

Cite this: DOI: 10.1039/xxxxxxxxxx

Silica/methacrylate class II hybrid: Telomerisation vs. RAFT polymerisation[†]

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Received Date
Accepted Date

DOI: 10.1039/xxxxxxxxxx

www.rsc.org/journalname

Inorganic-organic co-networks prepared by the sol-gel method are a promising class of materials due to their unique physical and biological properties, especially when covalent bonds are formed between the networks. The polymer structure and composition can have a drastic effect on the synthesis and properties. Here, we compared reversible addition fragmentation chain-transfer (RAFT) with telomerisation (TL), for synthesis of the polymer, to investigate whether refining the polydispersity of polymethacrylate could lead to better and more tailorable properties. 3-(Methoxysilyl)propyl methacrylate was used as a model and successfully synthesised by RAFT and TL using 2-cyano-2-propyl benzodithioate and thioglycerol as chain transfer agents, respectively. The polydispersity of the polymer had a significant effect on the sol-gel process with an increase in gelation time as the polydispersity decreased. Direct correlation was made between the gelation time and M_z , suggesting that the gelation of hybrids followed the percolation model. However, regarding the properties, it is a tie. No statistical difference in silica release and mechanical properties of the resulting hybrids was observed, regardless of the polydispersity of the polymer.

1 Introduction

Silica class II hybrids are glassy materials that consist of covalent co-networks of silica and organic polymers with covalent bonds between the networks.[?] They can be synthesised via the sol-gel process through the addition of an alkoxy silane-functionalised polymer into a sol that contains hydrolysed sol-gel precursors, such as tetraethyl orthosilicate (TEOS), allowing their co-condensation and co-existence at a molecular level. Mechanical properties, optical properties, chemical durability and degradability can be tuned as a function of synthesis parameters and by a careful selection of the organic matrix.^{????} Among the possible candidates, methacrylate polymers present multiple advantages, compared to other polymers, as their structure, molecular weight and functional pending groups can be selected and controlled independently. In addition, using monomer such as 3-(methoxysilyl)propyl methacrylate (TMSPMA), sol-gel precursors can be easily built in the polymer struc-

ture during its polymerisation.[?] Due to their high tailorability, silica class II hybrids made with methacrylate polymers have gained considerable interest in the field of biomaterials, especially as potential bone implant materials.^{??????} Most reports describing the synthesis of silica class II hybrids intended for this application used polymers synthesised from free radical polymerisation, despite the multiple reports on the synthesis of similar polymers using controlled radical polymerisation techniques such as reversible addition-fragmentation chain-transfer polymerisation (RAFT),^{????} atom-transfer radical-polymerisation (ATRP)^{????} or nitroxide mediated radical polymerisation (NMP)^{????}. Using advanced polymerisation techniques could potentially add another degree of tailorability for the silica class II hybrids as polymers can be designed with structures that cannot be obtained with free radical polymerisation.^{??} For instance, Chung *et al.* reported an increase in modulus of toughness using star poly(methyl methacrylate₉₀-co-TMSPMA₁₀) as compared to its linear equivalent at 70 wt% of polymer using TEOS as an inorganic precursor.[?]

Despite the progress recently made in the use of well-defined polymers in silica class II hybrids, no direct comparison between linear polymers made by free radical polymerisation and controlled polymerisation, at similar average molecular weight, has been reported in the literature. Polymers synthesised by free radical polymerisation inherently give larger molecular weight distribution as compared to controlled radical polymerisation

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[†] Electronic Supplementary Information (ESI) available: [details of any supplementary information available should be included here]. See DOI: 10.1039/b000000x/

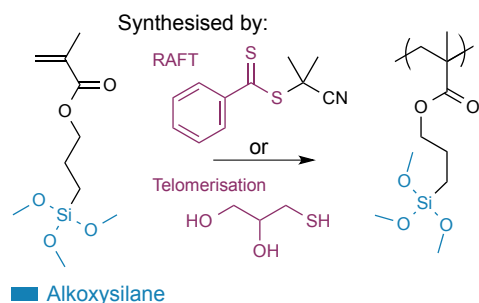


Fig. 1 Schematic representing the polymerisation of 3-(trimethoxysilyl)propyl methacrylate by RAFT using 2-cyano-2-propyl benzodithioate and by TL using thioglycerol as chain transfer agent.

techniques. Our hypothesis is that lowering the polydispersity could significantly affect the sol-gel process and refine the resulting hybrids properties. In addition, if hybrids are developed as regenerative tissue substrate, non-degradable polymer such as polymethacrylate must be designed with a hydrodynamic radius falling below the excretion limit of the kidney, a criterion which could be fulfilled using a controlled radical polymerisation technique.² Herein, we have investigated whether the hypothesis made above can be validated or not. Thus, homopolymers of poly(TMSPMA) were synthesised here using two different polymerisation techniques, yielding to polymer of similar average molecular weight but different polydispersity. The effect of the monomer purity on the polymerisation processes was investigated. Moreover, the effect on the sol-gel process, the mechanical properties and the chemical durability were evaluated.

2 Experimental section

2.1 Materials

All reagents were purchased from Sigma-Aldrich UK and used without further purification unless stated. 3-(Methoxysilyl)propyl methacrylate (TMSPMA), which did not contain any inhibitor, was purified by distillation under reduced pressure to remove hydrolysed monomers. 2,2'-Azobisisobutyronitrile (AIBN) was recrystallised in cold methanol before use. Tetrahydrofuran (THF) and toluene were dried using 3 Å molecular sieves prior to any polymer synthesis.

2.2 Polymerisation and kinetics protocols

Prior to any synthesis, the glassware was washed in an alkaline bath overnight, then rinsed with tap water and dipped into an acid bath for 2 h and subsequently dried at 120 °C for 2 h.

