Colloid Polym Sci (2002) 280: 783–788
DOI 10.1007/s00396-002-0702-3

ORIGINAL CONTRIBUTION

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Gelation of "catanionic" vesicles by hydrophobically modified polyelectrolytes

Received: 17 June 2001
Accepted: 11 March 2002

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Abstract The gelation of mixed cationic/anionic surfactant vesicles of sodium dodecyl sulfate/didodecyldimethylammonium bromide and sodium dodecylbenzenesulfonate/cetyltrimethylammonium tosylate by hydrophobically modified sodium polyacrylate is studied rheologically. When the vesicles are cationically charged, mixtures with this anionic polyelectrolyte form precipitates. When the vesicles are anionically charged, however, these mixtures display a progression from a Maxwell fluid to a critical gel to a solid-like gel with increasing vesicle and/or polyelectrolyte concentration. Consideration of the viscous behavior with increasing vesicle and polymer volume fraction indicates that the gel network is formed by the bridging of the hydrophobically modified polymer between vesicles. The similarity between the gelation results for the two anionic systems suggests the results can be generalized to other similarly charged mixtures.

Keywords Vesicles · Hydrophobically modified polymers · Gels

Introduction

Surfactant vesicles can be regarded as models for biological cells or membranes and, as such, have been the subject of intensive biophysical and colloidal research. While vesicles typically are stable at low volume fractions, they fuse and lamellar phases predominate at higher surfactant concentrations. The viscosification of vesicle phases that could extend the application range of these microstructures in, for example, controlled delivery is thereby limited. A notable exception are recently discovered vesicles composed of sodium oleate and octanol which form closed-packed vesicle gels [1, 2]. These gels, however, form at surfactant concentrations of 25 wt%, limiting their utility. Alternatively polymers can be added to enhance the solution rheological properties. Simple hydrophilic polymers tend to drive intervesicle attractions and fusion owing to depletion forces [3, 4, 5]. Hydrophobically modified (HM) polymers which can be anchored in the vesicular bilayer, on the other hand, can serve as steric stabilizing groups shielding the vesicles from one another and prevent their coalescence into a lamellar phase. This strategy has been used to stabilize liposomes and control the membrane permeability of liposomal drug delivery vehicles [6]. While stabilizing the vesicle morphology, the modified polymers can also bridge vesicles to form aggregated structures. Such an approach has been used to develop thermally sensitive gels of nonionic surfactant vesicles and HM polyelectrolytes [7]. In addition, cholesterol end-capped poly(ethylene oxide) has been shown to gel surfactant vesicles and induce agglomeration of living biological cells [8].

Presently, we report the gelation of mixed cationic/anionic (catanionic) surfactant vesicles by a HM polyelectrolyte. In particular, we examine the interaction of HM sodium polyacrylate (HM-NaPA) with vesicles composed of sodium dodecyl sulfate (SDS)/didodecyldimethylammonium bromide (DDAB) and sodium dodecylbenzensulfonate (SDBS)/cetyltrimethylammonium tosylate (CTAT). The HM-NaPA is randomly decorated with 3 mol% octadecyl groups, lending the hydrophobic functionality. The ternary phase diagrams for these two surfactant mixtures display anionic and cationic vesicle lobes which are spontaneous and stable [9, 10, 11, 12]. This permits us to examine the effect of the net vesicle charge on the phase behavior and rheology of the vesicle polyelectrolyte mixtures. Previous studies have focused only on interactions with oppositely charged vesicles [13, 14] or cases where only the polymer or vesicle carries a net charge [7, 8]. We find the polyelectrolyte readily gels the similarly charged anionic vesicles displaying a progression from a Maxwell fluid to a solidlike gel. Moreover, the similarity between the gelation results for the two anionic systems suggests the results are general and can be extended to other vesicle systems.

