

Report of the
Board of Regents

National Library of Medicine
Long Range Plan

Electronic Imaging



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Electronic Imaging

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Chairman
Board of Regents
National Library of Medicine

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Foreword

The 1987 Long Range Plan of the Board of Regents* recommended that the National Library of Medicine should "...thoroughly and systematically investigate the technical requirements for and feasibility of instituting a biomedical images library." It encouraged NLM to consider building and disseminating medical image libraries much the same way it acquires, indexes, and provides access to the biomedical literature. Early last year under the direction of the Board of Regents, an ad hoc planning panel was convened to explore in-depth the proper role for NLM in this rapidly changing field.

The Panel was chaired by Dr. Donald West King of the University of Chicago, and represented both the producers and potential users of biomedical images in medical education, research and clinical practice. In charging the Panel, the Board wished to know whether such image libraries would be used by students, faculty and clinicians; what standards and data exchange arrangements would be needed; and whether the proposed 3-D Visible Human Project, a very compelling idea that emerged from an earlier NLM workshop, would be a good place to begin.

On January 18, 1990, the Board of Regents reviewed the draft report prepared by the Panel and unanimously approved the incorporation of its recommendations as part of the NLM Long Range Plan. The Board applauded the leadership of Dr. King and commended Dr. Daniel R. Masys, Director of the NLM's Lister Hill National Center for Biomedical Communications, for his outstanding assistance to the work of the Panel. This report and the recommendations contained therein, presents exciting new challenges to the National Library of Medicine in advancing our fundamental knowledge and use of computerized representations of biomedical structural data, and its transmission across national networks in support of the needs of the biomedical community.

Don E. Detmer, M.D.
Chairman
Board of Regents
National Library of Medicine

*National Library of Medicine, Long Range Plan; report of the NLM Board of Regents. Bethesda, Md.: National Library of Medicine, January 1987.

Preface

The concept of building electronic image libraries, and providing for their transmission across high speed digital networks, presents a special opportunity for biomedical science in general and for the National Library of Medicine in particular. Much of our understanding of complicated processes of health and disease lies in images, pictures of body systems, organs and molecules which cannot effectively be described in words. The NLM Planning Panel on Electronic Imaging has defined a role for the Library which capitalizes on its unique technical capabilities, its very considerable stature in the biomedical community, and its position as a government agency with a Congressionally-mandated mission to acquire and disseminate biomedical knowledge -- in all its forms.

I am indebted to the serious discussion and diligent work on the part of the entire Panel membership during its two meetings in Bethesda, and its between-meeting deliberations. I thank them on behalf of the Library for their excellent contributions. I am also grateful for the support of Dr. Donald A.B. Lindberg, NLM Director; the staff of the Office of Planning and Evaluation, its Director, Dr. Elliot R. Siegel, and Ms. Susan B. Slater who served as Executive Secretary to the Panel; and to the other capable NLM staff who assisted us.

Donald West King, M.D.
Chairman
Planning Panel on Electronic Imaging

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Executive Summary

Background

Images are an important part of biomedical knowledge. Pictures facilitate the understanding of biological structure and function, and are an essential component of education, research, and health care delivery. New computer-based technologies are providing an unprecedented opportunity to supplement the traditional two dimensional images of medicine, such as pictures in textbooks and plain radiographs, with dynamic three dimensional images. These images can be viewed, rotated, and reversibly dissected in a manner analogous to the physical objects they represent, providing valuable instruction to the student, insight to the researcher, and critical treatment planning information to the practitioner.

The National Library of Medicine (NLM) has long been a world leader in the archiving and distribution of the print-based images of biology and medicine. NLM has also been a pioneer in the use of computer systems to encode and distribute the textual knowledge of the life sciences. The NLM's Long Range Planning effort of 1985-86 foresaw a coming era where NLM's bibliographic and factual database services would be complemented by libraries of digital images, distributed over high speed computer networks and by high capacity physical media. This planning panel was convened to recommend when and how the NLM might proceed in the development of such digital image libraries.

Findings

Acquiring and providing access to digital image libraries is entirely consistent with NLM's institutional mandate to acquire, organize, and make available the knowledge of biology and medicine.

