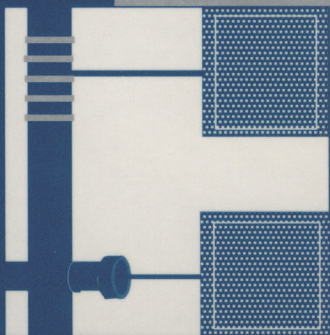
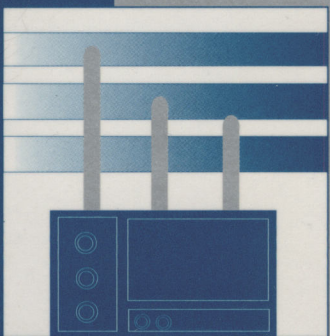
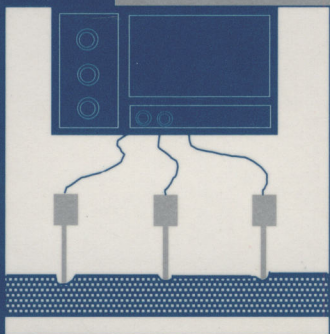


# PROCESS ANALYTICAL CHEMISTRY

*Edited by*  
*F. McLennan*  
*and*  
*B.R. Kowalski*



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# Process Analytical Chemistry

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## Preface

Traditional methods for controlling chemical manufacturing processes have relied exclusively on the measurement of temperature, pressure and flow rate. Only when more information was essential for the safe operation of a plant would the addition of other types of process analysers be considered. Measurement of oxygen in the manufacture of ethylene is a case in point, since oxygen can lead to runaway reactions and the loss of lives and equipment.

More recently, the manufacture of new polymers, materials and other complex products has demanded more timely composition data in order to ensure that the highest possible quality product be made at the lowest possible cost. Better process control with the use of detailed, real-time chemical measurements has become the key to lowering quality costs, i.e. costs associated with reprocessing, destroying or selling off-spec material. Quality costs in chemical and materials manufacturing are estimated to be ten per cent of sales!

Sophisticated on-line and in-line chemical analyses are also required when it is necessary to determine not only product composition, but also product performance during manufacturing. For example, octane numbers for gasoline, and several other performance parameters for all fuels, are today determined on-line during blending from near infrared spectral data analysed by multivariate calibration methods. Another application involves spectral data acquired during polymerization processes to predict quality parameters such as hardness, elongation or dyeability of the polymer product.

Finally, recent environmental regulations require data on aspects such as impurities, solvents and wastewater, to ensure that chemical manufacturing is safe for workers, for communities near chemical plants, and for the environment. These demands for real-time quantitative chemical information on a growing list of manufacturing processes present new challenges to analytical chemists, instrument engineers and plant supervisors.

In response to these needs, the Center for Process Analytical Chemistry was established in 1984 at the University of Washington to work with industry to identify, prioritize and address generic needs in the newly emerging area of Process Analytical Chemistry. Since then a journal (*Process Control and Quality*) has been introduced, several International Forums on Process Analytical Chemistry (IFPAC) have been held, and

in 1993 the *Application Reviews* issue of *Analytical Chemistry* contained the first review on the field, authored by chemists from Dow Chemical Company.

Although a few books are available on process analysers, these focus primarily on commercially available technology. This is the first book on *Process Analytical Chemistry* to cover the present and future of this new field. Our international team of contributors has been brought together from academia, equipment suppliers and different sectors of the chemical industry, to produce a volume which covers a list of topics currently under development as well as in real-life applications. Written for a broad range of scientists and engineers educated in the physical sciences and working in the chemical and allied industries, the book can also be used as the basis for a course at advanced undergraduate or graduate level. Some familiarity with standard laboratory chemical analysis is assumed. The editors hope that the book will provide the basis for more academic involvement in the field. The future of analytical chemistry calls for a partnership between analytical laboratories filled with the most sophisticated instrumentation and in-field chemical sensors/analysers capable of long-term, maintenance-free operation even in the most hostile environments.

