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COMMUNICATION

## Orthogonal alignment of DNA using hexafluoroisopropanol as solvent for film castings

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The use of the fluorinated alcohol, 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP) as a processing solvent for orthogonal alignment of DNA-surfactant complex is reported herein. 1-butanol (BuOH) was used as the control. At low frequencies, films of DNA-CTMA cast from HFIP exhibited higher, more consistent dielectric constant and lower dissipation factor compared to films cast from BuOH.

Deoxyribonucleic acid (DNA), an anionic polyelectrolyte, has been shown to form a highly organized assembly with cationic surfactants that is soluble in alcohols, chloroform, hexane, benzene and/or a mixture of such.<sup>1</sup> The sudden growth of research in this area commenced with the report of Okahata<sup>1e</sup> on the complex formation of DNA with the synthetic cationic amphiphile, *N,N,N*-trimethyl-*N*-(3,6,9,12-tetraoxadocosyl) ammonium (TTOA). The DNA-TTOA complex was found to be soluble in most polar organic solvents and could be cast into films. With the purpose of finding a simpler method for preparing high quality films of DNA-cationic surfactant complexes, Wang, *et al.*,<sup>2</sup> focused on using commercially available cationic surfactants that had a sixteen carbon (C<sub>16</sub>) alkyl tail. These surfactants imparted mechanical properties to give the DNA-surfactant complex quality film and fiber formation. In most literature reports, cetyltrimethylammonium (CTMA) is the most popular surfactant of choice.

Processing techniques such as spin-coating,<sup>3</sup> ink-jet printing,<sup>4</sup> doctor-blading, dip-coating, drop-casting and electrospinning<sup>5</sup> can be used to make films and fibers of DNA-CTMA with ethanol and butanol, being the most commonly used processing solvents.<sup>3a, 6</sup> Many of the material properties of DNA-CTMA such as electrical resistivity, transparency, optical loss, dielectric constant, band gap and index of refraction, were determined after casting from said solvents. In this study, the halogenated alcohol, 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP), was used as casting solvent and compared with butanol (BuOH). As mentioned earlier, there is fundamental understanding of DNA in BuOH and the respective material properties. Therefore, BuOH becomes a reasonable benchmark and control. HFIP is frequently used to process both synthetic and natural polymers. For example, HFIP has a long history of use in size-exclusion chromatography of crystalline polyesters and polyamides.<sup>7</sup> It has also been used to

electrospin poly( $\epsilon$ -caprolactone) as a bone grafting material<sup>8</sup> and polymethylmethacrylate and silk fibroin to make contact lenses.<sup>9</sup> In fact, recent reports use a similar system of processing DNA films from solutions of HFIP and BuOH for optical fiber waveguide applications, although, microstructure characterization was not evaluated<sup>10</sup>

Because of the unique material properties of DNA-CTMA, in addition to flexibility, light weight, low cost, low temperature processing, ease of fabrication and easily modifiable properties,<sup>11</sup> it has been incorporated in many optoelectronic devices such as organic light emitting diodes,<sup>6c</sup> quantum dots<sup>12</sup> and organic field-effect transistors.<sup>13</sup> We have also demonstrated its use as a matrix for dyes that resulted in fluorescence enhancement, fluorophore stabilization, and long-range Förster energy transfer.<sup>3b, 5, 14</sup> The dielectric properties of DNA-CTMA have also been characterized at the microwave frequencies using structures such as coplanar waveguides<sup>3a, 6a, 6b</sup> and variable capacitors.<sup>15</sup>

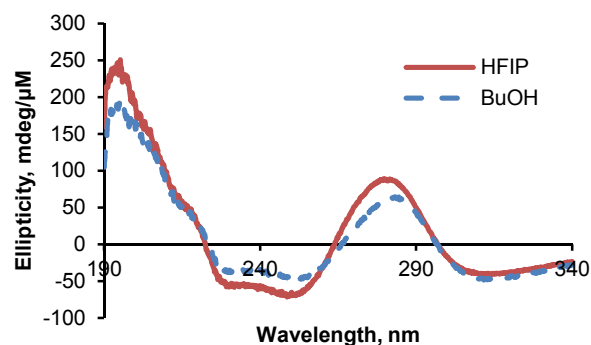


Fig. 1 Circular dichroism spectra of DNA-CTMA films deposited from solution in HFIP (—) and BuOH (---). ‡

