CPACT News

Issue No. 3
Spring 2001

CENTRE FOR PROCESS ANALYTICS AND CONTROL TECHNOLOGY

IN THE KNOW-HOW

Members of CPACT were delighted to learn that their proposal for funding under the Foresight LINK Award Scheme had been successful. The award, totalling £1.25M, has been granted to fund "Knowledge Driven Process Manufacturing" (KNOW-HOW) and this backing, together with commitment from industrial members, equips CPACT to forge ahead with Phase II early in 2001.

In Phase II, CPACT will help companies achieve and sustain competitive advantage by providing solutions to problemsin areas such as:

- drying
- scale-up
- fermentation
- sampling
- impurity monitoring
- end point detection
- mixing and blending
- process modelling

This will involve innovation in a range of technologies including,

- microwave, NMR, mass, NIR, uv-vis and Raman spectrometries
- data mining
- dynamic performance monitoring
- multivariate process tracking
- acoustic monitoring
- signal processing
- process chemometrics
- process optimisation

Meetings and discussions are currently taking place with members to finalise plans for research in the different project areas. Recruitment of postdoctoral researchers and PhD students is also underway.

Learn More at the Beardmore!

Conference 3/4 April 2001

ADVANCES IN PROCESS ANALYTICS AND CONTROL

It is not often that conferences of interest to both engineers and scientists are arranged. However, in most high technology industries, analytical scientists, process chemists, process engineers, control engineers and plant managers are required to work together to ensure manufacturing excellence. This can be assisted by implementing advanced methods of process monitoring, control and optimisation. The aim of this meeting is to provide a forum for the presentation and discussion of recent advances in engineering and scientific topics relevant to process analytics and control technologies.

The conference is open to all interested participants and will provide opportunities for workers in academia and industry to present their research to an informed multi-disciplinary audience. The programme will be of interest to those involved in the development and implementation of procedures for on-line analysis, signal processing, plant performance monitoring and process optimisation and control.

The programme will include invited and contributed lectures, poster presentations and a CPACT members' exhibition.

Set in expansive grounds, the Beardmore Conference Hotel is an independent four star hotel with purpose built conference facilities including a 170 seat tiered auditorium. Centrally located just 20 minutes from Glasgow city centre, the hotel is a ten minute drive from Glasgow Airport. Frequent trains connect to Glasgow city centre from the local station of Dalmuir. Car parking is available. For more hotel information visit: www.beardmore-hotel.co.uk

Registration

Registration leaflets can be obtained from - Natalie Driscoll
Tel: +44 (0) 141 548 4836
Email: natalie.driscoll@strath.ac.uk
Deadline for registrations - 23 March 2001

Congratulations on JIF Award from the Chancellor

Front row: Sudipta Roy, John Backhurst, Rt. Hon. Christopher Patten CH, Elaine Martin
Back row: Julian Morris, Keith Scott, Galip Akay, Colin Ramshaw, Roshan Jachuck

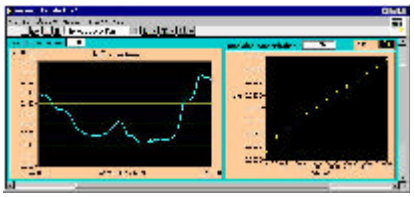
A Joint Infrastructure Fund (JIF) award (£1.6M) has been made to the University of Newcastle to establish the necessary Infrastructure for an Innovative Responsive Processing Unit within the Department of Chemical and Process Engineering. This initiative will bring together three internationally acknowledged research centres: the Process Intensification and Innovation Centre (PIIC), the Electrochemical and Materials Processing Centre (EMPC) and the Foresight Centre for Process Analytics and Control Technology (CPACT). It will provide a focus for a comprehensive multi-disciplinary experimental facility that will establish the UK at the world leading edge in "Responsive Process Manufacturing" and at the international forefront in the development and demonstration of intensified processing plant. A key aspect of this facility will be access to world class process engineering, mathematical and statistical modelling, signal processing and chemometrics, advanced process control and performance monitoring technologies.

