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Alginate/PEO-PPO-PEO Hydrogels**

Journal:	<i>Soft Matter</i>
Manuscript ID	SM-ART-09-2020-001628.R1
Article Type:	Paper
Date Submitted by the Author:	10-Nov-2020
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ARTICLE

Techniques to Characterize Dynamics in Biomaterials Microenvironments: XPCS and Microrheology of Alginate/PEO-PPO-PEO Hydrogels

Received 00th January 20xx,
Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

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Many recent studies have highlighted the timescale for stress relaxation of biomaterials on the microscale as an important factor in regulating a number of cell-material interactions, including cell spreading, proliferation, and differentiation. Relevant timescales on the order of 0.1–100 s have been suggested by several studies. While such timescales are accessible through conventional mechanical rheology, several biomaterials have heterogeneous structures, and stress relaxation mechanisms of the bulk material may not correspond to that experienced in the cellular microenvironment. Here we employ X-ray photon correlation spectroscopy (XPCS) to explore the temperature-dependent dynamics, relaxation time, and microrheology of multicomponent hydrogels comprising of commercial poly(ethylene oxide)-poly(propylene oxide)-poly(ethylene oxide) (PEO-PPO-PEO) triblock copolymer F127 and alginate. Previous studies on this system have shown thermoreversible behavior in the bulk oscillatory shear rheology. At physiological temperatures, bulk rheology of these samples shows behavior characteristic of a soft solid, with $G' > G''$ and no crossover between G' and G'' over the measurable frequency range, indicating a relaxation time > 125 s. By contrast, XPCS-based microrheology shows viscoelastic behavior at low frequencies, and XPCS-derived correlation functions show relaxation times ranging from 10 – 45 s on smaller length scales. Thus, we are able to use XPCS to effectively probe the viscoelasticity and relaxation behavior within the material microenvironments.

Introduction

It has long been acknowledged that the presence of mechanical stimuli can influence cell growth and differentiation in a microphysiological environment. Studies from as early as Wang et al.¹ have demonstrated a physiological process known as mechanotransduction, whereby cells can sense and respond to mechanical stimuli and convert them into biochemical signals which then elicit specific cellular responses. Vogel et. al. reported that the initial interaction and mechanosensing events occur on the subsecond to second timescale, while early cell responses occur between seconds to minutes.² Darnell et. al. also showed that fast-relaxing hydrogels ($t_{1/2} \approx 50$ s) show significantly more new bone growth than those that received slow-relaxing hydrogels with similar gel stiffness.³ This has encouraged many recent studies^{2–6} to explore the stress relaxation of biomaterials as they have demonstrated to be a regulator for cell spreading, proliferation, and differentiation. These recent studies have also made an effort not only to

understand the rigidity of these biomaterials by examining the compressive modulus, but also their viscoelastic properties and timescales for stress relaxation through measurement of the storage and loss moduli.^{3, 5} An additional consideration is that many soft biomaterials have heterogenous structures and may exhibit different rheological properties and dynamics on small length scales as compared to the bulk. Therefore, a proper understanding of the dynamic and rheological response of soft biomaterials, and specifically using techniques that can capture dynamics over the time scales relevant to cell spreading (e.g., roughly 0.1–100 seconds) for smaller length scales corresponding to the cellular microenvironment is crucial as these materials are developed for biomedical applications.

X-ray photon correlation spectroscopy (XPCS) has recently emerged as a powerful tool for gaining insight into the microstructural dynamics of soft materials. Similar to dynamic light scattering (DLS) with visible light, XPCS can provide information about a material's dynamics by tracking the fluctuations in its coherent scattering intensity. However, the much shorter wavelength of X-rays allows XPCS to probe motions over significantly shorter distances, giving it advantageous access to smaller length scales and longer time scales that are outside the capabilities of DLS. XPCS can thus be used to make connections between rheology and nanoscale dynamics, whereby it is capable of accessing structural dynamics that range over length scales from nanometers to hundreds of nanometers and over a range of time scales from

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Electronic Supplementary Information (ESI) available: XPCS results on additional samples. See DOI: 10.1039/x0xx00000x

milliseconds to hundreds of seconds. Additionally, XPCS can easily be applied to cloudy and opaque materials, unlike DLS.

