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Analytical Survey

The Microcomputer Revolution

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Abstract: The role of microcomputers in the analytical laboratory is growing rapidly as applications software becomes more generally available. In this survey, the impact of microcomputers on the practice of analysis in pharmaceutical and biomedical areas is examined in the context of available hardware. The advent of 16-bit microcomputers and the implications of computer access to networked data bases are also discussed.

Keywords: *Microcomputer; application software; graphics; multicomponent analysis; high-performance liquid chromatography.*

Introduction

Readers of this new Journal, no less than other scientists, are likely to feel the impact of the recent revolutionary development of the small computer industry. Many scientists have, of course, utilized large computer centres in some aspect of their work, and laboratory minicomputers are commonly incorporated in large and expensive instruments and experiments. But during the last decade, advances in microelectronics have led to the development of a new breed of small, low-cost, yet remarkably capable microcomputers. This has led to a dramatic increase in the number of computer owners and users, drawing in many who had little or no previous computer experience, perhaps because they could not afford the hardware, were intimidated by it, or had no real use for computers. These new users demanded systems which were more 'user-friendly', to which the manufacturers and software authors have responded by creating hardware and software that is much easier to use. Moreover, the new users have brought with them a fresh influx of application ideas, so that we are now seeing many new and imaginative uses of small computers.

Chemists and other scientists have many uses for computers: word processing, information management, education, data acquisition, signal processing, experiment control and data reduction. Indeed, the management of this new Journal is based on specially-designed programs run on a microcomputer. This article aims to present an overview of the present situation and to direct the reader to some useful resources.

Hardware

The minimum useable configuration of a small computer system consists of a central processing unit (CPU) with read–write memory (often called RAM, for random access memory), a 'terminal' consisting of a keyboard and a cathode ray tube (CRT) screen, together with some sort of mass storage device. The most popular mass storage device is the floppy disk, either in the 5.25 or 8 inch size. Although cassette tape is less costly, it is slower and often less reliable. The hard disk is much faster than floppy disk and has much greater storage capacity. Even the smallest hard disk units are rather more expensive than floppy disks, but prices can be expected to continue to fall.

To this basic configuration numerous peripheral units for additional applications can be added. The more popular microcomputers offer all the following peripherals, often a selection from several vendors: graphic display on the terminal CRT screen; printers; plotters; modem (for telephone communication); serial and parallel digital input/output (I/O); analog I/O (analog-to-digital converter, multiplexer, instrumentation amplifiers); real-time clock–calendar; graphics tablet; light pen; bar-code reader; speech I/O; hardware math cards; image input (via TV camera interface); power control.

An important consideration in selecting a system is that it should be capable of expansion by the addition of as many such peripheral devices as possible. All these devices must be properly interfaced to the computer, either by means of an interface card that plugs into the system bus (backplane) or by means of well-defined 'universal' interface protocols (such as the RS-232C serial or the IEEE-488 Hewlett–Packard instrumentation bus). In the former case the interface is particular to the system bus structure and cannot be expected to work with other bus systems. For this reason there is a distinct advantage in selecting either a system with the 'standard' S-100 bus, which is used by several computer manufacturers, or one of the very popular microcomputers such as the Apple, for which many plug-in compatible peripherals are available from a large number of vendors. In fact, all the above-mentioned devices are now available both for S-100 computers and for the Apple, but many are not yet available for other microcomputers, including several of the newest models.

Software

Ultimately the investment in software may far exceed that in hardware, especially considering the high cost of writing custom software. Generally, there are two categories of software to consider; software bought commercially and custom software, written or commissioned by the user. By and large, if commercial software will do the job, it should be used in preference to custom software, which is much more expensive. The amount and quality of commercial software varies greatly from one system to another and is not necessarily correlated to the power of the hardware itself. In fact, the most extensive software is generally available for systems which are no longer state-of-the-art in terms of hardware such as, for example, those based on the popular 8-bit microprocessors Z-80 and 6502. The new generation of systems based on 16-bit microprocessors is currently somewhat limited by the range of commercial application software available, but this imbalance will soon be redressed.

The major types of commercially available application programs which the scientific user may wish to have available include: a word processor (possibly including form-letter and mailing list capabilities); spread-sheet program for manipulating large arrays of numeric data; alternative or special-purpose computer languages; educational and tutorial programs; statistics (including curve fitting); communication package (for use with modem); data acquisition/manipulation (for use with analog-to-digital converter).

Although computer graphics are highly effective in many applications, they can be very challenging to program. Fortunately several types of graphic utilities now available are of considerable use for graphical presentation of data; of these, some are more commercially oriented (bar charts, pie charts, etc.), while others are more oriented to scientific work (logarithmic coordinates, error bars, etc.). These graphics utilities are available both as stand-alone programs (usually menu driven) and as utilities to be appended to or incorporated into the user's own custom program to facilitate the generation of graphics.

