

Small angle neutron scattering measurements of synthetic polymer dispersions in matrix-assisted laser desorption/ionization matrixes[†]

Barry J. Bauer*, H. C. Michelle Byrd and Charles M. Guttman

National Institute of Standards and Technology, Polymers Division, 100 Bureau Dr., Stop 8541, Gaithersburg, MD 20899-8541, USA

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SPONSOR REFEREE: Dr. Charles N. McEwen, E.I. Dupont De Nemours & Co., Wilmington, DE, USA

Small angle neutron scattering (SANS) is used to measure the size and the dispersion of synthetic polymers in matrix-assisted laser desorption/ionization (MALDI) matrixes. Deuterated polystyrene (DPS) and dithranol in tetrahydrofuran were deposited by electrospray onto a substrate for small angle neutron scattering (SANS) measurements. DPS with 6050 and 27000 g mol⁻¹ molecular masses were prepared at mass fractions between 0.2 and 6%. All samples contained large aggregates of DPS with characteristic sizes >200 Å that represent hundreds of aggregated chains. Samples of mass fraction 1% DPS (6050 g mol⁻¹) in 2,5-dihydroxybenzoic acid, *all-trans*-retinoic acid, and sinapinic acid also have large zero angle scattering characteristic of large aggregates. The morphological trend obtained from the SANS measurements of the DPS aggregate size in the four matrixes is dithranol > 2,5-dihydroxybenzoic acid > *all-trans*-retinoic acid > sinapinic acid. These measurements indicate that DPS in dithranol exhibits the most strong phase separation, while DPS in sinapinic acid shows considerable domain mixing. All of these matrixes produce MALDI signal strength under appropriate conditions, suggesting that strong phase separation does not diminish the signal-to-noise ratio. DPS (188000 g mol⁻¹) in biphenyl was used as a model system of a matrix that can be either crystalline or amorphous. SANS data shows that above the biphenyl melting point, a conventional solution is formed that has molecularly dispersed polymers. Upon crystallization, there is strong aggregation of the DPS into large domains. Therefore, the crystalline matrixes commonly used in MALDI measurements probably cause large aggregations of polymers to be present during the MALDI process. Published in 2002 by John Wiley & Sons, Ltd.

Matrix-assisted laser desorption/ionization (MALDI) time-of-flight (TOF) mass spectrometry (MS) of synthetic polymers can yield qualitative information about end groups and repeat units, and also quantitative information, such as molecular masses and molecular mass distributions.^{1,2} The function of the matrix is to disperse the polymer and to adsorb optical energy from a laser, ablating the sample into a plume. The ionized polymers are then separated by mass/charge and detected.

The matrix disperses and supports the polymer molecules and, therefore, sample preparation is crucial to the success of the technique. The size scale of the dispersion can vary from millimeter heterogeneity that is often visible to the naked eye, to molecular dispersions of individual chains dissolved in the matrix, as they would be in a conventional solvent.

Additionally, the matrix needs to have low volatility under the high vacuum conditions of the experiment, so it is most commonly a highly crystalline aromatic molecule. The sample preparation therefore involves a complicated system of polymer/matrix/solvent that undergoes simultaneous evaporation/crystallization/phase separation that can produce a wide variety of morphologies.

There are two common approaches to sample deposition for synthetic polymers onto the target surface: hand-spotting and electrospraying. In both preparation methods the polymer, the salt and the matrix are dissolved in a common or miscible solvents. In one approach, the solutions are hand-spotted from a microliter pipette onto a target plate; 0.5–2 µL of solution are used to deposit micrograms of polymer, matrix, and salt mixtures onto the plate. The solvent is allowed to evaporate forming crystals of the matrix. This technique has the advantage of requiring little additional equipment, but the samples can have large signal variations across the target plate.³

In the electrospray technique, the solutions are drawn into a micro-syringe that is placed into a syringe pump. The needle of the syringe is held at a potential of 3–7 kV to the

*Correspondence to: B. J. Bauer, National Institute of Standards and Technology, Polymers Division, 100 Bureau Dr., Stop 8541 Gaithersburg, MD 20899-8541, USA.

