Catching individual molecules in a million with optical antennas inside nano-boxes

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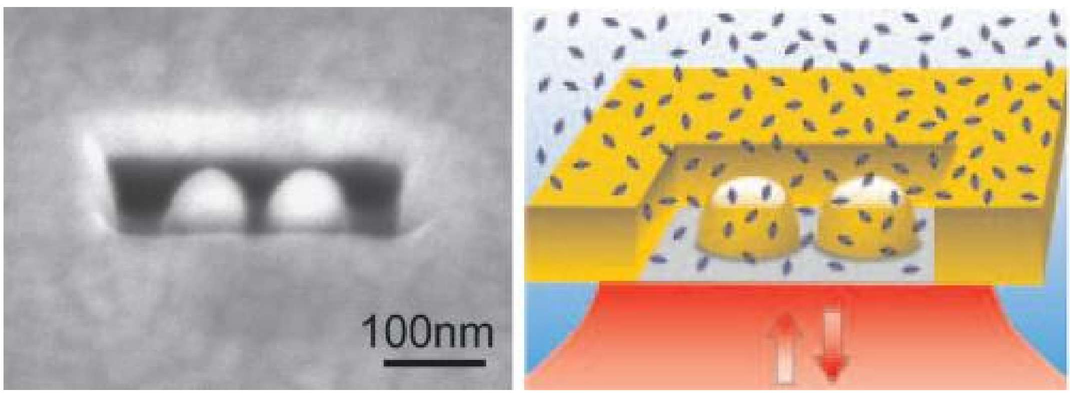

This is a dimer antenna inside a nanobox for single biomolecule analysis at high concentrations. Credit: ICFO

A single cell in our body is composed of thousands of millions of different biomolecules that work together in an extremely well-coordinated way. 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 advancing our knowledge in molecular and cell biology.

This knowledge is of central and fundamental importance in the quest for the detection of the earliest stages of many human diseases. As such, one of ultimate goals in Life Sciences and Biotechnology is to observe how individual molecules work and interact with each other in these very crowded environments. Unfortunately, detecting one molecule amongst millions of neighbouring molecules has been technically impossible until now. The key to successfully detecting the single molecule lies in the conception and production of a working device that shrinks the observation region to a tiny size that is comparable to the size of the molecule itself, i.e. only a few nanometres.

Researchers at the Fresnel Institute in Marseille and ICFO-the Institute for Photonic Sciences in Barcelona report in *Nature Nanotechnology* the design and fabrication of the smallest optical device, capable of detecting and sensing 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 dimer antenna made out of two gold semi-spheres, separated from each other by a gap as small as 15nm. 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. A second trick that the researchers used to make this device work was to embed the dimer antennas inside boxes also of nanometric dimensions. "The box screens out the unwanted "noise" of millions of other surrounding molecules, reducing the background and improving as a whole the detection of individual biomolecules.", explains Jerome Wenger from Fresnel Institute. 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 = 10-21L), i.e., the smallest observation volume in the world.

The antenna-in-a-box offers a highly efficient platform for performing a multitude of nanoscale biochemical assessments with single molecule sensitivity at physiological conditions. It could be used for ultrasensitive sensing of minute amounts of molecules, becoming an excellent early diagnosis device for biosensing of many disease markers. "It can also be used as an ultra-bright optical nanosource to illuminate molecular processes in living cells and ultimately visualize how individual biomolecules interact with each other. This brings us closer to the long awaited dream of biologists", concludes ICFO researcher Prof. Maria Garcia-Parajo.

More information: D. Punj, M. Mivelle, S. B. Moparthi, T. S. van Zanten, H. Rigneault, N. F. van Hulst, M. F. Garcia-Parajo, J. Wenger, "A plasmonic 'antenna-in-box' platform for enhanced single-molecule analysis at micromolar concentrations" *Nature Nanotechnology* DOI: 10.1038/NNANO.2013.98

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