Pattern-dependent, simultaneous plasticity differentially transforms the input-output relationship of a feedforward circuit

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Supporting Information

Files in this Data Supplement:

Supporting Data
Supporting Figure 5
Supporting Figure 6

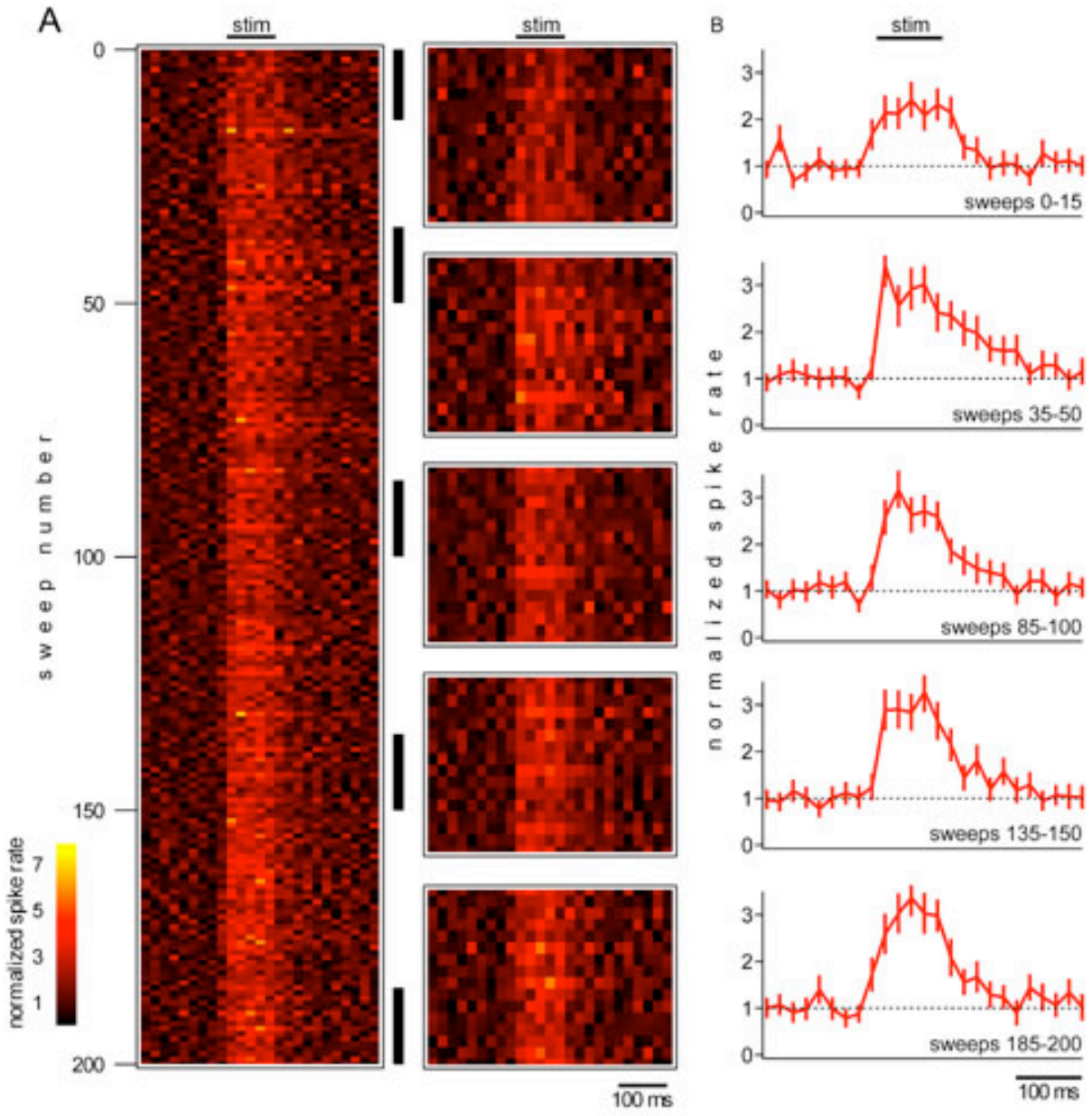

Fig. 5. Rapid changes in spike output induced by PF bursts. During PF burst stimulation, the Purkinje spike response to the stimulation evolves rapidly in time. The first thing to occur is a potentiation of spike output. Later the spike response is sharpened in time by returning to baseline more quickly. (A) Each horizontal line of pixels represents one sweep binned and averaged over eight cells. The firing rate has been normalized and is represented as a color. (B) Excerpts marked in A are expanded and shown with an averaged time course ± SEM.

