



Rapid Communication

Maintaining Stable Zeolitic Imidazolate Framework (ZIF) Templates during Polyelectrolyte Multilayer Coating



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A B S T R A C T

Equipping ZIF particles with a polyelectrolyte membrane provides functional groups at their interface, enabling further conjugations necessary for applications such as targeted drug delivery. Previous approaches to coat ZIF particles with polyelectrolytes led to surface corrosion of the template material. This work overcomes previous limitations by performing a Layer-by-Layer (LbL) polyelectrolyte coating onto ZIF-8 and ZIF-67 particles in non-aqueous environment. Using the 2-methylimidazolium salt of polystyrenesulfonic acid instead of the acid itself and polyethyleneimine in methanol led to intact ZIF particles after polyelectrolyte coating. This was verified by electron microscopy. Further, zeta potential and atomic force microscopy measurements confirmed a continuous polyelectrolyte multilayer built up. The here reported adaption to the well-studied (LbL) polyelectrolyte self-assembly process provides a facile method to equip ZIF particles with a nanometer thin polyelectrolyte multilayer membrane.

1. Introduction

Zeolitic imidazolate frameworks (ZIFs) are a subclass of metal organic frameworks (MOFs) where metal centers are coordinated by deprotonated imidazole derivatives [1]. ZIF-8 and ZIF-67 that have been investigated in this study are isostructural representatives of the ZIF family. ZIF-8 comprises of zinc cations while ZIF-67 comprises of cobalt cations that are coordinated by 2-methylimidazolate anions in both cases. Both, ZIF-8 and ZIF-67 share most of the material characteristics [2] that are relevant to this study. These material characteristics relate to the stability of the ZIF particle interface and are mainly determined by ionic dissociation and protonation equilibria of the imidazole ligand. Possible commercially relevant applications of ZIFs have been proposed and include their use for gas separation, gas storage, and chemical sensing devices as well as catalyst for chemical reactions [3–5]. Of particular interest to the present study is the fact that ZIFs and in particular ZIF-8 have been used to entrap small molecular weight drugs, proteins, and even enzymes [6]. ZIF-8 was of particular interest for these earlier studies since it only comprises of zinc ions and an imidazole derivative. Both components are precursors for several pharmaceutical preparations. Hence, ZIF-8 was envisioned to be a suitable candidate to realize MOF-based drug delivery approaches. Targeted drug delivery using ZIF-8 carriers would, however, require stabilization

against early dissolution in aqueous environment and functionalization on ZIF particle surfaces with e.g. antibodies. Native ZIF-8 particle surfaces are, however, not suitable for conjugation of antibodies due to their lack of functional groups. Functional groups might be introduced through the use of e.g. amino reactive imidazole derivatives [7]. However, this likely gives rise to material properties that differ from that of native ZIFs. Alternatively, a nano-meter thin polyelectrolyte coating around ZIF particles was envisioned to provide functional groups at the interface. Traditionally, polyelectrolyte coating was performed by using oppositely charged polyelectrolytes in aqueous environment [8] or by using solutions of their free acid and amine forms in organic solvents. The polyelectrolyte pair poly(4-styrene sulfonate) (PSS) and poly(allylammonium) (PA) is well-established for Layer-by-Layer (LbL) polyelectrolyte self-assemblies onto colloidal and micro particles. Reported properties of PSS/PA films include stability under a wide pH range (1 – 11), their tuneable permeability towards proteins [9], their tuneable thickness by number of LbL deposition steps and the possibility to functionalize their surface with low fouling polymers or antibodies [10]. Notably, PA and polyethyleneimine (PEI) share many properties except that PEI is highly branched, which often results in better adsorption on lowly charged interfaces [11], as it is the case for matured ZIF particle surfaces. The assembly of polyelectrolytes in organic solvents was shown to be valuable for water soluble materials

