CENTRE FOR PROCESS ANALYTICS AND CONTROL TECHNOLOGIES

CPACT NEWSLETTER April 2010

APACT 10

The APACT conference will take place on 28-30 April 2010 at the Hilton Deansgate Hotel in Manchester
If you wish to register please visit: www.apact.co.uk

CPACT Research Day

We had an excellent CPACT Research Day held at the Chemistry Innovation site in Runcorn on Tuesday 9th March 2010.

There was a good variety of presentations on different topics and a nice mix between academia and industry. The day also included an enjoyable poster session.

For those who were unable to attend this event, please note that the presentations are now available on the 'members only' section of the CPACT website, to view visit:
http://www.strath.ac.uk/Other/cpact/mo/themes.htm

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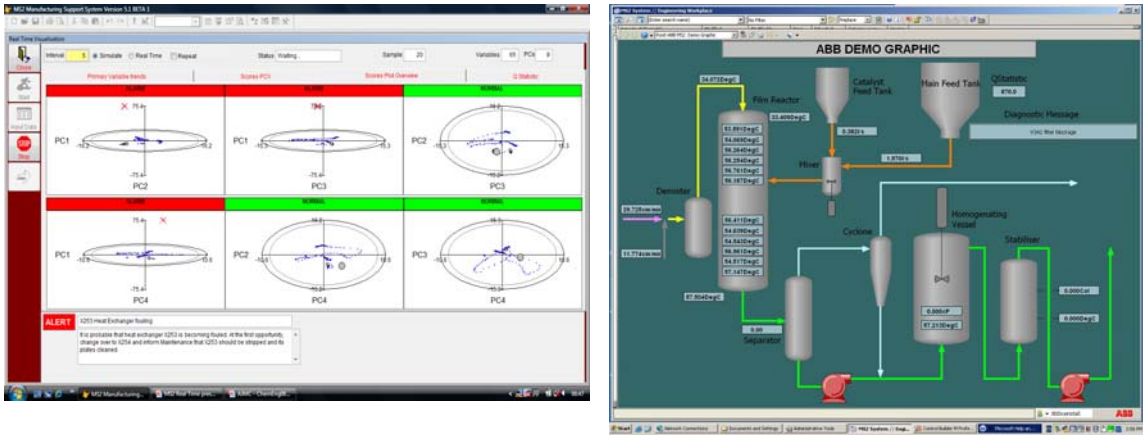
Developments in the MS2 Process Diagnostics System

AJM Consulting Services Ltd, the process diagnostics specialist and CPACT member company, is pleased to announce that ABB, one of the world's leading engineering companies, is now a reseller for MS2, the process diagnostics system developed by AJM Consulting. ABB will offer the Pinnacle version of MS2, which includes on-line data analysis, as part of its range of solutions for productivity improvement including asset management. In particular, it will focus on applying MS2 as an early event warning facility to reduce downtime. ABB will also be responsible for integration, including configuration and maintenance of the communication link between MS2 and ABB's System 800xA distributed control system.

MS2 combines advanced data analysis with powerful visualisation and other tools to provide a highly flexible tool for enabling productivity improvements including higher quality and yield. It was developed in conjunction with the Centre for Process Analytics and Control Technology at Newcastle University, and with funding from the European Union. MS2 is in use in many industries including nuclear, chemicals, oil, pharmaceuticals and biotechnology.

AJM Consulting will be demonstrating the on-line version of MS2, linked to System 800xA, at APACT.

In addition to the agreement reached with ABB for implementing the real-time MS2, its off-line functionality continues to become more powerful and easier to use. In June, the latest version, 5.2, will be released and some of the new functions will also be exhibited at APACT. MS2 now has around 45 users in a range of industries including nuclear, pharmaceuticals, chemicals, oil, biotechnology and advanced materials. A recent new user is Pharma Solutions (a division of Piramal Healthcare Ltd), one of the world's leading pharmaceutical manufacturing companies offering unique full lifecycle partnership and drug development services to small/virtual and big pharma companies. Its Morpeth site is engaged in the supply of advanced intermediates and commercial APIs to a number of European customers.



MS2 (shown on the left) performs the multivariate analysis and sends its results, together with appropriate operator advice, to the ABB System 800xA (shown on the right).

