Supporting Information

Subcellular Neural Probes from Single Crystal Gold Nanowires

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Experimental

Fabrication of Au NW Electrodes. Vertically grown single-crystalline gold (Au) nanowires (NWs) were synthesized on a *c*-cut sapphire substrate in a horizontal quartz tube furnace system by using previously described vapor transport method.[1] Briefly, the sapphire substrate was placed a few centimeters downstream from an alumina boat filled with pure Au slug. Argon gas flowed at a rate of 100 standard cubic centimeter per minute, maintaining the chamber pressure at 5 ~ 15 Torr. The high temperature zone of furnace was heated to 1100 °C. Au NWs were grown on the substrate for ~ 30 min of reaction time. They are well-faceted by single-crystalline Au (111) surfaces with no twins or defects as shown in transmission electron microscope (TEM) and high-resolution TEM (HRTEM) images and selected area electron diffraction (SAED) patterns were taken on a JEOL JEM-2100F TEM operated at 200 kV (Figure S1). To fabricate a Au NW electrode, a conducting adhesive-coated tungsten (W) tip mounted on a nanomanipulator was approached to a single Au NW on a sapphire substrate (Figure S2a) and picked it up by softly touching (Figure S2b). The Au NW-attached W tip was then insulated with nail varnish (Figure S2c). For the complete insulation, a middle area of W tip was immersed in nail varnish solution, moved back and forth several times, and dried in ambient environment. Scanning electron microscope (SEM) images of vertically grown Au NWs on a sapphire substrate and a fabricated Au NW electrode as shown in Figure 1 were taken on a Phillips XL30S operated at 10 kV.

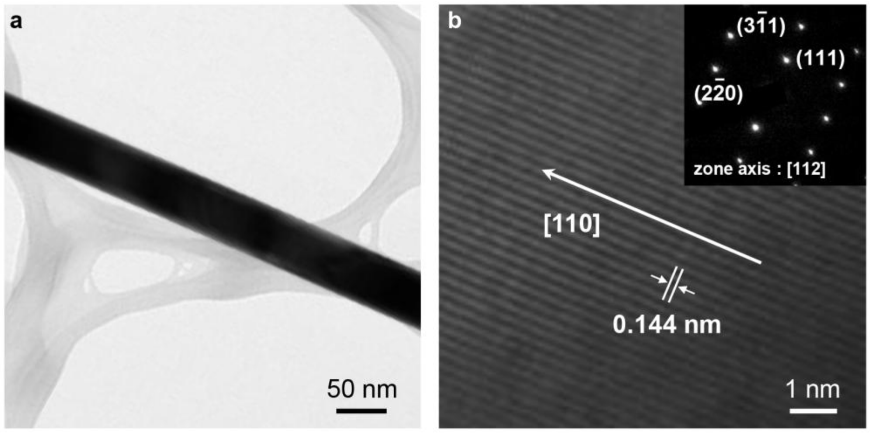

Figure S1. (a) TEM image, (b) HRTEM image and SAED pattern (inset) of a Au NW. The Au NW is single-crystalline without twins or defects.

