JOHN B. GARRISON and ROBERT E. JENKINS

AUTOMATING MEDICAL IMAGE ANALYSIS

A minicomputer-based image analysis system has been assembled at APL and a duplicate has been delivered to the Johns Hopkins Medical Institutions for their continuing use. The design and implementation of this system evolved as a result of our experience in a number of diverse areas of data processing and system design for military, space, and biomedical engineering systems.

INTRODUCTION

By image analysis we mean the operation of extracting a relatively small amount of quantitative information from a two-dimensional image. Typically, a two-dimensional image, in digital form, consists of an array of 512×512 eight-bit digital words. The quantitative information to be extracted consists of a few thousand digital words. These words may describe, for example, the contours of cell cross sections as seen in optical or electron microscope pictures, or contours of the heart wall as seen with a two-dimensional echocardiographic system.

A system for interactively extracting the quantitative data has been developed at APL. A duplicate version has been in operation at the Johns Hopkins Medical Institutions for the past year in support of cardiology research programs. The design of the system has been strongly influenced by the fact that we are concentrating on the class of image analysis problems that requires the processing of a few hundred to a few thousand images for a meaningful medical study. This imposes a requirement for rapid entry of pictures into the system and computerized handling of the data extracted from the pictures.

Pictures can be entered from 35-mm film, hard copy, video tape, or digital tape. Except for digital tape entry, the picture is entered in standard (analog) video format and is digitized and stored for display and processing in a commercial video image processor interfaced with a minicomputer. Digitizing a picture requires one frame time (1/30 second). The system also provides means for identifying the data by a character header and placing it on disk file in a central computer (IBM 3033). This approach permits ready access to the data for analysis by use of a high-level interactive language called APL.

The input picture is displayed on a cathode ray tube (CRT) and the user controls the system by means of a digitizing tablet that has a 16-button cursor. The operating modes of the system are selected by the push buttons. Moving the cursor over the surface of the digitizing tablet causes an electronic cursor, which appears superimposed on the picture displayed on the CRT, to move a corresponding amount. This provides a convenient and flexible means for the user to tell the system what to do and where to do it. With this control the operator can use manual, semiautomatic, or fully automatic methods of extracting the desired quantitative information. Since judgment decisions, which are notoriously difficult to implement in a fully automatic way, are almost always required in image analysis, the ability to use fast but imperfect computer assistance is essential. This is achieved by having the computer present the results of automatic decisions to the operator for approval. His task is to detect erroneous decisions and, after deleting them, to provide the correct decisions.

A simple example of this type of computer-aided image analysis is establishing the inner and outer boundaries of a cell wall as seen in a light microscope picture of a tissue section. In its simplest form, assuming an algorithm for contouring a selected cell, the user would designate the cell by moving the cursor to the interior of the cell and, by depressing the appropriate button, tell the system to contour that cell. The computer-generated contour is presented for operator approval; if he approves, he moves the cursor to the next cell and repeats the process. If the contouring is incorrect, he deletes the computer-generated contour and manually contours the cell by moving the cursor around the inner and outer boundaries of the cell wall. If he does not like his contour, he can delete it and try again.

While we expect that each image analysis task will have very similar requirements for picture entry, operator control of information extraction, and archiving and analysis of the extracted information, the specific algorithms used for the "image analysis" will differ from task to task. It is highly desirable to use an interactive language like APL in the development of these algorithms. We expect to have this capability by late 1981 by means of a 100 kilobit-per-second link being installed between our system and the IBM 3033, via a PDP 11/70. This will permit transfer of a full picture in approximately 25 seconds, with correspondingly shorter times for subsets of a picture. The algorithms will usually be installed in the system minicomputer; in some cases, we may wish to use the computing power of the larger computers beyond the algorithm development stage. The PDP 11/70 is an integral part of a general-pur-
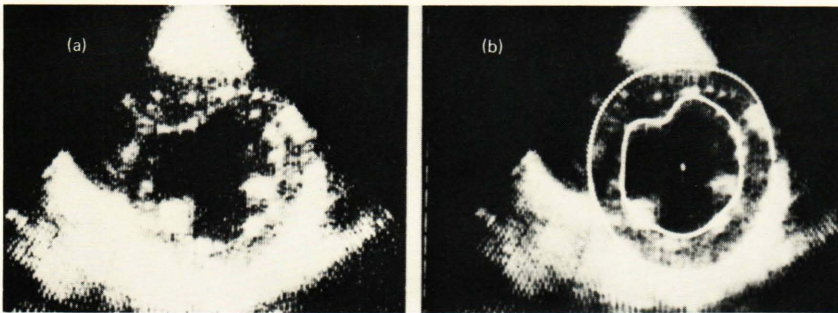
Fig. 1— A typical two-dimensional echocardiogram without (a) and with (b) superimposed contours of the inner and outer walls of the heart ventricle.

