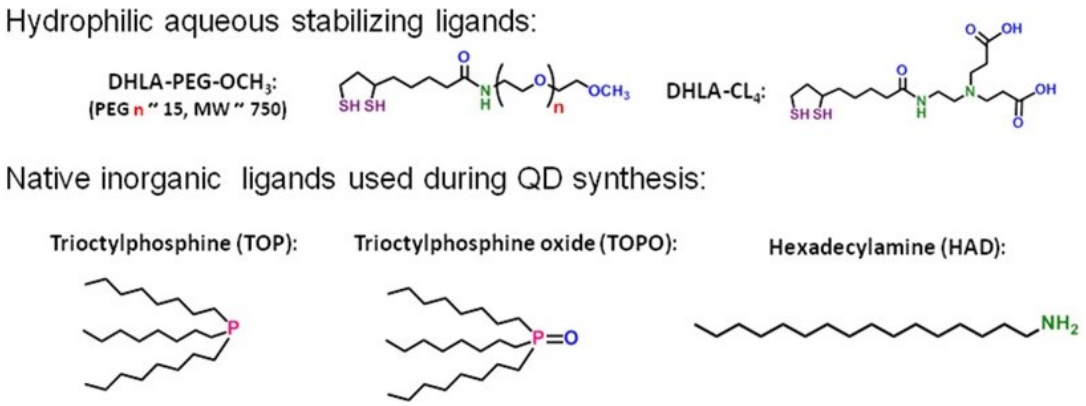
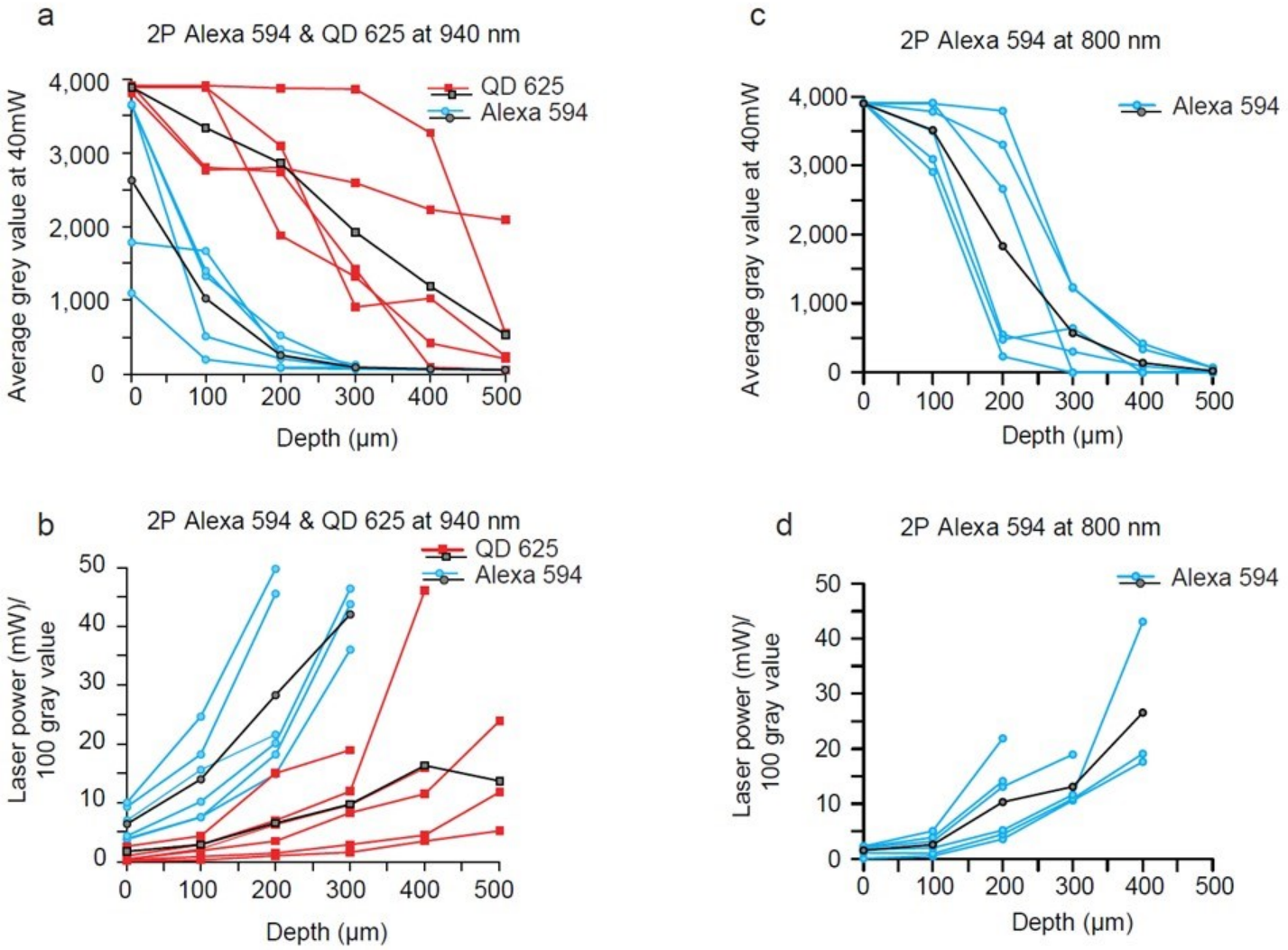


