

# Supplementary Information

## Orchestrated Excitatory and Inhibitory Learning Rules Lead to the Unsupervised Emergence of Up-states and Balanced Network Dynamics

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August 12, 2021

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## 1 Summary of results

### 1.1 *Homeostatic* learning rule

The equations for the Homeostatic learning rule are

$$\begin{aligned}
 \frac{dW_{EE}}{dt} &= +\alpha_{EE} E(E_{set} - E) \\
 \frac{dW_{EI}}{dt} &= -\alpha_{EI} I(E_{set} - E) \\
 \frac{dW_{IE}}{dt} &= +\alpha_{IE} E(I_{set} - I) \\
 \frac{dW_{II}}{dt} &= -\alpha_{II} I(I_{set} - I)
 \end{aligned} \tag{1}$$

and the condition for the Up state to be stable under this rule is

$$\begin{aligned}
 (R^2\alpha_3 + \alpha_4)(W_{EEup}g_E - 1)g_I \\
 < (R^2 + \alpha_2)(W_{IIup}g_I + 1)g_E
 \end{aligned} \tag{2}$$

where

$$R = E_{set}/I_{set}$$

$$\alpha_2 = \alpha_{EI}/\alpha_{EE}$$

$$\alpha_3 = \alpha_{IE}/\alpha_{EE}$$

$$\alpha_4 = \alpha_{II}/\alpha_{EE}$$

which is satisfied for biologically backed parameter values only if  $\alpha_{IE}$  and  $\alpha_{II}$  are small enough (slow inhibitory weights). See the step-by-step derivation of this stability condition in Section 2.3.

### 1.2 *Cross-Homeostatic* learning rule

The equations for the Cross-Homeostatic learning rule are

$$\begin{aligned}
 \frac{dW_{EE}}{dt} &= +\alpha_{EE} E(I_{set} - I) \\
 \frac{dW_{EI}}{dt} &= -\alpha_{EI} I(I_{set} - I) \\
 \frac{dW_{IE}}{dt} &= -\alpha_{IE} E(E_{set} - E) \\
 \frac{dW_{II}}{dt} &= +\alpha_{II} I(E_{set} - E)
 \end{aligned} \tag{3}$$

This rule is stable for any set of parameter values because the stability condition of the Up state can be written as:

$$(R^2\alpha_3 + \alpha_4)W_{EIup} + (R^2 + \alpha_2)W_{IEup} > 0 \tag{4}$$

(where  $R$  and  $\alpha_{2,3,4}$  are defined as in the previous subsection). This condition is always satisfied as the

weights and the parameters are all positive definite. See the step-by-step derivation of this stability condition in Section 2.4.

### 1.3 *Two-Factor* learning rule

The equations for the Two-Factor learning rule are

$$\begin{aligned}\frac{dW_{EE}}{dt} &= +\alpha E(I_{set} - I) + \beta E(E_{set} - E) \\ \frac{dW_{EI}}{dt} &= -\alpha I(I_{set} - I) - \beta I(E_{set} - E) \\ \frac{dW_{IE}}{dt} &= -\alpha E(E_{set} - E) + \beta E(I_{set} - I) \\ \frac{dW_{II}}{dt} &= +\alpha I(E_{set} - E) - \beta I(I_{set} - I)\end{aligned}\quad (5)$$

and the condition for the Up state to be stable under this rule is

$$(a - b)\beta < (a' + b' + c)\alpha \quad (6)$$

where

$$\begin{aligned}a &= (W_{EEup}g_E - 1)E_{set}I_{set}g_I \\ a' &= (W_{EEup}g_E - 1)E_{set}^2g_I \\ b &= (W_{IIup}g_I + 1)E_{set}I_{set}g_E \\ b' &= (W_{IIup}g_I + 1)I_{set}^2g_E \\ c &= (I_{set}\Theta_I - E_{set}\Theta_E)g_Eg_I\end{aligned}$$

Condition Eq. 6 is satisfied for biologically backed parameter values. See the step-by-step derivation of the stability condition in Section 2.5.

### 1.4 *SynapticScaling* learning rule

The equations for the SynapticScaling learning rule are

$$\begin{aligned}\frac{dW_{EE}}{dt} &= +\alpha_{EE}(E_{set} - E)W_{EE} \\ \frac{dW_{EI}}{dt} &= -\alpha_{EI}(E_{set} - E)W_{EI} \\ \frac{dW_{IE}}{dt} &= +\alpha_{IE}(I_{set} - I)W_{IE} \\ \frac{dW_{II}}{dt} &= -\alpha_{II}(I_{set} - I)W_{II}\end{aligned}\quad (7)$$

and the condition for the Up state to be stable under this rule is

$$(W_{EEup}g_E - 1)a < (W_{IIup}g_I + 1)b \quad (8)$$

where

$$\begin{aligned}a &= (I_{set}W_{II}\alpha_4 + \Theta_I\alpha_3)g_I \\ b &= E_{setup}W_{EEup}g_E \\ &\quad + ((W_{EEup}g_E - 1)E_{set} - \Theta_Eg_E)\alpha_2 \\ &\quad - (W_{EEup}g_E - 1)I_{set}\alpha_3\end{aligned}$$

(where  $\alpha_{2,3,4}$  are defined as in previous subsections). This stability condition does not hold for biologically backed parameter values unless the dynamics of the weights onto the inhibitory neuron are slow enough (and in a few fine-tuned cases). See the step-by-step derivation of the stability condition in Section 2.6.

## 2 Detailed calculations

### 2.1 Overview

We analyze the whole neural+synaptic system for every synaptic learning rule considered in this work, and study their stability. In every case, the general prescription is:

1. Take the combined neural+synaptic system and nondimensionalize all variables [see Sections 1.2 and 1.4 of Ref. 1][see Section 3.5 of Ref. 2], so that the two different time scales are evident (fast neural, slow synaptic).
2. Make a quasi-steady state (QSS) approximation of the neural subsystem [1, 2]. This means we will consider the neural subsystem is fast enough so that it converges “instantaneously” (when compared to the synaptic subsystem) to its corresponding fixed point. For this we will require that the stability conditions of the neural subsystem are satisfied (see below).
3. Find the steady-state solution of the synaptic subsystem, i.e. the Up state fixed point; compute the Jacobian of the synaptic subsystem at

the Up state; compute the eigenvalues of the Jacobian [2, 3]. Two out of the four eigenvalues are expected to be zero because the Up state is not an isolated fixed point of the system but a continuous 2D plane in 4D weight space.

4. Address (linear) stability. If both nonzero eigenvalues have negative real part, then the Up state is stable under the learning rule; if at least one of the nonzero eigenvalues has positive real part, then the Up state is unstable [2, 3]. (A note on abuse of notation: we might say indistinctly “the Up state is stable/unstable” and “the learning rule is stable/unstable”)

Eigenvalues and stability in the presence of continuous, i.e. non-isolated, attractors have been discussed in the context of neural networks for eye position control [4, 5] (keep in mind that their eigenvalues’ critical value is 1 instead of zero because they consider eigenvalues of the connectivity matrix alone, whereas we consider eigenvalues of the full system). As the Up state is a collection of non-isolated fixed points that form a 2D plane, there is no dynamics along the plane, and the linear stability analysis is enough to fully address stability—we do have two zero eigenvalues, but there is no need to compute the center manifold [3] because the other two eigenvalues represent the whole dynamics around the fixed point and have nonzero real part.

In order to apply the tools from Dynamical Systems’ theory for flows in a unified way for both the neural and synaptic subsystems, we will switch from a discrete-time description of synaptic weight dynamics (where the change in weight  $W$  is represented by  $\Delta W$  applied every certain time interval) to a continuous-time description (where the weights are continuously evolving albeit with a long time scale  $\tau_0$ ):

$$\Delta W \rightarrow \tau_0 \frac{dW}{dt}$$

In the following we first define the neural subsystem and compute its stability conditions (next subsection). Then we consider every learning rule in detail (following subsections).

**Paradoxical regime.** We show detailed calculations of the stability conditions for every learning rule in the paradoxical regime only; see Section 2.7 for the non-paradoxical case.

## 2.2 Neural dynamics

For the neural+synaptic system in the QSS approximation to be stable under a specific synaptic learning rule, it is necessary that the neural subsystem is stable so it remains in its QSS solution as the weights evolve. In this section we define the neural subsystem and compute its stability conditions.

(SageMath code in the Supplementary Material: `up states - Neural subsystem stability.ipynb`)

### 2.2.1 System’s equations and fixed points

We consider a two-subpopulation model with firing-rate units  $E$  and  $I$  with ReLU activation functions (gain  $g_X$ , threshold  $\Theta_X$ , with  $X = E, I$ ). The dynamics for synaptic currents above threshold is given by:

$$\begin{aligned} \frac{dE}{dt} &= \frac{1}{\tau_E} (-E + g_E (W_{EE} E - W_{EI} I - \Theta_E)) \\ \frac{dI}{dt} &= \frac{1}{\tau_I} (-I + g_I (W_{IE} E - W_{II} I - \Theta_I)) \end{aligned} \quad (9)$$

All variables and parameters are definite positive. In this subsection the synaptic weights  $W_{XY}$  are fixed.

**Up state** The Up state is the non-trivial fixed point of the system (i.e. a steady-state solution where  $dE/dt = dI/dt = 0$ ):

$$\begin{aligned} E_{up} &= (W_{EI} g_I \Theta_I - (W_{II} g_I + 1) \Theta_E) g_E / C \\ I_{up} &= ((W_{EE} g_E - 1) \Theta_I - W_{IE} g_E \Theta_E) g_I / C \end{aligned} \quad (10)$$

where

$$C = W_{EI} W_{IE} g_E g_I - (W_{II} g_I + 1)(W_{EE} g_E - 1) \quad (11)$$

The activity of the excitatory and inhibitory subpopulations at the Up state,  $E_{up}$  and  $I_{up}$ , depend on all weight values. Only some of the combinations, however, lead to a stable steady state. We compute the stability conditions in the following subsection.

