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Journal of Chromatography A 817 (1998) 287–295

JOURNAL OF CHROMATOGRAPHY A

Pluronic copolymer liquid crystals: unique, replaceable media for capillary gel electrophoresis

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Abstract

Liquid crystalline solutions of Pluronic copolymers are versatile alternatives to solutions of entangled, random coil polymers as replaceable media for capillary gel electrophoresis (CGE). Pluronic copolymers are tri-block polymers of poly(ethylene oxide) [$(EO)_x$] and poly(propylene oxide) [$(PO)_y$] with the general formula $(EO)_x(PO)_y(EO)_x$. Large micelles form in aqueous solutions in which central, hydrophobic cores of $(PO)_y$ segments are surrounded by ''brushes'' of hydrated $(EO)_x$ tails. Solutions of Pluronic F127 (BASF Performance Chemicals) in a concentration range of about 18–30% are liquids at refrigerator temperatures ($\leq$5°C) and are easily introduced into capillaries. A self-supporting, gel-like liquid crystalline phase is formed as the temperature is raised to $\geq$20°C. This liquid crystalline phase consists of spherical micelles with diameters of 17–18 nm which pack with local cubic symmetry. CGE in Pluronic F127 liquid crystals separates species within several chemical classes as varied as nucleoside monophosphates and organic dyes, oligonucleotides of 4–60 nucleotides, DNA fragments of 50–3000 base pairs (bp), and supercoiled plasmid DNAs of 2000–10 000 bp. Mechanisms of molecular sieving in polymer liquid crystals must differ in fundamental ways from separations in random polymer gels because molecules move around uncrosslinked obstacles that are larger than the smallest dimensions of typical analytes. Molecular sieving in Pluronic liquid crystals is envisioned to occur as molecules squeeze between hydrated $(EO)_x$ strands of micelle brushes, or through brushtips and interstitial spaces between micelles. Small molecules such as nucleotides appear to separate by a different mechanism involving partitioning between hydrophilic and hydrophobic environments. This process is termed ''hydrophobic interaction electrophoresis''. The unique structures of Pluronic copolymers and their liquid crystalline phases provide new challenges and opportunities in separations science.

Keywords: Liquid crystals; Pluronic F127; Hydrophobic interaction electrophoresis; Gel electrophoresis, capillary; DNA; Deoxynucleoside monophosphates; Nucleotides

1. Introduction

Capillary gel electrophoresis (CGE) is a powerful means for separating biological macromolecules with efficiencies far greater than conventional electrophoresis, or high-performance liquid chromatography. Separations in CGE are dominated by molecular sieving, which depends on the pore structure of the medium in relation to the molecular mass, shape and flexibility of the analyte. Crosslinked polyacrylamide gels used in early applications have been largely supplanted by replaceable solutions of flex-

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0021-9673/98/$19.00
PII: S0021-9673(98)00522-6

ible, random polymers as molecular sieving agents (e.g., see Refs. [1–5] and references therein). The ability to replace the medium improves reproducibility and eliminates uncertainties of polymerizing crosslinked gels in thin capillaries.

Polymer solutions for CGE are normally used above the concentration where chains entangle. Entangled polymers form a dynamic sieving network which acts much like a traditional, crosslinked hydrogel network. Several polymer types have been adopted for CGE, but in all cases the polymer chains are random coils and the effective pore size distributions are broad. The Ogston description of polymer networks as randomly oriented, long, thin, cylindrical fibers [6] provides an excellent description of pore size distributions in crosslinked gels [7–17], and should approximate entangled polymer solutions. Separation mechanisms of most molecule classes are expected to be similar in crosslinked gels and solutions of entangled random polymers.

Replaceable solutions of a distinctly different, self-organizing class of polymers were recently described as media for CGE [18–20]. Often these are referred to as ''Pluronic'' copolymers, which belong to a large family of commercial triblock copolymers with the general formula $(EO)_x(PO)_y(EO)_x$, where $(EO)_x$ is poly(ethylene oxide) and $(PO)_y$ is poly(propylene oxide). (Pluronic is a registered trade name of BASF) Some representative copolymers of this class are described in Table 1. Pluronic copolymers are uncharged and highly miscible with water. They are surfactants and self-associate into large micelles [21–25], a distinctly different behavior from random coil polymers used to form entangled polymer solutions. Self-association is favored by increasing concentration and temperature. The less polar poly(propylene oxide) chain segments are desolvated and segregate into a hydrophobic micelle core surrounded by a soft ''brush'' of highly hydrated, flexible poly(ethylene oxide) chains (Fig. 1).

