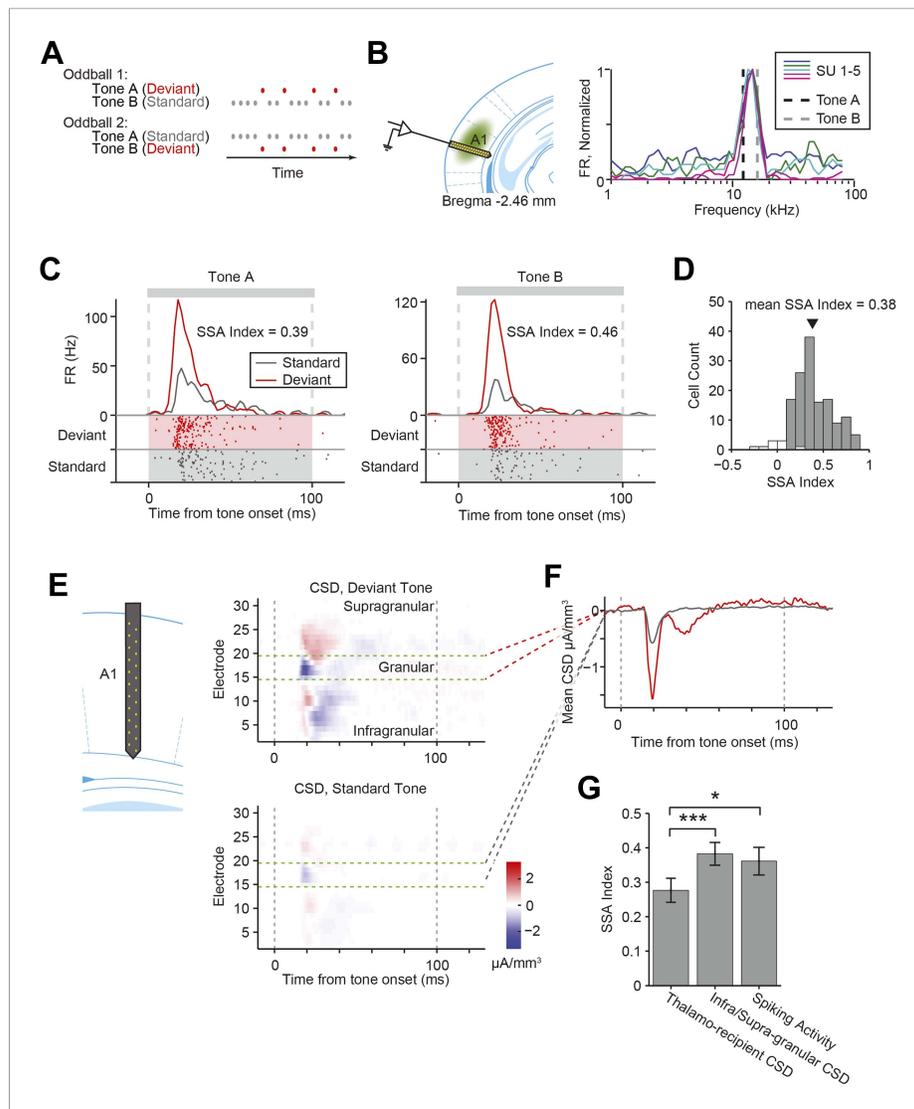


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## Figures and figure supplements

Complementary control of sensory adaptation by two types of cortical interneurons

**Ryan G Natan, et al.**



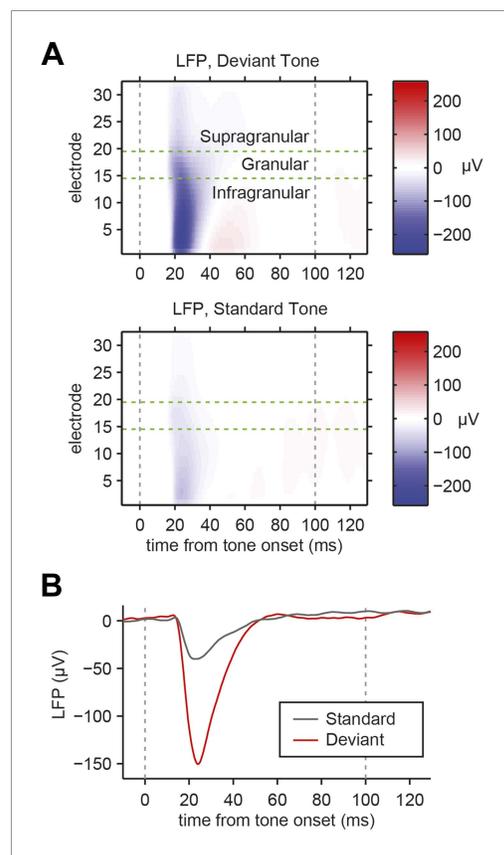
**Figure 1.** Nearly all recorded A1 neurons exhibit stimulus-specific adaptation. **(A)** Diagrams of oddball stimuli; oddball stimuli are composed of a 2.5-Hz train of 100-ms long sine-wave tone pips separated by 300 ms of silence (gray and red dots). Each tone pip is at one of two frequencies, tone A or B. In oddball stimulus 1, 10% of all pips are tone A and 90% of pips are tone B. In oddball stimulus 2, the tone probabilities are reversed. The less frequent tone is referred to as the deviant tone (red dots). The more frequent tone is referred to as the standard (gray dots). **(B)** Left: diagram of recording. Electrode was lowered perpendicular to the brain surface. Virus was injected in A1. Right: the frequencies of tones A and B (dashed black and gray lines) are selected based on the frequency response functions of neurons of interest. Mean firing rate (FR) of five co-tuned neurons (colored lines) recorded simultaneously in a single session in response to 65 dB tone pips at 50 frequencies logarithmically spaced from 1 to 80 kHz. FR is normalized to the peak response of each neuron. **(C)** A representative neuron exhibited suppressed responses to a tone presented as a standard (gray raster and PSTH) compared to the same tone presented as a deviant (red raster and PSTH). Left: responses to tone A, presented as a deviant in oddball stimulus 1, and a standard in oddball stimulus 2. Right: responses to tone B. Shaded regions indicate standard (gray) and deviant (red) tones trials. Gray dashed lines indicate tone onset and offset times. **(D)** Population histogram of stimulus-specific adaptation (SSA) index exhibited by all neurons included in the analysis. Gray and white bars indicate neurons expressing significant and non-significant SSA, respectively. Spike count for response to deviant tones was significantly greater than for response to standard tones (Wilcoxon rank sum test, one tail,  $p < 0.05$ ). The black marker indicates the population average SSA index. **(E)** Left: diagram of electrode spanning A1. Right: representative peri-stimulus current source density (CSD). Top: mean response to deviant tones. Bottom: mean response to standard tones. Gray dashed lines indicate tone onset and offset. Green dashed lines indicate the location of the granular layer. Negative CSD values (blue) indicate current sinks, while positive CSD values (red) indicate current sources. **(F)** Mean CSD  $\mu\text{A}/\text{mm}^3$  vs Time from tone onset (ms). **(G)** Bar graph of SSA Index for Thalamo-recipient CSD, Spiking Activity, and Infra/Supra-granular CSD. Statistical significance is indicated by asterisks (\*, \*\*\*, p < 0.05).

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Figure 1. Continued

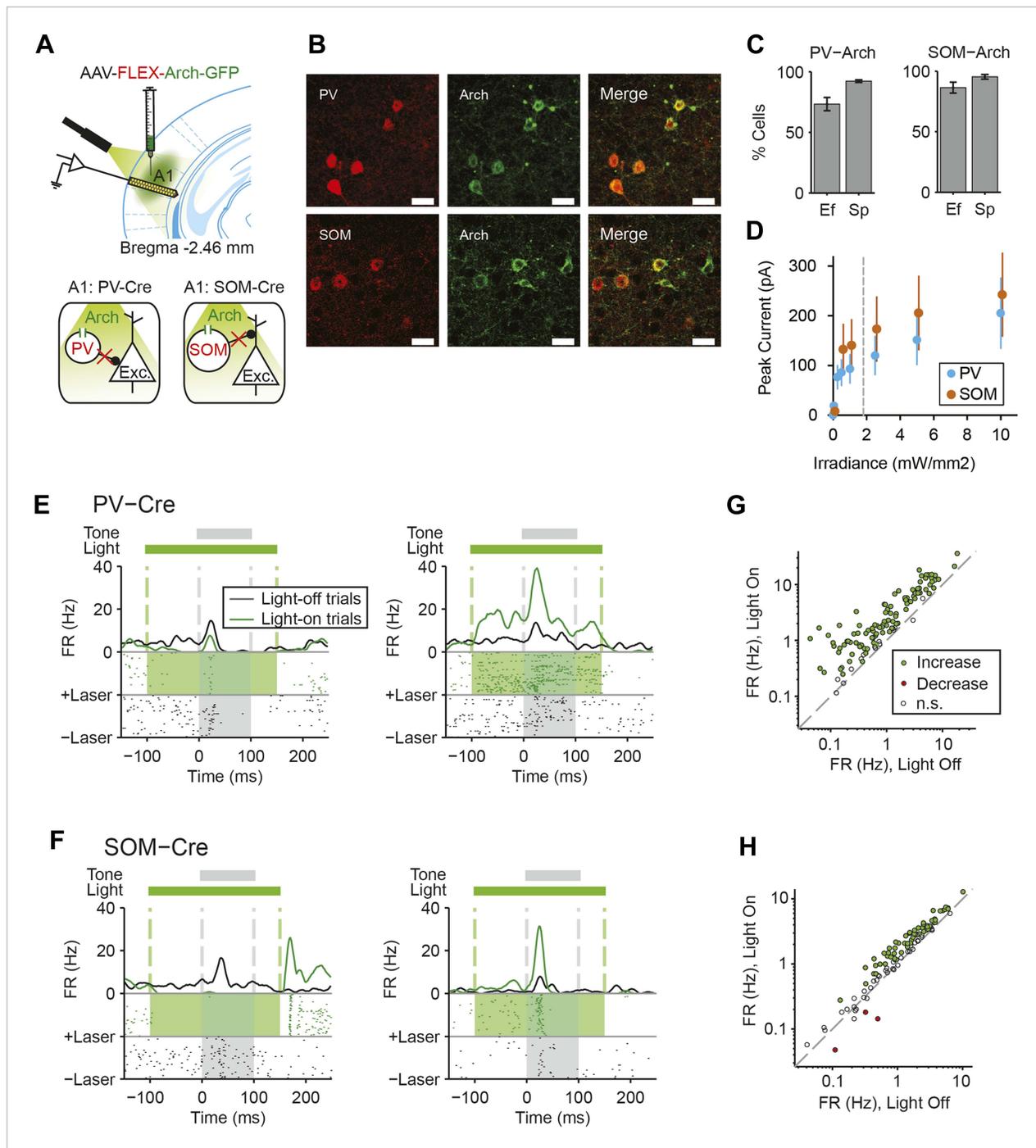
indicate current sources. (F) Mean CSD collected from the thalamo-recipient layer, in response to standard (gray) and deviant (red) tones. Gray dashed lines indicate tone onset and offset. (G) Mean SSA index across sessions measured from thalamo-recipient granular layer CSD, infra- and supra-granular layer cortical CSD and mean neuronal spiking activity SSA index averaged over sessions.

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**Figure 1—figure supplement 1.** Local field potentials recorded in A1 exhibit SSA. (A) Representative peristimulus local field potentials (LFPs) across cortical layers. Top: mean response to deviant tones. Bottom: mean response to standard tones. Gray dashed lines indicate tone onset and offset. Green dashed lines indicate the margins between cortical layers. (B) Mean LFP collected from the thalamo-recipient granular layer, in response to standard (gray) and deviant (red) tones. Gray dashed lines indicate tone onset and offset.

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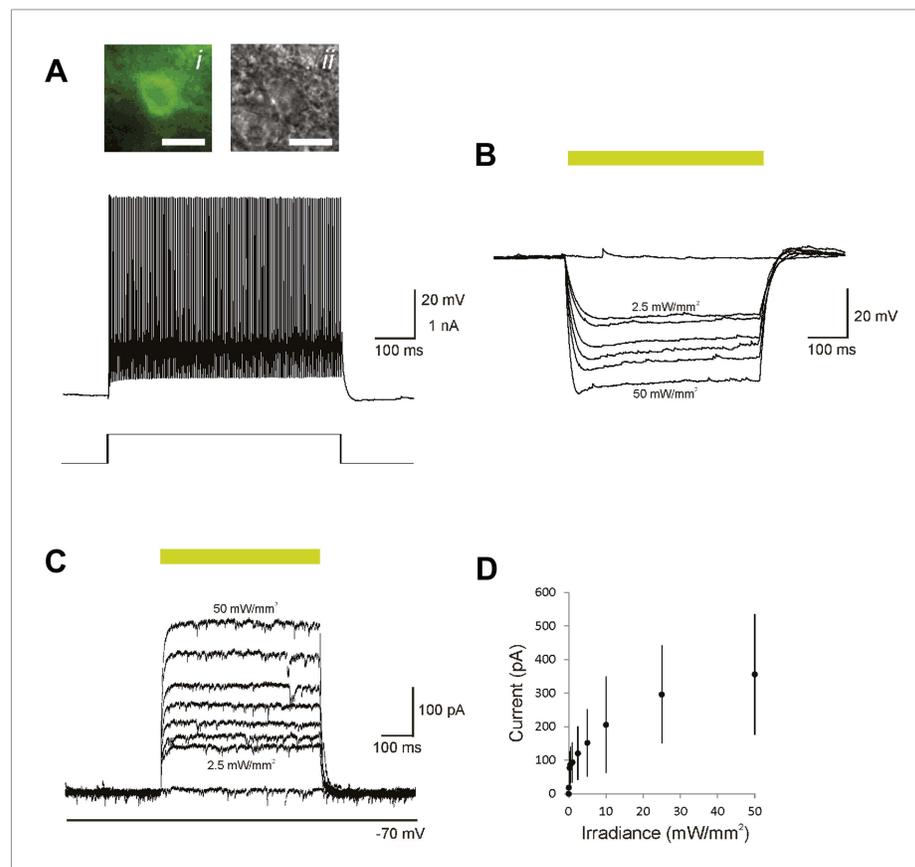
**Figure 2.** Cell type-specific optogenetic suppression of parvalbumin-positive and somatostatin-positive neurons. **(A)** Optogenetic methods diagram. Top: A1 was injected with AAV-FLEX-Arch-GFP. During experiments, an optic fiber was positioned to target A1 and neuronal activity was recorded using a multichannel silicon probe in A1. Bottom: green light (532 nm) suppresses PVs in PV-Cre mice or SOMs in SOM-Cre mice. **(B)** Transfection of interneurons with Archærhodopsin (Arch). Immunohistochemistry demonstrating co-expression of the Arch and an interneuron-type reporter in A1. Top: PV-Cre mouse A1. Red: anti-body stain for parvalbumin. Green: Arch-GFP. Merge; co-expression of Arch and parvalbumin. Bottom: SOM-Cre mouse A1. Red: anti-body stain for somatostatin. Green: Arch-GFP. Merge; co-expression of Arch and somatostatin. Scale Bar = 25  $\mu$ m. **(C)** Efficiency and specificity of transfection of interneurons with Arch. Bar Plots: efficiency (Ef) and specificity (Sp) of visual transfection of PVs (top) and SOMs (bottom) with Arch. Ef, percent of labeled interneurons expressing Arch. Sp, percent of Arch-expressing cells, which are also labeled interneurons. **(D)** Mean Arch-mediated outward current evoked in response to increasing photostimulation power, recorded in vitro by whole-cell patch recording in putative excitatory neurons from PV-Cre (blue, N = 5) and Som-Cre (orange, N = 5) mice. The gray dashed line indicates the level of irradiance expected in in vivo experiments at the deepest recording sites, in cortical layer 6. **(E, F)** Tone responses of representative neurons, which are suppressed (left) or activated (right) by

