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Review Paper

Medical Image Processing in an Era of High-Performance Computing

Abstract: Advanced radiology practices are already benefiting from powerful and increasingly more economical computing and networking facilities. Medical image processing methods have improved dramatically over the past five years, with sophisticated 3D display, visualization and analysis techniques allowing increased integration of multiple modalities of imaging, flexible environments for imaging analysis, and PACS (picture archiving and communication systems) for ease of transmission and retrieval. Emerging directions involve teleradiology and telesurgery virtual reality applications, the development of new image database techniques, and the building of large visual databases like that of the Visible Human Project. Challenging problems of image segmentation, registration, and multimodal image fusion are still with us. Building dynamic, flexible electronic atlases will have a profound effect on the understanding of structure and function from the level of cellular physiology to gross anatomy, but requires the development of new techniques of visual knowledge representation and more standardized ways of defining the conceptual and linguistic constructs of visual objects in biomedicine, for linkage to medical records, research results, and educational materials. Methods for reasoning with visual information in the context of multimedia information systems present an inviting challenge to the upcoming generation of researchers in medical informatics.

Keywords: Medical Image Processing, Informatics, Image Segmentation, 3D Image Visualization, Medical Image Databases

1. Overview

Among the many scientific and technological advances related to high performance computing, medical imaging stands out for its powerful popular visual appeal in demystifying the inner structures of the human body. It is also a harbinger of automation in health care practice, biomedical research, and education. Medical imaging offers unparalleled opportunities for dramatically improving health care through technology by increasing the ways and sophistication with which we can non-invasively visualize, analyze, and interpret the processes of health and disease.

Advances in imaging instrumentation and the design of new modalities depend on high-performance computing for rapid reconstruction and display of large sets of images. New techniques of digital image processing, particularly in 3D, are the keys to effective visualization, manipulation, and analysis [1], seeking to extract and use the medical information content of the images. With such tools in hand, we can begin to discern the emergence of a new medical imaging informatics.

While the large amount of precisely localizable and measurable information in medical images is already immensely useful for individual patient diagnosis and therapy, the accumulated visual information contained in biomedical image databases [2-5] is a veritable treasure trove waiting to be mined for scientific and educational purposes. However, because medical images are concrete and patient-specific, they lack the abstract expressive power of language-based descriptions. As a result, their information content is much less easily defined, shared and communicated than are the traditional symbolic descriptions of patient conditions found in the medical record [6-8].

The integration of imaging information with other medical records within health information systems [9-12], in ways that will facilitate standardized communication and interpretation, can well be considered the central problem of medical imaging informatics. And, with the development of multimedia and virtual reality systems [13] that can capture voice, touch and other sensory information as well, we may even foresee the emergence of a more general "multimedia medical informatics" to study the problems of coherently representing and integrating such disparate sources of information.

As high-speed and high-bandwidth networking comes closer to reality [14], the transmission of multi-modality medical images between imaging and health care centers will become routine, profoundly affecting the practice of medicine. The ability of teleradiology to interactively monitor a measurement as it is happening and make it available remotely, as well as to retrieve medical images efficiently from image databases for comparison with other related images, not only promises to increase the productivity of radiological procedures [15], but also makes possible for the first time large-scale quantitative studies of the visualizable anatomical changes that occur in disease. Until recently, the 3D nature of human anatomy was difficult and prohibitively expensive to model on the computer. Advances in hardware, graphics, and imagery software and in modelling methods are finally making it possible to plan for real-time 3D anatomical modelling and matching to patient data. Sophisticated interactive 3D display and visualization methods [1,16-20] are being widely distributed and already proving their worth in advanced radiology research and demonstration projects.

Despite much progress in Picture Archiving Systems (PACS) [21,22], relatively few centers at present have fully integrated digital processing of all routinely performed imaging studies. But their numbers are increasing, and software environments designed specifically for medical image processing and analysis are also becoming more sophisticated and widely available [23-26]. The tool kit of techniques for image analysis is also growing: many more sophisticated processing and analysis techniques [27] and methods for image registration [28] are being increasingly developed, as are methods for lossless (as well as lossy) image compression and decompression [29], facilitating the effective transmission of the large numbers of image data now being generated [30].

From an informatics perspective, it is also crucial that parallel efforts are ongoing in the development of electronic patient record systems and the informational infrastructure for them - vocabularies and languages for describing medical knowledge and practice. The Unified Medical Language System (UMLS) [31,32] and standards for medical and radiological nomenclature [33,34] can help in describing the contents of medical images more uniformly and according to shared conventions. From a practical point of view, current research in modelling radiological concepts [35] is based on analysis of linguistic constructs within reports describing radiographic images.

