Research Article

Zheng Cao*, Yuyuan Chen, Qianpeng Zhang, Yanping Xia, Gang Liu, Dun Wu, Wenzhong Ma, Junfeng Cheng, Chunlin Liu*

Preparation and ion sensing property of the self-assembled microgels by QCM

https://doi.org/10.1515/nanofab-2017-0002
Received November 28, 2017; accepted January 4, 2018

Abstract: The polyanion polystyrene sulfonate (PSS), the polycation poly (allylamine hydrochloride) (PAH), and the anionic poly (*N*-isopropylacrylamide-*co*-acrylic acid) [P(NIPAM-*co*-AA)] microgels were self-assembled onto the polyethylene imine (PEI) adsorbed gold surfaces of quartz crystal microbalance (QCM) because of the electrostatic attractions. The interactions of various metal particles including Ca^{2+}, Bi^{3+}, Cu^{2+}, Zn^{2+}, Ni^{2+}, Sn^{2+}, Co2+, and Cd^{2+} with the obtained PEI/PSS/PAH/microgel layer in aqueous solutions were evaluated by QCM. The PEI/PSS/PAH/Microgel covered QCM sensor demonstrates the lowest detection limit of 0.1 ppm in aqueous solutions and the obviously linear connection between the frequency response and Ni^{2+} concentration from 0.1 to 20 ppm, which is due to the complexation of Ni^{2+} with the carboxyl groups of microgels. Atomic force microscopy (AFM) was used to reveal the morphology and stability of the self-assembled polyelectrolyte/microgel layer before and after adsorbing heavy metal ions. These self-assembled materials of polyelectrolyte/microgel layer will be helpful for manufacturing ion-selective materials for separation and identification purposes.

Keywords: anionic microgels; quartz crystal microbalance; self-assembly; metal ions; binding

1 Introduction

Polymeric microgel is a type of microsized hydrogel known as cross-linked polymeric particles in which the polymer chains are bonded by means of chemical bonds [1-3. It is normally dispersed in watery solutions and can embrace three-dimensional structures, and also experience conformational change because of different external stimuli, for example, magnetic field, ionic strength, pH, and temperature [4-8]. The stimuli-responsive microgels have been broadly researched because of their unlimited usage in the tissue designing fields,[9,10] catalysis,[11,12] drug controlled release,[13-15] separation,[16] and sensors [17,18]. Including different active groups, for example, organic groups (e.g., -COOH, $-NH_2$, $-C{=}ONH_2$), ionic groups ($-NH_3^+$, $-SO_3^-$), and hydrophobic groups ($-CH(CH_3)_2$) into the microgel systems gives extraordinary opportunities to interact with biomolecules,[19] small organic molecules,[20] and heavy metal ions [21] in the aqueous environments, which constantly plays a significant role in the area of identification, separation, and recovery of these objective molecules.

A lot of studies on the fabrication, stimuli-responsive properties, and structures of the microgel particles dispersed in the aqueous solutions and their binding properties with target molecules have been carried out extensively [21-23]. Yin et al. [21] revealed the preparation of the thermosensitive PNIPAM microgels containing Cu^{2+}-chelating acceptor and fluorescent reporter functionalities and discovered that the swelling microgels acquired can specifically interact with Cu^{2+} over other metal ions (Hg^{2+}, Mg^{2+}, Zn^{2+}, Pb^{2+}, Ag^{+}, and Al^{3+}), bringing about extinguishing of fluorescence emission strength. Heating the microgel solution above the phase transition temperature can significantly expand the detection sensitivity for Cu^{2+} because of the collapse of the thermo-instigated microgel.

***Corresponding authors: Zheng Cao, Chunlin Liu,** Jiangsu Key Laboratory of Environmentally Friendly Polymeric Materials, School of Materials Science and Engineering, Jiangsu Collaborative Innovation Center of Photovoltaic Science and Engineering, Changzhou University, Changzhou, Jiangsu, 213164, China, E-mail: caozheng0571@hotmail.com, chunlin301@hotmail.com
Yuyuan Chen, Qianpeng Zhang, Yanping Xia, Gang Liu, Dun Wu, Wenzhong Ma, Junfeng Cheng, Jiangsu Key Laboratory of Environmentally Friendly Polymeric Materials, School of Materials Science and Engineering, Jiangsu Collaborative Innovation Center of Photovoltaic Science and Engineering, Changzhou University, Changzhou, Jiangsu, 213164, China
Zheng Cao, Dun Wu, Wenzhong Ma, Junfeng Cheng, Chunlin Liu, National Experimental Demonstration Center for Materials Science and Engineering (Changzhou University), Changzhou, 213164, P.R. China
Zheng Cao, Yanping Xia, Chunlin Liu, Changzhou University Huaide College, Changzhou, 213016

Zhou et al. [23] prepared the 4-(2-Pyridylazo)-resorcinol (PAR) functionalized thermosensitive ionic microgels (PAR-MG) by a one-pot technique and discovered that the microgel suspensions displayed the feature of color with the presence of different trace of ions including Cu^{2+}, Mn^{2+}, Pb^{2+}, Zn^{2+}, and Ni^{2+}, which can be outwardly recognized by the eyes. They likewise revealed that the detection mechanism was attributed to the chelation between the nitrogen atoms and o-hydroxyl groups of PAR inside the microgels and heavy metal ions. Chen et al. discovered that the ionic microgel particles obtained have the capacity to retain and repel ion oxide nanoparticles (Fe_3O_4-NPs) upon pH variation [24].

Recently, the consideration has been progressively moved to study the preparation and properties of the two-dimensional structures made out of the highly organized layers,[25,26] and the self-assembled microgels on the surfaces and interfaces [27-30]. Serpe et al. researched the swelling behavior of P(NIPAM-*co*-AA) microgel based thin films under different pH condition utilizing surface plasmon resonance (SPR) spectroscopy and quartz crystal impedance (QCI) analysis. Serpe additionally reported the study of the thermally regulated uptake and release of the drug doxorubicin from microgel thin films [31]. Also, the PNIPAM microgel-based etalons for pH, optical, and humidity detection have been created [32-35]. Wang et al. reported that LbL assembled microgel films of chemically cross-linked PAH and confined between two surfaces. (named PAH-D) and PSS equipped for reversible release and loading of dyes that are negatively charged, for instance, fluorescein sodium, mercaptoacetic acid-stabilized CdTe nanoparticles, and methyl orange (MO), can be manufactured by a LbL deposition procedure [36,37]. Islam et al. reported the penetration of polyelectrolytes into charged PNIPAM microgel layers confined amid two surfaces [38]. The intensive research on the interactions of biomaterials with the surface-bound microgels by QCM with dissipation monitoring has additionally been completed [39,40]. In spite of these efforts, the dynamics of the microgel-heavy metal ion interactions at interfaces have not yet been explored. A thorough understanding of the microgel-metal ion interaction and its enhancement are fundamental for creating ion-selective materials for detection and separation of heavy metal ions in an aqueous environment.