Beneficiaries of this book include students and practitioners of analytical chemistry, process engineering, plant supervision and control/intelligence. The book opens the opportunity for analytical chemists to work closely with chemical engineers to design, build and operate safer and more efficient manufacturing processes for the present and future. The editors see this possibility as the key to manufacturing excellence as we move into the 21st century.

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# 1 Process analytical chemistry in perspective

F. McLENNAN

## 1.1 Introduction

Process Analytical Chemistry (PAC) is the application of analytical science to the monitoring and control of industrial chemical process [1,2]. This information may be used to both control and optimise the performance of a chemical process in terms of capacity, quality, cost, consistency and waste reduction.

PAC is not new. It has been applied in the petroleum and petrochemical industries since the 1950s but is presently going through a reincarnation and is a rapidly developing field in all areas of chemical production – petroleum, fine chemicals, commodity chemicals, petrochemicals, biotechnology, food, pharmaceuticals, etc. being fuelled by technological advances in analytical chemistry together with changing needs within the chemical industry.

In a traditional chemical manufacturing plant, samples are taken from reaction areas and transported to the analytical laboratory which is typically centralised. Here the samples are analysed by highly qualified technical staff using state-of-the-art equipment producing results typically in a few hours to a few days. Such analysis is generally used retrospectively to measure process efficiency, to identify materials which need to be reworked or discarded or in a multistage batch synthesis to assess the charge for the next stage. Where these results are critical to the continuation of the process, the process is usually designed to accommodate this time delay giving rise to longer cycle times and reduced plant utilisation.

Process control in this environment is effected by an experimental correlation of physical parameters during the process such as flow rates, times, temperatures, pressures with chemical composition, quality and yield of the derived material followed by subsequent control of these physical parameters.

Implementation of PAC dramatically changes this scene. PAC analysers are situated either in or immediately next to the manufacturing process. They are designed to withstand the rigours of a manufacturing environment and to give a high degree of reliability. They are operated either automatically or by non-technical staff such as process operatives

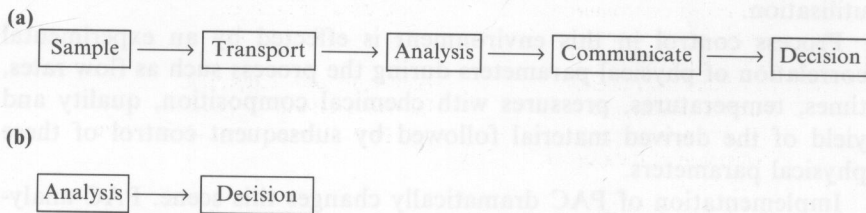
and produce real or near-real-time data which can be used for process control and optimisation.

The move towards PAC has been fuelled by two developments. Firstly, increasing international competitiveness within the chemical industry has led to the widespread adoption of 'right first time' and 'just in time' approaches to manufacturing and quality. This has placed the emphasis on building quality into all stages of the process, increased manufacturing flexibility, reduced inventory and improved control of processes. Secondly, during the past decade advances in analytical chemistry and in particular the development of the microcomputer and improved algorithms for data handling, have enabled almost instantaneous generation of information.

Moving from a traditional analysis approach to a PAC approach is not easy, not only does it require significant technical developments but it also requires a 'cultural' change. This change needs to be embraced not only by the analyst community, but also by manufacturing, R&D and engineering, etc. This change process requires a 'champion' or better still a number of champions at both the managerial and technical levels in order to be successful.

Figure 1.1 outlines the key differences between the traditional and PAC approaches to process control.

