SUPER-RESOLUTION RECONSTRUCTION OF WHOLE-BODY MRI MOUSE DATA: AN INTERACTIVE APPROACH

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ABSTRACT
Super-resolution reconstruction (SRR) is a post-acquisition method for producing a high-resolution (HR) image from a set of low-resolution (LR) images. However, for large volumes of data, this technique is computationally very demanding and time consuming. In this study we focus on the specific case of whole-body mouse data and present a novel, integrated, end-to-end approach to overcome this problem. We combine articulated atlas-based segmentation and planar reformation techniques with state-of-the-art in SRR to produce high resolution, interactively selected, localized isotropic volumes-of-interest in whole-body mouse MRI. With this method we overcome time and memory related limitations when applying the SRR algorithm to the entire dataset, enabling interactive visualization and exploration of anatomical structures of interest in whole-body MRI mouse data on a normal desktop PC.

Index Terms—Whole-Body, Articulated, Atlas-Based, Registration, Skeleton Segmentation, Image Processing, Molecular Imaging, Planar Reformation, Interactive, MOBY, MRI, Super-Resolution Reconstruction

1. INTRODUCTION
SRR is the process of producing a high-resolution (HR) image from a sequence of low-resolution (LR) images, where each LR image transforms and samples the HR scene in a distinct fashion. The idea was first introduced in the 1980s [1] and has since grown into a research field of its own. The first example of SRR applied to MRI was described in a 2001 patent [2]. SRR in MRI is a developing field, and encouraging results have been published showing its potential in resolution enhancement [3,4]. For an overview of SRR research in the biomedical field, see [5].

One drawback of the SRR technique is the demanding computation power and time that is necessary to reconstruct large volumes (whole-body mice datasets in this case). To overcome this impracticality, in this study we take advantage of recent progress in the areas of articulated atlas-based segmentation of whole-body small animal data [6–8] and MRI super-resolution reconstruction (SRR) [9,10].

We present a new integrated approach that enables global exploration of whole-body mouse MRI data, with local, interactive SRR enhancement of user selected volumes-of-interest (VOIs). The idea is similar to that of well-known web-based geographical maps, where it is possible from a global overview image to zoom in on a detail of interest. Such a functionality is relevant in a biomedical setting when working with high-resolution volumetric data. In the approach presented in this paper, data is loaded on a "just-in-time" basis: from a global low-resolution image the user is allowed to zoom in on a sub-volume of interest. The data needed to reconstruct the sub-volume at the requested level of resolution is collected from a database of low-resolution images and the sub-volume is reconstructed on the fly using SRR.

The sub-volumes of interest are obtained by segmenting one of the whole-body LR datasets using the semi-automatic whole-body articulated atlas-based method, first presented in [11] and applying the articulated planar reformation algorithm [8] which maps the data to a standardized atlas space.

The contributions of this paper are twofold:
• We present a new method for producing highly resolved, user selected, localized isotropic VOIs in whole-body mouse MRI. This enables interactive visualization and exploration of anatomical structures in whole-body MRI mouse data on a normal desktop PC.
• We realise this by combining recent progress in articulated atlas-based segmentation and planar reformation with state of the art in SRR.

In the following we describe the components of our approach and show that it enables interactive reconstruction of high-resolution volumes for interactive exploration of whole-body MRI mouse data.

2. METHODS AND MATERIALS
2.1. MRI mouse data
A whole-body scan of a post-mortem C57BL/6, 6 month old, male mouse was acquired on a 7T Bruker Pharmascan™ system using a recovery FSE (hFSE) sequence. TR was 6648 ms, TE was 33 ms, with Navg = 1 and NSP = 1. The 2D slice stack consisted of 64 slices (0.5 mm thick), with a FOV of 50 x 32 mm, and a resulting resolution of 0.125 x 0.125 x 0.5 mm. The scan time per stack was 213 s. The slice stack was rotated 24 times in uniform increments of 180/24 degrees. Due to the scanner’s limited FOV, the mouse was scanned in three sections (head, chest, lower abdomen).
2.2. Stitching

