and the distance for each pair of neurons within each network. Each dot represents data from one network.

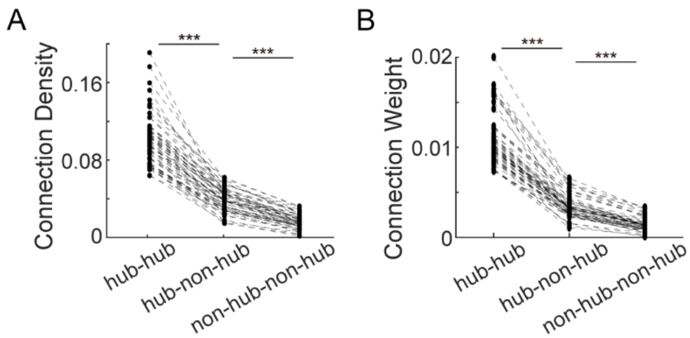

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Fig. S3. Hub neurons exhibit stronger and denser connections than non-hub neurons. (A) Comparison of connection density between hub-to-hub neurons, hub-to-nonhub neurons, and non-hub-to-non-hub neurons. **(B)** Comparison of connection strength (weight) across these groups. Each line represents the averaged result for one network. ***: P << 0.001.

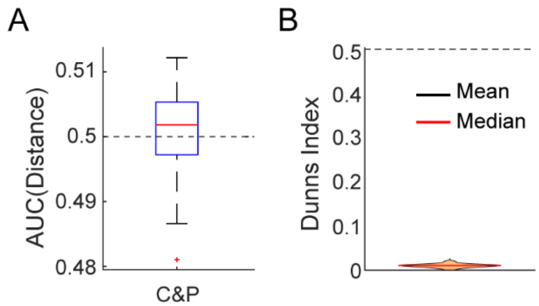

Fig. S4. Hub and non-hub neurons did not exhibit spatial overlapping. (A) An area under the curve (AUC) analysis was used to assess spatial distance differences between in-group (hub-to-hub, non-hub-to-non-hub) and out-group (hub-to-non-hub) neuron pairs. An AUC value close to 0.5 indicates no significant difference in spatial distance between these two classes of neuron pairs. **(B)** The Dunn Index was used to quantify intra-group distance relative to inter-group distance. A Dunn Index close to 0 indicates that the distance between groups is much smaller than the spatial scale of the groups themselves, suggesting spatial overlap for neither hub nor non-hub neurons.

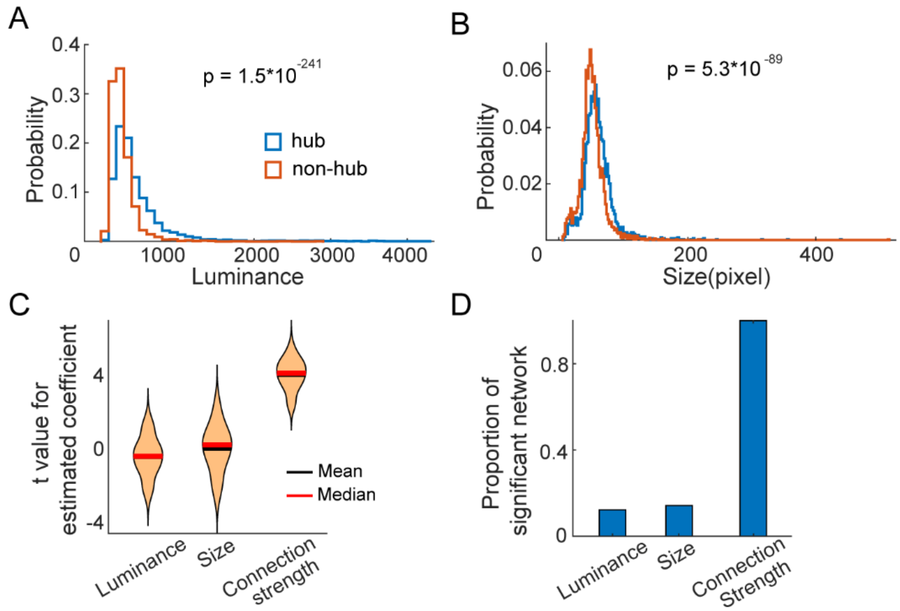

Fig. S5. Physiological Properties (Fluorescence Luminance and Size) Were Not the Primary Contributors to Neurons' Hub or Non-Hub Status. (A-B) Comparison of fluorescence luminance and size distributions between hub and non-hub neurons. On average, hub neurons exhibited higher fluorescence luminance and larger sizes than non-hub neurons. **(C-D)** A linear model was used to quantify the contributions of fluorescence luminance, size, and connection strength to neurons' hub/ non-hub status within each network. **(C)** t-values of the estimated coefficients from the linear model are shown separately for fluorescence luminance, size, and connection strength. **(D)** Proportion of networks in which each variable significantly ($p<0.05$) contributed to hub/non-hub status. Fluorescence luminance and size were significant contributors in only a small fraction of networks, whereas connection strength was a significant contributor in all networks.

