Mass Measurements Reveal Preferential Sorption of Mixed Solvent Components in Porous Nanoparticles

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Porous nanoparticles are a unique class of materials that open many new opportunities in fields ranging from drug delivery and sensing to catalysis, green chemistry, and energy conversion. Their physicochemical properties, in particular their morphology, surface charge, composition, porosity, and extremely high surface-to-volume ratio, are of paramount importance in defining their potential applications. Therefore, it is necessary to precisely control and measure these parameters.

Several characterization methods can be used to probe nanoparticles. Nano-meter-scale resolution on particle morphology and crystallinity can be obtained using solid-state approaches (e.g., electron microscopy and X-ray diffraction). However, these methods can only be used on dry samples, and thus they cannot account for interactions between the nanoparticles and the suspending solution. Mobility-based methods (e.g., dynamic light scattering) are commonly used to measure the hydrodynamic radius and zeta-potential of nanoparticles in liquids. Mobility, however, does not vary significantly with the internal state of nanoparticles, such as the filling of the pores. Therefore, pore volume, pore accessibility, and the internal affinity to specific gases are currently only probed in the dry state (e.g., nitrogen adsorption and helium pycnometry), or by the indirect measurement of the adsorption of probe molecules dissolved in solvents of different polarity.

To circumvent this limitation, we used nanomechanical mass correlation spectroscopy (MCS) to measure the effective mass density of metal–organic framework (MOF) nanoparticles in different solvent systems. In this approach, the MOF nanoparticles are dispersed in a range of binary solvent systems and the mass fluctuations resulting from the flow of this suspension through a suspended microchannel resonator (SMR) mass sensor of 10 pL volume are measured (1 pL = 10−12 L).

Figure 1. We used materials institute la voster (MIL)-101(Cr) MOF nanoparticles with different inner pore functionalizations and suspended them in binary mixtures of ethanol and water, and methoxyperfluorobutane (HFE-7100) and ethanol (EtOH). Based on geometry alone, these modifications of the solvent systems and of the functionalization of the pores are not expected to change the mass of the nanoparticles. The observed differences therefore provide new information about the specific interaction between the different solvent components and the internal surface.

MIL-101(Cr) nanoparticles are mesoporous MOF nanoparticles featuring two types of cages with respective diameters of 2.9 and 3.4 nm, and an accessible window of 1.2 and 1.4 nm. Here, we have examined the effective density of three different MIL-101(Cr) species: MIL-101(Cr) nanoparticles and MIL-101(Cr) derivatives functionalized at the coordinately unsaturated metal sites with pyridine or pyrazine using postsynthetic modification. The crystallinity, porosity, and morphology of the MIL-101(Cr) nanoparticle species were investigated with powder X-ray diffraction (PXRD) (Figure S3,
Supporting Information), nitrogen adsorption/desorption isotherms (Table S6, Supporting Information), transmission and scanning electron microscopy, TEM, Figures S4–S7, Supporting Information; SEM, Figures S8–S13, Supporting Information), respectively. We characterized the nanoparticles using both SEM of dried ethanolic suspensions, resulting in a size distribution of $d_{SEM} = (41 \pm 10)$ nm (Figures S14–S16, Supporting Information), and dynamic light scattering (DLS) in ethanol yielding in a hydrodynamic diameter of $d_{DLS} = (105 \pm 31)$ nm (Figure S18, Supporting Information).

The density of MIL-101(Cr) nanoparticles was measured using both apolar and polar solvents to probe the behavior of particles when exposed to different solvent mixtures (Figure 1). Surprisingly, the effective mass density of the particles depends significantly on the solvent system. In the relatively apolar mixture of HFE-7100 with EtOH, MIL-101(Cr) nanoparticles present a density $\rho_{HFE/EtOH}^{\text{eff}} = 1.25 \pm 0.02$ g cm$^{-3}$ (Figure 1b), while their density increases to $\rho_{EtOH/Water}^{\text{eff}} = 1.77 \pm 0.12$ g cm$^{-3}$ (Figure 1c) in the more polar mixture of ethanol with an aqueous buffer ($50 \times 10^{-3}$ M Glycine-HCl, pH 2.5). Both values are much larger than the mass density of the empty framework, which can be calculated from the crystal structure as $\rho_{\text{empty}} = 0.66$ g cm$^{-3}$ (Figure S21, Supporting Information).

