Quantitative Analysis of a Water-soluble Polymer Using the i-Raman EX Spectrometer

Vibrational spectroscopy is a well-established, powerful tool for polymer characterization.[1,2] Infrared and Raman spectroscopy are complementary techniques that provide a molecular fingerprint and are capable of both qualitative and quantitative analyses.[3] In general, infrared spectroscopy provides an excellent selection of functional groups associated with the polymeric composition, making it widely used in polymer identification and structural characterization. Raman spectroscopy also provides access to a selection of functional groups which enables determination of chemical composition and structure. Typically Raman spectroscopy probes non-polar chemical groups, such as multiple C-C backbone vibrations and strong characteristic aromatic bands. These characteristic Raman bands provide detailed information on chain conformation as well as easy discrimination of aromatic-based polymeric systems.[3]

A simple, robust quantitative analysis is required to determine the extent of functionalization of polystyrene to create a water-soluble polymer. The new generation of Raman instrumentation provides a small, cost-effective, user-friendly high-performing system. The strong characteristic Raman bands of the aromatic group along with the negligible signal from water enables the simple measurement of the final aqueous polymer to determine the extent of reaction.

INTRODUCTION

Initial evaluation of Raman spectroscopy to quantitate polymer functionalization reaction

The Raman spectra of the initial starting polymer and the fully functionalized polymer both show strong characteristic aromatic bands for the initial and fully functionalized polymers (see Figure 1). The strongest spectral features for the starting and fully functionalized polymers are observed as isolated bands at 1002 and 1132 cm^{-1}, respectively. These unique spectral features demonstrate that Raman spectroscopy is well suited for the desired analysis and will support either a simple classic univariate band ratio method or a PLS-based (Partial Least Squares) quantitative method.

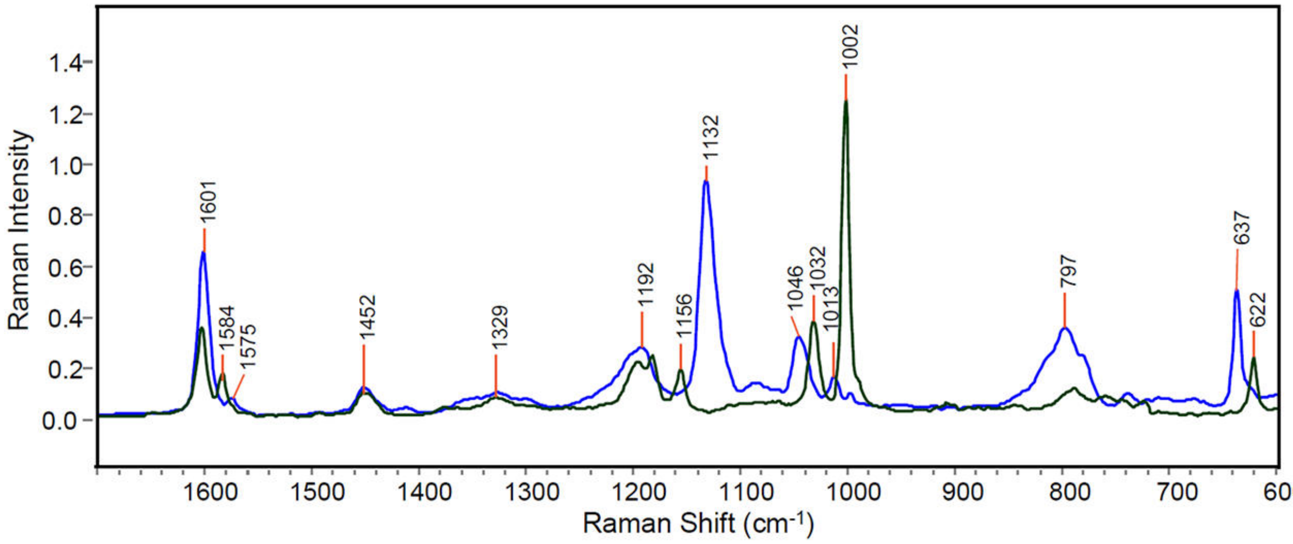

Figure 1. The FT-Raman spectra of the two pure polymer components: starting material polystyrene (green trace) and the fully functionalized polymer (blue trace) measured at 4 cm-1 resolution with 1064 nm excitation

Analysis deliverables

Well-designed chemometric analysis methods are needed that are appropriate for a plant quality control (QC) laboratory to determine the extent of the final polymer functionalization. This requires an expert-based system in which the interface for the QC analyst is a simple push-button work flow.