2.2.1 Telomerisation

In a 50 mL round bottom flask containing a magnetic stirrer, TMSPMA (6209 mg, 25 mmol), AIBN (61 mg, 0.37 mmol) and thioglycerol (TG) (269 mg, 2.49 mmol) were weighed out. THF was then added to the flask to reach a monomeric concentration of 1 mol·L⁻¹. The flask was then sealed using a septum and oxygen was removed by bubbling argon for 20 minutes. The reaction was started by placing the flask at 60 °C in preheated oil for 48 h at 500 rpm. The polymer was then precipitated in cold hexane 3 times to remove unreacted monomers, chain transfer agent and

initiator.

2.2.2 Reversible addition-fragmentation chain-Transfer polymerisation

In a 50 mL round bottom flask containing a magnetic stirrer, TMSPMA (9313 g, 37.5 mmol), AIBN (20.5 mg, 0.13 mmol) and 2-cyano-2-propyl benzodithioate (55.3 mg, 0.25 mmol) were weighed out. Toluene was then added to the flask to reach a monomeric concentration of 1.5 mol·L⁻¹. The flask was then sealed using a septum and oxygen was removed by bubbling argon for 20 minutes. The reaction was started by placing the flask at 70 °C in preheated oil for a maximum of 8 h at 500 rpm. The polymer was then precipitated in cold hexane 3 times to remove unreacted monomers, chain transfer agent and initiator;

2.2.3 Polymerisation kinetics

The kinetic studies were performed by taking aliquots of approximately 1 mL at given time points: 0.5, 1, 1.5, 2, 4, 8, 24 and 48 h for the TL and from 1 to 8 h, every hour for the RAFT polymerisation. They were taken under a flow of argon using a purged syringe and subsequently quenched in liquid nitrogen. The monomer conversion was calculated by comparing the integral values given by the protons of the unreacted vinyl from the monomer, H_{CIS} at δ5.45 and H_{TRANS} at δ6.02, to the singlet of 1,3,5-trioxane, Htrioxane at δ5.07, which was used as an internal reference. The concentration of thioglycerol (TL) was determined by iodometric titration using starch as an indicator. Starch was mixed with an aliquot at a 1:1 volume ratio in which iodine was added by 250 μL (0.002 mol·L⁻¹) up to a change in colour from transparent to a deep blue, indicating the formation of the iodine-starch complex. The concentration of TG is finally recovered using the following equation:

$$[RSH]_t = \frac{V_{ep}[I_2]_0}{V_{aliquot+starch,0}} \quad (1)$$

Where V_{ep} is the volume of iodine solution added to reach the end point, $[I_2]_0$ the concentration of the iodine solution and $V_{aliquot+starch,0}$ the volume after mixing an aliquot with the starch before adding iodine.

2.2.4 Polymer characterisation

¹H NMR spectra were recorded in CDCl₃ using a Bruker AV-400 spectrometer operating at 400 MHz. Spectra were then analysed using MestReNova 7.0 software. Prior to integration and chemical shift identification, the baseline was corrected using a built-in Whittaker algorithm and the spectrum calibrated to TMS (tetramethylsilane).

Size exclusion chromatography Molecular weight characterisation of the polymer synthesised by telomerisation was carried out by size exclusion chromatography using the Viscotek TDA 305 instrument (Malvern instrument, USA) equipped with a Viscotek D6000M and D2500M columns. The TDA module was fitted with a refractive index (RI) detector, a four bridge viscometer (VIS) and low and right angle laser scattering (LS) detectors. Linear polymethylmethacrylate was applied as a standard for universal calibration. Dimethylformamide with 0.075% of lithium bro-

Table 1 Summary of the polymerisation carried out here by telomerisation (TL) and reversible addition-fragmentation chain transfer.

Entry	Method ^a	[CTA]/[M] ^b	C ₇ ^c	Time (h)	Conv (%)	M _{n,target} (kg·mol ⁻¹)	M _{n,GPC} ^d (kg·mol ⁻¹)	D ^d
P1	TL	0.0083	0.693	48	>98	30.0	33.1	3.86
P2	TL	0.0166	0.730	48	>98	15.1	20.1	3.28
P3	TL	0.0331	0.749	48	>98	7.6	11.0	2.24
P4	TL	0.0994	0.707	48	>98	2.6	3.6	2.02
P5	TL	0.0413	-	24	98	6.0	5.7	1.61
P6	TL	0.0206	-	24	98	12.0	11.4	1.67
P7	RAFT	0.0066	-	1	8	6.0	6.1	1.13
P8	RAFT	0.0066	-	2	19	12.0	12.9	1.12

a) TL stands for telomerisation whereas RAFT stands for reversible addition-fragmentation chain transfer; b) Thioglycerol to TMSPPMA molar ratio; c) Chain transfer constant obtained from the O'Brien's law; d) Obtained by SEC relative to PMMA standards.

mide was used as a mobile phase flowing at 0.7 mL·min⁻¹, 35°C. The polymers synthesised by RAFT were characterised using an Agilent, SECurity GPC system, with a Polymer Standard Service (PSS) SDV analytical linear M column (SDA083005LIM), running in THF at 1 mL·min⁻¹. A single detection unit, consisting of an Agilent 1260 RID detector was used to measure the refractive index signal.

