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Q-Sense [Application Note] 34

Characterization of polymer layer swelling and collapse by the QCM-D technology

Surface coatings can be applied to a bulk material to add desirable properties such as biocompatibility, responsiveness to various stimuli, drug delivery capabilities and antibacterial qualities. Polymer brushes, which respond to changes in temperature, pH and ionic strength have been of great interest as surface coatings for biomedical and biological applications. In this study, the QCM-D technology was successfully used to track and understand the mechanism of swelling and collapse of polymer brushes.

Introduction

Chitosan (CH) brush layers are an attractive coating because chitosan is both bio-compatible and biodegradable. Chitosan is water-soluble at low pH but is a collapsed coil that is insoluble in water at pH above 6.5. The rheological properties, solubility and swelling of chitosan depend on pH and counter-anion size, because both parameters directly affect the extent of intra- and intermolecular electrostatic repulsions. Due to its limited solubility near physiological conditions (pH~7), chitosan has not been fully utilized as a biomaterial coating. To make chitosan water-soluble above pH 6.5 the molecule can be modified with quaternary ammonium salts (CH-Q). In the study reviewed here, the aim was to understand the mechanism of brush swelling for chitosan and modified chitosans. The Quartz Crystal Microbalance with Dissipation (QCM-D) technology was used to study the thickness of the polymer brushes as they were exposed to different ambient conditions.

Experimental

Reference measurements

The E4 QCM-D instrument was used with silicon dioxide sensors. The sensors were subjected to silane deposition and CH and CH-Q were grafted onto the silane layer. In order to calculate the extent of swelling in aqueous media, the initial dry thickness of the polymer brush was determined by QCM-D measurements and the Sauerbrey equation that relates mass changes to frequency changes.

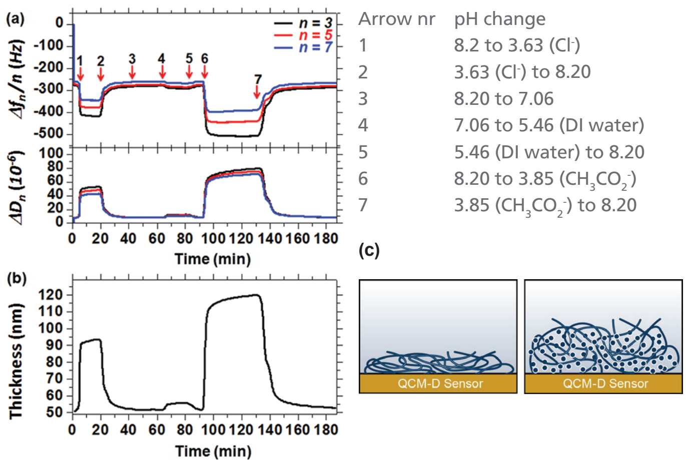
Results

In situ swelling of the polymer brushes – effect of pH and counteranion type

The chitosan polymer brush coated sensor was subjected to solutions of different pH and counter-anion type. The measured frequency (related to mass) and dissipation (related to rigidity) values were used in the Voigt viscoelastic model to determine the thickness of the layer during swelling and contraction (Figure 1). At low pH, the CH layer swells and becomes more viscous, whereas at higher pH (pH 7.06 and 8.20), the CH layer is elastic and rigid.

In order to study the effect of counter-anion type on the viscoelastic and swelling properties of the CH brush layer, it was exposed to a solution at pH 3.85 containing acetate anions ($CH_3CO_2^-$) (arrow 6) for comparison with the behavior when exposed to a solution at pH 3.63 containing chloride anions (arrow 1).

The larger counter-anions ($CH_3CO_2^-$) induce the layer to become more viscous and swell to a greater extent than the smaller counter-anions (Cl^-).

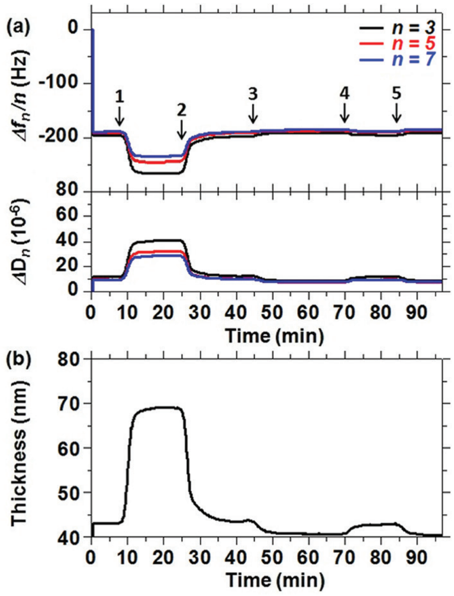


Arrow nr	pH change
1	8.2 to 3.63 (Cl^-)
2	3.63 (Cl^-) to 8.20
3	8.20 to 7.06
4	7.06 to 5.46 (DI water)
5	5.46 (DI water) to 8.20
6	8.20 to 3.85 ($CH_3CO_2^-$)
7	3.85 ($CH_3CO_2^-$) to 8.20

[Figure 1]: (a) Frequency (f) and dissipation (D) shifts (for overtone 3, 5 and 7) of a CH brush versus time as a function of sequential changes of solution pH and counter-anion type. (b) Thickness determined with the Voigt viscoelastic model versus time. (c) Illustrations showing collapsed (left) and swollen brushes (right), respectively.

