*Poster*

# OPTICAL AND BIOLOGICAL CHARACTERIZATION OF SURFACE MODIFIED QUANTUM DOTS

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Quantum dots (QDs) are gaining in popularity as fluorescent probes in the life sciences. Their popularity can be attributed to the unique optical properties of these colloidal nanoparticles (NPs). In most biological applications, the surface of QDs are modified with a small molecule, protein or antibody in order to lend specificity towards a biological target. The chemical, optical and biological properties of QDs can be drastically influenced by modification of their surface properties. In fact, this apparent drawback has been recently exploited for use in a broad range of sensing applications [1]. In our own work, we have shown that modification to the QDs with the small molecule dopamine (DA) can serve as an intracellular redox indicator [2].

In order to understand the effects of chemically modifying the surface of QDs. We have chosen the QD-DA construct as a model to investigate the optical and biological properties of QDs that have various levels of DA loading on the surface of the particles. To this end, we have developed and assay that can be used to asses the amount of dopamine that binds to the surface of the particles during the coupling reaction [3].

When DA is bound to the surface of CdSe/ZnS QDs, it quenches the fluorescent emission of the particles in a predictable manner. Figure 1 shows the quenching of the QD emission over a range of DA loading from zero to near saturation. Quenching is linear in this range and this is consistent with the notion that the quenching is due to a single molecular species. We have shown that the quenching of QD emission can be exploited for sensing applications. In the case of QD-DA, the probe is sensitive to oxidation by chemical and photo-related processes. The effect of oxidation is unquenching (restoration) of the QD emission. Our results also show that the kinetics of the QD unquenching by photo-oxidation are dependant on the level of DA loading [4].

The biological activity of QDs as a function of DA loading were investigated. The preliminary experiments suggest that the interactions of these bioprobes with cell lines expressing the D2 DA receptors are quite complicated in nature. First of all, there is a minimum level of DA loading that is required for visible association of QD-DA to cells. This requirement suggests that the bulk of the QD in comparison to DA may contribute to some steric hinderance and therefore restrict the activity of DA at its receptor on the cell surface. Another possibility is that with high DA loading, closely spaced DA ligands may be participating in multivalent interactions with the surface receptors. Qualitative information is hard to extract from fluorescence microscopy data as these results are skewed by various degrees of quenching and unquenching. We have designed a series of experiments that will reveal quantitative information on these interactions in a hope to elucidate the nature of the binding interactions of these probes with the surface receptors.

In summary, we have investigated the properties of QDs modified with a small molecule. The level of loading on the surface of the particles is an important parameter that modulates the optical and biological properties of the probes. These results are generalizable and valid for most NP based bioprobes.

**References:**


1. Medintz, I.L., et al., *Quantum dot bioconjugates for imaging, labelling and sensing.* Nat Mater, 2005. **4**(6): p. 435-46.

2. Clarke, S.J., et al., *Photophysics of dopamine-modified quantumdots and effects on biological systems.* Nature Materials, 2006. **5**(5): p. 409-417.

3. Clarke, S.J., et al., *Effect of ligand density on the spectral and affinity characteristics of quantum dot conjugates.* Submitted, 2007.

4. Khatchadourian, R., et al., *Fluorescence intensity and intermittency as tools for tracking bioconjugate processing in living cells.* Submitted, 2007.


**Figures:**

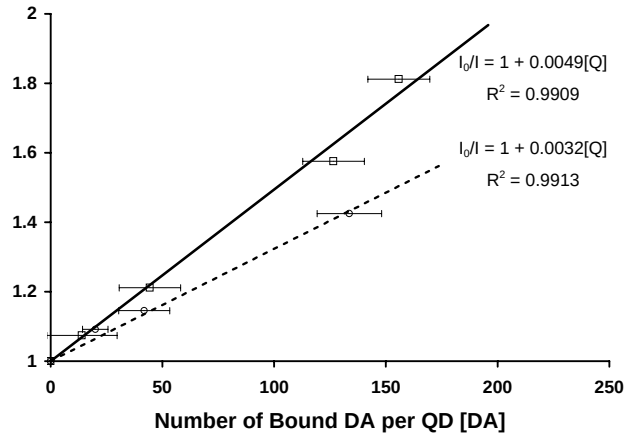


**Figure 1 - Relationship between the number of DA particles bound to the surface of the QD and the resulting emission quenching. For both green QDs (dashed line, cross marker) and red QDs (black line, square marker) the relationship can be fitted to the linear equations depicted on the graph.**

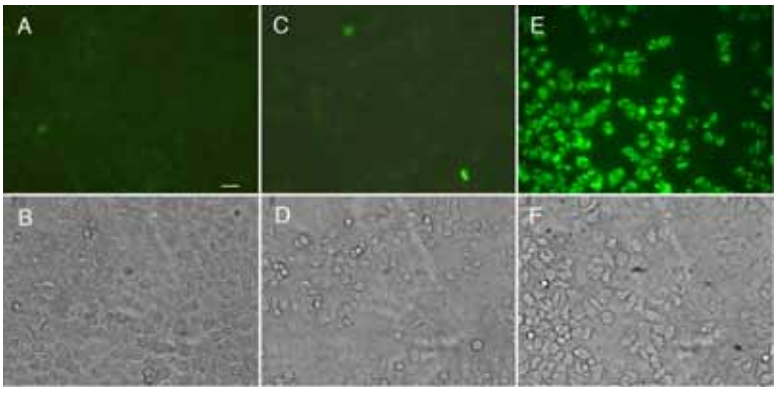


**Figure 2 - Incubation of green QD-DA with PC12 cells confirmed to have the D2 DA receptor. Cells were incubated with 2nM QD-DA for 30 minutes and washed extensively in PBS. Scale bar = 20 µm and applies to all panels. (A,B). QDs without DA do not associate with cells. (C,D) QD-DA with ca. 50 DA ligands has little specificity for cells. (E,F) With ca. 100 DA ligands, QD-DA had a high specificity for the surface D2 DA receptors.**