With the goal of ever-increasing improvements in yield and quality, Piramal has investigated the MS2 Process Diagnostics system and, with a team comprising in-house technologists augmented by specialists from AJM Consulting, has developed models which highlight subtle causes of process variability, enabling management to implement procedures which ensure improved productivity.

The complex manufacturing processes employed at Morpeth include state of the art batch manufacture. The advanced functions which the MS2 Process Diagnostics System provides for visualising the relationship between multiple batch step conditions and output parameters such as yield and individual quality parameters have been used to highlight complex cause and effect relationships. According to Jarrett Palmer, the Operations Director at Piramal:

"The high level of complexity of our processes means that investigations into performance are very time consuming. The advanced functions which MS2 provides enable us to rapidly understand this complexity, and to pinpoint subtle multivariate relationships which would otherwise be difficult to identify. We selected the MS2 Process Diagnostics system from AJM Consulting to assist in this because of its advanced visualisation tools and the batch and step profile analysis techniques which it provides.

The flexibility and ease of use of the MS2 system has been much appreciated by our process specialists. It has enhanced our understanding of our processes, enabling us to focus our improvement efforts on critical areas. We see this as a key tool to include in our continual efforts to improve production excellence."

Alan Mason
AJM Consulting

AJM Consulting

Work with Fibre Photonics

In October 2008 I began my PhD with Professor David Littlejohn in the Department of Pure and Applied Chemistry at the University of Strathclyde in collaboration with Fibre Photonics. This is a Scottish Funding Council SPIRIT funded studentship, designed to encourage Scottish universities to work on issues that are of importance to the industrial sector, especially, SMEs in Scotland. My research is targeted at the design, development and application of near and mid infrared *in-situ* probes for real-time analysis of chemical and biological systems.

To gain an understanding and knowledge of the different potential uses of near and mid IR spectrometry in process analysis, an applications assessment was completed. This included searching the literature for known applications and speaking to some potential users about their applications and needs of mid and near infrared spectrometry. Information about the application, sample composition, preferred analysis method and wavenumber range was collected and tabulated. Using this table of information has allowed a clearer idea of where the development of *in-situ* probes could best suit the needs of users in different industrial sectors.

In addition to the "desk" exercise, I have investigated the performance and predictive ability of a selection of polycrystalline silver halide fibre MIR ATR probes. The results showed where design changes had led to improvements and will help with future work in the design and development of probes. I hope to continue my interest in probe design through a period of research in Germany working with photonics specialists at Fibre Photonics. Here I will work alongside a design team helping to make improvements to IR probes based on the knowledge I have gained so far about customer requirements.

Figure 1: Fibre Photonics mid infrared ATR probes. 2.7, 6.3,

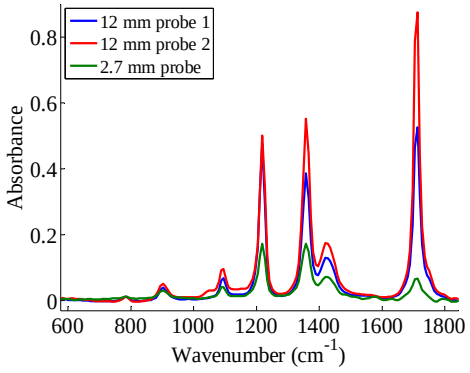


Figure 2: Overlaid plot of acetone analysed using a selection of probes.

The collaboration with Fibre Photonics has also enabled me to see some business aspects of running a small company as well as gaining scientific knowledge. I visited the Fibre Photonics manufacturing site at Livingston and toured around the facilities; I also attended the CPhI worldwide event in Madrid. CPhI is the world's largest dedicated pharma ingredients event that brings businesses face-to-face with potential customers and informs people about the latest advances in industry. CPhI was co-located with ICSE relating to both R&D and manufacturing outsourcing services. With an attendance of over 25,000 delegates, and 1800 exhibitors, this was a great opportunity for me to make new contacts, learn of the industries key challenges and establish connections with potential customers and collaborators.

My research so far has mainly focused on possible applications of *in-situ* infrared spectrometry and the knowledge gained will help with the design of probes for real-time analysis in a range of process applications. I now intend to use this knowledge to extend the range of measurements that can be achieved using Fibre Photonics' novel polycrystalline silver halide fibres.

