

Supplementary Information 1: *Influence of inhibition among bLNs on STDP of KC-bLN synapses (simulations and schematics).*

Unconstrained STDP drives network activity to saturation (Fig. 2a_{ii} and Fig. S1.1a_i; also ref 24). When we implement inhibition among model bLNs (according to experimentally determined parameters), network activity moves away from saturation and settles near the middle of the output range (Fig. 2d_{ii} and Fig. S1.1b_i). This is due to the fact that inhibition (from connected mbLNs) reduces the likelihood of potentiation of excitatory synapses from KCs onto mbLNs.

As described in ref 17, when bLNs fire at their expected phase (see also Fig. 2b), some active KC inputs are neither potentiated nor depressed; among those changed by STDP, potentiation and depression should be essentially balanced (Fig. S1.2a *top*). Whenever a bLN receives unduly strong synaptic input (causing it to spike early), more of its KC inputs are depressed (Fig. S1.2a *middle*), delaying subsequent spikes fired by this bLN (in response to the same stimulus). Conversely, when it receives very weak synaptic input, (and spikes late) more of its KC inputs are potentiated (Fig. S1.2a *bottom*), advancing subsequent spikes. This homeostatic mechanism maintains bLN firing phase¹⁷, but when

implemented in simulations, gives rise to uncontrolled synaptic growth, resulting in maximal network activation that is independent of the number of active inputs (Fig. 2a_{ii} and Fig. S1.1a_i). This is because even very weakly driven postsynaptic neurons fire occasionally (with the aid of a little noise) and, by virtue of being weakly driven, spike predominantly at a late phase. This potentiates a large fraction of their inputs and increases the likelihood of subsequent spiking, eventually giving rise to maximal network activation.

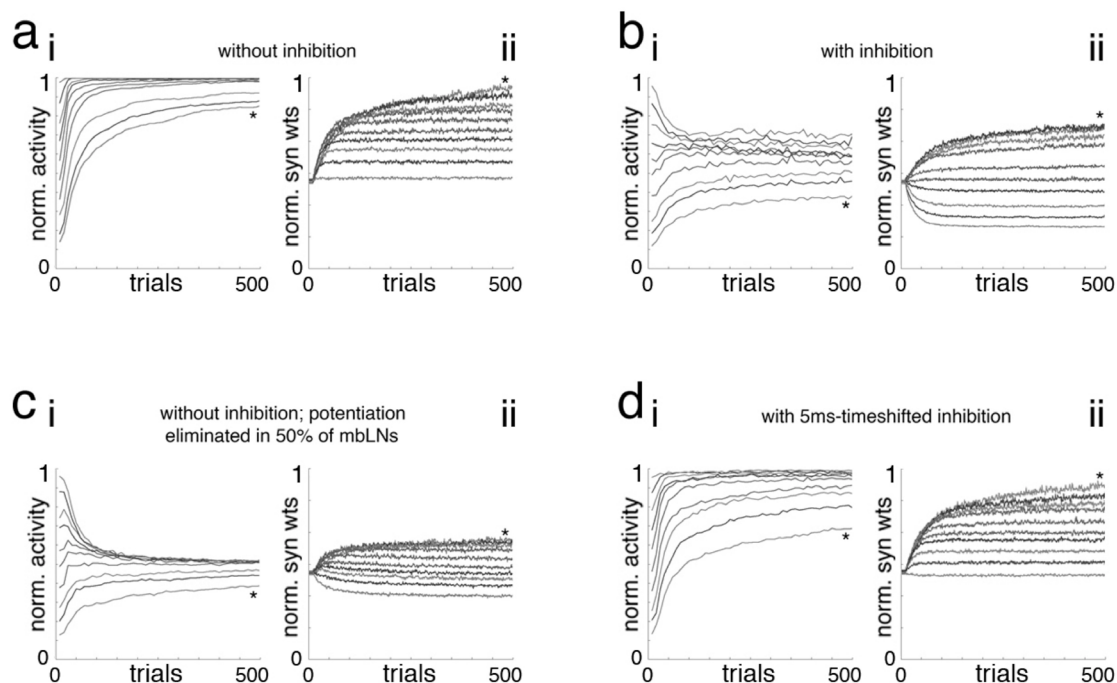
However, if very strong inhibition occurs immediately after the expected bLN firing phase, late bLN spikes will be rare (Fig. S1.2b, *bottom*). One solution to ensure that inhibition occurs at that time and with the appropriate strength (*e.g.*, reflecting total bLN activity) is to derive this inhibition from other bLNs. Such inhibition will predominantly affect potentiation and, as such, curb uncontrolled excitatory synapse enhancement and ultimately, saturation. This is illustrated in Fig. S1.2a and b: only late, net-potentiating spikes are affected (compare a and b, *bottom* vs. *top* and *middle*).

