



## Benefits of ABB's PAT Solutions

- Complete, vertically integrated solution for implementing Process Analytical Technology (PAT) and Quality by Design (QbD)
- Single configuration interface for defining PAT methods
- Data visualization, analysis and management
- Single, scalable platform that goes from R&D through pilot plant and scale up to manufacturing
- Advanced process control and closed loop control - with any DCS
- Enterprise connectivity and analyzer control, using open standards
- Product and solution expertise from one global supplier
- Wide range of analyzers supported

## Solution Description

Industrial IT eXtended Process Analytical Technology (xPAT) is a platform for integrating analyzers, control systems, data historians, enterprise systems (SAP, MES, LIMS...) and advanced process control within life sciences manufacturing. It can be applied to primary manufacturing of active ingredients, biotechnology and secondary manufacturing. The platform is scalable from a single unit operation to a whole process train and from R&D and pilot scale to full scale production.

This integration allows analyzers to become part of the manufacturing batch method by providing management of the analyzer configuration and complete control over the analyzer operation.

The ABB xPAT platform integrates the PAT method with the manufacturing batch. The batch can reside in any control system platform that includes batch management, such as ABB's System 800xA Extended Automation. All analyzer data is stored in an ISA-88 compliant manner against the batch ID.



## Introduction

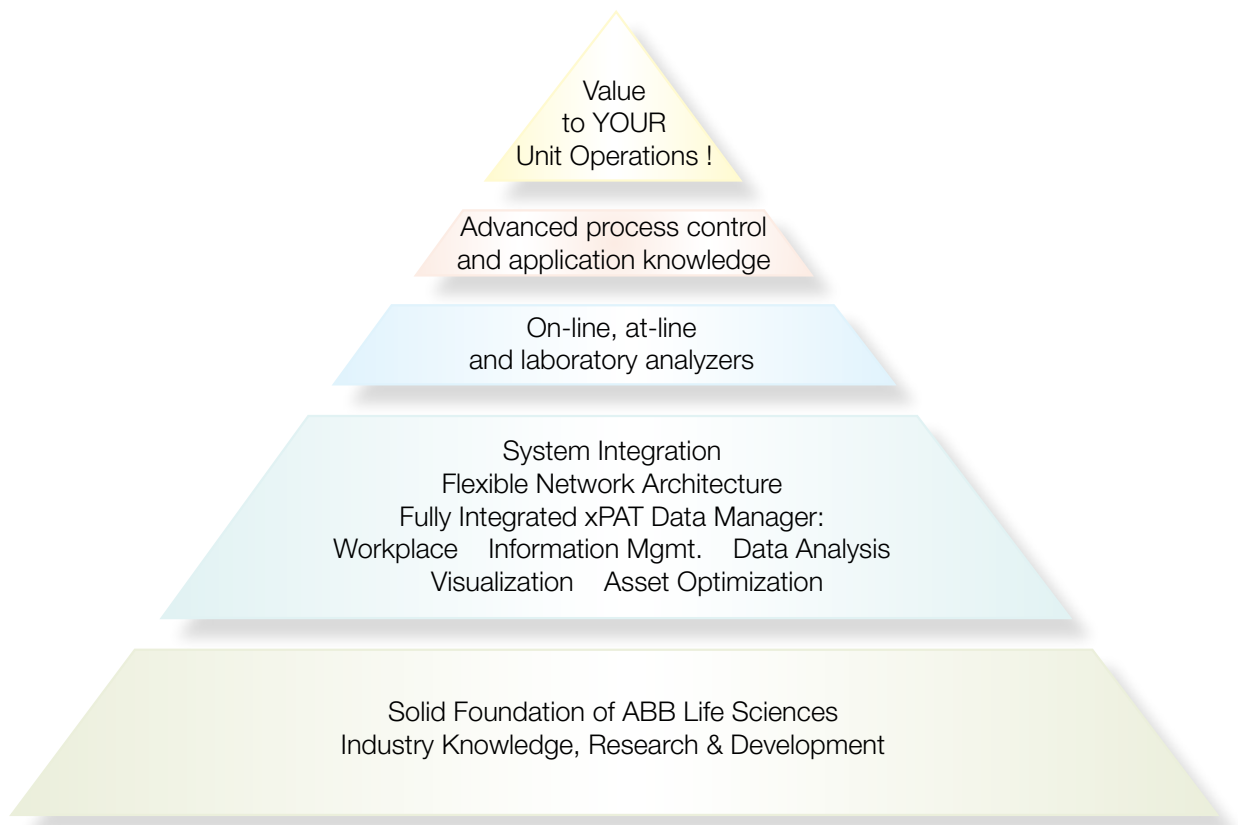
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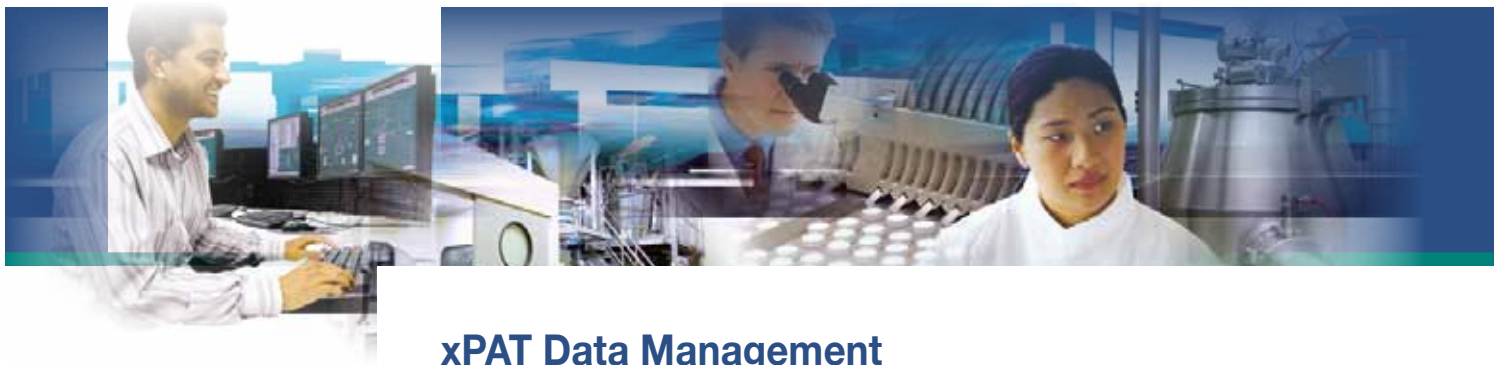
ABB offers one of the most complete solutions for optimized control and analyzer technology. The xPAT platform provides acquisition, management, visualization and analysis of the multivariate data typically generated by analyzers (spectra, histograms, chromatograms, etc.) and correlates it with process data for improved process understanding. This process understanding supports quality assurance, closed loop control and real-time product release.

