Clinical Biochemistry Department Specialist Portfolio Seminars

7.1 Laboratory Automation

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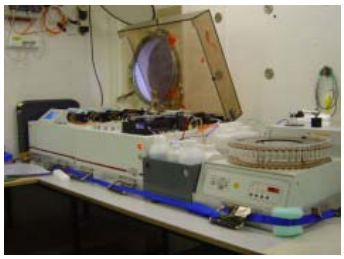
7.1 Introduction & Historical Setting

Growth in laboratory testing came with:

- Realisation test results can lead to diagnosis and treatment
- Analytical chemistry advances including equipment especially photometers such as the EEL and the Pye Unicam


AutoAnalyzer


EEL photometer


Cobas Bio Centrifugal Analyser


Kodak Vitros – dry slide analyser

As workload increased in the 1960s and 70s manual techniques – literally using test tubes, could not cope. We need to realise that many of our current colorimetric assays can be done in a test tube still. Labs were confronted with two big issues:

1. Analysing Increasing Numbers of Samples

A key solution of increasing workload came in 1957 when Professor Skeggs invented the Continuous Flow Analyser (CFA). For 20 years this was the main technique used to start the process of automation. After continuous flow came several newer approaches;

- **Centrifugal Analysers** – took over things such as enzyme assays which were not ideally suited to the AutoAnalyzer. Spun samples and reagents. Cobas Bio was the most popular and was used at City and Sandwell through the 1990s.
- **Kodak Analysers – became Ortho**: E700 – The first one was placed in the UK and went to Sandwell in 1988. Dry slide reagents. “No more liquid reagents forever” we were told! Used reflectance not absorbance.
- **Discrete Analysers:** Idea of three circles – reagents, samples and reaction curvettes. Our IL 600 is an excellent example of this early concept.

2. Handling the Data Entry and the Results Produced

Use of computers to help with data handling started in the 1960s with labs developing their own database approaches.

Automation and Mechanisation

- **Mechanisation:** Using devices to replace, refine or extend human effort
- **Automation:** Mechanisation with process control and use of computers helps with aspects of this.

See Ref 1 for further definitions

Which Tests can be Automated?
Any process can potentially be mechanised or automated. The key question is when to move from manual techniques and this can include:

- Workload gets too high – automating can save time, increase productivity, reduce cost and increase quality
- Mistakes are being made
- Processes safer

Constraints to automation – key issue is that for modern systems we are to some extent reliant on decisions of commercial companies on which tests to offer.

7.1.1 Considering Automation in Our Laboratory:

Common Photometric Tests and ISEs – Yes all available on automated platforms

Immunoassay Techniques – Most but not all available on our large analysers

Repertoire Governed By Company: Using large company analysers for blood spots is not easy. Can develop methods on photometric assays but immunoassay reagents are "locked" and not possible.

Key Decisions on Automation: When to add mechanisation or automation. Needs foresight and forward planning, including financial investment. The current issues in our laboratory:

Further Mechanisation of Vitamin D – 96 well plate approach lends to this.

Toxicology: Mechanisation depends on us developing systems.

Vitamins: Example of a high throughput test not yet automated. There are even aspects of mechanisation not fully in place.

TPMT: Very successful but is a manual test. Some evidence of mechanisation – types of pipette, HPLC has an autosampler. However, TPMT assay has complex steps needing close control. Together with a high workload suggests prime candidate for automation.

See Ref 2 for TPMT current method and a proposal to automate using a CFA approach.

7.1.2 Key Steps in an Automated System and Steps that can be automated

- **Mechanisation:** De-capping, centrifugation, analysis, re-capping and archival can all be seen as a flow of samples in a mechanised system.
- **Automation:** Two way interface with computer through some midware (AMS, Modulab) offers automation. Includes elements such as feedback – repeating high samples, retrieving samples from archive when new tests requested etc.
- **We have moved from off-line robotics (mechanisation) to on-line robotics** : A track system. Our approach allows more aspects which can be considered true automation to be incorporated. For example; feedback, automatic re-runs, add-ons etc. However track system automation has downsides as well. Such as when systems fail, have we got back ups? Can we get samples out of the archiver? – You may know some more!

