# Neuronal cell adhesion molecule L1 improves quality of chronic neural recording in mouse visual cortex

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**Statement of Purpose:**
The success of long-term functionality of implanted microelectrodes into the cortex for electrophysiological recording and stimulation depends on the stability of the interface between neural tissue and electrodes. One possible cause for electrode failure is inflammatory gliosis and neuronal loss in the surrounding microenvironment around the recording sites. L1, a neuronal specific cell adhesion molecule, has been shown to reduce the initial microglial attachment to the surface of neural implant when covalently bound [1]. Histological studies showed that L1 coating promote electrode-neuron integration and reduce gliosis at 1, 4 and 8 weeks [2]. We hypothesize that improved neural electrode-tissue integration will lead to high quality neural recording. In this study, the chronic recording performance of L1-coated neural electrode arrays was evaluated *in vivo* by implanting coated probes into V1m cortex of mice. The effect of L1 on brain tissue responses was evaluated with immunohistochemistry along with quantitative analysis.

**Methods:**
To test the L1 coating efficacy, linear, 16-channel silicon electrode arrays (NeuroNexus) were coated with L1 using silane chemistry and implanted into the visual cortex of C57BL/6 male mice. Neurophysiological recording (spontaneous and visually evoked) was performed weekly on anesthetized animals. Visual stimuli were presented to the contralateral eye of implantation through MATLAB-based Psychophysics toolbox. Spike sorting was done through a custom MATLAB script as previously published [3]. Electrode recording performance was determined by single-unit (SU) yield (% of channels measuring SU) and average signal-to-noise ratio (SNR). At the end time point (16W), animals were scarified for immunohistological studies.

**Results:**
Both groups had almost the same SU yield 6 hours to 1 week post implant (week 0 and 1 on the x-axis, $p>0.05$), but after week one, the SU yield of the L1 group was gradually increasing, while that of the control group decreased (Figure 1A). From week 2 through the end time point of study, electrophysiological recording from the L1 group presented significant improved single-unit yield compared to the control group. In addition, average SNR of single units (SUs) and signal amplitude also showed significant increases in the L1-coated group than those of the control animals on all time points after week 2 and week 1 respectively ($p<0.05$). The 1 kHz impedance for the L1 coated group was lower at the day of surgery and week one post implant suggesting that the L1 coating has decreased inflammatory cell infiltration and tissue swelling acutely. From week 3 until the end, 1 kHz impedance followed a similar profile for both groups suggesting the electrode was mechanically and electrochemically stable (Figure 1B). Additionally, by aligning the implant depth across animals between 2-16 weeks to layer IV depth, determined from current source density following the visual stimulus, electrode performance was further analyzed as a function of depth (Figure 1 C and D). From week 0 to week 2, in control group, electrodes at the depth of 300, 500, 600, and 1100 µm had high yield (above 80%), but from week 2, only electrodes at the depth of 200-900 µm had moderate recording yield (above 50%) (Figure 1C). However, the L1-coated group maintained high SU yield across multiple depth throughout the 16 weeks including the deeper regions (CA1) (Figure 1D).

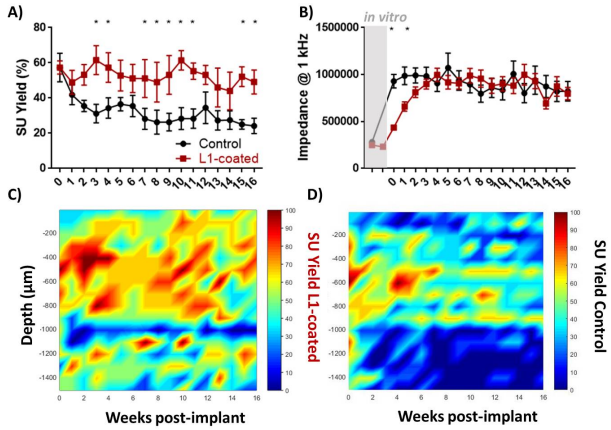


**Figure 1. Chronic neural electrode performance**

Finally, immunohistochemical staining and our quantitative image analysis demonstrated significantly reduced expression of microglia and astrocytes within 50 µm and 110 µm zones of around the L1 probes compared to the control at 16 weeks.

**Conclusions:**
This study demonstrated the potent effect of L1 coating in maintaining high quality single unit recording over long term implantation. The improvement in chronic recording performance may be a result of decreased inflammatory gliosis by the L1 protein. More comprehensive immunohistochemical and molecular analysis are necessary to further understand L1 coating's exact mechanism of action.

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**References:**
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