RECENT PUBLICATIONS BY THE CPACT ACADEMICS

If you are interested in receiving a copy of any of the papers listed below, please email your request to natalie@cpact.com

THE UNIVERSITY OF HULL

Development of a high throughput screening tool for biotransformations utilising a thermophilic L-aminoacylase enzyme, B. Ngamsom, A. M. Hickey, G. M. Greenway, J. A. Littlechild, P. Watts and C. Wiles, Journal of Molecular Catalysis B: Enzymatic, 2010, 63, 81-86.

The use of immobilised crown ethers as in situ N-protecting groups in organic synthesis and their application under continuous flow, G. P. Wild, C. Wiles, P. Watts and S. J. Haswell, Tetrahedron, 2009, 65, 1618-1629.

Enhanced Chemical Synthesis in Flow Reactors, C. Wiles and P. Watts, Chemica Oggi, 2009, 27(3), 34-36.

The development and evaluation of a continuous flow process for the lipase mediated oxidation of alkenes, C. Wiles, M. J. Hammond and P. Watts, Beilstein Journal of Organic Chemistry, 2009, 5(27), 1-12.

Microreactors as tools for high-throughput synthesis, C. Wiles and P. Watts, Speciality Chemicals Magazine, 2009, 40-41.

Continuous flow organic synthesis, a tool for the modern medicinal chemistry, C. Wiles and P. Watts, Future Medicinal Chemistry, 2009, 1593-1612.

A micro reactor for the study of biotransformations by a cross-linked gamma-lactamase enzyme, A. M. Hickey, B. Ngamsom, C. Wiles, G. M. Greenway, P. Watts and J. A. Littlechild, Biotechnology J., 2009, 4 (4), 510-516.

MANCHESTER 1824 The University of Manchester

Y. Yi, L. Guo and H. Wang. Adaptive Statistic Tracking Control Based on Two-Step Neural Networks With Time Delays. IEEE Transactions on Neural Networks. 2009 March; Vol. 20, No. 3: 420-429.

P. Afshar, H. Wang and T. Y. Chai. An ILC-Based Adaptive Control for General Stochastic Systems With Strictly Decreasing Entropy. IEEE Transactions on Neural Networks. 2009; Vol. 20, No. 3: 471-482.

Y Yi, L. Guo and H Wang. Constrained PI tracking control for output probability distributions based on two-step neural networks. IEEE Transactions on Circuits and Systems, Part 1, Regular Papers. 2009 July; 56: 1416-1426.

X. Dai, Z. Gao, T. Breikin and H. Wang. Disturbance Attenuation in Fault Detection of Gas Turbine Engines: A Discrete Robust Observer Design. IEEE Transactions on Systems, Man and Cybernetics - Part C. 2009 March; Vol. 39, No. 2: 234-239.

L Guo, L Yin, H Wang, T Y Chai. Entropy Optimization Filtering for Fault Isolation of nonlinear Non-Gaussian Stochastic Systems. IEEE Transactions on Automatic Control. 2009 April; 54: 804-810.

H Wang and P Afshar. ILC-based fixed-structure controller design for output PDF shaping in stochastic systems using LMI techniques. IEEE Transactions on Automatic Control. 2009 April; Vol. 54: 760 - 773.

P. Zhou, T. Chai, H. Wang. Intelligent optimal-setting control for grinding circuits of mineral processing process. IEEE Transact Automat science and Engineering. 2009 October; 6: 730-743.

A. Nobakhti and H. Wang. Noniterative N-infinity Based Model Order Reduction of LTI Systems Using LMIs. IEEE Transactions on Control Systems Technology. 2009 March; 17: 494-501.

X Dai, Z Gao, T Breikin and H Wang. Zero assignment for robust H_2/ H_infinity fault detection filter design. IEEE Transactions on Signal Processing. 2009 April; 57: 1363-1372.

J Zhou, D Zhou, H. Wang, L Guo and T. Y. Chai, Distribution function tracking filter design using hybrid characteristic functions, Automatica, Vol. 46, No. 1, pp. 101-109, 2010.

Newcastle University

Jeong, J.J, Jie Zhang and Julian Morris, "Enhanced Predictive Modelling Using Multi Block Methods", 19th European Symposium on Computer Aided Process Engineering - ESCAPE19, 2009.

