

**METHACRYLIC COPOLYMERS
FOR
COMPLEX COACERVATION**

**METHACRYLIC COPOLYMERS
FOR CONTROLLED PHASE SEPARATION
AND COMPLEX COACERVATION**

By

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COMPLEX COACERVATION**

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ABSTRACT

It is well known that complex coacervates can be prepared by combining aqueous solutions of oppositely charged biopolymers, such as gelatin and gum arabic. There are few examples of synthetic polyelectrolytes that produce complex coacervates, however. Two series of anionic copolymers capable of forming complex coacervates with branched polyethylenimine (PEI) in water have been prepared. One series consists of binary copolymers containing methacrylic acid (MAA) and poly(ethylene glycol) monomethyl ether monomethacrylate (PEGMA) in molar ratios ranging from 20:80 to 80:20, as well as the two homopolymers, poly(MAA) and poly(PEGMA). Another series contains an equimolar amount of MAA and PEGMA, together with between one and ten percent of a third, hydrophobic monomer, butyl methacrylate (BMA).

Both binary and ternary copolymers show lower critical solution temperatures, LCST's, ranging from 60.8°C to 1.5°C depending on composition. Furthermore, complex coacervation occurs upon addition of aqueous PEI to aqueous solutions of these copolymers. The percent volume of the liquid coacervate phase is independent of copolymer composition. However, with increasing MAA to PEGMA ratio in the binary copolymer, the concentration of the coacervate increases, reflecting an increased coacervation efficiency. The coacervate composition was not significantly affected by the BMA in the ternary copolymer series.

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1.0 INTRODUCTION

Water-soluble polymers include an enormously diverse class of biopolymers including polynucleotides (DNA), polyamides (proteins) and polysaccharides (starch, cellulose), which make up the essential building blocks of life. The structural features of these polymers control their molecular arrangement in aqueous media, allowing the formation of double helices, lipid bi-layers and complex globular shapes, for example, which enable them to perform very specific and highly controlled functions. These polymers arrange into their complicated ordered structures through hydrophobic interactions, hydrogen bonding and ionic associations. Taking their cues from nature, scientists have discovered that the self-assembly ability of biopolymers has many practical applications. For example, bi-layer vesicles generated from phospholipids may be useful in the pharmaceutical industry for drug delivery. Another important application is microencapsulation, where proteins have been employed in the formation of capsule walls to enclose water-insoluble molecules such as pigments, pesticides and perfumes. Such microcapsules are formed by the spontaneous assembly of the biopolymers, oil and water through a process called coacervation. In fact, coacervation has been suggested to have been involved in the origin of life in pre-biological times.¹

The coacervation process was first studied by the Dutch chemists, Bungenberg de Jong and Kruyt, who introduced the term. “Coacervation” is derived from the Latin word

for aggregation or heap, *acervus*, and the prefix *co* to signify a union between the macromolecules.² They used this term to describe the desolvation of macromolecules from a single homogeneous solution into two liquid phases. Usually, one of the phases is polymer-rich and initially appears as amorphous liquid drops called coacervate, which, under favourable conditions, may coalesce into a homogeneous liquid layer called the coacervate layer. The polymer-poor phase is referred to as the equilibrium liquid or coacervation medium.³ Coacervation is a remarkable colloidal phenomenon wherein two largely aqueous layers are immiscible. Theoretical treatments of this behaviour are thermodynamically based. Although entropy would favour dilution of the coacervate, the long-range interactions between the components in the coacervate layer inhibit dilution enthalpically.⁴ Conversely, complete desolvation does not take place because there are a number of possible arrangements of the macromolecules in a liquid phase, resulting in much greater entropy than if a precipitate were to form.⁵ Coacervation and precipitation are closely related phenomena, which can often be brought about upon the same system with miniscule changes in condition.

Coacervation can be further divided into two categories – simple and complex. An example of simple coacervation is the drop-wise addition of ethanol to a solution of gelatin in warm water. A phase separation similar to the process of fractionation occurs, and gelatin is concentrated in one of the phases.⁶ This transpires because the ethanol-water interactions are the most favourable in this ternary system, so that gelatin is excluded and becomes partially dehydrated. In contrast, precipitation occurs when exhaustive desolvation takes place. Precipitation can eventually be induced in this system

at a sufficiently high concentration of alcohol. One property of simple coacervates is that the addition of salts does not affect coacervation, indicating that charge effects are not involved.

A second type of simple coacervation can involve two macromolecules in solution, where the polymers partition exclusively between the two phases. If two concentrated solutions of gelatin, a protein, and gum arabic, a polysaccharide, are combined at a pH above the isoelectric point (IEP) of gelatin, two layers form, each enriched in only one of the polymer components.⁷ Under these conditions, the amphoteric gelatin is negatively charged, and the gum arabic is anionic also. Gelatin, which has a higher affinity for water, causes partial desolvation of the gum arabic. This process only occurs when the solutions are very concentrated. This method of generating two liquid phases in equilibrium has been applied as a separation technique for biological macromolecules, where it is necessary to have an aqueous solvent for each of the components being separated.⁸ In the case of dextran and polyethylene glycol (PEG), similar segregative phase separation takes place. It is believed to occur because of incompatibilities between the two polymers,⁹ and also due to the effects of the different polymers on the water structure, where the polarity of the water differs between the two phases.¹⁰

1.1 Complex coacervation

Complex coacervation, on the other hand, is an associative phase separation brought about by the interaction of oppositely charged macromolecules in solution. Unlike the concentrated gelatin-gum arabic system described earlier, an associative phase separation occurs when the pH of the solution is below the IEP of gelatin. In this circumstance, the gelatin has a net cationic charge and is attracted to the anionic gum arabic. The macromolecules form a polyelectrolyte complex (PEC) and separation into two liquid phases takes place. The coacervate phase is polymer-rich, and the equilibrium liquid is polymer-dilute. The coacervation process can take place over a wide range of concentrations, and is dependent on factors such as molecular weight, ionic strength, temperature, and particularly pH. In this system, the coacervation process is reversible, and the addition of base causes the coacervate phase to disappear. The cycle can be repeated by sequentially raising and lowering the pH, but eventually coacervation cannot occur even at low pH because the addition of the acid and base increases the salt concentration in the solution. The suppression of complex coacervation by the addition of salts is characteristic; the microions screen the ionic attractions between the macromolecules, preventing their electrostatic interaction to form a PEC.

An important application of complex coacervation is microencapsulation. In the 1950's, Green and Schleicher produced pressure-sensitive microcapsules containing pre-ink for carbonless copying paper.^{11,12} One popular technique used to produce gelatin-gum arabic microcapsules is to emulsify an oil in the presence of an aqueous solution of

gelatin and gum arabic. By lowering the pH, coacervate droplets are formed which coalesce at the surface of the oil drops, coating them. The hydrophobic phenyl groups on the gelatin drive the coacervate to the oil-water interface. As the temperature is then lowered, gelation occurs, and the hard shells can be crosslinked by the addition of formaldehyde, permanently solidifying the capsule walls.¹³ The oil phase may be released later by mechanical rupture or other means.

Although there is much patent literature on the application of complex coacervation to encapsulation and separation processes, the phenomenon is not very well understood or explained in the scientific literature. Various models have been proposed which attempt to elucidate the fundamental theory of complex coacervation, and while they are not all-inclusive, they do provide some insight into this process.^{14(a-d)} The merits of these theories have been analyzed by Burgess.¹⁵ It is commonly believed that the coacervate phase is liquid in nature partly because the electrostatic interactive forces are distributive rather than site specific, allowing the molecules to move around each other. However, some models suggest that initially a site-specific attraction occurs, and that the aggregates rearrange over time into a coacervate phase. This has been confirmed for certain systems by light-scattering experiments, which detected the initial presence of small flocculates which disappeared later. The theories predict that charge density is an important factor in complex coacervation. In order to obtain distributive charge interactions, the molecules must be able to adopt a random-coil configuration. If there is a high charge density on one of the macromolecules, coacervation may not occur as the molecule has a rod-like structure due to ionic repulsions along the polymer chain. Of

course, there is a lower limit to charge density also, in order to form a polyelectrolyte complex. Although high ionic strength suppresses coacervation, Burgess found that a certain minimum level of salt was necessary to maximize the coacervation for dilute gelatin-gum arabic mixtures. Gelatin and gum-arabic are highly charged polymers, which may be in an extended state at very low ionic strength. The molecules cannot adopt a random-coil configuration necessary for coacervation. Because the system is dilute, the molecules do not overlap, so precipitation does not take place either. A minimum level of salt is required to screen a fraction of the polyion charges in order for coacervation to take place. At high polyion concentrations, however, maximum coacervation occurs at zero ionic strength. In this case, the polyion segments can overlap to form neutral domains which entrap water to form a coacervate phase. The effects of polymer concentration and ionic strength on coacervation are strongly interrelated.

1.2 Hydrogen bonded complexes

The copolymers that will be described in this thesis include carboxylic acid and poly(ethylene glycol) (PEG) functionality. These functional groups can form hydrogen bonds to each other, and it is well known that homopolymers of this nature can form hydrogen-bonded complexes.¹⁶ For instance, a hydrogen-bond complex forms between poly(acrylic acid) (PAA) and PEG at appropriate pH and temperature conditions. This complex formation is suppressed above a certain critical pH value, because the dissociated acid groups are incapable of proton donation, which is necessary for complex

formation. There must be sufficient enthalpy from the hydrogen bonding to overcome the negative entropy of complexation. Below the critical pH, a stable complex between PAA and PEG can be formed.¹⁷ Simulations have shown that these complexes form in a 1:1 stoichiometric ratio with minimal bond strain.¹⁸

Peppas found that copolymers containing both carboxylic acid and PEG functional groups precipitate from water at low pH due to intramolecular hydrogen bonding, which is reversed by increasing pH.¹⁹ Klier et al. predicted that this intramolecular complexation would be enhanced in a random copolymer, but the efficiency would decrease for a block copolymer. To investigate this, they prepared copolymers of methacrylic acid (MAA) and poly(ethylene glycol) monomethyl ether monomethacrylate (PEGMA) by free-radical copolymerization in order to determine the monomer reactivity ratios.²⁰ When pure water was used as solvent, the ratios were determined to be $r_1=1.03$ and $r_2=1.02$ for MAA and PEGMA respectively. This would indicate a random copolymer, because both r values are very close to one. In a 50/50 ethanol-water mixture, however, the ratios were $r_1=2.0$ and $r_2=3.6$. This copolymer would be blocky, since both r values are much larger than one, and they predict that it would be less efficient at intramolecular complexation. The copolymerizations in this thesis research were carried out in tetrahydrofuran as solvent, and the reactivity ratios in these conditions are unknown, so the polymer architecture cannot be predicted.

Copolymers of MAA and PEGMA may have some interesting applications due to their ability to form intramolecular complexes. Klier et al. describe the reversible emulsifying properties of copolymers with a large excess of the MAA monomer relative

to ethylene glycol (EG) groups (10:1 and 20:1). The PEGMA comonomer had an average of 22 EG repeat units per monomer. Under basic conditions, intramolecular complexes are not formed, and the copolymer is hydrophilic. However, at low pH, the PEG side chains form intramolecular complexes with portions of the poly(MAA) backbone. The complexed segments are hydrophobic, while the remaining uncomplexed acid segments are hydrophilic. The molecular architecture is similar to hydrophilic-hydrophobic block copolymers, and the copolymers can stabilize oil emulsions under acidic conditions. It has been proposed that the emulsifying properties arise from stabilization against coalescence rather than reduction of interfacial surface tension.

Polymer networks of MAA/PEGMA copolymers have interesting pH and temperature sensitive properties as a result of intramolecular hydrogen bonding, which are greatly enhanced compared to the complexation between MAA and PEGMA homopolymers. Complexation is enhanced in the copolymers because the complementary functional groups are covalently attached to each other, so that the local concentrations of acid and EG groups are high, and complexation becomes highly probable. Peppas *et al.* prepared copolymer networks with MAA and PEGMA along with 2% of a dimethacrylate crosslinking monomer.²¹ The aqueous swelling behaviour of these gels was compared to the corresponding homopolymer gels at a pH of 4. At this pH, poly(MAA) gels are swollen due to the hydration of carboxyl anions and protons which are present due to partial dissociation of the acid groups. Pure PEGMA gels also swell independently of pH, due to hydration of the EG groups. In contrast, gels prepared with both MAA and PEGMA swelled considerably less, with a minimum swelling when

the ratio of MAA to EG groups was 1:1. This observation has been attributed to the hydrogen-bonded complexes formed within the network, which are hydrophobic. The swelling behaviour of the copolymer networks was also related to temperature. When the MAA:EG ratio was near 1:1, the networks were collapsed, independent of temperature. However, with excess EG to MAA, the gels were swollen at low temperature, but collapsed at high temperatures. At low temperatures, they attribute the gel swelling to the hydrophilic nature of the uncomplexed “free” EG sequences. When the temperature is raised, the interactions between the hydrophobic complexes cause the collapse of the gel. With decreasing EG, approaching stoichiometry, the transition temperature also decreases. Peppas *et al.* attribute this trend to an increased number of hydrophobic complexed segments, which tend to aggregate at higher temperatures. This network collapse at high temperatures may be analogous to the lower critical solution temperature observed with aqueous solutions of linear polymers such as poly(N-isopropylacrylamide).

