Supplementary Materials

Predictive Coding Models for Pain Perception

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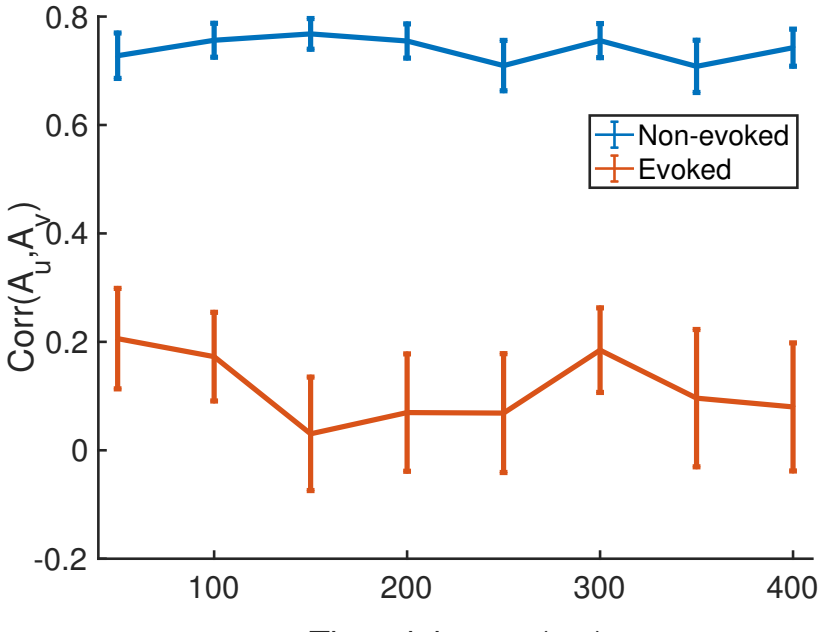
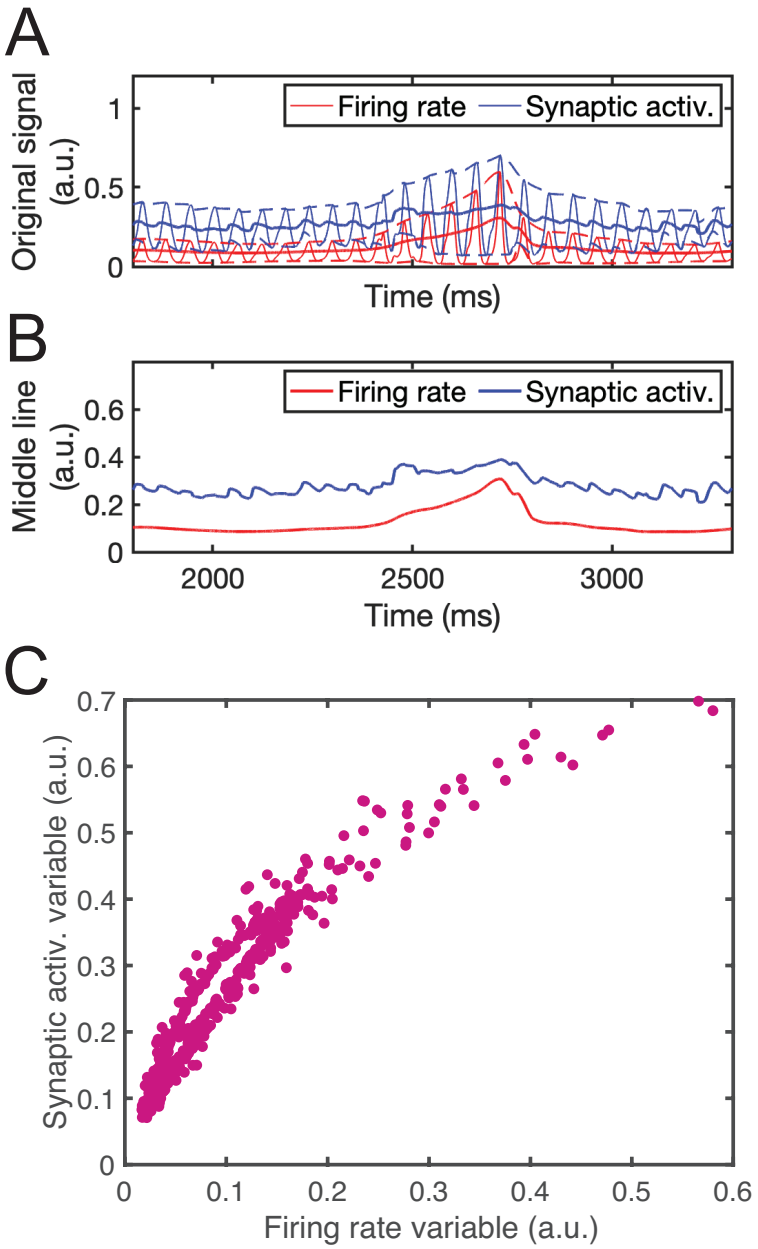
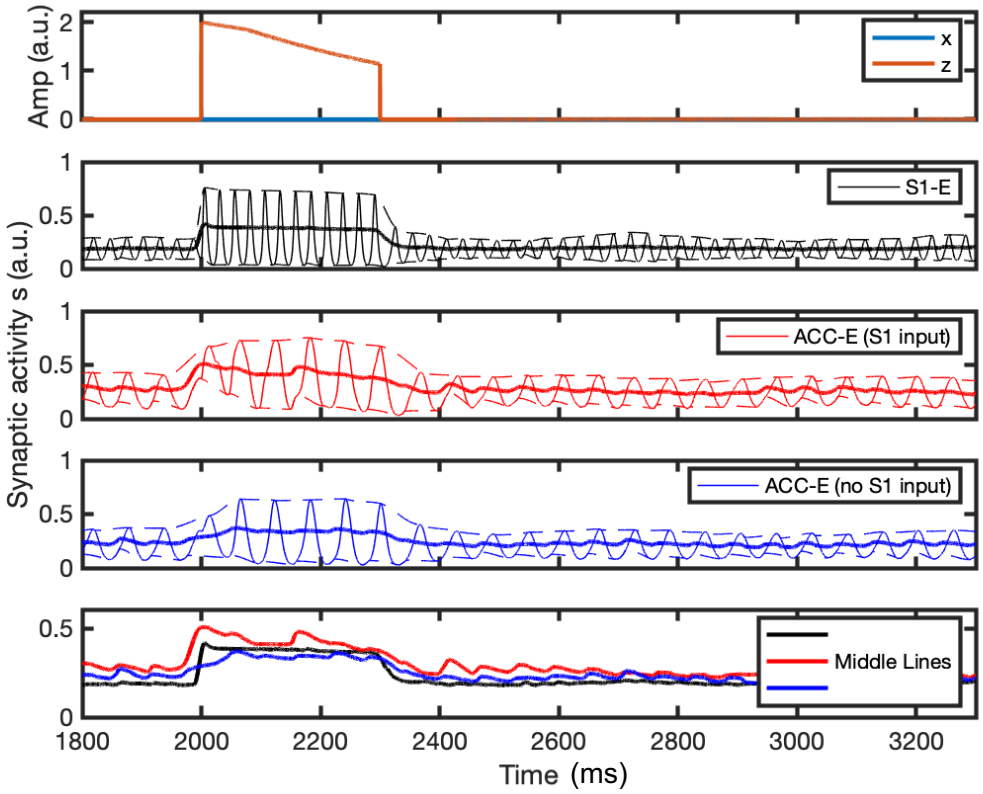