Next, we modified MIL-101(Cr) nanoparticles using a postsynthetic grafting approach. The coordinatively unsaturated chromium sites (Lewis acid sites) are used to coordinate Lewis bases, pyrazine or pyridine, to render the particles more hydrophilic or hydrophobic, respectively (Figure 2). As for the unfunctionalized MIL-101(Cr) nanoparticles,
The measurements were carried out in mixtures of HFE-7100/EtOH and of $50 \times 10^{-3}$ M Glycine-HCl/EtOH to detect both the particle densities and their permeability to the solvents in solution. Measurements in the HFE-7100/EtOH mixtures return an effective density of $1.31 \pm 0.03$ g cm$^{-3}$ for the pyrazine-functionalized particles and $1.30 \pm 0.05$ g cm$^{-3}$ for the pyridine-functionalized particles. These results are in line with the values found for the unfunctionalized MIL-101(Cr) nanoparticles. More pronounced differences are detected when measuring the density of the functionalized nanoparticles in the polar mixture. For the pyrazine-functionalized nanoparticles, we find a surprisingly high effective density of $1.42 \pm 0.06$ g cm$^{-3}$ in the mixture of ethanol and water (Figure 2b). As for the measurements of the unfunctionalized MIL-101(Cr) nanoparticles, the uncertainty on the effective density increases with the value of the estimated density. In contrast, the pyridine-functionalized nanoparticles show a drastic decrease in effective density to $1.12 \pm 0.02$ g cm$^{-3}$ when suspended in the same mixture (Figure 2d). The lower effective density may be due to an increased ethanol content within the particles. This could occur due to particle aggregation with concomitant inclusion of ethanol in the interstitial volume and/or due to the formation of an ethanol solvation layer surrounding the nanoparticles. In both cases, the ethanol fraction may be locally increased in the aqueous mixture because of the hydrophobic functional groups presented both on the inner and outer surface of the nanoparticles. This hypothesis is supported by DLS measurements of the nanoparticles suspended in the two mixtures: the nanoparticles in ethanol have a hydrodynamic diameter of 96 nm (polydispersity 18%), while their size increases to 149 nm (polydispersity 40%) in a 95% $50 \times 10^{-3}$ M Glycine-HCl/5% ethanol mixture.

The density estimations obtained for the different cases of MIL-101(Cr) nanoparticles when suspended in the different solvent mixtures are summarized in Table 1. The observed dependence of mass density on the chemical identity of the solvent in MOF nanoparticles can be understood by considering the possible interactions of the solvent components with the pore volume. Our measured correlation signal $C(0)$ represents the variance of the resonance frequency fluctuations of the SMR. This is directly proportional to the variance of mass fluctuations arising from Poisson statistics, i.e., $C(0) \sim c_0 V \frac{\partial \rho}{\partial c}$, where $c_0$ denotes the solid concentration, $V = 10$ pL is the volume, and $\frac{\partial \rho}{\partial c}$ is the density increment of the solution at constant chemical potential. In the simplest case, when particles are described as hard spheres, the density increment follows Archimedes’ law

$$\frac{\partial \rho}{\partial c} = 1 - \frac{\rho_s}{\rho_{\text{eff}}}$$

Table 1. Summary of density estimations for the functionalized and unfunctionalized MIL-101(Cr) MOF nanoparticles in the different solvent mixtures.

| MIL-101(Cr) functionalization | Solvent mixture | | | |
|-----------------------------|-----------------|-----------------|-----------------|-----------------|
|                             | EtOH/HFE [g cm$^{-3}$] | EtOH/50 $\times$ 10$^{-3}$ M Glycine-HCl [g cm$^{-3}$] |
| Unfunctionalized            | 1.25 $\pm$ 0.02 | 1.77 $\pm$ 0.12 |
| Pyrazine-functionalized     | 1.31 $\pm$ 0.03 | 1.42 $\pm$ 0.06 |
| Pyridine-functionalized     | 1.30 $\pm$ 0.05 | 1.12 $\pm$ 0.02 |
the following expression for the density increment by the fixed mass of adsorbed solvent molecules. This leads to solvent components. The dry mass of the particle is increased fixed and given by specific adsorption or exclusion of individual components (light yellow) can access a larger portion of the internal volume than the other.

\[ \rho'_{\text{eff}} = \frac{1 + B_A + B_B}{\rho_f + B_A \rho_A + B_B \rho_B} \]  

where \( \rho_f \) is the mass density of the solvent and \( \rho_{\text{eff}} \) denotes the mass density of the solid, which is equal to the inverse partial specific volume of the particles. In this case, the autocorrelation curve presents zero amplitude when the density of the suspending solution matches the density of the particles.

