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Meeting-report

Live-imaging and Quantification of Complex Nanostructure Hydrodynamic Motion in 3D Using Liquid Phase Transmission Electron Microscopy

Murat Nulati Yesibolati[1],*, Agnese Callegari[2], Jesús Pineda[2], Giovanni Volpe[2], Maciej Lisicki[3], and Kristian Mølhave[1]

[1]*National Centre for Nano Fabrication and Characterization, Technical University of Denmark, Lyngby, Denmark*
[2]*Department of Physics, University of Gothenburg, Göteborg, Sweden*
[3]*Institute of Theoretical Physics, Faculty of Physics, University of Warsaw, Warsaw, Poland*

*Corresponding author: nuye@dtu.dk

Brownian motion is essential to many diffusion and mass transport processes in physics, chemistry, and biology. It was only recently that theoretical models were developed for Brownian motion of non-spherical and simpler structures, such as rods, ellipses, and compared to experimental studies on micrometer-sized particles [1, 2]. Traditionally, imaging of such diffusion processes have been limited to optical microscopy (OM). However, the "particles", such as colloidal nanoparticles and their agglomerates, cells, bacteria, and viruses, has relatively complex structures and many are at or with features on the nanometer scale. It is straightforward to visualize the translational dynamics of arbitrary shapes with sub-nanometer precision using OM, however, it is far more challenging to directly visualize their rotational dynamics. The theoretical models may not be able to accurately predict translational and rotational processes on the nanoscale, particularly with arbitrary shapes in which translational and rotational motions often are coupled.

Liquid-phase transmission electron microscopy (LPTEM) has revolutionized the access to nanoscale, label-free imaging of a wide variety of processes in liquid with sub-nanometer spatial and millisecond temporal resolution [3]. Nanoparticle nucleation, growth, interaction, and diffusion near the liquid-solid interface [4] as well as in bulk liquid [5] have all been examined using LPTEM, which provides many intriguing details that are otherwise impossible to observe using other imaging methods [6].

This work presents for the first time the rotational and translational dynamics of complex nanostructures using LPTEM in a scanning mode. Capturing Brownian motion of complex nanostructures: Gold nanoparticle suspension (60 wt% glycerol/water solution) was drop-casted in a custom-made LPTEM cell as shown in Figure 1a. The electron beam was used to induce the formation of complex particle agglomerate nanostructures (dimer, trimer, tetramer, T shape or any other complex shapes as in Figure 1a). This step avoids pre-synthesizing complex nanostructures outside TEM, and provides flexibility for generating different complex shapes. The structures' Brownian motion was captured by a high-angle annular dark-field (HAADF) detector. To characterize the translational diffusion process of the moving complex nanostructures, we tracked them by determining their centroids in each frame of the time-lapse imaging as shown in Figure 1b (only the dimer is shown as an example) and calculated the translational diffusion constant. The diffusion constant in x,y directions is around 0.13 ± 0.02 um^2s^{-1}(Figure 1c) which is slightly smaller than the theoretical value based on a simple ellipsoid model [7].

Rotational dynamic: To estimate the rotational diffusion constant, 3D structures of the complex nanostructures were reconstructed using single particle analysis (SPA) which is commonly used in cryo-TEM [8]. For an arbitrary shape, there are three rotational diffusion coefficients. The dimer in Figure 1d, however, has high symmetry $D_{\infty h}$, and can be characterized by one the rotational diffusion coefficient of the major axis (unit vector Z as in Figure 1d) and the rotation around it which however is not resolved in the image series. The end of the Z unit vector was projected onto a unit sphere (Figure 1e) and used to calculate the mean square angular displacement (MSAD) as shown in Figure 1f. The rotational diffusion constant is 2.3 ± 0.2 s^{-1}, which is 3 times smaller than the simple ellipsoid model predictions of the major axis rotation [9].

Both the translational and rotational diffusion constants of a dimer are smaller than that of an ellipsoid model. Of course beam induced radiolysis may also have strong effects, but have so far only been seen to increase the diffusion constants [5], hence the actual rotational diffusion may be even lower. The lower diffusion is likely mainly caused by the geometrical confinement, and/or possibly because the simple ellipsoid model could not well describe the nanoscale diffusion process of a dimer, which may require improvements in hydrodynamic modelling [7]. This line of research aims to support developing such improved models, and with LPTEM one can measure translational and rotational correlation functions which can be directly compared to exact theoretical predictions [10, 11].

