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In partnership with:



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Biography

Niko Hildebrandt (www.nanofret.com) holds a diploma in Medical Physics (2001, Berlin, Germany) and a Ph.D. in Physical Chemistry (2007) from the University of Potsdam (Germany), where he also carried out postdoctoral research until 2008. From 2008 to 2010 he was groupleader at the Fraunhofer Institute for Applied Polymer Research in Potsdam. Since 2010 he is Full Professor at Université Paris-Sud in Orsay, France, where he is leading the group Nano-Bio-Photonics at the Institute for Integrative Biology of the Cell (I2BC) with a research focus on time-resolved Förster resonance energy transfer (FRET) spectroscopy and imaging for multiplexed biosensing. Since 2014 he is a member of the Institut Universitaire de France.

NANOPARTICLES AND NANOINTERACTIONS: A BEAUTIFUL COUPLE FOR MULTIPLEXED FRET BIOSENSING

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 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 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.²⁻⁵ Such FRET pairs have been successfully used for spectral and temporal multiplexing and highly sensitive detection of protein, peptide, DNA, and RNA biomarkers.⁶⁻¹⁰

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 spectral and temporal multiplexed luminescence detection. Then, recent applications 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.

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Keywords: Quantum Dots, Gold Nanoparticles, FRET, NSET, Time-Gating, Spectroscopy, Microscopy

11, 12 & 13 septembre

Session: Sensors

Keywords: 3D DNA origami, plasmonics, colorimetric sensing, nano-actuation

Colorimetric monitoring of DNA origami conformations with gold particles

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By combining gold nanoparticles and active DNA origamis, our aim is to design colorimetric sensors capable of reaching single-molecule sensitivities while maintaining a low-cost measurement strategy. DNA origamis are a flexible platform to produce complex organic nano-objects that shift their morphology when interacting with specific target biomolecules. To translate such conformational changes into a macroscopic optical signal, we assemble two gold nanoparticles on a 3D origami scaffold to exploit the nanoscale dependence of plasmon coupling. Indeed, darkfield microscopy allows the far-field monitoring of nanoscale distance changes in single gold dimers on a simple color camera.

In practice, we produce suspensions of origami-linked 40nm gold dimers in two different geometries (Figure 1-a-b). By studying typical plasmon resonance spectra of single gold particle dimers (Figure 1-c), we observe a spectral redshift associated with the reduced distance between the arms of the origami. A statistical analysis performed over more than 100 single nanostructures (Figure 1-d) demonstrates an average 25 nm redshift that is visible on a color camera (insets of Figure 1-a-b). This correlation between the morphology of the origami scaffold and darkfield optical signals opens exciting perspectives for the optical sensing of specific physicochemical stimuli that actively modify the conformation of DNA-templated gold particle dimers.

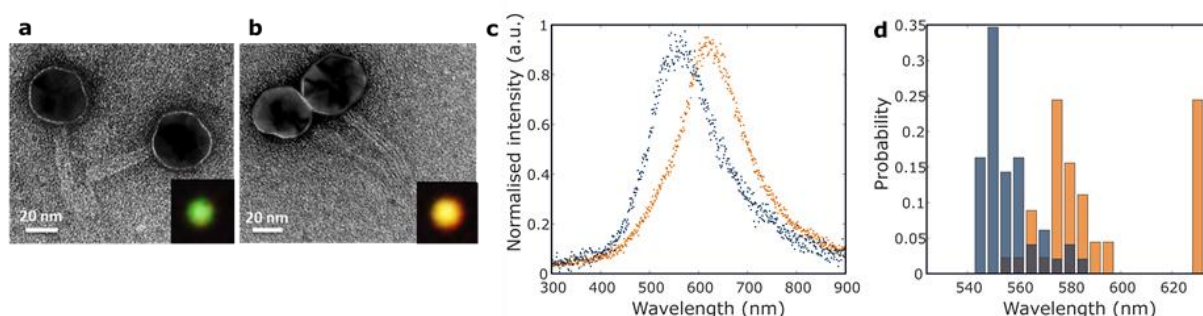


Figure 1: 40nm gold nanoparticle dimers assembled on DNA origami scaffolds: TEM images when the origami arms are separated by 42bp (a) and 126bp (b) DNA strands, insets: typical darkfield images. Typical scattering spectra (c) and plasmon resonance distributions (d) for 42bp (orange) and 126bp (blue) dimers.