Supplementary Figure 1

Chemical structures of the ligands.

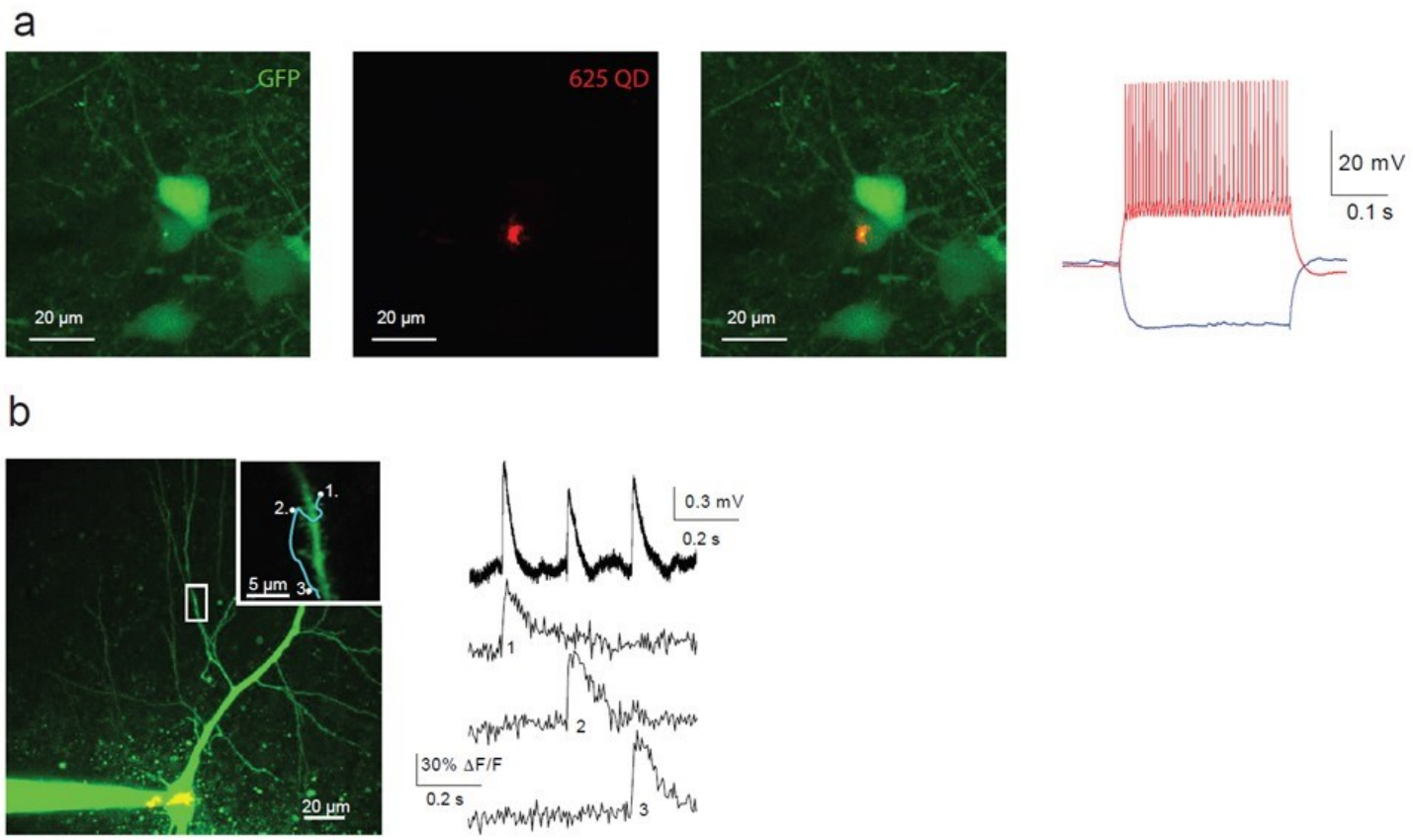
Chemical structures of the methoxy-terminated and PEG-appended dihydrolipoic acid (DHLA-PEG-OCH_3) and zwitterionic-compact ligand (DHLA-CL_4) ligands used to make the QDs hydrophilic and biocompatible. Structures are also shown for the hydrophilic-native inorganic ligands used during QD synthesis. These include trioctylphosphine (TOP), trioctylphosphine oxide (TOPO), and hexadecylamine (HDA).