Apart from single microgel particles dispersed in solution, the two-dimensional organized and surface-confined microgels can be produced by utilizing the electrostatic attraction driven LbL self-assembly method; this has the advantages that various functionalities embedded, stimuli-responsive properties, unique network structure, and microgel layer with tunable thickness at nanometer level that can be profoundly controlled to catch a particular metal ion. The subsequent layer of microgels onto a solid surface can be utilized as a simplified two-dimensional stage for unraveling the microgel-ion relationship. QCM comprising of a little α-quartz plate sandwiched between two gold electrodes is considered as an ordinarily utilized procedure. Since the frequency response of the quartz scales with the mass loaded on the surface of the crystal, mass changes at nanogram level can be recorded. Likewise, QCM can provide data on the viscoelastic properties of adsorbed layers. QCM has just been broadly utilized for evaluating the conformation of polymer chains [41], biomolecular interaction [42-44] viscoelasticity of hydrogel thin films [45,46], detection of metal ions using polymer films as sensing coating [47], and polyelectrolyte assembly [48]. The gold surfaces of QCM sensors can be simply tailored with microgels via the LbL self-assembly method as mentioned above.

In this research, we report a novel method to study the microgel-ion system, which makes use of the two-dimensional self-assembly containing microgels and the QCM method. The polyelectrolyte-microgel self-assembly was set up on gold surfaces of QCM sensors by means of LbL pathway driven by the electrostatic force. AFM and water contact angle measurements were utilized to describe the polyelectrolyte/microgel system in detail. The dynamics of the binding of various heavy metal ions with the polyelectrolyte/microgel system was examined with the assistance of the QCM immersed in the liquid environment.

2 Experimental Section

2.1 Chemicals and Materials

N-isopropylacrylamide (NIPAM, 99%, J&K Scientific Ltd., Beijing, China), acrylic acid (AA, 98%, Shanghai LingFeng Chemical Reagent Co. Ltd., Shanghai, China), *N,N'*-methylene bisacrylamide (MBA, 98%, J & K Scientific Ltd., Beijing, China), potassium persulfate ($K_2S_2O_8$, 99%, J & K Scientific Ltd., Beijing, China), polyethyleneimine (PEI, branched, M_w = 10 000, 99%, Alfa Aesar, Thermo Fisher Scientific Inc., Shanghai, China), polystyrene sulfonate (PSS, M_w =70 000, 98%), poly (allylamine hydrochloride) (PAH, M_w = 20 000, 98%), and nitrates (98%, J & K Scientific Ltd., Beijing, China) were bought and used as received. The dialysis tubing cellulose membrane (molecular weight cut off 14 000) was acquired from Sigma-Aldrich, Shanghai, China. Deionized water purified by a Millipore

Milli-Q system was employed in each experiment. QCM sensors with gold coating were bought from SuZhou SiJu Biomaterials company (Suzhou, China).

2.2 Synthesis of P(NIPAM-co-AA) microgels

The monomers of NIPAM (0.375 g), AA (0.125 g), and the crosslinker MBA (0.055 g) were dissolved in 38 mL deionized water at 70 °C under vigorous stirring. Oxygen was removed by bubbling nitrogen through the solution for 5 min. When the oil bath is heated to 70 °C and stabilized for about 15 min, 2 ml of $K_2S_2O_8$ solution with a concentration of 5 mg/ml was added to the solution to initiate the polymerization. The reaction was continued at 70 °C for 6 hours. The un-reacted molecules were separated by dialysis against Milli-Q water for 24 hours within which the outer Milli-Q water was refreshed every 6 hours. Lastly, the microgel solution was acquired and stored in a container for the following characterization and measurements.

2.3 Self-assembly of P(NIPAM-co-AA) Microgels

The self-assembly of P(NIPAM-*co*-AA) microgels on the gold surface of the QCM sensors was performed by the first deposition of PEI/PASS/PAH multilayer and afterwards the adsorption of anionic P(NIPAM-*co*-AA) microgels onto the adversely charged surfaces. The creation of PEI/PSS/PAH/P(NIPAM-*co*-AA) microgels on the gold surfaces of QCM sensors was monitored using a QCM (IQCM, Resonant Probes GmbH, Goslar, Germany) at 25 °C in a liquid medium. The QCM sensor is an AT-cut quartz crystal (fundamental resonant frequency f_0 = 5 MHz) covered with gold electrodes (100 nm thickness) on both surfaces. The frequency shift of the QCM sensors exposed in the deionized water without adding polymers was first recorded as the reference. After that, the liquid solution was pumped via the QCM flow cells at a flow rate of 10 µl min^{-1}. A layer of PEI (2 mg ml^{-1}) was firstly adsorbed, continued by the other deposition of PSS (1 mg ml^{-1}) and PAH (1 mg/l), lastly the adsorption of P(NIPAM-*co*-AA) microgel (0.025 mg ml^{-1}). After the adsorption of every single layer is finished, the surface was rinsed with deionized water. Note that multilayer samples marked with the code ‘‘PEI/PSS/PAH/MG’’, implies multilayer containing polyelectrolytes and microgels. Since the first harmonic had high-level noise, the QCM information was gained at third (15 MHz) overtone, and the frequency shift utilized here included the normalized changes in the frequency of the third harmonic. The normalization was accomplished by partitioning the adjustment in frequency by its harmonic number. Adsorbed mass change Δm during the layer-by-layer self-assembly was approximately calculated by the use of Sauerbrey equation as provided below:

$$\Delta m = \frac{-C\bullet\Delta F}{n} \qquad (1)$$

Where the constant C is 17.7 ng cm^{-2} Hz^{-1}, n is the overtone, and ΔF is the frequency change. The QCM frequency change (ΔF) were obtained at the third (15MHz) harmonic. To monitor the deposition of the polyelectrolyte and microgels, the frequency response of the uncovered sensors in water was first recorded as the reference, and afterwards, the frequency shift caused by the alternate adsorption of polyelectrolytes which includes PEI, PSS, PAH, and microgels onto sensor surfaces was achieved. To this end, the PEMs were washed with Milli-Q water and blow-dried in a surge of N_2 prior to subjecting them to characterization and estimation under ambient conditions.