Experimental

Three different catanionic vesicle stock solutions were prepared following the procedures and concentrations detail in Refs. [10, 11]. The first solution prepared was a 1.67 wt% surfactant solution of 0.71 mole fraction SDS (above 99%, Sigma) and 0.29 mole fraction DDAB (Acros). The resulting SDS-rich solution was bluish and turbid and lay well within the anionic vesicle lobe of the SDS/DDAB/water ternary phase diagram reported by Marques et al. [11]. The second solution prepared was a 2.25 wt% surfactant solution of 0.72 mole fraction SDBS (Fluka) and 0.28 mole fraction CTAT (Fluka). The resulting SDBS-rich solution was bluish and turbid and lay well within the anionic vesicle lobe of the SDBS/CTAT/water ternary phase diagram reported by Kaler et al. [10]. The final surfactant solution prepared was a 2.25 wt% surfactant solution of 0.69 mole fraction CTAT and 0.31 mole fraction SDBS. The resulting CTAT-rich solution was yellowish and turbid and lay well within the cationic lobe of the SDBS/CTAT/water ternary phase diagram reported by Kaler et al. [10].

HM polyacrylic acid ($\bar{M}_w = 250{,}000$, Aldrich) was prepared by the amide-formation reaction of octadecylamine (97%, Aldrich) with the polymer carboxylic acid group in an aprotic solvent, *N*-methylpyrrolidone (Fisher), in the presence of 1,3-dicyclohexylcarboiimide (99%, Aldrich). Reaction details are given in Ref. [15]. After the reaction, the remaining acid groups were neutralized by excess sodium hydroxide and the product was washed by extraction with methanol. The HM-NaPA synthesized was subsequently dried under vacuum. The degree of acid group modification as determined by ^{1}H NMR [15] was 3.0 mol%. From the prepared sample a 5.00 wt% polymer stock solution was prepared at pH 7.

Surfactant/polymer sample mixtures were prepared from the stock solutions. Samples were prepared along constant surfactant concentration, constant polymer concentration, and proportional surfactant/polymer concentration mixing pathways. The surfactant concentrations were kept within the vesicle region of the reported anionic surfactant/cationic surfactant/water phase diagrams. The samples were equilibrated for at least 1 week before rheological tests were performed. The samples remained in solution for several months without changing their visual appearance, suggesting no additional changes after the initial preparation.

Rheological measurements were performed using a Rheometrics RFS II controlled-strain rheometer in a Couette geometry. The sample temperature was maintained at 25 ± 0.2 °C by a circulating water bath and evaporation was minimized by a solvent trap. Prior to performing the frequency-sweep measurements to determine the sample storage, G', and loss, G'', moduli, a strain-sweep measurement was performed for each sample at a frequency of 0.5 rad/s to ensure that the tests were carried out in the linear viscoelastic regime with a large enough strain to minimize instrumental noise.

Results and discussion

To begin, we examined the behavior of the mixtures of the cationic SDBS/CTAT vesicles (i.e., CTAT rich) with HM-NaPA along a constant total-surfactant-concentration mixing path. As might be expected for oppositely charged species, these mixtures were cloudy and form a precipitated surfactant/polyelectrolyte complex. Complex precipitation is greatest at the point of charge neutralization when the net surfactant charge concentration equals that of the polyelectrolyte. Like the SDBS/CTAT system, the SDS/DDAB system displays a cationic vesicle lobe [12]. We expect similar behavior if HM-NaPA is added to these vesicles as well. Since this precipitation behavior is not of interest in the present study, we do not discuss it further.