In this work, we employ the use of XPCS to explore the temperature-dependent microstructural dynamics of multicomponent hydrogels as well as their relaxation process, relevant to cell spreading in biomaterials. Moreover, we use the generalized Stokes-Einstein relation to examine the microrheological response of the hydrogel as it compares to bulk rheology. We focus on multicomponent gels containing two well-studied biomaterials, alginate and the triblock Pluronic® F127. Pluronic® or poloxamers are poly(ethylene oxide)-poly(propylene oxide)-poly(ethylene oxide) (PEO-PPO-PEO) triblock copolymers that have been widely studied for pharmaceutical applications. Pluronic® F127 (F127), with the approximate formula of PEO₁₀₀-PPO₇₀-PEO₁₀₀, is one member of this family that has been approved by the FDA to be used in the human body. The rich phase behavior of F127 has been the main attraction of this polymer for a long time. F127 has been known to exhibit thermoreversible gelation behavior with respect to concentration and temperature. This is because the difference in hydrophobicity between PEO and PPO leads to the micellization of the triblock copolymer in water, and the micelles have been known to self-assemble into crystal lattices that result in stiffer gels.^{7, 8} Many have taken advantage of the amphiphilic characteristic of F127 for drug delivery, whereby the cores can carry and deliver hydrophobic antibiotics and other active ingredients for various applications.⁹⁻¹² F127 is especially promising for wound healing and soft tissue repair because its solution is known to form gels at physiological temperatures. Even so, the mechanical strength of F127 in the gel state is relatively weak and has become a major drawback for wound dressing applications.

Alginate, a mechanically stable hydrogel, can be physically incorporated with the F127 polymer to achieve the desired mechanical strength for wound dressing. It is a naturally occurring polysaccharide and is already used in wound dressing materials today because of its biocompatibility, hydrophilicity, and relatively low cost. Alginate chains consist of 1,4-linked-β-D-mannuronic acid and α-L-guluronic acid that are ionically bridged through cooperative binding of calcium cations, which is the reason for its mechanical stability. Even though alginate alone does not display thermoresponsive gelation behavior, we have previously demonstrated thermoreversible capabilities in alginate-F127 multicomponent hydrogels and reported the mechanical properties of these materials in low-amplitude oscillatory shear.^{8, 13}

Experimental

Materials and Methods

Alginic acid sodium salt from brown algae (CAS 9005-38-3, Batch # 067K0145), ethylenediaminetetraacetic acid calcium disodium salt (CaEDTA), and cell culture grade Pluronic® F127 were purchased from Sigma-Aldrich. D-Glucono-δ-lactone

(GDL) was obtained from MP Biomedicals. All reagents were used without further purification.

Alginate hydrogel preparation

A previously reported calcium ion release method was used to prepare alginate hydrogel gels.^{13, 14} A 0.5 % (w/v) alginate solution was first prepared by dissolving the respective amount of sodium alginate in water and stirring for 24 h. A final concentration of 0.05 M CaEDTA was stirred into the solution for 5 min, followed by the immediate addition of 0.05 M GDL. The slow release of Ca²⁺ is activated upon addition of GDL. Because GDL is added after CaEDTA, the rate at which CaEDTA is added to the alginate solution does not impact the alginate gel morphology. The final solution was dispensed into a mold to form a thin film.

