

The History of the AutoChemist®: From Vision to Reality

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Summary

Objectives: This paper discusses the early history and development of a clinical analyser system in Sweden (AutoChemist, 1965). It highlights the importance of such high capacity system both for clinical use and health care screening. The device was developed to assure the quality of results and to automatically handle the orders, store the results in digital form for later statistical analyses and distribute the results to the patients' physicians by using the computer used for the analyser.

Results: The most important result of the construction of an analyser able to produce analytical results on a mass scale was the development of a mechanical multi-channel analyser for clinical laboratories that handled discrete sample technology and could prevent carry-over to the next test samples while incorporating computer technology to improve the quality of test results. The AutoChemist could handle 135 samples per hour in an 8-hour shift and up to 24 possible analyses channels resulting in 3,200 results per hour. Later versions would double this capacity. Some customers used the equipment 24 hours per day.

Conclusions: With a capacity of 3,000 to 6,000 analyses per hour, pneumatic driven pipettes, special units for corrosive liquids or special activities, and an integrated computer, the AutoChemist system was unique and the largest of its kind for many years. Its follower – The AutoChemist PRISMA (PROgrammable INDIVIDUALLY SELECTIVE MODULAR ANALYZER) – was smaller in size but had a higher capacity. Both analysers established new standards of operation for clinical laboratories and encouraged others to use new technologies for building new analysers.

Keywords

History of medical informatics, high capacity clinical analyser system, discrete sample technology, medical information technology, large scale laboratory automation, mass analysis equipment for health screening.

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1 Introduction

The largest clinical analyzer system created for clinical laboratories, called the AutoChemist, was developed in the mid-1960s and used until the late 1980s. Its development started when Gunnar Jungner, MD, PhD, Associate Professor in Clinical Chemistry at the University of Gothenburg, Sweden, was a Visiting Scientist at the National Institute of Health (NIH) in the US. He became a member of a team working on the automation of hospital laboratories at the Department of Clinical Pathology, Clinical Center, which was headed by Dr George Z Williams [1-5]. Another notable member of the working team was Earnest Cotlove [6-7]. Ingmar Jungner, MD PhD, a younger brother of Gunnar Jungner, visited NIH at the autumn 1959 and took part of their plans to make the laboratory work more efficient through the use of laboratory robots and by directing their work towards an automated hospital laboratory through an “electronic brain”. An unforgettable event during his stay was a visit together with the working team to the aircraft manufacturer Boeing, whom NIH had commissioned to construct an automated blood analyzer. The project was lead by Jordan J Baruch, a genial technical consultant for NIH [8]. In 1966, Dr Williams, Dr Cotlove, Mr Baruch, and Gunnar Jungner presented the results of their work at the International Conference on Automated Data Processing in Hospitals in Elsinore (Denmark) [9-13].

2 History of the AutoChemist The Start – 1960

When Gunnar Jungner returned to Sweden, he created interest in the improvement of laboratory performance in Sweden. The Swed-

ish Agency for Health Services Development (SJURA) appointed Gunnar Jungner as the President of their working group on Clinical Chemistry. Hence, the Jungner brothers started to improve laboratory efficiency using tempo-automation and automation of single analyses. In parallel they developed a multi-channel equipment for large-scale health screening, which later resulted in the Värmland equipment [13-15].

The Värmland Survey

Following the initiative of the Jungner brothers, Swedish authorities decided in 1962 to apply on a large scale chemical analysis in the county of Värmland (300 kilometres northwest of Stockholm). 100,000 persons older than 25 years were screened from late 1962 to late 1964 [13-20] with a battery of twelve blood analyses. The apparatus system used in the project was built by the Jungner brothers [13-15]. More than one million analyses were performed during this two-year period. For the Jungner brothers, the Värmland project was an incentive to continue the technical development. It was rather challenging for two years when several hundred blood specimens were arriving for processing at the Stockholm laboratory by the night train from Karlstad four to five days a week. Every time the home-grown system was in a crisis, there were discussions about how to construct a safer installation.

Hospital for Infectious Diseases Project (SJURA 404)

A project for hospital automation was also initiated with the support of SJURA [21-23]. The Jungner brothers in collaboration with Hans Peterson, MD PhD [23] realised that

there was a need for a hospital service, a service whereby automated units (i.e. wards, laboratories, storage facilities, etc.) could be connected through telecommunication and the automated transport of material. They considered hospital wards and other clinical entities as consumers demanding support from their service departments and identified the need for a communication system to provide clinical information and material. However, to automate this communication, consumer and service units needed to be equipped with in- and out-functions.

