nanoVista

NEWSLETTER #2

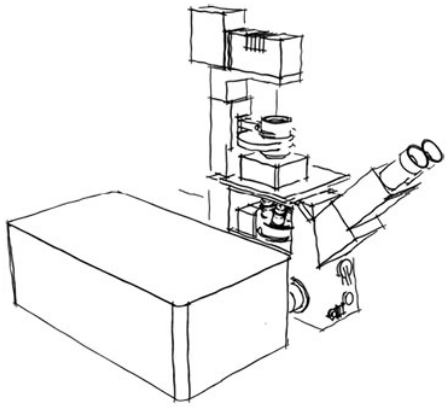
PHOTONICS ANTENNAS FOR BIOLOGY
Tools for biosensing and cellular imaging

OBJECTIVES

- The first objective of NanoVista is to pioneer the technological development of **novel photonic antenna** geometries (probes & 2D arrays) for both **ultrasensitive detection** at **high sample concentrations** in fluids and simultaneous spatial **nanometric resolution** and **sub-ms** time resolution in living cells.
- The second objective of the European project is to develop **high-throughput large-scale nanofabrication** of photonic antenna arrays fully compatible with biomolecule detection and live cell nanoimaging.
- The third objective of the consortium is to demonstrate the bionanophotonic technology for **ultra-sensitive detection of biomolecules for diagnostic** purposes and for **nanospectroscopy on living cells**.

NEWS

- COSINGO, Spanish tech. SME, entered the consortium with the aim of developing a compact, robust and highly sensitive instrument for biosensing and nanospectroscopy on living cells. Current efforts are focussed on the development of a lab-on-a-chip based on 2D nano-antennas and microfluidics and a stand-alone instrument to perform fluorescence correlation spectroscopy (FCS).



- EPFL investigated and improved the selective assembly of metallic nanoparticles over large areas with inter-particle distances below 2nm. The technique allows achieving strong field enhancement, as with usual Electron beam Lithography (EBL) technique of fabrication, but with the potential of large scale production compatible with commercial exploitation in term of cost and throughput.

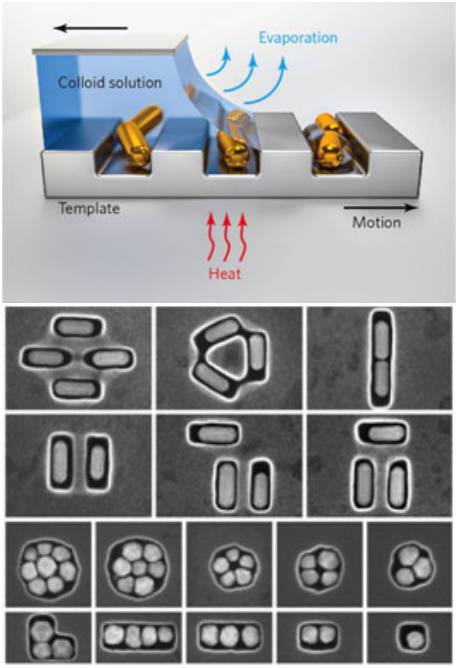


Fig. A solvent drop is dragged over a patterned template and the particles assemble in the grooves.

- ICFO, Fresnel Institute and RUNMC paired to demonstrate superresolution capacity of dual-colour nanoantennas excitation to resolve fluorescent molecules. as close as 2.1nm, with 4Å accuracy, opening the possibility of addressing multi-molecular complexes at the molecular scale.

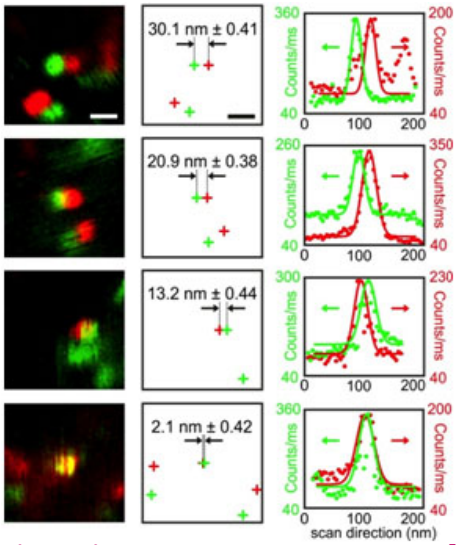


Fig. Distance measurements of dual-colour hybrid nanoantennas.

