Advancing Technology of Clinical Laboratory Practice*

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In spite of the temporary antitechnology attitude of a portion of our society, the future will be an era of automated technology. Buckminster Fuller (1) has reviewed the progress of industrial technology and points out that continuing scientific advances are inevitable and that technical applications will provide more equitable distribution of wealth, more time, more opportunity for education and intellectual pursuits. He predicts that technology will produce enough for all of mankind by efficient use of energy. He observes that the overall efficiency of the use of energy by man was 1% until the turn of the century; it has grown to 4% since then. Some modern devices and systems of energy conversion to productive work reach 10–15% and the potential of such machines as rockets is 75–80%. By 1900 the industrial revolutions of civilization had provided their benefits to approximately 1% of mankind, spreading to 5% of the world's population by 1920, 20% by 1940 and 44% by 1970. The growth curves depicting several technological indices in figure 1 provide convincing evidence of the remarkable accomplishments to be expected by extrapolation into the next several generations. The advances in communication up to the Telstars presently encircling the earth, in transportation by rocketing to the moon and in the scientific discoveries exemplified by the use of the chemical elements, illustrate the accelerated expansion of the benefits of science to man. A similar curve could be constructed for the advancement of medical science and its miraculous achievements when compared to health conditions in past centuries.

Science and technology have brought us to where we are and can be credited for all the "good" things we have. If scientific advances are not used for the benefit of mankind, the fault lies with the users, the people, not with the technology of science. Technology has brought a distribution of wealth to larger and larger numbers of the world's population in terms of food, communication, education and medicine. Today, fewer starve than ever before; the average life expectancy in developed countries has increased from 42 years to 80 years. Few in the world are ignorant of the happenings over the planet; radio and television are worldwide, and air transportation now reaches all points. Fuller reminds us that if we discarded all these advances at their present state, two-thirds of the world's population (two billion) would starve within six months, all communications would stop, people would be isolated into intolerable pockets of high density and cities would become inescapable centers of anarchy and violence. On the other hand, it is amusing to conjecture that if we discarded all the political ideologies, politicians and bureaucratic systems but retained our technological advances, the world would, in all probability, go on progressing, probably with less difficulty and turmoil. Nuclear energy was discovered by scientists, bombs were dropped by politicians. The thought occurs—is it rational to leave the decisions of the future to the politicians, or should they be left to those whose intellects, judgment and industry have bettered the physical and intellectual life of half the world beyond their fondest expectations of a short century ago? Recognition of what science has so far accomplished for man justifies the optimism that scientists will continue to mold a better life tomorrow for all the world's people.

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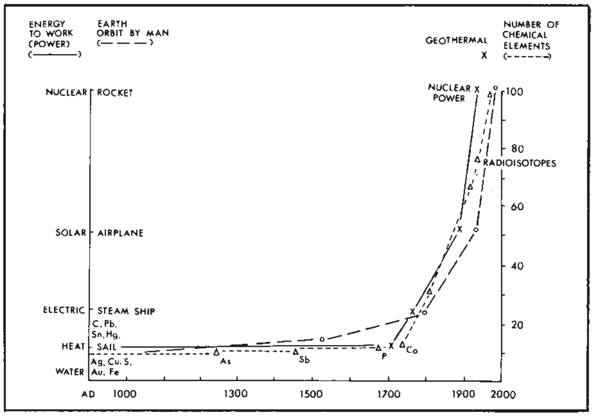

Fig. 1—Exponential growth curve of man's utilization of technology and scientific discovery.

Focusing on health and medical care, although development in medicine has necessarily lagged somewhat behind industry, there has been a parallel upswing of remarkable advances in the fields of human genetics, chemistry, physiology and mental capability. There is no question but that the sciences of physics, chemistry, physiology, morphology, psychology, logic and computer applications will continue to rapidly advance health knowledge. Automation must inevitably utilize fewer resources at a lower cost to provide more and better health and medical care to all.

