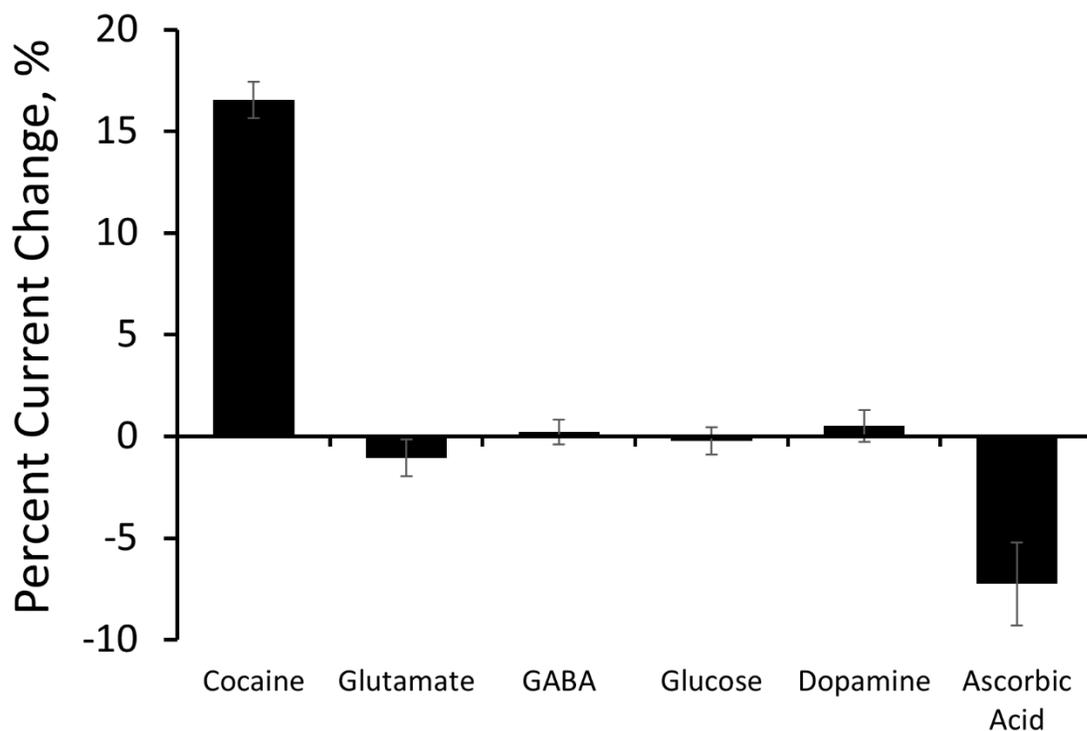
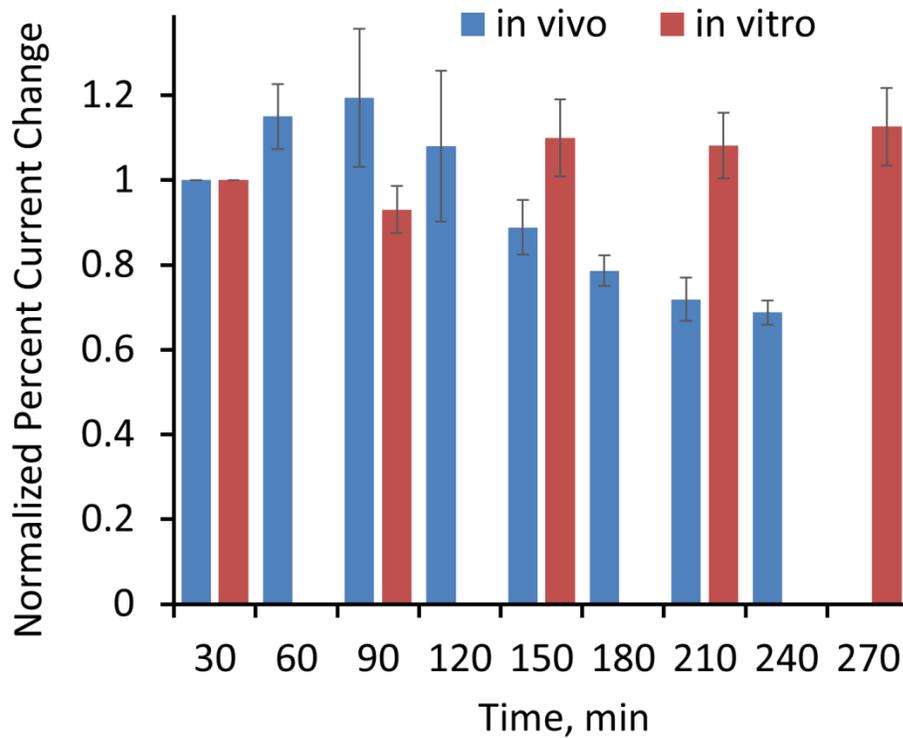