## Building on ABB's Solid Foundation

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ABB provides the Life Science industries with a comprehensive range of leading-edge technologies, solutions and services that improve the efficiency, quality and safety of pharmaceutical development and manufacturing processes. Our extensive industry knowledge and research and development efforts produce robust, process-specific solutions that ensure users of low lifecycle costs and optimized results. At the heart of our portfolio of solutions is Industrial IT eXtended PAT (xPAT) – the fully scalable and most complete PAT process control solution in the market today (for more detail see system diagrams, pg. 14 – 15).





## xPAT Data Management

All analytical and process data is stored in a structured manner and linked to a batch identification and batch hierarchy according to the ISA-88 model. This allows storage of scalar (univariate) and array (multivariate) data along with metadata. Array storage is used for analytical data (spectra, chromatograms, histograms).

The data is held live in the Data Management server for a period of time (which can be determined by the end-user) before being moved to long term archival storage. The xPAT platform provides tools for data mining to allow extraction and export of data according to specific criteria both from the current live data, online historical data and long term data archives. The extracted data can then be visualized and analyzed either with the xPAT visualization tools or with third party data analysis tools like Umetrics SimcaP+, Thermo Galactic GRAMS or Matlab.

xPAT stores configuration information from the workplace alongside the actual data in its archives so that the link between the data and the PAT method that produced it is never broken.

### Benefits of QbD and PAT

- Improve manufacturing cycle times
- Reduce product quality variations and waste
- Reduce work in progress inventory
- Enable real-time product release
- Reduce laboratory testing and associated paperwork
- Allow flexible, multi-product manufacturing
- Reduce regulatory overhead and compliance costs with traceable data
- Reduce time to market for new products by enabling early process understanding
- Improve health and safety by limiting operator exposure to pharmaceuticals

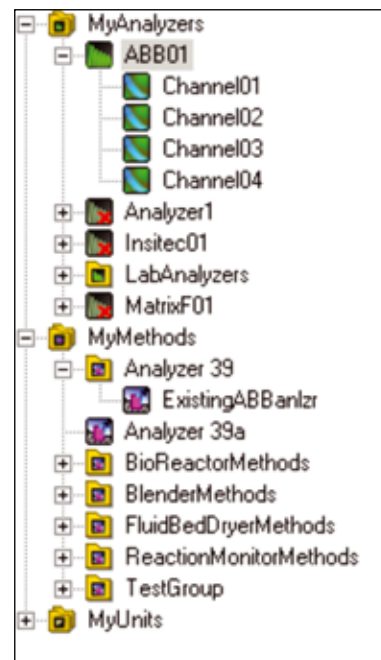
## xPAT Method Engineering - The Workplace

The xPAT Workplace is a unified user interface that runs on the data management server. It provides support for configuring applications and for monitoring operation in real-time. It includes:

- Visual method editing
- Encapsulation of all logic involved in data acquisition, analyzer control and data analysis, including chemometrics within a method
- Analyzer instance creation and configuration
- Standard face plates for supported analyzers
- Creation of process units
- Association of analyzers and process values to process units
- Process graphics

The workplace implements full version management for methods, with digital signatures for method approval. Using the workplace it is possible to import/export all assets (analyzer instances, methods and units) in a single operation, greatly simplifying migration between xPAT systems; e.g. from pilot plant to manufacturing.