The New Era of Scientific Medicine. Science is the systematic study of nature; bioscience applies scientific methods to the understanding of animate nature. Applications of scientific methods of discovery and analysis and the synthesis of knowledge concerning the nature of man have just begun. Growth ahead will be as rapid and phenomenal as advances in energy use, transportation and communication have been in the past. The computer potential in the study of man is in its initial exploratory phase, and practical applications in medicine have barely begun.

It is understandable that the laboratory, in its role of providing standardized and quantitative scientific measurements, will continue to grow as the primary source of reliable information concerning health and disease. To realize the importance of further advances, we can remind ourselves that, as with the technology of food distribution and communication in society, if we should destroy all modern applications thus far accomplished in medicine, chaos would reign. Think of the plight of today's dense population centers with no vaccines, no public health control of water, of insect disease vectors or food, no medical instruments, no drugs, no hormone or vitamin biologics, no antibiotics. The resulting disaster is unimaginable.

The laboratory of the future will probe not only deeper with newer tools of medical research, but it will apply the burgeoning new knowledge to maintain health and more effective therapy as well as to improve early diagnosis. To accomplish this at acceptable costs, however, automation, miniaturization, computerization and systemization are necessary.

Primary Laboratory Functions. The laboratory is the facility for the measurement of body functions and states of various constituents and for such activities as testing chemical reactions. Quantitative information is extracted from body fluids, products and tissues. Blood and urine contain enormous amounts of chemical and physiological information, which Dr. Irvine Page (2) compares with the use of coded computer tapes. This "coded information" must be discovered, identified and decoded. The data must be correlated and synthesized into understandable information, describing in medical terms the whole integrated organism of man during his varying reactions in health and disease. This task is only in the design stage. Our tools are still relatively crude. There are many steps in the development of this expanded role of the future laboratory. Immediate needs include:

1. New tests for functions and constituents yet undiscovered;
2. Frequently repeated sets of test measurements to reveal the kinetic nature of physiological and chemical activities and to delineate the limits of variation;
3. Improvement of precision and accuracy;
4. Limitation of blood and tissue samples to micro amounts for large batteries of analyses;
5. Miniaturization of equipment;
6. Automation for speed and elimination of error and laboratory bias (variability);
7. Computerized instant and long-term quality control;
8. Computerized data collection, correlation and reconstitution into usable physiological and biochemical information;
9. Identification of deviated test results which warn of trouble;
10. Standardization of methodology and inter-

pretation to permit comparability of data;

11. Regional health and medical data banks to prevent wasteful and costly duplications of examinations and testing and to provide lifetime health records.

The direction of development of the clinical laboratory in the future is already apparent. Mechanization and automation of the repetitive manipulations such as sample transport, pipetting, mixing, temperature control, end-point determination and reaction rate measurement are greatly improving precision and eliminating human errors. New transducers for detecting changes in constituents—their states and rates of change—are being devised and applied. Advances in gas-liquid chromatography, thermal microcalorimetry, laser beam technology, nuclear beam technology, nuclear magnetic resonance measurements, x-ray spectrography, radioimmune assay, mass spectrography and ion-electrode devices remain to be miniaturized, standardized, automated and calibrated. In one decade, the amount of blood sample required for a set of 10 or 12 analyses has been reduced from 100 to 1 ml—two orders of magnitude! Crude dual channel test instruments have advanced to 20 and 22 channels. Rates of measurements of reactions have shortened from minutes to seconds; precision has improved from 10% to less than 1% error for many tests.

Automation has amplified the productivity of the technical staff by factors of two, four and ten for different types of tests, and occasionally, by a factor of 100 for some, such as antibiotic sensitivity microtiter automation and the newer instruments for enzyme reaction rate analysis. At the laboratories of the National Institutes of Health, even the earlier phases of automation permitted doubling the test work load without increasing the technical staff.

