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**3D Informatics: A Research Program in
High Performance Computing;** A report to the
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3D Informatics: A Research Program in High Performance Computing

This report describes ongoing efforts at the Lister Hill National Center for Biomedical Communications and the National Library of Medicine to promote, advance, and to provide leadership in non-text, data-intensive informatics. This program concentrates heavily on information science surrounding image data of 2, 3, and higher dimensions.

Our mission reaches beyond high dimensional image processing or medical computer graphics; it attempts to synthesize semantic information and dynamic user navigation with visualizations created from real medical data. In the cases where we use models of biological structures, all of these models are generated from sources of real data, firmly grounding this work in the practical aspects of medicine.

We have developed a 3D Informatics research program for the gathering, manipulation, classification, storage, retrieval, representation, navigation, and display of complex, high-dimensional medical data. We consider the entire enterprise of medical visualization from data storage and retrieval to the rendering of the final visual presentation; conceived as a pipeline, the process is seen to be connected and yet divisible into separate subfields that can be studied and improved (See Figure 1). Our intention is to perform cutting edge scientific research in particular areas of this pipeline and to incorporate the latest technologies where the application of advanced engineering is appropriate.

This program is not limited to just three dimensions, and we routinely invoke time varying data and multimodal radiological information in our investigations. Much of our work has been performed in collaboration with faculty and research scientists from across the country. One of our aims is to create a laboratory environment that accommodates visiting research faculty, postdocs, and students. Our recent work has been focused in low-level high-dimensional image processing, multiscale geometry and shape analysis, and complex digital modeling using implicit surfaces. We integrate this work with advanced rendering techniques and display technologies to leverage state of the art equipment available at the Lister Hill Center.

1 Background

In 1989, the NLM Board of Regents empowered an ad hoc panel of experts to recommend the position that NLM should take in the rapidly evolving field of electronic imagery.

In August of 1991, the University of Colorado School of Medicine was awarded a contract resulting in the acquisition of the NLM Visible Human Male and Female (VHP) data sets.

NLM then made the data sets available under a no-cost license agreement over the Internet. The VHP male data set contains 1,971 digital axial anatomical images obtained at 1.0-mm intervals (15 Gbytes), and the VHP female data set contains 5,189 digital images obtained at 0.33-mm intervals (39 Gbytes). The optical data is supplemented by a complete series of clinical radiographic data including multiple MRI studies as well as X-ray CT images [Spitzer 96]. Since the introduction of the data sets and the initial licensing by over 1000 worldwide users, four VHP Conferences have been supported by

the NLM. These Conferences have highlighted the importance of sponsoring development of applications of the Visible Human Project.

These data illuminate the need for software tools and methods that admit the analysis, rendering, and visualization of large data that does not fit in core memory. The multi-channel nature of the data also suggests an increasing need for managing multi-valued, rather than scalar, volume data. Beyond the basic processes of rendering anatomical structures from annotated data, there remain the fundamental problems of aligning multimodal data and the extraction of valuable features from the disparate streams of information. Finally, pressure is mounting from quarters such as developmental biology to find new ways to utilize static data such as the VHP male and female datasets in dynamic models that can demonstrate the progression and regression of disease, portray patterns of gene expression over time, and represent physiological processes from biomechanics to electric field propagation in the study of cardiac and neural function. Our emerging program is positioned to address these diverse concerns.

2 Project Objectives

As shown in Figure 1, the flow of information from data acquisition through analysis to presentation can be conceived as a pipeline, passing several stages along the way to visualization. Ultimately, the representation of that information is presented to a human consumer through a digital display. The user can provide cognitive and semantic feedback to the visualization system through interactive user interfaces. A hallmark of the research investigators working on this project is that they each understand the technologies associated with computer graphics and digital displays, allowing us to apply advanced human-computer interface engineering where appropriate. However, technology alone is not sufficient for the visualization of complex, high-dimensional data.

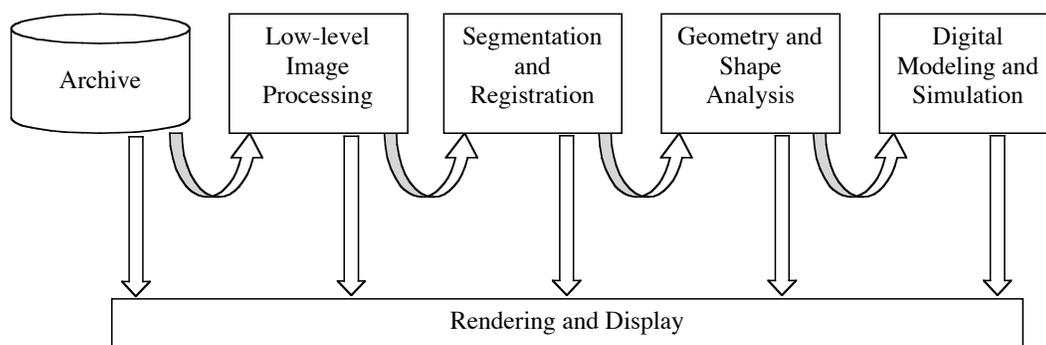


Figure 1. An idealized view of the medical visualization pipeline. The 3D Informatics group is working to study the process of medical visualization by research in the four core areas of Volume Image Archives, Low-level Image Processing, Geometry and Shape Analysis, and Digital Modeling and Simulation. A software toolkit is being created to cover a fifth area in Segmentation and Registration, under the direction of LHC investigators. Please note that the results of many of the subfields can be directly rendered, revealing the information that is hidden within the dataset at different levels of abstraction. One of our goals is to study the progressive abstraction of volume information from image to model.

What is needed is a coherent study of the refinement of the image information through the series of abstractions from data to useful, presentable information, culminating in the synthesis of this information into new knowledge for the user. The general goals of visualization are to create models and abstractions that convey the information buried within the data. We frame the problem as a progression of abstractions:

data \square features \square segments \square shape \square models

Our group has therefore pursued targeted tasks in applied mathematics of specific core areas:

1. Low-level High Dimensional Image Processing
2. Differential Geometry and Shape Analysis
3. Digital Modeling and Simulation
4. Volume Image Archives

A fifth area is being addressed through the development of an open-source toolkit of software components, the Insight Toolkit (ITK). This development is covering the following area:

5. Segmentation and Registration

By covering these core areas, this project is yielding new ideas in the connections between the stages from raw data to new knowledge. Although presented as separate subfields, each of the areas from image processing to digital modeling are interlinked with complex mathematical relationships. By pursuing a comprehensive project, we can study the process itself and the relationships between its many information abstractions.

3 Project Significance

Text-based informatics is far ahead of its visual analogs. No specific disciplines are driven to understand two-dimensional or volume image data in the same way that text may be processed with lexical analysis, parsed for its syntax, and studied using methods for natural language processing to devolve the semantic meanings within. What are available are a series of early models for extracting features from images using transfer functions and low-level image processing, partitioning datasets into cohesive, contiguous regions using segmentation, studying the shape properties and generating digital models of objects, and presenting these objects to expert users for study and knowledge integration. It is the passing of information along this progression: feature extraction to segmentation to shape analysis to digital modeling that is not well studied today. We hope to contribute new techniques in the management of the interfaces and abstract models passed along this progression, thus contributing significantly to the field of image understanding. We believe that the area of connecting medical volume data, visualization, user interaction, and data modeling is relatively young, making leadership and salient change possible from a project such as ours.

Our success in attracting visiting researchers and sponsoring collaborative research has been demonstrated in the past few years as our program has been building upon a collection of completed studies. Over the past four years we have successfully brought in two visiting computer science associate professors in a total of four summer appointments; we have conducted a research study with two NLM Library Associate Fellows; we have executed and published a case study with a medical doctor who is now in residency in radiology at the Mayo Clinic; and we have pursued and published at peer-reviewed conferences individual projects with summer graduate and undergraduate student interns. For the summer of 2003, our project attracted direct applications from two computer science faculty members, three graduate students, and three summer undergraduate interns. Leadership and significance of this research area may be reflected in the growing interest in this project.

4 Low-Level High-Dimensional Image Processing

A first task in medical visualization is the extraction of image features for higher level processing. This is an elementary analysis of the data, providing the building blocks for greater associations and abstractions to be constructed. In the context of complex multichannel data such as the color cryosections of the Visible Human Project data, low-level image processing problems become non-conventional arising from the relatively unique properties of the input dataset.

4.1 Multiscale Image Statistics

Instead of concentrating directly on the geometric analysis of image intensities in areas such as edge detection and watershed feature analysis, our current research has been developing *multiscale image statistics*, a new model for low-level vision. This model is a scale-space approach to low-level vision. Specifically, we have been working to understand how an image understanding model can employ a variety of resolutions governed by a regular tempered distribution, suggested by the Gaussian function as a regularizing sampling kernel. This approach precludes other approaches such as the coarse-to-fine pyramid analysis systems and wavelet based methods. Koenderink suggested applying a Gaussian filter at multiple apertures as a method for generating a rich higher dimensional space for analyzing structure. This mechanism has been suggested as a vehicle for emulating the overlapping visual fields of a retinal vision system [Koenderink 87]. Scale space methods are supported by an extensive mathematical structure [Lindeberg 92, Eberly 94]. Unlike related methods based on the scale-space derivative models of Florack and ter Haar Romeny, [ter Haar Romeny 91, Florack 94] our research incorporates local statistics of image intensities [Yoo 96].

This characterization, that low-level vision can be studied as a multilocal statistical process is a novel idea, though with firm grounding in earlier theoretical discussions of biological vision. What we have added are solvable implementations for applying these models to medical data. Moreover, it is important to introduce the calculus of statistics in order to capture the behavior of non-Euclidean information represented by multichannel (e.g., RGB color) or multimodal data (e.g., registered CT and MRI

information). The concept of *derivative* or *vector*, may not be sensible in nonlinear data spaces. However, the statistical notions of *correlation*, *covariance*, and *entropy* have been proven to be very powerful in describing the behavior of collections of data values. This study has investigated the relationships between local geometry and local statistics, attempting to extract image features for high level aggregation into segments, partitions, and image models.

Procedures and Methods for Multiscale Image Statistics

We begin with the notion that the common convolution operation can be used to create measurement of local population of image values. Written mathematically, convolution is an integration of a kernel function φ , with an image function, I .

Consider a set of observed values, $I(x)$ $\in \mathbb{R}$, where for purposes of discussion the location $x \in \mathbb{R}^n$, but can easily be generalized to \mathbb{R}^n . The values of $I(x)$ may be sampled over a local neighborhood about a particular location x using a weighting function, $\varphi(x)$, and the convolution operation, $I(x) \otimes \varphi(x)$, where

$$I(x) \otimes \varphi(x) = \int_{\mathbb{R}^n} \varphi(\Delta) I(x + \Delta) d\Delta = \int_{\mathbb{R}^n} \varphi(x - \Delta) I(\Delta) d\Delta \quad (1)$$

To avoid a preference in orientation or location, the sampling function should be invariant with respect to spatial translation and spatial rotation. Arguments put forward by the scale-space community [Koenderink 87, ter Haar Romeny 91, Florack 94] suggest that the optimal sampling function is the Gaussian $G(\Delta, x)$, where the parameter Δ is the sampling aperture.

$$\varphi(x) = G(\Delta, x) = \frac{1}{\Delta \sqrt{2\pi}} e^{-\frac{x^2}{2\Delta^2}} \quad (2)$$

Let the scale-space measurement comprising a sum of the original image intensities weighted by a Gaussian sampling kernel be the average or expected value of $I(x)$ over the neighborhood with an aperture of size Δ . Thus:

$$\begin{aligned} \langle I(x); \Delta \rangle &= \int_{\mathbb{R}^n} G(\Delta, x + \Delta) I(\Delta) d\Delta \\ &= I(x) \otimes G(\Delta, x) \end{aligned} \quad (3)$$

where $\langle I(x); \Delta \rangle$ is read as mean or the expected value of $I(x)$ measured with aperture Δ .