The polystyrene functionalization reaction includes both an organic and aqueous phase where the desired water-soluble polymer is present in the aqueous phase. The analysis must include a preliminary qualitative (classification) model to confirm the correct phase has been sampled for the final analysis. The subsequent quantitative analysis for the aqueous functionalized polymer will use a partial least squares for a single variable (PLS1) analysis to determine the percent functionalized polymer with well-defined accuracy and precision. This strategy ensures the analysis provides a simple, easy-to-use system appropriate for the multiuser plant analytical laboratory environment.

Instrumentation

The Raman spectra are measured using 1064 nm excitation at ca. 495 mW, 180° backscattering geometry, and a spectral range from 250 to 2500 cm^{-1} with a resolution of 9.5 cm^{-1} at 1296 nm. The instrument components included a B&W Tek i-Raman EX spectrometer with a thermoelectrically cooled 512 element InGaAs detector array. A fiber optic is interfaced to an enclosed cuvette/vial sample compartment (NR-LVH, B&W Tek). The aqueous polymer samples (ca. 10-20 weight percent solids) are transferred into borosilicate screw cap vials (height 4.5 cm, Outer Diameter 1.5 cm, Inner Diameter 1.1 cm) for the Raman measurements. Data acquisition is made using BWSpec v4.04 and includes a dark subtraction. Solutions are measured using an exposure time of 500 ms and 264 accumulations for a total measurement time of five minutes.

Software

A multivariable analysis software package, BWIQ version 3.0.6 (B&W Tek) was used to develop both the qualitative discrimination and quantitative analyses methods. The software included standard pattern recognition, classification and quantitative chemometric tools.[4]

Data analysis

A classification model is used to ensure that the sample consisted of the aqueous layer containing the polymer rather than the aliphatic organic layer. The analysis used to develop the PCA-MD classification model included: sample partition (Kennard-Stone algorithm), spectral preprocessing (mean centering, max value normalization), variable selection (spectral range) and classification (Principal Component Analysis-Mahalanobis Distance). The parameters selected for the final chemometric PCA-MD classification model for the measured Raman spectra are shown below (see Table 1):

Table 1. Parameters for the PCA-MD classification model for the measured Raman spectra.

Parameter	Component
Data Pretreatment	Center
Normalization	Max value normalization
Regression	PCA_MD
Principal components	3
Wavenumber	650 – 1700 cm$_{-1}$

Once the measured Raman spectra are confirmed to match that of the water-soluble polymer, a partial least squares model is employed to determine the extent of the polymer functionalization. Sixty different water-soluble polymers with varying extents of polystyrene functionalization were selected. The systems varied in the degree of functionalization from 65-98% as determined by ^{1}H NMR spectroscopy. The parameters selected for the final chemometric PLS1 % quantitation model for the measured Raman spectra of the functionalized water-soluble polymer are shown below (see Table 2).

Table 2. Parameters for the PLS1 quantitative model for % functionalized polymer based upon Raman spectra.

Parameter	Component
Data Pretreatment	Autoscale
Spectral derivative	Savitzky-Golay second derivative order = 3, window size = 5
Regression	PLS1
Principal components	6
Wavenumber region	995-1200 cm_{-1}

The developed methods were saved in chemometric modeling markup language (CMML) for easy transfer to the manufacturing site.

RESULTS AND DISCUSSION

Initial evaluation of the functionalized polymer Raman data

The Raman spectra measured with the i-Raman EX spectrometer of the low, medium and highly functionalized polymer exhibits excellent specificity in the 900-1300 cm^{-1} region (see **Figure 2**). An additional feature observed at 981 cm^{-1} derives from an inorganic species. A second derivative spectral pretreatment provides a well-defined baseline and resolution of the desired aromatic peaks for the initial and functionalized polymer.

A simple peak height ratio analysis is used to evaluate the quality of the Raman data to determine polymer functionalization. Twelve samples that varied in the extent of polymer functionalization as determined by ^1H NMR spectroscopy were selected. Next the single point peak height intensities of the second derivative spectra at 1126 and 1005 cm^{-1} are determined. The peak height analysis of the two components (i = initial, f = final) utilized the ratio of these two unique bands for component band f divided by the sum of the two component bands (i + f). The expected range of this ratio will be 0 to 1, where 1 corresponds to a 100% functionalized polymer. This simple univariate band ratio analysis resulted in very good linearity (see **Figure 2**) confirming the suitability of the Raman spectral data to develop a robust quantitative PLS1 model.