Computational capability has advanced in two decades from the use of the mechanical desk calculator and slide rule to the programmed electronic calculator first, and more recently, the minicomputer. Five years ago, a laboratory processing a million tests per year needed a million dollar computer system. With the application of computer technology and economy, the same laboratory today, needs only ten tiny preprocessing computers, each built into a set of specific instruments, at a comparable computer capability at a cost of less than $300,000. Nowhere is economic efficiency progressing as rapidly as in computer automation technology. Five years ago, computers served laboratories as expensive data collection, storage, calculation and printing machines. Today, they are beginning to be used for their true value in high speed correlation analyses, process control and conversion of data into information.

Several examples may serve to indicate the trends for the future. In figure 2, the rate and character of aggregation of human platelets are recorded on a chart; this is partial mechanization. Pipetting and transport are still manual as is the conversion of the charted analog curve to numerical representation. This exciting new test of platelet activity, which detects hyperactive or deficient platelet functions, and thereby identifies high risk "clotters" and "bleeders," requires automation and integration into the computer system so that one technologist can more precisely perform ten tests in the time now required for one. The model "S" electronic blood cell counter, now a familiar instrument in many larger laboratories, provides four measurements and three derived results (total of seven results) in hematology with a precision at least ten times that of the traditional manual methods and at a speed and capacity which can approach a hundredfold improvement if need be.

Enzyme rate reactions used to be very slow and tedious to measure by stopwatch, water bath and manual colorimeter. Precision was difficult to obtain. The semiautomatic bichromatic reaction rate analyzer improves precision to less than 1% error for some enzyme tests and at rates of 60–120 multiple

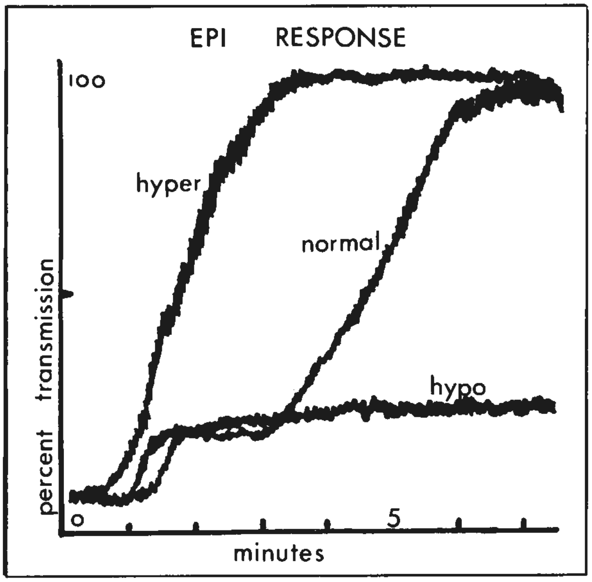

Fig. 2—Measurement of the rate and degrees of platelet aggregation by mechanized instrumentation.

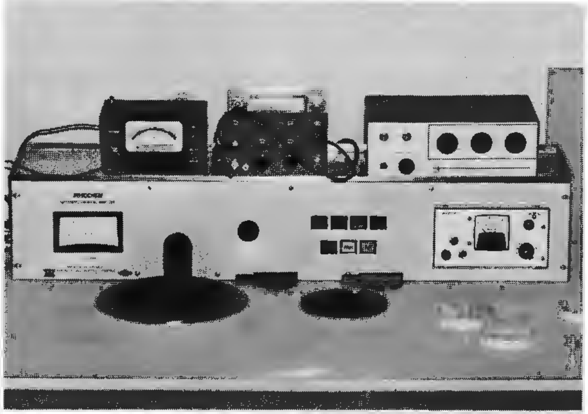

Fig. 3—Automated chemical analyzer console containing centrifuge and controls for speed, temperature and automatic washout of cuvettes.

point analyses per hour. With computer processing, human reading, calculation and transcription errors can be eliminated.