The local variance over the neighborhood specified by the scale parameter is easily generalized from the basic definition of central moments. Equation (4) describes the local variance of intensity about a point x at scale Δ .

$$\begin{aligned} \langle I^2(x); \Delta \rangle &= \left\langle (I(x) \otimes \langle I(x); \Delta \rangle)^2; \Delta \right\rangle \\ &= \int_{\mathbb{R}^n} G(\Delta, x + \Delta) (I(\Delta) \otimes \langle I(x); \Delta \rangle)^2 d\Delta \\ &= G(\Delta, x) \left(I(x)^2 \otimes \langle I(x); \Delta \rangle^2 \right) \end{aligned} \quad (4)$$

The significance of these derivations is that higher-order local statistical moments can be described as an algebraic combination of convolution or filtering operations. Such filtering operations are mathematically tractable and can be accelerated through common software methods or improved through the application of commonly available graphics and image processing systems.

Results of Image Statistics from Single Channel Images

Local variance of pixel or voxel values has a straightforward interpretation. In local regions with only intensity variations arising from scanner noise, the operation measures the variation in what should otherwise be a uniform signal. However, at boundaries between two signals, as in the interface between two biological tissues or the boundary between air and the scanned subject, the variance increases dramatically as the histogram of the local pixel values becomes distinctly bimodal. This behavior of the variance operator causes it to act like an edge detector. Figure 2a shows an axial Proton Density-Weighted MRI image from the Visible Human Project male datasets. After applying a variance filter with a Gaussian aperture with $\sigma=2$ pixels, the resulting output is shown in Figure 2c. Similarly, Figure 2b shows the red channel of the VHP male cryosection from a comparable slice, and Figure 2e shows the output after a variance filter is applied. In both cases, the output of the variance filter can be seen to act as an edge detector.

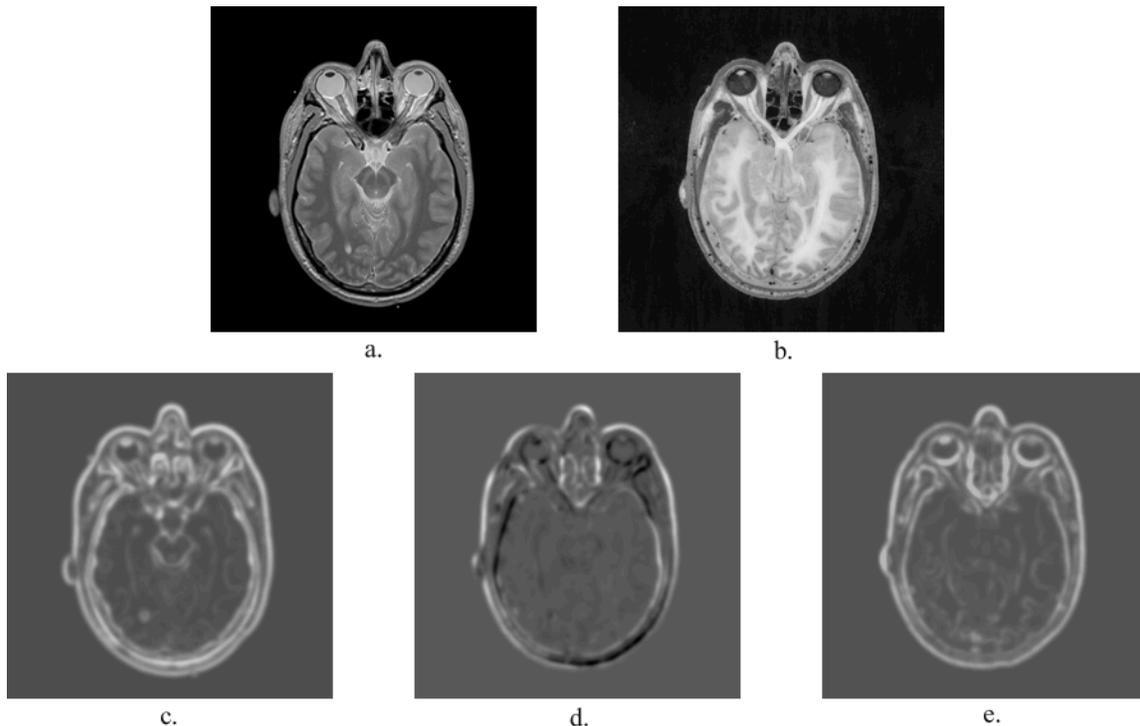


Figure 2. Multiscale statistics of a multimodal image from the Visible Human Project data. Figs. 2a and 2b are a PD weighted MRI image and the red channel of the corresponding cryosection data, respectively. Figs. 2c and 2e are variance measures of the respective source images. Fig. 2d is the local covariance measure of the two data slices. In all cases, $\sigma=2$ pixel-widths.

4.2 Multimodal Scale-Space Image Statistics

The power of applying statistical methods to multiscale image analysis arises when complex, multivalued data are considered. Multimodal image processing requires alignment or registration of the multiple scans. The physics of different scanning modalities guarantees that the values for the separate data values have nonlinear, incommensurable values. Image statistics have been successfully applied to whole datasets, using the entire image as the input domain when mapping one image scan to another. In cases where the alignment of the multiple datasets requires a warping or deformable map, more robust registration metrics are required.

Multimodal Procedures and Methods

Statistical pattern recognition techniques are commonly used on multivalued data; however, they rely on registered datasets. Viola and Wells show how statistical metrics have been devised to measure the quality of a registration. Mutual information has been applied to the histograms, scatterplots, and feature spaces of multimodal data as a metric to measure the fit between the two images [Viola 1997]. Figure 3 shows a framework for an iterative registration scheme; in the Viola-Wells method, a mutual-information metric is applied to measure the match between the two input images. Progressive refinement of the transform that is applied to the moving image incrementally improves the match until the two images converge and the algorithm reaches its stopping threshold.

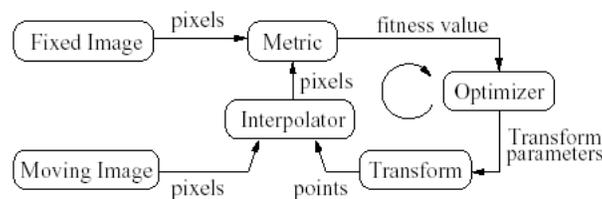


Figure 3. Schematic of an iterative approach for the registration of two images. The term image is not limited to two dimensions. Rather it is most commonly applied in three dimensions in medical cross-sectional data.

Most of the published literature on image-to-image registration techniques apply rigid or affine transforms to match one image to another. Deformable registration techniques, which warp one image to another are largely landmark based, using thin-plate splines to create continuous, deformable warps or transforms from one image to another. Image-to-image techniques perform better than landmark-based methods; image-to-image registration metrics employ the entire image in computing the quality of the fit. We are attempting to blend the best qualities of deformable point-based registration methods and image-based metrics. We are applying multiscale image statistics to create a framework for deformable image-to-image registration.

Results of Multimodal Covariance between Images

The equation for variance within an image can be extended to compute the covariance between images. This value can be computed and combined with the intra-image variance. Figure 2d shows the multiscale covariance image between the PD-MRI image

(Figure 2a) and the red channel of the color cryosection data (Figure 2b). Dark areas reflect negative covariance, and bright areas show positive covariance. The inter-image covariance data reveals not only misregistration between the two images, it reflects the direction of the shift. Local multimodal image covariance is the basis for a new image-to-image deformable registration method. This work was published in an invited paper at the international High Care 2000 conference in Bochum, Germany [Yoo 2000].

4.3 Image Processing of Color Spaces

Beyond multiscale image statistics, low-level image processing of complex multi-channel data can also be addressed by analyzing the parameterization of the inherent data spaces. Color spaces and color representations have been exhaustively studied, and their parameterizations can be used in feature extraction and image analysis. The color channels generated as part of the Visible Human Project data represent valuable information that is often difficult to exploit. We have undertaken the exploration of rendering color image data, using the multiple channels in the representation. This work was executed in collaboration with Dr. Ebert (Purdue University) and Dr. Rheingans (University of Maryland Baltimore Count) who together had an existing software rendering system and expertise in color space manipulation, respectively. Dr. Yoo provided the mathematical foundations for understanding volume gradients of color images.

The original digital photographic Visible Human Project data is composed of 8-bit R, G, and B color values. While structures of interest are readily apparent to the anatomically trained eye, automatically identifying image features is more difficult. We base our approach on the characteristics of human vision, not because that is the only possible approach, but because human vision demonstrably works on these images. Our approach draws from the functions of very low-level vision, concentrating on basic changes in the visual field.

Since the RGB color space does not correspond to human visual perception, we chose to explore the CIE $L^*u^*v^*$ (abbreviated CIELUV) color space to obtain a perceptually uniform representation of the color volume. A perceptually uniform color space has the characteristic that equal distances in the color space correspond to equal perceptual differences, at least for reasonably small distances. This allows us to computationally estimate the perceptual difference between two image samples by simply computing the Euclidean difference in color space. Using a perceptually uniform color space for feature calculations allows us to emphasize those features which are noticeable in the photographs, providing an analysis that is more consistent with features detected by human vision than an analysis generated from a device-derived color space such as RGB which would over-emphasize changes in blue content and bright regions. The CIELUV color space, also offers the advantage that chromatic and achromatic components of color are described by orthogonal color space dimensions. This feature allows us to experiment with biased weighting of the chromatic and achromatic color components, just as the human visual system performs certain scene understanding tasks with segregated achromatic and chromatic color information.

Procedures and Methods for Feature Extraction from Multichannel Color Images

Color space conversions were performed using the methods of Hall [Hall 1989]. Because precise specifications of the color primaries of the image data were not directly available, we approximated them by the NTSC standard primaries. Specification of the image data color primaries is indirectly available from the color calibration card included in each photograph. Analysis of the RGB values for these physically measurable colors could provide the required calibration information. Although deviations of actual primaries from these are expected to be modest, this approximation does not guarantee the correct absolute CIELUV coordinates for voxels, compromising the device independence of the color space. For color reproduction applications, this would be a problem, but, for the purposes of detecting color structure in an image, it is not. We require relative differences.

