Recent Progress of Near-Infrared (NIR) Imaging —Development of Novel Instruments and Their Applicability for Practical Situations—

Daitaro ISHIKAWA,*1 Hideyuki SHINZAWA,*2 Takuma GENKAWA,*3 Sergei G. KAZARIAN,*4 and Yukihiro OZAKI*1†

*1 Department of Chemistry, School of Science and Technology, Kwansei Gakuin University, Sanda, Hyogo 669-1337, Japan
*2 Research Institute of Instrumentation Frontier, Advanced Industrial Science and Technology (AIST), Nagoya, Aichi 450-0002, Japan
*3 Faculty of Life and Environmental Sciences, University of Tsukuba, Tsukuba, Ibaraki 305-8572, Japan
*4 Department of Chemical Engineering, Imperial College London, London, SW7 2AZ, United Kingdom

The purpose of this review article is to outline the recent progress in near-infrared (NIR) imaging technology with particular emphasis on new instrumentation. Superior features of NIR imaging such as suitability for nondestructive and in-situ analysis, transmission ability, availability of optical fibers, high-speed monitoring and stability are very attractive not only for laboratory-based studies but also for diverse practical applications. In this review, introduction to chemical imaging is described, and then, a comparison among NIR, infrared (IR) and Raman imaging are made. Furthermore, the features of new NIR imaging instruments developed by our research group in collaboration with Yokogawa Electric Corporation and Sumitomo Electric Industries, Ltd. are discussed. Finally, some examples of applications of NIR imaging are introduced. Particularly, the performance and usefulness of the newly-developed imaging devices are demonstrated through their applications to pharmaceutical tablets and polymers.

Keywords Chemical imaging, chemometrics, near infrared spectroscopy (NIRS), new instrumentation, pharmaceutical tablet, polymer, dissolution

(Received September 25, 2013; Accepted October 12, 2013; Published January 10, 2014)

Daitaro ISHIKAWA received his Ph.D. (Agriculture) in 2010 at the United Graduate School of Agricultural Sciences, Kagoshima University. He worked there as Research Fellow of the Japan Society for the Promotion of Science for the Promotion of Science (2010 – 2011) and then, as a Ph.D. Fellow at Kwansei Gakuin University (2011 –). His main concern is to develop environmental conservation systems by using non-destructive methods. Currently, he engages in the development of new near infrared (NIR) imaging instrumentation and its application for the pharmaceutical and polymer industry.

Hideyuki SHINZAWA received his Ph.D. in 2008 at Kwansei Gakuin University. He worked at RIKEN as Research Fellow of the Japan Society for the Promotion Science (2008 - 2009) and as Research fellow at National Institute of Advanced Industrial Science and Technology (2009 –). His research interest is vibrational spectroscopy to derive an in-depth understanding of the supermolecular structure of polymers.

† To whom correspondence should be addressed.
E-mail: ozaki@kwansei.ac.jp
1 Introduction

The distribution and morphology of components in two- or three-dimensional objects are main concerns in diverse practical situations because they affect the quality of final products directly. Visible imaging technology that uses the 400 - 750 nm region has been utilized and being regarded as one of the most important tools for monitoring distribution of an analyte.\(^1\)\(^,\)\(^2\) However, this technology only provides information about the target distribution on the surface of samples. Therefore, a more popular approach to gain more detailed information about the distribution of components employs chemical imaging using vibrational spectroscopies.\(^3\)\(^,\)\(^4\) Chemical imaging or vibrational spectroscopic imaging as a combination of vibrational spectroscopy with digital image processing provides a three-dimensional data set, i.e., a spectral hypercube with the X- and Y-axes representing spatial information and the Z-axis representing spectral information. To handle the hypercube, one uses a variety of chemometrics methods, such as principal component analysis (PCA).\(^3\)\(^,\)\(^10\)

Based on different imaging colors, the spatial distribution of the components that comprise a sample can possibly be visualized via vibrational spectroscopic imaging. Moreover, with array-based spectral sensing, the quantitative information about a trace sample can be obtained by parallel collection of the spectral records.

