

Single molecule biosensing at the quantum limit

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Sensors that are able to detect and track single unlabelled biomolecules are an important tool both to understand biomolecular dynamics and interactions, and for medical diagnostics operating at their ultimate detection limits. Recently, exceptional sensitivity has been achieved using the strongly enhanced evanescent fields provided by optical microcavities and plasmonic resonators [1,2]. However, at high field intensities photodamage to the biological specimen becomes increasingly problematic [3]. Here, we introduce a new approach to evanescent biosensing that combines dark field illumination and heterodyne detection in an optical nanofibre-based platform [4]. This allows operation at the fundamental precision limit introduced by quantisation of light. We achieve state-of-the-art sensitivity with a four order-of-magnitude reduction in optical intensity. This enables quantum noise limited tracking of single biomolecules as small as 3.5 nm and surface-molecule interactions to be monitored over extended periods. This opens the door to study the nanoscale machinery of life in its native state, without requiring either labels or photointrusion, including motor molecules such as myosin, kinesin and ATPase. By achieving quantum noise limited precision, our approach provides a pathway towards quantum-enhanced single-molecule biosensors.

- [1] M. D. Baaske, M. R. Foreman and F. Vollmer, *Nature Nanotechnology* 9 933-939 (2014).
- [2] Y. Pang and R. Gordon, *Nano Letters* 12 402-406 (2012).
- [3] See e.g. U. Mirsaidov, W. Timp, K. Timp, M. Mir, P. Matsudaira and G. Timp, *Phys. Rev. E.* 78 021910 (2008).
- [4] N. P. Mauranyapin et al. arxiv:1609.05979 (2016).