For color photographic volume data represented in CIELUV space, every voxel location is mapped to a color, represented by three separate values. Given $\text{color_vol}[x][y][z]$, a volume of color datapoints, imagine its image generating function $C(x, y, z)$ such that for every voxel location $[x_i][y_i][z_i]$,

$$\text{color_vol}[x_i][y_i][z_i] = C(x_i, y_i, z_i) = (L_i, u_i, v_i), \quad (5)$$

As we mentioned before, CIELUV space has reparameterized color space so that for unsaturated colors, the perceptual distances between two colors is, to a good approximation, proportional to the length of the straight line joining them. In other words, the color space is approximately locally linear. We therefore consider color values in CIELUV space as color vectors. Given this assumption, color differences can be measured with respect to spatial location. For instance consider the difference between a color voxel value $C(x_i, y_i, z_i)$ and the color from a neighboring location measured at a distance, h , along the x direction, $C(x_j, y_j, z_j)$ where $x_j = x_i + h$, $y_j = y_i$, and $z_j = z_i$. The color difference is expressed as:

$$C(x_j, y_j, z_j) - C(x_i, y_i, z_i) = C(x_i + h, y_i, z_i) - C(x_i, y_i, z_i) = (L_j, u_j, v_j) - (L_i, u_i, v_i) \quad (6)$$

Note that the difference of two adjacent colors is itself a color vector. That is:

$$(L_j, u_j, v_j) - (L_i, u_i, v_i) = (L_j - L_i, u_j - u_i, v_j - v_i), \quad (7)$$

As h is reduced and made infinitesimally small, we derive the partial derivative of $C(x, y, z)$ with respect to x . That is,

$$\frac{\partial}{\partial x} C(x, y, z) = \lim_{h \rightarrow 0} \frac{C(x, y, z) - C(x + h, y, z)}{h} = \left[\frac{\partial}{\partial x} L(x, y, z), \frac{\partial}{\partial x} u(x, y, z), \frac{\partial}{\partial x} v(x, y, z) \right] \quad (8)$$

As in the case with volume of scalar values, the combined partial derivatives of $C(x, y, z)$ in the x , y , and z directions results in $\nabla C(x, y, z)$, the gradient of $C(x, y, z)$. Since each partial derivative is a color vector, $\nabla C(x, y, z)$ is a tensor, a vector of 3 color vectors.

$$\nabla C(x, y, z) = \begin{bmatrix} \frac{\partial}{\partial x} C(x, y, z) \\ \frac{\partial}{\partial y} C(x, y, z) \\ \frac{\partial}{\partial z} C(x, y, z) \end{bmatrix} \quad (9)$$

Extending the analogy from the scalar case, we can evaluate the magnitude of $\nabla C(x, y, z)$ by taking its tensor dot product. This is accomplished by multiplying $\nabla C(x, y, z)$ with its transpose $\nabla C(x, y, z)^T$, resulting in \square , the “magnitude matrix,” a 3 \times 3 matrix. Mathematically:

$$\square = (\nabla C(x, y, z))(\nabla C(x, y, z))^T = \nabla C(x, y, z) \cdot \nabla C(x, y, z) \quad (10)$$

We can extract useful geometry from the tensor gradient magnitude matrix \square . Diagonalizing the gradient magnitude matrix generates the eigenvalues that represent the primary measure of boundariness, denoting interfaces and natural partitions in the color volume data.

Results of Color Feature Extraction

Figure 3 shows some resulting images from the volume rendering of color data using the transfer functions created from our color space analysis functions. We compare the color

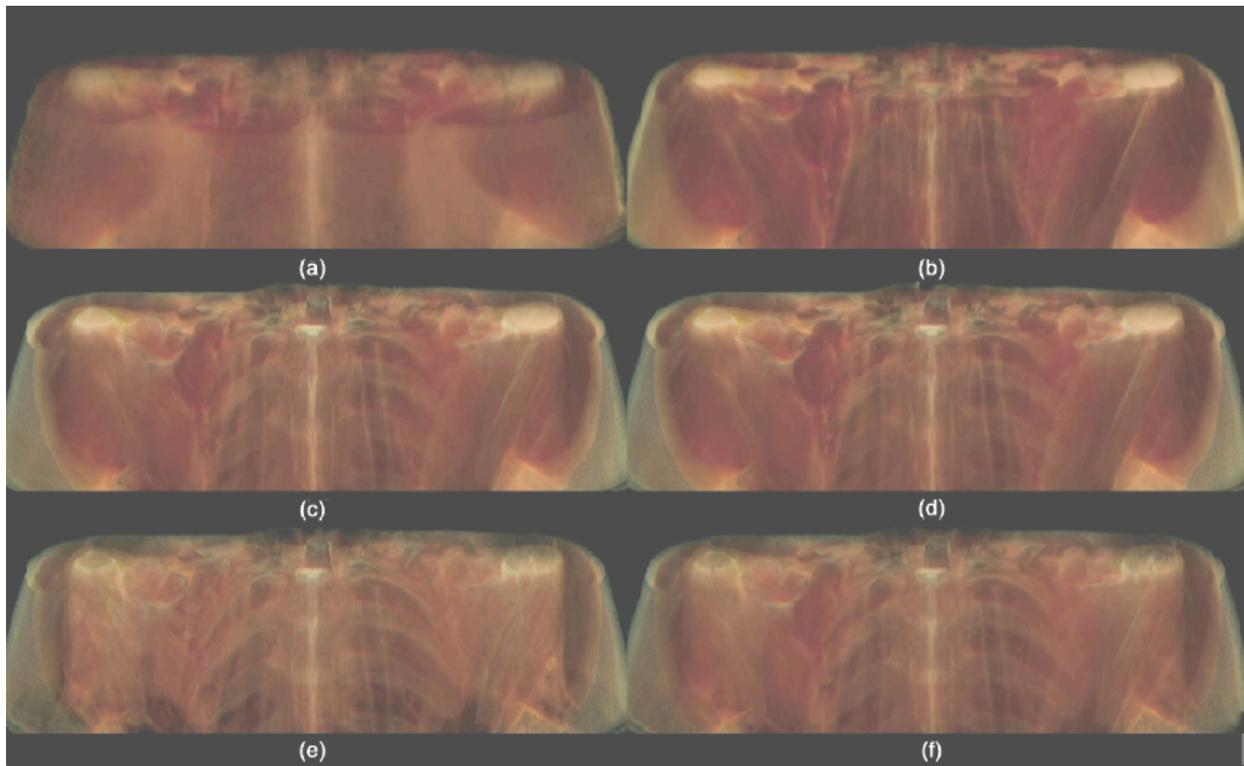


Figure 3. Volume Rendering of 64 slices of the Visible Human Project male dataset. (a) Opacity determined by CIE $L^*u^*v^*$ color component. (b) More opaque rendered, cutaway view with opacity determined by CIE $L^*u^*v^*$ color component. (c) Cut away view with opacity for RGB color distance gradient and product. (d) Cut away view with opacity from CIE $L^*u^*v^*$ color distance gradient dot product. (e) More transparent cut away view with opacity from RGB color gradient dot product. (f) More transparent cut away view with opacity from CIE $L^*u^*v^*$ color gradient dot product.

gradient magnitude matrix as applied to CIELUV perceptually uniform color space with the color gradient magnitude of RGB machine-derived color space. Figure 3 shows different transfer functions applied to the upper thoracic region of the Visible Human Project male dataset, highlighting musculature, bone, and other tissue types differently. While there are subtle differences between the color spaces and their color gradients, the behavior of the transfer functions from the RGB color gradient is not always predictable, while the perceptually uniform CIELUV color gradients yielded less capricious more intuitive results. This work was published at both the IEEE TCVG Symposium on Visualization [Ebert 2000] as well as in the journal, IEEE Transactions on Visualization and Computer Graphics [Ebert 2002].

5 Differential Geometry and Shape Analysis

In the progression of information abstraction from raw data to higher-level representation, shape analysis must follow the low-level extraction of features based on local statistics or the geometry of local image intensities. The concept of *features* does not have sufficient power to circumscribe the problems of shape description. Features generated by low level vision can support the next higher process of shape analysis, but cannot alone serve as the primitives or building blocks of shape description. Shapes are described, not by brightness differences, but rather by the manifolds and surfaces that bound them. In this work, we extend the descriptive power of multiscale methods to the study of surface geometry.

5.1 Multiscale Shape Operators for Sampled Manifolds

Computer vision attempts to create models from input images, while computer graphics attempts the inverse process of using models to generate output images. Our shape analysis work applies scale-space concepts to neither the input nor output images, but to the geometric models that are the intermediate abstractions of both fields. We have developed a multiscale shape operator for sampled manifolds based on Monte Carlo sampling and numeric differentiation. By varying the aperture of our differential geometric measuring tool, we analyze second-order properties of the surface, discriminating surface features from noise as well as ranking features according to shape saliency across scale. The resulting differential attributes allow the scale-space of shape to be considered in computer graphics algorithms such as polygonal simplification, geometric smoothing, and constraint selection for implicit surfaces used in medical visualization.

5.2 Design of Scale-Space Shape Operators

By exploiting the linear properties of the shape operator, we construct a least-squares approximation. A similar formulation has been described in Taubin [Taubin 1995] and Meyer *et al.* [Meyer 2002]. Our method differs by using Monte Carlo sampling that avoids the need to weight the approximations by their area, and incorporates the linear properties of the shape operator to enable the inclusion of sample points that are further

away. Previous least squares methods have been robust in principal direction estimation, but this new method, while similarly robust, also explicitly has scale as a parameter. Given a manifold, M , to compute the shape operator at a point $\mathbf{p} \in M$, we begin by computing the local neighborhood of points around \mathbf{p} . This set will be $Q = \{\mathbf{q}_i : 0 \leq i < m_q\}$. Initially consider Q to be all the sampled points that are “near” to \mathbf{p} .

The point \mathbf{p} has an associated normal vector n_p in the tangent space $\{U_1(\mathbf{p}), U_2(\mathbf{p}), U_3(\mathbf{p})\}$. We then choose another basis for the tangent space $B_1 = \{n_p, e_1(\mathbf{p}), e_2(\mathbf{p})\}$ where $e_1(\mathbf{p})$ and $e_2(\mathbf{p})$ are arbitrarily chosen only to form an orthonormal basis. Then the tangent plane of \mathbf{p} , T_p is the space spanned by $\{e_1(\mathbf{p}), e_2(\mathbf{p})\}$. Consider the differentiable situation where $N(\mathbf{p}) = n_p$ is the unit normal vector field. The shape operator of $(\mathbf{p} - \mathbf{q}_i)_p$, a vector in the tangent plane T_p is

$$S_p((\mathbf{p} - \mathbf{q}_i)_p) = S_p(\mathbf{v}_p) = \begin{bmatrix} \frac{\partial(N(\mathbf{p}) \cdot e_1)}{\partial e_1} & \frac{\partial(N(\mathbf{p}) \cdot e_1)}{\partial e_2} \\ \frac{\partial(N(\mathbf{p}) \cdot e_2)}{\partial e_1} & \frac{\partial(N(\mathbf{p}) \cdot e_2)}{\partial e_2} \end{bmatrix} \begin{bmatrix} \mathbf{v}_p \cdot e_1 \\ \mathbf{v}_p \cdot e_2 \end{bmatrix} \quad (11)$$

We then can apply numerical difference methods to differentiate our sampled manifold, resulting in

$$S_p((\mathbf{p} - \mathbf{q}_i)_p) \approx \begin{bmatrix} \frac{(\mathbf{n}_p - \mathbf{n}_{q_i}) \cdot e_1}{(\mathbf{p} - \mathbf{q}_i) \cdot e_1} & \frac{(\mathbf{n}_p - \mathbf{n}_{q_i}) \cdot e_1}{(\mathbf{p} - \mathbf{q}_i) \cdot e_2} \\ \frac{(\mathbf{n}_p - \mathbf{n}_{q_i}) \cdot e_2}{(\mathbf{p} - \mathbf{q}_i) \cdot e_1} & \frac{(\mathbf{n}_p - \mathbf{n}_{q_i}) \cdot e_2}{(\mathbf{p} - \mathbf{q}_i) \cdot e_2} \end{bmatrix} \begin{bmatrix} 2\mathbf{n}_{q_i} \cdot e_1 \\ 2\mathbf{n}_{q_i} \cdot e_2 \end{bmatrix} \quad (12)$$