The technologies underlying the computer-based representation and display of complex three dimensional biological structure are sufficiently mature that the NLM can proceed with the building of prototype digital image libraries.

The digital image requirements of education, research and clinical practice differ from one another. Education may profitably employ established teaching collections of representative normals and abnormals. Research requires laboratory tools which empower an investigator to make and test hypotheses based on numerical, conceptual and image data, to share that data easily with collaborators, and contribute it to

shared national resources when appropriate. Clinical practice imaging is often focussed on the diagnostic and treatment planning considerations for a single patient, and uses images representing that patient's unique condition.

There remain fundamental research problems in the domain of computerized representation of biomedical structural data, and its linkage to related text and numeric data. Additional research support is needed to facilitate progress in this emerging subsdiscipline of medical informatics.

NLM connection to and use of high speed computer networks is an essential prerequisite for the efficient distribution of computer-based digital images.

Recommendations

The panel makes five principal recommendations:

1. NLM should undertake a first project, building a digital image library of volumetric data representing a complete normal adult human male and female. This "Visible Human" project would include digital images derived from computerized tomography, magnetic resonance imaging, and photographic images from cryosectioning of cadavers. A working group should be assembled from experts in anatomy, clinical imaging, and computer science to establish standards for acquisition, and computer representation of the data. Technical guidelines for this phased project are offered. The panel views this project as a cornerstone for a future set of related image libraries, and a test platform for developing methods and standards.
2. The NLM should support a follow-on research effort to develop methods, tools and standards for classification of anatomic image data from the Visible Human Project, so that applications may be developed which can extract, manipulate and display image subsets on the basis of organs, tissues, body systems and biologic function.
3. NLM should expand upon initial image libraries composed of normal structure to encompass specialized image collections which represent related structural information, such as embryological development, normal and abnormal variations, and disease-related images. In this regard, NLM should collaborate with appropriate professional societies and other organizations to identify

and pursue worthy examples of specialized image collections which have been developed by subject experts.

4. NLM should encourage and support investigator-initiated research into methods for representing and linking spatial and textual information (and other relevant datatypes), and support efforts to introduce computer reconstructed anatomical imaging technologies into health professions curricula nationwide.
5. The NLM should develop and enhance its wide area computer network connections to provide an efficient electronic distribution mechanism for large digital files such as those encoding biomedical images. In the development phase of imaging projects, NLM should continue and enhance its connectivity to NSFnet and the research Internet. NLM should consider developing image-based applications which make use of the proposed gigabit speed National Research Network.

Resources

In the short term, the costs of undertaking the data acquisition phase of the Visible Human project can be derived from existing technologies and similar projects undertaken on a smaller scale. The panel estimates that Phase I of this project would require approximately \$1 million and yield a uniquely valuable image data set.

Phase II of the Visible Human Project--the classification of the image data--is considerably more labor and time intensive if undertaken using current manual or semi-automated methods, such as contour tracing by skilled anatomists. Between 40 and 50 man-years of effort would be required, at a cost of approximately \$5 million, to fully classify the anatomic data.

Research to develop new methods for representing and linking structural and symbolic data in the life sciences would benefit greatly from support for 5-10 high quality investigator-initiated grants annually at an estimated annual cost of \$3 million.

NLM connection to high speed computer networks is an extension of its current connections to NSFnet and the research Internet through the Lister Hill Center. The panel believes that over the next several years incremental improvement in bandwidth should be available to the NLM at approximately the same costs as it now bears (approximately \$100,000 per year). Experimental projects involving commercial telecommunications networks should be pursued under collaborative cost-sharing agreements.

Background

The visual nature of biomedical knowledge

Human vision provides an extraordinarily powerful and effective means for acquiring information. Much of what we know about ourselves and our environment has been derived from images processed by various instruments, ranging from microscopes to telescopes which extend the range of human vision into realms beyond that which is naturally accessible.