Near-infrared (NIR) spectroscopy and imaging has the following advantages:\(^3\)\(^,\)\(^4\)

1) It is suitable for in-situ analysis and inherently nondestructive.
2) It enables non-contact analysis and analysis using an optical fiber.
3) It can be applied to samples of various physical states, shapes and thickness.
4) It is much easier to study and analyze an aqueous dispersion with NIR imaging than with infrared (IR) imaging. NIR radiation can penetrate much deeper into a sample than IR radiation because of the much smaller molar absorption coefficient in the NIR region.\(^3\)\(^,\)\(^11\)\(^-\)\(^15\) Thus, NIR imaging is also very useful for probing thick samples or bulk materials with little or no sample preparation required, even when the sample contains a large volume of water. IR spectra consist of many sharp bands assignable to specific functional groups, and thus, development of IR imaging is frequently performed by measuring well-defined peak heights or peak areas of spectral bands corresponding to fundamental transitions. On the other hand, NIR bands arise from overtones and combinations, so developing an NIR image using well-defined peak heights or peak areas is not always easy. Chemometrics is usually employed for this purpose.

Raman imaging has a significant advantage over IR and NIR imaging,\(^3\)\(^,\)\(^4\)\(^,\)\(^6\)\(^,\)\(^8\) the former can achieve a higher spatial resolution easily compared with the latter two approaches. In conventional spectrometers, the spatial resolution of Raman spectroscopy is ca. 1 μm while those of IR and NIR imaging are 10 and/or several μm. In tip-enhanced Raman scattering (TERS) imaging one can develop imaging with the spatial resolution of ca. 10 nm or so.\(^16\)\(^,\)\(^17\)

Most currently, a number of interesting studies which use advantages of NIR imaging have been reported for diverse applications. However, in comparison with IR and Raman spectroscopic imaging, NIR imaging is a relatively new analytical technique in many research and application fields.\(^3\)\(^,\)\(^10\)

2 Development of New NIR Imaging Instruments

The performance of an imaging instrument is a constraint factor for NIR imaging technology and methodology. Therefore, the development of NIR imaging devices with high sensitivity of detection has been a matter of interest. However, improving of the sensitivity often comes at the expense of a decrease in the measurement speed and the imaged area. The potential for wide area measurements at high speed is one of the integral parts of a newly developed NIR imaging device for diverse practical situations such as on-line process monitoring. Since NIR imaging devices with such advantages are still in progress, an evaluation method for component distribution in a target using NIR imaging has not yet been fully established for practical purposes.

During the past decade, several kinds of novel NIR imaging devices have been developed.\(^18\)\(^-\)\(^21\) Our research group together with two instrumentation companies, developed two newly developed NIR imaging devices.\(^20\)\(^,\)\(^21\) Their most notable features are not only high sensitivity and high speed but also portability and wide area monitoring.

2-1 A portable NIR imaging device with high sensitivity and high speed

An NIR imaging device, D-NIRs, has been developed by Yokogawa Electric Corporation together with our research group for on-line process monitoring of pharmaceutical tablets

---

**Takuma Genkawa** received his Ph.D. in 2009 at Kyushu University. He worked at Kyushu University as Research Fellow of the Japan Society for the Promotion of Science (2009 – 2010) and as a Ph.D. Fellow at Kwansei Gakuin University (2010 – 2011), and as Assistant Professor at University of Tsukuba (2011 –). His current research theme is process analytical technology for postharvest engineering using vibrational spectroscopy and chemometrics.

**Sergei G. Kazarian** is Professor of Physical Chemistry in the Department of Chemical Engineering at Imperial College London, United Kingdom. He is a Fellow of the Royal Society of Chemistry. His research encompasses the fields of vibrational spectroscopy, supercritical fluids, intermolecular interactions and materials. In recent years his research has mainly been focused on the development and applications of spectroscopic imaging to materials, biomedical samples and pharmaceuticals (www. imperial.ac.uk/vsci). He has published over 180 articles and reviews in leading scientific journals.