At the Hospital for Infectious Diseases (Stockholm, Sweden), where Ingmar Jungner headed the Chemistry Department, our team started in 1964 a project with an automated requisition and report system [12] adapted to a teletypewriter as an in- and output unit, an order box for simple requisition and a patient record system for the reports produced. The referral contained patient identification information and a short summary of the case history together with information about the laboratory requisitions.

The requisition was sent to the laboratory via the order box, from where reports were then returned to the wards with information on date and lab results. A paper printout was produced to fit patient's medical records

allowing easy access for clinicians. Moreover, small cards were produced providing a summary of all relevant clinical information for health professionals to optimise patient management. The teletypewriter was equipped with a reader and a punch for an eight-channel paper tape approved for connection to the regular telephone network.

The AutoChemist System at the Hospital for Infectious Diseases

The AutoChemist System used at the Hospital for Infectious Diseases was constructed around a large multiple robot analyzer (Fig. 1), wherein one central unit could execute up to 40 different analytical methods (Fig. 2). Special connected measuring stations (satellite stations) were available for those analyses not suitable for full automation. The system was computer-based and worked online through a connection with the central unit and a telecommunication system. This system provided an automated requisition and reporting system using the previously described teletypewriters as well as boxes. These boxes were connected with the teletype of the ward which allowed correct identification of patients by room and bed.

The teletype and its connected cables allowed a simple push-button to provide the correct identification details for a patient, automatically extracted from the computer memory. The push-button of the Order box then allowed requesting of the appropriate analyses from the relevant laboratory and/or examination. This information was also sent to the laboratory computer, which then received data to print out an order form for the right requisition (e.g. sample taking). A requisition could easily be extended through manual input on the teletypewriter.

Computerisation and Software Development for the Hospital for Infectious Diseases

The technical developments of the AutoChemist continued after 1964, but the greatest improvements came from information technology. Until then, computers were not available for standard use, as they were considered too progressive and too expensive for the market and small data units were still under development. Eurocomp LGP 21, a German manufactured minicomputer, was used along with a prototype of the AutoChemist. At that time,



Fig. 1 AutoChemist: Automatic Multi- Channel Analyser for large scale analysis



Fig. 2 Inside AutoChemist

core memories were not in use yet and cycle times were measured in milliseconds rather than in microseconds. Further improvements were thus required to obtain an access time between 8 and 41 milliseconds. However, one still had to add the time needed to perform the tasks. The AutoChemist delivered 20 reports every 20 seconds. As a result, the time required to read the value on a digital voltmeter was too long. This problem was temporarily solved by manually inserting every second instruction diagonally on the disc, thus achieving twice the speed.

The LGP 21 was then replaced by a Digital Equipment Corporation's PDP-5, which was equipped with core storage, a programme controlled Multiplexer, an A/D converter and a double magnetic tape station, which was shown to be very useful for the telecommunication system in the hospital. Computer development was accelerating [24] and in 1965 Digital presented its first mass-produced mini computer PDP-8 [25].

At this time, the software rather than the hardware became a problem for the further enhancement of the AutoChemist. In 1965, a relatively simple programme, MACH – Main Program, was developed to handle all procedures of the AutoChemist [26].

The Development of the Mass Analyzer AutoChemist – the First Automated and Computerised Multichannel Analyzer (1965)

The previously described Värmland project [13-20] encouraged the Jungner brothers to continue the technical development of the AutoChemist. Repeated failures of the home-grown system revealed the need for a safer installation of mass analyses based on new ideas and technical solutions, without abandoning existing techniques. This required a system with high capacity, versatility, and compactness, but easy maintenance and low labour-intensity. This thus called for automated printing under minimal supervision. The existing equipment at that time did not respond to the high degree of mechanising needed to provide an essential advance in laboratory automation. The demand for an industrial production of

analyses and reagents was the subject of multiple debates in the field of biochemistry, and the task was theoretically possible since the pharmaceutical industry had already provided pipetted fluids for many years. The Jungner brothers and their team realised that automation needed to allow the processing of a large number of different analytical procedures whereby different specimens, including whole blood, serum, urine, cerebrospinal fluid or extract, were analysed simultaneously. They estimated that 20 to 40 different analyses of a much larger quantity were required, thus highlighting the need for a computerised mass analyzer.

