Scientific Visualization in Small Animal Imaging

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1 Introduction

Biomedical applications of small animal imaging are creating exciting opportunities to extend the scientific impact of visualization research. Specifically, the effective pairing of non-linear image filtering and direct volume rendering is one strategy for scientists to quickly explore and understand the volumetric scans of their specimens. Microscopic computed tomography imaging is an increasingly popular and powerful modality for small animal imaging [3]. This column highlights early work from collaborations at the University of Utah between the Scientific Computing and Imaging (SCI) Institute and the Department of Bioengineering, and between the SCI Institute and the Department of Pediatrics. In the first instance, volume rendering provides information about the three-dimensional configuration of an electrode array implanted into the auditory nerve of a feline. In the second instance, volume rendering shows promise as a tool for visualizing bone tissue in the mouse embryo, although the signal-to-noise characteristics of the data require the use of sophisticated image pre-processing.

Figure 1: University of Utah Small Animal and Microscopic Computed Tomography Core Facility

The data for both of these investigations was acquired with a General Electric EVS RS-9 computed tomography scanner with an 80 kilovolt X-ray source at the University of Utah Small Animal Imaging Facility, seen in Figure 1. The scanner generates 16-bit volumes roughly one gigabyte in size, with a spatial resolution of $21 \times 21 \times 21$ microns.

2 Implanted Electrode Arrays

Drs. Norman and Badi are studying advanced methods of restoring hearing to profoundly deaf individuals. Current cochlear implant technology can enable hearing by stimulating the auditory nerve with an array of electrodes placed within the cochlea. The cochlea is a spiral channel wrapped around the modiolus, a bone which encloses the auditory nerve along its central axis. Because electrical currents from the implant must pass through the thick modiolar bone to stimulate the auditory nerve, many patients with cochlear implants experience poor low frequency response, and a limited number of frequency channels. An array of penetrating electrodes, inserted directly into the auditory nerve, may overcome these limitations. By directly contacting the auditory nerve fibers, the implanted electrode tips should allow much more precise and efficient stimulation.

Figure 2: The 4-by-4 version of the Utah Electrode Array, photographed on a penny for scale, was implanted in the feline skull.

The Utah Electrode Array (Figure 2), has been implanted into the cochlear nerve of felines, to develop the delicate surgical technique required, and to test the stability of the implant for long periods of time. Non-invasive imaging is required to assess the correct location of the electrode array within the auditory nerve and in relation to the modiolus. Some representative slices of the CT scan are shown in Figure 3. The resolution of scanner is just sufficient to capture the electrode shafts and tips in the array. The streaking around electrode leads and contacts is a tomography artifact.

The feline auditory nerve itself is not discerned by CT imaging, but it is positioned at the center of the modiolus, the "bore" of the cochlea. Thus, the visualization task for this dataset is to determine whether the tips of the electrode array are correctly positioned with respect to the path of the nerve, as indicated by the surrounding bone surfaces. Because of the different radio-opacities of bone, air, and the electrode array, direct volume rendering provides a way of visualizing the objects in the dataset. In this case, the one-dimensional transfer function which determines opacity and color was generated by inspecting a histogram of the CT values.

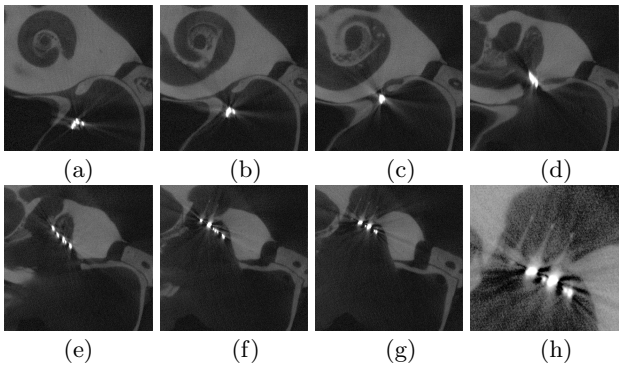

Figure 3: Sample slices of CT data. Slices (a), (b), (c) cut through the spiral turns of the cochlea while showing the approach of the electrode array leads, which pass through a hole in the modiolar bone (d), (e), ending with the array itself. Slices (f), (g) and final close-up (h) show the electrode shanks and tips as faint segments extending up and right from the electrode lead contacts (white spots).

We experimented with three different rendering methods as shown in Figure 4. The top row is rendered with opaque surfaces, which clearly shows the spiral shape of the cochlea, as well as the tips of the electrode array. The spatial relationship between the two, however, is better shown with translucent surfaces (in the second row). The translucency was created by modifying the transfer function that assigns opacity as a function of CT image value. As an alternative, the images in the third row also show the position of the electrode, and are very good at showing the internal structure of the cochlea. These images are nice examples of how informative visualizations can come from simple rendering algorithms: there is no shading, no transfer function, and no compositing. Instead, the sum of the CT image values along each ray are linearly mapped to green, and a sum of the gradient magnitudes are mapped to magenta.

