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Quasi-Quantitative Analysis by Multivariate Curve Resolution in Chemical Reaction and Blending Study

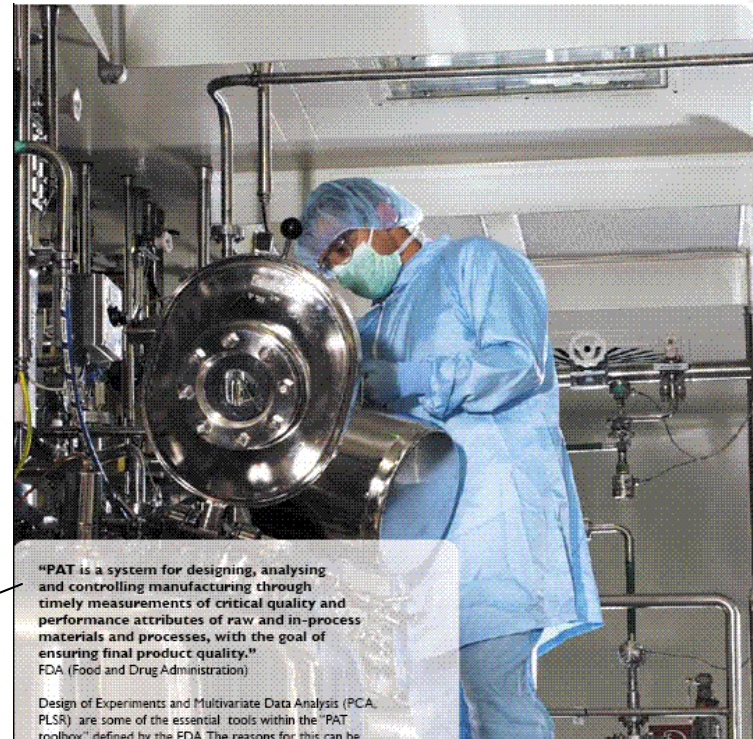
Dongsheng Bu, Martin Kermit and Valerie Lengard
Camo Software Inc

For EAS 2006

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Contents

- Introduction to Multivariate Curve Resolution
- Application Examples
 - FTIR: Process control at low temperature
 - NIR: Blending uniformity monitoring
 - UV/Vis: Chemical Reaction intermediates
- Conclusions



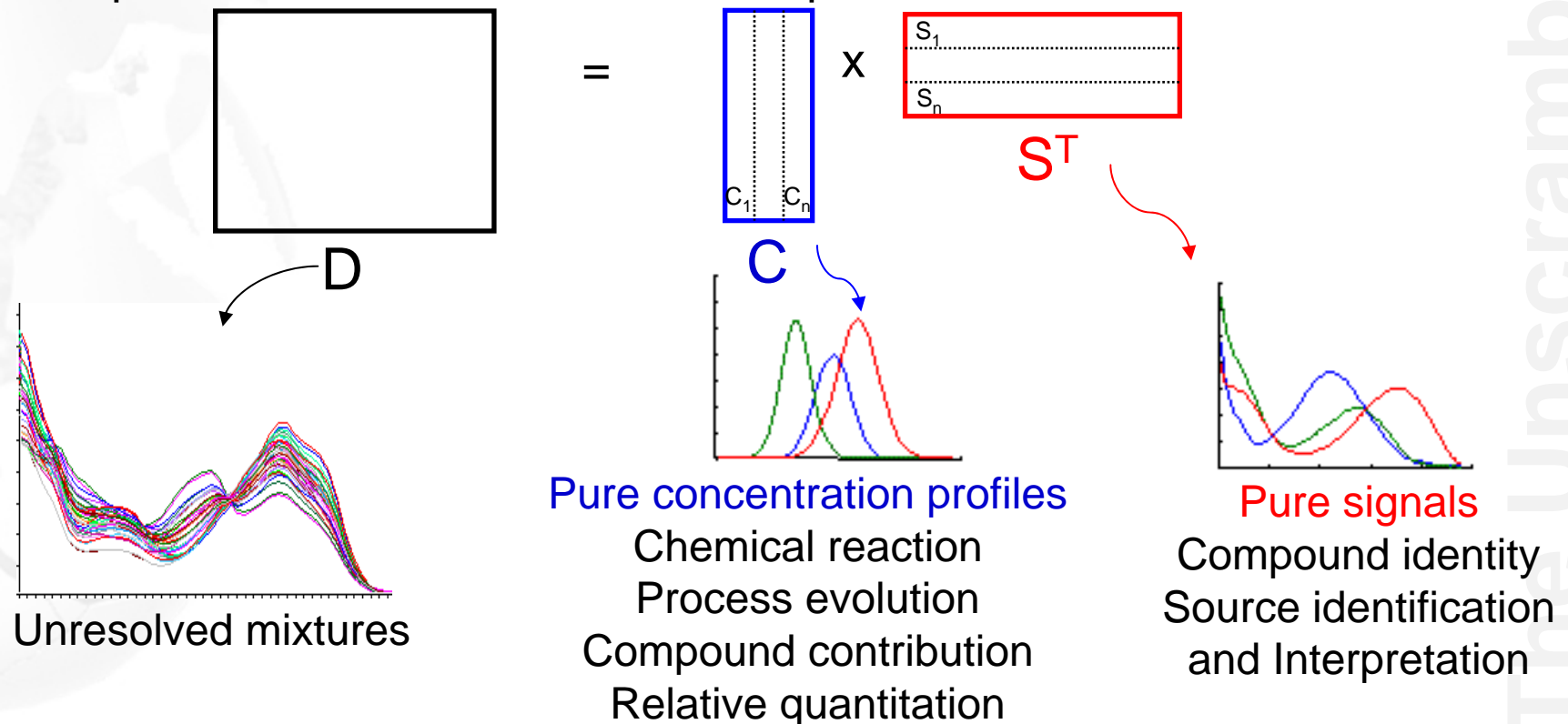
“PAT is a system for designing, analysing and controlling manufacturing through timely measurements of critical quality and

“PAT is a system for designing, analysing and controlling manufacturing through timely measurements of critical quality and performance attributes of raw and in-process materials and processes, with the goal of ensuring final product quality.”
FDA (Food and Drug Administration)

Design of Experiments and Multivariate Data Analysis (PCA, PLSR) are some of the essential tools within the “PAT toolbox” defined by the FDA. The reasons for this can be

(Self-Modeling) Multivariate Curve Resolution (MCR)

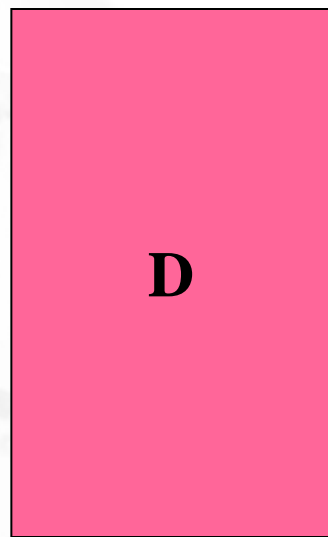
MCR methods may be defined as a group of techniques which intend the recovery of **concentrations** and **response profiles** of the components in unresolved mixtures using a minimal number of assumptions about the nature and composition of these mixtures.



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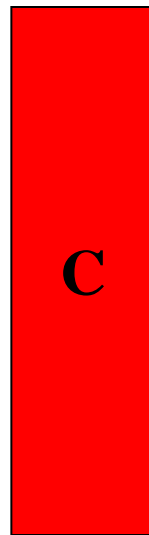


(Self-Modeling) Multivariate Curve Resolution (MCR)



Data matrix

=



Concentration
Matrix

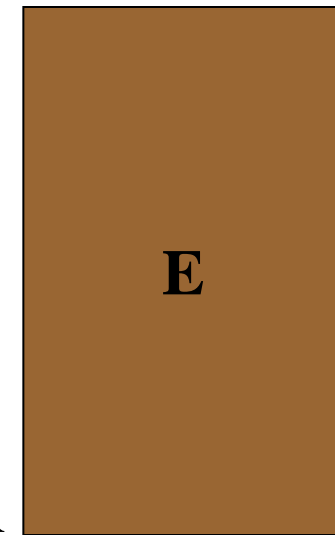


Pure
Spectra Matrix

N

+

NR



Residual Matrix
(Noise, Error)

Tauler R, Kowalski B, Anal. Chem. 65, 2040 (1993)
Windig W, Guilment J, Anal. Chem. 63, 1425(1991)
Bu D, Brown C, Appl. Spectrosc. 54, 1214 (2000)