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Session Nanobiology

Key words: SERS, Molecular Imprinted Polymers, Chemometrics, sensor

Détection du paracétamol par un capteur hybride SERS-MIP

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Les polluants émergents sont une classe de substances chimiques d'usage courant et qui se retrouvent dans l'eau après leur utilisation. Leur toxicité sur les écosystèmes est peu ou pas étudiée notamment à cause de la difficulté de les détecter et de quantifier leur présence. Leur concentration est très faible et leur petite taille les rend difficiles à détecter par les techniques classiques. De plus, les méthodes d'analyse de l'eau sont complexes et prennent souvent du temps. Il est également compliqué d'étudier les fluctuations temporelles et spatiales des concentrations de ces polluants. Nous proposons ici une nouvelle stratégie permettant de fabriquer un capteur *in situ* dont la manipulation autorisera une analyse rapide sur site. Ce capteur est basé sur l'exploitation de la spectroscopie Raman exaltée de surface (SERS) offrant une forte sensibilité pour la détection de molécules traces ; la surface nanostructurée est une assemblée de nanocylindres obtenus par lithographie électronique. Ces structures d'or sur ITO sont ensuite fonctionnalisées par des polymères à empreinte moléculaire (MIP) pour obtenir une plateforme de reconnaissance hautement sélective et spécifique. Les MIP sont des polymères qui sont synthétisés en présence d'une molécule cible qui est rincée en fin de la synthèse. Une empreinte est ainsi formée qui laisse la possibilité de piéger cette molécule si elle entre à nouveau en contact avec le MIP. Nous présenterons des résultats sur la détection du paracétamol, car il est l'un des médicaments les plus prescrits au monde. Cette molécule est détectée dans les rivières et les mers à environ 100 µg.l⁻¹. Une voie originale pour la synthèse MIP sur les nanostructures a été utilisée, basée sur une première fonctionnalisation avec un sel de diazonium, puis une photopolymérisation. Nous montrerons comment l'utilisation de méthodes statistiques (analyse en composantes indépendantes) permet d'obtenir une tendance de la sensibilité d'un tel capteur.

11, 12 & 13 septembre

Session: Nanobiology

Keywords: magneto-plasmonics, thin films, Kerr effect, surface functionalization, biosensors

Magneto-Optical Surface Plasmon Resonance Architecture for Cardiac Troponin Detection

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Surface plasmon resonance (SPR) is a surface-sensitive analytical technique used in a variety of biological sensors.¹ The main problem with classical SPR technology is associated with the existence of a lower physical limit of detection (LOD) with respect to fluorescence. Various approaches have been proposed to overcome this limitation by developing different sensing concepts including phase-sensitive detection schemes, use of metallic nanostructures, line gratings and others. More recently, the addition of active functionalities to the SPR based devices have been proposed to enhance the intrinsic sensitivity of the SPR system. A magneto-optical (MO) SPR sensor, based on a magneto-plasmonic modulation technique produced in multilayers of noble and ferromagnetic metals has been lately proposed.² The use of trilayered thin film structure (e.g. Au/Ferro/Au) allow to provide a transverse magneto-optical Kerr effect (TMOKE) of p-polarized light. This TMOKE signal exhibit improved physical sensitivity over classic SPR measurements thanks to the non-reciprocal modification of the surface plasmon wave vector induced by the applied magnetic field.³

Here we propose a novel combination of metals based on ferrimagnetic thin films composed of TbCo₂ stacked with FeCo providing a magnetic uniaxial anisotropy and giving rise to an easy and a hard magnetization axis in the structure. The combination of theoretical and experimental studies shows a significant increase of sensitivity when used in a magneto-plasmonic configuration. The interest of this novel sensing device for the detection of cardiac biomarkers such as troponin I⁴ will be shown.

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Session Nanobiology

Keywords: biosensors, nanoprobcs, light-harvesting, nanoantenna, fluorescent nanoparticles.

Fluorescent organic nanoantennas for ultrasensitive detection of nucleic acid cancer markers

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Diagnostics of early stages of diseases, such as cancer requires detection of ultra-low concentration of mRNA in biological samples. Nowadays the only technique used in clinics for detection of nucleic acid cancer markers is polymerase chain reaction (PCR), a multi-step molecular multiplication process that requires complex mixture of expensive reagents, sophisticated equipment and well-trained staff. Our goal is to develop alternative signal amplification strategy to achieve simple one-step ultrasensitive detection of RNA.

To this end, we developed ultrabright dye-loaded polymeric nanoparticles^{1,2}, which feature controlled small size and exceptional brightness because they encapsulate >1000 dyes per particle. We found that these nanoparticles operate as light-harvesting nanoantenna capable to amplify emission of single dye molecules >1000 fold, which enables for the first time detection of single molecules in sunlight excitation conditions.³

Based on these nanoantennas we developed the nanoprobcs for nucleic acids, by covalent modification of the polymer nanoparticles with oligonucleotides. In this nanoprobe, 3-5 hybridization events switches energy transfer from of thousands donor dyes, thus providing strong amplification. Detection can be performed in solution and on the surface with limit of detection reaching 0.25 pM, which is >1000-fold lower than that of conventional fluorescence molecular probes for nucleic acids.⁴ We currently study entry of DNA-functionalized nanoparticles into eukaryotic cells and explore their capacity to detect cancer markers in different biological samples.

The developed nanoprobcs constitute a new powerful platform for rapid and ultra-sensitive detection of cancer biomarkers.

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