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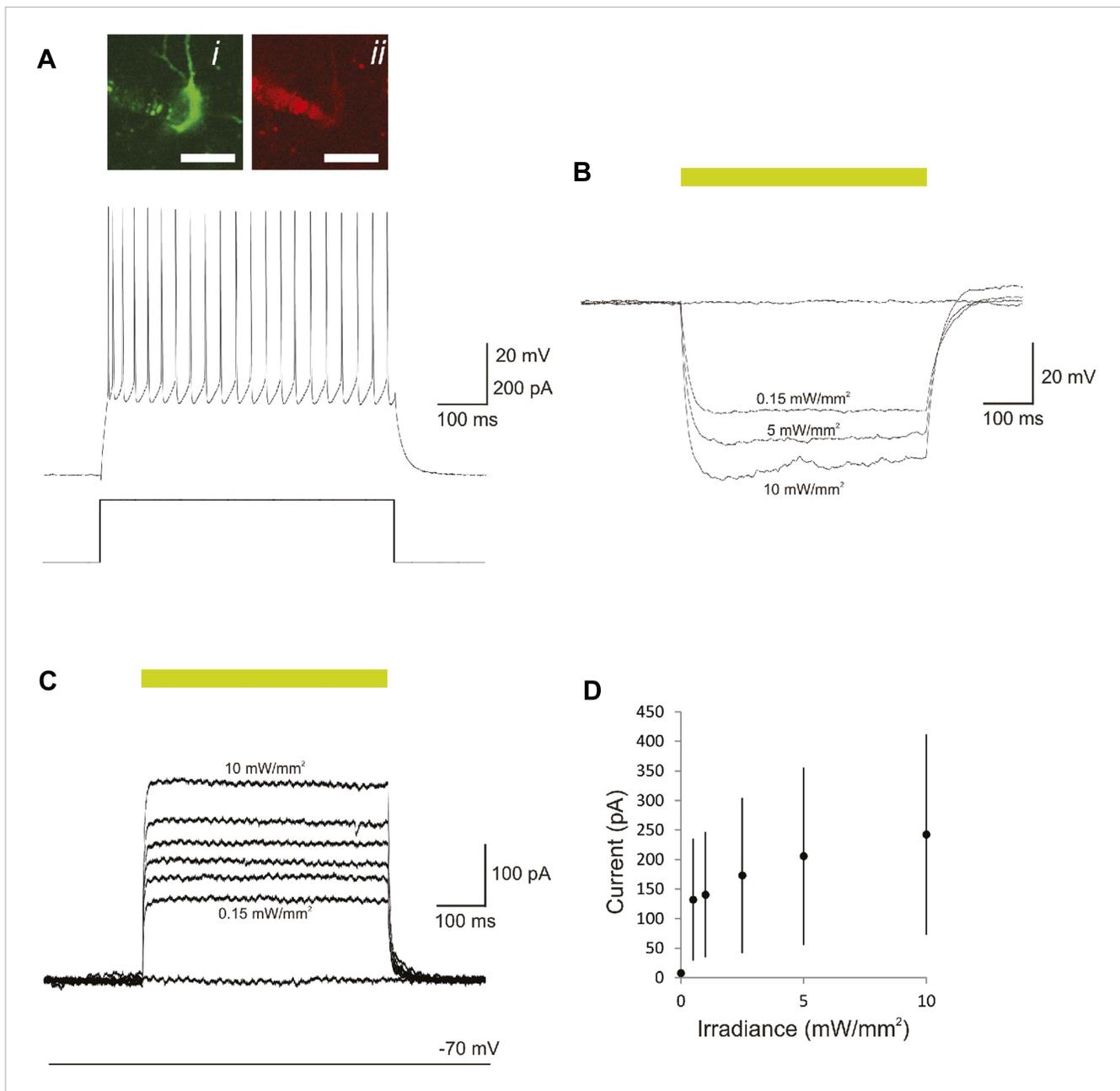
photostimulation, from PV-Cre (E) and SOM-Cre (F) mice. Raster plot of spike times (bottom) and PSTH (top) of a single neuron response to a 100-ms long tone (gray dashed lines, shaded region) on light-on (overlapping 250-ms light pulse, green shading) and light-off trials. Light-on trials: green. Light-off trials: black. (G, H) Modulation of spontaneous FR by interneuron photosuppression recorded in PV-Cre (G) and SOM-Cre (H) mice. Each neuron is represented by a circle that is filled for those with significantly increased (green) or decreased (red) FR or unfilled for those without significant modulation. Gray dashed line, identity line.

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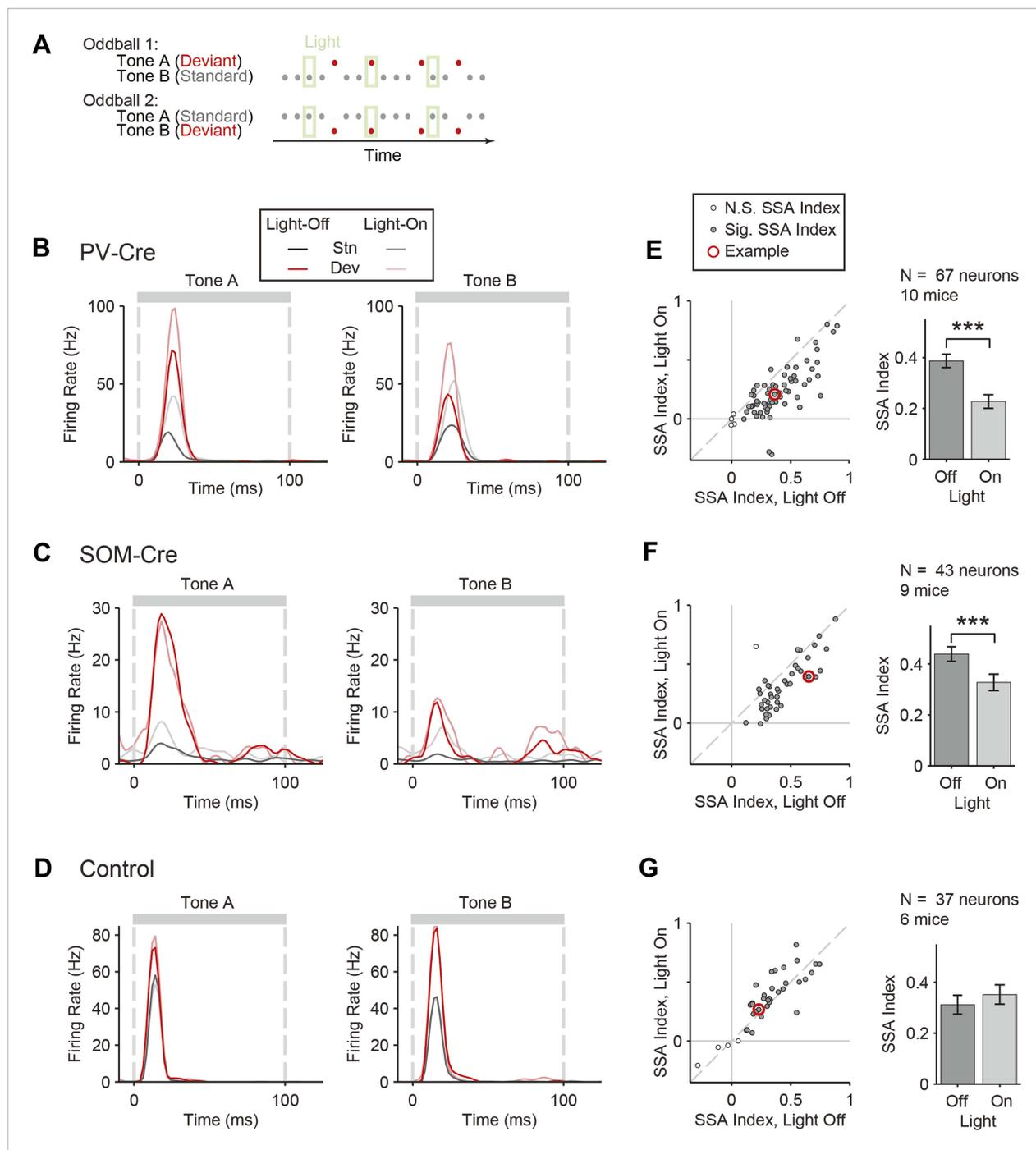
**Figure 2—figure supplement 1.** Optogenetic control of PVs in mouse primary auditory cortex via photostimulation of Arch in acute slices. (A) Sustained high-frequency firing pattern typical of a PV-positive FS cell (top) in response to rectangular current injection (bottom; 600 pA) recorded in vitro via whole-cell patch clamp. Inset, epifluorescence (i) and corresponding IR-DIC image (ii) of the depicted cell. Scale bar, 20  $\mu\text{m}$ . (B) Membrane hyperpolarization mediated by 532-nm light. (C) Outward current mediated by photoactivation of Arch. (D) Plot of light-induced outward current vs. illuminance ( $\text{mW}/\text{mm}^2$ ). Error bars, standard deviation.

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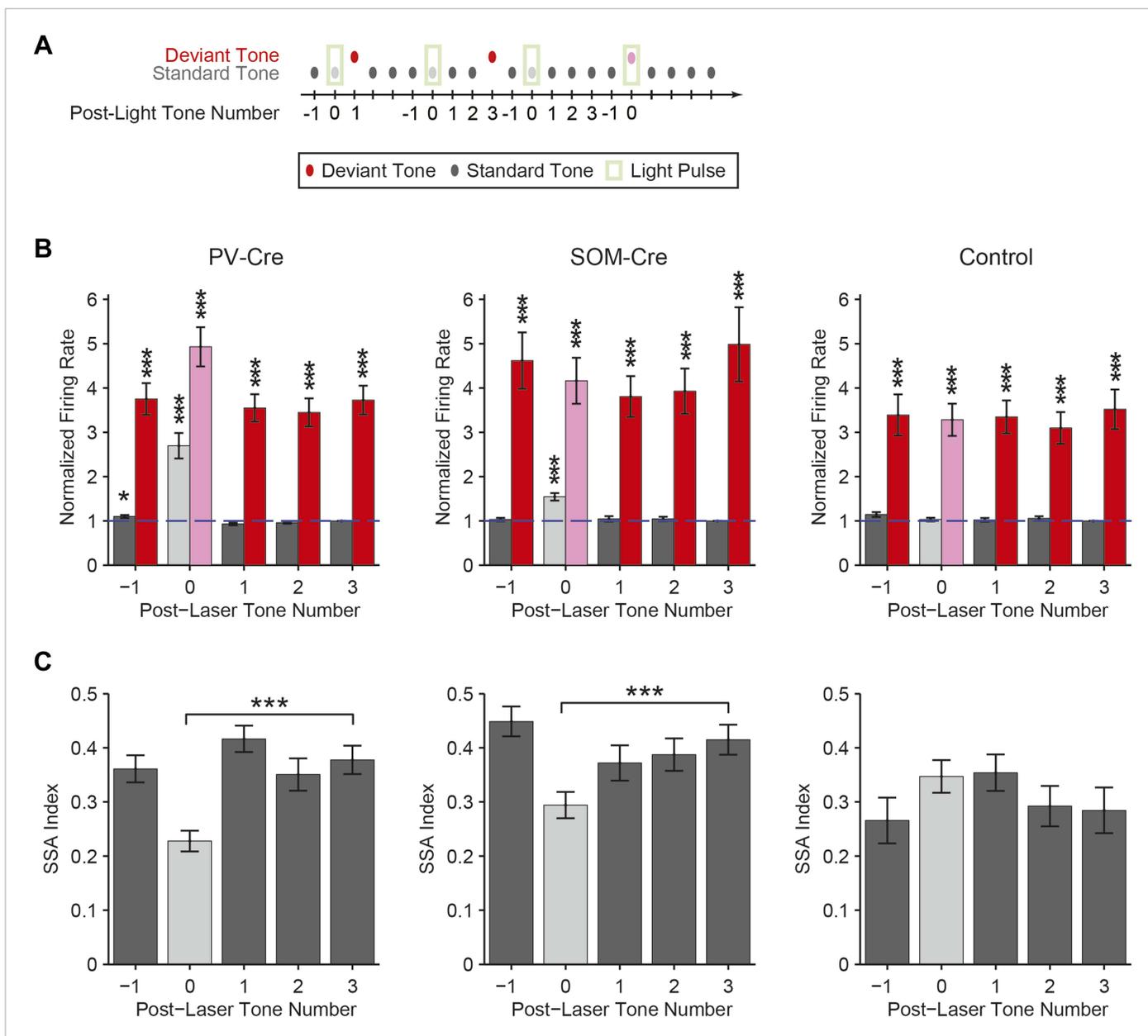
**Figure 2—figure supplement 2.** Optogenetic control of SOMs in mouse primary auditory cortex via photostimulation of Arch in acute slices. **(A)** Adapting discharge pattern typical of a somatostatin-positive cell (top) in response to rectangular current injection (bottom; 200 pA) recorded in vitro via whole-cell patch clamp. Inset, endogenous GFP fluorescence of the recorded cell illustrating AAV9.Arch.GFP expression (i) filled with Alexa 594 (ii) and imaged using a two-photon microscope. Scale bar, 20  $\mu\text{m}$ . **(B)** Membrane hyperpolarization mediated by 532-nm light. **(C)** Outward current mediated by photoactivation of Arch. **(D)** Plot of light-induced outward current vs illuminance ( $\text{mW}/\text{mm}^2$ ). Error bars, standard deviation.

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**Figure 3.** Optogenetic suppression of either PVs or SOMs reduces SSA in putative excitatory neurons in the auditory cortex. **(A)** Diagram of oddball stimuli with light; two oddball stimuli are presented (as in **Figure 1A**), with 250-ms light pulses (green bars) delivered during every fifth tone, starting 100 ms before tone onset. **(B–D)** Representative neuron PSTH in response to tone A (left) and B (right) as a standard (gray) or deviant (red) on light-on (light colors) and light-off trials (dark colors). Neurons recorded in PV-Cre **(B, E)**, SOM-Cre **(C, F)**, and control **(D, G)** mice. **(E–G)** Effect of interneuron photosuppression on SSA. Left: SSA index on light-on vs light-off trials. Each neuron is represented by a circle that is filled if the neuron exhibits significant SSA, that is, its FR in response to deviant tones is greater than that to standard tones. The respective representative neuron in **B**, **C**, and **D** is indicated by a red circle. Gray dashed line, identity line. Right: mean SSA index on light-on (green) and light-off (gray) trials over neuronal population.