These renderings confirm that the electrode array was implanted at the correct location, and that it maintained its configuration during the six months between implantation and CT imaging.

3 Non-Linear Filtering of Bone Scans

The mouse is an important animal model for the biomedical sciences. Developmental biologists study the growth of bones in mouse embryos, aiming to quantify size and shape as a function of different environmental and genetic factors. The traditional means for observing bone formation is by sacrificing and skinning the animal, followed by a lengthy chemical staining process, resulting in a specimen suitable for photo-microscopy. Within the resolution and contrast constraints imposed by the size and density of the bones, CT imaging may provide a way of inspecting embryo bones with much less effort. Similarly, volume rendering may offer an effective way to rapidly explore and interpret the CT data without the time-consuming task of segmentation, since for large scans segmentation usually is either a manual or (at best) supervised process. A major impediment to creating informative visualizations is noisy data.

While visualization practitioners often consider CT datasets as being less noisy than other modalities such as ultrasound or clinical MRI, small animal imaging CT scans can present significant signal-to-noise challenges. One problem is with contrast: the tissues of interest do not always have markedly different radio-opacity than their surroundings. The developing bones of a mouse embryo, for example, are partially and unevenly calcified. Regions which consist solely of cartilage are essentially indistinguishable in their CT value from the nearby soft tissue. A related issue is that the size of some features can approach the limits of the imaging resolution. In combination with the effects of partial voluming, it can become difficult to distinguish CT values inside and outside small features. This hampers the creation of a meaningful visualization.

Non-linear filtering methods from image processing are one way to mitigate noise while preserving important features. A standard method is *anisotropic diffusion*, wherein the image values are blurred by an amount governed by a function of the gradient magnitude [4]. This function, called the "conductance", decreases with high gradient magnitudes, to lessen the amount of blurring near edges or boundaries. Unfortunately, the conductance function often requires careful trial-and-error adjustment. A recent improvement on the basic anisotropic diffusion method, called *modified curvature diffusion*, operates on the space of image level sets (rather the image height-field), and tends to be both more accurate and easier to use [5]. The improved method moves image levels sets along their normal at a speed governed by both mean curvature and the conductance function of gradient magnitude. Modified curvature diffusion has been applied to the CT scans of a mouse embryo.

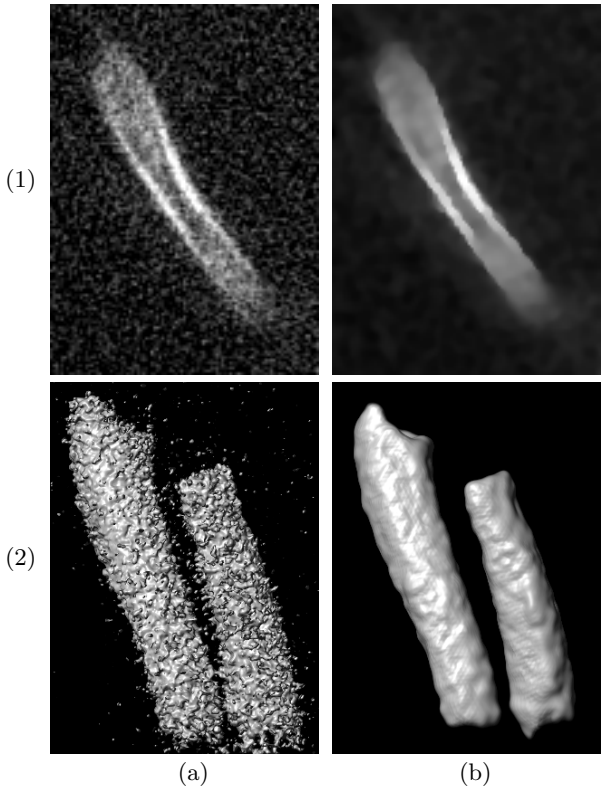

Figure 5: A slice (row 1) and an isosurface (row 2) of a portion of a CT dataset before (column a) and after (column b) modified curvature diffusion.