pose Laboratory image-processing facility that has available a wide variety of conventional image-processing programs.

BACKGROUND

An increasing number of techniques used in clinical diagnosis as well as in research provide information in the form of images and patterns rather than as a number or a simple "yes" or "no" answer. Typical examples are:

1. Two-dimensional echocardiograms,
2. Serial-section determination of cell morphology,
3. Biplane ("stereoscopic") X-ray pictures using implanted markers, and
4. Computerized axial tomography (CAT scan).

Figures 1, 2, and 3 show images from these methods. In Figs. 1 and 2, (a) is the initial image and (b) is the image with boundary contours superimposed. In Fig. 3, which shows implanted markers, the "contour" (not shown) consists of the points at the center of each marker.

These images are from three-dimensional structures, and both the short- and long-term time histories are important. In two-dimensional echocardiography, a "slice" through the heart is imaged at a rate of 30 pictures per second. The organ can be reconstructed in three dimensions by recording and analyzing an appropriate number of slices.

This reconstruction permits analysis of the performance of the heart over a cardiac cycle. It is necessary to measure performance as a function of time following a heart attack in order to assess the effects of various therapeutic interventions. Long-term studies are important in order to evaluate progressive changes in cardiac function due to aging and other factors. Similar long-term three-dimensional studies are required in the evaluation of tumor dynamics by both CAT techniques and more conventional X-ray imaging methods. The technique of implanting metallic markers to determine both rapid and long-term motion of various organs has been in use for about 50 years. We have applied modern computer techniques to permit accurate three-dimensional location of such markers when many are implanted in the organ. Studies of cell morphology in the cen-
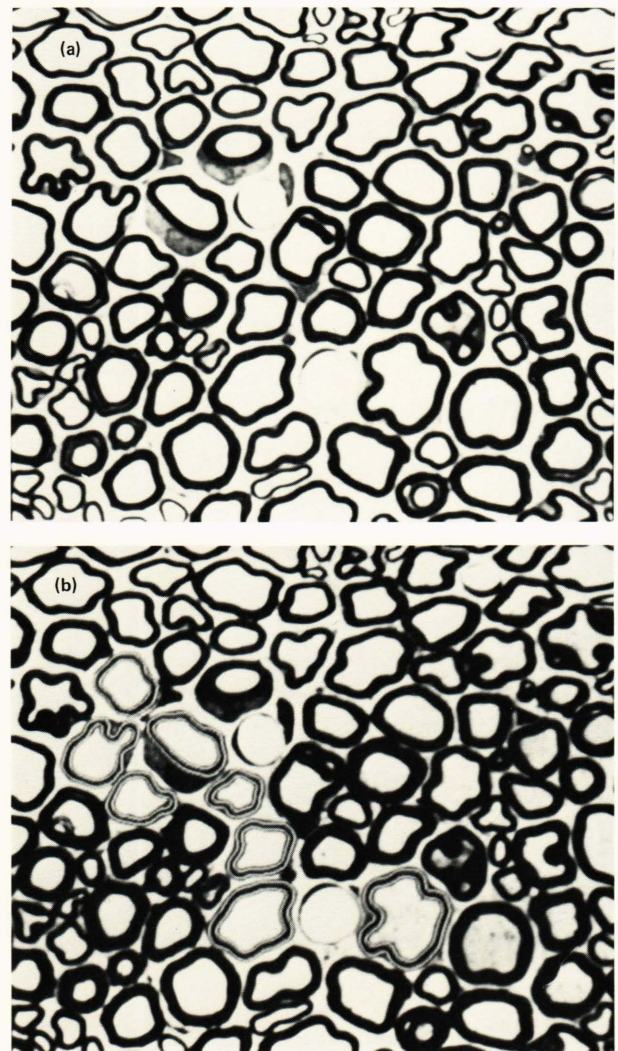