The workplace organizes methods, analyzers and units into multiple folders and subfolders.



xPAT Method Engineering – The Workplace

### Benefits of the xPAT workplace are:

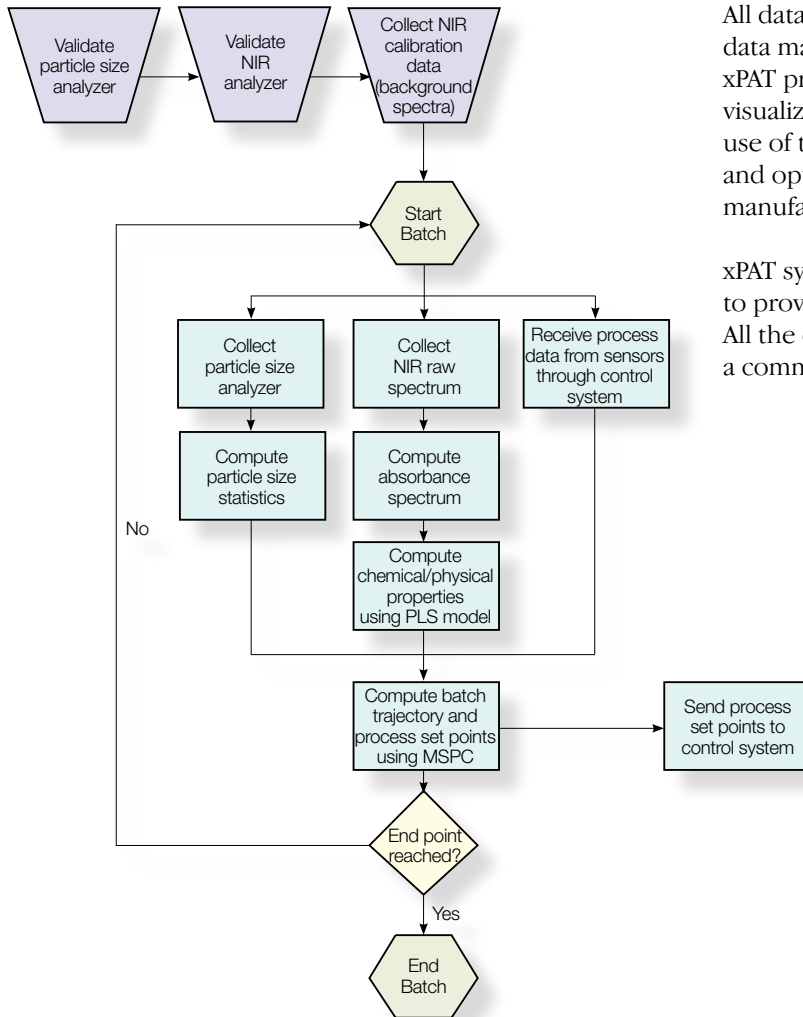
- Streamlined configuration of new analyzers; the whole process can be completed in minutes. PAT methods are developed through simple point and click operations
- Migration of configuration assets between xPAT systems is easily accomplished using import/export



## xPAT Data Analysis

xPAT provides both real-time and historical data analysis capabilities. Real-time data analysis capabilities include: processing raw data from different analyzers, mapping that raw data to chemical and physical properties, merging analytical data with process data and determining set points for closed loop control.

Additionally, xPAT integrates with Multivariate Statistical Process Control (MSPC) packages to provide batch trajectory monitoring for quality assurance, process monitoring, process improvement and advanced process control.



All data collected in real-time is held in the xPAT data management server for post analysis purposes. xPAT provides sophisticated data mining, data visualization, and data export capabilities, enabling use of this data for continuous improvements and optimization of pharmaceutical manufacturing processes.

xPAT synchronizes and “time aligns” all the data to provide coherent data sets for post-analysis. All the data is held in a common repository in a common format.

Real-time data analysis flowchart – batch process with NIR and particle size analyzers

## xPAT Data Analysis

Category	Algorithm	Description
<i>Spectral Computations</i>	Fast Fourier Transform	Convert interferogram to raw spectrum
	Absorbance Spectrum	$-\log_{10} \left( \frac{\text{Raw Spectrum} - \text{Black Background}}{\text{White Background} - \text{Black Background}} \right)$ <p>For FT instruments this becomes</p> $-\log_{10} \left( \frac{\text{Raw Spectrum}}{\text{Background Spectrum}} \right)$
	Spectral Math	Math expressions using +, -, x, ÷, exp, log, abs
	Spectral Statistics	Computation of mean, standard deviation, multiplicative scatter correction, mean centering, standard normal variate, etc., using equations
	Spectral Manipulation	Clip to a min or max, extract region, combine fragments
	<i>Spectral Preprocessing</i>	Scale Correction
Thickness Correction Normalization		Normalize spectrum to correct for path length variations
Baseline Correction		Flat, sloping or multipoint (piecewise linear or linear regression) baseline subtraction
Derivative		Savitzky-Golay derivative calculations
Smoothing		Savitzky-Golay smoothing
<i>Spectral Analysis</i>	Peak Height	Compute the height or area of a peak, the ratio of the height or area of two peaks
	PLS/PCA Models	Apply a Partial Least Squares model to map the spectrum into Physical or chemical properties. PLS/PCA models generated by Thermo Galactic PLSplus/IQ and Umetrics SimcaP+ are supported
<i>Particle Size Analysis</i>	Particle Size Distribution Statistics	Characterize the shape and spread of the distribution



## xPAT Data Visualization

xPAT provides a series of visualization tools that allows both real-time data presentation and visual analysis of historical data. Additionally, it is possible to overlay historical and real-time data for batch to batch comparison purposes.

