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On-line acquisition of the output of AutoAnalyzers

P. D. GRIFFITHS AND N. W. CARTER

From the Department of Clinical Chemistry, University of Dundee, The Royal Infirmary, Dundee

SYNOPSIS A computer-based system of on-line acquisition of the output from AutoAnalyzers is described and discussed. Early experience suggests that many advantages accrue from such a system.

The rapidly rising work load familiar to all pathologists has been felt particularly in the chemical pathology and cytology services (Association of Clinical Pathologists Working Party on Data Processing, 1968). In the larger chemical pathology laboratories much of the increased work load has been absorbed by the introduction of AutoAnalyzers; in this laboratory about 70% of all tests are carried out in this way. Although this has ameliorated the situation to some extent, there are still two major problems outstanding. The first is the handling of the vast amount of data emanating from such laboratories and the second is the wastage of skilled technicians' time involved in reading AutoAnalyzer charts. The advent of the computer offers an opportunity to overcome both.

One part of a computer experiment currently being pursued by our department is the use of a small digital computer and data acquisition unit to collect and process the output of AutoAnalyzers. The use of a computer for this purpose alone, of course, would be uneconomic, but the introduction of a computer into the laboratory provides the potential for its application to many other tasks (Wootton, 1968). The problem of reading charts has been tackled in various ways (*eg*, Flynn, Piper, and Roberts, 1966; Blaivas and Mencz, 1967) but is was thought that the recording of some of our experiences with the system to be discussed here would be of interest to other workers in the field.

EQUIPMENT ('HARDWARE')

The hardware comprises an Elliott 903C computer (8K store, paper tape reader and punch and two Teletypes), together with a data acquisition unit produced by Elliott-Automation, which includes facilities for analogue to digital conversion (Fig. 1).

The signals from the AutoAnalyzer colorimeters and flame photometer are read by tapping voltages arising from the photocells before their transmission to the recorder amplifiers, routing part of the signal via one of three small bench consoles, the remainder proceeding to the recorders to retain an important visual monitor.

Each console has facilities for tapping a maximum of eight AutoAnalyzer channels and is connected to the data acquisition unit in the computer room by overhead cables. The measuring and reference cell voltages are then amplified and applied through a logic switchboard to a single-channel analogue-to-digital converter, the output of which is acceptable by the computer.

In the data acquisition unit are provided not only the switchboard and digital converters but also facilities for two-way communication with the consoles. The channels governed by each console are assigned to two groups, the number in each group being fixed by the user, *eg*, three and five, or four and four, etc, each group corresponding to one sampler. There is a program-controlled fault lamp and a program-readable function switch for each group.

There is also a timer which is designed to provide an interrupt stimulus to the computer processor at two-second intervals; this is used to initiate a section of program to take one reading from each operative channel by forming a ratio of the measuring and reference cell voltages. Provision of two standard voltages derived within the data acquisition unit read at the beginning of each scan permits a check of the function of the analogue to digital converter.

This hardware, therefore, apart from accepting output from AutoAnalyzers, is also suitable for attachment to other equipment such as recording spectrophotometers or patient monitoring apparatus.

METHODS ('SOFTWARE')

A flow diagram of the overall procedure is shown in Figure 2.

COMPUTER 'CHART READING' The operations between and including reading the numerical input each two seconds, and the punching of results as concentrations on paper tape, are carried out by the computer under the control of a program produced for the purpose in this department.

This program not only detects the peaks, corrects them for drift, and calibrates them against peaks produced by