Fig. 2—Typical light microscope photographs of a nerve section without (a) and with (b) superimposed contours.

tral nervous systems of man and a variety of experimental animals are essential for the understanding of a variety of central nervous system disorders.

These images arise from diverse equipment and require different fields of expertise for the scientific analysis of their important features. In some cases they are used to reach a decision as to whether the
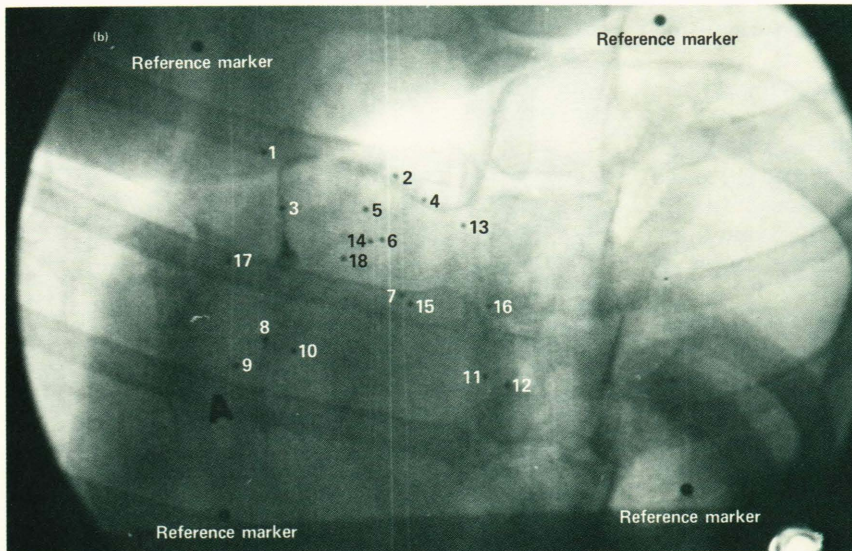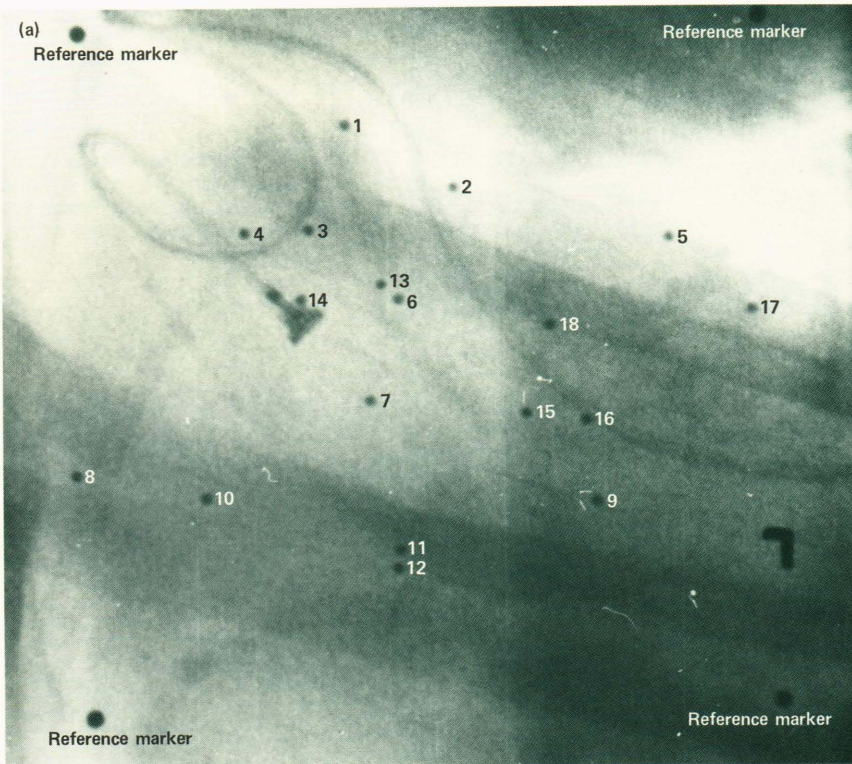
Fig. 3—Two orthogonal views of 18 markers implanted in a dog's heart. Numbers identify corresponding markers.