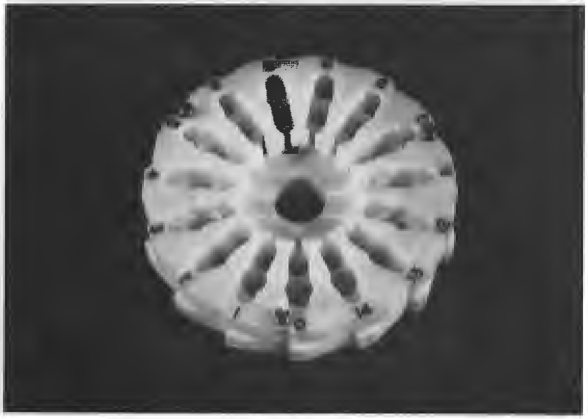

Fig. 5—Automated chemical analyzer. Transfer disc of centrifuge head showing the two well chambers placed in radial position for each of the 15 positions. The serum sample placed in the inner well is run into the reagent in the outer well and mixed by centrifugal force and finally forced into the peripheral quartz cuvette chambers of the rotor (not shown).

A new and innovative breakthrough in high speed, microsample handling and multisample analysis was developed at the Oak Ridge National Laboratory by Dr. Norman Anderson, Director of the Molecular Anatomy Program. Although precision for the tests adapted to this instrument, so far, is equal only to the best conventional methods, the sample size of 1–10 ml, comparably small amounts of reagent and high speed performance promise remarkable improvements in multitest microanalysis for the future. Figures 3, 4 and 5 illustrate the innovative principles and operation of this device which, with its built-in computer, exemplifies future automation in the laboratory. This device is a high-speed centrifugal analyzer using centrifugal forces to mix a series of samples and reagent in microchambers and to transfer them into quartz window cuvettes oriented radially in a teflon rotor. Computer-controlled synchronization permits serial multiple readings of density or color reaction changes within each cuvette. The rate of change in each sample is depicted graphically on an oscilloscope or CRT screen (fig. 6) and is computed as a digital result printed on an attached teletypewriter or via the computer system. Pipetting of sample and reaction is performed with a mechanized autopipetter of high precision.

Fig. 4—Systems Reaction-Analyzer—control panel, minicomputer and oscilloscope and television type screen displays of chemical reactions occurring in each cuvette of centrifugal head.

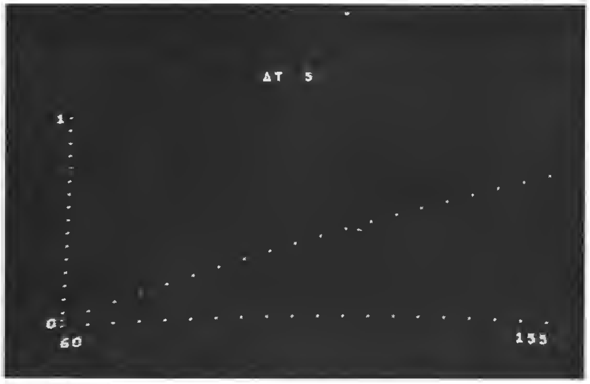

Fig. 6—Enzyme reaction rate curve depicted immediately on cathode ray tube screen.