### Visualization

Direct numerical display

Name	Value	Type
BatchState_DCS	Stopped	String
ReadTrigger_DCS	False	Boolean
BatchId_DCS	daf_022709_8	String
BatchScheduledStatus_	Active	String
ReadFeedback_DCS	2	Integer
ControlFeedback_DCS	2	Integer
LaunchFeedback_DCS	2	Integer
LaunchTrigger_DCS	False	Boolean
ControlTrigger_DCS	False	Boolean
StartScheduled_DCS	False	Boolean
MethodId_DCS	DemoFBMethod	String
Parameters_DCS		String
Start_DCS	False	Boolean
Stop_DCS	False	Boolean
Pause_DCS	False	Boolean
Resume_DCS	False	Boolean
End_DCS	False	Boolean
Stream_DCS	0	Integer
Acknowledge_DCS	False	Boolean

### Data types

Numerical values, small arrays can be displayed as a series of numerical values

### Availability

Real-time on xPAT workplace, real-time on desktop client, off-line in visualization tool, values can be exported to ASCII file

### Visualization

Faceplates



### Data types

Numerical values and status indicators

### Availability

Real-time on xPAT workplace

### Visualization

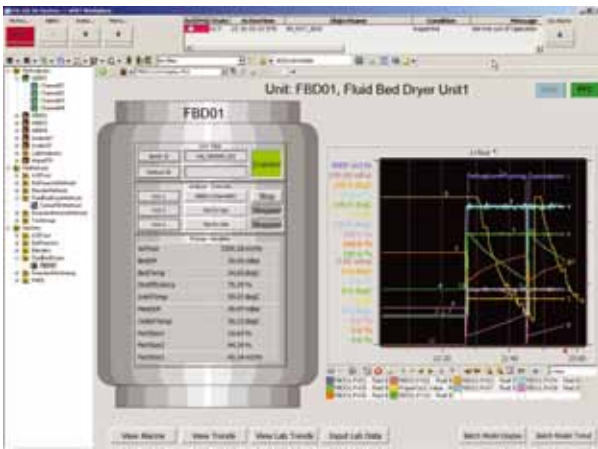
Process graphics

### Data types

Numerical values can drive process graphics

### Availability

Real-time on xPAT workplace



### Visualization

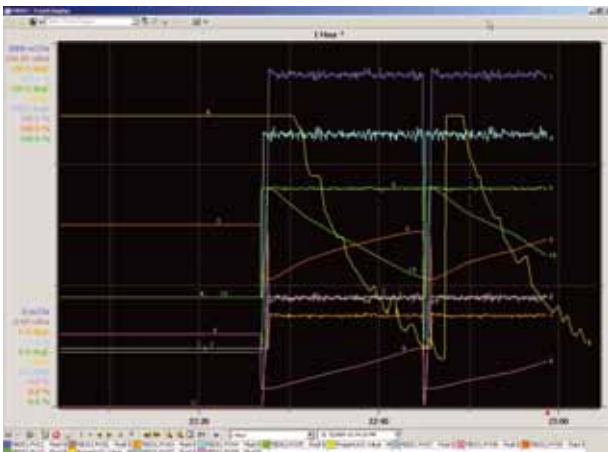
Trend Charts

### Data types

Numerical values with time stamps

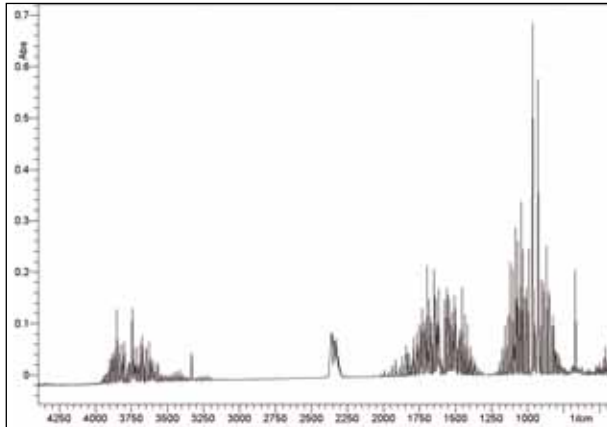
### Availability

Real-time on xPAT workplace, Real-time on desktop client, off-line in visualization tool, values can be exported to ASCII file





**Visualization**  
Spectral display



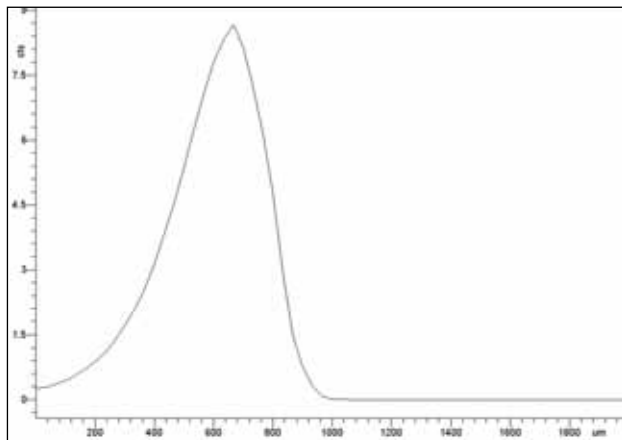
**Data types**

Data structure with x and y units, x min/max values and an array of y-values representing a spectrum with evenly spaced x values. The x values are either the wavelength, wavenumber or frequency of the light. The y values are either the intensity or absorption of the light