results represent a normal or abnormal condition or to estimate the seriousness of the condition. These are qualitative decisions.

In other cases, it is necessary to obtain a quantitative measure of some set of parameters such as area, dimensions, and their rates of change in order to assess changes from day to day and to establish the statistical significance of potentially valuable indices of performance.

Our initial effort was the development of a computer-aided contouring system to permit the extraction of quantitative information about wall motion and wall thickness in the left ventricular region

from two-dimensional echocardiographic images. This system[1,2] permits the operator to display and manually contour the walls of the left ventricle as seen on a typical two-dimensional echocardiogram. The contours are defined by a number of "control" points whose positions are set by the operator. After the definition of the inner and outer walls of the ventricle in the first frame selected for analysis, the contours on the successive frames in the sequence are constructed by moving these control points to follow the motion of the heart walls. We typically use 16 points spaced at equal angles with respect to the center of the ventricle. In regions of high curvature,

the operator can add additional points as required to obtain a satisfactory match. After these control points are set, the system computes a smoothed curve containing 128 points for the inner and outer walls and displays these curves for operator approval. The curves are saved and are used as the starting approximation for the next frame in the sequence. The system has provision for positioning eight markers that can be used to indicate the positions of anatomical features such as the papillary muscles and the ends of the septum.

This system was developed as a collaborative program between the Cardiology Division of the Johns Hopkins Medical Institutions (JHMI) and APL. Initial development was done with an experimental system at APL that was assembled from existing available components. A stand-alone system, which was delivered for use at JHMI in mid-1980, can be used with a transducer locating system to provide six-degree-of-freedom information regarding the position of the echocardiographic ("echo") transducer with respect to the patient. Three acoustic sources (small spark gaps of the type used in some digitizing tablets) are mounted in a triangular configuration on the echo transducer, which is hand held on the patient's chest by the echo technician. This arrangement gives the echocardiographer full freedom in moving the transducer to obtain the desired heart scan. The microphones that detect the acoustic impulses from the spark gaps are mounted a few feet away in a plane that is approximately parallel to the front wall of the patient's chest. With three microphones in a known configuration, the range from each spark gap is determined by measuring the transmission time from each source to each receiver. This permits calculations of the position and orientation of the echo transducer with respect to the array of three receivers.

In our case, we record these ranges on each frame of the video tape used for recording the two-dimensional echo pictures. This ensures that we have position data available for all recorded echo data. The information is used to compute transducer position for those frames selected for later analysis. We expect to use the information for three-dimensional reconstruction of heart motion.

The output of the contouring system is on magnetic tape and includes the operator-defined contours, marker positions, acoustic ranges for determining transducer position and orientation, and complete patient and test documentation. The tapes are sent to APL, where the information is transferred to a disk file on the APL central computer for computing cardiac performance indices and archiving the basic data. At a later date, this part of the operation may be transferred to a computer system at JHMI. The value of this method of obtaining quantitative information from two-dimensional echocardiograms has been proven. The process requires approximately two minutes for each frame of two-dimensional echo data. If a full cardiac cycle is to be analyzed at a heart rate of 60 beats per minute using an echo system that scans at a rate of 30 per second, this requires approximately one hour of a skilled echocardiographer's time. This time is satisfactory for research studies but is prohibitively long for clinical applications. The manual method has two distinct parts. The first is the selection of the frames to be contoured, entry of patient data and the operating conditions of the system, and definition of the initial contour. The second part consists of "tracking" the initial contour by moving the control points to follow the small frame-to-frame changes in the position of the heart walls.

