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Measuring the micro-polarity and hydrogen-bond donor/acceptor ability of thermoresponsive *N*-isopropylacrylamide/*N*-tert-butylacrylamide copolymer films using solvatochromic indicators.

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ABSTRACT

Thin polymer films are important in many areas of biomaterials research, biomedical devices, and biological sensors. The accurate, in-situ, measurement of multiple physicochemical properties of thin polymer films is critical in understanding biocompatibility, polymer function, and performance. In this work we demonstrate a facile, spectroscopic methodology for accurately measuring the micro-polarity and hydrogen-bond donor/acceptor ability for a series of relatively hydrophilic thermoresponsive copolymers. The micro-polarity of the *N*-isopropylacrylamide (NIPAM) and *N*-tert-butylacrylamide (NtBA) co-polymers was evaluated by means of the $E_T(30)$, α , β , and π^* empirical solvatochromic polarity parameters. The data shows that increasing the NtBA fraction in the dry copolymer film reduces polarity and hydrogen-bonding ability. Within the Kamlet-Taft polarity framework, the NIPAM/NtBA copolymer films are strong hydrogen-bond acceptors, strongly dipolar/polarisable, and rather moderate hydrogen-bond donors. This characterization provides a more comprehensive physicochemical description of polymers, which aids the interpretation of film performance. Comparison of the measured $E_T(30)$ values with literature data for other water-soluble polymers show that dry NIPAM/NtBA copolymers are slightly more polar than poly(ethylene oxide), less polar than polyvinylalcohol, and approximately the same polarity as poly(*N*-vinyl-2-pyrrolidone). These findings indicate that this spectroscopic method is a facile, rapid, and non-destructive methodology for measuring polymer properties in-situ, suitable for most biomaterials research laboratories.

INDEX HEADINGS: Thermoresponsive copolymer films; *N*-isopropylacrylamide, *N*-tert-butylacrylamide; Polarity; Solvatochromism;

1. INTRODUCTION

Micron scale thin polymer films are a key technology area in modern medical device manufacturing. In particular, significant interest is being invested in designing medical devices coated with drug-eluting polymers, for example to achieve local delivery of potential anti-restenosis therapy.¹ The choice of polymer is very important, as device efficacy is determined by the elution profile, coating stability, and other parameters, which are directly related to the physicochemical properties of the polymer coating. One area of current activity is in the area of stimuli-responsive polymers, where polymer properties can be modulated by external factors, *e.g.* temperature, light, or pH.²⁻⁷

Poly(*N*-isopropylacrylamide) (pNIPAM) is one of the most widely studied temperature responsive polymers. Its suitability for drug delivery applications arises from the fact that it undergoes a reversible and sharp, coil-to-globule transition in water at 32 °C.² Thus, drugs or therapeutic agents may be loaded into the polymer matrix at lower temperature and can then diffuse out at the higher body temperature when deployed due to the morphological change in the polymer structure. The temperature at which the phase transition occurs, the Lower Critical Solution Temperature (LCST) can be adjusted for specific biomedical applications by the introduction of hydrophilic or/and hydrophobic groups to the pNIPAM chain.⁸⁻¹¹ The properties of these polymer types can be further engineered for multi-parameter responses (temperature and pH) by copolymerization with ionisable co-monomers.^{12,13} Copolymers of *N*-isopropylacrylamide (NIPAM) and *N*-tert-butylacrylamide (NtBA) with different NIPAM to NtBA molar ratios are one model where the polymer structure has been modified to mediate LCST behavior. These NIPAM/NtBA copolymers are currently being investigated as potential drug elution matrices and for cell culture applications.¹⁴⁻¹⁶

To better understand the physicochemical performance of these hydrophilic polymers it is necessary to accurately measure the polarity of these materials. Polarity in its broadest sense will impact on aspects of polymer behavior such as water uptake, processability, surface energy, drug elution profiles, and mechanical properties. Polarity is a complex phenomenon and therefore it cannot be described quantitatively by any single physical parameter.¹⁷⁻¹⁹ The measurement of polarity is difficult and is usually implemented using optical spectroscopy methods where various empirical polarity scales have been established in order to characterize quantitatively all types of solvent-solute interactions.²⁰ From these scales, the most widely used and well-established are those based on solvatochromic measurements, *i.e.* $E_T(30)$ scale of Dimroth and Reichardt,^{21,22,23} α (hydrogen-bond donor) and β (hydrogen-bond acceptor) scales of Kamlet and Taft,²⁴ and π^* (dipolarity / polarizability) scale of Kamlet, Abboud, and Taft.²⁵ These scales utilize the shift of the

longest wavelength UV-Vis absorption band maximum in the absorption spectrum of various solvatochromic indicators, caused by the differential solvation of the solute molecule in the excited and the ground states. In analogy to solvents, Harris *et al.*^{26,27} showed that empirical polarity parameters for solid polymers can be obtained by measuring the electronic absorption spectra of carefully selected solvatochromic indicators when molecularly dispersed in polymers. This spectroscopic methodology is therefore well suited to either hydrophilic or hydrophobic polymers; furthermore because it is an optical method, the scope exists to apply the measurement to micrometer or millimeter size scales, and under different environmental conditions. Understanding the polarity behavior in detail of thin polymer films is important from the standpoint of fully understanding how films will behave in many biomedical applications. For example, changes in polarity will have significant impact on the water uptake and retention rates in polymers, which in turn affect the mechanical and chemical properties.

In this work, UV-visible absorption spectroscopy was used to assess the micro-polarity of dry NIPAM/NtBA copolymer films by means of the $E_T(30)$, α , β , and π^* empirical solvatochromic polarity parameters. We use the term micro-polarity in this context to represent the location of the probes within the polymer matrix, since there is a possibility that the probes can be located in a variety of different sites within these co-polymer systems. To our best knowledge, no previous work on direct measurements of the solvatochromic polarity parameters for polymer films of this type have been carried out. It is shown that the method is a useful non-invasive tool to assess not only the micro-polarity, but also the hydrogen-bonding and dipolarity/polarizability of hydrophilic polymers. Furthermore, it is a procedure that can easily be adapted to operate under a wide variety of environmental conditions, offering clear insights into (and rapid monitoring of) changes in thin polymer film properties under physiological conditions.

2. EXPERIMENTAL

2.1. Materials.

Reichardt's betaine dye 2,6-diphenyl-4-(2,4,6-triphenylpyridinium-1-yl)phenolate (I), 4-nitroanisole (III), 4-nitroaniline (IV), and ethanol of spectroscopic grade were purchased from Sigma-Aldrich. *N,N*-dimethyl-4-nitroaniline (II) was obtained from Acros Organics. All probes were used as received without further purification.