2.3 Hybrid synthesis

2.3.1 Polymer selection

Poly(TMSPPMA) was synthesised targeting 6 and 12 kg·mol⁻¹, by stopping the polymerisation at 1 and 2 h for RAFT polymerisation, respectively, and using R₀ = 0.04 and R₀ = 0.02, respectively, for TL. The molecular weight characterisation of the purified polymers is summarised in Table 1 and values were close to the values targeted. All polymers were purified 3 times by precipitation in n-hexane before being re-dispersed in ethanol and subsequently used for the sol-gel synthesis.

pTMSPPMA/SiO₂ hybrids were synthesised using the sol-gel process with tetraethyl orthosilicate (TEOS) and pTMSPPMA as precursors using acidic catalysis at room temperature.² The mass of TEOS hydrolysed was calculated based on the mass of the polymer (m_{polymer}) and the intended inorganic to organic mass ratio (I_h), using Eq 2:

$$I_h = \frac{m_{SiO_2} + m_{SiO_{1.5}}}{m_{SiO_2} + m_{SiO_{1.5}} + m_{Org}} \Leftrightarrow \quad (2)$$

$$m_{TEOS} = \left(\frac{I_h}{1 - I_h} * \frac{m_{polymer}}{M_{w,TMSPPMA}} * M_{w,Org} - \frac{m_{polymer}}{M_{w,TMSPPMA}} * M_{w,SiO_{1.5}} \right) * \frac{M_{w,TEOS}}{M_{w,SiO_2}}$$

The backbone of the polymer was considered part of the organic component of the class II hybrid. Hydrochloric acid (HCl) and water were added relative to the number of alkoxy silane groups in TEOS and pTMSPPMA according to the following ratios: R_{HCl} = n_{HCl}/n_{SiOR} = 0.01 and R_{H₂O} = n_{H₂O}/n_{SiOR} = 1. Water from HCl was subtracted according to the final amount of distilled water added. The solution was stirred at 1000 rpm, for 30 min, allowing TEOS to be hydrolysed, after which the purified polymer was added into the beaker. The mixture was allowed to mix for 30 s and cast into poly(tetrafluoroethylene) (PTFE) moulds and subsequently sealed. After 3 d of ageing, the lids were loosened for the solvent to evaporate. pTMSPPMA/SiO₂ hybrids monoliths were considered to be dried when their mass stabilised. Gelation point was measured by tilting at 45° the aging sol every 5 minutes until the meniscus no longer remained horizontal.² The

relative concentration of TEOS to the polymer (I_h) was varied to produce hybrids with inorganic to organic weight ratios of 29% (cross-linked polymer chains), 50%, 75% and 100%, termed I₂₉, I₅₀, I₇₅ and I₁₀₀, respectively.

2.4 Hybrid characterisation

2.4.1 Dissolution test

pTMSPPMA/SiO₂ hybrids were immersed in 5 mM TRIS-HCl buffered water using a ratio of 75 mg glass to 50 mL of media in an airtight polyethylene container.² Dissolution vessels were placed in an incubating orbital shaker held at 37 °C, agitated at 120 rpm. The pH (7.4) and temperature of the media were verified before use. The samples were incubated for 4 h, 8 h, 24 h and 72 h (n = 3). At the end of each time period, the samples were removed from the incubator and the solids were collected by filtration (filter paper with particle retention of 5-13 μm). The powder was immediately washed with DI water and subsequently with acetone to terminate any reaction. The filtered solution was collected to determine the ion concentrations using an inductively coupled plasma (ICP) analysis; the pH of the solution was also measured. The same protocol was applied to the media alone as a control. Elemental concentrations in solution were measured with a Thermo Scientific iCAP 6300 Duo inductively coupled plasma-optical emission spectrometer (ICP-OES) with auto sampler. Sample solutions were prepared by diluting the samples by a factor of 10 with analytical grade 2 M HNO₃. Silicon standard solutions were prepared at 0, 2, 5, 20 and 40 μg·mL⁻¹ for the calibration. Silicon was measured in the axial direction of the plasma flame.

2.4.2 Mechanical test

Measurements were performed using a NanoTest Vantage (Micro Materials Ltd, UK) mounted with a Berkovich pyramidal tip. Prior to measurement, samples were mounted in epoxy resin with a clearance of at least 5 mm between the bottom of the sample and the bottom of the resin. Load was applied on the sample at a rate of 5 mN·s⁻¹ to a maximum load of 50 mN. The tips were unloaded at a rate of 10 mN·s⁻¹ after a dwell of 20 s, at a rate of 15 mN·s⁻¹ down to 5 mN when a final dwell for 60 s was also applied to determine the thermal drift contribution of the indentation system to total displacement measured by a capacitive transducer.