**Yukihiro Ozaki** received M.S. (1975) and Ph.D. (1978) degrees in chemistry from Osaka University. Currently, he holds a position of professor in the Department of Chemistry, School of Science and Technology, Kwansei Gakuin University. He has been an Associate Editor of Applied Spectroscopy since 2009. His research program has been concerned with basic studies and applications of far-ultraviolet (FUV), infrared (IR), Raman, and near-infrared (NIR) spectroscopy. He has received many awards, including the 1998 Thomas Hirschfeld Award, the 2001 EAS Award for Achievements in Near Infrared Spectroscopy, the Spectroscopical Society of Japan Award (2002), the 2005 Science and Technology Award of Japanese Government (Ministry of Education, Culture, Sports, Science and Technology), and the Japan Society for Analytical Chemistry Award (2008).
A schematic diagram of D-NIRs is shown in Fig. 1. D-NIRs combines a newly-developed NIR spectrometer (P-NIRs) with an imaging unit. Although conventional NIR spectrometers are generally equipped with an InGaAs-photodiode (PD) array that has 256 or 512 elements, P-NIRs is equipped with a PD array that has 640 elements. P-NIRs, therefore, can measure spectra in the 900 - 1700 nm region with a wavelength resolution of 1.25 nm. Moreover, a new charge-amplifier-array-type integrated circuit also contributes to improve the high-speed of measurements and the high sensitivity of D-NIRs.

Furthermore, the imaging unit of D-NIRs is compact and has portability. The installation space of D-NIRs is $500 \times 300 \times 250 \text{ mm}^3$; however, the size of the imaging unit is only $151 \times 93 \times 102 \text{ mm}^3$, and its weight is less than 2 kg.

2-2 A wide area NIR imaging device with high-speed performance

Compovision is a wide area NIR imaging camera developed by Sumitomo Electric Industries Ltd. (Fig. 2). It should be noted that this imaging system can obtain NIR imaging with an area of $150 \times 200 \text{ mm}^2$ at high-speeds. This wide-area and high-speed monitoring has become possible by the development of a new detector. Specifically, the detector used in Compovision is the newly-developed InGaAs detector. To expand the spectral region and improve sensitivity, the detector is equipped with InGaAs/GaAsSb Type-II quantum wells (QWs) laminated on an indium phosphide (InP) substrate. The development of this detector enables the acquisition of high quality spectra data in the wide NIR spectral region (1000 - 2350 nm). Consequently, Compovision allows one to measure NIR imaging in a wide area (approximately $150 \times 200 \text{ mm}$) for the whole NIR region within shorter than approximately 5 s. Since conventional NIR imaging instruments require approximately 5 - 10 min or even more for the same pixel size, and their measurement area is 1000 times smaller than that of Compovision, it is clear that Compovision is a powerful instrument for practical monitoring of diverse industrial applications.

3 Applications

Recently, NIR imaging has been employed in polymer science and technology, the pharmaceutical industry, for agriculture, food research and technology, biomedical research and clinical applications. In polymer science and technology it has been used to investigate the phase separation, miscibility, and morphology of polymer blends. With this technique, researchers can easily obtain information about the distribution of different components or the different polymer morphologies in blends. For example, Suttiwijitpukdee et al. explored the effects of intermolecular hydrogen bonding interactions on the crystal spherulite of poly-(R)-3-hydroxybutyrate (PHB) and...
cellulose acetate butyrate blends by using IR and NIR imaging spectroscopy. Additionally, it is possible to explore dynamic processes such as polymer dissolution and crystallization. Unger et al. investigated the diffusion process of butanol (OD) into polyamide 11 using variable-temperature NIR imaging spectroscopy.