The DNA conformation is affected by its environment. Circular dichroism (CD) was used to confirm that the DNA double-helix configuration is kept intact after casting from the solvents used. Figure 1 shows the characteristic CD spectra of the B-conformation of DNA in the DNA-CTMA films cast from both solvents. The CD spectrum of DNA-CTMA cast from HFIP showed a negative band at about 249 nm and a positive band at about 280 nm while that cast from BuOH exhibited a negative band at about 253 nm and a positive band at about 283 nm. As

such, films from HFIP yielded slightly blue-shifted and more intense CD signals than those deposited from BuOH. Although the DNA assumes a B-conformation in both solvents, there could be some slight structural differences, *e.g.*, distance between base pairs and number of bases per helical turn. In literature, the addition of methanol to an aqueous solution of calf thymus DNA changed the B form from 10.4 bases pairs per turn to 10.2 base pairs per turn and lowered the dielectric constant.<sup>16</sup> From this, it can be inferred that there was an increase in the spacing between the stacked DNA bases. It must be noted, however, that in this study, the DNA is encased in CTMA layers, which plays a significant role in the solvent interaction and DNA structure.

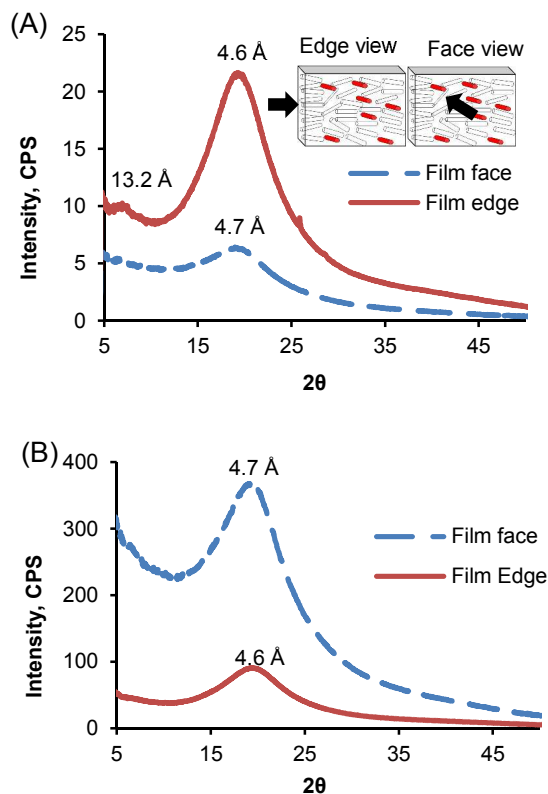


Fig. 2 Wide-angle X-ray diffraction of DNA-CTMA films deposited from HFIP (A) and BuOH (B).

Figure 2 shows one-dimensional wide-angle X-ray diffraction (WAXD) measurements of DNA-CTMA films with the incident X-ray beam oriented both perpendicular, “face view”, and parallel to the face, “edge view”, of the material. Both systems show broad but noticeable diffraction intensity from  $2\theta \approx 10^\circ$  to  $20^\circ$  due to the DNA base pair spacing. Base pair spacing from face and edge view,  $\sim 4.7 \text{ \AA}$  and  $4.6 \text{ \AA}$ , respectively, remain the same when using either solvent. Base pair spacing is slightly smaller, from edge view, indicating that the structure is more compact. Base pair spacing can change slightly as it has been reported right-handed helical DNA structures can vary  $0.2 \text{ \AA}$  due to the amount of water present.<sup>17</sup> A much weaker diffraction peak is seen,  $2\theta \approx 7^\circ$ , *ca.* d-spacing  $\approx 13 \text{ \AA}$ , which is likely the average diameter within a DNA double helix.<sup>18</sup> When using BuOH, stronger diffraction intensity is present from the face view, whereas HFIP, exhibits a stronger diffraction intensity from the edge view.

