

# *Chemometrics for On-Line Process Analytics*

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COPA



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## *The Need*

- In the 20<sup>th</sup> century, the analytical chemist controlled quality – bring a sample to the lab and determine if it is within specs.
- As we move instruments on-line, we bring the instruments to the sample and, as a result, enter a very data-rich environment.
- We can choose to ignore the changes, use this source of data haphazardly or process the data systematically.

Bill Winniford, DOW: We have to make do with a lot fewer people and they will have more to do. We are entering a time we have never seen before. My chief frustration is in data processing; we are simply not good at capturing knowledge from the experienced workforce

Randy Shearer, GE: We are faced with an ageing workforce worldwide and are graduating fewer scientists and engineers in the US. We need [among other things] quality standards for products, processes and services. We also need to apply the continuing improvements in computer technology.

# *Impediments to Wider Use of Chemometrics in Practice*

*Prof. Steven D. Brown  
University of Delaware*

- Training
  - chemists spend no time on training in data analysis
    - chemists' perception of the field is often unfavorable
    - chemometrics is method of “last resort” for intractable problems
  - chemists are ill-prepared in mathematics, statistics and quantitative computer skills
- Software
  - commercial chemometrics software is limited in capabilities and expensive
  - instrument-based chemometrics packages are non-standard in many respects
  - software is usually unavailable for many newer methods



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# *Impediments to Wider Use of Chemometrics in Practice*

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- Theory
  - chemometrics is algorithm-based
    - Poor connection to statistical principles limits development of inference
    - Lack of theory limits systematic discovery of newer approaches
  - many chemometric applications involve “one - off” methods
- Practical Issues
  - automation
  - standards for data transfer and presentation
  - difficulties with presentation of results
  - amounts of data and nature of data

# COPA

# *What is limiting implementation?*

## **People**

- Unrealistic user demands
- Fear of chemometrics (esp. by plant folks!)
- Mfg folks want simplicity
- Need software expert at plant
- Site champions transient

## **Technical capability**

- Limited pre-treatment and modeling options in analyzer S/W..., **but**
- Chemometrics S/W too complex for most users
- No consistent interface among vendor tools
- Absence of turn-key applications
- Incompatibility of modeling & analyzer S/W

## **Reliability**

- Poor long-term stability (PC system crash/hang)
- Custom solutions- long term support?...

## **Business strategy**

- Instrument vendors shield their data
- Vendors think that they must provide it all
- Few strategic partnerships

## **Cost/Resources**

- Insufficient time/\$ to develop custom solution
- Limited resources for site support
- Perceived higher cost of ownership compared to non-chemometrics apps
- Unwilling to invest time to develop robust apps

## **Regulatory**

- PAT regulatory concerns
- Reluctance to use chemometrics in GMP applications
- Need for consistent interpretation



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## *Poll of process users*

1. Analytical failure prediction
2. Result validation
3. More process-specific information (timely, higher quality, more focused)
4. Simplification of procedures
5. Reduction in the cost of ownership

*Driven in part by a dwindling workforce*

# *Chemometrics for On-line Process Analytics*

- *The COPA Goal is to facilitate successful application of existing and new chemometric techniques for on-line processes*

Why?

- Reduce the implementation costs for chemometrics technology
- Allow implementation of *new* chemometrics tools in a more timely manner
- Increase the repertoire of chemometrics tools to enable improved *Effectiveness, Reliability, and Maintainability*

## *History of the initiative*

- April 2000: Analect users meeting
  - Started as an on-line Matlab computing engine
- March and May 2001: Pittcon and CPAC meetings
  - Instrument and software vendor interest, fielded concerns
  - Formalized as CPAC initiative
- January 2002: IFPAC meeting
  - Gaining traction with end-users, vendors, academics
- January 2003: IFPAC meeting
  - Blended FDA-PAT initiative, Part 11 compliance
- January 2004: IFPAC meeting
  - Centered activities on creation of tools
- January 2005: IFPAC meeting
  - Three commercial solutions introduced for discussion
- February 2006: IFPAC meeting
  - Market feedback, postmortem on the original goals, advancing new goals



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## *COPA as a CPAC Initiative*

- Process control standardization
  - OPC Unified Architecture (Web Services)
  - IEC SC65D-62 chemometrics for process instruments
- ASTM
  - WK9191 (E55.02) standards for multivariate analysis
  - E1655-00 (E13-11) standards for IR quantitation
- Pharmaceutical (PAT) working groups
  - Chemometrics: Standardizing calibration algorithms, analyzer functionality, outlier detection
  - Process validation: Multivariate software validation
- CPAC NeSSI Initiative