Porous nanoparticles present a fundamentally different behavior. In solution, their effective density depends not only on their dry mass and volume but also on the ability of the solvent to access the pore volume. There can be significant differences in pore accessibility for different solvent components due to size exclusion and more complex interactions, such as solvation effects and gating. All of these phenomena may alter the effective mass density of the particles and necessitate an extension of the pure physical/geometric description, which is inherent to Archimedes’ principle.

To explain the range of the observed differences, we represent the pore volume by two compartments, as shown in Figure 3. Note that this is done only for modeling purposes; in reality, there need not be a defined physical boundary. In the first compartment (light blue) the solvent composition tracks the composition outside the pore exactly. In contrast, the composition in the second compartment (blue/yellow in Figure 3) is fixed and given by specific adsorption or exclusion of individual solvent components. The dry mass of the particle is increased by the fixed mass of adsorbed solvent molecules. This leads to the following expression for the density increment

\[ \frac{\partial \rho'}{\partial c} \bigg|_{A,B} = (1 + B_A + B_B) \left( 1 - \frac{\rho_f}{\rho'_{\text{eff}}} \right) \]  

Experimental Section

Density Measurements: Density of particles in solution is measured by detecting the variation of buoyant mass when the particles are suspended in mixtures of different concentrations of ethanol and 50 × 10⁻³ M Glycine-HCl (pH = 2.5) or ethanol and HFE-7100. The test solutions are injected into a suspended microchannel resonator featuring an embedded channel with a cross-section of 3 × 8 μm². The resonance frequency of the resonator is measured by using
an optical-lever detection scheme (see Figure S1, Supporting Information, for more information on the experimental setup). During the measurement, particle concentration is kept constant to simplify the subsequent data analysis process. As the buoyant mass of the particles is proportional to the induced frequency fluctuations, the time-domain mass signal is first high-pass filtered (cutoff frequency = 1 Hz) to remove slow-term-noise fluctuations, caused by temperature and/or mechanical variations. Frequency fluctuations are then analyzed by use of an autocorrelation analysis of the high frequency domain to minimize the effect of the uncorrelated readout noise background. The effective density of the particles is calculated after fitting the autocorrelation amplitude as a function of solution density, with the estimated particle density corresponding to the minimum of the fitting parabola. Therefore, the uncertainty on density estimation depends on the range of solution densities accessed during the measurement. More information on and validation measurements of the density characterization method are reported in the Supporting Information.

**Synthesis of MIL-101(Cr) Nanoparticles:** The synthesis of MIL-101(Cr) was conducted using microwave (MW) assisted synthesis.\(^2\)\(^3\) A mixture of Cr(NO\(_3\))\(_3\) · 9H\(_2\)O (1.48 g, 3.70 mmol) and terephthalic acid (0.615 g, 3.70 mmol) was added to water (20 mL) and stirred until all Cu(NO\(_3\))\(_3\) · 9H\(_2\)O was dissolved. Subsequently, the reaction mixture was placed in a Teflon vessel (80 mL) and sealed. The tube was placed in a microwave oven (Synthos 3000, Anton-Paar) along with 3 other vessels, two of them filled with water (20 mL) and one acting as control vessel and filled with an aqueous Cu(NO\(_3\))\(_3\) · 9H\(_2\)O (1.48 g, 3.70 mmol) solution. The solutions were first heated for 4 min to reach 210 °C and then were kept for 2 min at this temperature. A cooling phase of 1.5 h was then performed to allow the solutions to reach room temperature. The resulting nanoparticles were washed via centrifuging (20 500 rpm, 45 min), removal of supernatant, and then dispersing them in ethanol under sonication. The resulting modified nanoparticles dispersion was filtered to remove the excess terephthalic acid. This washing procedure was performed, in total, four times for ensuring complete wash of the produced particles.

**Postsynthetic Functionalization with Pyridine and Pyrazine:** MIL-101(Cr) nanoparticles were functionalized by linking of pyrazine or pyridine functional groups to the coordinatively unsaturated metal sites using a postsyntethic functionalization strategy. For the pyrazine functionalization, pyrazine (12.2 mL, c = 12.4 mg mL\(^{-1}\)) in addition to ethanol (2.2 mL). During the measurement, particle concentration is kept constant to take the opportunity to express his gratitude to Prof. Gérard Férey for his support and mentoring during S.W. postdoc stay in Versailles and who recently passed away.

**Conflict of Interest**

The authors declare no conflict of interest.

**Keywords**

mass correlation spectroscopy, mass density, metal–organic frameworks, porous nanoparticles, solvent permeability

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Supporting Information

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