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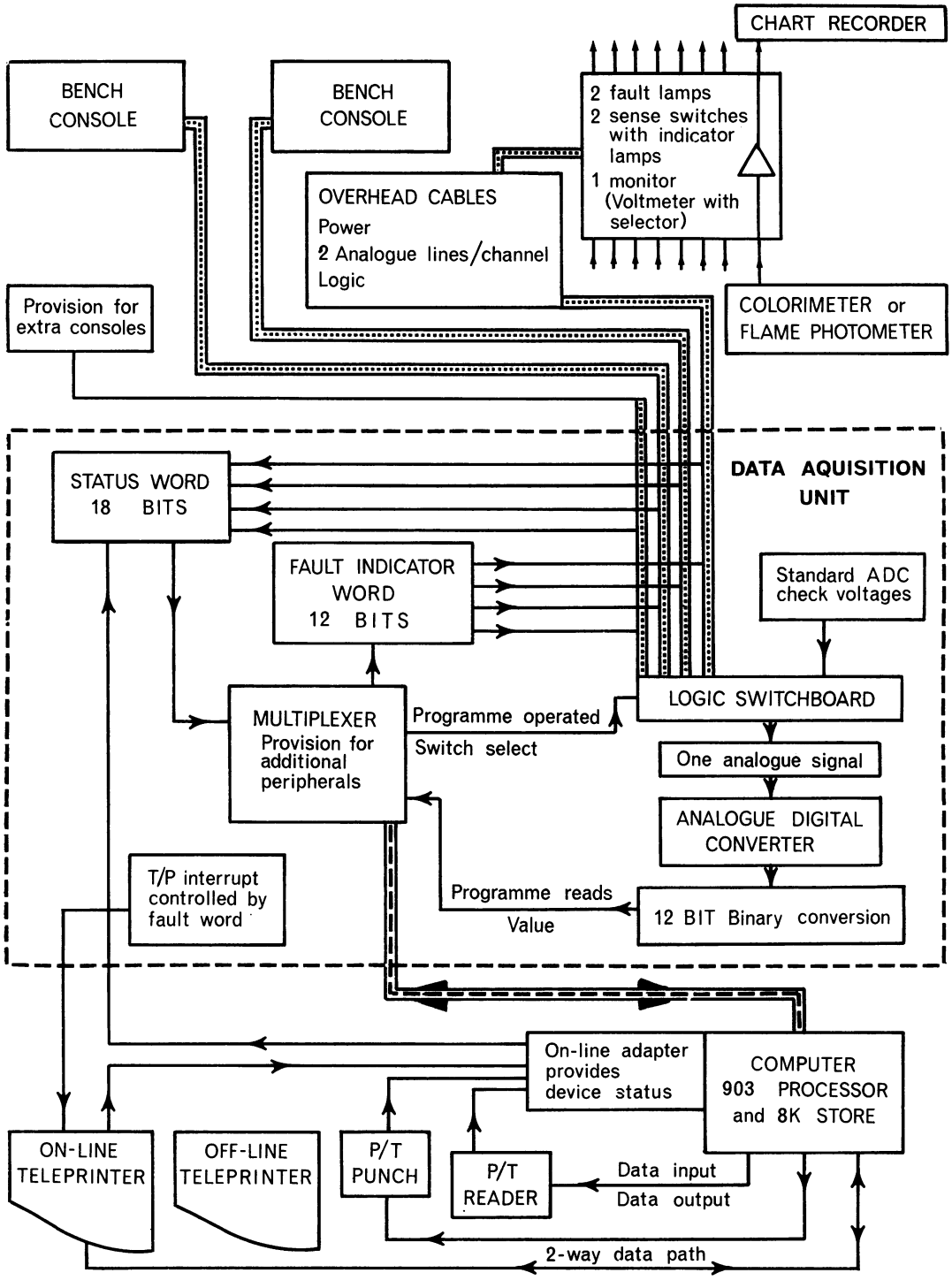