This is an approximation to the shape operator in one specific direction. We then construct an over determined set of linear equation with the rest of Q ,

$$\begin{bmatrix} (\mathbf{p} - \mathbf{q}_0) \cdot e_1 & (\mathbf{p} - \mathbf{q}_0) \cdot e_2 \\ (\mathbf{p} - \mathbf{q}_1) \cdot e_1 & (\mathbf{p} - \mathbf{q}_1) \cdot e_2 \\ \vdots & \vdots \\ (\mathbf{p} - \mathbf{q}_{m_q}) \cdot e_1 & (\mathbf{p} - \mathbf{q}_{m_q}) \cdot e_2 \end{bmatrix} S_p \begin{bmatrix} 2\mathbf{n}_{q_0} \cdot e_1 & 2\mathbf{n}_{q_0} \cdot e_2 \\ 2\mathbf{n}_{q_1} \cdot e_1 & 2\mathbf{n}_{q_1} \cdot e_2 \\ \vdots & \vdots \\ 2\mathbf{n}_{q_{m_q}} \cdot e_1 & 2\mathbf{n}_{q_{m_q}} \cdot e_2 \end{bmatrix} \quad (13)$$

We then use a least squares method to find the best shape operator for our approximations. Once the approximate S_p has been found, the principal curvatures and the principal directions can be computed. This is equivalent to solving for the eigenvalue and eigenvectors of S_p . Since S_p is a two by two matrix, a quadratic close form solution exists for the principal curvatures and the corresponding eigenvectors. Unfortunately our formation of the problem does not guarantee that S_p is a symmetric matrix; the principal curvatures could be the equal, making it impossible to solve. The symmetry problem is solved by averaging the appropriate elements.

This method is equivalent to least squares fitting a quadratic to the surface M that must go through p and have the normal n_p . It is not a fit for the points but rather a fit for the normal vectors, since each point is implicitly projected onto the tangent plane. We now refine the set Q . Each surface element is randomly resampled with a uniform distribution at a user defined density. The normal vectors are linearly interpolated between the samples. The user specifies the radius of the local neighborhood and the set Q is selected from the randomly generated points that are within the specified radius. This ensures the local neighborhood is uniformly sampled and the shape operator is the best fit for the surface in that neighborhood. The size of the neighborhood corresponds to a measurement aperture for the sampling process. Expanding the sampling radius decreases the compactness of the sampling operation. Increasing the sampling density increases the local support. These combined variables create control parameters that can be used to create a scale-space analysis of approximate shape.

5.3 Results of Scale-Space Shape Operators Applied to CT Data

We have begun exploring the use of these sampling operators of varying aperture to evaluate the saliency of shape features as tools for mesh modification or object registration. Figure 4 shows the structure of local geometry as a shape operator of increasing aperture is applied to a CT scan of a tooth. Viewing the figure from left to right shows that given noisy data, noise in the surface description can be suppressed and primary features extracted. The shape features to note are the persistence of the saddle shaped region at the top of the tooth that remains stationary even in the face of varying scale. Small features do not show the same scale invariance. This work is described in a manuscript that was submitted for publication at the international Scale Space 2003 symposium [Lowekamp 2003].

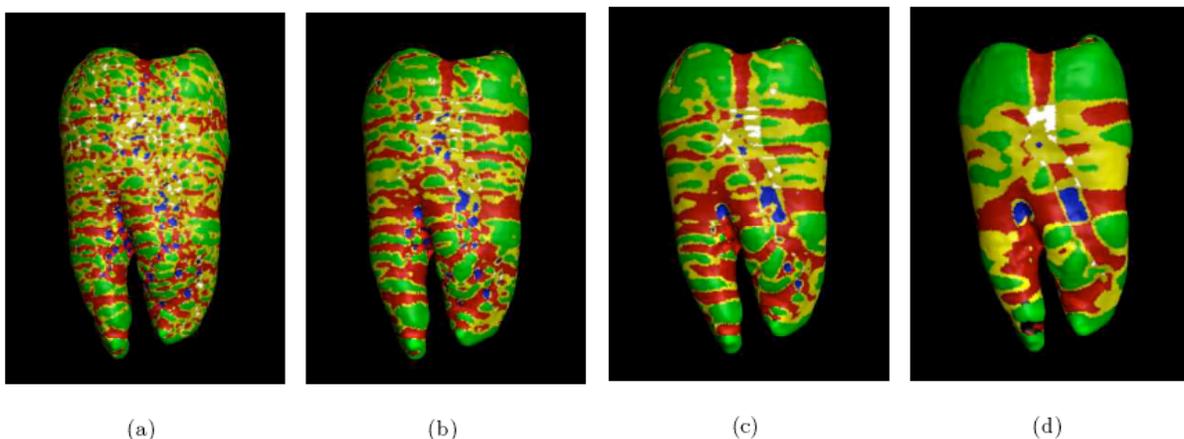


Figure 4. Classification of surface curvature with respect to scale on the tooth model. The original data was generated using an industrial CT scan of a human tooth. The sampled manifold model has been scaled to $_t$ in a unit cube. The data is courtesy of GE Aircraft Engines, Evendale, Ohio. Classification of the surface curvature is labeled by color, green is convex, blue is concave, yellow is cylindrical and red is saddle shape. The apertures for the figures: 3(a) 0.02, 3(b) 0.04, 3(c) 0.06, 3(d) 0.10. Note that although we are using a scale-space method to interrogate surface curvature, the object shape does not change with the scale parameter.

6 Digital Modeling and Simulation

To this point, we have described a progression from raw image data through local feature extraction to the description of geometric patches of surface shape. The topological properties of these surface shape patches have powerful descriptive properties of an object. However, we still require a compact description of objects themselves. The causal chain of object description and recognition must have a higher-level concept to encompass entire objects, and not just the patches that are used to construct them. The process of modeling objects is therefore part of our research domain in our comprehensive coverage of core areas of 3D informatics.

6.1 Data Driven Implicit Modeling

In recent years, implicit surfaces have emerged as an important method in computer graphics research. Most work in this area has been directed toward artistic modeling; however, Savchenko, *et al.* [Savchenko 1995] and Turk and O'Brien [Turk 1999] independently derived a method for creating interpolating implicit surfaces from constraints derived from real data. Their derivations begin with differing assumptions and base their mathematics on slightly different premises (Savchenko argues for the use of Green's function while Turk and O'Brien derive their work from the variational properties of thin-plate splines). However, their results are essentially identical yielding a linear algebraic method for solving a simultaneous system of equations to generate an implicit surface that interpolates constraining data points.

6.2 Variational Methods and Tools

An *implicit surface* is defined by $\{x: f(x) = k\}$, $k \in \mathbb{R}$, for some characteristic embedding function $f: \mathbb{R}^3 \rightarrow \mathbb{R}$. Given a set of surface points $C = \{\mathbf{c}_1, \mathbf{c}_2, \mathbf{c}_3, \dots, \mathbf{c}_n\}$, the variational implicit technique interpolates the smoothest possible scalar function $f(x)$ whose zero level set, $\{x: f(x) = 0\}$, passes through all points in C . That is, find the smoothest function f such that $f(x_i) = 0$ for each known surface point x_i , and $f(y_i) = 1$ for one or more points y_i known to be inside the shape. Following Turk and O'Brien's generalization of the problem, given a set of positions \mathbf{c}_i and corresponding values h_i , solve for an embedding function f such that $f(\mathbf{c}_i) = h_i$, by employing radial basis interpolating functions $\varphi(r)$ in a critically constrained linear system of n equations and n unknowns. Specifically, given a radial basis interpolating function $\varphi(r)$ and a series of known points where the desired function f is constrained to be $f(\mathbf{c}_i) = h_i$, solve the following equation for the unknown weights d_j .

$$f(\mathbf{c}_i) = \sum_{j=1}^n d_j \varphi(\|\mathbf{c}_i - \mathbf{c}_j\|) + P(\mathbf{x}) = h_i \quad (14)$$

Expanding $\mathbf{c}_i = (c_i^x, c_i^y, c_i^z)$, the entire linear system can be expressed as an $(n+4) \times (n+4)$ matrix M where:

$$\begin{bmatrix}
 \phi_{11} & \phi_{12} & \dots & \phi_{1n} & c_1^x & c_1^y & c_1^z & 1 \\
 \phi_{21} & \phi_{22} & \dots & \phi_{2n} & c_2^x & c_2^y & c_2^z & 1 \\
 \vdots & \vdots & \ddots & \vdots & \vdots & \vdots & \vdots & \vdots \\
 \phi_{n1} & \phi_{n2} & \dots & \phi_{nn} & c_n^x & c_n^y & c_n^z & 1 \\
 c_1^x & c_2^x & \dots & c_n^x & 0 & 0 & 0 & 0 \\
 c_1^y & c_2^y & \dots & c_n^y & 0 & 0 & 0 & 0 \\
 c_1^z & c_2^z & \dots & c_n^z & 0 & 0 & 0 & 0 \\
 1 & 1 & \dots & 1 & 0 & 0 & 0 & 0
 \end{bmatrix}
 \begin{bmatrix}
 d_1 \\
 d_2 \\
 \vdots \\
 d_n \\
 p^x \\
 p^y \\
 p^z \\
 1
 \end{bmatrix}
 =
 \begin{bmatrix}
 h_1 \\
 h_2 \\
 \vdots \\
 h_n \\
 0 \\
 0 \\
 0 \\
 0
 \end{bmatrix}
 \quad (15)$$

The resulting matrix is known to be positive semi-definite, and can be solved with a linear decomposition system. Once the weights d_i are found, the embedding function can be written as:

$$f(\mathbf{x}) = \sum_{j=1}^n d_j \varphi(\|\mathbf{x} - \mathbf{c}_j\|) + P(\mathbf{x}) \quad (16)$$

Depending on the differentiability of the radial basis function, $\varphi(r)$, $f(x)$ is an implicit surface generating function that can be resampled with arbitrary precision and remains invariant under rotation, translation, and zoom. (For most of this work, we have used the same radial basis function, $\varphi(r) = r^3$ for $r \geq 0$, used by Turk and O'Brien from related research on thin-plate splines.) If the constraints c_i for $f(x)$ are abstracted from either a grey-level or a binary bit mask volume sampled volume, the resulting variational implicit surface is a more compact analytical representation of the same data.

The radial basis function, $\varphi(r) = r^3$ for $r \geq 0$, advocated by Turk and O'Brien is infinite in extent. It has advantages when interpolating across unpredictable spans, making it ideal for morphing and shape interpolation. However, the infinite extent leads to ill-conditioned matrices and increased computational complexity. A naïve approach is easily order $O(n^3)$.

