Supporting Information for "A homeostatic rule for inhibitory synapses promotes temporal sharpening and cortical reorganization" by Moldakarimov, McClelland, and Ermentrout

Here we analyze the response time of the simple preliminary model described in the main text. Our analysis is predicated on the idea that our circuit is set up to produce a transient response to either a transient or sustained stimulus. To achieve this we use a negatively accelerated gain function for excitation like that shown in Equation 1 and a positively accelerated gain function for inhibition like that shown in Equation 2. Under these conditions, a transitory sensory response will be produced if the time constant of the excitation, τ_e, is smaller than the time constant for the inhibition, τ_i. Otherwise, for all but very weak stimuli the inhibition will simply prevent the excitatory response. Thus, we restrict our analysis to cases where τ_e is smaller than τ_i. We define the response time of the two-unit network as the period during which activity of the E cell is above a fixed threshold. In the simulations reported in the main text, we showed that if the connections along the self-inhibitory loop are fixed and we change only the strength of the self-excitatory connection this leads to a higher amplitude response but also a longer response time. We begin by considering the generality of this result.

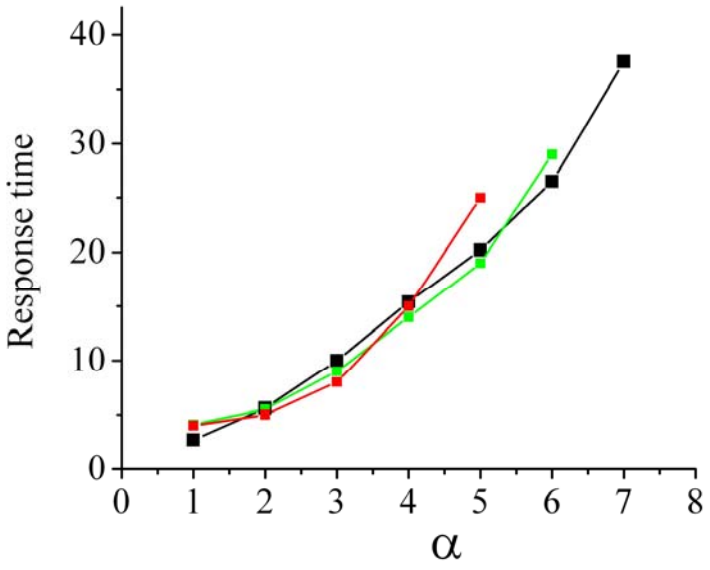

Figure S1. Response time as a function of the strength of the self-excitatory connection. Red: τ_e=3, τ_i=5; green: 2, 10; black: 1, 20. β=1.2 for all curves.

For the simulations of the simplified model in the text we used $\tau_e = 1$ and $\tau_i = 10$ or 20. These values probably exaggerate the differences between excitation and inhibition in the brain. To check that our results are not dependent on this choice, we first consider a case where the two time constants are far more similar: $\tau_e = 3$ and $\tau_i = 5$. As Figure S1 shows, even in this case the response time still increases as we increase the strength of the self-excitatory connection. Indeed, the size of the increase in response time for a fixed increase in alpha grows larger and larger as alpha increases, even in this situation.

In what follows we provide a mathematical analysis of this result based on phase plane analysis. As already indicated, the analysis assumes that the inhibitory unit is slower than the excitatory unit and that the inhibitory gain function is much steeper than the excitatory one. We also assume that the transient stimulus is very short in duration (a delta function), so that the locations of the nullclines in the phase plane will remain fixed, with the stimulus only setting initial conditions. For simplicity of the analysis we also apply the stimulus to the excitatory unit only. Since the inhibitory unit activates much later than the excitatory unit, it is not essential for the analysis, whether inputs to the inhibitory unit come from an external input or from the excitatory unit.

