



# Reliable spectroscopic process monitoring using an optimal acquisition time procedure determined by signal-to-noise ratio



J. Meyer-Kirschner, A. Mitsos, J. Viell\*

Aachener Verfahrenstechnik – Process Systems Engineering, RWTH Aachen University, Forckenbeckstr. 51, 52074 Aachen, Germany

## ARTICLE INFO

### Keywords:

Reaction monitoring  
Signal-to-noise ratio  
SNR  
Optimal acquisition time  
Indirect hard modeling  
IHM

## ABSTRACT

Monitoring chemical processes with optical spectroscopy involves a trade-off between high-frequency sampling to capture process dynamics and good signal-to-noise ratio (SNR). This contribution presents a strategy to maximize sampling frequency while maintaining a high SNR during in-line process monitoring.

To achieve this, a novel method to determine the analyte-specific SNR from a single multicomponent spectrum with overlapping peaks based on multivariate Indirect Hard Modeling (IHM) regression is presented. The method is extended to optimize the Raman acquisition time dynamically based on the current SNR. After each measurement, the acquisition time is adjusted to reach the target SNR of a component of interest. The method maximizes the number of individual measurements while sustaining the target SNR despite highly variable signal intensity.

The method is applied to monitor polymerization reactions showing that it is suitable for reliably monitoring high-rate reactions of multiple spectrally-similar components.

## 1. Introduction

Optical spectroscopy (i.e. UV/VIS, IR and Raman spectroscopy) is extensively used in process development and monitoring for identification and quantification of components in solid, liquid and gaseous samples. These samples can consist of single, homogeneous components or multicomponent mixtures and heterogeneous phases. The non-destructive nature of optical spectroscopy also qualifies for in-line reaction monitoring.

To monitor chemical reactions, high-sampling frequency of spectra and sufficient signal-to-noise ratio (SNR) of each spectrum are both necessary, which necessitates a trade-off in process monitoring. The SNR increases with the square root of the acquisition time [1] (i.e., the effective duration of sample irradiation and simultaneous signal collection). However, the sample composition changes due to reaction and therewith the signal intensities change, possibly enabling shorter acquisition times during the process.

An illustrative application is the synthesis of microgels [2], in which multiple weakly Raman-active and spectrally similar components at low concentrations polymerize at 80 °C to particles within 5–8 min [3]. The process dynamics mandate a sampling frequency of at least 5 spectra per minute to reveal differences in conversion between monomers. In practice, the acquisition time is set in advance and then kept constant during reaction. At high signal intensity, this procedure

generates less individual spectra than possible. At low signal intensity, it might generate spectra that cannot be quantified due to low SNR. Further, it does not account for non-chemical related changes in measurement signal such as foreign signal contributions (e.g., due to cosmic rays) or signal loss due to process probe fouling. Therefore, an adaptive adjustment of the acquisition time to reach and maintain a target SNR would be desirable.

The reliable identification and precise quantification of reaction mixtures requires the assignment and correlation of spectral peaks to the chemical components with regards to different intensity and (unwanted) noise. The SNR as a quantitative measure can be determined either using the intensity-variation of an analyte peak of multiple measurements or from remaining noise in the analyte peak region after subtraction of one spectrum from another [4]. During reaction, the analyte of interest might change, such as a change from monomer to polymer during polymerization. For SNR determination, this involves a change of the position of the signal peak. It is therefore necessary to determine the SNR individually for each component and to automatically select the component of interest during reaction monitoring.

Spectra are quantified typically using multivariate regression such as partial least squares (PLS) [5,6] or classical least squares (CLS) [7] regression. While both methods quantify concentrations from spectra of multicomponent mixtures, the CLS model contains the structure of pure component spectra. This allows to assign certain peak to individual

\* Corresponding author.

E-mail address: [joern.viell@avt.rwth-aachen.de](mailto:joern.viell@avt.rwth-aachen.de) (J. Viell).

components. A further development of CLS is Indirect Hard Modeling (IHM) regression [8,9]. In IHM, spectral pure component models are created by fitting multiple adaptive Voigt profiles to pure component spectra [10]. Mixture spectra can then be modeled by calculation of the sum of these pure component models using weights. As for CLS, the pure component model weights are optimized to minimize spectral differences (i.e., the sum of squared spectral residuals, RMS) between mixture model and measurement by a least squares optimizer [10]. IHM is reliable in the sense that the model is fitted to a broad wavenumber range, which compensates for random noise to a certain extent [8]. Further, each individual Voigt profile can account for nonlinear spectral changes, i.e., shifts and shape changes, which is termed peak-interaction. IHM reaches additional robustness by so-called ratiometric regression. Here, quotients of pure component weights are regressed while enforcing predicted fractions to sum up to unity to observe the mass balance. Since the pure component models preserve the spectral structure, the intensity of individual components can be extracted in case of overlapping peaks. However, SNR analysis has not been carried out before with IHM.

In this work, we define a component-specific SNR using IHM pure-component intensity as signal and spectral RMS as noise. We then optimize the acquisition time during process monitoring by comparison of the current SNR with a target SNR. The measurement setup is summarized in the Experimental Section. Then, the developed method is presented in the Methods Section, while its results are analyzed and discussed in the Results Section. As a case study, the method is demonstrated for Raman process monitoring of a microgel synthesis.