In the life sciences, the relationships between biological form and function have been central to the understanding of health and disease throughout recorded history. Indeed, illustrations of anatomy are the most enduring and informative relics of a medieval medical science whose theory has long since been discarded. An intimate understanding of biological structure and its implications for therapy remains a *sine qua non* for medical specialties such as surgery, neurology, and radiology, as well as a learning challenge for all health professionals. Until recently, a fundamental limitation in the teaching and understanding of three dimensional structure was that media for reproducing images was two dimensional, as exemplified by the printed page and the plain film radiograph. The attempt to convey three dimensional content by presentation of two dimensional views forces upon the viewer an exercise in mental model construction which can be difficult and possibly fraught with inaccuracy; it endures as one of the major hurdles in the curricula of all health professions. For the trained viewer, who has long experience in the "intuitive" correlation and interpretation of 2-D sections with 3-D images, it is hard to determine how and under what circumstances such expertise was developed, so that it can be analyzed and transmitted in a more systematic manner to the practitioner and scientist in training.

Early three dimensional photographic technologies were brought to bear on the problem of human anatomy. The Bassett collection of anatomy images used the popular Viewmaster technology of matched stereo pairs of color transparencies to convey the essential qualities of depth and spatial orientation of gross anatomic structure. Still, the user of such photographic collections is limited to the static content of the images acquired at the time of image capture. No facility exists to move the object of study, to change the perspective of one's viewpoint at

will in a manner analogous to having the physical object at hand, or to dynamically "enter" an object to disclose its internal representation.

New technologies

The emergence of the digital computer has provided a new technology for the acquisition, storage, manipulation, and display of complex images. Central to the capabilities of digital image display has been the development of large memory computers, specialized graphics processors, and high speed digital networks, along with robust and economical solid state scanning, high resolution display devices, and digital optical disks.

Pictures can be produced by computer in two fundamentally different ways¹. The first is the representation of pictorial elements as geometrical objects, such as a collection of polygons whose shape and surface qualities can be calculated to produce a likeness of a real world object; the underlying representation is based on mathematical formulas for the geometrical primitives which combined make up the complete object.

The second method of picture representation by computer is sample based (also called pixel-based or image-based). In this method, the pictorial data may be thought of as individual points (pixels) in a large two dimensional field, which taken together portray an object recognizable by the viewer. In this scheme, the computer generally does not have an independent representation of objects within the image.

The distinction between the two picture representation methods is crucial to computer-based biomedical imaging. Most clinical images are acquired using sample-based methods. Thus, although the varying x-ray patterns produced by the computerized tomographic (CT) scanner can be rendered into a display which a physician interprets as various anatomical structures, to the computer the pixel components of the image are not manipulable as objects (e.g. internal organs) except to the extent that some tissues share a unique and homogenous radiodensity (e.g., bone). Yet for purposes of understanding the content of complex medical images, the identification of objects and object boundaries within sample-based images is essential.

Classification, i.e., the assignment of a sample or pixel to an organ, is a fundamental and difficult problem. The problem is

typified by considering a CT sample that happens to fall at the boundary of bone and muscle tissue. The sample at that point represents some combination of both tissue types. Many classification techniques used today class such a pixel as one or the other tissue, thus introducing inaccuracies into the objects extracted from the sample set. Problems such as these may be overcome by better application of sampling methods, but the classification of objects within pixel sets remains a daunting problem.

NLM Long Range Plan

In 1985, the NLM commissioned a long-range planning effort involving over 100 experts in the fields of computer and library science, health professions education, and medical informatics research. Charged with looking five, ten and twenty years into the future, the planning panels identified major trends, impediments to progress, and "windows of opportunity" for the NLM to accommodate an information-rich future, or make elements of that future happen if appropriate to NLM's institutional mission.

Not surprisingly, the planning panels saw an increasing role for electronically-represented images in clinical medicine and biomedical research. As the world's foremost archive and distribution center for biomedical knowledge, the NLM was encouraged by the planning panel on Medical Education to explore the feasibility of building and making available electronic image libraries, much the same way that it maintains, indexes, and provides access to the biomedical literature².

However, the technologies to support such image libraries, associated high bandwidth communications, access and increasingly high resolution representation are new, and evolving rapidly in a number of disparate directions with heterogenous hardware and software requirements, and few if any standards for sharing of image data. To a public institution such as the Library, this flux translates into risk that prematurely launched programs will incur significant expense, yield image library data sets that are useable by only a small fraction of its constituency (or none at all), and be superseded by later developments which render its work obsolete and perhaps untransformable to new standards.