As for applications in the pharmaceutical industry, for each pharmaceutical process such as blending, granulation, drying and coating, the possibility of predicting quantity of components, evaluating the particle size and the determining distribution of mixing components has been reported. Lewis et al. investigated the blend uniformity of a tablet, which is one of the major NIR imaging applications in the pharmaceutical industry. The state of uniformity during the blend process was monitored using the histogram plot of the intensity of some significant bands. The standard deviation in the intensity of a tablet decreased as expected in a process where the blend is becoming more homogeneous. They also reported that the skew decreased with blending time; this means that these high target content domains are mixed with the bulk material and moving toward a mean blending value. Moreover, Awa et al. reported the ability to visualize and the quantitative result for target concentration with high accuracy during tablet dissolution. In the next section of this review we introduce some good examples of NIR imaging studies of pharmaceutical tablets and polymers, mainly from our studies using the new NIR imaging instruments.

3-1 Investigation of homogeneity for pharmaceutical tablets at/in line

The process analytical technology (PAT) and the quality by design (QbD) in the pharmaceutical field have been proposed to control the product by scientific understanding. It is widely known that NIR spectroscopy makes it possible to reveal physical or chemical mechanisms at the molecular level. Additionally, the quest for homogeneity in pharmaceutical tablets is generally a main concern in formulation development. Typical homogeneity is defined as uniform distribution of the active pharmaceutical ingredient within the other formulation components.

Cellulose is one of the most well-known excipients. The crystallinity of cellulose is an important factor and is closely related to solubility. The physical property of cellulose depends on the multiple hydroxyl group in glucose, and it can be influenced by a simple compression process. It is well known that the band positions of NIR spectra in cellulose tablet shift, representing amorphous or crystalline structures. In recent years, Shinzawa et al. have done a good work to investigate the variation of the cellulose crystalline structure in a tablet by the peak shift image of two dimensional spectra. Sample tablets
compressed at different pressures of 5 - 1250 kg were prepared. Two dimensional NIR spectra were measured by a commercially available imaging system named Spotlight (Perkin Elmer Co., Ltd.). Figure 3(a) and 3(b) show the images constructed by plotting the wavenumber position where an amorphous band was observed. The obvious difference between the two images suggests the structural variation caused by the compression of the tablets, mostly reflecting the disintegration of the crystalline structure.

On the other hand, Awa et al.34 demonstrated that NIR imaging combined with self modeling curve resolution (SMCR) can elucidate the change in the molecular structures of components in a tablet as well as their distribution induced by the grounding process. Pentoxifylline (PTX) and plamitic acid were ground for 0, 0.5, 1, 2, 10 and 45 min at a rotating time of 250 rpm rotating speed, and the powder was compressed. The concentration profile of PTX obtained by SMCR revealed that the grading process provides homogeneous distribution of PTX over the waxy matrix of tablet (see Fig. 4) which, in turn, provides, substantial delay in the sustained-release of PTX. Pure component spectra of the crystal structure of PIX, on the other hand, showed obvious changes in the spectral feature, suggesting disintegration of the crystalline structure. These results therefore, the distribution of PTX particles within the insoluble waxy matrix and the crystal structure change of PTX may be based on intermolecular hydrogen bonding, and are strongly related to sustained-release of PTX.

3·2 Potential of D-NIRs for pharmaceutical tablet monitoring

To investigate the performance of D-NIRs as a PAT and QbD tool, an experiment on distribution of talc in a tablet was carried out. Figure 5 shows a second derivative image (left) and a standardized image (right) for the distribution of talc in the tablet obtained by using a talc peak at 1391 nm.21 The standardized image was developed using the mean and standard deviation of second derivative readings at 1391 nm to enhance the pattern observed in the image. One can readily find the inhomogeneity of the component in the tablet. Moreover, the high portability of D-NIRs significantly enhances the potential as a PAT tool.

