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Enhanced Volume Rendering Techniques for High-Resolution Color Cryo-Imaging Data

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Abstract

We are developing enhanced volume rendering techniques for color image data. One target application is cryo-imaging, which provides whole-mouse, micron-scale, anatomical color, and molecular fluorescence image volumes by alternatively sectioning and imaging the frozen tissue block face. With the rich color images provided by cryo-imaging, we use true-color volume rendering and visually enhance anatomical regions by proper selection of voxel opacity. To compute opacity, we use color and/or gradient feature detection followed by suitable opacity transfer functions (OTF). An interactive user interface allows one to select from among multiple color and gradient feature detectors, OTF's, and their associated parameters, and to compute in live time new volume visualizations from within the Amira platform. We are also developing multi-resolution volume rendering techniques to accommodate extremely large (>60GB) cryo-image data sets. Together, these enhancements enable us to interactively interrogate cryo-image volume data and create useful renderings with "implicit segmentation" of organs.

Keywords

enhanced volume rendering; feature detectors; opacity transfer functions; multi-resolution rendering

1. INTRODUCTION

Color image volumes present many more opportunities for volume visualization than do gray-scale volumes such as those from CT or MRI, and we are exploring a variety of enhancements with regards to a particular application, cryo-imaging of mice. The cryo-imaging system at Case Western Reserve University provides ultra high-resolution, large field-of-view, anatomical color and molecular fluorescence image data by alternatively sectioning and imaging the block face [1-3]. The large volume of data generated (>60GB per adult mouse) necessitates fast, multi-resolution volume rendering to aid data interpretation. Multiple modalities (bright field color, fluorescence, multi-spectral imaging, etc.) provide

opportunities for renderings of fused data, which are very important for fast, efficient data interpretation.

Over the last two decades, direct volume rendering has been a key technology for visualization of large 3D datasets from scientific, engineering, and medical applications [4-11]. However, several factors still inhibit its widespread use including the complex interrelationship of rendering parameters, the lack of interactivity, and the design of a suitable transfer function to be used during volume rendering [12]. In applications such as cryo-imaging where high-resolution high-contrast true color information is available, we believe that true-color volume rendering using color and gradient features from the data along with an appropriate choice of an opacity transfer function (OTF) would help us make biologically useful inferences with minimal manual intervention. OTF's are crucial to the above process since they assign a "rendered opacity" to each voxel within the volume. For example, in routine medical visualizations of CT data it is often possible to use pre-defined 1D OTF's to highlight certain tissue types, such as bone or liver [6;13]. Further, a combination of data attributes such as color channel values, grayscale value, gradient of channels, and grayscale gradient can be mapped to a suitable opacity value as in the case of multidimensional OTF's reported in the literature [5;8;9]. In some previous studies [5;11], transfer function design was preceded by a tissue classification step. However, classification is a computationally demanding step especially with our extremely large cryo-imaging data sets (>60GB for a single high resolution color image data set of adult whole mouse) and is therefore not suited for on-the-fly visualization.

In this paper, we explore direct volume rendering techniques using natural colors and opacity values that depend upon both color of image data and gradients. Specific anatomical structures are enhanced using a two-step process - feature detection using color and gradient features from the data followed by rendering using suitable opacity transfer functions (OTFs). These techniques have resulted in volume renderings where tissue boundaries are better highlighted in color data. We have created a graphical user interface which allows the user to interactively choose opacity techniques and parameters. Multi-resolution volume rendering is provided to enable interaction with enormous (> 60 GB) cryo-image volumes. We use the Amira (company) [14] visualization/analysis platform.

2. METHODS

1.1 2.1 Color-based feature detectors

We exploit the rich color separation of cryo-images using color feature detectors. Below are examples of ratio-based feature detectors for Red, Blue, and Green, respectively, which we found useful for highlighting various tissues of interest.

$$\begin{aligned} cR &= R / (R+G+B) \\ cG &= G / (R+G+B) \\ cB &= B / (R+G+B) \end{aligned} \quad (1)$$

For example, cR , the red feature detector, helped highlight organs such as the liver, lungs, and heart; and cB was useful in an embryonic mouse cell lineage experiment for

highlighting blue skin cells expressing LacZ after staining with X-gal. These detectors can be combined to create a detector for any arbitrary color. For example, for detecting stomach and intestinal regions in adult mouse data set, which are predominantly brown in color, we exploited the fact that brown is composed of $0.5*R + 1.0*G + 0.0*B$. A brown feature detector is a weighted linear combination of red and green feature detectors:

$$cBR = (0.5*cR + 1.0*cG) \quad (2)$$

Similarly, by experimentation, we have developed a color feature detector for segmenting brain, which we refer to as cBRAIN.