Our interest in Pluronic polymers lies in their ability to form both isotropic and anisotropic liquid crystalline ''gels''. Liquid crystals occur at sufficiently high concentrations in order to efficiently pack micelles, minimizing their excluded volume. Many of these copolymers undergo transitions between two or three liquid crystalline phases to optimally utilize space as concentration or temperature change. A common progression, exemplified by Pluronic P104, is from a cubic phase of spherical micelles to a hexagonal phase of columnar micelles, and finally to a lamellar phase (Fig. 2). The detailed phase behaviors of different Pluronic polymers are highly dependent on chain composition and may vary significantly (Table 1).

Table 1
Some examples of Pluronic copolymers[a]

Type	Composition[b]	M_r	Phases[c]
P65	$(EO)_{20}(PO)_{30}(EO)_{20}$	3500	H, L
P104	$(EO)_{18}(PO)_{58}(EO)_{18}$	4950	C, H, L
P123	$(EO)_{20}(PO)_{70}(EO)_{20}$	5280	C, H
PF80	$(EO)_{73}(PO)_{27}(EO)_{73}$	7990	C
F68	$(EO)_{80}(PO)_{30}(EO)_{80}$	8780	C
F127	$(EO)_{106}(PO)_{70}(EO)_{106}$	13 400	C

[a] Pluronic is a copyrighted trade name of BASF Performance Chemicals (Mount Olive, NJ, USA) and can be purchased from Sigma (St. Louis, MO, USA). Only a few of many Pluronic and related $(EO)_x(PO)_y(EO)_x$ polymers are shown.

[b] (EO)=Ethylene oxide, (PO)=propylene oxide. Composition information was taken from Ref. [24].

[c] The major, uniform, lyotropic liquid crystalline phases formed in water are listed. C=Cubic phase of spherical micelles, H=hexagonal phase of columnar micelles, L=sheet-like, lamellar phase. Note that there are two general structural classes of $(EO)_x(PO)_y(EO)_x$ polymers, those with $x<y$, and those with $x>y$. The latter class tends to form a single, cubic phase; while the former class tends to form multiple phases, depending on the x/y ratio and overall molecular mass.

Pluronic liquid crystals are characterized by significant internal order over dimensions ranging from about 10 nm, the smallest dimensions of individual micelles, to 100 nm, the correlation length for intermicellar order [18,21,24,25]. In addition, the structure of individual Pluronic micelles is differentiated, consisting of a dehydrated $(PO)_y$ core surrounded by a hydrated ''brush'' of $(EO)_x$ chains. Liquid crystalline Pluronic solutions thus are ''nanostructured'' materials.

The marked structural differences between solutions of liquid crystalline Pluronic polymers and isotropic solutions of entangled, random coil polymers are expected to cause significant differences in molecular sieving behaviors. This expectation was confirmed using Pluronic F127, which has an approximate molecular formula $(EO)_{106}(PO)_{70}(EO)_{106}$, and molecular mass of about 13 000. Pluronic F127