2.4 Interactions of the self-assembled microgels with heavy metal ions

The polyelectrolyte/microgels interactions with various metal ions were studied utilizing QCM. To begin with, the self-assembled polyelectrolyte/microgel-coated QCM sensors mounted on the flow cells were opened to Milli-Q water for 1 hour within the formation stage. At that point, the QCM signal was recorded for up to 5 min, while as yet flushing with Milli-Q water to acquire the baseline. The aqueous solutions with the metal ion concentration of 20 ppm were infused into the QCM cells, and the frequency shift identified their interactions with the gathered microgels and deciphered by the mass change on the sensor surface. At long last, the salt solution was supplanted by Milli-Q water, and the signal was recorded.

2.5 Instruments and Characterization

2.5.1 Atomic Force Microscopy

The polyelectrolyte/microgel surface morphologies deposited on the gold surface of the quartz crystal were determined using tapping mode AFM (NanoMan VS, Veeco Instrument Inc., USA) at room temperature in air. A few places at each specimen were imaged.

2.5.2 Water Contact Angle

Water contact angle testing for the polyelectrolyte/ microgel modified gold surface was carried out at room temperature with 60% relative humidity and 1.0 µl drop size. A HARKE-SPCA instrument (Beijing Harke Experimental Apparatus Co., Ltd., China) was applied to calculate the contact angles.

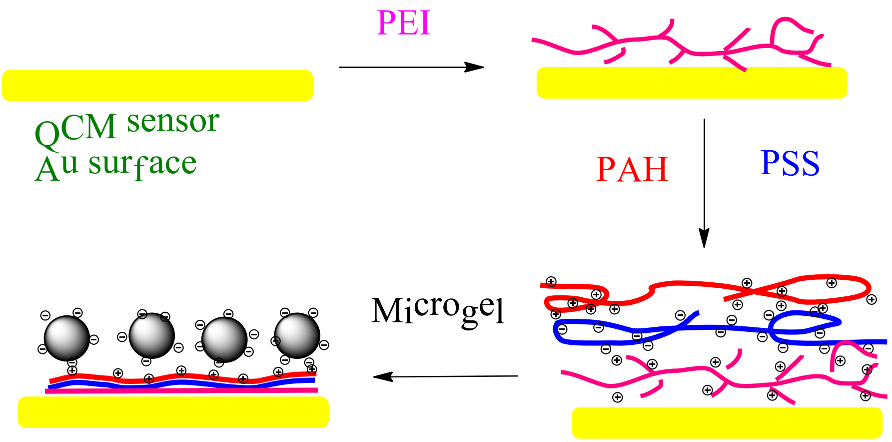
3 Results and discussions

3.1 The build-up of the self-assembled microgels on QCM sensor surface

P(NIPAM-*co*-AA) microgels were fabricated by surfactant-free emulsion polymerization using NIPAM and AA as monomers, MBA as the crosslinking agent, $K_2S_2O_8$ as an initiator. Figure S1 shows (supporting information) the particle size and particle size distribution of the microgel with the NIPAM/AA feed ratio of 3:1. It can be observed that the microgel has a particle size of 408 nm with a PDI value of 0.428. The Zeta potential of the microgels as measured by Zeta potential analyzer was -9.95 mV, indicating the presence of carboxyl groups and negative charges onto the surfaces of microgels. In combination with the oppositely charged polyelectrolyte chains, microgels with negative charges can work as building block for preparing the well-defined polyelectrolyte/microgel self-assembly on gold surfaces of QCM sensors, which is driven by the electrostatic force through the layer-by-layer pathway.

Following the three-step pathway on the gold surfaces of QCM sensors, the self-assembled PEI/PSS/ PAH/microgels were subsequently fabricated. Scheme 1 demonstrates the three stages of the formation, in particular, the modification of the surfaces with PEI chains containing amine groups in their main and side chains, which is followed by the deposition of the anionic PSS carrying negative charges onto the amino-functionalized surfaces, and along these lines connection of the cationic PAH carrying positive charges, at last the adsorption of the anionic microgels. In summary, the negatively charged microgels prepared were self-assembled onto the positively charged PEI/PSS/PAH multilayer coated gold surfaces of QCM sensors.

The QCM method can be used for the concurrent measurements of frequency shift (Δf) and half-band half-width ($\Delta\Gamma$) at the first, third, etc., overtone (n =1, 3 ,...; i.e., f = 5 MHz, 15 MHz). Since the signals received at the first harmonic are not secure and has a high noise level in aqueous solution, it will not be used for the QCM analysis. Figure 1 displays the variation of the normalized a) frequency shift (Δf_n/n) and b) half-band half-width ($\Delta\mathbf{\Gamma}_n$/n) at the third (n=3, 15 MHz), fifth (n = 5, 25 MHz), and seventh harmonics (n = 7, 35 MHz) for the formation of the PEI/PSS/PAH/MG in water. The frequency change, which is correlated with the mass adsorbed on the sensor surface and was recorded in real time. At first, a stable and flat baseline, which acts for the subsequent adsorption of polymer chains was achieved after flushing the QCM cell with MilliQ water. Then, a PEI solution with a concentration of 2 mg ml^{-1} was pumped into the QCM cell. Figure 1a demonstrates a decline in the frequency shift after adding the PEI solution, showing the adsorption of PEI onto the gold surfaces. After obtaining equilibrium, the PEI layer surface was rinsed with Milli-Q water to wash away the unstable PEI chains. Nonetheless, the solution was alternated to the watery PSS solution for absorbing the following layer. At that point, the deposition of PAH



Scheme 1. Self-assembly of the anionic microgels onto the PEI/PSS/PAH layer modified gold surfaces of QCM sensors driven by the electrostatic interaction.

and microgels took place because of the electrostatic attractions between the positively charged ammonium groups and negatively charged carboxyl groups. Note that the flushing strategy was completed before every deposition of the polymer layer. An immediate comparison of the frequency shift acquired at the third (15 MHz), fifth (25 MHz), and seventh harmonics (35 MHz) was observed, and these curves were somewhat spreading or did not demonstrate the indistinguishable value. That implies there is frequency reliance during the measurement, recommending that the self-assembled microgels were not an inflexible thin film but rather a delicate and viscoelastic layer.

