Regular and irregular deswelling of polyacrylate and hyaluronate gels induced by oppositely charged surfactants

Peter Nilsson *, Per Hansson

Department of Pharmacy, Uppsala University, Box 580, S-75123 Uppsala, Sweden

ABSTRACT

The deswelling kinetics of macroscopic polyacrylate (PA) gels in solutions of dodecyltrimethylammonium bromide ($C_{12}TAB$) and cetyltrimethylammonium bromide ($C_{16}TAB$), with and without added sodium bromide, as well as hyaluronate (HA) gels in solutions of cetylpyridinium chloride (CPC) are investigated. Additional data are also provided by small-angle X-ray scattering and microgel experiments. The purpose is to study the deswelling behavior of (1) regularly deswelling gels, for which the deswelling is successfully described using a core/shell model earlier employed for microgels, and (2) irregularly deswelling gels, where the gel turns into a balloon-like structure with a dense outer layer surrounding a liquid-filled core. For regularly deswelling gels, the deswelling of $PA/C_{12}TAB$ is found to be controlled by diffusion through both stagnant layer and collapsed surface phase, while for $PA/C_{16}TAB$ it is found to be controlled mainly by the latter. The difference in deswelling rate between the two is found to correspond to the difference in surfactant diffusion coefficient in the surface phase. Factors found to promote irregular deswelling, described as balloon formation, are rapid surfactant binding, high bromide and surfactant concentration, longer surfactant chain length, and macroscopic gel size. Scattering data indicating a cubic structure for HA/CPC complexes are reported.

© 2008 Elsevier Inc. All rights reserved.

1. Introduction

There are several descriptions in the literature of the deswelling of both macroscopic [1–7] and microscopic [8–10] charged polymer gels in the presence of oppositely charged surfactants. For some of these a non-uniform deswelling with the formation of a surface phase has been reported [1–3,5,6,8,9]. In general, a polyelectrolyte gel, such as a crosslinked polyacrylate (PA) or hyaluronate (HA) gel, is in its reference state swollen due to the swelling pressure provided by the counter ions present inside the gel [11]. When the gel is placed in a solution containing oppositely charged surfactant of a concentration exceeding the critical association concentration (*cac*), but of equal ionic strength, the surfactant monomers will diffuse into the gel and there form micelles [11]. This allows the release of the counter ions previously neutralizing the polymer charges and, due to the subsequent lowering of the swelling pressure, causes the gel to collapse [1,4,6]. As micelles form in the gel, the outer part will collapse first, causing a phase separation with a dense, outer, micelle rich surface phase and a still swollen, micelle lean core [1–3,5]. As more surfactant is absorbed into the gel, the surface phase will grow at the expense of the core [1,6]. The

regular deswelling behavior is that the gel continuously deswells as the collapsed surface phase grows, exerting higher pressure on the core, while the core is gradually converted to surface phase, until the entire gel has collapsed [1], see Fig. 1 (upper path). At this point the core may either have been completely converted to surface phase, or possibly remain to a lesser degree but in such a compressed state that it is hard to distinguish from the surface phase [12]. For microscopic PA gels in solutions of dodecyl- ($C_{12}TAB$) and cetyltrimethylammonium bromide ($C_{16}TAB$), it has earlier been shown that the deswelling kinetics can be described using ion-exchange kinetics for the surfactant transport from the bulk solution to the gel core. The liquid layer closest to the surface, where no convection takes place and only diffusion governs the transport, is called the stagnant layer. For microgels, transport through this layer becomes rate determining, as the collapsed surface phase remains thin in comparison for the major part of the deswelling [9,13]. For macroscopic gels, the kinetics have not been investigated in detail earlier, and there is reason to believe that the kinetics may be controlled by other processes, such as the diffusion of surfactant through the surface phase or the relaxation of the gel network and the reorganization of micelles in the surface phase. To determine this, we will investigate the deswelling of macroscopic PA gels in solutions of $C_{12}TAB$ and $C_{16}TAB$, as well as HA gels in solutions of cetylpyridinium chloride (CPC), and compare the results with values calculated using a surfactant-diffusion

---

* Corresponding author. Present address: Physical Chemistry 1, Lund University, Box 124, S-221 00 Lund, Sweden. Fax: +46 (0) 46 222 4413.
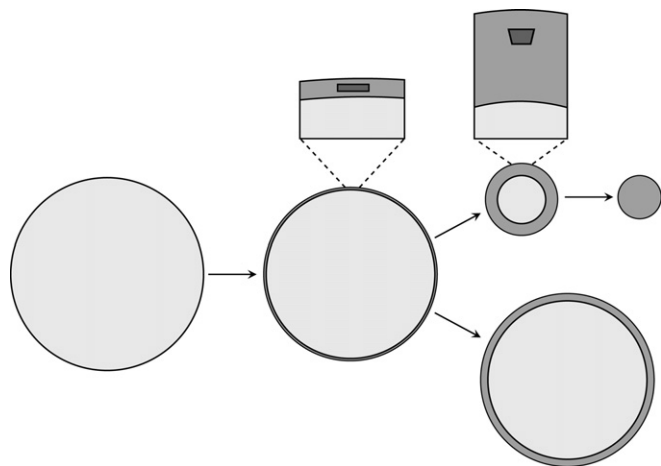*E-mail address:* Peter.Nilsson@fkem1.lu.se (P. Nilsson).

