Supplementary Methods

Estimation of Synaptic Conductances

Our strategy to estimate conductances is based on solving the parallel conductance model equation \(^1\) and measuring the total membrane conductance \((g_{\text{total}})\) and the reversal potential \((V_{\text{rev}})\) during the synaptic response. The measurements of \(g_{\text{total}}\) and \(V_{\text{rev}}\) are based on the current clamp data obtained during recordings with QX-314, in which the synaptic responses are recorded at multiple \(V_m\) levels by coupling the whisker deflection with current injection.

To estimate \(g_{\text{total}}\) we start with the standard parallel conductance equation \(^1\):

\[
C_m \times \frac{dV_m}{dt} = -g_{\text{total}} \times (V_m - V_{\text{rev}}) + I_{\text{inj}}
\]

where \(C_m\) is the membrane capacitance of the cell, \(g_{\text{total}}\) is the total membrane conductance, \(V_{\text{rev}}\) is the reversal potential of the combined membrane conductances, and \(I_{\text{inj}}\) is the injected current through the recording micropipette. The value of \(C_m\) is calculated from the time constant of the membrane measured from hyperpolarizing pulses applied at rest.

We rewrite the membrane equation in order to express \(V_m\) as a linear function of the injected current corrected for the capacitive current:

\[
V_m = \frac{1}{g_{\text{total}}} \times (I_{\text{inj}} - C_m \times \frac{dV_m}{dt}) + V_{\text{rev}}
\]

From the current clamp values of \(V_m\) under different levels of current injection, we construct V-I plots (using the corrected I value) where the inverse slope of the best-fit line at each time point is \(g_{\text{total}}\).

Next, we express the synaptic conductance \((g_{\text{syn}})\) as:

\[
g_{\text{syn}} = g_{\text{total}} - g_{\text{rest}}
\]
where the resting input conductance, $g_{\text{rest}}$, was measured as the average $g_{\text{total}}$ for the 50 ms prior to whisker stimulation.

We assume that $g_{\text{syn}}$ is initially composed of primarily glutamatergic inputs and chloride-mediated GABAergic inputs\(^2,3\):

$$V_E = 0 \text{ mV}, \ V_I = -75 \text{ mV}$$

$$g_{\text{syn}} = g_E + g_I \quad (1)$$

Again, we solve the parallel conductance model expressed for $g_E$ and $g_I$:

$$C_m \cdot \frac{dV_m}{dt} = -g_E(V_m - V_E) - g_I(V_m - V_I)$$

In the state of equilibrium, i.e., when $V_m = V_{\text{rev}}$, total membrane current is zero and therefore capacitive current is zero, we can then rewrite the equation as a function of $V_{\text{rev}}$:

$$V_{\text{rev}} = \frac{(g_E \cdot V_E + g_I \cdot V_I)}{(g_E + g_I)} \quad (2)$$

We estimate $V_{\text{rev}}$ as the x-intercept of the best fit line of the $V_m$ plotted against the value of baseline $V_m$. The value of $V_m$ was also adjusted to account for capacitive current:

$$V_m = R_{\text{in}} \cdot C_m \cdot \frac{dV_m}{dt}$$

From equations (1) and (2) we can solve for $g_E$ and $g_I$:

$$g_I = \frac{(g_{\text{syn}} \cdot (V_E - V_{\text{rev}}))}{(V_E - V_I)}$$

$$g_E = \frac{(g_{\text{syn}} \cdot (V_{\text{rev}} - V_I))}{(V_E - V_I)}$$

To calculate the Rms error of the predictions the following formula was used:
Any estimate of $g_{\text{input}}$ from a current clamp recording may incur in errors due to the space clamp of the recording and non-linearities in the V-I relationship. It has previously been shown that conductance estimates obtained with current clamp recordings are very similar to the values obtained in voltage clamp recordings \( ^3 \). As with voltage clamp recordings, a poor space clamp would result in an underestimation of the conductance induced by an electrotonically distant synaptic input, assuming a somatic recording; however, space clamp errors should not affect the relative timing of the conductance measures as much as their amplitudes \( ^4 \).

**Supplementary References:**