In related work, we address the computational complexity of variational implicit surface modeling. Instead of $\varphi(r) = r^3$ as the underlying interpolant, we select from among a family of radial basis functions to find a function with the necessary continuity but also with finite, compact local support. Figure 5 shows a comparison of the 3D thin-plate-spline radial basis function and the suggested compactly supported radial basis functions of our current research. The shift from a radial basis function of infinite extent to one that has compact local support has created dramatic gains in memory utilization and computational complexity. Previous work described solutions for systems of equations of order $O(n^3)$ complexity with iterative solutions capable of achieving order $O(n^2)$. The shift to finite interpolants and sparse matrices has shifted the bulk of the computation toward order $O(n)$, depending on the complexity of the model and the uniformity of the density of the surface constraints. We have measured the complexity of the matrix solution for some test cases as $O(n^{1.5})$. For more details, see Morse [Morse 2001].

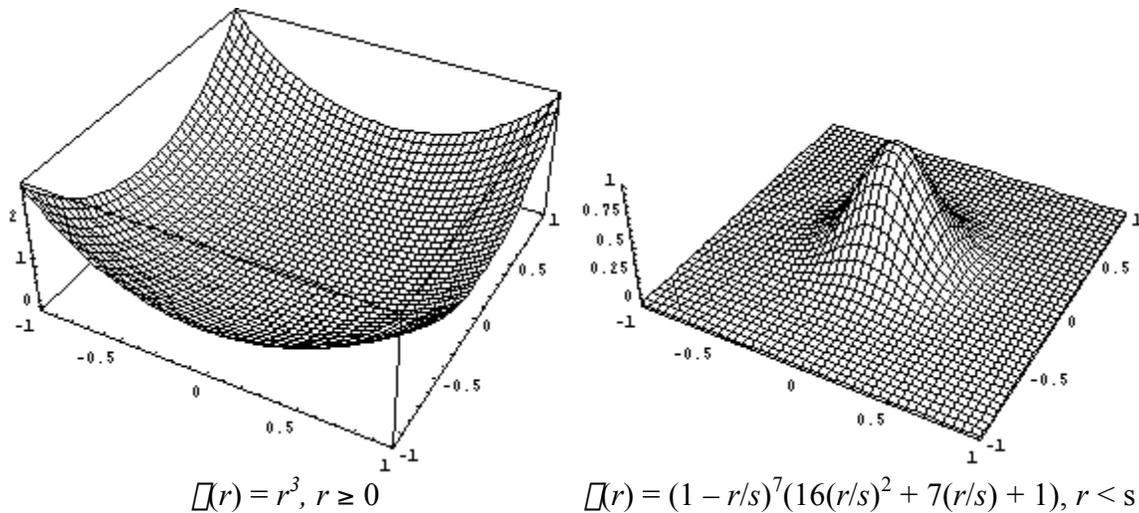


Figure 5. Two radial basis functions. The left function $\varphi(r) = r^3, r \geq 0$ has infinite extent. The right function $\varphi(r) = (1 - r/s)^7(16(r/s)^2 + 7(r/s) + 1)$ is clamped to zero outside a specified radius of support s , and is proven to be C^4 continuous. The compactly supported function on the right leads to more stable numerics and faster solutions of the variational implicit surface model.

The use of compactly supported radial basis functions imposes a restriction on the maximum distance allowed between systems of surface constraints. This trade-off between speed and the granularity of the surface samples is the topic of some of our future research in this area. The infinite radial basis function permits interpolation across wide spans and with arbitrary orientations to the subsets of constraints that comprise the initial surface description. However, the costs of using this system rise with the number of points required to faithfully represent the surface. This trade-off has ramifications in the choice and precision of the segmentation algorithm to be used and the complexity of the objects to be represented.

6.3 Results: Data Driven Implicit Surfaces

We have applied this method to the modeling of a bovine aorta from data acquired using an intravascularultrasound transducer. This particular modality acquires noisy 2D image slices, sampled at uneven intervals with non-parallel orientations. The transducer is drawn slowly through the vessel, acquiring cross-sectional sonographic images (see Figure 6).

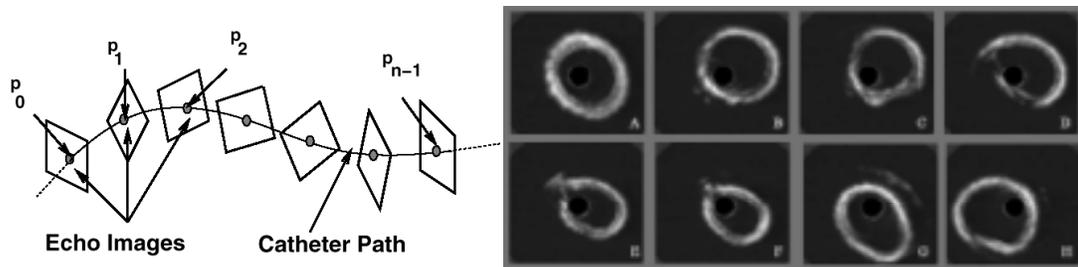


Figure 6. Cross-sectional ultrasound images of an ex-vivo bovine aorta. The slices are acquired at angles perpendicular to the endovascular catheter path. The imaging path is determined by the geometry of the blood vessel.

Each individual slice is then segmented, and the aggregate contours from the tilted slices are processed to form a variational implicit surface. The resulting analytic description can be sampled and rendered using volume rendering approaches, or it can be interrogated and tessellated into a polygonal or parametric surface representation. Figure 7 shows the two views of the interior surface of the bovine aorta from Figure 6 reconstructed as a variational implicit surface. The zero-set of the implicit model has been extracted using a surface tiler, rendering them as polygons at the resolution desired for the magnification shown. If close-up views are desired, the model can easily be re-interrogated and tiled in the surface rendering case or the model simply re-rendered in a direct volume rendering system with arbitrary precision, eliminating aliasing artifacts in the representation of the model.

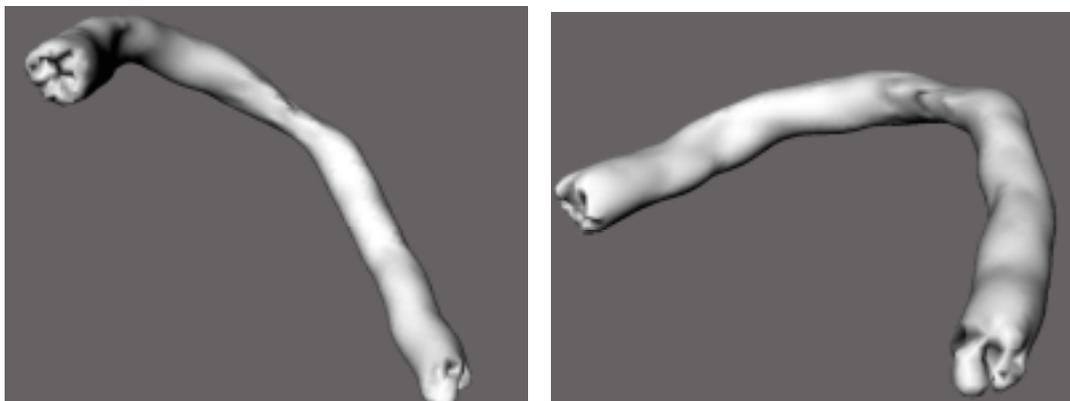


Figure 7. Surface renderings of the interior surfaces of the ex-vivo bovine aorta reconstructed as a variational implicit surface from intravascular ultrasound data. The models are not subject to aliasing artifacts generated by comparable surface or volume. In addition, these models are generated from sparse, non-uniformly sampled non-parallel ultrasound slices.

While these results have been very promising, the matrices that are created by this method are poorly conditioned and are difficult to solve. This leads to poor memory performance and increased computational complexity preventing the use of optimized solvers. Dr. Chen reimplemented the Turk and O'Brien code for the 3D Informatics Program, and visiting faculty Drs. Subramanian and Morse contributed new applications and mathematics, respectively. The result has been an improved technique for generating data-driven implicit models based on compactly supported radial basis

functions. The resulting, narrow-banded sparse matrices are amenable to accelerated solutions and data compression. The method has been published at the 2001 Shape Modeling International conference in Genova, Italy [Morse 2001], and has been solicited for publication in the journal ACM Transaction on Graphics. Medical applications based on these methods have been published at the 2001 Medicine Meets Virtual Reality conference [Yoo 2001c] and the 2001 International Medical Image Computing and Computer Assisted Interventions (MICCAI 2001) conference in Utrecht, the Netherlands [Yoo 2001a].

7 Volume Image Archives

We have covered the progression of information from raw data to object modeling through a series of abstractions of increasing complexity:

data \square features \square segments \square shape \square models.

Raw medical data, however, does not only come directly from scanners. Moreover, it does not come “naked” without significant metadata about the scan, including the quality, resolution, modality, anatomy, patient presentation, and history and physical information about the subject. Up to this point, we have treated this subject in a pure computer vision context, without the benefit of metadata. Framing the problem in this manner overlooks some of the most important resources available. Therefore, as part of our project we set about studying metadata associated with volume images.

7.1 Results: An Online Volume Archive

In 2002, the 3D Informatics group explored the concept of an online volume image database. Two library associates (C. Twose and T. Lee) accepted a spring project to study privacy, regulatory, and technical aspects of medical volume data collections. Their work included background investigations and interviews with a broad cross-section of potential users including internists, radiologists, anatomists, and computer scientists. They also explored the emerging HIPAA regulations, the commercial imaging standards such as DICOM 3.0, and existing examples of online public archives. The result was a design of a public archive including the necessary metadata for browsing, searching, and data entry. During the summer of 2002, two undergraduate interns (D. Leiman and A. Fletcher) joined the team and began the implementation of a pilot digital archive based on the design from the associates. The resulting initial modest collection has ten datasets, an HTML infrastructure, and an XML superstructure for organizing the collection. Figure 8 shows the data entry page for this site. This work resulted in an NLM Associates Project report as well as a refereed publication at the 2003 SPIE Medical Imaging Conference in San Diego [Leiman 2003].

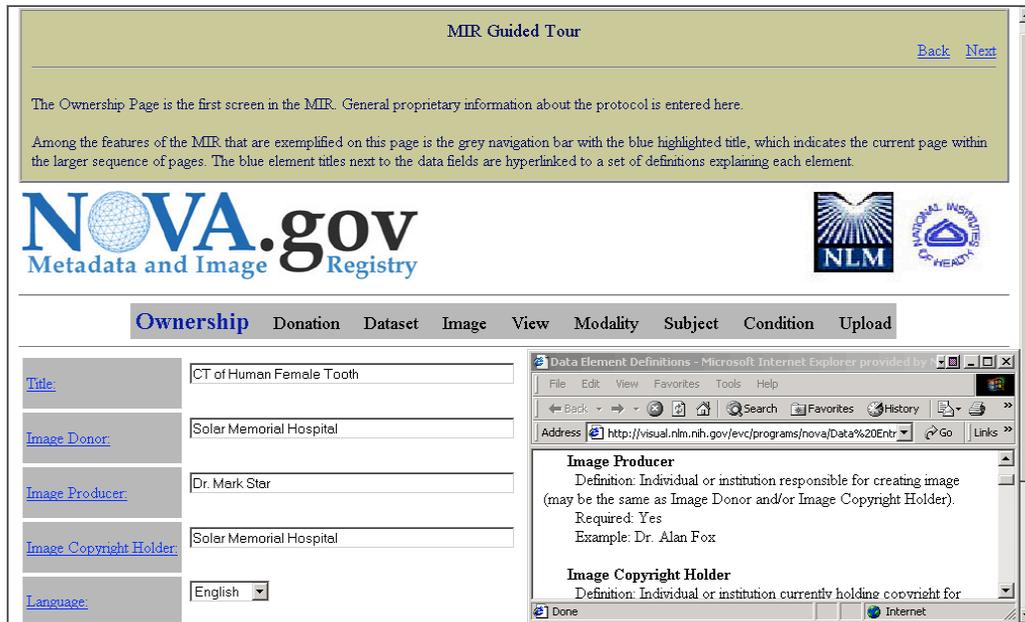


Figure 8: A screenshot of the Metadata Image Registry entry screen with Data Element Definitions present

8 The Insight Toolkit (ITK)

Between the abstractions of models and features, we study the problem of segmentation, the partitioning of data spaces into cohesive, contiguous regions. The three-year plan for our program included creating an imaging laboratory for the Lister Hill Center. An important element of creating this lab has been a software toolkit for the segmentation and registration of medical data. The Insight Toolkit, ITK, is the result. While the work for developing this software package has been the result of NLM contracts, Lister Hill Center personnel have served as collaborators as well as project officers. ITK is a unified software package rather than a loose collection of software routines. This development has required tight integration among the contractors and strong collaborative effort from the individual programmers. Dr. Yoo has served as the manager of this project, moderating every meeting of the group including the algorithm validation meeting at Columbia University Medical School in 2000. He supports this project in every aspect including soliciting involvement and financial support from other NIH Institutes and Centers and the other Federal Agencies.

