Chemometrics and model fitting in analytical chemistry

By

Matthew James Foot

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Department of Chemistry, Materials and Forensic Science
University of Technology, Sydney

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Certificate of Authorship / Originality

I certify that the work in this thesis has not been previously submitted for a degree nor has it been submitted as part of requirements for a degree except as fully acknowledged within the text.

I also certify that the thesis has been written by me. Any help that I have received in my research work and the preparation of the thesis itself has been acknowledged. In addition, I certify that all the information sources and literature used are indicated in the thesis.

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List of publications

Some of the work presented in this thesis has been published in the following refereed journal articles

1. Foot, M., M. Mulholland, and L. Kirkup, *Classification of the biopolymer sodium pemtosan polysulfate by infrared spectroscopy.* Chromatographia, 2003. **58**(1/2): p. 343-348.
2. Kirkup, L., M. Foot, and M. Mulholland, *Comparison of equations describing band broadening in high-performance liquid chromatography.* Journal of Chromatography A, 2004. **1030**(1-2): p. 25-31.
3. Foot, M. and M. Mulholland, *Classification of chondroitin sulfate A, chondroitin sulfate C, glucosamine hydrochloride and glucosamine 6 sulfate using chemometric techniques.* Journal of Pharmaceutical and Biomedical Analysis, 2005. **38**(3): p. 387-407.

Abstract

The aims of this project are to investigate the ability of advanced mathematical techniques and their contribution to the analysis of complex situations in analytical chemistry. The project falls into two areas. The first is the use of chemometrics to classify glycosaminoglycans (GAGs) such as chondroitin sulfates and glucosamines, substances that are being investigated for their potential use in the treatment of arthritis symptoms. This work is then expanded to the classification of novel anti-arthritis agents from different manufactures. The second part of this project looked at fitting different chromatographic band broadening models to real data. This work attempted to provide greater understanding of the processes involved in band broadening.

This classification work used different infrared spectroscopy techniques to analyse the molecules to which the classification systems were applied. Fourier Transform Infrared spectroscopy (FTIR), diffuse reflectance spectroscopy (DRIFTS) and Attenuated Total Reflectance spectroscopy (ATR) were evaluated for the classification of the chondroitin sulfates and glucosamines. The use of different spectral regions and derivative spectra were evaluated for their effect on the classification of the samples. It was found that FTIR coupled with derivative spectrums below 2000 cm^{-1} provided the best classification of these molecules.

The classification of sodium pentosan polysulfate was then considered using methods developed in the classification of chondroitin sulfates and glucosamines. Samples of the same material made by different manufacturers were provided to see if classification methods could distinguish them. Transmission spectroscopy coupled with the chemometric methods similar to those used for the classification of chondroitin

sulfate and glucosamines, were able to discriminate the samples by manufacturer and partially discriminate the samples by batch.

The second part of this thesis looks at fitting models to data as opposed to building classification models from data. This section looks at band broadening models in liquid chromatography followed by gas chromatography and finally looking at model fitting generally with some theoretical data. In this section a new model for band broadening in liquid chromatography is proposed. This model was found to be better able to predict band broadening behaviour in liquid chromatography at high flow rates. This model was then applied to gas chromatography; however it was found that previously published models best fit the data. The theoretical analysis highlighted the need for high quality data in order to draw conclusions about the model. It was also found that post column processes had the greatest effect on the band broadening.

Overall it was found that these advanced analytical techniques would be able to significantly improve the analysis of Glycosaminoglycan type compounds and provide further understanding of the band broadening process in liquid chromatography.

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