Stubbs, S, Jie Zhang, Julian Morris, "Fault detection of dynamic processes using a simplified monitoring-specific CVA state space approach", European Symposium on Computer Aided Process Engineering - ESCAPE19, 2009.

Zhang, J., J. Nguyan, and J. Morris, "Iterative learning control of a crystallisation process using batch wise updated linearised models identified using PLS", in (Eds) J. Jeowski and J. Thullie, Computer-Aided Chemical Engineering 26, Proceedings of the 19th European Symposium on Computer Aided Process Engineering, 14 - 17 June 2009, Cracow, Poland, PP387-392

Chen, Zengping and Julian Morris, Process analytical technology and compensating for nonlinear effects in process spectroscopic data for improved process monitoring and control, Highlighted Article, Biotechnol J. 2009 May;4(5), 610-619

Morris, A.J., D. Littlejohn and R. Benson, "Contributing to the Sustainability of the UK Chemicals and Pharmaceuticals Industries", European Pharmaceutical Review, February 2010.

Benson, R. and A.J. Morris, "What Goes Around Comes Around", Pharmaceutical Packing and Manufacturing Sourcer (PMPS), February 2010.

Invited to write an article for Chimica Oggi/Chemistry Today (International Journal of Chemistry and Biotechnology) Morris, A.J., "Multivariate Statistical Process Control: Moving Towards Model Based Approaches", Chimica Oggi/Chemistry Today (International Journal of Chemistry and Biotechnology, April 2010.

UNIVERSITY OF LEEDS

Multivariate statistical control of emulsion and nanoparticle slurry processes based on process tomography, dynamic light scattering, and acoustic sensor data. Li, R.F., Liu, L., Wang, X.Z., Tweedie, R., Primrose, K., Corbett, J., McNeil-Watson, F. 2009 Computer Aided Chemical Engineering (PSE'2009)27 (C), pp. 1317-1322.

Morphological population balance models for the dynamic evolution of particle shape and size distribution in protein crystallization. Liu, J.J., Ma, C.Y., Hu, Y.D., Wang, X.Z. 2009 Computer Aided Chemical Engineering (PSE'2009) 27 (C), pp. 1911-1916

Development of a morphological population balance model in principal component space. Ma, C.Y., Wang, X.Z. 2009 Computer Aided Chemical Engineering(PSE'2009) 27 (C), pp. 723-728

Inductive data mining based on genetic programming: Automatic generation of decision trees from data for process historical data analysis. Ma, C.Y., Wang, X.Z. 2009 Computers and Chemical Engineering 33 (10), pp. 1602-1616

Robust QSAR model development in high-throughput catalyst discovery based on genetic parameter optimisation. Wang, X.Z., Perston, B., Yang, Y., Lin, T., Darr, J.A. 2009 Chemical Engineering Research and Design 87 (10), pp. 1420-1429

Modelling protein crystallisation using morphological population balance models. Liu, J.J., Ma, C.Y., Hu, Y.D., Wang, X.Z. 2009 Chemical Engineering Research and Design. doi:10.1016/ j.cherd.2009.08.015

Morphological Population Balance Model in Principal Component Space. Wang, X.Z., Ma, C.Y. 2009 AIChE Journal 55 (9), pp. 2370-2381

Synthesis and characterization of doped nano-sized ceria-zirconia solid solutions. Weng, X., Perston, B., Wang, X.Z., Abrahams, I., Lin, T., Yang, S., Evans, J.R.G., Darr, J.A. 2009 Applied Catalysis B: Environmental 90 (3-4), pp. 405-415

UNIVERSITY OF LEEDS

Particle shape manipulation and optimization in cooling crystallization involving multiple crystal morphological forms
Wan, J., Wang, X.Z., Ma, C.Y. 2009 AIChE Journal 55 (8), pp. 2049-2061

Model-based Optimisation and Closed-loop Control of Crystal Shape in Cooling Crystallisation
Wan, J., Wang, X.Z., Ma, C.Y. 2009 Computer Aided Chemical Engineering (ESCAPE-19) 26, pp. 483-488