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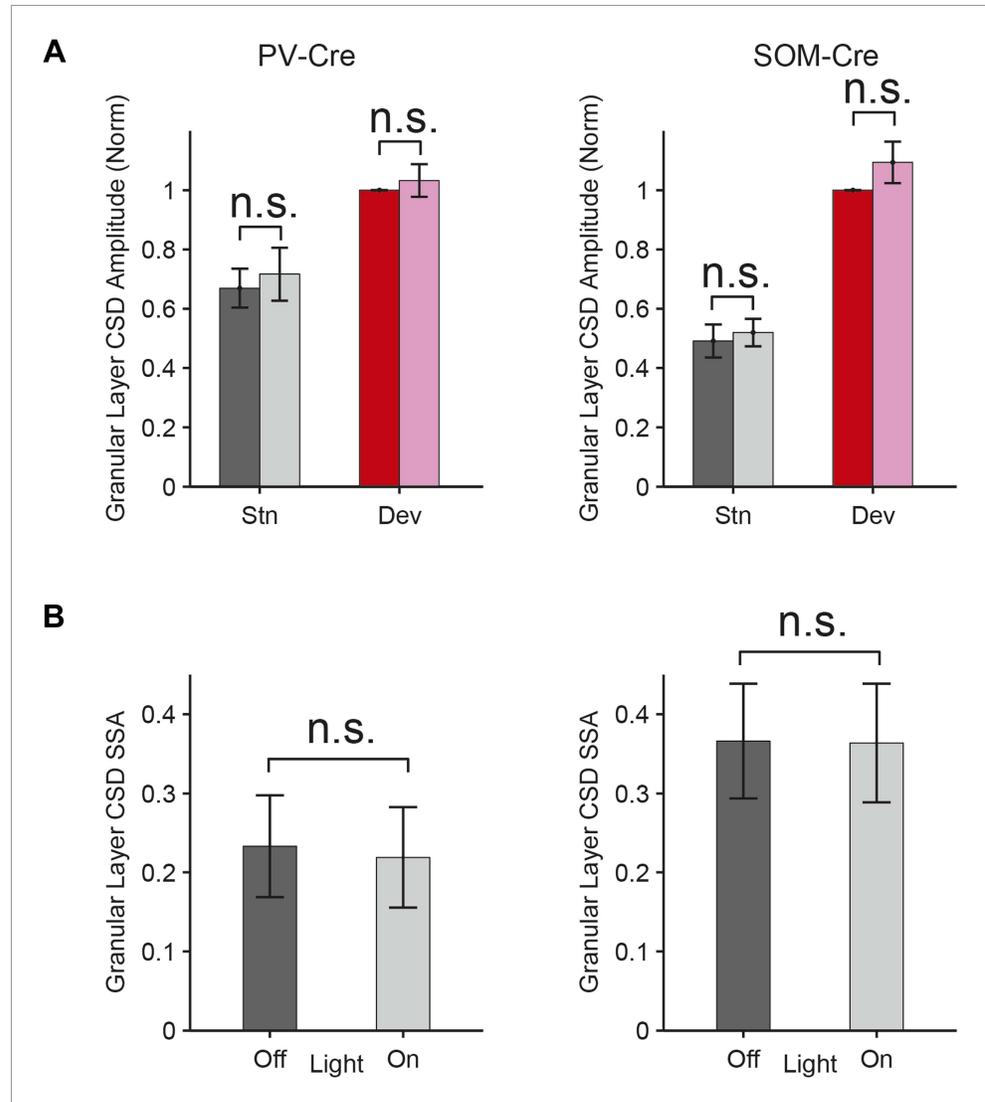
**Figure 3—figure supplement 1.** Photostimulation during standard tone does not affect SSA during subsequent tones on light-off trials. **(A)** Diagram of oddball stimuli illustrating post-photostimulation tone number: tones and light pulses indicated as in **Figure 3A**. Numbers indicate each tone position relative to light pulses as included in the analysis below. Any tones following deviant tones were excluded from the analysis. **(B)** The mean population firing rate in response to standard (gray) and deviant (red) tones subsequent to light-on trials is not affected by light presentation (dark bars: light-off, light bars: light-on). For each neuron, responses are normalized by the response to the third post-laser standard tone ( $T_3$ , indicated by blue dashed line). In PV-Cre mice, the standard tone-evoked FR with light-on ( $T_0$ ) and the tone preceding it ( $T_{-1}$ ) were significantly higher than that of standard  $T_3$  ( $N = 159$ ,  $T_{-1}$ :  $\Delta = 10\%$ ,  $p_2 = 0.037$ ,  $t(158) = 2.9$ ,  $C = 9$ .  $T_0$ :  $\Delta = 170\%$ ,  $p_2 = 2e^{-7}$ ,  $t(158) = 5.9$ ,  $C = 9$ ), while the two post-light tones ( $T_1$  and  $T_2$ ) were not significantly different ( $N = 159$ ,  $T_1$  and  $T_2$ :  $p_2 > 0.05$ ,  $t(158) < 2.6$ ,  $C = 9$ ). In SOM-Cre mice, the light-on standard  $T_0$ -evoked FR was greater than that of  $T_3$  ( $N = 114$ ,  $\Delta = 54\%$ ,  $p_2 = 4e^{-8}$ ,  $t(113) = 6.4$ ,  $C = 9$ ), while all light-off tones were not significantly different ( $T_{-1}$ ,  $T_1$ , and  $T_2$ :  $p_2 > 0.05$ ,  $t(113) < 0.9$ ,  $C = 9$ ). In control mice, no standard tones evoked greater FR than  $T_3$  ( $N = 107$ ,  $T_{-1}$  through  $T_2$ :  $p_2 < 0.05$ ,  $t(106) < 2.7$ ). In all three groups, deviant tones in all positions evoked greater FRs than standard  $T_3$  ( $\Delta > 209\%$ ,  $p_2 < 5e^{-5}$ ,  $t(106) > 4.7$ ,  $C = 9$ ). **(C)** Mean SSA index for each sequential tone position (for  $T_{-1}$ , 0, 1, 2, 3) calculated based on the pair of standard and deviant tones at each respective position. Each tone response, tone A or B, was used to calculate a separate SSA index:

$SSA\ Index = \frac{D_A - S_A}{D_A + S_A}$  or  $\frac{D_B - S_B}{D_B + S_B}$  Where S and D indicate mean FR evoked by standard and deviant tone probabilities, respectively, and their subscripts indicate the tone frequency condition. Compared to  $T_3$ , SSA index was significantly reduced only for  $T_0$ , the only light-on trial, in both PV-Cre and SOM-Cre mice. **Figure 3—figure supplement 1. continued on next page**

Figure 3—figure supplement 1. Continued

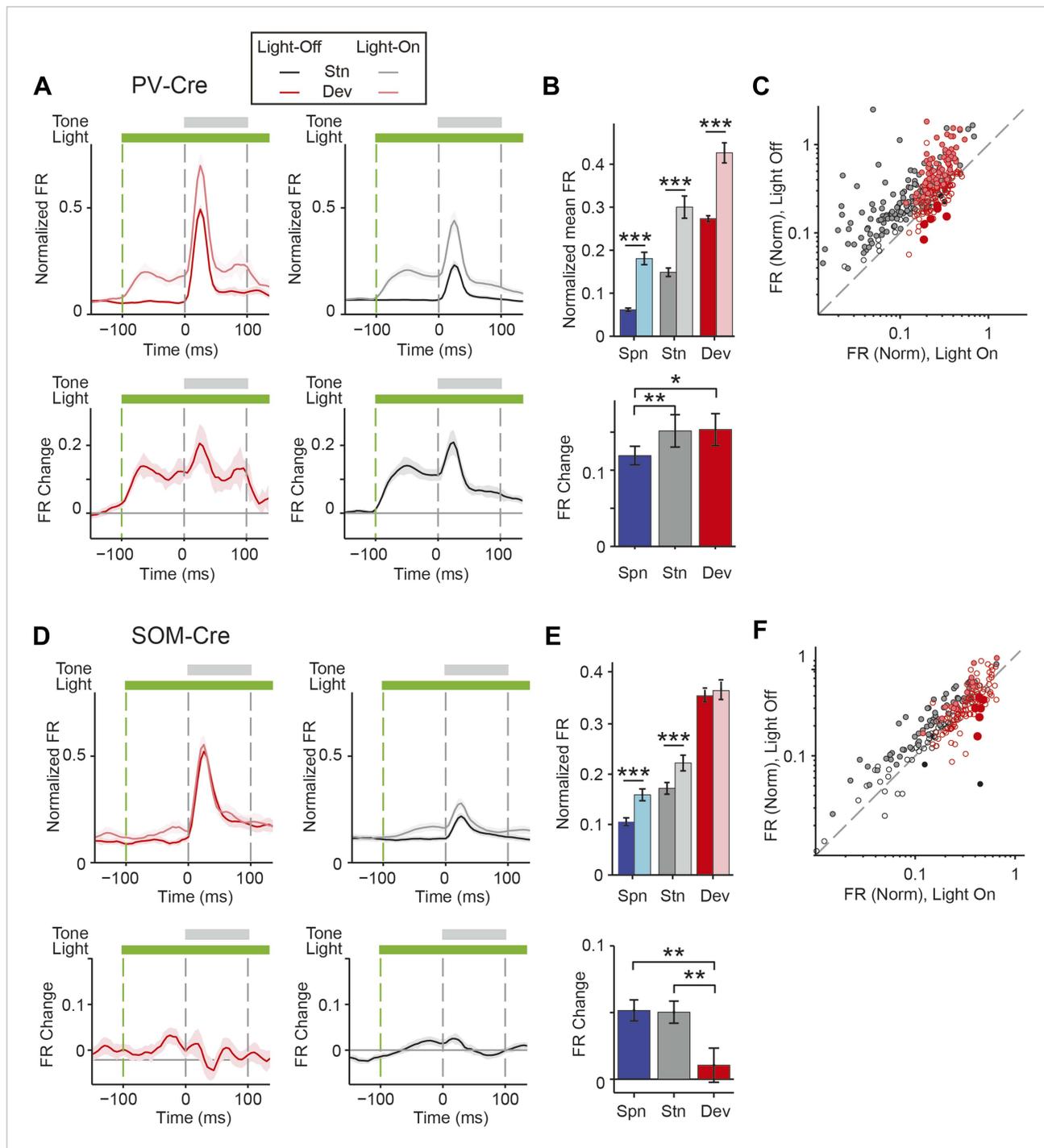
Cre mice (PV-Cre:  $\Delta = -40\%$ ,  $p2 = 4e^{-10}$ ,  $t(158) = -6.9$ ,  $C = 4$ . SOM-Cre:  $\Delta = -29\%$ ,  $p2 = 2e^{-7}$ ,  $t(158) = -5.8$ ,  $C = 4$ ), as expected from **Figure 3E–G**. In both PV-Cre and SOM-Cre mice, the SSA index at all of the other sequential tone positions,  $T_{-1}$  through  $T_2$  was not significantly different than that of  $T_3$  ( $p2 > 0.05$ ,  $t(113) < 1.9$ ,  $C = 4$ ), indicating that the effects of photosuppression were not detectable beyond  $T_0$ . In control mice, the SSA index was not different compared to  $T_3$  for any tone position, even  $T_0$  ( $p2 > 0.05$ ,  $t(106) < 1.8$ ,  $C = 4$ ). Together, this analysis demonstrates that the optogenetic effects are acute to illumination periods and unlikely to confound interpretation of effects observed during light-off trials. In all panels, single, and triple stars indicate  $p < 0.05$  and 0.001, respectively.

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**Figure 3—figure supplement 2.** Interneuron photosuppression does not affect thalamocortical responses to standard or deviant. **(A)** In PV-Cre and SOM-Cre mice, the mean granular layer CSD SSA index was not significantly different between the light-off and light-on conditions for standard or deviant tones ( $p2 > 0.05$ , for each condition; left, PV-Cre:  $N = 16$ . Center, SOM-Cre:  $N = 12$ ). **(B)** In both experimental groups, the mean granular layer CSD amplitude was not significantly different between the light-off and light-on conditions for standard or deviant tones ( $p2 > 0.05$ , for each condition; left, PV-Cre:  $N = 8$ . Center, SOM-Cre:  $N = 6$ ).

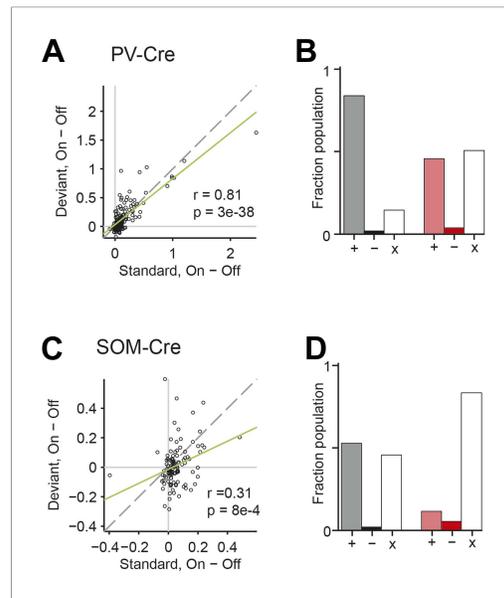
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**Figure 4.** PVs and SOMs differentially affect response to standard and deviant tones. **(A, D)** Top: mean response to deviant (left, red) and standard (right, black) tones, during light-on (light colors) and light-off trials (dark colors). Bottom: mean of the difference between responses on light-on and light-off trials for each neuron for deviant (left, red) and standard (right, black) tone. Each trace is a population average of putative excitatory neuron PSTHs normalized to each neuron’s maximum deviant tone-evoked FR on light-off trials. Shaded regions around traces indicate standard error (SE). Dashed lines indicate standard error (SE). Dashed lines indicate light onset (green) and tone onset and offset (gray). Neurons recorded in PV-Cre **(A)**, SOM-Cre **(D)** mice. **(B, E)** (Top) Mean population FR on light-on and light-off trials; (bottom) mean population FR difference between light-on and light-off conditions for deviant (red) and standard (gray) tones and spontaneous activity (blue). Normalization as in **A**. Neurons recorded in PV-Cre **(B)**, SOM-Cre **(E)** mice. **(C, F)** Modulation of PV-Cre mouse putative excitatory neuron FR response to tones by interneuron photosuppression. Neuronal responses to each tone are represented by two circles, one for standard (black) and one for deviant (red) tone responses. Filled circles represent significantly increased (gray, pink) or decreased (black, red) response; unfilled circles: responses without significant change. *Figure 4. continued on next page*