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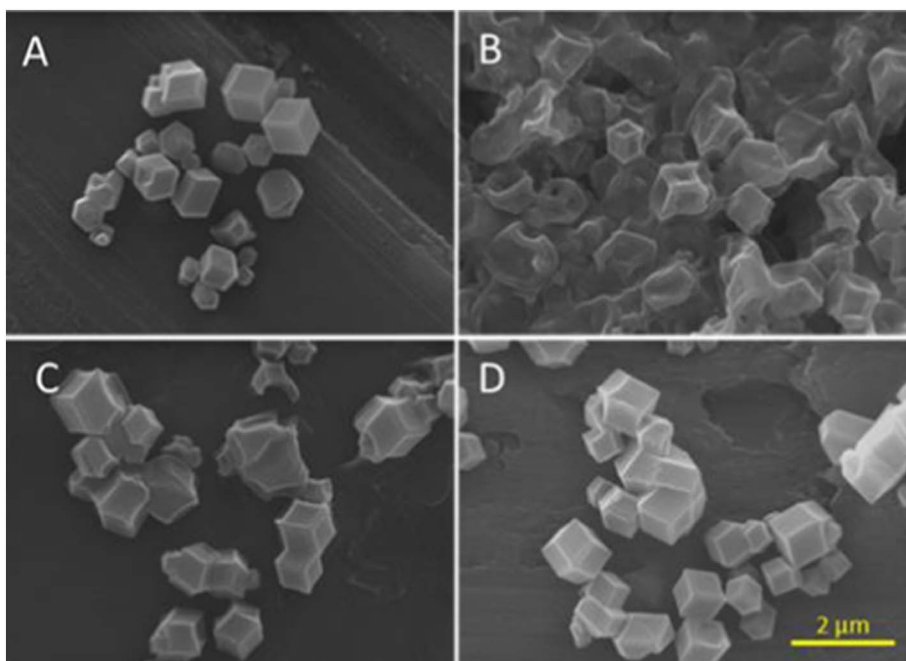


Fig. 1. Scanning electron micrographs depicting ZIF-67 crystals (A) that are coated with 4 double layers of each: PSA & PEI (B), PAA & PEI (C) and PSS-2MeIM salt & PEI (D).

[12–19]. In an earlier study by Ejima et al. ZIF-8 particles were used as template materials that were coated with polystyrenesulfonic acid (PSA) and PA polymers. As it was aimed to prepare multifaceted hollow polyelectrolyte microcapsules, this approach led to complete ZIF template material dissolution [20].

2. Results and discussions

Currently available LbL polyelectrolyte coating methods are unsuitable to provide a stable polyelectrolyte coating while maintaining intact ZIF particles. Hence, the scope of the current study was to establish a LbL polyelectrolyte coating procedure that overcomes these limitations. ZIF-8 and ZIF-67 were both utilized for this study and synthesized according to a previously established protocol [2]. The particle size distribution was generally between 500 nm and 1000 nm as shown by SEM imaging (Fig. 1A and supplemental data). Both ZIF-8 and ZIF-67 particles were dispersed in methanol for the LbL coating process since Zhang et al. [21] demonstrated that ZIFs have slight water solubility. Methanol more strongly prevents ionic dissociation and thereby lowers dissolution of ZIF-8 or ZIF-67 particles. Exact experimental procedures are described within the supplemental information. Firstly, the previously reported LbL polyelectrolyte self-assembly protocol to create multilayer of the strong acid PSA and polyethyleneimine (PEI) was evaluated. In accordance to Ejima et al. [20] this led to a complete template material dissolution and yielded hollow

polyelectrolyte microcapsules (Fig. 1B). As the ability of polyacids to dissolve the ZIF template during encapsulation depends on their acidity, the much weaker polyacrylic acid (PAA) was investigated as substitute for PSA in order to prevent template material dissolution. Interestingly, utilization of a weaker acid resulted in a concave morphology of the ZIF particles (Fig. 1C). This indicated surface etching. Thus, even weak polyacids led to corrosion of the ZIF material at particle interfaces. In order to completely avoid ZIF template dissolution, both polyacids were neutralized with 2MeIM to yield their 2-methylimidazolium salt. The attempt to neutralize PAA with 2MeIM led to precipitation in methanol. In contrast, the resulting polystyrene sulfonic acid-2-methylimidazolium (PSS-2MeIM) salt was soluble in methanol. And indeed, the PSS-2MeIM salt together with PEI allowed coating without dissolution or etching of template materials (Fig. 1D and Fig. S1 to S14).