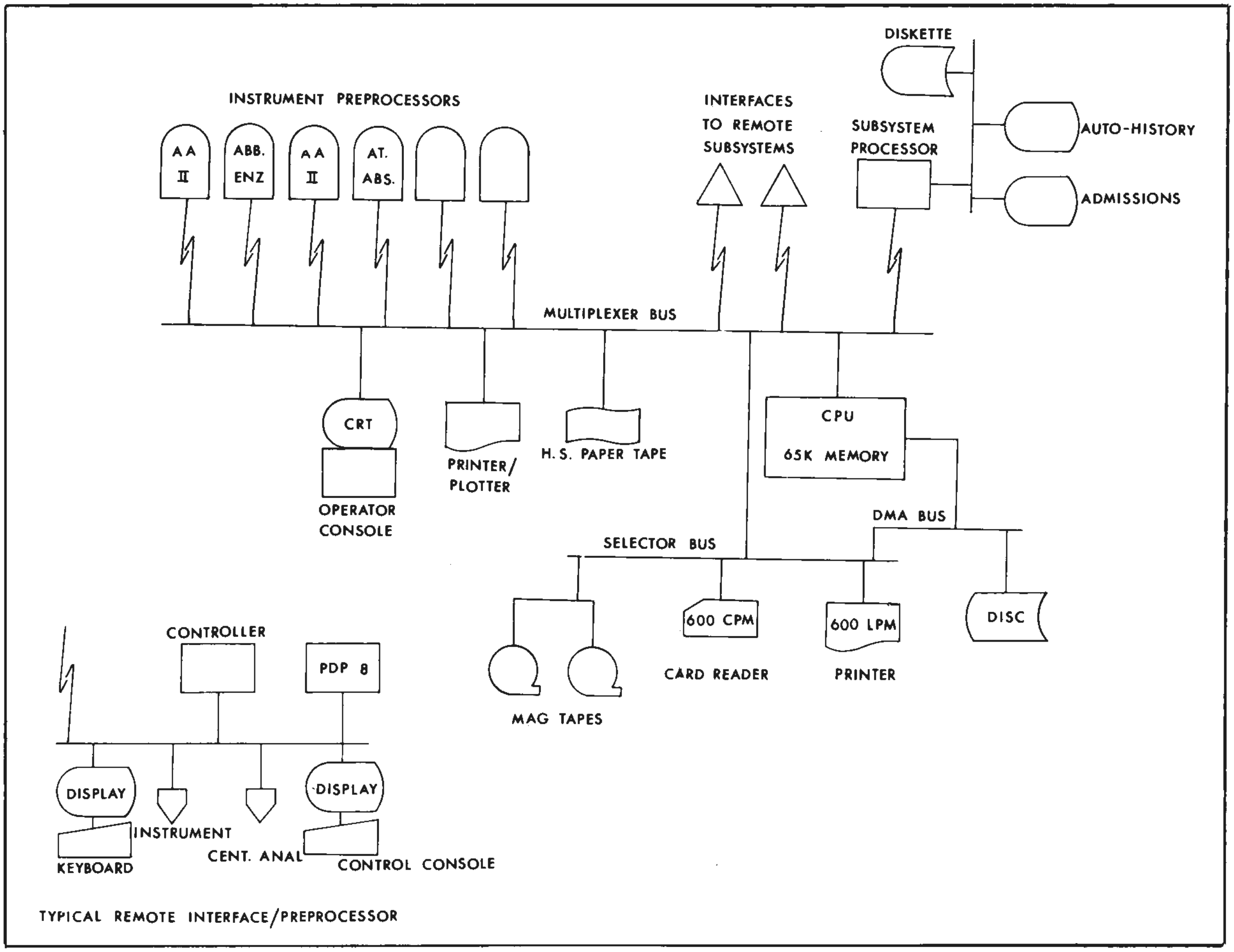

Fig. 7—Diagram of network of individual microcomputer preprocessors attached to each laboratory instrument and coupled to a control microcomputer for final processing, mass storage and report generation.

Finally, the heart of the laboratory of tomorrow—the computer. Due to the high costs of computer equipment and programming, initial attempts at application in the laboratory were designed to accomplish all possible operations with one large general purpose machine. As was discovered in industry, this was found to be expensive and inefficient in spite of the theoretical economic advantages of having one machine for the performance of many functions. With the exponential reduction in costs of processors and memories and the miniaturization of equipment, it is now feasible to employ many special-purpose mini-minicomputers, programmed to accomplish specific tasks for particular analytical instruments and to couple these in a network with one minicomputer for final processing, collation and report generation. This system frees the central coordinating minicomputer to accomplish the data correlation and interpretative functions while the other dedicated instrumental computers (buffered interfaces) are "baby sitting" the analyzers and preprocessing the raw data. Figure 7 depicts the diagram of such a system which is being installed in our new laboratory in San Francisco. Computers are here to stay because they can perform, at the speed of light, complex and repetitive computations, and can sort, coordinate and analyze large quantities of data too time consuming to be feasible if done manually. They can synthesize new information from multidimensional data, opening vast new areas of analytical potential.

REFERENCES

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