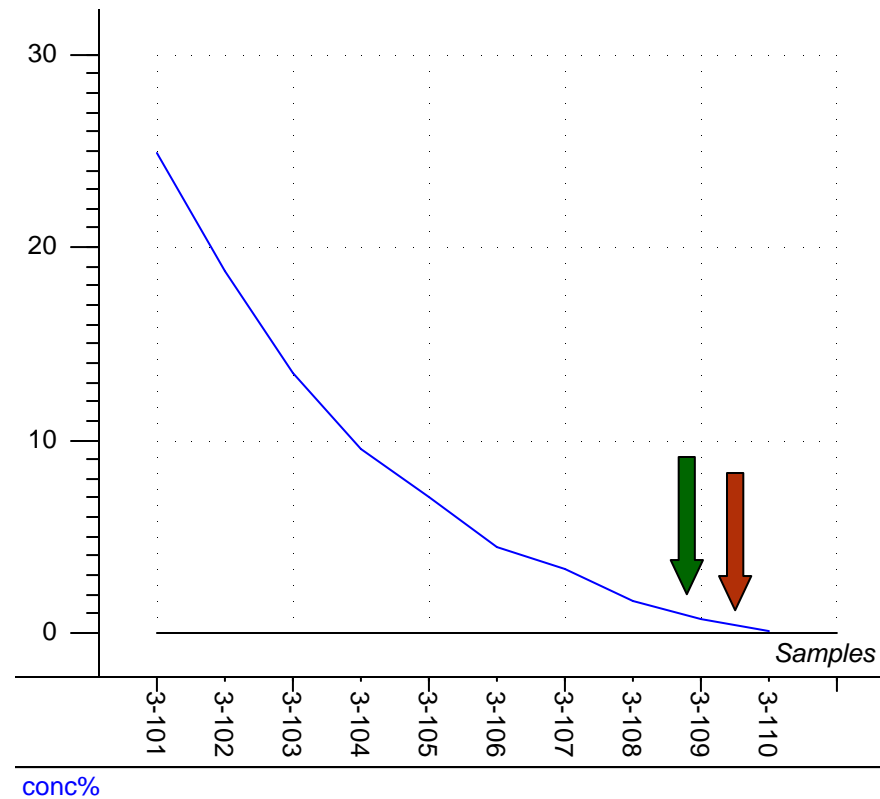
Part of MCR Talks in FACSS 06



- Water Sorption Process into a Biocompatible Polymer Film, MCR Analysis of ATR-IR Spectra.
- Interactive Self-Modeling Image Analysis
- Optical Sectioning of Live Cells via Hyperspectral Confocal Fluorescence Imaging and MCR.
- Incorporation of Practical Shape Constraints in the MCR-ALS Procedure for Analysis of Two-Way UV Resonance Raman.
- MCR and its Practical Use in Remote Sensing Applications
- MCR-ALS Analysis of Two-Way UVRR Spectra of Biologically Relevant Compounds.

Case 1- Chemical Process Ending Point Monitoring

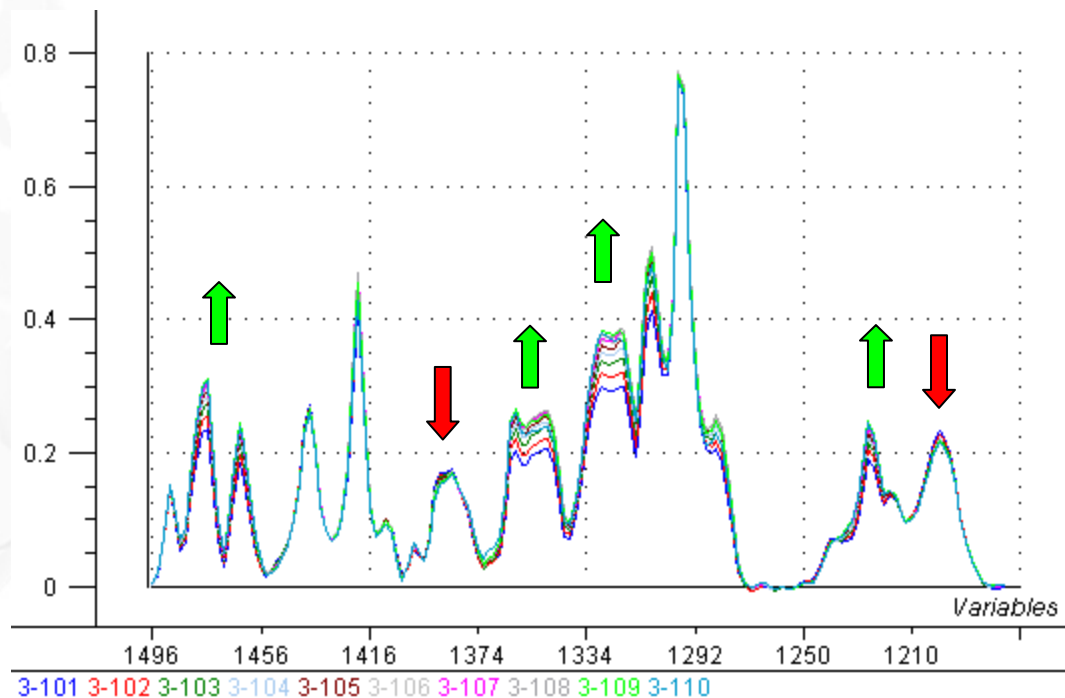
Real-time reaction monitoring by finding major reagent below **1%** and **0.5%**



Chemical Process

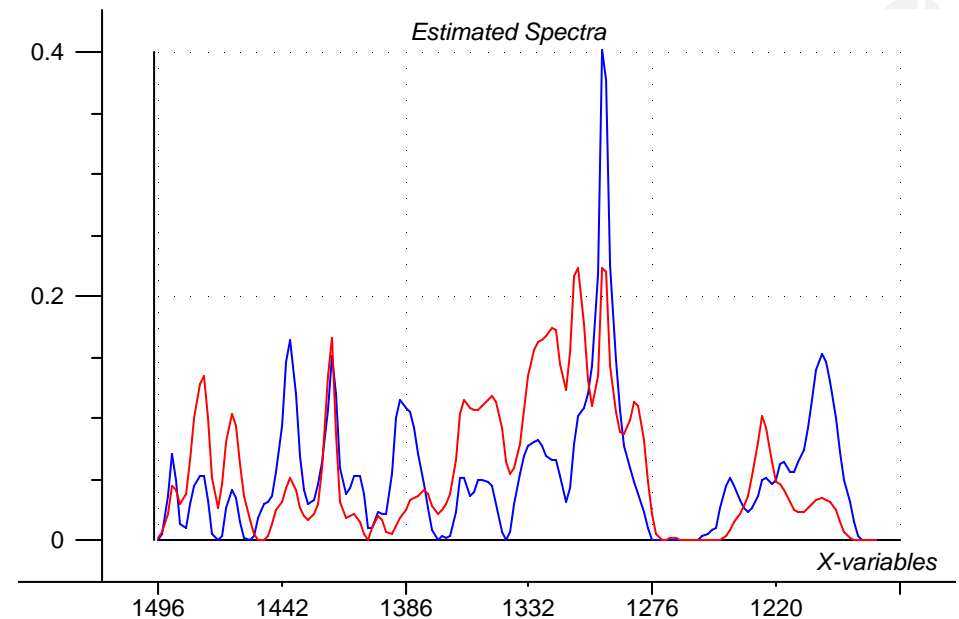
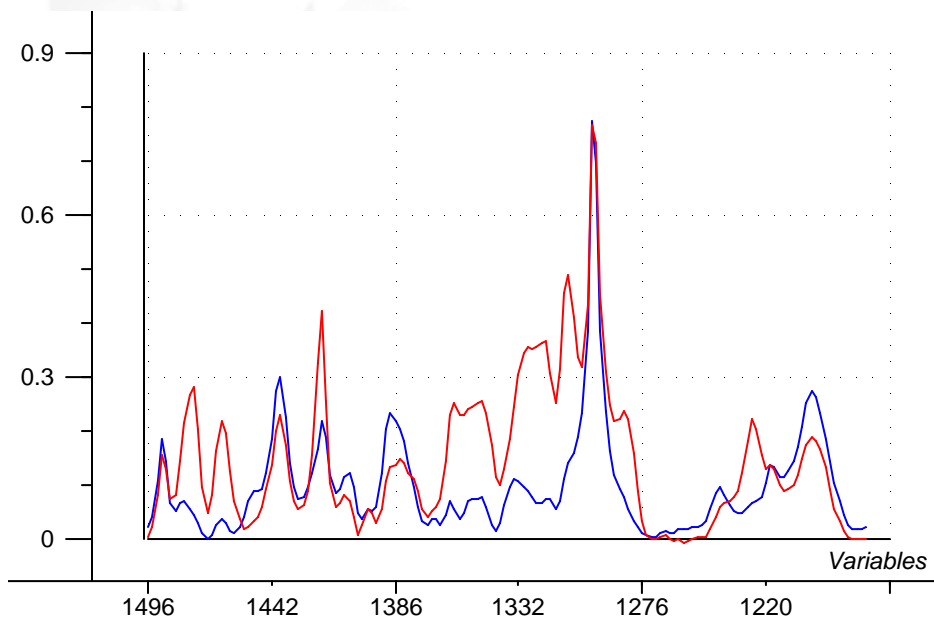
ATR-IR Spectra

