Towards Single Metal Ion Sensing by Förster Resonance Energy Transfer

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Abstract

Here we describe progress towards our objective of detecting single non-fluorescent hydrated metal ions.

1. Transition metal ions

Transition metal ions like copper and nickel play an important role in biology as nutritional microelements as well as important ligands in proteins e.g. manganese in the photosystem II of plant cells or copper in the regulation of intracellular transport [1]. Sensing transition metal ions in biological systems by chemical methods proves to be difficult for concentrations are small and chemical sensing often interferes with the very process one desires to monitor.

2. Light absorption by metal ions

When a transition metal ion interacts with one or more ligands the electrons of the ligand as well as the d-orbitals of the ion repulse each other. This raises the energy level of the electrons in the d-orbital and leads to a split into two distinct energy bands. With the d-orbitals incompletely filled, absorption of photons can lift an electron between the d-orbitals. Thus the ligand of the ion has an influence on the extent of the split of the d-orbitals and the subsequent absorption spectrum of the ion.

3. Quantum dots

The relatively small size, the long fluorescence lifetimes and the photostability of semiconductor nanocrystals or "quantum dots" are of great advantage for measurements in life sciences.

4. Förster Resonance Energy Transfer

In contrast to measurements that rely on direct binding of the ion the resonance energy transfer does not interfere with the process observed [2].

The fluorescence decay is measured then given by:

\[ I(t) = I(0) \exp\left(-\frac{t}{\tau} - 2\gamma \frac{t}{\tau_0} - \frac{t^2}{\tau_0^2}\right) \]

With \( \gamma \) being the transfer coefficient between donor and acceptor, defined as:

\[ \gamma = \frac{[A]}{C_A} \]

\([A]\) is the concentration of the acceptor and \(C_A\) is the critical acceptor concentration as calculated from the overlap integral between donor emission and acceptor absorbance.

The value of the spectral overlap integral between acceptor and donor \(R_0\) is

for Quantum Dot QDots525® with Cu²⁺ 13.9 Å
and Quantum Dot QDots800® with Cu²⁺ 20.3 Å.

These values of \(R_0\) allow measurements over considerable distances from the ion as for example probing through cell membranes (about 10 Å in thickness).

Calculations from measurements of the transfer coefficient \(\gamma\) and the acceptor concentration yield a \(R_0\) value of 14 Å for QDots800 with Cu²⁺.

6. Resolution of ion sensing

Recordings of the fluorescence lifetime of quantum dots emitting at 525 and 800 nm, show great sensitivity to addition of cobalt and copper ions respectively.

7. Quantum dots are potent sensors for metal ions

Semiconductor nanocrystals provide excellent sensors for transition metal ions in biophysical systems.

Quantum dots can be generated with precise spectral properties, allowing to target specific ions. Furthermore the surface-properties of quantum dots allow relatively easy modification for binding of antibodies or even directly to target proteins.

Quantum dots provide very advantageous fluorescent characteristics; namely a high photostability, allowing for prolonged monitoring, wide excitation spectra, giving flexibility in the excitation light source and narrow emission granting good distinction of the target ion from other acceptors.

In bulk measurements a single ion proves sufficient to yield a clear signal from a quantum dot.

A single quantum dot can be monitored using confocal microscopy.

References:

[1] Li J, Sauer A, Bost DD. "Regulation of Copper-Dependent Endocytosis and Vacuolar Degradation of the Yeast Copper Transporter, Ctr1p, by the Rsp5 Ubiquitin Ligase." Traffic. 2007