Cite this: Chem. Commun., 2011, 47, 12601–12603

www.rsc.org/chemcomm

COMMUNICATION

ATRP-mediated continuous assembly of polymers for the preparation of nanoscale films[†]

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Received 15th September 2011, Accepted 12th October 2011 DOI: 10.1039/c1cc15711f

The continuous assembly of polymers (CAP) *via* atom transfer radical polymerisation (ATRP) is reported as an efficient approach for the preparation of dense, cross-linked, nanoscale engineered films as surface coatings, hollow capsules and replica particles. These films can be reinitiated to allow the preparation of thicker films without loss of film growth efficiency while maintaining similar film density.

Facile techniques to synthesise tailored thin films and particles are integral to the development of the next generation of biomaterials,^{1,2} electronic devices,^{3,4} and stimuli-responsive surfaces.^{5–8} A number of approaches have been used to synthesise such films, including polymer grafting-to and grafting-from techniques.^{9–11} Both of these techniques allow the synthesis of thin films with a range of functionalities. Recently, we introduced a new approach called CAP,¹² which entails the one-step assembly of preformed polymers (referred to as macrocross-linkers) to form cross-linked, ultrathin films with tailored properties. The CAP approach is amenable to a diverse range of functional macrocross-linkers and generalisable to the modification of solid particles, which can then be removed to afford hollow polymer capsules. Such polymeric carriers have generated significant interest for applications in drug and gene delivery.^{2,13,14} Previously we demonstrated that ring-opening metathesis polymerisation (ROMP)-mediated CAP (CAP_{ROMP}) allowed efficient assembly of films of various composition on a range of substrates. However, ROMP is restricted to the polymerisation of strained cyclic monomers (e.g., norbornene), precluding the application of CAP_{ROMP} towards a wide range of common non-cyclic monomers such as alkene, acrylate and styrenic derivatives. Therefore, to further develop the versatility of the CAP process and thus design nanostructured films and capsules with unique properties, investigation of other polymerisation techniques is required. In this study we demonstrate the broad applicability of the CAP approach by employing ATRP as an alternative polymerisation technique. In comparison to the

 CAP_{ROMP} method, the CAP_{ATRP} approach leads to considerably denser (*ca.* 3-fold) and smoother (*ca.* 10-fold) thin films. Furthermore, application of the CAP_{ATRP} process to solid (non-porous) and mesoporous silica spheres is reported, which, after template removal, results in the formation of hollow capsules and replica spheres with enhanced mechanical stability.

ATRP is a facile polymerisation method, as it does not require stringent conditions, has high functional group tolerance and is applicable towards a large range of initiators, solvents and most importantly monomers.^{15,16} In the current study, CAP_{ATRP} was conducted under activator regenerated by electron transfer¹⁷⁻²⁰ (ESI[†]). In the CAPATRP process, preformed macrocross-linkers containing pendant polymerisable methacrylate groups were assembled on substrates functionalised with an initiating prelayer (surfaces grafted with ATRP initiators) (Scheme 1). The initiating prelayer was deposited onto substrates using a click chemistry strategy and was found to initiate CAP_{ATRP} more efficiently than conventional methods (ESI⁺). The single-step CAPATRP approach, via propagating radical species transferred through the film/surface via multiple radical additions across the pendant methacrylate moieties, results in surface-confined and cross-linked films with nanometre scale controlled thickness.

The kinetics of CAP_{ATRP} film formation was investigated on planar substrates modified with an initiating prelayer by immersing the substrates into a solution containing Cu(1) catalyst and a



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[†] Electronic supplementary information (ESI) available. See DOI: 10.1039/c1cc15711f



Fig. 1 (a) Evolution of the CAP_{ATRP} film thickness as a function of the polymerisation time, as measured by ellipsometry. (b) Evolution of CAP_{ATRP} film formation as a function of polymerisation time, as measured by OWLS. Arrow indicates rinsing of the OWLS chip with buffer. (c) 3D height mode AFM image of the CAP_{ATRP} film after 25 h polymerisation.

poly((2-hydroxyethyl) acrylate-*co*-(2-(methacryloyloxy) ethyl) acrylate) (P(HEA-*co*-MOEA)) macrocross-linker. Film growth was examined by ellipsometry on initiator-functionalised silicon substrates at predetermined exposure times (Fig. 1a). The resulting CAP_{ATRP} film thicknesses were obtained by subtracting the initiating prelayer thickness from the total measured thickness (Fig. S1, ESI†). The kinetic profile indicated asymptotic film growth with an average final thickness of *ca*. 12 nm (>10 h). Control experiments without catalyst or initiator confirmed that film growth results from ATRP of the macrocross-linker from the surface (Table S1, ESI†).