E-mail: barry.bauer@nist.gov

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sample target and the solution is delivered at 2–20 $\mu\text{L}/\text{min}$, producing a fine spray of charged droplets. The sprayed solvent evaporates from the droplets and the polymer/salt/matrix mixture is deposited on the sample plate nearly dry.^{3,4} This procedure keeps the crystals of the matrix small, ca. 2–5 μm diameter, with the components intimately mixed.^{5,6} The surface structure of MALDI samples has been investigated by microscopy^{7–9} and by mass spectroscopic imaging,¹⁰ and sub-millimeter heterogeneity has been detected.¹¹

The above examples show that if the size scale of the dispersion is larger than the laser beam, the results can be erratic. However, these studies did not actually measure the dispersion of the polymers on the molecular level. Crystallites can have characteristic sizes less than 1 μm , and phase separation on this size scale is more readily measured by techniques such as small angle neutron scattering (SANS).¹² In this paper we will describe measurements of domain size and composition of four common MALDI polymer/matrix combinations (polystyrene in dithranol, 2,5-dihydroxybenzoic acid, *all-trans*-retinoic acid, and sinapinic acid) prepared by the electrospray method. We also measure dispersion in a model matrix, biphenyl, which can be either crystalline or amorphous.

EXPERIMENTAL

Sample preparation

Deuterated polystyrenes (DPS) with reported molecular masses of 6050, 27000, and 188000 g mol^{-1} and narrow polydispersities were purchased from Polymer Source and Polymer Laboratories.* Dithranol, 2,5-dihydroxybenzoic acid, *all-trans*-retinoic acid, sinapinic acid, silver trifluoroacetate (AgTFA), tetrahydrofuran (THF), and biphenyl (BP) were purchased from Aldrich Chemical Company and used as received. Solutions were made at between 0.0001 and 0.0030 g DPS and 0.05 g matrix/1 mL THF and were electrosprayed at 5 kV potential with a flow rate of 4–10 $\mu\text{L}/\text{min}$. The spray was deposited onto thin copper windows until a thickness of approximately 0.2 μm was obtained. A mass fraction 1% solution of DPS in BP was made by heating the mixture to 90°C and the solution was placed in a 1-mm quartz cell for SANS analysis. Matrix/polymer samples for MALDI-MS analysis were electrosprayed in a similar manner but with the addition of AgTFA as a cationization agent.⁵

SANS

SANS experiments were carried out on the 8m (NG1) instrument of the National Institute of Standards Technology Cold Neutron Research Facility in Gaithersburg, MD, USA.¹³ The wavelength λ of the incident beam was 12 Å. The observed scattering intensity at a given temperature was

collected over a two-dimensional detector and was corrected for empty cell, background radiation and detector inhomogeneity. It was then normalized against H_2O , which serves as a secondary standard, to give the absolute intensity. Finally, it was circularly averaged to give the q dependence of the coherent scattering cross-section, $I(q) = d\Sigma/d\Omega(q)$, in absolute units (cm^{-1}). The uncertainties of the data presented are estimated as the standard deviation of the mean. In cases where the limits are smaller than the plotted symbols, the limits are left out for clarity. Fits of the scattering data are made by a least-squares fit of the data giving an average and a standard deviation to the fit. All temperatures reported are within $\pm 1^\circ\text{C}$, as determined by previous experience.

The electrosprayed samples were sealed in a neutron cell between the copper substrate and a quartz window. Mixtures on heptane and heptane- d_{16} were made to match the total average contrast of the DPS/dithranol mixture.¹⁴ This was done to eliminate any contribution by the sample-air surface that can have a surface roughness in the 1- μm range.

MALDI-MS

Experiments were performed on a Bruker Reflex II MALDI-TOF mass spectrometer operated in the reflectron mode. The matrix/polymer samples were irradiated using a 3-ns pulse generated by 337-nm wavelength nitrogen laser. The ions produced were then accelerated into the field-free region using delayed extraction (25 kV) and detected by a dual-MCP ion detection system. All mass spectra shown were collected in the positive ion mode and displayed without smoothing (see Results and Discussion for more details of MALDI-MS sample preparation).

Data analysis

Scattering techniques provide information on the organization of material in the scattering volume. Different materials have scattering contrast factors that depend on the atomic content of the materials and the type of scattered radiation. SANS contrast factors can be modified by substitution of deuterium for hydrogen in one of the components. The electrosprayed MALDI samples have contributions to the scattering from both the relative sizes of the organic matrix and polymer components and from the surface topography that results from the electrospray process. To make the contrast between the matrix/polymer components as intense as possible, a polymer is used with deuterium substitution for the hydrogen normally found in the polymer. Therefore, a matrix made from unlabeled material that contains hydrogen provides strong SANS contrast to the deuterated polymer and that contrast, thereby, produces a strong SANS signal.