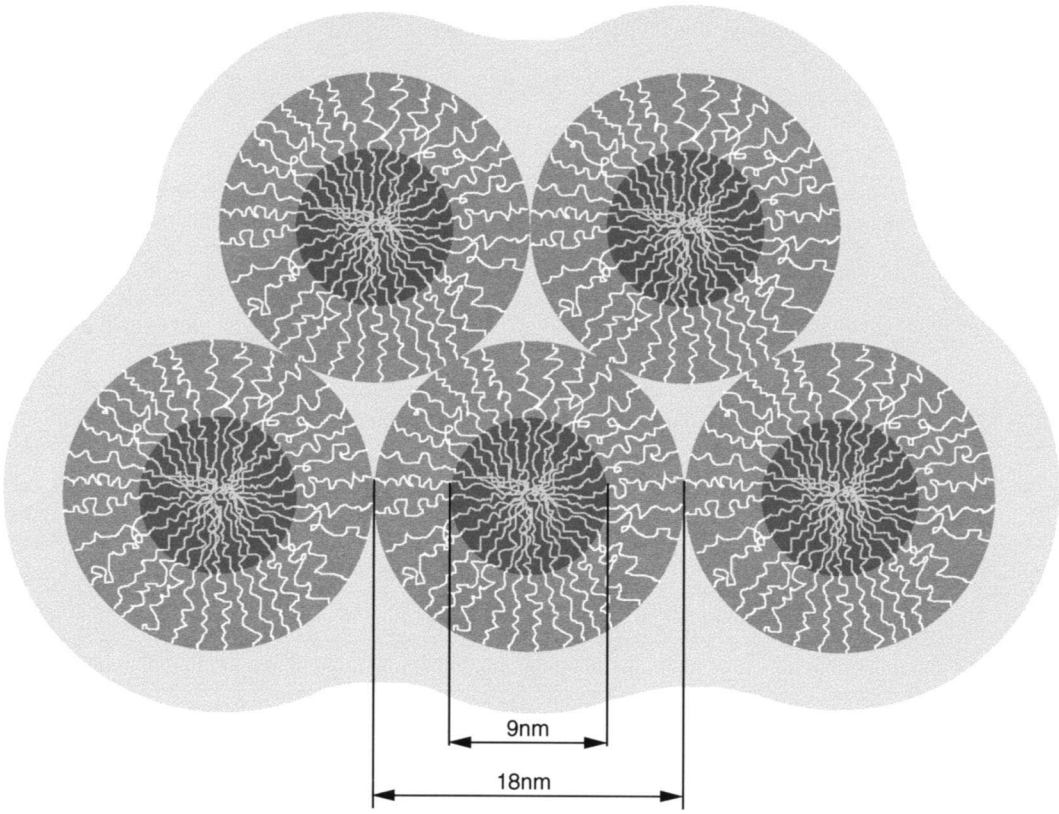

Fig. 1. Schematic of a plane of Pluronic F127 micelles in the liquid crystalline phase of a 20% solution. The central, darker grey region represents the approximate hard-core dimensions of the hydrophobic poly(propylene oxide) or $(PO)_{70}$ micelle core. The lighter grey region represents the approximate extent of the hydrated poly(ethylene oxide) or $(EO)_{106}$ micelle ''brush''. Individual $(EO)_{106}$ chains (curly lines) are flexible random coils, but will be more extended than an unperturbed random coil due to crowding near the micelle core surface. Interactions between micelles are expected to be repulsive [37]. Dimensions of the interstitial regions between micelle spheres depend on the packing geometry and degree of extension of $(EO)_{106}$ chains into this region. The approximate 9 nm hard-core diameter of the central, hydrophobic core was calculated from the molecular formula cited above based on an aggregation number, $N=54$ [24], and an assumed effective specific volume of 1.0 cm^3/g. This value is also consistent with recent estimates from small angle X-ray scattering (SAXS) data [18]. The inter-micelle distance of 18 nm is based on small angle neutron diffraction studies of 20% Pluronic F127 gels by Wanka et al. [24].

solutions at concentrations from 18 to 30% (w/w) are freely flowing liquids at refrigerator temperatures ($\leq$5°C) and are easily introduced into capillaries [18–20]. A self-supporting ''gel'' phase forms upon warming to room temperature ($\geq$20°C). This ''gel'' is not crosslinked, but instead is a cubic liquid crystalline phase in which spherical micelles are arranged with local cubic symmetry [18,21,24,25]. These gels were found to be suitable, convenient media for electrophoretic separations of a wide variety of biological macromolecules and other analytes.

2. Experimental

2.1. Materials

Pluronic F127 (manufactured by BASF Performance Chemicals, Mount Olive, NJ, USA), buffer salts, a double stranded ''Nx123 bp ladder'' DNA standard consisting of a collection of DNA fragments that are multiples of a 123 base pair (bp) sequence, ''poly U'' oligonucleotide standards, T_{12-18}, and T_{19-25} oligonucleotide standards, and nucleoside monophosphates were all obtained from Sigma (St.