**Availability**

Offline in visualization tool, values can be exported to ASCII file or Thermo Galactic GRAMS spc file

**Visualization**  
Particle size distribution display



**Data types**

Data structure with x and y units, an array of x-values and an array of y-values representing a frequency curve (histogram). The x values are the particle size. The y values are the relative number of particles for each size

**Availability**

Off line in visualization tool, values can be exported to ASCII file or Thermo Galactic GRAMS spc file

**Visualization**

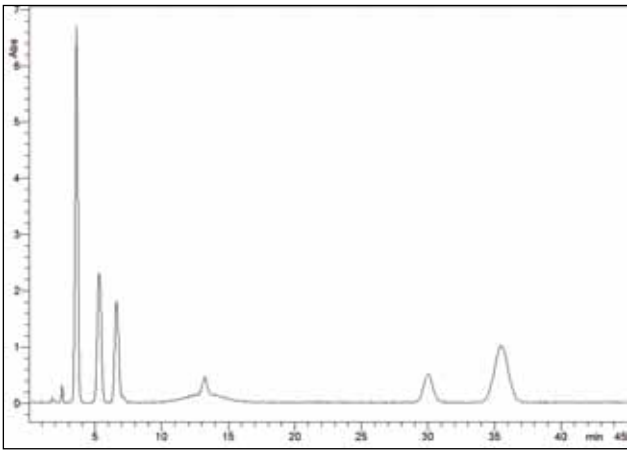
Chromatogram display

**Data types**

Data structure with x and y units, x min/max values and an array of y-values representing a chromatogram with evenly spaced x values. The x values are time. The y values are signal intensity

**Availability**

Off line in visualization tool, values can be exported to ASCII file or Thermo Galactic GRAMS spc file



**Visualization**

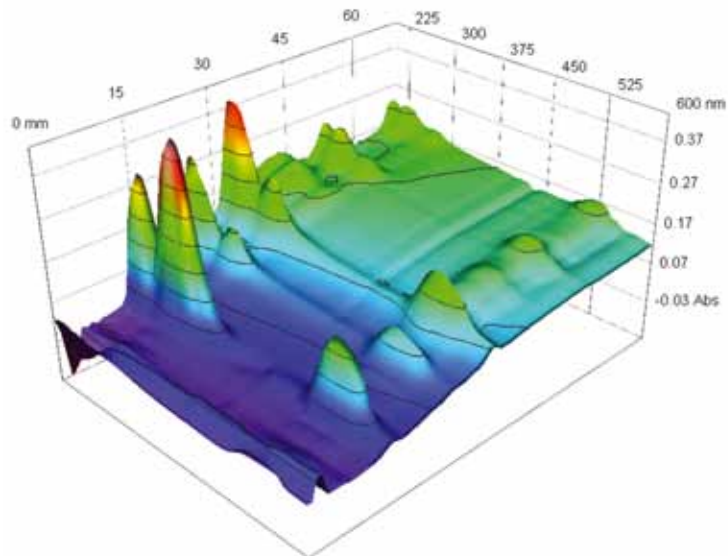
3D Trend Chart

**Data types**

Spectra, particle size distributions or chromatograms with time stamps

**Availability**

Off line in visualization tool, values can be exported to ASCII file or Thermo Galactic GRAMS spc files





## xPAT Data Export

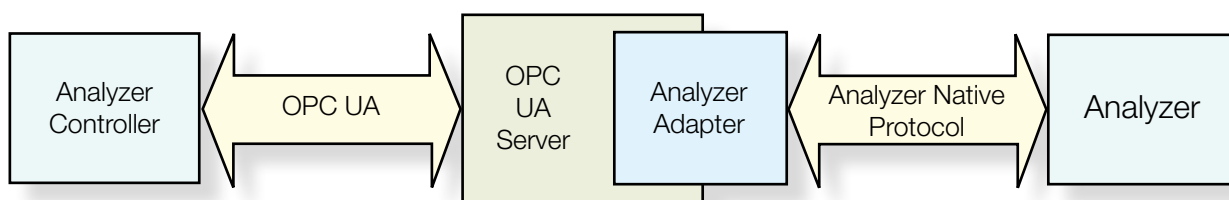
xPAT provides a data mining and export facility that enables data contained in either the data management server or the archives to be exported to either ASCII csv files or Thermo Galactic GRAMS spc files. Data is selected by browsing the ISA-88 structure and applying filters for specific characteristics including the batch name. The xPAT data export facility then builds a coherent data set from the selected data by using nearest neighbor interpolation to time align all the data. The data sampling time can be selected as an absolute time interval or can be aligned with the time intervals at which the data was originally collected. Additionally the export tool can apply preprocessing functions to exported spectral data to facilitate the building of chemometric models.