### 2.2.2 Stability of neural fixed point (Up state)

The Jacobian matrix, that is the matrix of first derivatives, gives information regarding the stability of fixed points: if the real parts of its eigenvalues are all negative, then the fixed point is stable.

The Jacobian of the neural system (Eq. 9) is

$$J = \begin{pmatrix} (W_{EE}g_E - 1)/\tau_E & -W_{EI}g_E/\tau_E \\ W_{IE}g_I/\tau_I & -(W_{II}g_I + 1)/\tau_I \end{pmatrix} \quad (12)$$

Its eigenvalues can be expressed as:

$$\lambda_{1,2} = \frac{1}{2} \left( Tr \pm \sqrt{Tr^2 - 4Det} \right) \quad (13)$$

where  $Tr$  and  $Det$  are the trace and determinant of the matrix, respectively. For eigenvalues either complex or purely real, their real parts are negative (and thus the Up state is stable) when  $Det > 0$  and  $Tr < 0$ , that is:

$$W_{EI}W_{IE}g_Eg_I > (W_{EE}g_E - 1)(W_{II}g_I + 1) \quad (14)$$

$$(W_{II}g_I + 1)\tau_E > (W_{EE}g_E - 1)\tau_I \quad (15)$$

Note that the positive determinant condition, Eq. 14, is equivalent to  $C > 0$  (Eq. 11).

In the following, we will require that the stability conditions of the neural subsystem, Eqs. 14 and 15, are satisfied.

### 2.2.3 Weight values consistent with an Up state

The Up state relationships, Eq. 10, are expressed as the  $E$  and  $I$  values resulting from a given set of weight values. If we set instead  $E$  and  $I$  to their target values  $E_{set}$  and  $I_{set}$  and solve for the weights, we get the weight values that are consistent with a given Up state activity:

$$W_{EIup} = \frac{(E_{set}W_{EEup} - \Theta_E)g_E - E_{set}}{I_{set}g_E} \quad (16)$$

$$W_{IIup} = \frac{(E_{set}W_{IEup} - \Theta_I)g_I - I_{set}}{I_{set}g_I}$$

Note first that any stable learning rule for the evolution of the weights for the neural subsystem (Eq.

9) must converge to weight values in accordance with these relationships (either in the form Eq. 16 or Eq. 10).

Second, note that the system is underdetermined and that is why two of the weights are free ( $W_{EE}$  and  $W_{EI}$ ). Note also that all weight values must be positive; specifically, requiring  $W_{EIup} > 0$  and  $W_{IIup} > 0$  leads to

$$W_{EEup} > \frac{\Theta_E g_E + E_{set}}{E_{set} g_E} \quad (17)$$

$$W_{IIup} > \frac{\Theta_I g_I + I_{set}}{I_{set} g_I} \quad (18)$$

We refer to these expressions as the “positive  $W_{EI}$ ” and the “positive  $W_{II}$ ” conditions, respectively.

### 2.2.4 Paradoxical effect

The paradoxical effect arises when an external depolarization of the inhibitory subpopulation (increase of  $I$ ) produces an actual *decrease* of  $I$ . In this model, an external depolarization of  $I$  can be mimicked by a decrease of its threshold  $\Theta_I$ , thus there is a paradoxical effect whenever the coefficient of  $\Theta_I$  in the numerator of  $I_{up}$  is positive. The coefficient is  $g_I (W_{EE}g_E - 1)/C$  and thus there is paradoxical effect if

$$W_{EE}g_E - 1 > 0 \quad (19)$$

The paradoxical effect can also be seen in a plot of the Up-state values  $E_{up}$  and  $I_{up}$  (Eq. 10) as a function of each individual weight. Specifically, from a naive point of view  $I_{up}$  should increase when  $W_{IE}$  is increased, and decrease when  $W_{II}$  is increased; however, it does the opposite in either case (see Figure S3).

## 2.3 Homeostatic learning rule

(SageMath code in the Supplementary Material: `up states - Homeostatic stability.ipynb`)

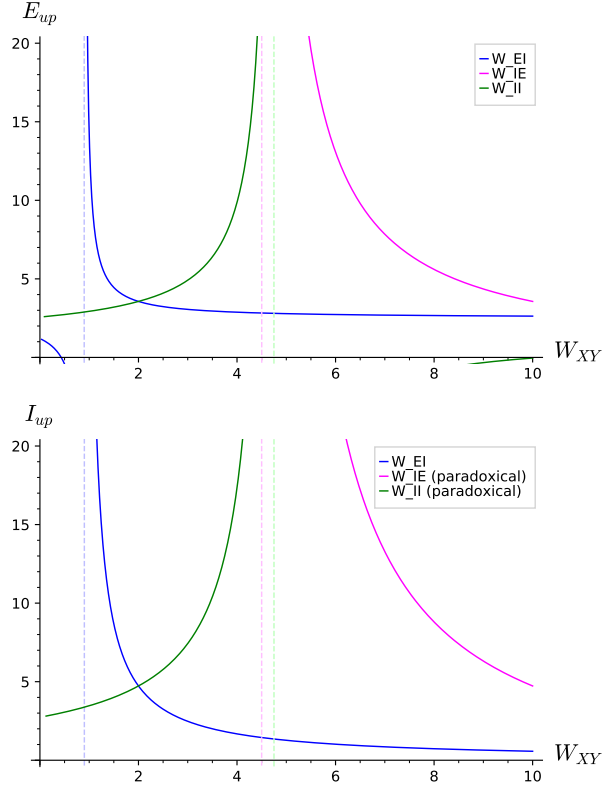


Figure S3: Paradoxical effect in the neural subsystem ( $W_{EE} = 5$ ; parameter values as in Table 1).  $E_{up}$  behaves as expected when each weight is varied.  $I_{up}$ , however, shows paradoxical behavior when either  $W_{IE}$  or  $W_{II}$  are varied. Dashed lines are the vertical asymptote of every case.

### 2.3.1 Definition of the learning rule

In continuous-time dynamics, the Homeostatic learning rule reads:

$$\begin{aligned}
 \frac{dW_{EE}}{dt} &= +\alpha_{EE} E(E_{set} - E) \\
 \frac{dW_{EI}}{dt} &= -\alpha_{EI} I(E_{set} - E) \\
 \frac{dW_{IE}}{dt} &= +\alpha_{IE} E(I_{set} - I) \\
 \frac{dW_{II}}{dt} &= -\alpha_{II} I(I_{set} - I)
 \end{aligned} \tag{20}$$

$I_{set}$	$=$	14	$E_{set}$	$=$	5
$g_I$	$=$	4	$g_E$	$=$	1
$\Theta_I$	$=$	25	$\Theta_E$	$=$	4.8
$\tau_I$	$=$	2	$\tau_E$	$=$	10

Table 1: Parameter values throughout the Supplementary Material. This set of parameter values makes the neural subsystem to be in the paradoxical regime (i.e. the Up state is an inhibition-stabilized fixed point [6]). For non-paradoxical conditions, see Section 2.7.

where  $\alpha_{XY}$  ( $X, Y = E, I$ ) are the learning rates (with appropriate units) setting the time scales of the weight dynamics, and  $E_{set}$  and  $I_{set}$  are the set points of the excitatory and inhibitory subpopulations, respectively.

The fixed points of the system (i.e. steady states) are determined by setting all derivatives to zero. There is a non-trivial fixed point compatible with the neural subsystem being above threshold: the Up state, that is the set of weight values such that:

$$\begin{aligned}
 E_{up} &= E_{set} \\
 I_{up} &= I_{set}
 \end{aligned} \tag{21}$$

The values of the weights corresponding to the Up state are given by the (underdetermined) system defined by equating Eqs. 21 and 10. Since it is a two-equation system for a set of four unknown weights, there are two free weights that we choose to be  $W_{EEup}$  and  $W_{IEup}$ . The values of the other two are given by Eq. 16. This means that the Up-state fixed point is actually a continuous set of non-isolated fixed points forming a 2D plane in 4D weight space. In other words, there is an infinite number of weight values compatible with the Up state (possibly not all stable, though).