We propose that lateral inhibition influences network output by interacting with STDP, thereby altering excitatory synaptic weights. This implies that changes observed in model network activity should be mirrored by changes in the excitatory synaptic weights. This is what we observe (Fig. S1.1a_{ii} and b_{ii}). Furthermore, if inhibition predominantly reduces the number of potentiating

events, then similar results should obtain when the number of potentiating events is artificially reduced, even in the absence of inhibition. This is illustrated in Fig. S1.2c. When potentiation is eliminated in 50% of mbLNs, the effect on synaptic weights and network output is qualitatively similar to the implementation of experimentally observed inhibition (Fig. S1.1ci and ii; note similarity to Fig. S1.1b, rather than Fig. 1.1a).

STDP is characterized by a very steep time-dependence. If lateral inhibition curbs network output by biasing STDP, then even very small time-shifts of the inhibitory inputs should significantly alter the effect of inhibition on excitatory weights and network activity. Such a change has little effect on spikes that occur at the expected or advanced phase (compare Fig. S1.2 b and d, *top* and *middle*, respectively), but by virtue of allowing spikes at a slightly delayed phase, still permit a slight excess of potentiation (compare Fig. S1.2b and d, *bottom*). We evaluate the effect of a 5-ms shift and observe a qualitative change, very similar to no inhibition at all (Fig. S1.1di and ii; compare to Fig. S1.1a).

Figure S1.1



Influence of inhibition among bLNs on STDP of KC-bLN synapses (simulations)

a. Simulation of 30 unconnected model bLNs receiving excitatory inputs from KC spiking distribution characterized by experimental parameters, as in Fig. 2a. Duration of simulation is one LFP cycle (50ms; different curves correspond to distinct simulations with different average number of KC inputs per bLN (range 22-56); 10% overlap of KC inputs among bLNs). Normalized network activity (**i**) and normalized excitatory synaptic weights (**ii**). Each curve is the average of 10 distinct simulations). **b.** Same as **a**, here with inhibitory connections among mbLNs, implemented according to experimental parameters, as in Fig. 2d; normalized network activity (**i**) and normalized excitatory synaptic weights (**ii**). Larger number of KC inputs per mbLN than in **a** so as to have equal levels of mbLN activity at onset of simulation as in **a** (range 25-125).

c. Same as **a**, here with potentiation turned off in 50% of mbLNs chosen at random at the onset of each simulation. As in **a**, no connections among mbLNs. **d.** Same as **b**, except inhibition is delayed by 5 ms. This is implemented at every trial with IPSPs based on mbLN spike trains of the preceding trial, delayed by 5 ms, thus preserving the distribution of times generated within the network. Absolute scale is identical for **a-d i**, and **a-d ii**, respectively.

Figure S1.2

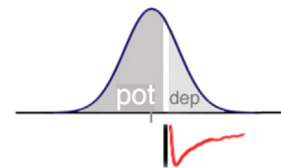


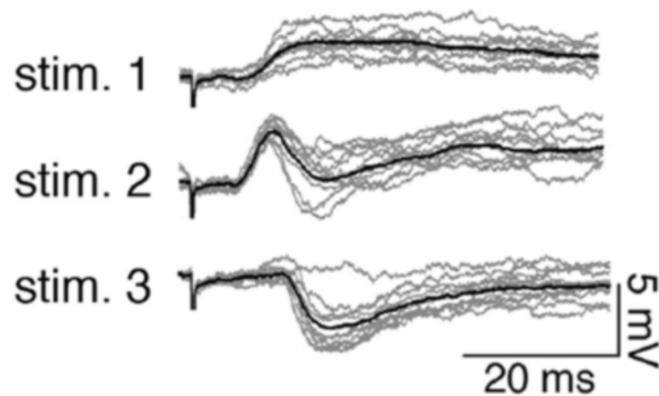
Figure S1.2 (figure on previous page)**Influence of inhibition among bLNs on STDP of KC-bLN synapses (schematics)**

