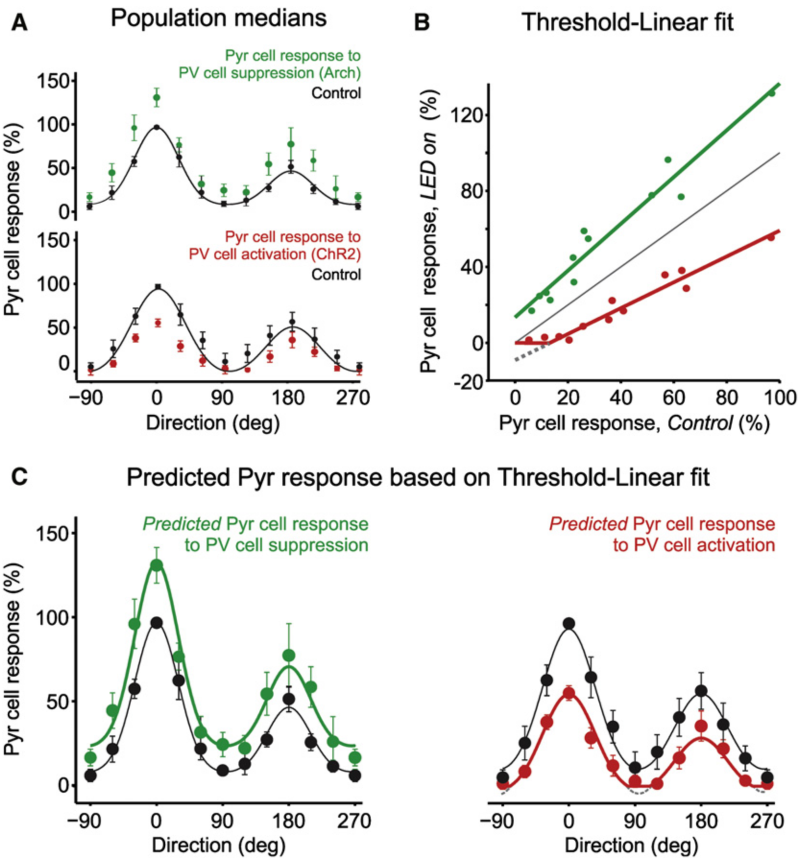

Figure 4. A Linear Function with a Threshold Describes How PV Cells Transform Pyr Cell Responses

(A) Median response of Pyr cell population to 12 directions under control conditions (black circles) and upon PV cell photo suppression (green circles; n = 31) or PV cell photo activation (red circles; n = 14). Error bars are bootstrapped 95% confidence intervals. Black solid lines: double Gaussian fits to median control response.

(B) Median response of Pyr cell population to 12 directions during PV cell photo suppression (green circles) or PV cell photo activation (red circles) plotted against control conditions (same data as A). Solid lines: threshold-linear function fit to data (green: slope of 1.2 and offset of 11%; red: slope 0.7 and offset of −13%). Gray dashed line extends the red linear fit to negative Pyr cell firing rates (i.e., the linear function without applying the threshold). Gray solid line is at unity.

(C) Same data as (A), with the addition of the quantitative prediction of Pyr cell tuning curves (green and red lines) based on the threshold-linear functions in (B).

Note the threshold-linear functions illustrates that activation/suppression of PV cells linearly scales Pyr cell responses regardless of stimulus orientation except where the responses are pushed below zero (gray lines). As a result, there is no change in HWHH and a small change in orientation and direction selectivity.

only must the decrease in inhibition result in a robust ~ 40% increase in Pyr cells response, but it must do so while having only slight impact on tuning properties and, in particular, tuning sharpness.

To set up the fundamentals of the model we first considered the orientation tuning under control conditions. To this end, we recorded excitatory and inhibitory conductances in layer 2/3 Pyr cells as a function of orientation. Stimulus-evoked excitatory currents (Figure 5C, red trace) recorded at the reversal potential for $GABA_A$ receptor-mediated inhibition showed clear tuning: they were on average 1.7-fold (n = 4) larger at the preferred orientation than at the nonpreferred orientation. In contrast, inhibitory currents (Figure 5C, blue trace) recorded at the reversal potential of glutamate-mediated synaptic excitation were less tuned, being only 1.2-fold (n = 5) larger at the preferred compared to the nonpreferred orientation (consistent with Liu et al., 2010). The membrane potential tuning was then calculated directly from these two opposing conductances (Figure 5D) and the model cell's intrinsic properties (Figure 5E). The spike generation threshold (dotted line, Figure 5E,F) was constrained such that the orientation selectivity and tuning sharpness of spikes matched experimentally measured Pyr cell spike tuning properties (modeled suprathreshold OSI = 0.7 and HWHH = 24 deg; Figure 5F, black trace).

To test the impact of PV cell suppression on model Pyr cell responses, we decreased the inhibitory conductance by 10%, as experimentally determined. Notably, this reduction in inhibition not only resulted in a substantial increase in the modeled spiking response (~50%) but did so in a manner that was strikingly consistent with the experimentally observed linear transformation—i.e., a small decrease in OSI (ΔOSI = 0.08) and no impact on tuning sharpness (ΔHWHH < 2 degrees; Figure 5F, Inset). The model robustly accounted for the transformation of Pyr cells over the wide range of Pyr cell orientation selectivity (Figure S3).

Thus, this conductance-based model provides insight into how even slight changes in PV cell-mediated inhibition can lead to robust changes in response of Pyr cells to visual stimuli without having a major impact on their tuning properties.

DISCUSSION

By manipulating the activity of PV cells bidirectionally we have determined that while these neurons minimally affect tuning properties, they have profound impact on the response of cortex to stimuli at all contrasts and orientations. We identified a specific and basic computation contributed by these neurons during cortical visual processing: a linear transformation of Pyr cell responses, both additive and multiplicative. This linear transformation of course operates in the presence of a threshold, as firing rates cannot be reduced below zero. The bidirectional control of PV cells during visual stimulation has also allowed us to demonstrate the consistency of this transformation over a range of PV cell activity levels, from ~20% below to 40% above control levels (Figure 2). While suppressing PV cell activity with Arch revealed their function under control conditions, increasing