The electrospray deposition leads to porous morphology that has structures in the range 100–10000 Å. These structures may cause scattering due to the fact that the average neutron cross-section of the sample differs from that of the surrounding air. This scattering obscures the signal of interest arising from the deuterated polymer and can be eliminated (minimized) by immersing the sample in a mixture of heptane- h_{16} and heptane- d_{16} . By mixing $-\text{h}$ and $-\text{d}$ versions of the same liquid which is polymer/matrix insoluble, the neutron contrast of the polymer and matrix

*Certain commercial materials and equipment are identified in this paper in order to specify adequately the experimental procedure. In no case does such identification imply recommendation by the National Institute of Standards and Technology nor does it imply that the material or equipment identified is necessarily the best available for this purpose.

can be changed to a value that enhances sample characteristics of interest. Consequently, deuterium substitution of the polymer and a contrast match liquid filling surface pores yields SANS data representative of the polymer and matrix components only.

SANS measurements can probe size scales in the range of 10–1000 Å and determine the organization of the chains. A solution of molecularly dispersed polymers in concentrations typical of MALDI samples has scattering of Ornstein-Zerneck¹⁵ type

$$I(q) = I(q = 0)/(1 + \xi^2 q^2) \quad (1)$$

where $I(q)$ is the scattered intensity at scattering vector $q = 4\pi \sin(\theta/2)/\lambda$ with θ being the scattered angle and λ the neutron wavelength and ξ is a characteristic size related to the radius-of-gyration of the polymer, as, $3\xi^2 = R_g^2$. At higher values of q , $I(q)$ obeys the characteristic power law of:

$$I(q) \propto q^{-2} \quad (2)$$

If the polymer is phase separated into two domains, one polymer-rich and one matrix-rich, with a random distribution of domain sizes,¹⁶ the Debye equation applies and the scattering follows Eqn. (3):

$$I(q) = 8\pi\phi(1 - \phi)\xi^3(\sigma_1 - \sigma_2)^2/(1 + \xi^2 q^2)^2 \quad (3)$$

where ϕ is the volume fraction of polymer, and σ_1 and σ_2 are the neutron contrast factors of the polymer and the matrix domains, respectively. At higher values of q , Eqn. (3) obeys a characteristic power law of:

$$I(q) \propto q^{-4} \quad (4)$$

Equation (3) can be used to determine the compositions of the two domains from the SANS measurements by assuming that there are two domains, one pure crystalline matrix and the other polymer mixed with a certain amount of matrix material. The total scattering would be a contribution of two structures, the two-phase domain structure, described above, and the internal structure of the polymer-rich domain. If the polymer-rich domain contains only a small amount of small molecules (i.e., matrix), the contribution of scattering from this domain to the total scattering is small. The neutron contrast factors are calculated from the domain compositions, one being that of pure matrix, $\sigma_2 = \sigma_M$, and the other being a volume average of polymer and matrix, $\sigma_1 = f\sigma_P + (1 - f)\sigma_M$, where σ_P is the polymer contrast factor, σ_M is the matrix contrast factor, and f is the volume fraction polymer in the polymer-rich domain. A fit of Eqn. (3) gives a characteristic domain size and the volume fraction of polymer in the polymer-rich domain. Fits of the data (Table 1) were made by nonlinear least squares and the uncertainties are single standard deviations and the uncertainties are propagated through the calculations by standard methods.

Equations (1) and (3) each describe a limiting morphology, molecular mixing and complete phase separation. In many cases a more complicated morphology may exist which is a combination of the two limiting cases. If there are two domains, and there is little mixing within the domains, Eqn. (1) dominates the scattering, as stated previously. But if one or both of the domains have considerable mixing of the two

components, then the scattering is described by a combination of Eqns (1) and (3). The low- q scattering due to the two domains is dominated by Eqn. (3) and the high- q scattering due to molecular mixing is dominated by Eqn. (1). In the q range accessible to the scattering experiments an intermediate power law often results:

$$I(q) \propto q^{-\nu} \quad (5)$$

where ν is a composite power law in the range $2 < \nu < 4$. Therefore, a fit of the data in the intermediate- q range provides information on the extent of phase separation with ν near 4 indicating strong phase separation and increases mixing of the domains as ν decreases to 2.