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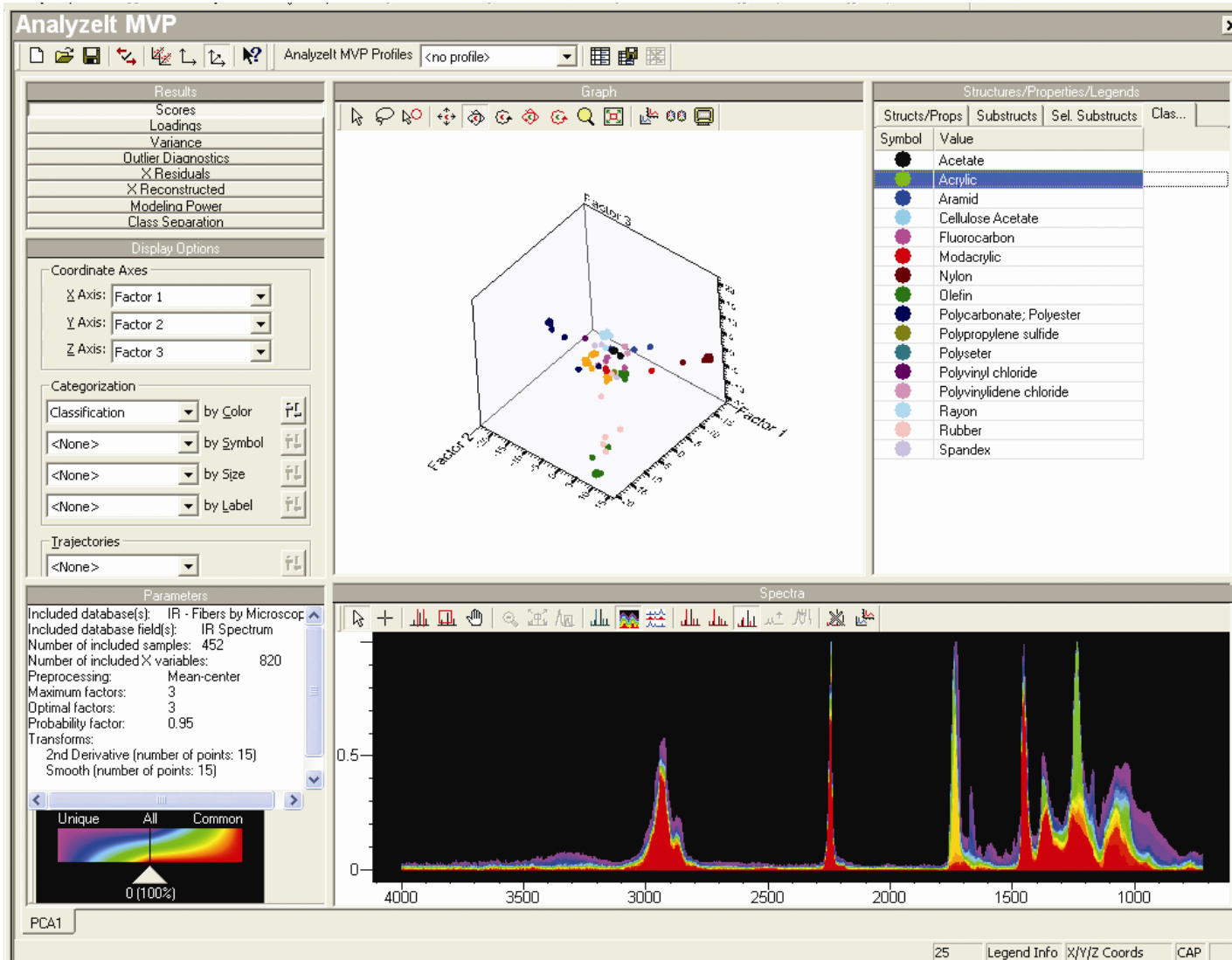
## *COPA Accomplishments To Date*

- Model formats are more accessible
  - Eigenvector Research has model formats that can be accessed in any Matlab system
  - Infometrix has enhanced their ASCII model from PLS/PCR predictions only to cover classification (KNN & SIMCA) plus outlier diagnostics
- Software has been created to allow use of chemometric models in a more flexible way
  - Symbion can run different models in parallel and handles the compliance issues
  - Infometrix introduced an ActiveX dll that enables any Windows-based software to execute a prediction without calling a separate user interface