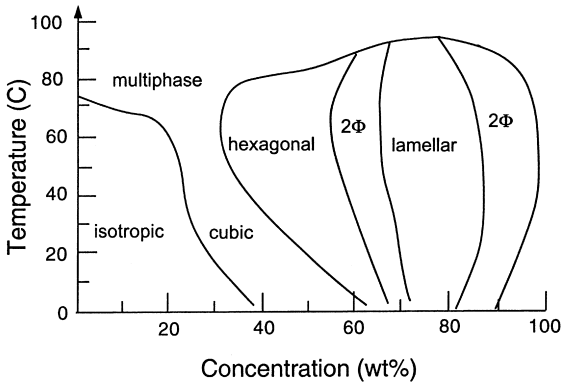

Fig. 2. Phase diagram illustrating the three common lyotropic liquid crystalline phases of Pluronic copolymers. The diagram shown (adapted from Ref. [24]) is for Pluronic F104 with the approximate molecular composition $(EO)_{18}(PO)_{58}(EO)_{18}$. The cubic phase consists of spherical micelles packed with local cubic symmetry. The hexagonal phase consists of columnar micelles packed with local hexagonal symmetery. The lamellar phase consists of layered sheets. The phase diagrams and phases available are variable and depend on the Pluronic molecular mass and composition [24].

Louis, MO, USA). A ''supercoiled DNA ladder'' and additional linear DNA standards were obtained from Promega (Madison, WI, USA). The supercoiled DNA ladder contained nine plasmids from 2000 to 10 000 bp (2–10 kbp), differing by 1 kbp.

2.2. Capillary electrophoresis

Electrophoresis was performed using a Beckman P/ACE 5010 instrument with UV absorbance detection at 254 nm (Beckman Instruments, Palo Alto, CA, USA). Temperature was controlled at the temperatures cited. Capillaries were 75 μm I.D., Celect-N columns from Supelco (Bellefonte, PA, USA) which have a surface coating reported to be exceptionally stable and to nearly eliminate electroosmosis [26]. No electroosmosis was noted in CE runs in Pluronic gels. The total capillary length was typically 36 cm (30 cm effective length). Some runs were done by introducing sample from the detector end of the capillary, in which case the effective length was usually 6 cm.

The electrophoresis buffer was Tris–borate–EDTA (TBE) buffer; which was 90 m*M* Tris, 90 m*M* boric acid, 2 m*M* Na_2EDTA, pH 8.3. Pluronic F127 solutions were prepared in TBE buffer and stored in the cold room (≤5°C). Capillaries in cartridges were filled with cold solutions of Pluronic F127 using modest hand pressure applied by a syringe, then placed on the instrument and equilibrated to room temperature for 5–10 min before use. Electrophoresis was performed in the reversed polarity mode. Samples were typically dissolved at concentrations of 1–2 mg total analytes/ml in Tris–borate–EDTA buffer which was diluted to one-tenth (1/10) the concentration cited above. Samples were injected electrokinetically. Highest reproducibility was attained by replacing the Pluronic gel after each electrophoretic run (see also Ref. [20]). The gel was replaced by transfering the capillary into the cold room, equilibrating to ambient temperature for 10–15 min, then flushing with TBE buffer before refilling with polymer solution.

3. Results

3.1. Double stranded DNA

Conventional and CGE electrophoresis experiments have demonstrated separations of double stranded DNA (dsDNA) fragments over the length range from about 100 to 3000 bp in Pluronic F127 gels over a range of polymer concentrations [18–20]. Increasing the Pluronic concentration from 18% to 30% increases resolution, but decreases the DNA size range of useful separations [19]. We obtained rapid CGE separations of double stranded DNAs in 20% Pluronic in a short (6 cm) capillary (Fig. 3). The size range of effective separation and resolution in this 12 min. CGE run approximated that obtained by conventional electrophoresis in 6 h [19].

Two unusual observations were described previously which support the suggestion that molecular sieving in Pluronic gels should be different in certain ways from sieving in random polymer gels or solutions ([19], see also Ref. [20]). The length range for effective separation of double stranded, linear DNA in 20% Pluronic F127 ended abruptly above 1000 bp, unlike the behavior expected from the reptation model, and observed in 6% polyacrylamide or 2% agarose gels (Fig. 4). Secondly, the inability