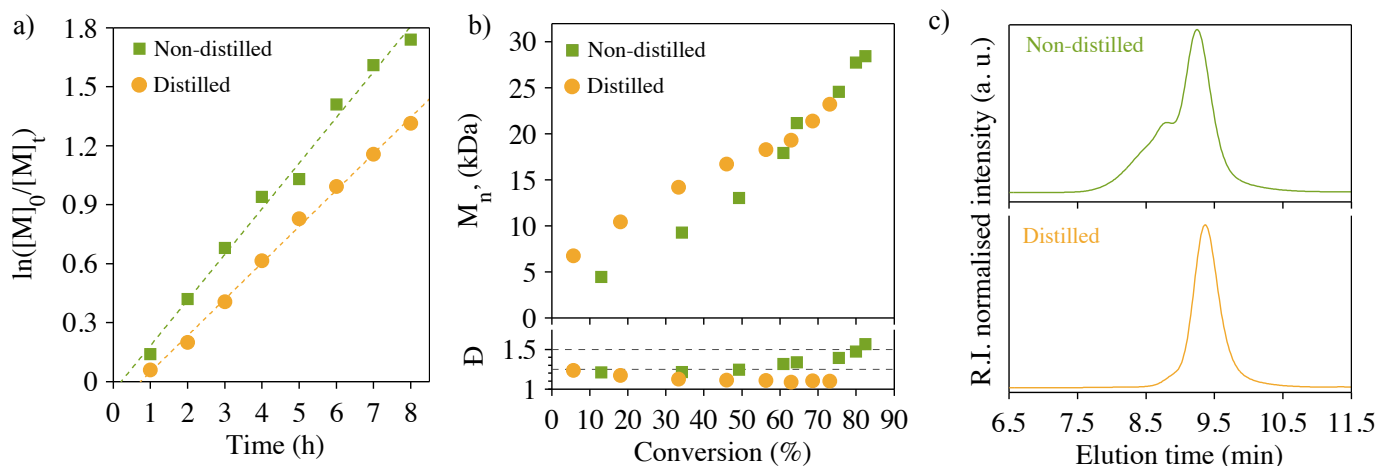


Fig. 2 RAFT polymerisation kinetics using non-distilled and vacuum distilled TMSPMA at 70°C (Monomer/CTA/initiator=150/1/0.5, molar ratio) in toluene with a) Their kinetic plots; b) Evolution of the molecular weights and polydispersities with monomer conversion; c) GPC traces at 82 % and 73 % conversion for the non-distilled and distilled monomer, respectively. GPC was conducted using THF as eluent at 1 mL·min⁻¹.

3 Results and discussion

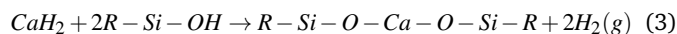
3.1 Varying the polydispersity of poly(TMSPMA)

Two radical chain transfer polymerisation techniques were used here (Figure 1), both allowing the synthesis of polymethacrylate with predefined molecular weights, yet with different span distributions. Wide molecular weight distributions ($1.5 < Đ < 2.0$) were obtained by telomerisation (TL) whereas reversible addition fragmentation chain transfer polymerisation (RAFT) was used to produce polymers with narrow molecular weight distribution ($Đ < 1.2$). A kinetic approach was selected for both polymerisation techniques, in order to stop the reaction at the desired molecular weight for RAFT and confirm the effectiveness of the chain transfer agent for TL. The molecular weights targeted for the hybrid synthesis (Section 3.2) were 6 and 12 kg·mol⁻¹ to respect the synthesis criteria of implant for tissue regeneration.^{??}

3.1.1 Dithiobenzoate mediated RAFT polymerisation

Polymers with low molecular weight distribution can be obtained with RAFT polymerisation due to the reversible deactivation of the propagating radicals, extending their lifespan to the extent of the polymerisation time.^{??} The protocol used here was adapted from the work of Mellon *et al.* who reported the successful polymerisation of TMSPMA using 2-cyano-2-propyl benzodithioate (CPBD) as a chain transfer agent (CTA).[?] Thus, kinetic experiments were performed using a constant TMSPMA:CTA:initiator ratio of 150:1:0.5, CPBD as CTA and AIBN as initiator at 70°C under argon. At first, and against the recommendations provided by Mellon *et al.*, TMSPMA was used as-received without any purification (*e.g.* vacuum distillation) to keep the synthesis as simple as possible. Figure 2 shows that a pseudo-first-order kinetic was obtained with apparent rate of propagation $k_{app,ND} = 6.45 \cdot 10^{-5} \text{ s}^{-1}$, reaching 82% of conversion at 8 h. Size exclusion chromatography revealed that the average molecular weight increased linearly with conversion, a characteristic of successful RAFT polymerisation (Figure 2-b). However, the polydispersity index greatly increased with conversion above 60%, reaching $Đ$

= 1.61 at 80% conversion, due to the formation of a distinctive shoulder peaks at lower elution time as shown in Figure 2-c, broadening the molecular weight distribution. This was unexpected as original reports on the polymerisation of TMSPMA did not observe such an effect. High molecular weight usually originates from undesired and inevitable termination reactions when reaching high conversion.^{???} However, the occurrence of these reactions can be significantly reduced by decreasing the radical flux, which could be achieved by reducing the initiator concentration or reducing the reaction temperature with respect to the initiator used.[?] Kinetics were performed at 60 and 80°C to test this hypothesis and resulted in a systematic increase in polydispersity occurring above 40% conversion regardless of the temperature (Figure S1). It was therefore likely that the increase in polydispersity originated from a lack of purity of the monomer. ¹H NMR of the crude TMSPMA, comparing the integral value of the SiO-CH₃ at 3.57δ and the chemical shift given by methanol at 3.47δ, revealed that the monomer was hydrolysed by 2%, which is within the manufacturer description (Figure S2). Hence, TMSPMA was vacuum distilled against calcium hydride (CaH₂) to yield to pure compound (Purity > 99.6% by ¹H NMR, Figure S2). Khan *et al.*[?] demonstrated that CaH₂ favourably reacts with silanol moieties (reaction enthalpy -1787 KJ·mol⁻¹), isolating the hydrolysed TMSPMA as follows:



The kinetic experiments were repeated with the purified monomer, yielding to similar apparent propagation rate, $k_{app,ND} = 5.14 \cdot 10^{-5} \text{ s}^{-1}$ and similar increase of degree of polymerisation as a function of conversion as shown in Figure 2-a and -b, indicating no change in the polymerisation kinetics. However, the purification of the monomer positively resolved the increase in molecular weight distribution at high conversion with a polydispersity of $Đ = 1.09$ at 73% conversion. Thus, we concluded that the shoulder peaks seen in Figure 2-c with the non-distilled monomer came from the branching of individual polymeric chains