Creating a Prototype

As a consequence, a prototype was created by the lab's own staff involving two instrument makers and about ten volunteer medical students. The resulting device was enormous as the installation was four meters long. It was two meters high and two meters wide (Fig. 1). This size was necessary to allow the transportation of thousands of centrifuge tubes (samples) in heavy metal racks hanging on motorcycle chains, supported by very thick beams (Fig.2). With

a capacity of 3,000 to 6,000 analyses per hour, pneumatic pipettes (see below), and an integrated computer, the AutoChemist was unique and the largest of its kind. This first AutoChemist was manufactured by AGA, Lidingö, Sweden.

3 Technical Specifications of the AutoChemist

The Operating System of the AutoChemist

Figure 3 depicts the operating system of the analyzer and Figure 4 illustrates the analyses occurring in one channel of the AutoChemist. Since the AutoChemist was mechanical [27-34], reagents were added by pipettes and transported with the sample within each analysis channel whereby a chain system was transported through the right incubation temperatures. The vertical movement allowed for changeable dimensions with sufficient reaction time at high analysis speed. All specimens and reagent mixtures were handled to avoid contamination of test samples, a technique called “discrete sample handling” which was in contrast with the

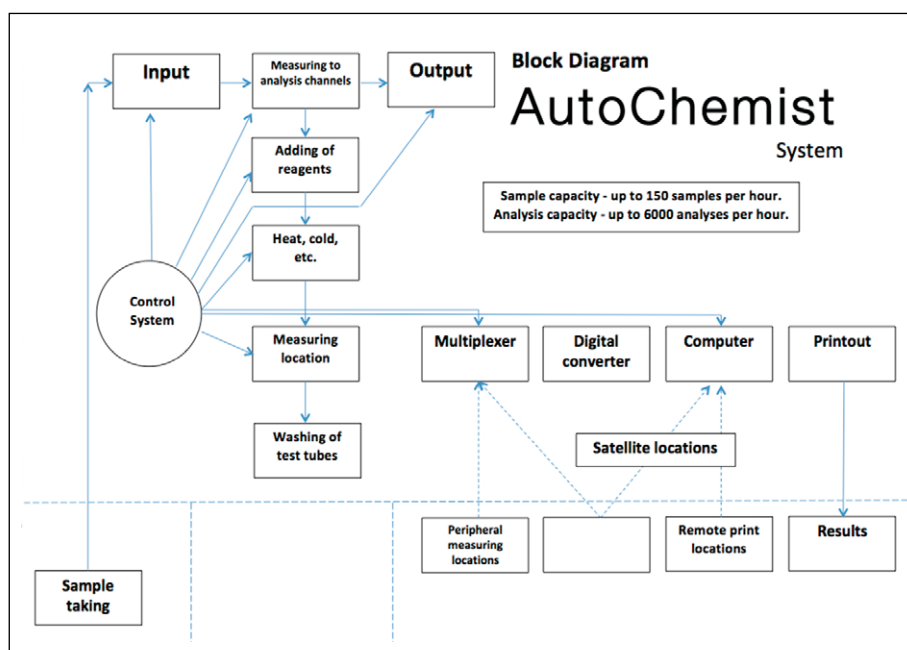


Fig. 3 Bloc diagram of the AutoChemist's operating system.