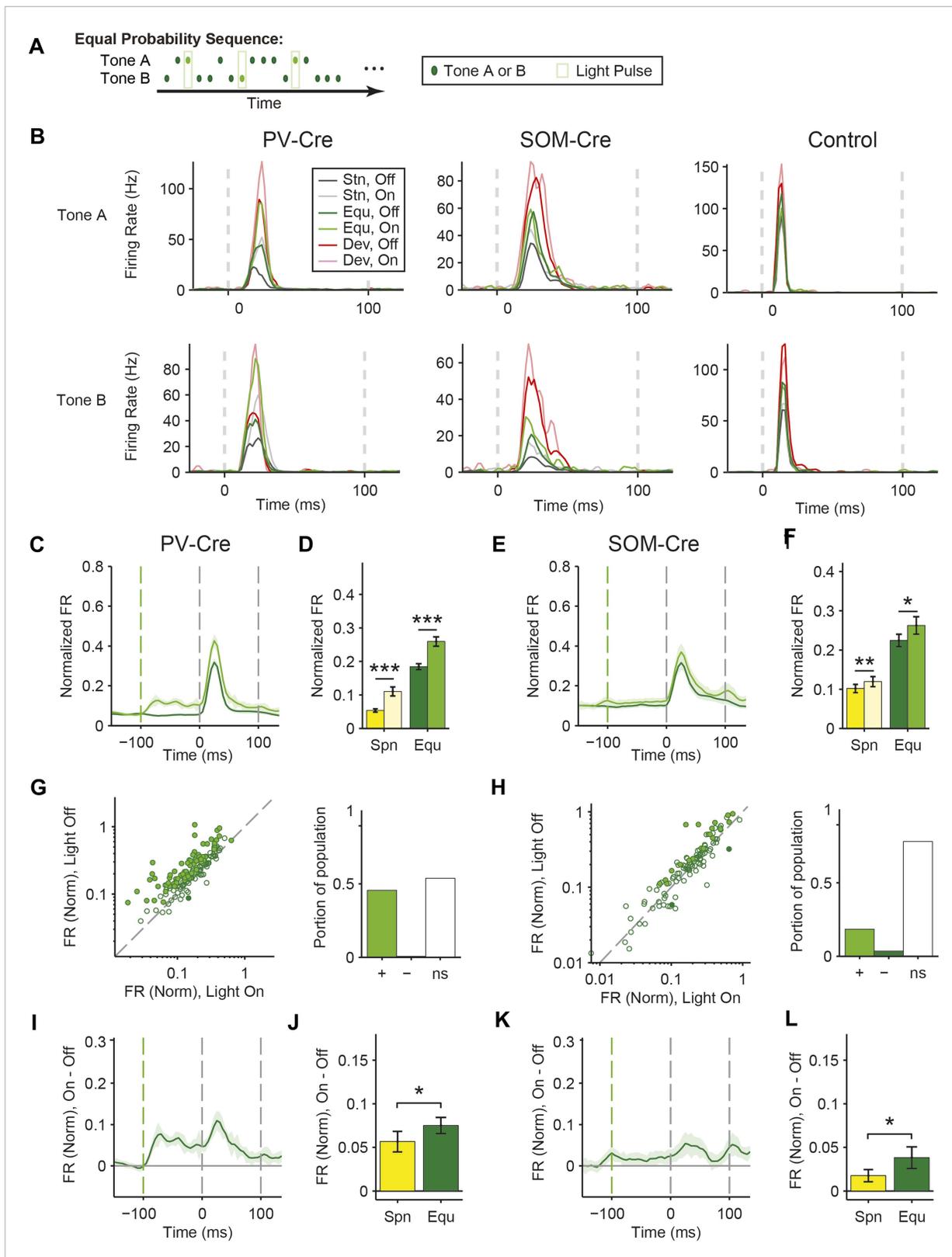
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significant modulation. Gray dashed line, identity line. Neurons recorded in PV-Cre (C), SOM-Cre (F) mice.  
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**Figure 4—figure supplement 1.** PVs and SOMs differentially affect response to standard and deviant tones. (A, C) Correlation between standard and deviant tone response change by photostimulation. Each neuron's response to each tone, A and B, is represented by one circle. Gray dashed line, identity line. Green dashed line, regression line. Neurons recorded in PV-Cre (A) and SOM-Cre (C) mice. (B, D) Proportion of putative excitatory population exhibiting significantly increased (gray, pink), decreased (black, red), or unchanged (unfilled) FR to standard and deviant tones due to photosuppression. Neurons recorded in PV-Cre (A), SOM-Cre (C) mice.

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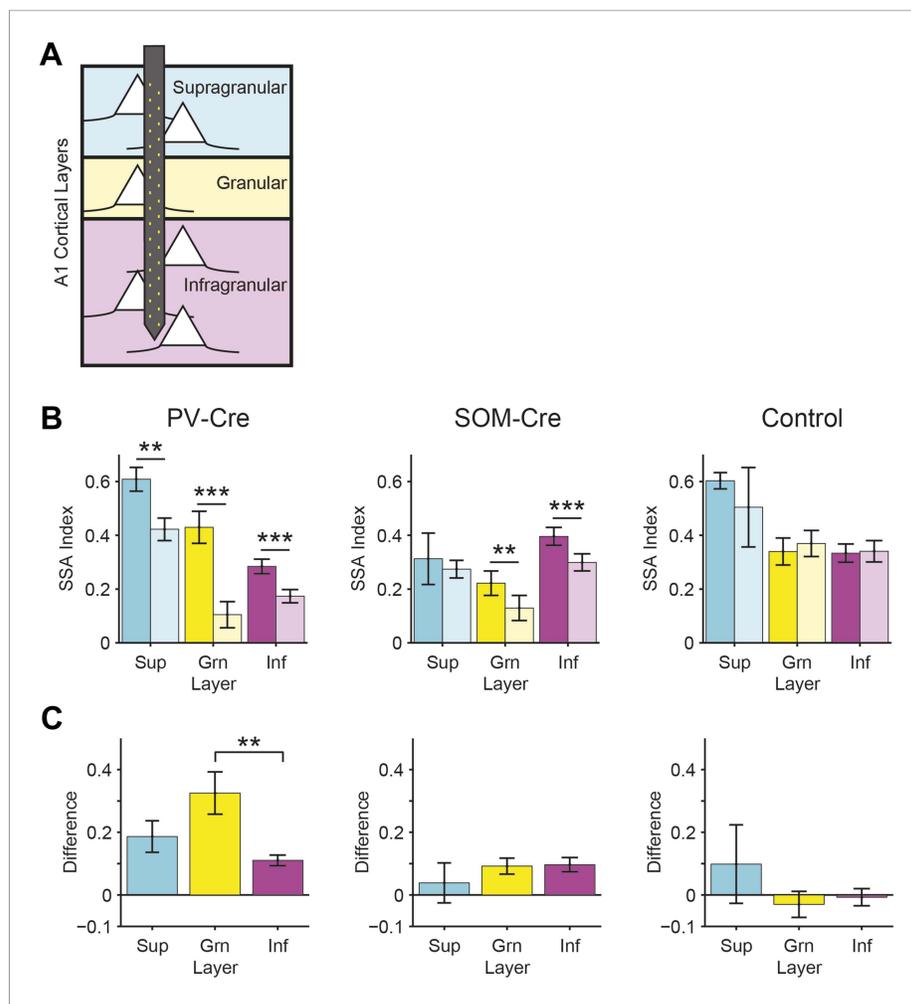


**Figure 4—figure supplement 2.** Consistent effects of PV and SOM suppression in response to equal probability tones. **(A)** Diagram of equal probability tone stimulus; an equal number of pseudorandom tones A and B are presented with 250-ms light pulses (green bars) delivered during every fifth tone, Figure 4—figure supplement 2. continued on next page

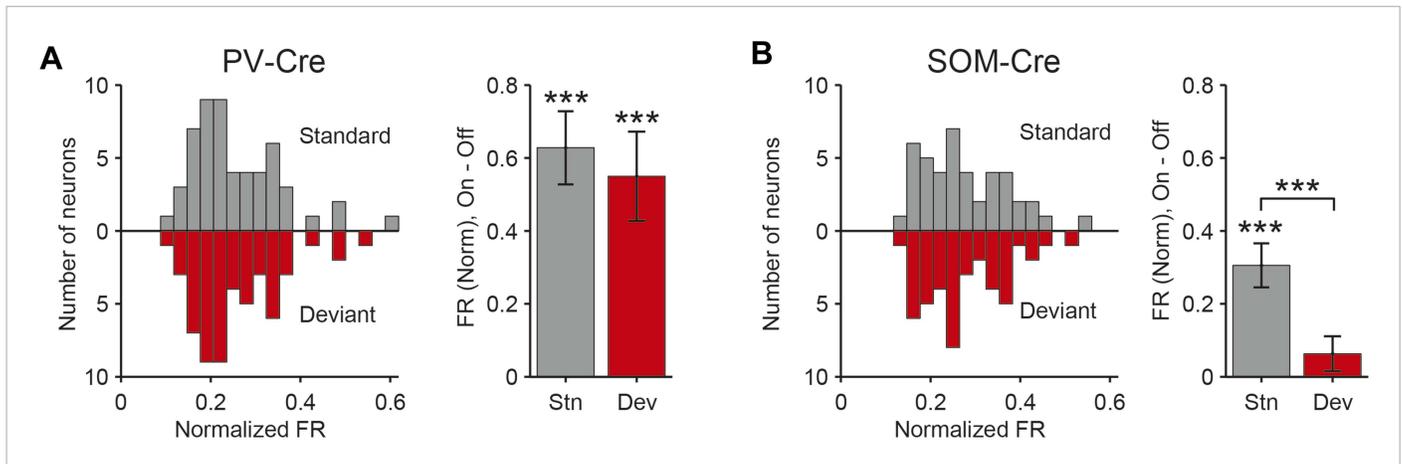
Figure 4—figure supplement 2. Continued

starting 100 ms before tone onset. **(B)** Effect of interneuron photosuppression on putative excitatory neuron responses to standard and deviant and equal probability tones. Mean FR of single neuron responses to standard (gray), equal (green), and deviant (red) tones on laser-off (dark colors) vs laser-on (light colors) trials. Top: responses to tone A. Bottom: responses to tone B. Left: neuron from PV-Cre mouse. Center: neuron from SOM-Cre mice. Right: neuron from control mouse. **(C, E)** PSTH of FR to equal probability tones, during light-on (light green) and light-off trials (dark green). Each trace is a population average of putative excitatory neuron PSTHs normalized to each neuron's maximum deviant tone-evoked FR on light-off trials. Shaded regions around traces indicate standard error (SE). Dashed lines indicate light onset (green) and tone onset and offset (gray). Neurons recorded in PV-Cre **(C, N = 160)** and SOM-Cre **(E, N = 114)** mice. **(D, F)** Population mean spontaneous FR (50 ms prior to tone onset, yellow) and equal-tone evoked FR (50 ms from tone onset, green) for light-off (dark colors) and light-on (light colors) trials. Normalized as in **C**. Neurons display an increase in spontaneous FR and equal tone-evoked FR with light-on for both PV-Cre **(D—Spn:  $\Delta 105\%$ ,  $p2 = 3e^{-6}$ ,  $t(159) = -8.1$ . Equ:  $\Delta = 41\%$ ,  $p2 = 1e^{-13}$ ,  $t(159) = 4.8$ )** and SOM-Cre **(F, Spn:  $\Delta = 17\%$ ,  $p2 = 0.002$ ,  $t(113) = -3.1$ . Equ:  $\Delta = 17\%$ ,  $p2 = 0.012$ ,  $t(113) = -2.54$ )** mice. **(G, H)** Modulation of PV-Cre mouse putative excitatory neuron FR response to tones by interneuron photosuppression. Left: circle: Response of each neuron to tone A and/or B. Filled: significantly increased (light green) or decreased (dark green) response; Unfilled: non-significant modulation. Gray dashed line, identity line. Right: fraction of neuronal tone responses in the population that increased (light green), decreased (dark green), or did not significantly change with light. Neurons recorded in PV-Cre **(G)**, SOM-Cre **(H)** mice. **(I, K)** Mean of the difference between light-on and light-off trials for each neuron for equal probability tones FR response PSTHs. Normalization and dashed lines as in **C**. Neurons recorded in PV-Cre **(I)**, SOM-Cre **(K)** mice. **(J, L)** Mean population FR difference between light-on and light-off conditions for spontaneous activity (yellow) and equal probability tones (green). Measured and normalized as in **D** and **F**. Neurons display a larger increase in equal-tone evoked FR than spontaneous FR with light-on for those recorded in both PV-Cre **(J,  $\Delta = 32\%$ ,  $p2 = 0.029$ ,  $t(159) = 2.2$ )**, SOM-Cre **(L,  $\Delta = 118\%$ ,  $p2 = 0.047$ ,  $t(113) = 2.0$ )** mice. In all panels, single, double and triple stars indicate  $p < 0.05$ ,  $0.01$  and  $0.001$ , respectively.