RESULTS AND DISCUSSION

Four combinations of commonly used linear polymer/matrix were examined, as well as a model polymer/matrix system. It is desirable to make the SANS measurements on commonly used polymer/matrix systems in which the polymer can be completely dissolved in one phase (Ornstein-Zerneck limit) and phase-separated in another (Debye limit). For example, we would like to dissolve DPS in the liquid state of dithranol, acquire the SANS data, and compare the data with SANS data acquired from the crystalline sample. DPS and dithranol are mutually soluble in several solvents; however, the solubility of DPS in molten dithranol is not known. Furthermore, dithranol has a reported melting point of 176–181 °C¹⁷ with considerable volatility at this temperature making it difficult to study the polymer molecule in molten dithranol. Therefore, we selected a “model matrix” material, biphenyl, where DPS is soluble in the liquid state and the sample can also be studied in the crystalline “matrix” state.

DPS in biphenyl exhibits the thermodynamic characteristics needed to establish the Ornstein-Zerneck and Debye limits. Biphenyl has a melting point of 69–71 °C¹⁸ forming a clear solution with DPS above the melting point, but a highly crystalline solid at ambient temperatures. Solutions were prepared as described in the Experimental section, and three measurements under different temperature conditions were made for both pure biphenyl and a mass fraction 1% DPS. Samples were measured at ambient temperature, 20 °C, heated to 90 °C, and then cooled back to room temperature.

Figure 1 is a plot of the scattering of the mass fraction 1% DPS, 188 000 g mol⁻¹, in BP. An incoherent contribution was subtracted based on the flat scattering of the BP in the melt. The shapes of the scattering curves change considerably when the crystalline sample is melted. At 20 °C, there is

Table 1. Debye analysis of SANS measurement of DPS/dithranol electrospayed samples

DPS – M_w (g mol ⁻¹)	W_{DPS} in whole sample	ξ (Å)	$N = \rho\xi^3/M$	f in DPS-rich domain
27000	0.002 ± 0.0001	420 ± 26	5200 ± 1000	0.960 ± 0.140
27000	0.007 ± 0.0001	294 ± 7	2600 ± 200	0.658 ± 0.093
27000	0.02 ± 0.0001	288 ± 5	2500 ± 100	0.660 ± 0.092
27000	0.06 ± 0.0001	337 ± 9	2900 ± 200	0.905 ± 0.125
6050	0.06 ± 0.0001	306 ± 6	9400 ± 600	0.992 ± 0.137

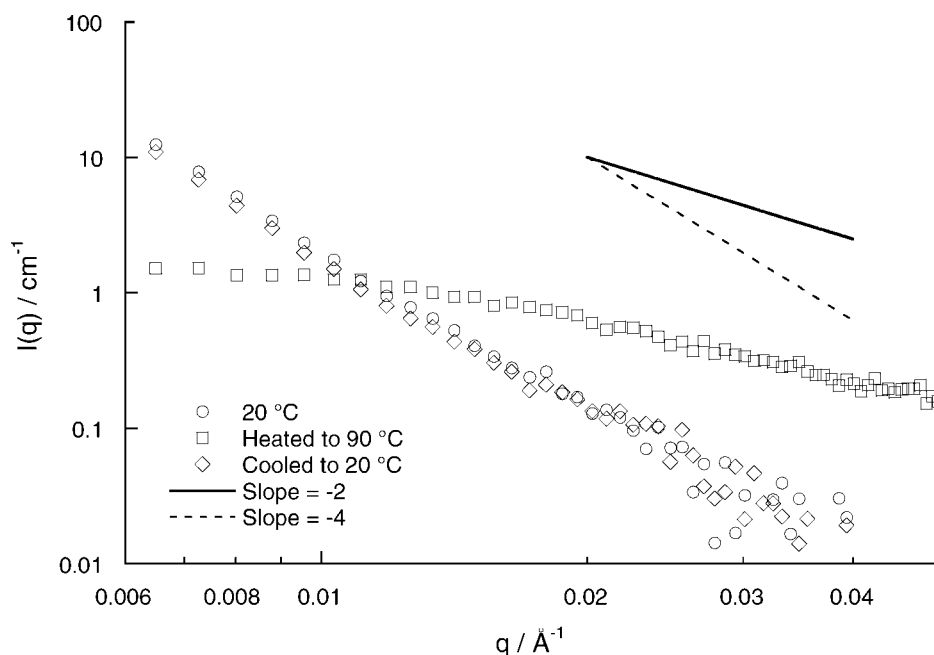


Figure 1. Log-log plot of SANS data of mass fraction 1% DPS $M_w = 188\,000\text{ g mol}^{-1}$ in biphenyl above and below the crystalline melting point.

much higher scattering at low q than at 90°C . The power law at higher q values is close to -2 in the melt and -4 in the crystalline state. These results are characteristic of a dissolved polymer chain in the melt, and large size scale phase separation in the crystalline state, respectively.