a. Illustration of effect of bLN spike timing on potentiation and depression of KC inputs. *Top*: balanced potentiation (pot, dark grey) and depression (dep, light gray) resulting from bLN action potential at preferred phase. No change to KC-bLN synaptic weights is indicated in white. KC input distribution, blue; bLN action potential, AP, black. *Middle*: excess of depression resulting from early bLN AP (advanced phase). *Bottom*: excess of potentiation resulting from late bLN AP (delayed phase).

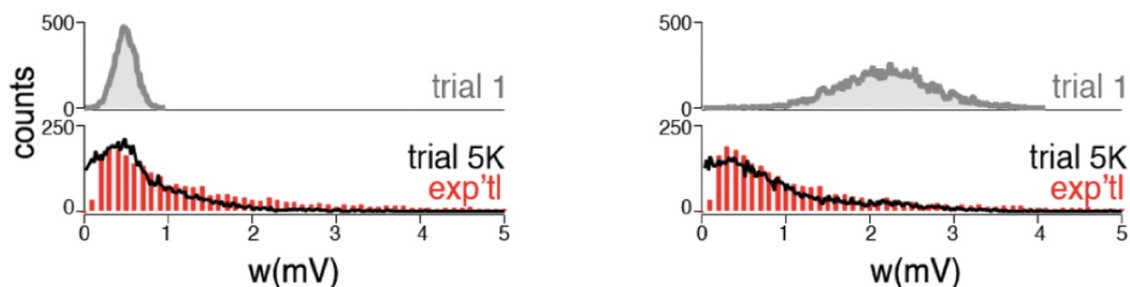
b. Illustration of effect of inhibition. *Top* and *middle*: essentially identical to **a**. *Bottom*: if inhibition is strong, late bLN spikes (delayed phase) are unlikely to occur. Since excess of depression due to early spikes (*middle*) can still occur, this implies a net bias towards depression. This bias is a function of the strength of inhibition, which is itself proportional to total network activity.

c. Illustration of a manipulation to directly test function of inhibition: potentiation (but not depression) is eliminated in 50% of mbLNs (**ii**) chosen randomly at onset of simulation. The remaining mbLNs (**i**) are identical to **a**.

d. Illustration of effect of time-shifted inhibition. While mbLN spiking at expected and advanced phase is unaffected (compare *top* and *middle* to **b**), mbLN spikes at delayed phase (*bottom*) are still permitted, removing (or drastically reducing) the bias towards depression illustrated in **b**.

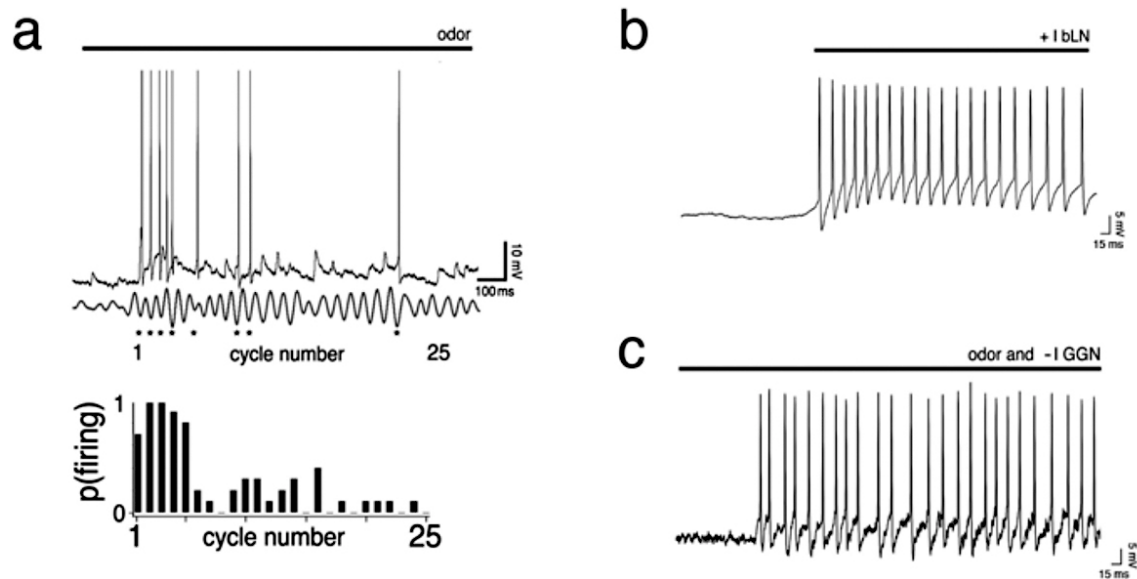
Figure S2**Indirect evidence for lateral inhibitory coupling between bLNs**