Multicomponent alginate / Pluronic® F127 (AP) hydrogel preparation

A previously reported soaking series was used to prepare multicomponent hydrogels with 0.5 wt% alginate and 20 wt% or 30 wt% F127.^{13, 14} The alginate hydrogels were soaked in a series of F127 solutions, whereby the first soak of the series was at a low concentration of 5 wt% F127 and sequentially increased to 10, 15, and 20 wt%, and also 30 wt% for the higher F127 concentration multicomponent AP hydrogel. The soaks were performed at a 9:25 volume ratio of alginate to F127 in accordance to the reported preparation method.^{14, 15} Each F127 soak solution was allowed to equilibrate at 4 °C for 7 days within the alginate matrix. Gravimetric analysis from the same study reported that the final F127 concentration is ~88% that of the final F127 soak solution.^{13, 14} DSC studies from White et al. report that the critical micelle temperature (CMT) in the composite system to be 14.4°C.¹⁴ Our previous SAXS studies on the composite gels show a clear indication of formation of F127 micelles at the temperatures and F127 concentrations that we consider in this paper;^{14, 15} and previous studies of neat F127 solutions report the critical micelle concentration (CMC) at 20 °C to be 4 %w/v.¹⁶ So, our systems are well above the CMT and CMC of F127.

Our XPCS data on the multicomponent alginate/F127 gel are compared with measurements taken on a gel comprising 30 wt% F127 alginate in water, with no alginate. Due to the low contrast of this system, silica nanoparticles with a radius of 6 nm were added as probe particles for the XPCS studies.

X-Ray Photon Correlation Spectroscopy (XPCS)

Dynamic studies were performed at the coherent hard X-ray (CHX, 11-1D) beamline at the National Synchrotron Light Source II (NSLS-II) located at Brookhaven National Laboratory, Brookhaven, NY. The X-ray energy was set to 9.65 keV (1.29 Å wavelength) delivered by a 3-meter long in-vacuum undulator with 20 mm magnetic period and a double-crystal monochromator. A partially coherent X-ray beam with a flux at the sample of ~10¹¹ photon/sec and a focused beam size of

$10 \times 10 \mu\text{m}^2$ was achieved by focused with a set of Be Compound Refractive Lenses and a set of Si kinoform lenses in front of the sample. The detector-sample distance was set to 4.91 m with 0.036 transmission of the full beam and an exposure time of 37.2 ms. The X-ray radiation dose on the sample was controlled by a millisecond shutter and filters of different thickness of Silicon wafers. The data acquisition strategy was optimized to ensure that the measured dynamics and structure are dose independent. Measurements were taken in a temperature-controlled environment in the 10–80 °C temperature range. To increase the signal to noise, the one-time correlation functions reported in this study are an average of 10 measurements at each temperature.

Microrheology

The Brownian motion of the micelles were monitored using XPCS and the mean-squared displacement (MSD), $\langle \Delta r^2(t) \rangle$, was extracted from the auto-correlation function, $g_2(\mathbf{q}, t)$, as the two relate by¹⁷,

$$g_2(\mathbf{q}, t) = 1 + \mathbf{b} \exp[-q^2 \langle \Delta r^2(t) \rangle / 3] \quad (1)$$

where q is the scattering vector and $\mathbf{b} = (g_2(\mathbf{0}) - 1)$ such that $g_2(\mathbf{0})$ is the auto-correlation function at low relaxation time (τ). The MSD can be related to the frequency-dependent complex shear modulus (G^*) of the surrounding fluid through the generalized Stokes-Einstein relation,

$$G^*(\omega) = \frac{k_B T}{\pi R \langle \Delta r^2(t) \rangle \Gamma(1 + \alpha(\omega))} \quad (2)$$

where k_B is the Boltzmann constant, T is the temperature, R is the tracer particle radius, and Γ is the gamma function. Silica ($R = 6$ nm diameter) tracer particles were used in the analysis for 30 wt% F127 sample, and the size of these particles is not expected to change with temperature. F127 micelles ($R = 5.5$ nm diameter) were considered to be the tracers in the analysis for alginate-F127 multicomponent samples. Previous studies of F127 micelles do not show a large change in micelle size with temperature for the temperature and concentration ranges that we consider.¹⁶ To evaluate eq. (2), we used the power-law approximation described by Furst and Squires¹⁸ where the MSD at each sampled time t_0 is a power-law function,

$$\langle \Delta r^2(t) \rangle \approx \langle \Delta r^2(t_0) \rangle (t/t_0)^{\alpha(t_0)} \quad (3)$$

where α is the logarithmic slope of the mean-squared displacement evaluated at t_0 ,

$$\alpha(t_0) = \frac{d(\ln \langle \Delta r^2(t) \rangle)}{d(\ln(t))} \Big|_{t=t_0} \quad (4)$$