Supplementary Figure 2

QD and Alexa 594 visibility *in vivo* under different laser power.

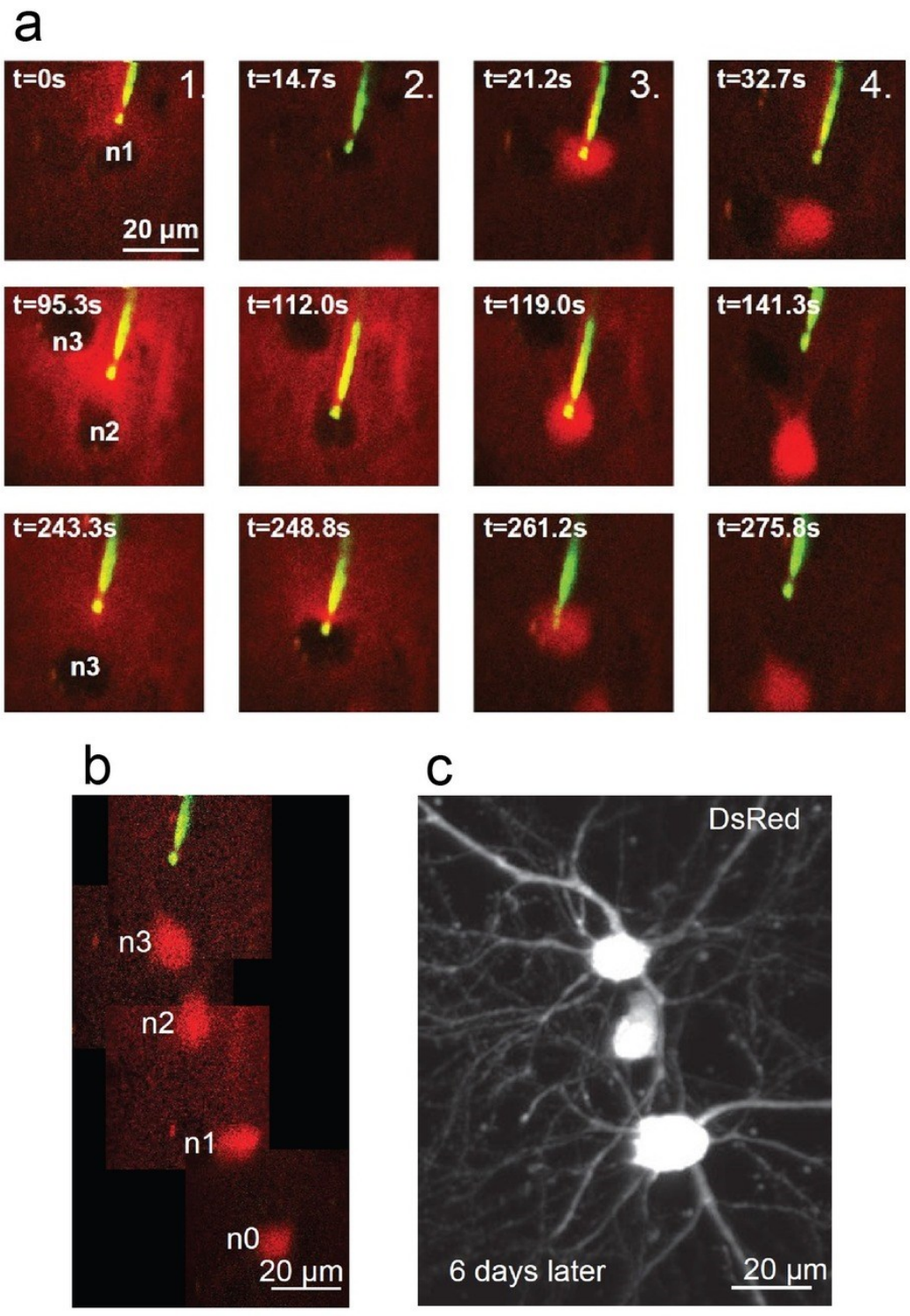
(a) Average gray value (10 frames) for Alexa Fluor 594 filled and 625 QD-coated pipettes across different depths at a fixed laser power of 40 mW. Rank Sum test $P < 0.01$.(b) Laser power required to obtain an average gray value of 100, corresponding to a visibly discernible fluorescence value. Blue circles: Alexa Fluor 594 filled pipettes, n = 6; red filled squares: 625 QD-coated pipettes, n = 6. Black lines correspond to respective averages. Alexa Fluor 594 filled pipette imaged at different depths (D) within in vivo brain of anaesthetized mice at the indicated laser power (LP). Rank Sum test $P < 0.05$. (c) Average gray value (10 frames) of Alexa Fluor 594 filled pipettes across different depths at a fixed laser power of 40 mW imaged at 800 nm. (d) Laser power required to obtain an average gray value of 100, corresponding to a visibly discernible fluorescence value



Supplementary Figure 3

Patching GFP labeled parvalbumin-positive interneurons and