## xPAT Analyzer Control

xPAT can support up to 20 analyzers with up to 4 measurement channels each; up to 6 analyzers can be used concurrently. xPAT Analyzer Control requires a dedicated Windows XP based computer for each analyzer. Analyzer control is integrated into the PAT method. It is completely automated. Manual control is available from the xPAT client using analyzer faceplates.

Connection to the analyzer is accomplished using an industry standard OPC UA driver to the analyzer native protocol over Ethernet TCP/IP. This approach allows complete control of all analyzer parameters and data acquisition of the raw multivariate array data coming from the analyzer.

Additionally xPAT can connect to analyzers for which an OPC UA driver is not available using simple I/O over industrial protocols like OPC DA and Modbus or ASCII CSV file exchange.

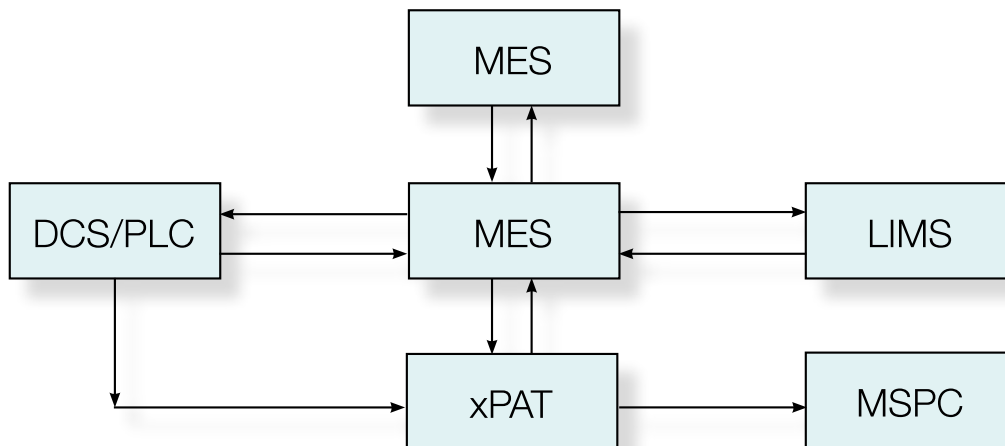


## xPAT Connectivity

xPAT uses open standards and follows the ISA-95 model to integrate with existing process and enterprise infrastructure. xPAT connects with real-time systems such as control systems and process historians using OPC DA. xPAT can also communicate with enterprise systems using ABB Industrial IT cpmPlus Enterprise Connectivity (ECS).

ECS provides generic connectivity using a series of connectors:

- Web services and SAP/R3 connectors provide ERP support
- Database Connector is a pre-built component that can connect with RDBMS Databases. This connector is used to provide connectivity from xPAT to LIMS and MES systems.
- OPC Connector allows real-time applications to directly connect to business systems or portals
- TCP/IP Connector provides integration with all TCP/IP based applications, such as Web servers and mail servers
- XML Connector provides processing of XML structures defined by a given XML schema