2.2. Copolymer synthesis.

N-isopropylacrylamide (NIPAM) (97%, Aldrich) and *N*-tert-butylacrylamide (NtBA) (purum, Fluka Chemie, Switzerland) were recrystallized from *n*-hexane and acetone, respectively. 2,2'-Azobis(2-

methylpropionitrile) (Phase Separation Ltd., U.K.) was recrystallized from methanol. All solvents were reagent grade and were purified before use.²⁸ A series of copolymers of *N*-isopropylacrylamide (NIPAM) and *N*-tert-butylacrylamide (NtBA) with ratios (w/w) of 100:0, 85:15, 65:35, and 0:100 were synthesized as described previously.²⁸ The chemical structure of the copolymers is shown in Figure 1.

2.3. Thin film preparation.

If a polymer film is to be used as a drug eluting coating then it must be of sufficient thickness to accommodate a therapeutic amount of a drug. It is generally accepted that a minimum thickness of approximately 5 to 10 μm is necessary to facilitate adequate loading of therapeutic agents into the polymer coating.²⁹ In our case, a casting method was used to make films of $\sim 10\ \mu\text{m}$ (after drying) in thickness. Quartz slides 12 mm x 45 mm x 1.5 mm (Lightpath Optical Ltd, UK) were used as a solid substrate to support the copolymer films. The slides were sonicated in deionised water for 15 minutes, washed at least three times with deionised water, acetone, and methanol, and dried in an oven at 70 °C before use. A weighed amount of the solid copolymer (5.4 mg) was dissolved in 137.5 μL of a 1×10^{-3} M ethanol solution of the requisite solvatochromic indicator. The prepared solution was then carefully spread on a quartz slide and the films were cured for 24 hours in a sealed environment with a source of ethanol. The ethanol was present to saturate the atmosphere above the polymer film and help prevent ingress of water into the film during curing. After 24 hours, the copolymer films were removed from the ethanol environment and placed into an oven at 70 °C for 48 hours to complete the drying process. The films thus obtained were transparent, smooth, and free of any physical inhomogeneities as verified under an optical microscope. The weight ratio of copolymer to dye for the dry films was calculated to be 100:1.4 for indicator (I), 100:0.42 for indicator (II), 100:0.39 for indicator (III), and 100:0.35 for indicator (IV). In general, the dye content in the film was approximately three times lower than that reported in the original work by Harris *et al.*²⁶ and 5-10 times smaller than reported elsewhere.³⁰ These low concentrations should ensure that there is minimal disruption to the native copolymer structure.

2.4. UV/Vis absorption measurements.

Absorption spectra of the copolymer films were recorded on a Varian Cary 50 spectrometer fitted with a temperature-regulated cuvette holder (CUV-TLC-50F, Quantum Northwest.). All measurements were made in triplicate at 20 °C and the reproducibility of recorded spectra was within 0.5 - 1 nm. The mean of the maximum wavelength values were used for the calculation of the polarity parameters. Data analysis and band fitting was carried out using the Origin software package. In the case of Reichardt's betaine dye-doped copolymer films, where spectra were found to

be very noisy, determination of the band maxima (λ_{\max}) and the Full Width Half Maximum (FWHM) of the absorption band was improved by using a Gaussian curve-fitting procedure. The absorption spectra of the solvatochromic indicators in polymer films (and hence the polarity parameters) are sensitive to water content and therefore, to prevent uptake of atmospheric moisture,^{26,27} all measurements were made with dry nitrogen gas passing through the cuvette holder.

2.5. Calculation of the empirical polarity parameters.

The $E_T(30)$ polarity parameter was calculated from the longest-wavelength UV-vis absorption band maximum of Reichardt's betaine dye (I) using Equation 1.^{22,26} Note that in this equation and from now on, $\tilde{\nu}_{\max}$ is reported in units of a 1000 wavenumbers units (1000 cm^{-1}).

$$E_T(30)[kcal.mol^{-1}] = 2.859 \times \tilde{\nu}_{\max}(I) \quad (1)$$

Dipolarity/polarizability (π^*), was determined from the longest-wavelength absorption band maxima of *N,N*-dimethyl-4-nitroaniline (II) and 4-nitroanisole (III) using Equation 2 and Equation 3 for indicators (II) and (III) respectively.^{25,26,31,32}

$$\pi_{(II)}^* = 8.0060 - 0.2841 \times \tilde{\nu}_{\max}(II) \quad (2)$$

$$\pi_{(III)}^* = \frac{\tilde{\nu}_{\max}(III) - 34.12}{-2.40} \quad (3)$$

The hydrogen-bond donor (α) ability was calculated from the longest-wavelength absorption band maxima of *N,N*-dimethyl-4-nitroaniline (II) or 4-nitroanisole (III) (poor hydrogen-bond bases) and Reichardt's betaine dye (I) (a good hydrogen-bond base) using Equation 4 for indicator pair (II)/(I), and Equation 5 for pair (III)/(I).^{26,32,33}

$$\alpha_{(II)/(I)} = \frac{\tilde{\nu}_{\max}(I) + 1.318 \times \tilde{\nu}_{\max}(II) - 47.70}{5.47} \quad (4)$$

$$\alpha_{(III)/(I)} = \frac{\tilde{\nu}_{\max}(I) + 1.873 \times \tilde{\nu}_{\max}(III) - 74.58}{6.24} \quad (5)$$

The π^* scale was originally constructed using several probes and averaging over several indicators and was recommended by Kamlet-Taft to reduce the contributions arising from solvent effect or spectra anomalies specific to any one probe. However, averaging over several solvatochromic probes has been recently criticized for masking physically meaningful differences in chemistry of the probes.^{34,35} In this work, both indicators, II and III are used independently to evaluate dipolarity/polarizability properties of the medium and the average π^* values are reported.