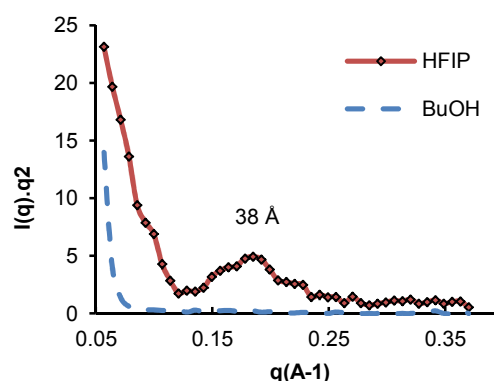
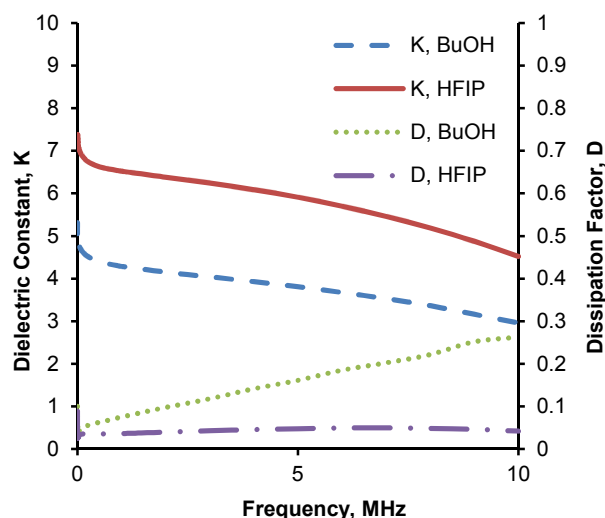


Fig. 3 Small-angle X-ray scattering of DNA-CTMA films deposited from HFIP (—) and BuOH (- - -).

Due to the different spacing observed face-on and edge-on, these results likely suggest a preferred orientation in both systems, although, orthogonal to one another. In HFIP, DNA-CTMA appears to align out of plane from the film surface while DNA-CTMA in BuOH aligns along the plane. To confirm this, small-angle X-ray scattering (SAXS), shown in Figure 3, was performed. Note that diffraction is seen from HFIP,  $q (\text{A}^{-1}) \approx 0.20$ , which corresponds to *ca.*  $38 \text{ \AA}$  inter-strand distances between DNA-CTMA, which cannot be seen with BuOH. This indicates that long range structural ordering is present in the HFIP system. Yang, *et al.*, reported a larger inter-strand distance of  $41 \text{ \AA}$  for stretched films of DNA-CTMA films exposed to water and a smaller,  $36 \text{ \AA}$ , for dried samples.<sup>19</sup>

To our knowledge, we are the first to report the use of HFIP as a processing solvent that gives orthogonal alignment to DNA-CTMA. Interestingly, as a result of this alignment, improved dielectric behaviour was observed for films of DNA-CTMA cast from HFIP versus BuOH as shown in Figure 4. In the frequency range  $10^{-3}$  to  $10^7$  Hz, the dielectric constant,  $K$ , values of DNA-CTMA cast from HFIP ( $K \approx 5-7$ ) were about two units higher than those cast from BuOH ( $K \approx 3-5$ ). However, for both solvents, the dielectric constant decreased as the frequency increased. The dissipation factor was lower for HFIP than BuOH. Across the said frequency range, the dissipation factor ( $\sim 5\%$  D) of the films showed a fairly constant behaviour when cast from HFIP, however, from BuOH, there was a linear increase in the dissipation factor ( $\sim 8$  to  $26\%$  D) as the frequency increased.



**Fig. 4** Dielectric constant and dissipation factor of DNA-CTMA films cast from HFIP and BuOH at various frequencies.

In a literature report, it was found that alkyl and halogenated alcohols have varying degrees of inducing an  $\alpha$ -helix conformation to the proteins  $\beta$ -lactoglobulin and melittin.<sup>20</sup> Halogenols, such as HFIP, were found to have stronger  $\alpha$ -helix conformation inducing property than alkanols, such as BuOH. This effect is increased significantly in the presence of multiple halogens. Since DNA also has a helical conformation, a similar approach was taken to understand the effects and interaction of the alcohols to the DNA-CTMA in this study.