Online monitoring of nanoparticle suspensions using dynamic light scattering, ultrasound spectroscopy and process tomography
Wang, X.Z., Liu, L., Li, R., Tweedie, R.J., Primrose, K., Corbett, J., McNeil-Watson, F. 2009 Computer Aided Chemical Engineering (ESCAPE-19)) 26, pp. 351-356

Online characterisation of nanoparticle suspensions using dynamic light scattering, ultrasound spectroscopy and process tomography
Wang, X.Z., Liu, L., Li, R.F., Tweedie, R.J., Primrose, K., Corbett, J., McNeil-Watson, F.K. 2009 Chemical Engineering Research and Design 87 (6), pp. 874-884

University of Strathclyde Glasgow

Non-invasive monitoring of the mixing of pharmaceutical powders by broadband acoustic emission, P. Allan, L.J. Bellamy, A. Nordon and D. Littlejohn, *Analyst*, 2010, **135**, 518-524.

Theoretical analysis of ultrasonic vibration spectra from multiple particle-plate impacts, G. Carson, A.J. Mulholland, A. Nordon, A. Gachagan and G. Hayward, *IEEE Transaction on Ultrasonics, Ferroelectrics and Frequency Control*, 2009, **56**, 1034-1041.

Estimating particle concentration using passive ultrasonic measurement of impact vibrations, G. Carson, A.J. Mulholland, A. Nordon, M. Tramontana, A. Gachagan and G. Hayward, *IEEE Transaction on Ultrasonics, Ferroelectrics and Frequency Control*, 2009, **56**, 345-352.

Analysis of the Rayleigh-Plesset equation with chirp excitation, E. Barlow, A.J. Mulholland, A. Gachagan, A. Nordon and K.G. Macpherson, *IMA Journal of Applied Mathematics*, 2009, **74**, 20-34.

Non-invasive monitoring of the mixing of pharmaceutical powders by broadband acoustic emission. Pamela Allan, Luke J Bellamy, Alison Nordon and David Littlejohn. Analyst, 2010, 135, 518-524.

IFPAC CONFERENCE 2010

The 24th International Forum for Process Analytical Chemistry (IFPAC) took place from the 31st January to 4th February, 2010, in Baltimore, USA. The conference programme covered a wide range of topics such as bioprocessing, process analysis, process Raman, chemometrics, quality by design, NeSSI, imaging, continuous processes, handheld instrumentation, knowledge management and particle characterisation.

CPACT was represented at the conference by Alison Nordon (CPACT Strathclyde) and Julian Morris (CPACT Technical Director). Julian gave a presentation in the session on applications of quality by design, entitled 'Smart Process Analytics and Process Systems Engineering - Contributions to Quality by Design'. Alison was invited to give a presentation on 'PhAT Raman analysis of pharmaceutical powders and tablets' in a process Raman session organised by Brian Marquardt from CPAC. This presentation covered some of the research carried out by recent CPACT Strathclyde PhD students (Luke Bellamy, Pamela Allan and Nicci Townshend) in collaboration with Clairet Scientific involving use of large-area illumination reflectance and transmission Raman spectrometry for the analysis of solids. Alison also gave a presentation entitled '*in situ* monitoring of liquids using mid infrared spectrometry' in a process analysis session. This presentation reviewed some of the opportunities for Mid Infrared (MIR) spectrometry following recent developments in robust fibre optics by Fibre Photonics.

Geir Rune Flaten (ex CPACT Hull researcher) from GSK gave a presentation on how he and colleagues (including Luke Bellamy, ex CPACT Strathclyde PhD student) had used the caterpillar algorithm for real-time detection of the end-point of powder blends in a compliant environment. The caterpillar algorithm was devised by Geir while working for CPACT.

Julian Morris was also invited by the IFPAC Organising Committee to give a one-day short course on "Process Control without equations". 10 people registered for the course.

The aim of this short course was to provide an introduction to closed loop process control for chemistry and biological scientists and engineers that have no background in process control and automation. Sufficient knowledge was provided to allow delegates to appreciate the scope of process control techniques and the challenges that need to be considered when implementing process control strategies within a PAT and QbD environment. The topics included were: classical feedback control with process examples; feedforward and inferential control; multi-loop control; analytical feedback control; and finished with an overview of more advanced control systems now being applied, and a brief review of control benefits analysis methods and practice.

View from Baltimore Marriott

Waterfront across the harbour area