The hydrogen-bond acceptor (β) property was determined from the longest-wavelength absorption band maxima of 4-nitroaniline (IV) (a good hydrogen-bond acid) and *N,N*-dimethyl-4-nitroaniline (II) (a poor hydrogen-bond acid) using Equation 6.^{26,36}

$$\beta = \frac{0.984 \times \tilde{\nu}_{\max}(\text{II}) - \tilde{\nu}_{\max}(\text{IV}) + 3.40}{2.67} \quad (6)$$

A variety of research groups have developed empirical correlations between Reichardt's $E_T(30)$ values and Kamlet-Taft parameters for both polymers³⁷ and solvents.^{38,39} Marcus^{38,39} has shown that for liquid solvents the $E_T(30)$ polarity parameter can be expressed in terms of the α and π^* parameters using a linear solvation energy relationship:

$$\begin{aligned} E_T(30) &= 31.2 + 15.2\alpha + 11.5\pi^* \\ n &= 166, r = 0.979, SD = 2.1 [kcal \cdot mol^{-1}] \end{aligned} \quad (7)$$

where n is the number of solvents, r is the correlation coefficient, and SD is the standard deviation. From the ratio of the coefficients in Equation 7 ($15.2 / 11.5 = 1.32$) it is clear that the hydrogen-bond donor (HBD) capacity (α parameter) of solvents contributes more strongly to the $E_T(30)$ value than the dipolarity/polarizability term (π^*), at least for HBD solvents.

A more detailed treatment (Equation 8) that incorporates a solvent polarizability correction term δ can also be applied:^{39,40}

$$\begin{aligned} E_T(30) &= 30.80 + 14.51\alpha + 13.68(\pi^* - 3.45\delta) \\ n &= 100, r = 0.984 \end{aligned} \quad (8)$$

where δ is 1.0 for aromatic, 0.5 for polyhalogenated aliphatic, and 0 for other solvents.

A modified scale for polymers was also proposed by Spange and co-workers from a correlation of experimentally obtained $E_T(30)$ parameters with independently determined α and π^* values for 23 different polymers:³⁷

$$\begin{aligned} E_T(30) &= 40.128 + 10.95\alpha + 3.55\pi^* \\ R &= 0.950, SD(E_T(30)) = 2.177, n = 23, \end{aligned} \quad (9)$$

3. RESULTS AND DISCUSSION

3.1. The $E_T(30)$ polarity parameter of poly(NIPAM-co-NtBA) films.

Figure 2 shows representative UV/Vis absorption spectra of Reichardt's betaine dye (I) dispersed in poly(NIPAM-co-NtBA) films. To facilitate comparison, the data were normalized to the maximum of the longest-wavelength absorption band. All of the spectra exhibit a single well-defined intramolecular charge-transfer (ICT) band and the position of this band depends strongly on the film composition; as the NtBA content increases the ICT band shifts toward longer wavelength. The λ_{\max} (Figure 3a) and Full Width Half Maximum (FWHM) of the absorption band (Figure 3b) plots show that the ICT band is red-shifted to longer wavelength and becomes broader with increasing NtBA fraction. The $E_T(30)$ values for the poly(NIPAM-co-NtBA) films calculated according to Equation 1 are plotted in Figure 4, which shows that increasing NtBA fraction reduces the overall micro-polarity.* The probe (I) has a highly dipolar zwitterionic ground state but its excited state is significantly less dipolar, so a red-shift in the absorption spectra indicates that in general the probe (I) is located in less polar environments. The broadening of the ICT band, however, indicates that the probe perceives a wider variety of microenvironments with subtly different polarities as the NtBA fraction increases. This is important because, although the gross polymer polarity decreases with NtBA fraction, the heterogeneity of the local microenvironment (polarity distribution) increases.³⁷ This is therefore a useful measure of film heterogeneity.

One of the main intermolecular interactions between the NIPAM/NtBA copolymers and (I) is formation of hydrogen-bonds between polymer N-H groups and the phenolate oxygen atom of the probe. Therefore, the drop in micro-polarity probably arises from more effective steric shielding of the amide groups (N-H groups) by tert-butyl groups than by isopropyl groups.¹⁶ Differences in the micro-polarity of the probes within the poly(NIPAM-co-NtBA) films could also be noticed visually as the pNIPAM films containing (I) appeared violet-blue whereas films of pNtBA were blue-green in color.

3.2. Dipolarity/polarizability (π^*) of poly(NIPAM-co-NtBA) films.

N,N-dimethyl-4-nitroaniline (II) and 4-nitroanisole (III) were used to probe the dipolarity / polarizability (π^* parameter) of the poly(NIPAM-co-NtBA) films. The position of the absorption maxima, $\tilde{\nu}_{\max}$, of (II) and (III) dispersed in the films of different composition are shown in Figure 5.

* In this work, polarity refers to the polarity of the sites in which the probes are located, i.e. the micro-polarity. This should correlate with bulk polarity of the polymer, however we cannot be sure that the probes are evenly distributed on a molecular scale within these copolymer films.

Increasing the NtBA fraction in the film results in the blue shift of $\tilde{\nu}_{\max}$ of both probes. It was observed that the signal to noise ratio of the absorption spectra was significantly lower in the case of (III) doped films than for the films with (II). This is attributed to the slightly lower concentration of (III) in the films in comparison to (II). Nevertheless, the π^* values obtained from both indicators are very similar (Figure 6) and it is clear that the NIPAM/NtBA copolymers films are strongly dipolar/polarisable. There is also a clear trend for a decrease in the π^* value with increasing NtBA fraction which can be explained by the increased steric effect of the tert-butyl groups with respect to isopropyl.

3.3. Hydrogen-bond donor ability (α parameter) of poly(NIPAM-co-NtBA) films.

The HBD ability (α parameter) of the poly(NIPAM-co-NtBA) films was estimated using two different pairs of solvatochromic indicators: *N,N*-dimethyl-4-nitroaniline/Reichardt's betaine dye, (II)/(I), and 4-nitroanisole/Reichardt's betaine dye, (III)/(I), and Equations 4 and 5, respectively. In Figure 7, the α values obtained with each pair are plotted as a function of NtBA content in the film. A pronounced decrease in the HBD ability of the poly (NIPAM-co-NtBA) films with increasing NtBA content is clearly seen for each indicator pair. We attribute this fact to better steric shielding of the copolymer's N-H groups by tert-butyl groups than by isopropyl groups.¹⁶ Due to an electron-donor inductive effect of the *N,N*-dimethylamino group, the basicity of indicator (II) is slightly higher than (III) and, as a consequence, is more sensitive to hydrogen-bonding. Therefore, the α values estimated with pair (II)/(I) are slightly higher than those obtained with (III)/(I). In the context of these co-polymers, the (II)/(I) pair gives a slightly wider range, and would be the recommended choice for routine measurements of relative changes in HBD ability.