1.3 Lower Critical Solution Temperatures

There are numerous examples of polymers possessing critical solution temperatures in various solvents. When a solvent-polymer system is heated, the polymer dissolves above the upper critical solution temperature, because the thermal motion of the solvent and polymer segments disrupts the attraction between like species. However, as the system is heated further, the polymer may again become insoluble above a critical temperature. This is called the lower critical solution temperature (LCST). It is the

temperature, called the lower critical solution temperature (LCST), where the polymer precipitates from solution. An LCST is entropy driven, and is usually a consequence of hydrogen bonding present in the system. The LCST behaviour of poly(N-isopropylacrylamide), or PNIPAAm, in water has been studied extensively.^{21,22} Below the LCST, the polymer-water interactions are favourable because of hydrogen bonding. However, the water molecules must orient themselves around the hydrophobic regions of the macromolecule in order to form hydrogen bonds with the polymer, which decreases the entropy of the system. As the temperature is increased, the entropic term dominates over the otherwise exothermic enthalpy of the hydrogen bonds. The interaction between the hydrophobic isopropyl groups increases, and is referred to as the hydrophobic effect. As the temperature is increased to the LCST, the free energy of mixing becomes positive, i.e. water-water and polymer-polymer interactions dominate over the polymer-water interactions, and the polymer precipitates.

Copolymers which can form intramolecular hydrogen bonds have been found to have varying LCST's depending on composition. For instance, the LCST of poly((N,N-dimethylamino)ethyl methacrylate-*co*-ethylacrylamide) in water varies from 50 to 4°C as the content of the ethylacrylamide comonomer varies from 0 to 50 mol%.²³ A shift to higher LCST is usually observed upon increasing polymer hydrophilicity. However, the incorporation of the hydrophilic ethylacrylamide comonomer in this situation decreases the LCST. FTIR was used to show that the ethylamide groups are hydrogen bonded to the amino groups of the comonomer. The authors conclude that the intramolecular hydrogen bonding prevents the formation of hydrogen bonds between the amine and

water, thus increasing the hydrophobicity of the copolymer and lowering the LCST. Furthermore, copolymers of ethylacrylamide exhibit a greater decrease in LCST than the corresponding acrylamide copolymers because of the hydrophobic contribution of the ethyl groups.

In a sufficiently concentrated solution, phase separation at the LCST is accompanied by precipitation, which is observed as a cloud-point once the polymer aggregates reach a certain size. Therefore, the LCST can be determined by measuring the macroscopic phase separation upon heating using UV-VIS spectrometry, and this is referred to as the cloud-point method. This experiment is quite popular due to its simplicity in execution, but it is a rather crude means of measuring the LCST, as it depends on the extent of precipitation and the size of the aggregates being formed. Dynamic light scattering offers a more precise means of measuring the onset of phase separation and provides structural information as well. Differential scanning calorimetry can also be employed to measure the LCST.²⁵ The transition at the LCST is accompanied by a small endotherm due to the energy required to break the hydrogen bonds between the polymer and water, which can be detected with sufficiently sensitive instruments. Transition temperatures measured by DSC agree well with cloud-point measurement results.

1.4 Design of system for complex coacervation

The subject of polyelectrolyte complexes has been studied extensively.²⁶

Complexes of poly(methacrylic acid) with ionene-type quaternary ammonium polycations were found either to be soluble, to phase separate as a coacervate, or finally to precipitate, all depending on polymer concentration, pH, and ionic strength.²⁷ These types of phase changes are usually observed in complexes between weak polyacids with strong polycations. There are few such examples of synthetic complex coacervate systems, however. We wish to investigate whether weak polyacids containing hydrophilic comonomers can form complex coacervates with weak polybases. It is necessary for the copolymers to have ionizable groups in order for complexation to occur, and hence methacrylic acid was chosen as a monomer for our system. A second characteristic of coacervate systems is that the polymers should be hydrophilic over the entire pH range. Thus, poly(ethylene glycol) monomethyl ether monomethacrylate (PEGMA) was chosen as the second comonomer, with four ethylene glycol repeat units per macromonomer. PEG groups have traditionally been used to impart water-solubility to otherwise hydrophobic polymers. Because coacervates are largely aqueous liquids, the PEG groups were expected to facilitate coacervation. Some coacervate systems are also enhanced by hydrophobic interactions. For example, the phenyl groups of gelatin may contribute to the polymer interactions in the coacervate phase. Thus, some of the copolymers in this thesis involved a third, hydrophobic comonomer, butyl methacrylate (BMA). This

monomer can be used to control the hydrophilic-hydrophobic balance of the copolymer, and facilitate interfacial applications of these copolymers.

Two series of methacrylic copolymers will be investigated. One series consists of binary copolymers containing MAA and PEGMA in molar ratios ranging from 20:80 to 80:20. Although similar to the copolymers prepared by Klier for emulsification, these copolymers will have an excess of ethylene glycol groups relative to MAA, and are expected to have different aqueous solution properties. Another series will contain an equimolar ratio of MAA and PEGMA, with from one to ten percent BMA comonomer. The aqueous solution properties of both binary and ternary copolymers, i.e. their lower critical solution temperature, LCST, and their ability to form complex coacervates with polyamines, will be discussed in this thesis.

In order to limit the number of variables involved, most of the coacervation experiments will involve branched poly(ethylenimine) (PEI) as the polybase. PEI is prepared commercially by ring opening polymerization of aziridine. Due to its highly branched structure, the ratio of primary to secondary to tertiary amines is approximately 1:2:1. The relative basicity increases from tertiary to secondary to primary amines, and it should be noted that the steric accessibility of these groups increases in that order also. Because of the different reactivities of the amines, as well as the branched structure, polyelectrolyte complexes with PEI are generally not stoichiometric.²⁸

2.0 OBJECTIVES

The objectives of this thesis research were to design a synthetic water-soluble polymer capable of forming complex coacervates with polyamines in aqueous solution, and to study the aqueous solution properties of these new copolymers. The polymer will be designed with separate ionic, hydrophilic and hydrophobic components, which can be varied in order to meet the first objective. Two copolymer series will be prepared. The binary copolymer series will contain methacrylic acid (MAA) and poly(ethylene glycol) monomethyl ether monomethacrylate (PEGMA) in molar ratios ranging from 20:80 to 80:20. The ternary series will contain an equimolar ratio of MAA and PEGMA, together with between one and ten percent of a hydrophobic monomer, butyl methacrylate (BMA). The solubility of these copolymers in water over the temperature range of zero to 100°C will be investigated. Polyelectrolyte complexes between these methacrylic copolymers and polyamines will also be studied, in order to determine whether complex coacervates can be prepared.

3.0. EXPERIMENTAL PROCEDURES

3.1 Materials

Methacrylic Acid, 99%, inhibited with 100-250 ppm monomethyl ether hydroquinone, Sigma-Aldrich Canada Ltd. The inhibitor was removed by distillation under vacuum

Poly(ethylene glycol) Monomethyl Ether Monomethacrylate, 200 Da, Polysciences Inc.

Butyl Methacrylate, 99%, inhibited with 10 ppm monomethyl ether hydroquinone, Sigma-Aldrich Canada Ltd.

Tetrahydrofuran, 99+%, Caledon Laboratories Ltd.

2,2'-Azobisisobutyronitrile, Kodak Chemicals, recrystallized from ethanol

Ethanol, 99%

Diethyl Ether, anhydrous, 99+%, Caledon Laboratories Ltd.

Solutions of **1N HCl** and **1N NaOH** were prepared by diluting analytical concentrates, (Anachemia Canada, Inc.) with deionized water. These stock solutions were further diluted to obtain concentrations of 0.5N and 0.1N. NaOH solutions were stored in Nalgene® polyethylene containers, and were titrated periodically with HCl to ensure that the NaOH concentration did not change.

pH Buffer Solutions, pH 4.00, 7.00, 10.00 used as received, Anachemia Canada, Inc.

Polyethylenimine, water-free, branched polymer, M_w 25,000 Da, M_n 10,000 Da, Sigma-Aldrich Canada Ltd, used as received.

Ethylenediamine, 99%, **Diethylenetriamine**, 99%, **Tetraethylenepentamine**, both linear and branched, Sigma-Aldrich Canada Ltd.

Poly(allyl amine hydrochloride), M_w 60,000 Da, Polysciences Inc.

Poly(allyl amine), obtained by dissolving 20g poly(allyl amine hydrochloride) in 120 mL 1N NaOH, which was distributed between four dialysis membranes with a molecular weight cut-off of 15,000 Da. The tubes were dialyzed against deionized water over a period of 16 days, and the water was replaced daily. The pH of the dialysis water was checked at the end of each day to monitor the removal of excess NaOH from within the membranes. After 16 days, the pH remained constant at about 6.

3.2 Solution polymerization of binary and ternary methacrylic copolymers

Solution Copolymerization:

In a typical procedure, tetrahydrofuran (THF, 75 mL) was magnetically stirred in a 250 mL three-neck round-bottom flask fitted with a condenser, nitrogen inlet and thermometer reaching below the liquid level. The temperature of the THF solution was maintained at 65°C using an oil bath. Methacrylic acid (MAA, 6.018 g, 0.0699 mol) and poly(ethylene glycol) monomethyl ether monomethacrylate (PEGMA, 13.982 g, 0.0699

mol) were transferred to the flask along with 15 mL THF, for a total of 20 g of monomer in 90 mL THF. The solution was stirred for 20 minutes under nitrogen to remove oxygen from the system. 2,2'-Azobisisobutyronitrile (AIBN, 0.230 g, 1.398 mmol) was dissolved in 10 mL THF and transferred to the flask. The solution polymerization reaction was allowed to proceed for 24 hours under nitrogen. In some cases, a 0.5 mL aliquot was removed after 6 hours for size exclusion chromatography (SEC) analysis, in order to verify that the polymerization was proceeding well. A second aliquot was removed at the end of each reaction to measure the conversion as well as the molecular weight of the final polymer prior to work-up. These aliquots were diluted to 10 mg/mL with distilled THF before injecting into the SEC apparatus.

The ternary copolymerizations were carried out as above. In a typical reaction, the 20 g of monomer added to 90 mL THF was composed of MAA (5.959 g, 0.0692 mol), PEGMA (13.843 g, 0.0692 mol), and butyl methacrylate, BMA (0.199 g, 0.0014 mol).

The homopolymer, poly(PEGMA) was synthesized as above in THF. The homopolymer poly(MAA) is insoluble in THF, and was hence synthesized as above but using 99% ethanol as solvent.

Yield and Work-up:

A 2.5 mL aliquot of the final polymer solution was diluted to 5 mL with THF and added drop-wise with stirring into cold ether (35 mL, 0°C) in a centrifuge tube. The tube was centrifuged at 3000 rpm for 10 minutes, and the polymer accumulated at the bottom of the tube. The ether was then decanted. The polymer was dried under vacuum at 70°C

for 24 hours and weighed. Yield: 86.8%.

The remaining polymer solution was diluted to 200 mL with THF (approx. 10% w/v), and precipitated into cold ether (1800 mL, 0°C). The mixture was magnetically stirred for 10 minutes to allow unreacted monomer to dissolve in the ether. The mixture was then allowed to stand covered for 2 hours, and the ether was decanted from the more dense and viscous polymer phase. The polymers with greater than 65% MAA precipitated as a flaky solid in ether, and were isolated by vacuum filtration. The polymers were allowed to dry overnight at 70°C and were then vacuum dried for 24 hours at room temperature (RT) and weighed. A 10 mg sample was removed for SEC analysis, and dissolved in 1 mL THF before injection. Typical SEC result: M_n 1.854×10^4 Da, M_w/M_n 2.4. A 15 mg sample was dissolved in deuterated dimethyl sulfoxide (DMSO-d6) for ^1H NMR analysis.

3.3 Characterization methods

3.3.1 ^1H NMR

Nuclear Magnetic Resonance (NMR) spectra were measured on a Bruker AC300, using DMSO-d6 as solvent. Occasionally, deuterated chloroform was used as solvent, and some spectra were measured on the AC200 instrument.

3.3.2 SEC

Size exclusion chromatography (SEC) was performed using a Waters 410 Differential Refractometer and Waters 441 Absorbance Detector, with three Waters Ultramicrostiyragel columns in series, calibrated using narrow-disperse polystyrene standards. THF was used as the mobile phase, at a flow rate of 1 mL/min.

3.3.3 Optical microscope

An Olympus BH-2, equipped with a Kodak DC 120 Zoom Digital Camera was used for the optical microscope pictures.

3.3.4 Photometric cloud point determination

The lower critical solution temperature (LCST) of each copolymer was measured by the cloud point method. A jacketed beaker maintained at constant temperature using a circulating water bath was charged with 30.0 mL of 3 % w/v [50-50-0] copolymer from the stock solution at 4°C. The temperature was increased quickly to 50°C in order to estimate the LCST to within 5°C. The solution was then cooled to about 10°C below the LCST, and the PC-Titrate photometric and temperature probes were placed in the solution. The solution temperature was ramped up at a rate of 0.5°C/min by manually changing the water bath set-point. A titration method was used which took readings from

both probes every ten seconds (the buret drive was disengaged). Once the temperature was about 5°C above the cloud point of the solution, the measurements were stopped. The photometric probe reads approximately -325 ± 50 mV in a clear solution, and approximately -10 ± 5 mV in very opaque liquids.