- Sanitized data
- Low temperature reaction
- References could be measured by HPLC, but it is not in-line monitoring



MCR-Estimated Spectra on Two Runs' Mixture Data

Reagent/Product spectra

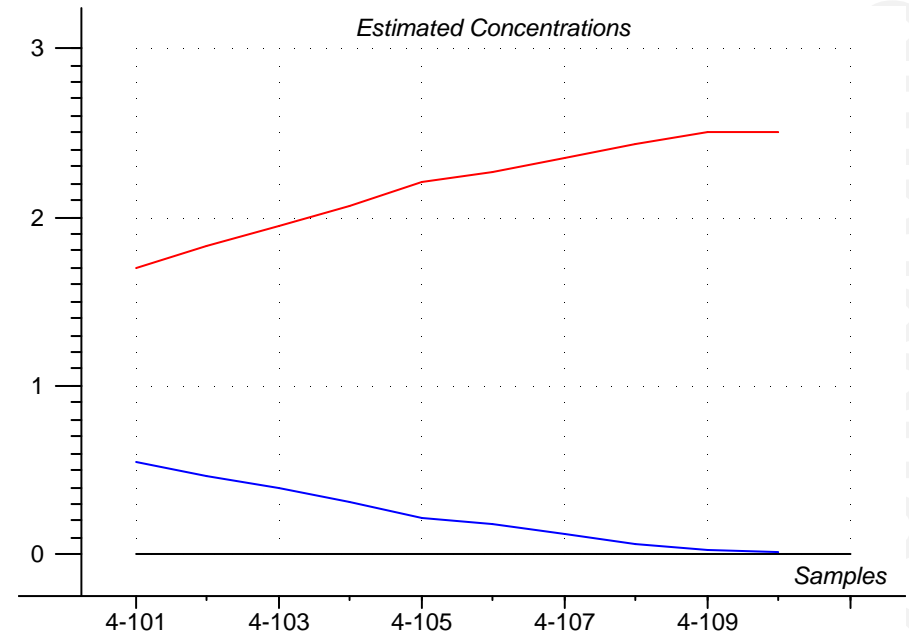
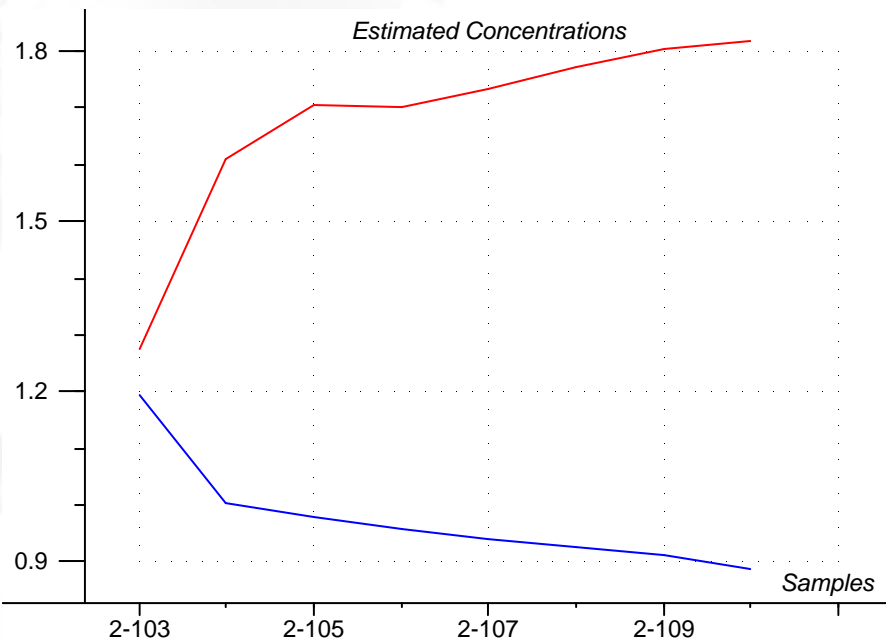


Useful information for selecting wavelength in modeling, studying chemical interaction and chemical structure transformation at extreme conditions

MCR-Estimated Concentrations on Two Runs' Mixture Data



Reagent/Product spectra

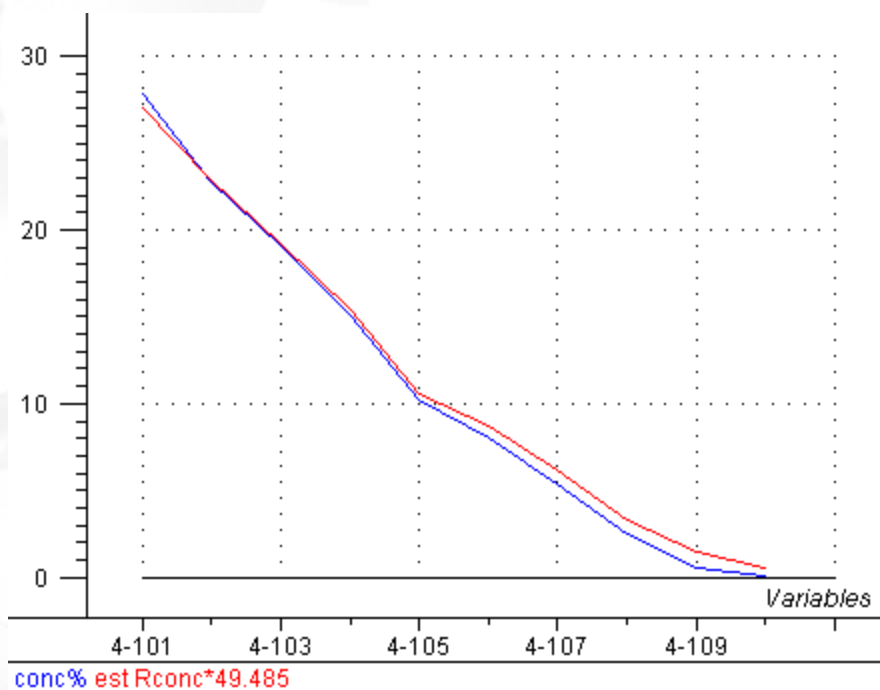


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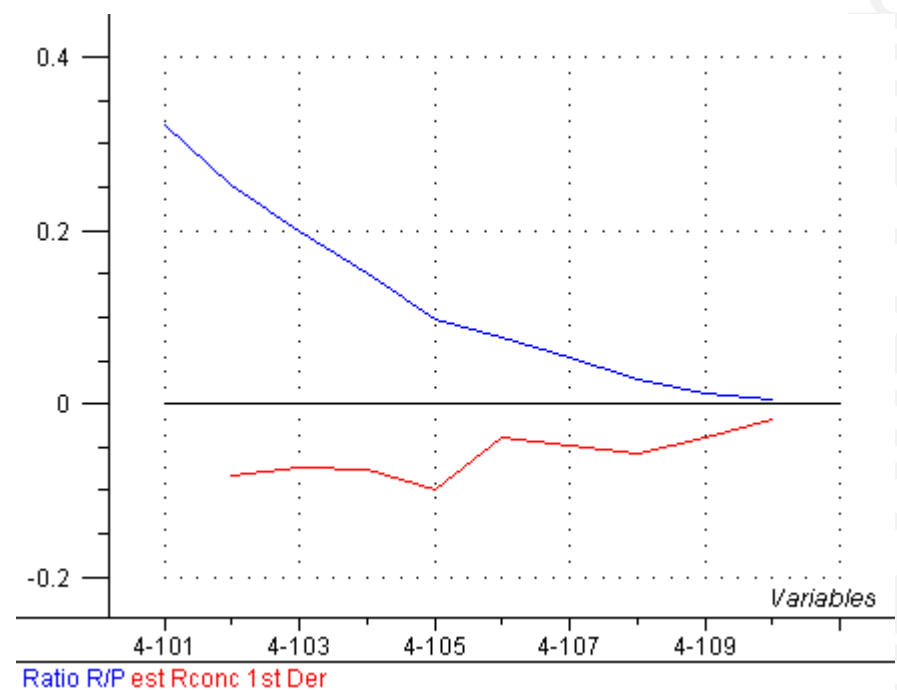