8.1 New Procedures: Distributed Software Engineering and Extreme Programming

The Lister Hill Center has pioneered the use of distributed software engineering methods to support a fast-track design process known as *extreme programming*. In this design model, software is proposed, implemented, and tested continuously throughout the evolution of a software system, rather than the monolithic, "Cathedral" approach for software development. Moreover, this development has been administered in the difficult organization of a geographically distributed, network-connected consortium of software developers.

The need to run ITK on multiple platforms and have the source code remain supportable and maintainable creates particular challenges. Although there is a large installed-base of workstations running Microsoft operating systems on Intel-type CPUs, much of the image processing, segmentation and registration algorithm development is still conducted on Unix-type systems. It is needful then to accommodate developers using a range of system types (Cygwin or Visual C++ on Windows, GNU C++ on Unix/Linux/Irix/Solaris/MacOSX, etc.) on a diverse spectrum of hardware which includes serial and multiprocessing architectures. ITK Developers chose to create a single base of source code that could be compiled for different system configurations. Older software development projects have experienced significant divergence in internal versions as some features are available on PC systems but not available for Macintoshes, for example. ITK is constructed from a single software effort that is continually checked so that it can be compiled and run on the range of system types supported by the project. At no point in the development and extension of ITK do we intend to have core features available only on some systems.

CMake and Dart - tools for Distributed Software Development

In order to support this mission, ITK has crafted new software engineering superstructure systems including CMake and DART. CMake is a system for configuring ITK (and other toolkit software) for compilation under different programming environments. DART is a distributed build and test system capable of continuously checking the source code for compilation and run-time errors and reporting them on a web-accessible dashboard illuminating bugs, design problems, and critical programming faults as they happen. The driving concepts behind these tools are not new; the tools are new implementations inspired by similar programs previously available. The refinements of these ideas, however, have led them to be re-incorporated into older programming projects including VTK, demonstrating that open-source programming can leverage itself benefiting more than just the narrow constituencies of individual projects. Both of these tools are essential to the operation of a distributed programming group and the maintenance of common, multi-platform core software. A complete discussion of these tools cannot be presented here. Please note that these tools have been created as versatile components, capable of integration in projects other than ITK. As a sponsored program in open-source software, both CMake and DART are available in the public domain in source code form, inviting adoption and refinement by a broad community of programming professionals.

8.2 Results: ITK

The Insight Software Consortium has completed design and development of an initial version of a public medical image segmentation and registration toolkit known as the Insight ToolKit (ITK). The goal is to create an application programmer's interface (API) that can be used by developers in medical programs and software products wherever the problems of image or volume segmentation and registration exist. Unlike other software development efforts, the goal is specifically NOT to create a single monolithic program. Rather, we are pursuing a software foundation from which a broad range of programs

can be supported. The ITK API has undergone continuous review and modification by the expert developers on the programming team. GE Corporate R&D along with Kitware, Inc. serve as the lead design groups, with GE CRD handling issues of testing and quality control during development and Kitware serving as system integrators for the project. Other teams from across the consortium are contributing new implementations of complex medical image processing algorithms, helping to refine the software architecture as the toolkit grows in complexity and mathematical sophistication.

At the current time, The Insight Toolkit (ITK) is available online (see the URL: <http://www.itk.org>). The ITK software has been downloaded over 3000 times, and the user's mailing list has over three hundred (300) subscribers in as many as 30 countries. Dozens of methods are represented in ITK including algorithms for segmentation and registration of clinical data. Validation studies are published with the software, testing a set of the software tools on a variety of data including MRI data from Alzheimer's patients, cases involving Multiple Sclerosis, ultrasound data, and volume studies for brain tumors. Current users include not only academic medical research groups, but also include commercial ventures including at least one company using ITK for handwriting recognition.

9 Surgical Templates: A Case Study in 3D Informatics

In this report, we have consistently described the medical visualization pipeline (see Figure 1) in comprehensive terms, following the progression of increasingly complex abstractions to final user presentation. However, we have studied only individual topics in depth. This depth-first study does not contribute to an overall understanding of the whole process, and it is susceptible to digression into complex applied mathematics that does not contribute to the overall goals of medical visualization.

To overcome possible tunnel vision, our group has undertaken a demonstration project, taking on a particular medical procedure, analyzing raw data, extracting features based on bone density, segmenting objects, analyzing shape, contributing information in the form of surgical plans, and creating tactile visualizations of the resulting combined information. Our lessons learned include a clear mandate to improve the interfaces between the levels of each type of abstraction. These may come in the form of file format standards. More likely, though, a new generation of markup and design languages will be required to overcome the communication barriers in imaging sciences.

9.1 Informatics for Posterior Lumbar Interbody Fusion

We are combining surgical planning techniques with computer aided manufacturing systems to create custom surgical aids for orthopedic surgery. Our application area is planning and controlling the trajectories of pedicle screws for spine surgery. The goal is to manufacture a physical jig that conforms to the contours of the patient's vertebrae. The jig is constructed with holes that correspond to the trajectories of the pedicle screws. These holes guide the drill placement and depth, increasing the accuracy and precision of screw placement (Figure 9). These devices are created for each individual patient, one

per segment, and improve accuracy without the introduction of navigation tools or increased fluoroscopic radiation dose. The intent is to use a jig to transfer the surgical plan directly to the operating room without introducing additional technology. Difficulties of computer-assisted surgery remain in the laboratory without intruding into the operating room.

We briefly describe our work in rapid prototyping for computer-assisted surgery. In this section we address the design issues for the surgical planning and template design workstation. Our prototype is an interactive modified texture-based volume rendering program [Cabral 1994] augmented with physical user interface devices, 3D stereo viewing, polygonal primitives, and tools for constructive solid geometry (CSG) to serve as the computer aided design foundation for modeling templates.

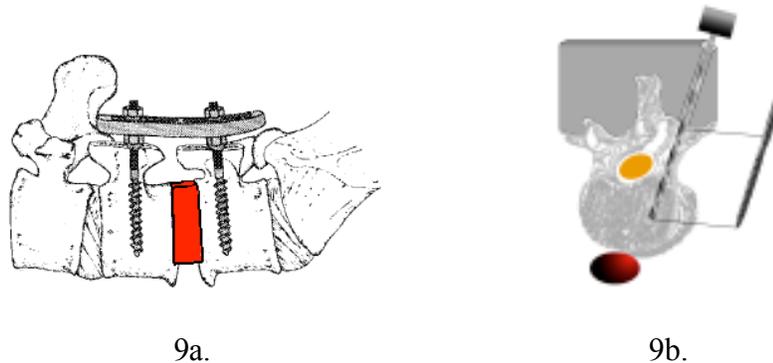


Figure 9. We are working on techniques for the precise placement of pedicle screws, required for many spine procedures. Figure 9a: lumbar plate secured with pedicle screws. Figure 9b: Our goal – a proposed template, guiding the drill path and depth. Structures such as the spinal cord, nerve roots, and the aorta must be avoided.

9.2 Background and Related Work

Figure 9a shows the basic problem faced in spine procedures. Appliances such as plates and rods require fixation through narrow channels called pedicles. Trajectories through these narrow isthmuses of bone have optimal placement and limited tolerances [Rampersaud 2001]. Complications can arise when the screws accidentally enter epidural or spinal spaces and transect the spinal cord, constrict the emerging nerve roots arising from the ganglion, drift through a disc, or by emerging out the anterior surface and cutting the aorta [Lin 1985].

Figure 9b shows the goal of our project, the creation of custom drill guides designed to mate closely with individual vertebrae that limit depth and provide for precise control of the screw path. Other groups have pursued templates for pedicle screw placement. Rademacher and Birnbaum have reported favorable results using numerically controlled (NC) machine tools to create plastic templates [Birnbaum 2001, Rademacher 1998].

Our approach differs from theirs in our use of Fused Deposition Modeling (FDM), an alternate technology for creating the templates. Many affordable NC machines are limited to three axes of control. This prevents many NC machines from supporting the

complex geometries required to create custom templates. By contrast, FDM is the successor to stereolithography in rapid prototyping technology. It is flexible and accurate, capable of creating a wide variety of geometries, well beyond those needed in pedicle screw placement procedures. Stratasys, a manufacturer of these rapid prototyping devices, has secured U.S. FDA approval for the generation of 3D models for diagnostic purposes. The requirements of high fidelity reproduction necessary for diagnosis are equally important in intervention. They also supply a production material that can be sterilized for use in medical procedures.

9.3 Design and Software Tools for Template Planning Workstation

We built our surgical planning workstation around an interactive volume rendering system. Recent trends in graphics workstations have led to the emergence of 3D transparent textures, enabling interactive volume rendering using conventional graphics primitives [Cabral 1994]. Figure 10 shows the process and the console.

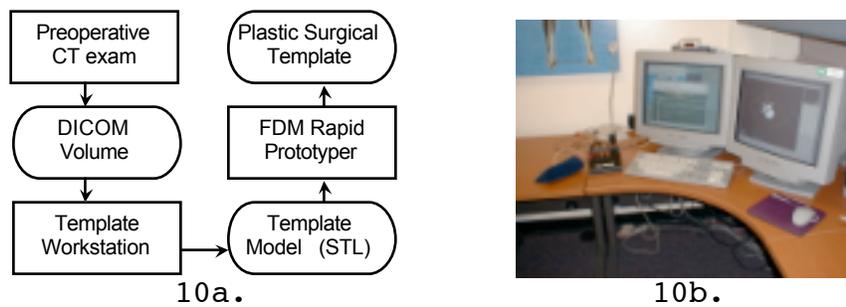


Figure 10. Procedure and console. Fig. 10a: The pipeline from exam to template. Fig. 10b: This paper describes the template design workstation: Joysticks, stereo viewing glasses, pushbuttons, and physical sliders provide more natural human interfaces than overloaded mouse controls.

To augment the interactive visualization of the vertebrae and the placement of tool paths, the workstation has recently been augmented with physical I/O devices including a 3D joystick, supplementing the overloaded mouse controls. A mouse is by definition a 2D input device, limiting its use for viewpoint control. Tactile coherence can be improved by the use of physical input devices.

