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Improved MOF nanoparticle recovery and purification using crosslinked PVDF membranes†

 Cédric Van Goethem,^a Matthias Mertens,^a Francisco G. Cirujano,^a
Jin W. Seo,^b Dirk De Vos^a and Ivo F. J. Vankelecom^{a*}

Crosslinked PVDF-membranes are demonstrated to offer a viable alternative for centrifugation in the preparation of MOF-particles, thus realising new opportunities at lab-scale and continuous production at large-scale. The membranes combine extreme-pH with solvent stability, thus enabling application in any MOF synthesis, demonstrated here for ZIF-8, ZIF-67, HKUST-1, UiO-66 and MIL-53(Al).

Metal–Organic Frameworks (MOFs) have attracted a lot of attention since their invention almost 20 years ago.^{1,2} The combination of different metal ions or clusters with various organic linkers leads to the formation of a wide array of crystalline materials, with many different topologies, pore sizes and chemical functionalities.³ Potential applications for MOFs include catalysis,⁴ separation processes,⁵ controlled release⁶ and gas storage.⁷ As many applications require tailored MOFs, many different synthesis strategies have been developed. The most common synthesis protocols are based on solvothermal synthesis in which a metal salt and organic linker are dissolved in a suitable solvent which is then kept at a certain temperature for a certain time.⁸ In addition, more advanced synthesis methods have been developed, such as mechano-chemical, interfacial, ultrasound-assisted and electrochemical synthesis.^{9–12} Each of these synthesis techniques holds their own advantages and disadvantages with respect to MOF purity, space-time-yield, scalability and ability to operate in a continuous way, each of which are key parameters to assess potential for large-scale commercial production.¹³ Literature shows examples of efforts made to go towards larger scale and continuous MOF production.^{14–16} However, very little attention has been paid to the separation and purification stage of MOF production.

Lab-made MOF particles are mostly separated and purified using cycles of centrifugation and re-dispersion in a washing solvent. Although centrifugation is very well suited for small-scale syntheses, it is very energy-intensive and impractical when applied at large scale, especially when involving nano-sized particles. However, it is exactly these nano-sized MOFs that are of high interest for mass-transfer limited applications, *e.g.* sorption or catalysis.^{6,7} In large scale MOF synthesis, both centrifugation and membrane filtration are used for the recovery of MOF particles.^{14,16} While centrifugation becomes really challenging for nano-sized particles because membrane filtration has so far been limited to soft conditions (*e.g.* methanolic synthesis) due to issues with membrane material stability. Membrane-based purifications offer an easily scalable and energy efficient separation process which can easily be tuned for the desired particle size and synthesis mixture.¹⁷ Indeed, many synthesis mixtures used in MOF synthesis are highly challenging for current polymeric membrane materials, as they often involve solvents that dissolve the membrane, sometimes in combination with inorganic acids that degrade it.⁶

Crosslinking of PVDF membranes was recently reported as a strategy to improve thermal¹⁸ and chemical stability of nano-filtration (NF) membranes, even in *e.g.* 5 M NaOH or HCl aqueous solutions. As the crosslinking also imparts solvent stability to the polymer membranes, crosslinked PVDF could provide an ideal material for the recovery of MOF nanoparticles. Therefore, in this work, crosslinked PVDF UF membranes were prepared *via* the phase inversion process and tailored for the recovery of MOF nanoparticles from different solvothermal synthesis mixtures, ranging from pure MeOH to (for membranes) highly challenging but common HCl/DMF.¹⁹ ZIF-8 (80–100 nm), ZIF-67 (250–500 nm), HKUST-1 (500–1000 nm), MIL-53(Al) (20–40 nm) and UiO-66 (50–100 nm) were chosen as prototypical MOFs. One of the advantages of membranes prepared *via* phase inversion is the ease with which the average pore size can be changed by tuning the phase inversion parameters (*e.g.* polymer concentration of the casting solution) and can thus be tailored to remove a desired particle size. As PVDF-based membranes can be prepared with pore sizes ranging from

^a Center for Surface Chemistry and Catalysis, KU Leuven, Celestijnenlaan 200F box 2461, 3001 Leuven, Belgium. E-mail: ivo.vankelecom@kuleuven.be

^b Surface and Interface Engineered Materials, Department of Materials Engineering, KU Leuven, Kasteelpark Arenberg 44, P.B. 2450, B-3001 Leuven, Belgium

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‡ C. V. G. and M. M. contributed equally.