*Current NLM digital
imaging projects*

Research and development involving digital images has been ongoing within the NLM's Lister Hill National Center for Biomedical Communications for several years. Appropriate to the Library's mission to serve as a national archive for biomedical information, investigations in the use of digital bit-mapped graphics to preserve page images of published material have been pursued in an Electronic Document Storage and Retrieval (EDSR) Program. The basic model for this research is the acquisition of high resolution (2,000 by 2,000 pixel) electronic images from biomedical texts, image enhancement and compression by computer algorithms, storage of page images on optical disk, and retrieval/display of page images linked to searches of NLM's bibliographic databases. The EDSR investigations have included extensive system software development and cost/throughput models to compare electronic archiving with more traditional modes of literature archiving such as microfilm.

An ambitious follow-on to the EDSR project is just beginning. Called the Machine Readable Archives in Biomedicine (MRAB), this project explores elements of document image "understanding", using automated algorithms to segregate text from graphics, and omnifont character recognition to convert printed text to machine readable character streams, while preserving nontextual regions in bitmapped form.

Color and monochrome digital representations of complex medical images such as microscopic tissue sections, 35mm dermatology slides, and clinical radiographs provide the focus for other Lister Hill Center projects. A key element of this research is the development of methods for automated assembly of overlapping digital image "tiles" into a composite high resolution image.

*1988 3-D Anatomical
Reconstruction
Workshop*

Innovative research on computer-based representation of three dimensional anatomic data is underway in a number of centers nationwide. In June of 1988 the National Library of Medicine convened representatives from eight academic medical centers involved with production and use of computer-based three dimensional anatomic imaging. The intent of this meeting was to review the current state of the art in 3-D imaging

techniques, and to identify possible contributions that the Library might make to this field as a public agency.

Each of the university groups presented an overview of the types of activities at their own centers. In the aggregate, it became clear that the power, graphical display capabilities, and affordability of current computers are sufficient for many educational and research applications in 3-D anatomical imaging, and that there are unique merits to images rendered from digitized anatomic databases. The most dramatic of these is the ability to isolate, highlight, "reversibly dissect", rotate, and view from multiple angles single and grouped tissues, organs, body regions, and physiologic systems. Anecdotal evidence of the enthusiastic acceptance of 3-D imaging, especially for complex anatomic systems such as the central and peripheral nervous system, and the use of 3-D images in surgical planning, was presented.

The meeting participants pointed to the time and labor-intensive qualities of anatomic data acquisition as significant impediments to the wider use of 3-D anatomic reconstruction data in health professions education, treatment, research, and patient education. No spatial data set of anatomic coordinates for the complete human body exists in the public domain, and the project to develop such a data set would require more resources than any single academic group could reasonably devote to it.

Accordingly, it was the consensus recommendation of the group that the Library could contribute substantially to the advancement of the field by supporting the development of an image data set of an entire human male and female. This "Visible Human Project" would be carried out in two phases. The first would be acquisition of enhanced computed tomography images of representative, carefully selected and prepared male and female cadavers. The original cadaveric material would be preserved. The second component of the initial image acquisition would involve selective cryosectioning of the same cadavers used for development of the CT data set, and production of photographic images from appropriately-spaced sections. The next phase would be the contouring and digitization by anatomy experts, to define organs, tissues, and other structural entities in both CT and cryosectioned images. In terms of the two fundamental image representation methods

discussed above, this phase would be the extraction of manipulable (geometric) objects from the pixel/sample based images obtained via radiography, magnetic resonance imaging, and photography.

The image library thus constructed would be made available by the Library in both electronic formats (such as CD-ROM discs) and as photographic image sets. A wide range of educational, diagnostic, treatment planning, and commercial uses was predicted by the group.