Figure 5 shows the original data (column a) and the data after modified curvature diffusion (column b), with a slice

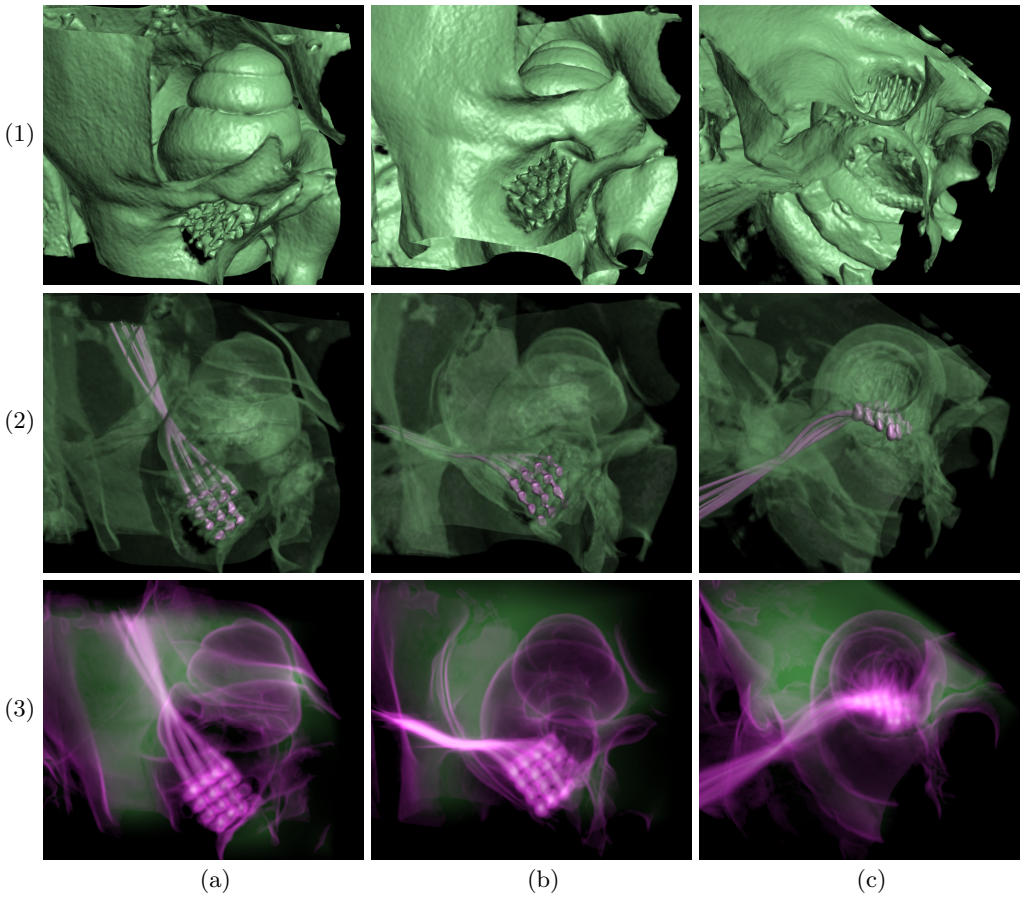

Figure 4: Volume renderings of electrode array implanted in feline skull. The volume is rotated gradually upwards in columns (a), (b), and (c), from seeing the side of the cochlea exterior in (a), to looking down the path of the cochlear nerve in (c). From top to bottom, each row uses different rendering styles; (1): volume renderings with opaque bone; (2): volume renderings with translucent bone, showing the electrode leads in magenta; and summation projections of CT values (green) and gradient magnitudes (magenta).

through the volume (row 1) and an isosurface rendering (row 2). These images show a portion of a mouse scan centered on the forearm. The noise, prominent in the original data, has been greatly reduced through non-linear filtering, while the bone boundary remains clear.

Figure 6: CT renderings (here of a mouse thorax) combine a two-dimensional opacity function (a), object contours (b), and depth cueing (c).

Figure 6 shows the cumulative effect of the different transfer function components we have used to visualize bones in the mouse, starting with the soft isosurfaces made possible by two-dimensional opacity functions [2]. Transfer functions based on surface curvature enable the rendering of feature contours with roughly constant image-space thickness, helping to clarify the shape and position of the individual bones (b) [1]. Finally, depth cueing is a simple but effective way to clarify the relationship between foreground and background objects (c). The renderings shown in Figure 7 combine these effects into a five-dimensional transfer function implemented as two two-dimensional lookup tables (for opacity and silhouettes) and one one-dimensional lookup table (depth cueing). These images successfully provide a vivid sense of the bone structure in the embryo, although the precise shapes and connections among bones would have to be confirmed by other means.