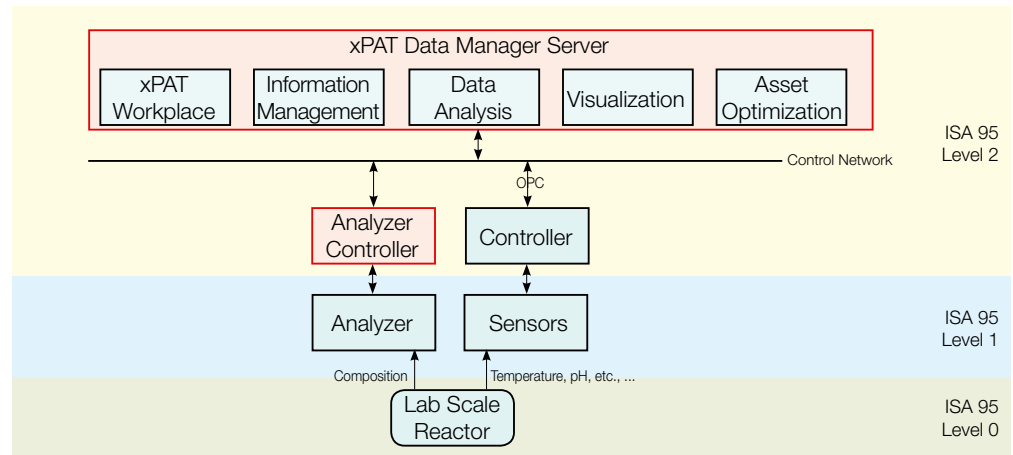




## xPAT Process Control

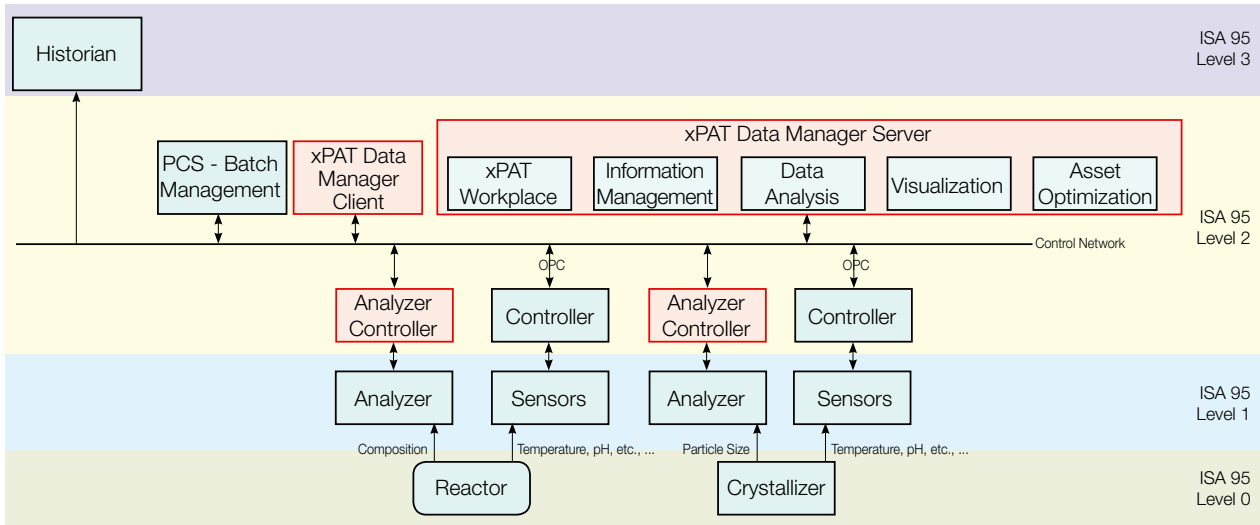
xPAT combines and synchronizes all the data coming from the process and from different analyzers to determine the current condition of the process. This data can be used for end point determination as well as for setting correct process parameters to predict and optimize yield.

xPAT can use a simple equation or advanced Multivariate Statistical Process Control (MSPC) to determine the process parameters. It integrates with existing control systems including ABB's System 800xA to provide closed control.

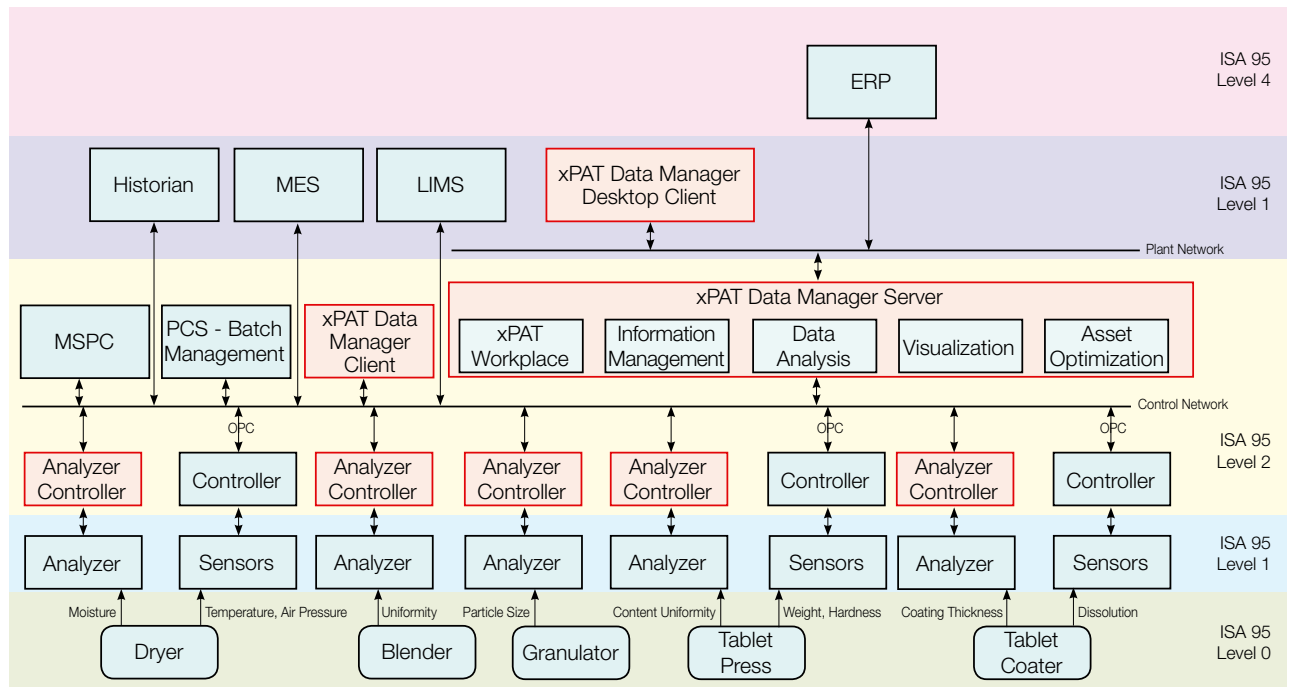


Products in ABB's xPAT Solution

xPAT Laboratory System (No clients, up to three analyzers, OPC connectivity)



xPAT Small Manufacturing System (Up to four clients, up to six analyzers, full connectivity)



xPAT Complete Manufacturing System (Up to four clients, up to six analyzers, full connectivity)