Stronger H-bonding is expected between HFIP and DNA-CTMA in comparison to BuOH. According to Kamlet-Taft solvent parameters, HFIP ( $\alpha = 1.96$ ) is a stronger H-bond donor than BuOH ( $\alpha = 0.84$ ). Inter- and intra-strand H-bonding between and within DNA chains is more disrupted in HFIP, which effectively solvates the DNA-CTMA and promotes a more expanded conformation. Furthermore, alkyl tails of alkanols tend to aggregate. The alkyl chains of the BuOH will associate more strongly with the CTMA phase of the DNA-CTMA, thereby reducing the chance of H-bonding and hindering the effective solvation of the DNA chains. It was previously reported that DNA-CTMA adapts a globular conformation in high concentrations of alcohols such as ethanol and butanol. The CTMA molecules construct a globule-like structure around the DNA mediating its dissolution.<sup>21</sup> DNA-CTMA has a less expanded conformation in BuOH than in HFIP. As the film dries, a different orientation of the DNA-CTMA strands is expected in HFIP than from BuOH. The interaction between HFIP and DNA can potentially be causing DNA to align out of plane as well. Similar to what was reported by Hiszpanski and Loo,<sup>22</sup> a preferred molecule-solvent, as opposed to molecule-substrate, interaction can potentially be occurring causing this particular kind of molecular orientation. Future studies will need to be done to evaluate surface energy effects of substrates on molecular orientation.

Materials have varying degrees of response to an applied electric field and involve the redistribution of component charges (electrons and protons) to some degree in the material, with negative charges being attracted towards the positive electrode and vice versa. This polarization effect, greatly affects the

dielectric behaviour of a material. At the molecular level, polarization has three components: (1) electronic polarization, wherein an electric field causes a slight displacement of the electrons of any atom with respect to the positive nucleus, (2) atomic or ionic polarization, which involves the distortion on the arrangement of atomic nuclei or ion in the molecule or lattice due to the electric field, and (3) dipolar polarization, where molecules with permanent dipole moments are aligned with respect to the applied electric field resulting in a net polarization.<sup>23</sup> The difference in dielectric behaviour of DNA-CTMA films cast from HFIP and BuOH is explained by looking at the molecular polarization dominated by the dipole orientational component at the frequency range of interest.

Two main structural features appear to be responsible for the improved dielectric properties. Having a compact base pair stacking when DNA-CTMA aligns perpendicular to the film surface could possibly allow 1-D electronic charge transport through  $\pi$ - $\pi$  stacking of the base pairs. Also, as Takashima<sup>24</sup> reported, the direction of the dipole moment in DNA is longitudinal rather than transverse, particularly in DNA with high molecular weight. These rod-like DNA-CTMA structures aligning out of plane provide a larger contact area on both sides of the film and more importantly, align in the direction of applied electric field between electrodes that are placed on each side of the film face. This alignment of the net dipole moment makes it easier for the material to recover from oscillations induced by the applied electric field, which in turn results in an increase in dielectric constant. Energy is also dissipated, usually in the form of heat, when the dipoles attempt to align with the changing electric field. In HFIP, DNA strands are oriented perpendicular to the substrate but parallel to the applied electric field. This makes it easier for the dipoles to align with the changing electric field, thereby resulting in a lower and constant dissipation factor when DNA is cast from HFIP than from BuOH.

In conclusion, by simply changing the solvent from BuOH to HFIP results in orthogonally oriented DNA chains having a B-conformation with similar base pair spacing. Strands of DNA-CTMA align out of phase with respect to the film surface in HFIP while in BuOH, the alignment is along the film surface. In HFIP, the dipole moment of the DNA-CTMA is parallel to the applied electric field. Hence, the dielectric properties of DNA-CTMA films in the frequency range  $10^{-3}$  to  $10^7$  Hz improved significantly using HFIP versus using BuOH. This material is foreseen to have useful applications as electrical and electronic components such as capacitors, varactors, transistors, as well as optoelectronics.

## Notes and references

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‡ CD signals also show the presence of proteins adopting a  $\alpha$ -helix conformation between 190 nm and 250 nm, which overlaps with the DNA signal.



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