Medical Images and Signals IRC

Plenary meeting 19th and 20th October 2004

The Medical Images and Signals IRC (MIAS-IRC) started a 6 year programme in January 2001 with funding from the MRC and EPSRC. Processing of information from medical images and signals is having a major impact in healthcare and medical science.

– New advances in medical image computing are providing very accurate measurements of disease progression and response to therapy. Measurements that are currently undertaken by laborious interactive analysis of large datasets are poised to become completely automated using advances in anatomical atlas generation, image registration, physical modelling, shape modelling, motion modelling and segmentation propagation. Members of the IRC have pioneered many of these component technologies and are now working on effective integrated systems.

– Recent developments in MR, CT and 3D ultrasound have dramatically increased the volume of data that requires processing. In many routine procedures it is now impossible to interpret the images acquired just by viewing them on a workstation screen. Automating analysis provides the only solution.

– The rapid take-up of image based cancer screening methods has put an intolerable load on those who have to interpret the very large numbers of images generated. Members of the IRC are working on solutions to provide accurate and robust automated analysis systems.

– In the areas of intervention and therapy localisation requirements are becoming more precise, while procedures are becoming much less invasive. This is putting a much greater demand on information extracted from images and signals, methods for image registration and modelling tissue deformation and motion. Again the IRC is pioneering the development of the computational technologies required for these new applications.

– Modern scanners incorporate powerful computers to rapidly reconstruct images yet it is clinical information not images that the clinician requires. The IRC has been pioneering methods that incorporate sophisticated information processing close to the image acquisition process.

– In biomedical research imaging and signals provide an increasingly important source of experimental information. As an example, the IRC is developing new ways of representing and measuring the fibre tracts in the brain using MR imaging, which will have a major impact on understanding brain connectivity in health and disease. Integration of signals and images is providing new understanding of the mechanisms of the regulation of blood flow and cerebral function.

Our remit was to bring together four of the major UK groups working in medical image and signals analysis, KCL, the University of Manchester, the University of Oxford and UCL. After one year Imperial joined the Consortium and we reorganised our activity around three so-called Grand Challenges: Structure and Function, Multiscale Modelling and Intelligent Image Acquisition to better focus and manage our large consortium. The objectives within each of these grand challenges directed our work for the next 2 years. We presented our progress at the mid-term review (effectively 2 years into our
programme due to the time taken to ramp up our activity).

This booklet provides a collection of short papers that summarise our activity and achievements over the last 12 months. We now need to grasp the opportunities that have arisen across the grand challenge boundaries. The papers presented in this booklet have been arranged into topics showing that at least some of the contributions cross these boundaries. About half the papers were presented orally at the plenary meeting and half as posters with plenty of opportunity for informal discussion of the research they represent. This provides a useful snapshot of the breadth and depth of our activity and contributions to all the areas outlined above are represented in these papers. We are now just over half way through the lifetime of our IRC and it is time to define precisely what we aim to achieve over the remaining time. The future holds significant promise for major advances in our area of research.

Immediately following the plenary meeting the London Technology Network, in collaboration with MIAS-IRC, held a technology transfer event to promote and encourage dissemination of the results of research in medical image and signal analysis. This allowed us to present our research output to key players and decision makers in the industries that support imaging in healthcare and biomedical research.

Finally, all this would not have been possible without all the hard work of the IRC coordinator, Jennet Batten, who has proved extremely skilled at herding cats, and who prepared the programme and the booklet and organised the logistics of the event. Also Daniel Rueckert’s considerable help in producing the booklet is gratefully acknowledged. We are also grateful to the coordinator of the Industrial Advisory Board, Pauline Hobday, for organising the IRC’s input to the LTN event. The Board wishes to thank both Jennet Batten and Pauline Hobday for all their efforts.

David Hawkes, MIAS-IRC Director
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A Generative Statistical Model of Mammographic Appearance

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1 Introduction

Computer-aided detection (CADe) in mammography has traditionally been treated as a pattern recognition task, attempting to emulate radiologists’ interpretation strategies. We propose instead that CADe should be performed via novelty detection. This requires a model of normal mammographic appearance. Not only are there far more pathology-free than abnormal mammograms from which to learn, but novelty detection would detect all abnormal features, rather than specific classes. Models of entire mammograms have been proposed [1] previously, but tend to produce unrealistic images and cannot be used in the analytical mode. Models of image patches [2] can yield realistic synthetic images, and can be used in analytical mode, but are of limited value for analysing entire mammograms. We have developed a generative statistical model of entire mammograms that can be extended to perform novelty detection. The generative property is useful because it allows us to evaluate the model’s specificity. We briefly describe the model, show synthetic images generated using the model, and summarise results from qualitative and quantitative evaluations of the synthetic images.

2 Method

We would like to be able to treat a mammogram as a point in an appearance space so that statistical analysis could be applied. Unfortunately, because mammograms must be digitised at high-resolution, the dimensionality of the space would be so large that it could not be sufficiently populated. We seek to overcome this problem by treating the approximate appearance separately from the detailed local texture. We decompose each image in a training set of shape-normalised mammograms using a wavelet-like decomposition. The wavelet coefficients can be viewed as having a pyramidal structure: at the top is a representation of the coarse structure of the image, and at the bottom is a representation of the fine structure. We model the distribution of the coefficients in the top few pyramid levels (capturing the approximate appearance) and model the distribution of the coefficients in the bottom levels assuming spatial ergodicity. Finally, the joint distribution of shape and approximate appearance is modelled. We can then generate a synthetic mammogram by sampling from the appearance model, conditionally sampling from the ergodic model, computing the inverse wavelet transform and finally warping to a conditionally sampled shape.

3 Results and Discussion

Figure 1 shows a real mammogram and several synthetic mammograms generated using our model. Qualitative evaluation was performed by an expert mammography radiologist, who gave generally positive feedback. Quantitative evaluation was performed using a psychophysical forced-choice experiment. Five participants each viewed 49 pairs of real and synthetic reduced resolution mammograms. $\chi^2$ analysis showed that two participants did no better than random (one at the 95% level, one at the 99.9% level), while the others consistently mistook the real and synthetic images. The results show that, although further improvement is needed, the differences between the real and synthetic images were very subtle. Future work will seek to improve the model and extend it to perform CADe via novelty detection.

References

1 Introduction

Modelling the elastic properties of tissue and deformation under external loads has various applications in medical diagnosis and analysis: in understanding the mechanism of trabecular bone formation, elastic modelling can help understand the changes in structure under changing external forces, for example in the presence of a joint replacement, or the influence of bone deterioration in osteoporosis. In soft tissue modelling, an elastic deformation model can provide a tool to predict and validate deformations under application of surface and volume displacements. Examples are the modelling of breast tissue deformation under compression in mammography, or brain deformation during surgery. We have developed a three-dimensional finite element model of linear elasticity capable of calculating the volume displacement field of an elastic body with distributed inhomogeneous material properties under explicit boundary displacements, boundary or volume forces. The model can operate either with an unstructured mesh of tetrahedral elements obtained from segmentation information, or on a regular voxel mesh directly converted from an MRI image.

2 Finite element model

The objective of the model is to calculate the displacement field \( \mathbf{u}(\mathbf{r}) = \{u(r), v(r), w(r)\}^T \) at each point \( \mathbf{r} \) of an elastic body under the influence of boundary forces and volume loads. In the linear case the relationship between stress \( \sigma \) and strain \( \varepsilon \) is given by Hooke’s law

\[
\sigma = \mathbf{D}(\varepsilon - \varepsilon_0) + \sigma_0
\]

where the strain and stress tensors contain longitudinal and shear components

\[
\varepsilon = \begin{bmatrix}
\frac{\partial u}{\partial x} & 0 & 0 \\
0 & \frac{\partial v}{\partial y} & 0 \\
0 & 0 & \frac{\partial w}{\partial z}
\end{bmatrix}
\quad \quad
\sigma = \begin{bmatrix}
\sigma_x \\
\sigma_y \\
\sigma_z \\
\tau_{xy} \\
\tau_{yz} \\
\tau_{xz}
\end{bmatrix}
\]

with initial residual strain \( \varepsilon_0 \), initial residual stress \( \sigma_0 \), and the elasticity matrix \( \mathbf{D} \) incorporating the appropriate material properties. In the isotropic case, \( \mathbf{D} \) is symmetric and defined by two parameters, Young’s modulus \( E \) and Poisson’s ratio \( \nu \). Using the method of virtual work \([1]\) and discretising the problem by defining a basis \( N_i, i = 1..n \) over the domain, the elastic model for displacement field \( \mathbf{a} \) can be described by the linear system

\[
\mathbf{K}\mathbf{a} + \mathbf{f} = \mathbf{q}
\]

where

\[
\mathbf{K} = \int_V \delta \varepsilon^T \sigma d\mathbf{r} = \int_V \mathbf{B}^T \mathbf{D} \mathbf{B} d\mathbf{r}
\]

and \( \mathbf{f} \) is given by

\[
\mathbf{f} = -\int_V \mathbf{N}^T \mathbf{b} d\mathbf{r} - \int_A \mathbf{N}^T \mathbf{t} d\mathbf{s} - \int_V \mathbf{B}^T \mathbf{D} \varepsilon_0 d\mathbf{r} + \int_V \mathbf{B}^T \sigma_0 d\mathbf{r}
\]

where \( \mathbf{B} \) is the appropriate strain matrix, \( \mathbf{q} \) is the force acting under the influence of boundary loads \( \mathbf{t} \) and distributed volume loads \( \mathbf{b} \).

3 FEM in bone remodelling

Models of bone growth and depletion under external load iteratively apply an elastic model to obtain the volume distribution of strain energy density \( \rho(\mathbf{r}) = \mathbf{a}^T \mathbf{K} \mathbf{a} \) which is then used to grow the mesh in areas with \( \rho > \rho_i \)

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and deplete it in areas where $\rho < \rho_2$ with model-dependent threshold values $\rho_1 > \rho_2$. Figure 1 compares the distribution of $\rho$ for an X- and a H-shaped 3-D bone structure element under application of an oblique force vector at the top and bottom surfaces. Each of the two meshes consists of approx. 40000 regular 8-noded voxel elements. The use of a regular mesh grid facilitates the ability to grow and erode the mesh with minimal computational cost in the remeshing process. Dark regions represent areas of low $\rho$ which would be depleted by the growth algorithm, while bright areas represent high $\rho$ which would stimulate growth at the adjacent surface layers.

4 Soft tissue modelling

Finite element elastic modelling can also be used to predict structural volume deformations of soft tissue under external boundary displacements. An example is the deformation of breast tissue under compression during mammography. Figure 2 shows a mesh consisting of 680000 tetrahedral elements obtained from a segmented 3-D breast MRI image. Elastic properties were assigned to the adipose and fibrous parts of the mesh, and an external displacement simulating the compression between parallel plates was applied to the top and bottom surfaces. The middle image shows the resulting distribution of strain energy densities on the surface of the compressed mesh, with the maximum energy density along the edge of the compression plate clearly visible. The right images show the deformation of a lesion in the breast as a result of the deformation. It can be seen easily that compression has a major influence on the internal tissue distribution, an effect that must be taken into account when planning surgery on the basis of mammographic images.

Acknowledgements

We would like to thank Christine Tanner, King’s College London, for providing the segmented breast meshes used for the deformation studies.

References

Establishing skin surface correspondence in breast surgery

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1 Introduction

Breast cancer is the most common malignancy in women, affecting one in nine females. 70% of breast cancers are treated with breast conservation therapy, in which the lesion and a margin of tissue around it are removed. Unfortunately 15% of these operations require repeat surgery [1], usually because histology shows cancer at, or close to, the resection margins.

We are therefore developing an image guidance system to allow the surgeon to visualise the location and extents of the lesion during surgery. We propose a technique in which a finite element model of the breast, built from pre-operative MR images, is displaced according to the skin surface acquired during surgery to provide the surgeon with an updated location of the lesion. We present here a method for establishing correspondence between two skin surfaces, which will be used to match the surface of the breast acquired with a stereo camera during surgery to the surface of the biomechanical model. We demonstrate it here by matching two surfaces captured with a stereo camera.

2 Method

Surfaces of the breast were acquired during surgery, with the patient’s arm by their side (as it would be during MR scanning) and with their arm out at right angles (as it would be during an operation). The surfaces consisted of approximately 3500 node points, with 3.5mm spacing and a localisation accuracy of 0.1mm over the region of interest. In addition to the node point a texture map was acquired. This could be overlaid on the surface to allow texture features, such as the henna markings that were used as fiducial markers, to be localised. Triangulated meshes were built from the node points. Seven fiducial markers were located in the coordinate frame of each mesh, and the closest vertex to each of these fiducials was adjusted into their position. The superior, inferior, medial and lateral extremes of the nipple were also localised as fiducial locations.

Figure 1. Acquiring surfaces in theatre. The stereo camera can be seen in the foreground

The meshes were aligned by performing a rigid registration of the fiducial marker locations [2]. The deformable mesh was then trimmed to ensure that it was smaller than the target mesh, and that only relevant skin surfaces (rather than, for example, the drapes) were being matched.

A mass-spring model was built from the deformable mesh, with the spring rest-lengths equal to the length of each triangle side and a mass located at each vertex. In addition to the spring forces, force was applied to each mass towards the target surface. A stronger force was applied to each fiducial towards its known location in the target mesh. No angular springs were used to prevent the surface bending, as changes in curvature should be allowed.

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The second order equations of motion of the mesh were simulated using an explicit Euler procedure. Initially the stiffness constants of the springs were set to be inversely proportional to their distance from the closest fiducial, with an upper limit on their value to prevent numerical instability. This prevented folding of the mesh despite relatively high forces being applied to the individual masses representing fiducial markers. Once all the fiducials in the deformable mesh were close to their target positions they were moved to be exactly at their target position, without the risk of folding. The stiffness constants for all springs were then set to the same value and the mesh was allowed to relax, whilst constraining the fiducials to lie at their target positions and applying forces, as before, to keep the mesh aligned with the target surface.

3 Results

The ability of the mesh to recover surface correspondences was assessed by treating each fiducial (excluding those marking the extremes of the nipple) in turn as a target, and attempting to recover its location based on the location of the remaining fiducials.

<table>
<thead>
<tr>
<th>Registration method</th>
<th>Mean (mm)</th>
<th>Maximum (mm)</th>
<th>Std Deviation (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rigid</td>
<td>4.0</td>
<td>5.7</td>
<td>1.3</td>
</tr>
<tr>
<td>Spring-mass</td>
<td>2.6</td>
<td>4.0</td>
<td>1.1</td>
</tr>
</tbody>
</table>

Table 1. Accuracy of recovering target locations

4 Discussion and future work

Based on this limited test case, it appears that a spring mass model might be able to capture surface correspondences to an accuracy suitable for driving a finite element model of the breast. We found that the points on the extreme of the mesh were less accurately recovered than those in the centre of the mesh, so judicious positioning of fiducial markers will be required for our application. We now intend to examine the effect of mesh design on accuracy. We will then more rigorously validate our method, and validate it for matching meshes derived from MR images to stereo camera meshes. Finally we will use it to drive a volumetric finite element model of the breast.

Acknowledgements

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References

1. NHSBSP “An audit of screen detected breast cancers for the year of screening April 2002 to March 2003”, *ABS at BASO*, 26th May 2004
Parametric Surfaces and Three-Dimensional Shape-Based Reconstructions in Medical Imaging

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1 Introduction

The routine use of 3D imaging methods by the medical community, such as MRI and CT is creating a vast amount of volumetric data. The usual way of storing these data is voxel images that allow visual capturing of the objects, but lack structural description since they are based on huge lists of numbers. On the other hand new medical imaging modalities, such as Optical Tomography and Electrical Impedance Tomography require precise and smooth models of human tissues. In this work a parametric description of closed volumetric surfaces is described and employed in a shape reconstruction algorithm for Optical Tomography. Parts of the human anatomy with interest in the research of the brain are initially parameterised using a mapping algorithm to a unit sphere and then meshed using regular meshes defined on the sphere. Then a Boundary Element numerical solution of the diffusion equation for the propagation of light in media with homogeneous optical properties is constructed. Finally, the numerical forward solution is utilised in an shape parameter’s optimisation Inverse Problem for the reconstruction of region boundaries for simulated non invasive light measurements.

2 Parametric surfaces

A mapping \( f_x(\theta, \phi) \) from the surface of a volumetric voxel object(head) to a unit sphere is constructed using a method similar to [1].

\[
f_x(\theta, \phi) = \sum_{l=0}^{\infty} \sum_{m=-l}^{l} C_{l,m}^{x} \times Y_{l,m}^{m}(\theta, \phi),
\]

Where \( Y_{l,m}^{m}(\theta, \phi) \) are Spherical Harmonics functions defined on the sphere surface and \( C_{l,m}^{x} \) the coefficients, that comprise the shape parameters, \( 0 \leq \phi \leq 2\pi \) and \( 0 \leq \theta \leq \pi \) are coordinates defined on the sphere, and \( x \in \mathbb{R} \) the cartesian coordinates in the volumetric object space.

A triangular mesh defined on a sphere with nodes \( \{\theta_i, \phi_i\} \) and elements defined by nodes \( n_j, j \in [1, 6] \), can be easily mapped on the surface of the object using (1).

Figure 1. The original head MRI image and the constructed parametric description

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3 Forward Problem

Having constructed triangular meshes for the boundaries of the disjoint domains of the head, and assuming the optical properties, $\mu_a$ absorbing and $\mu_s$ reduced scattering coefficient, constant in the different types of tissue, we can form a model and solve the diffusion approximation to the transport equation [2]

$$\nabla^2 \Phi(r, \omega) - k^2 \Phi(r, \omega) = q_0(r, \omega) \quad \forall r \in \Omega \quad (2)$$

Equation 2 describes the light transport in scattering tissue, which is commonly used for Optical Tomography. $\Phi$ stands for the photon density, $\omega$ is the modulation frequency of the source, $k = \sqrt{\mu_a D - i \omega / c}$ the wave number and $D = \frac{1}{2(\mu_a + \mu_s)}$, $c(r) = c_0 / \nu(r)$ is the speed of light, $\nu(r)$ is the refractive index and $c_0$ the speed of light in a vacuum, $q_0$ is a source of light. On the surface under consideration we impose the Robin boundary conditions:

$$\Phi(r, \omega) + 2\alpha D \frac{\partial \Phi(r, \omega)}{\partial n} = 0, \quad \forall r \in \partial \Omega \quad (3)$$

where $\alpha$ depends on refractive index. A Boundary Element Method BEM is used to solve (2) and (3) on the surface of the elements [3].

