Hyper-bright nanoparticles made from molecules: new tools for bioimaging

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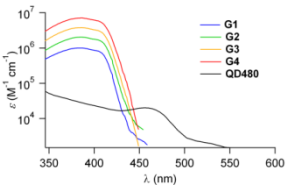
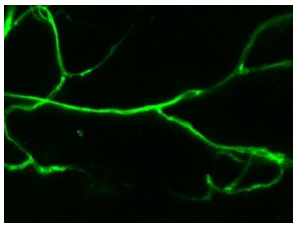
Among various probes, semiconductor quantum dots have been shown to provide a particularly powerful approach to luminescent nanoobjects for bioimaging purposes. However, these inorganic systems suffer from several drawbacks such as toxicity, blinking and raise a number of questions with respect to environmental issues (clearance, biodegradability…). With this in mind, we have developed ***molecular-based bottom-up*** approaches towards luminescent nanoparticles showing exceptional both one- and two-photon brightness. These fully organic nano-emitters of controlled nature are obtained from rational routes and differ from QDs in both their design and in the origin of their luminescent properties opening an innovative alternative avenue towards new nanoprobes for bioimaging.

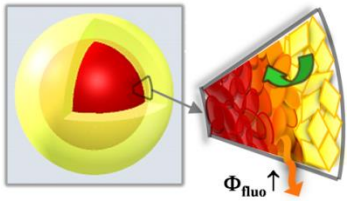
Two alternative and complementary routes will be presented. The first one is based on the control, at the single nano-object level, of the optical responses via the design of *covalent* molecular structures of highly confined chromophores within hierarchical architectures (dendrimers) in which interactions between chromophoric subunits are impeded and their relative positioning is fully controlled. This covalent bottom-up strategy led to tuneable nano-objects (typically 2-6 nm in radius) which can outcome semiconductor quantum dots in terms of brightness by orders of magnitude,[1], show cooperative enhancement of nonlinear absorption cross-sections,[2] and allow fast intra- and inter- nanodot excitation energy transfer in films[3a]. These tuneable, *soft* organic nanodots (ONDs) have been proven to be of major interest as luminescent nanoparticles for *in vivo* bioimaging[3b-c] as well for sensitive detection of explosives.[3a].



Absorption of blue-emitting OND as compared to QD480



In vivo two-photon imaging of blood vessels of stage 53 *Xenopus laevis* tadpole, after intracardiac injection of 1.5 pmol of green-emitting OND (excitation at 860 nm)



"Molecular Plasmonics": Luminescence enhancement and confinement at organic-organic nanointerface in core-shell FONs made from dedicated polar and polarizable complementary dyes

The second route is based on the spontaneous assembly of *specially designed multipolar* insoluble dyes in water. This *non-covalent* approach led to Fluorescent Organic Nanoparticles (FONs) showing record one- and two-photon brightness (up to 10^8 $M^{-1}cm^{-1}$ and 10^6 GM).[4] Interestingly, in such molecular-based nanoparticles, both the luminescence and the nonlinear optical responses can be tuned and enhanced via molecular confinement control.[4c] These luminescent molecular-based nanoparticules (having radius of 5-50 nm) can be readily prepared using simple, expeditious and green protocols. Their color, biocompatibility, colloidal and structural stability can be tuned thanks to a subtle bottom-up strategy, yielding biocompatible ultrasensitive nanotracers for *in vivo* two-photon angiography.[4a] This approach also opens the way to markedly enhanced photostability resulting in innovative multicolor FONs (including Hyperbright NIR-emitting FONs named HiFONs[4b]) which can be used for multicolor single particle tracking within cells.[5] Finally, striking luminescence enhancement and spatial confinement at the nano-interface can be achieved in core-shell binary nanoparticles made from dedicated complementary dyes, in relation with the generation of large interfacial electric fields. This opens an intriguing route towards "molecular plasmonics".[6]

[1] a) M. Blanchard-Desce, M. Werts, O. Mongin, J.-P. Majoral, A.-M. Caminade, R. K. Thatavarthy, *PCT Int. Appl*., 2007, WO 2007080176; b) O. Mongin, C. Rouxel, J.-M. Vabre, Y. Mir, A. Pla-Quintana, Y. Wei, A.-M. Caminade, J. P. Majoral, M. Blanchard-Desce, *Proc. SPIE-Int. Soc. Opt. Eng*, 2009, **7403**, 740303-1-12; O. Mongin, R. K. Tathavarty, M. H. V. Werts, A.-M Caminade, J-P. Majoral, M. Blanchard-Desce, *Chem. Commun*., 2006, 915-917

[2] F. Terenziani, V. Parthasarathy, A. Pla-Quintana, T.;Maishal, A.-M. Caminade, J.-P. Majoral, M. Blanchard-Desce, *Angew. Chem. Int. Ed.*, 2009, **48**, 8691-8694.

[3] a) A. Narayanan, O. Varnavski, O. Mongin, J.-P. Majoral, M. Blanchard-Desce, T. Goodson III, *Nanotechnology*, 2008, **19**, 115502; b) T. R. Krishna, M. Parent, M. H. V. Werts, L. Moreaux, S. Gmouh, S. Charpak, A.-M. Caminade, J.-P. Majoral, M. Blanchard-Desce, *Angew. Chem., Int. Ed.* 2006, **45**, 4645-4648; c) O. Mongin, C. Rouxel, A.-C. Robin, A. Pla-Quintana, Tathavarathy Rama Krishna, G. Recher, F. Tiaho, A. -M. Caminade, J.-P. Majoral, M. Blanchard-Desce, *Proc. SPIE-Int. Soc. Opt. Eng*. 2008, **7040**, 704006, 1-12.

[4] a) V. Parthasarathy, S. Fery-Forgues, E. Campioli, G. Recher, F. Terenziani, M. Blanchard-Desce, *Small*, 2011, **7**, 3219-3229; b) E. Genin, Z. Gao, J. A. Varela, J. Daniel, T. Bsaibess, I. Gosse, L. Groc, L. Cognet, M. Blanchard-Desce, *Adv. Mater*. 2014, **26**, 2258-2261. c) J.-B. Verlhac, J. Daniel, P. Pagano, G. Clermont, M. Blanchard-Desce, *C. R. Chimie*, 2016, **19**, 28-38.

[5] J. Daniel, A. Godin, M. Palayret, B. Lounis, L. Cognet, M. Blanchard-Desce, *J. Phys. D: Appl. Phys*., 2016, **49**, 084002-084012.

[6] a) E. Campioli, C. Rouxel, M. Campanini, L. Nasi, M. Blanchard-Desce, F. Terenziani, *Small*, 2013, **9**, 1982–1988; b) E. Campioli, D.-M. Nikolaidou, V. Hugues, M. Campanini, L. Nasi, M. Blanchard-Desce, F. Terenziani, *J. Mater. Chem. C*, 2015, **3**, 7483-7491.