Optofluidic microstructured fibers: a nanoparticle tracking analysis platform for understanding nanoscale objects such as SARS-CoV-2

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Abstract: Understanding nanoscale processes at the single-species level is highly relevant for many areas. Here, we will present the details of fiber-assisted nanoparticle tracking analysis and show various experimental results relying on microstructured fibers.

Introduction: Unlocking processes of entities with nanometer dimensions at the single species level is of utmost importance for a vast number of applications, examples of which include virus-induced infectious diseases or the development of novel vaccinations. Therefore, concepts for detecting and identifying individual nanoscale species that are unlabeled and exposed to their natural environment are in high demand to reach new levels in understanding nanoscale processes, which cannot be achieved by state-of-the-art technology. Here, optical technology principally allows for the non-invasive and fast detection of minuscule objects, while current methods reveal drawbacks such as immobilization or object labeling. Moreover, direct microscopic characterization of nanoparticles (NPs) is unfeasible if the diameters of the nano-objects fall below the diffraction limit. One approach applied in this context is dynamic light scattering (DLS), evaluating the diffusive properties of ensembles of NPs, and thus not allowing obtaining information at the individual NP level.

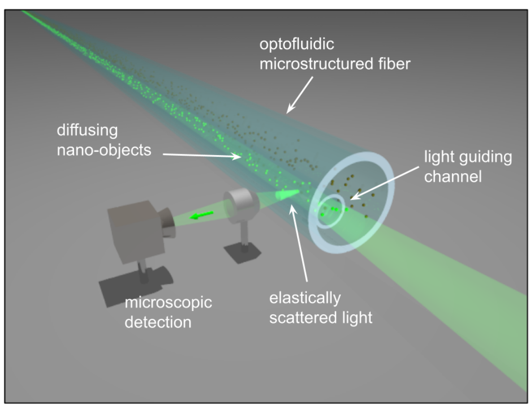

Fig. 1: Sketch of one realization of fiber-assisted NTA (FaNTA), including nano-objects that diffuse into the light-guiding channel, elastically scattered light and microscopic detection.

A conceptually different approach that operates at the single species level is nanoparticle tracking analysis (NTA). This technology statistically evaluates individual NP trajectories, making it possible to characterize small NP concentrations and polydisperse samples. Examples of successful NTA applications include characterization of viruses, extracellular vesicles or nanomotors, or pharmaceutical quality control. Note that crucial to NTA is the correlation between achievable accuracy of determined diameter and trajectory length (i.e., no. of frames per trajectory), suggesting to use approaches that enable the acquisition of as-long-as-possible trajectories.

Elastically scattered light has proven to be advantageous for NTA. Here, the scattered light from individual NPs is microscopically detected, allowing to follow the NPs with fast time resolution to obtain the NP's trajectory. As mentioned, the accuracy of the statistical analysis depends on the length of the trajectory, representing one of the main challenges in the field. It is crucial that the NP is kept in the microscope's field-of-view for as long as possible, which is a major challenge, especially in freely diffusing systems.

A novel NTA approach introduced by the author is based on tracking NPs in microstructured optical fibers (Fig. 1) [1], defining the concept of fiber-assisted NTA (FaNTA). The key feature of FaNTA is the confinement of NPs in fiber-integrated microchannels, leading to high-intensity light line illumination through the optical mode. Particularly relevant is confinement of the NPs to the light-guiding sections, preventing NPs from leaving the illuminated field-of-view or the focal plane of the microscope. This results in exceptionally long observation times (i.e., trajectories with very large number of frames) of rapidly diffusing objects, leading to high statistical significance in determined diameter, even for very small NPs [2]. In the following, we will outline our key achievements in the field of FaNTA:

3D tracking in modified step index fibers [3-5]: In conventional NTA experiments, the position of NPs can normally only be detected in the image plane, while it is not possible to determine the position along the axis of the microscope. By correlating the intensity of scattered light and position in the evanescent fields, optical fibers enable axial position retrieval within microfluidic channels that run parallel to an optical core. This method enables the acquisition of information about diffusing nanoscale objects in all three spatial dimensions at an acquisition rate of kHz over several seconds. With this method, we achieve spatial localization accuracies of <3 nm along the transverse and <21 nm along the retrieved directions.

Tracking in flat field fiber [6]: A typical challenge in commonly used NTA implementations is a transversally decreasing intensity of the excitation light, which can lead to insufficient scattering intensities. Here, we present a solution by generating flat fields in optofluidic fibers that contain a central nanohole. By adjusting the waveguide parameters, i.e., reaching a situation in which the effective mode index equals the refractive index of the cladding, it is possible to generate a constant intensity in all three spatial directions - a light strand - within a liquid-filled nanochannel. The advantageous properties of this light strand in the context of FaNTA will be demonstrated.