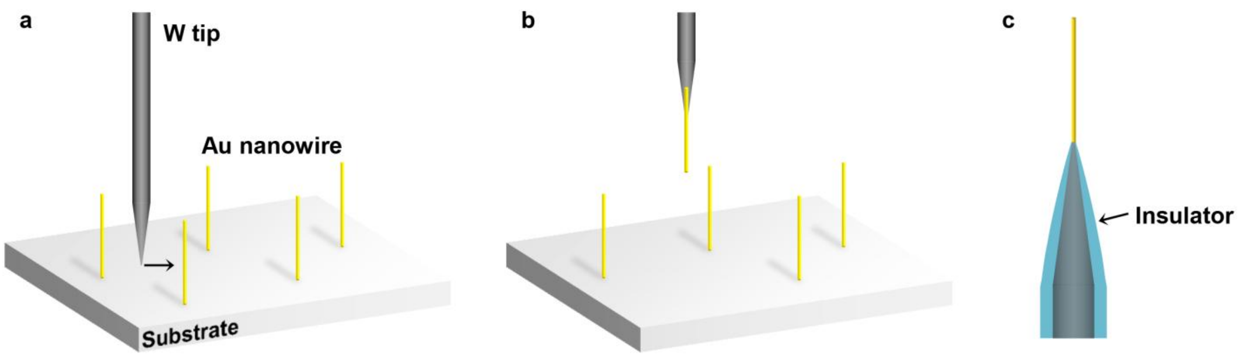

Figure S2. Schematic illustration of the fabrication process of a Au NW electrode. W tip was manipulated to approach to a single Au NW on a sapphire substrate (a) and pick it up by softly touching (b). The W part was insulated with nail varnish (c).

Electrochemical Measurements. All electrochemical measurements were performed by using a potentiostat (CHI 660D, CH Instruments) with a homebuilt three-electrode cell under optical microscope monitoring (Figure S3). To control a Au NW electrode precisely, we mounted a Au NW electrode on a three-dimensional piezoelectric stage (Sigma-Koki). Platinum wire and mercury/mercurous sulfate electrode (MSE, Hg/Hg_2SO_4) were used as counter and reference electrodes, respectively. H_2SO_4, $CuSO_4/H_2SO_4$, and $K_3Fe(CN)_6$ solutions were prepared with distilled water. All chemicals were purchased from Sigma-Aldrich and used as received.

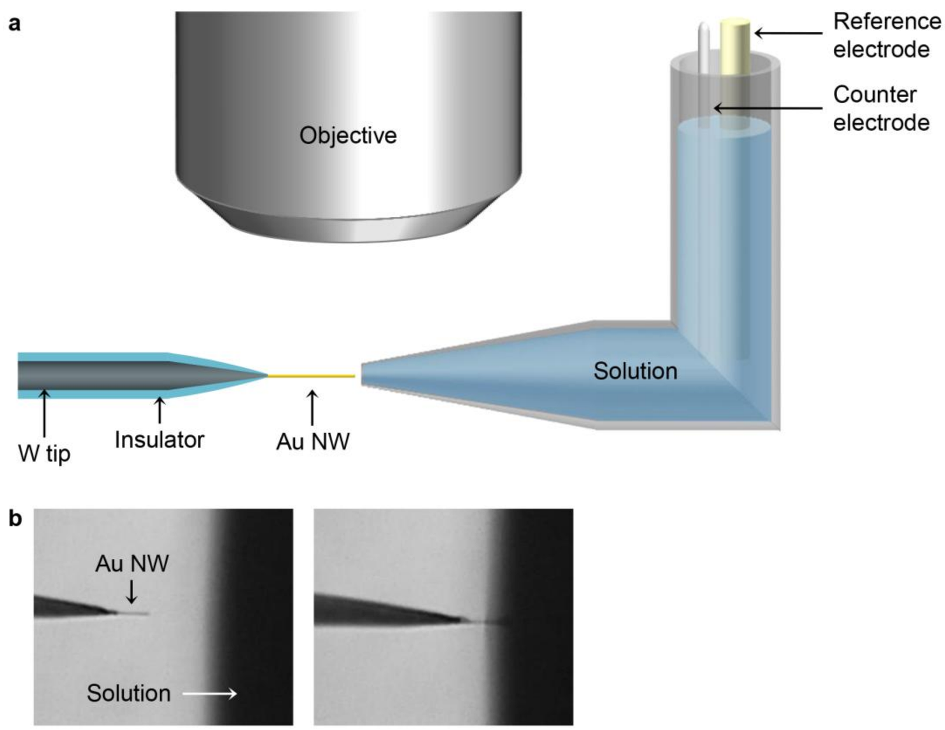

Figure S3. (a) Schematic illustration of a homebuilt three-electrode cell. (b) Optical microscope images of a cell before (left) and after (right) immersion of a Au NW electrode into a solution.