It was observed that the zeta potential changed in accordance to the adsorbed polymer for all polymer combinations that were investigated. It is important to note that PEI likely acquired charges only due to interaction with PAA, PSA or PSS-2MeIM salt. The coating was therefore referred to be a polyelectrolyte multilayer while the precursor material was referred to as polymers due to their little or no charge while in solution. Alternating polyelectrolyte layers resulted in an altered zeta potential for all polymer combinations investigated, although the magnitude of the acquired potential varied strongly between the different combinations. Alternate coating of PSA and PEI resulted in strong

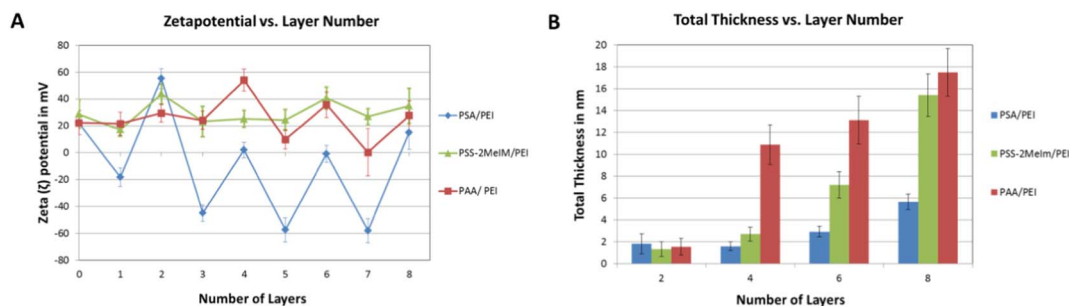


Fig. 2. Zeta-potential measurement in methanol (A) and AFM measurements of polymer layer total thickness (B), depicted as relation to the number of adsorbed polyelectrolyte layers. Blue indicates PSA & PEI. Red indicates PAA & PEI. Green indicates PSS-2MeIM & PEI. (For interpretation of the references to colour in this figure, the reader is referred to the web version of this article.)

and truly alternating zeta potentials (Fig. 2 A, blue line) that is in accordance with earlier observations [20]. As it is well established that polyacids cause protonation of the amine groups in polyamines and hence induce positive charges, the multilayers that were fabricated by sequential adsorption of these polymers therefore were held together by electrostatic interactions. In contrast, PAA being a very weak polyacid did not achieve a significant change in surface charge for the first 3 layers (Fig. 1 A, red line). This observation implied that multilayer build-up between PAA and PEI might have been governed by non-charged hydrogen bonds to a certain extent. The low positive zeta potential that was observed for ZIF particles with PEI as outermost layer could be explained by excess adsorption of non-charged polyamines. The positive zeta potential of particles with PSS-2MeIM as outermost layer suggested low dissociation of the salt (Fig. 1 A, green line). However, zeta potential measurements only allow for tentative conclusions on multilayer build-up. Thus, fluorophore labelled PEI was utilized to observe a continuous increase of fluorescent signal with increasing number of coatings in fluorescence images of LbL coated ZIF-8 particles (Fig. S15 and S16 of the Supplemental information). Increasing fluorescence intensity together with alternating zeta potentials has been established as a good indication of multilayer build-up [22]. Of note, earlier works distinguished between multilayer architectures that exhibit a linear layer thickness and exponential layer thickness growth. Thus, we aimed to investigate the layer thickness of the various polyelectrolyte pairs during multi-layer build-up by experimental Atomic Force Microscopy (AFM). Silicon supports were coated with polyelectrolyte multilayers and measurements were performed at the edge of a scratch through the multilayers to reveal the total thickness (Fig. 2 B, Fig. 3 B & C) of the coating. The single layer thickness was calculated by dividing the total thickness of the coating by the number of assembled polyelectrolyte layers. Since the single layer thicknesses that were determined for PSA together with PEI were the same regardless of the number of layers that were assembled, this polymer pair was assumed to exhibit a linear layer growth (Fig. 2B, blue bars). The layer growth of PAA and PEI on the other hand, was rather exponential and ranged from 0.78 nm for 2 polyelectrolyte layers to 2.19 nm for 8 layers, respectively. Interestingly, the layer growth kinetics of PSS-2MeIM appeared to be also rather exponential and comparable to that of PAA rather than to that of PSA. The single layer thickness for PSS-2MeIM and PEI increased from 0.68 nm for two layers to 1.91 nm for 8 layers. Figs. S17 to S27 (Supporting information) show representative AFM images depicting the surface topology. Previously it was established that the charge density and hence polyacid conformation in solution directly influences architecture (e.g. thickness) of the multilayer coating [23]. Since charge density on polyacids depends on the