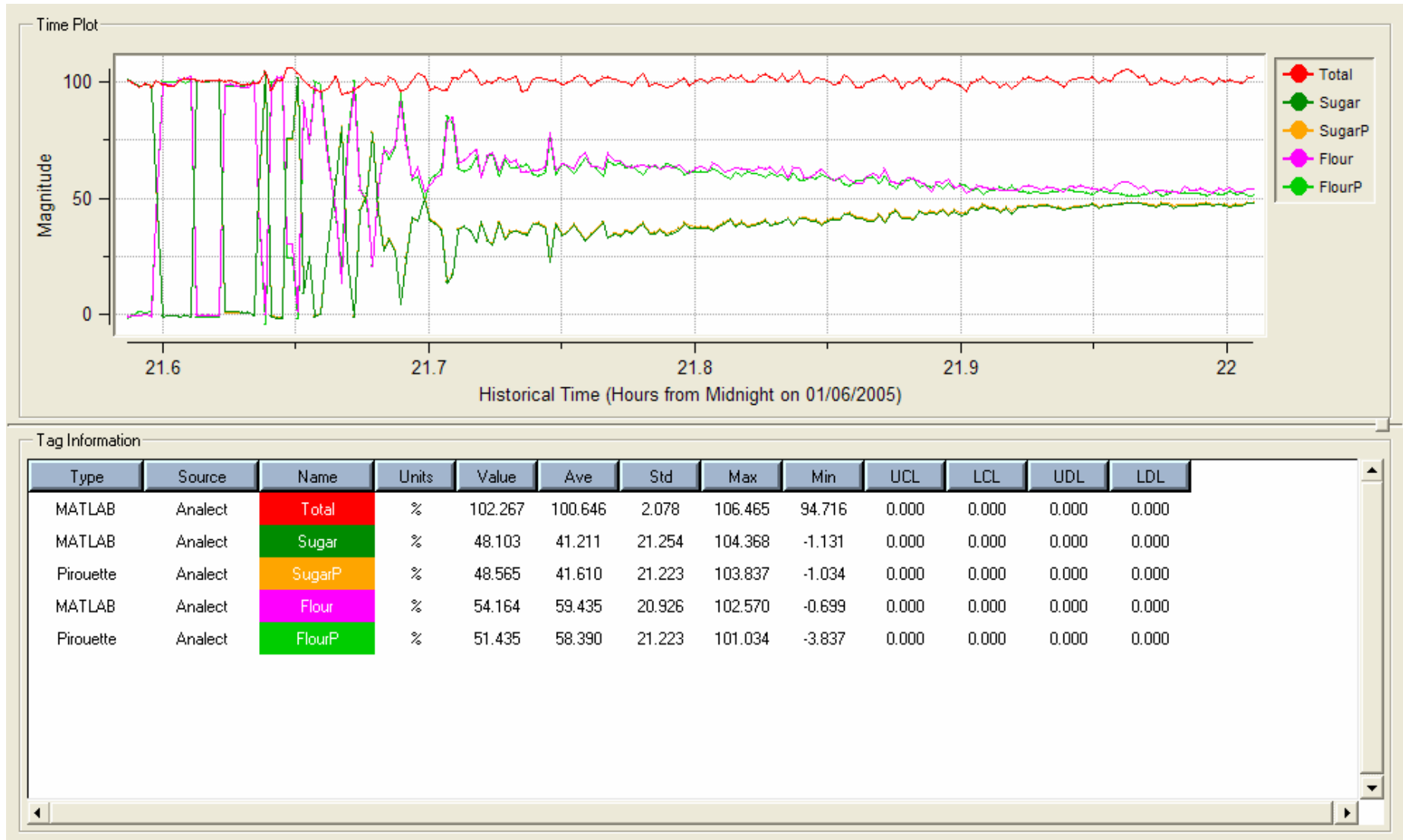


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# Chemometric Integration



# Blending Sources of Chemometric Information



## *The 7-Year Summary*

- Prior to the COPA Initiative, the chemometrics software allowed chemometric interpretation of analytical signals reliably and in real time.
- The first seven years of COPA effort extended the above capability to encompass custom systems and simplified the matching of a Vendor A instrument with chemometrics software supplier B.

## *FDA's Free Pass*

- Pharmaceutical companies were essentially blocked from deploying NIR (and other) instruments for process use.
- With PAT, companies can implement new technologies in parallel with legacy monitoring and control approaches with no penalties.
- This leads to a gain in process understanding which, in turn, leads to the option of better control of the process and of product quality.

## *PAT Changes the Bottlenecks*

No sensible decision can be made any longer without taking into account not only the world as it is, but the world as it will be.

-Isaac Asimov, scientist and writer (1920-1992)

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- **January 2007: IFPAC meeting**
  - Troubleshooting chemometrics in process settings
  - Incorporating process companies



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## *IFPAC 2007*

- **Bio-Rad** – Integrating salient chemometric features into an existing product
- **Yokogawa** – Process system supplier perspective on deploying chemometrics where legacy systems abound
- **GSK** – A user perspective on taking the leap from laboratory feasibility to on-line process chemometrics
- **Eigenvector Research** – multi-year case study (spectroscopy)
- **GE** – Process system supplier perspective on integrating chemometrics into the PAT world
- *Calibration Transfer Discussion*
- **Infometrix** – multi-year case study (chromatography)