An important consideration in selecting commercial software is data compatibility. Very often it is desired to use the output of one program as the input of another. This can be conventionally arranged if the first program writes its output data to disk (or other mass storage device), while the second program reads its input data from disk. The trouble is that commercial software packages are sometimes written 'in a vacuum', using their own non-standard and often undocumented file structures which cannot be read by other programs. It is better to select software that reads and writes standard files which run under the standard operating system of the computer in question. For example, many programs use standard disk text files (strings of alphanumeric characters) for data input and output. For this reason it is extremely convenient to use a word processor which also uses standard text files. This would allow the very powerful text-editing capabilities of the word processor to be used to edit assembler, BASIC or other language source files, or numerical data files. Another example relates to graphic utilities which read and write the graphics screen memory to disk as a binary image. This would allow a graphics image generated by one program to be input into and further manipulated by another.

In addition to commercially available software, many users will want to develop custom software for particular special applications. To this end, there are a number of program development tools available, including quite a few computer languages. In addition to the BASIC interpreter usually provided, there are BASIC compilers (to convert BASIC programs into faster-running machine code), assembler-editors, FORTRAN, FORTH (a language optimized for control and data acquisition applications), PASCAL (a highly structured language), plus a variety of less common languages. For applications which involve primarily the preparation and maintenance of specialized data bases, there are even program-writing programs, which actually write programs based upon the user's answers to an interactive dialogue. The BASIC language is easily learned and is familiar to many scientists, but it is generally too slow for some data acquisition purposes. For this reason some vendors of analog interfaces also supply a modified BASIC or a software module which can be appended to BASIC, which effectively adds special high-speed data acquisition commands to the BASIC language.

As a practical example of what can be expected at the current state-of-the-art, it is possible now to put together a very useful system from several vendors consisting of: a popular 8-bit CPU with a 64 Kbyte RAM, a single 5.25 inch floppy disk drive, medium-resolution graphics (*ca* 200 × 300 characters), a black-and-white CRT monitor, a dot matrix printer (80 columns, upper and lower case, with capability for printing a hard copy of the graphics screen), a real-time clock, a 16-channel 12-bit analog-to-digital converter with programmable gain, and software consisting of a disk operating system, BASIC interpreter and compatible compiler, macro-assembler, PASCAL, FORTH, a word processor, data base system, spreadsheet program, a scientific plotting and curve-fitting package, graphics utilities and a data acquisition/manipulation program. A second disk drive, a modem and a graphics tablet could be added at a later date. All the components of such a system can be expected to be well documented, plug-compatible and easily assembled without a knowledge of electronics.

There is one exception to this, however, where electronics expertise may be required. In order to use the analog-to-digital converter (ADC) for data acquisition from a laboratory instrument, it will be necessary to prepare a shielded cable with suitable connectors to match the instrument output and the ADC. Moreover, if the instrument output signal voltage is too high or too low for the voltage ranges available on the ADC, it will also be necessary to construct a voltage divider or amplifier. Some instruments may require that their output signals be buffered by using a low-pass filter to prevent sampling errors. To this end, some knowledge of operational amplifiers, filters, grounding, and shielding will be very useful. Such information can be found in 'electronics for scientists' textbooks [1].

Resources

There is already an extensive popular small computer literature, including many monthly, fortnightly and weekly magazines; some of these are devoted entirely to one manufacturer's computer. A fairly comprehensive overview of available personal computers has been published [2], though it is inevitably out of date already. Critical reviews of software can also be of considerable help in sorting through the current offerings [3]. Several collections of BASIC programs for science and engineering have been published [4–7]. Some [4, 7] include useful tutorial material on the principles of numerical techniques, such as least-squares curve-fitting and the solution of simultaneous equations.

Of the material more directly related to chemical applications, the book edited by Lykos [8] presents an interesting collection of articles by chemists describing a wide range of laboratory applications. The short course on Laboratory Automation [9] developed by R. E. Dessy is excellently done. Three new journals emphasize computers and automation: *Computers and Chemistry*, the *Journal of Automatic Chemistry* and the *Journal of Clinical Laboratory Automation*. The *Journal of Chemical Education* has featured a 'Computer Series' since 1979 with several excellent reviews and overviews [10, 11]. *Analytical Chemistry* has published several A-page reviews on computers and automation [12–14] and has recently begun a 'computer column' [15].

Of course, many descriptions of computer applications can be found in the chemical research literature. However, the lag-time between equipment purchase and research publication is long, particularly in view of the rapid development of the small computer field. As a result, it is understandable that many research articles describe microcomputer equipment which is below the current state-of-the-art, such as computers built from kits, obsolete computers, or elaborate self-constructed interfaces which can now be obtained commercially.