For the quality control of a product, i.e. QbD, we also investigated the dissolution in a tablet by using NIR imaging.40 A model tablet including 20% ascorbic acid (AsA) and 80% hydroxypropyl methylcellulose (HPMC) was prepared, and the tablet was sealed by a special tablet cell. Figure 6 illustrates absorbance and its second derivative spectra of the tablet during the dissolution process.40 A band at 1361 nm may be due to the first overtone of an OH stretching vibration of AsA and the band at 1354 nm decreases according to the dissolution process. Figure 7 shows NIR images developed by the intensity ratio of two bands at 1361 and 1354 nm of the second derivative spectra respectively. Of note is that a two-dimensional change of AsA concentration in the tablet due to water penetration is clearly shown by using the ratio-based image. This result demonstrates the novel potential in pharmaceutical applications of this new portable NIR imaging instrument, D-NIRs.

3·3 Evaluation of inhomogeneity polymer by using NIR imaging

Poly-lactic acid (PLA), which is a class of biodegradable polymer, has already been used in various industrial fields such as medical and agricultural industry since it has superior environmental compatibility.41–43 Copolymers and blends of PHB are also promising biodegradable polymers.44 Crystalline polymers such as PLA and PHB should have different
crystallinity depending on the annealing conditions, and the spatial distribution of components within a sample can also be affected by such conditions. Thus, the quest for homogeneous crystallinity of these polymers is a main concern for quality evaluation.

Furukawa et al.\(^3\) tried to clarify the inhomogeneity due to the difference of component concentrations in the PLA/PHB blend polymer using NIR imaging. NIR images were measured using a conventional NIR spectrometer (Spotlight; Perkin Elmer, Co., Ltd.). Figures 8(a) and 8(b) respectively, depict the raw and second derivative NIR spectra of PHB and PLA in the 1200 – 2400 nm region.\(^{33}\) Bands due to the first overtones of CH\(_3\) stretching vibrations and the second overtones of C=O stretching vibrations appear at 1690 and 1720 nm, and 1910 and 1950 nm in the PHB and PLA spectra, respectively. Since in the case of PLA/PHB blends, the bands in the 1200 – 2400 nm region are somewhat overlapping even in the second derivative spectra, chemometric analysis was employed to investigate the inhomogeneity of the components.

To summarize the spectral changes among the samples, the score value was calculated by partial least square regression (PLSR). The scores of PLSR include information about both the spectral variable and response variable (the blending ratio). The score image developed by two dimensional spectra of PLA/PHB blend indicates the difference between each component (Fig. 9). Additionally SD of the score values in the PLA/PHB blends noticeably shows a normal distribution except in the 40/60 ratio blend. They concluded that the homogeneity of the 40/60 blend may differ from those of other blends.\(^{33}\)

3·4 Crystal evolution with wide area by using Compovision

We investigated the inhomogeneity of crystallinity in a PLA film by using the spectra obtained by Compovision.\(^{45}\) PLA film with an area of 6.25 × 50 mm\(^2\) was prepared. A crystallinity distribution can be made due to the temperature slope of 70 – 105\(^\circ\)C across the film. Figure 10 depicts a visible image of the sample and an NIR image developed by standard normal variate (SNV) spectra\(^{45}\) (As for the details of the SNV, one should refer to previous familiar articles).\(^{46,47}\) One can find that the contrast of the center part in the sample coincides with crystal evolution. Also in many cases, the spectra representing the high crystallinity part, namely, the upper part of the image is saturated so that the estimation of inhomogeneity in that part is difficult. However, the high accuracy of the spectra obtained by Compovision may lead to the evaluation of the high crystallinity part of a polymer film in over wider area.

4 Future Prospects

As reported in the present article, NIR imaging instruments and applications of NIR imaging are progressing. Newly developed
NIR imaging devices can solve several issues such as the long acquisition times and relatively low sensitivity of detection. In particular, the working place of the high portability and wide area enabled devices will become wider and wider since it has the high potential for the diverse application situations. Simultaneously, they will lead the potential of the development of a quality control method for target in/at line. As we all know, the progress of the image analytical technology combined with the chemometrics is expected, but also the introduction of the statistical distribution analytical method such as kurtosis and/or skewness will strongly enhance the NIR imaging technology.