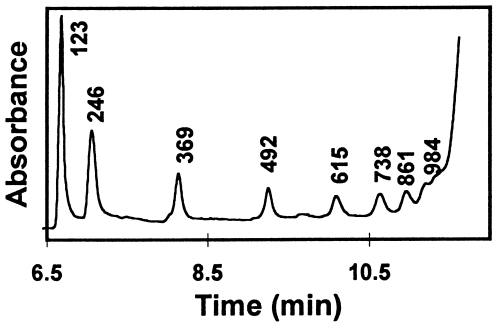

Fig. 3. Rapid CGE separation of double stranded DNA. The Nx123 bp standard of double stranded, linear DNA was electrophoresed in 25% Pluronic F127 in TBE buffer (total capillary length 36 cm, effective capillary length 6 cm, 30°C, 300 V/cm). Sample was injected electrokinetically for 5 s at an applied voltage of 10 000 V.

of 20% Pluronic gel to separate dsDNA fragments ≥3000 bp is due to unusually rapid, coincident electrophoresis of the large DNAs. By contrast, loss of resolution of large DNAs on polyacrylamide gels is due to their strong retardation.

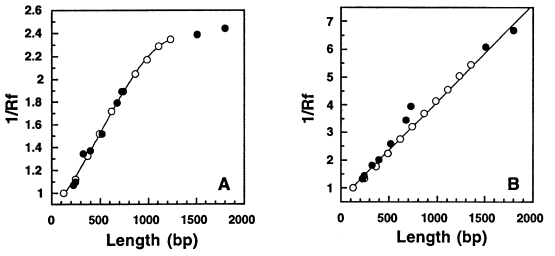

Fig. 4. Dependencies of inverse mobilities on length of double stranded DNA observed for electrophoresis in gels of (A) 20% Pluronic F127 and (B) 5% crosslinked polyacrylamide. Samples were electrophoresed in conventional format at room temperature in gels cast in 13 cm long glass tubes with 5 mm internal diameter. Gels contained TBE buffer and were electrophoresed with an applied voltage of 5 V/cm (Pluronic) or 2 V/cm (polyacrylamide). The linear dependence expected from DNA reptation theory was observed over the whole length range for 5% polyacrylamide, but over only a short range for 20% Pluronic. Open circles (○) represent Nx123 bp ladder fragments, filled circles (●) represent restriction endonuclease fragments of plasmid pGEM 3Zf (Promega). Mobilities (R_f) were normalized to the mobility of the 123 bp fragment. Solid line for polyacrylamide in frame (B) is a linear least-squares fit to all points. Solid line for Pluronic gel in (A) is a best-fit third order polynomial to data for the Nx123 bp fragments only. $R^2 \geq 0.999$ for both lines.

3.2. Supercoiled DNA plasmids

Extraordinary separations of the components of a 2 to 10 kbp supercoiled DNA ladder standard were obtained by CGE in Pluronic F127 solutions. This ladder contains nine components from 2 to 10 kbp, differing by 1 kbp, with the 5-kbp fragment in 3–4-fold excess of the others. The expected electrophoresis pattern of nine, well-resolved bands was observed in a 1% agarose gel (not shown). CGE on a short capillary of 20% Pluronic F127 provided poor resolution of perhaps nine components (Fig. 5a). Adjustments in column length, temperature and Pluronic concentration progressively resolved each of these broad bands into several components (Fig. 5b,c). A total of about 68 components, many represented by sharp peaks, were distinguishable when conditions were reasonably optimized (Fig. 5d). Curiously, better separations were obtained in 30% Pluronic than in lower concentration gels.

Origins of the microheterogeneity of supercoiled species have not been determined, but many components are likely to be topoisomers. Topoisomers are plasmids with the same DNA length, but different numbers of superhelical turns. Topoisomers of small plasmids can be separated on agarose gels [27], but separations of topoisomers of 8–10 kbp plasmids would be extraordinary. The banding patterns do not have a simple Boltzmann distribution of intensities [27], suggesting that more components than topoisomers may be separating. Some components may be conformers which interconvert slowly on the electrophoresis time scale. High-resolution separations of plasmid topoisomers or conformers have not been attained in solutions of random polymers, to our knowledge.