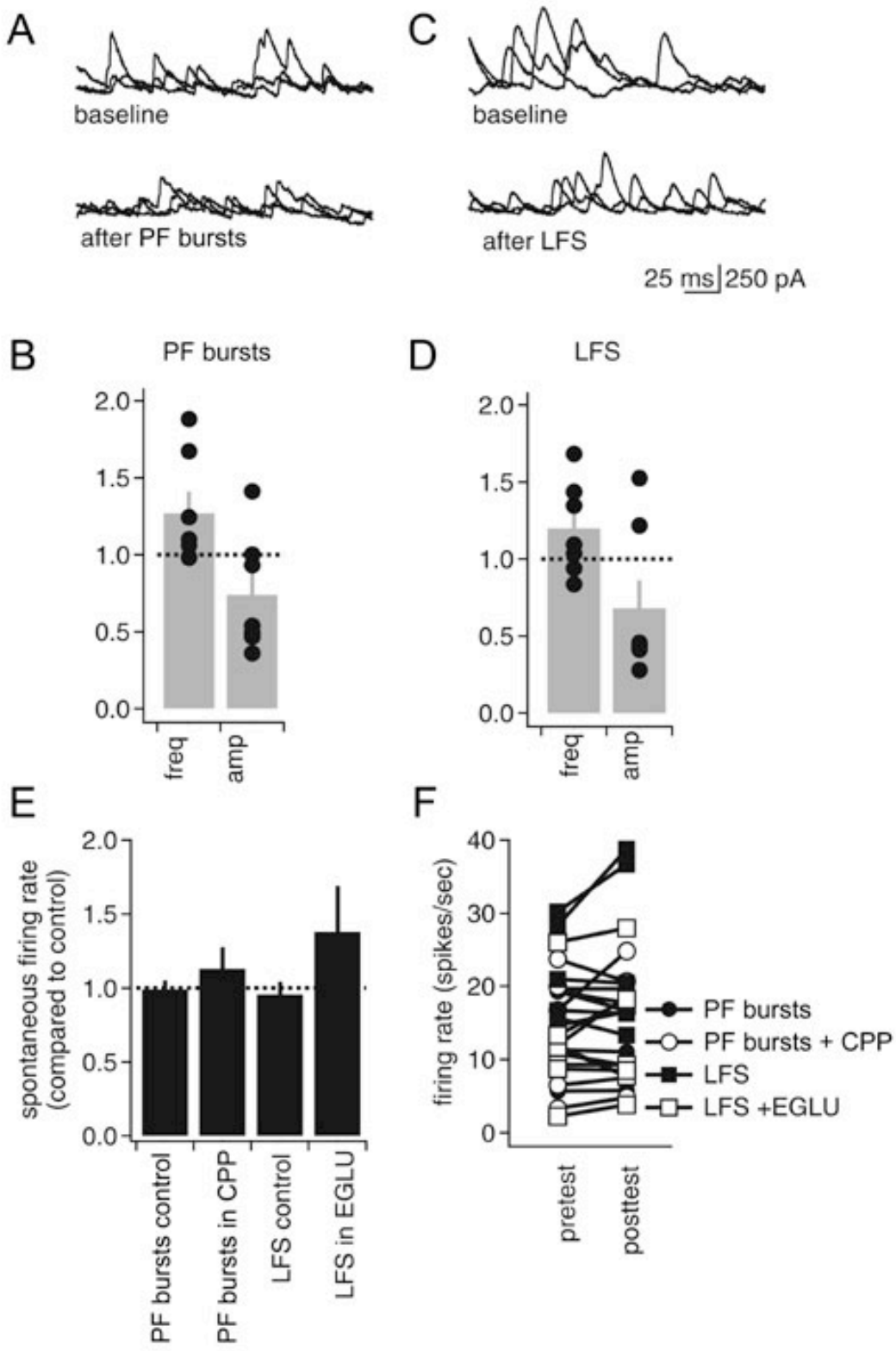
A
baseline
after PF bursts
C
baseline
after LFS
25 ms
250 pA
B
PF bursts
2.0
1.5
1.0
0.5
0.0
freq
amp
D
LFS
2.0
1.5
1.0
0.5
0.0
freq
amp
E
spontaneous firing rate (compared to control)
2.0
1.5
1.0
0.5
0.0
PF bursts control
PF bursts in CPP
LFS control
LFS in EGLU
F
firing rate (spikes/sec)
40
30
20
10
0
pretest
posttest
PF bursts
PF bursts + CPP
LFS
LFS +EGLU