ΔΓ, which can uncover the alterations in the structures and viscoelastic performance of the thin polymer layers loaded on the quartz crystal were recorded progressively and in real time. As a rule, the development of a delicate layer on the sensor surface prompts an increased **ΔΓ** value when distorted within the period of the oscillation of quartz crystal. Contrastingly, the deposition of a compact and strong polymer thin film on the sensor surface yields reduced **ΔΓ** values. As revealed in Figure 1b, the rise in **ΔΓ** at three harmonics with the deposition of PEI, PSS, PAH, and P(NIPAM-*co*-AA) microgels was accomplished, indicating the formation of the soft and non-rigid layers on the gold electrode surface of quartz crystal. This can be explained by the attributes of the hydrophilic and hydrated polyelectrolyte chains and the swollen microgels containing water molecules.

The mass of the rigid homogeneous thin films can be evaluated utilizing the Sauerbrey formula. Notwithstanding, in this case, the mass values generally computed in this form are not so exact but rather still supportive for semi-quantitatively analyzing the deposited materials in each layer adsorbed on the sensor surface. Table 1 demonstrates the frequency shift and the corresponding mass change for each layer deposited on the QCM sensor surfaces. From the table underneath it is obvious that the reduction in the frequency shift at third harmonic was observed achieving saturation -41.3 Hz, -30.6 Hz, -93.7 Hz and -275.5 Hz, corresponding to the deposition of PEI, PSS, PAH and microgels, respectively. The mass values calculated by the Equation 1 were 0.731, 0.542, 1.658, and 4.876 μg cm^{-2}. According to the test results, it was obvious that the negatively charged microgels were connected to the positively charged surface of the PEI/PSS/PAH multilayer because of the electrostatic interactions.

3.2 Interactions of the self-assembled microgels and heavy metal ions by QCM

The interactions are between the microgels self-assembled on the QCM sensor and the heavy metal ions. Figure 2 shows the real-time frequency shift at the third harmonic, recorded for the microgels on QCM sensors which is subsequently exposed to numerous heavy metal

Table 1. The frequency shift and the corresponding mass change for polyelectrolyte and microgels deposited on the QCM sensor surfaces.

Layer	**1**	**2**	**3**	**4**
Material	PEI	PSS	PAH	Microgel
Δ*f* (Hz)	41.3	30.6	93.7	275.5
Δm (μg/cm^2)	0.731	0.542	1.658	4.876

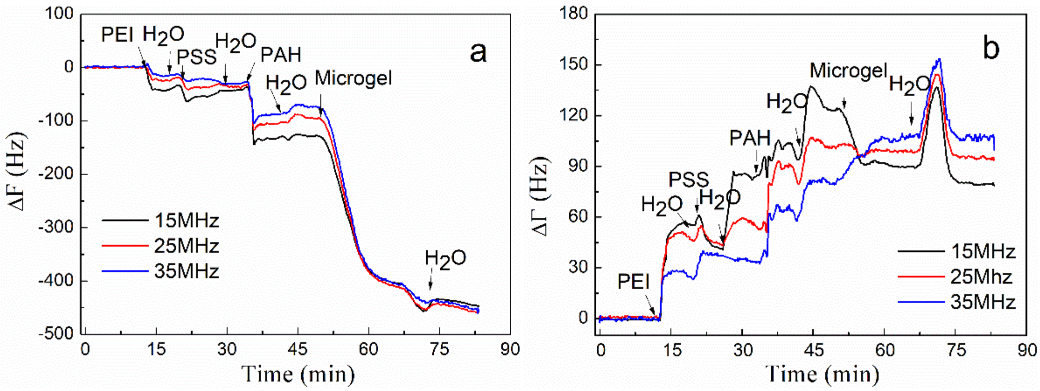


Figure 1. Variation of the a) **Δf** and b)ΔΓ at the 3rd, 5th, and 7th harmonics for the formation of the self-assembled multi-layers made with PEI, PSS, PAH, and P(NIPAM-*co*-AA) microgels in water.

ion solutions, such as 20 ppm of Ca^{2+}, Sn^{2+}, Zn^{2+}, Cu^{2+}, Ni^{2+}, respectively. Note that the microgel-deposited QCN sensor resonance frequency in Milli-Q water was used as the reference state for estimating the frequency shift in light of the heavy metal ions. It can be observed that when exposing the microgel-deposited QCM sensors to various metals ion solution, the resonance frequency reduced simultaneously, thereby, showing the complexation or adsorption of metal ions onto the surface of the microgel modified sensor. It was observed that the 20 ppm Ca^{2+}, Sn^{2+}, Zn^{2+}, Cu^{2+}, and Ni^{2+} in aqueous solution cause the frequency shift of 5.6, 50.3, 38.6, 40.4, and 113 Hz, respectively. The -COOH groups of the microgels might conceal the heavy metal ions successfully, and the stable complexes can be framed among the multivalent metal ions and anionic groups [49]. The microgel-covered sensors frequency response for Ca^{2+} was rather weak, hence, demonstrating the weak adsorption and complexation between Ca^{2+} and microgels. Likewise, the frequency responses of microgel-deposited QCM sensors exposed to some other heavy metal ions including Bi^{3+}, Co^{2+}, and Cd^{2+}, were also investigated. The corresponding areal densities (nmol cm^{-2}) of heavy metal ions obtained by the Sauerbrey equation and the molecular weight of each metal ion were displayed in Figure 2b. It is much more reasonable and exact to use the number of heavy metal ions instead of mass to describe the adsorbed metal ions because of the difference in the molecular weight of various metal ions. Note that the relative molecular weights for Ca^{2+}, Bi^{3+},Cu^{2+}, Zn^{2+}, Ni^{2+}, Sn^{2+}, Co^{2+}, and Cd^{2+} are 40, 208.98, 63.5, 65.4, 58.7, 118.7, 58.9, and 112.4, respectively. From Figure 2b, it is obvious that areal density of Ni^{2+} is around 34.1 nmol cm^{-2}, which is higher when compared to the values of the other heavy metal ions. These outcomes displayed that the microgel-coated QCM sensors shown high selectivity for the identification of Ni^{2+} over other heavy metal ions in aqueous solutions, which will guarantee making metal ion materials that are selective and building up the sensing framework for the detection of Ni^{2+}.