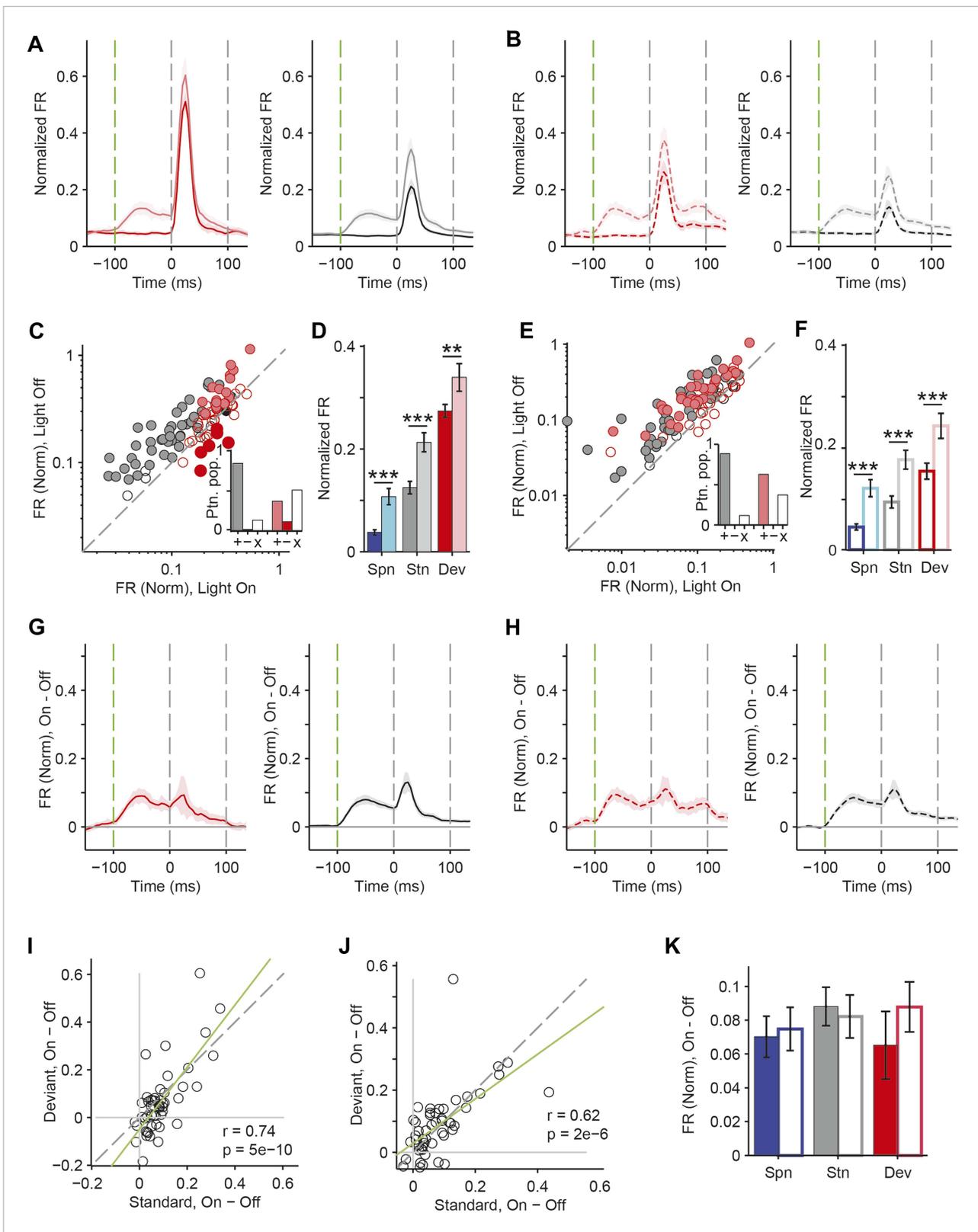
DOI: [10.7554/eLife.09868.013](https://doi.org/10.7554/eLife.09868.013)



**Figure 4—figure supplement 3.** PVs and SOMs have differential effects on SSA across different layers of cortex. **(A)** Diagram of multi-electrode recording across the supra-granular, granular, and infra-granular layers of A1. **(B)** SSA index for cortical supra-granular (Sup, cyan), granular (Grn, yellow), and infra-granular (Inf, magenta) layers on light-off (dark colors) and light-on (light colors) trials. **(C)** Difference in SSA index between responses on light-on and light-off trials for each layer as shown in **B**. Suppressing PVs reduced SSA throughout all cortical layers (**B** left, Sup: N = 15,  $\Delta = -31$ ,  $p_2 = 0.002$ . Grn: N = 27,  $p_2 = 2e^{-4}$ ,  $z = 3.8$ . Inf: N = 79,  $\Delta = -39\%$ ,  $p_2 = 1e^{-8}$ ,  $z = 5.7$ ). Notably, the effect of PVs was significantly stronger in the granular than in the infra-granular layers (**C** left— $\Delta = 194\%$ ,  $p = 0.014$ ,  $C = 2$ ) but was not different between the supra-granular and the granular or infra-granular layers ( $p > 0.05$ ,  $z < 1.8$ ,  $C = 2$ ). In the controls, SSA index was not significantly reduced between light-on and light-off trials in any layer (**B** right, Sup: N = 3. Grn: N = 21. Inf: N = 75. For each layer:  $p_2 > 0.05$ ,  $z < 1.4$ ), demonstrating that the light-induced effects required Arch. In contrast, suppressing SOMs reduced SSA in the granular (N = 7,  $\Delta = -42\%$ ,  $p_2 = 0.031$ ) and infra-granular (N = 63,  $\Delta = -24\%$ ,  $p_2 = 6e^{-7}$ ,  $z = 5.0$ ) layers but did not have a significant effect on SSA in the supra-granular layers (N = 3,  $p_2 > 0.05$ ) (**B**, center). In SOM-Cre mice and controls, there was no difference between effects of photosuppression on SSA index in different layers (**C**, center and right,  $p > 0.05$ ,  $z < 1.1$ ). Signed rank test for **B** and ranked sum test used for **C**. In all panels, double and triple stars indicate  $p < 0.01$  and  $0.001$ , respectively.  
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**Figure 4—figure supplement 4.** Differences between PV and SOM effects on standard and deviant tones are preserved for subsets of neurons matched for FR. **(A)** Left: two subsets of neurons recorded in PV-Cre mice with matched FR response magnitude to standard (gray, above x-axis) and deviant (red, below x-axis) tones on light-off trials. Right: difference between light-on and light-off FR in response to standard (gray) and deviant (red) tones for the respective subsets of neurons. **(B)** Same as **A** for neurons recorded in SOM-Cre mice. In all panels, triple stars indicate  $p < 0.001$ .  
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**Figure 4—figure supplement 5.** Effects of PV suppression are identical for tones that evoke strong or weak responses in putative excitatory neurons. Each neuron's response to oddball tones A and B is pooled according to their response strength. The tone which evokes a higher peak FR as a deviant is Figure 4—figure supplement 5. continued on next page

## Figure 4—figure supplement 5. Continued

pooled across neurons as the 'strong tone' response, while the tone which evoked a lower peak FR is pooled as the 'weak tone' response. (**A–J**) Data are presented as in **Figure 4**. Strong tone response data are presented on the left (**A, C, D, G, I**) with solid lines and filled bars, and weak tone response data are presented on the right (**B, E, F, H, J**) with dashed lines and unfilled bars. All data are from PV-Cre mice. (**K**) Mean population FR difference between light-on and light-off conditions for deviant (red) and standard (gray) tones and spontaneous activity (blue) for strong (filled) and weak (unfilled) tones. Measured and normalized as in **D** and **F**. Photosuppression of PVs led to increased spontaneous FR (Spn) and standard (Stn) and deviant (Dev) tone-evoked FR for both strong (**D**—Spn:  $\Delta = 187\%$ ,  $p2 = 4e^{-7}$ ,  $t(50) = -5.8$ . Stn:  $\Delta = 71\%$ ,  $p2 = 3e^{-10}$ ,  $t(50) = -7.8$ . Dev:  $\Delta = 24\%$ ,  $p2 = 0.002$ ,  $t(50) = -3.3$ ) and weak tones (**F**—Spn:  $\Delta = 171\%$ ,  $p2 = 3e^{-7}$ ,  $t(50) = -5.9$ . Stn:  $\Delta = 89\%$ ,  $p2 = 2e^{-8}$ ,  $t(50) = -6.5$ . Dev:  $\Delta = 58\%$ ,  $p2 = 2e^{-7}$ ,  $t(50) = -6.0$ ) ( $N = 51$ ). There were no significant differences between strong and weak tones for the change in spontaneous FR and standard and deviant tone-evoked FR (**K**, Spn, Stn and Dev:  $p > 0.05$ ,  $t(50) < 2.0$ ). In all panels, double and triple stars indicate  $p < 0.05$ ,  $0.01$  and  $0.001$ , respectively.

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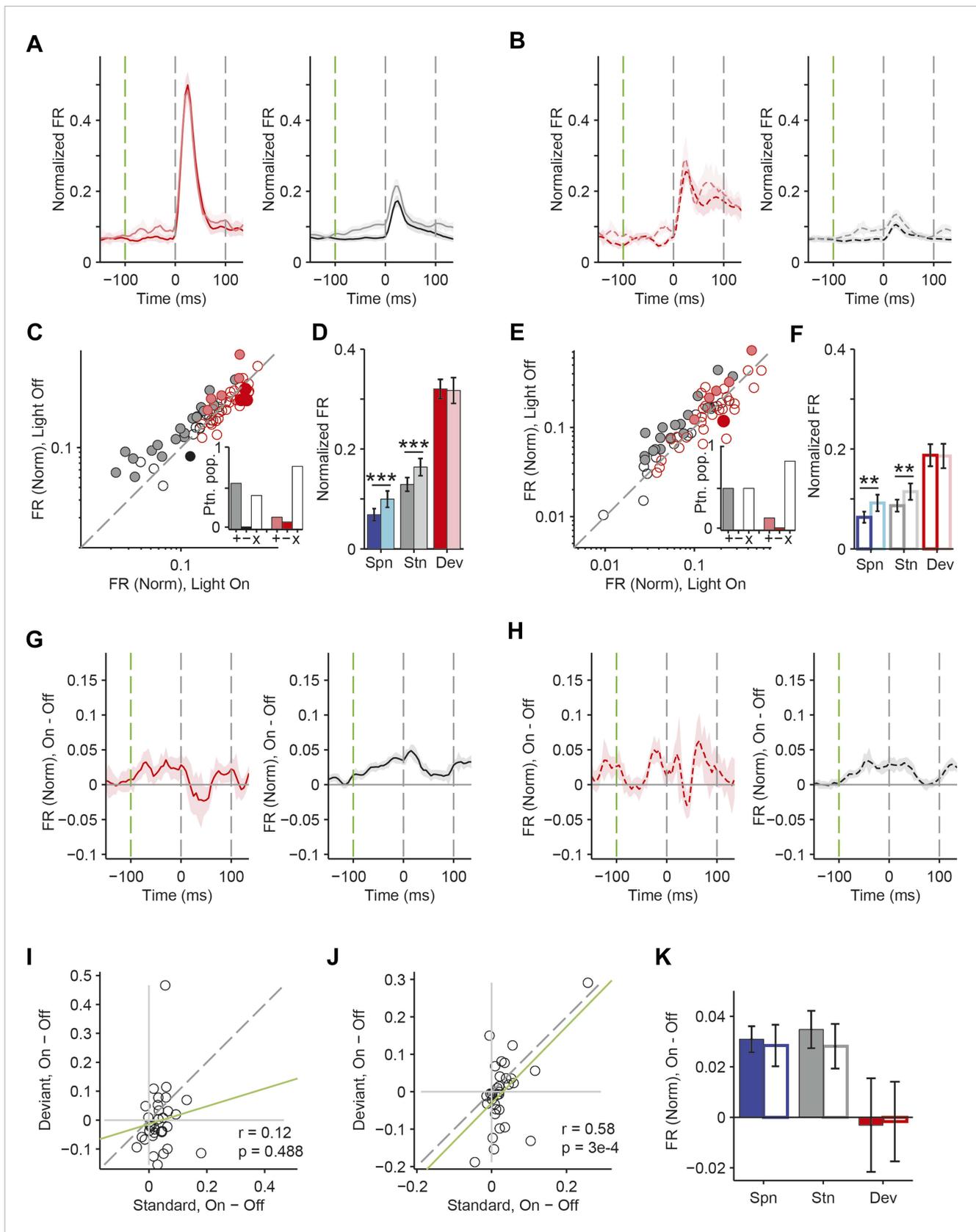
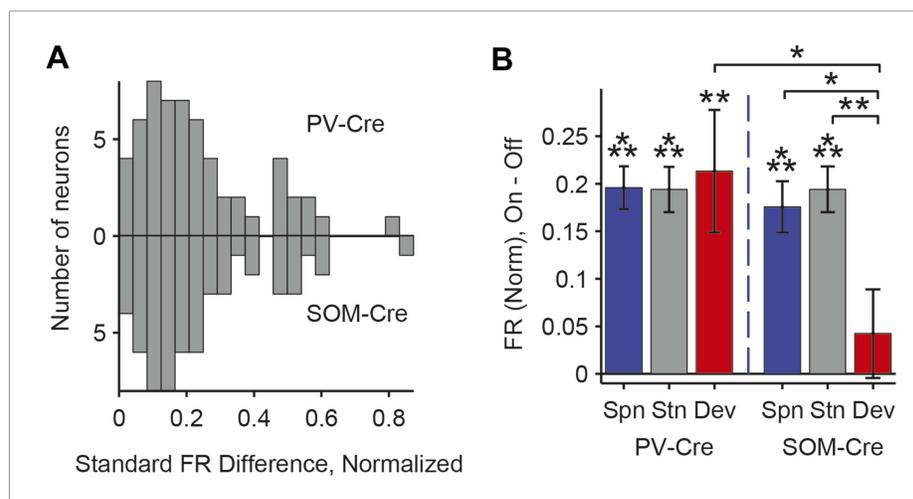


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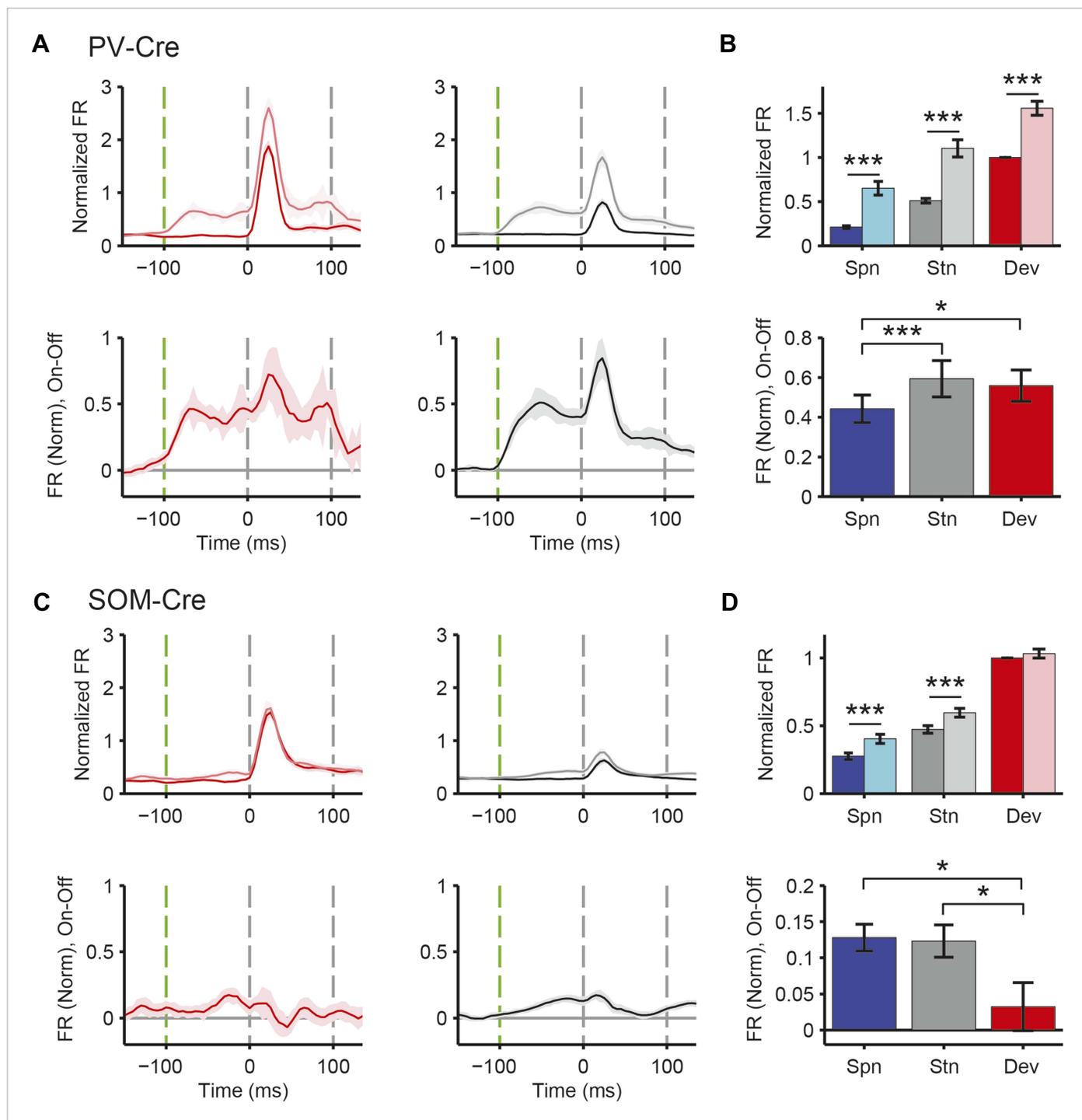
**Figure 4—figure supplement 6.** Effects of SOM suppression are identical for tones that evoke strong or weak responses in putative excitatory neurons. (A–K) Data are presented as in **Figure 4—figure supplement 5**. All data are from SOM-Cre mice. Photosuppression of SOMs lead to increased spontaneous FR and standard tone-evoked FR and did not change deviant tone-evoked FR for both strong (D—Spn:  $\Delta = 45\%$ ,  $p2 = 7e^{-7}$ ,  $t(33) = -6.1$ . Stn:  $\Delta = 27\%$ ,  $p2 = 4e^{-5}$ ,  $t(33) = -4.7$ . Dev:  $p2 > 0.05$ ,  $t(33) = -0.2$ ) and weak tones (F—Spn:  $\Delta = 45\%$ ,  $p2 = 0.001$ ,  $t(33) = -3.5$ . Stn:  $\Delta = 32\%$ ,  $p2 = 0.003$ ,  $t(33) = -3.2$ . Dev:  $p2 > 0.05$ ,  $t(33) = -0.1$ ) (N = 34). There were no significant differences between strong and weak tones for the change in spontaneous FR and standard and deviant tone-evoked FR (Spn, Stn, and Dev:  $p > 0.05$ , 0.28 and 0.95,  $t(33) < 1.2$ ). In all panels, double and triple stars indicate  $p < 0.05$ , 0.01 and 0.001, respectively.