Upon cooling, the biphenyl initiates crystal growth, forming a pure crystalline component that excludes the dissolved DPS. Eventually, the crystallization is complete with large crystalline domains separating the polystyrene domain. A Debye fit of the scattering over a wide q range gives a zero angle scattering and correlation length that is larger than can be measured in the q range available to the SANS measurement. It is therefore not possible to measure the domain size of the DPS/biphenyl system since it is too large. The largest size measurable from an experiment with a minimum scattering vector q_{\min} is $2\pi/q_{\min}$, which places a lower limit on the domain size of 1000 \AA . This is considerably larger than a single DPS molecule indicating that *at least hundreds of chains* are aggregated.

Five DPS/dithranol electrospayed films were examined containing DPS with 6050 and $27\,000\text{ g mol}^{-1}$ molecular masses and were prepared at mass fractions between 0.2 and 6% . Table 1 lists the compositions of the samples. These molecular masses and concentrations are in the range typical of the values used in a MALDI measurement.

Equation (3) can be transformed into Eqn. (6) in which a plot of $I(q)^{-1/2}$ vs. q^2 gives a linear relationship.

$$I(q)^{-1/2} = I(q=0)^{-1/2}(1 + \xi^2 q^2) \quad (6)$$

Figure 2 is a plot of $I(q)^{-1/2}$ vs. q^2 for the five samples in dithranol. All five show linear relationships. The linear relationship proves that there is strong phase separation present in all samples. The scattering was fit to Eqn. (3) to obtain the characteristic correlation length and the volume

fraction of DPS in the DPS-rich domain and the results are shown in Table 1.

In all cases, ξ is greater than 200 \AA and there is no strong correlation between either the molecular mass or the concentration with the size formed. A characteristic aggregation number, N , can be calculated from the molecular mass, M , and the correlation length, ξ , from Eqn. (7):

$$N = \xi^3 \rho / M f \phi \quad (7)$$

where ρ is the DPS density. In all cases this number is in the thousands exhibiting that the aggregation is very strong.

The volume fraction of DPS in the DPS-rich domain is high in all cases. There are considerable uncertainties in the calculations due to uncertainties in the absolute intensity calibration largely due to uncertainties in the sample thickness. It does seem, however, that the composition of the DPS-rich domain is primarily polymer indicating that the phase separation is strong.

It is not practical to determine if there are a small number of chains dispersed in the dithranol matrix domain, because we do not have SANS results from a sample in which molecular dispersion is present. However, we do have this situation for the model system of DPS in biphenyl. Figure 1 shows the results of SANS measurement above and below the crystalline melting point of biphenyl. As described earlier, the DPS dissolves in liquid biphenyl. The SANS data of this sample is greatly flattened and, at higher q , the scattering is considerably stronger than from SANS measurement of the crystalline material. The scattering from the dispersed DPS is more than 10 times greater than the scattering from the phase-separated morphology. If there were more than 10% of the DPS chains molecularly dispersed in the crystalline domain, the high q scattering would be