4 Discussion

Basic questions about three-dimensional structure and configuration are often central to a biological inquiry. In our collaborations, we have tried to answer two such questions: Was the electrode array implanted in the feline skull in the correct location and orientation relative to the auditory nerve? What are the shapes and sizes of bones in a living normal mouse embryo? The combination of small animal imaging, image processing, and volume rendering may help provide answers. Following acquisition, image filtering (such as the

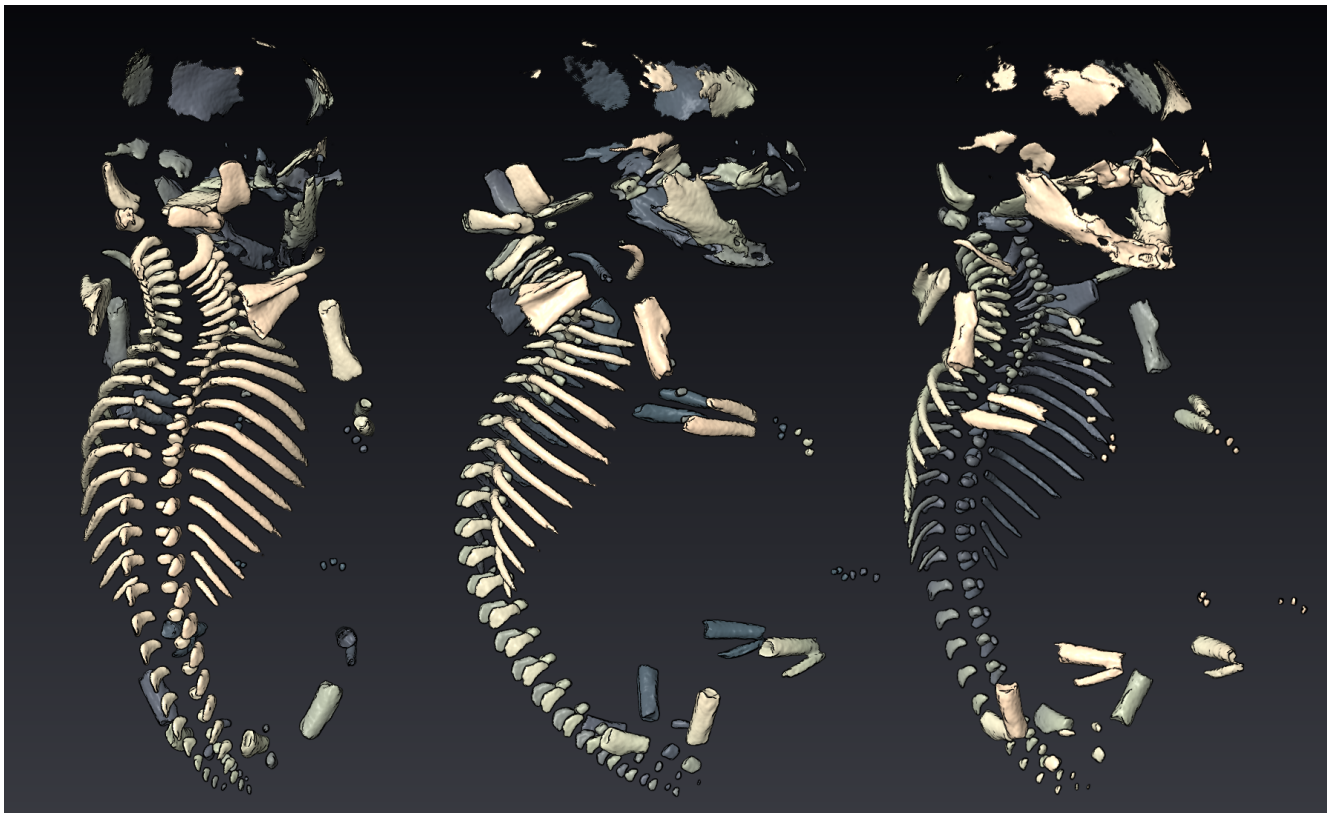

Figure 7: Renderings of the mouse embryo skeleton (18 day gestation) using the transfer function developed in Figure 6.

modified curvature diffusion demonstrated here) plays the vital role of removing noise that would slow or confound further processing. At this point, segmentation and feature quantitation may be required to test particular scientific hypotheses, but we feel that the two studies described in this column are good examples of how direct volume rendering can make scientifically informative visualizations without the computation expense of segmentation.

The effectiveness of direct volume rendering as a tool of scientific visualization depends on the action of the transfer function, which maps from the numerical properties of the acquired volume data to the colors and opacities making the final rendering. The complexity of the transfer function can be adapted according to the dataset and the visualization goals, ranging from the one-dimensional transfer functions used in visualizing electrode array, to the five-dimensional transfer functions used to visualize the mouse bones. The interplay between image acquisition, image processing, and visualization can generate a better understanding of the physical properties of structures being studied, which in turn can inform the application and optimization of subsequent segmentation algorithms. Our continued experience in applying these methods to real-world scientific problems will hopefully lead to improvements in their efficiency, flexibility, and ease of use.

5 Acknowledgments

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