### 2.3.2 Nondimensionalization

Next we nondimensionalize all variables in order to have a simpler system and make the QSS approximation in a safe way. We define new (nondimensional) variables  $e, i, \tau, w_{EE}, w_{EI}, w_{IE}$ , and  $w_{II}$ , and their corresponding scaling parameters. We substitute the

new variables into the full system (neural+synaptic, Eqs. 9 and 20) and choose the values of the scaling parameters such that all nondimensional variables are of order 1 (see attached SageMath code). With this, the full system reads:

$$\begin{aligned}
\epsilon_E \frac{de}{d\tau} &= -e + Rew_{EE} - \frac{iw_{EI}}{R} - \theta_E \\
\epsilon_I \frac{di}{d\tau} &= -i + \frac{Rew_{IE}}{g} - \frac{iw_{II}}{Rg} - \theta_I \\
\frac{dw_{EE}}{d\tau} &= -e(e-1) \\
\frac{dw_{EI}}{d\tau} &= +\alpha_2 i(e-1) \\
\frac{dw_{IE}}{d\tau} &= -\alpha_3 e(i-1) \\
\frac{dw_{II}}{d\tau} &= +\alpha_4 i(i-1)
\end{aligned} \tag{22}$$

where we defined the new parameters

$$\begin{aligned}
\epsilon_E &= \tau_E / \tau_0 \\
\epsilon_I &= \tau_I / \tau_0 \\
\tau_0 &= 1 / (\alpha g_E E_{set} I_{set}) \\
R &= E_{set} / I_{set} \\
g &= g_E / g_I \\
\alpha_2 &= \alpha_{EI} / \alpha_{EE} \\
\alpha_3 &= \alpha_{IE} / \alpha_{EE} \\
\alpha_4 &= \alpha_{II} / \alpha_{EE} \\
\theta_E &= (g_E / E_{set}) \Theta_E \\
\theta_I &= (g_I / I_{set}) \Theta_I
\end{aligned}$$

### 2.3.3 Quasi-steady state approximation

Neural dynamics evolves in a much shorter time scale ( $\tau_E$  and  $\tau_I$ ) than synaptic dynamics ( $\tau_0$ ):

$$\begin{aligned}
\tau_E \ll \tau_0 &\implies \epsilon_E \ll 1 \\
\tau_I \ll \tau_0 &\implies \epsilon_I \ll 1
\end{aligned}$$

which implies

$$\begin{aligned}
\epsilon_E \frac{de}{d\tau} &\sim 0 \\
\epsilon_I \frac{di}{d\tau} &\sim 0
\end{aligned} \tag{23}$$

thus we can safely assume  $e$  and  $i$  very quickly reach quasi-equilibrium values, i.e. practically instantaneous convergence to quasi-steady state (QSS) values as if the weights were fixed, while the synaptic weights evolve according to their slow dynamics. This allows us to reduce the system's dimensionality from six to four.

In the QSS approximation, the values of the nondimensionalized excitatory and inhibitory activities instantaneously track the slow dynamics of the learning rule. They are determined by applying Eq. 23 to the first two rows of Eq. 22; solving for  $e$  and  $i$  leads to

$$\begin{aligned}
e_{qss} &= (g\theta_I w_{EI} - (w_{II} + Rg)\theta_E) / c \\
i_{qss} &= (Rg\theta_I (Rw_{EE} - 1) - R^2\theta_E w_{IE}) / c
\end{aligned} \tag{24}$$

where

$$c = Rw_{EI}w_{IE} - (w_{II} + Rg)(Rw_{EE} - 1)$$

The full system in the QSS approximation reads

$$\begin{aligned}
\frac{dw_{EE}}{d\tau} &= -e_{qss}(e_{qss} - 1) \\
\frac{dw_{EI}}{d\tau} &= +\alpha_2 i_{qss}(e_{qss} - 1) \\
\frac{dw_{IE}}{d\tau} &= -\alpha_3 e_{qss}(i_{qss} - 1) \\
\frac{dw_{II}}{d\tau} &= +\alpha_4 i_{qss}(i_{qss} - 1)
\end{aligned} \tag{25}$$

where  $e_{qss}$  and  $i_{qss}$  are nonlinear functions of the weights as defined by Eq. 24.

Note that the Up state fixed point, defined by making all derivatives equal to zero, can be expressed as

$$\begin{aligned}
e_{qss} &= 1 \\
i_{qss} &= 1
\end{aligned} \tag{26}$$

which is the nondimensionalized version of Eq. 21. The weight values compatible with this condition are defined by equating Eqs. 24 and 26:

$$\begin{aligned}
w_{EIup} &= R(Rw_{EEup} - 1) - R\theta_E \\
w_{IIup} &= R(Rw_{IEup} - g) - Rg\theta_I
\end{aligned} \tag{27}$$

( $w_{EEup}$  and  $w_{IEup}$  are free). This is the nondimensionalized version of Eq. 16.

### 2.3.4 Stability condition

The program for assessing linear stability of the Up state is as follows: a) compute the Jacobian (the matrix of first derivatives) of Eq. 25 and evaluate it at the Up state; b) compute the eigenvalues of the Jacobian (two of them will be zero because the fixed points form a continuous 2D plane in phase space); c) If the real part of the two nonzero eigenvalues is negative then the Up state is stable; if at least one of the nonzero eigenvalue has positive real part then the Up state is unstable.

**Jacobian matrix** Let the full system in the QSS approximation (Eq. 25) be written as

$$\begin{aligned}\frac{dw_{EE}}{d\tau} &= f_{EE}(e_{qss}, i_{qss}) \\ \frac{dw_{EI}}{d\tau} &= f_{EI}(e_{qss}, i_{qss}) \\ &\text{etc} \dots\end{aligned}$$

where  $e_{qss}$  and  $i_{qss}$  are functions of the weights as defined by Eq. 24. By applying the chain rule the elements  $J_{ij}$  ( $i, j = 1 \dots 4$ ) of the Jacobian matrix can be expressed as

$$\begin{aligned}J_{11} &= \frac{df_{EE}}{dw_{EE}} = \frac{df_{EE}}{de_{qss}} \frac{de_{qss}}{dw_{EE}} + \frac{df_{EE}}{di_{qss}} \frac{di_{qss}}{dw_{EE}} \\ J_{12} &= \frac{df_{EE}}{dw_{EI}} = \frac{df_{EE}}{de_{qss}} \frac{de_{qss}}{dw_{EI}} + \frac{df_{EE}}{di_{qss}} \frac{di_{qss}}{dw_{EI}} \\ J_{13} &= \dots \\ J_{21} &= \frac{df_{EI}}{dw_{EE}} = \frac{df_{EI}}{de_{qss}} \frac{de_{qss}}{dw_{EE}} + \frac{df_{EI}}{di_{qss}} \frac{di_{qss}}{dw_{EE}} \\ J_{22} &= \dots \\ &\text{etc} \dots\end{aligned}$$

In order to have the Jacobian specialized in the Up state, these expressions are to be substituted by Eqs. 24-27.

**Eigenvalues of the Jacobian matrix** The Jacobian matrix has two zero eigenvalues and two nonzero eigenvalues. The nonzero eigenvalues have the form:

$$\lambda_{\pm} = \frac{A \pm \sqrt{A^2 - DC}}{C} \quad (28)$$

where

$$\begin{aligned}A &= R^2 g\theta_I + (R^2 \alpha_3 + \alpha_4) R w_{EEup} \\ &\quad - (R^2 + \alpha_2) R w_{IEup} + \alpha_2 g\theta_I - R^2 \alpha_3 - \alpha_4 \\ C &= 2R(Rg\theta_I w_{EEup} - R\theta_E w_{IEup} - g\theta_I) \\ D &= 2(R^2 \alpha_3 + \alpha_4)(R^2 + \alpha_2)/R\end{aligned} \quad (29)$$

**Sign of the eigenvalues** To determine the sign of the real part of Eq. 28, first note that the factor  $D$  is positive definite. Second,  $C$  must be positive because it is related to one of the stability conditions of the neural subsystem (Eq. 14, after substituting back to dimensionalized quantities). Note next that  $A^2 - DC$  is less than  $A^2$  (since  $C$  and  $D$  are positive), and thus the square root is either real and less than  $|A|$  or imaginary, both cases leading to  $\text{Re}(A \pm \sqrt{A^2 - DC}) < 0$  if  $A < 0$ . The learning rule is then stable (both eigenvalues have negative real part) if  $A < 0$ , which in terms of the original parameters and free weights  $W_{EE}$  and  $W_{IE}$  reads:

$$\begin{aligned}(E_{set}^2 \alpha_{EE} + I_{set}^2 \alpha_{EI}) E_{set} g_E W_{IEup} \\ > (E_{set}^2 \alpha_{IE} + I_{set}^2 \alpha_{II}) I_{set} (W_{EEup} g_E - 1) \\ &\quad + (E_{set}^2 \alpha_{EE} + I_{set}^2 \alpha_{EI}) \Theta_I g_E\end{aligned} \quad (30)$$

### 2.3.5 Analysis of the stability condition

It is hard to determine whether the stability condition Eq. 30 is satisfied for a general set of parameter values (see numerical analysis below). However, by using the Up state relationship Eq. 16, this condition can be re-expressed in a more useful form in terms of  $W_{EE}$  and  $W_{II}$ :

$$\begin{aligned}(R^2 \alpha_3 + \alpha_4)(W_{EEup} g_E - 1) g_I \\ < (R^2 + \alpha_2)(W_{IIup} g_I + 1) g_E\end{aligned} \quad (31)$$

Note that learning rates values of the same order lead to  $\alpha_{2,3,4} \sim 1$  and that biologically backed parameter values satisfy:

$$\begin{aligned}I_{set} &> E_{set} \\ g_I &> g_E\end{aligned}$$

both likely preventing the condition to hold.

On the other hand, small enough values of  $\alpha_3$  and  $\alpha_4$  (by making the dynamics of the weights onto the inhibitory neuron  $W_{IE}$  and  $W_{II}$  slower) would help satisfy the condition thus making the system stable.

### 2.3.6 Numerical analysis

As an illustration of the results above, in Figure S4(top) we plot the stability condition Eq. 30 with parameter values as in Table 1 and learning rates  $\alpha_{XY} = 0.02$ . It is clear that the learning rule is stable in a region with little overlap with the stability region of the neural subsystem.

The stability region can be enlarged by making the dynamics of the weights onto the inhibitory neuron slower, as in Figure S4(bottom) where  $\alpha_{EE} = \alpha_{EI} = 0.02$  and  $\alpha_{IE} = \alpha_{II} = 0.001$  (the stability boundary of the learning rule coincides with the trace condition of the neural subsystem).