FIG. 1. *Block diagram of hardware configuration.*

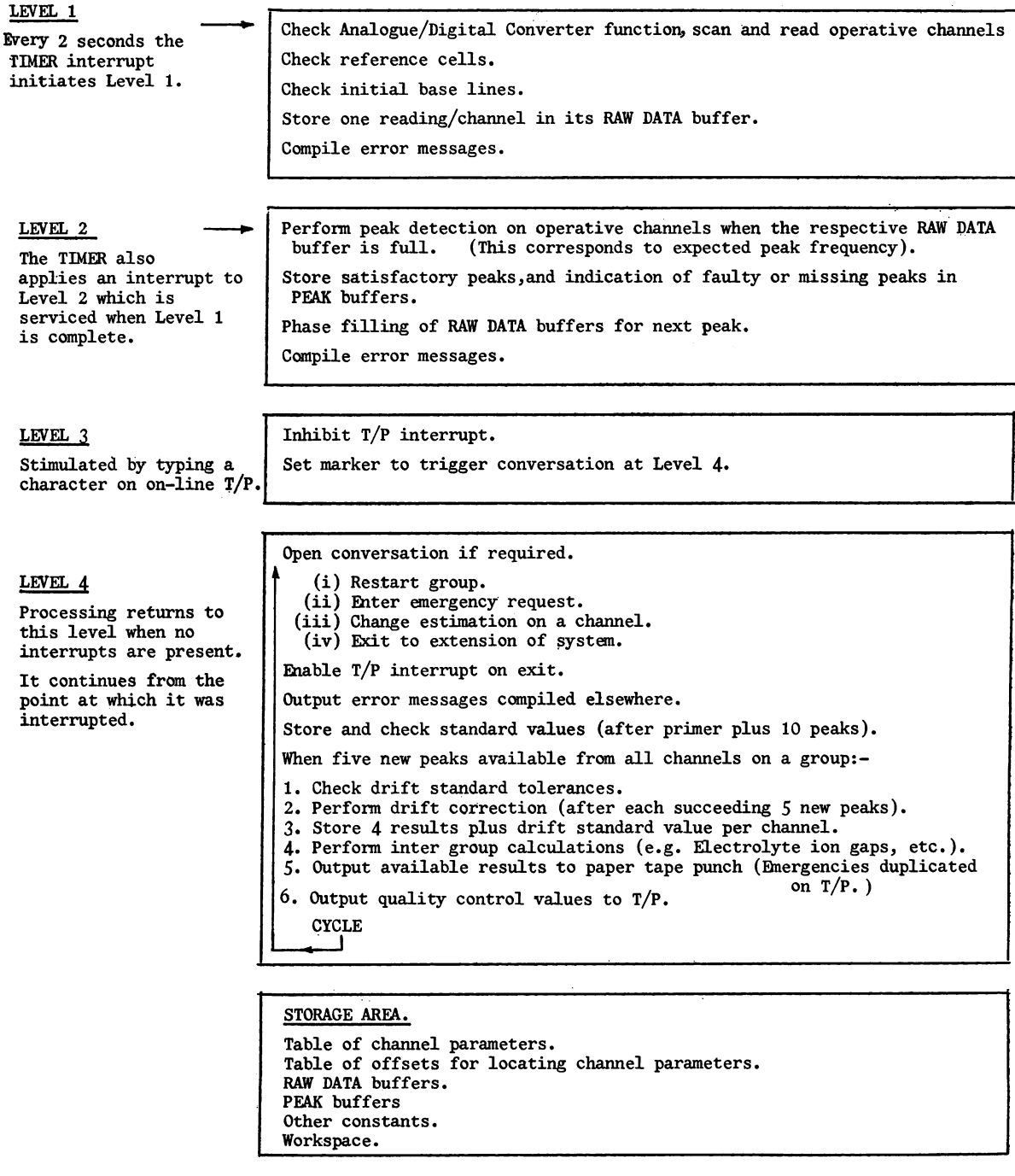

FIG. 2. *Schematic diagram of the distribution of functions to the respective priority levels for on-line AutoAnalyzer reading and interpretation. (It consumes approximately 3,500 words for 12 channels; additional channels approximately 90 words each.)*

standards, but also provides an immediate monitor by means of error messages. The program is divided into four sections.

The computer has the capacity to run these four sections under a priority interrupt system such that the voltage reading on level 1 and peak detection on level 2, which are initiated by the two-second timer interrupt, are performed when stimulated, whereas the calculations and the putting out of results and error messages assigned to level 4, proceed in the intervening periods. However, it should be pointed out that the task of chart analysis requires so little processor time that most of its time is available for the work on level 4.

