equations. Our predictions are in line with existing measurements in a range of model systems including the squid giant axon and the garfish olfactory nerve. We expect our model to serve as a framework for understanding the physical origins and possible functional roles of these AWs in neurobiology. See arXiv:1407.7600 for details.

1037-Plat
Robust Optical Stimulation of Neuronal Activity using Functionalized Gold Nanoparticles
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It was recently shown that infrared light pulses can directly stimulate neuronal action potentials by quickly heating the cell membrane and inducing capacitive currents (Shapiro, et al., Nat Commun, 2012). While useful, this technique works by heating the entire aqueous environment around a cell, rendering it nonspecific and incapable of stimulating specific populations of cells. Furthermore, since water absorbs infrared, the light source must be near the target. Here, we sought to stimulate neurons with visible light, using the ability of 20 nm spherical gold nanoparticles (AuNPs) to absorb light and convert it into heat. By applying the AuNPs to painted lipid bilayers, we first confirmed that, upon 532 nm pulse stimulation, the membrane capacitance increases following the rate of temperature increase. The resulting currents are well-behaved, being linear with respect to both laser power and membrane potential. We next applied AuNPs to cultured dorsal root ganglion (DRG) neurons and demonstrated action potential initiation with 532 nm pulses of ≤1 ms. Finally, we obtained a dramatic improvement of this technique by functionalizing AuNPs with high-avidity ligands for DRG neuron membrane proteins. Non-functionalized AuNPs are cleared away from DRG neurons within seconds of starting a perfusion wash, causing the cells to lose optical excitability. However, AuNPs functionalized with Ts1 neurotoxin, or with anti-TRPV1 or anti-P2X3 antibodies, showed substantial resistance to washout; DRG neurons labeled with these functionalized particles remained light-sensitive after more than 20 minutes of perfusion washing. Furthermore, these particles required a lower concentration and less laser power to confer optical excitability. By appropriate selection of AuNP-conjugated ligand, this technique may enable improved cell-type specificity of neuronal photostimulation, such as ganglion cells in diseased retina where photoreceptors are non-functional. Support: R21-EY023430 and The Beckman Initiative for Macular Research.

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Ligand Fingerprinting in the Membrane Dynamics of Single TrkA and P75NTR Neurotrophin Receptors
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We have sought to investigate the responses of Nerve Growth Factor (NGF) receptors TrkA and P75NTR at the plasma membrane of living neuronal cells by single-molecule imaging and tracking. To this purpose we exploit the acyl carrier peptide and some of its shortened versions (A1 and S6 tags, labeled selectively by two different PPTases) to tag human p75NTR and TrkA. These tags were covalently conjugated to the biotin- or fluorophore-substituted arm of a coenzyme A (CoA) substrate.

This approach allows: (i) a precise control of stoichiometry and site of receptor conjugation; (ii) versatility of the tags used; (iii) studying two interacting molecules with orthogonal fluorolabels, at the single-molecule or single-interaction-complex level. This experimental toolbox is completed by fast microscopy (e.g. TIRF microscopy with a fast EM-CCD), and by a semi-automatic algorithm for the analysis of the trajectories. This novel algorithm separates self-similar from multimodal trajectories, divides the last ones in sub-trajectories, and calculates the combined distributions of parameters measuring the diffusivity, the localization or driftiness degree, and/or the number of molecules in tracked spots. We shall present results on the early response of TrkA upon binding different binding-irrelevant ligands (including NGF and proNGF); without ligands, TrkA is presently used as fast-diffusing monomers; ligand binding results in an increasing number of dimers and oligomers, which are typically slower and/or more confined. Each ligand promotes distinct trajectory patterns at the cell membrane, because of different receptor-binding affinities, intracellular effectors recruited and formation of signalling/recycling endosome precursors. We believe that this imaging toolbox and our results pave the way to the quantitative description of the kinetics, dynamics and stoichiometry of any binary or