Supporting Information for

The mechanics of correlated variability in segregated cortical excitatory subnetworks

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Network stability

The deterministic version of Eq. 8 (Fig. S1A)

$$\frac{d\boldsymbol{\Delta}\mathbf{r}}{dt} = (\mathbf{W} - \mathbf{I})\Delta\mathbf{r}(t)$$

is *asymptotically stable* if the eigenvalues λ_i of $\mathbf{W} - \mathbf{I}$ satisfy $\Re[\lambda_i] < 0$, meaning that a perturbation of the excitatory rates is quenched and rates are returned to their steady-state values (Fig. S1B, top) (1). An equivalent condition for stability is if the eigenvalues λ_i of $\mathbf{W}$ satisfy $\Re\{\lambda_i\} < 1$. We say that a network is stable if it admits a stable equilibrium solution, otherwise we say the network is unstable.

The inhibition-stabilized network (ISN). A linear network is an *inhibition stabilized network* (ISN) (2) if it satisfies two conditions:

(1) The network is unstable in the absence of (dynamic) feedback inhibition,

(2) The network is stable with sufficiently strong inhibition.

We consider the conditions under which the global inhibition motif (i.e., two excitatory populations with one shared inhibitory population) is an ISN. The corresponding weight matrix is

$$\mathbf{W} = \begin{bmatrix} W_{EE} & \alpha W_{EE} & W_{EI} \\ \alpha W_{EE} & W_{EE} & W_{EI} \\ W_{IE} & W_{IE} & W_{II} \end{bmatrix},$$

which has eigenvalues

$$\begin{aligned} \lambda_1 &= (1-\alpha)\cdot W_{EE}, \\ \lambda_{2,3} &= \frac{1}{2}\left[(1+\alpha)\cdot W_{EE} + W_{II} \pm \sqrt{(1+\alpha)^2 W_{EE}^2 + 8W_{EI}W_{IE} - 2(1+\alpha)W_{EE}W_{II} + W_{II}^2}\right]. \end{aligned}$$

We note that λ_1 does not depend on any of the inhibitory connections. As a result, if $\lambda_1 = (1-\alpha)\cdot W_{EE} > 1$ the system is unstable and inhibition is unable to stabilize it, so we necessarily require $(1-\alpha)\cdot W_{EE} < 1$. On the other hand, $\lambda_{2,3}$ do depend on the inhibitory connections. Absent feedback inhibition (i.e., $W_{EI} = 0$) these eigenvalues become

$$\lambda_2 = (1+\alpha)\cdot W_{EE} \text{ and } \lambda_3 = W_{II}.$$

In this work the latter is always less than 1. Meanwhile, it is possible to increase recurrent excitation such that $\lambda_2 = (1+\alpha)\cdot W_{EE} > 1$. Unlike the previous condition derived with λ_1, we can choose inhibitory parameters W_{EI}, W_{II} such that this eigenvalue decreases below 1, restoring the stability of the system. Thus, this system lies in the ISN regime when

$$(1+\alpha)\cdot W_{EE} > 1 \text{ and } (1-\alpha)\cdot W_{EE} < 1.$$

If the first condition is satisfied while the second condition is violated, the system exhibits winner-take-all dynamics where one excitatory population increases away from steady state while the second decreases away from it (Fig. S1B, bottom). All three regions (non-ISN, ISN, and winner-take-all) are shown in Fig. S1C. The same constraint to lie in the ISN regime can also be derived for the specific inhibition motif.

Positive correlations in segregated subpopulations

We prove here that if $|W_{EI}W_{IE}|$ is chosen such that the segregated E_i/I_i subpopulation model lying in the ISN regime is stable, then $C_{E_1E_2} > 0$. This is achieved by deriving first a condition on $|W_{EI}W_{IE}|$ that implies stability, and then one that implies $C_{E_1E_2} > 0$. We then show that the stability condition implies the positive covariance condition.