4 Inverse Problem

Using the prior knowledge of the optical parameters we can now solve the inverse problem of shape reconstruction. Denoting $F(C_{m_{lx}})$ as the Forward Problem, and $z_0$ the simulated data, we form the boundary recovery as a least square problem:

$$\Xi(C_{m_{lx}}) = \|z_0 - F(C_{m_{lx}})\|^2. \quad (4)$$

The results can be seen in the figure

![Figure 2. Boundary Reconstruction in head domain. Wireframed is the reconstructed surface, solid the simulated data surface.](image)

5 Conclusions

We introduced a method for the construction of a triangulation from the surface of a voluminous object with the topology of a sphere. Smooth objects like human organs can be modelled in multiresolution, which is an inherent property of the Spherical Harmonics representation. The creation of a mesh with any number of elements is now a straightforward process. Any object with the topology of a sphere can be modelled. The implementation of BEM is enabling the calculation of a forward solution on the parametric model and the shape coefficients could be used in a shape reconstruction problem.

References

Reconstruction of the heart boundary in undersampled cardiac MRI using basis functions

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1 Introduction

Cardiac MR acquisitions are time consuming because of the need to sample all of k-space at many time points throughout the cardiac cycle in order to reconstruct a fully sampled set of images. The analysis of these images typically involves first reconstructing an image and then segmenting the left ventricle at each phase of the cardiac cycle. The lack of automatic segmentation tools implies substantial user interaction. The work described here segments the endocardial boundary directly from highly undersampled MRI measurements, rather than first acquiring a fully sampled image, then reconstructing and finally segmenting. A model is used to approximate the background and interior intensity variation, and most important the shape of the endocardiac contours using basis functions. The classification of pixels is considered to be a mapping $G : P \to X$ from the space $P$ of the parameters of the model to the pixel space $X$. The data can be further considered to be a mapping $F : X \to Y$ from the pixel space to the measurement space $Y$. The benefit of this, is that the combined mapping $y = Z(p) = F \circ G(p), p \in P, y \in Y$, can be treated as a forward model for the measurement of the object. The inverse problem is to determine the parameters of the model that produce the best fit of the forward model to the measured data.

2 Method

2.1 Forward Model

If the intensity variation is considered to be sufficiently smooth, it can be represented with local basis functions on a regular grid, for example

$$B_j(r) = B_0(r + r_j) = B_0(r) \ast \delta(r - r_j),$$

where $B_0$ is the central basis function based on the Kaiser Bessel window function \cite{1}. The exact definition of the basis functions can be found in \cite{2}. The background and interior of the heart are modelled using two separate sets of coefficients, $p_b$ and $p_i$ respectively, implying two independent grids of local basis functions. The region boundary can be approximated with the use of basis functions:

$$C(s) = \left( \begin{array}{c} x(s) \\ y(s) \end{array} \right) = \sum_{n=1}^{N_n} \left( \begin{array}{c} \theta_n^b(s) \\ \theta_n^i(s) \end{array} \right), s \in [0,1], \gamma_n \in P,$$

In this paper we use trigonometric basis functions $\{\theta_n(s)\}$ as in \cite{3}. The image $x$ generated by the mapping $G$ can be described as follows:

$$x(r) = \sum_{k=1}^{N_{b_k}} p_{b,k} B_j(r)(1 - \Theta_\gamma(r)) + \sum_{k=1}^{N_{i_k}} p_{i,k} B_j(r) \Theta_\gamma(r),$$

where $\Theta_\gamma(r)$, is the characteristic function of the curve $C(s)$ indicating for every point whether it belongs in the background or interior of $C(s)$. The implementation of eq. 3 completes the mapping $G : P \to X$ from the space of the parameters $p \in P$ to pixels $x \in X$. Finally the mapping $F : X \to Y$ is a Radon transform $R$, that maps an image to its 1D projections.

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2.2 Inverse Problem

The combined mapping \( Z = F \circ G \) is non-linear, and the solution of the inverse problem will require an iterative approach. This is typically solved using the Levenberg-Marquardt method, which updates the solution estimate:

\[
p^{k+1} = p^k + (J^*(p^k)J(p^k) + \lambda I)^{-1}J^*(p^k)[g - Z(p^k)],
\]

where \( g \) is measured data, \( J(p^k) \) is the linearization of the combined mapping \( Z \), and \( \lambda \) is a control parameter.

Since \( F \) is linear we can write \( J = F \circ \frac{\partial G}{\partial p} \), where \( \frac{\partial G}{\partial p} \) is the Jacobian of the mapping \( G \). The Jacobian is separated in three parts \( J = [J_b | J_i | J_c] \), one for each of the parameter sets \( p_b, p_i \) and \( \gamma \). The parts of the Jacobian referring to the intensity variation parameters can be calculated as follows:

\[
J_{b|i} = \begin{cases} 
R[\beta_j(r) \Theta_j(r)] & j \in \mathbb{C} \cup \mathbb{I} \\
R[\beta_j(r)(1 - \Theta_j(r))] & j \in \mathbb{C} \cup \mathbb{B},
\end{cases}
\]

(5)

The part of the Jacobian of the shape parameters can be derived as in [5]:

\[
J_c = \begin{cases} 
R \left[ \int_{s_1}^{s_2} \dot{y}(s) \theta_n(s) \, ds \right] & n \in \gamma^x \\
-R \left[ \int_{s_1}^{s_2} \dot{x}(s) \theta(s) \, ds \right] & n \in \gamma^y,
\end{cases}
\]

(6)

where \( R \) is the Radon transform.

3 Results

In a proof of concept experiment, our technique was applied to short axis steady state free precession images (TE 1.6ms, TR=3.2ms, flip angle 50 degrees) with radial k-space sampling. A fully sampled image was acquired for reference, and a highly undersampled image was simulated by extracting eight projections. The algorithm was initialised with a circular region of interest approximately located over the left ventricle.

Figure 1. a) the original image \( f \) used to generate the Radon data, b) image reconstructed by an inverse Radon transform applied to the data projections of \( f \) at 8 angles, c) initial image \( x_0 \) for the start of the algorithm, d) final image \( x_f \), e) the final contour \( C_f \) overlaid of \( f \)

4 Conclusion

The presented method shows that the left ventricle can be segmented directly from undersampled MRI data, without the reconstruction of an image.

References

Five Reasons to use Local Phase for Registration

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1 Introduction

Recently, it has been proposed that by applying statistical similarity criteria, such as mutual information, to the local phase, rather than intensity, the properties of registration algorithms based on these criteria are significantly altered [1,2]. Here, we describe in more detail the properties of phase based registration, and describe how these properties are consequences of the properties of local phase itself. This leads to a list of five properties of local descriptors which may be used as the basis for application specific local descriptor design. We describe a few existing methods for obtaining local image descriptors with some of these properties and propose a new method for obtaining the remaining properties.

2 Five Properties of Phase Based Registration

2.1 Friendly Statistics

In practice, the performance of algorithms which require the estimation of statistical distributions is often very dependent on the method used to estimate the distributions. However, there is not one ‘best method’: this will depend on the data, and therefore the application. When choosing or designing a local descriptor, it may be possible to select one for which estimation of distributions is simple. Local phase has two properties that make it a good choice in this respect. First, phase is confined to a fixed range of values, and all values must be present to some extent in any image. Second, it is a property of phase that the distribution of phase in a typical medical (or other) image is approximately flat. These two properties mean that the size of the histograms can be fixed, removing a design parameter, and that the histograms contain no ‘dead space’. More importantly, it greatly reduces the effect of the choice of the statistical similarity measure. Mutual Information (MI), joint entropy and normalised mutual information, for example, only differ in the way in which they treat the marginal distributions. If the marginals contain very little information, and are unchanged by varying regions of overlap, the three methods behave in a very similar manner.

2.2 Predictable Joint Distribution

In addition to the above, for many applications it is possible to predict the joint distribution of the image phases. For example, in the case of MR-T1 to MR-T2 registration, there is an almost one-to-one correspondence between the phases of the two images, and the joint distribution exhibits a strong diagonal mode. These simple relationships reflect the very strong relationship between the appearances of the two images; specifically, that edge features coincide and that, they face in opposite directions. This property extends to other modalities as well. For example, in the case of ultrasound to MR registration, some of the structures that appear as edges in MR appear as ridges in the ultrasound image, due to specular reflection; again this relationship is nearly one-to-one and appears as a strong diagonal in the joint distribution, as seen in fig. 1. The simplicity and predictability of the joint distributions suggests that it is possible to create strong priors for the registration of these image types.

2.3 Simple Effect of Registration Error on Similarity

Local phase has the property that its gradient is slowly varying. This has implications for the behaviour of the joint distribution when the images are misaligned. If the registration error is modelled as a zero-mean Gaussian distributed displacement at each voxel, then, for a local descriptor with constant gradient, the effect of the registration error will be a Gaussian blur in the joint distribution. This guarantees that the only effect of registration error is dispersion of the joint distribution, not formation of new modes. This tends to reduce the number of local minima encountered during the registration procedure [2]. In practice, no meaningful local descriptor can have constant gradient. However, the more slowly the descriptor varies, the better the approximation.
2.4 Invariance to Slowly Varying Intensity and Contrast Variations

Arguably, mutual information is a sensible criterion for alignment of modalities such as MR and CT, because in these modalities intensity can be considered a noisy tissue class label. By maximising MI of intensity, MI of tissue type is approximately maximised. However, in some modalities slowly varying intensity errors may exist, which may cause a significant variation in intensity for tissue classes which are spread over a wide area in an image. Also, because this type of noise is so highly spatially correlated, it may cause unexpected behaviour in registration algorithms.

![Figure 1](image-url) Phase facilitates registration of ultrasound and MR. Left, centre: MR and US images. Right: joint phase distribution. The appearance of specular reflection in ultrasound is represented by the diagonal bar.

2.5 Detection of New Image Relationships

By looking for statistical relationships between local phases rather than intensities, new types of image relationships can be detected. For example, it is possible to detect the relationship between specular reflections in ultrasound (ridge like structures) with edges in MR. This is a difficult problem to solve using algorithms based on intensity MI, since the specular reflections appear to be a unique class; MI is then maximised by aligning the specular reflections with one particular tissue type, rather than allowing them to straddle tissue type boundaries. In this particular case, intensity MI algorithms will therefore consistently find an incorrect solution.

3 Designing Application Specific Local Descriptors

The properties listed above are not unique to local phase. We present the results of several algorithms which can be used to produce local descriptors with some of the properties of local phase. The friendly statistics property can be encouraged using histogram pre-processing techniques, such as histogram equalisation [3]. It is possible to produce descriptors which are slowly varying using the non-linear design principle of 'slowness' [4]. Invariance to slowly intensity variations may be introduced by high pass filtering the images prior to registration, and contrast invariance can be introduced through local normalisation procedures. However, the most interesting properties, the detection of new image relationships and the predictability of joint statistics cannot be supplied by existing procedures. We present some preliminary results of a procedure adapted from the slowness principle, which attempts to supply both of these properties by finding non-linear descriptors, which are approximately invariant to the difference in appearance between two modalities.

References

1. M. Mellor, M. Brady, Non-rigid Multimodal Image Registration Using Local Phase. MICCAI (1) 2004: 789-796
Abstract
The aim of non-rigid registration as applied to a group of images is to find a ‘meaningful’, consistent dense spatial correspondence across the whole set. There are many methods available for finding such a correspondence given a pair of images, but viewing the groupwise case as just successive pairwise registrations is rather naïve, since the correspondence so obtained for any given pair depends only on that particular pair, rather than on information from the entire group. If we wish to perform a statistical analysis of the spatial and pixel-value deformations across the set (as defined by the found correspondence), we obviously need these deformations to be defined with respect to a common spatial and pixel-value reference. This means that both the objective function that defines the optimal correspondence, and the reference with respect to which this correspondence is defined should be determined in a fully groupwise manner.

It is possible to construct such an objective function and such a reference by applying the Minimum Description Length (MDL) principle [1]. The key idea is to consider transmitting the dataset to a receiver, where the dataset has been encoded using some type of model. For the case of non-rigid registration, this model can be taken to consist of the following:

- A reference image or template – this defines the common spatial reference frame of the set.
- A set of spatial and pixel/voxel-value deformations – these are applied to the template by the receiver so as to reconstruct each of the images in the training set.

We then define an objective function as the total length of the transmission; this can be written symbolically in the form:

\[ L = L_{\text{model parameters}} + L_{\text{encoded deformations}} + L_{\text{residual deformations}}. \] (1)

The model parameters are the reference/template image itself, and the parameters for the combined model of the spatial and pixel-value deformations. The residuals allow for the fact that the total required deformation to reconstruct the training set may not be exactly represented by the model. The optimal model according to MDL is then that model with the minimum total transmission length/description length.

Modelling spatial and pixel-value deformations
In pairwise registration, many different image similarity measures have been used (e.g., sum-of-squared difference, mutual information, normalised mutual information) to define what is mean by the optimal pairwise correspondence. And in general, different image similarity measures will give different results for the optimal correspondence. We have shown [2] than many of these image similarity measures can be viewed, within the MDL framework, as different groupwise models of the pixel-value deformations across the imageset. So, the model selection property of MDL means that we are not limited to choosing one particular type of model (that is, one particular image similarity measure), but can instead compare different classes of models, and pick the optimum model for our particular dataset. In general, such a model can be a combined model of the spatial and pixel-value deformations, which is particularly interesting for the case of vector or tensor-valued images, where we would expect there to be a link between the applied spatial deformation and the re-orientation of vectors which correspond to actual physical structures in the image (e.g., the vector field(s) in diffusion tensor brain images which correspond to the direction of neural fibres).

The Reference Image
It is known from successive-pairwise approaches to groupwise registration that a different choice of reference image can greatly effect the final registration. In the MDL approach, the reference image (both the spatial and pixel-value references), is just another part of the model. Hence, full optimisation of the MDL model includes optimising the reference image itself.

Experiments
Full application of the MDL approach to non-rigid registration requires the solution of a very large optimisation problem – to the usual problem of optimising the spatial warps for all the images in the set, we have added the problem of optimising the reference image, and of optimising the combined model of spatial and pixel value
deformations. To study the nature of this optimisation problem, and the behaviour of the MDL objective function, we have performed the following series of experimental investigations:

**Algorithms:**

- A simple algorithm, without a groupwise model of deformations, which can be used to initialize other more complex algorithms. An example non-rigid registration using such an objective function is shown in the Figure. The training set consists of 5 2D MR image slices of the brain, taken from 5 normal subjects. The allowed spatial deformations were those that could be generated from the movements of a set of 10 knotpoints (as shown in the Figure). It can be seen that the structures in the proximity of the knotpoints (i.e., the skulls) have been brought into alignment.
- A more complex, self-bootstrapping algorithm, which analyzes the correlations in the unmodelled parts of the deformations in order to expand the current groupwise model.

See [3] for further details of the algorithms.

**Optimising the Reference Image:**

- One way to construct the reference is by averaging the aligned images. For the case of affinely misaligned examples of the same seed image, where each example has a different part of the image missing, we can show that MDL does not only correctly align the images, but prefers the median to the mean as reference, enabling us to recreate the original seed image.
- The number of colours/grayscale values in the reference need not be the same as that in the imageset. We considered the simple case of a single image corrupted by noise, and show that for high noise levels or a small number of images, the reference is in effect a simple sketch of the original image, with few greyscale values. As the noise is reduced, or the number of examples is increased, the reference becomes more detailed.
- The MDL approach is also able to consider the case where the input data may actually consist of two subsets, and compare the cases of using a single reference, or separate references for each subset. We can also use MDL to find the optimal splitting of the dataset into subsets.

**Non-Scalar Valued Images:** We have considered the registration of test sets of artificial vector-valued images, and shown that the study of correlations in the residuals lead to the construction of a combined model where the vectors transform orientation according to the Jacobian of the spatial transformation. The importance being that this was motivated by the data itself, rather than assumed a priori, as is the case for other approaches to the registration of vector-valued images. It also means we can have an extended ‘soft’ model, which models variations about this ‘hard’ linkage between spatial and vector deformations.

![Figure 1. Top: The training set. Bottom: The fixed knotpoint positions in the reference frame, and the mean of the aligned images after 0, 2, 6 and 10 iterations, with the transmission length per pixel shown.](image)

References

Computing Covariances for Mutual Information Coregistration

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Mutual information has become a popular similarity measure in multi-modality medical image registration since it was first applied to the problem in 1995. This paper describes a method for calculating the covariance matrix for mutual information coregistration. We derive an expression for the matrix through identification of mutual information as a biased log-likelihood measure. The validity of this result is then demonstrated through comparison with the results of Monte-Carlo simulations of the coregistration of T1-weighted to T2-weighted MR images of the brain obtained from a normal volunteer. We conclude with some observations on the theoretical basis of the mutual information measure as a log-likelihood measure.

Mutual information \( I(I; J) \) measures the Kullback-Leibler divergence between the joint probability distribution \( p(i, j) \) of two images \( I \) and \( J \) and the product of their marginal distributions \( p(i) p(j) \) [1],

\[
I(I; J) = \sum_{i,j} p(i,j) \log \frac{p(i,j)}{p(i)p(j)}
\]

i.e. the divergence of the joint distribution from the case of complete independence of the images: maximisation of this measure with respect to a set of coregistration parameters will therefore optimise the image alignment. Roche [2] has shown that, letting image \( I \) be the target image and ensuring that the data sampled from this image remains constant throughout the coregistration, the mutual information is a monotonic function of the probability of image \( I \) given image \( J \).

\[
\log P(I|J) = N(I(I; J)) + \text{const.}
\]  

(1)

In simple maximum likelihood techniques this probability would be the likelihood, and the covariances for such a technique would be given by the minimum variance bound (MVB) [3]

\[
C^{-1}_\theta \geq \sum_v (\nabla_\theta \log \mathcal{L})^T \otimes (\nabla_\theta \log \mathcal{L}) \bigg|_{\theta_0}
\]

where \( \theta \) represents the parameters of the model, \( \theta_0 \) represents the parameters for optimal alignment, \( \mathcal{L} \) is the likelihood function, and \( v \) is the index of the data terms (voxels). This bound becomes exact if the likelihood function is Gaussian: since, in the case of rigid coregistration of medical image volumes, the likelihood consists of \( \approx 100,000 \) data terms (voxels) the Central Limit Theorem should ensure that this Gaussian regime is attainable. However, in the case of mutual information the likelihood is “bootstrapped” from a joint image histogram, rather than generated from an explicit model. Therefore, the probability in Eq. 1 is not a properly normalised log-likelihood: for instance, it is dependent on the histogram bin size. The solution to this problem is to renormalise to the probabilities to the peak, rather than the area, of the distribution. It can be shown [4,5] that, under the Gaussian assumption, this produces a properly normalised log-likelihood that is a monotonic function of the \( \chi^2 \). The MVB can also be expressed in terms of the individual data terms \( \chi_v \) in the \( \chi^2 \) sum,

\[
C^{-1}_\theta \geq \sum_v (\nabla_\theta \chi_v)^T \otimes (\nabla_\theta \chi_v) \bigg|_{\theta_0}
\]  

(2)

In order to identify the equivalent \( \chi^2 \) term in the mutual information measure, Eq. 1 can be split into two terms

\[
\log P(I|J) = \sum_v \log p(i,j) = \sum_v \log \frac{p(i,j) p(i_{\text{max}}, j)}{p(j) p(i_{\text{max}}, j)} = \sum_v \frac{p(i,j)}{p(j)} + \sum_v \frac{p(i_{\text{max}}, j)}{p(j)}
\]

The first term on the RHS is the \( \chi^2 \) metric, normalised to the distribution peak as required: the second is a bias term dependent on the non-uniform normalisation of the likelihood distribution. This expression elucidates the behaviour of the mutual information measure: it is a maximum likelihood measure biased with a term that maximises the “peakiness” of the distributions in the joint histogram, in order to maximise the correlation between

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Figure 1. The standard deviations (square-roots of the diagonal elements of the covariance matrices) of the coregistration parameters, plotted against added noise in multiples of intrinsic image noise.

equivalent structures in the images. Assuming that the bias term varies slowly compared to the $\chi^2$ term, Eq. 2 can be applied: expanding using the chain rule and inserting the expression for $Y$ gives

\[
C_\theta^{-1} = -\sum_i \left( \frac{\partial p(i,j)}{\partial x} \frac{p(i,j)}{p(i\rightarrow j,j\rightarrow i)} \right)^2 \frac{1}{2p(i,j)^2 \log \frac{p(i,j)}{p(i\rightarrow j,j\rightarrow i)}} \left( \nabla_\theta J_i \right)^T \otimes \left( \nabla_\theta J_j \right) \bigg|_{\theta_0}
\]

(3)

The accuracy of the covariance estimate was tested through comparison with the results of Monte-Carlo simulations of rigid coregistrations between T1 and T2 weighted MR image volumes of the normal brain. One thousand coregistrations were performed at each of various levels of added Gaussian noise, allowing the calculation of the covariances on the parameters. The covariance estimate was also applied at each noise level, and the standard deviations of the parameters were compared. The results, shown in Fig. 1, demonstrate that the practical and estimated variances match closely. Discrepancies were investigated by plotting the likelihood function around the optimum, and were found to be due to numerical stability issues.