In order to reconstruct the complete mouse volume, one needs to know the relative positioning of each of the acquired subvolumes in the scanner. That requires registering two image stacks to each other, which, in case when only the translation is unknown, is usually done by using correlation-based methods. For the given type of data, the image gradient is the most complete and reliable source of information since MR is known to provide good contrast between different soft tissues, while direct usage of the intensity information might be hampered by possible field inhomogeneity and variations between different image stacks. In this work, we used a 3D extension of the gradient-correlation-based scheme recently developed by Tsimopoulos et al. [12] for recovering the translations between each two consecutive image stacks. After the relative positions of image stacks are known, the final volume is obtained by using the multiresolution method of Burt and Adelson [13] in the overlap areas, see Figure 1.

![Image of overlapping image stacks](image)

**Fig. 1.** Registration performance of the full volume reconstruction algorithm. One coronal slice from each of the three acquired image stacks (top 3 images) and from the final reconstructed volume (bottom) are shown. Image contrast is enhanced for visualization purposes.

2.3. MOBY atlas

The MOBY mouse atlas was used as the anatomical reference. Segars et al. [14] used a C77BL/6, 15 week old male mouse to generate a realistic 4D digital mouse phantom based on high-resolution 3D MRI data. For the bone segmentation described here, we used an articulated version of the MOBY skeleton [6,7], where all major bones or bone compounds like the paws were separately labeled and joint locations and types were defined. See Figure 2.(a).

2.4. Articulated atlas-based bone segmentation

To segment the mouse, the semi-automated bone approximation method first presented in [11] for whole-body µMRI mouse data was applied on one of the 24 datasets (Figure 2.(b)). This approach, where the user identifies 16 landmarks, considerably reduces the required user effort compared to a manual segmentation.

Using the Amira software and guided by an anatomical text book [15], the following 15 joint and bone landmarks were manually extracted in one of the mouse datasets: 2 knee joints, 2 hip joints, posterior and anterior extremities of the sternum, right and left anterior pelvic extremities, 2 elbow joints, 2 shoulder joints, 2 ankle joints and 2 wrist joints (Figure 2(c)). After the landmark selection in an arbitrary order the joints are automatically identified. Using the atlas (joint locations, anatomically realistic bone dimensions, anatomically realistic degrees of freedom for each joint) and a hierarchical anatomical model of the skeleton all joints can be labeled and the correspondent bones fitted to the data (see [11] for more details), (Figure 2.(d)).

2.5. Articulated planar reformation

Articulated planar reformation (APR), is a method first developed for follow-up data in [8]. This method uses the articulated registration approach described above and in [6] to reformat the data into segments corresponding to a mouse atlas and thus maps the data to a standardized atlas space. After applying APR to one of the low-resolution MRI datasets, the user can interactively select any sub-volume of interest for a subsequent interactive SRR of that volume, see Figure 2.(e, f).

2.6. Super-resolution reconstruction

After interactive selection of a sub-volume of interest in the low-resolution MR image, spatially corresponding volumes are extracted from all low-resolution datasets. These volumes differ, according to the acquisition scheme described above, in angular shifts in the sampling grid orientation. Our super-resolution technique then is applied to reconstruct the volume on a high-resolution grid.

The MRI acquisition process can be modeled by a linear system A encompassing a geometric transformation, blur and sampling operators, and a Gaussian noise model [16]. The $k^{th}$ acquisition in a series of LR images can thus be described by $y_k = A_k x + n_k$, where $x$ is the HR image to be reconstructed.

SRR is an inverse problem and involves recovering $x$ given the $y_k$ and $A_k$. Using additional prior knowledge about the solution, e.g. that it is smooth, the problem can be formulated as a regularized least squares problem:

$$\hat{x} = \arg\min_x \sum_{k=1}^N \| y_k - A_k x \|^2 + \lambda C,$$

where $C$ is a regularization term formalizing the prior, and $\lambda$ is a scalar weight.