The dynamics for E and I cells are described by equations

$$\tau_e \frac{dE}{dt} = -E + F_e(I_{exte} + \alpha \cdot E - \beta \cdot I) \qquad \tau_i \frac{dI}{dt} = -I + F_i(I_{exti} + \gamma \cdot E) \qquad \text{(A.1)}$$

In Fig. S2A we colored solid lines to show the nullclines of the system (lines on plane E and I where dE/dt=0 (red) and dI/dt=0 (green)). The I nullcline is a monotonically increasing function of E, whereas the E nullcline is a cubic function of E. It is easier to analyze the model for the idealized case in which the I cell is much slower than the E cell (singular perturbation approach). Fig. S2A shows why this is so. There are three trajectories on the phase plane superimposed on the nullclines, for three different choices of the time constant of the I cell. And as we can see as the I cell gets slower the trajectory moves closer to the E nullcline, in the limit, the trajectory will go along the E nullcline exactly. In this case it is easy to determine what amplitude and duration of the response are.

We start at point A in the Fig. S2B (a stable fixed point) and we apply a very short impulse to the *E* cell. If the impulse is strong enough to move the system beyond point B, the trajectory will continue until it reaches point C on the *E* nullcline. Since we have assumed that the *I* cell is much slower than the *E* cell, the variable *I* essentially does not change along the line from point A until it reaches point C. From point C the trajectory moves along the *E* nullcline toward point D. At point D the trajectory jumps back to the *E* nullcline (point F), then moves down along the E nullcline toward the fixed point A. Without loss of generality we can adjust the nullclines such that points A, B and C will lie on E axis (their coordinates will be $(E_A,0)$, $(E_B,0)$, $(E_C,0)$). Now it is easy to determine the amplitudes of responses: The amplitude of the *E* cell response now is indicated by point C, the point where the *E* nullcline crosses *E* axis. The amplitude of the *I* cell response is determined by point D which is local a maximum on the E nullcline.

Based on phase plane analysis we conclude that the amplitude of the response of the *E* cell is determined by the position of the point C along the E axis. The higher point C is along the E axis, the higher the amplitude of the response will be. As we have observed (Fig. 2B, the main paper), strengthening the self-excitatory connection alone leads to a stronger response. Now we can explain those observations. We draw nullclines with different strengths of the self-excitatory connection (Fig. S2C) and observe that point C is shifting to the right as we increase α, meaning more excitation leads to higher amplitude of the *E* cell response.

Let us now address the question of what determines response time of the model. Since we have assumed that the *I* cell is much slower than the *E* cell, it takes much more time for the trajectory to move from point C to point D compared to the time that it takes the system to jump from point A to point C. So the response time is determined mainly by the C-D part of the trajectory. As we increase the self excitation by increasing the *E-E* connection (α in the equations), the amplitude of activity of the *E* unit increases as a response to the external input (Figs. 2B of the main paper, and Fig. S2C of this supporting material). But the response time will also increase. On the phase plane this is indicated by the fact that point C has shifted to the right, and point D has shifted up, increasing the distance between C and D (Fig. S2C). In addition, now the C-D part of the trajectory comes close to the *I* nullcline, where the response of the system is quite slow.

To get a shorter duration we need to decrease the distance from C to D and keep the trajectory as far as possible from the *I* nullcline, since $dI/dt=0$ at the nullcline. These considerations do not involve any specific assumptions except the cubic form of the *E* nullclines. Cubic nullclines can be observed in systems with *f-I* curve in which frequency increases sublinearly for large currents, which is true for most neurons.

We also draw *E* nullclines with different self-excitatory and self-inhibitory connections (Fig. S2D). Here we see that increasing the excitatory connection with fixed inhibitory strength increases the amplitude of the response and also greatly extends its duration (compare dotted and solid curves). Increasing the inhibitory connection at the higher excitatory strength (dashed curve) does not affect the amplitude. In the regime where the inhibitory time constant is much slower than the excitatory time constant, strengthening the inhibitory to excitatory connection has negligible influence on the position of point C but determines the position of point D, moving it down, away from the *I* nullcline. This results in: 1) shortening the C-D path and 2) placing this path farther from the *I* nullcline. These two effects together result in faster dynamics of the model compared to the case with the fixed inhibition loop.