protolysis equilibrium, differences between the protolysis equilibria of the utilized polyacids were briefly estimated from the pKa values of their monomeric components. The acidity of monomeric benzenesulfonic acid ($pK_{a,water} \sim 0.7$) and acetic acid ($pK_{a,water} \sim 4.25$, $pK_{a,ethanol} \sim 6.9$) spans already several orders of magnitude indicating that the polyacids will significantly differ in acidic strength.

Polyacids are even weaker when compared to their monomeric counterparts due to their coupled protolysis equilibria. This indicates that PAA is barely charged and coiled in diluted solution while PSA is moderately charged and semi-stretched in diluted solutions. Consequently, the stretched PSA conformation explains why PSA and PEI yielded the thinnest polyelectrolyte coating. The membrane made of PAA with PEI, on the other hand, was thicker due to the lower charge density and more coiled conformation of PAA. The fact that polyelectrolyte membranes made of PSS-2MeIM and PEI were more similar in thickness to the membranes made of PAA & PEI than to that of PSA & PEI indicated a low charge density on the PSS-2MeIM salt. This was in line with the observations from zeta-potential measurements as was discussed above. The reduced charge density of the 2MeIM salt presumably led to a more coiled polymer in solution. This consequently also led to a thicker coating together with PEI, when compared to the free acid PSA. Thus, the presented results are in line with the theoretical understanding and earlier studies. Atomic force microscope measurements on hollow polyelectrolyte microcapsules that were generated with the here described protocol were not successful. In line with earlier observation by Ejima et al., the resulting hollow polyelectrolyte microcapsules did not fully collapse which is, however, necessary for AFM measurements to determine the polyelectrolyte layer thickness from microcapsules. In addition to the described enabling methodology to equip ZIF particles with a polyelectrolyte coating, this study also presented a novel alternative to established Layer-by-Layer coating protocols. The here described alternative used a polyacid salt together with a non-charged polyamine in an organic solvent. Our understanding of the discussed acid-base chemistry led to the hypothesis that PEI has a stronger proton affinity (expressed in pKa values) by roughly two orders of magnitude compared to 2MeIM [24,25]. Therefore, it appeared likely that the stronger base of PEI acquired the charge from 2MeIM by proton transfer. This chemistry would have furthermore allowed ionic pairing between PSS-2MeIM and PEI.

3. Conclusions

PSS-2MeIM and PEI in methanol constituted an excellent polymer pair for a self-assembly process that led to electrostatically bound polyelectrolyte multilayers around ZIF particles. This work is