*Charge to Image
Planning Panel*

To address the issues raised by the workshop on 3-D Anatomical Reconstruction, the current panel representing both the producers and potential users of computer-based biomedical images was convened. Members of the panel undertook presentations and discussion to answer the following questions:

1. What is the proper role for a public agency such as the NLM in relation to electronic imaging technologies? Should NLM change its current policy of exploring image library technologies to one of actually building and distributing image libraries?
2. Would such image libraries, if available today or in the near future, be used sufficiently by students, health sciences educators, and/or practitioners to justify the expense involved in their creation and maintenance?
3. Are new standards, data exchange conventions, or consortia arrangements needed to enhance the sharing of image data for purposes of education and health care?
4. Is the proposed 3-D visible human project a good start for undertaking the development of an electronic image library? If so, how should this project be pursued? Are there other equally or more compelling image projects the NLM should consider?

Findings

Digital Images: Clinical Applications

The panel notes that electronic imaging is having a major impact on the conduct of clinical medicine. Particularly affected are the disciplines of neurology, reconstructive surgery (especially facial and oral surgery), neurosurgery, orthopedics, radiology, and radiation therapy. A growing emphasis on 3-D spatial information for treatment planning now supplements the traditional role of radiologic studies in diagnosis.

In some specialties such as neurology, imaging studies serve as a screening procedure prior to requesting clinical consultation; clinical signs and symptoms are sometimes subordinated to imaging results in the management of patients, and referrals for asymptomatic abnormal imaging results are increasingly common. Stereotactic guidance for neurosurgical procedures using 3-D imaging data is under development.

Management of traumatic, degenerative and congenital bony abnormalities, be they located in the head, thorax, or major joints, now often includes pre-operative 3-D imaging as an adjunct to therapy planning. The uses of imaging in this area include visual displays intended to convey a clear anatomic model to the physician. In addition, computer imaging data can be linked to robotically controlled milling machines to produce models of pathologic tissue for practice operations, to build prosthetic devices to guide implantation and reconstruction, and to guide the selection and/or remodelling of artificial joint hardware to fit a particular patient. Industrial research is currently in progress to use such data to guide the actual robotic milling of bone and joint surfaces *in vivo*.

Additional therapy-planning uses of volumetric digital imaging include the matching of donor organ and recipient cavity sizes in cases of heart and liver transplant, the preoperative sizing of malignant tumors such as musculoskeletal sarcomas, and radiation therapy planning from 3-D volumetric tumor models.

Digital Images: Educational Applications

The panel recognizes that 3-D image reconstruction by computer provides a new and promising method for the education of health professionals. The understanding of complex structure-function relationships such as those in the central nervous system is a challenging educational problem which is

only poorly solved by two dimensional images, physical models, and cadaver dissections. The educational goal is the development of a clear three dimensional model in the mind of the student, and the integration of structural knowledge with physiological and biochemical function.

Just as the practicing surgeon might view abnormal, patient specific anatomy at a radiological workstation, the panel noted that a student's workstation would allow the display, rotation, selective "dissection" and reassembly of normal human anatomy by the student, controlled by graphical pointing devices and easy-to-use interface methods. Such methods would also greatly facilitate the understanding of congenital abnormalities and aid the planning of their corrections by rendering the existing collections of human embryos (e.g., Carnegie Collections, Blechschmidt Collection) in computer readable form. Initial work to develop both geometrical and image-based teaching files and control software is under way at several university centers.

*Digital Images:
Research Applications*

Biomedical research presents special requirements for digital imaging. The need to correlate biochemical and physiologic data with anatomic location is especially acute in the neurosciences, where the recent discovery of large numbers of neurotransmitters and investigational techniques such as monoclonal antibody staining are generating a flood of new information which requires spatial mapping and correlation within the nervous systems of man and model systems such as rat brain. The tools for manipulating and sharing laboratory data add special requirements: the need to develop standardized formats for exchange of text, numeric, and graphical data among investigators; the need for user interface software which allows an investigator to easily view, edit, and compare the data from biochemical and neurocircuitry mapping experiments. Unlike the educational requirements for consensus standard image sets, research requirements emphasize the variability and one-of-a-kind nature of particular experiments.

Research imaging requirements for a National Neural Circuitry Database are the object of a study currently being funded by the Alcohol, Drug Abuse and Mental Health Administration (ADAMHA) and conducted by the Institute of Medicine. The panel recognizes the importance of coordinating digital imaging projects among the federal agencies which sponsor biomedical

research, and making available the knowledge resulting from that research.