3.4. Hydrogen-bond acceptor ability (β parameter) of poly(NIPAM-co-NtBA) films.

The hydrogen-bond acceptor (HBA) ability (β parameter) of the poly(NIPAM-co-NtBA) films was estimated using 4-nitroaniline (IV) (a good hydrogen-bond acid) and *N,N*-dimethyl-4-nitroaniline (II) (a poor hydrogen-bond acid) probes. The position of the absorption maxima, $\tilde{\nu}_{\max}$, of (IV) dispersed in the films of different composition is shown in Figure 8A. The β values calculated according to Equation 6 are plotted in Figure 8B and it is obvious that films of the NIPAM/NtBA copolymers have relatively high HBA ability compared to organic solvents. It also appears that in general, increasing the NtBA fraction in the film does not significantly affect its HBA ability. This experiment also indicates one of the significant difficulties with this type of absorption-based measurement, namely the very small spectral shifts involved. In figure 8 we note that the full spectral range is only ~ 5 nm and, with an error of ~ 1 -2 nm, this leads to a large degree

of uncertainty. This is further exacerbated by the probe being in a heterogeneous (on the microscale) polymer environment where there is a distribution of polarities.

3.5. Correlation of Reichardt's $E_T(30)$ values with Kamlet-Taft parameters.

To verify whether the absorption probes in the copolymers behave in a similar manner to solvents, semi-empirical $E_T(30)$ values for poly(NIPAM-co-NtBA) films were calculated from Equations 7, 8, and 9, using the experimentally derived α and π^* parameters (note that averaged values for α and π^* parameters were used). Figure 9 shows the plot of the calculated versus experimental $E_T(30)$ values, and it is clear that the model with the correction term (Equation 8) gives the best agreement between measured and calculated values. The data also fits reasonably well to Equation 7 (the differences between measured and calculated parameters ($\Delta E_T(30)$) do not exceed the value of the standard deviation given for the solvent model). This demonstrates the robustness and reliability of the calculated parameters (α , β , π^*), and also confirms that the behavior of these solvatochromic indicators in the poly (NIPAM-co-NtBA) films is similar to that in solvents. The slightly different slopes of the fits for the Equations 7 and 8 arises from the relative weighting between HBD and polarizability, with an α/π^* ratio of 1.06 (Equation 8) giving the best correlation. This clearly indicates that the $E_T(30)$ parameter is almost equally sensitive to the polarizability/dipolarity of the polymer as the HBD ability. The fit can be further improved by setting the delta correction term to 0.005, to correct for small polymer matrix effects.

The better fit achieved with equation 8 indicates that the high weighting of the polarizability factor (and incorporation of a correction term) is important for the accurate characterization of these polymer systems. This is supported by the poor correlation found with the polymer model proposed by Spange,³⁷ particularly with polymers of moderate polarity ($E_T(30) < 47$ kcal.mol⁻¹). The high α/π^* ratio of 3.08 (Equation 9) puts less emphasis on dipolarity/polarizability than HBD ability to explain the spectroscopic trends. For example, with aromatic polymers and these aromatic solvatochromic dyes there is a high potential for some form of π - π stacking,⁴¹ which is more probable in less polar polymers. This physical interaction will distort the absorption spectra of the solvatochromic dyes by both subtly changing the ground and excited electronic states of the dye and altering the hydrogen-bonding. While we do acknowledge that these polymers do not have any aromatic constituents, the strong measured dipolarity/polarizability of the polymer makes it possible that the dye molecules may be interacting with hydrophobic microdomains.

3.6. Comparison of evaluated polarity parameters with solvent model systems

The classification of poly(NIPAM-co-NtBA) films on the $E_T(30)$ solvent polarity scale of Dimroth and Reichardt^{18,21} is shown in Figure 10. The polarity (or more precisely the micro-

polarity experienced by the probes) of the NIPAM/NtBA films cover a relatively small section of the $E_T(30)$ scale from ~ 45 to ~ 49 kcal.mol⁻¹, corresponding to the polarity range of aliphatic and cycloaliphatic alcohols such as tert-butyl alcohol ($E_T(30) = 43.3$ kcal.mol⁻¹) and isopropyl alcohol ($E_T(30) = 48.4$ kcal.mol⁻¹).¹⁸ However, it would be incorrect to judge the polarity of NIPAM/NtBA copolymers as having the same polarity as primary alcohols because the alcohols are generally very good hydrogen-bond donors. It is more correct, taking into consideration the polymer structure and the measured Kamlet-Taft parameters, to say that the polarity of poly(NIPAM-co-NtBA) films is similar to the polarity of *N*-alkyl-acetamides such as *N*-methylacetamide ($E_T(30) = 52$ kcal.mol⁻¹, $\alpha = 0.47$, $\beta = 0.8$, $\pi^* = 1.01$),³⁸ or to the polarity of cyclic amides such as 2-pyrrolidinone ($E_T(30) = 48.3$ kcal.mol⁻¹, $\alpha = 0.36$, $\beta = 0.77$, $\pi^* = 0.85$).³⁸

From the comparison of estimated $E_T(30)$ values with available literature data for other water-soluble polymers,^{26,30,37,42} it is evident that the NIPAM/NtBA copolymers are slightly more polar than poly(ethylene oxide) (PEO, reported $E_T(30) = 42.48$ – 45.7 kcal.mol⁻¹),^{30,37} less polar than polyvinylalcohol (PVA, $E_T(30) = 49.3$ kcal.mol⁻¹),²⁶ and have approximately the same polarity as poly(*N*-vinyl-2-pyrrolidone) (PVP, reported $E_T(30) = 45.1$ to 47 kcal.mol⁻¹).^{37,42} Within the α - β - π^* model, the observed differences are more significant since PVP ($\alpha = 0.01$, $\beta = 0.93$, $\pi^* = 0.93$)³⁷ is an aprotic polymer, PEO ($\alpha = 0$, $\beta = 0.65$, $\pi^* = 0.86$)³⁷ is an amphiprotic polymer, whereas PVA ($\alpha = 0.29$, $\beta = 0.52$, $\pi^* = 1.11$)²⁶ and NIPAM/NtBA copolymers are more protic systems. Thus, the solvatochromic α - β - π^* method offers a more discriminating method for assessing the polarity of hydrophilic polymers than by simple polarity or water contact angles.