PARTNERS

ICFO Institut de Ciències Fotòniques
Radboudumc university medical center
INSTITUT FRESNEL
EPFL ÉCOLE POLYTECHNIQUE FÉDÉRALE DE LAUSANNE
COSINGO Imagine Optic Spain S.L.
SEVENTH FRAMEWORK PROGRAMME

MORE INFORMATION: www.nanovista.eu

Project ref.: **288263**; Funded under: **Information and Communication Technologies**; Area: **ICT-2011.3.5**; Duration: **2011-2016**;

PROJECT MEETINGS

NanoVista roadmap is ensured by rigorous progress meetings organized periodically at partners premises:
July 7, 2014 at ICFO (Barcelona, Spain) when COSINGO has been officially introduced in the consortium. June 19, 2015 at EPFL (Lausanne, Switzerland) which has been the opportunity to organize simultaneously a Young Researchers Meeting, aiming at fostering brainstorming, exchanges and collaborations between students participating to NanoVista project.

Fig. 3D replica of a picture of the young researchers, taken during the meeting and printed into a temperature sensitive polymer by means of a thermal scanning probe. The overall AFM image is 17 µm size, which means that it could fit on a cell !

PUBLICATION HIGHLIGHT

A single cell in our body is composed by thousands of millions of different biomolecules that work together in an extreme coordinated manner. Likewise, many biological and biochemical reactions occur only if molecules are present at very high concentrations. Understanding how all these molecules interact with each other is key to advance our knowledge in molecular and cell biology. Unfortunately, detecting one molecule within millions of other neighbouring molecules has been technically impossible until now. The key to succeed relies on foreseeing a device that shrinks the observation region to a tiny size that is comparable to the size of the molecule itself, that is, only a few nanometres.

Researchers from the NANO-VISTA consortium, Fresnel Institute in Marseille and ICFO, have now conceived and fabricated the smallest optical device that can detect and sense individual biomolecules at concentrations that are similar to those found in the cellular context. The device called “antenna-in-a-box” consists on a tiny dimmer antenna made out of two gold semi-spheres and separated from each other by a gap as small as 15nm.

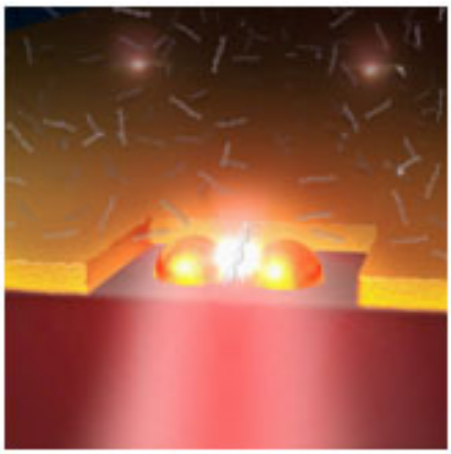


Fig. Antenna-in box platform for single-molecule analysis at high concentrations.

Light sent to this antenna is enormously amplified in the gap region where the actual detection of the biomolecule of interest occurs. Because amplification of the light is confined to the dimensions of the gap, only molecules present in this tiny region are detected. As additional trick, we embed the dimer antennas inside boxes also of nanometric dimensions. The box screens out the unwanted contribution of millions of other surrounding molecules, reducing the background and improving as a whole the detection of individual biomolecules. When tested under different sample concentrations, this novel antenna-in-box device allowed for 1100-fold fluorescence brightness enhancement together with detection volumes down to 58 zeptoliters (1 zL = 10^{-21}L), i.e., the smallest observation volume in the world. The work, supported by EU project *NanoVista*, was published in *Nature Nanotechnology,* 2013, **8**, 512–516.

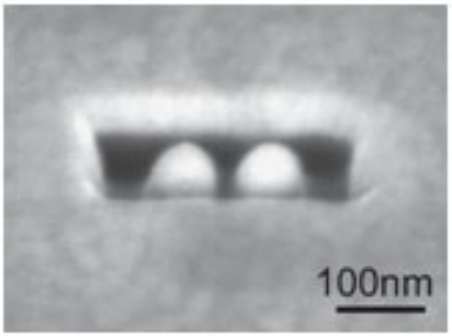


Fig. SEM image of a fabricated nano “antenna-in-a-box”.

Our antenna-in-a-box offers a highly efficient platform for performing a multitude of nanoscale biochemical assays with single molecule sensitivity at physiological conditions. It could be used for ultrasensitive sensing of minute amount of molecules, becoming an exquisite early diagnosis device for biosensing of many disease markers. It could be also used as an ultra-bright optical nanosource to lighten up molecular processes in living cells and ultimately watch how individual biomolecules interact with each other, a long awaited dream of biologists.