(a) Red 625 QD-coated pipette with only the tip labeled as used for patching a GFP-PV positive interneuron from a PV/GFP BAC mouse. Representative of 11 cells in 6 animals. Panels from left: z-stack 2P images obtained in the green channel, red channel, and merged; voltage responses to positive and negative current injections (200 pA) in the cells shown on the left. (b) Z-stack 2P image of a rat hippocampal CA1 pyramidal neuron loaded with 100 μM OGB-1 (green) through 625 QD-coated patch pipette in an acute slice. Inset shows 3 spines selected for 2P glutamate uncaging, along with the imaging line. Right, top: individual glutamate induced excitatory postsynaptic potentials (gluEPSPs) evoked at the indicated spines. Right, bottom: corresponding Ca2+ signals in the individual spines. Similar Ca2+ responses were evoked in 9 out of 11 spines in 3 dendrites from 2 neurons in one animal.



Supplementary Figure 4

(**a**) Repeated steps of *in vivo* single cell electroporation of fluorescent gene vector with QD coated pipette, demonstrated on L2/3 cortical neurons at ~300 µm depth. 1. Approaching the cell. 2. Seal formation on cell membrane. 3. Filling the cell. 4. Withdrawing pipette after successful electroporation. (**b**) Montage of electroporated cells. (**c**) Z-stack image of cells n1-3 six days later (75% success rate).