The Fourier Transformation of the power-law yielded the modulus amplitude,

$$|G^*(\omega_0)| = \frac{D k_B T}{3\pi R \langle \Delta r^2(t_0) \rangle \Gamma[\alpha(t_0) + 1]} \Big|_{t=1/\omega_0} \quad (5)$$

where D represents the number of dimensions tracked for the MSD.

Using G^* , the loss modulus (G'') and the storage modulus (G') can be obtained by

$$G'' = G^*(\omega) * \sin\left(\frac{\alpha(\omega)\pi}{2}\right) \quad (6)$$

$$G' = G^*(\omega) * \cos\left(\frac{\alpha(\omega)\pi}{2}\right) \quad (7)$$

Bulk rheology

Conventional bulk rheological properties of the multicomponent AP hydrogel systems were examined using a 40-mm steel plate geometry on a TA Instruments AR-G2 stress-controlled rheometer with a Peltier plate for temperature control. All temperature sweep and frequency sweep measurements were performed within the linear viscoelastic region, which was determined by conducting stress sweeps at 25 °C, 6.28 rad/s. All samples were run in triplicate, and results are from averages of three runs.

Results and Discussion

XPCS dynamics

In previous studies, we were able to use traditional bulk rheology and small angle X-ray scattering (SAXS) to demonstrate that alginate-F127 multicomponent hydrogels can transition in its mechanical properties between a weak gel and a stiff gel through the reorganization of the F127 micelles.^{8, 13} The multicomponent gel demonstrated a weak-stiff-weak gel transition with respect to temperature whereby the two transitions were referred to as the lower and upper transition temperatures (LTT/UTT).¹³ White et al. suggested that the LTT and the UTT roughly correspond to the lower and upper gelation temperatures (LGT/UGT) of F127.¹⁴ Shear rheology studies showed that the transitions corresponded with an increase in the storage modulus (G') of approximately two orders of magnitude as temperature is increased from 10 °C to 80 °C, whereby the gel is stiffest in the mid-range temperatures of about 25 °C to 70 °C for the alginate-F127 multicomponent hydrogel at 30 wt% F127 (~11,000 Pa) and about 36 °C to 50 °C for the multicomponent at 20 wt% F127 (3500 Pa).¹³ In this study, we focused our discussion on the multicomponent gel with 30 wt% F127 as the sample with 20 wt% F127 demonstrated weak scattering.

We performed XPCS measurements on the prepared alginate-F127 multicomponent hydrogels and the 30 wt% F127 gel in the temperature range of 10 °C to 80 °C to examine the dynamics of the material throughout these characteristic phase transitions. The autocorrelation functions, $g_2(\tau)$, measured from 10 °C to 80 °C resulted in different relaxation rates, as shown in Figure 1. The $g_2(\tau)$ in Figure 1 were normalized to 1 in order to better illustrate the relaxation times, τ , of the micelles. In Figure 1b, we find that the fastest dynamics occur at lower temperatures of 10 °C to 20 °C, as indicated by the quick decrease in $g_2(\tau)$ at low τ . We can see the dynamics slow down at slightly higher temperatures between 20 °C and 30 °C, and signs of speeding up again from 50 °C to 60 °C. This behavior corresponds to the previously discussed trend that was demonstrated in bulk rheology where we see faster dynamics,