*Digital Images and
Computer Networks*

The complex images of biology and medicine, as represented by digital volumetric data sets, constitute a challenge to currently available computer networks. Image files may range from hundreds of thousands to many millions of bits representing measures of volume (voxels) or points on a display screen (pixels). This contrasts with NLM's current bibliographic services where a database query may yield tens to a few thousands of alphanumeric characters, and wide area commercial networks providing 120 to 240 characters per second over voice-grade phone lines give acceptable response times. The transmission speed (bandwidth) necessary to accommodate image data will require that wide area networks be available with a capacity which equals or exceeds that currently found in local area networks (10-100 megabits/second).

*Digital Imaging and
the NLM*

The panel identifies a number of salient issues which bear upon National Library of Medicine involvement in digital image technologies and libraries. The most important of these are listed here.

Acquiring and providing access to digital image libraries is entirely consistent with the NLM's institutional mandate to acquire, organize, and make available the knowledge of medicine and biology. No such publicly available digital libraries currently exist. Clearly, the questions about this technology revolve around "when" and "how" the Library should proceed, not "if" the Library should proceed.

As noted by NLM's previous advisors, the greatest potential impact of NLM projects appears to be in the area of health professions education, where the establishment of image libraries representing normals and archetypal abnormals is an activity which cannot reasonably be undertaken by single academic institutions, and where there are few economic drivers in place to promote commercial development. However, educational institutions at the present time generally lack both the computer hardware of sufficient capacity, and the professional expertise among faculty to use 3-D computer images as a component of the curriculum. Indeed, the current emphasis upon molecular biological mechanisms of health and disease has led to a de-

emphasis of gross anatomy in the curriculum, and fewer hours dedicated to "structural biology." Faculty training and acceptance of new modalities such as computer-generated images is critical to the success of this technology in the educational process.

From a knowledge representation viewpoint, key issues remain in the development of methods to link spatial data--images and objects within images--to the symbolic data comprising the names, hierarchies, principles and theory which are the text-based understanding of visual things. The research group at the University of Washington has coined the term "Structural Informatics" to describe this field. Standards do not currently exist for such linkages among different data types, but this area of endeavor is new, rapidly changing, and the panel believes it is premature to insist upon such standards. In addition, much basic research is needed in the description and representation of morphological structures, and the connection of structural-anatomical to functional-physiological knowledge through the use of alternative modeling methods. Generalizable methods which support a hypertext-like model, where words can be used to find pictures, and pictures can be used as an index into relevant text, are needed.

Libraries of normal structures should be created so that they can be easily linked to related collections of diseased and abnormal structure, as well as those representing temporal variation (e.g., embryology). Research support by the NLM at key academic centers would assist in advancing the field, as would the convening of meetings to develop standards for data exchange and knowledge base sharing.

It is clear that the current environment is one of rapid change and new development in computers and algorithms designed for graphics manipulation and rendering. For this reason, the panel believes that NLM emphasize the creation, standardization, exchange and distribution of volumetric image databases, rather than the development of applications software which uses those databases.

Recommendations

The panel recommends the following:

1. NLM should proceed with the proposed project to acquire and make available an image dataset of a complete, carefully selected male and female cadaver using the modalities of CT, MR, and photographs of cryosections. There must be a first project, and the panel believes this one to be quite appropriate. It will be a project through which standards will be developed and set for the electronic image libraries to come. It will provide a cornerstone and point of reference for future image collections which are related but extend along various conceptual axes: diseases of body parts, normal and abnormal growth and development, and dynamic temporal processes such as normal and abnormal body part motions.

Guidelines for proceeding with this project are offered in Appendix A.

2. The NLM should support a follow-on research effort to develop methods, tools and standards for classification of anatomic image data from the Visible Human Project, so that applications may be developed which can extract, manipulate and display image subsets on the basis of organs, tissues, body systems and biologic function. NLM should support the development of object classification techniques, standards of rendering (e.g., degree of photorealism, how lit, how colored, how antialiased, etc.) for this subsequent phase of the project in which geometric representations are developed from the initial image data sets. NLM should develop detailed resource requirements based on its proposed standards, to determine the timing and feasibility of proceeding with the comprehensive object classification of the initial image data.