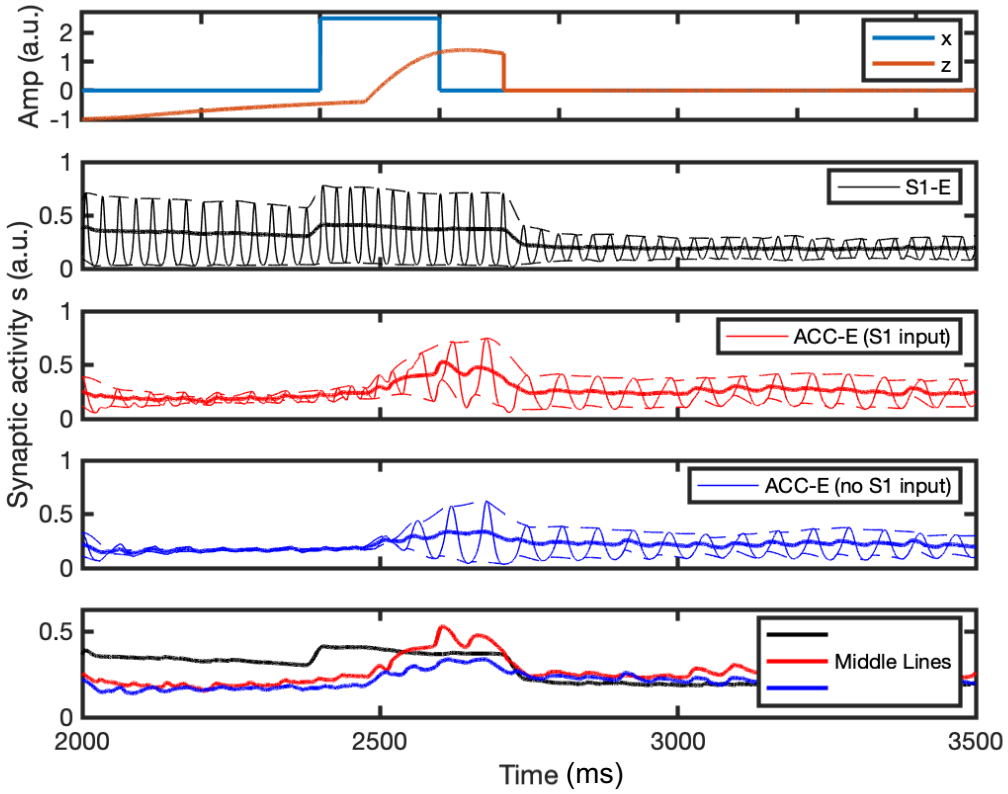
Supplementary Fig. 1: Sensitivity analysis of correlation between A_u and A_v with respect to the delay parameter Δ_u in the predictive coding model. The correlation statistics are relatively stable across a wide range of Δ_u in evoked pain (red) and non-evoked nociception (blue). Error bar denotes SEM ($n = 10$).