Volren 6.1, a texture-based volume rendering system running on a dual 250 MHz CPU Onyx2 with dual Reality Graphics™ raster managers was modified into a surgical planning workstation enabling the modeling of objects through constructive solid geometry (CSG). Texture based volume rendering naturally combines clipping planes and polygonal objects in a simplified volume rendering pipeline. The hardware accelerated graphics systems necessary to support these methods are available in PC cards today. Clip planes, polygonal models, and volume rendering combine to make a natural graphical interface for planning screw placement.

9.4 Results, Discussion, and Future Work

As a test of the technology and its precision, we selected a dry, dissected lumbar vertebrae and created a surgical plan for pedicle screw placement. Thin section CT scans

(1mm apart and 1mm thick) of 5 individual dry lumbar vertebrae were obtained on a GE Genesis High Speed RP Scanner. A block was modeled to fit tightly to the posterior surface of the vertebrae. Cylinders, that would ultimately be the drill guides, were then modeled through the block. The positioning of the cylinders, or trajectory planning, was accomplished with the aid of clipping planes and interactive control of the volume rendering transfer functions. This assured the authors that the planned trajectory was through the isthmus and along the axis of the pedicle, as shown in Figure 11. The 3-D drill guide block with trajectories was then divided into 2-D slices and converted to DICOM files. The 2-D slices were imported into Mimics v.6.3 (Materialise) and converted to STL files. The STL files were then used to generate the tool paths for the Fused Deposition Modeler (FDM) 2000 (Stratasys).

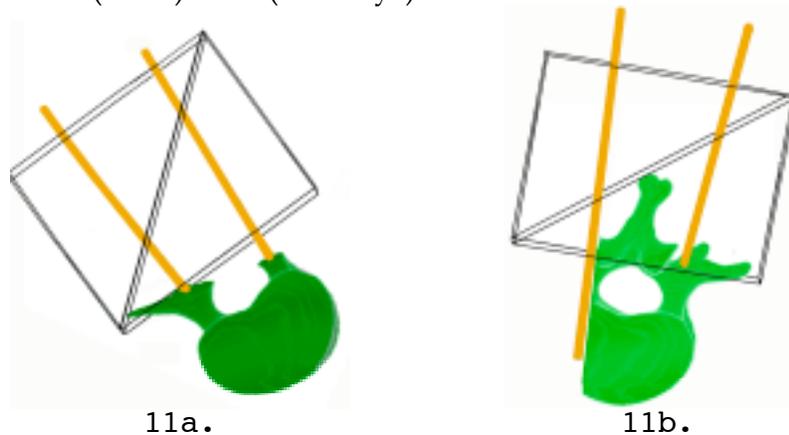


Figure 11. The template design, taken from the texture-based volume rendering based surgical planning workstation. Clipping planes, polygonal primitives, and volume data are easily combined using advanced graphics.

We have achieved frame rates on the order of 10 frames per second for interactive template design including rendering the medical volume. Drawing from experience with molecular modeling systems, physical I/O tools such as joysticks were added improving the intuitive feel of the workstation. Some overloading of the input devices still occurs, leading to occasional confusion. Stereo viewing does not appear to speed template design. The use of Open GL as a programming base significantly reduced software development costs and permitted the fast integration of CSG.

A drill guide was produced by the FDM 2000 with approximately 125.06 cm³ of non-medical ABS plastic at a slice interval of 0.2540 cm. The block, as designed, had an intricate area reserved for the posterior elements of the chosen lumbar vertebra. This first attempt was flipped in the x-axis due to an image format discrepancy. A second template was produced, correcting the defect, and pedicle pilot holes were drilled into the dry vertebrae. A CT scan was conducted to verify the placement of the pilot holes (Figure 12). Physical templates transfer the power of surgical planning workstations to the operating room without the need for complex technology. Confidence in the path planning will increase accuracy, speed procedures and reduce patient radiation dose by decreasing fluoroscopic verification.

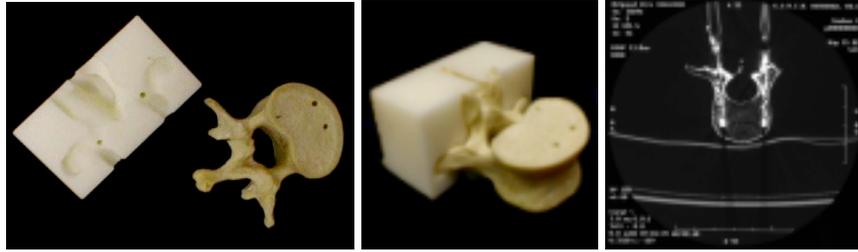


Figure 12. The prototype template and the dry spine test with a validating CT exam. (The pinholes in the top of the vertebrae are incidental, and leftover from the string connecting multiple vertebrae for its former use as an anatomy teaching tool.).

Dr. Jonathan Morris, now a radiology resident at the Mayo Clinic, handled the clinical aspects of the task, while Dr. David Chen handled the technical areas and Dr. James Burgess of Inova Fairfax Neurosurgery provided consultation and clinical guidance. The manufacturing for this project was performed with the help of the Bethesda National Naval Medical Center Radiology Department (Dr. Richardson). The idea, technical leadership, and the resource and personnel management was provided by Dr. Yoo.

This work was presented at the 2001 Computer Assisted Surgery Workshop in Nurnberg, Germany and published at the 2001 Workshop on Interactive Medical Image Visualization and Analysis in Utrecht, the Netherlands [Yoo 2001b].

10 Project Assessment and Future Work

Over the last four years, we have continued to work in core areas of image-based medical informatics. We have succeeded in pioneering new areas of individual research, contributing to individual subfields of our chosen research domain. However, we continue to struggle with crossing the boundaries and defining the languages and interfaces that divide these research subfields. They often share common mathematics, but integrating the research still proves daunting. Lessons from our case study indicate that the most likely place for errors to occur are when crossing informatics boundaries between technologies, between software systems, and consequently between intellectual research domains.

We propose two projects in integrating multiple subfields already under study by our group. We hope to pool resources and concentrate our effort in finding vehicles, software standards, and markup languages to bridge the gaps in image-based medical informatics. This means formally describing the abstractions shared by subfields and developing the languages, models, and interfaces to accurately describe them.

10.1 Assessment of Cardiovascular Stent Ingrowth Using Intravascular Ultrasound

This project is an extension and combination of existing efforts within the 3D Informatics Project. It combines three supporting strengths: (a) high dimensional image processing, (b) shape modeling, and (c) medical volume visualization. Previous work with intravascular ultrasound (IVUS) has been done in partnership with the University of North Carolina at Charlotte and their clinical associates. Our earlier work included the

use of implicit surfaces to model the interior of the coronary arteries. However, this data was taken on ex-vivo blood vessels in a laboratory setting.

New data being provided by Dr. Carl Jaffe and the Yale School of Medicine from live patients is providing an opportunity to advance our research toward clinical practice. The live data includes complicating factors not seen in our earlier work including cardiac motion and temporal noise arising from blood flow. The available data is from patients who have had a traditional angioplasty procedure and had stents placed at the site of the stenosis, the narrowing of the blood vessel wall. In some significant fraction of these patients, the endothelium grows through the stent and arterial plaques begin reforming within the mechanical structure, effectively reversing the intervention. The fundamental question posed by Dr. Jaffe is: Can we quantify the amount of encroachment? This question has particular ramifications for the follow-up procedures of radiation treatment of the affected areas. Figure 13 shows an example 2D cross section of this type of data.

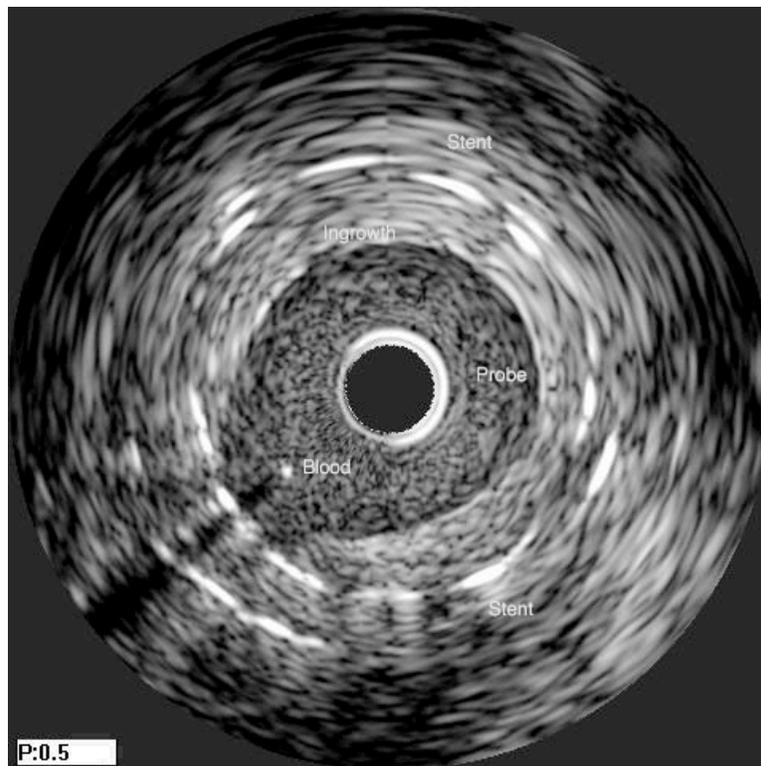


Figure 13. Intravascular ultrasound (IVUS) image of a coronary artery showing ingrowth through a stent, placed as an earlier intervention.

We are pursuing a combination of existing methods to address this problem. The structured noise of this complex 4D data suggests a modification of the multiscale statistical methods reported earlier. We are trying to discriminate between the anisotropic structure of the stationary tissues with the flowing blood that has both less structure and a greater temporal stochastic signature. This level of segmentation analysis will be combined with a quantitative filter to assess the degree of occlusion of the artery and thus measure the extent of the cardiovascular disease. 3D visualization of this data

is also being investigated to give clinicians spatial context for these pathologies. Drs. Yoo and Chen are the principals of this work, with clinical supervision by visiting researcher, Dr. Carl Jaffe.

10.2 NPR Shading Languages for Medical Illustration of Real Data

Non-photorealistic Rendering (NPR) is an important and sometimes overlooked domain of computer graphics. The emphasis in computer graphics has been on nearly-real imagery for the entertainment and gaming industries, while education and communication can often benefit more from schematic and cartoon images that suppress extraneous and often distracting details. The current NLM exhibit, *Dream Anatomies*, is a testimonial to the power of pen-and-ink renderings of anatomy.

We propose to investigate the pathway from volume data to non-photorealistic illustration of anatomical and biological objects. Early work in the differential geometry of shapes indicates that we have promising methods to pursue. Figure 14 shows the geometric analysis of a digital model of a real artifact. In this case, the imaging modality is a laser range camera, but the model could easily have been generated using a medical imaging modality such as X-ray CT or MRI. Although the model in this case is a small figure, it shares many of the surface properties of biological or anatomic objects including texture, relatively smooth overall shape, and bifurcating appendages. The digital model has been analyzed for its inherent geometrical properties, and invariant features such as principal and Gaussian curvature have been extracted. The example in figure 14 has been published [Morse 2001] and submitted for publication [Lowekamp 2003]. These invariant geometric features are necessary to facilitate the illustration of smooth surfaces. Hertzmann and Zorin use principal curvature in their computer graphic treatment of surface illustration [Hertzmann 2000]. We intend to use these same properties to illustrate anatomical structures.