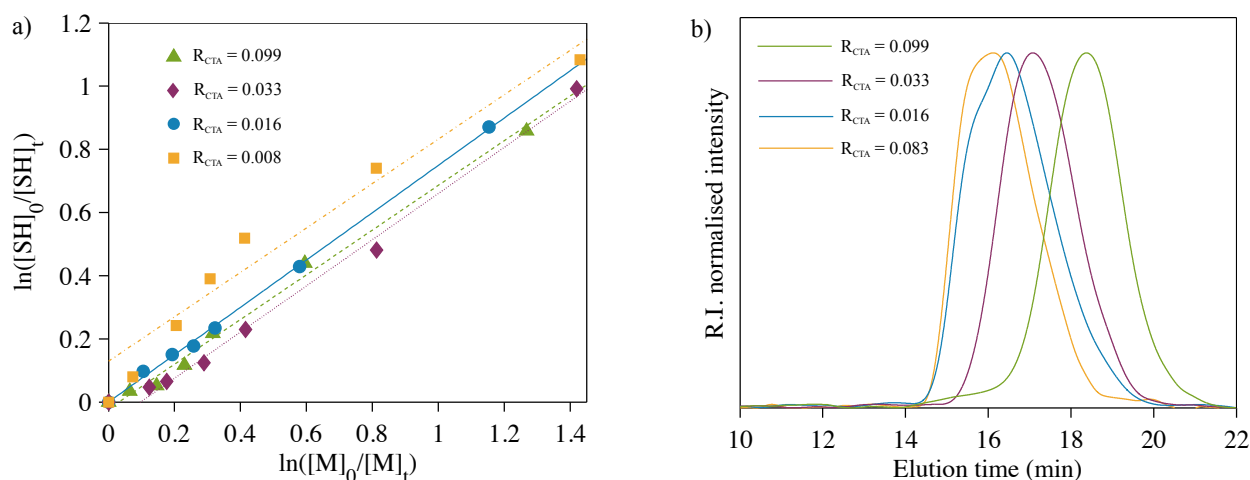


Fig. 3 a) Logarithm of the normalised concentration of TMSPMA against the logarithm of the normalised concentration of thioglycerol upon polymerisation in THF using AIBN as initiator, varying R_{CTA} and b) their respective size exclusion chromatographs after 48 h of polymerisation. SEC was conducted using DMF as eluent at $0.7 \text{ mL} \cdot \text{min}^{-1}$.

through the condensation of the silicate residues originating from the hydrolysed monomers as the viscosity increased. From this point onward, all polymerisation described in this report were performed using purified monomer.

3.1.2 telomerisation

In TL, thiols ($R-SH$) are used as chain transfer agents where their labile proton can irreversibly terminate a growing polymeric chain while reinitiating another chain from the thyl ($R-S\bullet$) formed.^{???} If the rate of transfer of radical to thiol is equal to the rate of propagation of the polymeric radical (i.e. monomer addition), the degree of polymerisation of the polymer is equal to the initial chain transfer agent (CTA) to monomer (M) molar ratio, R_{CTA} , as follows:[?]

$$DP_n = C_T \frac{[M]_0}{[CTA]_0} \xrightarrow{C_T=1} DP_n = \frac{1}{R_0} \quad (4)$$

Where C_T is the ratio of the propagating rate over the transfer rate and termed chain transfer constant. This can be achieved through a careful selection of the polymerisation parameters with regards to the polarity of the chain transfer agent. Here, thioglycerol and THF were selected as chain transfer agent and solvent, respectively, as this combination provided a good control over the molecular weight of methyl methacrylate.[?] In order to determine whether the same degree of control could be obtained with TMSPMA, the chain transfer constant C_T of the system was determined using the O'Brien's law[?]:

$$\ln\left(\frac{[RSH]_0}{[RSH]_t}\right) = C_T \ln\left(\frac{[M]_0}{[M]_t}\right) \quad (5)$$

varying R_{CTA} , the monomer to thioglycerol molar ratio, from 0.008 to 0.0994 targeting molecular weight between 2.6 to 30 $\text{kg} \cdot \text{mol}^{-1}$ as shown in Table 1. The stationary condition and invariance of the propagation rate as a function of the concentration of the chain transfer agent were first checked (see supplementary information for details). Then, the logarithm of the normalised concentration of the chain transfer agent was plotted against the

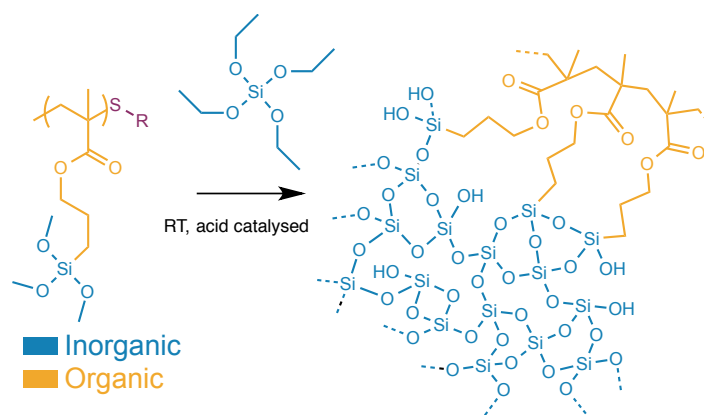


Fig. 4 Schematic representing the class II hybrid synthesis using pTMSPMA and TEOS as organic and inorganic precursor, respectively.