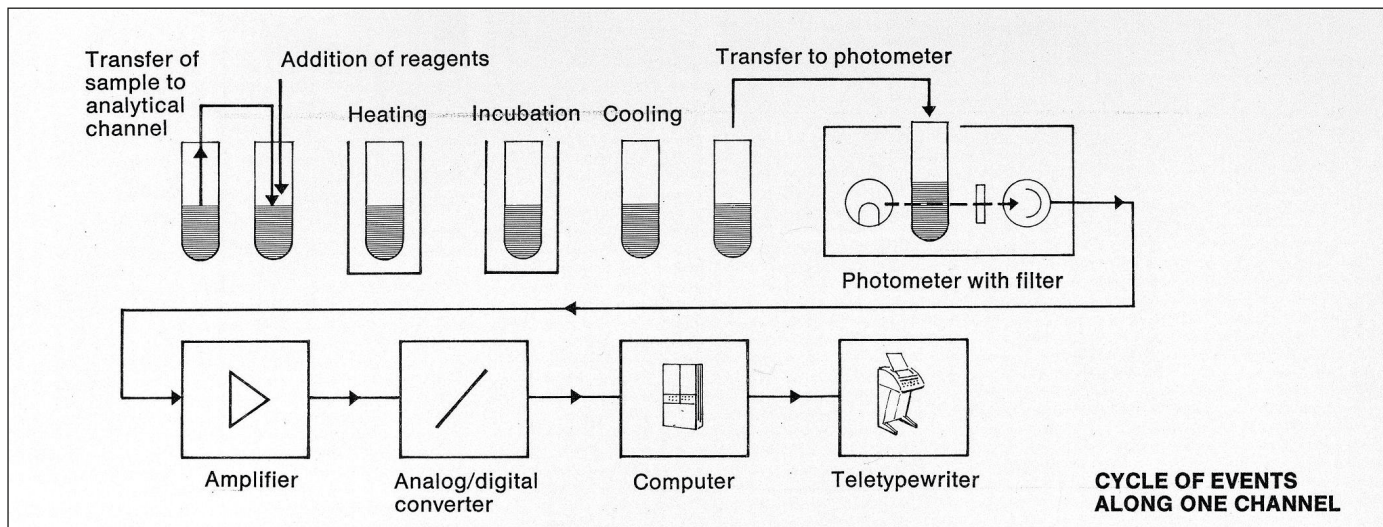


Fig. 4 The cycle of events along one channel in the AutoChemist

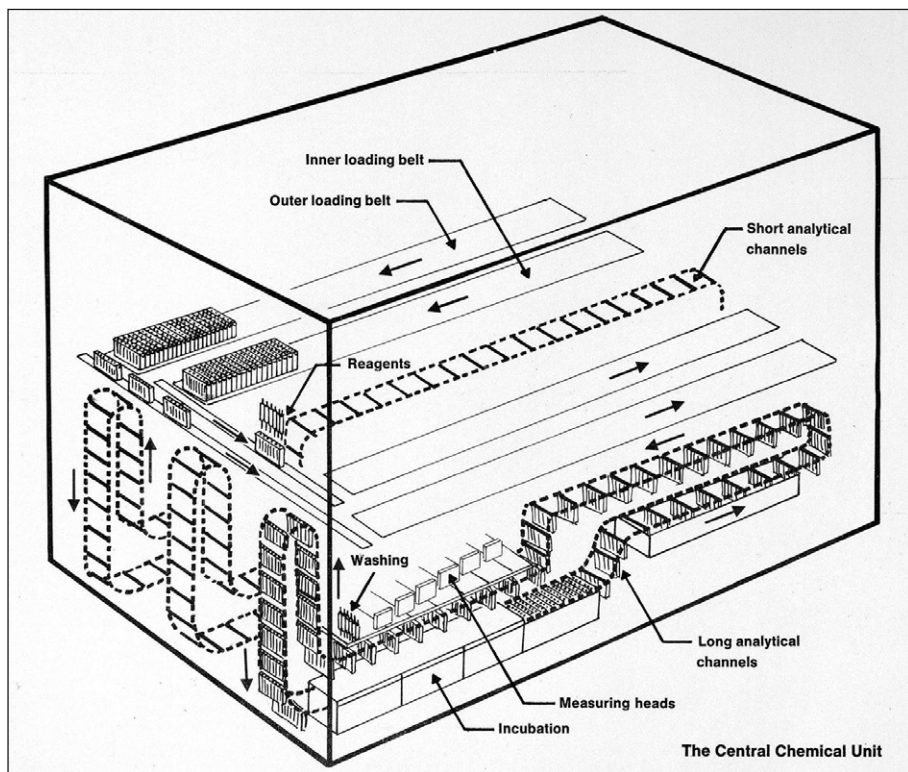


Fig. 5 AutoChemist's Central Unit: The transport system in the analyser

continuous flow system then used by the automated AutoAnalyzer® from Technicon.

An installation like the AutoChemist needed special constructions for photometric parts, automated filtration, printouts, etc. This equipment implied remote controlled

components with an automatic steering system whereby temperature control, ventilation, rinsing and removal of waste products were completely automated. The equipment was built to correct disruptions and to indicate errors.

The Central Processing Unit

The AutoChemist transported the samples, usually blood serum, on a loading belt of centrifuge tubes along a series of sample taking stations, where all tubes stopped at the same time, one at each station.

A pipette drew a calibrated volume of the serum, which was then transferred - at the same time the diluting fluid or reagent was added - to a new test channel of reaction tubes. These were then moved through the different required treatments of each test procedure. Thus every testing station was the first step for each test channel. The total number of tubes was around 6,000 tubes. The process was started while pressing a button on the control panel [35].

The AutoChemist had two loading belts for test samples (Fig. 5), one of which was used for less complicated procedures. More than 1,000 samples could be loaded simultaneously. The test samples were put into specially designed metal racks to allow identification and easy handling. This allowed for the selection of test channels requiring the same incubation temperature. Apart from the room temperature, the system also included three different incubation temperatures as well as a possibility to set the temperature as decided in a selection of special channels. The incubation time was normally up to 30 minutes (Fig. 6). The number of analytic channels varied between 20 and 40 types.