### 2.3.7 Relationship between the stability condition and the paradoxical condition

The boundary of the stability condition for this learning rule, Eq. 30, is a linear function in the  $(W_{EE}, W_{IE})$  space with a slope that tends to infinity as the excitatory learning rates ( $\alpha_{EE, EI}$ ) tend to zero:

$$\text{slope} = \frac{(E_{set}^2 \alpha_{IE} + I_{set}^2 \alpha_{II}) I_{set}}{(E_{set}^2 \alpha_{EE} + I_{set}^2 \alpha_{EI}) E_{set}}$$

while its root is a complicated expression (see SageMath notebook) that tends to  $W_{EE} = 1/g_E$ . The region of stability is to the left of the line. Thus, the boundary of stability in this limit coincides exactly with the boundary of the paradoxical condition ( $W_{EE} > 1/g_E$ ). This can be construed as an inconsistency/contradiction between the stability of the rule and the existence of the paradoxical effect.

## 2.4 Cross-Homeostatic learning rule

(SageMath code in the Supplementary Material: `up states - CrossHomeostatic stability.ipynb`)

In this section we follow a path analogous to the one in the previous section, so we will skip some details.

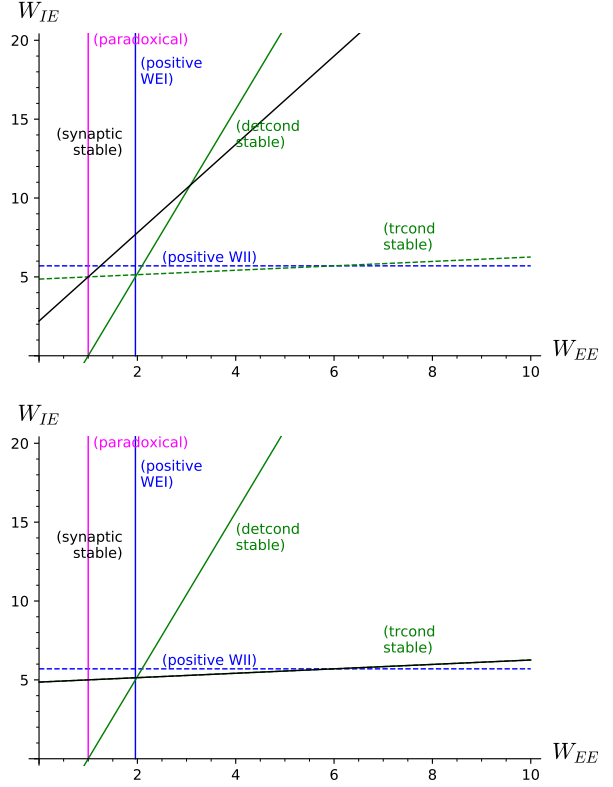


Figure S4: Regions of stability. (Top) For biologically backed parameter values and learning rates of the same value ( $\alpha_{XY} = 0.02$ ), the stability region of the Homeostatic learning rule has little overlap with the region where the neural subsystem is stable. (Bottom) Setting  $\alpha_{EE} = \alpha_{EI} = 0.02$  and  $\alpha_{IE} = \alpha_{II} = 0.001$  enlarges the stability region of the learning rule and makes it overlap with the stability region of the neural subsystem. Every label is on the side where the corresponding condition holds (synaptic stable: Eq. 30; paradoxical: Eq. 19; detcond stable: Eq. 14; trcond stable: Eq. 15; positive  $W_{EI}$ : Eq. 17; positive  $W_{II}$ : Eq. 18).



### 2.4.1 Definition of the learning rule

In continuous-time dynamics, the CrossHomeostatic learning rule reads:

$$\begin{aligned}\frac{dW_{EE}}{dt} &= +\alpha_{EE}E(I_{set} - I) \\ \frac{dW_{EI}}{dt} &= -\alpha_{EI}I(I_{set} - I) \\ \frac{dW_{IE}}{dt} &= -\alpha_{IE}E(E_{set} - E) \\ \frac{dW_{II}}{dt} &= +\alpha_{II}I(E_{set} - E)\end{aligned}\quad (32)$$

The only fixed point is the Up state and is the set of weight values such that:

$$\begin{aligned}E_{up} &= E_{set} \\ I_{up} &= I_{set}\end{aligned}\quad (33)$$

The values of the weights corresponding to the Up state are given by the (underdetermined) system defined by equating Eq. 33 and Eq. 10. Since it is a two-equation system for a set of four unknown weights, there are two free weights that we choose to be  $W_{EEup}$  and  $W_{IEup}$ . The values of the other two weights are defined by Eq. 16. This means that, as in Section 2.3, there is an infinite number of weight values compatible with the Up state (possibly not all stable, though).

### 2.4.2 Nondimensionalization

The full system (Eqs. 32 and 9) in nondimensionalized form reads:

$$\begin{aligned}\epsilon_E \frac{de}{d\tau} &= -e + ew_{EE} - \frac{iw_{EI}}{R^2} - \theta_E \\ \epsilon_I \frac{di}{d\tau} &= -i + R^2ew_{IE} - iw_{II} - \theta_I \\ \frac{dw_{EE}}{d\tau} &= -e(i - 1) \\ \frac{dw_{EI}}{d\tau} &= +\alpha_2 i(i - 1) \\ \frac{dw_{IE}}{d\tau} &= +\alpha_3 ge(e - 1) \\ \frac{dw_{II}}{d\tau} &= -\alpha_4 gi(e - 1)\end{aligned}\quad (34)$$

where we defined the new parameters

$$\begin{aligned}\epsilon_E &= \tau_E/\tau_0 \\ \epsilon_I &= \tau_I/\tau_0 \\ \tau_0 &= 1/(\alpha_{EE}g_E E_{set}I_{set}) \\ R &= E_{set}/I_{set} \\ g &= g_E e/g_I \\ \alpha_2 &= \alpha_{EI}/\alpha_{EE} \\ \alpha_3 &= \alpha_{IE}/\alpha_{EE} \\ \alpha_4 &= \alpha_{II}/\alpha_{EE} \\ \theta_E &= (g_E/E_{set})\Theta_E \\ \theta_I &= (g_I/I_{set})\Theta_I\end{aligned}$$

### 2.4.3 Quasi-steady state approximation

As before, we assume that the neural variables evolve in a much shorter time scale than synaptic variables. In the QSS approximation, the values of the nondimensionalized excitatory and inhibitory activities are

$$\begin{aligned}e_{qss} &= (\theta_I w_{EI} - R^2 \theta_E (w_{II} + 1))/(R^2 c) \\ i_{qss} &= (\theta_I (w_{EE} - 1) - R^2 \theta_E w_{IE})/c\end{aligned}\quad (35)$$

where

$$c = w_{EI}w_{IE} - (w_{II} + 1)(w_{EE} - 1)$$

The full system in the QSS approximation reads

$$\begin{aligned}\frac{dw_{EE}}{d\tau} &= -e_{qss}(i_{qss} - 1) \\ \frac{dw_{EI}}{d\tau} &= +\alpha_2 i_{qss}(i_{qss} - 1) \\ \frac{dw_{IE}}{d\tau} &= +\alpha_3 ge_{qss}(e_{qss} - 1) \\ \frac{dw_{II}}{d\tau} &= -\alpha_4 gi_{qss}(e_{qss} - 1)\end{aligned}\quad (36)$$

where  $e_{qss}$  and  $i_{qss}$  are nonlinear functions of the weights as defined by Eq. 35.

Note that the Up state fixed point, defined by making all derivatives equal to zero, can be expressed as

$$\begin{aligned}e_{qss} &= 1 \\ i_{qss} &= 1\end{aligned}\quad (37)$$

which is the nondimensionalized version of Eq. 33. The weight values compatible with this condition are defined by equating Eqs. 35 and 37:

$$\begin{aligned} w_{EIup} &= R^2(w_{EEup} - 1) - R^2\theta_E \\ w_{IIup} &= R^2w_{IEup} - \theta_I - 1 \end{aligned} \quad (38)$$

( $w_{EEup}$  and  $w_{IEup}$  are free). This is the nondimensionalized version of Eq. 16.

#### 2.4.4 Stability condition

Now we show that this learning rule is stable. The Jacobian matrix evaluated at the Up state has two zero eigenvalues (as expected) and two nonzero eigenvalues. The nonzero eigenvalues have the form:

$$\lambda_{\pm} = \frac{A \pm \sqrt{A^2 - DC}}{C} \quad (39)$$

where

$$\begin{aligned} A &= Rg(R^2\alpha_3 + \alpha_4)(\theta_E - (w_{EEup} - 1)) \\ &\quad - R(R^2 + \alpha_2)w_{IEup} \\ C &= 2R(\theta_I w_{EEup} - R^2\theta_E w_{IEup} - \theta_I) \\ D &= 2g(R^2\alpha_3 + \alpha_4)(R^2 + \alpha_2)/R \end{aligned}$$

To determine the sign of the real part of Eq. 39, first note that  $D$  is positive definite. Second,  $C$  must be positive because it is related to one of the stability conditions of the neural subsystem (Eq. 14, after substituting back to dimensionalized quantities). Note next that  $A^2 - DC$  is less than  $A^2$  (since  $C$  and  $D$  are positive), and thus the square root is either real and less than  $|A|$  or imaginary, both cases leading to  $\text{Re}(A \pm \sqrt{A^2 - DC}) < 0$  if  $A < 0$ . The learning rule is then stable (both eigenvalues with negative real part) if  $A < 0$ . The stability condition in terms of the original parameters and the free weights  $W_{EE}$  and  $W_{IE}$  then reads:

$$\begin{aligned} (E_{set}^2\alpha_{EE} + I_{set}^2\alpha_{EI})I_{set}g_E W_{IEup} \\ > -(E_{set}^2\alpha_{IE} + I_{set}^2\alpha_{II})E_{set}g_E W_{EEup} \\ &\quad + (E_{set}^2\alpha_{IE} + I_{set}^2\alpha_{II})(\Theta_E g_E + E_{set}) \end{aligned} \quad (40)$$

#### 2.4.5 Analysis of the stability condition

By switching  $W_{EE} \rightarrow W_{EI}$  via Eq. 16, the stability condition can be put in the simpler form

$$(R^2\alpha_3 + \alpha_4)W_{EIup} + (R^2 + \alpha_2)W_{IEup} > 0 \quad (41)$$

This condition is always satisfied because the weights and parameters are positive definite and thus the rule is stable for any choice of parameter values (as long as the neural subsystem is). Fig. S5 shows the stability region of the neural subsystem for the set of parameter values of Table 1. Any choice of values for the weights  $W_{EE}$  and  $W_{IE}$  within the stability region of the neural subsystem will lead to a stable Up state.