The new Responsive Processing Laboratories and Research Offices will be built during 2001 and will provide for CPACT access to revolutionary responsive processing experimental facilities. The development of these demonstration processes will be critical in moving the UK process manufacturing and biochemical industries from current continuous and batch-mode processing to the adoption of new methodologies that offer major advantages in terms of cost, energy consumption, environmental impact and processing flexibility. The new Responsive Processing unit will be capable of manufacturing novel, demonstration process plant with state-of-the-art analytical control and performance monitoring systems. This will bring to both global manufacturing companies and the increasingly important SME chemicals sector revolutionary "desk-top" processing and will contribute to the transition of the UK chemicals, bio-chemicals, pharmaceuticals, food and materials processing sectors from their present technology base into high added-value, highly responsive process manufacturing.

Batch Reactor Monitoring

A reactor facility has been established at the University of Strathclyde to allow the development and testing of procedures for the on-line monitoring, optimisation and control of batch reactions (**Figure 1**). Two model esterification reactions, involving a mono-basic acid (crotonic) and a di-basic acid (itaconic), have been used to evaluate the improvements achieved. The esterification of crotonic acid with butan-2-ol is homogeneous, whereas the reaction of itaconic acid with butan-1-ol is heterogeneous, with the mono-ester the preferred product. In order to carry out these reactions, a number of issues need to be addressed including the operation and control of the batch reactor and the choice of analytical technique for monitoring the reaction.

A LabView monitoring and control system has been developed, as an alternative to the existing proprietary system, to operate the batch reactor at Strathclyde. The LabView system provides greater flexibility for the monitoring of physical and analytical variables, and permits more complex or novel control algorithms to be implemented. For example, it is possible to export data from the analyser computers via a local area network onto the LabView control computer. This enables data from a number of different techniques to be displayed simultaneously on the one computer. Through the use of previously built and stored calibration models, on-line prediction of concentration can be achieved. **Figure 2** shows an example of on-line prediction of ester concentration using NIR data. The feasibility of having a link from LabView to the CPACT website has been investigated and this will allow reactions to be monitored via the internet.



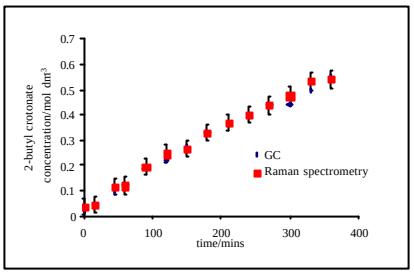
The problem of getting a representative sample is crucial for on-line analysis. This issue has been central to the design and construction of a fast sampling loop. The loop enables samples to be taken from the reaction mixture for off-line analysis. A secondary sampling loop has also been constructed to allow the reaction mixture to flow through a low-field process NMR spectrometer (Resonance Instruments) to permit on-line analysis.

A number of techniques have been used to monitor the esterification reactions. On-line analysis of the crotonic acid reaction has been carried out by Raman and NIR spectrometries by immersion of probes, which are connected to the spectrometers by fibre optic cables, into the reaction mixture. Calibration models were built for the Raman and NIR data using GC and LC data, respectively, obtained by off-line analysis of samples taken during a number of reactions. It was necessary to use a partial least squares (PLS) calibration model for the NIR data. In comparison, for Raman spectrometry, it was possible to build a univariate calibration model using the signal at 838 cm^{1} in the first derivative spectrum. The results obtained using both techniques were in good agreement with those obtained by the reference method. **Figure 3** shows a comparison of the concentration of butyl crotonate predicted using Raman spectrometry with that obtained by off-line GC analysis.

The itaconic acid reaction has been studied using on-line Raman spectrometry and at-line NIR and low-field ^{1}H NMR spectrometries. PLS calibration models were built for each of the techniques using off-line LC data from the analysis of a number of reactions.

In the case of low-field ^{1}H NMR spectrometry, it was possible to monitor the production of mono-ester from the shift in the spectral peak produced by the exchangeable proton that moves between the mono-ester carboxylic acid and butan-1-ol. This feature permits optimisation and reaction monitoring without the need for standards. The use of such model-free procedures is attractive as the need for construction, maintenance and update of calibration models can be avoided. Research in this area has proved encouraging with algorithms developed based on multivariate curve resolution methods.