Though essentially similar, each of the channels has certain parameters, *eg*, sampling rate, by which it differs from the others. The program is in the form of a generalized routine which is applied to each channel in turn invoking the respective channel parameters.

PEAK DETECTION The sampling rate indicates approximately the number of readings taken at two-second intervals, expected to cover one peak. When this number of readings has been accumulated in a block of locations in the computer store, the highest value is found and a check made that it lies within preset limits designating the centre of the 'block'. If the highest value falls outside these limits, the peak is deemed to be 'skew' and a message to this effect is output on the Teletype which is 'on line' to the processor.

The program also tests the continuity of a fixed number of rising and falling readings about this maximum. A 'kink' message is output if significant deviations are found from a smooth rise and fall.

A final check is made on the range of readings taken in order to eliminate the possibility of these conditions being satisfied by a shallow undulation such as that occurring when the unwanted CO_2 channel is being read by the computer when a urine is run for estimates of the other components of a five-channel 'electrolyte' configuration employing one sampler, *ie*, one console group.

A peak having been found and verified, the next block is examined similarly, the program characteristics being such that the peak 'centre' will be required to fall within limits appropriate to the rate of sampling of the group concerned. Thus, peak detection is kept in phase with the sampling rate.

When searching for the first peak of a run the above technique is modified to make quarter block shifts, until conditions for a peak are satisfied. The peak is then checked against a preset maximum value above the baseline voltage ratio. For this purpose, a priming standard of the highest concentration which will not cause carry over into the following peak (the first calibration standard) is employed. For most channels where increasing concentration of the measured constituent produces a reduction in percentage transmission, 'troughs' rather than peaks are produced. To allow for this, the measuring to reference cell voltage ratio is subtracted from unity and then treated as for peaks. Thus, a further variable has to be incorporated into the program.

THE STANDARD CURVE In the interests of economy of program and hence computer storage space, uniform treatment of all channels is desirable and the program has been written on this basis. The first 10 results, following the priming standard, are interpreted as calibrating standards, and every fifth result thereafter as a drift standard, and sampler plates have to be loaded accordingly. Concentrations of the standards, of course, for each channel have to be incorporated into the program.

Provision is made to allow a series of standards to be loaded in either a rising or falling sequence, and a check is incorporated to ensure that the corresponding peaks follow the correct sequence. Any further computer check upon the validity of the standard curve is difficult, unless the chemical method used is one in which the output is linear (or readily converted to this form). Other curves require mathematical analysis, introducing problems beyond the scope of this paper. Attempts to define the peak voltage ratio for individual standards have not proved satisfactory to date as analytical and electrical conditions are not sufficiently constant from day to day.

For the time being, therefore, though conscious of this deficiency, reliance is placed partly on a visual check by the technician of the recorder chart (and the computer is programmed to remind him to do this by means of an instruction appearing on the on-line Teletype) and partly on the result of control sera placed at irregular intervals in a run; these results are printed out on the on-line Teletype as soon as they become available.

DRIFT CORRECTION The 'drift' standards correspond to one of the calibration standards, so that a check can be made upon both drift from the corresponding initial calibrating standard and also between successive drift standards.

When a drift standard fails to fall within a preset tolerance, an error message is produced. Providing the drift standards fall within the approriate tolerance, the computer calculates a correction factor which is applied to the peak voltage ratios produced by the samples between them. Obviously, a rejected drift standard is not used to 'correct' a result, and the technician will investigate the cause of this rejection, and if necessary halt the run and restart when the cause of the fault has been corrected.

CALCULATION OF RESULTS When the corrected results are available from all channels of a group any necessary calculations are performed, *eg*, estimations of alkaline phosphatase where both test and blank channels are run, or cation-anion gaps for electrolyte checks. This task completed, a paper tape, containing the group and cup identification and concentration of sample in the latter, is produced by the 'on-line' punch. If desired, this tape can then be fed into an 'off-line' teleprinter to produce a listing of the results (Fig. 3).