3.3. Oligonucleotides

CGE separations of moderate length oligonucleotides in Pluronic F127 were exceptional. Optimum single base resolution of T_{19-24} standards in a 30 cm capillary ranged from 2.6 to 3.3 for CGE in 25% Pluronic at 30°C, while optimal resolution between T_{12-18} standards ranged from 3.9 to 4.5 [19,28]. This high resolution is also reflected in the separation of poly U shown in Fig. 6. In addition to the expected oligomers differing by a single base, two classes of

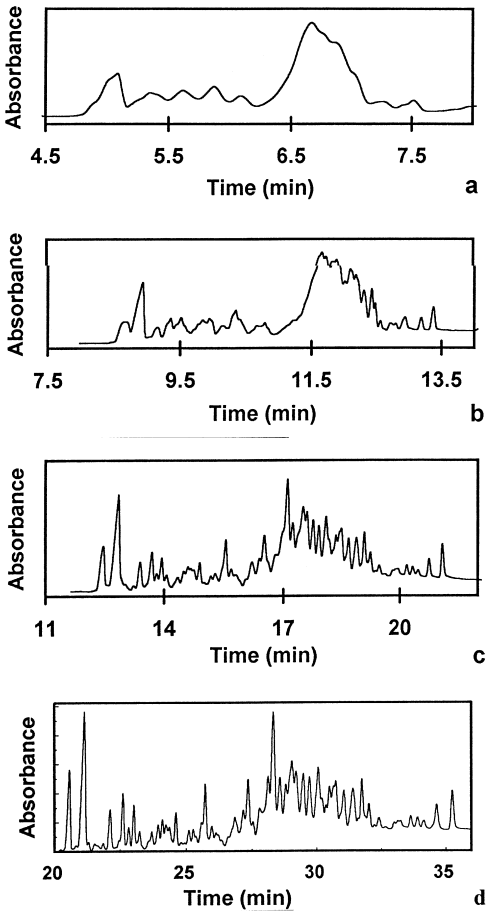

Fig. 5. Separation of supercoiled DNA plasmids by capillary gel electrophoresis in Pluronic gels. The standard from Promega contains nine plasmid DNAs from 2 to 10 kbp in length, differing by 1 kbp. The 5-kbp plasmid was supplied at about 3–4 times the abundance of other species. Progressive improvements in resolution are shown in frames (a) to (d). (a) Low-resolution electrophoresis in 25% Pluronic F127 (25°C, 300 V/cm, effective column length: 6 cm). (b) 25% Pluronic F127 (25°C, 300 V/cm, effective column length: 20 cm). (c) 30% Pluronic F127 (25°C, 500 V/cm, effective column length: 20 cm). (d) 30% Pluronic F127 (25°C, 500 V/cm, effective column length: 30 cm).

impurities were detected migrating between oligomers from 15 to 27 nucleotides (nt) long. As was found with double stranded DNA [19], the size separation range of oligonucleotides in 20–25% Pluronic seemed to be short, extending from about 4 to 60 nt. Fortunately the range of superior resolution includes the ≈20 nt to 35 nt size range most

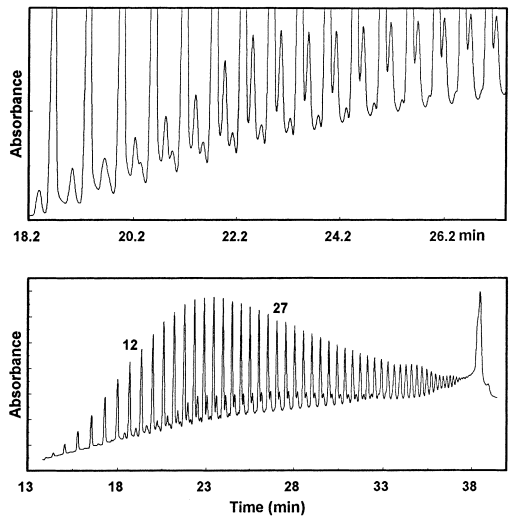

Fig. 6. Bottom: CGE separation of components of ''poly U'' (Sigma) in 25% Pluronic F127. Top: Note the resolution of two contaminants between each of the oligonucleotides from about 15–27 nt long in this expanded section of the bottom electropherogram. Electrophoresis was performed in 25% Pluronic F127 in TBE buffer (25°C, 500 V/cm, effective column length 30 cm).

commonly used for DNA sequencing primers and therapeutic oligonucleotides.