7.1.3 Scientific Principles of Analytical Techniques

Electrochemistry - Ion Selective Electrodes: Use the change in signal and the Junction Potential of electrochemical cell to make measurements. Examples; Na^+, K^+ Cl^- $Ca2^+$ (blood gas analysers).

Photometric Assays: Measure concentration and activity using change in Absorbance.

- Relies on **Beer Lambert Law** where Absorbance is a quantitative measure expressed as a logarithmic ratio between the light falling upon a material and the radiation transmitted through a material.

  $$A_\lambda = -\log_{10}\left(\frac{I_1}{I_0}\right),$$

  Where A_λ is the absorbance at a certain wavelength of light (λ), I_1 is the intensity of the light passing through and I_0 is the initial intensity of the light.

Reagents in our large AutoAnalysers offer many different ways of using photometry to measure something in a sample. For example:

End Pont Reaction: The reaction goes to completion ***Example: Total Protein***

Rate of Change: Enzymes and also some other assays where enzyme reactions are used. *Examples: All enzymes, urea, creatinine.*

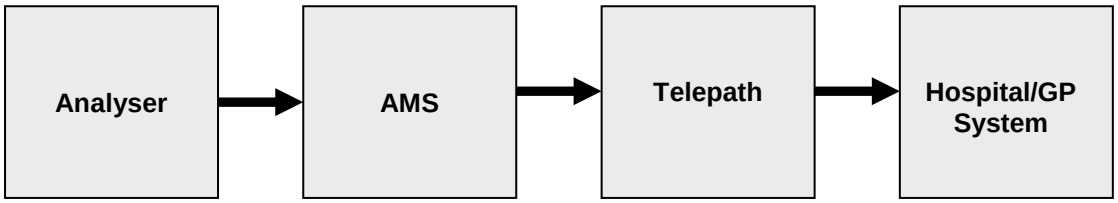
Immunoassay: Here we use the antibody antigen reaction in different ways. We link these primary reactions to secondary reactions giving signals such as fluorescence and chemilinescence to measure the amount of substance. Key use is where we have low concentrations and need a lot of specificity. Examples: Hormones, tumour markers and Troponin T.

7.1.4 Range of Samples That can be Analysed

Most of our work in Biochemistry is on serum. Our track system also undertakes lots of analysis on urine and also some other fluids. We are also trying to adapt some of our assays to analyse blood spots – there are issues here relating to CE marking.

7.1.5 User Interface

Our track system uses AMS to interface with our Laboratory Information Management System (LIMS) which we call Telepath, and is supplied by iSoft. The Abbott system looks like this:



7.1.6 Basic Feature Of Our Automated Equipment

The original discrete analyser's research was conducted in the UK at Northwick Park Hospital and the Wolfson Research Laboratories in Birmingham. The Coulter Dacos was the direct output of this R&D. ***Reference 3 gives a view on this.*** You should be able to see how discrete analysis has moved on with regard to automation by comparing our current systems with the analyser assessed at Good Hope Hospital in 1985. Some of their comments will be familiar!

7.1.7 Sample Integrity and Corrective Action

Sample integrity means that the starting point of analysis is actually fit for purpose. Pre-analytical factors that can cause problems include:

Inherent things in the sample that can interfere: Lipaemic or icteric samples for example
Problems with sample collection: Incorrect phlebotomy – ***see Reference 5***

Problems with Samples Once In the Laboratory: Old samples or not stored correctly for example, without a cap and going round a track for prolonged periods.

7.1.8 Health and Safety Issues for Automated Systems

We do need to think holistically here, so:

- Laboratory Environment – noise, space, adequate facilities
- Working arrangements
- Physical Risks of Analysers- water and electricity, fire lifting and handling
- Reagents and Samples - COSHH, infection etc

7.1.9 Internal QC and EQA

Quality Control – Is used to check on a daily basis that the methods on all units are running OK. Also need to ensure that all units in a system give equivalent results and for us this includes across both sites. For large track systems with many different analytical units there are considerable issues in the area of QC.

External Quality Assurance – Much more about ensuring that the whole of what we do gives the right answers.

7.1.10 Maintenance and Housekeeping

Daily, weekly and monthly maintenance are all key to ensure we have systems that work efficiently for us.

Jonathan Berg
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