As described in Ref. 2, we have developed a correlation tracking algorithm that appears to meet the requirements for relieving the operator of the time-consuming task of "tracking" the contours from frame to frame in a sequence of pictures. This method, if successful, will greatly reduce the time required for analysis of a set of pictures without eliminating the requirement that the operator approve each contour.

During the development of this system, and as a result of both previous experience in related fields and the continuing close relationship and exchange of information between JHMI and APL, we have been investigating other applications of the basic technology. Based on our experience to date, we are cautiously optimistic that the methods developed for the echo system are applicable to other problems in image processing and that our present facility can be used to develop a family of special-purpose systems. This opinion is based on several new applications that, while still in the early stages, show encouraging results.

NEW APPLICATIONS

The most significant of the new applications is the Multiple Marker project with the Department of Biomedical Engineering at JHMI. In this program, multiple spherical markers are implanted in a dog's heart. Using high-speed (up to 90 frames per second) biplane X-ray pictures taken with a standard X-ray system, we have developed the necessary calibration and tracking techniques to permit accurate (0.1 millimeter root-mean-square error) recovery of the three-dimensional coordinates of a large number of such markers (up to at least 50 identical markers).

A potential use of this technique is to track the positions of markers implanted in the inner and outer walls of the heart muscle and to compute from the trajectories of these particles the effect of impaired cardiac blood flow on the mechanical behavior of the heart. The pilot studies and the technique development were done with general-purpose APL facilities, e.g., a production manual-digitizing facility for digitizing the positions of the markers as they appear on the X-ray film, and the IBM 3033 for algorithm development. This approach is satisfactory and desirable in the early phases of such a program because the turnaround time is short and no special equipment is required.

The heart is a complex, rapidly moving, three-dimensional pump. With 50 markers, a heart rate of 150 beats per minute (dog heart), and an exposure rate of 90 frames per second, we obtain 36 measurements of each marker position during each beat. This gives 1800 three-dimensional position measurements per beat. Considering the variety of experiments for which this technique is essential, it is apparent that more complete automation and provision of a standalone system at JHMI are desirable.

The correlation tracking method developed for tracking the motion of the control points in the echo system is directly applicable to tracking the motion of the individual markers in the X-ray system. When markers are used, higher accuracy is required, the number of points is larger, and more precise tracking is required. The image quality is much better in the X-ray system because the markers are high-contrast, symmetrical objects while the echo images are more diffuse and lower in contrast.

We conducted a pilot study using the correlation tracking method and found that it met the requirements for use in the Multiple Marker project. Both the Cardiology Division and the Department of Biomedical Engineering at JHMI are planning to use the multiple marker technique in continuing research and have agreed that the existing system at JHMI can be used for processing the multiple marker data. The major change required is to add a 35-mm projector and video camera to the system to permit entry of the 35-mm biplane multiple marker images into the system.

The tracking rate, using the correlation tracking algorithm in its present form, is approximately 2 seconds per marker per frame. Thus, for one beat as defined above, a processing time of $1800 \times 2 \times 2 = 7200$ seconds is required. (The extra factor of 2 comes from the fact that two views [biplane] are required to locate each point.) This means that it would be highly desirable to reduce the unit computational time from 2 seconds to 0.5 second or less. This may require the addition of an array processor.

We recently initiated a pilot study with the Department of Neurology at JHMI to contour cell processes as seen in light microscope images of tissue sections. Computer-assisted contouring will provide accurate data in sufficient quantity to support a variety of studies related to nerve growth, nerve regeneration, and pathologic conditions such as motor neuron diseases and Alzheimer disease. The shape, wall thickness, and inner and outer areas are the parameters of interest. Using the equipment at APL, we were able to demonstrate automatic contouring of operator-selected cells with only a few hours' work (see Fig. 2). This was possible because we already had a television camera and image digitizer (deAnza IP-5000) interfaced to our processing system as a result of the ongoing development of the correlation tracking system for echo and multiple marker work. The cell images are high contrast, and it appears that a simple edge-tracking algorithm will provide adequate accuracy. Initially, we will have the operator position a cursor somewhere inside the cell to be contoured. The system contours the cell, and the result is superimposed on the image. The operator then repeats the process for all cells he deems appropriate for contouring, and he must approve the result of each operation.