It might be expected in the case of similarly charged vesicle/polyelectrolyte mixtures that these samples would exhibit segregative phase separation between a surfactant-rich and a polyelectrolyte-rich phase [16]. Interestingly though, all the samples of anionic vesicles (i.e., SDS or SDBS rich) and HM-NaPA were one-phase, retained their bluish color associated with the pure vesicle system, and were stable over a period of several months. When we used an HM-NaPA with shorter dodecyl substituent hydrophobic groups with the same degree of modification (3.0 mol%) segregative phase separation was observed. This suggests that hydrophobic interactions must be sufficiently strong to overcome the electrostatic repulsion between the polyelectrolytes and vesicles. In support of our conclusion, it has been previously found from viscometric [17], cryogenic transmission electron microscopy [18], and fluorescence measurements [19] that the association strength between SDS micelles and anionic HM polyelectrolytes increases with increasing degree of hydrophobe substitution and length of the alkyl side chains along the polymer backbone.

Representative measurements of G' and G'' as a function of frequency, ω, for mixtures of the anionic SDS/DDAB vesicles with HM-NaPA along a constant polyelectrolyte concentration mixing path are shown in Fig. 1. At low surfactant concentrations (Fig. 1a) G'' is greater than G' over a wide range of ω and the mixtures behave as a Maxwell fluid with characteristic power law exponents of 2 and 1 for the dependence of G' and G'' on ω, respectively. At intermediate surfactant concentrations (Fig. 1b), G'' still dominates G' over the frequencies of interest, indicating that the mixture is still behaving as