microfiltration (MF) to nanofiltration (NF), any (nano)particle size can be recovered.^{20,21} PVDF UF membranes prepared from casting solutions containing 14, 16, 18 or 20 wt% PVDF in NMP were therefore prepared and crosslinked. While pure MeOH fluxes declined when the polymer concentration increased from 14 to 16 wt%, they levelled off thereafter. This is presumably due to the swelling and subsequent polymer chain rearrangements during the crosslinking.²² All membranes ultimately showed a 99.9+% retention for 80 nm ZIF-8 nanoparticles. The initial permeate of the 14 wt% membrane was however clearly not transparent, indicating incomplete retention of the nanoparticles. However after 10 min (at 250 l m⁻² h), the retention increased to 99.9+%. This phenomenon is well known and attributed to the formation of a cake-layer of ZIF-8 particles on the membrane surface, which forms a dynamic selective layer to retain the remaining nanoparticles.²³ Because retention in continuous operation should intrinsically arise from the membrane itself, the 16 wt% membrane was used for further experiments.

For most applications, the synthesized nanoparticles need to be sufficiently purified from the remaining reagents. Diafiltration potentially provides a process allowing combined separation and purification of MOF nanoparticles. In contrast to the discontinuous nature of centrifugation and re-dispersion cycles, diafiltration can be operated continuously. In diafiltration, the permeate that is removed from the nanoparticle suspension is continuously replaced with fresh solvent. The UF membrane shows full retention for the nanoparticles but no rejection at all for the linker and metal salt, hence the remaining impurities/reagents are removed continuously. Such a process can easily be modelled (and thus controlled flexibly) as a continuously stirred tank reactor, allowing to predict how many diavolumes (permeate to filtration cell volume ratio) are required to reach a certain impurity level. This principle was demonstrated for the synthesis of ZIF-67 particles synthesized from Co(NO₃)₂ and HMim in MeOH. Fig. 1 shows the permeate absorbance and purification level of the ZIF-67 nanoparticles as function of the number of diavolumes. As the membrane is equally unselective for the metal salt as for the organic linker, the removal efficiencies for metal complex and linker are equal. It can be seen

that 5 diavolumes are sufficient to reach $\pm 99\%$ impurity removal. When the desired purity level is reached, the addition of fresh MeOH is stopped and the suspension is filtrated until no solvent is present anymore. The nanoparticles can then easily be recovered at lab-scale by scraping them off the membrane surface. Fig. 1 also shows that the modelled absorbance nicely fits the experimental data, confirming that the level of impurity removal can easily be predicted. In addition, also large scale production using these membranes should be straightforward. Typically, a 10" single module of 18 wt% XL-PVDF membrane should be sufficient for the purification of 2.5 t day⁻¹ ZIF-8 (see Table S1, ESI†).

After the ZIF-67 diafiltration, XRD on the membrane coupon showed the presence of crystalline material, *i.e.* remains of the MOF on the membrane surface. After a simple 1 h treatment in 1 M HCl, the XL-PVDF membrane coupon remained intact, confirming the extreme pH stability of this membrane. In addition, all reflections associated with ZIF-67 were gone, confirming thorough membrane cleaning.

The range of conditions used for solvothermal MOF synthesis is very diverse. Solvents that are more stringent to a polymeric membrane, such as DMF (ZIF-8 synthesis) or DMF/HCl (UiO-66) are often encountered.^{6,8} Especially stability in the latter type of conditions, combining a strong polar solvent with an inorganic acid, is extremely challenging for either polymeric or ceramic membranes. However, crosslinked PVDF is stable in virtually any solvent and acid/base or combinations thereof (see ESI†, Section 4). 4 commonly used MOFs were synthesized (ZIF-67 in MeOH, HKUST-1 in H₂O/EtOH/DMF, ZIF-8 in DMF and UiO-66 in DMF/HCl), purified using diafiltration and compared using transmission electron microscopy (TEM, Fig. 2) and X-ray diffraction (XRD, Fig. 3 and Fig. S4–S7, ESI†) to determine particle size and crystal phase respectively. All results were benchmarked to MOF nanoparticles conventionally purified through centrifugation. From the XRD patterns, no differences in number, position nor width of the peaks could be observed. The TEM images however did show some differences. The syntheses in conditions that allow crystallization and nucleation at room temperature (ZIF-67 and HKUST-1) showed slightly larger and more uniform particles with a

Fig. 1 (left) Methanol permeance and retention of 80–100 nm-size ZIF-8 nanoparticles as function of polymer concentration in the membrane casting solution. (right) Experimental and modelled purification of 250–500 nm-size ZIF-67 particles *via* diafiltration, showing the absorbance of Co(NO₃)_x(Mim)_y (with $x + y = 2$) at 562 nm as function of the diavolumes filtered.