3.3.5 pH and conductometric titrations with NaOH

The carboxylic acid content of the copolymers were measured on a PC-Titrate instrument, simultaneously reading from pH and conductometric probes. The instrument was first calibrated using buffer standards of pH 4.00, 7.00 and 10.00. The buret was then purged once with deionized water, and twice with 1N NaOH. Copolymer stock solutions of 3 % w/v were prepared by dissolving 7.500 g of copolymer in 250 mL deionized water. A jacketed beaker, maintained at constant temperature with a circulating water bath, was charged with 30.0 mL of stock solution. The temperature was chosen to be 5°C below the polymer lower critical solution temperature (LCST). The [65-35-0] copolymer was an exception, because the temperature could only be set 1°C below the onset of the LCST, without freezing the solution. The instrument was programmed to calculate the volume of titrant to inject based on the previous increase in pH, so that the volume would be reduced if the change in pH was greater than 0.05 pH units. The program would wait between injections for the pH to stabilize to ten consecutive readings within ± 1 mV (± 0.018 pH units).

In a typical experiment, 30 mL of 3 % w/v [50-50-0] copolymer was titrated with 1N NaOH. An endpoint was detected both in the pH and conductometric curves at 2.97 mL, indicating 0.00297 mol carboxylic acid groups in the 0.9 g sample of polymer, or 0.00330 mol/g, or 302.9 g/mol. The polymer was predicted to have an acid content of 0.00349 mol/g, based on the monomer loading in the polymerization reaction.

3.3.6 Determination of T_g

A Rheometrics Dynamic Mechanical Analyzer (DMA) instrument was used to measure the glass transition temperature, T_g of each polymer. The polymer sample was pressed between two flat plates oscillating at 1Hz. The function tan delta was measured versus temperature, and the maximum tan delta indicates the T_g . The T_g was also measured by differential scanning calorimetry (DSC). When the polymer undergoes a transition from glassy to rubbery, an endotherm is detected by the calorimeter at the T_g .

3.4 Titration of methacrylic copolymers with amines

[50-50-0] with various amines:

A series of 3 % w/v amine solutions were prepared, including butyl amine, BA, ethylenediamine, EDA, diethylenetriamine, DETA, branched tetraethylenepentamine, b-TEPA, linear tetraethylenepentamine, l-TEPA, poly(allyl amine), PAA and branched polyethylenimine, PEI, all in deionized water. For each titration, 30 mL of 3 % w/v [50-

50-0] copolymer was maintained at 18°C using a jacketed water bath. The PC-Titrate potentiometric, photometric, conductometric and temperature probes were placed in the solution. The buret drive was flushed twice with the amine solution. The standard base-to-acid titration method described in section 3.3.5 was used to titrate the copolymer with the amine solution.

All copolymers with PEI:

Solutions of 1 % w/v were prepared for each of the methacrylic copolymers synthesized, as well as the PEI. In a typical titration, 30 mL of 1 % w/v [50-50-0] copolymer was maintained at about 5°C below the LCST using a jacketed water bath. The PC-Titrate potentiometric, photometric, conductometric and temperature probes were placed in the solution. The buret drive was flushed twice with the PEI solution. The standard base-to-acid titration method described in section 3.3.5 was used to titrate the copolymer with the PEI solution. The titrations were ended when about 35 mL of the polyamine had been added.

3.5 Determination of properties of polyelectrolyte complex coacervates

All polymers were used as 3 % w/v solutions. First, the volume ratio of coacervate to equilibrium liquid ratio was determined. 12 mL or 15 mL samples were prepared containing copolymer and PEI solutions in various ratios, chosen based on the titrations carried out in section 3.4. The samples were prepared in calibrated glass

centrifuge tubes, and were centrifuged at 2000 rpm for 20-30 minutes, until both phases were clear. The volumes of the upper and lower liquids were read from the calibrated tube. The upper liquid was carefully decanted into a pre-weighed aluminum pan. The aluminum pans containing the equilibrium liquid and the centrifuge tubes containing the coacervate liquid were dried in a vacuum oven for 24 hours, and weighed. These weights indicate the relative masses of polymer in each of the two phases.

4.0 BULK PROPERTIES OF BINARY AND TERNARY COPOLYMERS

4.1 Synthesis of binary and ternary copolymers

Two series of copolymers were prepared by free-radical solution copolymerization in tetrahydrofuran (THF). First, a series of binary copolymers containing methacrylic acid (MAA) and poly(ethylene glycol) monomethyl ether monomethacrylate (PEGMA) in molar ratios ranging from 20:80 to 80:20, as well as the two homopolymers, poly(MAA) and poly(PEGMA), were prepared. Secondly, a series was synthesized which also included a third monomer component, butyl methacrylate (BMA). In the ternary series, the MAA and PEGMA monomer molar ratios were maintained at 1:1, and the BMA content was varied from one to ten percent of the total moles of monomer. A copolymer structure including all three monomers is shown in Figure 4.1.

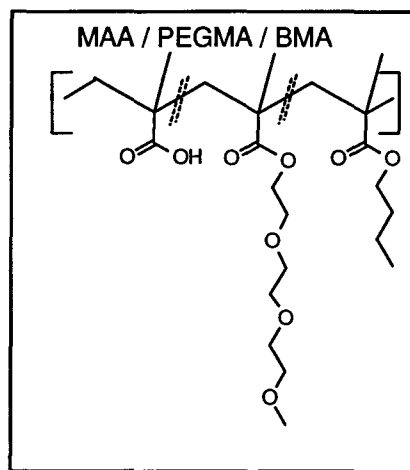


Figure 4.1: Ternary copolymer structure

Table 4.1 summarizes the series of binary and ternary copolymerizations carried out as described in the experimental section. In every case, a total of 20 g of monomer and 100 mL THF was used, along with 1 mol % AIBN initiator, relative to the total moles

of monomer.

Table 4.1: Binary and ternary methacrylic copolymer series

Copolymer Name	Mol % Monomers			$^{\dagger}M_n$, Da	$^{\dagger}M_w/M_n$	† Yield %
	MAA	PEGMA	BMA			
[100-0-0]	100	0	0			97
[80-20-0]	80	20	0	1.2×10^4	2.3	96
[65-35-0]	65	35	0	1.4×10^4	2.5	92
[50-50-0] [†]	50	50	0	1.9×10^4	2.4	87
[35-65-0]	35	65	0	2.2×10^4	3.5	93
[20-80-0]	20	80	0	2.2×10^4	2.4	82
[0-100-0]	0	100	0	1.0×10^5	3.0	85
[49.5-49.5-1]	49.5	49.5	1	2.5×10^4	2.5	96
[48.5-48.5-3]	48.5	48.5	3	1.8×10^4	2.7	93
[47.5-47.5-5]	47.5	47.5	5	2.0×10^4	2.3	94
[46.5-46.5-7]	46.5	46.5	7	1.9×10^4	2.4	99
[45 - 45 - 10]	45	45	10	1.2×10^4	2.0	81

[†]Additionally, the solution polymerization of the [50-50-0] copolymer was carried out at concentrations of 10 and 50 wt. % in THF. [‡]Molecular weights and yields measured after work-up

4.4 Molecular weight

The number average molecular weights (M_n) of the copolymers were reported in Table 4.1. The weight average molecular weights (M_w) were also measured. The polydispersity values (M_w/M_n) were typical of free-radical solution polymerizations. The SEC results for the [50-50-0] copolymer are shown in Figure 4.2, and are typical of all the copolymer chromatographs. The chromatographic signals from the crude reaction mixture (1) and after precipitation into ether (2) are overlaid.

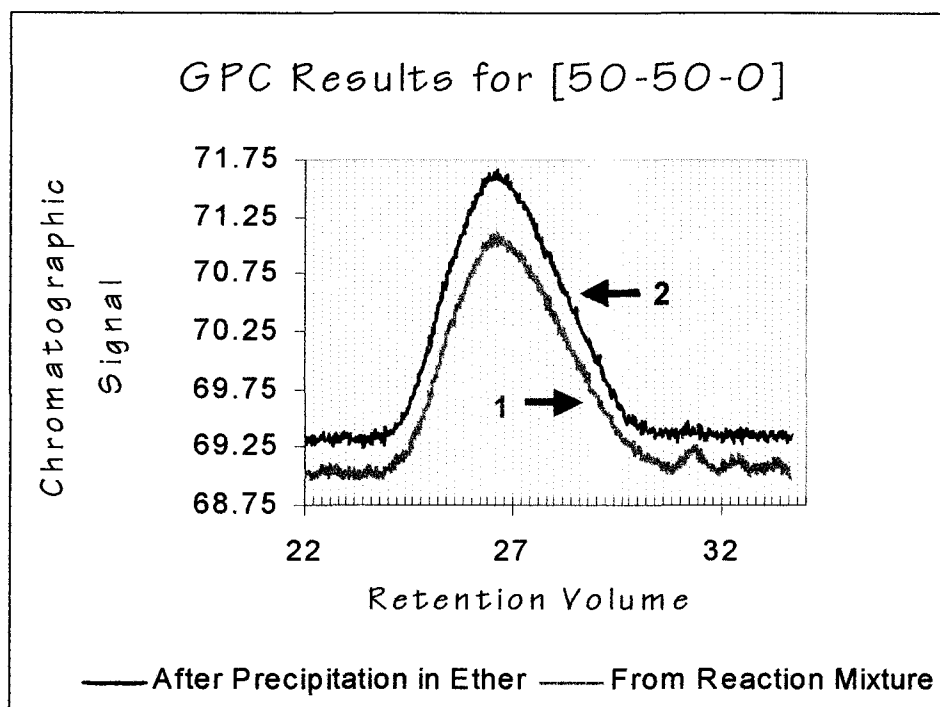


Figure 4.2: SEC Traces (1) before work-up (2) after work-up

Signal 1 has two small peaks at high retention volume, which correspond to the lowest molecular weight components. These peaks are absent in the chromatograph taken after work-up, 2, showing that there is some residual monomer at the end of the reaction which is removed by precipitation in ether. Ether is a good solvent for the monomers, and it may also dissolve low molecular weight oligomers. The SEC results indicated that M_n increased from 1.5×10^4 to 1.9×10^4 and the polydispersity decreased from 2.8 to 2.4 upon work-up. This confirms that some of the lower molecular weight polymer has been removed during the work-up, thereby increasing the molecular weight and lowering the polydispersity. The molecular weights of the copolymers decreased slightly with decreasing MAA content, and with increasing BMA content.

4.5 Effect of copolymer composition on Glass Transition Temperature

The glass transition temperatures (T_g) of selected copolymers were measured by either a dynamic mechanical analyzer (DMA) or by differential scanning calorimetry (DSC). It was found that the DMA results differed significantly from the DSC results, but the DSC results may be more accurate, since the transitions in the curve are more pronounced and more easily measured. The error in the DMA results is about $\pm 30\%$, and the error in the DSC measurements is approximately $\pm 10\%$ of the given value.

Table 4.2: Measured T_g and observed macroscopic properties of the methacrylic copolymers

Copolymer Name	T_g ($^{\circ}\text{C}$)	Observed properties after work-up
[100-0-0]	228 [†]	solid: very brittle, white, opaque
[80-20-0]	62 [†]	solid: fine powder, white, opaque
[65-35-0]	51 [†]	solid: chunky powder, white, opaque
[50-50-0]	38 [*]	solid: brittle, poor elasticity, sticky, white, opaque
[35-65-0]	6 [*]	soft solid: plyable, tacky, elastic, semi-transparent
[20-80-0]	-38 [†]	soft solid/liquid: viscous gel, sticky, clear
[0-100-0]	-57 [†]	Viscous liquid: very sticky, clear
[49.5-49.5-1]	30 [*]	solid: slightly sticky, not plyable, white
[48.5-48.5-3]		solid: plyable, white
[47.5-47.5-5]	38 [*]	solid: hard, brittle, white, opaque
[46.5-46.5-7]		solid: hard, brittle, white, opaque
[45-45-10]	35 [†]	solid: hard, brittle, white, opaque

[†]Values measured by DSC, ^{*}Values measured by DMA

The T_g data is presented in Table 4.2. A correlation can be made between the observed physical properties of the polymers and the T_g data. The MAA homopolymer [100-0-0] is brittle, and has a high T_g , while PEGMA homopolymer [0-100-0] is a viscous liquid, and has the lowest T_g . The copolymer T_g values vary within this range,

depending on the composition. The MAA homopolymer is a brittle white solid, and the PEGMA homopolymer is a very viscous, sticky liquid. As the monomer content varies between these two extremes, the copolymer properties also vary between hard, brittle solids and soft viscous materials with properties between solid and liquid. The ternary copolymers became slightly harder and less sticky as the BMA content was increased, but the T_g values were not significantly different from the [50-50-0] binary copolymer.