3. NLM should expand upon initial image libraries composed of normal structure to encompass specialized image collections which represent related structural information, such as embryological development, normal and abnormal variations, and disease-related images. In this regard, NLM should collaborate with appropriate professional societies and other organizations to identify and pursue worthy examples of specialized image collections which have been developed by subject experts. The dissemination and use of these digital library collections should be promoted.
4. NLM should encourage and support investigator-initiated research into methods for representing and linking spatial and textual information (and other relevant datatypes), and support efforts to introduce computer reconstructed anatomical imaging technologies into health professions curricula nationwide.

Fertile areas for grant support include:

- 1) Structural Informatics
- 2) Computer Graphics Technology as applied to biomedical images
- 3) Basic biomedical research applications
 - a. Developmental Biology, Embryology
 - b. Neurobiology
 - c. Cell and Tissue Biology
 - d. Molecular and supramolecular structure
- 4) Clinical applications
 - a. Stereotactic procedures
 - b. Radiation therapy
 - c. Anesthesiology
 - d. Radiology
 - e. Organ systems imaging
 - f. Orthopaedics
- 5) Center Grants for computer-based imaging
- 6) Program Projects
- 7) Instrumentation grants

5. The NLM should develop and enhance its wide area computer network connections to provide an efficient electronic distribution mechanism for large digital files such as those encoding biomedical images. In the development phase of imaging projects, NLM should continue and enhance its connectivity to NSFnet and the research Internet. NLM should consider developing image-based applications which make use of the proposed gigabit speed National Research Network.

Resource Recommendations

Visible Human Project Phase I

The panel recognizes that its recommendations include a specific first project in building digital image libraries, and a more general endorsement of support for research to enable the fullest usage of such libraries. In the short term, the costs of undertaking the data acquisition phase of the Visible Human Project can be derived from existing technologies and similar projects undertaken on a smaller scale. The panel estimates that Phase I of this project would require approximately \$1 million and yield a uniquely valuable image data set.

Phase II

Phase II of the Visible Human Project--the classification of the image data--is considerably more labor and time intensive if undertaken using current manual or semi-automated methods, such as contour tracing by skilled anatomists. Between 40 and 50 man-years of effort would be required, at a cost of approximately \$5 million, to fully classify the anatomic data.

Structural Informatics Research

The panel encourages the NLM to provide research support to develop automated image processing tools for improving the speed and efficiency of biomedical image classification. Research to develop new methods for representing and linking structural and symbolic data in the life sciences is also needed. Support for 5-10 high quality investigator-initiated grants annually would greatly facilitate progress in these areas, at an estimated cost of \$3 million.

Computer Networks

NLM connection to high speed computer networks is an extension of its current connections to NSFnet and the research Internet through the Lister Hill Center. The panel believes that over the next several years incremental improvement in bandwidth should be available to the NLM at approximately the same annual cost as it now bears (approximately \$100,000 per year). Experimental projects involving commercial telecommunications networks should be pursued under collaborative cost-sharing agreements.

Appendix A: The Visible Human Project

The panel recommends that a cooperative working group be formed from respondents to a competitive solicitation or request for proposals. The working group would be made up of representatives from several different institutions whose strengths and capabilities complement one another and make the Visible Human project feasible at a reasonable cost, with the greatest potential for widespread benefit to the biomedical community.

The working group would be formed from successful applicants who develop proposals to work on one or more of the several tasks outlined below. It is understood that no single group would necessarily perform all of the tasks working in isolation as effectively and efficiently as a cooperative group who work on various tasks and coordinate their efforts. This could be done through either a contract or grant mechanism, but it is understood that not all of the costs would necessarily be borne by the NLM. If groups had existing support for similar or related work which could be adapted to these requirements, or their institutions would co-fund and underwrite some of the development costs, this would be most effective.

Stage I: Acquisition of "Raw" Image Data

The first step avoids all issues of classification by not identifying specific objects within the image data sets. It is therefore far short of clinical application, but guarantees feasibility and reliability. It provides the "raw truth" on which all subsequent elaborations can be built.