$|W_{EI}W_{IE}|$ **condition implying stability.** Consider the connectivity matrix that corresponds to the segregated four population network configuration

$$\mathbf{W} = \begin{bmatrix} W_{EE} & \alpha W_{EE} & W_{EI} & 0 \\ \alpha W_{EE} & W_{EE} & 0 & W_{EI} \\ W_{IE} & 0 & W_{II} & 0 \\ 0 & W_{IE} & 0 & W_{II} \end{bmatrix}.$$

Assume that the individual excitatory-inhibitory subunits lie in the ISN regime (i.e., $W_{EE} > 1$) and that there exist values of W_{EI} and W_{IE} such that the system is stable. Note that together, these two conditions imply that the segregated four-population network is an ISN. Here, we derive a condition involving W_{EI} and W_{IE}, specifically a condition on $|W_{EI}W_{IE}|$, that guarantees the system's stability.

We start by noting that while this matrix has four eigenvalues, it can easily be shown that the largest eigenvalue, and the one that determines the stability of the system, is given by

$$\lambda = \frac{1}{2}\left[(1+\alpha)W_{EE} + W_{II}\right] + \frac{1}{2}\sqrt{\left[(1+\alpha)W_{EE} - W_{II}\right]^2 + 4W_{EI}W_{IE}}.$$

Since $W_{EI}W_{IE} < 0$, we can rewrite λ explicitly as a function of $|W_{EI}W_{IE}|$,

$$\lambda(|W_{EI}W_{IE}|) = \frac{1}{2}\left[(1+\alpha)W_{EE} + W_{II}\right] + \frac{1}{2}\sqrt{\left[(1+\alpha)W_{EE} - W_{II}\right]^2 - 4|W_{EI}W_{IE}|}, \qquad \text{[S1]}$$

which emphasizes that it is a decreasing function of $|W_{EI}W_{IE}|$.

For the system to be an ISN, we require $\Re(\lambda(|W_{EI}W_{IE}|)) > 1$ for low levels of feedback inhibition (i.e., the system is unstable) and $\Re(\lambda(|W_{EI}W_{IE}|)) < 1$ for high levels (i.e., the system is stable). To derive a stability condition that relies explicitly on $|W_{EI}W_{IE}|$, we can then set Eq. S1 equal to one and solve for $|W_{EI}W_{IE}|$. However, we first must show that it is possible to solve this corresponding equation. We will do this by showing that values of $|W_{EI}W_{IE}|$ exist such that $\Re(\lambda(|W_{EI}W_{IE}|)) > 1$ and $\Re(\lambda(|W_{EI}W_{IE}|)) < 1$.

First, note that the maximum value of $\lambda(|W_{EI}W_{IE}|)$ occurs when $W_{EI}W_{IE} = 0$, so we have that

$$\max_{|W_{EI}W_{IE}|\geq 0} \Re(\lambda(|W_{EI}W_{IE}|)) = (1+\alpha)W_{EE} > 1, \qquad \text{[S2]}$$

where the last inequality follows from the fact that $\alpha > 0$ (by definition) and $W_{EE} > 1$ (since we are assuming that the individual excitatory-inhibitory subunits are ISNs).

Second, note that $\lambda(|W_{EI}W_{IE}|)$ is complex for all values of $|W_{EI}W_{IE}|$ such that

$$|W_{EI}W_{IE}| > \frac{1}{4}\left[(1+\alpha)W_{EE} - W_{II}\right]^2,$$

and that this parameter regime coincides with values where $\Re(\lambda(|W_{EI}W_{IE}|))$ reaches its minimum. A quick calculation therefore yields

$$\min_{|W_{EI}W_{IE}|\geq 0} \Re(\lambda(|W_{EI}W_{IE}|)) = \frac{1}{2}\left[(1+\alpha)W_{EE} + W_{II}\right].$$

Since $\Re(\lambda(|W_{EI}W_{IE}|))$ is a decreasing function of $|W_{EI}W_{IE}|$ and we are assuming there exist values of W_{EI} and W_{IE} such that the system is stable (again, since we are assuming the network is an ISN), this minimum must be less than 1, leading to the condition

$$\min_{|W_{EI}W_{IE}|\geq 0} \Re(\lambda(|W_{EI}W_{IE}|)) = \frac{1}{2}\left[(1+\alpha)W_{EE} + W_{II}\right] < 1. \qquad \text{[S3]}$$