Estimated Concentrations Post-Processing

1) Projection Method with 1st and 4th HPLC reference

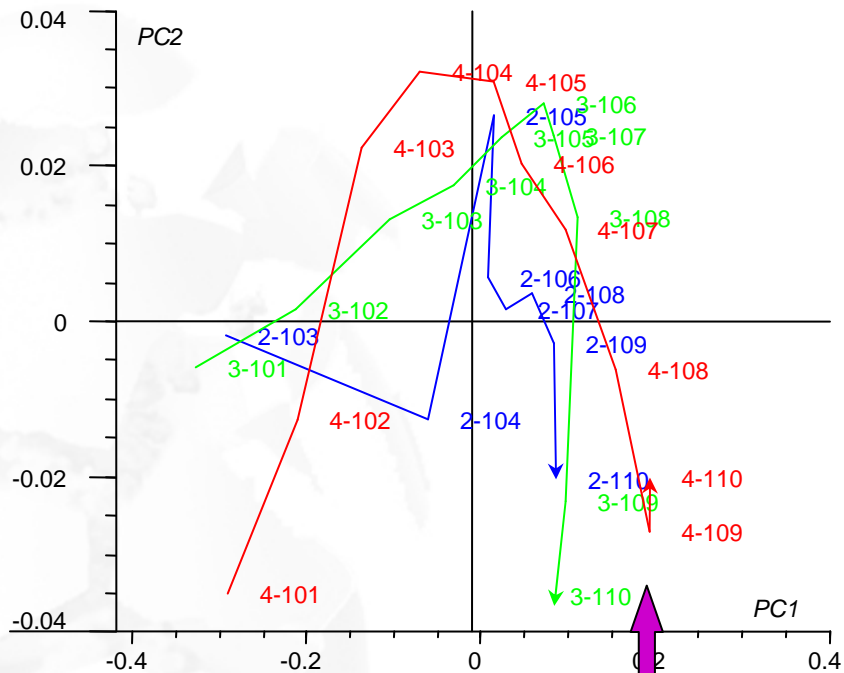


2) Ratio of Reagent/Product 3) Derivative of Reagent Conc



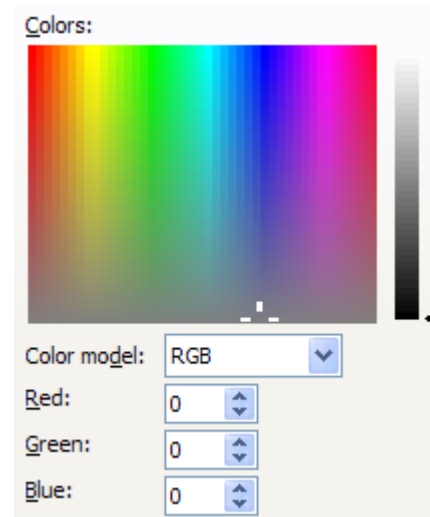
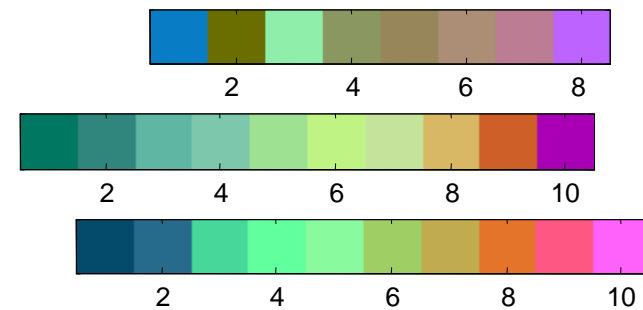
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PCA for 3 Runs



Ending area indicated
In scores scatter plot

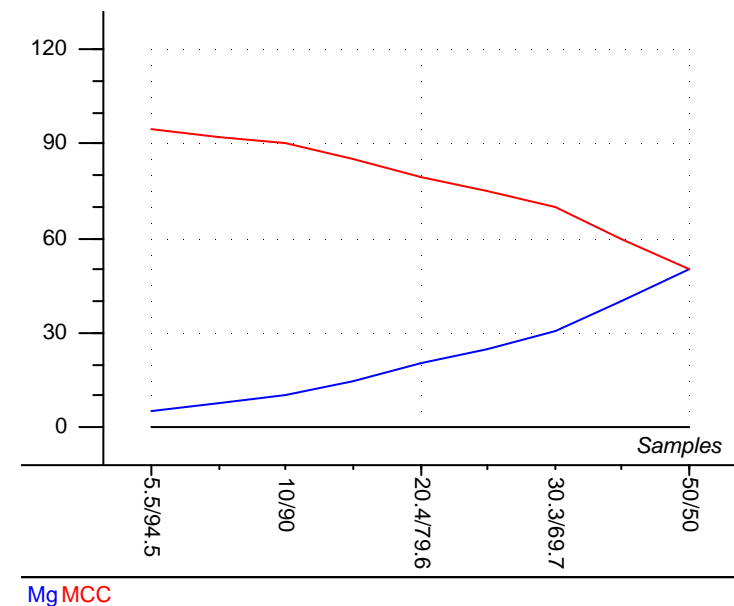
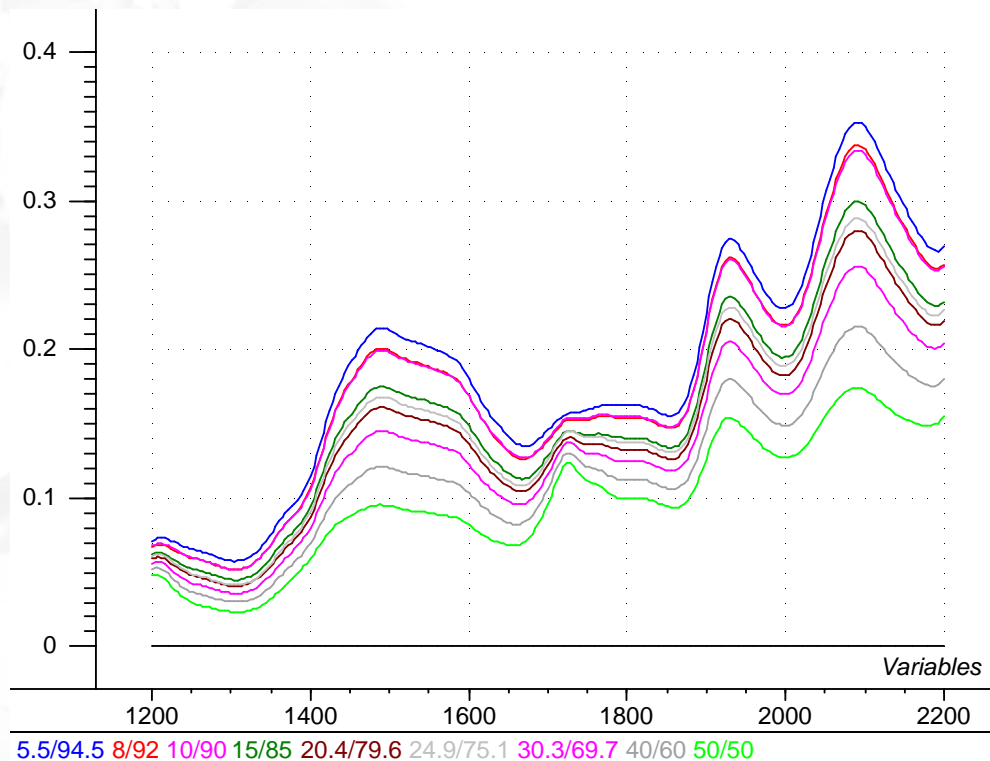
Ending color indicated
In scores RGB plot