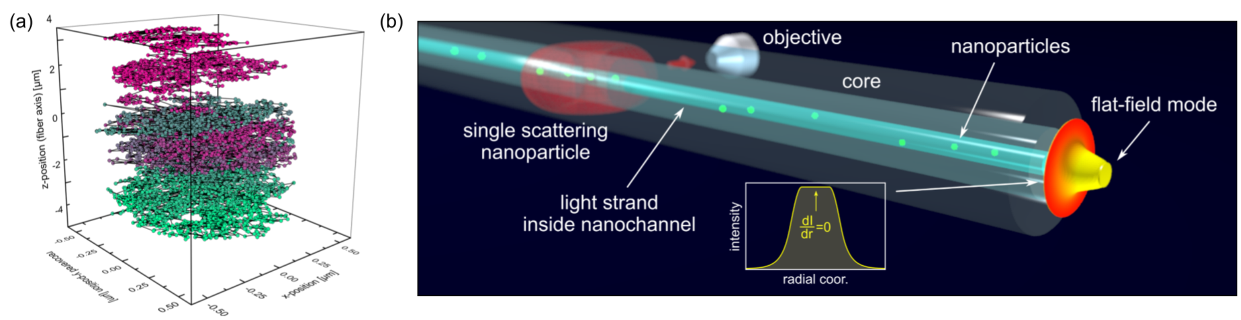

Fig. 2: Examples of tracking with evanescent field. (a) Record-long 3D trajectory of a 40nm gold nanosphere diffusing inside a step-index fiber that contains a nanochannel that runs parallel to an optical fiber core [3]. (b) Illustration of flat-field formation inside the optofluidic channel of a nanobore step-index fiber [6].

Tracking in anti-resonant fibers [2, 7, 8]: In addition to tracking with evanescent fields, hollow-core fibers provide an important and promising platform for FaNTA. Here, diffusing NPs are detected directly in the light guiding microchannel by illuminating them with the optical core mode, enabling the detection of the trajectories through elastic light scattering. In contrast to fibers with nanochannels, these fibers enable the analysis of ensembles of NPs due to the significantly larger core diameter, which is particularly interesting from an application standpoint. The recording of exceptionally long trajectories of a large-scale ensemble of NPs is possible. Here, an effective single-mode antiresonant element fiber was employed to efficiently confine NPs to the light-conducting channel and track them individually over more than 1000 images. Unique features of the approach are (i) the high-precision determination of the size distribution of monodisperse nanoparticle ensembles and (ii) the accurate characterization of individual components in a bimodal mixture with very closely spaced mean diameters.

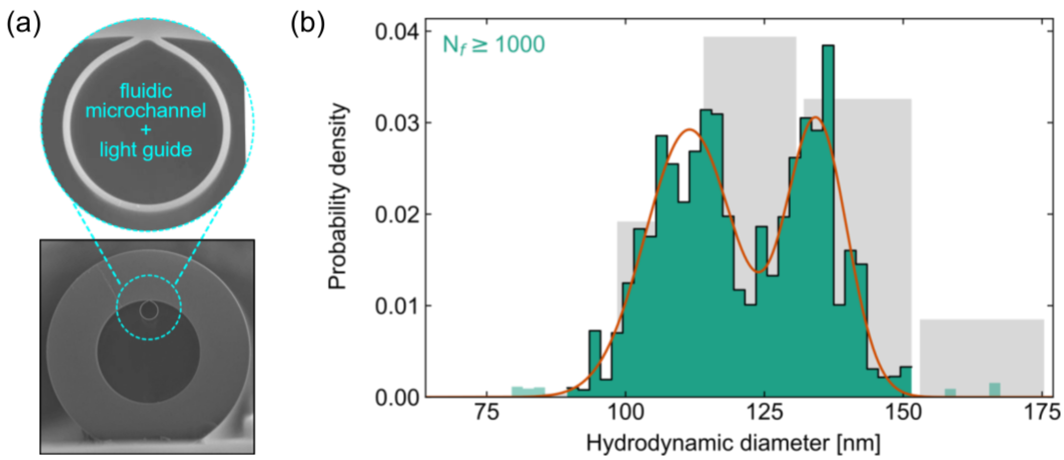

Fig. 3: Tracking inside a fiber that contains one anti-resonant element [8]. (a) SEM of the cross-section of the fiber. (b) Characterization of a bimodal solution of polymeric nanoparticle having very close mean diameters (100 nm and 125 nm).

Conclusion: In this presentation, the recent results of our group in the field of tracking single nano-objects in optofluidic microstructured optical fibers using elastic light scattering - FaNTA - have been discussed. Based on the unique properties of FaNTA, application of this concept can be envisioned in a multiple of fields, including life science, nanomedicine, or nanorheology.

References

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