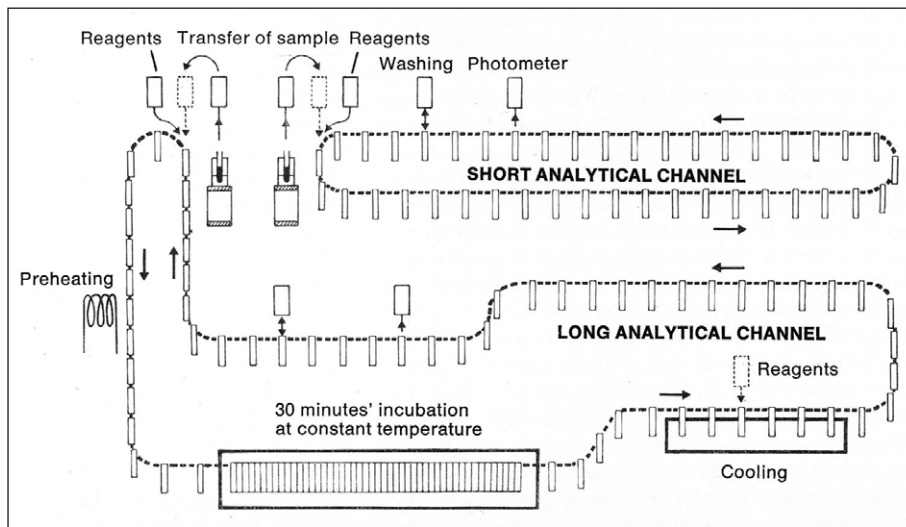


Fig. 6 AutoChemist: Analytical channels

Control Unit, Power and Electronic Cabinets

Except for the computer, all procedures were managed in the central unit by a special control unit distributing the incoming electric power to the central unit and to all other cabinets. The control unit had semiconductor components and thus no mechanical or moving parts.

Measuring Devices

Most of the measurements of laboratory analyses were made by photometer-supported colorimetric analyses of solutions. The photometers in the AutoChemist were two-ways photocell colorimeters with an interference filter (Fig. 7). In contrast to the conventional techniques, the AutoChemist was equipped with separate measuring de-

vices (photometers) for each analytical channel, where the colour solution was pumped in and out by a pneumatic driven pipette.

New Pneumatic-driven Pipettes

Pneumatic driven pipettes (Fig. 8) were crucial for this analyzer because pipetting was essential for very high precision and reliability. These pipettes did not exist yet and it became a difficult and expensive challenge to AGA to develop them. However, they did succeed and the pneumatic-driven pipettes were marketed worldwide for different types of laboratory work including the dispensation of corrosive and acid solutions. The AutoChemist contained 300 pipettes, able to process up to 20 million operations each.

Mini-cube and Satellite Stations

Analyses requiring high incubation temperatures or reactions with strongly corrosive or foul-smelling liquids were preferably handled separately. An enclosed analytical robot, called Mini-cube (Fig. 9a, b), was developed for this purpose. It was made of