5 Acknowledgements

The development of D-NIRs by Yokogawa Electric Corp. and our group was supported ‘Innovation Promotion Program’ by New Energy and Industrial Technology Development Organization (NEDO), Ministry of Economy, Trade and Industry, Japan. We also thank Sumitomo Electric Industry Ltd. for the collaboration of developing Compovision.
6 References

1. P. Gao and R. H. Meury, *J. Pharm. Sci.*, 1996, 85, 725.
2. K. J. Zuzak, M. D. Schaeberle, E. N. Lewis, and I. W. Levin, *Anal. Chem.*, 2002, 74, 2021.
3. Y. Ozaki, *Anal. Sci.*, 2012, 28, 545.
4. S. Šašić and Y. Ozaki (eds.), “Raman, Infrared, and Near-Infrared Chemical Imaging”, 2009, Wiley, New York.
5. J. van der Werd and S. G. Kazarian, “Multivariate movies and their applications in pharmaceutical and polymer dissolution studies” in “Techniques and Applications of Hyperspectral Image Analysis”, ed. H. F. Grahn and P. Geladi, 2007, Chap. 10, John Wiley and Sons Inc., Chichester, 221.
6. R. Salzer and H. W. Siesler (eds.), “Infrared and Raman Spectroscopic Imaging”, 2009, Wiley-VCH, Weinheim.
7. J. L. Koening, in “Spectrochemical Analysis Using Infrared Multichannel Detectors”, ed. R. Bhargava and I. W. Levin, 2005, Chap. 5, Blackwell Publishing Ltd., Oxford, 115.
8. B. Boldrini, W. Kessler, K. Rebner, and R. W. Kessler, *J. Near Infrared Spectrosc.*, 2012, 20, 483.
9. E. N. Lewis, J. Schoppelrei, and E. Lee, *Spectroscopy*, 2004, 19, 28.
10. C. Genèrin, Y. Roggo, and C. Collet, *J. Pharm. Biomed. Anal.*, 2008, 48, 533.
11. T. Nishii, T. Genkawa, M. Watari, and Y. Ozaki, *Anal. Sci.*, 2012, 28, 1165.
12. Y. Miyamae, Y. Yamakawa, M. Kawabata, and Y. Ozaki, *Anal. Sci.*, 2012, 28, 1159.
13. L. Zhang, I. Noda, B. Czarnik-Matuszewicz, and Y. Wu, *Anal. Sci.*, 2007, 23, 901.
14. M. Kahiara, M. Satoh, and M. Satoh, *Anal. Sci.*, 2007, 23, 921.
15. Z. Chi, M. Wang, L. Yang, X. Li, X. Cong, S. Liu, and B. Cai, *Anal. Sci.*, 2013, 29, 661.
16. T. Yano, P. Verma, Y. Saito, T. Ichimaru, and S. Kawata, *Nat. Photonics*, 2009, 3, 473.
17. L. Opilik, T. Schmid, and R. Zenobi, *Annu. Rev. Anal. Chem.*, 2013, 6, 379.
18. S. J. Erickson and A. Godavarty, *Med. Eng. Phys.*, 2009, 31, 495.
19. I. Y. Son and B. Yazici, in “Advances in Sensing with Security Applications 2”, ed. J. Byrnes and G. Osthheimer, 2005, Springer, Berlin, 341.
20. D. Ishikawa, K. Murayama, T. Genkawa, K. Awa, M. Komiyama, and Y. Ozaki, *NIR news*, 2012, 23, 19.
21. D. Ishikawa, T. Nishii, F. Mizuno, S. G. Kazarian, and Y. Ozaki, *NIR news*, 2013, 24, 6.