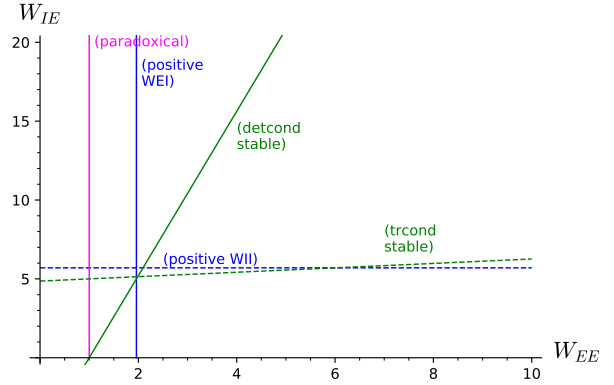


Figure S5: Regions of stability, *Cross-Homeostatic* rule. The rule is stable for any parameter value; the full neural+synaptic system is thus stable where the neural subsystem is stable, i.e. in the upper right triangular region between the two green lines. Every label is on the side where the corresponding condition holds (paradoxical: Eq. 19; detcond stable: Eq. 14; trcond stable: Eq. 15; positive  $W_{EI}$ : Eq. 17; positive  $W_{II}$ : Eq. 18).

#### 2.5 Two-Factor learning rule

(SageMath code in the Supplementary Material: `up states - Two-Factor stability.ipynb`) In this section we follow a path analogous to the one in previous sections, so we will skip some details.

### 2.5.1 Definition of the learning rule

In continuous-time dynamics, the Two-Factor learning rule reads:

$$\begin{aligned}\frac{dW_{EE}}{dt} &= +\alpha E(I_{set} - I) + \beta E(E_{set} - E) \\ \frac{dW_{EI}}{dt} &= -\alpha I(I_{set} - I) - \beta I(E_{set} - E) \\ \frac{dW_{IE}}{dt} &= -\alpha E(E_{set} - E) + \beta E(I_{set} - I) \\ \frac{dW_{II}}{dt} &= +\alpha I(E_{set} - E) - \beta I(I_{set} - I)\end{aligned}\quad (42)$$

The only fixed point compatible with the neural subsystem being suprathreshold is the Up state:

$$\begin{aligned}E_{up} &= E_{set} \\ I_{up} &= I_{set}\end{aligned}\quad (43)$$

The values of the weights corresponding to the Up state are given by the (underdetermined) system defined by equating Eqs. 43 and 10. Since it is a two-equation system for a set of four unknown weights, there are two free weights that we choose to be  $W_{EEup}$  and  $W_{IEup}$ . The values of the other two are given by Eq. 16. This means that the Up-state fixed point is actually a continuous set of non-isolated fixed points forming a 2D plane in 4D weight space. In other words, there is an infinite number of weight values compatible with the Up state (possibly not all stable, though).

### 2.5.2 Nondimensionalization

The full system (Eqs. 42 and 9) in nondimensionalized form reads:

$$\begin{aligned}\epsilon_E \frac{de}{d\tau} &= -e + ew_{EE} - \frac{iw_{EI}}{R^2} - \theta_E \\ \epsilon_I \frac{di}{d\tau} &= -i + \frac{R^2 ew_{IE}}{g} - \frac{iw_{II}}{g} - \theta_I \\ \frac{dw_{EE}}{d\tau} &= (1 + R\gamma)e - ei - R\gamma e^2 \\ \frac{dw_{EI}}{d\tau} &= -(1 + R\gamma)i + R\gamma ei + i^2 \\ \frac{dw_{IE}}{d\tau} &= -(1 - \frac{\gamma}{R})e - \frac{\gamma}{R}ei + e^2 \\ \frac{dw_{II}}{d\tau} &= (1 - \frac{\gamma}{R})i - ei + \frac{\gamma}{R}i^2\end{aligned}\quad (44)$$

where we defined the new parameters

$$\begin{aligned}\epsilon_E &= \tau_E / \tau_0 \\ \epsilon_I &= \tau_I / \tau_0 \\ \tau_0 &= 1 / (\alpha g_E E_{set} I_{set}) \\ R &= E_{set} / I_{set} \\ \gamma &= \beta / \alpha \\ g &= g_E / g_I \\ \theta_E &= (g_E / E_{set}) \Theta_E \\ \theta_I &= (g_I / I_{set}) \Theta_I\end{aligned}$$

### 2.5.3 Quasi-steady state approximation

As before, we assume that the neural variables evolve in a much shorter time scale than synaptic variables. In the QSS approximation, the values of the nondimensionalized excitatory and inhibitory activities are

$$\begin{aligned}e_{qss} &= (R^2 \theta_E (w_{II} + 1) - g \theta_I w_{EI}) / (R^2 c) \\ i_{qss} &= (R^2 \theta_E w_{IE} - g \theta_I (w_{EE} - 1)) / c\end{aligned}\quad (45)$$

where

$$c = (w_{II} + g)(w_{EE} - 1) - w_{EI} w_{IE}$$

The full system in the QSS approximation reads

$$\begin{aligned}\frac{dw_{EE}}{d\tau} &= (1 + R\gamma)e_{qss} - e_{qss}i_{qss} - R\gamma e_{qss}^2 \\ \frac{dw_{EI}}{d\tau} &= -(1 + R\gamma)i_{qss} + R\gamma e_{qss}i_{qss} + i_{qss}^2 \\ \frac{dw_{IE}}{d\tau} &= -(1 - \frac{\gamma}{R})e_{qss} - \frac{\gamma}{R}e_{qss}i_{qss} + e_{qss}^2 \\ \frac{dw_{II}}{d\tau} &= (1 - \frac{\gamma}{R})i_{qss} - e_{qss}i_{qss} + \frac{\gamma}{R}i_{qss}^2\end{aligned}\quad (46)$$

where  $e_{qss}$  and  $i_{qss}$  are nonlinear functions of the weights as defined by Eq. 45.

Note that the Up state fixed point, defined by making all derivatives equal to zero, are the weight values that satisfy

$$\begin{aligned}e_{qss} &= 1 \\ i_{qss} &= 1\end{aligned}\quad (47)$$

which are the nondimensionalized versions of Eq. 43. The weight values compatible with this condition are defined by equating Eqs. 45 and 47:

$$\begin{aligned}w_{EIup} &= R^2(w_{EEup} - 1) - R^2\theta_E \\ w_{IIup} &= R^2w_{IEup} - g\theta_I - g\end{aligned}\quad (48)$$

( $w_{EEup}$  and  $w_{IEup}$  are free). This is the nondimensionalized version of Eq. 16.

### 2.5.4 Stability condition

Now we show the conditions for which this learning rule is stable. The Jacobian matrix of Eq. 46 evaluated at the Up state has two zero eigenvalues (as expected) and two nonzero eigenvalues. The nonzero eigenvalues have the form:

$$\lambda_{\pm} = \frac{(A \pm \sqrt{A^2 - DC})(R^2 + 1)}{C}\quad (49)$$

where

$$\begin{aligned}A &= (\gamma - R)(w_{EEup} - 1) \\ &\quad - (R\gamma + 1)Rw_{IEup} + g\gamma\theta_I + R\theta_E \\ C &= 2R(g\theta_Iw_{EEup} - R^2\theta_Ew_{IEup} - g\theta_I) \\ D &= 2(\gamma^2 + 1)/R\end{aligned}$$

To determine the sign of the real part of Eq. 49, first note that  $(R^2 + 1)$  and  $D$  are positive definite.

Next note that  $C$  must be positive because it is related to one of the stability conditions of the neural subsystem (Eq. 14, after substituting back to dimensionalized quantities). With that, note that both eigenvalues have negative real part if  $A < 0$ : the argument of the square root is less than  $A^2$ , and then the square root itself is either real and less than  $|A|$ , or imaginary. In any case, both eigenvalues have negative real part. The stability condition is then  $A < 0$ , which can be written in terms of the original parameters and free weights  $W_{EE}$  and  $W_{IE}$  as

$$\begin{aligned}(I_{set}\alpha + E_{set}\beta)g_EW_{IEup} \\ > (I_{set}\beta - E_{set}\alpha)g_EW_{EEup} \\ &+ (\Theta_Eg_E + E_{set})\alpha + (\Theta_Ig_E - I_{set})\beta\end{aligned}\quad (50)$$

### 2.5.5 Analysis of the stability condition

The stability condition above can be rewritten in a more useful form by using Eq. 16 to switch  $W_{IE} \rightarrow W_{II}$ :

$$(a - b)\beta < (a' + b' + c)\alpha\quad (51)$$

where

$$\begin{aligned}a &= (W_{EEup}g_E - 1)E_{set}I_{set}g_I \\ a' &= (W_{EEup}g_E - 1)E_{set}^2g_I \\ b &= (W_{IIup}g_I + 1)E_{set}I_{set}g_E \\ b' &= (W_{IIup}g_I + 1)I_{set}^2g_E \\ c &= (I_{set}\Theta_I - E_{set}\Theta_E)g_Eg_I\end{aligned}$$

Note that the following is satisfied for a biologically backed set of parameter values:

$$\begin{aligned}I_{set} &> E_{set} \\ \Theta_I &> \Theta_E\end{aligned}$$

and thus it is likely that  $c > 0$ . In addition,  $b$  and  $b'$  are positive definite, and  $a, a' > 0$  in the paradoxical regime ( $W_{EEup}g_E - 1 > 0$ ). All this makes the stability condition likely satisfied, and thus the learning rule stable. Finally, a small enough  $\beta$  would make the condition more likely to hold.

