

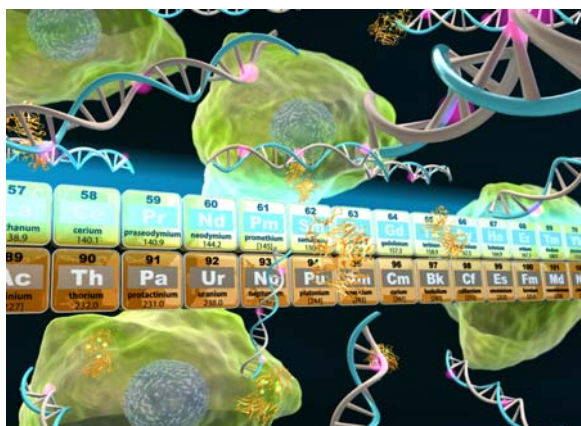
Time-gated FRET biosensing: Rapid, sensitive, and multiplexed absolute quantitation of biomarkers

Niko Hildebrandt

NanoBioPhotonics, Institute for Integrative Biology of the Cell (I2BC), Université Paris-Saclay / Université Paris-Sud / CNRS / CEA, Orsay, France (www.nanofret.com, niko.hildebrandt@u-psud.fr)

Determination of biomolecular recognition via Förster Resonance Energy Transfer (FRET) plays an important role for quantifying concentrations and distances in many fields of the life sciences.¹ The application of time-gated photoluminescence spectroscopy and microscopy for the analysis of FRET systems offers several advantages concerning versatility, sensitivity, and specificity. Luminescent lanthanide complexes, and in particular Tb complexes, exhibit extremely long luminescence lifetimes and multiple narrow emission peaks over a broad spectral range. These photophysical features make them highly interesting FRET donors in combination with different FRET acceptors, such as organic dyes or semiconductor quantum dots.²⁻⁸ Such FRET pairs have been successfully used for the multiplexed and highly sensitive detection of protein, peptide, DNA, and RNA biomarkers.

The presentation will give an introduction to time-resolved and time-gated FRET and explain the specific benefits of lanthanide/dye/quantum dot FRET pairs for luminescence detection. Then, the application of these FRET pairs in different homogeneous single-step FRET biosensors for the sensitive and specific detection of multiple biomarkers from low-volume liquid samples or on cell membranes and inside cells will be discussed. These Tb-based FRET biosensors provide a rapid, simple, selective, and sensitive tool for multiplexed detection of various oligonucleotides or proteins, which makes them highly interesting for clinical diagnostics and other biosensing applications.



References:

1. I. Medintz and N. Hildebrandt (editors). FRET – Förster Resonance Energy Transfer. From Theory to Applications”, Wiley-VCH, Germany **2014**, ISBN 978-3-527-32816-1.
2. N. Hildebrandt, C. M. Spillmann, W. R. Algar, T. Pons, M. H. Stewart, E. Oh, K. Susumu, S. A. Díaz, J. B. Delehanty, and I. L. Medintz. Energy Transfer with Semiconductor Quantum Dot Bioconjugates: A Versatile Platform for Biosensing, Energy Harvesting, and Other Developing Applications. *Chemical Reviews* **2017**, 117 (2), 536-711.
3. M. Sy, A. Nonat, N. Hildebrandt, and L.J. Charbonnière. Lanthanide-based luminescent biolabelling. *Chemical Communications* **2016**, **52**, 5080-5095.
4. M. Cardoso Dos Santos and N. Hildebrandt. Recent Developments in Lanthanide-to-Quantum Dot FRET Using Time-Gated Fluorescence Detection and Photon Upconversion. *TrAC – Trends in Analytical Chemistry* **2016**, **84**, 60-71.
5. D. Geißler and N. Hildebrandt. Recent developments in FRET diagnostics using quantum dots. *Analytical and Bioanalytical Chemistry* **2016**, 408 (17), 4475-4483.
6. K.D. Wegner and N. Hildebrandt. Quantum Dots: Bright and Versatile In vitro and In vivo Fluorescence Imaging Biosensors. *Chemical Society Reviews* **2015**, **44**, 4792-4834.
7. N. Hildebrandt, K. D. Wegner, and W. R. Algar. Luminescent Terbium Complexes: Superior Förster Resonance Energy Transfer Donors for Flexible and Sensitive Multiplexed Biosensing. *Coordination Chemistry Reviews* **2014**, 273-274, 125-138.
8. D. Geißler, S. Lindén, K. Liermann, K. D. Wegner, L. J. Charbonnière, and N. Hildebrandt. Lanthanides and Quantum Dots as Förster Resonance Energy Transfer Agents for Diagnostics and Cellular Imaging. *Inorganic Chemistry* **2014**, **53**, 1824-1838.
9. W. R. Algar, H. Kim, I. L. Medintz, and N. Hildebrandt. Emerging non-traditional Förster resonance energy transfer configurations with semiconductor quantum dots: Investigations and applications. *Coordination Chemistry Reviews* **2014**, 263-264, 65-85.