The present review highlights research in medical image processing. Despite slower-than-expected progress in the central problem of automated image segmentation [36], developments in interactive visualization and analysis software have more than compensated for this by providing effective tools for radiology practice and research [1]. The present convergence of technological, scientific, and societal factors makes it very likely that imaging will be increasingly important to medical informatics in coming years [37].

2. 2-D Medical Image Processing: Preprocessing and Segmentation

Medical imaging systems almost never provide the radiologist with "raw" image signal data. Instead, various computational preprocessing methods are used to reconstruct an image that will give the greatest amount of diagnostic information to the practitioner. Reconstruction methods are specific to the particular form of imaging (whether CT, MRI, PET, or other). Other preprocessing typically involves general low-level vision methods for filtering and transforming the image data so that they are better visualized and easier to analyze.

Since the early days of computing, researchers have been beguiled by the promise of using computers for automating the recognition of visual patterns. Analogies between human vision and machine vision motivated Rosenblatt's Perceptron [38], the ancestor of today's artificial neural networks. Numerous other pattern recognition methods followed [39] with many being applied to visual problems such as handwriting recognition. In medical imaging, Lodwick [40] used Bayes' theorem for the computer-aided diagnosis of bone tumors with great success, after painstakingly and manually extracting features characterizing these tumors in radiographic images from 2000 cases stored in the Bone Sarcoma Registry of the American College of Surgeons. It is natural to characterize visual objects by sets of features extracted from the natural scene (the X-ray image) in which they are found. Objects are most easily classified by comparing their patterns of features. When the features are noisy and uncertain, this classification approach to pattern recognition is closely related to statistical decision making [39].

When computers became powerful enough, features began to be extracted from image data automatically. In grey-level images, typical features could include measures of the intensity level of an object, descriptions of its boundary, shape, texture, size, etc. It was recognized early that segmentation of an object from its background (everything else in the scene) could be accomplished by either identifying a region in the image corresponding to the object or by first identifying the boundary of the object and then extracting the enclosed region.

Region-based segmentation approaches became popular because they could be easily implemented by thresholding of individual pixel intensity values. This works when object regions have uniformly high contrast in relation to their background (high signal-to-noise ratio), and well-defined edges. Otherwise different strategies of region growing or splitting need to be tried. A recent review can be found in [41]. Boundary-based segmentation is usually more complex, since it requires defining an object boundary in terms of edges detected in the image [42]. Edges can be defined in many ways, the simplest being by thresholding some measure of discontinuity in the intensity values of the image, such as the gradient. In images of natural scenes, edges are frequently complex and noisy, so simple step or ramp models of discontinuities prove to be unrealistic. They may also present in different sizes or scales in different parts of a scene, with resulting difficulties if we wish to apply a single edge-extracting operator during preprocessing to the entire image. An alternative is to detect the most rapidly changing part of an edge through zero crossings of a second derivative function (Laplacian) of the image. To reduce susceptibility to noise it can be combined with a low pass Gaussian filtering function [43]. A further, more tunable improvement is the Canny filter [44]. Besides edges, tissues in medical images may exhibit differences in texture, color, or other more complex features which can be used for discrimination, preferably by multiresolution methods [45,46]. But regardless of the definition of edges and other features, medical images with multiple complex objects and various sources of noise are rarely directly segmentable in their entirety by any single method.

For simple segmentation methods to have a chance of succeeding, images must be filtered first to smooth out noisy (high frequency) edges by low-pass filtering and to enhance true edges by high- or band-pass filtering [39]. The problem, of course, is that it is hard to know a priori how to distinguish true from spurious edges. Despite the availability of many sophisticated statistical models for edges, their applicability to and superiority over other models for particular problems can be ascertained only by carefully controlled empirical testing - which may be feasible with phantoms, but is frequently costly and not practical in clinical situations.

Given the complex dependencies between image formation processes and environments it is hardly surprising that attempts to solve the general automatic segmentation problem have not been very successful. A recent survey of methods for object recognition in 2D images of natural scenes from aerial photometry, industrial inspection, and medicine illustrates the difficulties of choosing computational strategies for solving problems of this type [47]. After characterizing recognition problems in terms of data and matching-model complexity, the authors distinguish four different classes of computational strategies:

1. *Feature vector classification methods*: These apply only to the simplest problems with low data and model complexity (no noise and simple object labeling). They can work directly with the raw data (pixel classification) or with abstracted features or regions derived from them.
2. *Fitting models to noisy image data*: Here spatial constraints describe the expected structure of objects to be recognized and can be either fixed or flexible. In fixed models (like the Hough transform), mathematical operators with predetermined global characteristics must be parameterized for recognition. Flexible models are specified by generic constraints and delineate contours or surfaces of an object. In medical imaging various elastic deformation methods are used to model surface contours [48].
3. *Fitting models to symbolic structures*: Scenes containing multiple and different types of objects are best modeled by descriptions of subparts which are, on the one hand, easily detected from the data and, on the other, easily assembled into the whole scene (i.e., the problem is decomposable, or reasonably so). Recognition can then be carried out by finding efficient search strategies for the best assembly of sub-

parts (or intermediate symbolic structures) that may have generated the image. In medical imaging such situations are rare.

