ICFO



# THESIS DEFENSE: Advanced Nanoantenna Platforms for Enhanced Single-Molecule Detection at High Concentrations

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September 13, 2024

10:00

Auditorium

The ability to study the dynamics of individual biomolecules is crucial to understanding the complex organization of biological systems beyond what can be learned from ensemble averages. These single-molecule dynamics often occur at high micro- to millimolar concentrations, where conventional optical techniques cannot isolate single molecules anymore due to fundamental physical laws. This thesis explores the design, fabrication, and application of advanced nanoantenna platforms to detect individual fluorescent molecules at such high concentrations with increased sensitivity.

Here, the theoretical groundwork is provided to understand the interactions between

fluorescent molecules and nanoantennas. It is discussed how the single-molecule detection sensitivity of nanoantenna platforms can be quantitatively assessed through analytical models and numerical simulations. Based on these quantitative models, antenna-in-box platforms are identified to provide superior sensing performance and suitable lithography processes for their fabrication are established.
Both computational and experimental evidence are presented that cleverly combining materials in hybrid antenna-in-box platforms enhances single-molecule detection sensitivity at micromolar concentrations. This improvement is attributed to decreased background signals and the use of previously unexplored coupling mechanisms inherent in the antenna-in-box architecture. Furthermore, hexagonal close-packed antenna-inbox platforms are introduced to enable highly parallelized single-molecule detection at micromolar concentrations. Notably, these hexagonally ordered platforms constitute the first demonstration of antenna-in-box platforms capable of single-molecule detection across the visible spectral range. Lastly, a correlative approach is presented that combines nonlinear fluorescence and vibrational spectroscopy to study the organization of receptor proteins in the cell membrane of living cells using nanoantennas. Measures to protect both the nanoantennas and the living cells are discussed and their effectiveness is validated. Overall, this thesis presents novel approaches for studying single-molecule dynamics at high concentrations with enhanced sensitivity. The development of these approaches was enabled through analytical and numerical modeling, the creation of new fabrication processes, and the use of appropriate experimental methods.
These advancements promise to offer previously inaccessible insights into dynamics within biological systems.

**Friday September 13, 10:00 h. ICFO Auditorium**
**Thesis Director: Prof. Dr. Maria Garcia-Parajo**
**Hosted by:** Prof. Dr. Maria Garcia-Parajo