

## Stimuli responsive multilayer films based on host-guest interactions between biocompatible polymers

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### Experimental section

#### General

The chitosan used has a weight-average molecular weight  $M_w$  of 195000; it is a commercial sample from Pronova (Norway) with a degree of *N*-acetylation equal to 0.12. It was purified by solubilization in aqueous  $\text{CH}_3\text{COOH}$  and reprecipitation by  $\text{NaOH}$  at neutral pH. The polysaccharide was finally washed with deionized water and ethanol and then dried. The  $\beta$ -cyclodextrin was kindly supplied by Roquette Frères (Lestrem, France). Cyclodextrin grafted chitosan (average degree of substitution (DS) = 0.07) and adamantane grafted chitosan (DS = 0.05) were synthesized in the laboratory as described previously.<sup>1,2</sup> 1-adamantane acetic acid and all other chemicals were purchased from Fluka (Buchs, Switzerland).  $^{13}\text{C}$  NMR spectra were recorded using a Bruker DRX400 spectrometer operating at 100 MHz. Chemical shifts are given relative to external tetramethylsilane (TMS = 0 ppm) and calibration was performed using the signal of the residual carbons of the solvent as a secondary reference. Electron impact mass spectra were measured in the positive mode on a Varian MAT 311 mass spectrometer.

#### Synthesis of adamantane acetamidoethanethiol (AD-SH)

To a solution of adamantane acetic acid (0.5 g, 2.57 mmol) in dry DMF (15 mL), hydroxybenzotriazole (0.35 g, 2.57 mmol), 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (0.64 g, 3.35 mmol) dissolved in DMF (5 mL) in the presence of *N*-ethyldiisopropylamine (1.05 mL, 6.18 mmol) and cysteamine hydrochloride were successively added under nitrogen. After 14 h of stirring at room temperature under nitrogen, the solvent was evaporated under vacuum. The residual oil was dissolved in diethyl ether (200 mL) and the resulting organic phase was washed with  $\text{H}_2\text{O}$  (2×30 ml and 1×20 ml) and dried ( $\text{Na}_2\text{SO}_4$ ). Solvent was evaporated under vacuum to yield AD-SH as a white powder (0.38 g, 1.50 mmol).

Yield: 58 %

$^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  (ppm): 28.8 (3 CH adamantane), 32.9 (1 C 4° adamantane), 36.9 (3  $\text{CH}_2$  adamantane, 1  $\text{CH}_2\text{SH}$ ), 42.5 ( $\text{CH}_2\text{CO}$ ,  $\text{CH}_2\text{NH}$ ), 48.9 (3  $\text{CH}_2$  adamantane), 178.4 (CO)

EI-MS:  $m/z$  253.1503 [ $\text{C}_{14}\text{H}_{23}\text{NOS}$ ]<sup>+</sup>

#### QCM-D experiments

All experiments were performed on a quartz microbalance from Q-sense, Gottenburg, Sweden. The measurements were realized at 24 °C in a batch mode using 0.3 M  $\text{CH}_3\text{COOH}$  /0.03 M  $\text{CH}_3\text{COONa}$ , the usual solvent of chitosan.<sup>1-3</sup> This solvent has been proved to be the more appropriate to chitosan elution, preventing aggregation phenomena.<sup>4</sup> Salt was added in order to screen the long range electrostatic repulsions between positively charged chains. The dissolution time was at least 12 h at room temperature to allow a correct dilution of the adamantyl- and cyclodextrin grafted polysaccharides. Several injections of the solution were performed in order to overcome depletion phenomena. Polymers were injected at increasing concentration (from 0.05 g/L to 1 g/L) in order to ensure saturation for the initial surface and for each layer. Gold-coated quartz crystal were cleaned and functionalized according to the following procedure. After a 10 min UV/ozone treatment, the crystal were immersed in a 1:1:6 (v/v/v) solution of  $\text{NH}_3$  (25%)/ $\text{H}_2\text{O}_2$  (30%)/ $\text{H}_2\text{O}$  and heated to 70 °C for 10 min followed by rinsing with water and drying in a stream of nitrogen gas.<sup>5</sup> A self-assembled monolayer (SAM) made from a mixture of ethanethiol and adamantane acetamidoethanethiol (thiol-adamantane) was used to obtain a defined gradient of the interfacial composition. Crystals were soaked in ethanolic solution of the desired thiol mixture for 18 hours at room