### 2.5.6 Numerical analysis

In Figure S6 we plot the stability condition of this rule, Eq. 50, for three different parameter values:

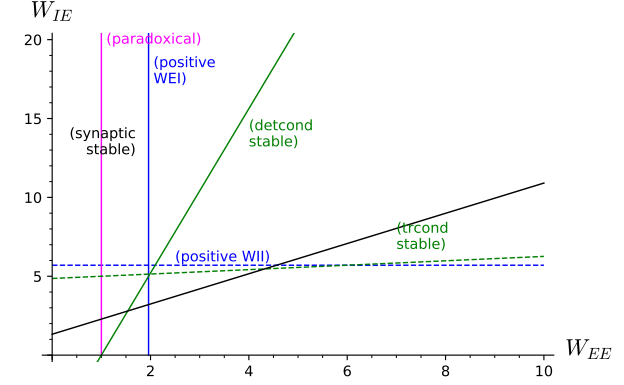
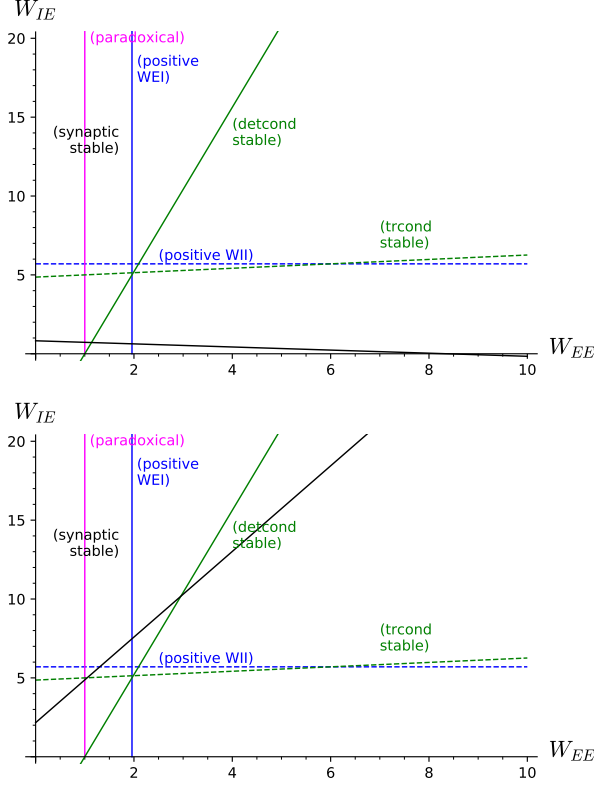


Figure S6: Regions of stability, *Two-Factor* rule. (Top Left)  $\alpha = 0.02$ ,  $\beta = 0.005$ . (Top Right)  $\alpha = 0.01$ ,  $\beta = 0.02$ . (Bottom Left)  $\alpha = 0.0002$ ,  $\beta = 0.02$ . Every label is on the side where the corresponding condition holds (synaptic stable: Eq. 50; paradoxical: Eq. 19; detcond stable: Eq. 14; trcond stable: Eq. 15; positive  $W_{EI}$ : Eq. 17; positive  $W_{II}$ : Eq. 18).

$\alpha \gg \beta$  (the “Cross-Homeostatic” terms dominate over the “Homeostatic” terms, and the rule is stable with the largest stability region);  $\alpha \sim \beta$  (the two terms are of comparable size); and  $\alpha \ll \beta$  (the “Homeostatic” terms dominate instead, and the stability region of the rule is as small as that of the Homeostatic learning rule).

## 2.6 *SynapticScaling* learning rule

(SageMath code in the Supplementary Material: `up states - SynapticScaling stability.ipynb`)

In this section we follow a similar path as in previous sections, so we will skip some details.

### 2.6.1 Definition of the learning rule

In continuous-time dynamics, the SynapticScaling learning rule [7] reads:

$$\begin{aligned} \frac{dW_{EE}}{dt} &= +\alpha_{EE}(E_{set} - E)W_{EE} \\ \frac{dW_{EI}}{dt} &= -\alpha_{EI}(E_{set} - E)W_{EI} \\ \frac{dW_{IE}}{dt} &= +\alpha_{IE}(I_{set} - I)W_{IE} \\ \frac{dW_{II}}{dt} &= -\alpha_{II}(I_{set} - I)W_{II} \end{aligned} \quad (52)$$

The only fixed point compatible with the neural subsystem being above threshold is the Up state and is the set of weight values such that:

$$\begin{aligned} E_{up} &= E_{set} \\ I_{up} &= I_{set} \end{aligned} \quad (53)$$

The values of the weights corresponding to the Up state are given by the (underdetermined) system defined by equating Eq. 53 and Eq. 10. Since it is a two-equation system for a set of four unknown weights, there are two free weights that we choose to be  $W_{EEup}$  and  $W_{IEup}$ . The values of the other two weights are defined by Eq. 16. This means that there is an infinite number of weight values compatible with the Up state (possibly not all stable, though).

### 2.6.2 Nondimensionalization

The full system (Eqs. 52 and 9) in nondimensionalized form reads:

$$\begin{aligned}
\epsilon_E \frac{de}{d\tau} &= -e + ew_{EE} - iw_{EI} - \theta_E \\
\epsilon_I \frac{di}{d\tau} &= -i + ew_{IE} - iw_{II} - \theta_I \\
\frac{dw_{EE}}{d\tau} &= -(e - 1)w_{EE} \\
\frac{dw_{EI}}{d\tau} &= +\alpha_2(e - 1)w_{EI} \\
\frac{dw_{IE}}{d\tau} &= -\alpha_3(i - 1)w_{IE}/R \\
\frac{dw_{II}}{d\tau} &= +\alpha_4(i - 1)w_{II}/R
\end{aligned} \tag{54}$$

where we defined the new parameters

$$\begin{aligned}
\epsilon_E &= \tau_E/\tau_0 \\
\epsilon_I &= \tau_I/\tau_0 \\
\tau_0 &= 1/(\alpha_{EE}E_{set}) \\
R &= E_{set}/I_{set} \\
g &= g_E/g_I \\
\alpha_2 &= \alpha_{EI}/\alpha_{EE} \\
\alpha_3 &= \alpha_{IE}/\alpha_{EE} \\
\alpha_4 &= \alpha_{II}/\alpha_{EE} \\
\theta_E &= (g_E/E_{set})\Theta_E \\
\theta_I &= (g_I/I_{set})\Theta_I
\end{aligned}$$

### 2.6.3 Quasi-steady state approximation

As before, we assume that the neural variables evolve in a much shorter time scale than synaptic variables.

In the QSS approximation, the values of the nondimensionalized excitatory and inhibitory activities are

$$\begin{aligned}
e_{qss} &= (\theta_I w_{EI} - \theta_E (w_{II} + 1))/c \\
i_{qss} &= (\theta_I (w_{EE} - 1) - \theta_E w_{IE})/c
\end{aligned} \tag{55}$$

where

$$c = w_{EI}w_{IE} - (w_{II} + 1)(w_{EE} - 1)$$

The full system in the QSS approximation reads

$$\begin{aligned}
\frac{dw_{EE}}{d\tau} &= -(e_{qss} - 1)w_{EE} \\
\frac{dw_{EI}}{d\tau} &= +\alpha_2(e_{qss} - 1)w_{EI} \\
\frac{dw_{IE}}{d\tau} &= -\alpha_3(i_{qss} - 1)w_{IE}/R \\
\frac{dw_{II}}{d\tau} &= +\alpha_4(i_{qss} - 1)w_{II}/R
\end{aligned} \tag{56}$$

where  $e_{qss}$  and  $i_{qss}$  are nonlinear functions of the weights as defined by Eq. 55.

Note that the Up state fixed point, defined by making all derivatives equal to zero, can be expressed as

$$\begin{aligned}
e_{qss} &= 1 \\
i_{qss} &= 1
\end{aligned} \tag{57}$$

which is the nondimensionalized version of Eq. 53. The weight values compatible with this condition are defined by equating Eqs. 55 and 57:

$$\begin{aligned}
w_{EIup} &= w_{EEup} - 1 - \theta_E \\
w_{IIup} &= w_{IEup} - 1 - \theta_I
\end{aligned} \tag{58}$$

( $w_{EEup}$  and  $w_{IEup}$  are free). This is the nondimensionalized version of Eq. 16.

### 2.6.4 Stability condition

Now we show that this learning rule is unstable for biologically backed parameter values. The Jacobian matrix evaluated at the Up state has two zero eigenvalues (as expected) and two nonzero eigenvalues. The nonzero eigenvalues have the form:

$$\lambda_{\pm} = \frac{A \pm \sqrt{A^2 - DC}}{C} \tag{59}$$

where

$$\begin{aligned} C &= 2R(\theta_I w_{EEup} - \theta_E w_{IEup} - \theta_I) \\ D &= 2(\alpha_2(\theta_E + 1) - (\alpha_2 + 1)w_{EEup}) \\ &\quad (\alpha_4(\theta_I + 1) - (\alpha_3 + \alpha_4)w_{IEup}) \end{aligned}$$

and  $A$  is a long expression that can be found in the corresponding Jupyter notebook.