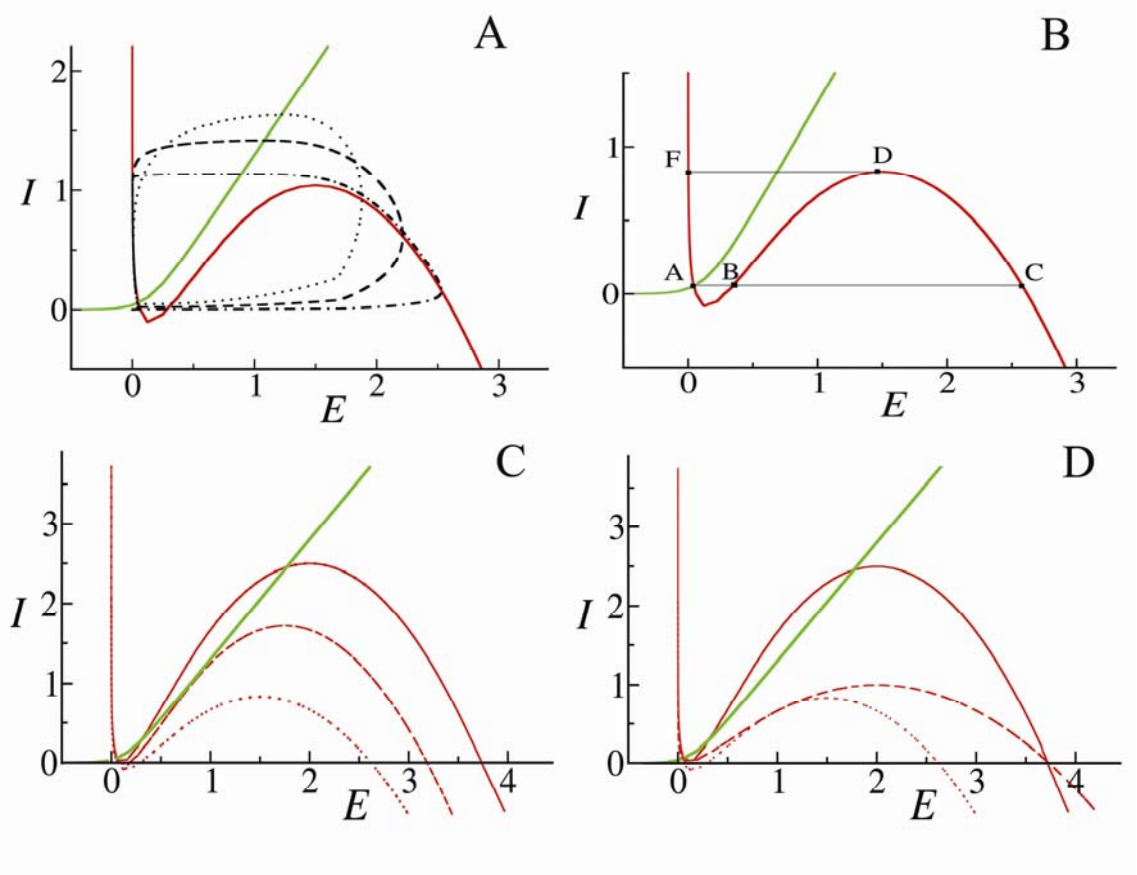

Figure S2. Phase plane analysis.

A. Nullclines and trajectories for different time scale of the inhibitory unit. Solid lines represent E and I nullclines. Dotted line represents a trajectory with time scale of the inhibitory unit $\tau_i = 5$, dot-dash line is for $\tau_i = 20$, and dashed line is for $\tau_i = 80$. All connections are fixed at the values α=3 and β=1.2. Other parameters fixed and had values: $\tau_e = 1$, $\varepsilon_e = 0.2$, $\varepsilon_i = 0.15$, $th_e = 1$, $th_i = 0.2$, $I_{exte} = 5$.

B. Phase plane of the model. The red line is the nullcline of the variable E (points where dE/dt=0), green line is nullcline of the I variable (dI/dt=0). Point A is a stable fixed point. (A-B-C-D-F-A is the trajectory of the system stimulated by a short impulse applied to the E cell.

C. The dotted line is the basic E nullcline with α=3 and β=1.2. The dashed line represents the E nullcline with a stronger self-excitatory connection, α=3.5 and β=1.2. The solid line is the E nullcline with α=4 and β=1. All other parameters are fixed and had values as above.

D. Dotted line is the basic E nullcline with α=3 and β=1.2, solid line represents E nullcline with stronger self-excitatory connection (α=4 and β=1.2), and dashed line is E nullcline for strong self-excitatory and strong self-inhibitory connections (α=4 and β=2.5). All other parameters are fixed and had values as above.