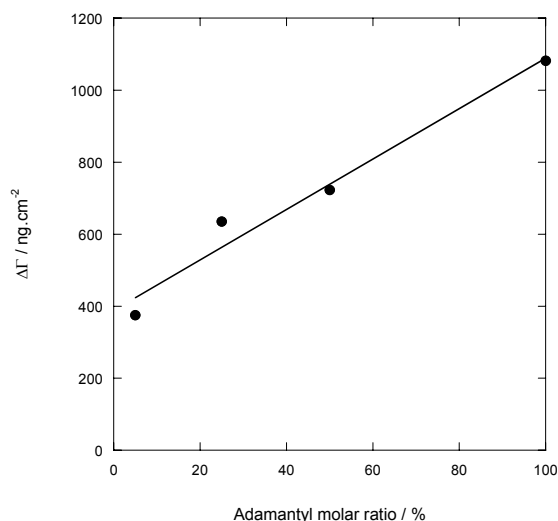
temperature. Thiol solutions were prepared with 1 mM stock solutions of ethanethiol and acetamidoethanethiol. The mole fraction of acetamidoethanethiol adsorbed on surface, in default to be the same, is supposed to increased with its bulk molar fraction, in all the range of concentrations.<sup>6</sup> *To simplify the lecture of the manuscript, the SAMs adamantane densities mentioned in the text are the thiol-adamantane bulk concentration.* After rinsing with ethanol and water followed by drying in a stream of nitrogen gas, the quartz is mounted in the QCM-D chamber. Therefore,  $\Delta f$  and  $\Delta D$  recorded for the 5 MHz fundamental frequency and for the 3<sup>rd</sup>, 5<sup>th</sup> and 7<sup>th</sup> overtones, equal 0 for all surfaces prior the deposition of the first layer. Data were fitted, according to the viscoelastic model described by Voinova, using Q-tools modelling software. Each value, except for experiments concerning the ionic strength influence, is taken after rinsing with solvent to remove solvent effect on frequency and dissipation.

**Table 1** Analysis of the QCM-D response according to the Voinova's model<sup>7</sup> with  $\Delta\Gamma$  the mass,  $\mu$  the shear elastic modulus and  $\eta$  the shear viscosity of the polymer adsorbed layer.

Layer nb	Polymer	AD-SH molar ratio of the adsorption solution								
		50%			25%			5%		
		$\eta$ (kg/ms)	$\mu$ (Pa)	$\Delta\Gamma$ (ng/cm <sup>2</sup> )	$\eta$ (kg/ms)	$\mu$ (Pa)	$\Delta\Gamma$ (ng/cm <sup>2</sup> )	$\eta$ (kg/ms)	$\mu$ (Pa)	$\Delta\Gamma$ (ng/cm <sup>2</sup> )
1	Chi-CD	$1.38 \times 10^{-3}$	$5.73 \times 10^4$	1368	$1.34 \times 10^{-3}$	$5.59 \times 10^4$	907	$1.39 \times 10^{-3}$	$5.55 \times 10^4$	951
2	Chi-Ad	$1.30 \times 10^{-3}$	$4.98 \times 10^4$	530	$1.31 \times 10^{-3}$	$5.06 \times 10^4$	657	$1.38 \times 10^{-3}$	$5.53 \times 10^4$	946
3	Chi-CD	$1.36 \times 10^{-3}$	$5.35 \times 10^4$	-288	$1.25 \times 10^{-3}$	$4.44 \times 10^4$	437	$1.36 \times 10^{-3}$	$5.47 \times 10^4$	85

### Competition experiments with free $\beta$ -CD

Chit-CD layer was formed by adsorption of a 1g/L polymer solution on the various SAMs (a 2g/L solution was used on the 50% adamantyl SAM). 5mM solution of free  $\beta$ -CD was then injected on this layer. Competition between free CD and CD moieties grafted to the polymer adsorbed on the adamantyl surfaces induced partial desorption of the chit-CD layer. A last step of rinsing with solvent was then performed. Masses remaining on the different SAMs in function of the surface-adamantyl ratios are represented on Figure 1.



**Fig 1** Masses remaining on the surface after injecting 5 mM free  $\beta$ -Cd solution on a chit-CD layer formed by adsorption of a 1g/L (2g/L for 50%) polymer solution on the different SAMs.

Effect of the ionic strength variation onto a multilayer built on the 5% and 25 % adamantyl surfaces

**Table 2** Variation of the characteristic parameters on the multilayer, formed on 5% adamantyl-modified surface, upon ionic strength variation of the solvent ( $\Delta\Gamma$  the mass,  $\mu$  shear elastic modulus,  $\eta$  the shear viscosity of the adsorbed layer and  $\Gamma$  the mass of the entire assembly).

	$\eta$ (kg/ms)	$\mu$ (Pa)	$\Delta\Gamma$ (ng/cm <sup>2</sup> )
Solvent A	$1.42 \times 10^{-3}$	$6,72 \times 10^4$	/
Solvent B	$1.846 \times 10^{-3}$	$1,31 \times 10^5$	-403
Solvent A	$1.42 \times 10^{-3}$	$6,89 \times 10^4$	576
Solvent B	$1.847 \times 10^{-3}$	$1,26 \times 10^5$	-557
Solvent A	$1.42 \times 10^{-3}$	$6,90 \times 10^4$	592
Solvent B	$1.852 \times 10^{-3}$	$1,25 \times 10^4$	-584
Solvent A	$1.43 \times 10^{-3}$	$6,84 \times 10^4$	662

**Table 3** Mass variation  $\Delta\Gamma_s$  of the 3-layer assemblies built on a 5% and on a 25% adamantyl SAM exposed to solvent of different ionic strength.  $\Delta\Gamma_s$  is the mass difference between the assembly at each solvent exposure and the initial assembly in solvent A.

	$\Delta\Gamma_s$ (ng/cm <sup>2</sup> )	
	5% adamantyl surface	25% adamantyl surface
Solvent A	0	0
Solvent B	-403	-67
Solvent A	173	98
Solvent B	-385	-53
Solvent A	208	141
Solvent B	-377	
Solvent A	286	

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