4.3 ^1H NMR

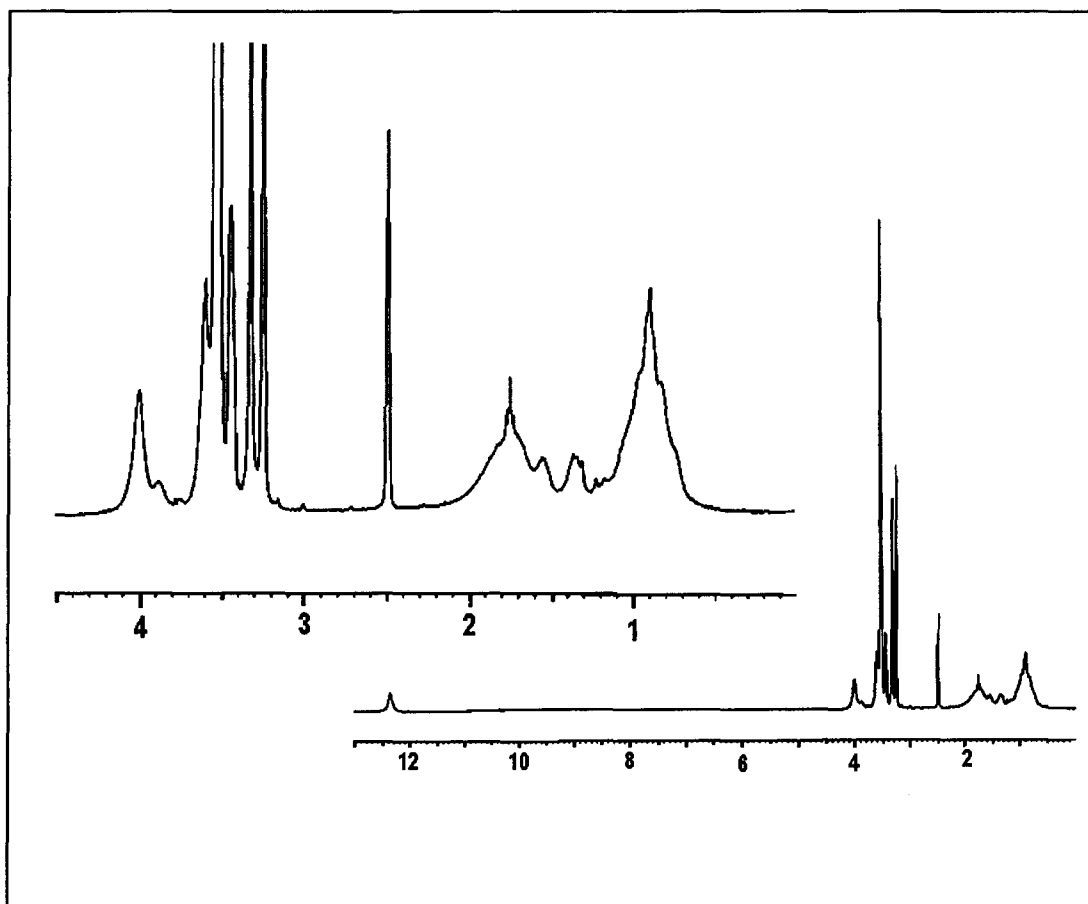


Figure 4.3: 300MHz ^1H NMR Spectrum of [46.5-46.5-7] Ternary Copolymer

A typical ^1H NMR spectrum for the ternary copolymer [46.5-46.5-7] is shown in Figure 4.3. The multiplet at 2.49 ppm is the solvent DMSO- d_6 reference peak. Most of the major peaks can be assigned to the copolymer structure. It was difficult to assign the backbone methylene and methyl protons (2.0-0.5 ppm), due to the atactic nature of the polymer which gives each methylene a different chiral environment. One feature of interest in the ^1H NMR spectra is the presence of a broad acid peak at 12.35 ppm. At the low MAA content of 20%, this peak is very small, but as the MAA content is increased, the peak becomes much larger and more distinct. The largest peak at 3.53 ppm is assigned to the methylene protons on the PEG side chains. The methylene protons adjacent to the carbonyl on PEGMA appear upfield at 4.0 ppm. There are also two methylene protons on the butyl side chains neighbouring a carbonyl, and these have been assigned at 3.75 ppm. This peak is absent in the binary copolymer series. The last methylene group of the PEG chain, as well as the terminal methoxy protons, appear at 3.44 and 3.29 ppm respectively.

4.6 Carboxylic acid content

The carboxylic acid content of the binary and ternary copolymers was measured by titration with a strong base, NaOH. Both potentiometric and conductometric measurements were made. In order to study the polyelectrolyte characteristics of the copolymer, it is useful to compare the characteristics of a monoprotic acid/base titration. Both types of titration are illustrated in Figure 4.4.

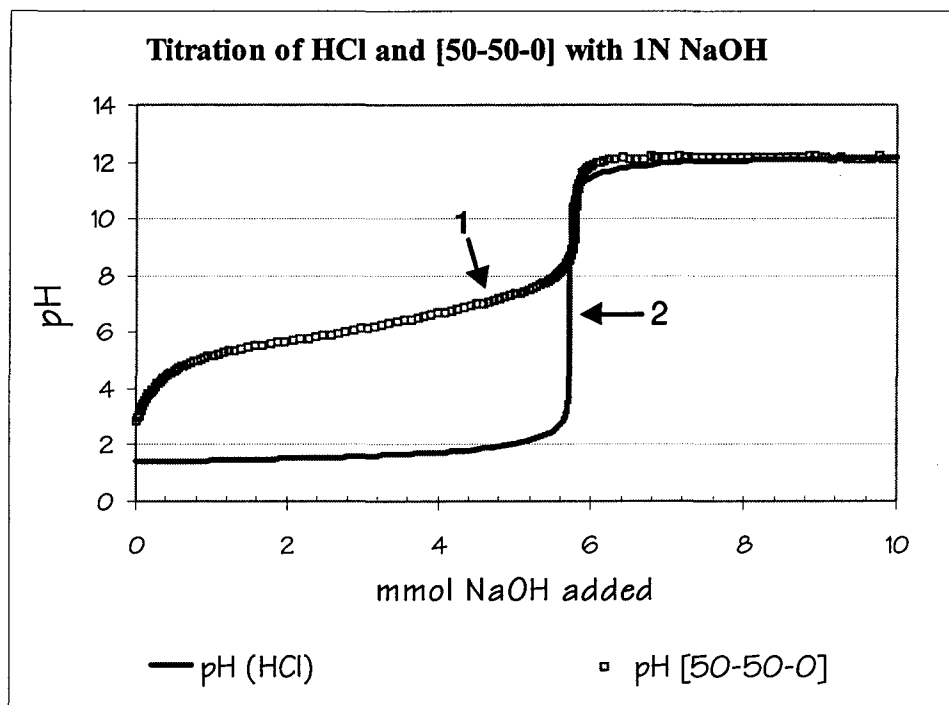


Figure 4.4: Potentiometric titration of strong acid (HCl) and weak polyacid [50-50-0] with 1N NaOH

Curve 1 is the potentiometric titration of a 3% w/v solution of [50-50-0] with 1N NaOH. For comparison, curve 2 is the titration of 0.1N HCl with 1N NaOH. The pH at the start of curve 2 is 1.4, standard for a strong acid, since all of the HCl dissociates into H^+ and Cl^- . The pH remains relatively constant as NaOH is added, rising by only 0.5 pH units, until the end-point is approached (when 5 mmol NaOH is added). By contrast, curve 1 begins at pH 2.8, which rises very sharply to pH 4.5. The initial pH is determined by the partial dissociation of the weak acid in water. The pH rises sharply at first because the base rapidly reacts with the dissociated protons. Then, the pH increases more gradually from 4.5 to 7.5 until the end-point is approached (at around 5.2 mmol NaOH). Curve 1 is

more sloped in this region than curve 2 because as each carboxylic acid group along the chain is deprotonated, the accumulation of negative charges makes it successively more difficult to remove the next proton from the chain. This is standard polyelectrolyte behaviour. The repulsion of charges along the polymer chain have many consequences, which are commonly referred to as the “polyelectrolyte effect”. For example, the radius of gyration and the hydrodynamic volume of the polymer increase. The polyelectrolyte changes from a random coil to an extended rod configuration due to the ionic repulsions between the charged polymer segments.

Between the addition of 5.2 mmol NaOH and 5.8 mmol, the slope of both curves increases rapidly, going to infinity at the endpoint, when 5.8 mmol NaOH has been added. There is a significant difference between the pH values at the end-points (at the inflection points of the pH curves). The HCl titration has an end-point at $\text{pH } 7.08 \pm 0.10$ but the [50-50-0] copolymer end-point is at $\text{pH } 10.29 \pm 0.10$. Strong acid/base titrations have end-points at pH 7, which is simply determined by the dissociation of water at 25°C. Weak acids usually have pH end-points above 7, because the conjugate base is present at the equivalence point, and thus the solution is basic. In this case, the polyelectrolyte effect also increases the end-point pH: the conjugate base of the polyacid is strong due to the cooperative action of the neighbouring anions on the chain.

Figure 4.5 illustrates the conductometric behaviour of both titrations (curves 3 and 4). The initial conductivity of the HCl solution (curve 4) is high, because HCl fully dissociates in solution. As the strong acid is titrated, the H^+ and OH^- ions form neutral water. The net effect is that H^+ ions are replaced with Na^+ ions which are less

conductive, so the conductivity decreases. Protons are more conductive than other ions because they can move in aqueous solution by transfer between water molecules, and are therefore much more mobile. However, there is a break in the curve at the end-point, because now excess Na^+ and OH^- ions are being added, so the total number of ions in solution increases, and the conductivity rises.

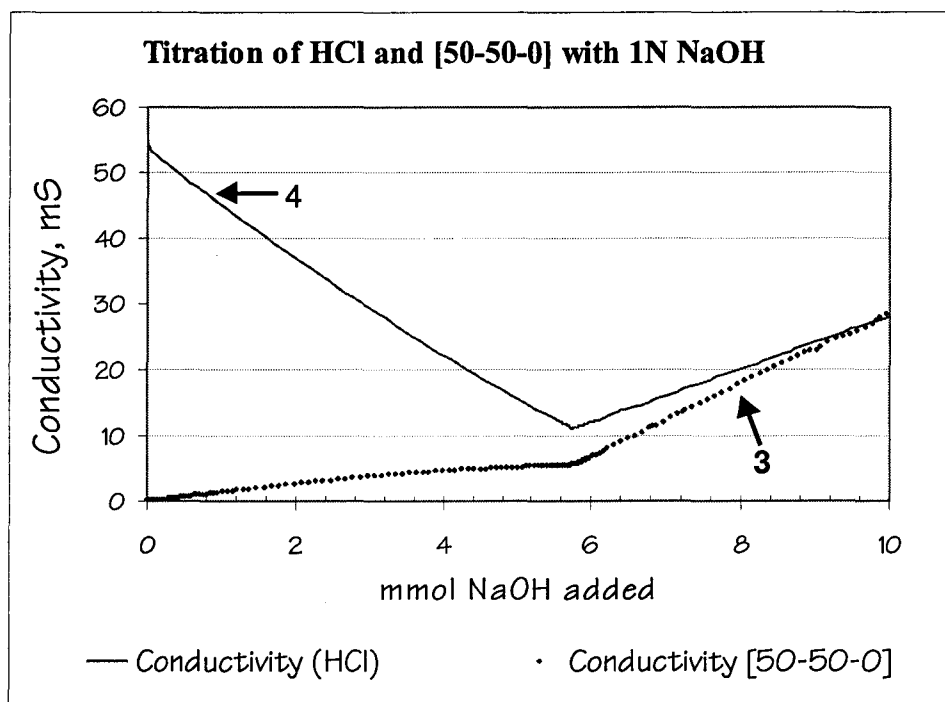


Figure 4.5: Conductometric Titration of Strong Acid (HCl) and Weak Polyacid [50-50-0] with 1N NaOH

On the other hand, the conductivity of the [50-50-0] solution (curve 3) begins near 0 mS, because the polymer is a neutral chain in deionized water. The polymer partially dissociates because it is a weak polyacid, so there is a low concentration of ions initially in solution. During the titration, the conductivity increases gradually. Anions build up on the polymer chain, and these macroions make the solution more conductive. However,

the increase is slight because the macroions have limited mobility compared to microions. After the end point (the break in the curve), the excess NaOH increases the concentration of microions (Na^+ and OH^-) in solution, so the conductivity rises sharply. It was observed that the potentiometric and conductometric end-points coincided exactly.

Generally, the titrated carboxylic content was slightly lower than the theoretical content based on the monomer feed ratio in the polymerization reaction. The final MAA content in each copolymer was lower by about 10% of the original MAA mol%. For example, the copolymer with the [50-50-0] feed ratio may have an actual composition of [45.1-54.9-0] according to the titration results. It should be noted, however, that the polymer is very hygroscopic due to the PEG groups. Therefore, the polymer which was weighed out to prepare the solutions may have been wet, so the amount of polymer and thus carboxyl groups present would be underestimated by about 5%. Because of this factor, the actual composition of the copolymer cannot be measured accurately by this method. Nevertheless, the actual concentrations of carboxylic acid in each polymer stock solution can be determined to an accuracy of $\pm 1\%$. The carboxylic acid content as determined by titration was used in all calculations involving the copolymer acid groups; however, the original mol% feed ratios were used for nomenclature purposes.

5.0 SOLUTION PROPERTIES OF BINARY AND TERNARY METHACRYLIC COPOLYMERS

As discussed in the introduction, the copolymers studied in this thesis were designed to incorporate different amounts of acidic, neutral hydrophilic and hydrophobic methacrylate units. The ultimate purpose is to study their electrostatic association with polybases in aqueous solutions. Furthermore, the unique structure of these polymers was also expected to result in interesting aqueous solution characteristics, including surfactant properties and critical solution temperatures. In order to study the solution properties, it is necessary to know the conditions where the polymer will be soluble in water, so the first task was to investigate the lower critical solution temperatures (LCST's) of these new binary and ternary copolymers.

As described in the introduction, polymers which can form hydrogen bonds with water often possess an LCST. In the example of poly(N-isopropylacrylamide), it is the amide protons which can form hydrogen bonds with water. The methacrylic copolymers in this research also contain hydrogen-bonding functionality: the ethylene oxide groups, as well as the acid groups. By analogy with poly(NIPAAM), these polymers may have an LCST in water. If this is the case, there is a certain temperature above which hydrogen bonding between the polymers and water would be disrupted, resulting in polymer

precipitation. Therefore, the phase behaviour of the new methacrylic copolymers in aqueous solution over a range of temperatures was investigated.