## 2. Experimental

Raman spectra were acquired using a RXN2 Process Analyzer from Kaiser Optical Systems. It is equipped with an Invictus 785 nm laser with 400 mW excitation power. The Raman signal was collected using a long-focus immersion optic. The device was controlled using the software Analyzer Control SDK (Version 5.0.9.1, Kaiser Optical Systems Inc.), which includes setting of acquisition parameters, taking of spectra and saving of measurement files.

For model calibration, Raman spectra were taken from 20 mixtures of monomers N-vinylcaprolactam (VCL), N-Isopropylacrylamide (NIPAM) and PVCL-PNIPAM-microgels in water. Sample composition is given in Table S1 in the Supplementary Material. For SNR determination, seven of these samples were measured at acquisition times 1, 2, 5, 10, 15, 20, 30 and 60 s with 10 repeated measurements of each sample and acquisition time. In-line process spectra were taken during microgel syntheses via precipitation polymerization [11] as described in Meyer-Kirschner et al. (2016) [3]. In brief, 4.43 g of VCL and NIPAM at different ratios were dissolved in 300 ml water together with a surfactant and crosslinker and heated to 60–80 °C. After addition of an initiator, the monomers polymerize to turbid microgel particles within 5–20 min. Further details for using microgel synthesis as application example are given in the Supplementary Material.

## 3. Methods

IHM regression was carried out in Peaxact 4.0.0 (S-Pact GmbH, Germany, 2015). All other data processing was conducted in Matlab R2015b (MathWorks Inc., Natick, MA, 2015). This includes computation of analyte-specific SNR as well as communication with the Analyzer Control SDK to control of the spectrometer for dynamic adjustment of the Raman acquisition time.

### 3.1. Model development and calibration

To determine sample composition and SNR from Raman spectra of the microgel system, IHM pure component models were created for the components water, the monomers VCL and NIPAM as well as PVCL-

PNIPAM-copolymer microgel. The pure component models for water and VCL were taken from a previously published model [3]. The models for NIPAM and copolymer were created analogously to previous pure component models using complementary hard modeling (CHM) [9]. To this end, calibration spectra of aqueous NIPAM and microgel were taken in small glass vials. To extract pure component models from these binary-mixture spectra, first the previously created water model was imported and then further peak functions were added to fit the analyte peaks. Removing the water model resulted in the pure component models. The mixture model contains the pure component models and a linear baseline. Apart from a range selection of 1000–2000  $\text{cm}^{-1}$ , no further pretreatment or standardization was done on the spectra. The model was calibrated using ratiometric regression, with peak-interaction and leave-10%-out cross-validation.

### 3.2. Analyte-specific signal-to-noise ratio

For single-component spectra, the SNR is given as  $SNR = \frac{\bar{s}}{\sigma} = \frac{\bar{s}}{\sqrt{\sigma^2}}$ , where the intensity  $\bar{s}$  is the average intensity of the analyte peak above the baseline.  $\sigma$  is the intensity standard deviation and  $\sigma^2$  the corresponding variance. The standard deviation  $\sigma$  can be determined from the intensity variation of the analyte peak from multiple measurements. Therefore, several measurements of an unaltered sample are necessary. It can also be determined from subtraction of two spectra, leaving only noise.  $\sigma$  is then defined as standard deviation of the remaining difference signal in the analyte peak region divided by  $\sqrt{2}$  [4].

The analyte signal can only be determined if the selected analyte peak is not superimposed by signal from other components. For overlapping multicomponent spectra, care has to be taken to exclusively extract the analyte intensity. Instead of using the baseline-corrected peak intensity as analyte signal, in this work the signal is determined for each analyte individually as the intensity of the strongest peak of the particular fitted pure component model. When using the pure component (PC) intensity as signal, the corresponding noise can either be determined using the variation of the model intensity or from the spectral residuals between model and measurement. In the latter case, only one spectrum is necessary to determine a SNR value. A performance comparison of established and IHM-based methods regarding the resulting SNR and the amount of input measurements necessary is given in the Supplementary Material. The IHM-based method is found to reach identical SNR values compared to the established methods using only a single spectrum. In the remainder of this work, the SNR is determined using the pure component intensity as signal and the spectral residuals as noise.

### 3.3. Optimal acquisition time

Based on the insight that SNR varies during reaction, we propose a procedure for dynamic adjustment of the acquisition time during reaction by continuous comparison of the current SNR to a target SNR that is required for reliable spectral quantification. The procedure is shown in Fig. 1. An initial acquisition time needs to be specified, determined for instance from experience or lab analysis. A spectrum is acquired, processed and stored. Next, a check is made if the experiment is finished. Common criteria are the passage of a specified time, detection of a desired product concentration or external intervention. If the experiment is not finished, the established route (dashed line) is to acquire the next spectrum with identical acquisition time. Instead, using optimal acquisition time, the spectrum is checked for validity. Common criteria are a threshold for minimum Raman signal and absence of foreign spectral contributions such as peaks from other components or cosmic rays. When using IHM the latter can be verified by absence of pronounced peaks in the spectral residuals. If the spectrum does not pass, another spectrum is acquired. Otherwise, the SNR of the component of interest is determined. The current SNR is then compared

Download English Version:

<https://daneshyari.com/en/article/7121203>

Download Persian Version:

<https://daneshyari.com/article/7121203>

[Daneshyari.com](https://daneshyari.com)