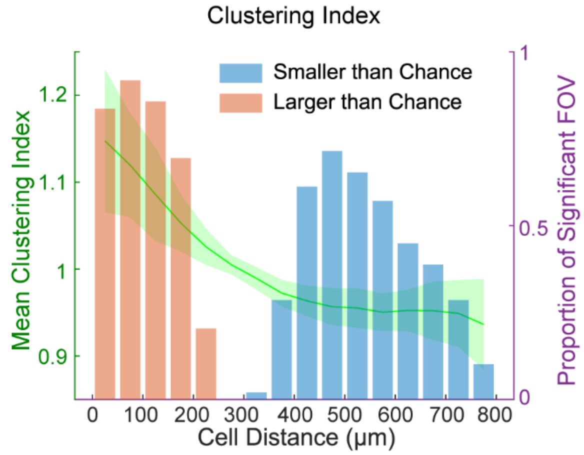

Fig. S6. Neurons within each network module exhibit significant spatial clustering. This figure presents the modular spatial clustering index for all PPC neuron networks. The spatial clustering index was calculated based on the probability that two neurons belong to the same module. Values greater than 1 indicate that neuron pairs are more likely to be in the same module than expected by chance (modular affinity), whereas values smaller than 1 indicate that neuron pairs are less likely to be in the same module than expected by chance (modular exclusion). The spatial clustering index was computed for neuron pairs within each distance bin (50 µm bins from 0 to 800 µm). The mean ± standard deviation (green line, left Y-axis) of the spatial clustering index across all PPC networks is overlaid with the proportion of sessions (right Y-axis) that exhibited significant modular affinity (red bars) or modular exclusion (blue bars) at each distance bin. The results demonstrate that most networks exhibit significant spatial clustering of modular organization.

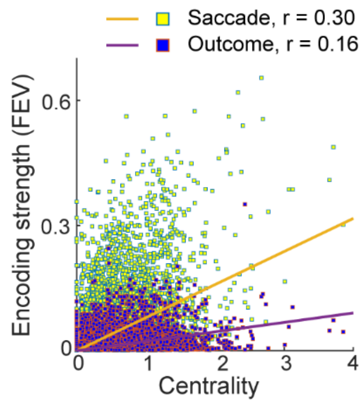

Fig. S7. The neurons' encoding strength for key task variables correlated with their hub/ non-hub status in the network. The centrality was calculated for measuring the connection strength for each neuron in the network. Neurons form all network were pooled together. The brown and purple lines represent the linear fits of neurons' saccade direction encoding and trial outcome encoding, respectively, based on their centrality in the network.