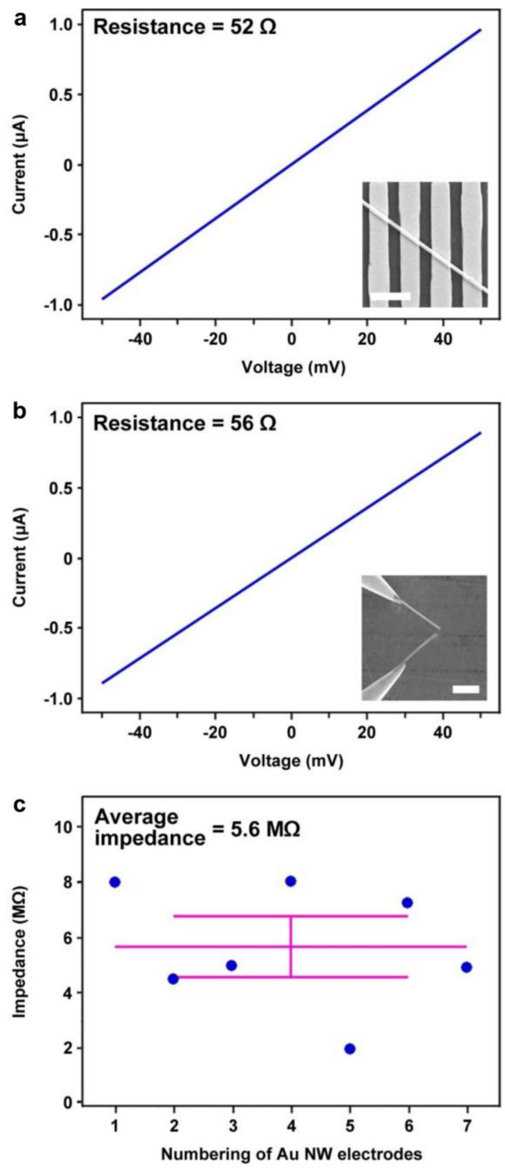

Figure S4. (a) *I*-*V* curve recorded on a single Au NW device, exhibiting Ohmic behavior and low resistance of 52 Ω. Inset shows the SEM image of four-probe Au NW device from which we obtained the data. The scale bar denotes 2 μm. (b) *I*-*V* curve recorded on a Au foil by using two Au NW electrodes, exhibiting Ohmic behavior and low resistance of 56 Ω. Inset shows the SEM image of two Au NW electrodes contacted to a Au foil. The scale bar denotes 5 μm. (c) The impedances of seven Au NW electrodes measured at 1 kHz. The averaged impedance is 5.6 MΩ and the error bar (lines in a magenta color) represents standard deviation.

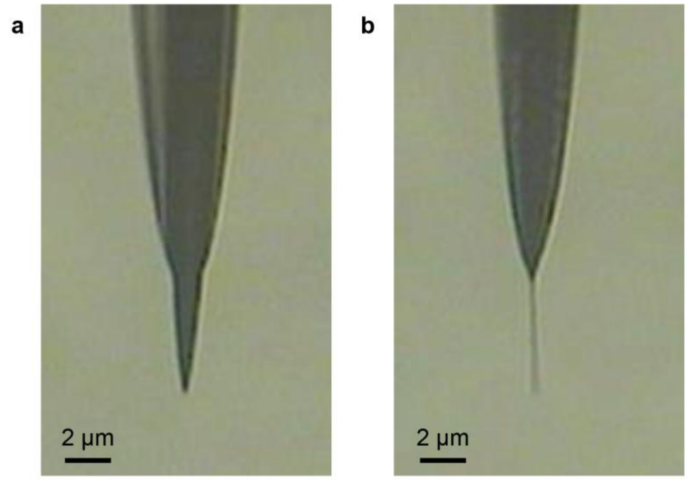

Figure S5. Optical images of typical W (a) and Au NW (b) electrodes for recording neural signals.