Response time calculation

From figure S2D it is not obvious that the "high amplitude response" is faster than the original "low amplitude response". In this section we show that for a given value of the strength of the self-excitatory loop it is possible to find a value of the strength of the inhibitory connection that makes the "high amplitude response" last for a shorter time than the original "short amplitude response".

What determines the response time of the network? Using notations from figure S2B, it is roughly the time that it takes the system to move from point C to point D. Without loss of generality we have chosen the fixed point A (which is the initial point as well) to be on the E axis. In the limit of very slow I cell dynamics, point C has coordinates (E_C, δ), where $\delta << 1$ and we can assume that the coordinates are (E_C, 0). This allows us to find E_C as the point where the E nullcline crosses the E axis.

Since we apply as an external stimulus a very short impulse we can write an equation for the E nullcline without the external input term

$$E = F_e(\alpha \cdot E - \beta \cdot I) \qquad \text{(A.2)}$$

On the outer branch of the E nullcline $E >> 1$, and therefore $F_e(x) >> 1$. Since F_e is a monotonically increasing function of its argument, we can conclude that $x >> 1$. Due to the fact that $\varepsilon_e << 1$, the excitatory gain function can be approximated as $F_e(x) = \sqrt{x - \theta_e}$ for $x >> 1$.

$$Q(E,I) = E^2 - (\alpha \cdot E - \beta \cdot I - \theta_e) = 0 \qquad \text{(A.3)}$$

E_C (point C on Figure S2C) can be found as $Q(E,I)=0$ for I=0, which gives us

$$E^2 - (\alpha \cdot E - \theta_e) = 0 \qquad \text{(A.4)}$$

By solving this equation we obtain that

$$E_C = (\alpha + \sqrt{\alpha^2 - 4 \cdot \theta_e}) / 2 \qquad \text{(A.5)}$$

E_D (point D on Figure S2C) can be defined as $\frac{\partial Q(E,I)}{\partial E} = 0$

$$\frac{\partial Q(E,I)}{\partial E} = 2 \cdot E - \alpha = 0 \qquad \text{and} \qquad E_D = \frac{\alpha}{2} \qquad \text{(A.6)}$$

By inserting E_D in equation A.3 we can find I_D .

$$I_D = \frac{\alpha^2 / 4 - \theta_e}{\beta} \qquad \text{(A.7)}$$

As we already pointed in discussing the simulation of the simple rate model, strengthening the excitatory connection alone increases the amplitude and the duration of the response. Now we can observe the basis for that behavior. First, E_C (the amplitude of the response) increases as α (the strength of excitatory connection) increases. Second, the response time of the network is roughly the time that it takes the system to move from point C to point D. By increasing α we also increase the distance between points C and D.

We have also shown that by strengthening the inhibitory connection we decrease the response time of the network. As we have shown, E_C and E_D depends only on the strength of the excitatory connection, and the strength of the inhibitory connection

influences only I_D. Strengthening the inhibitory connection moves point D down closer to the E axis, and this leads to two effects: first, a path along the E nullcline from point C to point D becomes shorter, and second, point D is now farther away from the I nullcline. This also shortens the response time of the network.

The actual time that it takes for the network to move from point C to point D in figure S2B can be found by solving the equation

$$\tau_i \frac{dI}{dt} = -I + F_i(\gamma \cdot E) \tag{A.8}$$

with an initial point (E_C,0) and an end point (E_D, I_D).

Again if we assume that for E>>1, $F_i(x) = x - \theta_i$

$$\tau_i \frac{dI}{dt} = -I + \gamma \cdot E(I) - \theta_i \tag{A.9}$$

where E(I) is the E nullcline

$$E(I) = (\alpha + \sqrt{\alpha^2 - 4 \cdot (\theta_e + \beta \cdot I)}) / 2 \tag{A.10}$$

We approximated the E nullcline between points C and D as a linear function.

$$I = (E_C - E) \cdot \varphi \tag{A.11}$$

Where φ is $$\varphi = I_D /(E_C - E_D) \quad \text{(A.12)}$$

By substituting A.11 and A.12 into A.9 we obtain

$$\tau_i \frac{dI}{dt} = -I + \gamma \cdot (E_C - I/\varphi) - \theta_i \quad \text{(A.13)}$$