1.2 Gradient-based feature detectors

Data gradients are useful in visualization and interpretation of internal structures and surfaces within volumetric data. Many possibilities exist. First, one can compute gradients on grayscale image data I_g . Using the central difference operator, a numerical estimate of grayscale gradient at voxel location (x, y, z) is obtained:

$$\begin{aligned} \nabla(I_g) &= (I_{gx}, I_{gy}, I_{gz}) \\ \text{where} \\ I_{gx} &= I_g(x-1, y, z) - I_g(x+1, y, z) \\ I_{gy} &= I_g(x, y-1, z) - I_g(x, y+1, z) \\ I_{gz} &= I_g(x, y, z-1) - I_g(x, y, z+1) \end{aligned} \quad (3)$$

A useful gradient function for rendering is a normalized magnitude of the grayscale gradient vector:

$$gGRAY = \frac{|\nabla(I_g)|}{|\nabla(I_g)|_{max}} \quad (4)$$

Similarly, gradients can be computed from each color channel by substituting I_g with R, G, or B in equations (3) and (4) resulting in color gradient feature detectors gR, gG, and gB. Yet another approach is to compute gradients directly from color vector data. Color vector data can be represented using several color spaces such as RGB, $L^*u^*v^*$, YCbCr, HSV, YIQ, etc [15]. It has been reported that the $L^*u^*v^*$ color space is perceptually linear unlike the more commonly used RGB space [6;9], thereby making it more appropriate for computing gradients. Following a color space transformation from RGB to $L^*u^*v^*$, we computed two gradient measures pertaining to the color data vector: color distance gradient magnitude (CDGM) and color distance gradient dot product (CDGDP) [6;9]. We have found them to be useful for highlighting boundaries between tissue types with different color attributes.

1.3 Opacity transfer functions (OTFs)

The color (c) and gradient (g) feature detectors defined in previous sections serve as inputs to opacity transfer functions (OTF's), denoted by o , which finally assign α -opacity values to

each voxel for rendering. We have investigated threshold, sigmoidal, and power-law OTF's. Below, we list the threshold and sigmoidal OTF's in equations (5) and (6) respectively.

$$\alpha=o(T, w, c, g) = \begin{cases} w.c + (1+w).g, & w.c + (1-w).g > T \\ 0, & w.c + (1-w).g \leq T \end{cases} \quad (5)$$

with $0 \leq T \leq 1, 0 \leq w \leq 1$

where T is a threshold, and w is a weighting factor for combining the effects of color and gradient.

$$\alpha=o(T, \gamma w, c, g) = \frac{1}{1+e^{-\gamma[w.c+(1-w).g]-T}} \quad (6)$$

with $0 \leq W \leq 1, 0 \leq T \leq 1$, and $\gamma > 1$

where w is a weighting factor as above, T is a threshold, and γ controls the shape of the sigmoid.

Sometimes, we have found it advantageous to apply the OTF separately to color and gradient feature detectors and then linearly combining them. In other cases, a multiplicative combination of color and gradient OTF's has proved to be efficient in terms of memory and computation time.

1.4 User Interface

We have created an intuitive, interactive user interface for volume rendering of color data (Fig 1). The crop interface at the top allows one to interactively identify a rectangular solid or ROI for “slab” volume rendering. The ROI can be modified by dragging the small spheres identifying the bounding box in the figure. This interface provides an easy way to eliminate extra structures which limit our ability to visualize a tissue of interest. The main rendering interface (Fig 1-middle) allows one to select an appropriate color feature detector. The Red, Green, and Blue selections correspond to cR , cG , and cB in Eq(1), respectively. One or more of the above selections can be chosen at the same time. In addition, we provide preset detectors (e.g., “brain”, brown, etc.). Gradient feature detectors can be computed from R, G, B, or grayscale channels, or from color vector data using CDGM and CDGDP. Finally at the bottom of the interface in Fig 1, one can choose the OTF and its parameters for volume rendering. Choices include threshold, sigmoid, and power law OTF. Using radio buttons, one chooses either a weighted sum or multiplicative method for combining color and gradient detectors. A weighting factor w lets the user chose the relative contribution of color and gradient. The color volume rendering program was created using Amira TCL scripting along with the Amira volume rendering engine.

3. RESULTS

We produced a baseline true-color volume rendering of the whole mouse where the opacity was simply set to the inverse of grayscale value (Fig 2a). We then applied CR feature detector [Eq. (1)] with $w = 1$ (no gradient enhancement). Empirically, we determined a threshold of $T = 0.6$ to be appropriate. The resulting rendering clearly highlighted vasculature, lungs, heart, liver and kidneys in the whole mouse (Fig 2b). We next used gR ,

the red gradient feature detector with $w = 0$ to provide only gradient (and no data) enhancement. Again, a threshold based OTF was used. The resulting volume rendering is shown in Fig 2d. We then used *cBRAIN*, a color feature detector derived especially for brain. A sigmoid OTF with $\gamma=50$ with $w = 1$ (only color-based enhancement) and $T = 0.55$ was used. This highlighted brain, spinal cord, eyeballs, and olfactory bulbs (Fig 2c). We applied gradient enhancement to the rendering in Fig 2c using the multiplicative combination technique discussed in section 2.3. The resulting gradient enhanced volume rendering highlighting pale red is shown in Fig 2e.