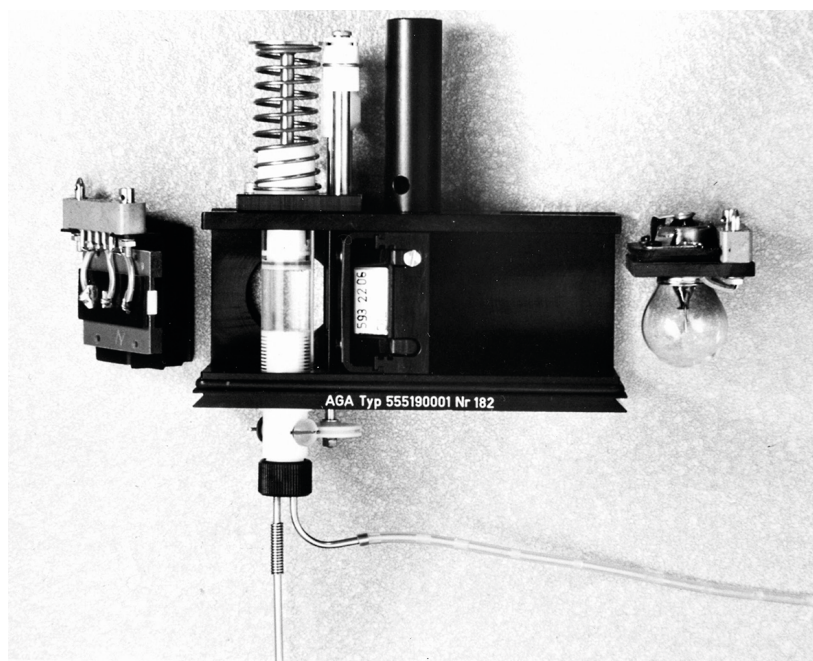


Fig. 7 AutoChemist: Photometer

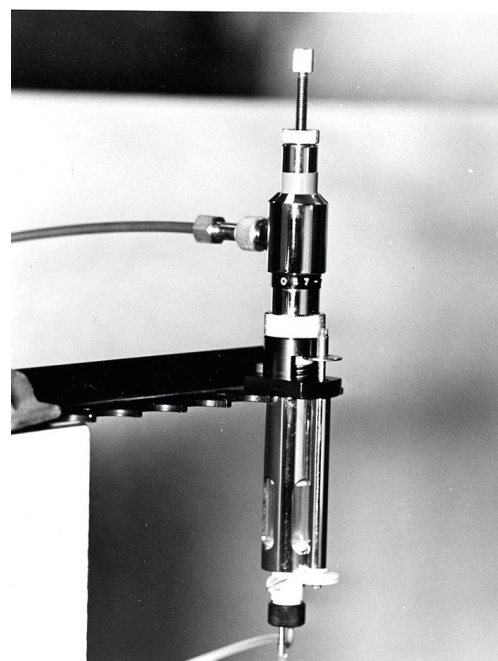


Fig. 8 AutoChemist: Pneumatic pipette

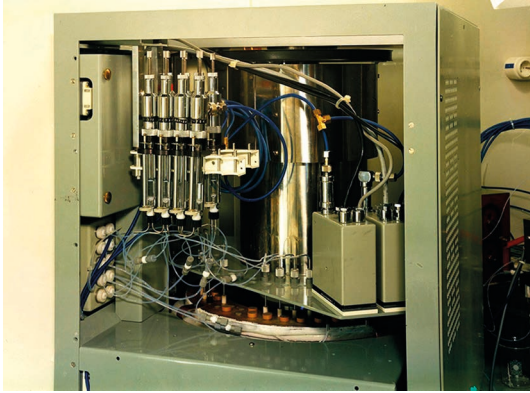


Fig. 9a MiniCube



Fig. 9b MiniCube in AutoChemist inspected

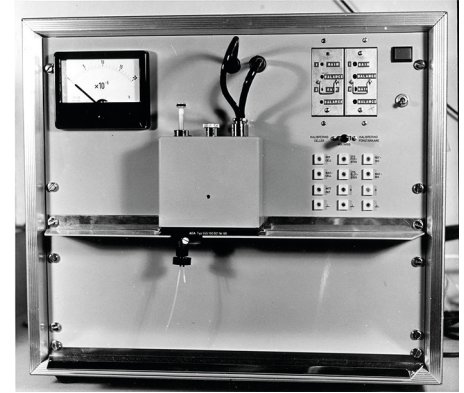


Fig. 10 Satellite station

a corrosion safe material and could be enclosed in the central unit where there was room for four such cubes. The incubation temperature could be set up to 110 degrees Celsius. One advantage of the automated laboratory was that it could connect to other activities within or outside the laboratory through other satellite stations. This satellite (Fig. 10) could even be a station for a completely different measuring instrument, directly attached to the AutoChemist computer. It could provide assistance in analytic measurements, corrections, and controls, as well as use the same requisition and reporting system of automatic analyses. As a result, hospital wards were in a way also in- and output satellite stations.

Computer, Software, Registration, and Printout

In the project at the Hospital for Infectious Diseases, a more sophisticated program than the already existing MIACH 3 was developed for the AutoChemist [26]. At the hospital, the analyzer was supported by a PDP-8 computer and an ASR Teletype Writer teleprinter. In 1975, an upgrade of the software was released, the MIACH 4 with a Quality Control Program, which soon after became the MIACH 5 [26] (See Fig. 11).

Gradually MIACH 4 became the skeleton of a further development whereby the AutoChemist was incorporated in an entire computer system for clinical laboratories

and the new PDP-12 computer from Digital Equipment [26]. The resulting new system, called the Clinical Laboratory System (CLACH), made the AutoChemist adaptable to any laboratory system. It became a flexible, independent, and easily modifiable system that could be extended to 8K cores. As the software was written in sections, it provided the possibility for CLACH to be

used with two computers to meet the high demand for reliability in a real-time system.