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Case 2-NIR Blending

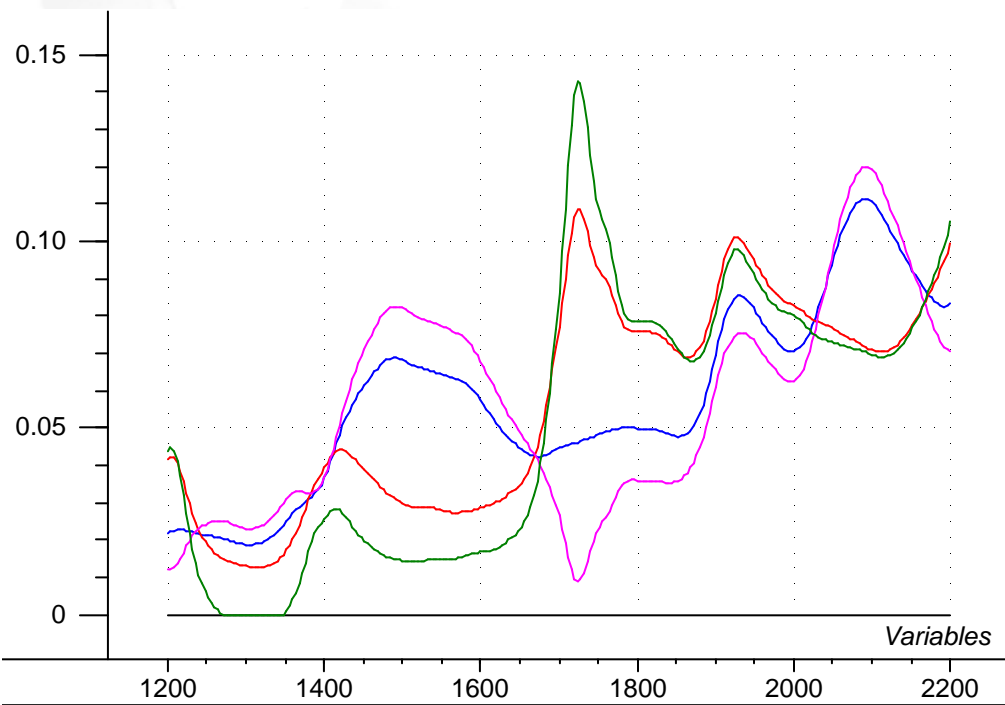
Feasible Study with mixtures of two excipients MCR on Pre-treated NIR data



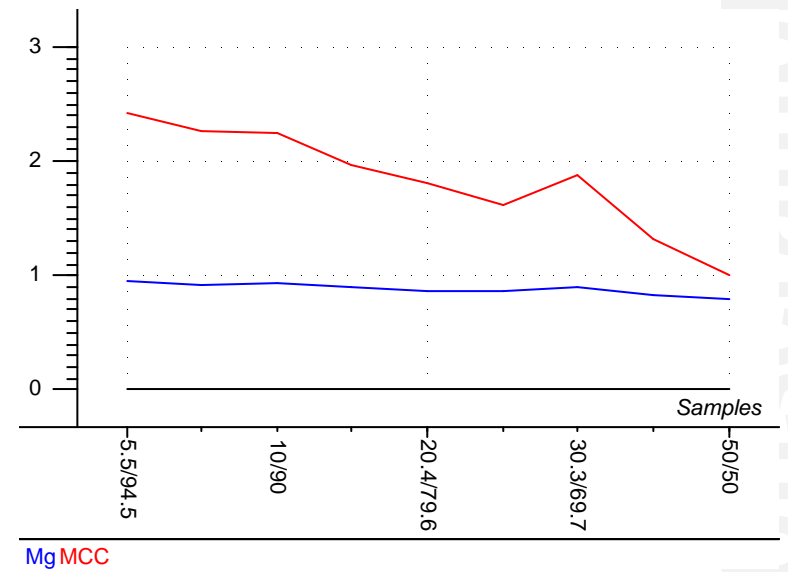
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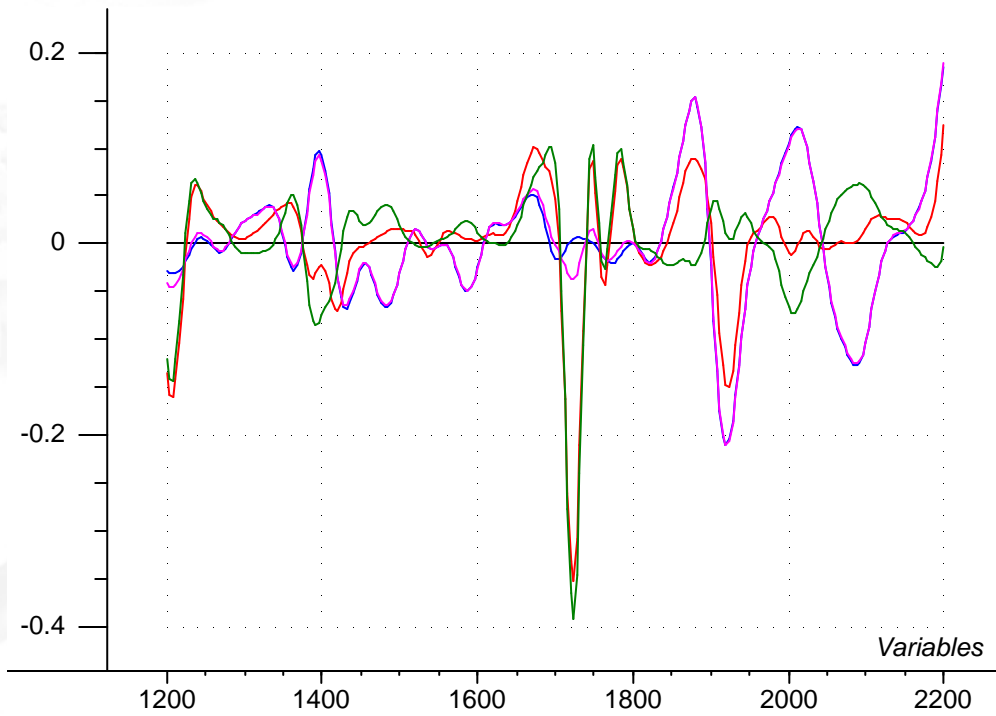
MCR-ALS with Raw Data