5.1 LCST of methacrylic copolymers

Cloudpoints were measured by heating a 3% polymer solution at a constant rate of 0.5°C/min in presence of a photometric probe, and plotting the photovoltaic output against temperature. A typical cloud-point curve is shown in Figure 5.1.

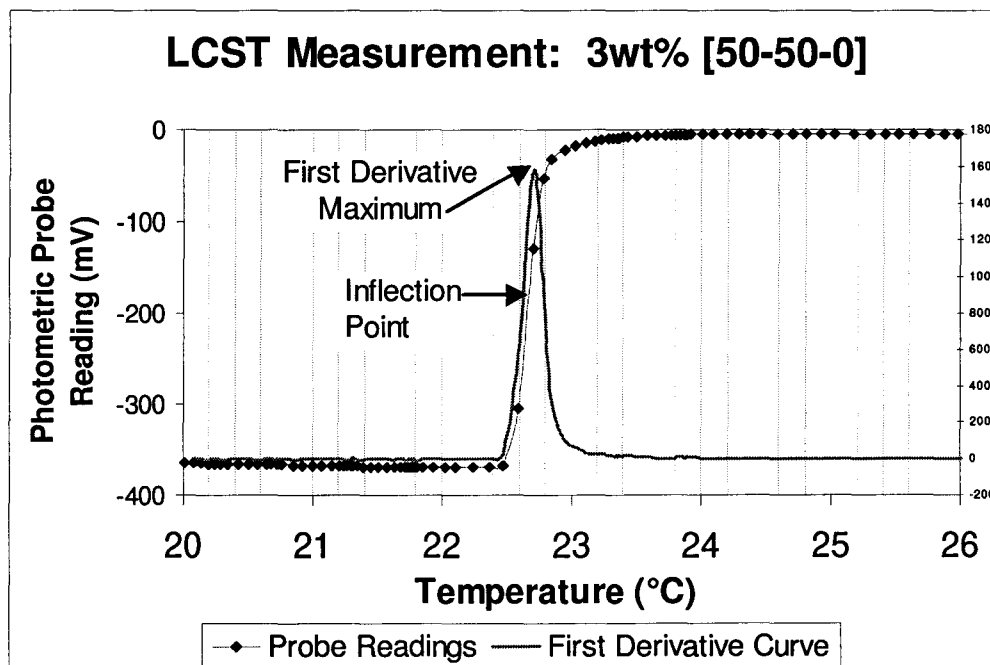


Figure 5.1: Cloud-Point curve for [50-50-0]

Initially, the polymer solution is clear, and the photometric probe reading is near -375 mV. As the solution is heated, the polymer begins to phase separate over the temperature range 22.2 to 23.1 °C. The solution becomes cloudy, and the photometric probe reading

increases. When the solution is opaque, the probe reads close to 0 mV. Because phase separation occurs over a temperature range, the LCST temperature was defined as the inflection point in the photometric curve, where a maximum in the first derivative occurred. On the curve in Figure 5.1, the LCST occurs at $22.7 \pm 0.5^\circ\text{C}$ by this definition. The rate of heating affects the measurement of the LCST, and thus $0.5^\circ\text{C}/\text{min}$ was used in all experiments for consistency.

5.2 Effect of molecular weight on LCST

Due to the nature of free radical solution polymerization, there is an inherent variation in the molecular weights of the polymers, depending on the reaction conditions. Even those produced under near identical reaction conditions can vary. The molecular weight is particularly affected by the total concentration of monomers, or monomer loading, in the original reaction mixture. Increasing the monomer loading can increase the molecular weights significantly. The [50-50-0] copolymer was prepared at different concentrations in solution, and Table 5.1 shows how the LCST varies with molecular weight. The LCST shows a decrease of only 1.5°C as the molecular weight increases almost four-fold. All of the other copolymers were

Table 5.1: Effect of molecular weight on LCST

<i>Total Monomer loading [w/v%]</i>	M_n	<i>LCST, °C</i>
10	1.1×10^4	26.3
20	2.3×10^4	25.6
50	3.9×10^4	24.8

synthesized at 20% monomer loading. Even so, Table 4.1 shows that there is variation in the molecular weights of the copolymers as their compositions change, all within the

range examined in Table 5.1. Therefore, changes in LCST of more than 1.5°C in the following LCST studies can be considered significant, and assumed to be independent of molecular weight.

5.3 Effect of binary copolymer composition on LCST

The LCST values for the binary copolymers are shown in Figure 5.2 below.

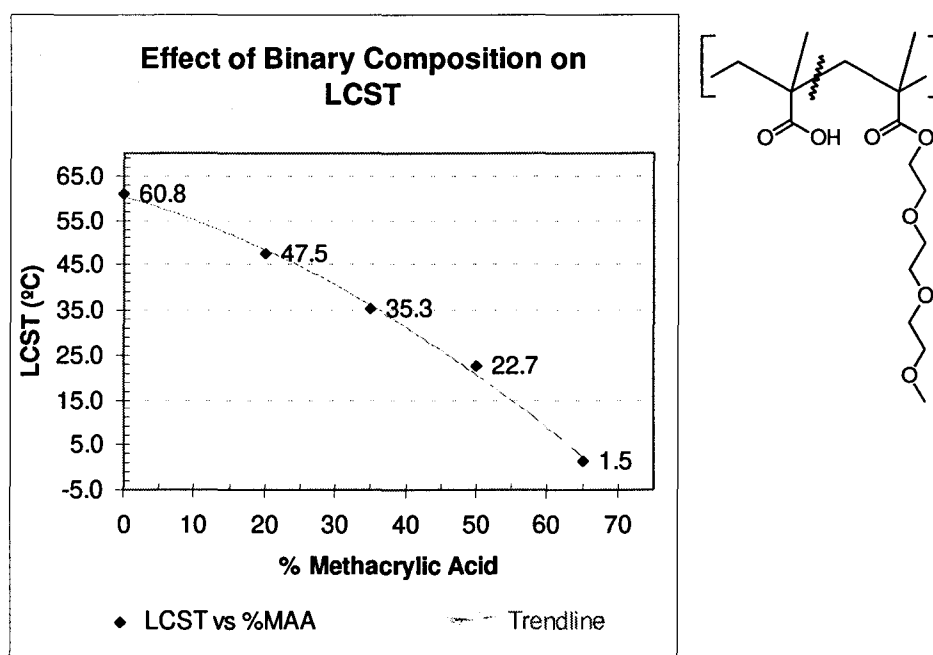


Figure 5.2: Effect of binary copolymer composition on LCST

The PEGMA homopolymer, [0-100-0], has an LCST of $60.8 \pm 0.5^\circ\text{C}$. This is lower than the LCST of poly(ethylene oxide), 95°C ,²⁹ likely due to the added hydrophobicity of the methacrylic backbone, which self-associates more easily with increasing temperature.

Incorporation of the MAA comonomer further decreases the LCST in the binary copolymer, down to $47.5 \pm 0.5^\circ\text{C}$ for the [20-80-0] copolymer and decreasing to $1.5 \pm 1.0^\circ\text{C}$ for the [65-35-0] copolymer. The [80-20-0] copolymer containing 80% MAA comonomer does not dissolve in water at all within the range from 100 to 0°C . However, the poly(MAA) homopolymer, [100-0-0], is again soluble in water over the whole range from 0°C to 100°C , and also does not have an LCST in water at STP. Presumably, copolymers with MAA mole fractions between 80 and 100% do show LCST's, increasing rapidly from 0 to 100°C .

The decrease of LCST down to its minimum at an MAA content of about 80% is likely due to the optimal cooperative nature of the intramolecular hydrogen bonding of the PEO side chains. There are approximately four ethylene oxide groups per PEG side chain, and thus the ratio of acid to ether group in the overall copolymer is one to one. It is possible for the PEG side chains to hydrogen bond to either water or backbone acid groups. This competition is affected mostly by entropy, since the enthalpic difference would be expected to be small. When the PEG chain H-bonds to water, there is an entropy loss for water. There is also an entropy loss if the outermost methoxy H-bonds to an acid on the backbone, since the PEG chain loses translational mobility. However, there is now a cooperative effect because there is little further entropy loss for the other ether oxygens to form H-bonds with the polymer acid groups. A simple cartoon of this effect is shown in Figure 5.3. The result is that intermolecular H-bonding is favoured over H-bonding to water, and since there are no excess ethylene oxide or acid groups, the

polymer cannot H-bond to water at all. The H-bonding orients the backbone methyl groups, as well as the side-chain ethylene groups, towards the outside of the polymer coil, resulting in a very hydrophobic polymer which cannot dissolve in water.

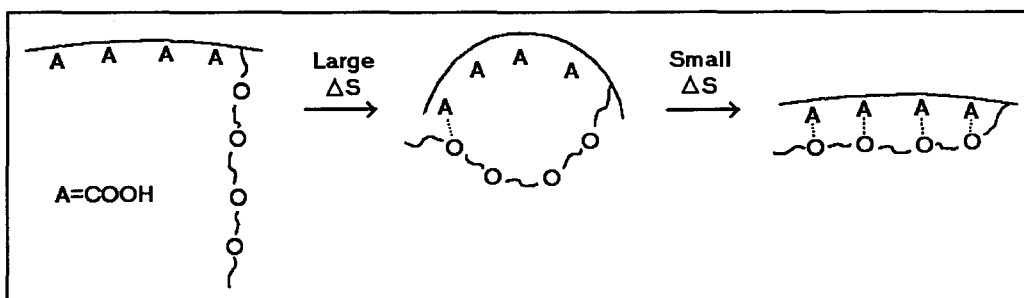


Figure 5.3: Cooperative intramolecular hydrogen bonding for the [20-80-0] copolymer

As the ratio of MAA to PEGMA decreases, there are eventually enough excess ethylene oxides, not involved in H-bonding to the chain, which can form hydrogen bonds with water and dissolve the polymer below the LCST, as shown in Figure 5.4 (water molecules omitted for clarity). Also, the cooperative effect is decreased because the

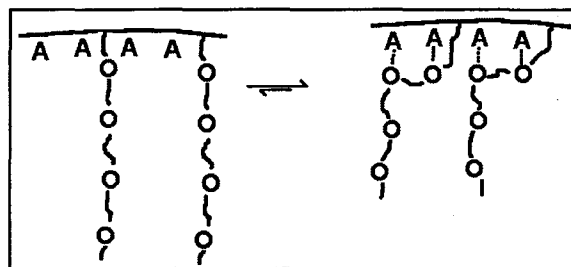


Figure 5.4: Intramolecular hydrogen bonding for the [65-35-0] copolymer

complexed segments become shorter, so the competition between acid groups and water for the PEG groups is more balanced entropically and the equilibrium would shift more to the left in Figure 5.4. The curve in Figure 5.2 is non-linear, which is further evidence for the cooperativity. As the ratio of acid groups to ether groups approaches 1:1 (going from left to right on the curve) the drop in LCST becomes larger for each point.

Above the LCST, the polymer precipitates from solution. The thermal motion of the water molecules increases, and they can no longer form hydrogen bonds with the PEG chains. The enthalpy of mixing decreases dramatically without this hydrogen bonding, and the overall free energy of mixing becomes positive. Without the hydrogen bonds to water, the otherwise hydrophobic polymer must precipitate out of solution. Also, the hydrophobic interactions between the intramolecularly complexed segments increases with increasing temperature, further driving the precipitation. This precipitation occurs at higher temperatures (higher LCST) as the MAA content decreases because more H-bonds between water and the PEG chains exist which must be broken. Also, the LCST increases because fewer intramolecular complexes are present, and the polymer is less hydrophobic.

5.4 Effect of ternary copolymer composition on LCST

There is also a trend in the case of the ternary copolymers, where the MAA and PEGMA comonomers are present in a 1:1 molar ratio, and only the BMA content is varied (Fig. 5.5). In the case of the binary copolymer [50-50-0], the LCST is 22.7°C. The addition of only 1 mol% BMA reduces the LCST to 18.8°C for the copolymer [49.5-49.5-1]. The LCST continues to decrease as the BMA content increases. This is because the copolymer becomes successively more hydrophobic as BMA groups are added, and fewer H-bonds between the polymer and water need to be broken for the polymer to precipitate. In this case the curve is linear and does not show any cooperative effects.