We conclude that our approach provides an accurate method for estimating the covariances on the parameters of mutual information coregistration. Furthermore, it indicates that the theoretical origin of the mutual information measure lies in its link to standard likelihood methods, rather than to information theory.

References

Abstract. The need to establish correspondence across groups of images has for long been recognised. This problem is referred to as non-rigid registration. To enable comparative analysis of images depicting a similar object, analogous object structures must be identified and a practical way of doing so is by aligning these structures. The alignment is achieved by treating each image as a deformable object and transforming it to match another. One image is said to match another when it appears similar, i.e. objects within it overlap. A framework for a registration scheme comprises a measure of similarity (the objective function), a method of applying warps and an optimisation regime. Similarity measures assign an evaluative score to a collection of images that are subjected to transformations. That score reflects how good the alignment is and when it can no longer improve, convergence (i.e. registration) is assumed.

There is no agreement in the literature on what to consider a powerful family of transformations. It is also unclear what correctly defines similarity and which images should be compared when measuring that similarity. Popular methods are based on heuristics and results are difficult to validate. Our work addresses these issues, not by finding good registration schemes empirically, but by providing a well-founded approach to the problem. Since registration is known to reduce variation within groups of images, a model which represents these images will be accordingly affected. By looking at a model, we can derive similarity across the entire set, without the need for a reference. In a sense, the model is used here as a global similarity measure. Moreover, when models are used in the process of registration, statistical models are created, allowing variability in the dataset to be broken down into meaningful ‘components’ – the principal modes of model variation, which highlight attributes of interest. This functionality can aid identification of pathology symptoms in an autonomous manner. By registering raw sets of images of different groups, models can be built to find where greater variability lies.

The objective function presented in this work obtains similarity indirectly. It does so by calculating the complexity of a combined model of shape and intensity, namely by looking at the covariance matrix of that model. To efficiently evaluate model complexity, we obtained \( \sum_{i=1}^{n} \log(\lambda_i + \delta) \) where \( \lambda_{1 \leq i \leq n} \) are the \( n \) Eigen-values of the covariance matrix whose magnitudes are the greatest. This approximates

\[
det(M + \delta) \approx \prod_{i=1}^{n} (\lambda_i + \delta) \propto \sum_{i=1}^{n} \log(\lambda_i + \delta) \equiv \log(det(M + \delta)) \tag{1}
\]

where \( M \) is the covariance matrix under consideration. The algorithm makes the registration purely model-driven so that no reference is required. The objective function leads to one distinct solution without dependence upon individual images. This resolves the recurring issue of having to select a reference image and treat the problem as if it relies primarily on that one image.

Figure 1. On the left: Example bump data is displayed in its initial form. Each bump on the surface represents a 1-D vector. On the right: Example of the early results of registration (200 iterations). The edges of the bumps clearly begin to align.

To transform images, we chose to employ clamped-plate splines as they address known flaws often encountered when thin-plate splines and the B-splines are used. The clamped-plate splines prevent any of the regions in an images from being torn or folded, hence they preserve the existence and integrity of all
image regions. Particularly in the bio-medical domain, visibility of all constituent structures becomes crucial.

To demonstrate the advantages gained by the model-based approach, we experimented with one dimensional synthetic data where the correct solution is known. Generated data depicted a bump, a half-ellipse, which varied in height, width and position (see Figure 1). The sets were stochastically generated with significant variability that makes the problem challenging. We define a solution to be good when we observe proper alignment of the bumps and a resulting registered set that is distinct from any of the original images. At the same time, we are continuously delivered statistical models (as shown in Figure 3) of variable bumps. A combined model is derived from the shape model and the intensity model. Well-founded ways exist to visualise and evaluate them and it can be seen that the combined model is refined in the process, even after as little as 200 iterations.

After only a few minutes, good alignment amongst all bumps was obtained. Sets comprising dozens of bumps could be successfully handled by the algorithm and a statistical model of their appearance emerged even after as little as 200 iterations.

As well as a basic model-based objective function, we investigated the use of subsets to speed up the process. Subsets are chosen stochastically every 100 iterations, thereby the problem is simplified and the algorithm becomes more effective in dealing with large sets. It is worth adding that choice of warps was random at all stages so no data-bias or a-priori knowledge was involved.

![Figure 2](image.png)

**Figure 2.** On the left: The correct warps that align given data and that same data with the warps applied. On the right: The value of the objective function as convergence is approached.

The results we have seen thus far suggest that our approach works properly while addressing common difficulties. It can handle large sets and provide a solution that does not depend on any arbitrary selection of images. Future work will apply this approach in a real-world problem by treating 2-D images and 3-D volumes of the human brain.

![Figure 3](image.png)

**Figure 3.** At the top, from left-to-right: Combined, shape, and intensity models of 10 data instances at the start. The principal modes are shown with up to ±2 standard deviations away from the mean. At the bottom: corresponding models after registration.
Oxygen saturation as a measure of myogenic and metabolic changes in cerebral function

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1 Introduction

The mechanisms underlying cerebral autoregulation, traditionally defined as the maintenance of adequate Cerebral Blood Flow (CBF) despite external stimuli, are many and complex and are still far from being understood properly. The monitoring of cerebral behaviour is thus vital if our understanding of the underlying mechanisms is to be improved. However, non-invasive measurements are few and still not completely understood. One of the confounding factors is that there are several possible stimuli, Figure 1, including changes in Arterial Blood Pressure (ABP) (the myogenic response) and metabolic rate (the metabolic response). Any measurement of cerebral performance is thus a mixture of the two responses. In this paper, the theoretical response of oxygen saturation to changes in both the myogenic and the metabolic behaviour is examined. This is done using two expanded models of the cerebral system.

2 Myogenic response

There have been a number of models proposed to model the myogenic response. Here, the model proposed by Ursino et al., 2000, is used. This model has previously been examined in detail and shown to mimic the accepted static and dynamic behaviour of the cerebral system, Payne and Tarassenko, 2004a. It is now expanded to model the response of the parameters measured using Near Infra-Red Spectroscopy (NIRS), although only Tissue Oxygenation Index (TOI) is considered here. TOI is defined as the ratio of oxygenated to total haemoglobin, which can be expressed as a volume-weighted fraction of the arterial and venous saturations, the capillary network being assumed negligible. Payne and Tarassenko, 2004b, show that steady state TOI, for constant metabolic rate of O2, is given by:

\[
TOI = 1 - \frac{V_v}{V_a + V_v} \left( \bar{S}_{O2,a} - \bar{S}_{O2,v} \right).
\]

The resultant steady state variation in TOI with ABP, Figure 2a, shows almost negligible change within a very wide range of ABP, approximately -50% to +40%. The variations in CBF and in arterial and venous volumes essentially cancel each other out: around the basal conditions, TOI changes by only -0.01% for every 1% change in ABP. TOI is thus almost insensitive to changes in ABP. This is not the case for changes in oxy and deoxyhaemoglobin, which are well known to drop and rise respectively.

3 Metabolic response

There have also been a number of models proposed to model the response to increases in Cerebral Metabolic Rate of Oxygen (CMRO2). However, none of the models include the effects of changes in arterial volume, which are necessary if the NIRS variables are to be simulated accurately. The model proposed by Zheng et al.,
2002, is used and extended here by modelling the arterial compartment in a similar manner to the venous compartment. Conservation of arterial volume, in non-dimensional form, gives:

\[
\tau_a \dot{V}_a = f_{in,a} - f_{out,a},
\]

the flow-volume relationship for flow into the arterial compartment being assumed to follow a power law:

\[
f_{in,a} = (v_a)^{\beta}.
\]

where the exponent is assumed to be -1 as a first approximation. The results presented are relatively insensitive to the precise value. The concentration of arterial oxygenated haemoglobin is then assumed constant and the resulting expression for oxygen saturation can be derived:

\[
S = 1 - \frac{(1-r_v)E_o v_f h_f}{r_v v_a + (1-r_v)v_f o_v (1-E_o) + E_o h_f}.
\]

Since this is defined in exactly the same way as TOI, the two are equivalent: essentially both S and TOI are volume-weighted oxygen saturations. The resultant steady state variation in S with CMRO2, Figure 2b, shows a near linear change. Around the basal conditions, S changes by 0.60% for every 1% change in CMRO2: a 60-fold increase over the response to changes in ABP.

4 Conclusions

Existing models of cerebral responses to both myogenic and metabolic stimuli have been extended to model oxygen saturation, also known as TOI when measured using NIRS. These models predict a negligible change with ABP but a significant change with CMRO2 in the steady state. This means that TOI can be interpreted solely as a measure of metabolic demand within a wide range of ABP, rather than myogenic response, and is thus the only known non-invasive signal that is essentially only dependent upon one of these effects. This raises the possibility of using changes in oxygen saturation as a direct measure of changes in O2 metabolic rate: something that has not previously been considered.

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure2.png}
\caption{Variation in O2 saturation with (a) ABP; (b) CMRO2}
\end{figure}

References

Modelling noise-based fibre-orientation error in Diffusion Tensor MRI

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1 Introduction

Diffusion-weighted magnetic resonance imaging allows in-vivo imaging of diffusing water molecule populations as they interact with microscopic cellular structures. The diffusion tensor (DT) is proportional to the covariance matrix of a Gaussian diffusion process in three dimensions. The eigen system of the DT contains three eigenvectors $e_1, e_2, e_3$, and their corresponding eigenvalues, $\lambda_1 \geq \lambda_2 \geq \lambda_3$. The eigenvalues are proportional to the mean squared displacements along the corresponding eigenvector. Within brain white matter the diffusion is anisotropic, and when the fibres are organized into a single bundle, the DT is prolate, $\lambda_1 \gg \lambda_2 \approx \lambda_3$. When two fibre bundles cross at right angles within a single voxel, the tensor becomes oblate, $\lambda_1 \approx \lambda_2 \gg \lambda_3$. The fibre orientations cannot be resolved from the tensor, but the orientations lie close to the plane defined by $e_1$ and $e_2$, perpendicular to $e_3$. Tractography reconstructs complete fibre pathways from voxel measurements of the fibre orientation. It is simple to trace a streamline by following the principal diffusive direction $e_1$ in each voxel. However, each voxel measurement is subject to error because of noise and other artefacts, such as patient motion. Probabilistic tractography methods define an orientation density function (ODF) of any fibre orientation $x$ in a voxel given the measured data. The Probabilistic Index of Connectivity (PICo) [1] uses Monte-Carlo streamline generation to create maps of connection probability. For each Monte-Carlo iteration, $e_2$ of each tensor is aligned with a sample from the voxel ODF, and a streamline is tracked from a manually selected seed point. After many iterations, the probability of connection between the seed point and a voxel $p$ is proportional to the number of streamlines that pass through voxel $p$.

Parker and Alexander [2] use a one-dimensional normal distribution on the angle between $x$ and $e_1$. This ODF is designed to model the uncertainty in prolate, cylindrically symmetric diffusion tensors, caused by noise in the imaging process. We use standard statistical methods to model the noise-based error in the primary directions of symmetric and non-symmetric tensors. We also model the fibre-orientation error when the tensor is oblate, where the diffusion tensor gives an estimate of the plane containing the fibre orientation, rather than the fibre orientation itself. We demonstrate that these methods provide more accurate models of noise-based fibre-orientation error in crossing fibres and in the presence of asymmetric diffusion.

2 Methods

The Watson distribution [3] generalises the cylindrically-symmetric ODF proposed by Parker et al. The Watson ODF is $f(x) \propto \exp[\kappa (\mu^T x)^2]$. The parameter $\kappa$ describes the concentration of the distribution and the unit vector $\mu$ describes its orientation. For $\kappa > 0$, the density has maxima at $\pm \mu$. For $\kappa < 0$, the distribution is concentrated around the great circle orthogonal to $\mu$, which models the dispersion of $e_1$ in regions of crossing fibres where the DT is oblate. The Bingham distribution [3] is a model for tensors with or without cylindrical symmetry. It is defined by two orthogonal axes and two scaling parameters, where $f(x) \propto \exp[\kappa_1 (\mu_1^T x)^2 + \kappa_2 (\mu_2^T x)^2]$.

We test our models in synthetic data, as described in our recently published work [4]. The first image consists of anisotropic, prolate diffusion tensors aligned so that the primary eigenvectors trace out a circular path. The second image contains two straight, perpendicular anisotropic paths, which form a region of oblate tensors where they cross. We vary the anisotropy of tensors in both images, and compare the ODFs for each anisotropy. We also test asymmetric tensors in the circular path, with $\lambda_2 \lambda_3^{-1} = 0.5 \lambda_1 \lambda_3^{-1}$. We synthesize an MR acquisition of each image using a standard imaging protocol, (3 unweighted and 60 diffusion-weighted measurements spread evenly on the sphere). We add complex Gaussian noise to each measurement, with noise variance chosen to give a signal to noise ratio of approximately 16 in the unweighted measurements within the anisotropic tensors. We compute the DT with a nonlinear least-squares fit to the noisy data.

We construct a lookup table for each ODF, indexed by the tensor anisotropy (for the Gaussian model) or by the ratio of the eigenvalues, $\lambda_1 \lambda_3^{-1}$ and $\lambda_2 \lambda_3^{-1}$ (for the Watson and Bingham models). For each tensor shape, we add noise to the MR measurements, fit the diffusion tensor, and extract the primary eigenvector. We repeat this...

...add noise to the MR measurements, fit the diffusion tensor, and extract the primary eigenvector. We repeat this...
5000 times to get a large sample of noisy eigenvectors. We then fit the maximum-likelihood estimate of the model parameters, and store the parameters in the lookup table.

As a gold standard, we create a probability map using noise in place of ODF samples. For each Monte-Carlo iteration, we add noise to the ideal measurements and fit the tensor in each voxel, before tracking a streamline. We compute the normalized cross-correlation between the probability map from each ODF and the gold standard.

3 Results

In the circular path, there was no detectable difference between the Gaussian, Watson and Bingham models. In the fibre crossing, the Watson model provided the best correlation to the gold standard. The Gaussian model, lacking any ability to handle oblate tensors, performed worst. In the asymmetric circular path, the Bingham model correlated better to the gold standard than the Watson and Gaussian models. Figure 1 shows the difference in correlation between each model, averaged over 50 different noisy images.

Noise causes an error in the DT orientation and shape. This introduces an error in the ODF orientation and concentration, since the lookup tables are indexed by tensor shape. We test the contribution of each source of error by fixing one of the model parameters at the correct value in the symmetric circular path. The variation in correlation between images is not significantly different when the tensor shape is fixed at the correct value, but when the orientation is fixed, the correlation becomes significantly higher. We find no advantage to enforcing symmetry by using the Watson model in symmetric prolate regions. In fibre crossings, the Watson model performs slightly better than the Bingham model.

4 Discussion

The Bingham and Watson ODFs improve the Gaussian ODF by modelling asymmetric and oblate DTs, and our current work is to extend these models to deal with multiple fibres in each voxel. We also plan to use bootstrap MRI experiments to compare the total uncertainty with our noise-based models.

Acknowledgements

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References

A computational model of the cerebral circulation: model predictions with experimental data during a CO$_2$ challenge

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1 Introduction

The brain circulation is a highly dynamic system that responds in a complex way to a wide range of different stimuli (both physical and chemical), on a variety of time scales and using different interconnecting pathways. A single integrated physiological model of the cerebral physiology has been constructed [1] by combination of an existing model of the biophysics of the cerebral circulatory system [2], a basic model of brain metabolic biochemistry, and a model of the functioning of vascular smooth muscle (VSM).

In this study, the model is used to predict the time pattern of changes in the cerebral haemodynamics in young healthy volunteers in response to maneuvers affecting the arterial concentration of CO$_2$, which is known to cause changes in cerebral blood flow (CBF) and cerebral blood volume (CBV). The consequences of 5% inspired CO$_2$ (moderate hypercapnia) on the cerebral vasculature were both modelled and experimentally investigated by the application of cranial near-infrared spectroscopy (NIRS). The study purpose was to compare results from the computational model with measured experimental data to investigate the predictive strength and clinical significance of the additional information the model provides.

2 Method

12 healthy volunteers of mean $\pm$SD age 32 $\pm$4 years were investigated (the local ethics committee approved the protocol for the study, and all subjects gave informed consent for participation). Each study involved three physiological phases. These include an initial rest period, a 5% inspired CO$_2$ stimulus (moderate hypercapnia) and a final rest period. Cerebral oxygenation was monitored in a continuous, direct, and non-invasive manner using NIRS, an optical technique, which when applied to the head provides information on cerebral tissue oxygenation (TOI) and haemodynamics [3]. Additionally, systemic variables such as arterial blood pressure (BP), arterial saturation (SaO$_2$), end tidal CO$_2$ ($\text{EtCO}_2$), inspired CO$_2$ ($\text{InspCO}_2$) and heart rate (HR) were monitored continuously.