Investigation on the Status of Au NW Electrode in a Brain-Like Material and a Brain Slice. Since it is difficult to observe the shape of a single Au NW as it penetrates into an intact brain which is not transparent, we first examined the mechanical properties of a Au NW electrode using 0.4% agarose gel which is transparent and reportedly shows dynamic mechanical behavior similar to a neural tissue.[2] We inserted a Au NW electrode in transparent 0.4 ~ 0.6% agarose gel and observed the structure of the NW using an optical microscope (Figure S6a). Although we used the Au NW electrodes as long as ~5 μm for recording neural signals (Figure S5), to clearly observe the status of a NW we inserted a long Au NW electrode (~ 20 μm) into the gel by 45° to the gel surface and observed the whole process above the gel. As the Au NW touched gel, it immediately bent and then recovered to its straight form during further insertion into the gel (Movie S1) and after it was withdrawn from the gel (Movie S2). From this observation, it is expected that a Au NW electrode is not broken during the insertion into brain and keep its straight structure (as shown in a blue circle in middle of Figure S6b). Furthermore, we performed the above experiment using mouse brain slice which was 350 ~ 400 μm thick instead of agarose gel. We could not examine the structural status of a Au NW electrode when it was inside the nontransparent brain slice, but observed its straight form after we withdrew it from the brain slice (Figure S6c,d). Circular feature pierced by a Au NW electrode is a single neuron. The reason that a ~ 100 nm thin Au NW was able to maintain its straightness when implanted into a brain-like material and a brain slice was its special mechanical property, namely superb flexibility and strength, originating from the perfect crystallinity of Au NWs.[3]

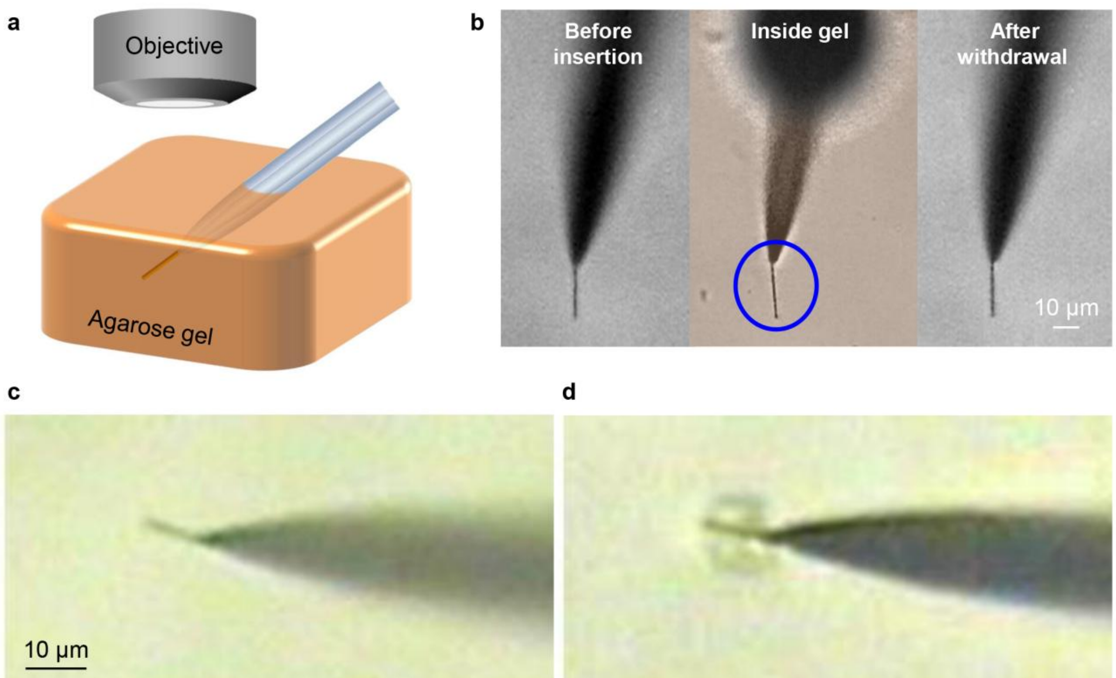

Figure S6. (a) Experimental setup for the insertion of a Au NW into a agarose gel (or brain slice). (b) Structure of a Au NW electrode inserted in a transparent 0.4% agarose gel. Photographs of a Au NW electrode were taken before it was inserted into a gel (left), while it was inside a gel (middle), and after it was taken out from the gel (right). A Au NW electrode kept its straight structure inside the gel (as shown in a blue circle). Optical images of a Au NW before insertion into (c) and after withdrawn from (d) a brain slice. Straight structure of a Au NW electrode was maintained after withdrawal from the brain slice. Circular feature is a single neuron pierced by a Au NW electrode.