22. M. Komiyama, Y. Sanpei, A. Miura, K. Sakakibara, T. Yakihara, T. Fujita, S. Kobayashi, S. Oka, and Y. Akasaka, US Patent, 2003, 6, 552, 325 B1.
23. K. Murayama, T. Genkawa, D. Ishikawa, M. Komiyama, and Y. Ozaki, *Rev. Sci. Instrum.*, 2013, 84, 023104.
24. H. Ishikawa, T. Takahashi, F. Mizuno, T. Suzuki, E. Yamada, Y. Ozaki, and D. Ishikawa, *SEI Tec. Rev.*, 2013, 76, in press.
25. L. Alvarz-Jubete, J. Mishura, I. Jones, P. J. Cullen, and C. Sullivan, *J. Near Infrared Spectrosc.*, 2013, 21, 173.
26. L. C. Enfield and A. P. Gibson, *J. Near Infrared Spectrosc.*, 2012, 20, 185.
27. H. Kobori, H. Yonenobu, J. Noma, and S. Tsuchikawa, *Appl. Spectrosc.*, 2008, 62, 854.
28. G. Polder, G. Van der Heijden and, I. Young, *Real-Time Imaging*, 2003, 9, 253.
29. M. Manley, G. Toit, and P. Geladi, *Anal. Chim. Acta*, 2010, 686, 64.
30. H. Shinzawa, M. Nishida, T. Tanaka, and W. Kanematsu, *Appl. Spectrosc.*, 2012, 66, 470.
31. N. Suttiwijipukdee, H. Sato, M. Unger, and Y. Ozaki, *Macromolecules*, 2012, 45, 2738.
32. M. Unger, Y. Ozaki, and W. H. Siesler, *Appl. Spectrosc.*, 2011, 65, 1051.
33. T. Furukawa, H. Sato, H. Shinzawa, I. Noda, and S. Ochiai, *Anal. Sci.*, 2007, 23, 871.
34. K. Awa, T. Okumura, H. Shinzawa, M. Otsuka, and Y. Ozaki, *Anal. Chim. Acta*, 2008, 619, 81.
35. H. Shinzawa, K. Awa, and Y. Ozaki, *J. Near Infrared Spectrosc.*, 2011, 19, 15.
36. E. N. Lewis, J. E. Carroll, and F. M. Clarke, *NIR news*, 2001, 12, 16.
37. J. M. Amigo and C. Ravn, *Eur. J. Pharm. Sci.*, 2009, 37, 76.
38. K. A. Bakeev, “Process Analytical Technology-Spectroscopic Tools and Implementation Strategies for the Chemical and Pharmaceutical Industries”, 2002, Blackwell Publishing Ltd., Oxford.
39. C. D. Hinze, *Anal. Bioanal. Chem.*, 2006, 384, 1036.
40. D. Ishikawa, K. Murayama, K. Awa, T. Genkawa, M. Komiyama, S. G. Kazarian, and Y. Ozaki, *Anal. Bioanal. Chem.*, 2013, 405, 9401.
41. H. Tsuji and Y. Ikada, *Macromol. Chem. Phys.*, 1996, 197, 3483.
42. H. Tsuji and Y. Ikada, *Appl. Polym. Sci.*, 1998, 67, 405.
43. Y. Ikada and H. Tsuji, *Macromol. Rapid Commun.*, 2000, 21, 117.
44. Y. Hu, J. M. Zhang, H. Sato, Y. Futami, I. Noda, and Y. Ozaki, *Macromolecules*, 2006, 39, 3841.
45. D. Ishikawa, T. Nishii, F. Mizuno, H. Sato, S. G. Kazarian, and Y. Ozaki, *Appl. Spectrosc.*, 2013, 67, 1441, in press.
46. R. J. Barnes, M. S. Dhanoa, and S. J. Lister, *Appl. Spectrosc.*, 1989, 43, 772.
47. M. S. Dhanoa, S. J. Lister, R. Sanderson, and R. J. Barnes, *J. Near Infrared Spectrosc.*, 1994, 2, 43.