The objective of the pilot study is to get a quantitative measure of the speed and accuracy of this method as compared to the present manual method. The initial tracking algorithm needs to be improved to provide interactive operator control of the parameters that define an edge. The JHMI investigators will use the system to determine if it is promising for their applications. It appears that the computer-aided method is also applicable to electron microscope section analysis. In addition, there is strong interest in following cell processes through a set of serial sections to investigate the three-dimensional aspects of cell morphology. We anticipate that the correlation tracking method, with suitable modifications and operator assistance, will permit the computer-aided tracking of cell processes through serial sections in order to obtain three-dimensional information.

Our last example is a project with the Oncology Center at JHMI. The problem in this case is to use a set of CAT scans of the liver to estimate tumor and liver shape and volume as a function of time in order to evaluate the efficacy of therapy. We conducted a short feasibility study in which we entered some of the CAT scans (from magnetic tape) into the APL central computer (IBM 3033) and, using the APL language, conducted some experiments. The pictures had previously been manually contoured by an expert. We tried some simple automatic contouring based on intensity levels and found the agreement between these automatic contours and the manual results sufficiently encouraging to make us optimistic about the long-range possibilities of automating the contouring operation.

For immediate application, the contours are drawn by Oncology Center personnel on 5 × 7 inch glossy prints and are digitized in the APL production facility. The contour data are placed on a disk file in the IBM 3033 and used to compute liver and tumor volumes. We are currently using a 1-centimeter slice thickness with a separation of 1 centimeter between successive slices; a calibration phantom is included in each set of scans. To date, 49 sets of data have been archived. Together with the Oncology Center, we have proposed the construction of a system similar to the Cardiology system for production work.

SYSTEM DESCRIPTION AND CONCLUDING REMARKS

Based on the above experience, we believe there is a market for suitably sized general-purpose image analysis systems. The remainder of this article

describes the characteristics of such systems as we see them and our philosophy concerning the design and implementation of the systems. It is clear that they are not general-purpose image-processing systems but are designed for the extraction of small quantities of quantitative information from relatively large numbers of pictures. We are extracting information that a skilled observer could obtain by drawing curves on a photograph. He can therefore judge the suitability of computer-generated curves. We may need to do some spatial filtering, edge enhancement, and color coding if it helps the skilled operator make his decisions, but these are not the primary objectives of the program.

The system has the following major components:

- Minicomputer (PDP 11/34)
- Digital disks
- Digital tape drive
- Image digitizer (deAnza IP-5000)
- Digitizing tablet (Altec)
- Television monitor
- High-resolution wideband monitor (Kratos)
- Video disk
- 35-mm projector (Vanguard)
- Television camera (RCA)
- Video tape recorder (IVC)
- Computer terminal(s).

It occupies about two standard 6-foot racks and requires a separate table for the displays, digitizing table, and computer terminal(s). Figure 4 shows the system. Figure 5 is a functional block diagram. The digitizing tablet has a cursor containing 16 buttons that are used by the operator to control the system operation. The computer terminal has a CRT that prompts the operator regarding choices of operating modes. Most users are medical personnel who spend a few hours a week using the system. As in the case of any part-time user, prompting is essential for effi-
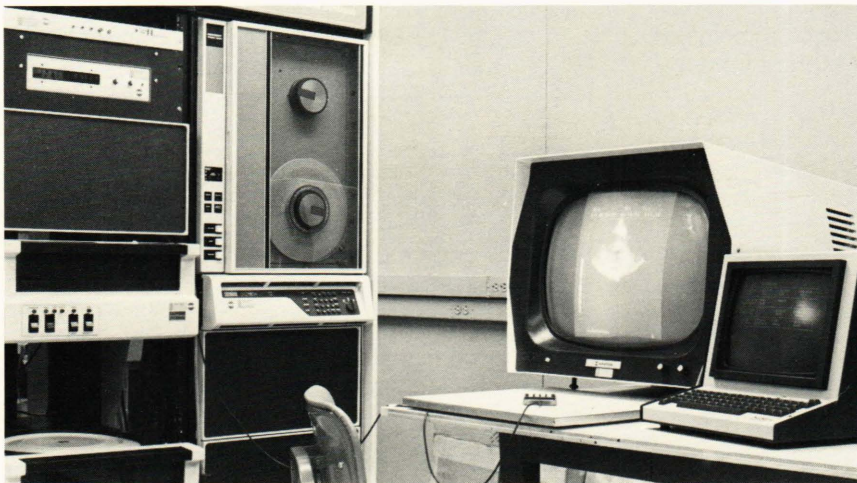