Simulations were performed for each study using the individual measured time traces of $\text{EtCO}_2$, ABP and SaO$_2$ as input parameters to the model after being down-sampled and converted to appropriate units.

Figure 1. Representative data collected from one volunteer.
3 Results

Figure 2 shows a comparison between the measured and simulated cerebral TOI signal on one volunteer. The mean values of EtCO$_2$, measured TOI and predicted TOI for all 12 subjects were calculated for a 1 minute interval at the end of the rest and the hypercapnia phases. These results are shown in Figure 3.

![Figure 2](image)

**Figure 2.** Qualitative comparison between measured and simulated TOI for one volunteer.

![Figure 3](image)

**Figure 3.** (a) Mean EtCO$_2$ values. (b) Mean measured TOI values. (a) Mean simulated TOI values.

4 Conclusions

Understanding the complexity of the relationships between intracranial and systemic quantities is essential to reach a deeper understanding of cerebral homeostasis. An extensive computational model of the cerebral circulation is being developed and tested. We present results from a hypercapnia challenge and show comparisons between model predictions and experimental data. Preliminary results show a qualitative agreement between model predictions and measured physiological data. The next stage is to find ways of customising the model for a given individual, which should improve the quantitative accuracy of the predictions.

References


Dynamic 3D Under-Sampled Reconstruction by Temporal Registration
Pablo Irarrazaval, Redha Boubertakh, Derek Hill, Jo Hajnal

Introduction
There is no doubt about the clinical utility of procuring the temporal and 3D evolution of the Magnetic Resonance Imaging (MRI) signal. This poses a difficult challenge for the current MRI technology, due to the need to acquire large quantities of data in short time intervals. Under-sampling $k$-space is one possibility to speed up the acquisition [1]. In this paper we present a new technique to reconstruct under-sampled data which exploits the information redundancy of the object from time frame to time frame. The proposed technique is based on predicting how the image should look like for a particular time, and based on the incompletely sampled data correcting the prediction to match the actual object. The method works by reconstructing first a rough estimate of the images (with a sliding window reconstruction [2]) which is assumed to be a good estimate for some of the frames, when there is little movement. These well estimated frames are the base used to predict the badly estimated frames, when there is large motion.

Method
The proposed algorithm is described in five stages: Computation of an Initial Estimate; Time registration of frames; Classification of frames in moving and not-moving; Prediction of moving frames; and Ensuring consistency of data. A summary of the first four stages is shown in the figure.

In this description $m(x,t)$ is the desired 3D movie and $M(k,t)$ its Fourier transform. The under-sampled data is $M_U(k,t) = S(k,t)$. $M(k,t)$, where $S(k,t) = \sum_i \delta(k - k_i, t - t_i)$ represents the sampling function. We used an under-sampled scheme in which the data is uniformly distributed in $k$-space [3].

Initial Estimate. From the under-sampled data $M_U(k,t)$ an initial estimate in $k$-space $M_T(k,t)$ and in object space $m_T(x,t)$ are computed. This is done by convolving in time the data with a triangular kernel of size $2q - 1$ (a simple linear interpolation, $q$ is the acceleration factor): $M_T(k,t) = \delta(k) \wedge (t/(2q - 1)) * M_U(k,t)$

Frame Registration. We register, non-rigidly, every frame of $M_T(k,t)$ to every other, such as to obtain all the transformation parameters that allow the conversion of one frame into any other, with the VTK CIGS 3D Registration Toolkit [4].

Frame Classification. Using reference points, we compute a “motion measurement” for each frame, by counting the number of points whose displacement in any dimension crosses the mean value for that dimension. This index is used to classify the frames as either moving or not-moving with a simple threshold (manually set).

Frame Prediction. We substitute the moving frames with the predicted frame $m_P(x,t)$, computed as the median of several predictions $m_P^j(x,t)$ for that frame. Where $m_P^j(x,t)$ is frame $s$ transformed to time $t$ with the registration transformation. Frames $s$ are not-moving frames as close as possible to time $t$.

Data Consistency. To ensure data consistency, we force the acquired samples into the predicted images. This is done, in the Fourier domain, by letting $M_A(k,t) = M_P(k,t) +
\( M_E(k, t) \) where the error \( M_E(k, t) \) is \( S(k, t) \cdot \{ M_U(k, t) - M_P(k, t) \} \), the difference between the effectively acquired samples and the Fourier transform of the predicted image. Effectively, this means that the prediction is used only for the non-acquired samples and the acquired data is used without modification.

**Results**

A 3D movie of the knee is an ideal application for the proposed algorithm. It is relatively easy to control the movement and it is an interesting application from the clinical point of view. We simulated the under-sampling from a 3D fully sampled acquisition (with a Steady State Free Precesion sequence, \( 256 \times 100 \times 10 \) voxels) of a volunteer’s moving knee. The acquired data was under-sampled by a factor of \( q = 5 \). The algorithm reconstructs the images without the blurring and artifacts of the sliding window reconstruction, as shown in the figures (cuts for a given time and evolution in time).

**Conclusion**

The main advantages of the proposed reconstruction method are that (1) it does not require the motion to be spatially localized (no restrictions on the FOV); (2) it does not require any particular under-sampling pattern; and (3) it is perfectly applicable to any trajectory. The only restriction on the data is that there exists enough time to reconstruct with sliding window at least one frame free of motion blur or aliasing. There is no restriction on the fraction of the FOV that is moving. This makes the method useful for a great variety of applications. In particular for those in which it is easy to control the movement, like joint imaging. On the other hand it places a limit on the under-sampling factor for situations in which the object is still only for a limited time, like the heart. Finally, this algorithm has the potential to automatically quantify dynamic changes in the sequence of images which could be exploited in a combined reconstruction/analysis of the data.

**References**

Multiple Coils for the Reduction of Flow and Motion Artefacts in MRI

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1 Introduction

Blood flow and other physiological processes can result in the ghosting and blurring of MR images. In addition to the blurring, these artefacts can introduce additional features that are not present in the object. This can be problematic, for example, difference images from registered serial brain volumes can be corrupted by flow artefacts from the carotid and middle cerebral arteries.

Multiple coils have previously been used to detect and reject motion-corrupted phase encode lines [1]. The remaining data was then reconstructed using a generalised SMASH [2] approach. Odd and even echos in EPI images have been used for flow artefact reduction [3]. Here we apply a new, more general, technique to the problem of artefacts from flowing blood and motion [4].

2 Method

In the absence of any artefacts, the image $s^\gamma$ obtained from receiver coil $\gamma$ with spatial sensitivity $c^\gamma$ is given by

$$s^\gamma = c^\gamma \cdot r$$

(1)

where $r$ is the underlying object. This can be expressed in k-space as a convolution which in turn can be written as the matrix multiplication $S = CR$. Here $S$ and $C$ can contain data relating to either one or all coils. In the presence of flow or motion artefacts, the k-space representation of the object and the acquired k-space change to $\tilde{S}$ and $\tilde{R}$ respectively. If the artefact can be parameterised as a change to the coils, rather than the object, we can write $\tilde{S} = CR = \tilde{C}R$. In the case of flowing blood, we assume that the coil profile at the position of the artery can be multiplied by one complex term for each discrete time step during the scan. For rigid-body motion, the motion is parameterised by a motion of the coils. Solving for $\tilde{R}$ with one or all coils [2] enables us to minimise the cost function

$$F = \sum_{\gamma,\gamma'} |r^\gamma - r^G|^2,$$

(2)

where $r^\gamma$ are the (image domain) reconstructions from each coil $\gamma$ and $r^G$ is the reconstruction using data from all coils at once. The sum is over all coils and all image-domain pixels. In the absence of artefacts, $r^\gamma$ and $r^G$ should differ only by noise.

3 Results and Conclusions

Figure 1 shows an axial slice from a volunteer acquired on a Philips 1.5T Eclipse using a 4-element body array coil (128 x 128, TR/TE of 250/10 ms, breath-hold, no cardiac gating, 128 discrete time points). Ghosts can be seen in the spinal body and intestine region as well as outside the body. We use the MATLAB [The MathWorks] least squares nonlinear optimisation routine with 256 unknowns (128 complex multiplicative factors). After processing with our algorithm, the ghosts are reduced and image quality is comparable to a similar slice acquired with saturation bands (which would not be effective for multi-slice acquisitions).

Figure 2 shows a volunteer head image corrupted by motion in the phase encoding direction. The motion parameters in the optimisation routine were the phase encode displacement at each of the eight shots in the acquisition (giving eight unknowns). The algorithm clearly reduces the motion artefacts.

We have demonstrated a method for the removal of artifacts that uses the extra information provided by multiple coils. The technique compares reconstructions of the object using various combinations of coils. In principle the method is applicable to any artifact whose physical cause can be parameterised and expressed as an equivalent change to the coil sensitivity profiles. No modifications to the pulse sequences are required.

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Figure 1. Slice corrupted by flow in aorta (left), corrected (middle) and a similar slice acquired using saturation slabs in a different breath-hold (right).

Figure 2. Head image corrupted by motion in phase encode direction (left) with artifacts arrowed, the corrected image (middle), and a similar slice with the subject stationary (right).

Acknowledgements

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References

Signal Analysis for the Diagnosis of Vasovagal Syndrome

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1 Introduction

Vasovagal syndrome – the frequent occurrence of vasovagal syncope – is a problem affecting people of all ages. Often occurring from several minutes to an hour after the subject assumes the upright position, episodes of vasovagal syncope are characterised by a loss of consciousness resulting from a temporary reduction of cerebral blood flow. Blood flow falls as a consequence of a sudden drop in blood pressure, with or without a decrease in heart rate, probably caused by a dysfunction of the nervous control of heart and blood vessels [1]. Analysis of the appropriate physiological signals monitored noninvasively can inform the cardiovascular system can influence models of the mechanisms of syncope, consistent with the theme of the IRC Multi-Scale Modelling Grand Challenge.

A common method to investigate vasovagal syndrome is head-upright tilt table testing (HUT). Patients lie flat on a specialised bed for several minutes, before being tilted to an angle of 60-80 degrees from horizontal. If syncope occurs after characteristic symptoms are observed, the patient is diagnosed with vasovagal syndrome. The aim of the current work is to classify patients as vasovagal or normal early in the test, based on signal processing of the first few minutes of ECG data.

One of the most popular classes of metrics under exploration has been heart rate variability (HRV). However, a significant limitation is the effect of ageing on the autonomic system; this effect is one of the reasons that traditional HRV metrics tend to fail in the elderly [2]. An interesting HRV development in the late 1990s has focused on the investigation of ICF (instantaneous centre frequency) [3]. The present research explores the use of an extension of ICF, known as ICFV (ICF variability), to predict vasovagal syncope in the elderly. Although the initial discussion addresses its application to the ECG, ICFV can be applied to other time series as well, such as blood pressure or cerebral perfusion data.

2 Calculation of ICFV

“RR tachograms” are sequences of unevenly sampled beat-to-beat intervals derived from the ECG. In this application, RR tachograms of elderly patients undergoing HUT are created, before cubic spline interpolation at a sampling rate of 3 Hz is employed to produce an evenly-sampled instantaneous heart period signal $y(n)$. The Smoothed Pseudo Wigner-Ville Distribution (SPWVD) [4] is then applied to calculate a time-frequency map, $W(n,m)$, where $n$ is the time coordinate and $m$ is the frequency coordinate. The discrete version of the SPWVD is defined as

$$W(n,m) = \frac{1}{2} N \sum_{k=-N+1}^{N-1} |h(k)|^2 \sum_{p=-M+1}^{M-1} g(p) z(n+p+k) z^*(-n+p-k) e^{-j\pi m k}$$

where $z(n) = y(n) + i H[y(n)]$.

$N$ and $M$ are parameters determining the length of the frequency-smoothing window $h(k)$ and time-smoothing window $g(p)$, respectively. The asterisk denotes complex conjugation and $H[·]$ the Hilbert transform. The purpose of the transform here is to remove the negative frequencies from $y(n)$ and hence create an analytic signal which is less susceptible to aliasing. Finally the smoothing functions $g(p)$ and $h(k)$ can take a number of forms. For the present SPWVD, a Hamming window function was selected and the lengths of the windows selected using least-squares optimisation on a training set [5].

The ICF of a signal is the “mean” frequency at any point in time; it is the time-dependent frequency average of $W(n,m)$. The variability of this signal across a given time duration is defined as the variance of the ICF (square of the standard deviation) and is named ICFV. ICFV during the first few minutes of tilt is examined, after the first 60-90 seconds. The initial response is excluded to allow $y(n)$ time to settle; during the first minute or so after tilt, it is typical for $y(n)$ to increase sharply as part of the natural autonomic response to adopting an upright position.

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3 ICFV and Elderly Patients

Sample results from vasovagal and nonvasovagal patients are presented in Figure 1. In general, ICFV tends to be higher in vasovaginal patients, and this can be used to classify patients. In Table 1, ICFV is compared with two traditional techniques, in a leave-one-out classification of 50 patients (18 vasovaginal, 32 nonvasovagal; 10 male; mean age 79 ± 7). Two traditional HRV analysis techniques, successful on datasets involving a broad range of patients, perform poorly classifying the elderly. The objective of using ICFV was to improve the classification, and indeed ICFV does perform better.

<table>
<thead>
<tr>
<th>Predictive Test</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICFV during the first 90-180 s after tilt (Ebden et al.)</td>
<td>0.77</td>
</tr>
<tr>
<td>LF/HF ratio in the first 240 s after tilt (after Kochiadakis et al.)</td>
<td>0.71</td>
</tr>
<tr>
<td>LF in the first 300 s after tilt divided by the last 300 s of baseline recording (after Kouakame et al.)</td>
<td>0.52</td>
</tr>
</tbody>
</table>

Table 1. Vasovagal syncope prediction from analysis of the RR tachogram. NPV=Negative Predictive Value.

Results of HRV analysis of elderly patients are often harder to interpret than for young patients [2], due in part to comorbidity (simultaneity of diseases) and in part to autonomic degeneration. Since the elderly suffer from comorbidity more than any other age group, it is difficult to find patients with vasovagal syndrome and no other disorder. As to the issue of autonomic degeneration, it is well known that ageing decreases autonomic activity. Hence, traditional autonomic indicators such as the LF/HF ratio of the RR time series spectrum are less effective in predicting syncope results in the elderly.

The motivation for examining the variability of ICF was to identify autonomic instability, rather than assess the magnitude of particular spectral bands. The hypothesis is that patients with greater variability in their ICF (i.e., higher ICFV) might experience greater difficulty in controlling their autonomic response to tilt, and hence could be more prone to fainting. The lack of reliance on spectral bandwidth power magnitudes should have a normalising effect to combat the results of ageing on HRV analysis.

4 Conclusions

Using RR tachograms, ICFV represents a tool with which to explore systemic cardiovascular rhythms. ICFV can next be applied to cerebral time series from near infrared spectroscopy, for instance in the search for trends associated with the onset of syncope.

References

Ultrasound Pulse-shaping Optimisation for Displacement Estimation

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1 Introduction

Advances in digital ultrasound technology enable programmatic pulse shaping, which can be used to reduce errors in displacement estimation. The discipline of elasticity imaging is characterised by using images from soft-tissue sensitive modalities to derive tissue material properties such as Young’s modulus. Frequently, simpler measures such as strain also appear to hold clinically relevant information. Ultrasound is a popular modality for elasticity imaging benefiting from its availability, low cost, and real-time performance.

The common method of elasticity imaging examined in this work requires, at minimum, a pre- and post-compression image. A key requirement of this ‘quasi-static’ method is accurate tissue displacement estimation. Improvements in displacement estimation, even on the order of 1%, can realise significant improvements in many post-processing stages. These improvements apply in particular to full elasticity reconstruction. Currently, the most successful displacement estimation methods are based upon block-matching techniques employing basic similarity measures such as sum-of-squared-differences or correlation. The two main benchmarks of these algorithms are bias and variance. Typically, both of these measures are found experimentally under additive-noise test conditions, despite it being commonly understood that such overly simplified testing conditions result in incomplete analyses of algorithms.

To reduce variance and increase the range of measurable tissue strains, algorithms typically attempt to correct for tissue compression through post-compression signal stretching [1]. It appears, however, that under more realistic elasticity imaging conditions these common algorithms are indeed biased and underperforming.

This work endeavours to find a theoretically correct technique by which stretching-based algorithms can perform closer to their potential. This is achieved through the optimisation of ultrasound pulse fundamental frequency. At the cost of increased acquisition time and data storage size, increases in accuracy and effectiveness of ultrasound elasticity imaging are obtained.

2 Background and Theory

A modern ultrasound imaging workstation is an extremely complex system with hundreds of variable parameters. Previously, commercial workstations were closed systems, containing fine-tuned proprietary algorithms. As ultrasound technology matured and research-based users became increasingly interested in machine control, workstations became more open. The advent of fully digital systems has enabled vendors to provide a programmatic interface to all aspects of the signal processing pipeline. One such system used at the Wolfson Medical Vision Laboratory in Oxford, is the Analogic CasaEngine [2]. While its pipeline topology remains fixed, the vast majority of tuneable parameters are accessible programmatically.

To understand the improvements attainable through ultrasound pulse-shaping optimisation, we must first examine the approximations made when applying temporal stretching algorithms. Here basic linear systems theory provides insight. The ultrasound processes can be simplified into the convolution of a system point-spread function (PSF), (a concept taken from optical systems theory) and a tissue scattering function. The applied tissue compression is modelled as a compression in the tissue scattering function. However, this post-compression image is still obtained with the original PSF, a parameter of the ultrasound system. To increase correlation, temporal stretching algorithms interpolate the post-compression image to better match the pre-compression image. As a consequence the underlying PSF is similarly stretched resulting in a sub-optimal match.

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This sub-optimality has been previously identified and considered a suitable compromise. In addition to the compromised variance, however, a bias error also appears to exist. As discussed, additive-noise testing has not previously revealed this phenomenon.

3 Pulse Shaping Technique

Any algorithm utilising temporal stretching can be optimised by shaping the ultrasound pulse prior to imaging either the pre- or post-compression tissue. This, in turn, similarly shapes the PSF. The pulse is either stretched when imaging the pre-compression tissue, or compressed if imaging the post-compression tissue. We refer these independent techniques as pulse pre-stretching (PPS) and pulse pre-compression (PPC) respectively. They are applied in practice by modifying the fundamental frequency of the excitation waveform.

If the amount of PPS or PPC matches the tissue strain exactly, then the temporal stretch applied to the post-compression image will optimally recover the pre-compression image. In practical applications, the tissue experiences an unknown, spatially varying strain. Consequently, iterative strain estimates are made locally throughout the image in a manner such as described in [3]. As the strain estimates approach the actual tissue strain, an estimate strain error is evident. To fully understand the gains afforded by PPS or PPC, we must examine their effects under positive, negative and zero strain estimation error.