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**Figure 4—figure supplement 7.** Differences between PV and SOM effects on standard and deviant tones are preserved for subsets of neurons matched for strength of laser effects on standard tones. (A) Two subsets of tone responses (N = 66) matched across PV-Cre (above x-axis) and SOM-Cre (below x-axis) mice for standard tone-evoked FR difference between light-on and light-off conditions. (B) Difference between light-on and light-off FR for spontaneous FR (blue) and standard (gray) and deviant (red) tone-evoked FR and for the PV-Cre (left) and SOM-Cre (right) subsets. With PV photosuppression, spontaneous FR, standard, and deviant tone-evoked FR increased (Spn: 20%,  $p2 = 1e^{-12}$ ,  $t(65) = 8.8$ , Stn: 19%,  $p2 = 1e^{-11}$ ,  $t(65) = 8.2$ , Dev: 21%,  $p2 = 0.001$ ,  $t(65) = 3.3$ ), and there were no significant differences between spontaneous and tone-evoked FR changes (Spn vs Stn:  $p2 > 0.05$ ,  $t(65) = 0.1$ , C = 3, Spn vs Dev:  $p2 > 0.05$ ,  $t(65) = -0.3$ , C = 3, Stn vs Dev:  $p2 > 0.05$ ,  $t(65) = -0.3$ , C = 3). With SOM photosuppression, spontaneous FR and standard tone-evoked FR increased (Spn: 17%,  $p2 = 1e^{-8}$ ,  $t(56) = 6.6$ , Stn: 19%,  $p2 = 2e^{-11}$ ,  $t(65) = 8.1$ ), while deviant tone-evoked FR did not change ( $p > 0.05$ ,  $t(65) = 0.9$ ). These changes were not significantly different between spontaneous FR and standard tone-evoked FR (Spn vs Stn:  $p > 0.05$ ,  $t(65) = -1.2$ ), but both were greater than the change in deviant tone-evoked FR (Spn vs Dev: 309%,  $p2 = 0.022$ ,  $t(65) = 2.8$ , C = 3, Stn vs Dev: 360%,  $p2 = 0.003$ ,  $t(3.5)$ , C = 3). By design, the change in standard tone-evoked FR was nearly identical between PV-Cre and SOM-Cre mice ( $p1 > 0.05$ ,  $t(65) = -0.1$ , C = 3). Spontaneous FR was also similarly modulated by PV and SOM photosuppression ( $p1 > 0.05$ ,  $t(65) = 0.8$ , C = 3). However, deviant tone-evoked FR was more strongly modulated by PV photosuppression than by SOM photosuppression (405%,  $p1 = 0.029$ ,  $t(65) = 2.4$ , C = 3). In all panels, single, double and triple stars indicate  $p < 0.05$ , 0.01 and 0.001, respectively.

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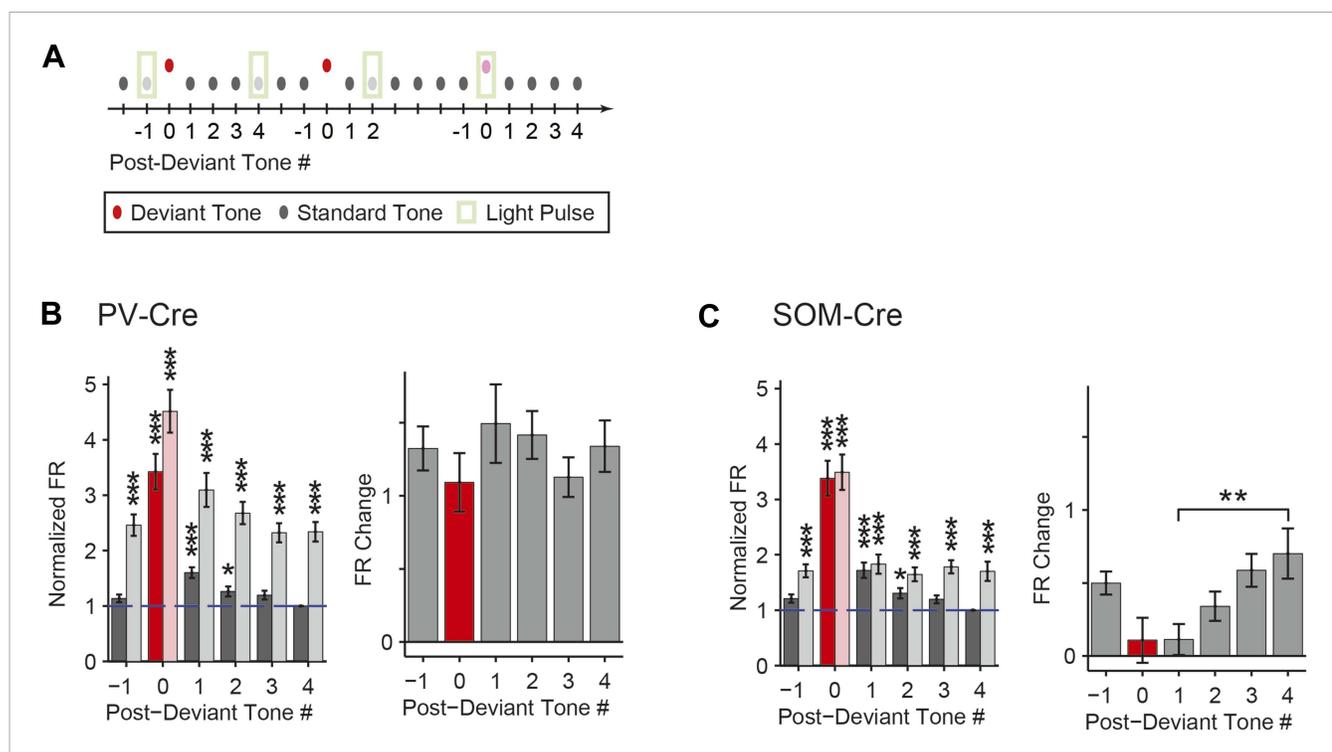


**Figure 4—figure supplement 8.** Differences between PV and SOM effects on standard and deviant tone responses are preserved when FRs are normalized by the mean onset response. **A, B, C,** and **D** as in **Figure 4A,B,D,E**, respectively. **(A, B)** In PV-Cre mice, spontaneous FR and standard and deviant-tone evoked FR increased with light (**B** top—Spn:  $\Delta = 210\%$ ,  $p2 = 2e^{-9}$ ,  $t(159) = -6.4$ . Stn:  $\Delta = 116\%$ ,  $p2 = 9e^{-10}$ ,  $t(159) = -6.5$ . Dev:  $\Delta = 56\%$ ,  $p2 = 5e^{-11}$ ,  $t(159) = -7.1$ ). For FR changes between light-on and light-off conditions, there was no difference significant difference between standard and deviant-tone evoked FRs (**B**, bottom, Stn vs Dev:  $p2 > 0.05$ ,  $t(159) = 0.7$ ,  $C = 2$ ), but both were great than the difference in spontaneous FR (Spn vs Stn:  $\Delta = 34\%$ ,  $p2 = 1e^{-4}$ ,  $t(159) = -4.1$ ,  $C = 2$ . Spn vs Dev:  $\Delta = 26\%$ ,  $p2 = 0.029$ ,  $t(159) = -2.5$ ). **(C, D)** In PV-Cre mice, spontaneous and standard tone-evoked FRs increased with light (**D** top—Spn:  $\Delta = 46\%$ ,  $p2 = 2e^{-10}$ ,  $t(113) = -7.0$ . Stn:  $\Delta = 26\%$ ,  $p2 = 2e^{-7}$ ,  $t(113) = -5.5$ ), but deviant tone-evoked FRs did not (Dev:  $p2 > 0.05$ ,  $t(113) = -1.0$ ). For FR changes between light-on and light-off conditions, there was no difference between spontaneous and standard tone-evoked FRs (Spn vs Stn:  $p2 > 0.05$ ,  $t(113) = 0.7$ ,  $C = 2$ ). **Figure 4—figure supplement 8. continued on next page**

Figure 4—figure supplement 8. Continued

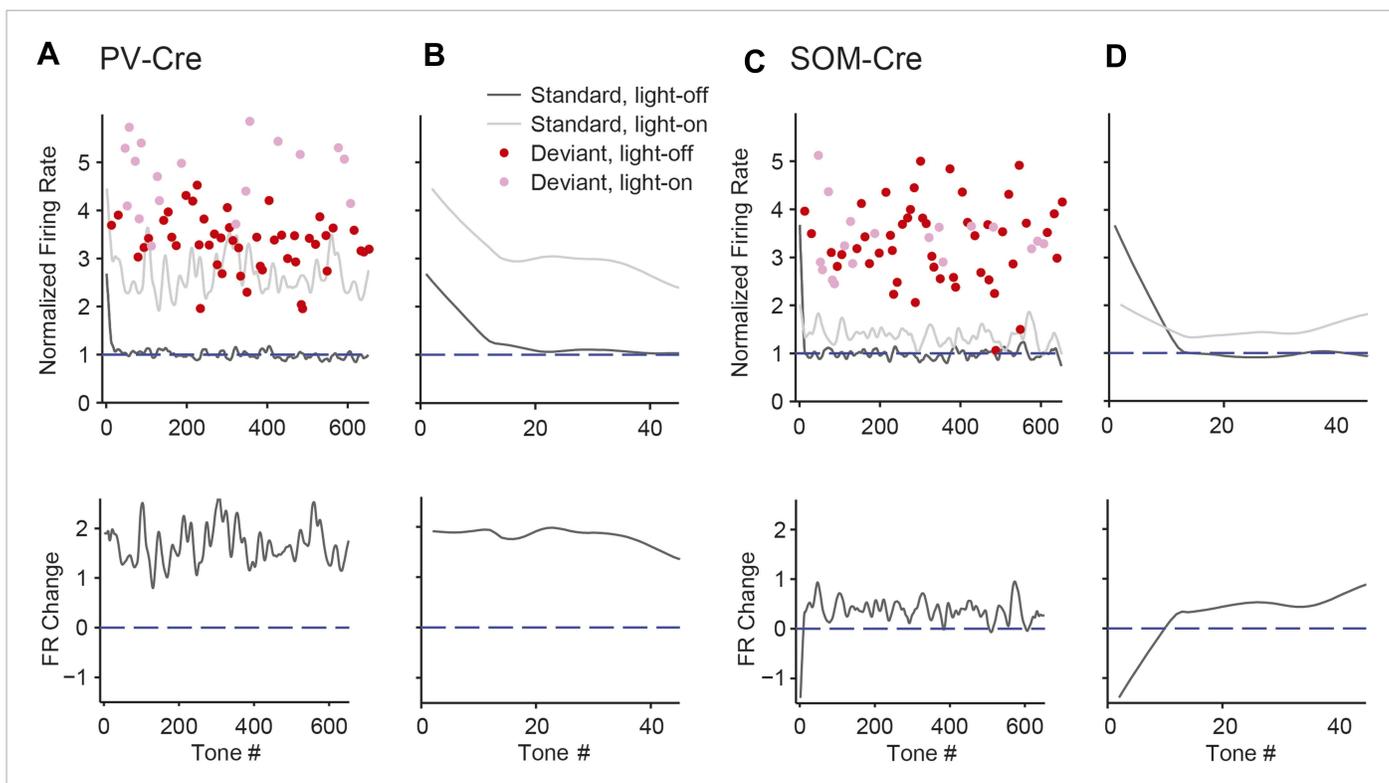
FR (D, bottom, Spn vs Stn:  $p_2 > 0.05$ ,  $t(113) = -0.3$ ,  $C = 2$ ), but both were significantly greater than deviant tone-evoked FR differences (Spn vs Dev:  $\Delta = 298\%$ ,  $p_2 = 0.011$ ,  $t(113) = 2.8$  Stn vs Dev:  $\Delta = 282\%$ ,  $p_2 = 0.016$ ,  $t(113) = 2.7$ ,  $C = 2$ ). In all panels, single, and triple stars indicate  $p < 0.05$  and  $0.001$ , respectively.