Statistical Analysis of Neural Signals during Behavioral Experiments.

To compare the neural signals from the Au NW and tungsten electrodes during the experiment of social interaction, power intensities of the neural signals were analyzed. In the experiment of pilocarpine-induced seizure, averaged first-peak values of cross-correlation among the neural signals were used for the statistical analysis. Student's *t*-test was used, and all data obtained from behavioral experiments are presented as means ± standard error of mean (SEM). A P-value < 0.05 was considered to indicate statistical significance.

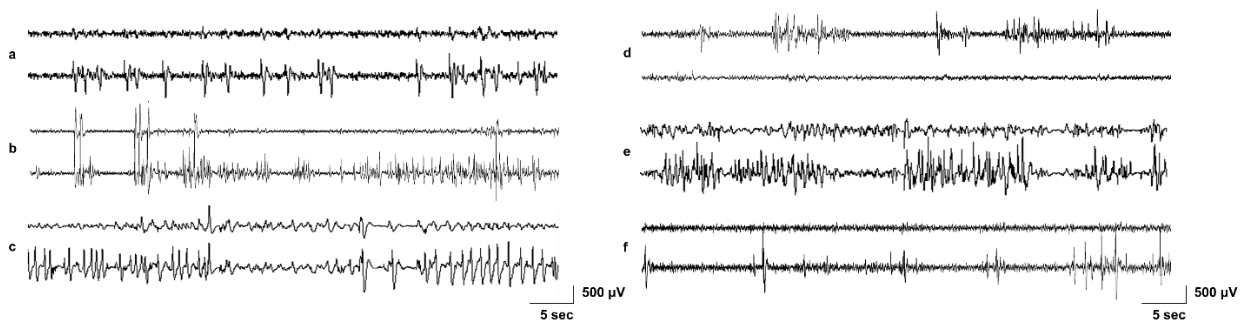

Figure S7. (a-f) The traces of each measurement from two Au NW electrodes located 1 mm apart from each other in the hippocampal CA1 region of a living mouse brain.

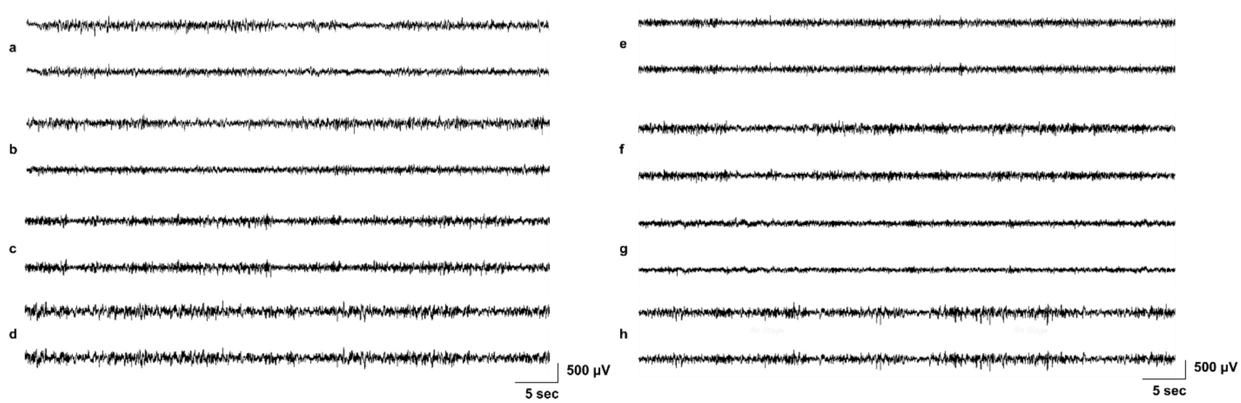

Figure S8. (a-h) The traces of each measurement from two tungsten electrodes located 1 mm apart from each other in the hippocampal CA1 region of a living mouse brain.