ERROR MESSAGES In order that the output of error messages to the relatively slow teleprinter (10 characters/second) shall not hinder the taking of readings, the messages are coded, stored, then decoded and output when time becomes available on level 4. The actual delay resulting from the production of an error message is only a matter of milliseconds. In the case of major faults

GROUP	CUP NO.	RESULTS					GAPS
ELS	31	141	4.7	111.4	19.6	59.2	15
ELS	32	130	4.5	97.1	21.8	29.9	16
ELS	33	138	5.2	109.7	17.4	120.7	16
ELS	34	136	3.4	98.6	27.1	27.6	14
ELS	35	133	4.3	96.5	26.7	70.8	14
GLU	41	235.2					
GLU	42	230.6					
GLU	43	151.7					
GLU	44	165.6					
GLU	45	157.2					
CAP	26	4.4	2.1				
CAP	27	4.8	1.7				
CAP	28	4.2	1.9				
CAP	29	6.9	2.6				
CAP	30	2.9	3.0				
CTN	16	1.3					
CTN	17	4.0					
CTN	18	5.1					
CTN	19	4.4					
CTN	20	2.9					
PRO	11	6.4					
PRO	12	8.2					
PRO	13	6.8					
PRO	14	6.6					
PRO	15	7.2					
ELS	36	143	4.3	111.2	21.9	36.1	15
ELS	37	131	3.1	89.9	27.0	131.9	17
ELS	38	135	4.6	104.9	18.8	40.8	16
ELS	39	142	4.8	101.6	26.6	125.1	18
ELS	40	131	4.3	96.2	26.2	72.5	13

FIG. 3. *Typical list of results. Group codes:* ELS *Sodium, potassium, chloride, bicarbonate, urea;* GLU *Glucose;* CAP *Calcium, phosphate;* CTN *Creatinine;* PRO *Total protein. Cup numbers 15, 20, and multiples of 5 are drift standards.*

eg, excessive variation of the reference voltage, the program also lights the corresponding group fault lamp on the bench console and the data acquisition unit.

OPERATING PROCEDURE To facilitate operation it has been arranged that once the daily program has been loaded, control over the computer is by means of the 'on-line' teleprinter, *ie*, a 'conversational' mode is adopted.

Depressing any teleprinter key produces an interrupt stimulus on level 3 where note is taken that intervention has been made. On returning to level 4, the program in that level causes a conversation to be opened with the operator. The required control effect is achieved by use of a question-answer routine where at each stage the computer poses a question and provides a selection of answers from which the operator must choose the appropriate one.

RESTARTS In the event of, say, an AutoAnalyzer failure or blockage of a flow-line when it becomes necessary for a technician to restart a sampler (and hence all channels in that group), it is necessary either to re-run the standard curve or resume at a drift standard. This has to be intimated to the computer by entering into 'conversation' with it, selecting the group restart option and indicating the group concerned and the cup number of the first peak which will appear once the baseline conditions have been re-established.

CHANGE OF ASSAY Although it is preferable for a given channel always to be concerned with a particular assay, facilities are available to permit a change of assay on a given AutoAnalyzer channel. This is provided for in the program in such a way that the computer can be informed by means of 'entering into conversation' with it.

URGENT SPECIMENS If an urgently required assay is submitted after a run has commenced, the late specimen can be substituted for a specimen already in a cup on the sampler plate, the displaced specimen being added to the end of the run. The 'conversation' procedure is adopted first to inform the computer of the substitution, and secondly, to instruct it to print out the results as soon as they become available on the 'on-line' teleprinter, allowing a preliminary report to be sent to the clinician. The results also appear on the output of the paper tape punch to be processed with the batch in due course.

DISCUSSION

The introduction of a computer-controlled data acquisition unit for the 'on-line' acquisition of AutoAnalyzer outputs has brought with it some benefits to the laboratory, but has also produced a number of problems which have forced a re-examination of, and in some instances changes in, previous laboratory practice.