At present, it is not possible to monitor the pH of the batch reactions at elevated temperatures in non-aqueous media using standard commercially available pH probes. To overcome this problem thermally grown iridium oxide electrodes have been developed for pH monitoring in harsh environments. The sensors show a stable Nernstian response in buffers and respond faster than a glass electrode. Promising results have also been obtained when studying the response of the electrodes to dichloroacetic acid in toluene or ethanol.



Acknowledgements

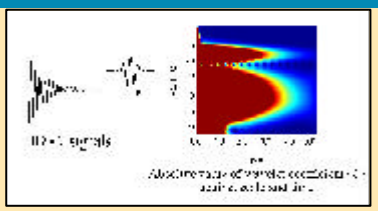
This work has been carried out at the University of Strathclyde by CPACT researchers Alvaro Diez-Lazaro, Danladi Mamman, Colin McGill, Alison Nordon, Kamal Setarehdan and Manori Weerasinghe with the support of BSc and MSc project students Viv McAlpine, Angus Nicholson, Claire Ordoyno, Jan Vos, Claire Watt and Steve Wilson. For further information contact Colin McGill (colin.a.mcgill@strath.ac.uk) or Alison Nordon (alison.nordon@strath.ac.uk)

Process NMR Spectrometry

A low-field NMR spectrometer (with an operating frequency of 29 MHz for ^{1}H), manufactured by Resonance Instruments, has been evaluated for use in process analysis. At low fields, spectral resolution can be poor particularly in ^{1}H NMR spectra, and hence overlapping signals are likely to result. Traditional approaches to the analysis of overlapping signals include the construction of multivariate calibration models using e.g. partial least squares (PLS), which are then used to predict the concentration of components in unknown samples. However, any procedure that utilises calibration models requires continual model maintenance and update. Hence, it is desirable to employ procedures that are model-free. The use of model-free quantification is of particular interest in NMR spectrometry, as the NMR signal is inherently quantitative. Usually, NMR signals are analysed in the frequency domain, after Fourier transformation. However, the information contained within the spectrum is identical to that contained within the time domain, i.e. the initial free induction decay (FID) signal. A number of data processing steps are involved in going from the time to frequency domain. Analysis of signals in the time domain would enable those data processing steps that are difficult to automate reliably, such as phasing, to be eliminated. This is particularly important for at-line and on-line applications of process NMR spectrometry.

A number of potential methods for the extraction of quantitative information from low-field NMR signals in the time domain have been investigated. The methods include the continuous wavelet transform and modifications of the generalised rank annihilation method (GRAM). The work involving GRAM has been carried out in collaboration with Paul Gemperline (Measurement and Control Engineering Centre, University of East Carolina).

A wavelet is a waveform of effectively limited duration that has an average value of zero. To analyse the NMR FID with the continuous wavelet transform, the FID is multiplied by scaled and shifted versions of the original



wavelet to generate a time-scale representation of the original signal (see figure 1). From this, it is then possible to determine the parameters of interest; namely frequency (V), signal amplitude (A) and the transverse relaxation time (T_2). It is the amplitude parameter that can be used to determine component concentrations. The method used has previously been applied to high-field NMR signals, where the signals obtained are of superior resolution to those that can be obtained at low fields. Hence, the first stage in this work was to investigate the limitations of the method in terms of the effects of phase, frequency, signal-to-noise ratio and resolution on predictive accuracy. This was achieved using simulated data, with the parameters chosen to simulate the data, such as linewidths, being comparable to those in spectra obtained with the low-field NMR instrument.

An important feature of the continuous wavelet transform is that phase correction of the NMR signal prior to analysis is not required. In NMR, the frequency of a particular signal is dependent upon the composition of the sample and hence during a reaction, a peak may shift. Although the amplitude determined using the continuous wavelet transform is dependent upon scale, which is related to frequency, this can be corrected for. There are some limitations on the frequencies that can be analysed. It is not possible to analyse signals at 0 Hz, which means in practical terms that the transmitter in the NMR experiment would have to be positioned to one side of the spectrum.

The ability to analyse overlapping signals can be enhanced by increasing the frequency of the analysing wavelet, although some of the approximations used in the method limit the maximum frequency of the wavelet that can be used. Current research will improve the ability of the method to analyse poorly resolved signals.