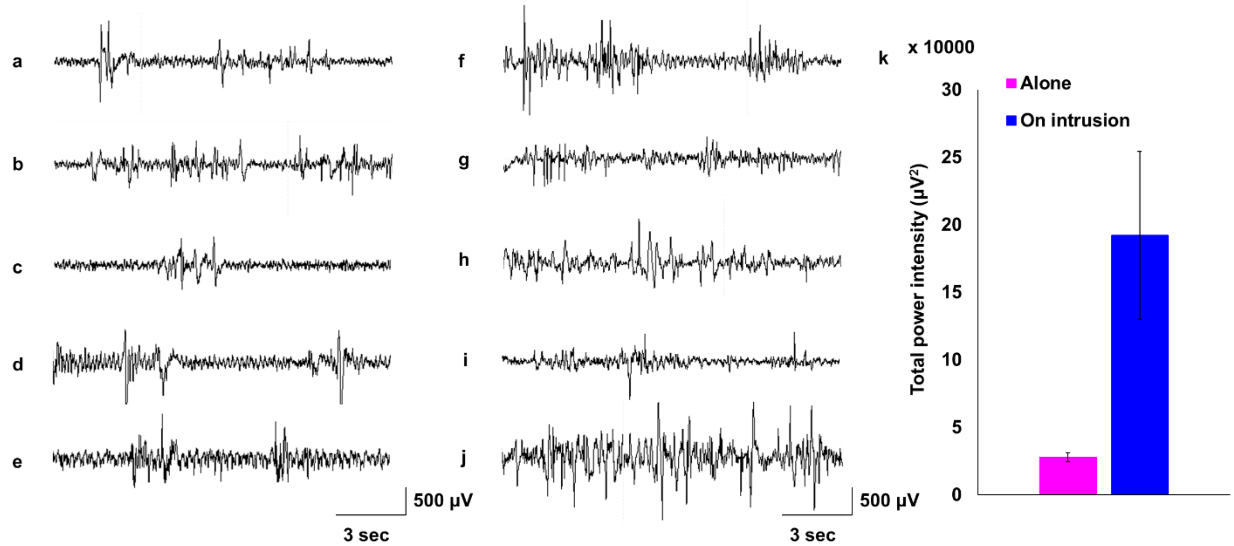

Figure S9. The traces from Au NW electrodes (n = 5) (a-e) before and (f-j) after interaction with an intruder mouse. (k) Total power intensity of neural signals was significantly increased after the social interaction ($p < 0.05$, Student's t-test).