Responses of one b-LN recorded intracellularly from a dendrite in the beta-lobe to single-pulse stimuli from 3 electrodes embedded among KC somata at 3 different locations (10 trials each, 0.1/s, averages in black). Stimulus 1 evoked a pure EPSP; stimulus 2 evoked a mixed E-IPSP; stimulus 3 evoked a pure IPSP (with one failure). Our interpretation of these data is as follows: electrode 1 stimulated KCs directly connected to the recorded bLN; electrode 3 stimulated KCs not directly connected to the recorded bLN, but to at least one interposed inhibitory neuron, which was brought to threshold by the KC stimulation in 9 out of 10 trials. Electrode 2 stimulated KCs directly connected to the recorded bLN, as well as to one or more interposed inhibitory neuron(s), brought to threshold by the KC stimulation. We hypothesized that the interposed inhibitory neurons in these recordings could be other bLNs; the existence of lateral inhibitory connections between bLNs was tested directly, and established, with paired recordings (Fig 2C).

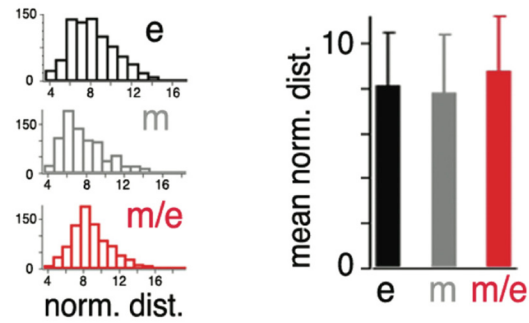
Figure S3**Synaptic weight distributions**

Comparison between distribution of synaptic weights to our model b-LNs (grey: starting condition; black: after STDP) and EPSP amplitudes, taken from intra- dendritic bLN recordings (obtained in the absence of odour stimulation, 16 bLNs). Model distributions are shown for two simulations: starting with low (0.5mV, top left) or high (2.2mV, top right) mean weights. The experimental distribution (red histogram, 0.1mV bins, bottom left and right) is shown superimposed with the model distributions after 5,000 trials (bottom). Regardless of whether the simulation starts with low (left) or high (right) mean weight, the model converges to a distribution that is similar to the experimental distribution. As described in the methods and ref 24, the value of μ determines the shape of the weight-distribution at equilibrium. We used the experimental EPSP size distribution to constrain the value of this parameter.