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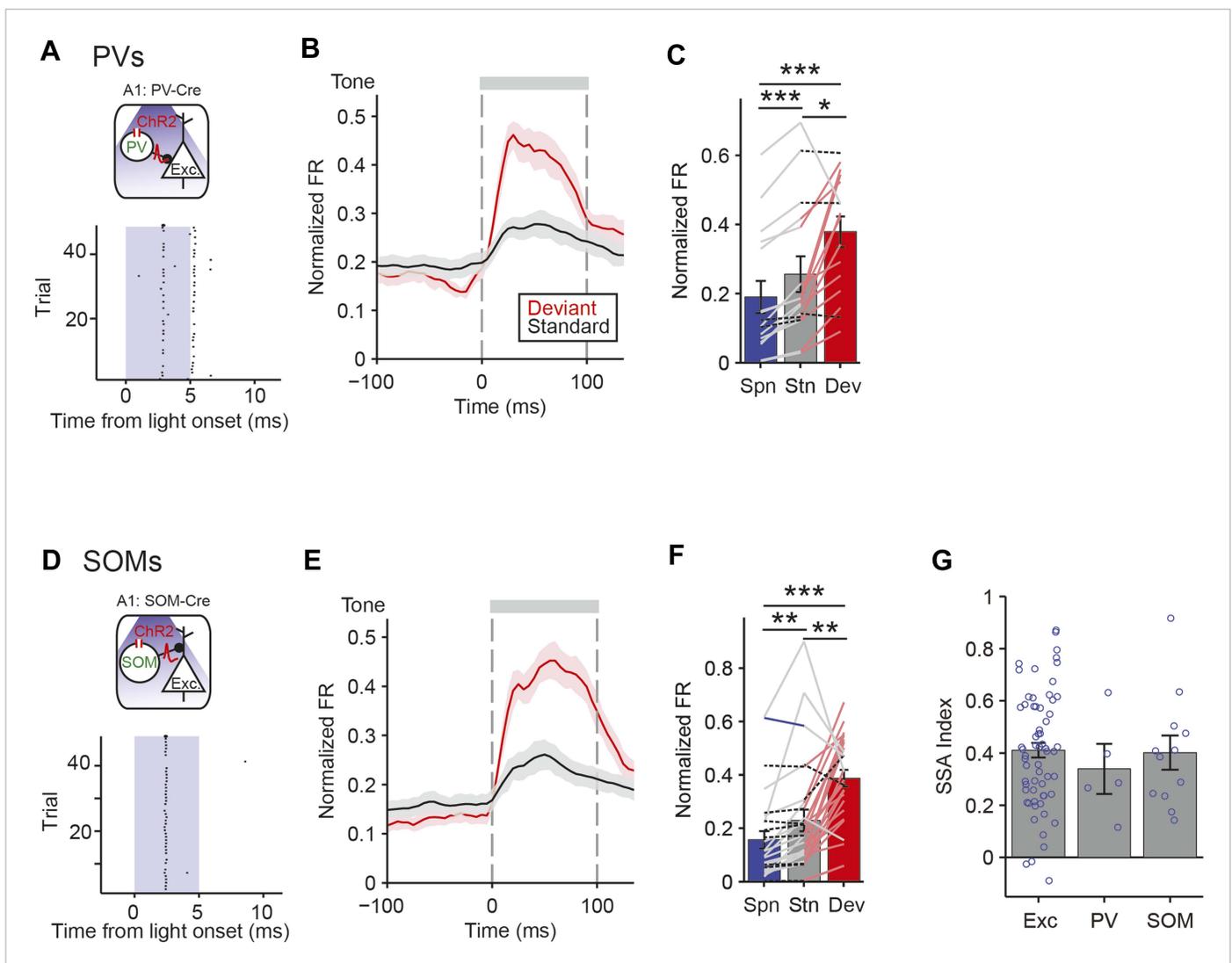
**Figure 5.** Post-deviant time course of interneuron-mediated effect on SSA. (A) Diagram of oddball stimuli illustrating post-deviant tone number used in subsequent analysis; Tones and light pulses are as indicated in **Figure 3A**. Numbers indicate each tone position relative to deviant tones. Responses to any standard tones following light-on standards were excluded from the analysis. (B, C) Left: mean population FR in response to standard tones (gray) subsequent to deviant tones (red) within the oddball sequence on light-off (dark colors) and light-on (light colors) trials. All responses are normalized to the response to the fourth post-deviant standard tone on light-off trials (green dashed line). Right: difference between FR on light-on and light-off trials in response to standard (gray) and deviant (red) tones. (B): PV-Cre mice. (C): SOM-Cre mice.

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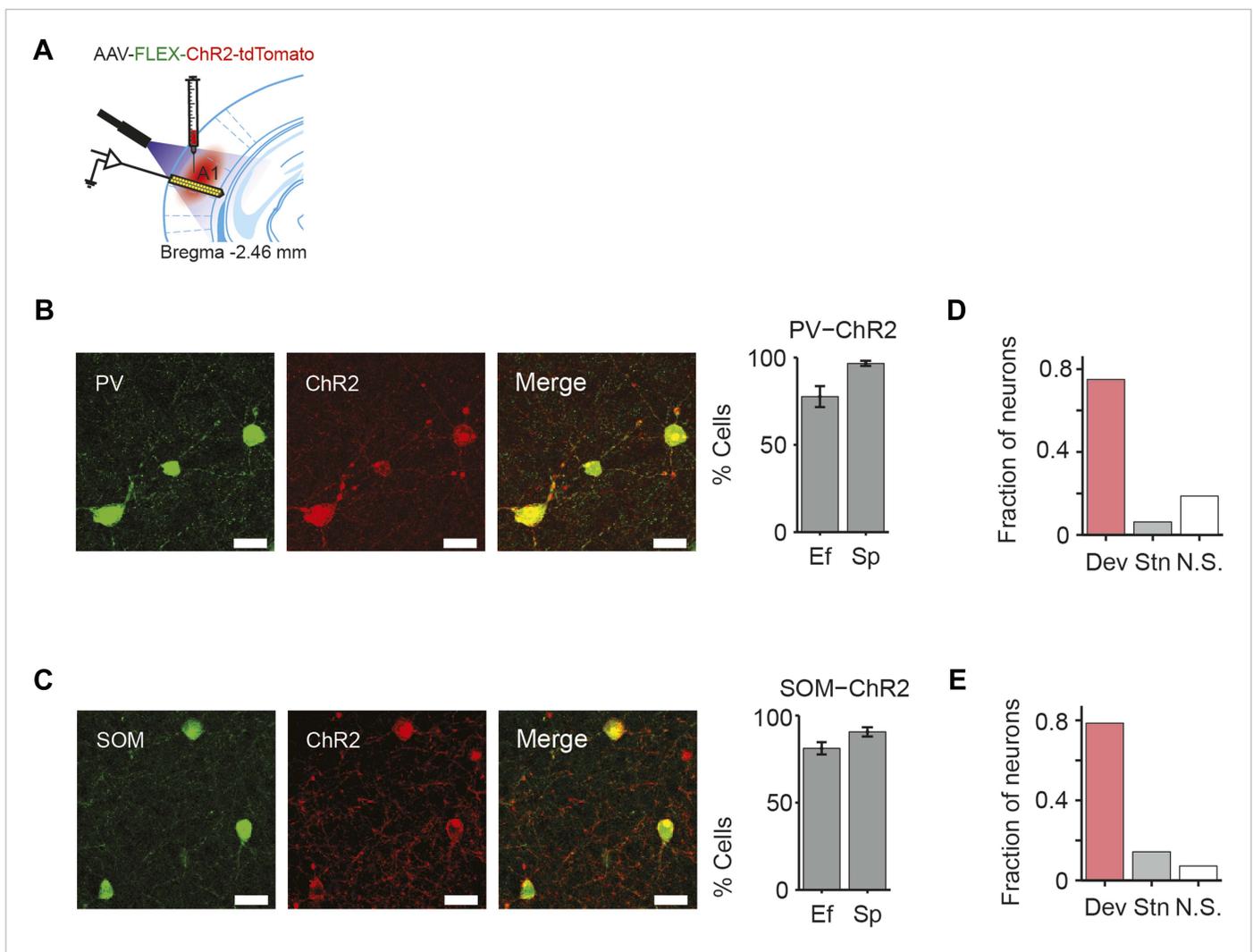
**Figure 5—figure supplement 1.** Initial time course of interneuron-mediated effect on SSA. The inhibitory influence of PV+ interneurons is persistent while that of SOM+ interneurons builds up over the first 40 tones. (A, B, C, D) Top: mean population FR in response to consecutive tones of the oddball sequence. Lines represent FR to standard tones on light-off (dark gray) and light-on (light gray) trials, interpolated to continuous lines. Dots represent FR to deviant tones on light-off (red) and light-on (pink) trials. Bottom: difference between FR on light-on and light-off trials to standard tones of the oddball sequence. Left: whole-oddball sequence. Right: first 50 tones of each sequence. A, B: PV-Cre mice. C, D: SOM-Cre mice.

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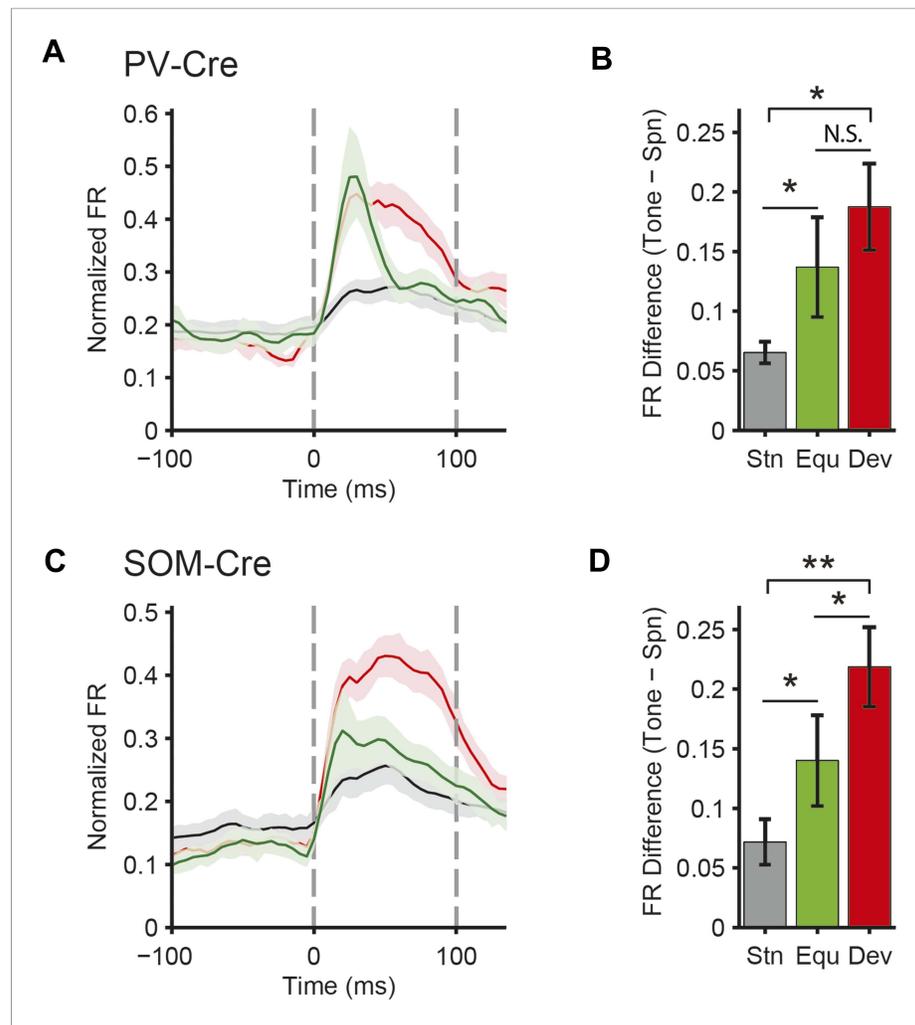
**Figure 6.** PV and SOM interneurons exhibit SSA. **(A, D)** Optogenetic methods. A1 was injected with AAV-FLEX-ChR2-tdTomato. During experiments, an optic fiber was positioned to target A1 and neuronal activity was recorded using a multichannel silicon probe in A1. Top diagram: blue light (473 nm) excites PVs in PV-Cre mice or SOMs in SOM-Cre mice. Bottom: peri-stimulus spike raster of a representative optogenetically identified PV (top) or SOM (bottom). Shaded region, blue light on. **(A)** PV-Cre. **(D)** SOM-Cre. **(B, E)** PSTH of PVs **(B)** or SOMs **(E)** FR response to deviant (red) and standard (black) tones. Normalization and dashed lines as in **Figure 4A,B**. **(C, F)** Mean PVs **(C)** or SOMs **(F)** FR response over the 100 ms of deviant (red) and standard tones (gray), and 100 ms of spontaneous activity prior to tone onset (blue). Each line represents a single neuron's response to each conditions, and its color indicates the magnitude of significant differences between two conditions; pink, gray, blue, and dashed black lines indicate a greater response to deviant tone, standard tone, silence and no significant change, respectively. **(G)** Mean SSA index of putative excitatory neurons, PVs, and SOMs. Circles represent SSA index values of individual neurons.

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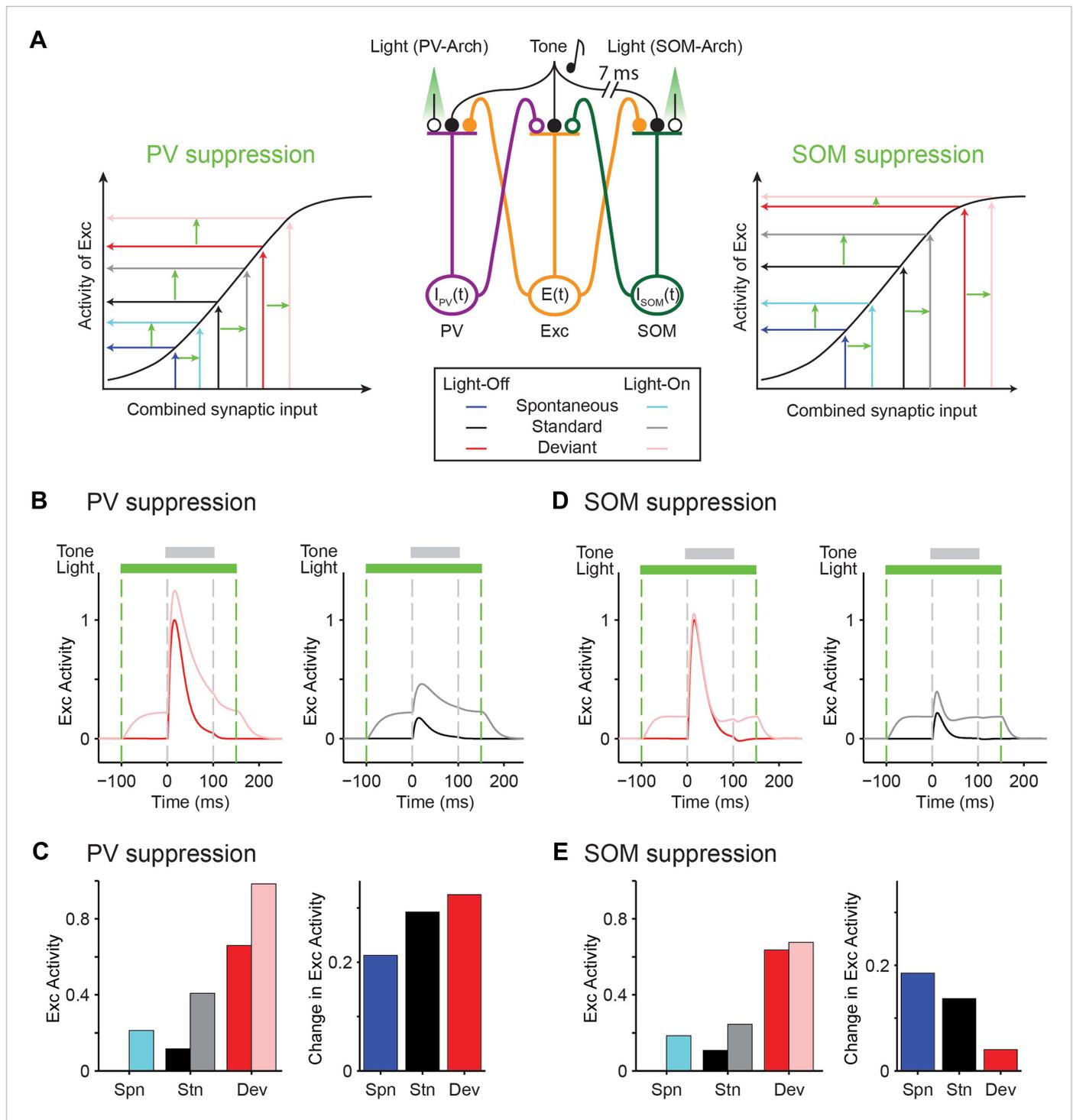
**Figure 6—figure supplement 1.** Optical tagging of PVs and SOMs. **(A)** Diagram of optogenetic methods. A1 was injected with AAV-FLEX-ChR2-tdTomato. During experiments, an optic fiber was positioned to target A1 and neuronal activity was recorded using a multichannel silicon probe in A1. **(B, C)** Transfection of interneurons with Channelrhodopsin-2 (ChR2). Images: immunohistochemistry demonstrating co-expression of ChR2 and an interneuron-type reporter in A1. Bar plots: efficiency (Ef) and specificity (Sp) of visual transfection of PVs (top) and SOMs (bottom) with ChR2. Ef, percent of labeled interneurons expressing ChR2. Sp, percent of ChR2-expressing cells, which are also labeled interneurons. **(B)** PV-Cre mouse A1. Green; anti-body stain for parvalbumin. Red; ChR2-tdTomato. Merge; co-expression of ChR2 and PVs. **(C)** SOM-Cre mouse A1. Green; anti-body stain for somatostatin. Red; ChR2-tdTomato. Merge; co-expression of ChR2 and SOMs. Scale Bar = 25  $\mu$ m. **(D, E)** Fraction of PVs **(D)** or SOMs **(E)** exhibiting a greater response to deviants than standards (pink), the reverse (gray), or neither (white).