Simulation results indicate PPS provides gains regardless of strain error. Under all conditions it is advantageous to have stretched the ultrasound pulse by an amount on the order of the expected tissue strain. The gains are twofold: first, there is a gain in image correlation that increases proportionally with tissue strain. While only marginal gains are attainable for small tissue strains (<2%), gains of several percent (1-10%) have been found for larger strains (5-10%). Secondly, PPS dramatically reduces bias (2% to 0.2% of window size) for large tissue strains (>5%).

Interestingly, PPC actually worsens signal correlation when the strain is overestimated. Consequences of strain overestimation are likely magnified by the increased PSF mismatch. The mechanism of this failure is not thoroughly understood at this time.

Implementation of PPS or PPC requires multiple pre- or post-compression images recorded with the modified pulse to account for the various tissue strains present. This entails both increased storage and acquisition time, which impose significant constraints on imaging protocols and may prove impractical. However, if a suitably small region of interest is identified, a feedback system could be designed to iteratively optimise the pulse shape during acquisition reducing the required acquisitions. These extensions are currently under investigation.

Acknowledgements

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References

2. Analogic Corporation, 8 Centennial Drive, Peabody, MA 01960, Tel: 1-978-977-3000.
Pressure-dependent attenuation of microbubbles at low mechanical index

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Abstract. It has previously been shown that the attenuation of ultrasound by microbubble contrast agents is dependent on acoustic pressure \cite{1}. While previous studies have modelled the pressure-dependence of attenuation in single bubbles, this paper investigates this subject by considering a bulk volume of bubbles together with other linear attenuators. Specifically, a new pressure-dependent attenuation model for an inhomogeneous volume of attenuators is proposed. In this model the effect of the attenuation on ultrasound propagation is considered. The model was validated using experimental measurements on the ultrasound contrast agent Sonovue\textsuperscript{TM} (Bracco S.p.A. Milan, Italy). The results indicate, at low acoustic pressures, a linear relationship between the attenuation of Sonovue\textsuperscript{TM}, measured in dB, and the insonating acoustic pressure.

1. Introduction

 Quantification of tissue perfusion in ultrasound contrast imaging enables a number of important clinical and physiological indices of the microvasculature to be measured. These include the relative vascular volume, flow velocity and relative perfusion rate\cite{2}. Although efforts have been made to develop techniques for quantifying tissue perfusion\cite{3,4} the accuracy of the quantification is still largely compromised by artefacts caused by inaccurate attenuation compensation. Attenuation correction for linear attenuators such as tissue has been studied by Hughes and Duck\cite{5}. However, microbubbles attenuate ultrasound quite differently to soft tissues. In this study we investigate the nonlinear attenuation arising from a bulk volume of bubbles combined with other linear attenuators and propose an attenuation model. Preliminary validation of this model through in-vitro single-element transducer experiment is also presented.

2. Method

 An attenuation model for a volume of bubbles with local variations in concentration is developed. The model is expanded to include linear attenuators such as tissue. An ultrasound pulse is modelled as an impulse travelling along the $x$ axis at a constant speed. Propagation of the impulse through a suspension of bubbles from point $x$ to point $x + \Delta x$ results in attenuation of the signal $S(x)$ to $S(x + \Delta x)$. If $\Delta x$ is small, the properties of the solution can be assumed to be constant. If $\alpha(x, S(x))$ represents the fractional loss in amplitude per unit distance between $x$ and $x + \Delta x$, noting that the signal amplitude $S(x)$ is the local acoustic pressure and the fractional loss $\alpha(x, S(x))$ is signal-dependent and takes a value in the range 0 to 1, then

$$S(x + \Delta x) = (1 - \alpha(x, S(x))\Delta x)S(x).$$

(1)

Through experiment the attenuation, $\alpha(x, S(x))$, was found to be linearly related to bubble concentration $c(x)$, for a specific acoustic pressure $S(x)$. Thus:

$$\alpha(x, S(x)) = \alpha_{ave}(S(x))c(x),$$

(2)

$\alpha_{ave}(S(x))$ is the average bubble attenuation, per unit volume of bubbles. The dependence of the average bubble attenuation on the local acoustic pressure $S(x)$ can thus be modelled using a polynomial,

$$\alpha_{ave}(S(x)) = \sum_{i=0}^{n} \alpha_i S(x)^i.$$

(3)

The parameters $\alpha_i$ ($i=0$–$n$) are the attenuation coefficients of the bubbles. In the case of first order polynomials:

$$\alpha(x, S(x)) = (\alpha_0 + \alpha_1 S(x))c(x)$$

(4)

and,

$$S(x + \Delta x) = (1 - \alpha_0 c(x)\Delta x - \alpha_1 c(x)S(x)\Delta x)S(x).$$

(5)

Rearranging equation (5), dividing both sides by $\Delta x$, then letting $\Delta x \to 0$...
\[ \frac{dS}{dx} = -\alpha \cdot c(x) \cdot S(x) - \alpha_1 \cdot c(x) \cdot S^2(x) \]  
(6)

Solving this equation, integrating over the path length from \( x_0 \) to \( x \), and letting \( S(x_0) = S_0 \) gives:

\[ S(x) = \frac{S_0 \exp(-\alpha \int_{x_0}^{x} c(v) dv)}{1 + S_0 \alpha_1 \int_{x_0}^{x} c(v) \exp(-\alpha \int_{x_0}^{v} c(u) du) dv} \]  
(7)

Equation (7) relates the signal amplitude at point \( x \) to the original signal amplitude \( S_0 \) at \( x_0 \), and the bubble concentration distribution \( c(x) \) and forms the basis of our attenuation-transmission model. In-vitro experiments were conducted to verify this model. The experimental setup consisted of a pair of broadband 3.5MHz focused single element transducers driven by an arbitrary waveform generator and a power amplifier. The transducers were aligned and submerged in a large water bath, maintained at 37°C. A sample chamber containing a solution of Sonovue™ diluted in saline (0.09% w/v) was placed at the focus. On either side of the sample chamber a large thin plastic window allowed passage of the ultrasound with minimal attenuation. A ramped burst of Gaussian enveloped sinusoidal pulses of 4 cycles at 3MHz with a range of 16 increasing levels of amplitude was emitted by one transducer. The attenuated transmission signal received by the other transducer, was recorded on a digital oscilloscope. Typically the largest peak negative pressure measured was 219±2 kPa, corresponding to an MI of 0.13 at 3MHz. At such low pressures the chance of bubble destruction is greatly reduced. Experiments were performed with three levels of bubble concentration, 77ul/1000ml, 154ul/1000ml and 310ul/1000ml, and with three sample chambers of different acoustic path length, 4cm, 6cm and 8cm, which makes a total of 9 test conditions. In addition the effects of bubble destruction and concentration were measured in similar experiments.

3. Results

The attenuation coefficient was obtained by firstly fitting the measurements from each concentration to the model to get \( \alpha_0 \) and \( \alpha_1 \) for each concentration. The results confirmed a clear linear relationship between the attenuation and bubble concentration. In-vitro experiments also confirmed that significant bubble destruction occurs when MIs above 0.13 are used. When a higher concentration of microbubbles were used the effects of this destruction was minimized. For all the experiments the pressure-dependency of the overall attenuation of the bulk of contrast solution was found to be significant. The measurements of the transmitted signal were fitted to the proposed model. The goodness of fit for all the measurements was assessed by the R² test. The mean and standard deviation of R² are 0.999±0.001, suggesting a good fit. The goodness of fit was improved when a bigger sample chamber was used.

4. Discussion & Conclusions

The experiments demonstrate that the pressure-dependency of a contrast agent solution is significant even at low insonating pressures. Therefore ignoring this pressure-dependency in any attempt at attenuation correction in ultrasound contrast imaging may introduce significant errors. The in-vitro data generally provided a good fit to the proposed model. The attenuation coefficients \( \alpha_0 \) and \( \alpha_1 \), as defined in the model, are constants depending solely on the physical acoustic properties of the microbubbles. Our results show that both coefficients vary with dosage and sample chamber. The likely cause of this is destruction of the bubbles at higher insonating pressures. The development and characterisation of this model is the first step towards a comprehensive method for automatic compensation of attenuation in microbubble contrast imaging. Such a method is required to improve the consistency and accuracy of ultrasonic measurements. In particular it is essential for any quantitative study involving microbubble ultrasound contrast agents.

6. References

Cerebral Blood Flow Measurement from a Rotational Angiographic Sequence

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1. Introduction

The aim of this project is to investigate new ways of measuring three-dimensional cerebrovascular blood flow which has applications in the field of neurosurgery. In particular, it can be used as an aid for the treatment and embolisation of cerebrovascular diseases such as aneurysms and arteriovenous malformations (AVMs). Previous approaches include matching distance-concentration curves obtained from biplanar sequences of digitally-subtracted angiograms [1] and mapping a series of fixed-view X-ray images depicting the flow variation onto a 3D rotational angiographic volume [2].

Our proposed method involves capturing a rotational sequence of contrast-enhanced digitally-subtracted X-ray images of blood flowing through an artery. We then estimate the 2D blood flow velocity between successive pairs of these images and then backproject these into 3D space using as a guide a computed tomographic 3D reconstruction created from the same rotational image sequence.

To obtain this form of data, we use the Siemens Axion Artis X-ray machine situated at the Radcliffe Infirmary, Oxford which has a dual C-arm setup that allows rotational capture as well as a biplanar setup. The machine is also capable of computing tomographic 3D reconstructions.

A major advantage of this type of method is that it is not very invasive and can be carried out during an operation. Hence, for treatments where the repeated monitoring of blood flow is necessary - for example, the embolisation of AVMs (Figure 1) - this could reduce treatment times where normally magnetic resonance angiography methods may be used as there is no need to move the patient to another room.

This project is in collaboration with Dr. James Byrne from the Department of Neuroradiology at the Radcliffe Infirmary, Oxford.

Figure 1. Treatment of AVM. Left-to-right, i) pre-embolisation, ii) post-1st embolisation, iii) post-2nd embolisation. One of the feeding arteries has been successfully blocked off.

2. Computing 2D flow estimations between image pairs

In order to compute a flow estimation between pairs of images, we propose to use an optic flow-based method which has previously been developed for measuring fluid flow from image sequences. Due to the tortuous nature of cerebral blood vessels, it was decided that this method is suitable as it is capable of producing a 2D flow map rather than the more common 1D-based videodensitometric methods [3].

The fluid flow model used is a combination of the optic flow brightness constancy equation and the flow continuity (conservation of mass) equation.

\[ I(\nabla \cdot \mathbf{v}) + \nabla I \cdot \mathbf{v} + I_t = 0 \]
A regularising term to minimise the spatial variation of the flow is added, and minimisation and discretisation of the resulting equation leads to an iterative solution [4]. This method of solution is based on that used by Horn and Schunck for obtaining optic flow [5].

Additionally, there is a constraint that at the boundary of the vessel being imaged, there is no fluid flow normal to the boundary. This constraint is derived from 3D space, but is also applicable to a corresponding 2D transmittance image. The vessel boundary in the 2D image can be found by using an edge detector.

3. Compensating for the difference between image pairs taken from a rotational sequence

The method described so far is suitable when both images are taken from the same fixed angle. However, the image sequence is captured over a range of angles and so successive images will have been taken from slightly different angles (a difference of approximately 1 degree), and so there is a small variation between the images in terms of the location of the vessel and its boundary.

To compensate for this, a warp is applied to one of the image pair so that the two are aligned without significantly altering the intensity distribution of the fluid. The warp is estimated from a pair of maximum-intensity projections (MIPs) of the 3D reconstructed volume (as provided by the machine) created from the same angle directions as the image pair.

4. Backprojection of flow vectors into 3D

We intend to investigate this part of the problem by combining the flow vectors measured from a range angles to create a 3D flow vector with a weighted least squares approach. This would give an average velocity over that time period rather than reproduce a representation of the pulsatile nature of blood flow through vessels.

5. Experiments

The 2D flow estimation was initially tested with synthetic data (a simple cylinder containing many particles which were moved in a direction parallel to the cylinder axis under a parabolic velocity profile) with some successful quantitative results. Testing these algorithms with real angiogram data (at a resolution of 512 by 512 pixels) resulted in the flow being quantitatively detected.

We have recently run some experiments using a phantom of a bifurcating vessel. Water was channelled through the phantom using a simple constant flow-rate pump and an iodine-based contrast was injected into the stream. The C-arm apparatus was then used to capture a rotational sequence of 1024 by 1024-pixel images over a range of approximately 200 degrees with 1 degree steps over a period of 7 seconds. 3D reconstructions of these data sets have also been created.

While the data has not been fully tested to date, the initial results show that the method is vulnerable to diffusion of the contrast agent and that a pulsatile flow which is more similar to that in cerebral vessels would be more detectable with our current algorithm.

Acknowledgements

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References

Pathways of control in the cerebral vasculature

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1 Introduction

A variety of stimuli are known to cause direct or indirect changes in the calibre of cerebral resistance vessels, both in vitro and in situ, via effects involving vascular smooth muscle (VSM), the vascular endothelium, and other cell-types in brain tissue. These stimuli include changes in:

- physical quantities, primarily shear stress and pressure [1], [2]
- oxygen and CO₂ levels [3], [4]
- levels of neurotransmitters such as noradrenaline and acetylcholine [1], [5], [6]
- levels of metabolic by-products such as lactate and adenosine [4], [7], [8], [9]
- levels of substances associated with pathologies (e.g., angiotensin II during hypertension and extracellular oxyhaemoglobin during subarachnoid haemorrhage) [10], [11], [12]
- pharmacological agents such as glibenclamide and forskolin [10]

The pathways by which many of these stimuli take effect are under active investigation, and there is little quantitative data. There is a high degree of variability in experimental results depending on species, organ from which the tissue is taken, experimental conditions, etc. Various subtleties complicate experimentation: for example a stimulus can have a modulatory effect which only manifests in the presence of some other stimulus.

2 A computational graph theoretic approach

At this point, the data needed to construct a full quantitative model of the system using differential equations does not exist. In [13] we attempted to bypass this problem using simple caricatures of many of the processes, and omitting others. Here we adopt a different approach: Rather than constructing a quantitative but incomplete model, we attempt to construct a more qualitative, but also more complete, model of cerebral vessels. The main tool used is computational graph theory.

To illustrate the potential of such an approach, in Figure 1 we present a diagram which has been constructed automatically from a large database of processes and represents a subgraph of a larger graph. The figure maps out all the pathways by which nitric oxide (NO) can influence VSM tone once it has entered the VSM cells. In this instance there are ten paths, all of which decrease tone.

It is easy to use graph-theoretic algorithms to ask what the effect of deleting a node (inhibition of a quantity) or an edge (inhibition of a path) would be, or how the system might respond to two simultaneous stimuli. For example, application of an inhibitor of sGC could be represented as the removal of the node sGC in the graph. In this situation, five inhibitory pathways survive suggesting that we might still get some vasodilatory action.

3 Conclusions

Although the work is at a very preliminary stage, the results are promising, in that we can qualitatively reproduce the outcomes of a number of experiments available in the physiology literature. We speculate that including further information, for example some weighting of the edges representing the relative importance of processes, would allow more detailed predictions.

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1We do not suggest either that this pathway diagram is complete, or that all pathways are equally important in the cerebral circulation: the diagram represents possibilities.
Figure 1. The way that nitric oxide which has entered vascular smooth muscle (VSM) cells can influence VSM tone. Solid lines are activatory steps, while dashed lines are inhibitory steps.

**Variables:**

- **force**: the active tension developed by VSM cells
- **pRMLC**: phosphorylated regulatory light chains of myosin
- **MLCP**: myosin light chain phosphatase
- **MLCK**: myosin light chain kinase
- **CPI17**: a smooth-muscle specific protein inhibitor of MLCP
- **NO**: nitric oxide
- **sGC**: soluble guanylate cyclase
- **sGCreac**: the reaction catalysed by soluble guanylate cyclase
- **cGMP**: guanosine 3’,5’-cyclic monophosphate
- **CYP4A**: cytochrome p450 enzymes
- **CYPreac**: reaction catalysed by cytochrome p450 enzymes
- **HETE20**: 20-HETE (20-hydroxyeicosatetraenoic acid) - a product of arachidonic acid
- **PKG**: cGMP-dependent protein kinases
- **RhoA**: a G protein of the Rho family
- **ROK**: Rho-associated kinase
- **HSP20**: small heat shock protein
- **SERCA**: sarcoplasmic/endoplasmic reticulum Ca$^{2+}$-ATPase
- **PKC**: protein kinase C
- **Ca**: calcium
- **gCa**: conductivity of calcium channels
- **Vmem**: VSM cell membrane potential
- **gKtot**: total potassium channel conductivity
- **BKCa**: Conductivity of large calcium sensitive potassium channels

**References**

The effectiveness of physiological challenges in the testing of cerebral autoregulation

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1 Introduction

An experiment was conducted to investigate the effect of various physiological challenges which affect the systemic circulation upon a sample of normal volunteers. The chosen were all standard tests found in the literature routinely used in the assessment of cerebrovascular autoregulation. The purpose was to compare the physiological response to each of the tests and to select a subset that were candidates for use in the bore of a magnetic resonance imaging scanner.

2 Data Collection and Analysis

Five male and three female volunteers aged 18 to 50 (mean ± S.D. 33.4 ± 4.5 years) were recruited through a poster campaign and word of mouth. All were healthy and had no history of cardiovascular disease. The urine of all female participants was tested for β-HCG, which returned negative results in all cases. Ethical approval was granted by the Salford and Trafford Local Research Ethics Committee (ref 03/ST/150). The physiological parameters that were continuously monitored were

- bilateral cerebral blood flow velocity in the mid-cerebral artery using transcranial Doppler ultrasound,
- bilateral changes in concentration of oxygenated, de-oxygenated haemoglobin and cytochrome oxidase as well as tissue oxygenation index using near-infrared spectroscopy,
- arterial blood pressure using a tonometer located over the radial artery,
- end-tidal carbon dioxide using a near infrared capnograph,
- leads I and II of an electrocardiogram,
- and arterial oxygen saturation using a pulse oximeter.

The analogue outputs of these channels were digitised to 16 bits using a CED micro1401 mk II and were sampled at rates from 6 Hz to 500 Hz using Spike2 software.

2.1 Experimental protocol

The protocol consisted of a series of physiological challenges conducted in a fixed order, separated with recovery time. The challenges used were

- transient hyperaemic response (THR): unilateral occlusion of the carotid artery lasting 5 seconds [5];
- carotid sinus massage (CSM): unilateral longitudinal massage performed over the site of the carotid sinus lasting 5 seconds [4];
- Valsalva manoeuvre: expiration against a load sufficient to raise the pressure at the mouth to 6 kPa for at least 15 second [3];
- head-up tilt test: volunteer passively tilted from supine to 80 for ten minutes [2];
- lower-body negative pressure (LBNP): the lower body of the volunteer was sealed in an air-tight box and the pressure in the box was then lowered in steps of 1.5 kPa to -4.5 kPa, each step lasting 150 s, from where the pressure was returned to atmospheric in steps of 1.5 kPa lasting 150 s each [1].