Film growth was also measured in situ by optical waveguide lightmode spectroscopy (OWLS) and dual polarisation interferometry (DPI) on chips modified with the initiating prelayer. Evolution of the surface mass of a CAPATRP film with time (Fig. 1b) obtained from OWLS analysis of the film refractive indices (Fig. S2, ESI⁺) and subsequent mathematical modelling yielded a deposited mass of 8 mg m⁻² and a thickness of 10 nm after 10 h polymerisation. The film density, determined by DPI, is 0.56 g cm^{-3} . This value compares favourably with cross-linked poly(methacrylic acid)/poly(vinylpyrrolidone) layer-by-layer (LbL) films (5 bilayers), which were found to have a density of 0.6 g cm⁻³ at pH 7.²¹ In contrast, DPI measurements of a $\mathrm{CAP}_{\mathrm{ROMP}}$ film prepared using similar PHEA-based macrocross-linkers¹² revealed significantly lower densities (0.17 g cm⁻³). It is postulated that the CAP_{ATRP} approach provides denser films as a result of the smaller interlayer spacing resulting from ATRP of pendent methacrylate groups (Scheme 1, X') as compared to the relatively large interlayer spacing provided by ROMP of pendent norbornene groups in CAP_{ROMP}.¹² Ellipsometry, OWLS and DPI all revealed asymptotic film growth, which is attributed to steric constraints of the polymer network limiting diffusion of polymer

to the film isolated reactive sites. Atomic force microscopy (AFM) of the cross-linked PHEA-based film obtained *via* CAP_{ATRP} (25 h) revealed a smoother and more homogenous topography (surface roughness ≤ 3 nm) (Fig. 1c) compared to the PHEA films obtained previously *via* CAP_{ROMP} (surface roughness *ca*. 50 nm). AFM scratch analysis (Fig. S3, ESI†) confirmed the thickness data obtained from ellipsometry and OWLS. Gel permeation chromatography (GPC) of the P(HEA-*co*-MOEA) macrocross-linker solution before and after the CAP_{ATRP} process showed a negligible change in the polymer molecular weight characteristics (Fig. S4, ESI†), demonstrating that polymerisation is confined to the substrate surface.

To facilitate further film growth, CAPATRP films can be reinitiated, thus leading to the formation of thicker polymer films and potentially compositionally diverse films if different macrocross-linkers are employed for each step. New initiating moieties can be attached to the CAPATRP films via esterification of the pendant hydroxyl groups of the surface-bound PHEA with *α*-bromoisobutyryl bromide, followed by submersion into a fresh solution of P(HEA-co-MOEA) containing Cu(I) catalyst (Fig. 2a). Evolution of the CAPATRP film thickness as a function of reinitiation step was monitored via ellipsometry (Fig. 2b) and ranged from 12 nm for the first CAP layer (L1) to 75 nm after 4 CAP layers (L4), with an average thickness increment of 21 nm per reinitiation and CAP step. DPI revealed that the film density remained consistent $(0.55-0.60 \text{ g cm}^{-3})$ with each reinitiation and layering step. Analysis of these films by AFM confirmed the thickness data and revealed uniform film formation with low surface roughness values (L2 \leq 4 nm; $L4 \leq 8 \text{ nm}$) (Fig. S5, ESI[†]).

The enhanced CAP reinitiation efficiency can be attributed to the surface densities of initiating groups. The substrate initiating prelayer has an initial alkyl bromide surface concentration of approximately 12% (NMR analysis of polymeric initiator), whereas subsequent initiating surfaces were saturated with initiating groups through reaction of α -bromo*iso*butyryl bromide with the pendant hydroxyl groups of surface-bound PHEA. This also likely explains the thinner initial CAP_{ATRP} film (12 nm), compared to CAP films formed following reinitiation (average increase of 21 nm). Importantly, linear and consistent growth is observed for each reinitiation and CAP step, demonstrating that repeated regeneration of the film surface can be conducted without loss of film growth efficiency.