To determine the sign of the real part of Eq. 59, first note that  $C$  must be positive because it is related to one of the stability conditions of the neural subsystem (Eq. 14, after substituting back to dimensionalized quantities). Next note that  $D$ , after switching  $w_{EE} \rightarrow w_{EI}$  and  $w_{IE} \rightarrow w_{II}$  by means of Eq. 58, reads

$$\begin{aligned} D &= 2(\alpha_3(\theta_I + 1) + (\alpha_3 + \alpha_4)w_{IIup}) \\ &\quad ((\alpha_2 + 1)w_{EIup} + \theta_E + 1) \end{aligned}$$

which is positive definite

Note next that  $A^2 - DC$  is less than  $A^2$  (since  $C$  and  $D$  are positive), and thus the square root is either real and less than  $|A|$  or imaginary, both cases leading to  $\text{Re}(A \pm \sqrt{A^2 - DC}) < 0$  if  $A < 0$ . The condition for the stability of the learning rule (both eigenvalues with negative real part) is then

$$A < 0 \quad (60)$$

( $A$  is a long expression and can be found in the Jupyter notebook).

### 2.6.5 Analysis of the stability condition

It is illustrative to consider the particular case where all learning rates are equal. Then the stability condition Eq. 60 doesn't depend on the learning rates and takes the simpler form:

$$\begin{aligned} (W_{IIup}g_I + 1)a &> (W_{EEup}g_E - 1)a' \\ &\quad + (W_{EEup}g_E - 1)(W_{IIup}g_I + 1)b \end{aligned} \quad (61)$$

where

$$\begin{aligned} a &= (E_{set}W_{EEup} - \Theta_E)g_E \\ a' &= (I_{set}W_{IIup} + \Theta_I)g_I \\ b &= I_{set} - E_{set} \end{aligned}$$

Note that in a biologically backed set of parameter values the following is true:

$$\begin{aligned} I_{set} &> E_{set} \\ g_I &> g_E \\ \Theta_I &> \Theta_E \end{aligned}$$

This makes  $b > 0$  and likely  $a' > a$  (in addition,  $a'$  is a sum of positive terms while  $a$  is a difference). Then in the paradoxical regime where  $(W_{EEup}g_E - 1) > 0$  it seems likely that the stability condition is not satisfied, because the right-hand side is a sum of positive terms and one of them is likely greater than the left-hand side. The SynapticScaling rule is then likely unstable when the learning rates are equal.

A more general case with different learning rates can be analyzed by grouping terms in the following way:

$$\begin{aligned} &(I_{set}W_{IIup}\alpha_4 + \Theta_I\alpha_3)g_I(W_{EEup}g_E - 1) \\ &< (((W_{EEup}g_E - 1)E_{set} - \Theta_Eg_E)\alpha_2 \\ &\quad - (W_{EEup}g_E - 1)I_{set}\alpha_3 \\ &\quad + E_{set}W_{EEup}g_E)(W_{IIup}g_I + 1) \end{aligned}$$

If  $(W_{EEup}g_E - 1) > 0$  (paradoxical regime), then decreasing  $\alpha_3$  and/or  $\alpha_4$  (slow dynamics of the weights onto the inhibitory neuron) helps satisfying the condition and thus making the rule stable.

### 2.6.6 Numerical analysis

As an illustration of the reasoning above, we express the stability condition Eq. 60 in terms of the free weights  $W_{EE}$  and  $W_{IE}$  and plot it with parameter values as in Table 1 and equal rates ( $\alpha_{XY} = 0.02$ ; Figure S7 top left). The stability condition is a homographic function (i.e. a hyperbola) with stability regions in its upper-left and lower-right quadrants—entirely outside the stability region of the neural subsystem. If the dynamics of the weights onto the excitatory neuron are made slower, the homographic function is even steeper (bottom left); if the weights onto the inhibitory neuron are made slower instead, the rule is stable (top left).

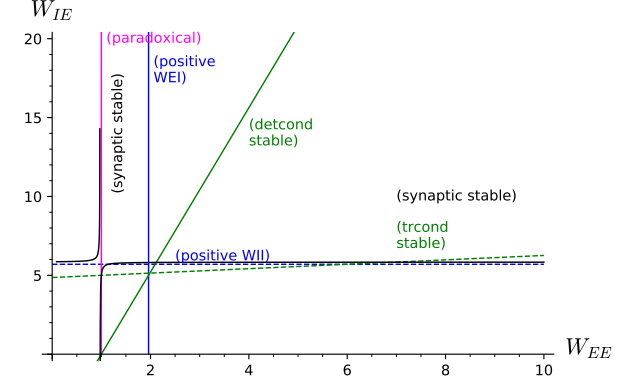
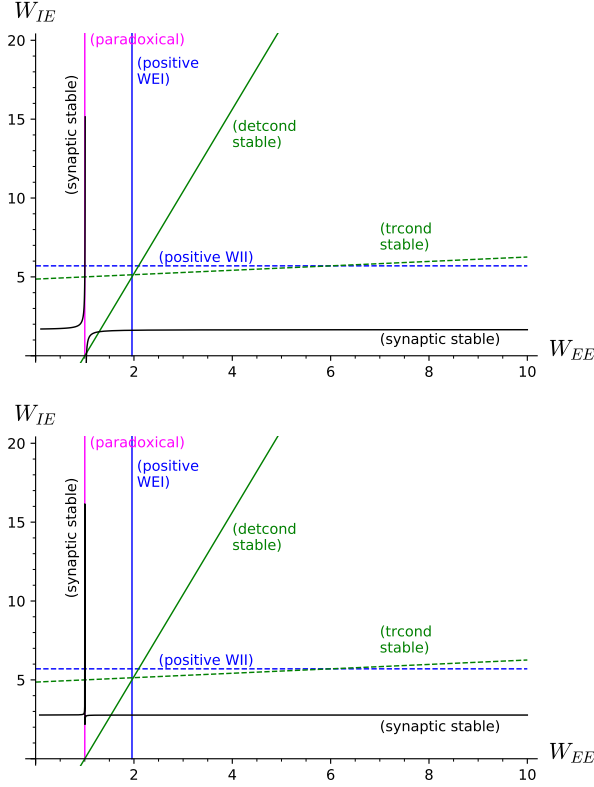


Figure S7: Regions of stability, *SynapticScaling* rule. (Top Left) Equal rates ( $\alpha_{XY} = 0.02$ ). (Top Right) Slow inhibitory ( $\alpha_{EE,EI} = 0.02$ ,  $\alpha_{IE,II} = 0.002$ ). (Bottom Left) Slow excitatory ( $\alpha_{EE,EI} = 0.002$ ,  $\alpha_{IE,II} = 0.02$ ). Every label is on the side where the corresponding condition holds (synaptic stable: Eq. 60; paradoxical: Eq. 19; detcond stable: Eq. 14; trcond stable: Eq. 15; positive  $W_{EI}$ : Eq. 17; positive  $W_{II}$ : Eq. 18).

## 2.7 Stability of the rules in a non-paradoxical regime

All results above were developed with the neural subsystem set in the paradoxical regime—that is, the region in  $(W_{EE}, W_{IE})$  leading to a stable Up state was completely within the paradoxical region ( $W_{EE}g_E > 1$ ). In order to show the importance of the paradoxical behavior for the stability of the learning rules, we also computed the stability conditions of every learning rule in a more general setting where the excitatory subpopulation in the neural subsystem has an external, constant, excitatory input current  $I_{ext}$ . This allows the neural subsystem to display both paradoxical and non-paradoxical stable behavior (in the second case, at the expense of the Up state not being an inhibition-stabilized fixed point). The results can be found in the following SageMath-Jupyter notebooks:

- up states - Neural subsystem stability - with `ltext.ipynb`
- up states - Homeostatic stability - with `ltext.ipynb`
- up states - Two-Factor stability - with `ltext.ipynb`
- up states - SynapticScaling stability - with `ltext.ipynb`

(The stability condition of the Cross-Homeostatic learning rule doesn't depend on  $I_{ext}$ .)

## 3 Learning rule from loss function

(SageMath code in the Supplementary Material: up states - Loss function.ipynb)



Here we show how to compute the learning rule starting from a loss function. Then we make an approximation by considering the weight values are small, and take that as input to interpret several learning rules that don't come from a loss function.

### 3.1 General prescription

We consider the full neural+synaptic system in the QSS approximation (see e.g. Section 2.3). In this approximation the neural subsystem is represented by the quasi-steady-state values

$$\begin{aligned} E &= E_{up}(W_{EE}, W_{EI}, W_{IE}, W_{II}) \\ I &= I_{up}(W_{EE}, W_{EI}, W_{IE}, W_{II}) \end{aligned} \quad (62)$$

where the functions  $E_{up}$  and  $I_{up}$  are defined by Eq. 10 (see [8] for a related discussion on quasi-steady state, synaptic plasticity, and gradient descent).

The synaptic subsystem, that is the learning rule, will be obtained as a result of considering a specific loss function, and the general prescription to compute the learning rule from a loss function  $L$  is the following:

1. Consider a loss function depending on  $E$  and  $I$  (which in turn depend on all weights):

$$L = L(E, I)$$

Conditions to be satisfied by the loss function are, for instance, to be smooth enough (i.e. continuous and differentiable) and to have a minimum when the activities  $E$  and  $I$  are at the set points  $E_{set}$  and  $I_{set}$  (i.e. homeostatic plasticity).