Next, we applied our enhancements on slabs (sub-volumes) to enhance internal organs and tissue interfaces. A thick slab from thoracic region was extracted from whole mouse volume using the cropping tool. *cR* feature detector was applied to detect deep red with $w = 1$ (data enhancement alone). A sigmoid OTF with $\gamma = 50$ was chosen with $T = 0.6$ (Fig 3a). An axial MPR cutaway view highlighted pulmonary arteries and heart compartments (Fig 3b). A coronal cutaway through the same volume showed structure of the lung (Fig 3c). We then used *cBRAIN* feature detector with $w = 1$, $T = 0.58$, and a sigmoid OTF with $\gamma = 50$ for a slab chosen in the head region (Fig 4). Fig 4 (a-c) shows different views of this region. The brain, spinal cord, cochlea and olfactory bulbs can be clearly visualized in these views. Next, the “special” brown feature detector *cBR* [Eq. (2)] was applied in the abdominal region with $w = 1$ with the same sigmoidal OTF as above (Fig 5). The resulting volume rendering was visually evaluated for different values of T , and a choice of $T = 0.6$ clearly highlighted stomach and colon in the slab.

We next applied gradient detectors to slabs extracted from the mouse volume. We used gradients multiplicatively with *cBRAIN* feature detector and a sigmoid OTF with $\gamma = 50$ (Fig 6). In the resulting volume rendering, the boundaries around brain, brain stem, and spinal cord have been clearly enhanced.

4. DISCUSSION

Our user interface has been designed keeping usability, simple interactivity, and flexibility in mind. It covers a wide range of choices for feature detectors and OTFs, along with volume editing/cropping and multi-resolution interaction options. Our experience with the adult and embryonic mouse volumes has revealed that, due to its shape, the sigmoidal OTF is most effective in producing volume renderings with smoothly highlighted edges (Fig 2-4). Further, the parameter γ controls the behavior of sigmoid around the threshold value T , approaching a step function for very large γ . A larger γ is desirable when sharp delineation is required; a smaller γ would provide a more gradual transition between feature and background. Normalized feature detectors permit us to define thresholds (T) in a uniform fashion across different data sets and across different sub-regions from the same volume. One of the major challenges during volume visualization is the efficient handling of large data sets. A tiled acquisition with an adult whole mouse using a 4×5 tiling configuration and $40\mu\text{m}$ section thickness generates >60 GB of data, a prohibitively large size for volume rendering purposes even with recent advancements in graphics processor design. To remedy this problem, we have designed a multi-resolution volume rendering approach. Briefly, we

render whole mouse at reduced resolution and then indicate a smaller ROI from which to produce a high resolution volume rendering.

To summarize, we have developed enhanced volume rendering techniques, choosing color cryo-imaging data as example, for highlighting features based on color properties and gradients obtained from both scalar and vector (color) data. Our feature detectors and OTFs have been successful in producing anatomically interesting visualizations from adult and embryonic mouse data sets. We have built in user interactivity into our system. We have also developed a multi-resolution volume rendering scheme to address the extreme data challenge. We believe our enhanced rendering techniques along with the intuitive user interface will enable interactive interrogation of cryo-image data.

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Fig. 1. Screenshot of user interface for volume rendering. The user clicks on the crop button in (a) to load interactive cropping panel (b). The data can be cropped to a required slab within the volume (c). Color and gradient feature detectors can then be applied (a, middle) along with OTFs (a, bottom) for producing enhanced volume renderings.

Figure 2.

Enhanced true color volume rendering using color and gradient magnitude based opacities on whole mouse data set. A baseline volume rendering scheme is shown in (a) where the opacity is set to be equal to the grayscale value. Volume rendering using simple threshold OTF after “deep red” detection (b), and sigmoidal OTF after applying “pale red” detection (c). (d) and (e) show volume renderings obtained using the same feature detectors as in (b) and (c) but with gradient enhancements.

Figure 3.

Enhanced volume rendering from a thick slab in adult mouse thoracic cavity. The heart, lung, aorta, vena cava and coronary arteries can be clearly seen in (a). Additionally, a cutaway view through this slab volume shows heart, pulmonary artery, and pulmonary vein (b). Another cutaway view clearly reveals the structure of the lung (c).

Figure 4.

Slab-based volume rendering from the head region of adult mouse. (a) View of the anterior of the head showing brain, eyeballs and olfactory bulbs. (b) Posterior view of head showing spinal cord and cochlea (c) Top view showing brain and eyeballs.

Figure 5.

A slab-based volume rendering from the abdominal region of an adult whole mouse. (a) A brown feature detector clearly shows GI, e.g., the stomach and colon. (b) A red feature detector shows lower blood vessels along with kidneys.

Figure 6.

A gradient-enhanced volume visualization from a slab chosen from head region in adult mouse clearly highlights tissue interfaces and edges around brain, eyeballs, cochlea, and olfactory bulbs. The gradients were combined multiplicatively with data attributes.