lower τ , at temperatures where the G' is low and slower dynamics, larger τ , where the G' is higher.¹³ As the corresponding LTT and UTT are also observed in the $g_2(\tau)$ trends, we believe that the dynamic behavior shown in Figure 1 is a result of the inter- and intra- micellar changes that can take place with respect to temperature. It stands to reason that the phase behavior of F127 is still prominent in the alginate-F127 multicomponent hydrogel, as F127 micelles have demonstrated the ability to rearrange themselves within the alginate matrix in previous SAXS studies.¹³ We believe that the fast dynamics observed at lower temperatures are evidence of freely moving F127 micelles and the dynamic slowdown at mid-range temperatures can be attributed to the cubic lattice arrangements of the F127 micelles. Shear rheology studies often show that the viscoelastic moduli of F127 decreases at much higher temperatures. It has long been suggested that higher temperatures can reduce the solubility of the PEO blocks in the F127 micelles.^{14, 19} This can lead to shorten PEO coronas, which reduces corona entanglements and allows for F127 micelles to be more loosely arranged.^{14, 19} As discussed above, even though the alginate may alter the arrangement of micelles, we still expect formation of micelles at these concentrations and temperatures; we are above the measured CMT of the composite gel of 14.4°C,¹⁴ of the composite gel, and previous SAXS results show evidence of micelle formation.^{14, 15} However, as a result of the alginate chains interfering with the structural ordering of micelles, we observe slightly faster dynamics and lower viscoelasticity at much higher temperatures. These results are also illustrated in Figure 1c where the data were fitted to a modified stretched exponential,

$$g_2(q,t) \sim \beta \exp\left[-2\left(\frac{\tau}{\tau_0}\right)^a\right] + c \quad (8)$$

where a is the stretching exponent, τ is the relaxation time, and c is the baseline.

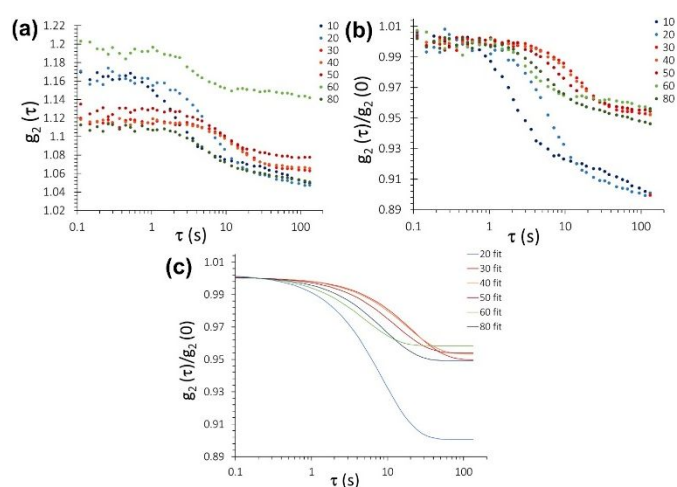


Fig 1. (a) Autocorrelation functions and (b) normalized autocorrelation functions of alginate-F127 multicomponent hydrogel with 0.5 wt% alginate and 30 wt% F127 at different temperatures, measured at $q = 7.59 \times 10^{-3} \text{ \AA}^{-1}$ and (c) the corresponding fits

to Eq. (6). Normalized values were reported as $g_2(\tau)/g_2(0)$, where $g_2(0)$ is the auto-correlation function at low relaxation time (τ).

Microscale relaxation time as compared to bulk rheology

The temperature dependence of the alginate-F127 multicomponent hydrogel's relaxation time, τ_0 , was investigated in this thermoresponsive material. The relaxation time with respect to temperatures between 10 °C to 80 °C, as shown in Figure 2, corresponds to viscoelastic behavior of the multicomponent at those respective temperatures. In Figure 2, we also see that the relaxation time more than doubles between 20 °C and 30 °C from 17.2 s to 41.3 s and proceeded to decrease as temperature continues to increase. We attribute this behavior to the cubic lattice arrangements of the F127 micelles at the LTT. When compared to neat 30 wt% F127, the relaxation time of the multicomponent appeared to be slower, which can be a result of the presence of the alginate network. Previous studies have reported the mesh sizes of alginate hydrogels of similar systems to be 10-12.4 nm, which can restrict the movement of F127 micelles, which are approximately 11 nm in diameter, resulting in slower relaxation times.^{20, 21} The relaxation time for alginate-F127 multicomponent hydrogel from 20 °C to 80 °C occurs between ~10 s to ~45 s. This timescale spans a range that is relevant to cell behaviors, as cells have been reported to respond to force oscillations over a timescale of $O(1)$ seconds,² and undergo cell spreading over a timescale of minutes to hours²². Additionally, although the length scale probed in our XPCS experiments is many times smaller than a typical mammalian cell (10-20 μm), our results highlight the large differences that can occur in these complex gels between the dynamics on small scales versus what is observed on larger scales by conventional bulk rheology. Experiments are underway to probe the effect of larger probe particles on the microscale dynamics.