2. The dynamics of the weights is such that it follows a gradient descent on the loss function towards its minimum. In vector notation :

$$\Delta \mathbf{W} = -\alpha \nabla L \quad (63)$$

with learning rate  $\alpha$ . The unfolded learning rules, that is the equations that govern the

weights' dynamics, are then

$$\begin{aligned} \Delta W_{EE} &= -\alpha \frac{\partial L}{\partial W_{EE}} \\ \Delta W_{EI} &= -\alpha \frac{\partial L}{\partial W_{EI}} \\ \Delta W_{IE} &= -\alpha \frac{\partial L}{\partial W_{IE}} \\ \Delta W_{II} &= -\alpha \frac{\partial L}{\partial W_{II}} \end{aligned} \quad (64)$$

3. The partial derivatives of the loss function in Eq. 64 are:

$$\begin{aligned} \frac{\partial L}{\partial W_{EE}} &= \frac{\partial L}{\partial E} \frac{\partial E}{\partial W_{EE}} + \frac{\partial L}{\partial I} \frac{\partial I}{\partial W_{EE}} \\ \frac{\partial L}{\partial W_{EI}} &= \frac{\partial L}{\partial E} \frac{\partial E}{\partial W_{EI}} + \frac{\partial L}{\partial I} \frac{\partial I}{\partial W_{EI}} \\ \frac{\partial L}{\partial W_{IE}} &= \frac{\partial L}{\partial E} \frac{\partial E}{\partial W_{IE}} + \frac{\partial L}{\partial I} \frac{\partial I}{\partial W_{IE}} \\ \frac{\partial L}{\partial W_{II}} &= \frac{\partial L}{\partial E} \frac{\partial E}{\partial W_{II}} + \frac{\partial L}{\partial I} \frac{\partial I}{\partial W_{II}} \end{aligned} \quad (65)$$

or, in vector notation:

$$\nabla L = \frac{\partial L}{\partial E} \nabla E + \frac{\partial L}{\partial I} \nabla I \quad (66)$$

Here we use the chain rule for the derivatives because it gives us much more compact expressions at the end.

4. The partial derivatives in the gradients  $\nabla E = \left( \frac{\partial E}{\partial W_{EE}}, \dots \right)$  and  $\nabla I = \left( \frac{\partial I}{\partial W_{EE}}, \dots \right)$  etc. are to be taken from the quasi-steady-state values of  $E$  and  $I$ , Eq. 62. We will, however, compute the partial derivatives from the implicit expressions given by setting  $dE/dt = dI/dt = 0$  in Eq. 9 without solving for  $E$  and  $I$ .

### 3.2 Detailed calculation

**Loss function** We choose a very general loss function that depends homeostatically on both  $E$  and  $I$  activities:

$$L(E, I) = \frac{1}{2}(E_{set} - E)^2 + \frac{1}{2}(I_{set} - I)^2 \quad (67)$$

This loss function is an elliptic paraboloid in  $(E, I)$  space with a global minimum at  $(E_{set}, I_{set})$  so a gradient descend learning rule as above should converge to that minimum (see Liapunov function and gradient systems: [3, Section 1.1B][9, Sections 9.3 and 9.4][2, Section 7.2]. Keep in mind, however, that  $L$  has a different shape when expressed as a function of the weights, and that  $E$  and  $I$  are not necessarily monotonic functions of the weights, so the conditions for the set point of  $L$  to be stable or a global minimum or even unique are not necessarily satisfied.

**Partial derivatives of  $L$**  The partial derivatives of  $L$  with respect to  $E$  and  $I$  are simply

$$\begin{aligned}\frac{\partial L}{\partial E} &= -(E_{set} - E) \\ \frac{\partial L}{\partial I} &= -(I_{set} - I)\end{aligned}\quad (68)$$

**Partial derivatives of  $E$  and  $I$**  We compute the partial derivatives  $\partial X / \partial W_{XY}$  ( $X, Y = E, I$ ) by first equating the neural subsystem (Eq. 9) to zero:

$$\begin{aligned}E &= g_E(W_{EE}E - W_{EI}I - \Theta_E) \\ I &= g_I(W_{IE}E - W_{II}I - \Theta_I)\end{aligned}\quad (69)$$

then differentiating the implicit functions:

$$\begin{aligned}\frac{\partial E}{\partial W_{EE}} &= g_E(E + W_{EE} \frac{\partial E}{\partial W_{EE}}) - g_E W_{EI} \frac{\partial I}{\partial W_{EE}} \\ \frac{\partial E}{\partial W_{EI}} &= g_E W_{EE} \frac{\partial E}{\partial W_{EI}} - g_E(I + W_{EI} \frac{\partial I}{\partial W_{EI}}) \\ \frac{\partial E}{\partial W_{IE}} &= g_E W_{EE} \frac{\partial E}{\partial W_{IE}} - g_E W_{EI} \frac{\partial I}{\partial W_{IE}} \\ \frac{\partial E}{\partial W_{II}} &= g_E W_{EE} \frac{\partial E}{\partial W_{II}} - g_E W_{EI} \frac{\partial I}{\partial W_{II}} \\ \frac{\partial I}{\partial W_{EE}} &= g_I W_{IE} \frac{\partial E}{\partial W_{EE}} - g_I W_{II} \frac{\partial I}{\partial W_{EE}} \\ \frac{\partial I}{\partial W_{EI}} &= g_I W_{IE} \frac{\partial E}{\partial W_{EI}} - g_I W_{II} \frac{\partial I}{\partial W_{EI}} \\ \frac{\partial I}{\partial W_{IE}} &= g_I(E + W_{IE} \frac{\partial E}{\partial W_{IE}}) - g_I W_{II} \frac{\partial I}{\partial W_{IE}} \\ \frac{\partial I}{\partial W_{II}} &= g_I W_{IE} \frac{\partial E}{\partial W_{II}} - g_I(I + W_{II} \frac{\partial I}{\partial W_{II}})\end{aligned}\quad (70)$$

and then solving for the derivatives:

$$\begin{aligned}\frac{\partial E}{\partial W_{EE}} &= -(EW_{II} g_E g_I + E g_E) / C \\ \frac{\partial E}{\partial W_{EI}} &= (IW_{II} g_E g_I + I g_E) / C \\ \frac{\partial E}{\partial W_{IE}} &= EW_{EI} g_E g_I / C \\ \frac{\partial E}{\partial W_{II}} &= -IW_{EI} g_E g_I / C \\ \frac{\partial I}{\partial W_{EE}} &= -EW_{IE} g_E g_I / C \\ \frac{\partial I}{\partial W_{EI}} &= IW_{IE} g_E g_I / C \\ \frac{\partial I}{\partial W_{IE}} &= (EW_{EE} g_E - E) g_I / C \\ \frac{\partial I}{\partial W_{II}} &= -(IW_{EE} g_E - I) g_I / C\end{aligned}\quad (71)$$

where

$$C = W_{EI} W_{IE} g_E g_I - (W_{II} g_I + 1)(W_{EE} g_E - 1)$$

**Exact learning rules** Putting everything together, the learning rules Eq. 64 are:

$$\begin{aligned}\Delta W_{EE} &= -\frac{\alpha}{C}((I_{set} - I)EW_{IE} g_E g_I \\ &\quad + (E_{set} - E)E(W_{II} g_I + 1)g_E) \\ \Delta W_{EI} &= +\frac{\alpha}{C}((I_{set} - I)IW_{IE} g_E g_I \\ &\quad + (E_{set} - E)I(W_{II} g_I + 1)g_E) \\ \Delta W_{IE} &= +\frac{\alpha}{C}((E_{set} - E)EW_{EI} g_E g_I \\ &\quad + (I_{set} - I)E(W_{EE} g_E - 1)g_I) \\ \Delta W_{II} &= -\frac{\alpha}{C}((E_{set} - E)IW_{EI} g_E g_I \\ &\quad + (I_{set} - I)I(W_{EE} g_E - 1)g_I)\end{aligned}\quad (72)$$

Note that these are very complicated, nonlinear expressions because both  $E$  and  $I$  depend on all weights via Eq. 69. Also the denominator  $C$  depends on all weights (see previous paragraph).

**Small weights approximation** We want simpler expressions for the learning rules. Note that the ex-

act expressions above all have a homeostatic factor (either  $E - E_{set}$  or  $I - I_{set}$ ) and a presynaptic factor ( $E$  in  $\Delta W_{EE}$  and  $\Delta W_{IE}$  and  $I$  in  $\Delta W_{EI}$  and  $\Delta W_{II}$ ). Despite their complicated dependence on the weights, both factors have simple interpretations so we want to keep them as they are while expanding the rest of the expressions (explicit dependence on the weights including  $C$ ) as a first-order Taylor series around zero. Although this is not a textbook Taylor expansion of the full expressions, it is very informative because the results can be much more easily interpreted (for a similar approach see [8]:

$$\begin{aligned}
\Delta W_{EE} &= +\alpha((E_{set} - E)E g_E \\
&\quad + (E_{set} - E)EW_{EE} g_E^2 \\
&\quad + (I_{set} - I)EW_{IE} g_E g_I) \\
\Delta W_{EI} &= -\alpha((E_{set} - E)I g_E \\
&\quad + (E_{set} - E)IW_{EE} g_E^2 \\
&\quad + (I_{set} - I)IW_{IE} g_E g_I) \\
\Delta W_{IE} &= +\alpha((I_{set} - I)E g_I \\
&\quad - (I_{set} - I)EW_{II} g_I^2 \\
&\quad - (E_{set} - E)EW_{EI} g_E g_I) \\
\Delta W_{II} &= -\alpha((I_{set} - I)I g_I \\
&\quad - (I_{set} - I)IW_{II} g_I^2 \\
&\quad - (E_{set} - E)IW_{EI} g_E g_I)
\end{aligned} \tag{73}$$

Note that the first terms of these expressions (corresponding to the zeroth order in the approximation) are exactly the standard Homeostatic learning rules, Eq. 20. Also note that the homeostatic factors in the third terms have the sign corresponding to the Cross-Homeostatic rules, Eq. 32.

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