To confirm the microgel-deposited QCM sensors detection limit and uncover more information on changes in the structures and viscoelastic properties of microgels on the gold surfaces, Δf and $\Delta\Gamma$ at the third harmonic were investigated as function of time when exposing the microgel-deposited sensors to a series of Ni^{2+} solutions with a lower concentration of 0.1, 1, and 5 ppm. As shown in Figure 3, with the consecutive replacement of Ni^{2+} aqueous solutions, the frequency shift of microgel deposited QCM sensor decreased, and each Ni^{2+} aqueous solution obtained a stable adsorption equilibrium. The lowest detection limit of the microgel modified QCM sensor

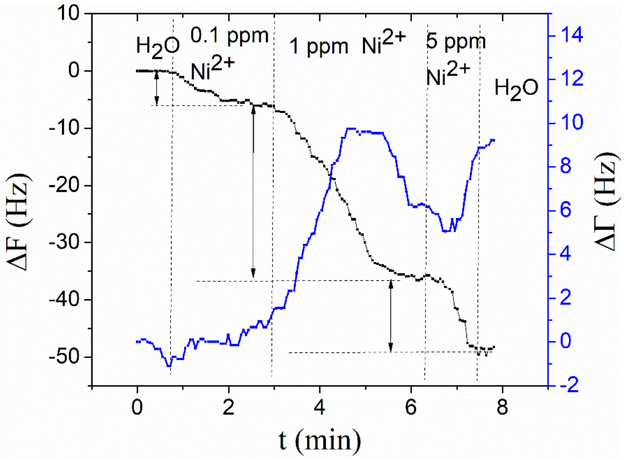


Figure 3. Frequency shift (Δf) and half-band half-width (ΔΓ) at the third harmonic as a function of time for the adsorption of Ni^{2+} at a progressively expanded concentration (0.1 ppm, 1 ppm, 5 ppm) onto microgel modified QCM sensor surfaces.

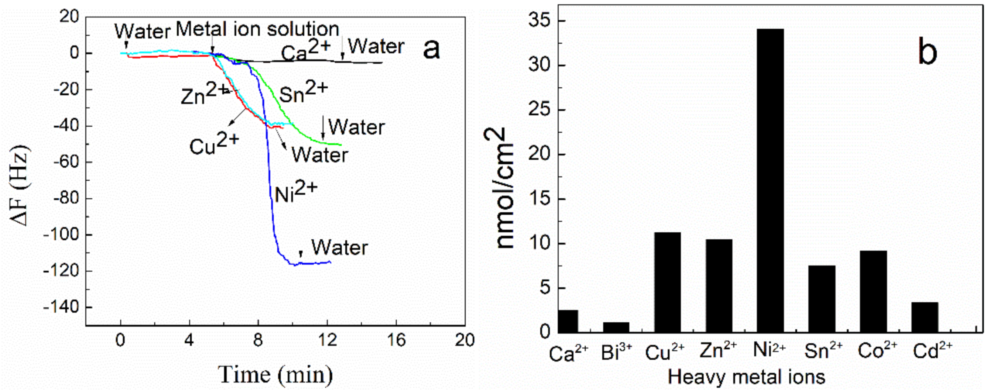


Figure 2. a) The net frequency shifts of the PEI/PSS/PAH/Microgel deposited QCM sensors in numerous heavy metal ion solution with the same concentration of 20 ppm as a function of time. b) The corresponding areal densities (nmol cm^{-2}) of heavy metal ions obtained by the Sauerbrey equation and the molecular weight of each metal ion after rinsing with water.

for Ni^{2+} can be as low as 0.1 ppm in an aqueous solution. The 0.1 ppm Ni^{2+} in the aqueous solution prompted the frequency shift of 6.1 Hz. It was increased to 48.6 Hz for 5 ppm Ni^{2+} in aqueous solution. Upon introduction to the Ni^{2+} solution, it was discovered that $\Delta\Gamma$ of the microgel adjusted sensor ascends to a positive value. The high $\Delta\Gamma$ shift for Ni^{2+} studied for the microgels can be clarified by the solid connections between anionic groups and Ni^{2+}. As reported in the literature, the stable complexes can be formed between the multivalent metal ions and anionic groups. As the Ni^{2+} is not totally dehydrated and consistently conveys water molecules into microgels, this gives rise to the soft and hydrated structures.

Figure 4 plots the Ni^{2+} concentration versus frequency shift for the information of Figure 3. The obvious linear connection between the Ni^{2+} concentration and frequency shift was achieved in the scope of 0.1 ppm to 20 pm for the microgel modified QCM sensors. This outcome shows that the microgel modified QCM sensor can be utilized for detecting Ni^{2+} in aqueous solutions.

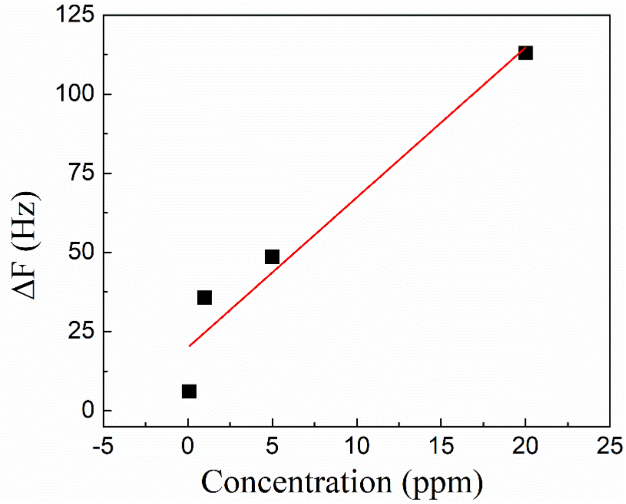


Figure 4. The total frequency shifts at the third harmonic of the microgel-coated QCM sensors in Ni^{2+} aqueous solutions as a function of the Ni^{2+} concentration (0.1, 1, 5, and 20 ppm).

Figure 5 shows the AFM morphologies of the bare and microgel covered gold surfaces of QCM sensors with the scanning area of 5 µm×5 µm. The images of water contact angles on the bare and microgel modified gold surface of QCM sensors were also inserted. From Figure 5, it can be observed that the bare gold surface of QCM sensor seems rather flat and smooth. Compared to the bare gold; the microgel modified surfaces are rather rough. It can be obviously observed that the microgel particles with a size of about 500 nm were dispersed on the gold surface. The microgel particles did not completely cover the gold surface. That is because in our case, the concentration of microgel solution was in a lower concentration range and was not high enough to form the continuous microgel film during the LbL self-assembly procedure. Note that the height of microgels shown in Figure 5c is 117±5 nm. The water contact angles on the bare gold surface of QCM sensors is 88.6 °, indicating the hydrophobic nature of the gold. After modifying the gold surface, the contact angle was decreased to 76.9 °, confirming the formation of the self-assembly on gold made with the anionic and hydrophilic polyelectrolyte and microgels. The contact angle on microgel modified surface seems not much lower than that of hydrophobic gold due to the partial coverage of the microgels on gold, which is consistent with the results generated by AFM.