The CAP_{ATRP} process is also applicable to the synthesis of polymeric hollow capsules and replica particles.^{21–23} CAP_{ATRP} film



Fig. 2 (a) Reinitiation of the CAP film with bromo*iso*butyryl bromide and subsequent CAP_{ATRP} leading to thicker films. (b) Evolution of the film thickness with reinitiation and CAP_{ATRP} step onto planar surfaces, as measured by ellipsometry.



Fig. 3 (a) Fluorescence intensity evolution of film growth on SiO₂ particles after each CAP_{ATRP} step, as followed by flow cytometry. (b) Fluorescence microscopy images of P(HEA-*co*-MOEA)-FITC capsules in solution after 4 reinitiation and CAP_{ATRP} steps; inset corresponds to a bright field microscopy image. P(HEA-*co*-MOEA) capsules in dehydrated states by (c) SEM and (d) AFM. Fluorescence microscopy images of (e) MS particles coated with a single CAP_{ATRP} film of P(HEA-*co*-MOEA)-FITC and (f) polymeric replica spheres obtained after template removal; insets show corresponding bright field microscopy images. Scale bars are 5 µm (b, e, f) and 2 µm (c, d).

growth and reinitiation was performed on nonporous silica (SiO₂, 5 µm diameter) particles and mesoporous silica (MS, 5 µm diameter) particles, which were used as sacrificial templates. Fluorescence intensity data obtained from flow cytometry illustrates the continuous growth of fluorescein isothiocyanate (FITC)-tagged P(HEA-co-MOEA) assembled via CAP_{ATRP} with increasing number of reinitiation steps (Fig. 3a) onto SiO₂ particles. After four reinitiation and CAP layering cycles, the underlying SiO₂ template was removed by exposure to hydrofluoric acid (HF) to form stable, robust and well-dispersed polymer capsules (Fig. 3b). Control experiments performed without ATRP initiator or catalyst did not result in capsule formation. Scanning electron microscopy (SEM) and AFM images of the capsules confirmed the formation of homogenous polymer capsules (Fig. 3c and d). The limited shrinkage ($\leq 10\%$) of the cross-linked PHEA-based capsules obtained via the CAPATRP approach compared to the CAPROMP approach (ca. 50%) indicates the enhanced mechanical stability obtained for these materials, most likely as a result of the higher film density and/or cross-linking. An estimated wall thickness of 15 ± 1 nm was determined by AFM analysis (Fig. S6, ESI[†]). Compared to planar substrates, a significant reduction of film thickness was observed (more than 50 nm over 4 reinitiation steps). Similar differences in film coating thicknesses have been previously observed between planar and particle systems.12,24,25 Applicability of the CAPATRP process to different surface morphologies was also explored via the coating of MS particles. A single CAPATRP coating of P(HEA-co-MOEA)-FITC onto MS particles afforded uniform CAPATRP films (Fig. 3e) and dissolution of the template with HF yielded homogenous polymeric replica spheres (Fig. 3f). Uniform fluorescence before and after template removal demonstrates the successful infiltration and covalent assembly of the CAP_{ATRP} polymer matrix.

In summary, application of CAP_{ATRP} provides access to substrate-supported, cross-linked, nanoscale films with tailorable

film thicknesses. These films exhibit low surface roughness and film densities comparable to LbL films. Applied to particle templates, CAP_{ATRP} affords robust hollow capsules or particle replicas following template removal. ATRP allows facile single-step CAP film formation at room temperature without stringent air-free conditions and supports the utilisation of a wide range of pendant vinylic functionalised macrocrosslinkers to afford compositionally diverse films. Current studies are focused on applying the CAP process to macrocrosslinkers with complex architectures to prepare films not readily accessible *via* traditional grafting approaches, as well as the application of the CAP approach towards the development of nanoengineered films and particles for a range of applications, ranging from membranes to drug delivery.

This work was supported by the Australian Research Council under the Federation Fellowship (F.C., FF0776078) and Discovery Project (F.C., G.G.Q, DP1094147) schemes. We thank C. R. Kinnane for help with SEM.

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