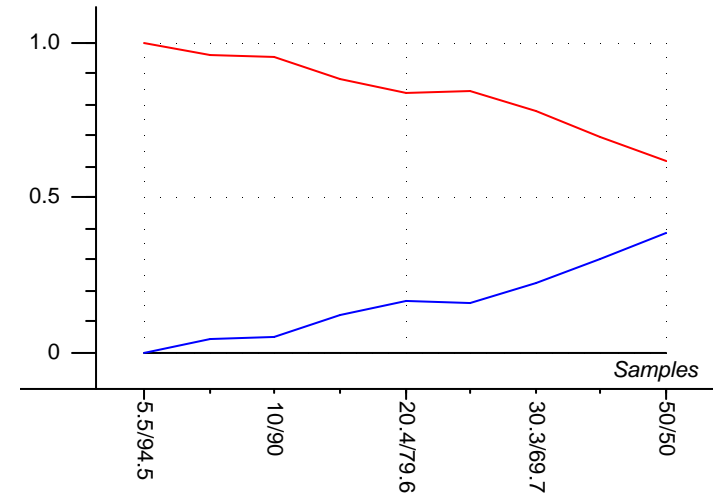
0/100 100/0 s1 s2



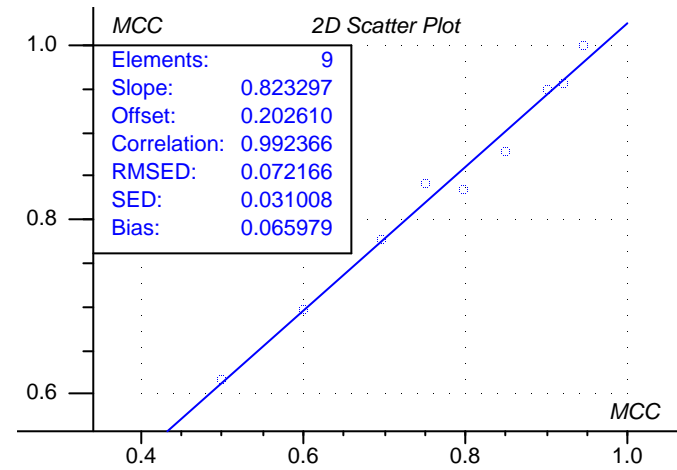
MCR-ALS with 2nd Der



0/100 100/0 s1 s2



Mg MCC



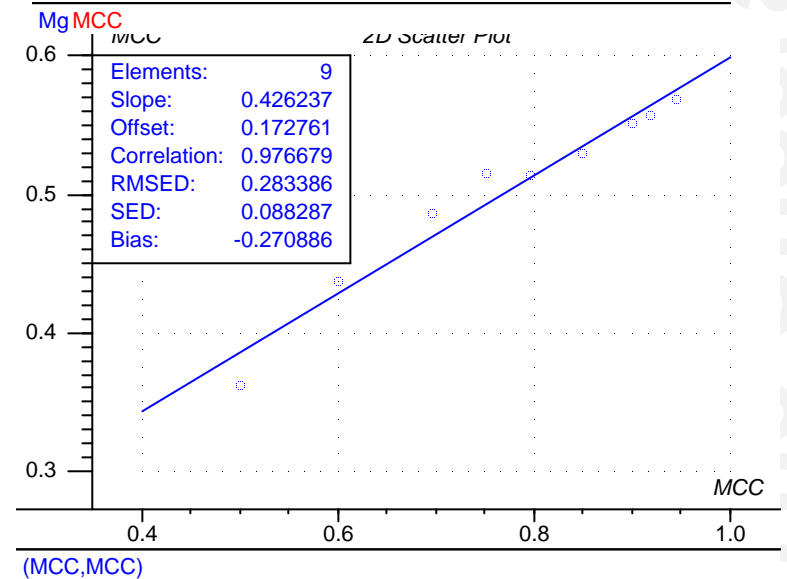
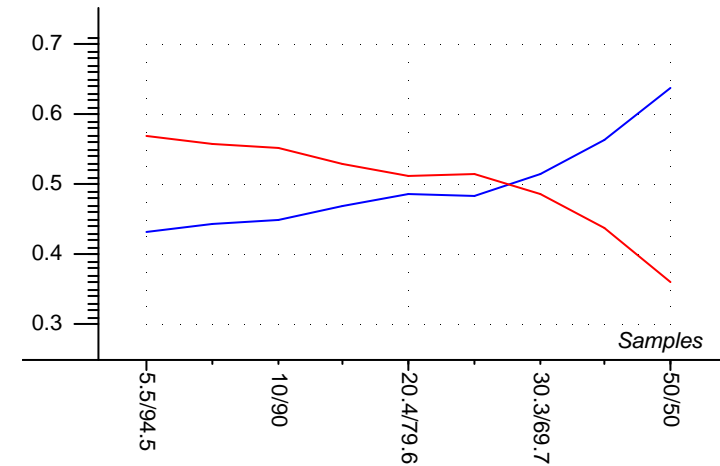
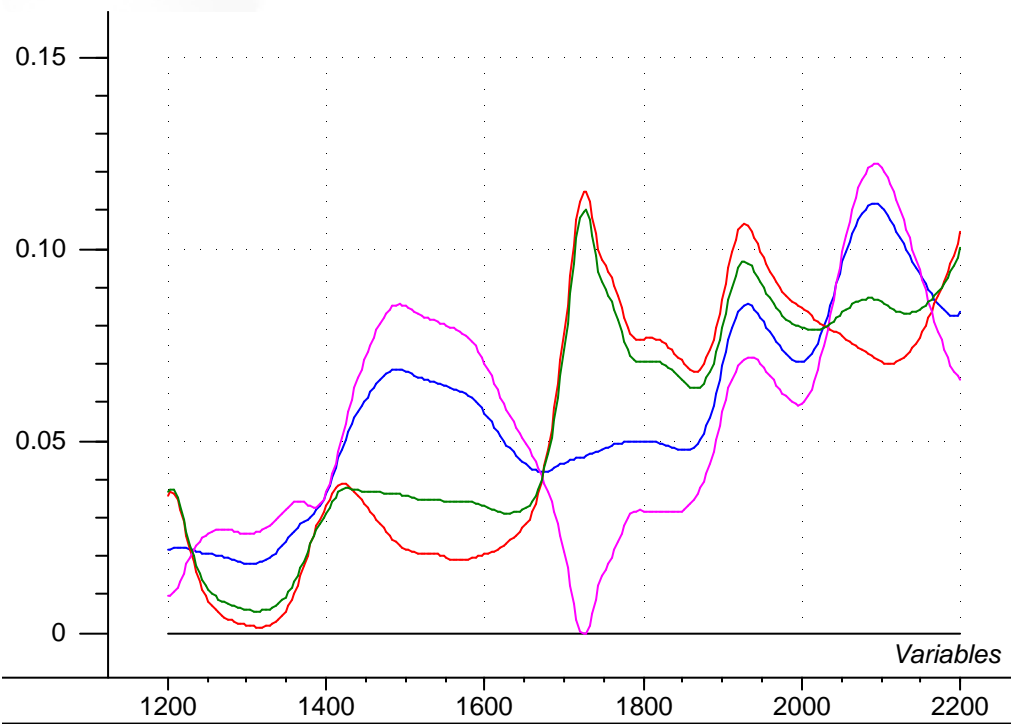
(MCC, MCC)

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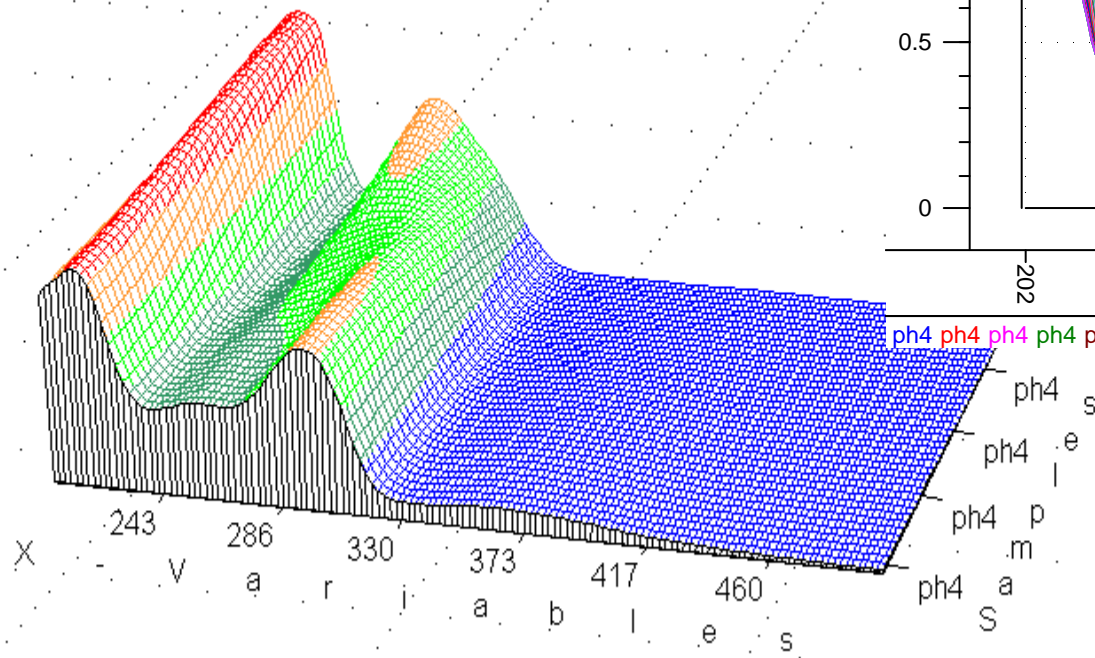
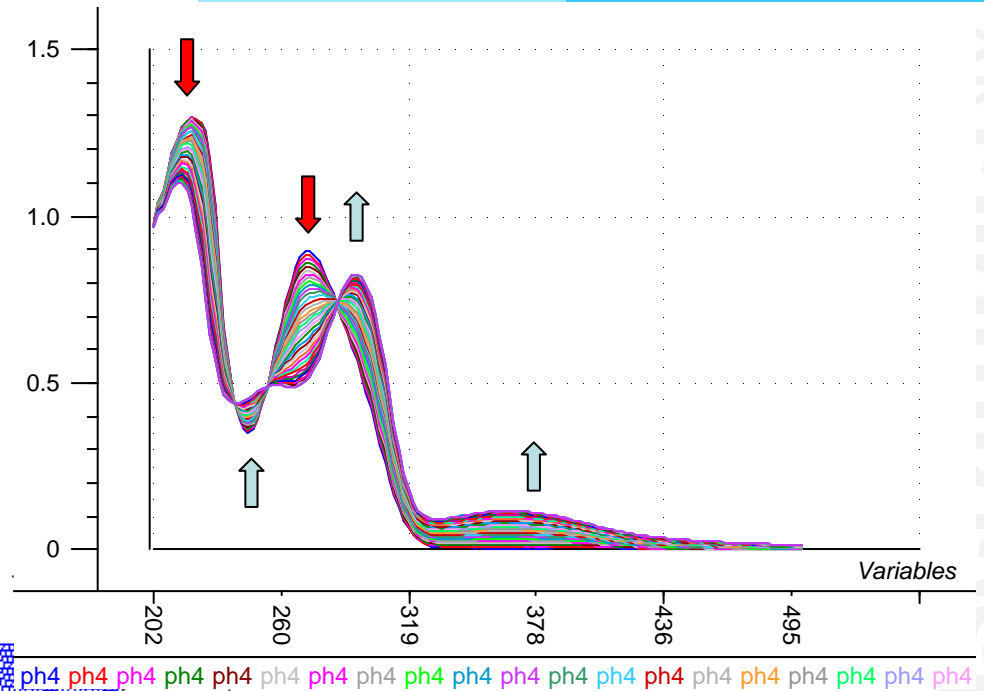
MCR-ALS with MSC