Figure 6 shows the AFM morphologies of P(NIPAM-*co*-AA) microgel deposited on the gold surface of QCM sensors after exposing to Cu^{2+}, Ni^{2+}, and Zn^{2+} with the scanning area of 5 µm×5 µm. It can be observed that the morphologies of the microgel deposited surface after exposing to heavy metal ions were quite similar to that of the microgel covered surface before exposing it to heavy metal ions. This signifies the exceptional stability of the PEI/PSS/PAH/microgels adsorbed on the QCM sensor's gold surface.

4 Conclusions

The self-assembled microgels were deposited on the QCM sensor surface by the LbL procedure with polyelectrolytes and anionic microgels because of the electrostatic interactions. QCM estimations including frequency and $\Delta\Gamma$ signals confirmed the formation of PEI/PSS/PAH/Microgel self-assembled and formation of the hydrated viscoelastic structures. The self-assembled microgel-containing networks with –COOH groups were permitted to absorb the heavy metal ions, which can be observed by the same QCM procedure. This two-dimensional microgel modified QCM sensors is one perfect platform for specifically detecting Ni^{2+}, with the most minimal detection limit of 0.1 ppm in aqueous solution and the obvious linear relationship between the frequency shift and Ni^{2+} concentration (0.1-20 ppm). The images of AFM likewise revealed that in contrast to the exposed surface of QCM sensor, the microgel-coated QCM sensors had a high surface roughness. It can be discovered that the microgel particles with a size of around 500 nm were dispersed on the gold surface. The morphologies of the microgel deposited surface after exposing to heavy metal ions were similar to that of the microgel covered surface prior to exposing it to heavy

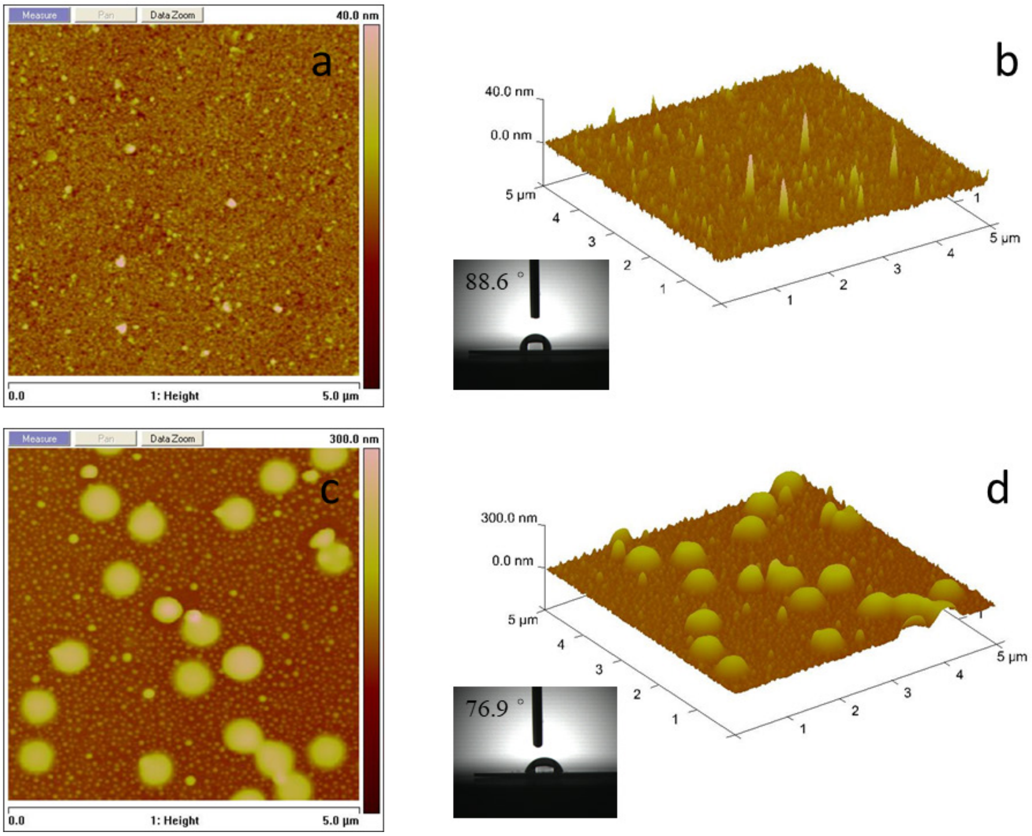


Figure 5. AFM morphologies of the bare (a two dimensional, b three dimensional) and microgel modified (c two dimensional, d three dimensional) gold surfaces of QCM sensors with the scanning area of 5 μm×5 μm. The images of water contact angles on the bare and microgel modified the gold surface of QCM sensors were also inserted.

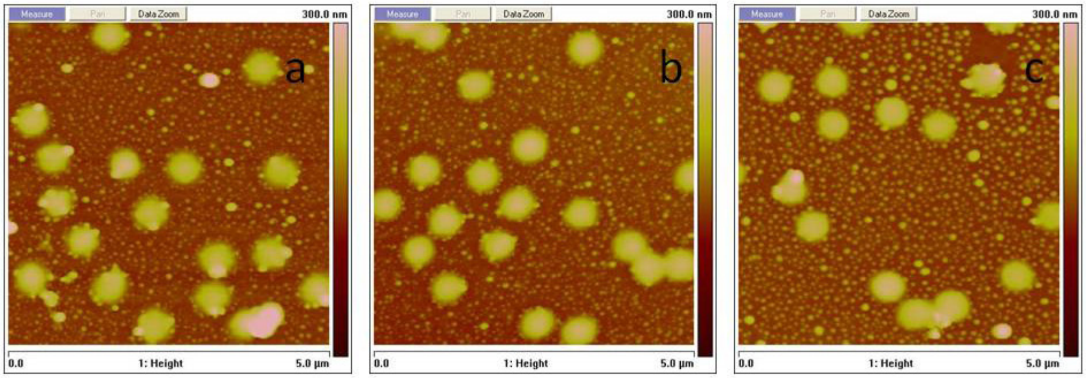


Figure 6. AFM morphologies of P(NIPAM-*co*-AA) microgel deposited on the QCM sensors gold surface after exposing to Cu^{2+}, Ni^{2+}, and Zn^{2+} with a concentration of 20 ppm and the scanning area of 5 μm×5 μm and the height of 115±10 nm, 121±3 nm, and 125±3 nm, respectively.

metal ions, demonstrating the excellent stability of the microgels modified QCM sensors. We reported a novel method of studying the microgel-ion system, which employs the use of two-dimensional self-assembly containing microgels deposited on surfaces and the QCM strategy. This will guarantee manufacturing sensing materials with the assistance of QCM procedure for detection purposes.