The most obvious benefit is the saving of skilled technicians' time by relieving them of the need to read charts. This is particularly important where, in heavily loaded laboratories, a number of assays may be grouped together, *eg*, sodium, potassium, chloride, bicarbonate, and urea, so that five charts will have to be read in rapid succession. Apart from the time involved, a combination of fatigue and hurry, particularly towards the end of the day, tends to produce errors. The danger can of course be reduced by double-reading charts but this is even more costly in skilled time. In our experience, despite the presence of drift standards, control sera, and double reading, errors still occur (usually transcription errors). When the computer system was initially under test, whenever there were disagreements between results of charts read by technicians and computer results, on re-checking the errors were always those of technicians.

It has been customary for correction to be made for drift and this has not always proved to be as objective in practice as it should be, as subject bias is inevitably introduced. This is again overcome by the use of computer correction. The validity of the procedure for drift correction in any case may be questioned, and testing the validity of this practice will become much easier using the computer facilities.

An unlooked-for benefit resulted from our attempts to lay down standard conditions and tolerances for each channel. This led us to re-examine each assay procedure in detail in an endeavour to improve the chemical techniques employed and thus produce a more consistent output. This re-appraisal brought to light a number of unofficial modifications to methods, some of which proved undesirable while others were helpful. As a result, it has become necessary to lay down firm instructions for the operation of each AutoAnalyzer channel and to adopt a much more rigid system of supervision of operating staff to ensure that the instructions are faithfully adhered to.

The need for continuous surveillance of AutoAnalyzers has been emphasized by the instruction to the technician to check the calibration curve as soon as it has been produced, the flow of error messages, and printing out of results for control sera. Thus there is a built-in system of early-warning devices to indicate malfunction of an AutoAnalyzer. This prevents the situation which sometimes arose in the past of a complete batch of assays having to be repeated because malfunction only became apparent when the chart was read at the end of a run. Admittedly, a good technician should have noticed malfunction during a run, but with the current shortage of trained staff and rapid turn-over of student technicians, the required standard of supervision of AutoAnalyzers is not always achieved.

It will be apparent that the availability of the computer provides an easy means of statistical analysis

of the quality of the work produced. While there has been no addition to existing methods of quality control, the tedium of the maintenance and processing of quality control data is markedly reduced and has released additional time of skilled personnel for other purposes.

The chief problem that has arisen is a rigidity of operation that has been imposed on the laboratory. The setting up of a sampler plate now has to conform to a pattern dictated by the computer—indeed the order of loading of samples will also be computer-controlled through the production of work sheets. It follows that, during the induction period of computer operation, many changes had to be made, and in a laboratory working to capacity, introducing changes is not always popular. Much of the uniformity between channels was introduced in order to save space in the limited computer store, and a larger, but more expensive, computer configuration would of course permit a greater degree of flexibility. Once the modified running conditions had been implemented and the staff adjusted to them, the rigidity has been advantageous, *eg*, a change of operator from one channel to another is now simpler.

A corollary to the adjustment of laboratory routine to meet computer requirements is an explanation to the technical staff of the reasons for it. This has resulted inevitably in having to instruct them in computers and their appreciation, which is to their ultimate advantage. They also had to learn the simple procedure of 'conversing' with the computer, but most of them are enjoying the process.

One minor problem that arose was of a more technical nature, and this was the handling of the output from the sodium line of the electrolyte group. On this channel, the working range occurs only in the top two-fifths of full-scale output. In the design of the flame unit, the earth from the output of the sodium side is floated, thereby increasing the measuring/reference cell voltage ratio. Only a fixed fraction of the output is then transmitted to the recorder, but this is amplified two-and-a-half times to produce an adequate graph. When this output is connected to the analogue-digital converter this offset effect was lost as the unit re-earthed the floating earth rail. To overcome this, the offset was bypassed within the flame unit and generated in the link between analogue to digital converter and recorder by floating the earth at that point (the level being variable to permit of a hitherto unavailable flexibility in its setting). As a result, the computer is presented with the full scale, but the visual record is produced as before; the slight loss in accuracy resulting from this manoeuvre is compensated for by the greater accuracy of the computer readings and calculations.