Fig. 2 TEM comparison of ZIF-67 (MeOH), ZIF-8 (DMF), UiO-66 (DMF/HCl), HKUST-1 (H₂O/EtOH/DMF) and MIL-53(Al) (DMF) recovered and purified via centrifugation and diafiltration.

Fig. 3 (left) XRD comparison of UiO-66 nanoparticles recovered *via* diafiltration and centrifugation. (right) Reaction scheme and yield-*vs.*-time plot for the synthesis of a substituted indole (**1**) and oxindole (**2**) in the presence of no catalyst or UiO-66 obtained *via* diafiltration or centrifugation.

more regular shape after diafiltration. This indicates that the crystal growth process continued longer in the diafiltration process than with centrifugation.²⁴ Indeed, under the implemented conditions, centrifugation presented a faster initial drop in leftover reagent concentration compared to diafiltration. In addition, Ostwald ripening can still occur during the diafiltration, as MOF particles are often purified using MeOH which shows good solubility for both linker and metal ions/clusters. This residence time can obviously be adjusted by changing the filtration pressure or the installed membrane area (see ESI,[†] Section 5), depending on the desired size of the MOF-particles. In contrast, the syntheses that proceed at higher temperature in a solvent that doesn't favor spontaneous nucleation (ZIF-8, UiO-66 and MIL-53(Al) in DMF) show similar particle size and shape, indicating that cooling down the synthesis mixture in these cases is sufficient to stop, or at least significantly slow down, the above outlined processes. XRD only reveals the structural integrity of a material. Most applications (*e.g.* catalysis) however, require a sufficiently pure and active material. The UiO-66 nanoparticles were therefore tested as heterogeneous catalysts.

Substituted indoles and oxindoles are important pharmaceutical intermediates in the synthesis of drugs for the treatment of

neurological pathologies and cancer.^{25–30} Due to the necessity of cleaner organic transformations in such syntheses, the use of non-toxic, recoverable and reusable solids is highly interesting to reduce the amount of toxic waste resulting from the isolation and purification steps in a traditional homogeneous catalytic processes. The UiO-66 MOF contains Zr–O acid–base pairs and can thus be employed as heterogeneous catalyst in the acid–base catalysed reaction steps in the synthesis of such (ox-)indole pharmaceutical intermediates.^{31,32} On the one hand, the UiO-66 nanoparticles were used for the Friedel–Crafts alkylation of indole with electron-deficient alkenes (such as *e.g.* nitrostyrene) to produce compound **1** which forms an intermediate in the synthesis of tryptamine analogues. Almost 80% yield for **1** was obtained after 15 min reaction of indole with benzaldehyde under neat and mild (80 °C) reaction conditions when using UiO-66 as catalyst (Fig. 3 left). In the absence of catalyst, only 42% yield for **1** was obtained after 15 min reaction. On the other hand, the reaction between oxindole and benzaldehyde, generating compound **2** which is an intermediate for the synthesis of tumor suppressor spirooxindoles gave quantitative yields with UiO-66 after 2 h of reaction under neat and mild (80 °C) conditions (Fig. 3 right). In the case of the

blank reaction, only 41% for 2 is obtained after 2 h. In both cases, the UiO-66 obtained *via* diafiltration performed equal to UiO-66 obtained *via* centrifugation, confirming the potential for diafiltrated MOF nanoparticles in this type of application. Comparison of the XRD patterns before and after catalysis confirmed that both UiO-66 samples were stable during both catalysis experiments (Fig. S9, ESI†).

In conclusion, ultra-stable crosslinked PVDF membranes were prepared for the recovery and purification of a wide set of MOF nanoparticles (ZIF-8, ZIF-67, HKUST-1 and UiO-66), synthesized in diverse conditions (including HCl/DMF) that require an extremely inert membrane material. 80 nm ZIF-8 nanoparticles were recovered with 99.9+% efficiency and easily recovered from the membrane surface by scraping. A diafiltration procedure was optimized for the purification of the synthesized nanoparticles, easily reaching 99.9+% removal of unreacted metal ions and linker molecules. Application of the UiO-66 nanoparticles as heterogeneous catalysts showed no difference between the nanoparticles obtained *via* diafiltration and the conventional centrifugation route. Diafiltration using XL-PVDF membranes is thus a viable alternative for the recovery and purification of MOF nanoparticles at lab-scale with straightforward upscaling potential which, in contrast to repeated centrifugation and redispersion, can easily be automated. Moreover, in the preparation of very small nanoparticles or when the particle density is very similar to the synthesis mixture, centrifugation becomes very challenging. Size-based membrane separation can offer a versatile way out here.

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Conflicts of interest

There are no conflicts to declare.

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