Fig. 6. Many parameters of the circuit are unchanged by PF burst and low-frequency stimulation (LFS). (A and C) Spontaneous inhibitory events (sIPSCs) offer a way to screen for global changes in the IN-Pkj synapse. (B and D) The average amplitude of sIPSCs did not significantly change and neither did the frequency, which reflects the firing rate of INs. Furthermore, the trends in the data were not different between the two conditioning paradigms, PF burst (A and B) and LFS (C and D). Therefore, changes in the circuits are likely occurring predominantly at the PF-IN and PF-Pkj synapses. (E) Pkj excitability also did not significantly change in these experiments, with either PF burst of LFS. Spontaneous firing rates are shown as posttest firing rates normalized to pretest rates. (F) Absolute firing rates during pretest and the last 5 min of posttest are shown. There was no systematic variation in the firing rate among the experimental conditions.

Supporting Data

The Spike Output in Response to Bursts Evolves Rapidly. It is of interest to determine how the spike output in response to parallel fiber (PF) burst evolves in time. In particular, we wanted to measure how rapidly it developed and whether the inhibitory and excitatory changes had different kinetics. For this purpose, we used repeated presentations of PF burst stimulation (Fig. 5A) to condition the circuit while recording Purkinje neuron spike responses. We found that the spike output of the system evolved rapidly in time with significant changes occurring within the first few stimulus presentations. Potentiation of spike output during the train occurred early with a significant increase in spike output detected in the first 50 sweeps (1.26 ± 0.041, $P < 0.05$, $n = 8$; Fig. 5B). The rate at which the firing rates returned to baseline after the stimulus greatly lengthened after potentiation (from 360 ms for sweeps 1–15 to 600 ms for sweeps 35–50; Fig. 5B). However, this rate of return to

baseline decreased significantly by later sweeps (320 ms during sweeps 135–150; Fig. 5B) with no decrease in the potentiated firing rate during the stimulus (sweeps 135–150 as compared with sweeps 1–15: 1.26 ± 0.036, $P < 0.05$, $n = 8$; Fig. 5B). This result suggests that the potentiated inhibitory response, which contributes to the reestablishment of baseline firing rate, takes longer to develop than the potentiated excitatory response.

Other Circuit Parameters. We explored other circuit parameters [interneuron (IN)–Purkinje (Pkj) synapses, intrinsic excitability of Pkjs] that might be expected to change in known forms of plasticity in the cerebellar circuit. To test for changes in IN–Pkj synapses, we analyzed the spontaneous inhibitory postsynaptic currents (IPSCs) that occurred during the 5-s periods between test stimuli during the intracellular experiments described in Figs. 3 and 4. With either conditioning paradigm, the average amplitude of spontaneous IPSCs decreased slightly, whereas the average frequency increased slightly between the pretest and posttest (Fig. 6 A and C). However, these changes were not statistically significant ($P > 0.05$, Fig. 6 B and D).

To test for changes in intrinsic excitability of Pkjs, we examined the spontaneous firing rate of Purkinje neurons before and after PF burst and LFS stimulation (Fig. 6E). Again, no significant changes were observed in Pkj firing frequency after either protocol under a variety of conditions. Although our previous work has shown that PF activity can cause a persistent increase in the spontaneous firing rate of Purkinje neurons (1), the stimulus intensities used in those experiments (and thus the numbers of PFs stimulated) were much greater. These experiments do not rule out a possible role for input-specific changes in excitability (2).

1. Smith, S. L. & Otis, T. S. (2003) J. Neurosci. **23,** 367–372.

2. Frick, A., Magee, J. & Johnston, D. (2004) Nat. Neurosci. **7,** 126–135.