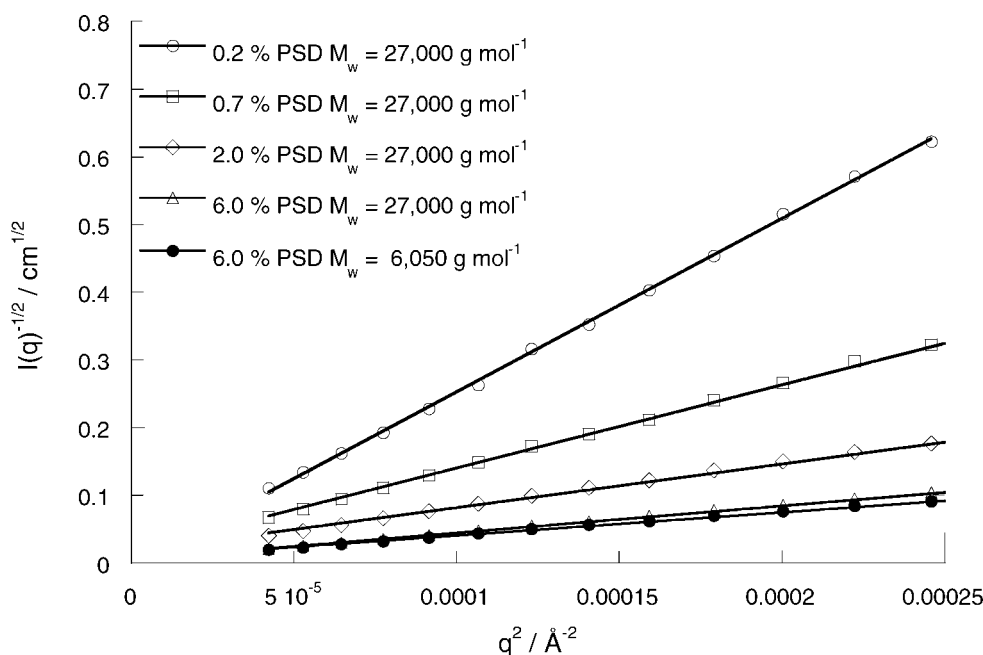


Figure 2. Debye plot of SANS data of DPS $M_w = 6050$ and 27000 g mol^{-1} in dithranol at concentrations from mass fraction 0.2–6.0%.

seen. Therefore, if polymer chains exist in the crystalline domain, they can only be present in quite small quantities.

MALDI-MS data was collected of the DPS 6050 prepared with each of the four matrixes, *all-trans*-retinoic acid, dithranol, 2,5-dihydroxybenzoic acid, and sinapinic acid. The analyte and matrix were mixed together as powders and dissolved in tetrahydrofuran. For the initial procedure, silver trifluoroacetate (AgTFA), dissolved in tetrahydrofuran, was added to the matrix/polymer solution to yield a 1:100:1 ratio by mass (analyte/matrix/AgTFA), and the solution was deposited onto the MALDI target using electrospray conditions described for the SANS measurements (See Experimental section for MALDI-MS protocol).

In order to prepare a sample for SANS measurements, a thick sample layer was necessary that required electrospraying for a long duration (15–20 min). Under these conditions, AgTFA was found to react strongly with dithranol and to a lesser extent with sinapinic acid and DHB in tetrahydrofuran even in the presence of the radical inhibitor 2,6-di-*tert*-butyl-4-methylphenol. This reaction likely leads to silver reduction, since, at times, silver clusters were observed on the sample surface. To reduce the duration of exposure to silver and keep the sample preparation similar to that used for SANS measurement, the matrix/polymer solution, in the absence of silver, was deposited onto the MALDI target for 10–12 min. Then a second solution containing the matrix/polymer in THF and AgTFA dissolved in ethanol was sprayed for a shorter duration ~3–5 min on top of the original matrix/polymer layers.

Figure 3 shows MALDI mass spectra acquired for the four matrix/polymer samples. Each spectrum was collected using a laser setting 50% above the threshold laser energy (TLE). The threshold energy is defined, for the present study, as the energy that yields a nominal signal-to-noise (S/N) ratio of 5:1. The sample surface was sampled using a

random-surface laser sampling method, i.e., ablating a pristine area of the sample surface for each MALDI-MS acquisition. Each spectrum shown is a sum of 128 mass spectral acquisitions using a 2-ns timebase.

Although the SANS measurements demonstrate that the DPS 6050 forms discrete domains in all four matrixes, MALDI analysis shows intense polymer ion signals for all four polymer/matrix samples (Fig. 3). Therefore, commonly used and highly successful MALDI matrixes do not result in complete solvation of individual oligomers by the matrix molecules as is often assumed. While some of the polymer molecules may be intimately mixed with matrix molecules, the large majority is segregated into large agglomerations.

The S/N ratio might be considered a measure of the quality of the MALDI-MS analysis of a synthetic polymer. In the present study, the S/N ratio is defined as the ratio of the signal height at the maximum of the polymer ion distribution to the average noise value. Interestingly, the polymer ion S/N ratio does not correlate with the degree of polymer dispersion in the MALDI matrixes determined from the SANS measurements. For example, dithranol and sinapinic acid can yield similar average S/N ratios at 50% TLE although polystyrene is more strongly phase separated in the former than the latter (Table 2, Fig. 3), while the S/N ratios of all four of the matrixes are all in the range 26–39.