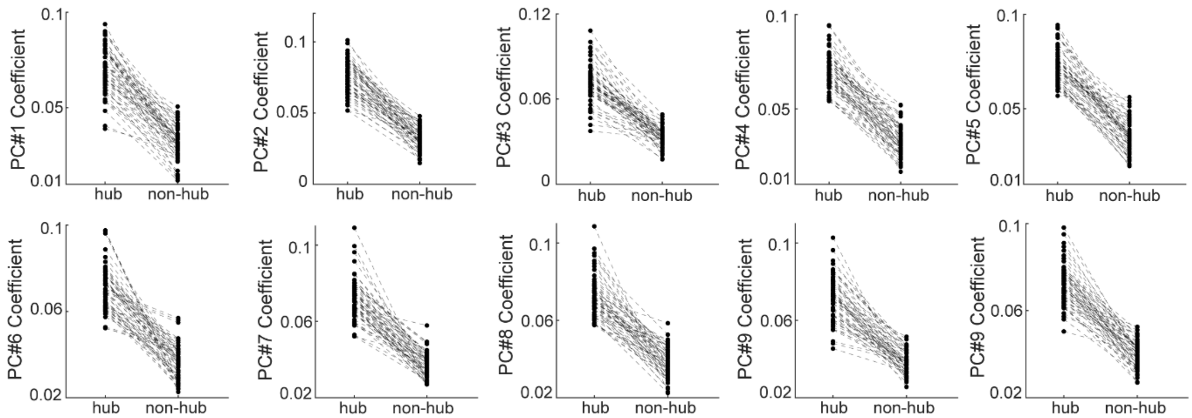

Fig. S8. Hub neurons contributed significantly more to population activity dynamics than non-hub neurons. Principal component analysis (PCA) was used to reduce the dimensionality of neuronal population activity within each network, projecting it onto the top 10 principal components (PCs). The averaged absolute PC coefficient, which quantifies each neuron's contribution to the corresponding PC of population activity, was compared between hub and non-hub neurons across networks.

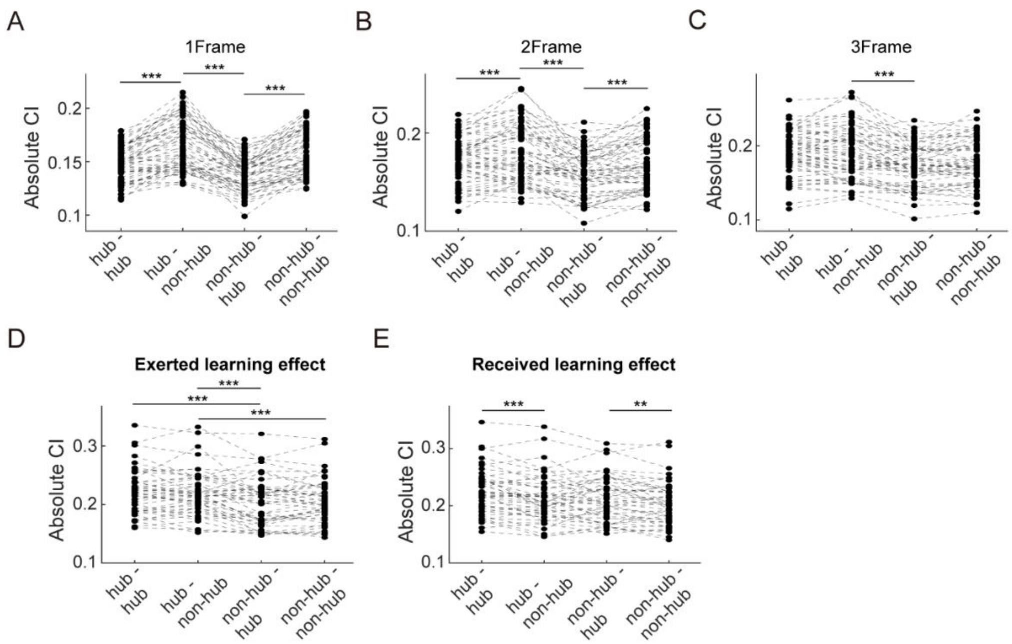

Fig. S9. Hub neurons play a central role in driving activity dynamics and shaping the evolution of neural encoding during monkeys' task performance and learning. (A-C) Hub neurons exhibit a greater causality index (CI) toward non-hub neurons than non-hub neurons exhibit toward hub neurons across time lags of 1 (A), 2 (B), and 3 (C) recording frames. **(D)** Comparison of the exerted learning effect between hub and non-hub neurons across PPC networks. The exerted learning effect, measured using the CI, is defined as the influence of each neuron's activity on other neurons' selectivity to key task variables in the following session (day). Hub neurons exhibited a significantly greater exerted learning effect than non-hub neurons. **(E)** Comparison of the received learning effect, which quantifies the influence of a neuron's selectivity to key task variables is influenced by the activity of other neurons in the previous session (day). Hub neurons also exhibited a significantly greater received learning effect than non-hub neurons. ***: P << 0.001.