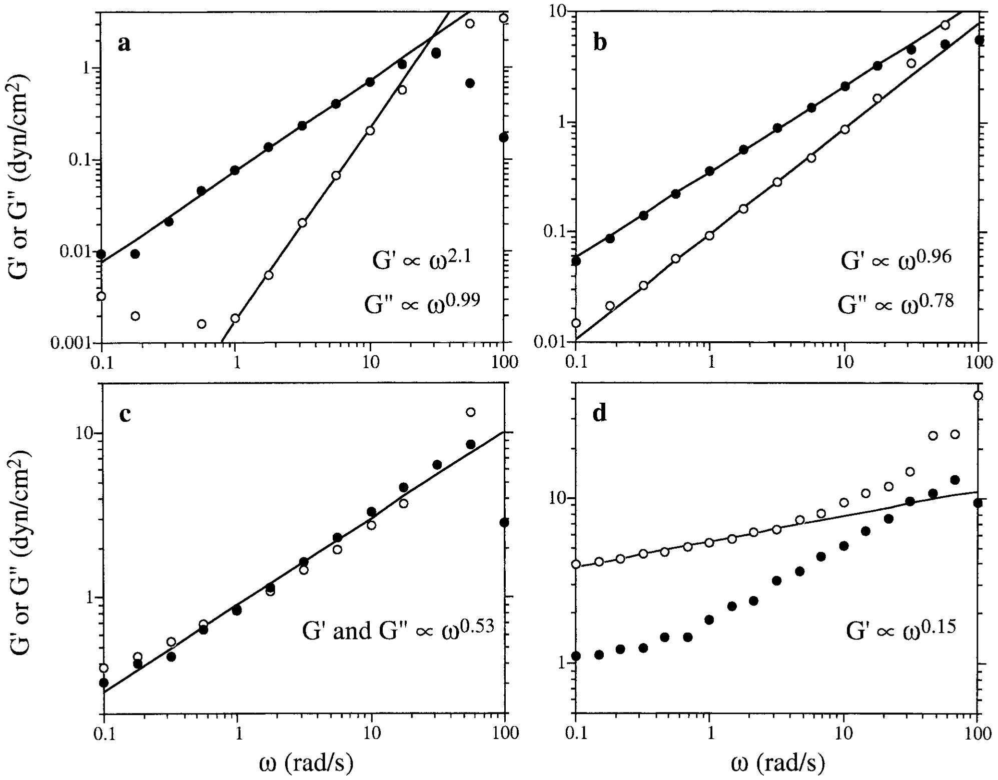

Fig. 1. Storage, G', and loss, G'', moduli as a function of frequency, ω, for anionic sodium dodecyl sulfate (*SDS*)/didodecyldimethylammonium bromide (*DDAB*) vesicle mixtures with hydrophobically modified sodium polyacrylate (*HM-NaPA*) with increasing surfactant concentration at constant polyelectrolyte concentration. The *open* and *closed symbols* denote G' and G'', respectively. The *lines* indicate power fits of the dependence of the moduli on ω, i.e., G' or $G'' \propto \omega^n$. The concentrations at which each measurement was taken are indicated in Fig. 2. Progression in surfactant concentration shows: (**a**) a low surfactant concentration solution that behaves like a Maxwell fluid with characteristic exponents of around 2 andaround 1 for the dependence of G' and G'', (**b**) a non-Maxwellian fluid at intermediate surfactant concentrations whose exponents are decreasing and approaching one another, (**c**) a critical gel with G' and G'' equal over nearly 3 orders of magnitude in ω with a characteristic power-law exponent of around 0.5, and (**d**) a vesicle/polymer gel with G' greater than G''over the range of ω and G' increasingly independent on ω

a fluid. The power-law exponents in this case, however, are less than their idealized Maxwell values and approach one another for G' and G''. At still greater surfactant concentrations, a critical gel is formed with G' and G'' equal to each other over a wide range of frequencies (Fig. 1c). Moreover, the power-law exponent for the moduli is 0.5, indicating that the gel results from the formation of a percolating vesicle/polyelectrolyte network with a fractal dimension of 2 [20, 21, 22]. Finally, above the critical gel concentration (Fig. 1d), G' dominates the rheological response and is less sensitive to frequency, indicating elastic solidlike behavior for these gels.

Similar fluid-to-gel behavior is observed along constant surfactant concentration and proportional surfactant/polyelectrolyte concentration mixing paths for the anionic SDS/DDAB vesicle mixtures with HM-NaPA. The results for these rheological measurements are summarized in Fig. 2a. The results shown here extend beyond this particular system as comparable results are found for mixtures with the anionic SDBS/CTAT (SDBS-rich) vesicles. To compare the results for these two systems we calculate the vesicle, ϕ_v, and polyelectrolyte, ϕ_p, volume fractions in solution. ϕ_v can be shown to be

$$\phi_v = \bar{A}_s R_v N_A C_s / 6, \tag{1}$$

where $\bar{A}_s = x_- A_- + x_+ A_+$ is the mole average surfactant head group area of the anionic and cationic species, R_v is the average vesicle radius, N_A is Avogadro's number, and C_s is the molar surfactant concentration. We note that when the surfactants are paired in the vesicle bilayer, the head group area is probably less than that calculated assuming additivity. Thus, Eq. (1) serves as an upper estimate of ϕ_v. ϕ_p is given by

$$\phi_p = 4\pi R_g^3 N_A C_p / 3, \tag{2}$$

where R_g is the polymer radius of gyration and C_p is the molar polymer concentration. The surfactant head group areas and vesicle/polyelectrolyte radii used in our calculations are given in Table 1 [23, 24]. The HM-