4. *Combined strategies*. With high complexity of both (noisy) data and model, combinations of data-driven and model-driven strategies are suggested, with optimization of some subproblems (like feature extraction) feasible within a generic scheme for recognition. Such approaches characterize the solution of more abstract medical imaging problems - the composition of image processing processes [49], the planning, experimental design, and learning of such compositions [50], and the indexing and retrieval of images according to their subpart arrangements [51].

Based on the above categorization, most 2D medical image recognition work falls into categories 1 and 2, since applications of recognition techniques have traditionally been demonstrated on very specific (and often highly delimited and idealized) imaging problems. While combining strategies has become more frequent in recent years, the computational complexity of most realistic medical image interpretation problems has tended to make their application very specific, and generalizations about broader applicability less than obvious.

A very different perspective from recognition was taken by Marr [52] in his computational theory of vision. Using an information processing approach, he differentiated the issues of vision research according to whether they are at the level of (1) computational theory, (b) representation and algorithm, or (c) hardware. This approach has had a strong influence on the active or purposive vision methods applied particularly in robotics, where a reconstructive, top-down, model-based approach is frequently taken to the design of experiments in machine vision. Such approaches will have increasing relevance to medical imaging when it is embedded within surgical, robotic, and other controlled environments [53]. General mathematical models of vision illustrate clearly how most 2D image recognition problems are ill-posed inverse problems for which we cannot expect to find solutions without severely limiting their generality by problem-, method-, and domain-specific constraints [54].

3. 3-D Medical Image Processing

In contrast to general natural scene recognition, medical imaging does provide fairly strong constraints, particularly if we use a 3D model that corresponds to the true underlying patient environment. Tomographic measurements in particular, yield highly accurate volume-averaged estimates of the values of actual physical properties of the tissue being imaged within each volume element, or voxel, of the body [55].

Unlike general-purpose imaging like photography, medical imaging modalities have usually been specifically refined to discriminate between target tissue types [56]. While still subject to various sources of noise, instrument-induced error, field-of-view artifacts, slicing approximations, inadequacies in resolution, and scene complexity/scaling problems for certain tasks, the interpretation of sets of 2D slice data from most 3D medical image acquisitions presents few problems for the experienced human observer. Automatic 3D object recognition, while still unfeasible, except for very simple objects in standard settings, may finally be on the horizon due to the recent dramatic advances in imaging/computing hardware, graphics, modeling, and visualization software.

For 3D visualization and analysis, 2D data slices must be combined by interpolation [57,58], and corresponding images of different modalities, views or times of acquisition registered [28, 59-61].

Various sophisticated methods for viewing the inherently 3D data on 2D screens have been developed, but generally fall into one of two categories: surface and volume renderings [62-65], though a new shell rendering method combines elements of the two [66]. Fusion of data [67,68] from multiple modalities is also frequently required for display and analysis purposes. Machine architectures that take account of the needs of these computationally intensive methods are reviewed in [69].

A comprehensive overview of 3D imaging can be found in [1]; and [70] lists how various imaging transformations are specified according to their applicability to the acquired data (scene space), the data extracted for viewing (object space), their rotations, scalings, and transformations (image space), and 2D representation on a screen (view space). Transformations for each of these spaces (of scene, structure, geometry, and image, respectively) and mappings between them are described. Mappings are mostly bidirectional, reflecting the emphasis of this work on practical interactive techniques for user-controlled selection of different operators by which images can be transformed for more effective analysis (in a parameter space of chosen models). These operators may be mathematical (such as filtering or feature selection) or graphical (selection of views, subscenes, or rendering methods). The choice of analysis method (segmentation, image transformation) is left largely to the user.

