# NON-LINEAR REGISTRATION OF HISTOLOGICAL IMAGES FOR 3-D MIDDLE-EAR MODELLING

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# 1. INTRODUCTION

Hearing loss is the most common sensory impairment. It has been estimated that more than 560 million people worldwide suffer from mild or worse hearing loss (Davis, 1995). Conductive hearing losses involve middle-ear disorders. Advances in otology and biomechanical engineering have led to new surgical techniques and to developments in the design of implantable hearing aids. Further advances will demand detailed analyses of the acoustical and mechanical properties of the middle ear.

A comprehensive and reliable finite-element model of the human middle ear can provide a better understanding of the biomechanics of its many interrelated structures. The middle ear, situated within a physiologically complex milieu, consists of an air-filled cavity extending from the eardrum (tympanic membrane) to the oval window (the interface with the inner ear). The cavity contains three bones, two muscles and several ligaments and other structures. Geometries of models are often based on microscopic X-ray computed tomography (microCT) or magnetic resonance microscopy (MRM). Due to the limited contrast and resolution of these imaging modalities, however, it is not possible to distinguish details like the different tissue types in the ear canal, the fine details of the middle-ear ligaments and joints, and the distinct ossified and cartilage components of the bones. Histological images offer much better image contrast and resolution, and permit one to identify the sub-structural intricacies of the middle ear. Such details are important for realistic finite-element modelling of middle-ear mechanics and acoustics. However, serious spatial misalignments and distortions are introduced at the time of histological tissue processing. The usual approach is to employ a suitable registration technique to account for the misalignments. Various warping strategies are available. Linear transformations are most commonly used to align the images with one another, but this cannot correct for all of the distortions. Non-linear registration techniques also exist and one such algorithm, developed at the Brain Imaging Centre (BIC) at McGill University, has been used for the creation of a brain atlas from serial histological data (Chakravarty et al., 2003). In this paper, we investigate the adaptation of the above non-linear warping algorithm for registration of a human middle-ear histological data set. Preliminary results are presented, with an emphasis on the

long-term goal of obtaining a reliable and refined finiteelement model of the human middle ear.

# 2. METHODS

#### 2.1 Histological data acquisition

The histological data set of the adult human middle ear was acquired from C. Northrop (Temporal Bone Foundation, Boston). The histological block was cut into 20-µm-thick sections and every tenth slice was stained with hæmatoxylin and eosin to yield a total of 56 slices. Each slice was digitized using a slide scanner to form images of size  $3644 \times 2152$  pixels. The histological images were then downsampled by a factor of 4 for speed of processing.

#### 2.2 Non-linear registration algorithm

The non-linear warping algorithm used is a variant of the Automatic Nonlinear Image Matching and Anatomical Labelling (ANIMAL) algorithm (Collins and Evans, 1997). The aim is to maximize the slice-to-slice (source-to-target) anatomical consistency between adjacent slices in order to achieve global 3-D consistency. The ANIMAL algorithm defines a 2-D regular lattice of control nodes and computes a vector for each node that maximizes the correlation ratio for the local intensity neighbourhood centred at each of these lattice points. The non-linear spatial registration transformation is computed in a hierarchical fashion: deformations are first estimated on slices blurred with a Gaussian kernel having a large full width at half maximum (FWHM) and then the transformations are further refined by estimating deformations on slices with Gaussian kernels having smaller FWHM's. This blurring is done three times, and for each step the ANIMAL algorithm is applied iteratively. The transformations are represented by deformation fields which are defined to be locally translational, so the deformation vector at each node can be considered independently from its neighbours. This is followed by a smoothing step to ensure continuity of the deformation fields. Both the local and smoothing processes are carried out iteratively to achieve global optimization. The overall optimization is thus achieved by amalgamation of all the local optimizations computed at each lattice point. The quality of the non-linear transformation can be altered by three parameters: the similarity cost ratio, the stiffness and the weight. The transformation thus obtained can be applied to the coördinates of the segmented contours, the surface triangulation of which yields a 3-D model.

## 3. **RESULTS**

Here we present preliminary results of the application of the algorithm described above. Sample histological images are shown in the figures to illustrate the registration principle. Fig. 1 shows the source slice, which is registered onto the target slice (Fig. 2). Fig. 3 shows the source slice after registration.

Some of the anatomical parts of the temporal bone are marked in the figures: semicircular canal (a), stapes footplate (b), cochlea (c) and external ear canal (d). The geometry of the stapes footplate in the source slice seems to have been registered well onto the target, as seen in Fig. 3. The smooth rounded outlines of the semicircular canal and cochlea, however, have been seriously distorted, and the region of the ear canal has become smeared.



Fig. 1: Source slice of human temporal bone.



Fig. 2: Target slice.



Fig. 3: Registered slice.

## 4. CONCLUSION

The preliminary application of the registration algorithm led to good results for some structures but poor results for other structures. Various approaches can be taken to improve the outcome. For example, the 2-D slice-to-slice algorithm relies on a set of parameters that was initially optimized by Chakravarty et al. (2006) for certain areas of the human brain (basal ganglia and thalamus). The optimization was done by using an exhaustive search strategy to minimize the mean chamfer distance between the source and target contour data. Redoing this parameter optimization for the middle-ear histological data may allow more successful registrations, leading to more accurate mechanical and acoustical models and thus to new insights into the function of the middle ear.

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