GRAM was originally developed for the analysis of two-dimensional data sets such as LC-UV spectrometry data. In order to analyse FIDs using GRAM, it is first necessary to transform the FID, a vector, into a Hankel matrix. Application of the GRAM algorithm to Hankel matrices formed from test and reference FIDs, resolves the FIDs into their constituent frequencies and calculates the amplitude ratio of each frequency in the test and reference FIDs. As with the continuous wavelet transform, the FID does not have to be phase corrected prior to application of the GRAM algorithm. There are no limitations on the frequency of the signal that can be analysed, although a major disadvantage of GRAM is that the frequency of a particular signal must be identical in both the reference and test FIDs. At present, the ability of GRAM to resolve overlapping signals is far superior to the continuous wavelet transform. The results obtained using GRAM have also been compared to those obtained by PLS analysis of Fourier transformed spectral data. The performance of GRAM was found to be comparable to PLS, despite the fact that only one reference sample was needed for GRAM whereas PLS analysis required a number of calibration samples.

Achnowledgements

This work has been carried out at the University of Strathclyde by CPACT researchers Colin McGill, Alison Nordon and Kamal Setarehdan. For further information contact Colin McGill (colin.a.mcgill@strath.ac.uk) or Alison Nordon (alison.nordon@strath.ac.uk).

Chemometrics in Analytical Chemistry Conference

The 7th International Conference on Chemometrics in Analytical Chemistry took place from 16th to 20th October at Antwerp, Belgium.

A number of presentations and posters were presented which are of particular relevance to process analysis. Multivariate curve resolution was the subject of a number of presentations, with one describing automated application of the technique to resolve complex multicomponent data. The use of in-situ UV-visible spectrometry and multivariate curve resolution was presented as a method for forecasting batch endpoints without the need for calibration. On-line NIR and NMR spectrometries in combination with multivariate analysis were discussed in relation to prediction of polyolefin properties in polypropylene and high-density polyethylene production. Other presentations described the estimation of uncertainty in sampling, smoothed PLS regression, and the use of similarity measures for clustering spectra that exhibit peak shifts.

Fountain at Province House, Antwerp

Alison Nordon (CPACT Strathclyde) gave a presentation entitled 'Quantitative analysis of process NMR signals in the time domain'. The talk gave an overview of some of the work carried out by Alison and Colin McGill (CPACT Strathclyde) in collaboration with Kamal Setarehdan (CPACT Strathclyde) and Paul Gemperline (MCEC, University of East Carolina). The methods investigated so far include the continuous wavelet transform and the generalised rank annihilation method (see article on Page 2). Such methods are of particular interest, as neither technique requires construction of calibration models nor application of a phase correction to the NMR signal prior to analysis.

For further information contact Alison Nordon (tel: 0141 548 2073, email: alison.nordon@strath.ac.uk).

IFAC Adchem 2000 Conference

CPACT was represented at the International Federation for Automatic Control Conference, ADCHEM'2000, held in June 2000 in Pisa, Italy by Manori Weerasinghe and Julian Morris. Manori, a researcher at CPACT Strathclyde, presented a paper on Modelling and Simulation of a Laboratory Scale Esterification Process. Professor Julian Morris presented a paper co-authored by Elaine Martin and Giuseppe Baffi (CPACT Newcastle) on Dynamic Non-linear Modelling. Dr Baffi also presented a joint paper on the extension of this work to model based predictive control at the International Conference on Process Control and Instrumentation 2000, Glasgow UK.

Left to right - Eliana Zaprogna (University of Podova), Manori Weerasinghe (CPACT Strathclyde), Faisal Uppal (University of Podova)

New Project in Assured Food Processing

An article 'Multivariate Statistical Process Monitoring – The Answer for Assured Food Manufacturing?' appeared in the Food LINK News, No. 33, December 2000. CPACT is planning to submit a proposal for a MAFF Food LINK project associated with the integration of spectroscopic and process information for performance enhancement in food manufacturing processes. A MAFF Bridge LINK scoping project with Unilever and Tetley is nearing completion and will lead to the formation of a consortium to address those issues. Interested food manufacturing companies, analytical equipment vendor companies and control systems provider companies, should contact Julian Morris on +44 191 222 7342 or by email at julian.morris@ncl.ac.uk.