Between each test there was a period of recovery, where the measured parameters were allowed to return to pre-test baselines.

2.2 Data analysis

The data was analysed using Matlab 6.5. The first task undertaken was QRS detection using the data from the ECG leads. From there it was possible to average the other physiological parameters over single heart cycles. Each test was then segmented identically, either by time or physiologically. Once that had been completed it was possible to perform analysis on the data from each volunteer.

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3 Results

![Figure 1: Locus of BP and CBFv caused by the Valsalva manoeuvre (left) and a summary of test results for one volunteer (right)](image)

Figure 1 shows the effect of each of the tests on mean arterial pressure and cerebral blood flow velocity for one volunteer. Each of the crosses corresponds to a value averaged over the each of the segments in each of the tests, and the lines a simple linear regression for each test.

4 Discussion

Some of the tests used in the protocol were inconsistent due to technique. This notably affected the carotid sinus massage and the transient hyperaemic response tests, both of which require a clean occlusion of the carotid artery. Although positioning of the volunteer was not ideal, the results show that even experienced clinicians could not occlude it successfully every time. The tilt test also caused problems due to the degree of movement involved in the test. This introduced artefact in to the blood pressure recording and frequently caused the TCD to lose the signal from the mid-cerebral artery. On the other hand both the Valsalva manoeuvre and the lower-body negative pressure were easy to control and produced physiologically consistent results between volunteers.

The results show that changes in mean arterial blood pressure and cerebral blood flow velocity due to the tilt test are comparable to those achieved using LBNP.

5 Conclusion

This experiment shows that tests that repeatably produce the most significant change in physiological state are the Valsalva manoeuvre and lower-body negative pressure. The others were prone to either movement artefact or inconsistencies in the technique used to conduct the test.

Taking this subset of tests into the bore of the MR scanner would be viable since the challenges can be run without moving the volunteer and equipment needed can be designed to be MR compatible. The results from this experiment enables us to continue with the next step in the project: combining the signals from the near infrared spectrometer with the images produced by the MR scanner.

Acknowledgements

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References

Multi-Resolution Fluid Registration: Evaluation in Motion Correction of MR Mammography

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1 Introduction

Fluid registration is a potentially powerful framework for solving correspondence problems due to its ability to cope with large deformations and reluctance to produce deformation fields that fold (i.e. for which the Jacobian determinant < 0) [1]. However it has not been widely adopted for reasons that include (i) a perceived complexity compared with more intuitive Free-Form-Deformation methods (ii) a belief that it is computationally slow and (iii) the fact that it is susceptible to local minima problems. In this paper we describe a multi-resolution fluid registration designed to improve computational speed and robustness. The new algorithm is evaluated on magnetic resonance images of simulated breast deformation for which the applied displacement is known.

2 Methods

Fluid registration models the response of a hypothetical compressible viscous fluid, velocity \( v \), to a set of forces, \( f \), derived from image similarity and uses it to update a displacement field \( u \) (equation 1).

\[
\mu \nabla^2 v + (\mu + \lambda) \nabla (\nabla \cdot v) + f(u) = 0
\] (1)

Different numerical strategies have been employed to solve equation 1. The most well known are Successive Over Relaxation (SOR) [1], Full Multi Grid (FMG) [2] and the convolution filter (CF) [3]. FMG approaches are intuitive and solve large 3D registration problems in a few hours (typically 5-15) on contemporary desk-top processors. However previous implementations have solved equation 1 in a dimensionless form with images resampled to isotropic voxel dimensions. For anisotropic images this has either meant super-sampling low-resolution dimensions or sub-sampling high-resolution dimensions, neither of which make the best use of the data. The alternative is to treat anisotropic voxels as isotropic which introduces directional bias into the flow. Also, naïve implementations of FMG use the same hierarchy of grids in each coordinate direction dependent on the dimension with the smallest number of voxels.

We first recast equation 1 to explicitly incorporate the mm voxel-dimensions which involves scaling the interaction of the different derivative terms. Then, to improve computational efficiency in very anisotropic images, a semi-coarsening strategy [4] is incorporated into the FMG solver to allow the resolution of the FMG grids to be different in different coordinate directions. Gaussian smoothing with variance related to the multi-resolution scale in each coordinate direction is applied at each grid level. Finally, we exploit the structure of the FMG for an efficient multi-resolution strategy by retrieving the solution first at coarse resolutions and then at full resolution.

<table>
<thead>
<tr>
<th>FMG Grid</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>No SC</td>
<td>289x113</td>
<td>145x57</td>
<td>73x29</td>
<td>37x15</td>
<td>19x8</td>
<td>-</td>
</tr>
<tr>
<td>SC</td>
<td>289x113</td>
<td>145x113</td>
<td>73x57</td>
<td>37x29</td>
<td>19x15</td>
<td>10x8</td>
</tr>
</tbody>
</table>

Table 1. The Effect of Semi-Coarsening on Full Multi-Grid. In this 2D example, the grids used by the FMG are shown with semi-coarsening (SC) and without SC. Note that with SC, there are more grids to solve but the full solution is obtained on a coarser more isotropic grid.

Images acquired during dynamic contrast-enhanced MR mammography were used for evaluation. A biomechanical model of 6 tissue deformations, varying in displacement magnitude and range, produced a series of deformed breast images for 5 patients where the displacement at each voxel is known [5]. The registration task is to recover the deformation field by matching the deformed and undeformed images. In this work we are interested in motion correction so intensity changes due to contrast enhancement are not considered. Thirty registrations (5 patients x 6 scenarios) constituted a single test set. We ran the following fluid cases 33, 23, 13,
where the first digit denotes the finest resolution level and the second digit denotes the coarsest resolution level with smaller numbers implying finer resolution e.g. 02 means start at level 2 (¼ resolution) and finish at level 0, (original resolution). In each case 200 fluid iterations were divided equally between the number of multi-resolution levels with the registration at a particular level stopping earlier if no further improvement to the image similarity could be obtained.

Figure 1. The Mean Registration Error and Computation Time. The 2-digit labels indicate the multi-resolution scheme; see text for details. (a) N0 is the mean applied displacement. (b) The mean computation time.

3 Results

Table 2 shows the computational speed per iteration for each multi-resolution level for an example data-set. Figure 1a shows the mean displacement error in mm over the breast for each fluid registration case evaluated over 5 patients and 6 deformation scenarios with the error bars showing one s.d.; the associated run-times are in Figure 1b. The most dramatic reduction in error and compute time is between 00 and 01. Note that even the slowest case runs on average inside 1 hour. The error goes down as the available degrees of freedom goes up i.e. from 33 to 22 to 11 to 00. The s.d. also reduces but is smaller for 11 than 00 indicating that the multi-resolution scheme is not affecting registration accuracy. The mean error is nearly constant for cases 03, 02, 01, 00 indicating that the multi-resolution scheme is not affecting registration accuracy. The mean (s.d.) error is less than 0.5 (0.25) mm for all multi-resolution cases, compared with a mean (s.d.) applied displacement of 2.1(1.2)mm and maximum of up to 10mm.

<table>
<thead>
<tr>
<th>Multi-Resolution Level (0=Finest)</th>
<th>3</th>
<th>2</th>
<th>1</th>
<th>0</th>
</tr>
</thead>
<tbody>
<tr>
<td>FMG(Total) Time Per Iteration / s</td>
<td>0.17 (0.25)</td>
<td>1.3 (2.3)</td>
<td>10 (15)</td>
<td>45 (60)</td>
</tr>
</tbody>
</table>

Table 2 : Timings for Multi-Resolution Fluid Registration. The timings were obtained on a 1.8GHz Athlon CPU. The images were 256x256x64 voxels of sizes 1.3x1.3x2.5mm padded to 289x289x113 for computation.

4 Conclusions

Fluid registration benefits from an efficient multi-resolution scheme in terms of speed but we have not demonstrated improved accuracy – which is already very good - in this relatively straight-forward registration task. The results suggest that in some applications it might be better to run fluid registration at a coarser scale to reduce the influence of noise. Further evaluation on a completely different registration problem, inter-subject MR brain registration using the overlap of corresponding neuroanatomy is underway.

References

Elasticity Imaging From Displacement and Strain Estimation of Ultrasound Radio Frequency Signals

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Recent years, Ultrasound (US) elastography has drawn much attention as a low cost and risk imaging modality to derive information about the biomechanical properties of soft tissues and to understand how changes in these properties correlate with pathological developments. So it will provide new opportunities for detection and diagnosis of cancers in the breast, prostate, coronary artery and other sites by assessing the elastic characteristics of soft tissue. Most of these techniques can be classified into the direct or inverse approaches. The inversion elasticity imaging approaches have been widely investigated because of their robustness, while the noises of displacement estimates in solving the ill-posed inverse problem has become an impediment to restrict its diagnostic effectiveness, especially for ultrasound images with limited spatial and contrast resolution.

In a recent paper [1] we developed a multi-frame elasticity reconstruction approach that will lead to a more robust reconstruction solution on simulated data (displacements). Currently we have extended the approach to work on radio frequency (RF) data. An iterative phase zero estimation algorithm is performed to obtain temporal displacements between pre- and post- compression RF images [2]. And then, strain field is estimated by the Least-Squares strain estimator (LSOSE) [3]. To render the solution of the inverse elastography problem to be unique and stable, a finite-element based inverse split-and-merge strategy is applied for elasticity reconstruction [1].

The performance of the developed method has been tested by simulated data of a one inclusion phantom. The mechanical characteristics of the simulated phantom is that the Young’s modulus of the inclusion is twice less than that of background. The Field II software specifically dedicated to simulate RF US data was used to compute RF signals of the phantom. The simulation results shown that although multi-frame processing is computationally intensive, the presented method shows promise to give significantly higher accuracy for elasticity imaging than previously reported work.

Preliminary experimental works will be also performed on agar and gelatin phantom.

REFERENCE


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http://www.robots.ox.ac.uk/~mvl/external/mvl-html/
Segmentation of foetal cardiac data

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1 Introduction
Congenital heart disease affects about 8 in every 1000 births [1] and its signs can be diagnosed with prenatal echocardiography [2]. As with the adult heart, functional volume estimation of the left ventricle provides quantitative information about the state of the myocardium. However, in the foetus the blood flow in both sides of the heart is allowed to mix and so both ventricles are important for clinical assessment. One important application of foetal cardiac segmentation is for measurement of the absolute size of the chambers. This can be used for evaluation of the function of the heart, compromised either by cardiac malformations or by non cardiac diseases such as immuno-haemolysis. In this condition the maternal immune system can kill foetal blood cells and so the foetal heart grows larger to compensate.

In the past Navaux’s group have published their work on segmentation of the 2D foetal heart by classification via neural networks [3], [4]. Lassige et al used a level set snake based on the fast marching method to measure the size of the septal defects in echocardiographic images. In 2003 Dindoyal and co-workers presented an explicit Gradient Vector Flow (GVF) snake algorithm with rigid body motion constraints to segment and track ventricles in 2D motion-gated foetal cardiac data [5].

2 Method
Acquisition of the foetal heart by 2D slices was carried out by an online motion gated method pioneered in the group [6] using paired Acuson scanners (25 frames per second and a pixel spacing of 0.26mm). 3D acquisition of the foetal heart was performed with the Live 3D ultrasound scanner from Phillips. The imaging system is capable of capturing 20 volumes per second and can output a resampled voxel resolution of 1.47mm³.

A level set model based on the snake equation from Sarti et al 2002 [7] uses the edge flow diffusion properties of the GVF snake. Datasets with signal dropout were segmented by Sarti’s algorithm using the properties of the mean curvature and edge flow terms. In this report a new term was added to this evolution equation to incorporate region growing based on local deviations from the interior and exterior regions using the image part of the Mumford Shar (MS) functional. This term is useful in images without clear boundaries [8]. In this implementation the MS force is heavily penalised by curvature and inter-snake collision detection to reduce inter-chamber leakage. This is shown in (1) where Sarti’s geometric model for boundary completion is enclosed in curly braces.

\[
\phi = \left\{ \alpha g \nabla \frac{\nabla \phi}{|\phi|} + \beta g \nabla \phi \right\} \|\nabla \phi\| + \left( \lambda_1 (I - \mu_i)^2 - \lambda_2 (I - \mu_o)^2 \right) \exp \left( -\kappa \nabla \frac{\nabla \phi}{|\phi|} \right) \|\nabla \phi\| (1 - \xi) \|\nabla \phi\| \quad (1)
\]

Where \( g = (1 + |\nabla G F|) \) is an edge detector that returns a value between 0 and 1, with \( G \) denoting Gaussian filtering and \( F \) is the image. In equation (1) \( \phi \) is the level set function, \( I \) is the current voxel intensity under investigation. \( \mu_i \) and \( \mu_o \) are the means of the internal and outside regions of the dataset defined by the level set front. \( \xi \) is a function that tests if any of the enclosed regions from individual snakes overlap. If there is overlap \( \xi \) returns 1 and 0 otherwise. \( \alpha, \beta, \lambda_1, \lambda_2, \kappa \) are empirically determined weighting coefficients for the respective terms.

3 Results and Discussion
Inter-snake collision detection appeared to work most reliably if the seed points for the snakes are placed as close to the centres of their respective chamber as possible. This increases the likelihood that snakes in

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adjacent chambers will meet at the shared partial boundary at the same time. An example of inter-snake detection is shown in Figure 1.

![Figure 1 Example segmentation in 2D and 3D (central slice). The atria appear at the top of the images and the ventricles below. The two snakes meet at open boundaries or at wall drop outs and the inter-snake collision detection prevents the two fronts from leaking into adjacent chambers.]

In 3D the segmented boundary has a maximum root mean square (rms) error of 9 voxels when projected on the manual tracings. Segmentation of the 2D slices yielded an rms error of under 4 pixels over 33 slices.

In many images the front stopped short of the desired boundary and this shows up in the high rms errors. Whilst high curvature penalisation was partially responsible, premature stopping of the level set front was also due to contributions from the type of image forces used. The MS term models unchanging mean intensities both inside and outside of a small sphere or circular seed placed inside the chamber. If the mean was updated as the snake evolved the front could come to rest closer to the boundary. The edge flow term requires a diffusion equation to be applied to an edge map and so broadens edges. The Gaussian prefiltering used a broad kernel of length 9 pixels and this could contribute to the edge broadening.

4 Conclusion

A level set snake was formulated to segment foetal heart data with drop out and shadowing artefacts. Future work will involve correction of the under segmentation of the cardiac chambers and application of the snake to additional datasets.

Acknowledgements

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References

FMRI simulator and its application in modelling

$B_0$-inhomogeneities and $B_0$-motion interactions

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Introduction

$B_0$-inhomogeneities occur at interfaces of materials with different magnetic susceptibilities, such as tissue-air interfaces. These differences lead to distortion in the local magnetic environment, causing signal loss and geometric distortion of the image. Current methods for modelling and correcting these artifacts involve acquiring a field map (i.e. an image of the perturbed field) and transforming the image by warping from distorted to undistorted voxel positions. However, acquiring field maps at each time point is not practical in FMRI. Hence a more quantitative and analytical approach is needed to examine the interaction of $B_0$ distortions and motion. We propose an FMRI scanner simulator to model motion, $B_0$-inhomogeneities and their interactions.

Methods

A general MRI simulator was constructed in C++ to solve the Bloch equations for each element of the object (small rectangular voxels). The perturbed field $\tilde{B}_z^{[1]}$ was calculated from known susceptibility distribution by using a perturbation approach to solve Maxwell’s equations [1] and then was implemented in the Bloch equations. In order to model the object motion, two coordinate systems are introduced, the scanner coordinate system $\mathbf{x}$ and the object coordinate system $\mathbf{x}_{ob}$. Motion parameters (three translations $T_x, T_y, T_z$ and three rotations $R_x, R_y, R_z$) are specified by an input matrix at a sparse set of (user-specified) discrete time points. It is then interpolated between these in order to evaluate the position for each time point of interest. The interpolation assumes a constant linear and angular velocity between each pair of discrete time points and is implemented using quaternions. The two coordinate systems are related with a rigid body transformation $\mathbf{x} = R(t)\mathbf{x}_{ob} + T(t)$. Integrating the magnetisation vector in time for each tissue type separately in a voxel element in object space gives the MR signal as

$$S(t) = \iiint |M_{xy}(t_{rf})| \exp \left( -\frac{t}{T_2} \right) \exp \left( i\gamma \int_{t_{rf}}^t \mathbf{G}_{sc}(t')(R(t')\mathbf{x}_{ob} + T(t'))dt' \right) \exp \left( i\gamma \int_{t_{rf}}^t \tilde{B}_z^{[1]}(\mathbf{x}_{ob}, t')dt' \right) d\mathbf{x}_{ob}$$

where $t_{rf}$ is the time of the last RF pulse, $M_{xy}(t_{rf})$ is the transverse magnetization following the last RF excitation, $\mathbf{G}_{sc}(t)$ is the applied gradient vector (in the scanner coordinate frame) at time $t$, and $\tilde{B}_z^{[1]}(\mathbf{x}_{ob}, t)$ is the perturbed magnetic field. $\tilde{B}_z^{[1]}(t)$ is evaluated at the center of each voxel of the object as:

$$\tilde{B}_z^{[1]}(t) = [0 \ 0 \ 1] R(t) \begin{bmatrix} \tilde{B}^{[1]}_z(1, 0, 0) & \tilde{B}^{[1]}_z(0, 1, 0) & \tilde{B}^{[1]}_z(0, 0, 1) \\ \tilde{B}^{[1]}_y(1, 0, 0) & \tilde{B}^{[1]}_y(0, 1, 0) & \tilde{B}^{[1]}_y(0, 0, 1) \\ \tilde{B}^{[1]}_x(1, 0, 0) & \tilde{B}^{[1]}_x(0, 1, 0) & \tilde{B}^{[1]}_x(0, 0, 1) \end{bmatrix} R^{-1}(t) \begin{bmatrix} 0 \\ 0 \\ 1 \end{bmatrix}$$

where $\tilde{B}^{[1]}_p(\hat{q})$ is the field calculated in the object coordinate system with the $p$ direction ($x, y$ or $z$) specifying the component of the field resulting from an applied field $B^{[0]}_p = \hat{q}$ (where $\hat{q}$ is a unit axis vector). Calculated values are trilinearly interpolated to form $\tilde{B}_z^{[1]}(\mathbf{x}_{ob}, t)$. The total signal is the sum of the contributions from each voxel.