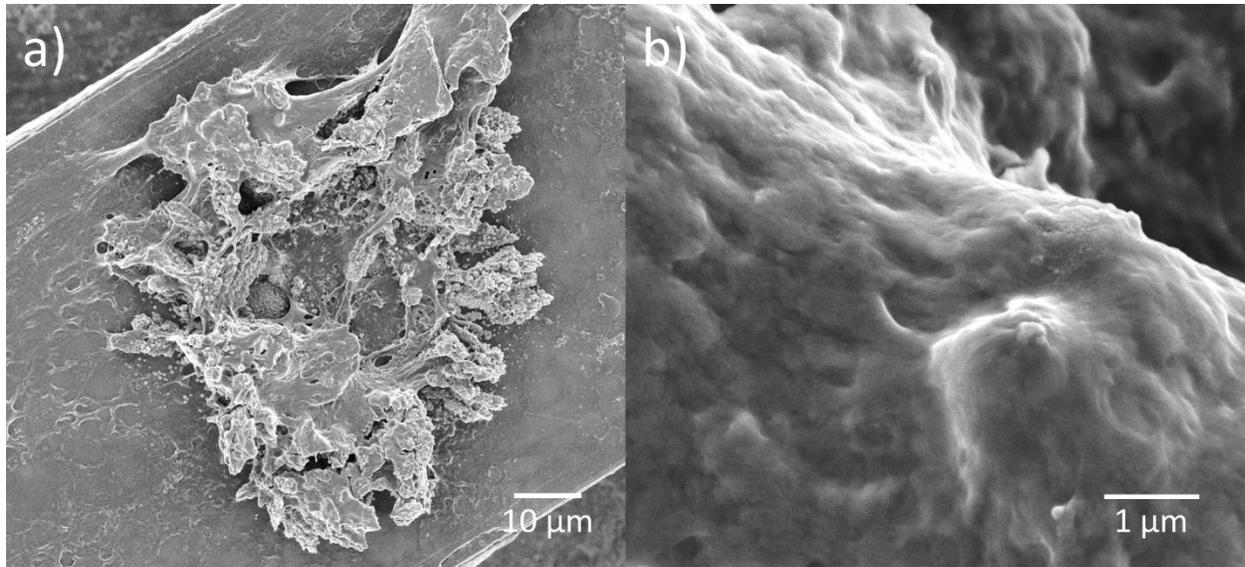
Supplementary Information



Supplementary Figure 1. Cocaine sensor selectivity. The aptamer-based cocaine sensor is selective for cocaine over five common neurochemicals in aCSF. All species were tested as individual 100 μ M solutions. Cocaine induced a 16.5 ± 1.9 % increase in percent current change, GABA, glucose and dopamine did not induce any average percent current change from baseline and glutamate and ascorbic acid resulted in -1.0 ± 0.9 % and -7.3 ± 2.0 decreases in percent current change respectively. The negative signals resulting from glutamate and ascorbic acid are likely due to decreases in solution pH. Both negative detection events were accompanied by notable right-shifts in methylene blue peak potential (indicative of an acidic shift).



Supplementary Figure 2. Cocaine sensor stability *in vivo* and *in vitro*. The average (\pm SEM, $n=2$) normalized percent current change resulting from *in vivo* direct local cocaine infusion (blue, data also presented in Figure 5b) significantly decreases upon the 6th cocaine infusion replicate (180 min, one way ANOVA, $F(7,15) = 7.214$, $p < 0.01$, Bonferroni post hoc comparison, $p < 0.05$ compared to infusion 1). The average (\pm SEM, $n=3$) normalized percent current change resulting from the repeated detection of a 1 mM cocaine solution in PBS (red) does not significantly change over 270 minutes using identical SWV data collection conditions used for *in vivo* testing (one way ANOVA, $p > 0.05$). At 210 minutes, the normalized percent current change due to *in vitro* cocaine detection is significantly higher than the normalized percent current change due to *in vivo* cocaine detection (one way ANOVA, $F(1,4)=12.28$, $p < 0.05$).



Supplementary Figure 3. Additional SEM images of an electrode site post explant. Representative scanning electron microscopy images of the aptamer functionalized electrode following *in vivo* explantation. The images show substantial biological tissue encapsulation (a and b). The lower magnification image (a) clearly shows intact dendritic gold structures following probe explantation.