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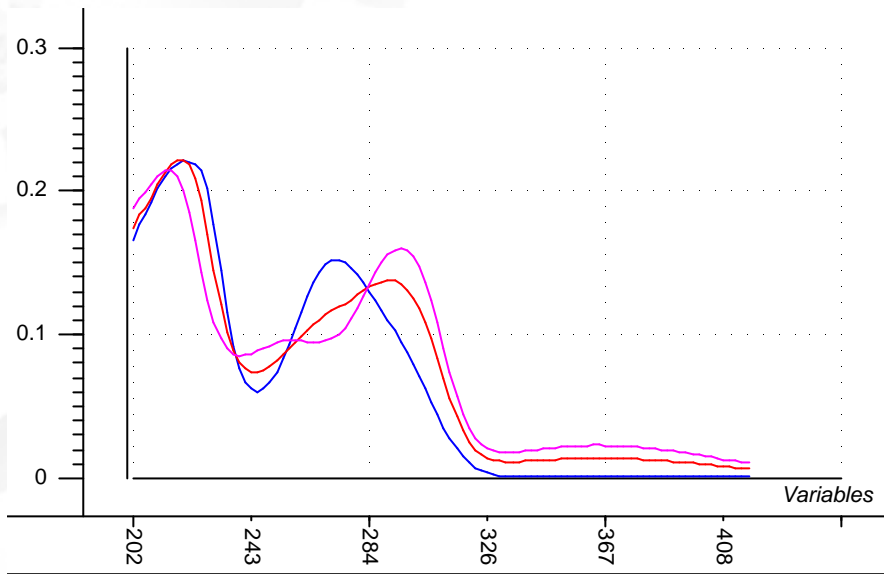


Case 3 – Reaction of Syringic Acid with Laccase, UV/Vis Data

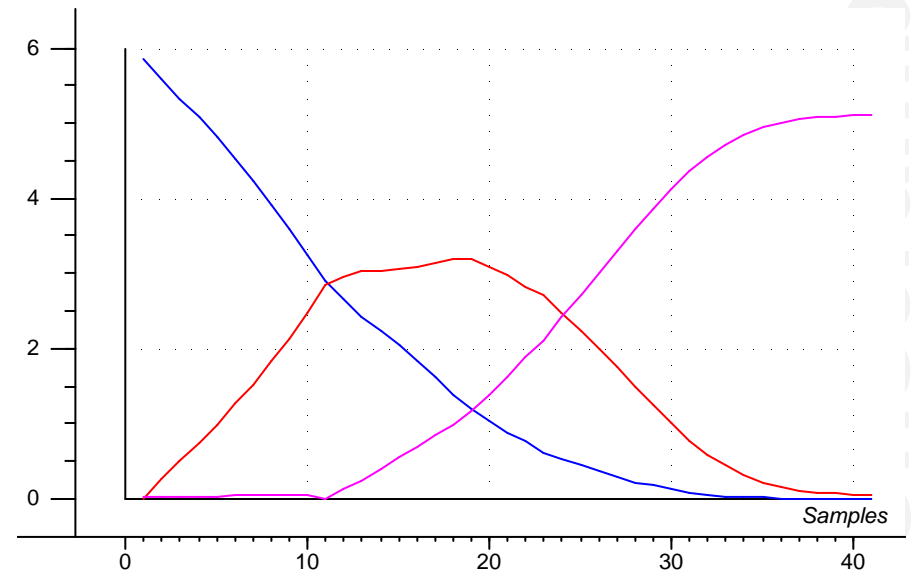


pH4

- Syringic Acid
- Intermediate
- End Product



pH4-1 pH4-2 pH4-3

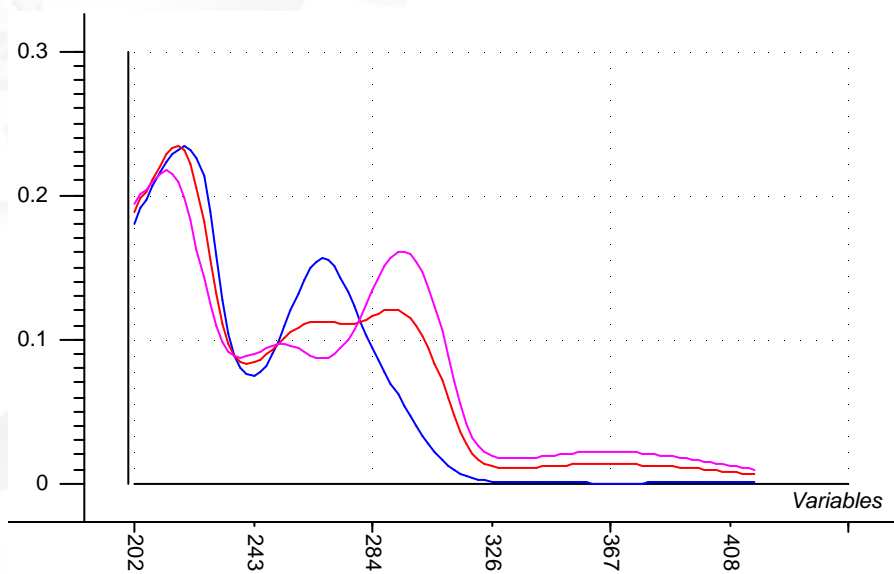


C1 C2 C3

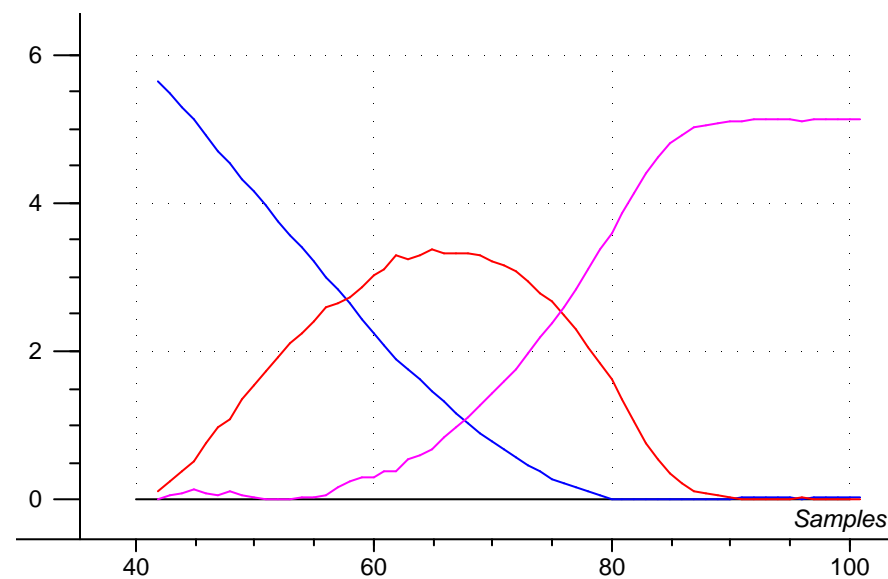
pH5



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pH5-1 pH5-2 pH5-3



C1 C2 C3

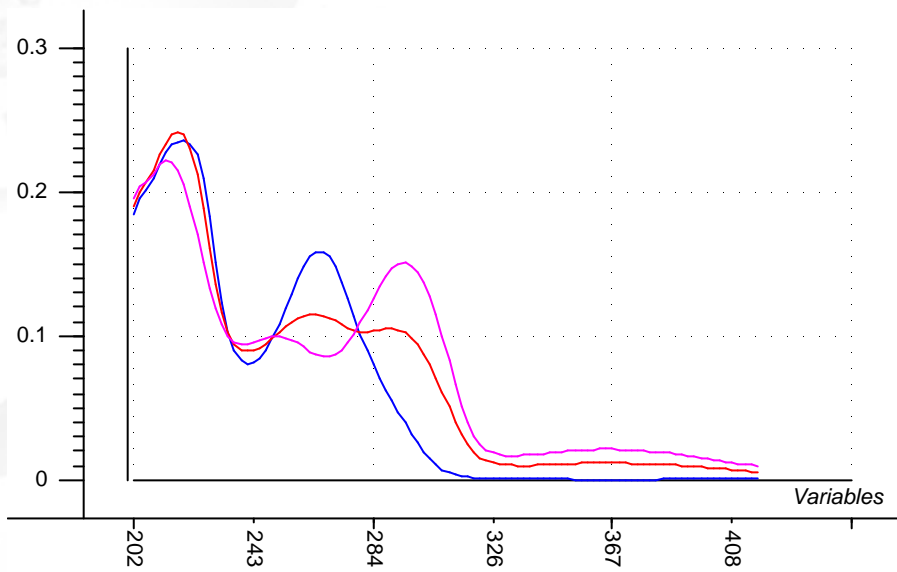
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pH6