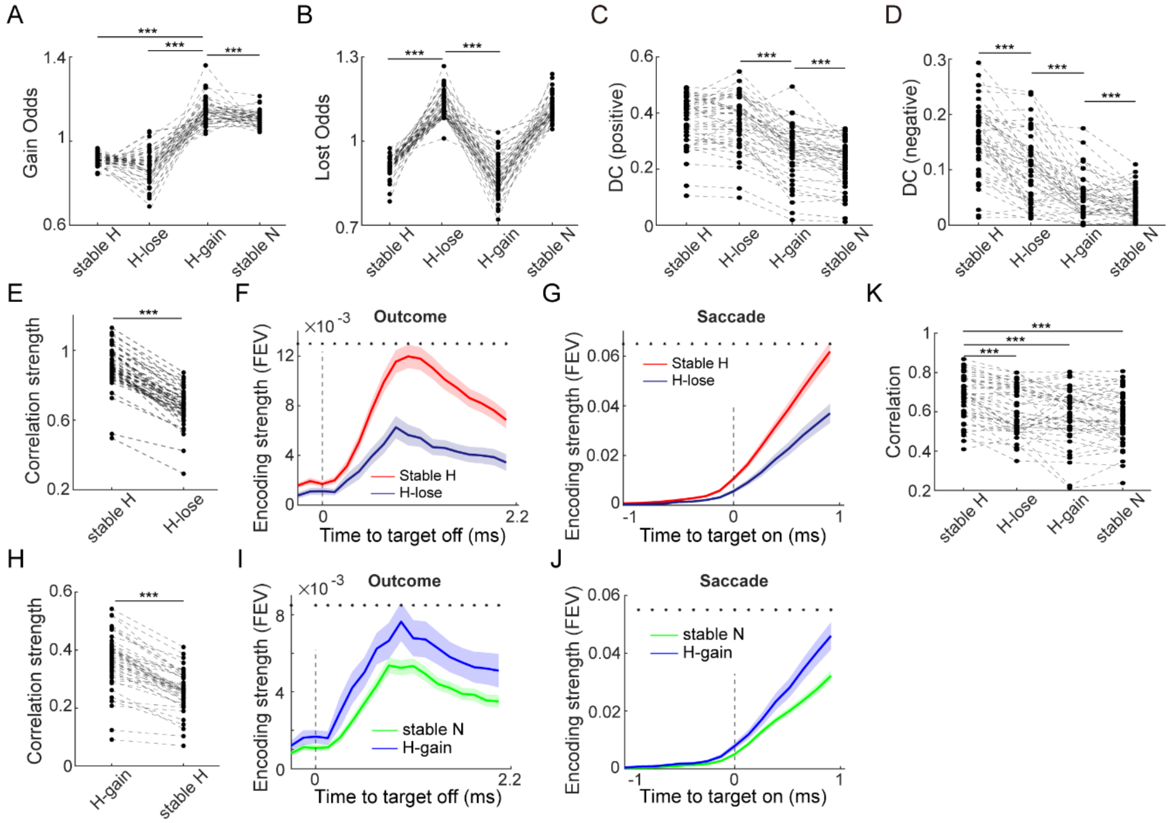

Fig. S10. Transitions in neurons' hub/non-hub status are associated with network topology and neuronal function. (A) Comparison of the odds of gaining significant connection weight across two successive learning days among four neuron groups: stable hub neurons (stable H), hub-losing neurons (H-lose), hub-gaining neurons (H-gain), and stable non-hub neurons (stable N). Hub-gaining neurons acquired more network connections than the other groups. **(B)** Comparison of the odds of losing significant connection weight across two successive learning days among the four groups. Hub-losing neurons lost more network connections compared to stable hub or hub-gaining neurons. **(C-D)** The transition of hub/non-hub status was correlated with inter-module connectivity within the network, measured by the diversity coefficient (DC). Positive and negative DC comparisons among different neuron groups are shown in (C) and (D), respectively. **(E)** Comparison of connection strength between stable hub neurons and hub-losing neurons. **(F-G)** Comparison of the encoding strength of key task variables between stable hub neurons and hub-losing neurons. The encoding strength for trial outcome and saccade direction is shown in (F) and (G), respectively. **(H)** Comparison of connection strength between stable non-hub neurons and hub-gaining neurons. **(I-J)** Comparison of key task variable encoding strength between stable non-hub neurons and hub-gaining neurons. **(K)** Comparison of the stability of neuronal encoding among different neuron groups, quantified by the correlation of neural selectivity across two successive learning days. Stable hub neurons exhibited the highest encoding stability among all groups. ***: $P << 0.001$.