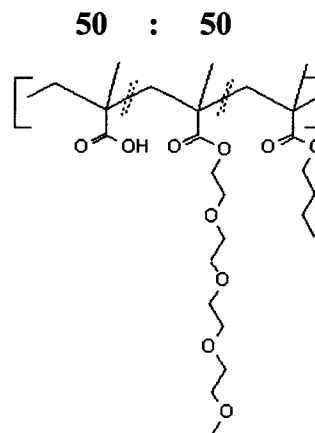
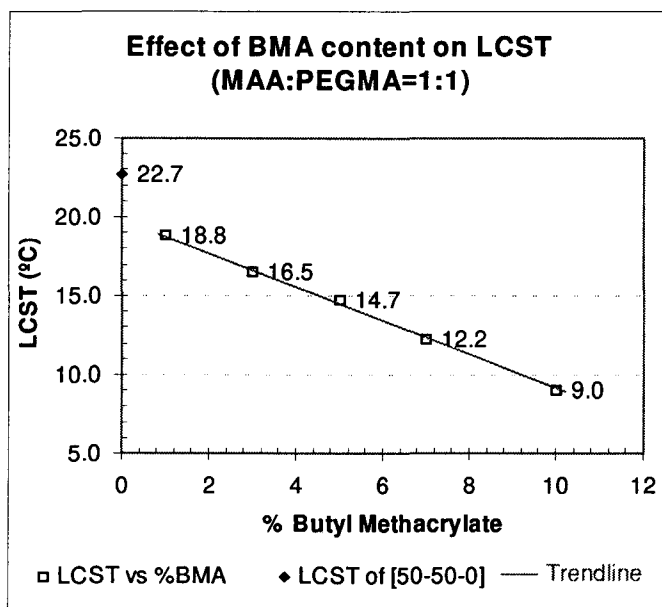


Figure 5.5: Effect of ternary copolymer composition on LCST

6.0 POLYELECTROLYTE COMPLEXATION

With the exception of the PEGMA homopolymer, all of the polymers synthesized in this thesis contained carboxylic acid functionality due to the presence of the monomer methacrylic acid (MAA). The primary objective was to study how these new polyacids interact with polybases in aqueous solution. Amines were chosen as weak bases for this project. Prior to studying how polyamines interact with the entire copolymer series, the complexation between a representative copolymer and simple oligobases was examined. The interaction between the [50-50-0] polymer with mono-, di-, tri-, tetra-, and penta- amines was compared with two polyamines; one linear, and one branched.

6.1 Complexation of the [50-50-0] copolymer with amines

Solution pH behaviour during titration:

The potentiometric curves for titration of the [50-50-0] copolymer with various amines is shown in Figure 6.1. The vertical line indicates a stoichiometric ratio between amine and carboxylic acid functional groups. In general, these titration curves were sloped with no clear end points. However, the monofunctional butylamine (BA) curve does exhibit a well-defined end-point. This curve can be compared to the earlier titration of the [50-50-0] copolymer with NaOH, which is a strong base. The end-point is more

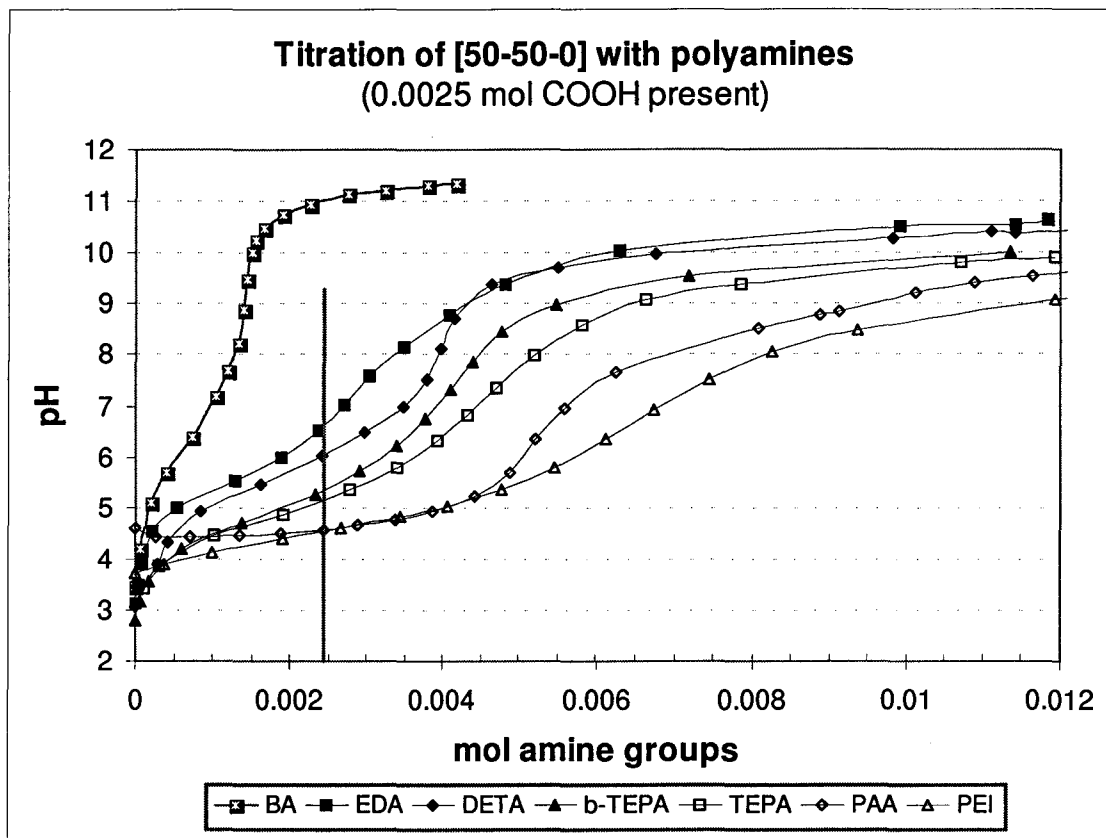


Figure 6.1: Potentiometric curves for complexation of [50-50-0] with amines

Legend abbreviations (Fig 6.1, 6.2)	
BA Butylamine	TEPA Tetraethylenepentamine {linear}
EDA Ethylenediamine	PAA Poly(allyl amine) {linear}
DETA Diethylenetriamine	PEI Poly(ethylenimine) {branched}
b-TEPA Tetraethylenepentamine (branched)	

gradual in the BA case, and the final pH is lower because of the weaker amine base.

Upon going from BA to EDA, a difunctional amine, the end-point becomes too gradual to be detected. As the functionality of the bases increase, there is a double polyelectrolyte effect, with multiple end-points for both the acid and the base that merge together and cannot be distinguished. Whereas a strong, monofunctional base can titrate the entire weak polyacid, the weak multifunctional bases cannot be fully deprotonated, and the

weak polyacid is never fully neutralized either. The pH curves for the polymeric amines hence show the smallest slopes.

Solution conductivity during titration:

The conductivity curves shown in Figure 6.2 may further explain some of the factors involved in these titrations.

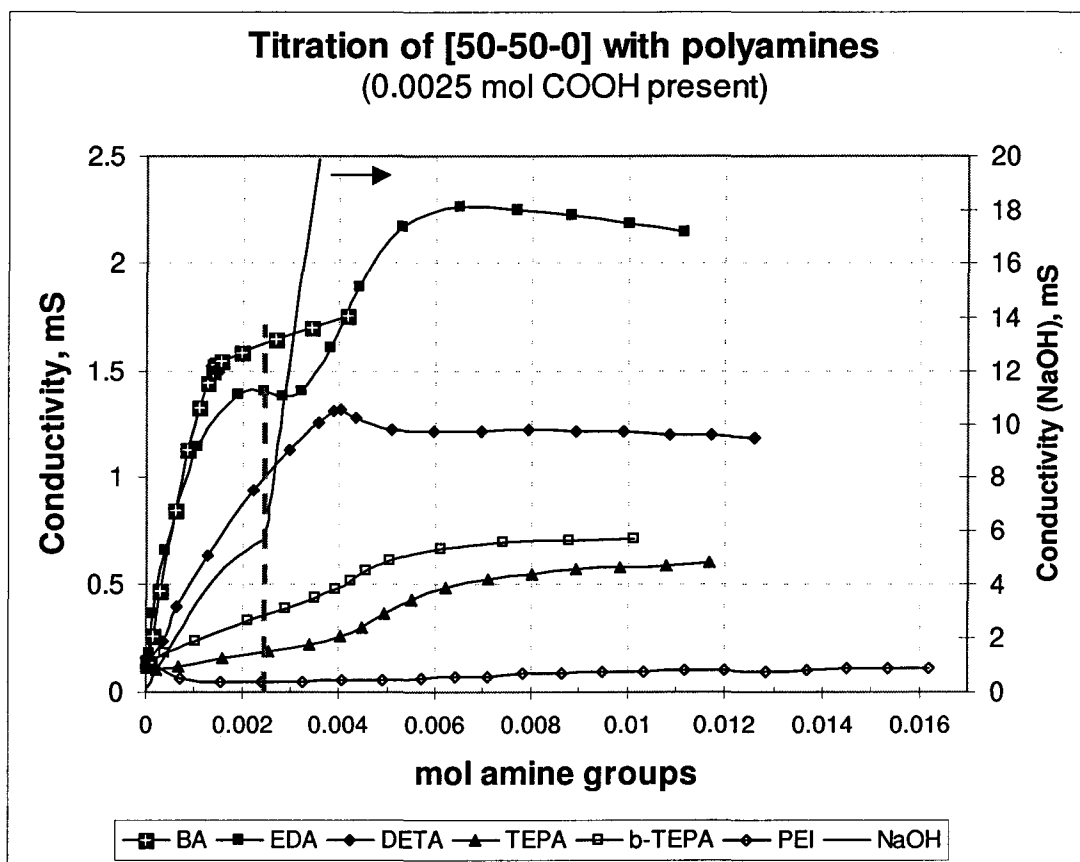


Figure 6.2: Conductivity curves for titration of [50-50-0] with polyamines

The titration curve with NaOH has been included in Figure 6.2 for comparison, and the conductivity is shown on a secondary axis. The solution becomes much more

conductive in the NaOH case than with any of the weaker amines. Titration with BA causes the initial solution conductivity to rise moderately, because the mono-amine becomes protonated, and the polyacid becomes deprotonated, so the overall number of micro and macroions in solution increases. The conductivity increase is much greater with NaOH as the titrant, because the more mobile Na^+ ions contribute more to the conductivity than the butylammonium ions. At the end-point in the NaOH titration, the conductivity rises sharply and continuously due to excess Na^+ and OH^- ions in solution. This is not the case for the amine titrations. At first, the conductivity does continue to rise slowly as excess amine is added, because of the increased ammonium and OH^- ions. The curve eventually levels off, even though excess amine is still being added after the end-point (especially the EDA curve). At this point, the solution pH may be above the pK_b of the amine, so the excess remains neutral in solution and does not increase the conductivity. This trend continues for the other amines, and the break-points in the conductivity curves become less distinct. In spite of these general observations, the conductivity curves in Figure 6.2 are quite complex, and cannot be further elucidated without additional research.

Solution phase behaviour during titrations:

The lower molecular weight series with one, two, three, and five amines per chain did not cause phase separation during the titration. These curves represent a titration between a weak polyacid and a weak base. Therefore, not all of the base amines are protonated by the weak carboxylic acids. While a portion of each oligo-amine molecule

is ionically bound to the polyacid chain, another portion remains free, and can form hydrogen bonds with water, maintaining the solubility of the complex (Fig. 6.4a).

Phase separation was observed, however, for the macromolecular polyamines: poly(allyl amine) (PAA), which is linear, and poly(ethylenimine) (PEI), which is branched. In this case, the titration is between a weak polyacid and a weak polybase. The amines are protonated by the carboxylic acid groups, and the polymers become oppositely charged polyelectrolytes, which form a complex due to the coulombic attraction. These bases are polymers, so the chains are long enough to interact with more than one polyacid chain. Both intra- and intermolecular polyelectrolyte complexes can form, which can range from a coiled, “scrambled egg” structure to a more linear “ladder-like” structure. In the case of a ladder structure, each polyamine chain is paired up with one polyacid chain, with the opposite charges holding the two polymers together like a zipper. In the scrambled egg structure, the polymers are entangled and each polyamine is complexed at different points along the chain with many different polyacid chains. These structures are sketched in Figure 6.3. In either case, phase separation may occur because the transient

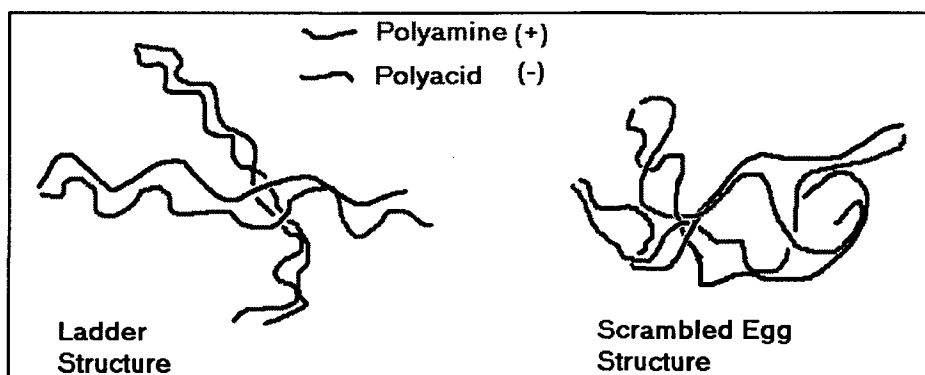


Figure 6.3: Possible structures of polyelectrolyte complexes

because the transient ion-pair connections limit the polymer motions and decrease the entropy of the system. The PAA complex phase-separates as a solid precipitate. This complex exists between two linear polyelectrolytes, and may have a ladder-like structure. Each polyelectrolyte pair becomes more hydrophobic as the charges pair up, and in spite of the hydrophilic PEG chains, precipitation occurs (Fig. 6.4b). The PEI/[50-50-0] complex, on the other hand, phase separates as a second liquid phase, or coacervate. Since PEI is branched, it is conceivable that this polyelectrolyte complex has a scrambled-egg structure. The structure may be similar to a network, cross-linked with transient ionic bonds rather than covalent bonds, and therefore liquid in nature. Furthermore, the branched and highly charged nature of PEI makes it physically impossible for each charge on PEI to be paired with a carboxylic acid on the linear methacrylic copolymer (Fig. 6.4c). The uncomplexed amines, along with the PEG chains, incorporate sufficient water into the complex to form a coacervate.