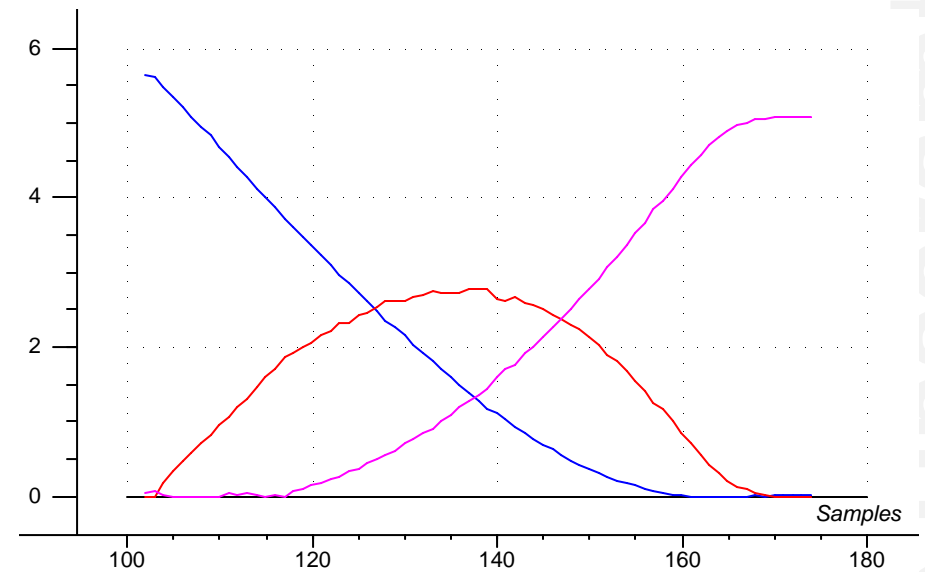


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pH6-1 pH6-2 pH6-3



C1 C2 C3

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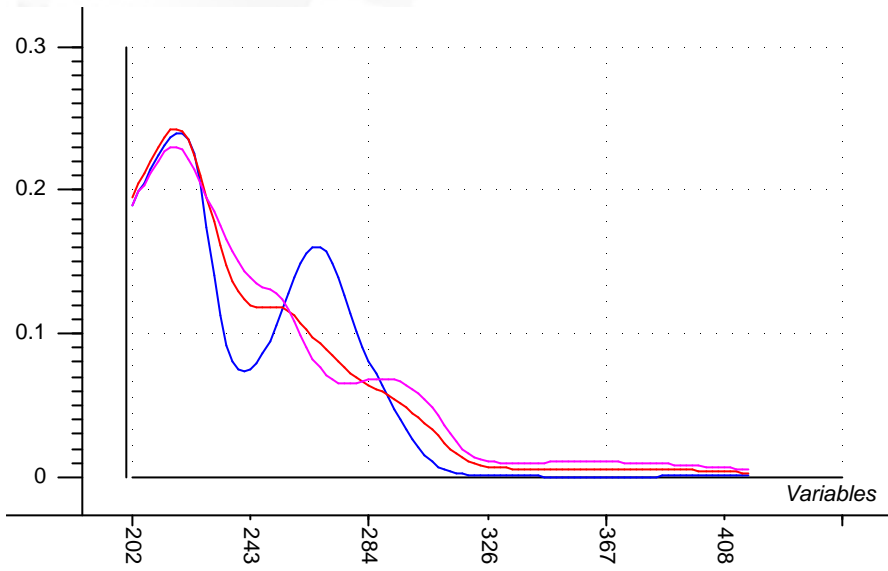


pH7

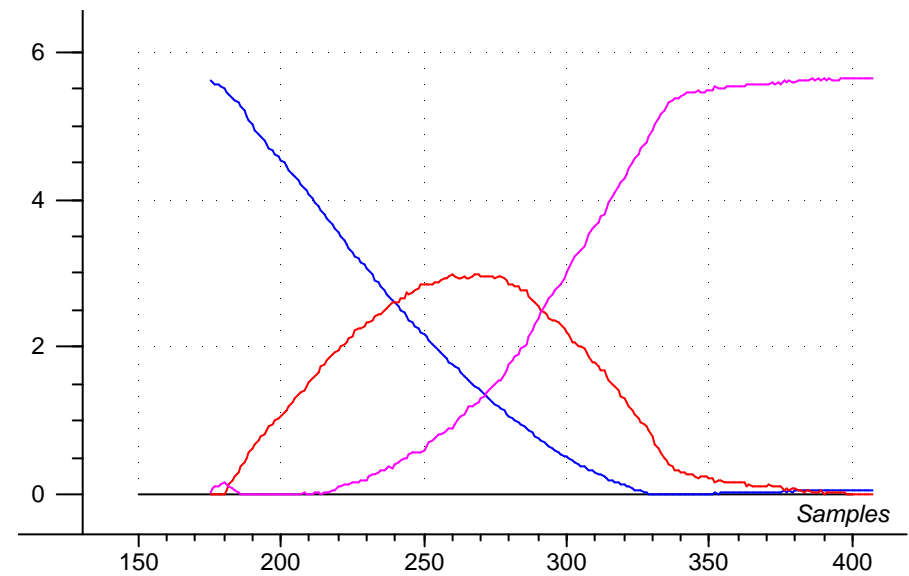


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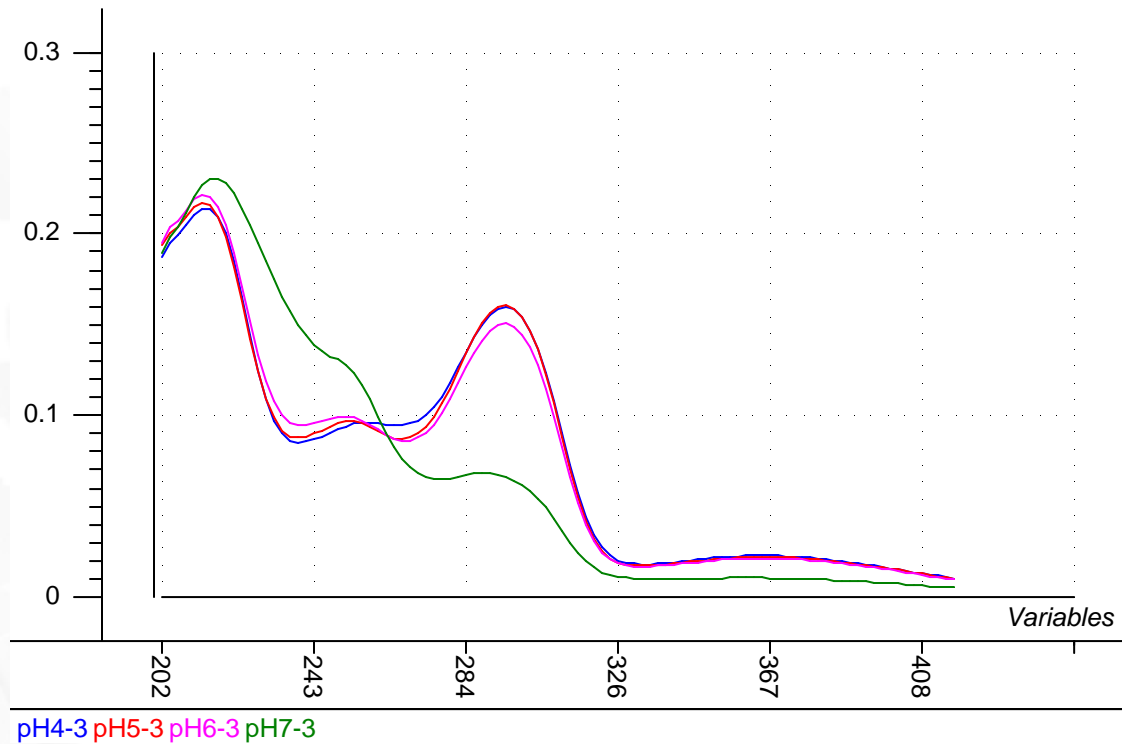
pH7-1 pH7-2 pH7-3



C1 C2 C3

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Estimated Syringic Acid Profiles



Useful information for the study of reaction kinetics and pH effects

Conclusions



- MCR could improve efficiency and reliability of real-time process monitoring.
- MCR can be used for quasi-quantitative analysis while regression-prediction approach is costly, or not feasible.
- Pre-treated NIR data is suitable for MCR, but right constraints settings needed.
- MCR could provide information of reaction intermediates.

Acknowledgements



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Camo Team

Unscrambler Customers

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