4. CONCLUSIONS

We have evaluated the polarity and hydrogen-bonding ability of dry poly(NIPAM-co-NtBA) films by means of the $E_T(30)$, α , β , and π^* solvatochromic polarity parameters. From these results (see Table 1 for summarized data) it is clear that dry NIPAM/NtBA copolymers fabricated into micron scale thin films are generally rather moderate hydrogen-bond donors (α), strong hydrogen-bond acceptors (β), and strongly dipolar/polarizable (π^*). The hydrogen-bond accepting ability (β parameter) was found to be relatively independent of the film composition whereas the $E_T(30)$, α , and π^* values were found to decrease linearly with increasing NtBA fraction. Finally, the experimental $E_T(30)$ values were found to correlate well with independently determined α , β , and π^* values. This confirms the accuracy of calculated parameters, and confirms that the behavior of the solvatochromic indicators in the poly(NIPAM-co-NtBA) films is similar to that observed in solvents. It should also be pointed out that because these measurements are made with visible light and because of the wide variety of sampling accessories (either in transmittance or reflectance

mode) available for most absorption spectrometers, the method can be easily adapted to study the properties of thin polymer films under different environmental conditions (e.g. humidity, temperature, etc). Finally, we also note that the UV/VIS absorption spectroscopy method does require relatively high probe concentration (10^{-3} M or more) to obtain accurate $\tilde{\nu}_{\max}$ values. This may cause some minor disruption to some polymer architectures but more importantly this concentration may be too high for use in-vivo or with live cells. Therefore, a more sensitive methodology may be required to supplement this method particularly where one needs to monitor physicochemical changes occurring in-situ in an in-vitro or in-vivo environment. Despite this caveat, this method is suitable for a wide variety of hydrophilic polymer types.

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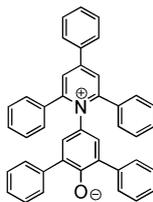
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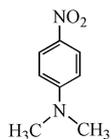
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FIGURES & CAPTIONS

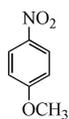
a)



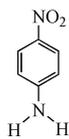
2, 6-diphenyl-4-(2,4,6-triphenylpyridinium-1-yl)phenolate (I)



N,N-dimethyl-4-nitroaniline (II)



4-nitroanisole (III)



4-nitroaniline (IV)

b)

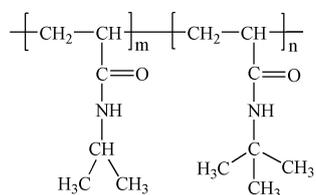


Figure 1: Molecular structure of (a) the solvatochromic indicator dyes I-IV used in this work, and (b) of the *N*-isopropylacrylamide/*N*-tert-butylacrylamide copolymers.

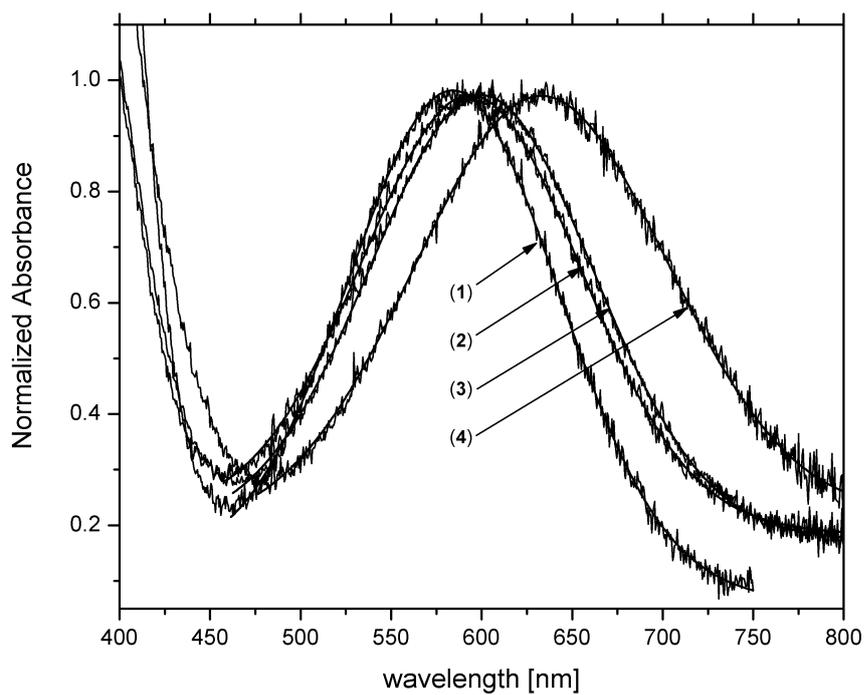


Figure 2. Normalized absorption spectra of Reichardt's betaine dye dispersed in pNIPAM (1), P85 (2), P65 (3), and pNtBA (4) films. Black solid curves (—) represent the Gaussian fit to the intramolecular charge-transfer (ICT) band. **P85** = (85% NIPAM, 15% NtBA), **P65** = (65% NIPAM, 35% NtBA).

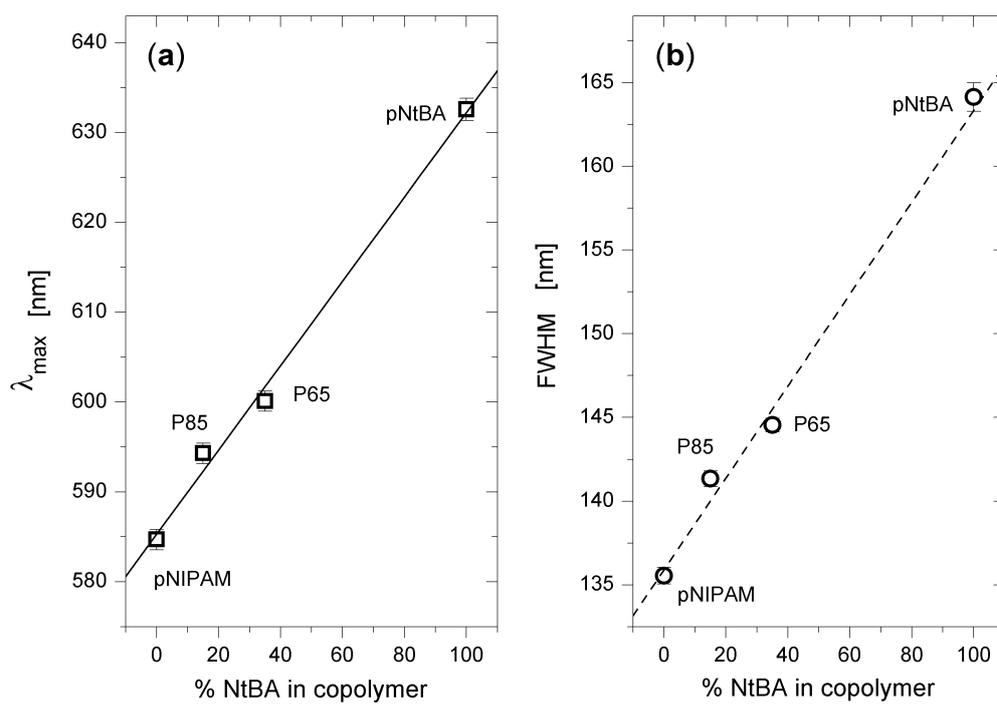


Figure 3: The UV/Vis absorption maxima, λ_{\max} , (a) and the full width at half maxima, FWHM, (b) of the intramolecular charge-transfer band of Reichardt's betaine dye dispersed in poly(NIPAM-co-NtBA) films plotted against polymer composition.