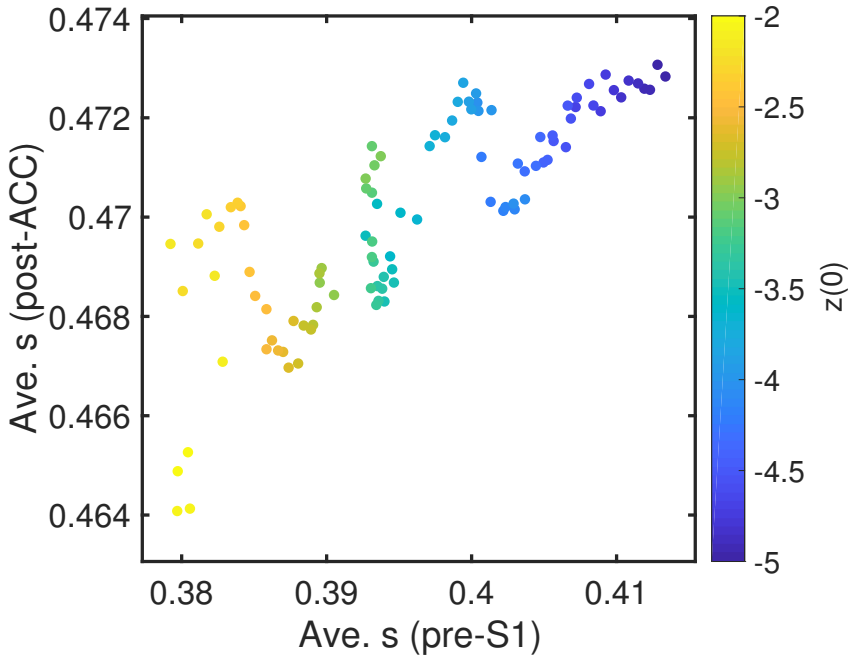
Supplementary Fig. 2: Comparison of firing rate variable r and synaptic activation variable s in evoked pain based on the mean field model. (A) Representative simulated traces of firing rate (red) and synaptic activation (blue) of ACC population $E_{2\text{-}1}$ in one evoked pain trial. Dashed lines show the upper and lower envelope of the oscillation. (B) Replot the midline of the envelopes in panel A. (C) Scatter plot of firing rate variable and synaptic activation variable in panel A. Two variables are highly correlated (Spearman's correlation 0.969, $p < 10^{-10}$).