Figure 4 is a power law plot of the SANS measurement of 6050 DPS in each of the matrixes between $0.006 \text{ \AA}^{-1} < q < 0.03 \text{ \AA}^{-1}$ showing power laws between 3.7 ± 0.2 and 2.1 ± 0.2 . The dithranol power law is close to 4 suggesting strong phase separation with only a small amount of mixing (See Data Analysis). The sinapinic acid sample has a power law close to 2 indicating extensive mixing of the polymer and the matrix. However, the low- q portion of the sinapinic acid scattering indicates that there is a two-phase structure present. In Fig. 1, the 90°C sample for DPS dissolved in BP

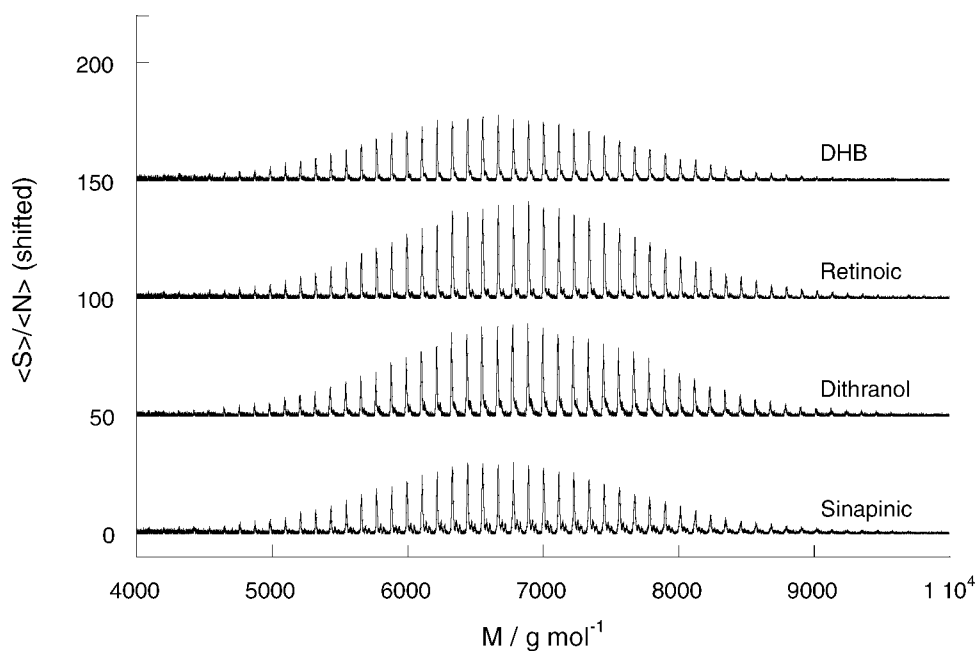


Figure 3. MALDI mass spectra of DPS 6050 in 2,5-dihydroxybenzoic acid, *all-trans*-retinoic acid, dithranol, and sinapinic acid (top to bottom) acquired at 50% TLE with 1% mass fraction of the polymer to matrix show intense signals for all four samples. The spectra were normalized by dividing the polymer ion signal by the average noise value of the spectrum.

Table 2. Power law fits of DPS in dithranol, 2,5-dihydroxybenzoic acid, *all-trans*-retinoic acid, and sinapinic acid matrixes in the range $0.0065 \text{ \AA}^{-1} < q < 0.03 \text{ \AA}^{-1}$

Matrix	SANS power law
Dithranol	3.7 ± 0.2
2,5-Dihydroxybenzoic acid	3.6 ± 0.2
<i>all-trans</i> -Retinoic acid	3.0 ± 0.2
Sinapinic acid	2.1 ± 0.2

shows a low- q flattening of the SANS data due to the functional form of Eqn. (1). On the other hand, Fig. 4 shows no flattening of the data for the sinapinic acid sample in the same q range. The flattening of the SANS data occurs at a transition point that can be estimated from the Ornstein-Zernike equation (Eqn. (1)). In Eqn. (1), the transition between 0 and -2 power law occurs at a q value of approximately $1/R_g$, where R_g is the radius of gyration of the polymer. This transition region ($0.01 \text{ \AA}^{-1} < q < 0.015 \text{ \AA}^{-1}$) is