Figure S4

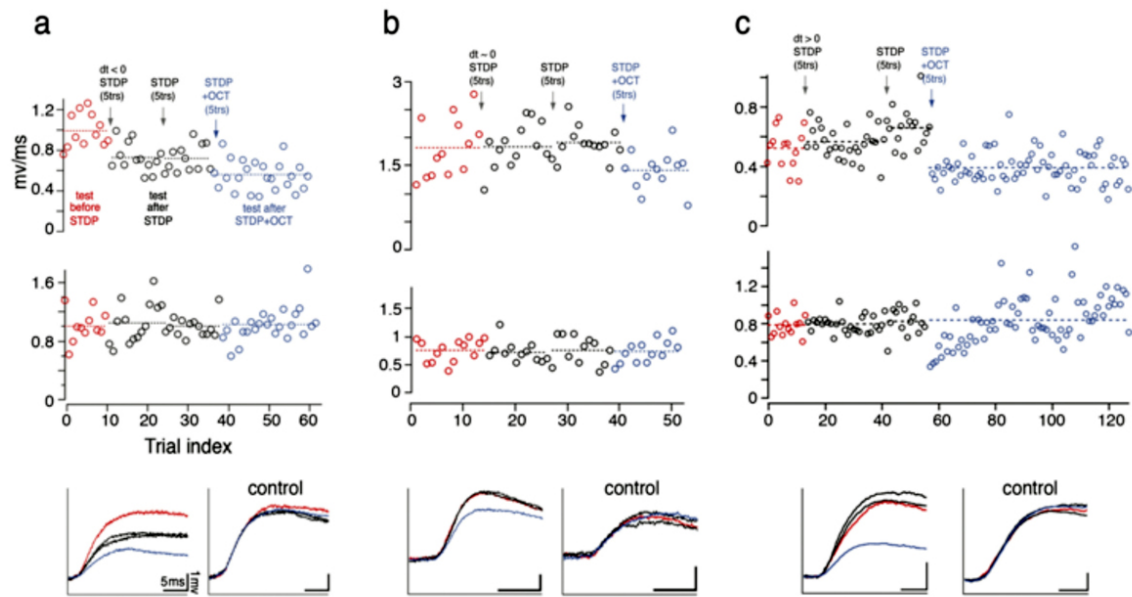


a. Top: Intra-dendritic bLN and LFP recording during odour stimulation, used to generate histograms in Fig 2f. Asterisks mark cycles where bLN fired at least one action potential. Bottom: Probability of firing as a function of LFP cycle, computed over ten trials. **b.** Intra-dendritic bLN recording illustrating that bLNs are intrinsically capable of firing at rates well exceeding the average rates observed during odour stimulation, here due to depolarizing current injection. **c.** Intra-dendritic bLN recording illustrating that excitatory input to bLNs is not saturated during odour stimulation. In this experiment we simultaneously recorded from a bLN and from a giant GABAergic neuron (GGN, experiment carried out together with Maria Papadopoulou), which provides feedback inhibition to KCs. For the recording shown in this panel, we presented an odor stimulus and simultaneously injected negative current into GGN. As described in ref 16, this manipulation results in the activation of a larger set of KCs than would occur due to odor stimulation alone, giving rise to a high firing rate in the bLN.

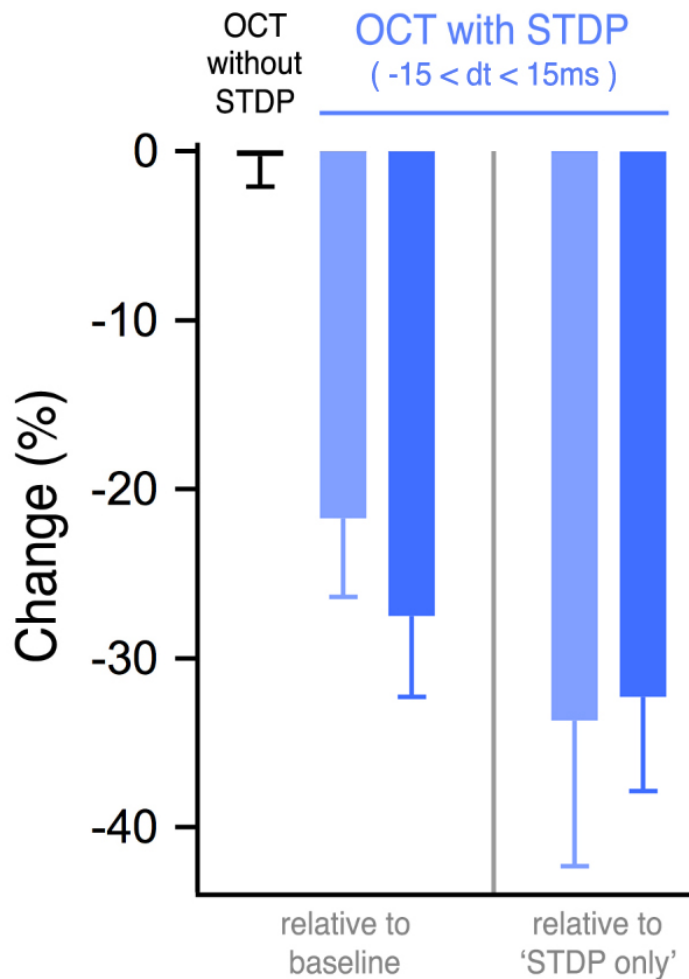
Figure S5

Quantification of similarity between model and experimental p(firing) histograms in Fig 2C. Euclidean distance distributions are shown for experimentally recorded bLNs (e), model units (m), and pairwise experimental-model comparisons (m/e). Mean distances for the three comparisons are also shown (right).