normalised monomeric concentration, as a function of R_{CTA} as shown in Figure 3-a. The average C_T was extracted from the slopes, giving a value of 0.72 ± 0.03 with $R^2 \geq 0.95$. Individual values are available in Table 1. The values obtained for C_T fell in the region allowing a good regulation of the molecular weight with a mono-modal distribution.[?] However, with the polymerisation using the least amount of chain transfer agent, $R_{CTA} = 0.008$, and after two hours, the concentration of thioglycerol was too low to allow for a complete solubilisation of starch. Thus, the end point was solely observed by the presence of iodine, introducing a substantial human error, which in turns did not guarantee that the polymerisation followed a 1st order kinetic.^{??} Pardal *et al.*[?] reported the telomerisation of TMSPMA using acetonitrile as solvent at 70°C and thioethylene glycol as a chain transfer agent. A good regulation was obtained with TMSPMA ($C_T < 1$) from a kinetic analysis, however, it was not validated by SEC analysis. Figure 3-b shows the chromatographs obtained from the size exclusion after 48 h of polymerisation and purification. Regardless of the molecular weight targeted, all distributions were mono-modal, which corroborated the observations made previ-

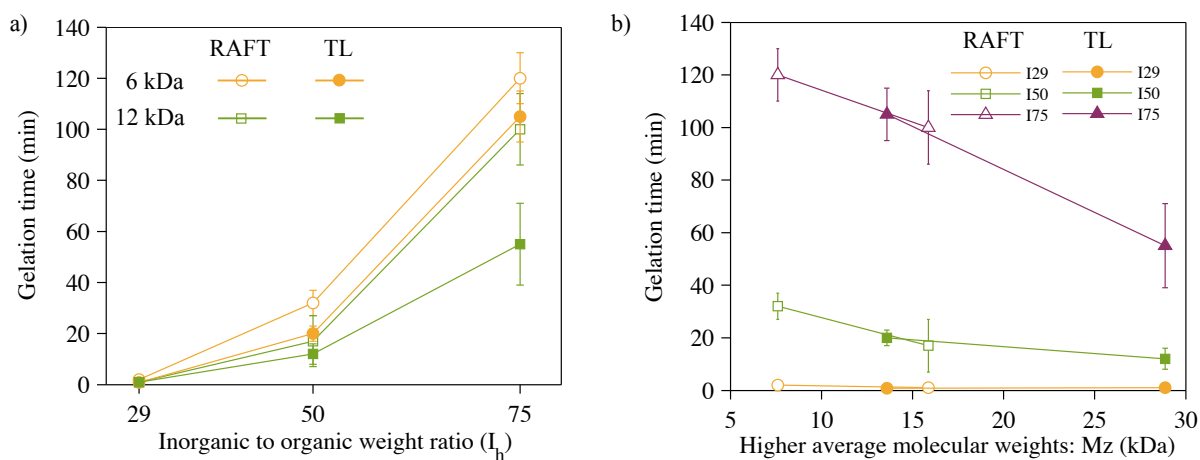


Fig. 5 Gelation time of the hybrid sol comprised of hydrolysed TEOS and poly(TMSPMA) synthesised either by RAFT or TL at 6 and 12 kDa: a) as a function of the inorganic to organic ratio; b) as a function of the higher average molecular weight M_z , which was obtained by SEC using THF as eluent at $1 \text{ mL}\cdot\text{min}^{-1}$.

ously. The measured average molecular weights were in good agreement with their kinetically re-evaluated estimations (See Table 1). The polydispersity index (\mathcal{D}), characterising the span of a polymeric distribution, increased with the molecular weight. For the smallest molecular weight with $R_{CTA}=0.1$ and $R_{CTA}=0.03$, $\mathcal{D} = 2.02$ and 2.24 , respectively, which is typical of a conventional free radical polymerisation when termination occurs solely by disproportionation, or radical transfer.[?] However, for $R_{CTA}=0.016$ and $R_{CTA}=0.008$, \mathcal{D} exceeded 3. This could be explained by the concentration of chain transfer agent verging on or dropping below that of the initiator. At these concentrations of CTA, slightly more polymeric chains could be initiated than CTA present. Thus, radical transfer was not the exclusive chain-stopping reaction and conventional termination was competitively taking place, broadening the molecular weight distribution.[?]

3.2 Silica class II hybrid synthesis: effect on the gelation time

Silica class II hybrids were prepared using the same experimental conditions described previously.[?] The relative concentration of TEOS to the polymer (I_h) was varied to produce hybrids with inorganic to organic weight ratios of 29% (cross-linked polymer chains), 50%, 75% and 100%, termed I_{29} , I_{50} , I_{75} and I_{100} , respectively. Once the polymer was mixed with the acidic TEOS, fast hydrolysis of the pending alkoxy silane groups occurred, subsequently followed by the co-condensation of free-silicate moieties, forming a glass network with silicon bridging oxygen (Si-O-Si). The formation of these bridges led to the gelation of the precursor solution as shown in Figure 4. The time that the sols took to reach the gel point, or gelation time, decreased as the inorganic to organic ratio decreased, regardless of the molecular weight or polymerisation method used (Figure 5-a). In addition, at a fixed inorganic to organic weight ratio, as molecular weight increased, the gelation time decreased, regardless of the polymerisation method used. These observations are in agreement with our previous report.[?] However, the polymerisation method