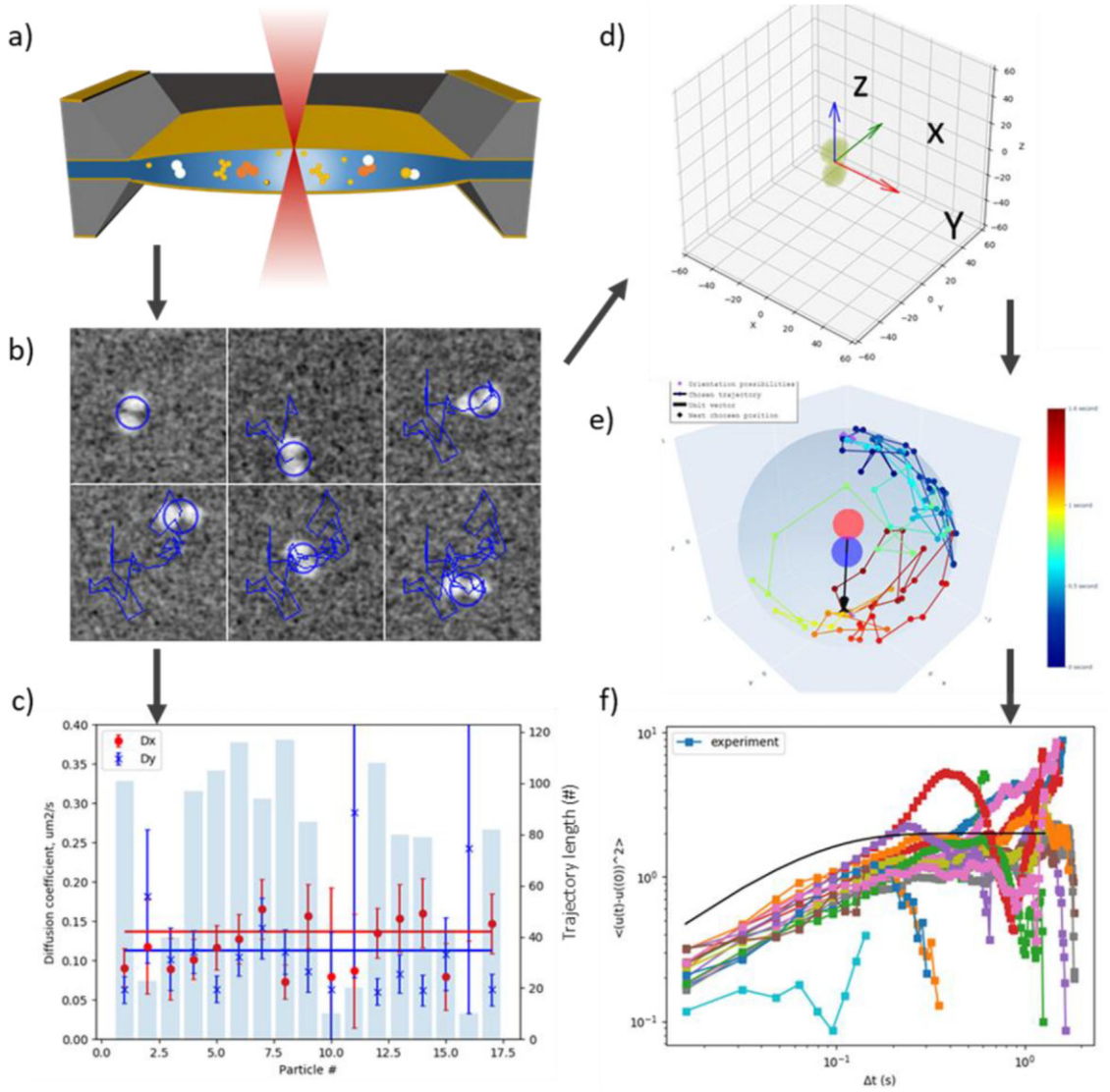

Fig. 1. a) A custom-made LPTEM cell, nanostructures with complex shapes are shown in between two electron transparent silicon nitride membranes with a scanning beam. The dimensions are not scale. b) time series and trajectories of a dimer nanoparticle rotating and diffusing in a liquid cell. The frame rate is 63 FPS, and the pixel resolution is 9 nm. c) Diffusion coefficients and trajectory lengths of individual dimer. d) Reconstructed 3D model of the dimer from images sequences from b. e) MSAD of the unit vector Z, the black solid line is theoretical MSAD from a simple ellipsoid model.

References

1. A Chakrabarty *et al.*, *Physical Review Letters* **111** (2013), p. 160603. doi:10.1103/PhysRevLett.111.160603
2. Y Han *et al.*, *Science* **314** (2006), p. 626. doi:10.1126/science.1130146
3. FM Ross, *Science* **350** (2015), p. aaa9886. doi:10.1126/science.aaa9886
4. SW Chee *et al.*, *The Journal of Physical Chemistry C* **120** (2016), p. 20462. doi:10.1021/acs.jpcc.6b07983
5. MN Yesibolati *et al.*, *Nano Letters* **20** (2020), p. 7108. doi:10.1021/acs.nanolett.0c02352
6. SF Tan *et al.*, *Accounts of Chemical Research* **50** (2017), p. 1303. doi:10.1021/acs.accounts.7b00063
7. M Hoffmann *et al.*, *ACS Nano* **3** (2009), p. 3326. doi:10.1021/nn900902b
8. T Wagner *et al.*, *Communications Biology* **2** (2019), p. 218. doi:10.1038/s42003-019-0437-z
9. J Fung *et al.*, *Optics Express* **19** (2011), p. 8051. doi:10.1364/OE.19.008051
10. B Cichocki *et al.*, *The Journal of Chemical Physics* **142** (2015), p. 214902. doi:10.1063/1.4921729
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