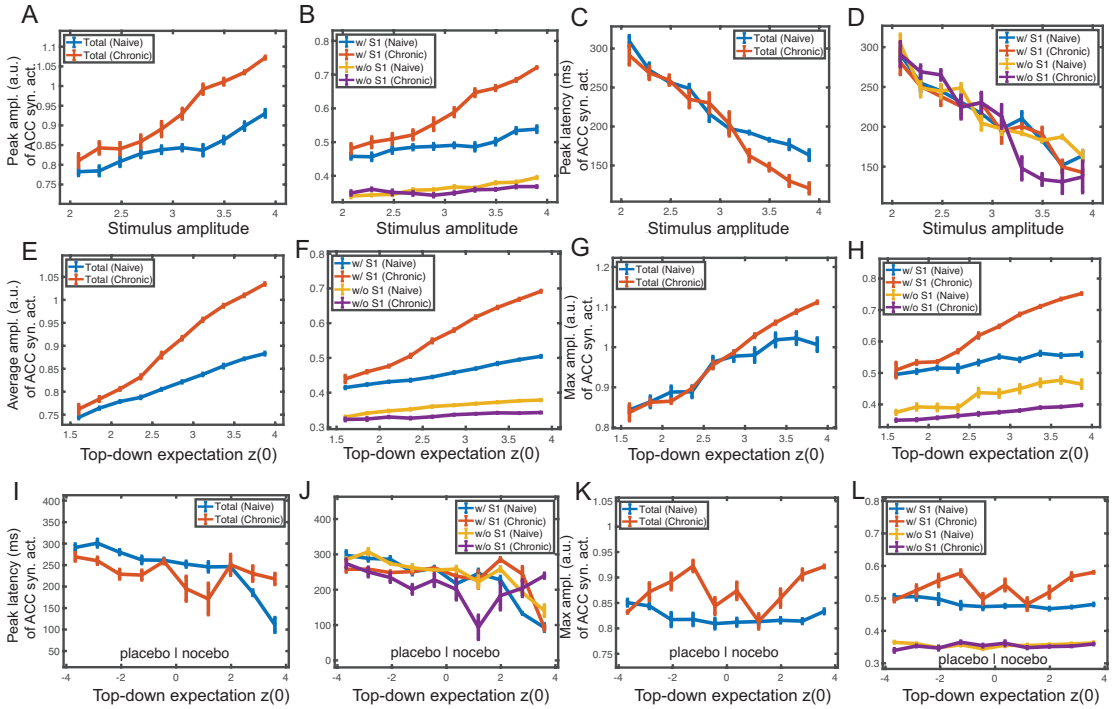
Supplementary Fig. 3: Mean-field activity (synaptic activation s) for three different excitatory neuronal populations in one representative non-evoked nociception simulation. Notations are the same as Fig. 6*A*,*B*.



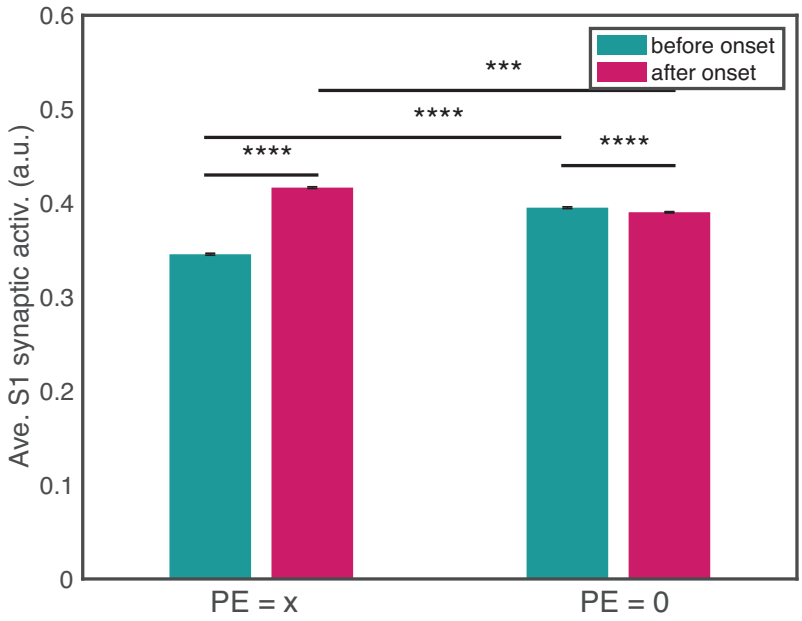
Supplementary Fig. 4: Mean-field activity (synaptic activation s) for three different excitatory neuronal populations in one representative placebo condition simulation. Notations are the same as Fig. 6*A*,*B*.