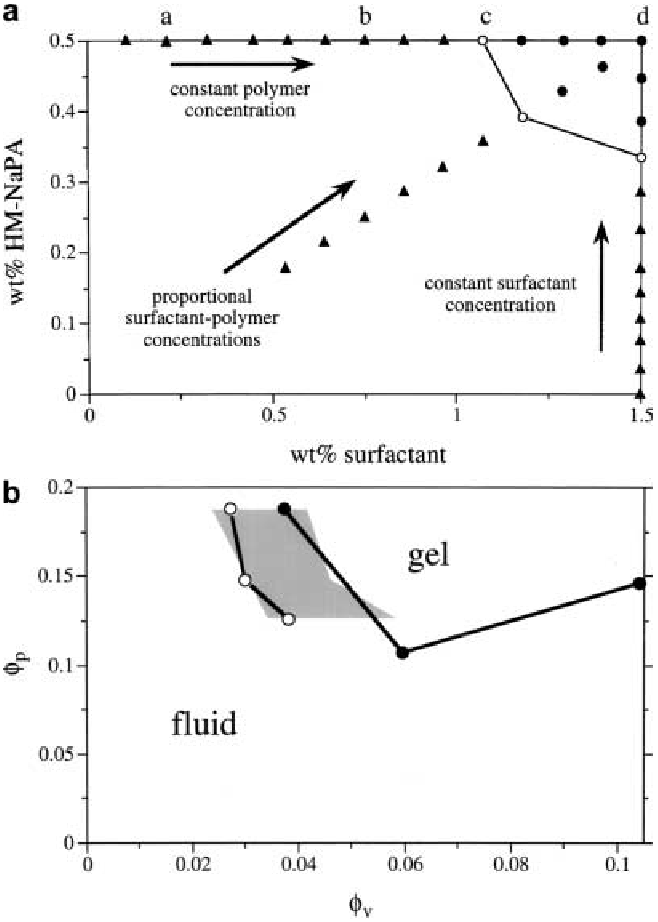

Fig. 2. (**a**) Gel phase diagram for mixtures of anionic SDS/DDAB vesicles and HM-NaPA. The gel boundary was determined along three mixture paths: along a constant 1.5 wt% surfactant concentration path, a constant 0.5 wt% polymer concentration path, and a constant 3:1 surfactant-to-polymer weight proportion. The *closed triangles*, *open circles*, and *closed circles* indicate fluid, critical gel, and gel phases as determined rheologically. The *solid line* demarks the gel boundary. The *letters* correspond to the points along which the sample measurements shown in Fig. 1 were taken. (**b**) Comparison of the gelation behavior of net anionic vesicles of SDS/DDAB and sodium dodecylbenzensulfonate (*SDBS*)/cetyltrimethylammonium tosylate (*CTAT*) by HM-NaPA. The *open* and *closed symbols* demark the gel boundaries for the SDS/DDAB and SDBS/CTAT vesicles, respectively. The shaded area indicates the overlap region between the SDS/DDAB and SDBS/CTAT vesicle gelation boundaries ($\pm\sigma_{\phi_v}$, Eq. 3) when the polydispersity of the vesicle radii is taken into account

NaPA induced gelation of these two anionic vesicle mixtures are compared in Fig. 2b. While the gelation patterns are similar, the gel boundaries for these two different vesicle systems do not fall directly on top of one another. When the vesicle volume fraction was calculated by Eq. (1), however, it was assumed that the vesicles were monodisperse. The measured standard deviation in the SDS/DDAB and SDBS/CTAT anionic vesicles indicates that in fact the size distributions are polydisperse (Table 1). When this polydispersity is taken into account by assuming to a first approximation that the volume fraction dispersity is

$$\sigma_{\phi_v} = \bar{A}_s \sigma_{R_v} N_A C_s / 6 \tag{3}$$

following Eq. (1), the gelation boundaries are more diffuse. In Fig. 2b we show that the region over which the gelation boundaries for these two vesicle systems overlap with increasing surfactant concentration when polydispersity is included in the calculation of ϕ_v. Thus, while the gelation boundaries for these two systems are not exactly the same, it is reasonable to expect that they have a similar origin when the vesicle size distribution is taken into account. Additional differences between these two systems include specific molecular interactions between the polymer and surfactant species as well as the surfactant head group areas and surface charge density.