While this chapter and most of this book will concentrate on the role of in-plant analysis, this does not mean that there is not a place for the specialised analytical laboratory and it is the author's belief that an integrated approach to process analysis is essential to meet all the needs of a modern chemical plant [3, 4]. It also does not mean that manufacturing processes are the only processes to benefit from moving analytical chemistry from its centralist role to the in-situ or distributed role. The human body, the air over a city and a mountain lake all represent complex chemical processes, the study of which would benefit from on-line, real-time and even non-invasive analysis.



**Figure 1.1** (a) Traditional approach to process control. Analysis employs technical staff, high-tech equipment and typically takes several hours. (b) Process analytical chemistry approach to process control. Analysis is either automatic or employs non-technical staff, utilises rugged and reliable equipment and takes seconds or minutes.

## 1.2 Terminology

For the purpose of this volume, we propose to use the following definitions (Figure 1.2).

**Off-line analysis:** This involves manual removal of the sample, transport to the measurement instrument which is located in a specialised central laboratory using highly qualified technical staff. This is typified by relatively low sample frequency, complex sample preparation, flexible and complex analysis. The advantages of this approach arise from the economy of sharing expensive instruments and skilled staff.

**At-line analysis:** Many of the deficiencies of off-line analysis—time delay, administration costs, prioritisation of work—may be addressed by carrying out the analysis at-line. This still involves manual sampling but in this case the measurement is carried out on a dedicated analyser by the process operative. At-line analysis is usually accompanied by significant method development work to simplify the sample preparation and to modify the measurement technique to permit the use of robust, reliable instrumentation. It is a mistake to simply transfer the laboratory analysis to the plant floor – time and effort spent in the evaluation of what information is required to control the process invariably leads to the development of a more robust solution.

**On-line analysis:** We use this definition to describe all examples of fully automated analyser systems. Other authors have subdivided this further into on-line, in-line and non-invasive analysis but we will consider all these as one group.

Table 1.1 highlights the pros and cons of each of these approaches.

**Table 1.1** The pros and cons of each approach

	Advantages	Disadvantages
Off-line	Expert analysts available. Flexible operation. Controlled environment. Sophisticated instrumentation. Low unit costs/test.	Slow. Lack of ownership of data. Conflicts of priorities. Addition admin costs.
At-line	Dedicated instrument. Faster sampling process. Simpler instrumentation. Ownership of data by production personnel. Control of priorities.	Low equipment utilisation. Equipment needs to be robust to cope with production environment.
On-line	Fast. Automatic feedback possible. Dedicated analyser.	Minimum downtime required. Long/expensive method development. 24 h troubleshooting/maintenance resource required. Electrical classification required.

