Title: Gold-core nanoparticles for non-invasive tracking of neuroreceptor distributions

Author list: Elleard Heffern[1], Jason Fuller[2], and Russell W. Hanson[3,*]

[1]Department of Genetics, Harvard Medical School, Boston, MA, 02115, USA
[2]Ginkgo BioWorks, 27 Drydock Avenue Floor 8, Boston, MA, 02210, USA
[3]Children's Hospital Informatics Program at the Harvard–Massachusetts Institute of Technology Division of Health Sciences and Technology, Harvard Medical School, Boston, MA, 02115, USA

* E-mail: Russell.Hanson@childrens.harvard.edu

300-word Summary:

Development of technologies to image neuronal cell surfaces can provide much insight into neuronal function in vivo. To this end we have developed a novel method based on gold nanoparticle aptamer sensors that can be injected directly into tissue, imaged in chemically induced phases in tissue, and retrieved after phase cycling to garner path information recorded in exchange events.

Nanoparticles have been specifically designed with several components. To mediate phase initiation, aptaswitches conceal i) the barcoded sequences designed for inter-particle exchange, ii) higher-affinity sensor sites for barcode retrieval, and iii) the mating sequences designed for subsequent receptor binding. Upon exposure to a phase-specific reagent, these aptaswitches are dissociated to reveal all three sequence sets simultaneously. Each prior phase's receptor-mating sequence attaches to the nanoparticle via the concealing aptaswitch for the next phase's barcode retrieval site, so phase initiation frees particles from prior bound receptors, in addition to exposing barcode exchange and receptor binding sites (see Figure 1, Individual nanoparticle schematic).

During a given phase, exchange events proceed until nanoparticles reach and bind to their next receptor targets – high receptor binding affinity contributes to preventing particle aggregation. Oligocap sequences are added to the environment in order to re-conceal unused sites. Prior to next-phase initiation, brief tissue imaging using PET provides overall receptor binding event distribution.

Following cycling through all phases, particles are retrieved from tissue. DNA strands are cleaved from the nanoparticles using an enzyme. Sequencing the cleaved DNA strands identifies which particles exchanged barcodes to which other particles and between which receptor binding events. Using this information the network of events can be reconstructed on the computer using swarm computing techniques. The reconstructed information includes spatiotemporal particle-particle exchange events and nanoparticle receptor binding events.

Additional Detail:

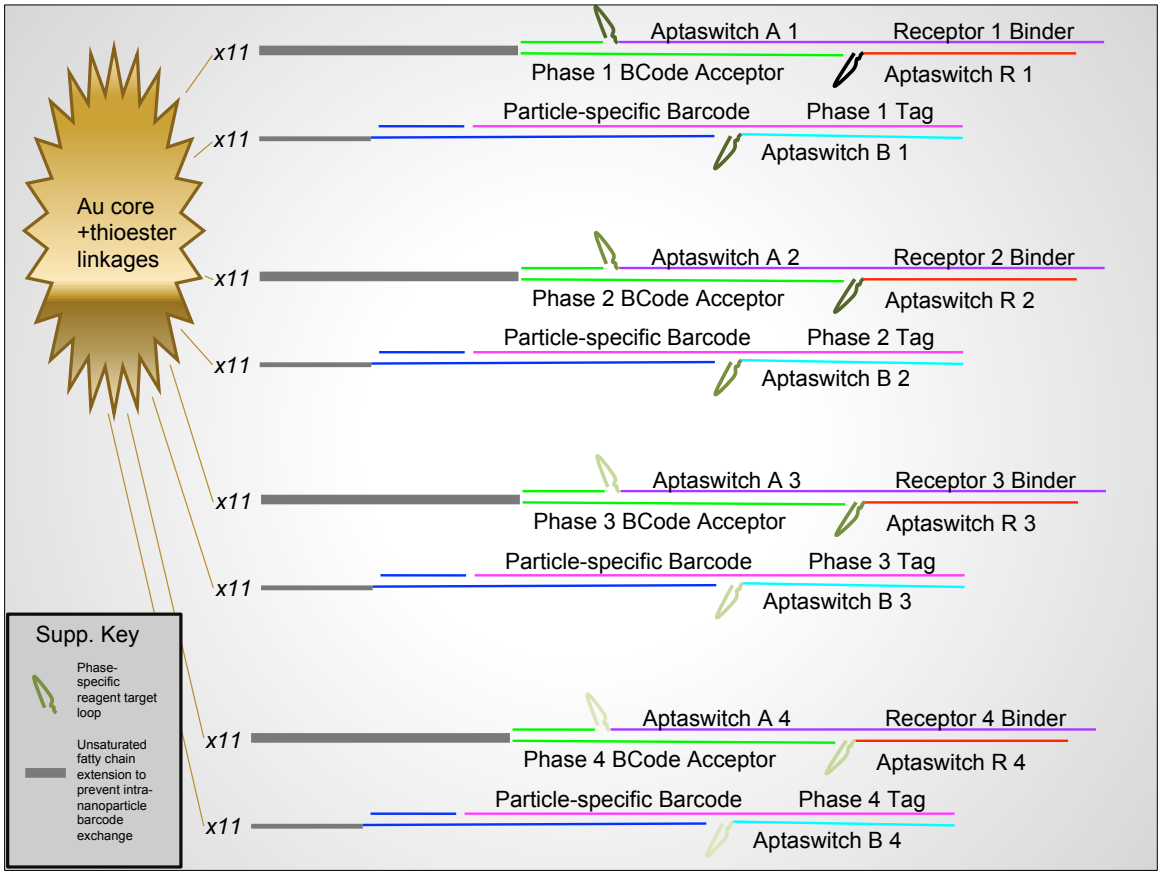

Figure 1. Individual nanoparticle schematic.

This work "Gold-core nanoparticles for non-invasive tracking of neuroreceptor distributions" extends ideas and techniques developed in the paper below of Liu et al. (2006) and provides much needed applications and technology for neurological sensing and imaging. The citation is provided as a background reference to supplement the abstract.

Liu, J. W. & Lu, Y. Fast colorimetric sensing of adenosine and cocaine based on a general sensor design involving aptamers and nanoparticles. *Angewandte Chemie-International Edition* **45**, doi:10.1002/anie.200502589 (2006).