CPACT IN DEMAND - Worldwide

Over the past few months, considerable interest has been shown in the research conducted at the CPACT universities, with developments in MSPC and Performance Monitoring Techniques featuring strongly in several presentations. Elaine Martin and Julian Morris (CPACT Newcastle) were invited to Washington to give a keynote paper at the "Biocontaminants and Biological Production Issues" Conference held at the Cambridge Healthtech Institute. Research on Feature Extraction in Bioprocess Technologies (Jarka Glassey, Newcastle University) and Impurity Monitoring in Pharmaceutical Processes (Nicola Fletcher, CPACT Newcastle) was also presented at other meetings during 2000.

Interest in manufacturing control in the food industry is growing and Julian and Elaine gave keynote presentations on "Assured Food Manufacturing through Process Performance Monitoring" at a Foresight Meeting in London. A poster highlighting research in Manufacturing Performance Monitoring in Food Processing was also presented at an IEE event on "Engineering in Food Manufacturing".

Developments in On-line Process Analysis are also attracting the attention of researchers worldwide. In September 2000, David Littlejohn (CPACT Strathclyde) was invited to present a keynote lecture at the Spanish National Conference on Spectroscopy, held at Leon University. Particular interest was shown in the research in at-line and on-line process NMR spectrometry and in the use of in-reactor Raman measurements for batch reaction monitoring. David was also invited to participate in a colloquium on Optical Spectroscopy and Chemometrics in Process Oriented Analysis at the Institute of Spectrochemistry and Analytical Spectroscopy (ISAS) in Dortmund, Germany. Again the main interest was in the use of NMR, Raman and NIR spectrometries for at-line and in-line process analysis.

In addition to the technical developments, there is growing awareness of the CPACT method of collaboration between universities and industry. During 2000, David Littlejohn was asked to explain the CPACT philosophy at several events including a Scottish Enterprise meeting in Glasgow, the Pharmaceutical Analysis Science Group meeting in Warwick, an RSC event in Huntingdon and the ISAS colloquium in Dortmund. It has been suggested that CPACT's success represents a "good practice guide" to consortium development and many of our ideas are now being adopted by other organisations.

Technology Transfer Workshop

A two day meeting was held at Hull University on 12/13 December 2000 to give CPACT members a hands-on session with some of the deliverables from the Chemometrics project team.

The meeting format was very informal and followed a general pattern of a 30-40 minute presentation of the algorithm and the background to its development. This was followed by a short demonstration of the algorithm, and then after a short break for orientation, there was a hands-on session coordinated by Kalin Stoyanov and Tony Walmsley (CPACT Hull). During the hands-on session attendees could work through the demonstration and try out the software on either their own data or new data that had been provided.

The meeting was well attended with representatives from six CPACT companies. Feedback from the meeting was very positive and possible in-house applications were clearly identified. The themes chosen for the workshop were:

- **Maintenance of Calibration Models**
- **Using Experimental design to construct a calibration model**
- **Univariate Monitoring of process based upon spectral data (without calibration)**
- **The use of E-optimality to develop calibrations with natural data (spectral data)**

The general feeling from the meeting was that it was useful to see and discuss the algorithms, brainstorm possible applications, and then feed those back into CPACT Phase II. This forum was seen to be a very important deliverable in itself, and those present expressed their thanks to Kalin Stoyanov for his hard work in delivering the workshop.

For further information contact Tony Walmsley (tel: 01482 465470, email: a.d.walmsley@chem.hull.ac.uk)

CONGRATULATIONS

John Green, Technical Specialist in Process Analysis at BP Chemicals, and a member of the CPACT Steering Committee, was appointed President of the Analytical Division of the Royal Society of Chemistry (RSC) in July 2000. John will hold this appointment for two years.

David Littlejohn

The RSC has also awarded David Littlejohn (CPACT Strathclyde) the Theophilus Redwood Lectureship for 2001, in recognition of his contribution to teaching and research in a range of areas in Analytical Chemistry. David will present a lecture on recent developments in process spectroscopy at several locations in the UK during 2001.