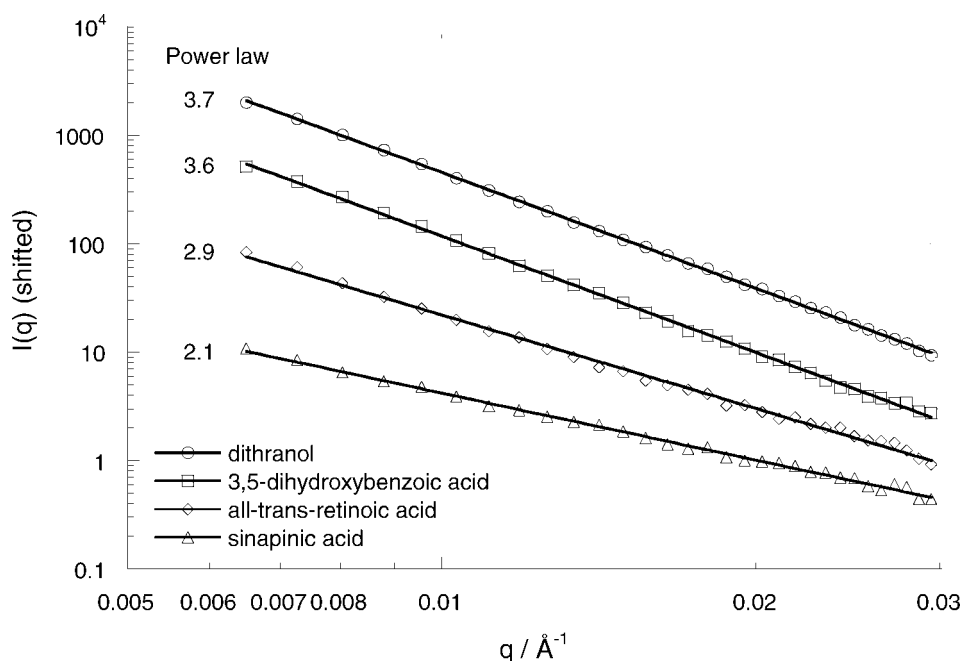


Figure 4. SANS high- q power laws for DPS in dithranol, 2,5-dihydroxybenzoic acid, *all-trans*-retinoic acid, and sinapinic acid.

clearly seen in Fig. 1 for $M = 188\,000\text{ g mol}^{-1}$ DPS. Since the DPS in Fig. 4 has a lower molecular mass of 6050 g mol^{-1} , the transition should be at a q value of $(188\,000/6050)^{1/2}$, approximately five times higher, i.e., greater than 0.05 \AA^{-1} . Figure 4 shows the 2.1 power law at much lower q suggesting that there is a relatively large two-phase morphology present in the sinapinic acid sample.

Overall, our results suggest that separated polymer molecules may not be necessary to obtain a strong signal during MALDI-MS. These results are consistent with the findings of Trimpin *et al.*,^{19,20} who demonstrated that a solvent-free matrix/polymer preparation which contains large aggregates of both polymer and matrix leads to strong MALDI-MS signals.

CONCLUSIONS

SANS analysis can be used to measure the size and the dispersion of polymers in MALDI matrixes. DPS with 6050 and $27\,000\text{ g mol}^{-1}$ molecular masses were electrosprayed at mass fractions between 0.2 and 6% in dithranol for SANS measurements. All of the samples contained large aggregates of DPS with characteristic sizes $>200\text{ \AA}$ representing at least hundreds of aggregated chains. A DPS sample in biphenyl was used as a model of a matrix that can be either crystalline or amorphous. SANS analysis shows that above the biphenyl melting point, a conventional solution is formed that has molecularly dispersed polymers. Upon crystallization, there is strong aggregation of the DPS into large domains.

Other common MALDI matrixes, 2,5-dihydroxybenzoic acid, *all-trans*-retinoic acid, and sinapinic acid also have large zero angle scattering characteristic of large aggregates. DPS in the four matrixes show limiting SANS power laws from 3.7 to 2.1 in the order dithranol $>$ 2,5-dihydroxybenzoic acid $>$ *all-trans*-retinoic acid $>$ sinapinic acid, which indicates the morphological trend of strong phase separation to considerable domain mixing. MALDI analysis demonstrates that an intense polymer ion signal may be generated from all four

matrixes. Therefore, the crystalline matrixes commonly used in MALDI measurements probably cause large aggregations of polymers in the matrix.

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