Supporting Information

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SI Results

Here, we extend the argument to how evolution naturally selects the conservation law of synaptic strength. The selection process operates on phenotype, which is a physical manifestation of genotype and—in a modeling approach—determines the set of the model's parameter values. To avoid unnecessary complexity, we consider that all parameters have assumed their optimal values except z (assumption *iii*). If parameter z were such that the synaptic strength of some individuals changes in a nonconservative manner, thus having a tendency to increase or decrease, the fitness of these individuals would be seriously diminished. We finalize the model construction with an auxiliary assumption.

Assumption *Si*. Synaptic strengths take values only from interval (S_{min}, S_{max}). The more z deviates from the optimal value, the higher proportion of synapses is impaired, thus compromising the fitness. Put alternatively, the population growth rate of individuals with a particular value of parameter z is a decreasing function of the fraction of impaired synapses.

To see how fitness diminishes, let us first establish that synaptic strength has a minimum (S_{min}) and a maximum (S_{max}), which together define the interval of all possible synaptic strengths, (S_{min}, S_{max}). The minimum synaptic strength is in fact self-evident and without any loss of generality we set $S_{min} = 0$. The maximum synaptic strength arises as a result of fatigue (38). Namely, the strengthening of synapses intensifies glutamate signaling, which means that the increasing quantities of glutamate end up in the extracellular space of a strengthened synapse. This glutamate needs to be cleared by the surrounding astrocytes. However, if the brain has been extremely active for a long period, astrocytes may ultimately be overwhelmed and unable to scoop all of the glutamate from the extracellular space. Evidence pointing to the described sequence of events is astrocyte swelling and subsequent unspecific interneuronal signaling that accompany highly strengthened synapses. Even more importantly, neurons are for a period left without the much-needed glutamate, resulting in the decreased overall activity that slows down further increases in synaptic strength (38). In our model, at the synaptic level, fatigue is included as incompetence of particular synapse to learn (16).

That fitness can diminish depending on the value of z is readily seen by interpreting the role of this parameter. If z is set to a relatively low value, synaptic strength will tend to increase during the excited phase, yet poorly recover during the resting phase, causing many synapses to maintain their strength close to S_{max}. However, such synapses must shut down even after short periods of activity, which forces the model to transition from the excited to the resting phase—the organism has to spend an excessively long time inactive. If, by contrast, z is set to a relatively high value, learning is impaired because synaptic strengths may be difficult to increase from around S_{min} even in the excited phase and with certainty get completely reset during the short episodes of resting. Fitness is therefore determined by a trade-off between excessive inactivity and impaired learning.

Optimal fitness implies better feeding and more offspring and thus a higher population growth rate. Let us consider the evolution of two subpopulations of the same species (the argument readily generalizes to any number of subpopulations). We denote N_i $(i = 1, 2)$ the number of individuals in subpopulation i and r_i the corresponding population growth rate, where arbitrarily we choose that for $i = 2$ the z value deviates more from the optimal value, implying $r_1 > r_2$. Here we assume that the offspring inherits the value of z from parents (i.e., replicator dynamics). Using

$$N_1(t+1) = r_1 N_1(t),$$

$$N_2(t+1) = r_2 N_2(t),$$

and

$$N(t) = N_1(t) + N_2(t),$$

we obtain the fraction x_i of individuals from subpopulation i in the total population. Specifically

$$x_i(t+1) = \frac{N_i(t+1)}{N(t+1)} = \frac{r_i x_i(t)}{r_1 x_1(t) + r_2 x_2(t)} = \frac{r_i}{\langle r \rangle} x_i(t),$$

where $\langle r \rangle = r_1 x_1(t) + r_2 x_2(t)$ is the average fitness of the entire population. It is now evident that subpopulation $i = 1$ will dominate if $r_1 > \langle r \rangle$, which is certainly met due to $r_1 > r_2$. A conclusion is that, when inheritance and population growth are included, no matter what the initial position in the phase space is, evolution naturally selects the exact value of z that leads to a statistical conservation law of synaptic strength (Fig. S1). Thus, in our approach natural selection mimics self-organized criticality (17, 41).

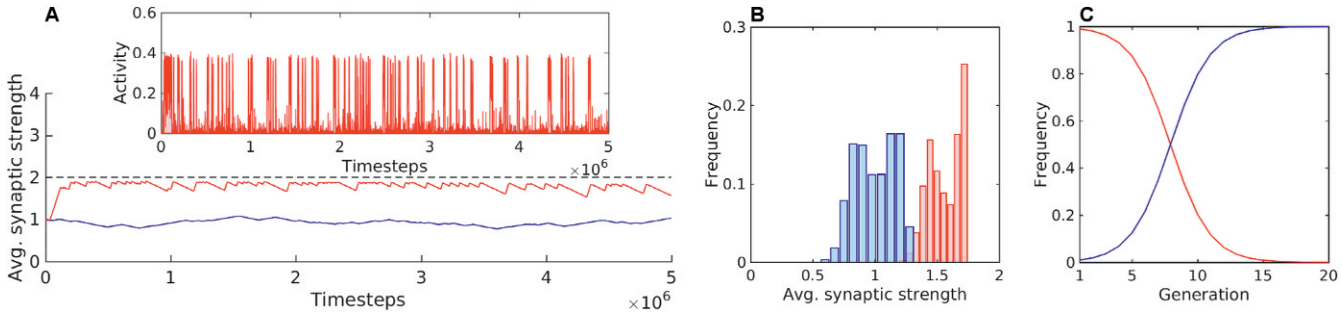

Fig. S1. Natural selection of homeostatic plasticity. (*A*) Mutants with the appropriate value of parameter z maintain homeostatic plasticity (blue; $z = 1/16$) and compete against natives with a lower value of this parameter (red; $z = 1/70$). The average synaptic strength of natives is close to the maximum value, S_{max} (dashed line; arbitrarily set to double the initial average strength), thus increasing the time spent resting at the expense of activity (*Inset*; compare with Fig. 3). (*B*) The distributions of the average synaptic strengths of mutants (blue) and natives (red), showing that the mutants truly establish homeostatic plasticity, while the natives have their synaptic strength pushed toward maximum. (*C*) Mutants need a relatively small number of generations, even if their initial fraction is very low (here 1%), to successfully invade a population of natives.