Fig. 1. Schematic showing the regular (upper) and the irregular (lower) deswelling paths, as well as the changes taking place in a segment of deswelling gel. Note that in addition to the surface phase growing, a rearrangement of the already formed surface phase must take place to enable gel deswelling, during which any arbitrary segment will become thicker in the direction perpendicular to the gel surface, and shorter laterally, as the gel radius decreases.

controlled deswelling model, earlier employed for PA microgels [8, 9,13]. In addition, we will also investigate the HA/CPC system more closely, establishing binding/swelling isotherms and looking at the microstructure using small-angle X-ray scattering (SAXS).

In parallel to this, we will also take a closer look at a previously largely neglected area of gel/surfactant interaction, namely the deswelling behavior where the gel at some point during deswelling forms a balloon-like structure, which then shows slight or no further deswelling, even though it still absorbs surfactant. In this irregular deswelling case, the surface phase does not contract as expected, but instead forms a dense balloon-like shell around a liquid core, empty of polymer network, see Fig. 1 (lower path). Some references to irregular deswelling can be found [1,2], but we will now try to give a more comprehensive picture of when this deswelling behavior can be expected and a plausible explanation as to why it occurs.

2. Experimental

2.1. Materials

Acrylic acid (99%) and *N*-dodecylpyridinium chloride monohydrate (98%) from Aldrich, dodecyltrimethylammonium bromide (99%), ammonium persulfate (AP) ($\geqslant$98%), *N*,*N*′-methylenebis-acrylamide (NMBA), tris(hydroxymethyl)aminomethane (Trizma® base) (99.9%) and *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (TEMED) (99%) from Sigma, sodium hydroxide (NaOH) from Eka Chemicals, *N*-cetyl-*N*,*N*,*N*-trimethylammonium bromide (p.a.) from Merck, hydrochloric acid (FIXANAL®) and cyclohexane (p.a.) from Riedel-de Haën, Span 60 from Carl Roth OHG, methanol (HPLC grade) from Fisher Scientific, sodium chloride (NaCl) (Baker analyzed) from Tamro and sodium bromide (NaBr) from Kebo were all used as received. Crosslinked hyaluronate gels [14] were a kind gift from Q-Med AB. Solutions were prepared using high-quality Millipore water.

2.2. PA macrogel synthesis

A solution of 1.6 M acrylic acid, 14 mM NMBA (crosslinker), 6 mM TEMED (accelerator) and 6 mM AP (initiator) was prepared and degassed in vacuum. The solution was transferred into glass capillaries (ca. 5 cm length, one end capped) or tubes (length

40 mm, ⌀ 7 mm) and heated to 65 °C for 3 h. The gels were removed from the capillaries/tubes and transferred to a 0.5 M NaOH solution over night. After washing (3×12 h) in large excess of water the gels were dried to prevent degradation.

2.3. PA microgel synthesis

Submillimeter gels were prepared using an adaptation of the inverse suspension polymerization method used by Wang et al. [15]. A 10 mL portion of the reaction mixture containing acrylic acid, 1% crosslinker (NMBA), radical initiator (AP), accelerator (TEMED), NaCl (s), and 2 M NaOH was injected into 30 mL cyclohexane (with 0.3 wt% SPAN 60), in a round-bottom flask under heavy stirring. The polymerization was allowed to continue at 60 °C for 15 min under a nitrogen atmosphere, after which the suspension was poured into excess amounts of methanol. The precipitated gels were redissolved in water and bubbled with nitrogen to remove organic solvent, after which they were repeatedly washed with water on a 0.80 μm filter.

2.4. HA/CPC equilibrium experiments

Cylindrical HA gels ($\sim$0.8 g, length $\approx$ diameter $\approx$ 1 cm) were autoclaved in 1 mM phosphate buffer with isotonic salt concentration, after which they were washed repeatedly with water and equilibrated in 12 mM TRIS buffer pH 7.4. The polymer content of the gels in their reference state was determined by freeze-drying. After weighing, the appropriate amount of CPC was added and the gels were allowed to equilibrate for three weeks. The gels were then weighed again and the remaining CPC concentration of the solution was measured at wavelength 259 nm using a Spectronic Genesys 5 spectrophotometer. For ease of reference, these samples will be referred to as equilibrium samples, as opposed to the samples from the kinetic experiments (Sections 2.6 and 2.7).

2.5. Micromanipulation and light microscopy

Single gels were studied using a light microscope (Olympus BX-51) equipped with a micromanipulator (Narishige ONM-1). All micropipettes were pulled and polished using a Narishige PC-10 Puller and a MF-9 Microforge. All gels were in contact with a bulk solution containing NaBr and small amounts of NaOH (to ensure pH > 10 and thereby a fully charged network). All experiments were performed at room temperature. For each experiment, a small sample of gels was allowed to equilibrate in a petri dish with surfactant free solution until no change in gel size could be observed. After equilibration C_{16}TAB was added to the solution and the gel deswelling was studied using an Olympus DP-50 digital camera connected to the microscope. The images were analyzed with respect to gel size using the Olympus DP-Soft software. The micromanipulator equipped with a sharpened micropipette was used to puncture suspected balloon gels.

2.6. PA/C_{12}TAB and PA/C_{16}TAB kinetics

All experiments were performed at room temperature and under heavy stirring unless otherwise noted. The gels synthesized in tubes were cut to cubes of approximate volume 1 mL, while the ones synthesized in capillaries were allowed to retain their cylindrical shape. PA macrogels were equilibrated in NaBr solution (surfactant free), pH > 10 (to ensure a fully charged network) of the appropriate ionic strength. For each experiment, a gel was placed in a wire basket and lowered into a solution containing surfactant, NaBr, and small amounts of NaOH under stirring. The solution volume was chosen so that fully saturating the gel with surfactant would change the surfactant concentration of the solution by less