Results and Discussion

Results are acquired by simulating an EPI pulse sequence and using the BrainWeb partial volume tissue estimates [2] as an object model. Figure 1 shows the effect of rotation about $z$-axis during the acquisition of one slice (TR=120ms) - including the readout points. From left to right, no motion, blurring and distortion due to rotation about $z$ axis in one direction, and striping due to back and forth rotation, $R_z$. Figure 2 shows the effects of the $B_0$-inhomogeneities in the case of no motion, where the biggest distortion is in the frontal lobe as it is close to a large air/tissue boundary. Figure 3 shows the intensity (after motion correction) in the voxel with the maximum

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We have presented a MRI simulated scanner which, for any gradient echo pulse sequence and any object model, simulates the effects of motion, B0-inhomogeneity, BOLD [3], and their interactions. Therefore it will be extremely useful in several areas such as: motion correction techniques, quantifying the performance of analysis software, testing and comparing different physiological models and in examining the effect of different acquisition techniques, especially in separating the effects of different artifacts.

Figure 1. Example of motion during the readout time of the acquisition of one slice. The line under each picture represents the timing of the rotation $R_z$ that occurred during the imaging of the slice (max rotation is 9 degrees, which is artificially large in order to emphasize the effects visually).

Figure 2. Simulation of the EPI acquisition of one slice with $B_0$-inhomogeneity present (left), and with no $B_0$-inhomogeneity present (right).

Figure 3. Simulation of the EPI time series for one voxel with $B_0$ inhomogeneity (left figure), and without $B_0$ inhomogeneity (middle figure). Red and black lines correspond to continuous motion (including motion during the readout points) and abrupt motion (between the readout periods) respectively. Motion sequence is represented in the right figure.

Acknowledgements

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References

Characterization of Novel Microbubble Contrast Agents

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Abstract. An exciting recent development in ultrasound microbubble contrast agent technology is their extension from non-specific diagnostic tools to targeted and therapeutic agents. This involves attachment of targeting, or otherwise active, ligands to the microbubbles. The aim of this work was to evaluate the effect of these additional ingredients on the acoustic properties and stability of microbubbles with shells consisting of either albumin or phospholipids. Non-conjugated bubbles were found to behave comparably to their commercial equivalents. Both albumin and phospholipid bubbles show reduced stability following conjugation. Cross-linking of the albumin shell was found to improve bubble stability. For the lipid bubbles improvement in stability was also recorded upon conjugation via polymeric spacers. This work demonstrates that the acoustic characterisation of novel bubbles is crucial in refining the manufacturing process. The results presented show that conjugation of large molecules into the bubble can affect the acoustic behaviour of the bubbles. The approaches employed in this work allow testing of chemical hypotheses in the design of novel targeted agents.

1. Introduction

Through combination with appropriate anti-bodies it is possible to target microbubbles to specific tissue or cell types, enabling targeted imaging of pathology e.g. inflammation [1]. Furthermore, the combination of microbubbles with therapeutic agents has potential for improving the efficiency of drug delivery [2, 3]. These extensions of the utility of microbubbles in biomedical ultrasounds from non-specific contrast agents to targeted and therapeutic agents are currently of much interest. A number of strategies for labelling and/or loading microbubbles have been proposed (e.g. [4]). Typically these involve the addition of large molecules such as DNA segments or anti-bodies to the microbubbles. It is important if these are to be successful that the effect of the physical and chemical changes in the microbubble composition on the acoustic properties is quantified and understood. Varied and wide ranging approaches to the challenges of microbubble characterization [5-7] have been described. In our laboratory we have embarked on a program of producing targeted and therapeutic microbubbles with ligands attached to their shells. As part of this program we have developed a series of acoustic characterization tests and tools. With reference to previous approaches, four aspects of microbubble acoustic behaviour were selected for our investigations: I) the attenuation, II) the backscatter, III) the longevity at physiological dilution under low power insonation, and IV) the bubble stability at higher power. In this paper we describe these tools and present initial results obtained from applications of these tools to microbubble production.

2. Method

Novel microbubbles were produced in our laboratory with shell materials comprising albumin or phospholipid blends. In each case both targeted bubbles and non-conjugated (naked) versions were manufactured. Laboratory made microbubbles were compared to commercially available equivalents, Optison® (Amersham Health, UK) and Sonovue® (Bracco UK Ltd.). Initially, samples of each bubble type were optically sized and the concentration of the sample assessed from photographs taken through a standard light microscope. The acoustic properties of the bubbles were measured through a series of tests designed to provide information on the attenuation, backscatter, strength and stability. This was performed with two separate experimental set-ups. Attenuation and backscatter were measured using a semi-automated laboratory set-up controlled through MATLAB® via a GPIB interface. Additional backscatter and stability measures were obtained using commercially available clinical ultrasound equipment. For the attenuation measurements the frequency of the peak in attenuation, the mean attenuation level, full width half maximum of the attenuation were all measured from the frequency spectrum. In addition, the slope of a straight line fitted to the mean attenuation level plotted against time was recorded for each sample. For the backscatter experiment the results from all repeats were combined to provide a measure of backscatter versus acoustic pressure. The mean difference in signal level between pulse 1 and pulse 50 for each pressure level were also recorded and compared against threshold levels as a measure of the bubble shell strength. The backscatter signal level was divided by the mean attenuation measurement (both obtained at the same pressure level) to determine a relative measure of the backscatter to attenuation ratio [8] at 3.5MHz. A straight line fit was used to reduce the grey-scale data (measured as the mean...
dB level in the region of interest). The slope of this line was used as a measure of the microbubble stability. To avoid bias, the data was collected and analyzed with the relevant author blinded to the specific details of each bubble sample.

3. Results

**Albumin based bubbles:** The major difference observed with the albumin based bubbles was in their stability, which was reduced by the conjugation process. The inclusion of an additional cross-linking stage was found to improve the stability during the attenuation test by a factor of 10 (from -2.3dB/min to -0.24dB/min). This coincided with an increase in the 3dB destruction threshold from an MI of 0.23 to 0.29. There was no significant difference in the initial backscatter measured for all albumin bubbles (all measured at 40 ± 2 dB). The ratio of scattering to attenuation was found to be higher in the conjugated bubbles (8 ± 2 µV dB-1) compared to the equivalent naked sample (5 ± 1 µV dB-1), both measured at 3.5MHz. Compared with Optison® the acoustic properties of the cross-linked bubbles were not significantly different except the 3dB destruction threshold for Optison® was lower at 0.12MI. **Phospholipid based bubbles:** Without the inclusion of the polymeric spacers the bubble yield and stability where generally too poor to allow acoustic testing. The inclusion of macromolecules was found to reduce both the strength and stability of the microbubbles 3dB destruction MI >0.6 for naked bubble vs. MIs of 0.06, 0.12, 0.46 for three bubbles containing macromolecules. In the grey-scale stability test the naked bubbles were found to decay at 0.07 ± 0.03 dB/min vs. 0.30 ± 0.02 dB/min. By comparison, in the same test Sonovue® was found to decay at a rate of 0.20 ± 0.03 dB/min. Similar results were obtained for the ratio of scattering to attenuation as in the albumin-shelled case. This was found to be higher in the conjugated bubbles (20 ± 7 µV dB-1 and 27 ± 10 µV dB-1) compared to the naked equivalent (11 ± 3 µV dB-1), both measured at 3.5MHz.

4. Discussion & Conclusions

Similar trends in the results were obtained for both the albumin and phospholipid bubbles tested. These results show that addition of large molecules reduces microbubble stability. In the case of the albumin bubbles this was additionally reflected in the 3dB destruction threshold. The attenuation and backscatter measurements for the microbubbles yielded scattering to absorption ratios, which increased with the conjugation process. Although a broadband attenuation measurement was obtained, backscatter measurements were only performed at a single fixed frequency. In future work we plan to enhance the testing system to include feedback from the attenuation measurement to select the most appropriate frequency for subsequent measurement. We plan to use measurements of the attenuation spectra to aid in driving the bubble manufacture process. By combining knowledge of the bubble size and the attenuation we hypothesize that it should be possible to generate bubbles designed for use at a specific frequency. We have developed a series of acoustic tests for evaluating microbubble properties. The results presented show that conjugation of molecules into the bubble can affect the behaviour of the bubbles. These approaches allow the testing of chemical hypotheses in the design of novel targeted agents.

6. References

Automatic Segmentation of Liver from Computerised Tomography (CT) Images

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Abstract

Most attempts at automatic segmentation of liver tissue to date have relied on 2D, low-level segmentation techniques, such as thresholding and mathematical morphology, to obtain the basic liver structure. The derived boundary can then be smoothed or refined using more advanced methods. Here we present results that improve greatly on this previous work by using a topology adaptive active contour model, or snake, to accurately segment the liver outline from CT images.

1 Introduction

As part of the diagnosis of liver disease, a Computerised Tomography (CT) scan is taken of the patient, which the clinician then uses to assist in determining the presence and extent of the disease. Frequently the clinician is required to hand segment the liver tissue, in order to obtain further information such as liver volume, or to quantify the extent of diseased tissue. As hand-segmentation is slow and time-consuming, an automatic segmentation tool for the liver could greatly reduce the workload for the clinician. The automatic detection of the liver from CT scans is considered one of the harder segmentation challenges in medical image processing. The difficulties arise due to large variations of liver geometry between patients, the limited contrast between the liver and the surrounding organs, and image noise [1]. Previous work on liver segmentation [2,3,4] usually relies on initial boundary estimation, for example using thresholding or previous knowledge, before refining and smoothing the boundary with higher level techniques. However, the irregular shape of the liver can greatly vary the accuracy of the initial boundary placement, and thus the correct segmentation of the liver. Our solution to this problem is to segment the liver using an inflationary active contour model, which reparameterises to a grid imposed on the image, similar to the topology adaptive snake (T-snake) first proposed by McInerney and Terzopoulos [5].

2 Methods

The active contour model we have developed is a modified version of the T-Snake [5]. As the contour moves under the internal and external forces, it is reparameterised, at regular intervals, to a grid superimposed upon the image. This reparameterisation overcomes aliasing problems that naturally occur with inflationary contours, and allows the contour to ‘flow’ into the complex shape of the liver. Our technique differs from that presented in [5], in that the resolution of the grid changes depending on the curvature of the snake at each individual node. The major advantage of this novel technique is that the resolution of the snake increases at complex and highly irregular areas of the shape to be segmented, thus enabling the inflating contour to push itself into sharp corners and avoid aliasing effects that might otherwise cause a false segmentation result. By using this inflationary model to segment the liver, we avoid the initialisation problems that affect other methods of liver segmentation, as described above.

3 Results

Complete scans from four different patients, giving a total of 501 separate liver slices, were used to test the proposed segmentation method. All the images used were 512x512 pixels and reduced 256-level greyscale. The accuracy of the segmentation can be measured by comparing to the hand-segmented data in two ways; by comparing the area enclosed by the segmented contours, and by calculating a root-mean-square (RMS) error for the Euclidean distance between the automatic segmentation contour and the nearest point of the hand segmented contour. To compare areas, a paired t-test was used, and the null hypothesis in each case was “There no difference in the areas of the snake segmented liver and the hand segmented liver.”, and the significant probability level (p) was set to 0.05. Table 1 shows the results of the t-tests and RMS errors. For each dataset, the t-value obtained is less than the t-statistic presented in the data tables. This means that we cannot reject the null hypothesis at the 0.05 level of significance, and must therefore assume that there is no detectable change, at
this level of significance, in the values of the snake segmented and hand segmented data. The low RMS errors are comparable with those expected from hand segmentation.

<table>
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<th>Patient Number</th>
<th>Slices</th>
<th>T-value (experimental)</th>
<th>Critical T-value (p &lt; 0.05)</th>
<th>RMS Error (pixels)</th>
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</tr>
<tr>
<td>2</td>
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</tr>
<tr>
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<td>±1.990</td>
<td>5.83</td>
</tr>
<tr>
<td>4</td>
<td>50</td>
<td>-1.347 ±2.009</td>
<td>±2.009</td>
<td>10.22</td>
</tr>
</tbody>
</table>

Table 1. Results of paired t-test comparing segmented areas;

The two images in figure 1 show the effect of reducing grid size at areas of high curvature. One immediately observed difference between Figure 1(a) and 1(b) is that the snake in 1(b) has not inflated into the lobe at the top right hand side of the liver. The likely reason for this is that the relatively low resolution of the grid (8 pixels) has not enabled points to cluster around the narrow area of tissue connecting the lobe to the main bulk of the liver (in this slice).

Figure 1: Two images showing the same liver slice segmented by different snakes. (a) is segmented using a varying resolution reparameterising grid, (b) is segmented using a constant grid size. c) compares the hand segmented area (top) against a close up of the same areas from image a) (middle) and image b) (bottom).

4 Conclusion

This paper presents a new method for the automatic segmentation of the liver from CT scans. It avoids the main problem affecting previous segmentation techniques, that of initialising the snake in an efficient manner, by employing an inflationary snake which reparameterises at certain iterations of the snake movement. It has also been demonstrated that the ability to reparameterise to a smaller grid at areas of high curvature ability enables more accurate segmentation. While our preliminary segmentation results are very encouraging, our current work concerns the development an active surface model in 3D. We predict that this would further improve the accuracy of the segmentation of the liver, and form a firm basis for further work concerning abnormal livers.

References

Dynamic Models for Biomedical Time Series
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1 Introduction

Time series arise naturally in many areas of biomedical engineering. Common examples include the electrocardiogram (ECG), the electroencephalogram (EEG), and the tissue oxygenation index (TOI) from near infra-red spectroscopy. In addition, modern functional imaging techniques such as the BOLD response from fMRI also give rise to time series data. Developing effective techniques for analysing such data is a challenging problem, with many important applications in medical image and signal analysis.

In this paper we present a principled framework for the dynamic modelling of biomedical time series data. Our approach is based upon a novel hidden Markov model architecture, which makes use of prior physiological information (in the form of a set of “duration constraints”) to match the statistical properties of the model to those of the signal. In addition, we show how the undecimated wavelet transform offers an effective representation of the signal for subsequent modelling. Finally, we discuss how this framework can be extended to both multi-channel and multi-modal data fusion problems.

2 Representation

For many biomedical signals of interest, the salient features are most easily identifiable in the frequency domain. Unfortunately, these signals also tend to exhibit non-stationary behaviour, such that the informative spectral content of the signal varies with time. This property therefore prohibits the use of classical Fourier analysis techniques as an effective representation. In order to analyse successfully such non-stationary time series data, it is necessary to make use of a technique which is well-suited to the time-varying spectral properties of the signal. One such technique is given by the wavelet transform.

Wavelets are a class of functions that possess compact support and form a basis for all finite energy signals. They are able to capture the non-stationary spectral characteristics of a signal by decomposing it over a set of atoms which are localised in both time and frequency. These atoms are generated by scaling and translating a single mother wavelet.

The standard wavelet transform algorithm is the discrete wavelet transform (DWT), which uses the set of dyadic scales (i.e. those based on powers of two) and translates of the mother wavelet to form an orthonormal basis for signal analysis. In the context of biomedical signal analysis, the DWT is most suited to applications such as compression where a compact description of the signal is required. An alternative transform to the DWT is derived by allowing the translation parameter to vary continuously, whilst restricting the scale parameter to a dyadic scale (thus, the set of time-frequency atoms now forms a frame). This leads to the undecimated wavelet transform, or UWT.

The UWT is particularly well-suited to time series analysis since it provides a time-scale description of the signal on a sample-by-sample basis. Thus, at each time sample in the signal, the UWT generates a vector of transform coefficients which are associated with the spectral properties of the signal within a local neighbourhood of that time sample. A further advantage of the UWT is that the resulting coefficients are translation-invariant, such that a time-shift of the signal gives rise to an identical time-shift of the UWT coefficients. This property (which is not shared by the DWT) is particularly important for subsequent signal modelling.

3 Modelling

Given the UWT representation of the biomedical time series, it is necessary to choose a suitable model for characterising this representation. Many popular modelling techniques (such as neural networks) assume that the data is independent and identically distributed (iid). However for time series analysis this assumption is clearly incorrect, and it is therefore necessary to make use of dynamic models which incorporate the temporal nature of the time series (i.e. the “dynamics”) into the modelling process.
There are two forms of dynamic models which are most commonly used in practice. These are the Kalman filter and the hidden Markov model (HMM). With the former, the underlying state space is assumed to be continuous in nature, whereas with the latter it is assumed to be discrete. Discretising the state space is advantageous since it allows the model parameters to be learnt efficiently from the data using the Expectation Maximisation (EM) algorithm. In addition, the use of a discrete state space enables the model to be used for the purposes of segmentation.

The HMM architecture is comprised of a “hidden” state sequence, which is stochastically related to an “observed” signal (corresponding to the set of UWT coefficients). The model is parameterised by an initial state distribution $\pi$, a state transition matrix $A$, and a set of observation densities $b_i$ (for each model state $i$). These parameters can be learnt in a supervised fashion from “labelled” data, or from the raw time series alone using the EM algorithm.

A significant limitation of the standard HMM is the manner in which it models state durations. For a given state $i$ with self-transition coefficient $a_{ii}$, the probability mass function for the state duration $d$ is a geometric distribution, given by $p_i(d) = (a_{ii})^{d-1}(1 - a_{ii})$. For many biomedical signals, this state duration distribution is inappropriate [1]. In particular, the distribution naturally favours state sequences of a very short duration. Conversely, real-world state sequences do not occur for arbitrarily short durations, and there is typically a minimum duration for each state resulting from the underlying physiological mechanisms. In practice this “mismatch” between the statistical properties of the model and those of the time series limits the effectiveness of the model for many applications.

In order to improve the suitability of the model for biomedical signal analysis, it is necessary to incorporate a set of duration constraints into the HMM architecture. More precisely, each duration constraint takes the form of a number specifying the minimum duration for a particular state in the model. Such values can be estimated in practice using either prior knowledge, or a labelled data set of signals.

Once the duration constraints have been chosen, they are incorporated into the model in the following manner: for each state $k$ with a minimum duration of $d_{\min}(k)$, we augment the model with $d_{\min}(k) - 1$ additional states directly preceding the original state $k$. Each additional state has a self-transition probability of zero, and a probability of one of transitioning to the state to its right. Thus taken together these states form a simple left-right Markov chain, where each state in the chain is only occupied for at most one time sample. The most important feature of this chain is that the parameters of the observation density for each state are identical to the corresponding parameters of the original state $k$ (this is commonly referred to as “tying”). The overall procedure is illustrated in figure 1.

4 Fusion

This framework can be extended to multiple time series (with potentially different dynamic ranges and sampling rates) by using a separate model for each time series and then “coupling” the state spaces of the various models (so called coupled HMMs). Recently it has been demonstrated that this approach can be extended to the more general problem of multi-modal data fusion [2]. Much of this work has focused on the problem of audio-visual speech recognition, however the same techniques offer promise for problems in joint medical image and signal analysis.

References

Empirical Validation of Cerebrospinal Fluid Pulsatility Model

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1 Introduction

The brain is surrounded by a rigid skull and an incompressible fluid, the CSF (cerebrospinal fluid). The pulsations pass directly into the CSF and the Monro-Kellie doctrine predicts that the CSF pulse will be dissipated by shifting CSF out of the cranial cavity and/or compressing venous structures to eject venous blood.