Control of shading and rendering requires the specification of a variety of parameters to guide the illustration process. The realm of non-photorealistic visualization extends these problems to a host of illustrating primitives such as cross-hatching, stippling, brush stroking, and other artistic devices for rendering images. Effective communication through images often requires the use of several techniques in the same work. Elaborating all of this structure will require new languages for crafting and shaping visualizations.

We propose to build on our shape analysis work in differential geometry for volume illustration. We describe this initiative as NPR Shading Languages for Medical Illustration of Real Data. Beginning with Visible Human Project data, we will adopt segmented volumes, extract digital models, analyze the differential geometric shape properties, and develop a shading language for illuminating these shapes with computer generated artistic elements. The principal investigators for this work are Dr. Yoo and Mr. Lowekamp with support from Dr. Chen. We are seeking collaborative support from an expert in shading and rendering languages, Dr. T. Marc Olano from the University of Maryland, Baltimore County.

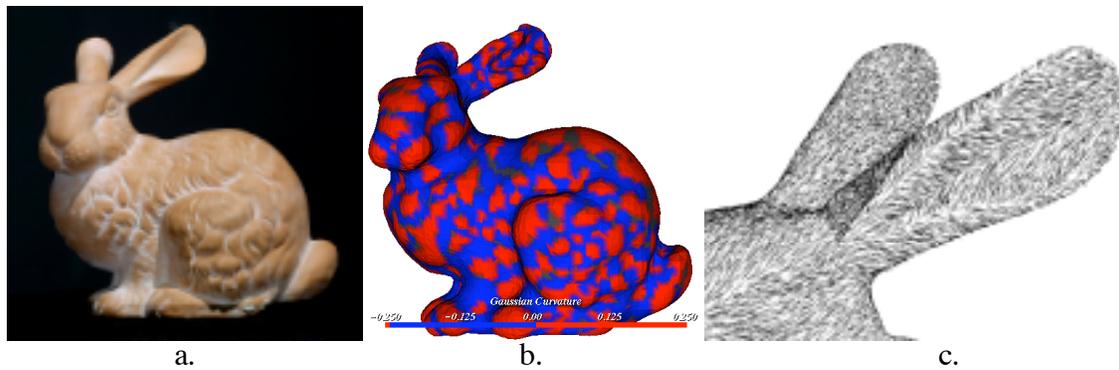


Figure 14. Example analysis and evolution of real data toward non-photorealistic rendering of object shape. (a.) This is a photograph of the Stanford Bunny, a terracotta figure later scanned using a laser range finder to create a digital model. (b.) This is a geometric analysis of the digital model of the bunny. Red areas show elliptical patches on the object, while blue indicate hyperbolic or saddle-shaped regions. (c.) This is a detail of the digital model of the bunny ears. This view shows the representation of one of two principal curvature directions associated with the geometric analysis of the solid shape. Though suggestive of fur, this is a visualization of surface shape. Similar techniques for analysis and representation are proposed for our research on 3D Informatics of medical data.

11 Evaluation

The different areas of this program are at different stages of their development. Each area works to support the broader research program that we are developing. Evaluation criteria for the separate parts of the research program are divided into appropriate validation approaches. Each area of research will be executed in phases. A hypothesis or proposed approach will be adopted and milestones or interim goals that validate the research approach will be chosen. Attainment of the milestone or goal will signal the start of a new phase of the research. The collection of milestones will be a measure of overall progress.

11.1 Evaluation Plan: Assessment of Cardiovascular Stent Ingrowth Using IVUS

The IVUS data associated with this project is already part of a clinical sequence that is routinely analyzed and evaluated for clinical interventions. Dr. Jaffe is our clinical advisor for this project, and he will provide us with the results of the analysis that is routinely done in the clinic today. Our project will create a more comprehensive analysis of the condition, but the existing metrics can be compared to rudimentary measurements that we will be making. This will permit us to evaluate our segmentation and show that we are *at least* as accurate and repeatable as existing tools. Improvements in the evaluation of the cardiovascular condition will come from other quantitative analysis of the segmentation that we are performing, adding benefits to the planning of clinical treatment of chronic cardiovascular disease.

11.2 Evaluation Plan: NPR Shading Languages for medical illustration of real data

It is difficult to evaluate the efficacy of an illustration or visualization, but it is possible to study the correctness of the mathematics upon which the shading and texturing procedures are based. The development of these techniques will be applied to synthetic

objects first. Later, rendering of simple physical objects derived from laser range data and X-ray CT scans of simple physical artifacts will help verify that the geometric underpinnings of the shading procedures are consistently correct. Finally, the non-photorealistic rendering methods can be applied to objects derived from medical data. This serial progression is necessary to permit a logical series of validating experiments. The validation of visualizations of medical information is often a subjective task. By confirming geometric values such as Gaussian curvature of known mathematically generated objects and simple physical artifacts, the validity of these methods can be supported when they are applied to real medical data.

11.3 Evaluation Plan: Continuing Production of the Insight Toolkit

The Insight Software Consortium has met to discuss the problems of validation of segmentation and registration algorithms. A validation framework derived from this workshop was published at the 2000 MICCAI Conference in Pittsburgh, PA. Ten algorithm validation case studies have been performed by the Insight developer team. These studies compare, contrast, and measure the accuracy, precision, and efficiency of different segmentation and registration algorithms. This framework will be extended by the 3D Informatics group and applied to the IVUS work as well.

12 Project Plan

The project plan is divided among short range targets, mid-range targets, and long range targets. These divisions represent the most probable, low risk targets, medium risk initiatives, and longer range guiding research directions for the group.

12.1 Short Range Targets (1 year projection)

Assessment of Coronary Arteries using IVUS (Image Proc., Modeling, Visualization)

The work in intravascular ultrasound is dependent on making progress in several areas. Image processing research is the critical path of this work, to be followed by new methods for volume visualization for the noisy data generated by the ultrasound modality.

- May 2003 – Begin statistical image processing of the temporal and spatial noise structure of IVUS data.
- July 2003 – Apply volume rendering techniques to segmented IVUS data.
- November 2003 – Begin clinical assessment of the resulting analysis.
- March 2004 – Submission of first manuscript on IVUS to MICCAI 2004.

Differential Geometry and NPR Languages (Shape Analysis and Visualization)

A study of non-photorealistic rendering methods is already underway within our group. Also, as reported, we have been conducting studies for geometric analysis of shape. These elements will be combined with rendering techniques and computer languages to create flexible rendering and medical illustration tools. This work will begin immediately and will be punctuated by submission of our earliest results in early 2004 to the ACM SIGGRAPH conference.

- May 2003 – Begin specification of artistic devices for NPR shading and texturing. This will become the language specification for the rendering tools.
- July 2003 – Begin implementation of software systems that parse the shading language, accept input data, and generate rendered images.
- October 2003 – Refinement of specific illustration techniques begins with the most successful image representation methods. Begin draft of manuscript.
- January 2004 – Submission of first manuscript on NPR shading languages.

12.2 Mid-range Target: An Image Research Laboratory (3 year projection)

Data Collection (Metadata Management and Foundation)

Research pressures of computer scientists will continue to increase the demand for sources of valued datasets. Essentially, computer science researchers are data starved, and the National Library of Medicine is an institution that is ideally positioned to serve this need. With the foundation of the Visible Human Project data and the structure of our previous work on volume data collections, we will naturally collect data through our research efforts. Organization and distribution of this ad hoc data will be required. In addition, organized collection of data will likely arise in the course of the work on the future Visible Human Project.

- Fall 2003 – Establish an operational archive of biomedical volume data.
- Spring 2004 – Commence active solicitation of research data for distribution.
- June 2004 – Summer project for faculty and interns on content based retrieval of volume data.
- January 2005 – Submission of first manuscript volume image archives and content based retrieval.

12.3 Directions for Long Range Plans (beyond 3 years)

Long-range projections include the establishment and management of new leveraged projects for advancing 3D Informatics. Research in simulation and modeling of biological and physiological function should be supported. Middleware for uniting multiple disciplines and creating interoperable interfaces between multiple scales of representation will be necessary. Being able to correlate information between datasets (e.g., correlating structures between the visible human specimens and newly acquired data) and simulations will provide semantic handles on a broad range of problems in indexing and anatomical/physiological analysis.

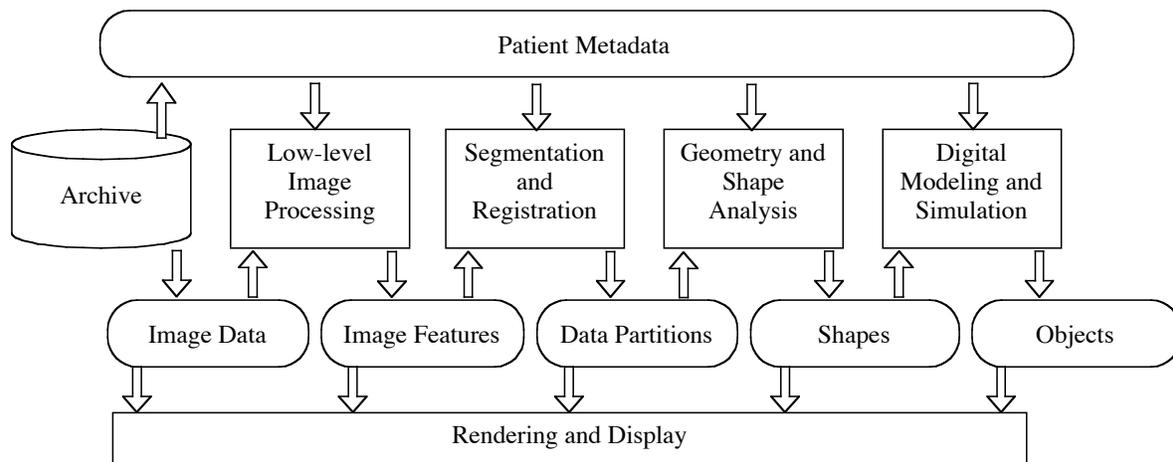


Figure 15. A more comprehensive view of the medical visualization pipeline to be read from left to right. Each subfield creates abstractions that form the input for the next higher level processing stage. Each abstraction can be individually rendered, but the aggregation of knowledge increases the complexity of the representation. We have been studying not only targeted research in the subfields, but the progression of abstractions from simplest to higher-order descriptions. Our proposed research is to integrate and combine research areas and study the informatics questions of passing information across scales.

Summary

The research area we call 3D Informatics is a synthesis of medical image processing, computer graphics, modeling, and data storage and retrieval. This concept is built up of multiple strengths with extensive study in particular core areas. It is our intention to continue to extend our integration of these subfields into a unified research project area through the development of shading languages and interfaces that describe the many abstractions in image-based medical informatics (See Figure 15). We believe that unless a program integrates the breadth of volume data analysis, modeling, and representation, it will focus too tightly on the narrow confines of the separate mathematics and techniques of its subfields, and so be incapable of adequately supporting the practice and research endeavors of medicine.

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Professional Activities

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1. Zhang Z, Hoffmann K, Walczak A: Curvature-vector pair and its application of displaying CT colon data with a pair of curvature-images. SPIE 2002, San Diego, USA.
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