A number of questions arise about the future of the approach to handling clinical chemical data outlined in this paper. Clearly, this is a very expensive way of reading AutoAnalyzer charts and would be difficult to justify if this were the only use to which the computer is to be put. If, however, the whole of the data processing from receipt of a request, production of work sheets, assembling and printing results to record filing is envisaged, then the addition of the data acquisition unit may be reasonable. Against this one must consider the advent of multichannel machines, which may produce either records suitable for direct transmission to the clinician or computer-orientated listings. Both types of machine currently being produced and developed rely on the availability of a linear calibration and therefore have not the flexibility available in the Elliott data acquisition unit which can be applied to other types of laboratory instrumentation.

It is premature at this stage to draw firm conclusions. What has been shown is the feasibility of utilizing equipment of this type, but longer experience is necessary before the overall reliability can be assessed. There is still too little practical experience of the use of computers in pathological laboratories in any case, and the problems which would arise from a computer breaking down in this context are daunting.

We are pleased to acknowledge the ready cooperation of the technical staff of this department in this project. The work was supported by grants from the Nuffield Provincial Hospitals Trust and the Court of the University (then St Andrews).

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ADDENDUM

In order to achieve adequate scale expansion for sodium estimations, a floating earth for the output from the sodium channel has been incorporated in the Technicon flame photometer unit. When this device is connected to the analogue digital converter of the Elliott automation data acquisition system, the floating earth is earthed in a normal fashion and the scale expansion effect is lost.

This problem can be overcome by a small modification. The offset network provided on the sodium channel in the flame unit is by-passed by turning the

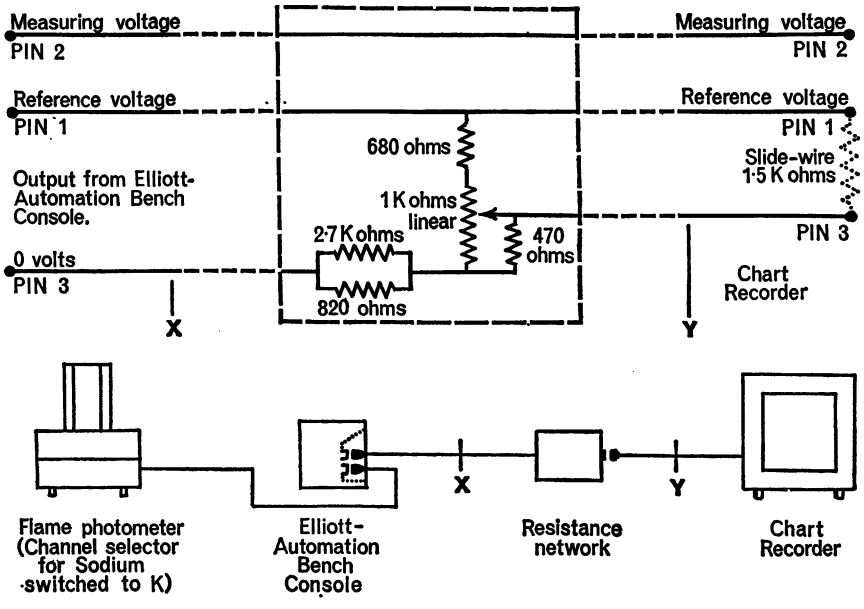

FIG. 4. *Diagram of the resistance network.*

appropriate selection switch to potassium. The resistance network, details of which are given in the diagram (Fig. 4), is inserted between the Elliott bench console and the chart recorder. This restores the offset to the sodium channel to provide the accustomed chart record. The component values chosen ensure that 1·5 K ohms is across the reference/0 volt lines in place of the recorder slide-wire, adjustment being provided by the 1 K linear potentiometer. In this way, it is possible to continue to operate the flame photometer without detriment to the normal working conditions.

The computer will continue to view the full range of readings unaffected by this offset.