Characteristic timescales for stress relaxation in gels can sometimes be observed in conventional oscillatory rheology through a frequency, ω_x , at which the G' and G'' values cross one another. The characteristic time is then equal to $1/\omega_x$. For the relaxation times we observe in XPCS, 10-45 s, we would expect to see crossover frequencies in the range 0.14-0.63 rad/s. In comparing the microscale relaxation time derived from XPCS to conventional oscillatory rheology (Figure 3), we see that on the macroscale, there is no crossover between G' and G'' at timescales corresponding to the relaxation times obtained from XPCS. At the macroscale, for samples at 25 °C and 40 °C, the samples exhibit behavior characteristic of a soft viscoelastic solid, with $G' > G''$ over the measurable frequency range, and G' fairly independent of frequency. For the sample at 25 °C (Figure 3b), G'' is also fairly independent of frequency, suggesting any crossover would be below the measurable frequency range, corresponding to a relaxation time > 125 s, about an order of magnitude larger than the time scale observed via XPCS. For the sample at 40 °C (Figure 3c), G'' shows some frequency dependence, but again no crossover is observed.

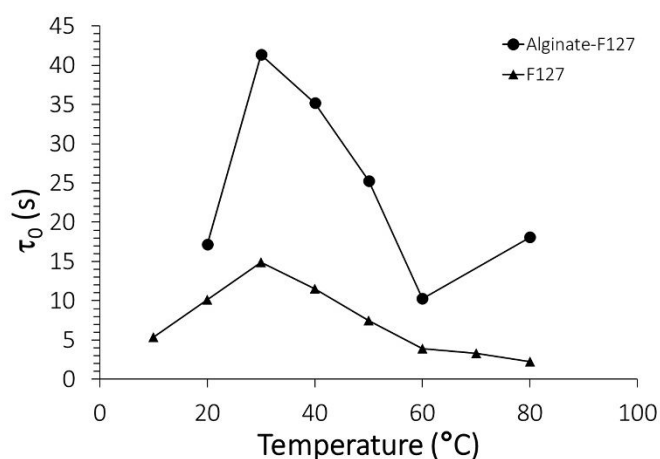


Fig 2. Relaxation time of alginate-F127 multicomponent hydrogel and neat 30 wt% F127 between 10 °C to 80 °C, derived from fitting XPCS data to Eq. 8.

If we consider the samples at 15 °C and 40 °C, extrapolating the trend in G'' to lower frequencies, we might expect a crossover near a frequency of 0.05 rad/s, although it is difficult to discern a trend in G'' for the sample at 40 °C due to noise in the data. A crossover of 0.05 rad/s would correspond to a relaxation time of about 125 s, again much larger than what is observed in XPCS. Only the sample at 15 °C (Figure 3a) shows significant frequency-dependence of G'' , with potential crossover points both above and below the measured frequencies. In other words, at physiologically-relevant temperatures, the microscale dynamics of these gels obtained from XPCS are much faster than those obtained by conventional rheology. This has important implications for uses of these materials for certain biomedical applications, due to the relevant timescales for cellular responses, as noted above.