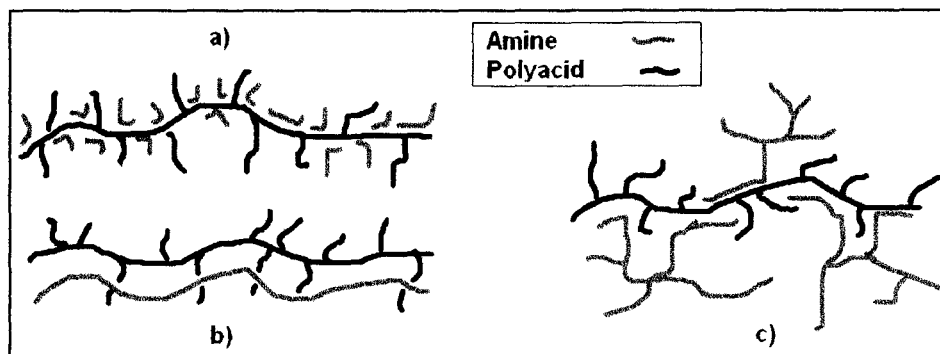


Figure 6.4: Sketch of possible structures of polyacid complex with a) oligoamines b) linear PAA c) branched PEI

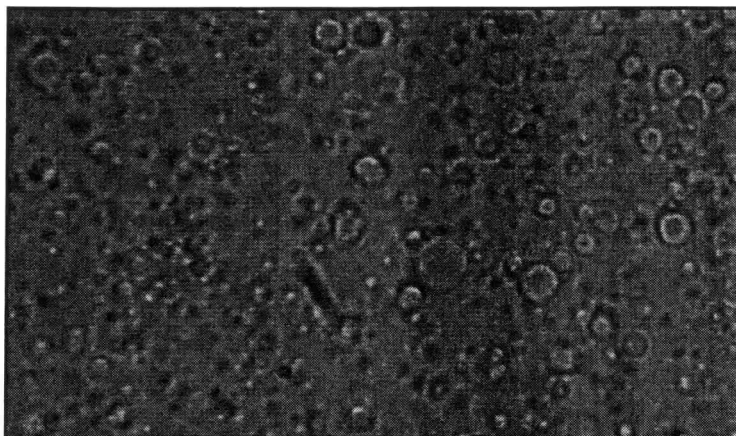


Figure 6.5: [50-50-0]/PEI complex coacervate droplets on optical microscope slide (droplets about 20-100 μ m)

Optical microscopy was used to examine the two phases present in the PAA and PEI systems. In the PAA case, the second phase was a curd-like, solid precipitate. However, the second phase in the PEI system was a liquid, and viscous coacervate droplets in a low-viscosity medium could be observed on the slide (Fig. 6.5). When both mixtures were allowed to settle overnight, the PAA complex was observed as a soft sticky solid, while the coacervate phase in the PEI system settled at the bottom of the container, and was indeed a second liquid phase.

6.2 Test of complex coacervation

In order to verify that a polyelectrolyte complex coacervate was formed in the PEI case, a solution of 0.07 M NaCl was slowly added to the mixture, with mechanical stirring. The second phase was observed to disappear slowly, and the mixture finally became a clear, homogeneous solution of low viscosity. The photometric curve is shown

in Figure 6.6. As salt is added to the system, the microions pair up with the ionic sites on the polyelectrolyte. The microions behave as an electrical double layer on the polymers, so the electrical potential near the polyelectrolytes is greatly decreased. This reduces their attraction for each other, so that the polyelectrolytes no longer form a complex. If phase separation were mainly due to another phenomenon, such as hydrogen bonding between the PEG side chains and the polyamine, then the salt test would not have caused the coacervate to disappear.

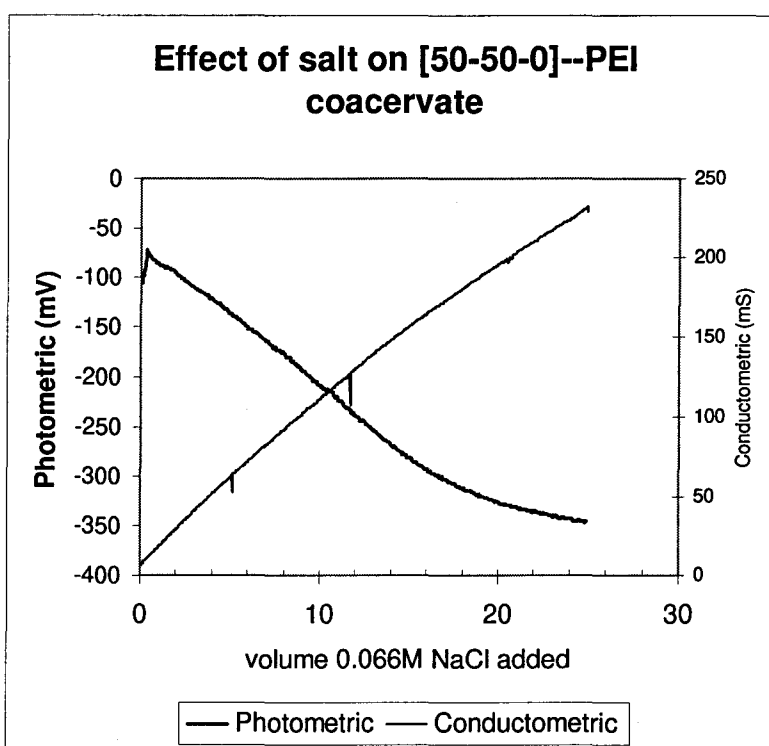


Figure 6.6: Effect of Salt on Coacervation

6.3 Polyelectrolyte complexation between the methacrylic copolymers and poly(ethylenimine)

In Section 6.1, it was found that both PAA and PEI formed polyelectrolyte complexes with the [50-50-0] methacrylic copolymer, resulting in a two-phase system for both cases. The PAA/[50-50-0] complex was observed as a solid phase dispersed in the equilibrium liquid. In contrast, the PEI/[50-50-0] complex was observed as a second liquid phase emulsified within the equilibrium liquid. This liquid-liquid phase separation was of particular interest, because it is a complex coacervate. While the subject of coacervation has been treated thermodynamically in the literature³⁰, there is not a great deal of information regarding the physical structure of coacervates. Therefore, the PEI complex system was further investigated in order to learn more about complex coacervation.

The pH profile for complexation of a 3% w/v solution of [50-50-0] with 3% w/v PEI was shown in Figure 6.1, at the far right of the graph. The experiment was repeated with both titrant and analyte solutions at 1% w/v and 5% w/v. In the case of the 1% w/v solutions, the photometric probe reading did not reach a 0mV reading at the point of phase-separation. The probe read a minimum at -34mV, and levelled off around -60mV, indicating that the solution was not completely opaque. The turbidity probe was saturated for the titrations at both 3% and 5% w/v (reading -6 mV). The 1% w/v concentration was therefore selected for further titrations so that minor differences in the turbidity at the point of coacervation could be detected.

6.3.1 Titration of methacrylic copolymer series with branched

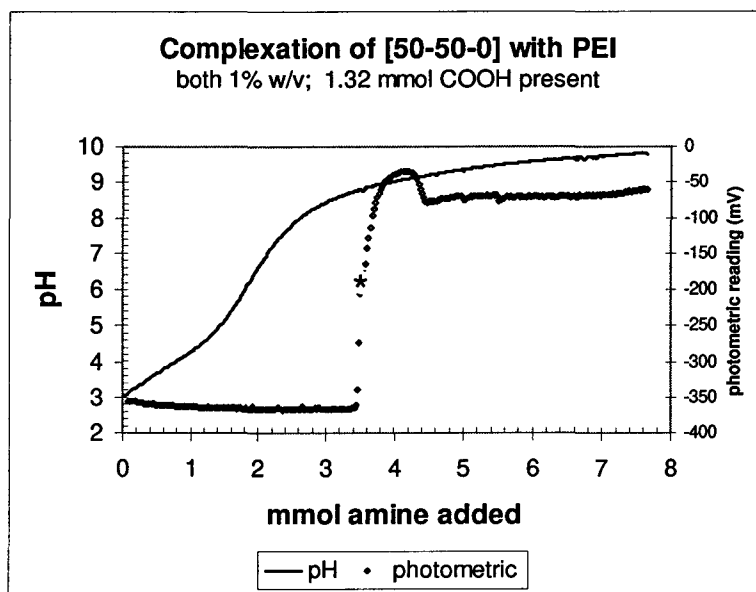


Figure 6.7: Complexation Between [50-50-0] and PEI polyethylenimine

It was hoped that since all of the copolymers in the series had both acid and PEG functionality, that they could each form complex coacervates with solutions of PEI. If this were the case, it would be a versatile system for complex coacervation. Therefore, each copolymer was titrated with a PEI solution at 1% w/v concentration. A typical pH/photometric titration profile for the complexation of the [50-50-0] copolymer with PEI is shown in Figure 6.7. The pH curve generally had the same shape for the other copolymers.

For every addition of the PEI solution to the polyacid solution, an initial phase separation was observed around the location of the added drop. The second phase quickly cleared as the solution was stirred. Thus, the early section of the photometric curve shows a clear solution (reading -360 mV). However, a permanent phase separation was observed to occur when 15 mL of the PEI solution had been added to the 40 mL [50-50-0] solution. Although both solutions are the same concentration by weight, the charge densities on the polymers are quite different. Thus the molar ratio of amine groups to carboxylic acid groups present at this point should be considered. When permanent phase separation occurred, the ratio of amine to carboxylic acid was about 2.6:1. A maximum in turbidity was observed when a three-times excess of amine had been added. It is interesting to note in Figure 6.7 that there is a maximum in turbidity just after the onset of phase separation, followed by a slight decrease, and then the turbidity levels off. It is possible that at the maximum in turbidity (minimum photometric reading), there are a large number of small coacervate droplets. As more PEI is added, some of these droplets coalesce, so that the turbidity decreases slightly.

It was found that all of the copolymers prepared for this project formed complex coacervates with PEI, except for the [80-20-0] copolymer which was insoluble in water. However, neither of the homopolymers formed complex coacervates. The poly(PEGMA) cannot form a polyelectrolyte complex with PEI. It may form a hydrogen-bond complex with PEI, but no phase separation occurred during the titration. It is possible that protonated PEI may form complexes with PEGMA. The homopolymer, poly(MAA) does form a polyelectrolyte complex with PEI, but the complex is a precipitate. Phase

separation permanently occurs for each addition of PEI during the titration. The results of the homopolymer titrations show that both acid and PEG functionality are necessary for coacervation in this system.

The conductivity curves also had similar profiles for each of the copolymers titrated with PEI. Figure 6.8 shows the curve for the [50-50-0] copolymer as an example.

The conductivity remains very low throughout the titration. However, it drops initially. This can be explained by considering that the analyte solution contains a weak polyacid which is partially dissociated. As the partially protonated polybase is added, the

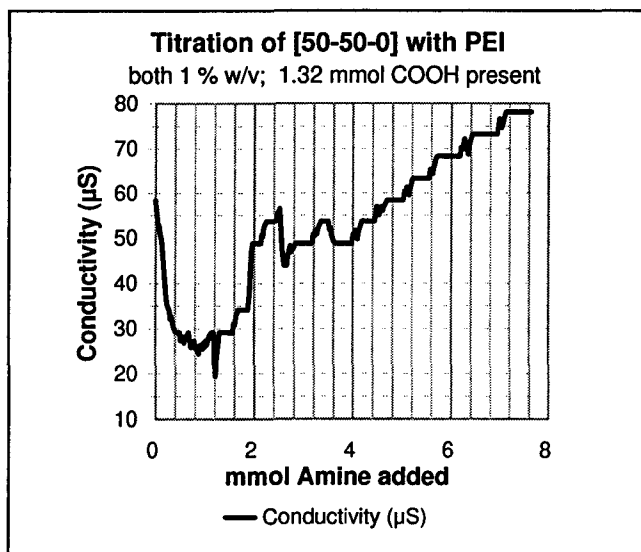


Figure 6.8: Conductometric titration of [50-50-0] with PEI

free hydroxyl ions in the titrant combine with the free protons in the analyte, forming water, and decreasing the concentration of ions in the solution. At this stage, the partially charged polymer chains attract each other, and also contribute less to the solution conductivity. Once these free ions are removed from solution, the acid-base reaction between the polymers begins to increase the total charge on each chain. As macroions are being generated in the solution, the conductivity then rises slowly. However, the increase is small because the newly formed charges on the polyacid chains are associated with opposite charges on the polybase chains. As well as shielding each others charges, the complexation between the

chains reduces their ionic mobilities.

The turbidity curves generally had the same shape for each of the other copolymer titrations, with minor variations. However, the location of the cloud-point varied significantly in each case. The cloud-point in Figure 6.7 occurs when 3.5 mmol of amine groups have been added, which is a 2.6 fold excess of amines relative to carboxylic acid groups present in the analyte solution. The point where the turbidity curve starts to increase is defined as the onset of coacervation. For some of the titrations, the onset of coacervation was not so sharply defined. In Figure 6.7, the photometric reading midway between minimum and maximum turbidity is marked by an asterisk. This point indicates the solution composition at 50% turbidity, and could be measured more consistently for each titration. The composition at 50% turbidity for each of the copolymers titrated with PEI is summarized in Table 6.1. The amine to carboxylic acid ratio is affected by the copolymer compositions. The MAA content has a significant effect; as the MAA content increases, the ratio of amine to carboxylic acid at the onset of phase separation decreases.