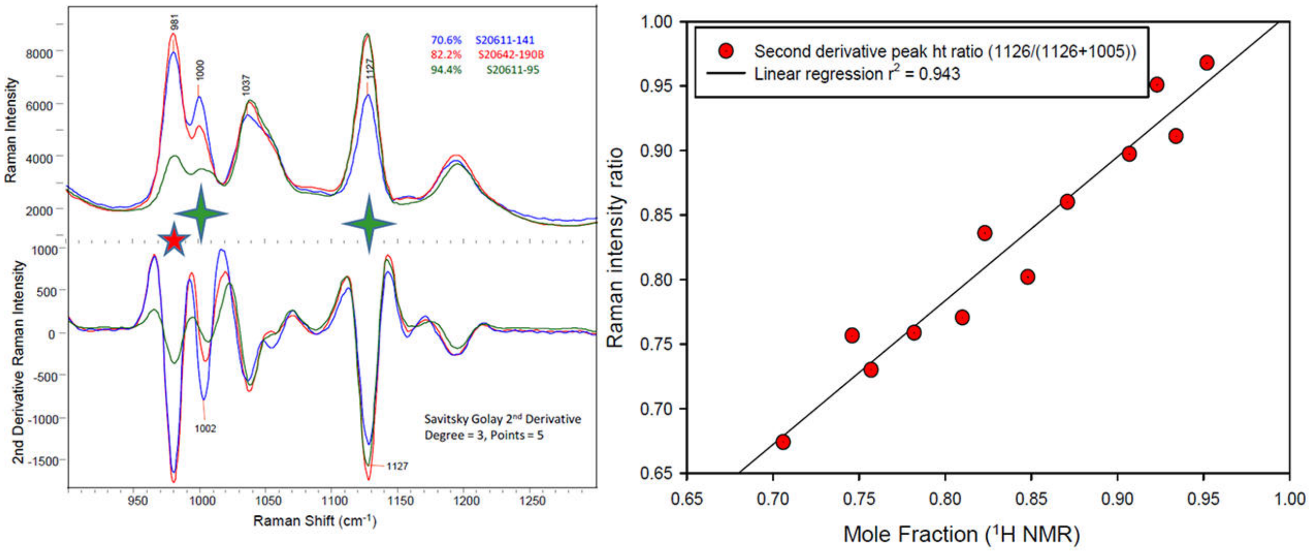

Figure 2. The spectral overlay on the left shows the Raman spectra and their second derivative spectra of three different polymers representative of low, medium and highly functionalized systems. The spectral feature at 981 cm-1 (red star) derives from varying amounts of an inorganic species. The highly diagnostic bands at 1002 and 1132 cm-1 from the starting and functionalized polymer species are identified with a green star. The correlation plot for the simple peak height ratio using the two diagnostic bands versus the 1H NMR determined extent of functionalized polymer is shown on the right.

RESULTS AND DISCUSSION

Standard selection

A well-designed calibration set includes the expected possible variation of future samples. This includes concentration ranges of constituents, as well as process-induced and environmental variability. For the PCA-MD classification of the organic and aqueous phase samples, this included multiple production samples from both the organic and aqueous phases. For the final PLS1 quantitative analysis this included over seventy samples from initial research lab design-of-experiments, pilot plant batches, and production lots that were fully characterized by the ^{1}H NMR spectroscopy.

PCA-MD Discrimination analysis of organic and aqueous phases

Principal component analysis (PCA) is a chemometric method in which the original spectral data is transformed into a new coordinate system, which condenses the information found in the original inter-correlated variables into a few uncorrelated variables, called principal components. The PCA can be used to reduce the dimensionality by zeroing out one or more of the smallest principal components. This results in a lower-dimensional projection of the data that preserves the maximal data variance.

This multivariate analysis reveals the internal structure of the data in a way that enables a simple explanation of the variance in the data. As such, it is a useful tool for visualization of datasets. In any principal component rotation, the first component accounts for the maximum proportion of the variance and subsequent components account for the remaining variance.

PCA clearly enables grouping or clustering the

Raman spectra into different classes. The cumulative explained ratio plot quantifies how much variance is explained in the first N components. In this application, three (N) variables explain 98% of the variance. Cluster analysis methods aggregate the Raman spectra stepwise, based upon the similarity of their spectral features (variables). A simple distance measurement of the individual spectrum relative to the various clusters provides the pattern recognition. A standard distance metric includes the Mahalanobis distance. Here, the Mahalanobis distance is a statistical tool that is coupled to PCA and can be considered as the distance of a point from the center of a principal component cluster. The smaller the Mahalanobis distance, the higher probability that the point belongs to the cluster.