Acknowledgements: This project is supported by the National Natural Science Foundation of China (Grant No. 21644002 and 21704008). Financial support was provided for this project by the Top-notch Academic Programs Project of Jiangsu Higher Education Institutions (TAPP) and the Priority Academic Program Development of Jiangsu Higher Education Institutions (PAPD). The Natural Science Foundation of the Jiangsu Higher

Education Institutions of China (Grant No. 16KJB150003), and Jiangsu Provincial University-Industry Cooperation Innovation Foundation Prospective Study of China (Grant No. BY2016029-21), and financial support from the MOE Key Laboratory of Macromolecular Synthesis and Functionalization, Zhejiang University (2017MSF01) are also acknowledged and appreciated accordingly.

References

[1] Saunders, B. R.; Vincent, B., Microgel particles as model colloids: theory, properties and applications. *Adv. Colloid Interface Sci.* **1999,** *80*, 1.

[2] Lyon, L. A.; Meng, Z.; Singh, N.; Sorrell, C. D.; John, A. S., Thermoresponsive microgel-based materials *Chem. Soc. Rev.* **2009,** *38*, 865-874.

[3] Ballauff, M.; Lu, Y., “Smart” nanoparticles: Preparation, characterization and applications. *Polymer* **2007,** *48*, 1815-1823.

[4] Tanaka, T.; Fillmore, D., Kinetics of swelling of gels *J. Chem. Phys.* **1979,** *70*, 1214-1218.

[5] Fernandez-Nieves, A.; Fernandez-Barbero, A.; Vincent, B.; de las Nieves, F. J., Charge controlled swelling of microgel particles. *Macromolecules* **2000,** *33*, 2114-2118.

[6] Nolan, C. M.; Serpe, M. J.; Lyon, L. A., Thermally modulated insulin release from microgel thin films *Biomacromolecules* **2004,** *5*, 1940.

[7] Senff, H.; Richtering, W., Temperature sensitive microgel suspensions: Colloidal phase behavior and rheology of soft spheres. *J. Chem. Phys.* **1999,** *111*, 1705-1711.

[8] Cao, Z.; Du, B.; Chen, T.; Nie, J.; Xu, J.; Fan, Z., Preparation and properties of thermo-sensitive organic/inorganic hybrid microgels. *Langmuir* **2008,** *24* (22), 12771-12778.

[9] Nicodemus, G. D.; Bryant, S. J., Next generation nerve guides: materials, fabrication, growth factors, and cell delivery *Tissue Eng.: Part B Rev.* **2008,** *14*, 149.

[10] Ahadian, S.; Sadeghian, R. B.; Salehi, S.; Ostrovidov, S.; Bae, H.; Ramalingam, M.; Khademhosseini, A., Bioconjugated hydrogels for tissue engineering and regenerative medicine. *Bioconjugate Chem.* **2015,** *26* (10), 1984-2001.

[11] Biffis, A.; Cunial, S.; Spontoni, P.; Prati, L., Microgel-stabilized gold nanoclusters: Powerful “quasi-homogeneous” catalysts for the aerobic oxidation of alcohols in water. *J. Catal.* **2007,** *251* (1), 1-6.

[12] Lu, Y.; Proch, S.; Schrinner, M.; Drechsler, M.; Kempe, R.; Ballauff, M., Thermosensitive core-shell microgel as a “nanoreactor” for catalytic active metal nanoparticles. *J. Mater. Chem.* **2009,** *19* (23), 3955-3961.

[13] Ranjha, N. M.; Mudassir, J.; Akhtar, N., Methyl methacrylate-co-itaconic acid (MMA-co-IA) hydrogels for controlled drug delivery. *J. Sol.-Gel Sci. Technol.* **2008,** *47*, 23-30.

[14] Rathna, G. V. N., Gelatin hydrogels: enhanced biocompatibility, drug release and cell viability. *J. Mater. Sci.: Mater. Med.* **2008,** *19*, 2351-2358.

[15] Choi, W. I.; Kim, M.; Tae, G.; Kim, Y. H., Sustained release of human growth hormone from heparin-based hydrogel. *Biomacromolecules* **2008,** *9*, 1698-1704.

[16] Li, B.; Jiang, X.; Yin, J., Multi-responsive microgel of hyperbranched poly(ether amine) (hPEA-mGel) for the selective adsorption and separation of hydrophilic fluorescein dyes. *J. Mater. Chem.* **2012,** *22* (34), 17976-17983.

[17] Romero, M. R.; Garay, F.; Baruzzi, A. M., Design and optimization of a lactate amperometric biosensor based on lactate oxidase cross-linked with polymeric matrixes *Sens. Actuators, B* **2008,** *131*, 590-595

[18] Kim, J. S.; Singh, N.; Lyon, L. A., Label-free biosensing with hydrogel microlenses. *Angew. Chem., Int. Ed.* **2006,** *45*, 1446-1449

[19] Mastour Tehrani, S.; Lu, Y.; Guerin, G.; Soleimani, M.; Pichugin, D.; Winnik, M. A., Temperature-invariant aqueous microgels as hosts for biomacromolecules. *Biomacromolecules* **2015,** *16* (10), 3134-3144.

[20] Fan, K.; Bradley, M.; Vincent, B.; Faul, C. F. J., Effect of chain length on the interaction between modified organic salts containing hydrocarbon chains and Poly(N-isopropylacrylamide-co-acrylic acid) microgel particles. *Langmuir* **2011,** *27* (8), 4362-4370.

[21] Yin, J.; Guan, X.; Wang, D.; Liu, S., Metal-chelating and dansyl-labeled Poly(N-isopropylacrylamide) microgels as fluorescent Cu2+ sensors with thermo-enhanced detection sensitivity. *Langmuir* **2009,** *25* (19), 11367-11374.

[22] Yi, X.; Xu, Z.; Liu, Y.; Guo, X.; Ou, M.; Xu, X., Highly efficient removal of uranium(vi) from wastewater by polyacrylic acid hydrogels. *RSC Advances* **2017,** *7* (11), 6278-6287.

[23] Zhou, X.; Nie, J.; Du, B., 4-(2-Pyridylazo)-resorcinol functionalized thermosensitive ionic microgels for optical detection of heavy metal ions at nanomolar level. *ACS Appl. Mater. Interfaces* **2015,** *7* (39), 21966-21974.

[24] Chen, H.; Dai, L. L., Adsorption and release of active species into and from multifunctional ionic microgel particles. *Langmuir* **2013,** *29* (36), 11227-11235.