3.4. Amphiphilic small molecules

Strong retention of bromophenol blue ''tracking'' dye was noted during conventional electrophoresis on Pluronic gels. Subsequently a series of singly charged cationic dyes (acridine orange, ethidium, methylene blue, toluidine blue, uniblue) were separated by conventional electrophoresis in 20% Pluronic in Tris–borate–EDTA buffer (pH 8.3) and in 50 m*M* acetate buffer adjusted to pH 5.0 with Tris (not shown). Excellent separations of smaller deoxynucleoside monophosphates (dNMPs) were obtained by CGE in 30% Pluronic F127 in 1×TBE buffer. The four common dNMPs were resolved well beyond baseline within 19 min on a 30 cm column. (Fig. 7). Optimization can considerably shorten the analysis time. At this pH all dNMPs carry the same charge, hence separations must depend on other molecule features. Electrophoretic mobilities decreased in the order dCMP>TMP>dAMP>dGMP.

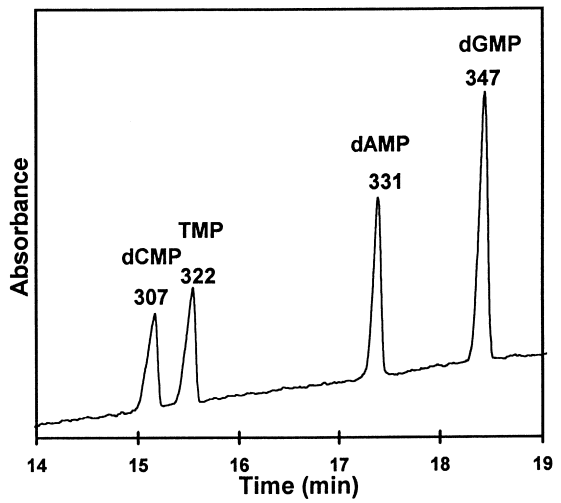

Fig. 7. Separation of deoxynucleoside monophosphates (dNMPs) in 30% Pluronic F127. Molecular masses of the dNMPs are indicated below the abbreviations. Electrophoresis was performed in Pluronic F127 in TBE buffer (25°C, 500 V/cm, effective column length 30 cm).

The band spacing between TMP and dAMP was much greater than between dCMP and TMP, or between dAMP and dGMP. This spacing pattern is consistent with the relative hydrophobicities of the bases, and not with the differences in molecular masses.

4. Discussion

Liquid crystalline ''gels'' of Pluronic F127 are easily and effectively used for CGE. They are also extremely versatile. A single medium at one concentration is not expected to provide high-performance separations of molecules as diverse as nucleoside monophosphates, organic dyes, oligonucleotides to 60 nt, double stranded DNA fragments to 750 bp, and supercoiled plasmid DNAs to 10 kbp. Pluronic gels can do this. All these separations have been done on 25% Pluronic F127, although the gel concentration for optimal separations with a given analyte class may be somewhat higher or lower. Preliminary studies have indicated that native proteins and sodium dodecyl sulfate (SDS)-coated proteins can also be separated with high resolution in 20–25% Pluronic F127 gels ([29] see also Ref. [18]).

How can such diversity be generated? We suggest that much is determined by the tripartite structure of Pluronic liquid crystals defined by the hydrophobic micelle cores, hydrated brushes, and interbrush domains (Fig. 1) [19]. Amphiphilic small molecules almost certainly interact with hydrophobic cores, since Pluronics are cleansing, emulsifying and drug delivery agents. The process of separation by equilibration between aqueous and hydrophobic domains during electrophoretic transport might appropriately be termed ''hydrophobic interaction electrophoresis'' (HIE or CHIE).

Highly charged nucleic acids are not expected to penetrate the hydrophobic cores, but can be sieved as they move within or between the hydrated brushes of $(EO)_x$ polymer chains that extend away from the core. The precise mechanisms of sieving of semiflexible, single and double stranded nucleic acids in Pluronic gels are uncertain. Simple considerations lead to the conclusion that sieving in polymer liquid crystals must be different from sieving in crosslinked polymer gels or entangled solutions of random polymers. Small nucleic acids are thought to separate in random polymer media by Ogston sieving, while longer nucleic acids separate by reptation when their effective radii are larger than the average pore size [30–33]. Very long molecules no longer separate according to length as they frequently ''hook'' on polymer fibers and stretch in the field [30–33]. Gel fiber dimensions, pore size distribution, frictional resistance of the gel matrix, and responses of the gel matrix to passage of the nucleic acid are not considered in most models of sieving through conventional random polymer media. These factors must play important roles in the migration of nucleic acids through Pluronic gels.