Applications

Many of the traditional uses of small computers, such as word processing, data base management and statistical calculation, are immediately applicable to the analytical laboratory and are supported by quite a few good commercial software packages. Thus, such common activities as the storage and searching of literature references and the fitting of non-linear analytical calibration curves can be accomplished readily in most instances using available low-cost software. The recent *Analytical Chemistry* biennial review on Chemometrics [16] reveals the extent to which analytical chemists have begun to utilize computers in the optimization of measurements and the interpretation of results. As it becomes more practical to perform such operations on laboratory microcomputers, it can be expected that application in the pharmaceutical and biomedical area will increase.

Many more possibilities for applications arise when analytical instruments such as spectrophotometers and liquid chromatographs are interfaced to microcomputers for on-line data acquisition and, where appropriate, instrument control [17, 18]. This can result in much greater flexibility in designing measurement protocols for research, method development and routine quality control. Some commercial application software is available, specifically for chromatographic peak integration and automated continuous-flow colorimetry, but for the most part this type of application will require some programming effort by the user. However, useful results can be obtained with modest effort by combining and modifying BASIC programs from published collections or from other laboratories. One specific example relevant to analysis in the pharmaceutical and biomedical field is the simultaneous multicomponent quantitative analysis of a mixture of known constituents by multiwavelength uv-visible spectrophotometry. Using microcomputer-controlled instrumentation based on conventional scanning instruments or based on the linear photodiode array, it is quite convenient to acquire a large number of absorbance values at very precise wavelengths and to compute the concentration of the constituents and their standard deviations by matrix methods for which programs have been published [4]. This technique is one of the features of a commercially available, diode array multichannel spectrophotometer [17]. It is quite practical, however, to carry out a similar operation using much less expensive instrumentation interfaced to a small personal computer. The author has found, for example, that using data acquired at 90 wavelengths, the concentrations and corresponding errors could be computed for a three-component mixture in about 10 sec, with the aid of an Apple II microcomputer programmed in BASIC.

The use of microcomputers for on-line data acquisition and post-run manipulation in HPLC will continue to increase, especially for automated method development utilizing simplex procedures in the pharmaceutical and related industries [19, 20]. Furthermore, the rapid development of commercially available rapid-scanning HPLC detectors, based on the linear photodiode array, will utilize microcomputers for data acquisition, processing and presentation. The impact of this technology is already apparent in the environmental, forensic and pharmaceutical fields [17, 18, 21]. In particular, the presentation of (A, λ, t) data as three-dimensional 'spectrochromatograms' generated by microcomputer opens up new approaches for HPLC detection in pharmaceutical and bioanalytical studies [18, 22].

Future Trends

It is safe to expect that the power of small computers will continue to increase for a given cost. The 16-bit CUP's will gradually squeeze out the 8-bit systems for most applications because of their superior speed and memory capacity. Hard disk prices will drop as the quantity manufactured increases. Systems will probably become more integrated, with many features previously considered as external peripherals available as standard built-in features (modems, analog I/O and speech I/O, for example). Very low-cost portable computers will be commonplace. Eventually speech recognition will be developed to the point that it will become a viable supplement to keyboard input in the laboratory environment. One problem that confronts the new system purchaser is just how close one should get to the state-of-the-art in hardware. For example, we now have a choice of several low-cost 8-bit systems with an extremely wide range of low-cost systems and application software, whereas the newer 16-bit systems feature good systems software but are limited by the variety of application software. There is no question that the 16-bit processors are more powerful than the 8-bit. The Motorola 68000, for example, can execute floating point arithmetic routines over ten times faster than a 6502. Moreover, the 68000 can directly address far more memory and its instruction set is much more sophisticated and powerful. Nevertheless, it must be admitted that, at the time of writing, there is much less 68000 software available. A similar problem confronts the user who has made a substantial investment in time and money in one of the popular 8-bit systems and is reluctant to discard this in order to up-grade to a 16-bit system, which may not be able to run much of his present software. One solution to this problem is to buy one of the new 16-bit co-processor cards now available for some 8-bit systems. These allow the 16-bit processor to run concurrently with the system's native 8-bit processor, the latter handling input/output through the host system's bus.

Software development always seems to lag behind hardware to some extent, but it is likely that standardized software will become more readily available and more user-friendly. Powerful programming languages and development tools will increase the productivity of programmers and allow people whose primary interests and abilities are in areas outside computer science to write useful programs. Certainly this will have the effect of broadening the scope of computer applications and possibly lowering the price of software. It seems likely that the present interest in computer networks will continue, so that scientists will soon have greater access to large data bases and inter-computer communication.

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