The AutoChemist was preliminary designed for photometric determination and registration of the analytic results. The measurement data from each test sample were converted to digital values and stored in the computer. When all the measurements of the patient had been made, the test results were

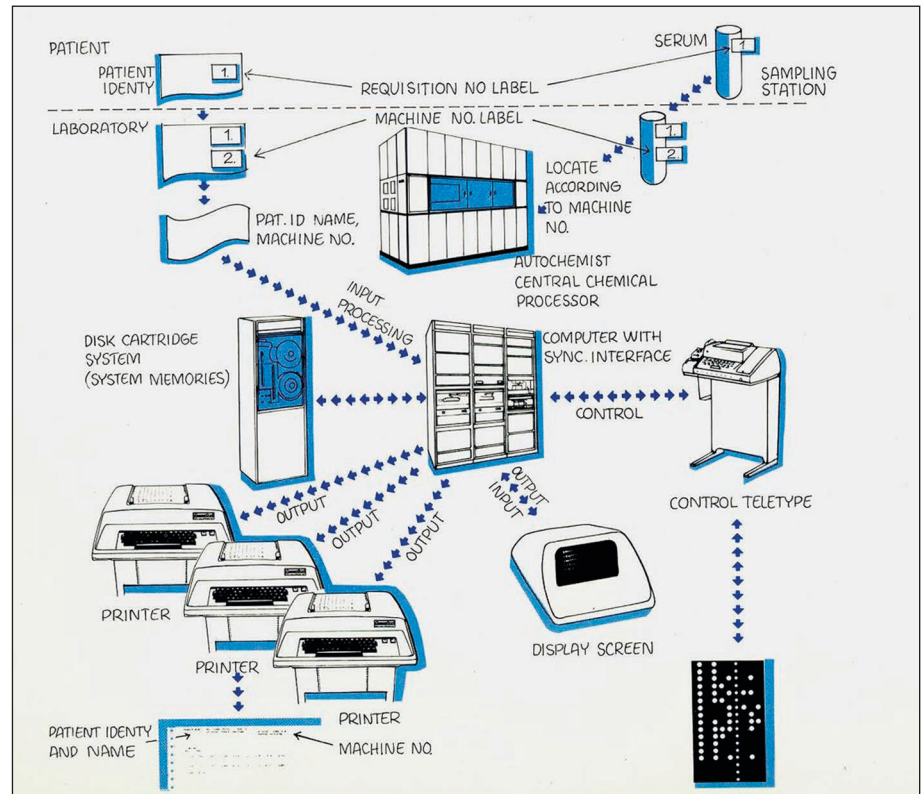


Fig. 11 Example of simultaneous time-sharing operations with the MIACH 4 programme.

printed out, collected, checked and punched to be stored for further data analyses.

The demands on the computer system were steadily increasing [26]. It was necessary to complete and introduce age/gender information to analytical results, printed in different columns for normal, slightly or strongly deferring results. Automatic corrections of all analyses and comments on the results, according to generally accepted guidelines, were also introduced.

Industrial Reagent Manufacturing

This multi-channel analyzer used reagents in volumes that were not seen before. In the early 1960s, it was common practice for laboratories to produce their own reagents in volumes of a few litres (L), but negotiations with chemical manufacturers resulted in the industrial production of reagents on a larger scale providing easy transportable containers for up to a-month storage. A 25L-container, easy to transport and handle, became a standard.

Analyses Programmes

The possibility to analyse different materials simultaneously was very important. The AutoChemist could for instance analyse blood serum on the outer belt and urine on the inner belt. One could thus chose an analytic combination representing a programme for serum involving more than 20 different types of analyses as well as a programme for urine. This then fulfilled the requirements for a variety of medical procedures including hospital analyses and health screening [14, 15, 32, 36]. The result was the introduction of "Chemical Health Screening". Chemical analyses of blood and urine were conducted to search for signs of illness (pathological changes). These screening tests could be performed as part of health check-ups, which could also include other medical procedures such as X-rays, or as part of a screening procedure for healthy individuals to identify those, who may need treatment [37].