[25] Cea, P.; Ballesteros Luz, M.; Martín, S., Nanofabrication techniques of highly organized monolayers sandwiched between two electrodes for molecular electronics. *Nanofabrication* **2014,** *1* (1), 96–117.

[26] Vafai, N.; Lowry Troy, W.; Wilson Korey, A.; Davidson Michael, W.; Lenhert, S., Evaporative edge lithography of a liposomal drug microarray for cell migration assays. *Nanofabrication* **2015,** *2* (1), 32-42.

[27] Serpe, M. J.; Jones, C. D.; Lyon, L. A., Layer-by-Layer deposition of thermoresponsive microgel thin films. *Langmuir* **2003,** *19* (21), 8759-8764.

[28] Clarke, K. C.; Lyon, L. A., Modulation of the deswelling temperature of thermoresponsive microgel films. *Langmuir* **2013,** *29* (41), 12852-12857.

[29] Seeber, M.; Zdyrko, B.; Burtovvy, R.; Andrukh, T.; Tsai, C.-C.; Owens, J. R.; Kornev, K. G.; Luzinov, I., Surface grafting of thermoresponsive microgel nanoparticles. *Soft Matter* **2011,** *7* (21), 9962-9971.

[30] Spears, M. W.; Herman, E. S.; Gaulding, J. C.; Lyon, L. A., Dynamic materials from microgel multilayers. *Langmuir* **2014,** *30* (22), 6314-6323.

[31] Serpe, M. J.; Yarmey, K. A.; Nolan, C. M.; Lyon, L. A., Doxorubicin uptake and release from microgel thin films. *Biomacromolecules* **2005,** *6* (1), 408-413.

[32] Islam, M. R.; Xie, S.; Huang, D.; Smyth, K.; Serpe, M. J., Poly (N-Isopropylacrylamide) microgel-based optical devices for humidity sensing. *Anal. Chim. Acta* **2015,** *898*, 101-108.

[33] Gao, Y.; Li, X.; Serpe, M. J., Stimuli-responsive microgel-based etalons for optical sensing. *RSC Advances* **2015,** *5* (55), 44074-44087.

[34] Islam, M.; Ahiabu, A.; Li, X.; Serpe, M., Poly (N-isopropylacrylamide) microgel-based optical devices for sensing and biosensing. *Sensors* **2014,** *14* (5), 8984–8995.

[35] Johnson, K. C. C.; Mendez, F.; Serpe, M. J., Detecting solution pH changes using poly (N-isopropylacrylamide)-co-acrylic acid microgel-based etalon modified quartz crystal microbalances. *Anal. Chim. Acta* **2012,** *739*, 83-88.

[36] Wang, L.; Wang, X.; Xu, M.; Chen, D.; Sun, J., Layer-by-Layer assembled microgel films with high loading capacity: reversible loading and release of dyes and nanoparticles. *Langmuir* **2008,** *24* (5), 1902-1909.

[37] Wang, X.; Zhang, L.; Wang, L.; Sun, J.; Shen, J., Layer-by-Layer assembled polyampholyte microgel films for simultaneous release of anionic and cationic molecules. *Langmuir* **2010,** *26* (11), 8187-8194.

[38] Islam, M. R.; Serpe, M. J., Penetration of polyelectrolytes into charged Poly(N-isopropylacrylamide) microgel layers confined between two surfaces. *Macromolecules* **2013,** *46* (4), 1599-1606.

[39] Sigolaeva, L. V.; Gladyr, S. Y.; Gelissen, A. P. H.; Mergel, O.; Pergushov, D. V.; Kurochkin, I. N.; Plamper, F. A.; Richtering, W., Dual-stimuli-sensitive microgels as a tool for stimulated spongelike adsorption of biomaterials for biosensor applications. *Biomacromolecules* **2014,** *15* (10), 3735-3745.

[40] Nyström, L.; Nordström, R.; Bramhill, J.; Saunders, B. R.; Álvarez-Asencio, R.; Rutland, M. W.; Malmsten, M., Factors affecting peptide interactions with surface-bound microgels. *Biomacromolecules* **2016,** *17* (2), 669-678.

[41] Wang, X.; Liu, G.; Zhang, G., Conformational behavior of grafted weak polyelectrolyte chains: effects of counterion condensation and nonelectrostatic anion adsorption. *Langmuir* **2011,** *27* (16), 9895-9901.

[42] Höök, F.; Kasemo, B.; Nylander, T.; Fant, C.; Sott, K.; Elwing, H., Variations in coupled water, viscoelastic properties, and film thickness of a Mefp-1 protein film during adsorption and cross-Linking: a quartz crystal microbalance with dissipation monitoring, ellipsometry, and surface plasmon resonance study. *Anal. Chem.* **2001,** *73* (24), 5796-5804.

[43] Wu, Y.; Ma, H.; Gu, D.; He, J. a., A quartz crystal microbalance as a tool for biomolecular interaction studies. *RSC Advances* **2015,** *5* (79), 64520-64525.

[44] Cao, Z.; Tsoufis, T.; Svaldo-Lanero, T.; Duwez, A.-S.; Rudolf, P.; Loos, K., The dynamics of complex formation between amylose brushes on gold and fatty acids by QCM-D. *Biomacromolecules* **2013,** *14* (10), 3713-3722.

[45] Cao, Z.; Du, B.; Chen, T.; Li, H.; Xu, J.; Fan, Z., Fabrication and properties of thermosensitive organic/inorganic hybrid hydrogel thin films. *Langmuir* **2008,** *24* (10), 5543-5551.

[46] Du, B.; Johannsmann, D., Operation of the quartz crystal microbalance in liquids: derivation of the elastic compliance of a film from the ratio of bandwidth shift and frequency shift. *Langmuir* **2004,** *20* (7), 2809-2812.

[47] Cao, Z.; Guo, J.; Fan, X.; Xu, J.; Fan, Z.; Du, B., Detection of heavy metal ions in aqueous solution by P(MBTVBC-co-VIM)-coated QCM sensor. *Sens. Actuators, B* **2011,** *157* (1), 34-41.

[48] Shen, L.; Chaudouet, P.; Ji, J.; Picart, C., pH-amplified multilayer films based on hyaluronan: influence of HA molecular weight and concentration on film growth and stability. *Biomacromolecules* **2011,** *12* (4), 1322-1331.

[49] Morris, G. E.; Vincent, B.; Snowden, M. J., Adsorption of lead ions onto N-isopropylacrylamide and acrylic acid copolymer microgels. *J. Colloid Interface Sci.* **1997,** *190* (1), 198-205.

Supplemental Material: The online version of this article
(DOI: 10.1515/nanofab-2017-0002) offers supplementary material.