## xPAT System Architecture and Specifications

### System Configurations

Node Type	Min./Max. per		Description
	Laboratory System	Manufacturing System	
<i>xPAT Data Manager Server</i>	1/1	1/1	The data management server is the heart of the xPAT system. It is where all the data and methods are stored. The server includes a built-in Engineering Client.
<i>xPAT Data Manager Operator Client</i>	1/1	0/4	The Operator Client can be used to visualize the operation of the system but does not allow any configuration/engineering. The system supports up to 4 Clients total (Operator or Engineering).
<i>xPAT Data Manager Engineering Client</i>	1/1	0/4	The Engineering Client allows both visualization and configuration/engineering of the xPAT system. The system supports up to 4 Clients total (Operator or Engineering).
<i>xPAT Analyzer Controller</i>	3/20	1/20	The xPAT Analyzer controller allows connection of controller analyzers to the system. The xPAT system supports up to 20 analyzer controllers (6 concurrently).
<i>xPAT Data Manager Desktop Client</i>	1/1	0/2	The Desktop Client consists of a software Client that runs on a non-dedicated PC which allows data retrieval from the Data Management server and limited process visualization.
<i>OPC Connections</i>	0/4	0/4	The system supports up to 4 OPC connections to process infrastructure systems like DCS, Process Historians, PLCs, etc.



### System Capacities

Maximum number of PAT methods	Determined by disk space
Maximum number of unit operations	Determined by disk space
Maximum number of units in a method	4
Maximum number of steps in a unit	4
Maximum number of ports in a unit	3
Maximum number of process parameters in a unit	10
Maximum number of analyzers	20
Maximum number of simultaneous analyzers	6
Maximum measurement channels per analyzer	4
Maximum number of properties per channel	5
Typical number of profile logs (array logs) per channel	1 measurement and 2 calibration/reference
Maximum number of chemometric statistics per property	13
Maximum analyzer data collection rate	1 sample measurement every 5 seconds
Maximum array size	32768 values
Maximum size of a profile log	64 gigabytes online; e.g. 4000000 arrays of 4096 values or about 5000 at a rate of 1 every 5 seconds



## xPAT System Architecture and Specifications

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### System Capabilities

Connectivity to External systems	OPC DA and Modbus for process values, OPC DA mapping for external batch management engines, Direct connection to LIMS and MES systems with ABB Enterprise Connectivity
Data Export	Time aligned export of all batch, process and analyzer data
Data Export formats	ASCII CSV, GRAMS SPC for spectral information
Multivariate Statistical Process Control	Umetrics Simca Batch On-Line
Data Visualization	Data displays are interactive (zoom, pan, etc.), printable and can be copied to the Windows clipboard <ul style="list-style-type: none"> <li>- Real-time and post analysis trend charts</li> <li>- Post analysis xy spectral displays</li> <li>- Post analysis 3D spectral displays</li> <li>- Real-time process graphics</li> </ul>
Connectivity to Analyzers	OPC UA
Analyzer classes supported	<ul style="list-style-type: none"> <li>- Spectrometers (IR/NIR, FT-IR/NIR, UV/VIS, Raman)</li> <li>- Particle size analyzers (Non-imaging, 1 dimensional particle size distribution)</li> <li>- Chromatographs (limited support for HPLC, GC)</li> <li>- Generic interface to receive analysis results as process values from other analyzers</li> </ul>

## System Capabilities

Mathematical processing for spectrometers	<ul style="list-style-type: none"><li>- Absorbance spectrum computation from calibration spectra and sample spectrum</li><li>- Frequency scale correction</li><li>- Thickness correction/normalization</li><li>- Baseline correction (1 point, 2 point, multipoint)</li><li>- Derivative (Savitzky-Golay algorithm)</li><li>- Smoothing (Savitzky-Golay algorithm)</li><li>- Spectral math</li><li>- Scalar math on spectral points</li></ul>
Chemometric model types supported for spectrometers	<ul style="list-style-type: none"><li>- GRAMS PLS/plus-IQ (single component PLS1, PCA, PCR models)</li><li>- Umetrics SimcaP+</li><li>- Peak height, peak area and peak height or area ratios with or without baseline correction</li><li>- Calculations with simple math expressions</li></ul>
Mathematical processing for particle size analyzers	Particle size statistics, array math, scalar math on particle size distribution points
Mathematical processing for chromatographs	Normalization against target chromatogram, quantile baseline correction, correlation optimized warping, spectral math, scalar math on chromatogram points
Multivariate Statistical Process Control (MSPC)	Umetrics Simca Batch On-Line using SimcaP+ batch models



### **Benefits of QbD and PAT**

- Improve manufacturing cycle times
- Reduce product quality variations and waste
- Reduce work in progress inventory
- Enable real-time product release
- Reduce laboratory testing and associated paperwork
- Allow flexible, multi-product manufacturing
- Reduce regulatory overhead and compliance costs with traceable data
- Reduce time to market for new products by enabling early process understanding
- Improve health and safety by limiting operator exposure to pharmaceuticals

**For more information on ABB's Life Sciences products, solutions and services, contact your local ABB representative or visit [www.abb.com/lifesciences](http://www.abb.com/lifesciences)**



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