Chemical Health Screening for the asymptomatic population thus provides many advantages:

<u>CAPACITY OF ANALYTICAL ROBOTS</u>			
VÄRMLAND PROJECT APPARATUS		AUTOCHEMIST	
NUMBER OF SAMPLES	NUMBER OF ANALYSES (12 CHANNELS)	NUMBER OF SAMPLES	NUMBER OF ANALYSES (40 CHANNELS)
40 per hour	480 per hour	150 per hour	6,000 per hour
700 per 24 hrs	8,400 per 24 hrs	2,500 per 24 hrs	100,000 per 24 hrs

Fig. 12 AutoChemist capacity compared with the Värmland equipment (1962): a tenfold increase

- Changes in blood usually appear before clinical symptoms arise
- Many clinical symptoms can often easily be explained by metabolic disturbances, which can be identified in the blood
- Blood serum is easy to take, also in primitive situations and on a large scale
- Blood serum can be long lasting and transported long distance for analysis
- Blood serum can be analysed on a large scale by robot analyzers
- A large number of analyses on each sample increases the medical value
- Analytical results can be processed by a computer or are readable through inexpensive mechanical methods

Analytical Capacity

The maximal test capacity in the first basic version of the AutoChemist was 135 samples per hour for each belt. This corresponded to an analytical capacity of 24 channels of at least 3,000 analyses per hour. An adequate margin for standard tests, calibration, emergency tests was included and the amount of channels was increased by driving two belts and/or using additive equipment such as mini-cubes, flame photometers, or fluorimeters. This doubled the analysing capacity to 6,000 analyses per hour, which was ten times more than the Värmland project implemented only a few years earlier (Fig. 12). Thus, a full eight-hour shift with 24 channels

could provide a production of seven million analyses per year. Several customers soon operated the AutoChemist in multi-shifts.

4 Applications

The AutoChemists were used in a variety of laboratories varying from health screening centres such as BUPA in London [38-41] and Kaiser Permanente in San Francisco, to university hospitals such as Odense in Denmark [42] and Toulouse [43] and Nancy in France, as well as regional hospitals in Sweden and Italy and commercial laboratories in Sweden, the US [44-46], and Japan [47-48].

The first AutoChemist for the US was delivered to the Kaiser Foundation/Multi-Phasic Clinic, Oakland, California, in December 1967 and attracted worldwide interest.

The second installation of three units started some months later at the United Medical Laboratories (UML) in Portland, Oregon [44-45]. Another unit was later installed with all four units running in two shifts. The UML Lab News claimed in March 1969 [44] that they were the world's largest and most automated laboratory. After more than two and a half years of research, the scientific staff of UML found in Sweden a revolutionary computer-controlled 30-channel mass testing system. UML's Operations Vice-President defines it as "An automatic analytical device designed with unusual flexibility for large

scale processing of discrete or completely chemically isolated samples – an analyzer which is one of the most precise pieces of automated equipment ever made, having a built-in monitoring system which practically eliminates the possibility of error”[44].

The next two units were installed in 1970 at the Metropolitan Laboratory Inc. (MetPath), New Jersey. MetPath called their AutoChemist-panel “Chem-Screen” which involved about 26 tests. In 1975, they performed close to 1.6 million screens with about 40 million analyses or > 100,000 per day. MetPath continued to expand and in 1978 they opened a large new laboratory in nearby Teterboro [46]. MetPath had ten AutoChemists, which later even increased to 11. Their Annual report for 1980 stated: “The capacity is now 12,000 Chem-Screen” or around 300,000 tests per day which means above 100 million tests per year. “MetPath is the largest clinical laboratory in the world”.

Japan was the first non-Swedish country showing an interest for the AutoChemist, as soon as in 1965. Japan Medical Laboratories (JML) ordered the first AutoChemist in the early 1970s. The first unit was installed in Osaka, and later three more at JML, two in Kyushu and one in South-Osaka. The head of the Osaka laboratory, Dr Masao Wakabayashi, was not only interested in test results but also in the technical solutions. The AutoChemist concept [47-48] was well-known in Japan with more than 35 published articles (1977).

Conclusions

The vision and the ideas of the Jungner brothers from the early 1960s to construct a unit both for mass analyses /health screening/ and batteries of analyses in hospitals were actively debated in Sweden by persistent detractors and keen supporters.

The idea has shown to be of high public health importance, but original units were not of acceptable size for customers. This work resulted in a smaller and lighter version, the AutoChemist-PRISMA® (PROGRAMMABLE INDIVIDUALLY SELECTIVE MODULAR ANALYZER) [49-50] and as of 1976 it became a successor for many AutoChemist customers

[34]. Companies such as MetPath bought as many as fifteen of these.

In summary, during the short time in which the AutoChemist was developed and operated in numerous locations around the world, it had a significant impact on the nature and operation of automated equipment in clinical laboratories. The demand for robust components capable of continuous operations for days, based on bulk reagent preparation and delivery, with innovative features of on-line monitoring and quality control, established new standards of operation for clinical laboratories and industry to meet. Overall, 31 AutoChemists and 44 AutoChemist PRISMA with one to three modules were sold worldwide.



Gunnar Jungner (1914-1982)

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