Task 1. Obtain a set of sample adult human cadavers, three each of males and females. These cadavers must be "fresh" or very well preserved with minimal structural abnormality at the time of death. They should be young or middle-aged and fall within norms for size.

Task 2. The preparation of the bodies must be done to fulfill stringent requirements for registration of serial sections obtained by medical imaging techniques or through serial sectioning. The bodies should be prepared with injection of radiodense fluid plastic to adequately define the arterial tree and fill the major vessels. Reference markers are required in an external plaster cast which should be applied to the specimen before processing. The required

preparation is a separate task, and may be performed by specially trained experts, not necessarily from the same site which provided the cadaver initially.

Task 3. Whole body imaging of the prepared specimens is performed at 1 mm. intervals, using computed tomography of the whole body and magnetic resonance imaging of the head. This should be performed on all six cadavers soon after their demise. The cadavers should be rigidly fixed spatially prior to CT and MR imaging, such as by a total-body rigid cast, to prevent any motion or gravity-induced deformation of fresh tissues. Data from these imaging sequences would be archived to optical disks in a working group specified format that would be readable by NLM and other members of the group. All cadavers must be frozen after imaging is completed. It is anticipated that the pre-specified MRI sequences would require one or two hours of scanner time, while the CT scanning process to be performed under working group-specified conditions would require twelve hours or more, including archiving.

The working group panel would review all images from the six cadavers at a collaborative meeting and select a single male specimen and single female specimen. The four remaining specimens might be used later in whole or in part for additional subprojects, or as a potential replacement in the event of an unforeseen problem with the ones selected first.

Task 4. Anatomic sectioning would be performed at submillimeter intervals with color photographs taken at each slice level. These photographs would be obtained on pin-registered color film on as large a color transparency as possible (ideally 4 x 5 or 8 x 10 inch), and might be printed or copied as part of their distribution. The color images should be represented in an appropriate archival form, such as three color separation onto black and white film. The photographs should be made using a color film with a normal rather than enhanced color balance, such as Kodak EPN-100 Ektachrome Professional 100 ASA sheet film. This is the current standard for anatomic photography.

Task 5. The photographic images would be archived, with a recognized color standard (e.g., MacBeth, Kodak Q-60C Paper Reproduction Guide, Kodak Q-50C Kodachrome Reproduction Guide for gray scale) in each photo. These photographs would be digitized at 300 pixels/inch (professional photography/publishing resolution), or 2400 x 3000 pixels, in RGB with 12 bits per color channel (R, G and B). They would also be archived at the same pixel density as the CT slices (either 512 x 512 or 1024 x 1024) to correspond as precisely as possible with the pixels of the CT scans. This resolution can be derived from the high resolution scans without redigitizing.

All digital data would be archived to optical disks in an appropriate format; the specification of this format should be obtained by consultation with experts in computer graphics and imaging. At this point, the entire working group would have access to all slice digital data and NLM would assist with distribution of it, after suitable reformatting to video disk, CD-ROMs, or other media as deemed practical and useful. A product would be available at this stage for outside groups, as the first result from the Visible Human Project. Outside groups could obtain the serial slice images and might use them in research or teaching.

Stage II: Classification into Objects

Task 1. Object definition would be performed on the slice data with segmentation, either manually or automatically. Quality control procedures and acceptance standards for the object definition results would be established by the working group and applied to the data sets at proof of performance. The object definition task may be restricted to a single body region or organ as proposed by each respondent to the solicitation. Ultimately, the entirety of the data sets should be segmented, but it is necessary that standards be established first, and in the early work associated with this initiative, it is understood that only specialized regions may be defined.

The object definitions would be distributed in the working group specified format, and could be made available expeditiously to outside groups by the NLM. The computer software tools used to implement the object definition would be available to accompany the raw slice data and object definitions. This should facilitate the generation of additional object definitions by outside groups who are studying specific areas of the body.

Task 2.

A hierarchical data base organization and associated retrieval functionality is required for the management of the very large amount of image data created in the Visible Human Project. The specification and implementation of the data base organization is a separate research task, and a successful outcome would involve a working retrieval system that operates at multiple levels and provides ties to additional sets of imagery such as nuclear medicine, ultrasound, histologic slice images, and text.

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