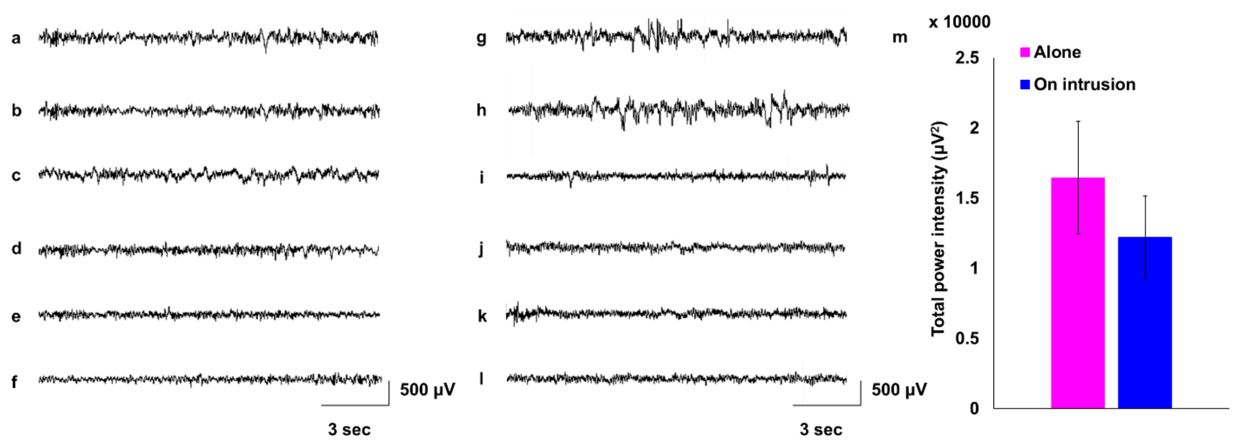

Figure S10. The traces from tungsten electrodes (n = 6) (a-f) before and (g-l) after interaction with an intruder mouse. (m) There was no significant difference in the total power intensity between before and after social interaction ($p = 0.4139$, Student's t-test).

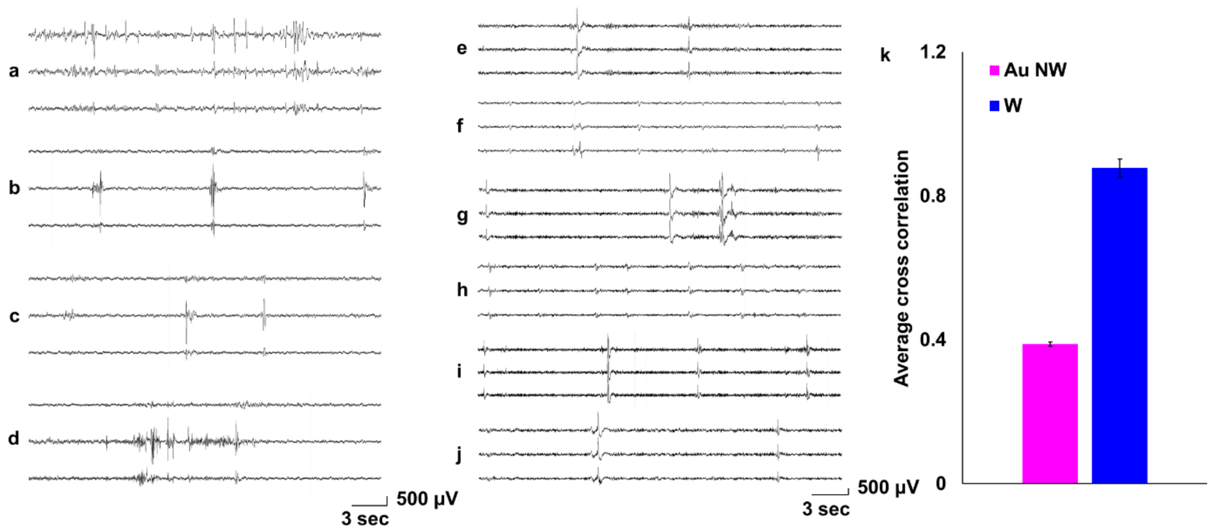

Figure S11. The traces from tungsten (n = 6) and Au NW (n = 4) electrodes after pilocarpine injection. (a-d) Neural signals from the three Au NW electrodes are distinguishable. However, (e-j) neural signals from three tungsten electrodes are all similar. (k) Cross-correlation analysis revealed that neural signals from Au NW electrodes displayed reduced correlation value (0.38) compared with the tungsten electrodes (0.87), indicating higher spatial resolution of Au NW electrodes. ($p < 0.01$, Student's *t*-test).

References

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2. Pervin, F. Dynamic Compressive Response of Soft Biological Tissues. PhD thesis, Purdue University (2010).

3. Seo, J. H.; Yoo, Y.; Park, N. Y.; Yoon, S. W.; Lee, H.; Han, S.; Lee, S. W.; Seong, T. Y.; Lee, S. C.; Lee, K. B.; *et al*. Superplastic Deformation of Defect-Free Au Nanowires *via* Coherent Twin Propagation. *Nano Lett.* **11**, 3499–3502 (2011).