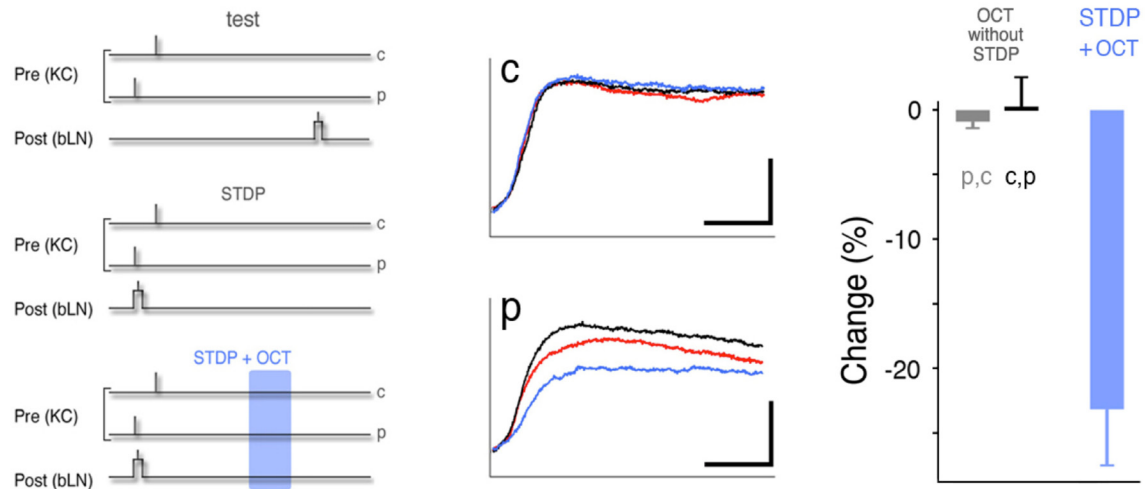
Figure S6



Time course of control pathway EPSPs recorded during experiments in Fig 3a-c. Note that even when a depression can be observed transiently for the control pathway, the overall effect is small compared to the paired pathway.

Figure S7

Quantification of effect of octopamine (OCT) in electrical stimulation experiments in figure 3 for $-15 < dt < 15\text{ms}$. Average effect (mean and SEM) of OCT without STDP (black, $n=10$). Average effect of OCT with STDP, relative to baseline (before STDP), for the subset of experiments (with $-15 < dt < 15\text{ms}$) in which we found KCs that converged from two locations onto the same recorded bLN (light blue, $n=10$); and for all experiments with $-15 < dt < 15\text{ms}$ (dark blue, $n=16$). Average effect of OCT with STDP, relative to 'STDP only', for control-matched experiments (with $-15 < dt < 15\text{ms}$; light blue, $n=10$) and for all experiments with $-15 < dt < 15\text{ms}$ (dark blue, $n=16$). The changes in the control-matched subset are not significantly different from the larger dataset (relative to baseline, $p > 0.39$; relative to 'STDP only', $p > 0.89$). Comparison to controls for the complete data set in figure 3 ($-25 < dt < 25\text{ms}$, $n=20$) is included in figure S8.

Figure S8

Control EPSPs are unaffected by reversal of the order of control (c) and paired (p) stimulations. Stimulation protocol (left): paired KC stimulation (p, which occurs within 25ms of the postsynaptic action potential evoked by current injection during STDP trials and during STDP+OCT trials) is followed by control KC stimulation (c, 300ms later; this order is reversed compared to Fig 3d). Example recording (middle; $dt = 12\text{ms}$). Comparison (mean and SE) of the two control conditions (right; $p > 0.66$; p followed by c, $n=3$; c followed by p, $n=10$). The effect in both control conditions is compared with the average effect of STDP+OCT (mean and SE) for the data in Fig 3f ($n=20$; $-25 < dt < 25\text{ms}$).