It remains to identify the gelation mechanism. Two potential routes for gel formation are illustrated in Fig. 3. In the first route, the vesicles and polymer pack together in a close-packed configuration with a net volume fraction of the order of $\phi \approx 0.7$, similar to the vesicle gels produced by Gradzielski and coworkers [1, 2]. The second possibility is that the vesicles act as network junctions with the HM polyelectrolyte bridging between them at volume. The complex viscosity, η^*, at $\omega = 0.1$ rad/s for the anionic SDS/DDAB vesicle mixtures with HM-NaPA is shown in Fig. 4 as a function of the total volume fraction, $\phi = \phi_v + \phi_p$. The viscosity is a strongly increasing function of ϕ, spanning nearly 4 orders of magnitude over the range examined. The gel boundary, however, does not occur at a fixed value of ϕ, as might be expected if gelation arose from close packing of the vesicles and polyelectrolyte coils. Moreover, the value of ϕ at gelation is in the range 0.14–0.20, 3–4 times less than the close-packing value. Perhaps most telling, however, is the behavior along the constant polyelectrolyte concentration mixing path. At the lowest surfactant concentration, the solution viscosity is just slightly greater than that of liquid water. Indeed at this point the polymer concentration, $\phi \to 0.18$–0.20, is well below the overlap concentration at which point the viscosity increases significantly owing to the packing of the polymer coils themselves. Adding the vesicles to this solution dramatically raises the viscosity over a relatively narrow window of volume fraction, $\phi_{max} = 0.20$. Thus, it could be concluded that the vesicles are acting as multifunctional network junctions in the gel. The dramatic viscosity increase arises in this case from the fact that each hydrophobic attachment of the polymers to the vesicles increases the number of elastically active polymer segments, which themselves contribute approximately ρkT to the elastic modulus [25], where ρ is the concentration of active chains and kT is the product of Boltzmann's constant and the temperature. Taken

Table 1. Surfactant and polymer physical properties for the volume fraction calculations. Substances: sodium dodecyl sulfate (*SDS*), didodecyldimethylammonium bromide (*DDAB*), sodium dodecylbenzensulfonate (*SDBS*), cetyltrimethylammonium tosylate (*CTAT*), and sodium polyacrylate (*NaPA*)

Substance	Variable	Value	Reference
SDS	Surface area	52 Å^2	[23]
DDAB	Surface area	70 Å^2 [a]	
SDBS	Surface area	66 Å^2	[23]
CTAT	Surface area	61 Å^2 [b]	
Anionic SDS/DDAB vesicle	Average radius	150 Å	[11]
Anionic SDS/DDAB vesicle	Standard deviation in vesicle radius	± 80 Å [c]	
Anionic SDBS/CTAT vesicle	Average radius	300 Å	[10]
Aionic SDBS/CTAT vesicle	Standard deviation in vesicle radius	± 110 Å	[10]
NaPA $\overline{M}_w^v = 250{,}000$	Radius of gyration	155 Å [d]	

[a] Upper bound estimate, experimental value not determined

[b] Taken from the value for the bomide salt (CTAB) reported in Ref. [23]

[c] Evaluated from the cryogenic transmission electron microscopy image reported in Fig. 4b of Ref. [11]. The vesicle radii were measured manually from the scanned image and the standard deviation evaluated as $\sigma_{R_v} = \left(R_v^2 - \bar{R}_v^2\right)^{1/2}$ from the vesicle size distribution

[d] Evaluated from the expression $R_g = K\bar{M}_w^{1/2}$ using K for NaPA reported in Ref. [24]. It is assumed that the hydrophobic groups do not significantly perturb R_g for the unmodified polyelectrolyte

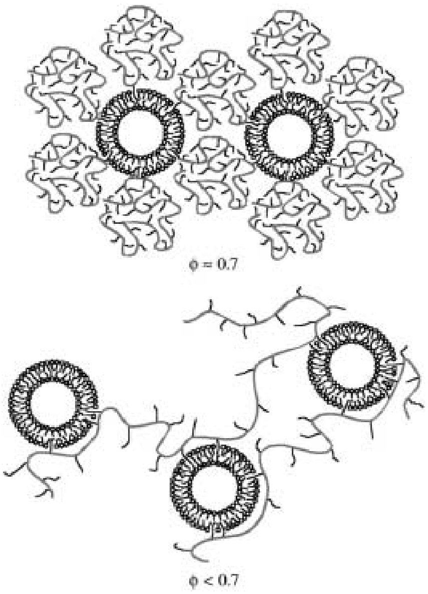

Fig. 3. Schematic illustration of possible gelation mechanisms. The *top* mechanism corresponds to gelation by close packing of the vesicles and polymer coils at total volume fractions of around 0.7. The *bottom* mechanism corresponds to the formation of a percolating network at volume fractions less than close packed with the polyelectrolyte chains bridging between vesicle network junctions