A simple PCA-MD classification model was successfully developed using 37 calibration and 34 validation Raman spectra. The model was 100% accurate in classification of the training set Raman spectra for both the organic and aqueous phases.

RESULTS AND DISCUSSION

PLS1-based quantitative determination of % functionalized polymer

The PLS regression is one of the most popular multivariate techniques presently used in vibrational spectroscopic methods for quantitative analyses. It is used to develop a linear model between two matrices, the Raman spectral data and the reference values. The PLS model finds the empirical relationship between the two matrices (X and Y) and enables prediction of a continuous property, such as the % polymer functionalization, from the training set. In the case of the Raman spectra of the standards, the variation in the 1002 cm^{-1} and the 1127 cm^{-1} spectral features are highly correlated with the % polymer functionalization.

The developed quantitative model for the % functionalized polymer employs a PLS1-based (partial least squares for a single variable) algorithm. The Raman spectrum uses the 995-1200 cm^{-1} spectral region which includes diagnostic bands from both the starting and reacted polymer. Data pretreatment included a second derivative. The overall performance of the final quantitative model is summarized in the plot of the predicted (PLS) versus known (^{1}H NMR) % functionalized polymer (see **Figure 3**). 29 calibration (blue symbols) and 31 validation (red symbols) standards where used. Excellent linearity was observed with an R^2 of 0.95 for the calibration standards and 0.87 for the validation standards. The RMSE (root mean square error) is based upon the residuals of the calibration data and provides a simple measure of the predicted values. This was calculated for both the calibration (RMSEC) and validation (RMSEP) standards, with an RMSEC of 1.22 and an RMSEP of 1.43. The RME less than two (<2) demonstrates the model exhibits good predictive performance.

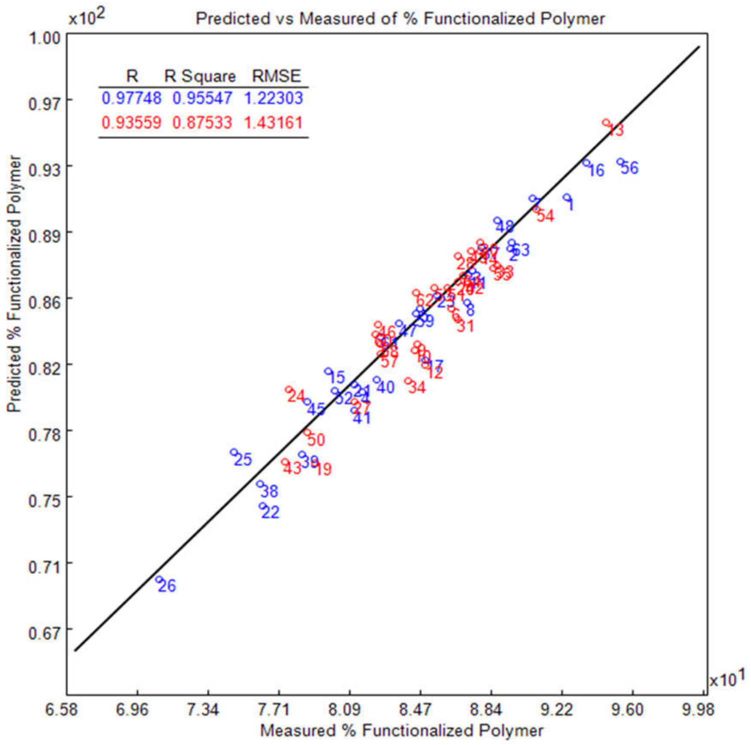

Figure 3. Plot of the predicted (PLS) versus the measured (1H NMR) % functionalized polymer. The blue symbols depict the calibration and the red the validation standards.

PLS1 quantitative Raman model accuracy and precision

The final developed model provides good linearity between the predicted (PLS) and assayed (^{1}H NMR) values for both the calibration and validation standards. Table 3 summarizes the precision and accuracy performance of the quantitative PLS Raman model. This includes the RMSEP from the validation standards (see Figure 4) a standard single-day and lot precision measurement and finally the average RMSE calculated for 16 subsequent manufactured lots (see Figure 4). The observed precision of 0.49% and the RMSE of 1.31 to 1.43 demonstrates the good statistical performance of this quantitative Raman method.

Table 3. Selected statistical measures of merit (precision, accuracy) for the PLS1 quantitative Raman model to determine polymer % functionalization.