used had two noticeable effects on the gelation time: i) regardless of the composition targeted, the sols containing poly(TMSPMA) synthesised by RAFT were slower to gel than those containing the polymers synthesised by TL. ii) The relative increase in gelation time as an increase in molecular weight, at a given I_h , was more significant with polymers synthesised by TL than by RAFT. These two observations highlight the influence of the polydispersity of the polymer onto the gelation and also suggest that the gelation mechanism needs to be refined accordingly; We previously hypothesised that when using high cross-linking density polymers, the gelation was induced by the co-condensation of alkoxy silane moieties from the polymer forming a macroscopic mesh in which TEOS condenses. The data collected here shows that the higher fraction of the molecular weight distribution had a preponderant effect in the formation of the polymeric mesh. Thus, the gelation time was plotted as a function of the higher average molecular weights M_z , third moment of the molecular distributions, which is more sensitive to the high molecular weight polymers as shown in Figure 5-b. At a fixed I_h , the gelation time decreased linearly ($R^2 > 0.97$) as M_z increased, regardless of the polymerisation method used, demonstrating that the gelation of the sols were solely due to the cross-linking of poly(TMSPMA) and reinforcing the observations made previously.[?] Based on these observations, it is likely that the gelation of class II hybrids, synthesised with high cross-linking density polymers, follow the bond percolation theory, where adjacent polymers are co-cross-linked randomly along their chains, forming 3-dimensional lattices, which upon reaching a critical size induces macroscopic gelation.^{??} Hence, poly(TMSPMA) acted as large preformed clusters, where the higher fraction of its molecular weight distribution caused gelation, at an earlier stage, with polymer synthesised with TL compared to RAFT due to higher polydispersity.[?] Understanding how the mechanism of gelation of these materials worked is important as physical properties of hybrid systems (alkane bridges) can be correlated and predicted using the bond percolation theory.[?] However, the data presented here are not sufficient to make

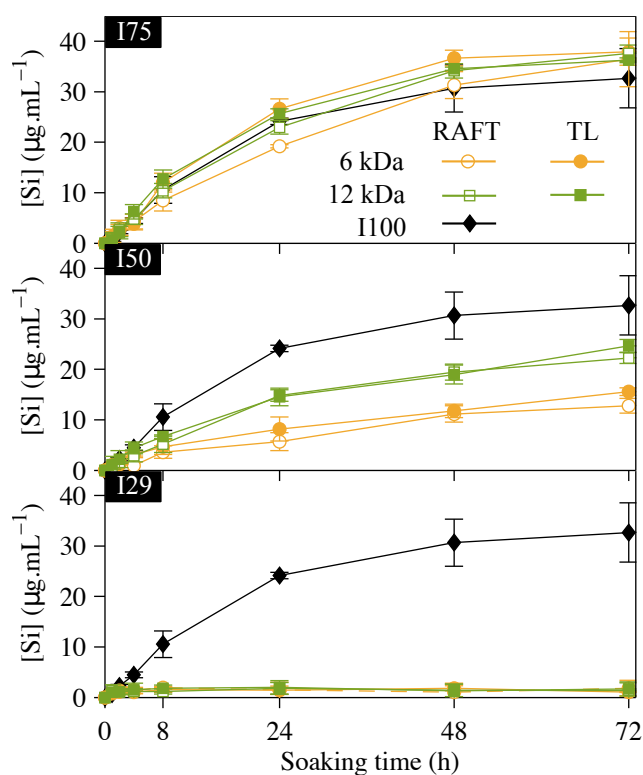


Fig. 6 Silicon concentration profiles upon immersion of pTMSPMA/SiO₂ hybrids synthesised with RAFT and TL in 5 mM TRIS solution buffered at a pH of 7.35 over 3 days. Each plot represents an inorganic to organic ratio with I₁₀₀ was plotted as a control.

such connection, but suggests its existence.

3.3 Polydispersity/properties relationship

Now that the influence of the polydispersity of poly(TMSPMA) on the sol-gel process has been established, the properties of the resulting hybrids were investigated by nanoindentation and immersion of the hybrid in buffered solution.

3.3.1 Chemical durability in buffered media

In order to study the chemical durability of the hybrids as a function of the polydispersity of poly(TMSPMA), immersion in 5 mM TRIS solution buffered at pH 7.35 over a period of 3 days was conducted (Figure 6). The silica release profile obtained for I100, pure silica glass, was plotted as a control. For the hybrid with inorganic to organic ratio of 75%, the silicon release profiles were statistically equivalent to I100, with a steady increase of the level of silicon reaching $39.1 \pm 3.9 \mu\text{g}\cdot\text{ml}^{-1}$. At I₅₀, the concentration of silicon did also increase over the 3 d of incubation, however, at a reduced level compared to I₁₀₀, reaching at 3 d, $22.3 \pm 1.1 \mu\text{g}\cdot\text{ml}^{-1}$ and $12.8 \pm 1.43 \mu\text{g}\cdot\text{ml}^{-1}$ for well defined poly(TMSPMA) at 12 kDa and 6 kDa, respectively. The values obtained at 3 d from the hybrids synthesised with poly(TMSPMA) obtained by TL were statistically equivalent to these obtained with well-defined polymers. At I₂₉, only $\approx 1.5 \mu\text{g}\cdot\text{ml}^{-1}$ of silica was released in solution, value close to the $1 \mu\text{g}\cdot\text{ml}^{-1}$ detection limit of the ICP-OES used here. The release of

Table 2 Reduced Young's modulus (E_r), hardness (H), and viscoelastic factor ($\alpha_3\eta_0$), extracted from nanoindentation data using the Viscous-Elastic-Plastic model at different inorganic to organic ratios. poly(TMSPMA)/SiO₂ hybrids with poly(TMSPMA) synthesised by RAFT at a M_n of 12 kDa. Mean and standard deviation are given with $n=50$. * given as a reference?