Supplementary Fig. 5: Scatter plot of the average pre-S1 synaptic activation s versus the average post-ACC synaptic activation s derived from the mean field model simulations ($n = 100$) in the placebo condition (Pearson's correlation coefficient: 0.80, $p = 7.7 \times 10^{-24}$).



Supplementary Fig. 6: Latency and maximum peak statistics of synaptic activation in ACC populations during evoked pain (*A-D*), non-evoked nociception (*E-H*) and placebo/nocebo (*I-L*) conditions. (*A*) Maximum of middle line of ACC synaptic activation variable s from total population during the duration T_s between the stimulus onset to withdrawal, for varying stimulus amplitude under naive (blue) and chronic pain (red) conditions. (*B*) Similar to panel *A*, except for two ACC subpopulations. (*C*) The latency from the stimulus onset to the maximum defined in panel *A* for varying stimulus amplitude under the naive and chronic pain conditions. (*D*) Similar to panel *C*, except for two ACC subpopulations $E_{2\text{-}1}$ (w/ S1 input) and $E_{2\text{-}2}$ (w/o S1 input). Mean and SEM for each group are shown. 100 Monte Carlo runs were run with random initial input amplitude $x \in [1.3, 5.0]$. (*E*) Average of middle line of ACC synaptic activation variable s from the total population during the duration T_s for varying top-down expectation $z(0)$ under naive and chronic pain conditions. (*F*) Similar to panel *E*, except for two ACC subpopulations $E_{2\text{-}1}$ and $E_{2\text{-}2}$. Mean and SEM for each group are shown. 100 Monte Carlo runs were run with random initial $z(0) \in [1.5, 4.0]$. (*G*) Maximum of middle line of ACC synaptic activation variable s from total population during the duration T_s between the stimulus onset to withdrawal, for varying top-down expectation $z(0)$ under the naive and chronic pain conditions. (*H*) Similar to panel *G*, except for two ACC subpopulations $E_{2\text{-}1}$ and $E_{2\text{-}2}$. The curves in panels *G* and *H* have similar shapes as in panels *E* and *F*. (*I*) The latency from the stimulus onset to the maximum of ACC synaptic activation for varying top-down expectation $z(0)$ under naive and chronic pain conditions. (*J*) Similar to panel *I*, except for two ACC subpopulations $E_{2\text{-}1}$ and $E_{2\text{-}2}$. Mean and SEM for each group are shown. 100 Monte Carlo runs were run with random initial $z(0) \in [-4.0, 4.0]$. (*K*) Maximum of middle line of ACC synaptic activation variable s from the total population during the duration T_s between the stimulus onset to withdrawal, for varying top-down expectation $z(0)$ under naive and chronic pain conditions. (*L*) Similar to panel *K*, except for two ACC subpopulations $E_{2\text{-}1}$ and $E_{2\text{-}2}$.



Supplementary Fig. 7: Comparison of average S1 synaptic activation at different periods (before vs. after onset) and PE values: PE= x (or $z = 0$) and PE= 0 (or $z = x$), with feedback from the ACC to S1. A total of 10 Monte Carlo trials were run with random stimulus input amplitude $x \in [1.8, 2.2]$. Mean and SEM were presented for each group. There was a significant difference in the average S1 synaptic activation variable between before and after the stimulus onset in both conditions. All p-values for pairs marked in the graph are less than 0.0001, expect for the $p = 0.0008$ between PE= x and PE= 0 after the onset (two pink bars). This indicates that the decrease in S1 firing intensity after the stimulus onset was slightly less significant with the presence of feedback. The pre-stimulus firing was averaged from the expectation z onset (from 0 if no expectation) to the stimulus x onset; the post-stimulus firing was averaged from the stimulus onset to withdrawal. Compared to Fig. 9*C*, the gap between before and after the stimulus onset was smaller here.