Statistical merit	Value	Comments
RMSEP	1.43%	Precision: Figure 3 PLS model$_1$
Precision	0.49%	Single day, single lot precision Raman
(Predicted - Assay) Avg. RMSE	1.31%	Accuracy: Figure 4 for 16 additional lots$_1$

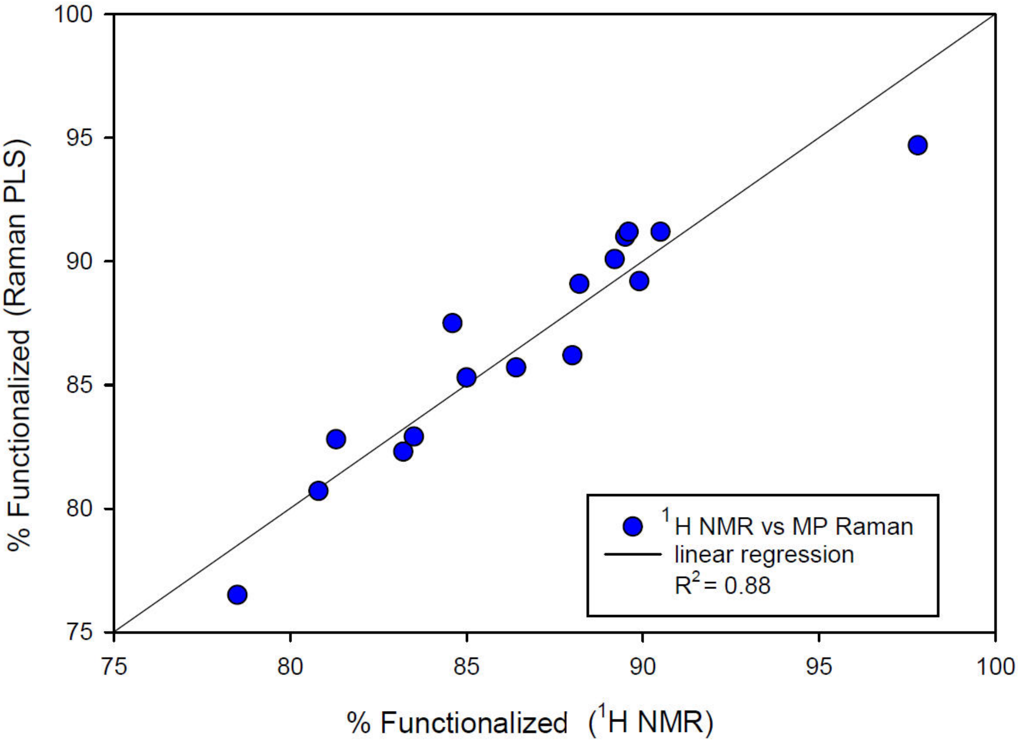

Figure 4. External validation of second manufacturing campaign batches. Raman predicted % functionalized polymer versus NMR determined value.

CONCLUSION

High-quality Raman spectra of an aqueous based water-soluble polymer (10-20% solids) are rapidly and easily measured using the i-Raman EX spectrometer. The Raman spectrum provides strong, unique bands for both the initial and fully reacted polymer. This enables development of a simple, robust quantitative analysis of the percent polymer functionalization using a PLS1 chemometric model with the vendor-supplied software (BWIQ). The final Raman method exhibits excellent linearity, accuracy and precision. This Raman method is now used routinely in a multiuser plant quality control (QC) laboratory.

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REFERENCES

1. N.J. Everall, J.M. Chalmers, P.R. Griffiths, "Vibrational Spectroscopy of Polymers: Principles and Practice", John Wiley & Sons, Chichester, 2007
2. J.L. Koenig, "Spectroscopy of Polymers" American Chemical Society, Washington, DC, 1991
3. P.J. Larkin, "Infrared and Raman Spectroscopy, Principles and Spectral Interpretation, SecondEdition", Elsevier, Cambridge, MA, 2018
4. M. Otto, "Chemometrics: Statistics and Computer Application in Analytical Chemistry", Wiley-VCHVerlag GmbH et Co. KGaA, Weinheim, 2017

CONTACT

Метром България ЕООД
12, Чипровци
1303 София
office@metrohm.bg

CONFIGURATION

Vial Holder Adapter

Vial holder adapter for use with the BAC100/BAC102 lab-grade Raman Probe with 9.5 mm shaft diameter. Compatible with vials with a diameter of 15 mm. Shipped with 6 vials made from borosilicate glass (15 mm).