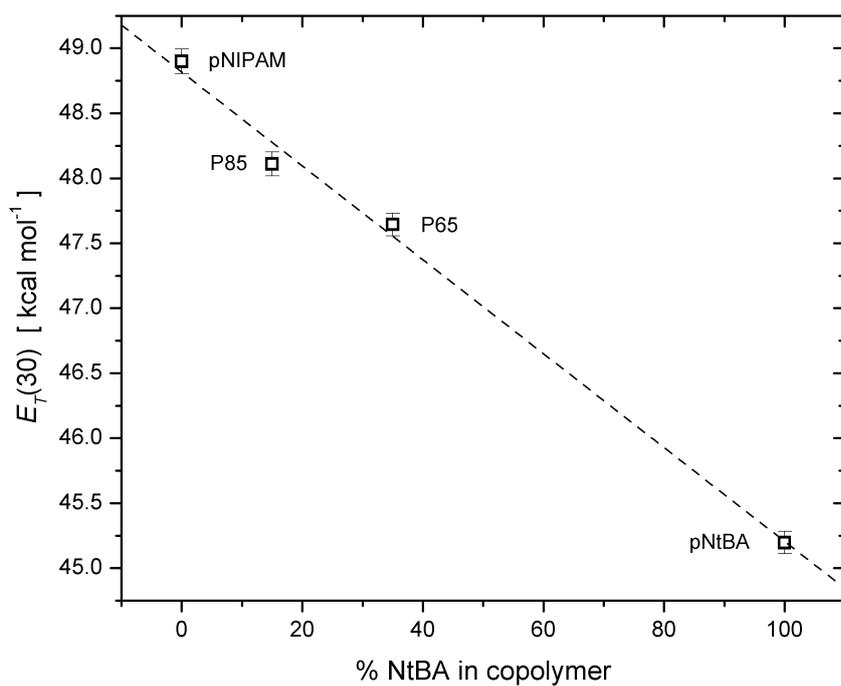


Figure 4. Dependence of the $E_T(30)$ polarity parameter on % of NtBA component. **P85** = (85% NIPAM, 15% NtBA), **P65** = (65% NIPAM, 35% NtBA).

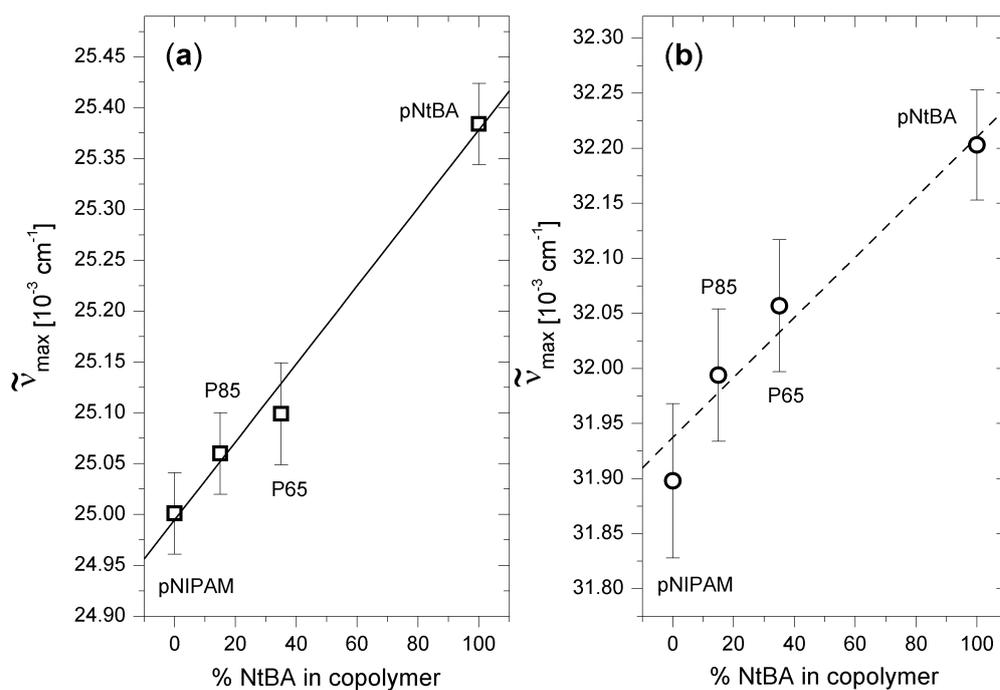


Figure 5. The UV/Vis absorption maxima, $\tilde{\nu}_{\max}$ [10^3 cm^{-1}], of *N,N*-dimethyl-4-nitroaniline (**a**) and 4-nitroanisole (**b**) dispersed in poly(NIPAM-co-NtBA) films.

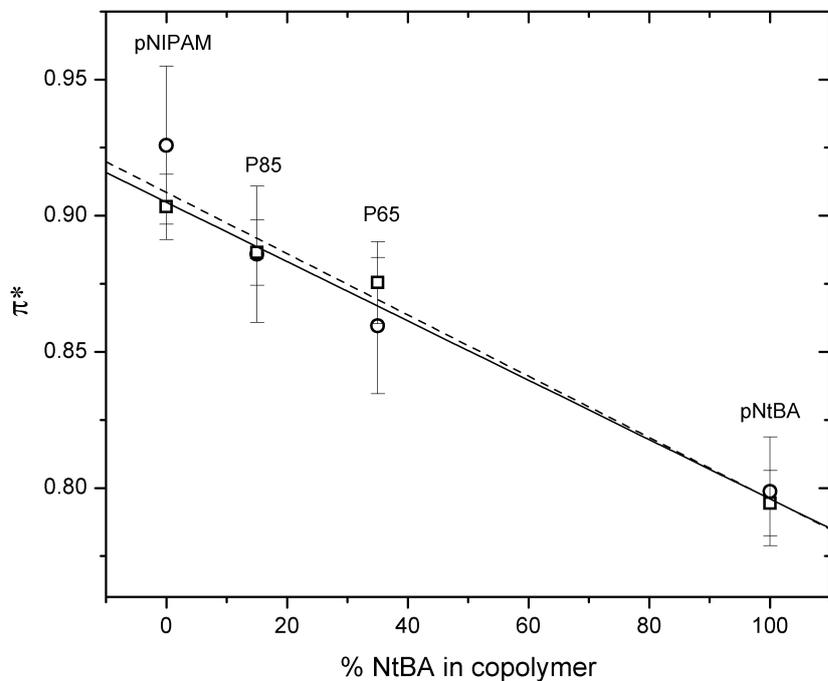


Figure 6: Dependence of dipolarity/polarizability (π^* parameter) of poly(NIPAM-co-NtBA) films on % of NtBA component. (○) values obtained with 4-nitroanisole, (◻) values obtained with *N,N*-dimethyl-4-nitroaniline as probe.