Microrheology

We were able to express the shear modulus of the alginate-F127 multicomponent hydrogel in terms of the Fourier Transform of the MSD using the generalized Stokes-Einstein relation in Eq (2). The corresponding G' of the multicomponent hydrogel consisting of 0.5 wt% alginate and 30 wt% F127 is shown in Figure 4a. The G' was evaluated from 10 °C to 80 °C within the angular frequency range of 0.008 rad/s to 0.05 rad/s. We note that it is challenging to obtain data at such low frequencies using conventional bulk rheology. In Figure 4a we see a similar behavior corresponding to the self-arrangement of the F127 micelles, whereby the hydrogel is weakest at low temperatures and stiffest past the LTT.

It is seen that the alginate-F127 multicomponent hydrogel exhibits shear-thinning behavior between 10 °C to 80 °C (Figure 4b). This is evident in the decrease in complex viscosity with increasing frequency. The complex viscosity increases with temperature and reaches a maximum viscosity at 60 °C. The complex viscosity decreases as temperature continues to increase.

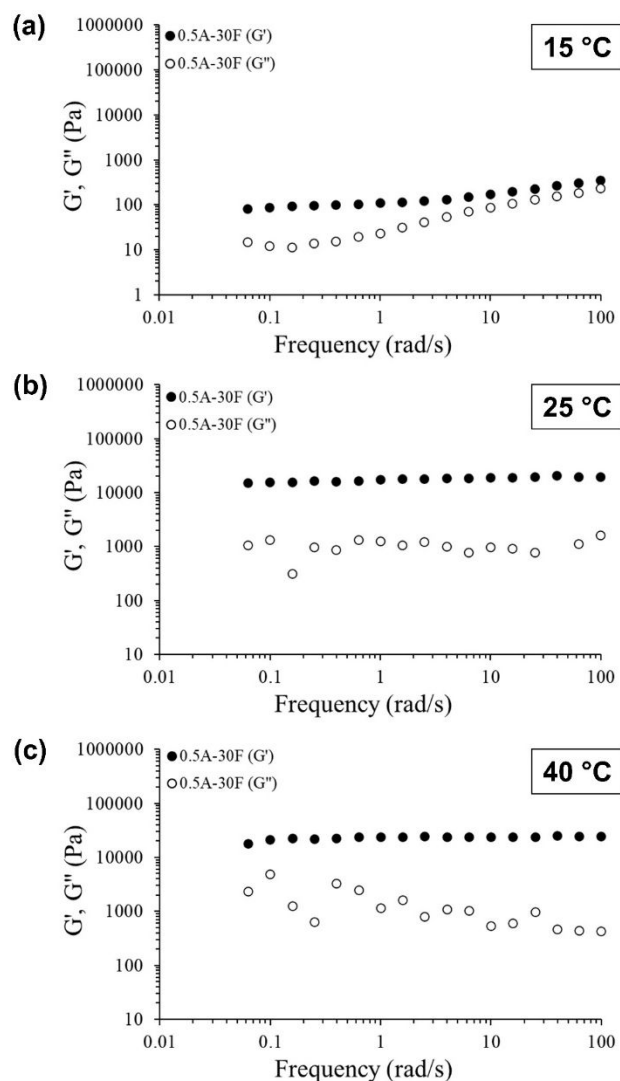


Fig 3. Results from conventional oscillatory shear rheological measurements on the alginate-F127 multicomponent hydrogel between at (a) 15 °C, (b) (a) 25 °C, and (c) 40 °C.

Temperature dependent G' at an angular frequency of 0.008 rad/s was reported as a comparison to the temperature sweep that was obtained through bulk rheology at 6.28 rad/s (1 Hz).

By contrast, microrheology shows a gradual increase in G' from 10 °C to 60 °C (Figure 5). This could indicate that at the microscale, the increase in stiffness is much more gradual than is led on by bulk rheology. We also note that the G' values for microrheology are about one order of magnitude lower than those obtained from bulk rheology. A similar phenomenon has been previously reported by Oppong et al. for disordered samples.²³ When considering the length scales of the F127 micelles and the alginate mesh size, one reason that the microrheology is lower than bulk rheology may be that the microscopic environment being probed is in part the internal pore of the alginate hydrogel. However, it is clear that the mesh is not large enough to allow for free motion of the F127 micelles; they are hindered by the presence of the alginate network, and this is supported by the fact that the relaxation

times of the 30 wt% F127 gel with no alginate are much lower than in the multicomponent system. Therefore, microrheology has several advantages over conventional bulk rheology including the ability to study systems that are intrinsically small, access to high-frequency dynamics, and sensitivity to special heterogeneity.