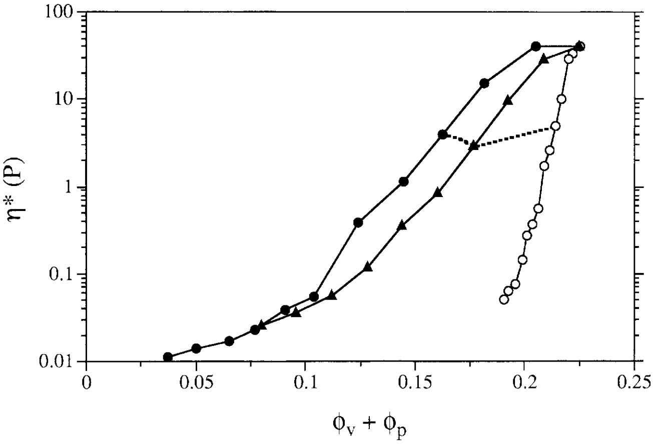

Fig. 4. Complex solution viscosity, η^*, for SDS/DDAB surfactant (SDS-rich) mixtures with HM-NaPA as a function of the total vesicle and polyelectrolyte volume fraction ($\phi_v + \phi_p$). The *closed circles*, *open circles*, and *closed triangles* denote measurements along the constant surfactant concentration, constant polymer concentration, and proportional surfactant/polymer concentration mixing paths in Fig. 2a. The *dashed line* demarks the gelation boundary

together, these observations support the idea that the percolating gel network is formed by the bridging of the HM polymer bridging between vesicles. While the gelation boundary for the anionic SDBS/CTAT vesicles lies at higher vesicle volume fractions, the total volume fraction at gelation is more than half the close-packed value (maximum ϕ at gelation about 0.25). Thus, we anticipate a similar vesicle/polyelectrolyte network structure at gelation.

In summary, we have demonstrated that stable vesicle gels can be made by mixtures of similarly charged vesicles and HM polyelectrolytes. The pendant hydrophobic groups must be of sufficient length, and presumably degree of hydrophobic modification, to overcome the electrostatic repulsion between the macromolecular species. The gels formed display a classical transition from a Maxwell fluid to a critical gel to an elastic solid with either increasing surfactant and/or polyelectrolyte concentration. Comparable gelation behavior was observed for these two different vesicle systems, suggesting the underlying results are general. The changes in the solution viscosity with changing vesicle and polymer volume fraction indicate the gel network arises from the bridging of the polyelectrolyte between the vesicles, which act as multifunctional network connections. Presently, we have only examined the phase behavior and rheological response of these systems. Our analysis of the network formation mechanism has assumed that the vesicle and polyelectrolyte do little to perturb their individual solution behavior, while this is not necessarily the case. Indeed polyelectrolytes can induce structural changes in the vesicle structures, such as faceting of the vesicle surface [13, 14]. It would be of interest, therefore, to investigate the structure of the vesicles in the gel by scattering and microscopy techniques. While we have focused on charged systems in this study, it is reasonable to expect that nonionic HM polymers can induce vesicle gelation as well [8]. Moreover, the absence of charge neutralization suggests such polymers will be able to simultaneously gel anionic and cationic vesicles.

Acknowledgements We thank Asani Phillips, who helped initiate this work during a summer NSF-REU work study fellowship, and Bing-Shou Yang, who assisted in the polymer modification as well as provided a sample of the dodecyl-modified polymer for comparison with the present results.

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