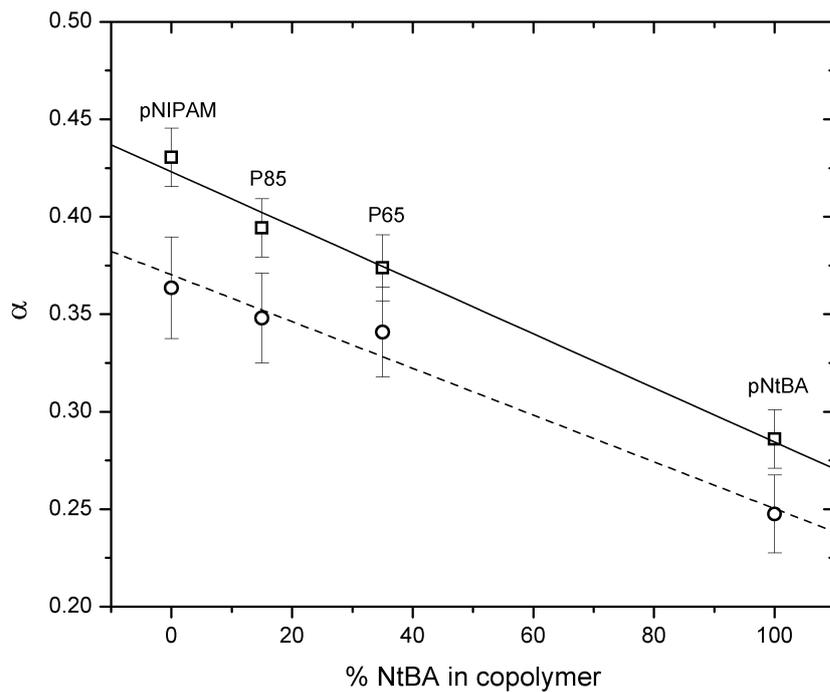


Figure 7: Dependence of hydrogen-bond donor ability (α parameter) of poly(NIPAM-co-NtBA) films on % of NtBA component. (○) values obtained with 4-nitroanisole/Reichardt's betaine dye according to Equation 5, (●) values obtained with *N,N*-dimethyl-4-nitroaniline/Reichardt's betaine dye by Eq. 4.

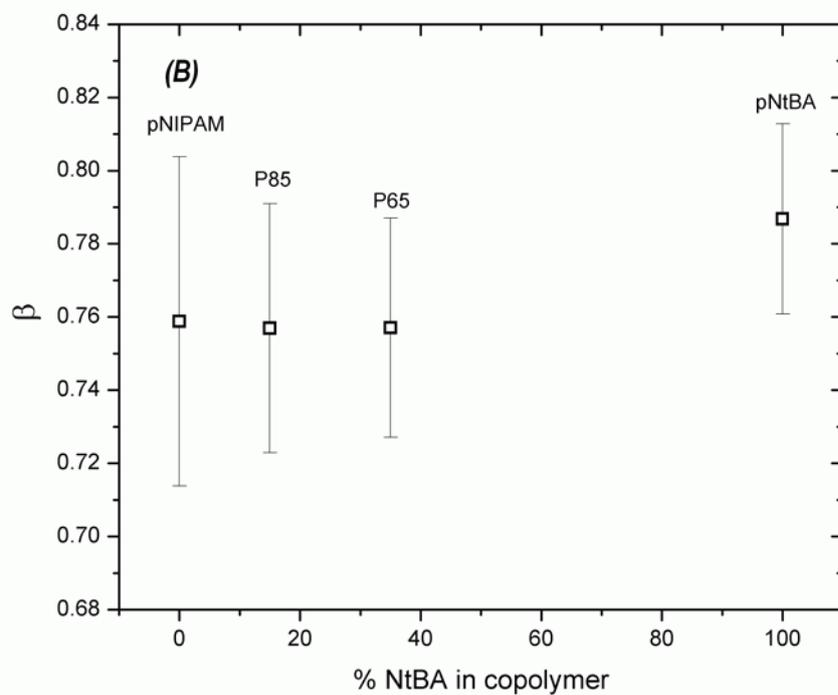
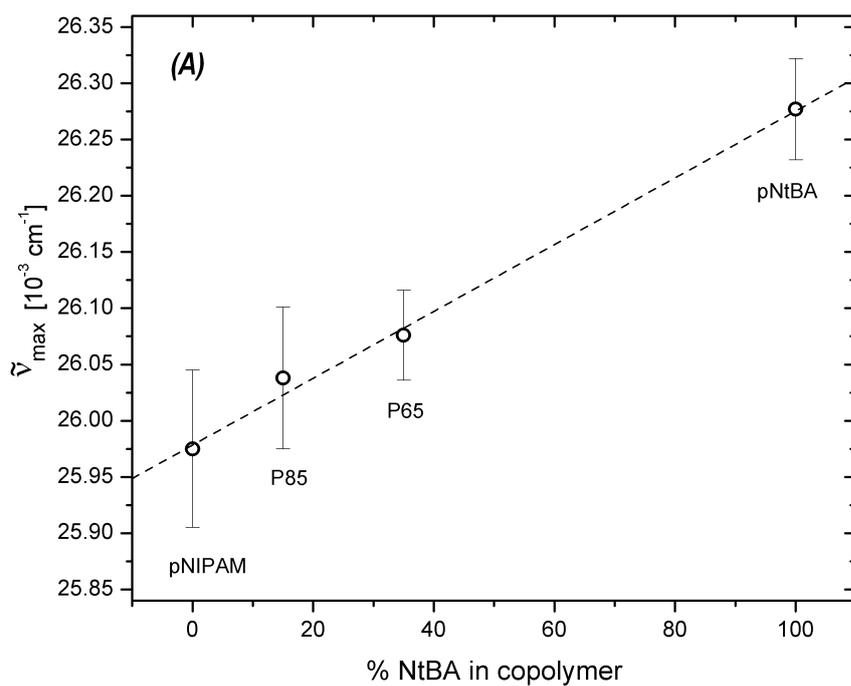


Figure 8: (A) The UV/Vis absorption maxima, $\tilde{\nu}_{\max}$ [10^3 cm^{-1}], of 4-nitroaniline dispersed in poly(NIPAM-co-NtBA) films. (B) Dependence of hydrogen-bond acceptor ability (β parameter) of poly(NIPAM-co-NtBA) films on % of NtBA component.

