

# Biofunctionalisation of core shell colloidal quantum dots for the tracking of synaptic receptors

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Functional bioconjugated colloidal quantum dots (cQDs) have already been used to track single molecules like synaptic receptors[1]. There are two main steps to transform the synthesized hydrophobic cQDs into ready-to-use biomolecule trackers, which are (1) the ligand exchange or encapsulation leading to an hydrophilic cQD and (2) the subsequent conjugation with a protein which specifically recognises the target molecule.

It is possible to buy commercial hydrophilic cQDs coupled with binding proteins like antibodies. However, their main drawback is the large size of the polymer capsule making the cQD soluble in water, which can become problematic for some applications. For example, in the tracking of synaptic receptors, the size of the synaptic cliff (distance between presynaptic and postsynaptic neurons) is thought to be between 30 to 40 nm and penetration of cQD-labeled receptors could be impeded if they are too large.

An alternative approach to give cQDs an affinity with water without dramatically increasing their size is to proceed to a ligand exchange using dihydrolipoic acid (DHLA) as the new ligand. This technique has successfully been applied in the past and is well described in the literature[2]. One must be aware that the new ligand is likely to deteriorate the photoluminescence (PL) properties of cQDs, such as quantum efficiency and photostability[3].

Here we perform a ligand exchange using DHLA on well-passivated low-strain CdSe/CdS/Cd<sub>0.5</sub>ZnS<sub>0.5</sub>/ZnS cQDs and demonstrate that this manipulation does not modify dramatically the photoluminescence properties of new hydrophilic cQDs. Shown on figure 1, PL of cQDs after photoactivation is almost constant during more than 4 hours of 488nm wavelength laser

excitation for both the hydrophobic and the DHLA capped cQDs.

We then conjugated these DHLA capped cQDs to streptavidin through the formation of an amide bond between the carboxylate (COO<sup>-</sup>) end of DHLA and free NH<sub>2</sub> amines of streptavidin. Since streptavidin is a protein known to have a high specific binding affinity with biotin, we used a technique previously reported [4] to express biotinylated calcium dependent receptors at cell surfaces in cultures of neurons. Finally, we exposed the cell culture to the appropriate concentration of biofunctionalised cQDs. This lead to a specific binding between biotin and streptavidin that allows the tracking of biotinylated receptors through cQDs PL.

The same cQD PL could also give more information than the position of a biological target. One application of interest is to use cQDs as voltage sensors. Designing cQDs with properties significantly dependent on the local electric field would give a powerful tool to follow ionic currents in a cell membrane vicinity where changes in ion distributions have a strong impact.

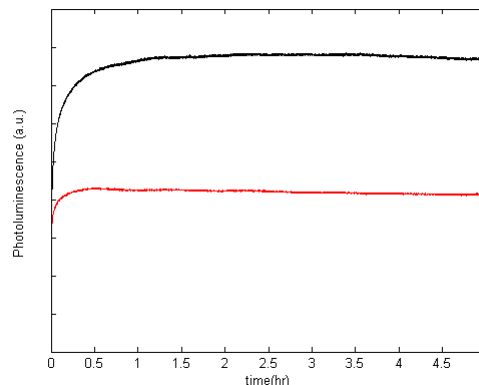


Figure 1: Weak photobleaching of cQDs (black for hydrophobic cQDs and red for DHLA capped cQDs)

## References

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- [2] H. Mattoussi et al., Nature Protocols **1**, p. 1258, 2006
- [3] S. Weiss et al., Proc. of SPIE **5704**, p. 57, 2005
- [4] A. Y Ting et al., Nature Protocols **3**, p. 534, 2008

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