A direct solution of Eq. (1) is generally infeasible. Instead, iterative methods are applied to approximate the solution. For the purpose of both effective and efficient reconstruction, the method developed in [10] was chosen for our pipeline. Based on the assumption that the HR image is mainly smooth, this method employs Tikhonov regularization using the $L_2$-norm of the second order derivative of the reconstruction as the regularization term:

$$C = \| \nabla^2 x \|^2 = \left( \frac{\partial^2 x}{\partial x^2} \right)^2 + \left( \frac{\partial^2 x}{\partial y^2} \right)^2 + \left( \frac{\partial^2 x}{\partial z^2} \right)^2,$$

where $v$ is the spatial dimension over which the partial derivative is taken. The regularized LS problem of Eq. (1) was solved by the conjugate gradient method and the transforms in $A_k$ and $A^*$ were implemented using a set of shear transforms that minimizes aliasing and spectral distortions [10].

3. EXPERIMENTAL RESULTS

The proposed SRR approach was tested for each segmented bone (femur, tibia-fibula, pelvis, sternum, humerus, ulna-radius), using an increasing number of LR images (2, 4, 8 and 12). The SRR times for each bone experiment were compared with the SRR times for the
Fig. 2. Overview of the proposed approach: (a) - MOBY mouse atlas: articulated skeleton [7,14]. (b) - Original, low-resolution, stitched MRI data. (c) - Manual landmarks selection: 2 knee joints, 2 hip joints, posterior and anterior extremities of the sternum, 2 elbow joints, 2 shoulder joints, 2 ankle joints, 2 wrist joints, right and left anterior pelvis extremities. (d) - Registered atlas bones to the data. (d-e) - APR of the LR, MRI mouse data. The user can now interactively select any LR bone of interest (left femur) from the standardized MOBY atlas space. (f) - The SRR algorithm applied to the selected left femur. From left to right: the selected LR image and the HR image reconstructed using 2, 4, 8 and 12 LR images respectively. The improvement in image quality is especially noticeable when using a high zooming factor. The red arrow indicates the distortion caused by the low sampling in the $z$ direction during the acquisition. Applying the SRR, results in HR volumes with isotropic sampling and this issue is resolved. Note: the $z$ axis of the volume shown is not aligned with the $z$ direction during acquisition but with the principal axes of the bone. The data has been resampled in order to align the bone to the reconstructed volume.
same experiments performed for the whole-body dataset. The times to perform each SRR experiment are shown in Table 1. All the experiments were implemented in MATLAB R2009b™ and performed on a 2.80GHz Intel Xeon® with 12GB of RAM, Windows® PC.

<table>
<thead>
<tr>
<th>Bone</th>
<th>2 LR</th>
<th>4 LR</th>
<th>8 LR</th>
<th>12 LR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Femur</td>
<td>52</td>
<td>55</td>
<td>140</td>
<td>222</td>
</tr>
<tr>
<td>Tibia-Fibula</td>
<td>59</td>
<td>94</td>
<td>184</td>
<td>286</td>
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<tr>
<td>Pelvis</td>
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<td>119</td>
<td>249</td>
<td>372</td>
</tr>
<tr>
<td>Sternum</td>
<td>64</td>
<td>99</td>
<td>150</td>
<td>249</td>
</tr>
<tr>
<td>Humerus</td>
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<td>56</td>
<td>117</td>
<td>170</td>
</tr>
<tr>
<td>Ulna-Radial</td>
<td>33</td>
<td>84</td>
<td>139</td>
<td>249</td>
</tr>
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The times in seconds, for each reconstructed bone and the whole-body, using 2, 4, 8 and 12 LR images. For the whole-body experiments, the SRR times using 12 LR images were not possible due to insufficient memory.

5. ACKNOWLEDGMENTS

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6. REFERENCES