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**Figure 6—figure supplement 2.** PVs and SOMs have different adaptation profiles for equal probability tones. **(A, C)** PSTH of PVs **(A)** or SOMs **(C)** FR response to standard (black), equal probability (green), and deviant (red) tones. Normalization and dashed lines as in **Figure 4A,B**. **(B, D)** Mean PV **(B)** or SOM **(D)** population FR response to standard (gray), equal probability (green), or deviant (red) tones over 100-ms tone duration. The mean spontaneous FR (during the 100 ms prior to all tones) of oddball and equal probability stimuli was subtracted from respective tone-evoked mean FRs. In PVs, equal probability tones evoked FRs greater than standard tones (**B**— $N = 16$ ,  $\Delta = 110\%$ ,  $p_2 = 0.030$ ,  $z = -2.4$ ,  $C = 2$ ) and not significantly different that deviant tones ( $p_2 > 0.05$ ,  $z = -1.7$ ,  $C = 2$ ). In SOMs, equal tones evoked higher FRs than standard tones (**C**— $N = 28$ ,  $\Delta = 95\%$ ,  $p_2 = 0.022$ ,  $z = -2.6$ ,  $C = 2$ ), and lower FRs than deviant tones ( $\Delta = -36\%$ ,  $p_2 = 0.049$ ,  $z = -2.3$ ,  $C = 2$ ). In both types of interneuron, deviant tones evoked higher FRs than standard tones (**B**, PV— $\Delta = 188\%$ ,  $p_2 = 0.010$ ,  $z = -2.8$ ,  $C = 2$ . **C**, SOM— $\Delta = 205\%$ ,  $p_2 = 0.002$ ,  $z = -3.3$ ,  $C = 2$ ). In all panels, single and double stars indicate  $p < 0.05$  and  $0.01$ , respectively.

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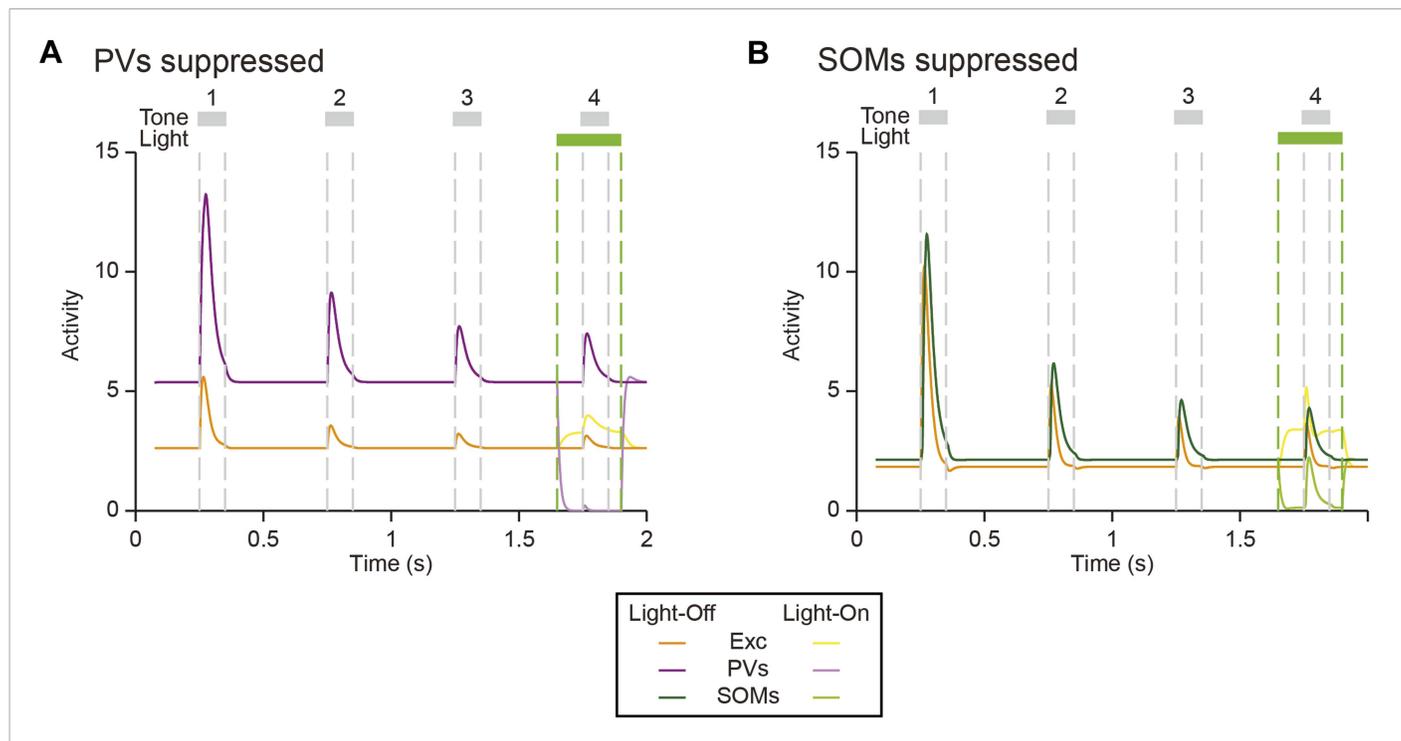


**Figure 7.** Mutually coupled excitatory-PV-SOM neuronal model accounts for differential effects of PVs and SOMs on SSA in putative excitatory neurons. **(A)** Center: diagram of coupled network model. Excitatory (Exc) and two types of inhibitory interneurons (PV and SOM) receive tone-evoked inputs. They make reciprocal connections on each other; Exc makes excitatory synapses on PV or SOM; PV and SOM inhibit Exc. Closed circles: excitatory synapses. Open circles: inhibitory synapses. Orange outlines: excitatory input-output pathway. Purple outlines: PV input-output pathway. Green outlines: SOM input-output pathway. The effect of optogenetic modulation was modeled as an additional input current delivered to inhibitory neuronal populations. Adaptation was modeled as decaying synaptic coefficient with slow adaptation. Left and right inset plots: combined input-output transfer function that represents the transformation between synaptic inputs and the activity of excitatory neurons. The values of inputs are depicted by arrows for the spontaneous and tone-evoked activity in response to deviant and standard tones under light-off (dark color) and light-on (light color) conditions, with *Figure 7. continued on next page*

Figure 7. Continued

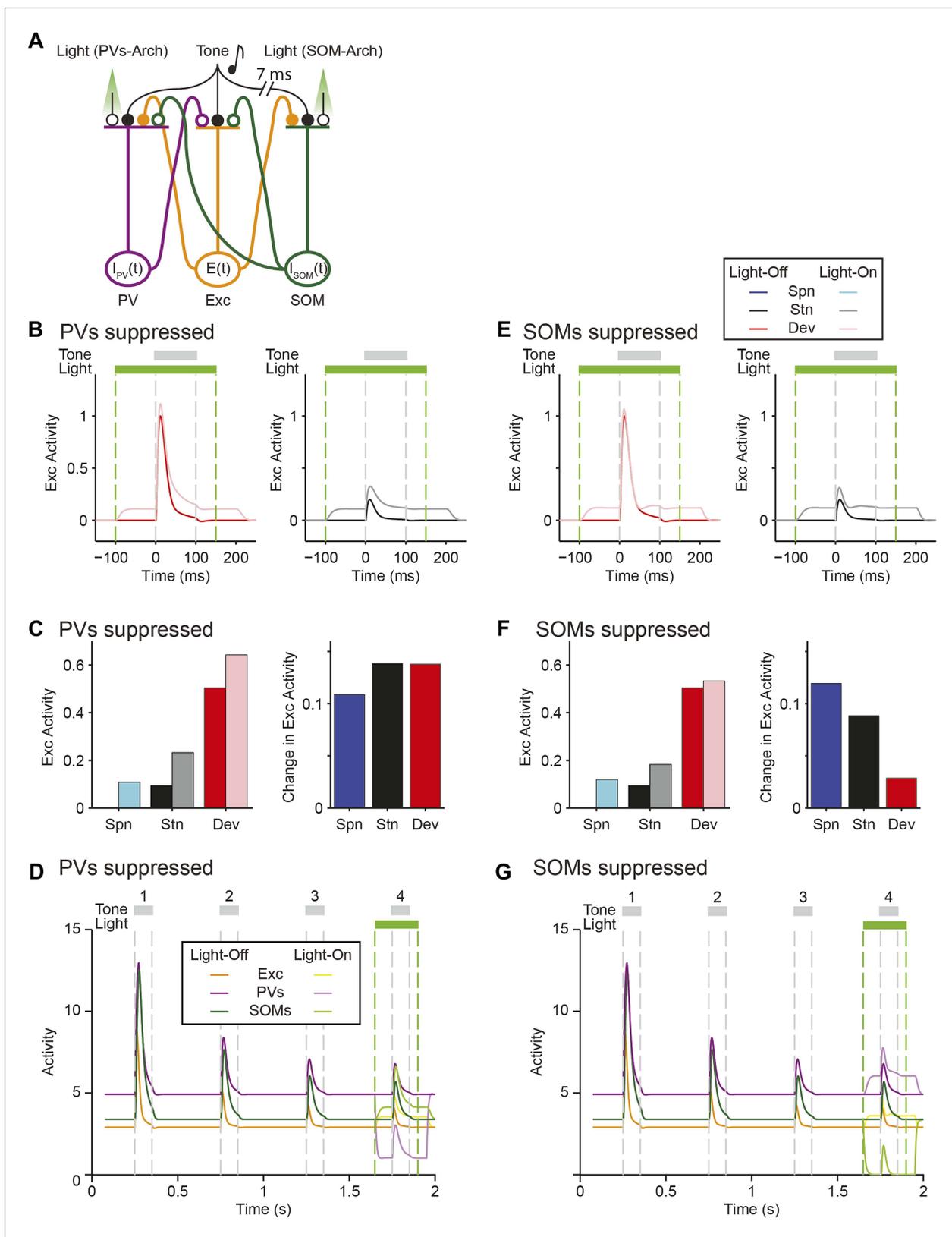
change due to light highlighted by light green arrows. **(B, D)** Tone-evoked responses of model neuronal excitatory population to deviant (red) and standard tones (gray), that is, the first and fourth consecutive tone presented, under light-off (dark colors) and light-on (light colors) conditions. Dashed lines indicate light onset and offset (green) and tone onset and offset (gray). **(B)** Light suppresses PVs. **(D)** Light suppresses SOMs. **(C, E)** Left: spontaneous FR (blue) and standard (black) and deviant (red) tone-evoked FRs on light-off (dark colors) and light-on (light colors) conditions. Right: mean difference between responses on light-on and light-off conditions. **(C)** Light suppresses PVs. **(E)** Light suppresses SOMs.

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**Figure 7—figure supplement 1.** Adaptation to repeated tones in model excitatory and inhibitory neurons. Responses evoked by four consecutive tones Exc (purple), PVs (orange, **A**), and SOMs (green, **B**). Note adaptation in the responses of both excitatory and inhibitory neurons. During fourth tone, there is light-evoked suppression of interneuron activity. Light-on: solid; light-off: dashed lines. **(A)** Light suppresses PVs. **(B)** Light suppresses SOMs.

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**Figure 7—figure supplement 2.** Excitatory–inhibitory model with inhibitory inputs from SOM to PV population accounts for differential effects of PVs and SOMs on SSA in putative excitatory neurons. **(A)** Center: diagram of coupled network model. Model is as in **Figure 7**, with additional inhibitory inputs from **Figure 7—figure supplement 2**. *continued on next page*

Figure 7—figure supplement 2. Continued

SOM to Exc population. **(B, E)** Tone-evoked responses of model neuronal excitatory population to deviant (red) and standard tones (gray), that is, the first and fourth consecutive tone presented, under light-off (dark colors) and light-on (light colors) conditions. Dashed lines indicate light onset and offset (green) and tone onset and offset (gray). **(B)** Light suppresses PVs. **(E)** Light suppresses SOMs. **(C, F)** Left: spontaneous FR (blue) and standard (black) and deviant (red) tone-evoked FRs on light-off (dark colors) and light-on (light colors) conditions. Right: mean difference between responses on light-on and light-off conditions. **(C)** Light suppresses PVs. **(F)** Light suppresses SOMs. **(D, G)** Responses evoked by four consecutive tones Exc (purple), PVs (orange), and SOMs (green). Note adaptation in the responses of both excitatory and inhibitory neurons. During the fourth tone, there is light-evoked suppression of interneuron activity. Dark traces: light-off. Light traces: light-on. **(D)** Light suppresses PVs. **(G)** Light suppresses SOMs.

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