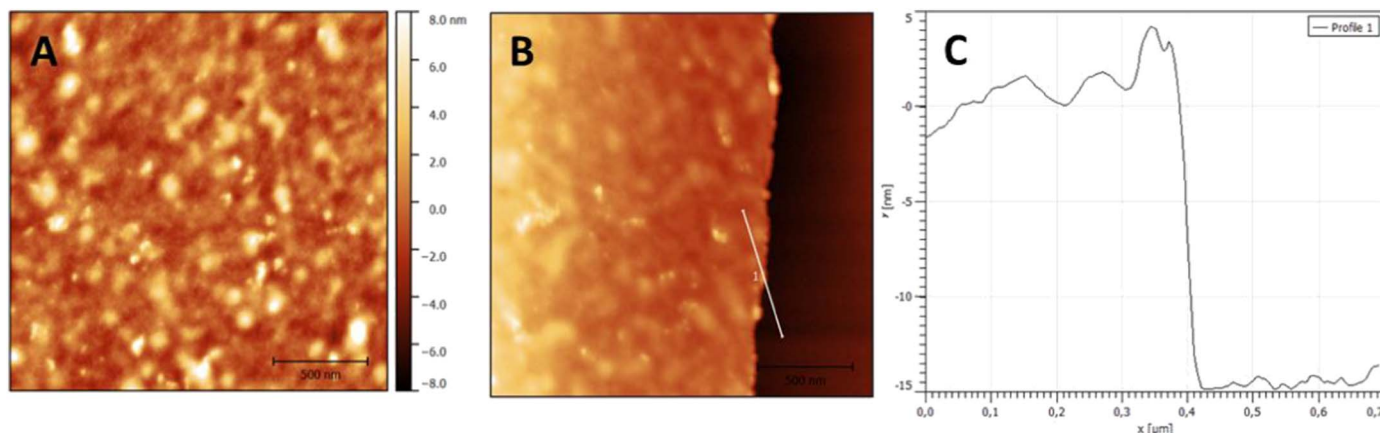


Fig. 3. Representative atomic force microscope images of Layer-by-Layer polyelectrolyte coated silica surfaces with 4 double layers of PEI and PSS-2-MeIM. The micrographs depict a coherent polyelectrolyte coating (A), the edge of a scratch for total layer thickness measurement (B). The line profile (C) reveals a total polyelectrolyte coating thickness of ~ 15 nm for 4 double layers of PEI and PSS-2-MeIM or 1.88 nm per single polyelectrolyte layer.

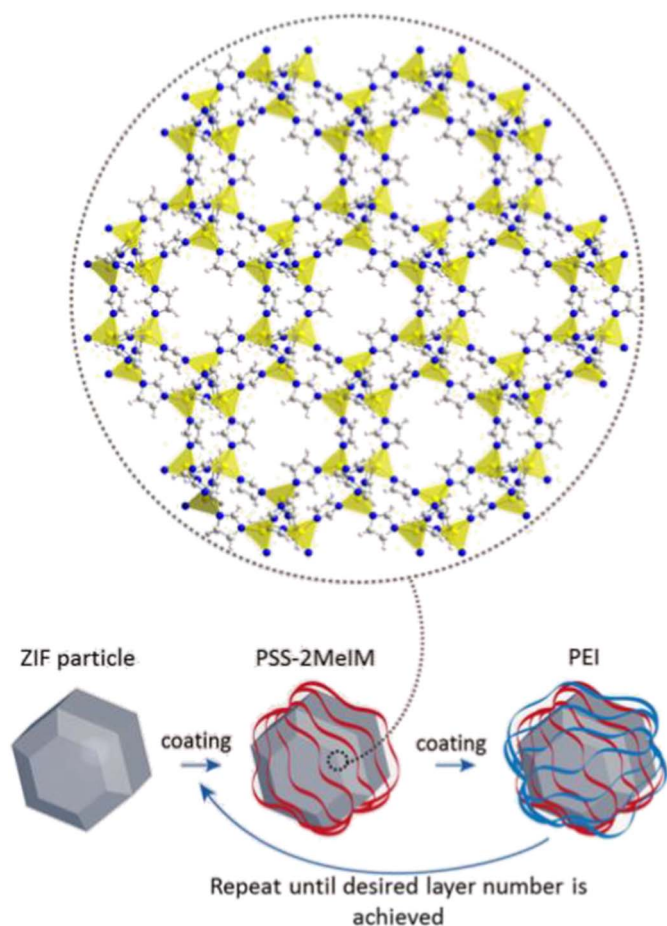


Fig. 4. Schematic representation of the process to encapsulate ZIF crystals with a nanometer thin polyelectrolyte membrane. Multilayer membranes are achieved by consecutively coating cycles of PSS-2M (red) and PEI (blue) until the desired number is reached. The magnification of the ZIF particle shows the six-membered rings of one-dimensional channels along the [111] direction of a ZIF-8 crystal. The yellow polyhedra indicate coordinated zinc ions. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

envisioned to provide a facile polyelectrolyte coating procedure for acid sensitive ZIF particles or generally ZIF interfaces (Fig. 4). Such a facile protocol would, for example, allow bioconjugation to facilitate future applications of ZIF-8 in targeted drug delivery or other application that require e.g. antibody conjugation.

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Appendix A. Supplementary Data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.colcom.2017.11.004>.