Table 6.1: Composition at onset of coacervation (at cloud-point)

Copolymer	Ratio Amine:COOH
[20-80-0]	7.7
[35-65-0]	4.6
[50-50-0]	3.0
[65-35-0]	2.6
[49.5-49.5-1]	3.2
[48.5-48.5-3]	3.2
[47.5-47.5-5]	3.0
[46.5-46.5-7]	3.4
[45-45-10]	3.2

The amount of MAA in the ternary copolymer series remains nearly constant, and likewise there is no trend in the amine to carboxylic acid ratio for this series. The BMA content in the copolymers does not appear to significantly affect this ratio at all.

6.4 Properties of polyelectrolyte complexes and coacervates

The results of Section 6.3 show that four of the binary copolymers and all of the ternary copolymers form complex coacervates with PEI. As the composition of the binary series had a greater effect on the coacervation in terms of stoichiometry, the properties of these coacervates were further examined for that series. In order to learn more about the coacervation process, measured volumes of PEI were combined with measured volumes of copolymer solutions. These volumes were chosen based on the titration curves. At the onset of coacervation, there is very little coacervate present, and so the properties at this point would be physically difficult to measure. However, it would be desirable to study the coacervate properties at a point very close to the initial cloud point. A point too far away from the onset of coacervation would have excess PEI, and this would offset the results. The amount of PEI required for 50% turbidity was measured, and increased by 10%. This ratio of PEI to polyacid was used to make 15 mL, 3% w/v samples. The samples were centrifuged and the relative volumes of both liquid phases read from the calibrated tubes. Then, the upper phase was carefully decanted into pre-weighed pans, and dried. Also, the lower liquid phase in the centrifuge tube was dried. The relative masses of polymer in each phase was calculated as a percentage of the total polymer weight in the combined solutions. Also, the concentration of polymer as % w/v in each phase was calculated.

6.4.1 Effect of concentration and ratio of PEI to [50-50-0] copolymer on coacervation

First, both the effect of carboxylic acid to amine ratio, as well as the effect of initial solution concentrations on the composition of the liquid phases were studied. In this experiment, the [50-50-0] copolymer was chosen as a representative sample. The polyelectrolyte solutions were combined in two ratios: the first was chosen near the onset of coacervation, as described in Section 6.4; the second mixture contained double that quantity of PEI (by volume). Also, solution concentrations of 3 and 0.5 % w/v were compared to observe how coacervate volume is affected by polymer concentration. Solutions of 0.1% w/v were also prepared, but these resulted in too little coacervation to be measured.

Table 6.2: Composition at onset of coacervation (at cloud-point) between [50-50-0] and PEI

A	B	C	D	E	F
COOH : Amine	Initial Conc'n	Top Vol %	Coac. Vol %	Top % w/v	Coac. % w/v
1 : 2.7	3 % w/v	90	10	1.6	17
1 : 2.7	0.5 % w/v	99	1	0.35	19.6
1 : 5.4	3 % w/v	86	14	1.37	15.6
1 : 5.4	0.5 % w/v	98	2	0.24	16.4

- A Molar ratio of COOH groups to amine groups after combining certain volumes of solutions
- B Concentrations of both [50-50-0] and PEI solutions (and of overall combined solution)
- C After phase separation and settling, % of liquid volume in top equilibrium layer
- D After phase separation and settling, % of liquid volume in lower coacervate layer
- E Concentration of polymer in top equilibrium layer before drying
- F Concentration of polymer in coacervate layer before drying

A comparison of the rows in Table 6.2 in pairs shows the effect of each of the two variables discussed above. The values in Table 6.2 columns C and D are accurate to about $\pm 2\%$ of the given value. The columns E and F are accurate to about $\pm 10\%$ of the given value, because it was difficult to remove all of the water during the drying process. Rows 1&2, as well as rows 3&4 compare the effect of the initial solution concentrations (column B), at a constant amount of PEI. When the solutions are more dilute, there is less coacervate liquid (column D). The concentration of polymer in the coacervate liquid (column F) increases. Now, compare rows 1&3 and rows 2&4, keeping the concentrations fixed, but varying the amount of PEI relative to [50-50-0] copolymer (column A). When a large excess of PEI is added, the volume of the coacervate increases. However, the concentration of polymer in the coacervate phase decreases.

6.4.2 Effect of binary copolymer composition on complex coacervation

The effect of copolymer composition on complex coacervation was studied. Solutions of 3% w/v concentration were used in order to have an easily measured quantity of coacervate. The ratio of PEI to polyacid was chosen near the point of 50% turbidity indicated on the titration curves for each copolymer, as described in Section 6.4. Figure 6.9 shows the effect of copolymer composition on coacervate volume. The coacervate volume is not significantly affected by copolymer composition.

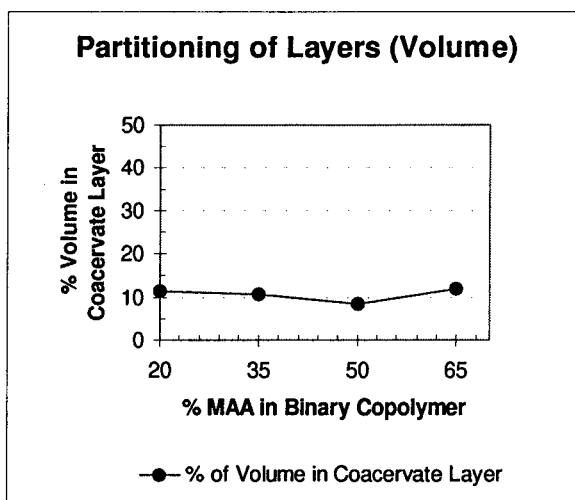


Figure 6.9: Effect of copolymer composition on coacervate volume

However, the composition of the coacervate layer was strongly affected by the composition of the binary copolymer. The coacervation efficiency increases with increasing percent MAA in the copolymer. That is to say, the concentration of the coacervate layer increases (Fig. 6.10). In the case of the [20-80-0] copolymer, 50% of the total polymer is present in the coacervate layer, which has a 12% concentration by weight (Table 6.3). Over 80% of the total polymer is found in the coacervate phase for the [65-35-0] system.

Table 6.3: Polymer Loading in Coacervate Phase

Copolymer Name	% Polymer in Coacervate
[20-80-0]	50.4
[35-65-0]	66.1
[50-50-0]	81.7
[65-35-0]	83.9

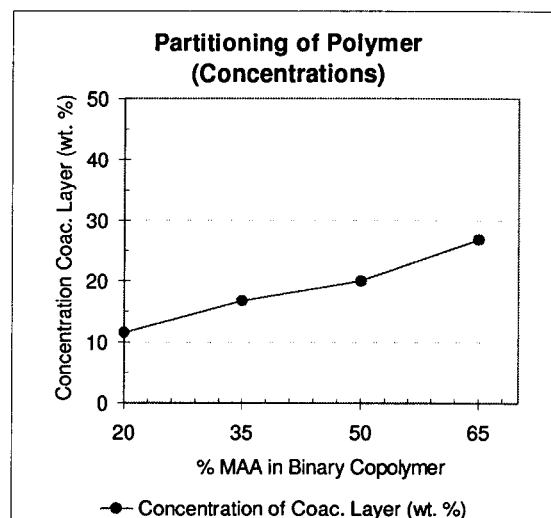


Figure 6.10: Effect of copolymer composition on coacervate concentration

These trends are caused by many factors. As the PEGMA content of the copolymers increase, their properties change also. They become more bulky, because the PEG chains are like short-chain branches. Furthermore, they are one of several groups present in the system capable of hydrogen bonding. Because the (protonated) amine groups on the PEI can also hydrogen bond, the excess PEGMA comonomer may have a secondary influence on the nature of the complexation. Moreover, as the MAA comonomer content is increased, the number of ionizable groups increase. One would expect that the minimum amount of PEI required to form complex coacervates would increase with increasing MAA. In fact, the converse is true, and the results were presented in Table 6.1. Figure 6.11 illustrates this trend. One possibility is that the side PEG chains interfere with the

efficiency of binding the PEI to the polyacid. As the PEGMA content increases, the PEG chains prevent the highly branched PEI from accessing the backbone acid groups on the methacrylic copolymer. Therefore, many PEI groups are necessary to access all of the MAA

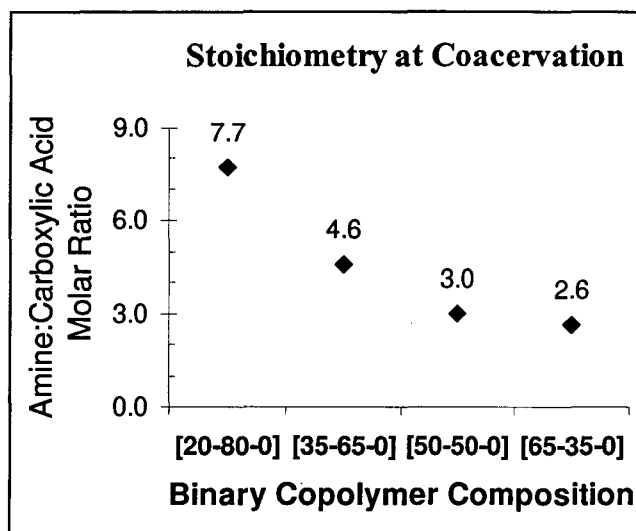


Figure 6.11: Binary series coacervation ratios

sites on the polyacid, and the amine to carboxylic acid ratio is high for this complex. As there are fewer PEG groups, the backbone becomes sterically more accessible, and one PEI molecule can neutralize several acid groups. The amount of PEI required for

coacervation thus decreases, even though the MAA content increases. This theory correlates well with the information in Figure 6.10. The copolymer with the high PEGMA content requires a large excess of PEI to form a complex coacervate. There are a large excess of amine groups not involved in complexation which may be protonated. These complexes would have an overall positive charge, and sterically as well as electrostatically repel each other. In other words, the coacervate structure would be expanded due to positive charge repulsions. The coacervate phase is thus more dilute for this system. As the PEGMA decreases, and the required amount of PEI decreases, there would be less repulsion between complexes, and the coacervate phase becomes more concentrated. This is a complicated system, however, and other factors may be involved as well.

7.0 CONCLUSIONS

Two series of anionic copolymers were prepared. One series consisted of binary copolymers containing methacrylic acid (MAA) and poly(ethylene glycol) monomethyl ether monomethacrylate (PEGMA) in molar ratios ranging from 20:80 to 80:20, as well as the two homopolymers, poly(MAA) and poly(PEGMA). The second series contained an equimolar amount of MAA and PEGMA, together with between one and ten percent of a third, hydrophobic monomer, butyl methacrylate (BMA). Except for the [80-20-0] copolymer, each of these copolymers were soluble in water. Both binary and ternary copolymers show lower critical solution temperatures, LCST's, ranging from 60.8°C to 1.5°C depending on composition.

Despite the wide range of copolymer composition, all of the water soluble copolymers formed complex coacervates with aqueous poly(ethylenimine). Thus copolymers of methacrylic acid, which include PEG side chains, are well suited to complex coacervation. The percent volume of the liquid coacervate phase depended on the component solution concentrations, and was independent of copolymer composition. However, with increasing MAA to PEGMA ratio in the binary copolymer, the coacervate density increased, while the molar ratio of amine groups relative to carboxylic acid groups at the onset of coacervation decreased. Steric factors may contribute to these trends. The PEG groups may limit the efficiency of complexation between PEI and the

methacrylic copolymers. The coacervate may be more dilute as a result of ionic repulsions between uncomplexed amine groups on the PEI chains. The coacervate composition was not significantly affected by the butyl methacrylate in the ternary copolymer series.

The linear poly(allyl amine) resulted in precipitated polyelectrolyte complexes. Furthermore, complexes between PEI and poly(MAA) were also precipitates. The results of this work show that the PEG groups and the branched structure of the polyamine both play an important role in the complex coacervation.

8.0 RECOMMENDATIONS

- This project demonstrated that coacervation efficiency increased with increasing methacrylic acid copolymer. However, the maximum MAA that could be incorporated was limited by the LCST. It is probable that copolymers with an excess of MAA relative to ethylene glycol groups would be water-soluble and that such copolymers may contribute to even greater coacervation efficiency.
- By studying the composition of the coacervate and equilibrium phases in more detail, the process of coacervation might be better understood. The relative amounts of PEI and methacrylic copolymer in each phase should be measured separately. One approach to this study would be elemental analysis.
- The effect of pH on coacervation should be investigated.
- All of the coacervates formed in this project involved branched poly(ethylenimine) as the polybase. There are many other polymers which could be considered for the role of polycation. Variations could include the spacing of the ionizable functional groups, the degree of polymer branching, and the incorporation of PEG into the polybase chain. Polyamines with only primary amine groups may eliminate some of the variables involved as well.
- The effect of copolymer composition on LCST should be studied in greater detail. By measuring changes in solution viscosity with temperature, more subtle effects may become apparent. It would be interesting to examine a wider range of copolymer composition. Each of the copolymers in this thesis had an excess of ethylene glycol groups relative to methacrylic acid. Further studies should be made on copolymers with excess methacrylic acid. Also, the effect of varying the PEG chain lengths on the macromonomer should be investigated in greater detail.

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