It is also observed that the swelling is reversible. To summarize, these studies demonstrated that the immobilized CH layer is chemically stable over a wide range of pH values and exhibit reversible swelling and contraction that can be tuned by varying the pH of the solution and counter-anion type.

The same kind of study was performed on CH-Q to compare with unmodified CH. The results for one kind of modification (CH-Q25) can be seen in Figure 2. As the pH decreases, the CH-Q25 brush becomes more viscous and swells, whereas at higher pH, in the range of 7.06 to 8.20, CH-Q25 is more elastic and rigid.



Arrow nr	pH change
1	5.46 to 3.63 (Cl-)
2	3.63 (Cl-) to 5.45
3	5.46 to 7.06
4	7.06 to 5.46 (DI Water)
5	5.46 to 8.20

[Figure 2]: (a) Frequency (f) and dissipation (D) shifts (for overtone 3, 5 and 7) versus time for grafted CH-Q25 as a function of sequential changes of the solution pH.
(b) Thickness determined with the Voigt viscoelastic model versus time.

At high pH, when the CH-Q25 wet film is at its minimum thickness, it is approximately 2 x thicker than the dry thickness of CH-Q25. For the CH layer, at high pH, the thinnest wet film is the same as the dry thickness. So, at pH values of 8.20 and 7.06, the CH-Q25 layer is swollen by water resulting in a viscous layer, whereas the CH layer contains very little water and behaves more like a solid-like film. By using another molecule, CH-Q50, high swelling at high pH can be achieved (data not shown).

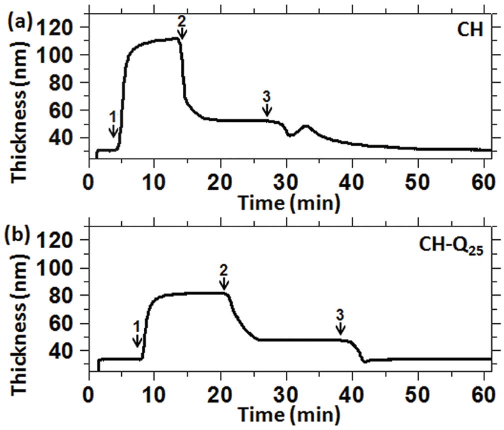
Collapse by cross-linking

The possibility to use multifunctional anions for crosslinking with cationic polymers was investigated. The polymer brush layer was subjected to different anions at similar pH and the effect of anion was noted.

In Figure 3, it can be seen that when the citrate anions are replacing the acetate anions, ionic cross-links are formed with the ammonium cations on the CH brush and the brush layer collapses. This reaction, illustrated in figure 4, is a facile method to trap/concentrate and release active agents and the capacity and dynamics of the brush can be further tuned by the quaternary ammonium content in chitosan.

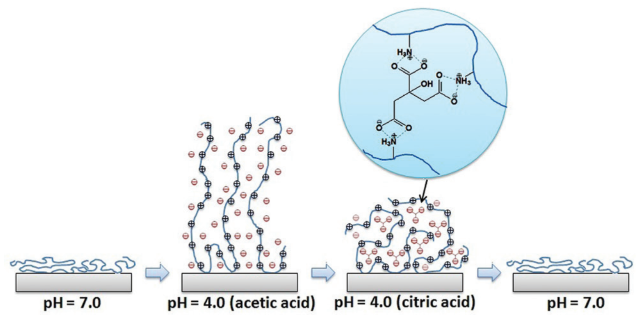
Conclusions

Here we have shown that QCM-D was successfully used to understand the mechanism of swelling and collapse of polymer brushes. This knowledge is crucial when designing surface coatings for biomedical and biological applications.



Arrow nr	pH change
1	7.06 to 4.05 (acetate)
2	4.05 to 4.08 (citrate)
3	4.08 to 7.06

[Figure 3]: Thicknesses of CH (a) and CH-Q25 (b) brush layers as a function of sequential changes in solution pH and counter-anion. The thicknesses of CH and CH-Q25 were determined with the Voigt viscoelastic model.



[Figure 4]: Schematic showing the structure of the chitosan brush layer as a function of pH and counter- anion type.

References:

[1] Hyun-Su Lee, Michael Q. Yee, Yonaton Y. Eckmann, Noreen J. Hickok, David M. Eckmann and Russell J. Composto. Reversible swelling of chitosan and quaternary ammonium modified chitosan brush layers: effects of pH and counter anion size and functionality. J. Mater. Chem, 2012, 22, 19605.

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