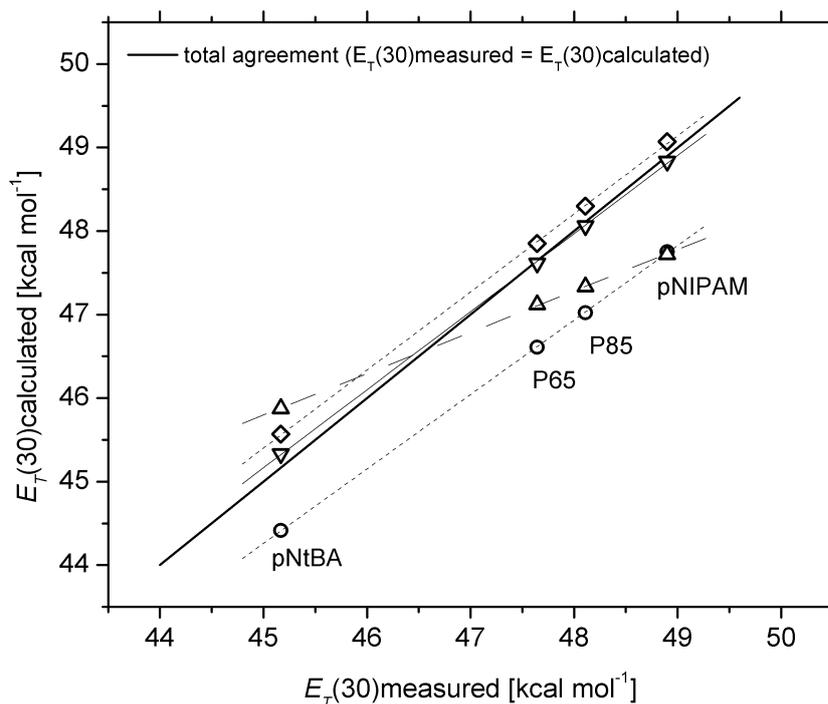


Figure 9: Plot of measured $E_T(30)$ versus calculated values for poly(NIPAM-co-NtBA) films. (O) values calculated with Equation 7, (Δ) values calculated with Equation 9, values obtained with Equation 8 (\diamond , $\delta=0$ and ∇ for $\delta=0.005$).

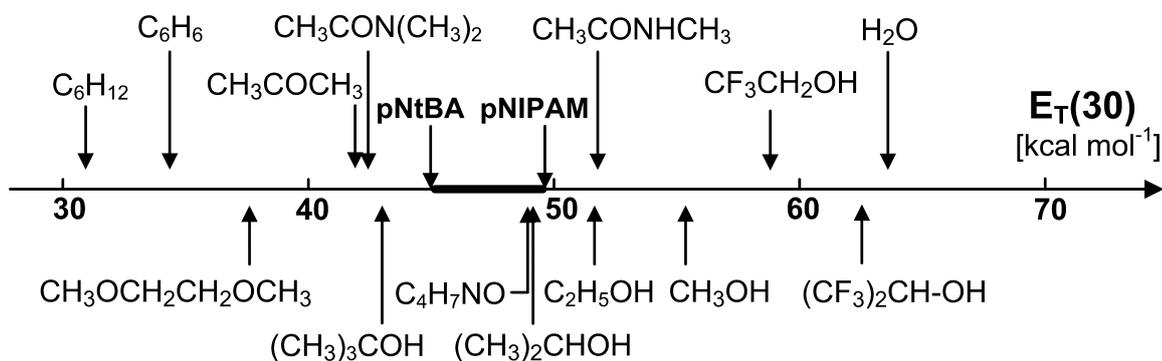


Figure 10: The categorization of poly(NIPAM-co-NtBA) films along the $E_T(30)$ solvent polarity scale of Dimroth and Reichardt. The $E_T(30)$ values for solvents were taken from Refs. [18, 35, 43].

Sample	$E_T(30)$	$\alpha_{(II)/(I)}$	$\alpha_{(III)/(I)}$	α_{AV}	β	$\pi^*_{(II)}$	$\pi^*_{(III)}$	π^*_{AV}
pNIPAM	48.9	0.43	0.36	0.40	0.76	0.90	0.93	0.92
	± 0.1	± 0.02	± 0.03	± 0.03	± 0.05	± 0.01	± 0.03	± 0.01
P85	48.1	0.39	0.35	0.37	0.76	0.89	0.89	0.89
	± 0.1	± 0.02	± 0.02	± 0.02	± 0.03	± 0.03	± 0.03	± 0.01
P65	47.6	0.37	0.34	0.36	0.76	0.86	0.86	0.87
	± 0.1	± 0.01	± 0.02	± 0.02	± 0.03	± 0.03	± 0.03	± 0.01
pNtBA	45.1	0.29	0.25	0.27	0.79	0.79	0.80	0.80
	± 0.1	± 0.01	± 0.02	± 0.02	± 0.02	± 0.03	± 0.02	± 0.01

Table 1: Empirical polarity parameters for dry poly (NIPAM-co-NtBA) thin films at 20 °C. P85 = (85% NIPAM, 15% NtBA), P65 = (65% NIPAM, 35% NtBA), $\alpha_{(II)/(I)}$ calculated with *N,N*-dimethyl-4-nitroaniline (II)/Reichardt's betaine dye (I) and Equation 4, $\alpha_{(III)/(I)}$ obtained with pair 4-nitroanisole (III)/Reichardt's betaine dye (I) using Equation 5, $\pi^*_{(II)}$ obtained with *N,N*-dimethyl-4-nitroaniline (II) and Equation 2, $\pi^*_{(III)}$ calculated from Equation 3 using 4-nitroanisole (III) as dipolarity/polarizability probe. $E_T(30)$ values in units of kcal mol⁻¹.