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Optoplasmonic detection of single particles and molecules in motion

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Conclusion and outlook

This thesis is focused on investigation of label-free detection of single molecules and proteins. We use high-speed optoplasmonic method to detect diffusing single particles and molecules. Chapter 2 introduces a photothermal spectro-microscopy as a tool for the characterization and optimization of optoplasmonic detection assays. In chapter 3, we used an immobilized gold nanorod as a plasmonic sensor and measure interferometric plasmonic scattering which enables us to detect single proteins as they diffuse through the near field. Chapter 4 provides an investigation and characterization of rotational diffusion of single gold nanorods. In chapter 5 we study plasmonic coupling of an immobilized gold nanorod as a sensor and tiny diffusing gold nanorods as analytes toward plasmonic goniometer.

Photothermal as benchmark for optoplasmonic bio-detection We provide a measurement of the optoplasmonic bio-detection as an assay to probe the response of plasmonic nanostructures by changes in their dielectric environment. In chapter 2 we introduce photothermal spectro-microscopy as a benchmarking tool for the characterization and optimization of optoplasmonic detection assays. We have performed this optimization for the case of gold nanorods and showed that the photothermal signal-to-noise ratio (SNR) scales directly with the SNR found for average perturbations caused by small nanodroplets entering and exiting a NR's near field.

Transient optoplasmonic detection of single proteins We read out changes in the resonantly scattered field of individual gold nanorods interferometrically and use photothermal spectroscopy to optimize the experiment's parameters. This interferometric plasmonic scattering enables the observation of single proteins as they

traverse plasmonic near fields of gold nanorods with unprecedented temporal resolution in the nanosecond-to-microsecond range. We think that analyzing such short unspecific interactions opens up a new pathway to gain physical properties and structural information of analytes. In chapter 3 we have performed transient detection of single proteins with 64 kDa mass passing through the plasmonic near-field volume of single gold nanorod during times as short as 100 ns and with an SNR exceeding 5.

Measurement of rotational diffusion We record dark-field scattering bursts of individual gold nanorods, freely diffusing in water suspension. We have performed the measurement and analysis with high enough statistics. The selection of resonant plasmonic nanorods based on the wavelength of the laser, produces comparatively narrow histograms of tumbling times. The narrow histogram provides sensitivity to changes in temperature, viscosity and hydrodynamic volume of the particles. We have extracted rotational diffusion constants from crossed- or parallel-polarization measurements, which have provided consistent results in good agreement with theory and dimensions of the nanorods measured by TEM. As an example of a local change of temperature and viscosity of the solvent, we investigated the effect of laser power on the rotational diffusion of the GNRs. The effect of heating is moderate at low power, but becomes more and more pronounced at high powers as a shortening of the tumbling times of the largest and/or most resonant rods, which also are the hottest ones. A second use of rotational diffusion we have investigated tumbling time histograms in presence of a very low concentration of PVA, which binds to gold nanorods. We find a saturation of adsorption at about 100 ppm, the process being well described by a Langmuir isotherm. These observations allows the possibility to use tumbling nanorods as probes for low concentrations of ligands, provided specific receptors can be attached covalently to their surface. We think detailed studies of rotationally diffusing plasmonic probes would reveal specific adsorption sites and local mobilities with high resolution in time and space.

Plasmonic goniometers In chapter 5 we examined the possibility to detect conformational changes through precise angle measurements, by so-called plasmonic goniometers. As building such a component is very challenging, we chose to study the rotational diffusion of plasmonic gold nanorods as analytes instead and demonstrate a study of rotational diffusion via opto-plasmonic sensing by a large gold nanorod as a sensor. The rotational diffusion of such analytes can be observed in dark-field scattering, in bright-field scattering close to an interface, or through opto-plasmonic coupling to another plasmonic particle, as a sensor gold nanorod. We found that

the detectivity for angle changes in these three configuration is of the same order, about $1 \times 10^{-3} \text{ deg}/\sqrt{\text{Hz}}$ with a slight advantage for the opto-plasmonic detection compared to the other two methods. Finally, we performed simulation and showed opto-plasmonic scattering signals of free rotational diffusion of dielectric nanoparticles such as protein molecules are about 500-1,000 times weaker than those of (resonant) plasmonic particles for comparable sizes, a few tens of nanometers. To directly discern 90° differences in molecular alignment would require integration times on the order of $\approx 60 \mu\text{s}$.