The approach articulated above can be viewed as a new "modular architectural phase" in the development of imaging systems. It has been pioneered by such systems as ANALYZE [23], 3D-VIEWNIX [24], OSIRIS [25] and

VIDA [26]. Various generic methods for visualization, manipulation, and analysis of images are provided as modular software options, reflecting the maturity of the field in recognizing the multiplicity of context-dependent modes of application that are possible for them and the need to have effective flexible imaging tools for use in the practice of radiology. The availability of systems on multiple platforms (from workstations to PCs) at a reasonable cost [71] promises to disseminate these advanced 3D imaging capabilities and methods widely.

While the above represents a retreat from the goal of fully automatic segmentation, it can be seen as a healthy reaction to what is an overambitious and impractical undertaking for most imaging problems. Instead, the user is encouraged to apply different segmentation methods to various subproblems in intermediate stages of processing. Because alternative geometrical models (surface vs. volume, projection vs. slice) can be used to fuse multimodal, multislice, and multiview data spatially at different stages of visualization and analysis, operations of applying filtering, segmentation, feature extraction, and surface or volume estimation and rendering can be applied in different sequences to obtain different results for a given problem [20]. Each sequence represents a different analysis strategy, and the expert image analyst must then choose which of the alternatives to trust the most, or else try to fuse them into a single coherent interpretation. This is currently left to the human expert.

Overall performance results for some combinations of techniques and studies of observer variability have been reported [72,73], but the technology is still too young and evaluation methodologies still inadequate for systematic and controlled experimentation comparing different strategies for a given problem. Just defining what constitutes a class of problems is difficult, as witnessed by the variability encountered in the literature. While evaluation methods from signal analysis in the form of ROC curves can be applied to individual segmentation/ recognition subproblems [74], more sophisticated strategies will be needed to assess complex system usage [75].

In the meantime, each imaging modality (and combination of modalities) continues to be analyzed with various filtering and transformation techniques for particular types of problems. Some applications are more general than others. For instance, an image Eigenfiltering method [76] is reported to be the optimal linear filter for correcting partial volume effects in the fusion of MRI modalities, while at the same time segmenting for a specified feature. Scale-space techniques have been successfully used for interactive segmentation [77], and multiresolution methods like wavelets are gaining in appliability [78]. Neural networks have been applied with increasing frequency to MRI segmentation [79,80]. Morphological [81], geometrical [82], knowledge-directed geometrical modeling [83-85], and knowledge-based frameworks [49,50,86] have been tested with generally successful results for prototype systems.

4. Medical Image Processing and Informatics Implications

All the techniques of medical image processing are directed to achieving goals in medical practice, research, and education. The most dramatic application of the new visualization and analysis capabilities are those involving computer-assisted surgery and teleradiology. This work builds on a decade of experience with surgical planning and simulation guided by 3D imaging [87-89]. With faster imaging modalities and high-performance computing and networking becoming more reliable, cost-effective and ubiquitous, plans are now underway for image-guided surgery through the superimposition of images from prior acquisitions, as well as acquisitions carried out during the course of the surgical procedure [53,90]. Another related area of high visibility and promise is the evaluation and design of prostheses [91], to which is now added the possibility of automatic milling of prostheses by robots.

From an informatics perspective, the explosion of imaging data from practical and research applications poses interesting opportunities and challenges. As cost-effective storage media capacity increases, so will the temptation to store all records digitally. Meaningful, intelligent retrieval can present problems with current techniques of data representation and storage. While ACR-NEMA conventions have helped standardize communication of images between devices, they do not standardize anything about the content of an image. A review of database issues in medical imaging is given in [92]. Indexing and retrieval of structures within images is difficult with most present techniques, which lack representations of visual objects. New methods of representing, indexing, and retrieving pictorial objects are beginning to appear [51,93] and much research is needed on this topic. Object-oriented techniques for representing and manipulating dynamic sequences of visual objects, currently being developed for multimedia applications [94] may well prove to be essential for handling the processes of visualization, manipulation, and analysis of images within an interactively controlled feedback loop of surgical intervention [53].

The construction of digital atlases [3-5] and other sets of visual reference data from the large amounts of imagery being recorded in the Visible Human Project [2] and from other anatomical collections, both human and animal [95], requires research into its registration, structuring, segmentation, visualization, and validation. Tools for navigating through the great volume of visual data are needed [96,97], since such collections can range from the level of gross anatomy down to the cellular level [98]. The possibilities for substantive morphometric analyses [99] increase as large digital image databases are built.

The greatest challenge is to develop techniques for injecting meaning into large image collections through flexible annotations and logs of our "journeys" through them, correlating different functional and structural observations with higher-level conceptual summarizations and interpretations. Developing knowledge-based methods for capturing the semantics of imaging sequences in their many facets and relating them to corresponding information from other sensory channels, promises to open a whole new chapter in informatics: that of imaging.

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