Together, Ineq. S2 and Ineq. S3 imply that there exists a value of $|W_{EI}W_{IE}|$ such that

$$\begin{aligned}\Re(\lambda(|W_{EI}W_{IE}|)) &= \lambda(|W_{EI}W_{IE}|)\\ &= \frac{1}{2}\left[(1+\alpha)W_{EE} + W_{II}\right] + \frac{1}{2}\sqrt{\left[(1+\alpha)W_{EE} - W_{II}\right]^2 - 4|W_{EI}W_{IE}|}\\ &= 1.\end{aligned}$$

Rearranging this equation yields

$$\sqrt{\left[(1+\alpha)W_{EE} - W_{II}\right]^2 - 4|W_{EI}W_{IE}|} = 2 - (1+\alpha)W_{EE} - W_{II}.$$

Solving this for $|W_{EI}W_{IE}|$, we find

$$|W_{EI}W_{IE}| = (-1 + (1+\alpha)W_{EE})(1 - W_{II}).$$

Thus, stability of the four-population system is guaranteed for all values of $|W_{EI}W_{IE}|$ such that

$$|W_{EI}W_{IE}| > (-1 + (1+\alpha)W_{EE})(1 - W_{II}). \qquad \text{[S4]}$$

$|W_{EI}W_{IE}|$ condition implying $C_{E_1E_2} > 0$. Using Eq. 2 for the long-time covariance matrix, we can calculate $C_{E_1E_2}$ directly (i.e., without using the expansion). We find that the covariance between E_1 and E_2 is given by

$$C_{E_1E_2} = \left[\frac{2\sigma^2}{\det(M)^2}\cdot \alpha W_{EE}\left(W_{EI}^2 + (1-W_{II})^2\right)\cdot(1-W_{II})\right]\cdot\Big[|W_{EI}W_{IE}| - (-1+W_{EE})(1-W_{II})\Big].$$

The first set of terms in the bracket are all positive. So it follows that for $C_{E_1E_2} > 0$ we require

$$|W_{EI}W_{IE}| - (-1+W_{EE})(1-W_{II}) > 0,$$

and so

$$|W_{EI}W_{IE}| > (-1+W_{EE})(1-W_{II}). \qquad \text{[S5]}$$

Stability implies $C_{E_1E_2} > 0$. Since $\alpha > 0$, we have that Ineq. S4 implies Ineq. S5, namely

$$|W_{EI}W_{IE}| > (-1 + (1+\alpha)W_{EE})(1 - W_{II}) \Rightarrow |W_{EI}W_{IE}| > (-1 + W_{EE})(1 - W_{II}),$$

Thus, we conclude that the stability of the segregated E_i/I_i system guarantees positive correlations between E_1 and E_2.

Covarying cross-population connections

It is possible that in the segregated E_i/I_i subpopulation model (Fig. 5A), covarying cross-population connections might induce synergetic effects different from those observed by adding singular bidirectional connections (Fig. 5C). We tested this numerically by adding pairwise combinations of $E \to I$, $I \to E$, and $I \to I$ (Fig. S2A-C). Only when ζ (scaling $I \to I$) dominated either β or γ was an increase in correlations observed; $E \to I$ and $I \to E$ connections always reduced correlations, consistent with the foregoing results.

