

LANTHANIDE-ION DOPED OXIDE NANOPARTICLES FUNCTIONALIZED FOR SINGLE BIOMOLECULE TRACKING

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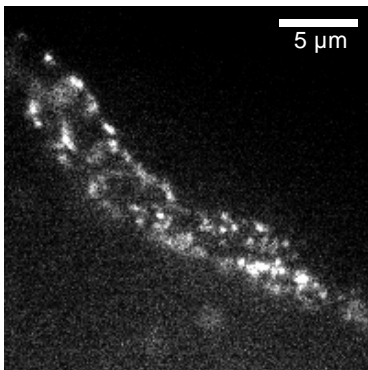
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Organic fluorescent labels are extensively used for studying molecular and cellular processes. The disadvantage of these organic chromophores is that they undergo rapid photobleaching. Semiconductor nanocrystals (quantum dots; QDs) have been proposed as alternative fluorescent labels and led to very promising results despite the fact that their water solubilization is complex and that long-term single-QD tracking is hampered by their fluorescence intermittency.

We here demonstrate functionalized lanthanide-ion doped oxide nanoparticles as a promising new class of biological fluorescent probes. This system possesses distinct advantages: (i) colloids are synthesized directly in water, which greatly facilitates their functionalization, (ii) no blinking behaviour is observed due to the large number of dopant ions present in one nanoparticle, which makes them interesting for sustained single-particle tracking.

We observed $\text{YVO}_4:\text{Eu}$ nanoparticles (doping: 20%; average diameter: 23 nm) in a widefield fluorescence microscope by direct excitation of the Europium ions. Nanoparticles as small as 10-15 nm in diameter could be detected. Owing to their photostability, individual nanoparticles could be imaged for durations superior to 15 minutes under continuous illumination.

We then demonstrated specific binding of these nanoparticles to sodium channels. The nanoparticles were functionalized with guanidium groups in order to mimick the blocking effect of saxitoxin on Na^+ channels. Electrophysiological measurements in frog heart auricular tissue confirmed that functionalized nanoparticles specifically target Na^+ channels and mimick the effect of saxitoxin [1].



We achieved imaging of individual functionalized nanoparticles on the membrane of live cardiomyocytes, revealing the distribution of Na^+ channels [1]. Moreover, we showed that a simple mechanical time-gated detection scheme can be used to take advantage of the long excited state lifetime of lanthanide ions (~1 ms) and filter out the short-lived cellular fluorescence (ns). See figure on the left (exposition time : 1 s; intensity at the sample 5 kW/cm^2).

Functionalized lanthanide-ion doped oxide nanoparticles thus appear as a versatile tool particularly attractive for long-term single-molecule tracking.

[1] E. Beaurepaire, V. Buissette, M.-P. Sauviat, D. Giaume, K. Lahlil, A. Mercuri, D. Casanova, A. Huignard, J.-L. Martin, T. Gacoin, J.-P. Boilot, A. Alexandrou, *Nano Lett.* **4**, 2079 (2004).