Success resounds with Resonance

When Resonance Instruments joined CPACT as a founder member in 1996, they had only 8 employees and a turnover of around £750,000. The last four years have seen a 300% increase in both employees and turnover, and the company has developed from a small start-up to an important world player in many niche areas of the NMR market.

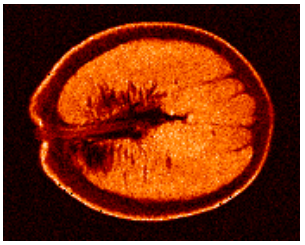
Resonance Instruments started by making a new range of benchtop low resolution instruments for quality control (QC) applications, with the very first instrument being bought by Weetabix for measuring moisture in breakfast cereals. Other QC applications rapidly followed, including density of polymers, fabric impregnation levels, fluoride in toothpaste, H/F ratios, and many others. A considerable number of research applications also developed, including studies of water behaviour, diffusion, and droplet size measurements.

RESONANCE

Barry Jones with a large magnet used for rock core studies

In the last few years the product range has expanded in many different directions, and now also covers such diverse areas as low-field instruments for rock core studies (used by most of the world's major oil companies), benchtop imaging systems, and advanced electronics for medical MRI applications.

Resonance Instruments joined CPACT for two main reasons: first, to gain exposure to potential customers and hear about their needs, and, secondly, to take part in the development of a new type of NMR instrument. The idea was to try to improve the resolution of benchtop NMR instruments so as to obtain more detailed spectral information without sacrificing the robustness which makes these spectrometers suitable for plant use. Some excellent work in the project has been done by Alison Nordon and Colin McGill at CPACT Strathclyde and significant technical advances were made. The next phase is to extend the R&D work into useable plant applications.



MRI image of an orange

Featured at the House of Commons

Nicola Fletcher

Nicola Fletcher, a PhD student at Newcastle, and working with Pfizer on a project relating to Process Feature Detection and Performance Monitoring, was invited to present a poster at a one day meeting of Special Presentations by Britain's Young Engineers at the House of Commons. She presented a poster on Feature Extraction and Performance Monitoring for Improved Bio-process Understanding and Supervision.

Process Analytics and Quality Technology

MSc PAQT

An EPSRC Masters Training Package in Process Analytics and Quality Technology (MSc PAQT) was awarded to Elaine Martin, Julian Morris and David Littlejohn. Funding of £573,891 was received to cover project studentships.

The objective of the course is to enhance the skills of engineers, scientists and mathematicians by providing them with competencies in chemical and process engineering, process control, process analytics, quality technology, statistics, chemometrics and business and project management and to develop skills that enable them to integrate the different disciplines to solve multi-faceted problems.

It comprises 12 taught modules, each of 1 week duration, plus a 6 month industrial placement. The modules comprise two foundation modules (Introduction to Analytical Chemistry and either Introduction to Mathematics and Statistics or Principles of Process Engineering), 6 compulsory modules (Quality Technology, Process Control Systems, Managing Complex Projects, Process Data Modelling, Design of Experiments and Multivariate Data Analysis and On-Line Process Analysis) and four optional modules from Waste Management and Effluent Treatment, Technology and Management, Time Series and System Identification, Chemometrics and Signal Processing, Model Based Predictive Control, Non-Linear Process Modelling, Mathematical Modelling and Process Optimisation in Practice.

The course is in its first year and CPACT member companies have been very supportive in terms of lecturing on the course and offering student placements. Continuing the role of CPACT in providing professional development courses, it is anticipated that from next year some of the week-long modules will be opened up to CPACT industrial companies, with some forming the basis of 3-day Professional Development Courses.

For further details see http://www.ncl.ac.uk/engmaths/paqt/

Why join CPACT?

Members of CPACT enjoy the benefits of

- shared cost research
- multidisciplinary collaboration
- immediate access to royalty-free innovative technology
- networking and benchmarking
- professional development of staff
- access to trained and motivated graduates

CPACT bridges the gap between science and engineering, academia and industry, vendor and end-user

Membership

Full Members:
End user companies
– £30,000 per annum plus in-kind contribution

Associate Members:
Vendor companies
– in-kind contribution only
Non-vendor SME companies
– £2k-£10k per annum by negotiation plus in-kind contribution

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