Fig. 4—Image analysis system: computer, video display, and operator controls.
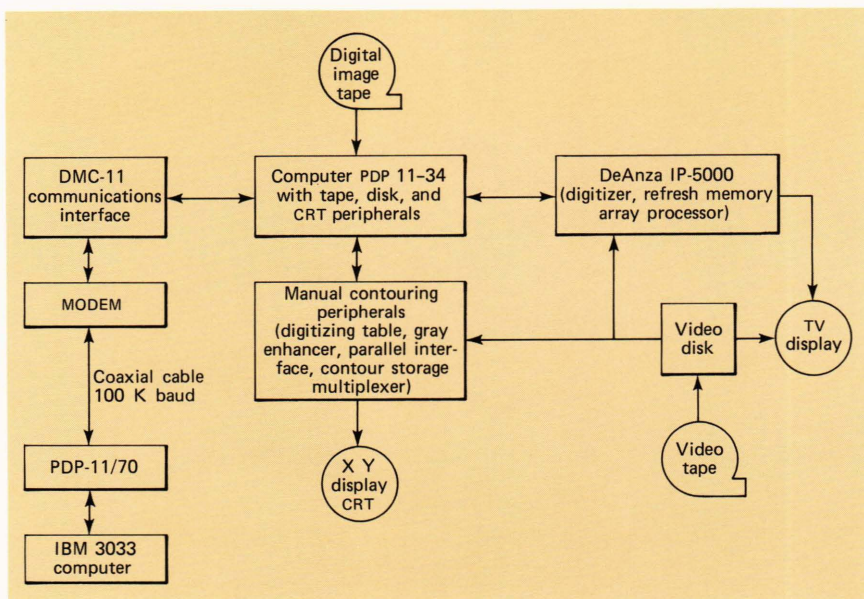

Fig. 5—Functional diagram of an image processing facility.

cient operation and minimization of frustration. We are adding a wideband link to the IBM 3033 in the APL system that will permit the transfer of digital images to the computer for interactive processing using the powerful APL language. This will greatly facilitate the development of new algorithms and thereby reduce the overall development cost and time. It will permit us to conduct feasibility experiments on possible new applications for our methods. Such trials are essential in order for APL and JHMI personnel to get a correct evaluation of the applicability of these methods to the medical problem in question.

One approach to providing a stand-alone system is to duplicate the essential features of the system we have at APL. This would put the cost between $100,000 and $200,000 and would require essentially no development cost. An alternative approach, provided there is an adequate market to warrant it, is to develop a new set of hardware tailored to the specific application. This approach, using microprocessors and modern integrated circuit technology, is likely to put the system's cost in the $20,000 to $50,000 range, depending on the exact requirements and anticipated market, and would require a large initial outlay for development.

REFERENCES

[1] J. B. Garrison, J. L. Weiss, W. L. Maughan, O. M. Tuck, W. H. Guier, and N. J. Fortuin, "Quantifying Regional Wall Motion and Thickening in Two-Dimensional Echocardiography with a Computer-Aided Contouring System," in *Proc. Computers in Cardiology*, IEEE, pp. 25-35 (1977).
[2] R. E. Jenkins and J. B. Garrison, "Automatic Contouring for Two-Dimensional Echocardiography," *Johns Hopkins APL Tech. Dig.* 1, 139-143 (1980).