NANOVISTA PUBLICATIONS

- **Dual color super-resolution microscopy reveals nanoscale organization of mechanosensory podosomes**
van den Dries K, Schwartz SL, Byars J, Meddens MB, Bolomini-Vittori M, Lidke DS, Figdor CG, Lidke KA, Cambi A.
Mol Biol Cell. 2013 May 1 (in press)
- **Interplay between myosin IIA-mediated contractility and actin network integrity orchestrates podosome composition and oscillations**
van den Dries K, Meddens MB, de Keijzer S, Shekhar S, Subramaniam V, Figdor CG, Cambi A.
Nat Commun, 2013. 4: 1412
- **Automated Podosome Identification and Characterization in Fluorescence Microscopy Images**
Meddens MB, Rieger B, Figdor CG, Cambi A, van den Dries K.
Microsc Microanal, 2013. 1-10
- **Nanoclustering as a dominant feature of plasma membrane organization**
M.F. Garcia-Parajo, A. Cambi, N. Thompson, K. Jacobson.
J. Cell Sci. 127, 4995–5005 (2014). Invited commentary
- **Hybrid photonic antennas for subnanometer multicolor localization and nanoimaging of single molecules**
M. Mivelle, T.S. van Zanten, M.F. Garcia-Parajo
Nano Lett. 14, 4895, (2014)
- **Enhanced receptor-clathrin interactions induced by *N*-glycan mediated membrane micropatterning**
J. A. Torreno-Pina, B. Castro, C. Manzo, S. Buschow, A. Cambi, M.F. Garcia-Parajo
Proc. Nat. Acad. Sci. USA 111, 11037, (2014). Chosen by the Faculty of 1000 as must-read paper
- **Priming by chemokines restricts lateral mobility of the adhesion receptor LFA-1 and restores adhesion to ICAM-1 nano-aggregates on human mature Dendritic Cells**
K. J. E. Borgman, T. S. van Zanten, C. Manzo, R. Cabezón, A. Cambi, D. Benítez-Ribas, Maria F. Garcia-Parajo
PLoS ONE 9, e99589 (2014)
- **Nanophotonic approaches for nanoscale imaging and single molecule detection at ultra-high concentrations**
M. Mivelle, T.S. van Zanten, C. Manzo, M.F. Garcia-Parajo
Microsc. Res. Techniq 77, 537, (2014) (Invited review)
- **Nonergodic subdiffusion from Brownian motion in an inhomogeneous medium**
P. Massignan, C. Manzo, J. A. Torreno-Pina, M. F. García-Parajo, M. Lewenstein, G. J. Lapeyre
Phys. Rev. Lett. 112, 150603 (2014)
- **PSF decomposition of nanoscopy images via Bayesian analysis unravels distinct molecular organization of the cell membrane**
C. Manzo, T. S. van Zanten, S. Saha, J. A. Torreno-Pina, S. Mayor, M. F. Garcia-Parajo
Sci. Rep. 4, 4354 (2014)
- **A plasmonic 'antenna-in-box' platform for enhanced single-molecule analysis at micromolar concentrations**
D. Punj, M. Mivelle, S. B. Moparthi, T. S. van Zanten, H. Rigneault, N. F. van Hulst, M. F. García-Parajó, J. Wenger
Nature Nanotechnol. 8, 512 (2013). Highlighted in *Nature Nanotechnol*. 8, 96 (2013)
- **Vectorial Nanoscale Mapping of Optical Antenna Fields by Single Molecule Dipoles**
A. Singh, G. Calbris, N. F. van Hulst
NanoLetters 14, 4715-4723 (2014); DOI:10.1021/nl501819k
- **A resonant scanning dipole-antenna probe for enhanced nanoscale imaging**
L. Neumann, J. van 't Oever, N. F. van Hulst
Nano Lett. 13, 550 (2013); DOI: 10.1021/nl402178b
- **Ultra-bright, free-standing bowtie nanoperture antennas probed by single molecule fluorescence**
M. Mivelle, T. S. van Zanten, L. Neumann, N. F. van Hulst, M. F. Garcia-Parajo
Nano Lett. 12, 5972-5978 (2012)
- **Plasmonic antennas and zero-mode waveguides to enhance single molecule fluorescence detection and fluorescence correlation spectroscopy toward physiological concentrations**
D. Punj, P. Ghenuche, S. B. Moparthi, J. de Torres, V. Grigoriev, H. Rigneault, J. Wenger
WIREs Nanomed Nanobiotechnol 6, 268 (2014)
- **Gold nanoparticles for enhanced single molecule fluorescence analysis at micromolar concentration**
D. Punj, J. de Torres, H. Rigneault, J. Wenger
Opt. Express 21, 27338-27343 (2013)
- **Plasmonic Band Structure Controls Single-Molecule Fluorescence**
Langguth L., Punj D., Wenger J., Koenderink F.
ACS Nano 7, 8840-8848 (2013)