Putting (for simplicity) θ_e=0, θ_i=0, and solving this equation we obtain the time it takes for the system to move from point C to point D.

$$T = \frac{\tau_i}{1+\frac{\gamma}{\varphi}} \log\left(\frac{\gamma \cdot E_C}{\gamma \cdot E_C - I_D \cdot \left(1+\frac{\gamma}{\varphi}\right)} \right) \quad \text{(A.14)}$$

Recalling that E_C=α, E_D=α/2 and I_D=α/4β, we find that

$$\varphi = \alpha / 2\beta$$

And therefore

$$T = \frac{\tau_i}{1+\frac{2\beta\gamma}{\alpha}} \log\left(\frac{1}{1-\frac{\alpha}{4\beta\gamma}\left(1+\frac{2\beta\gamma}{\alpha}\right)} \right) \quad \text{(A.15)}$$

T is a function of α/β, so if we increase α alone the period increases, but if we increase β with α, the period remains constant. Increasing β more will reduce the period. So for given initial α and β, we can easily find values of α and β that can both increase the amplitude of the response and reduce the response time of the system.

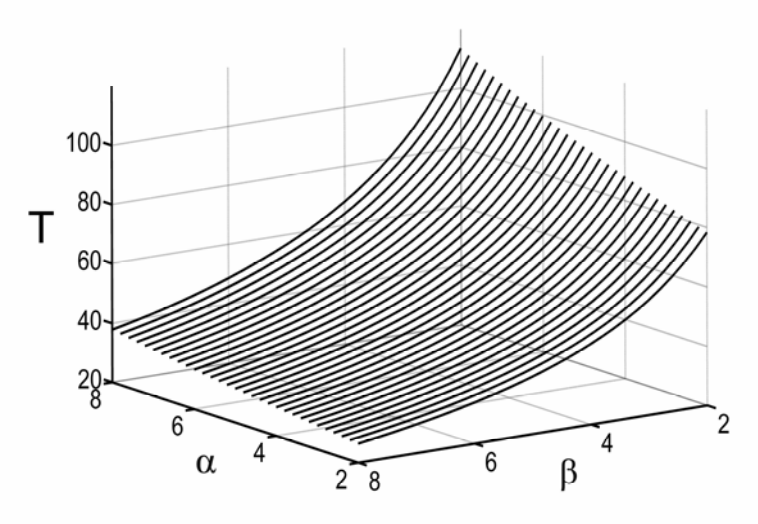

Figure S3. Response time as a function of the strength of the excitatory connection and the strength of the inhibitory connection. τ_e=1, τ_i=10, γ=2.5.

Strategy for connections adjustments

We have shown so far that the amplitude and the duration of the response can be adjusted by appropriate choices of the strengths of the self-excitatory and the inhibitory connections. If we want a response to have higher amplitude we need to increase the self-excitation and, in addition, if we want a shorter duration of the response we have to increase the strength of the inhibitory connection. Given the value of the parameter α Figure S3 shows how much we need to change parameter β in order to observe temporal sharpening in the simple rate model. All the adjustments we have discussed so far we performed manually. How would a network adjust its connections in order to show temporal sharpening (higher response with shorter duration)? Here we suggest a possible mechanism for such adjustments. If we assume that the network will adjust its connections in such a way that the total activity of the excitatory unit remains constant, then clearly, the higher-amplitude response must necessarily be shorter than the original low-amplitude response.

Total activity can be estimated as an integral over the area denoted by points A, C, D and F in Figure S2B. In a linear approximation the integral is

$$S = \frac{3}{4}\alpha \cdot T \qquad \text{(A.16)}$$

So to keep S constant for higher α we have to decrease T, which can be done by adjusting parameter β. From figure S3 we can observe that response time is an increasing function of α and a decreasing function of β. So if we start simulation with weak inhibitory and excitatory connections, and if we increase the excitatory connection, then in order to keep S constant we have to decrease T below it is initial value, which can be done by strengthening the inhibitory connection. The homeostatic rule for inhibitory connection adjustment that is described in the text ensures that the strengthening of the inhibitory connection is sufficient to produce the sharpening effect.