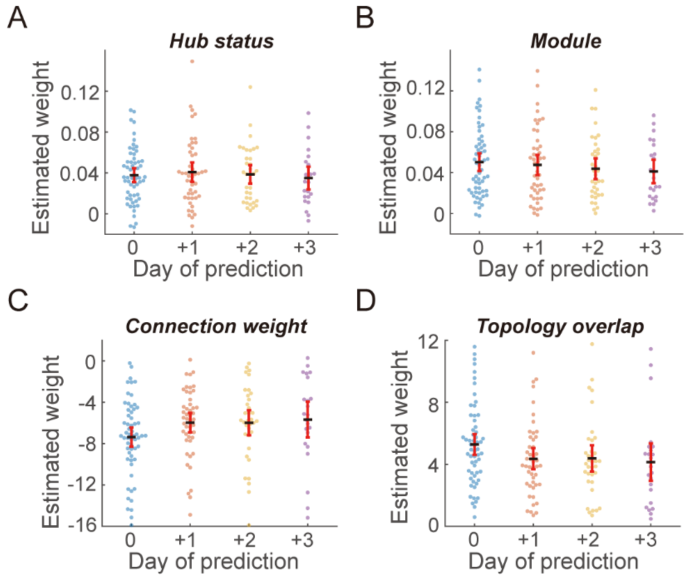

Fig. S11. Network properties predict the similarity of neuronal encoding within the PPC network. (A-D) A linear model incorporating four network parameters was used to predict signal correlation between all neuron pairs within each network, both on the current day and across successive learning days. The estimated coefficients for hub/nonhub status (A), modular organization (B), relative connection weight (C), and topology overlap (D) are shown separately. Each dot represents data from one network. Across different networks and time intervals, the sign of each estimated coefficient remains consistent.

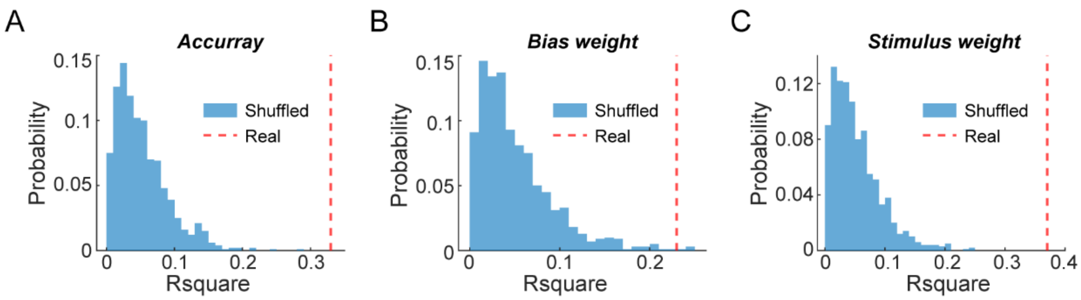

Fig. S12. Network topology predicts monkeys' daily behavioral performance during learning. We used a stepwise linear model incorporating multiple topological features of PPC neuron networks to predict the monkeys' daily behavioral performance. **(A)** Permutation test evaluating the relationship between network topology and daily performance accuracy. The histogram shows the distribution of model fit (goodness-of-fit) from linear models built on shuffling learning days for each network. The red dashed line indicates the model fit from real data, which was significantly higher than the shuffled distribution, indicating a meaningful predictive relationship. **(B-C)** We employed the dynamic 'PsyTrack' model to estimate two behavioral weights: stimulus weight ($W_{stimulus}$) and bias weight (W_{bias}), which quantify the influence of visual stimuli and internal bias on monkeys' saccade choices, respectively. Each weight was independently modeled using linear regressions based on network topological features. Permutation test results for the relationship between network topology and bias weight and stimulus weight are shown in (B) and (C), respectively.

Behavior	Variable	Estimate	SE	tStat	pValue
Accuracy	Q_{mod}	-4.3141	1.0663	-4.0459	1.6417e-04
	SPL	-10.7177	2.1733	-4.9316	7.8992e-06
	Q_{mod}**SPL*	16.5257	3.6126	4.5745	2.7588e-05
W_{bias}	Density	19.4007	8.1761	2.3729	0.0212
	Q_{mod}	6.7713	2.1758	3.1121	0.0029
	SPL	-6.3946	1.7027	-3.7556	4.1921e-04
$W_{stimulus}$	Q_{mod}	-34.8355	7.2571	-4.8002	1.2561e-05
	SPL	-83.5321	14.7913	-5.6474	5.9298e-07
	Q_{mod}**SPL*	134.0772	24.5871	5.4532	1.2079e-06

Table S1. Linear models with PPC neuron network parameters predict the monkeys' daily behavioral performance during associative learning. $W_{stimulus}$ and W_{bias} represent the extent to which the monkeys' saccade choice during each learning day was based on visual stimuli and internal bias, respectively. Q_{mod}: modularity; *SPL*: normalized short-path length; *Den*: averaged connection density.