Entry	E_r (GPa)	H (GPa)	$\alpha_3\eta_0$ ($10^{12}\text{Pa}\cdot\text{s}^2$)
Cortical Bone*	24.78 ± 3.07	2.21 ± 0.27	9.45 ± 1.01
I29	1.11 ± 0.67	0.32 ± 0.10	3.18 ± 3.66
I50	3.83 ± 0.27	0.41 ± 0.04	22.94 ± 1.90
I75	7.08 ± 0.75	2.32 ± 0.02	41.34 ± 0.95
I100	15.96 ± 0.73	1.40 ± 0.06	39.76 ± 1.34

silica from class II hybrid synthesised originates from the hydrolysis of condensed orthosilicate.² According to the mechanism of gelation from high cross-linking density polymers, the orthosilicate species are present within the polymer mesh formed upon intra-condensation of the polymer chains.²² Even though the kinetic of gelation varied with the polydispersity, the release of silica from the two sets of hybrids described here did not, suggesting that the spatial characteristic and interconnection of the polymer meshes in which TEOS condensed was principally defined by the average molecular weight which is similar for both polymerisation techniques.

3.3.2 Mechanical properties

As reported previously, poly(TMSPMA)/SiO₂ class II hybrids exhibit viscoelastic response under mechanical stress. Thus, appropriate tools need to be used to carefully extract their characteristic values. As a result, the mechanical properties were characterised by nanoindentation, which allows for an indirect measure of reduced Young's modulus (E_r), hardness (H) and quadratic viscosity ($\alpha_3\eta_0$).²² These values were extracted by fitting the experimental data using the Visco-Elastic-Plastic (VEP) model proposed by Oyen *et al.*²². It relies on a Maxwell modelisation of the mechanical deformation, where the response under the tip of an indenter can be represented as the sum of a purely viscous damper (h_v), a purely elastic spring (h_e) and an elementary friction block (h_p), where:

$$\frac{dh}{dt} = \sqrt{\frac{F}{\alpha_3\eta_0}} + \frac{1}{\sqrt{F}} \frac{dF}{dt} \frac{1}{2\sqrt{\alpha_2 E_r}} + \frac{1}{\sqrt{F}} \frac{dF}{dt} \frac{1}{2\sqrt{\alpha_1 H}} \quad (6)$$

Figure 7-a shows the experimental and the fitted load-displacement curves obtained from hybrid synthesis with well-defined poly(TMSPMA) of M_n 12 kDa as a function of the inorganic to organic weight ratio. I100 (pure silica gel) was plotted as a control. It noteworthy to mention that all samples at a fixed inorganic/organic weight ratio and poly(TMSPMA) molecular weight gave similar hysteresis and hence are not represented in this manuscript. Table 2 summarises the values extracted from the VEP model for the same samples. All hybrids underwent a crack-free deformation under the load of the indenter, regardless of the synthesis method used and the molecular weight. The polydispersity of the polymer did not have any significant effect on the general behaviour of the samples, under the load of the indenter,

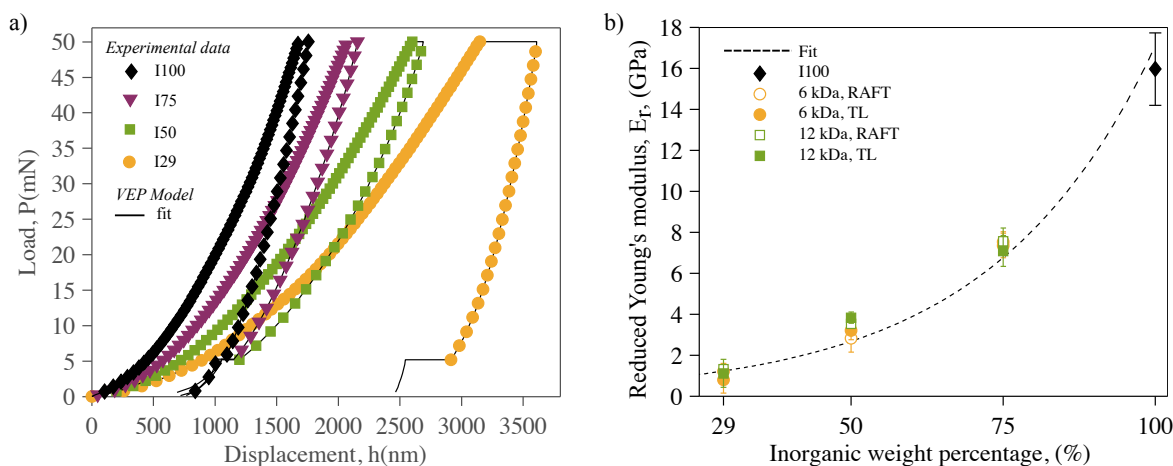


Fig. 7. a) Experimental and predicted load-displacement of pTMSpMA/SiO₂ hybrids with poly(TMSPMA) synthesised by RAFT at a Mn of 12 kDa as a function of the inorganic to organic ratios; b) Reduced Young's modulus as a function of the inorganic-organic weight percentage.

which can be seen in Figure 7-b, where no statistical difference could be seen in E_r at fixed I_h and molecular weight. The reduced Young's modulus was found to increase solely as the inorganic to organic weight ratio increased, the inorganic to organic weight ratio as shown in Figure 7-b with $E_r \approx 1, 3$ and 7.5 GPa at I29, I50 and I75, respectively.

4 Conclusions

Poly(TMSPMA) was successfully synthesised by RAFT and TL, yielding polymer of similar average molecular weight but different polydispersity. We demonstrate that the polydispersity of polymers with high cross-linking density has a significant effect on the sol-gel process, with a gelation driven by the higher fraction of the molecular distribution while the mechanical and chemical durability properties were not affected. These findings could be of a great interest for applications where longer gelation time is required as it increases the processability of the sol, which could be beneficial when synthesising 3D template, or scaffold, using electrospinning or 3D printing.

Acknowledgement

The authors thank the EPSRC for funding (EP/I020861/1 and EP/M019950/1). The raw data are available on request from julian.r.jones@imperial.ac.uk

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