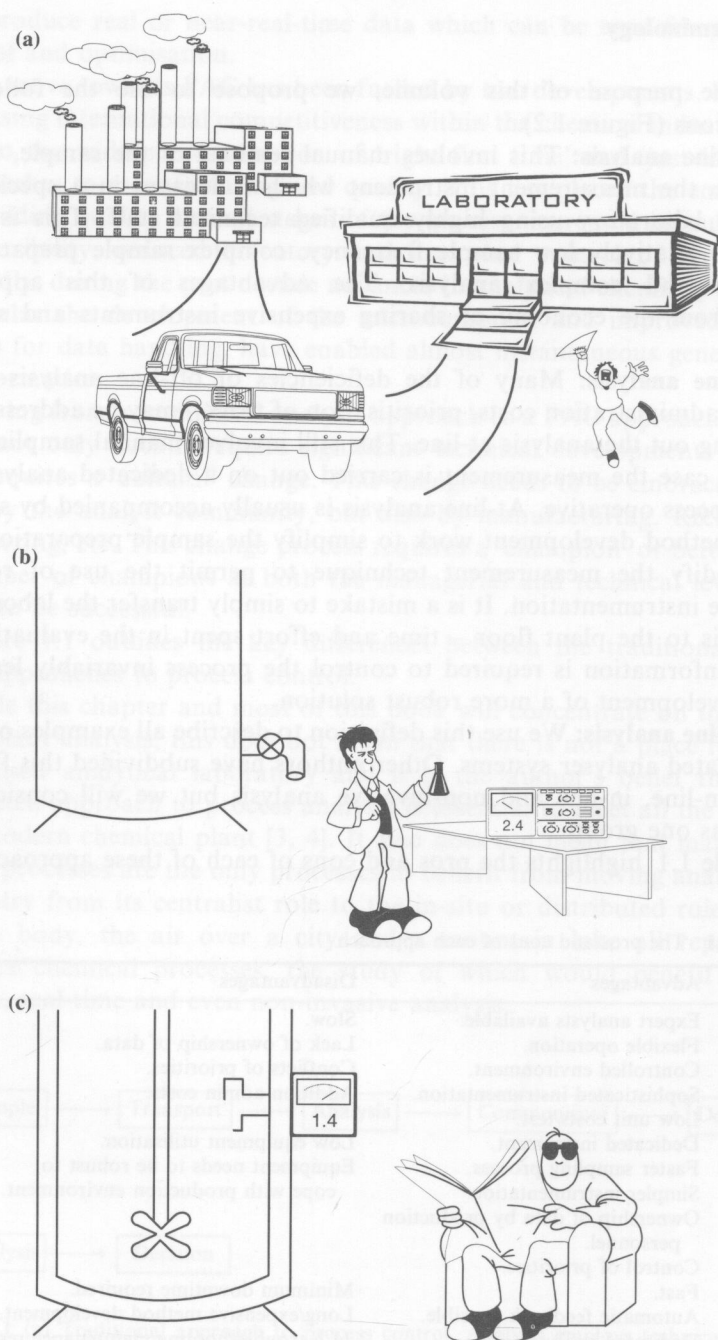


Figure 1.2 (a) Off-line, (b) at-line, and (c) on-line analysis.



### 1.3 An integrated approach

PAC is a truly multidisciplinary science. The aim of each project should be to define the optimum process control, measurement and analysis philosophy for the process. This key stage requires contributions from the analytical chemist, measurement engineer, control engineer, process development chemist, chemical engineer and production manager. In the past we have had on-line analysis teams and off-line analysis teams, often competing with each other and nobody looking at the important area of at-line analysis.

While the move from off-line to in-plant analysis can be retrofitted to a process and bring substantial benefits, experience has shown that the biggest impact comes when PAC is integrated with the process development and plant design (e.g. rapid on-line or at-line analysis may allow efficient manufacture without intermediate storages). In the former case, much of the in-built inefficiency (i.e. to cope with time consuming off-line analysis) cannot be recouped. An effective way of getting in at a sufficiently early stage, is to apply the PAC philosophy (especially on-line) to process research and development. Substantial gains in development time, process cycle times, materials efficiency and energy efficiency are achievable even where such work does not lead to process-scale PAC projects.

On a project by project basis, PAC should be problem rather than technique driven. It is nonetheless essential that high level research and development is undertaken to enhance the range of techniques available. This is especially true for on-line analysis where the application of even well established laboratory techniques may offer huge challenges. In addition to instrument development, the application of commercially available systems to specific process problems can also be complex. A progressive PAC organisation needs high calibre staff and support from senior management to ensure that project implementation against today's problems is undertaken in parallel with longer term research to solve tomorrow's problems. Such research should make full use of existing company research infrastructure; the PAC specialist cannot be an expert in all analytical techniques. It is therefore important that 'traditional' researchers embrace the PAC philosophy to some extent.

Great progress in PAC has clearly been made over the past 5–10 years. Most of the R&D has been undertaken by the world's major chemical companies; it was not easy to follow developments since much of the work is deemed proprietary and confidential. Over the years, this has been supported by relatively small 'niche' instrument companies, close to particular sectors of the chemical industry. More recently, the major suppliers of analytical instrumentation have become interested in PAC. The strategic alliance between Perkin Elmer and Dow Chemical, to develop and commercialise Dow's PAC expertise, is a good example.