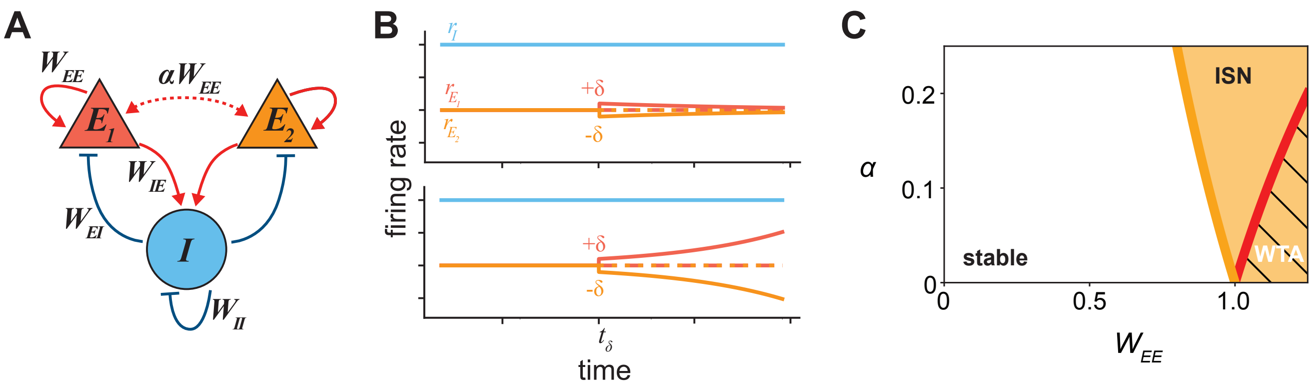

Fig. S1. Dynamical regimes and limitations on α. A: Network schematic. **B:** Illustrations of a small change in the input $+\delta$ to E_1 and $-\delta$ to E_2. Top: stable network regime; bottom: unstable (winner-take-all) regime. **C:** $W_{EE} - \alpha$ space. Yellow region: inhibition-stabilized (ISN); black hatched region: winner-take-all (unstable). Solid yellow line: $W_{EE} = 1/(1+\alpha)$. Solid red line: $\alpha = 1 - 1/W_{EE}$. Parameters as in Fig. 5. α changed to 0.1 for the unstable regime in B.

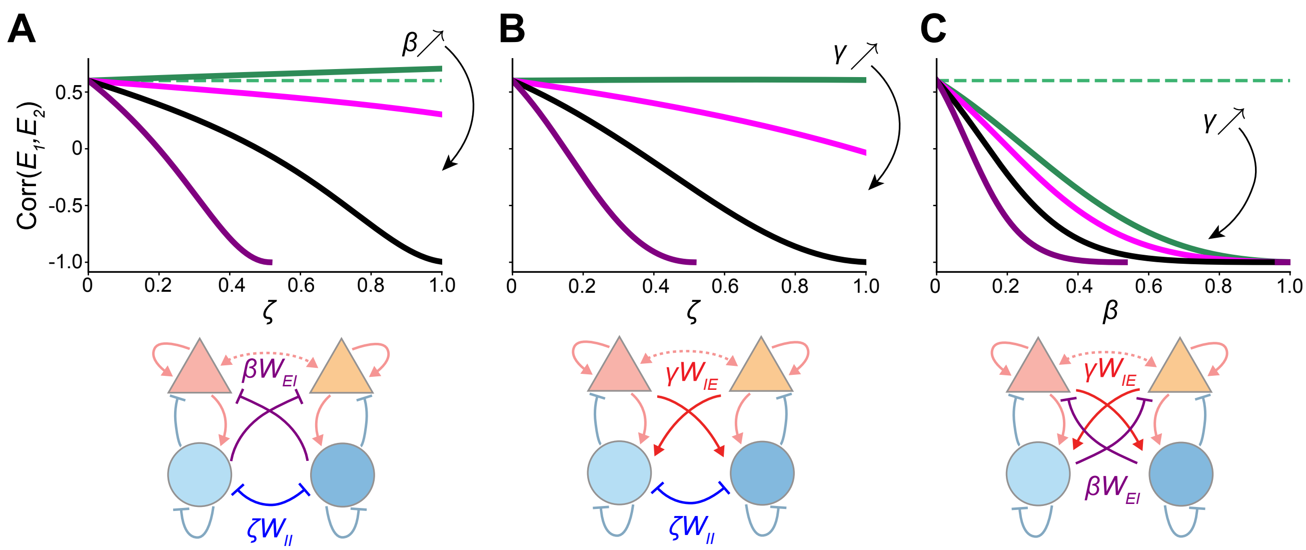

Fig. S2. Covarying cross-population connections in segregated ISN. A: Top: $Corr(E_1, E_2)$ as a function of ζ; colored lines indicate different values of β. Black line indicates when $\zeta = \beta$. Bottom: network schematics indicating connection weights co-varied in the above plot. Green dashed line indicates value of $Corr(E_1, E_2)$ for $W_{EI} = W_{IE}$. Parameters as in Fig. 5. **B:** same as (A) for ζ and γ. **C:** same as (A) for β and γ.

References

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2. H Ozeki, IM Finn, ES Schaffer, KD Miller, D Ferster, Inhibitory stabilization of the cortical network underlies visual surround suppression. *Neuron* **62**, 578–592 (2009).