Compact InP/ZnS nanocrstals through optimized aqueous phase transfer: high conservation of fluorescence and colloidal stability

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Semiconductor nanocrystals small enough to exhibit quantum confinement, also termed quantum dots, have shown to be very promising fluorophors for biological labeling owing to their size-dependent emission color, large absorption spectrum, high brightness and excellent photostability.[1] Most of the high quality quantum dots (e.g. CdSe, InP, InAs) are synthesized in organic solvents and are stablilized by surface ligands rendering them hydrophobic.[2] Therefore, in recent years a large number of different approaches for the aqueous phase transfer of quantum dots have been proposed, specially in view of biological application with these NCs. Among those, surface ligand exchange with small hydrophilic thiols has been shown to yield the lowest hydrodynamic diameter, on the order of 5-10 nm. Compact quantum dots are required for specific imaging applications (e.g. sentinel lymph node detection, study of synaptic signaling) and for maximizing renal excretion in *in-vivo* studies. Thiol-containing amino acids such as L-cysteine are of particular interest as capping ligands for hydrosoluble quantum dots as they exhibit low non-specific binding to serum proteins due to their zwitterionic character. However, cysteine is prone to dimer formation, yielding cistine, which limits the colloidal stability of the quantum dots.

We will demonstrate that the precise control of the pH value during aqueous phase transfer dramatically increases the colloidal stability of InP/ZnS quantum dots. While precipitation of the quantum dots in PBS buffer typically occurs within one day, DLS measurements show that no aggregation takes place even after several weeks in case of the correct choice of the pH during the transfer reaction. In addition to cysteine, various other bifunctional thiols have been tested. The pH has to be chosen in a range of 8-10 according to the pK_a value of the thiol function as only the thiolate ion exhibits strong binding to the quantum dot surface. The formation of disulfides has been prevented during phase transfer through addition of reducing agents, e.g. TCEP. Disulfides significantly diminish the fluorescence quantum yield (QY) of InP/ZnS quantum dots. To the contrary, in our procedure up to 90% of the initial QY is maintained. The obtained quantum dots emit at 650-720 nm with a QY of 15% at pH 7.4 and their hydrodynamic diameter is below 10 nm. The described procedure can equally be used for other types of nanoparticles, such as CdSe nanodots or nanorods, $CuInS_2$/ZnS quantum dots or $CuInSe_2$ nanoprisms.

Finally we will present the *in vitro* and *in vivo* behavior of the hydrosoluble quantum dots after surface functionalization with functional molecules (e.g. cell penetrating peptides).

References

[1] Medintz I. Q.; Uyeda, H. T.; Goldman, E. R.; Mattoussi, H. Nature Materials, **4** (2005**)**, 435-446.

[2] a) Reiss, P.; Bleuse, J.; Pron, A. *Nano Lett.* **2** (2002)**,** 781– 784; b) Li, L.; Reiss, P. J. Am. Chem. Soc. **130** (2008), 11588-11589; c) Allen, P.M.; Liu, W.; Chauhan, V. P.; Lee, J.; Ting, A. Y.; Fukumura, D.; Jain, R. K.; Bawendi, M. G. J. Am. Chem. Soc. **132** (2010), 470-471.

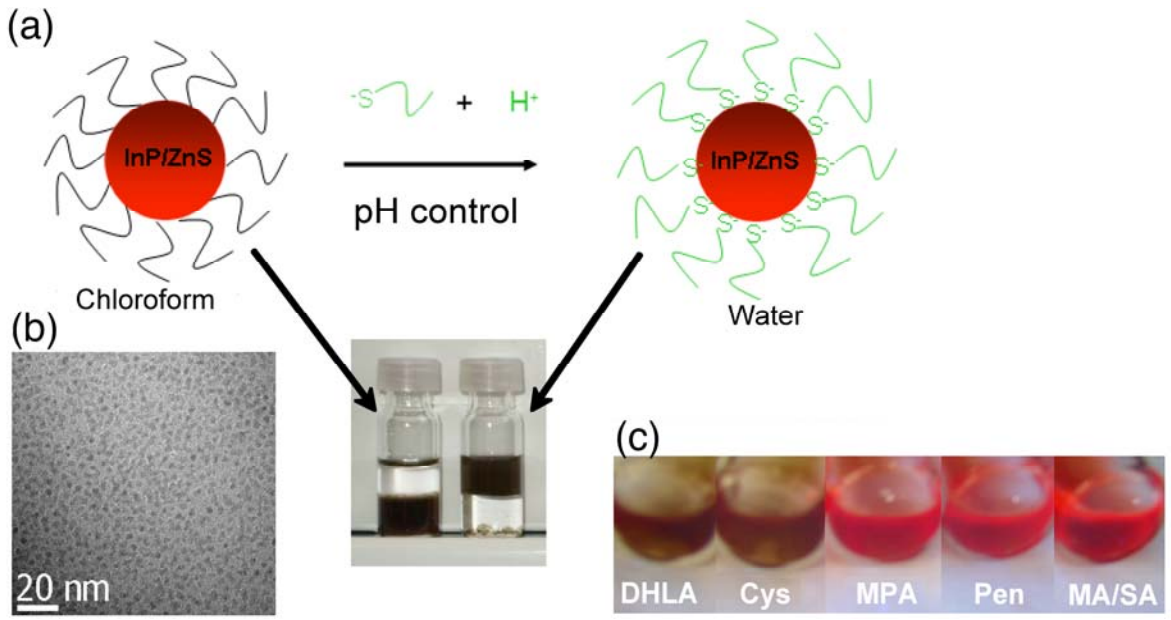

Figure 1: (a) Transfer of InP/ZnS quantum dots from the organic phase (chloroform, bottom) to the aqueous phase (DI water, top). (b) TEM image of the used quantum dots. (c) Photographs of samples transferred using different bifunctional thiols under UV light (DHLA: dihydrolipoic acid, Cys: L-cysteine, MPA: mercaptopropionic acid, Pen: D-penicillamine) compared to the sample in chloroform (MA/SA: myristic acid/stearic acid).