however, the bulk rheology experiments do not show a crossover between G' and G'' over comparable timescales. Moreover, the bulk rheology measurements yield storage and loss moduli that are orders of magnitude higher than our microrheology analysis. Thus, the hydrogels behave as a much softer material with more rapid dynamics on small length scales as compared to the macroscale. These experiments highlight the varying dynamics and mechanical properties of soft biomaterials when probed over different length scales. Recent studies implicate the timescale for stress relaxation as one factor regulating interactions such as cell spreading, proliferation, and differentiation. As the relevant timescales and length scales can be difficult to access via conventional rheology, XPCS may be regarded as a new tool to characterize these properties in soft biomaterials.

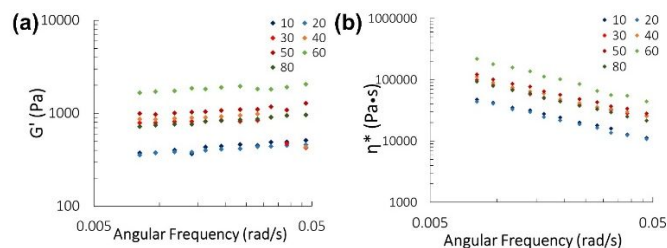


Fig 4. Frequency dependent (a) storage modulus behavior and (b) complex viscosity of alginate-F127 multicomponent hydrogel at temperatures between 10 °C to 80 °C from microrheology.

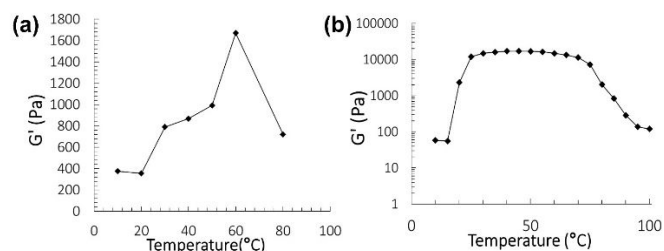


Fig 5. Temperature-dependent storage modulus of alginate-F127 multicomponent hydrogel from (a) microrheology at 0.008 rad/s and (b) bulk rheology at 6.28 rad/s from previous study¹³.

Conclusions

X-ray photon correlation spectroscopy (XPCS) was utilized to probe the microscale temperature-dependent dynamics of multicomponent F127/alginate hydrogels. Moreover, we utilized XPCS-based microrheology to explore the viscoelastic behavior of these materials. Both the XPCS experiments and macroscale rheology measurements show similar trends with temperature. However, correlation functions from XPCS yield relaxation times ranging from 10 – 45 s on the microscale for the composite alginate/F127 gel, as derived from fits to the correlation function to eq. (8), shown in Fig. 2. Relaxation times in this range are outside of the frequency range that is probed by our XPCS-based microrheology. By contrast, conventional bulk rheology experiments are within the frequency range where we should be able to measure these relaxation times;

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

Financial support for this work was provided by National Science Foundation awards DMR-1905547, CBET-1903189, DGE-1922639, and CHE-1609494; NIH R01GM097971; ACS PRF award 55729-ND9; and a Department of Education Graduate Assistance in Areas of National Need (GAANN) fellowship for S.P.Q. and B.Z., Award P200A160163. This research used resources of the National Synchrotron Light Source II, U.S. Department of Energy (DOE) Office of Science User Facilities operated for the DOE Office of Science by Brookhaven National Laboratory under Contract No. DE-SC0012704.

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Table of Contents Graphic and Sentence

X-ray photon correlation spectroscopy (XPCS) experiments provide insight into microscale dynamics of soft materials and biomaterials, differing from those observed through macroscale rheology, on time scales of relevance for some cell-material interactions.