References

- [1] K.S. Park, Z. Ni, A.P. Cote, J.Y. Choi, R.D. Huang, F.J. Uribe-Romo, H.K. Chae, M. O'Keeffe, O.M. Yaghi, *P Natl Acad Sci USA* 103 (2006) 10186–10191.
- [2] S. Beyer, C. Prinz, R. Schurmann, I. Feldmann, A. Zimathies, A.M. Blocki, I. Bald, R.J. Schneider, F. Emmerling, *Chemistry* 1 (2016) 5905–5908.
- [3] G. Lu, J.T. Hupp, *J. Am. Chem. Soc.* 132 (2010) 7832.
- [4] L. Mu, B. Liu, H. Liu, Y.T. Yang, C.Y. Sun, G.J. Chen, *J. Mater. Chem.* 22 (2012) 12246–12252.
- [5] U.P.N. Tran, K.K.A. Le, N.T.S. Phan, *ACS Catal.* 1 (2011) 120–127.
- [6] K. Liang, C.J. Coghlan, S.G. Bell, C. Doonan, P. Falcaro, *Chem. Commun.* 52 (2016) 473–476.
- [7] K. Eum, K.C. Jayachandrababu, F. Rashidi, K. Zhang, J. Leisen, S. Graham, R.P. Lively, R.R. Chance, D.S. Sholl, C.W. Jones, S. Nair, *J. Am. Chem. Soc.* 137 (2015) 4191–4197.
- [8] G. Decher, *Science* 277 (1997) 1232–1237.
- [9] Z. She, M.N. Antipina, J. Li, G.B. Sukhorukov, *Biomacromolecules* 11 (2010) 1241–1247.
- [10] C. Cortez, E. Tomaskovic-Crook, A.P.R. Johnston, A.M. Scott, E.C. Nice, J.K. Heath, *F. Caruso, ACS Nano* 1 (2007) 93–102.
- [11] V. Bosio, F. Dubreuil, G. Bogdanovic, A. Fery, *Colloid Surface A* 243 (2004) 147–155.
- [12] S. Beyer, W.C. Mak, D. Trau, *Langmuir* 23 (2007) 8827–8832.
- [13] J.H. Bai, S. Beyer, W.C. Mak, R. Rajagopalan, D. Trau, *Angew. Chem. Int. Ed.* 49 (2010) 5189–5193.
- [14] J.H. Bai, B. Sebastian, T.S. Yein, T. Dieter, *ACS Appl. Mater. Interfaces* 3 (2011) 1665–1674.
- [15] S. Beyer, J.H. Bai, A.M. Blocki, C. Kantak, Q.R. Xue, M. Raghunath, D. Trau, *Soft Matter* 8 (2012) 2760–2768.
- [16] J. Bai, S. Beyer, W.C. Mak, D. Trau, *Soft Matter* 5 (2009) 4152–4160.
- [17] L.Y. Lin, S. Beyer, T. Wohland, D. Trau, D. Lubrich, *Angew. Chem. Int. Ed.* 49 (2010) 9773–9776.
- [18] H.M. Pan, S. Beyer, Q.D. Zhu, D. Trau, *Adv. Funct. Mater.* 23 (2013) 5108–5115.
- [19] H.M. Pan, A. Subramanian, C.J. Ochs, J.Y. Dewavrin, S. Beyer, D.W. Trau, *RSC Adv.* 4 (2014) 35163–35166.
- [20] H. Ejima, N. Yanai, J.P. Best, M. Sindoro, S. Granick, F. Caruso, *Adv. Mater.* 25 (2013) 5767.
- [21] H.F. Zhang, D.F. Liu, Y. Yao, B.Q. Zhang, Y.S. Lin, *J. Membr. Sci.* 485 (2015) 103–111.
- [22] G.B. Sukhorukov, E. Donath, S. Davis, H. Lichtenfeld, F. Caruso, V.I. Popov, H. Mohwald, *Polym. Adv. Technol.* 9 (1998) 759–767.
- [23] B. Schoeler, G. Kumaraswamy, F. Caruso, *Macromolecules* 35 (2002) 889–897.
- [24] H.K. Hall, *J. Am. Chem. Soc.* 79 (1957) 5441–5444.
- [25] H. Walba, R.W. Isensee, *J. Organomet. Chem.* 26 (1961) 2789.