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Single molecule diffusion studies of mesoporous materials: From material science to drug-delivery applications

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Diffusion is an essential process in chemistry, physics and biology. The investigation of these processes is mostly accomplished by measuring a large number (ensemble) of the diffusing species. Therefore, diffusion dynamics, such as the diffusion coefficient, are obtained by averaging over the properties of many particles measured at the same time. Recently, single molecule (SM) experiments, where the motion of a single particle is directly observed over a sufficiently long time interval, provided a totally new view on diffusion. In detail, subpopulations, rare events and the influence of heterogeneities of the structural surrounding on the diffusing particles can be revealed.

A thorough understanding of the diffusing particles within their surrounding is vital for the development of customized host-guest systems for nanotechnology applications. Mesoporous silica materials are ideally suited as host systems with possible applications ranging from molecular sieves, catalysts, nanosensors to drug delivery systems. Here, we investigate these host-guest interactions using single molecule spectroscopy (SMS) and study the dynamics of single terrylene diimide (TDI) dye molecules in mesoporous silica films, filaments and particles.[1,2] The diffusion behaviour in the mesoporous host is represented by the trajectories of the single molecules. These trajectories are highly structured and thus provide information about the host structure, such as domain size or the presence of defects and dead-ends (Fig.1a).

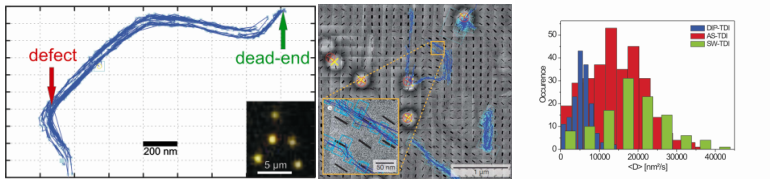

Figure 1: a) Highly structured trajectory of a single TDI molecule travelling inside hexagonal mesoporous channels. The inset displays a wide-field fluorescent image extracted from a movie showing single TDI molecules diffusing in a hexagonal mesoporous film. b) Overlay of single molecule trajectories on TEM images obtained by fitting and overlaying the positions of polystyrene bead markers. c) Histogram of the mean single molecule diffusion coefficients *D* extracted from the linear part of the individual MSD plots for three TDI derivatives in a hexagonal mesoporous film.

Moreover, the obtained single molecule trajectories can be directly compared to the real structure of the mesoporous host by plotting an overlay of the trajectories and TEM images of the same area of interest (Fig.1b).[3]

The diffusion coefficient for each single molecule can be extracted from the linear part of the mean square displacement (MSD) plots according to the Einstein-Smoluchowski relation $< r^2 (t) > = 2dDt$, where d indicates dimensionality (Fig.1c).

Mesoporous materials can be structurally tuned to a large degree and also functionalized at the pore walls with numerous chemical functional groups. Therefore, they are able to incorporate a large variety of different guest molecules. We used mesoporous filaments as carriers for fluorescently labeled ss- and ds-DNA. Förster-Resonance-Energy-Transfer (FRET) measurements showed that the DNA is still intact inside the mesopores. Moreover, we were able to observe DNA diffusion inside the mesopores of the filaments. In another approach, mesoporous silica nano-particles were used as drug-delivery devices for controlled colchicine release into HuH7 cells.[4,5] After about 2h, the microtubules were depolymerized and finally the cell morphology was completely disintegrated (Fig.2).

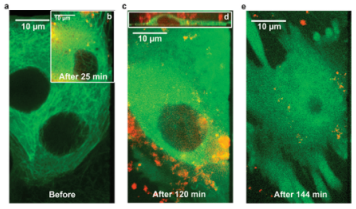

Figure 2: Drug delivery by colchicine loaded silica nanoparticles to HuH7 liver cancer cells. a) Untreated HuH7 cells with a GFP-labeled well-structured microtubule network (green). b) HuH7 cells were exposed to colchicine-loaded silica nanoparticles for 25 min. The microtubule network still appears to be intact. c) After 120 min, the microtubule network disappeared and a diffuse fluorescence due to microtubule depolymerization was observed. d) Side view of the HuH7 cell represented in panel c, where the internalized nanoparticles (yellow) are visible. Several other nanoparticles (red) are on the top of the cell. e) After 144 min the cell morphology was disintegrated, confirming cell death.

References

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