When migrating through Pluronic gels, nucleic acids must travel around and between large, spherical obstacles. The pore size distribution in Pluronic gels is intrinsically bimodal since accessible volume elements occur within two distinctly different, but interconnected structures – the intrabrush and interbrush domains. The spaces between $(EO)_x$ strands within the hydrophilic brushes are small, on the order of 0.5 to 2 nm [34]. These spaces should be accessible only to small or thin molecules, perhaps

including oligonucleotides. ''Thick'' molecules, including dsDNA in linear and supercoiled forms, must migrate through the interbrush regions and interstices between micelles (Fig. 1).

Unlike the case of random polymer gels, geometry and packing requirements dictate that there cannot be continuous pathways or ''tubes'' in ≥20% Pluronic F127 gels which can fit, without substantial contact, molecules with the stiffness and effective diameter of dsDNA. In other words, dsDNA cannot move without distorting the gel structure (micelle brushes) and experiencing frictional drag from these distortions. On the other hand, DNA chains should be able to slide around the uncrosslinked micelles. For these reasons the simple reptation model and concepts such as hooking do not seem appropriate for describing migration of dsDNA in Pluronic gels. Indeed, the observed functional form of the dependence of dsDNA mobility on length is consistent with a reptation model over only a very short length range (Fig. 4, see also Refs. [19,20]).

A comparison of some of the features distinguishing Pluronic liquid crystals from conventional media used for CGE is given in Table 2. The discovery of hydrogel media which differ substantially from conventional molecular sieving media offers new opportunities for optimizing separations. To date, Pluronic F127 gels appear uniquely suited for superior CGE separations of oligonucleotides up to about 40 nt [19,28], and supercoiled plasmids to at least 10 kbp. HPCE separations of this size oligonucleotides are of special interest in biotechnology because of the expanding importance of PCR primers and oligonucleotide therapeutics [35,36]. Pluronic F127 gels in capillaries are more easily replaced than the concentrated solutions of random polymers required to provide highest performance separations of modest length oligonucleotides [2]. Ease of replaceability is a major consideration for highly automated CGE or related microchip technologies. High-performance CE separations of supercoiled plasmids, now achievable in Pluronic gels, may be important to gene therapy. The proposed ''hydrophobic interaction electrophoresis'' mode of separating small molecular ions deserves more investigation and comparison to capillary zone electrophoresis (CZE) and capillary electrochromatography (CEC). A major virtue of Pluronic F127 gels for some laboratories may be the ability to analyze a variety of analytes using the same medium with little or no change in medium concentration or other conditions.

Possible applications of Pluronic liquid crystals have barely been tapped. The wide variety of commercially available Pluronic and related liquid crystal-forming block copolymers offer many opportunities for optimizing specific separation parameters. The micelle geometries and dimensions of the hydrophobic and hydrophilic domains of liquid crystal phases are determined by the Pluronic composition. Properties of a given Pluronic can be tuned over narrow ranges by adjustments in concentration and temperature [18,24]. Much also remains to be discovered about relationships between structure and separation mechanisms on Pluronic liquid crystals. These unique media pose both challenges and opportunities for separations science.

Table 2
Comparison of solutions of random coil polymers and Pluronic liquid crystals for CGE

Polymer solutions	Pluronic liquid crystals
Structure random, thin fibers	Structure regular, thick elements
Single disordered phase	Several ordered phases
Limited choice of materials	Extensive choice of materials
Continuous pore size distribution	Bimodal pore size distribution
Moderate selectivity over broad size ranges	Enhanced selectivity over narrow size ranges
High viscosity polymer solutions	Low viscosity polymer solutions
Some solutions not easily replaced	''Gels'' easily replaced
Little temperature effect	Structure tunable by temperature
Weak non-covalent interactions	Strong hydrophobic interactions
Single format (CE)	Dual formats (CE and micro-preparative)

Acknowledgements

We thank Dr. Leonore C. Witchey-Lakshmanan (Schering-Plough Research Institute, Kenilworth, NJ, USA) for bringing our attention to the Pluronic polymers. We also thank Dr. William Cooper (Florida State University) and Beckman Instruments for generously providing access to capillary electrophoresis equipment. This work was supported in part by NSF grant BES-951381 and the FSU Center for Materials Research and Technology (MARTECH).

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