In this paper, we derive a model for CSF pulsatility in the head due to the passage of blood through the brain in one cardiac cycle in the form of an equivalent electrical circuit. Also we try to validate the model using data from MR (magnetic resonance) images of normal volunteers.

2 Analysis of Model

We assume that fixed values for compliances and impedances within system (Figure 1(a)) then we can obtain an equivalent model as an electrical circuit (Figure 1(b)). Flow paths with impedance are modelled as resistors and elastic surfaces between any two pressure reservoirs (arteries, brain, vein, CSF, ventricles and spine) are modelled as capacitors. As we can see this system has 10 free parameters and 6 possible measurements. We can represent all time varying signals in the Fourier domain and analyse the equivalent circuit at a fixed set of frequencies $\omega$. We can then analyse the circuit using conventional means by specifying current flows and writing down the equations describing current and voltage (Figure 1 (c)).

By solving the above equations, we obtain a complex constraint equation for the free parameters of the form: $\frac{1}{\omega} \frac{d}{\omega} - a_1 \frac{d}{\omega} + b_1 = 0$ ... (2) where $\alpha, \beta, \gamma$ are found appropriately. Applying the variational method to Eq. (2), we can say that the complex residual on the constraint for each Fourier amplitude $\omega$ in the measured current is: $\frac{1}{\omega} \frac{d}{\omega} F_n - \frac{1}{\omega} R_n = 0$

3 Results

We have measured CSF flow at AQ (aqueduct, $I_3$), FM (foramen of magnum, $I_4$) and blood flow at CAB (carotid artery, $I_1$), and then fed them into our model to obtain parameters ($R_i$ & $C_i$), to estimated errors and

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obtain the rest of Is. Figure 2 shows comparison of the flow data measures and the flow data obtained from the model with estimated error corrected. Figure 3(a) shows the rest of flow data obtained from the model for one cardiac cycle (16 MR images are obtained). Figure 3(b) shows a typical graph obtained from optimal parameter estimation. Because we do not know scales or typical values for some of the parameters, we initialised the optimisation process with random set of values. After having obtained all the parameter values for 14 volunteers, we run the process again with median values of parameters’ minimum as initial starting point. Parameters C1 & C2 does not appear to have any effect on the model, however we expect patients with CSF circulation disorder might have different behaviour of parameters, e.g. Hydrocephalus.

4 Discussion & Conclusion

The model identified is the simplest we can manage at this stage. We note that it is very difficult to identify specific parts of the anatomy as separable parameters. Further refinement might include splitting the arteries to model the effects on the ventricular and extra-cortical compliances separately [2]. This model does not include time variation in impedance in arteries and veins. Eq. (1) tells us that once we have measured any two of arterial flow, venous flow and flow through the FM, measurements of the third one does not help to determine the model parameters. The only things estimated using the above approach are arterial compliance, brain compliance, ventricular compliance, venous compliance, arterial impedance, brain impedance and the impedance of the cerebral aqueduct. We cannot estimate arterial impedance, spine compliance, static pressure or scale the 7 estimated parameters without pressure measurements. Also the equivalence between compliance and capacitance is not straight forward. However, the primary concern must be the accuracy of the measured flow data. It is crucially important that we determine the ability to estimate the statistically significant amplitudes at three different frequencies from the data available. Given the compliances and impedances of the system and the arterial and AQ flow, other flows and pressures can be computed starting from Eq. (2) and working backward. The model could thus be used in a forward manner in order to determine the effects of parameter changes on flow and pressure curves.

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References

Wavelet-based Analysis and Classification of Liver CT

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Abstract. This paper presents a study on classification of Liver CT images, using wavelet transform analysis in conjunction with statistical pattern recognition techniques. We seek to establish which statistical measures clearly distinguish between the normal/abnormal classes, when applied to a large dataset.

1. Introduction.

Wavelet theory is a mathematical tool for hierarchically decomposing functions. Wavelet transform analysis has been applied to medical images mainly for compression, and mammographic image analysis [1]. This paper attempts an investigation on the usage of statistical features collected from the spatial and wavelet transform domains, using several different classifiers, for applications on Liver CT image classification and retrieval.

2. Results and Discussion.

In this study we used 720, 32x32x8 bit, image extracts from the 13 Liver CT scans (360 normal and 360 cancer), for the training stage of the classification procedure. The images were analyzed in Spatial domain, and using the three levels of decomposition of the overcomplete wavelet transform [2][3][4] architecture. The Daubechies 4-TAP wavelet filter was used, in all the wavelet architectures.

The usage of statistical features for the analysis and classification of textured images has been extensively demonstrated in the literature. Overall twenty-two statistical image features were collected from each image, given by category as: First Order Statistics [5], i.e. Mean, Variance, Skewness, and Kurtosis. Second Order Statistics [6], i.e. Angular Second Moment, Correlation, Entropy, Sum of Squares: Variance, Inverse Difference Moment, Sum Average, Sum Variance, Sum Entropy, Entropy, Difference Variance and Difference Entropy. Grey Level Run Lengths [7], i.e. Short Runs Emphasis, Long Runs Emphasis, Gray Level Non-Uniformity, Run Lengths Non-Uniformity, and Run Percentage.

Three statistical classifiers were constructed and employed in this study. The classifiers used are: 1) the Minimum Distance Classifier (MDC) [8], which employs as classification criterion the minimum Euclidean distance between the unknown entry and the mean values of each of the other classes, 2) the Quadratic Classifier (QC) [9][10], which employs the same decision rule as the previous classifier, but using a quadratic equation within the least squares method, and 3) the Bayes Classifier (BC)[11][12], which minimizes the expected cost of misclassified data.

The performance of the classifiers was evaluated by using the Leave-One-Out method. This involves the re-classification of all the signals (one at the time) to their a priori known categories (or classes). In addition, for each set of features all possible combinations were tested up to four-dimensional decision space. Those features, which achieve the best classification rate, were used in the pattern recognition process. This phase is called feature selection, and aims to reduce the features set to a subset, which consists only of meaningful information (i.e. features which characterize best) about the images we want to classify.

The classification accuracy results presented in this paper are those, which fulfil all of the three requirements: a) the classification accuracy of the normal class (specificity) is more than 70%, b) the classification accuracy of the abnormal class (sensitivity) is more than 70%, c) the overall accuracy is more than 70%.

3. Results and Discussion.

In the Spatial domain the best overall classification accuracy result achieved was 99.03% (specificity 99.44%, sensitivity 98.61%), using the feature combination Skewness-Sum Average-Sum Variance-Difference Entropy from the 1st and 2nd Order statistics. In the first level of wavelet transform domain, the best overall classification accuracy was 90.56% (specificity 85.28%, sensitivity 95.83%), using the feature combination of Mean-Sum of Squares: Variance-Sum Average-Difference Entropy. In the second level of the wavelet transform domain, the overall best classification accuracy was 90.14% (specificity 83.06%, sensitivity 97.22%).
using features from the 1\textsuperscript{st} and 2\textsuperscript{nd} Order statistics (Mean-Sum of Squares: Variance-Sum Average-Difference Variance). Finally from the third level of the wavelet transform domain, the best overall classification accuracy was 90.14\% (specificity 85.28\%, sensitivity 95.00\%), using the 1\textsuperscript{st} and 2\textsuperscript{nd} Order statistics feature combination of Mean-Correlation-Sum of Squares: Variance-Sum Average.

<table>
<thead>
<tr>
<th></th>
<th>Specificity (%)</th>
<th>Sensitivity (%)</th>
<th>Overall (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spatial</td>
<td>99.44</td>
<td>98.61</td>
<td>99.03</td>
</tr>
<tr>
<td>1\textsuperscript{st} Level</td>
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<tr>
<td>3\textsuperscript{rd} Level</td>
<td>85.28</td>
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In terms of the performance of the Classifiers employed in this study, we concluded that: the Quadratic Classifier outperformed all of the other classifiers used, in respect to its high classification accuracy, and the number of feature combinations it used. The classification accuracy results from all the classifiers were improved by increasing the dimensionality of the decision space.

The usage of statistical features for the analysis and classification of textured images has been extensively demonstrated in the literature. Our results suggest that features from the 2\textsuperscript{nd} Order Statistics achieved the best classification accuracy results, since such measurements focus on the overall nature of the texture such as homogeneity, contrast, the presence of organised structure, complexity, and the grey tone transitions within the image. Although numerous publications have presented and evaluated different Computer Aided Diagnosis schemes, one has to keep in mind that the detection accuracy of any CAD system depends upon the set of images used. This includes the number of images used throughout the training stage of the classification scheme, as well as properties of the images, such as resolution and depth, type of abnormalities included etc.

References

Inverse Elasticity Reconstruction Based on Similarity measures of Ultrasound Image

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The inversion elasticity imaging techniques have been widely investigated. So far, the commonly used inverse approaches compute the elasticity parameters by minimization of the sum of squared differences between measured and calculated displacements over the entire tissue [1]. However, the noises of displacement estimate in solving the ill-posed inverse problem has become an impediment to restrict its diagnostic effectiveness, especially for ultrasound images with limited spatial and contrast resolution. Recently, a novel approach to elastography using mutual information and finite elements is introduced that considers the inverse reconstruction problem as a non-rigid image registration problem and can combine the inverse reconstruction method with the recent advanced mono and multi-modal non-rigid image registration techniques [2].

In this preliminary study, we consider the inverse elasticity problem as a global optimal problem based on the similarity measures of ultrasound images. First the ultrasound images before and after deformation are acquired. A forward model that simulates the deformation process is built. To simplify the problem, small deformation condition is assumed. The calculated deformed image (Deformation transform of the pre-compressed image) is then obtained from the forward model with known boundary conditions and pre-set elasticity distribution, which is the optimization variable of the inverse problem. The inverse problem is defined as minimization of the similarities (cross-correlation coefficients in our study) of the observed and calculated deformed image at every block centered at the observing pixels. A split-and-merge approach [3] is employed based on the local mismatch of the calculated and deformed source image and the inverse problem is solved iteratively.

By converting the displacement-based inverse problem into the similarity-based problem, the optimal elasticity distribution will be the one that find the calculated deformed image with best registration result with the observed deformed image. An obvious advantage of the proposed method is that no displacement calculation is needed. The displacement calculation is actually embodied in the optimal process itself. Thus there will be no displacement error introduced in the inverse solution. The main error sources are the validity of the deformation model and accuracy of the observed image itself. Preliminary simulation experiments are then carried out using ultrasound images simulated by Field II package.

REFERENCE


Multi-local statistics of gradient directions in natural images

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Abstract. In image analysis, areas of particular interest may contain missing or ambiguous data which makes correct interpretation difficult. It is our hypothesis that a multi-local approach is required; this entails using cues at multiple locations and analyzing those cues as a group, rather than as separate entities.

With this approach in mind, a study of multi-local natural image statistics has been undertaken. Such statistics will help determine what, if any, regularities of images are uniquely accessible by a multi-local approach. Furthermore, such prior statistics can be exploited by image analysis algorithms. In particular, the statistics of gradient directions have been studied. These are important because:

- they are geometric measure, which means that, unlike luminance or gradient magnitudes, they are invariant to monotonic transformations of the image intensities.
- they are suitable for studying multi-local statistical dependence.
- their distributions of values are roughly uniform over a finite range. This is in contrast to image statistics such as filter responses which are highly kurtosed. This makes for easier statistical analysis.

As is already known, if one simply collects all the gradient directions from a set of natural images, one finds an excess of horizontal and vertical contours. This is an example of a finding from 1-point statistics. We go beyond this to consider what effect knowledge of the gradient direction at one point has on one’s expectation of the gradient directions at other points (2-point statistics). We have found that one gains more information at points which are (i) nearby, and (ii) in a direction perpendicular to the known gradient direction. Furthermore, this pattern is not found in our analysis of Gaussian noise images, where the decrease in information falls off more quickly with point separation and more isotropically than for natural images. For phase-randomized natural images, the pattern is similar to that for natural images but with a rate of information fall-off between that of gaussian and natural images.

However, the properties highlighted for natural images are for an average of many such images. Individual natural images can exhibit statistics more characteristic of noise, if for example the images contain scenes of dense foliage, or more correlated statistics, if for example the image contains a substantial region of cloudless sky.

We have started a study 3-point statistics. It is worth noting here that to establish the significance of n-point interactions, removal of components due to (n-1)-point statistics must be done. Preliminary results show that the 3-point case is significantly different to 2-point interactions, indicating 3- or more point interactions should be modelled to fully capture the regularities of natural images.

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A compact physiologically based model of cerebral autoregulation

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1 Introduction

Current one-dimensional models of the cerebral circulation and its autoregulation are either based on very crude approximations to the underlying physiology or are extremely complex. However, if these models are to be expanded to examine three-dimensional, i.e. spatially-resolved, behaviour, which is crucial if different pathologies, such as stroke, are to be addressed, models must be found that are based on the underlying physiological processes but compact enough to be expanded spatially without excessive computational cost. This will be key to the future integration of models that can be used by both the signal and image analysis communities: an important feature of the IRC.

The work of the Grand Challenge “Multi-Scale Modelling” has resulted in the production of a comprehensive physiologically based model of cerebral blood flow control, Banaji et al., 2004. This model is an extremely detailed model of the biochemistry behind the response of vascular smooth muscle to changes in arterial pressure. Mathematically it is represented as a system of differential equations involving around 80 chemical species. Models of this form serve a vital purpose in enabling extensive simulation and hypothesis testing to be performed, in the manner of a virtual patient. However the large number of parameters mean that attempts to optimise the model to fit specific patient data are virtually impossible and it becomes difficult to make use of them for diagnostic purposes. In this paper, a significantly more compact model is presented that is still based on the key physiological mechanisms, allowing for a future expansion to a spatially-resolved model.

2 Model description

Biologically, the local autoregulatory response of cerebral blood vessels to changes in pressure is thought to originate from the action of two major signalling pathways; endothelial production of nitric oxide (NO) in response to increased shear stress in the vessel wall, causing dilation of vascular smooth muscle, and pressure induced membrane depolarisation, causing increased intracellular calcium, $[\text{Ca}^{2+}]$, and contraction of vascular smooth muscle. The model presented here is a first attempt to isolate these system dynamics in a compact form.

Figure 1 is a schematic description of the model. The haemodynamic network and wall mechanics models are taken from Ursino and Lodi, 1998, and the vascular smooth muscle tension modulated through the phosphorylation state of the light chain of myosin. The vascular smooth muscle cell behaviour is only dependent upon arterial pressure and wall shear stress, which are physiologically meaningful, rather than flow, as assumed by Ursino and Lodi, 1998. The resulting model is still comparable in size to the Ursino and Lodi model, having only 13 state variables but with the unknown cerebral autoregulation dynamics replaced by a physiologically accurate model.

Figure 2(a) shows the dynamic cerebral blood flow response of the model to a simulated 30 mmHg drop in blood pressure for our model and the models presented by Banaji et al., 2004, and Ursino and Lodi, 1998. Figure 2(b) compares the static autoregulation curves of the three models. The static autoregulation curves are all in close agreement, and the Oxford and Banaji et al. models are in good agreement for the dynamic behaviour, with the Ursino and Lodi model showing slightly different behaviour. Experimental data presented elsewhere, Payne and Tarassenko, 2004, indicates that the cerebral autoregulation system is essentially second order, which agrees with the Oxford and Banaji et al. models.

3 Conclusions

Modelling work within the IRC has previously yielded a comprehensive physiologically based model of the mechanisms responsible for cerebral autoregulation. This study now builds on this work to provide a greatly reduced system based on consideration of the underlying biological processes. Future work will involve improving the vessel wall mechanics model and integrating it more closely with the autoregulation model. This
will then enable further work to be performed to develop the first anatomically based spatially-resolved models of the cerebral vasculature, which will allow modelling of conditions such as stroke, since a simple biochemically-based feedback mechanism is required to incorporate autoregulation into these detailed three-dimensional models. This will provide a valuable link between current signal processing studies using near infrared spectroscopy and image processing data obtained using MRI.

Figure 1. A schematic diagram of the model

Figure 2. (a) Dynamic CBF responses; (b) Static autoregulation curve

References

Reconstruction of Undersampled Cardiac MRI

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1 Introduction

The use of MRI in cardiac imaging has great clinical potential but is still in limited use due mainly to the amount of time and expertise needed to perform clinically useful scans. Standard fully sampled cine 3D (4D) scans involving 10 or more slices at 20 or more time points (phases) currently requires segmented k-space data acquired over several breathholds at a position repeatable to within low tolerance. These exams are time-consuming and exhausting to patients with cardiovascular disease. Clinically, full 4D anatomy is needed to diagnose only certain pathologies such as congenital defects. A much more common use of CMRI is assessment of cardiac function through metrics such as stroke fraction to indicate compliance, and wall motion abnormalities indicating areas of infarcted heart muscle. Both of these normally involve the segmentation of the left ventricular myocardial boundary.

This abstract presents work-in-progress for a PhD project the main aim of which is to improve the quality of images and clinical data obtained from undersampled k-space data. This involves the investigation and development of current methods that normally reconstruct images, and also the development of novel methods that attempt to concurrently reconstruct and segment ventricular myocardial boundaries directly from raw data.

2 Method

2.1 Fourier Snakes

The project so far has been investigating two separate yet related approaches to the problem. The first method is in collaboration with I Kastanis and S Arridge of UCL. The aim of the work is to fit a shape model of an object of interest in the scan to very undersampled data. The primary candidate for the object of interest is the roughly circular myocardial boundary of the left ventricle, having high intensity contrast in ‘bright blood’ BFFE scans. The shape model used is a ‘Fourier Snake’ in which a contour is modelled with polar/circular harmonics. An algorithm was developed in which the contour parameters are iteratively updated to minimise the difference between the data being reconstructed and the corresponding data produced by the model.

To produce data corresponding to the acquired data, firstly an image is produced by choosing the contrast properties for the boundary. This produces very simple approximations to the actual images seen. This image is then transformed into the space of the acquired data by Fourier transform and appropriate sampling, in our case radial sampling. A linearised inverse of the forward model is computed and the difference between the measured and predicted data is then used to iteratively update the model parameters until the differences converge.

In close connection to this work, spectrographic techniques such as Short-Time Fourier Transforms are being investigated in an attempt to provide automated selection of phases with the least motion in order to find the most stable and highly sampled parts of a dataset from which images may be produced. This is similar to self-gating and ties in to the next stage of the development of the Snake algorithm, namely dynamic data reconstruction.

2.2 Motion Correction and Acquisition Strategies in KT-BLAST

The other major area of investigation is the acquisition and reconstruction technique KT-BLAST. KT-BLAST uses undersampled acquisitions that are skewed in time and k-space. The current work aims to use these sampling schemes to produce novel reconstruction methodologies. A skewed acquisition produces fully sampled yet motion blurred ‘DC’ images, i.e. images at the zero-frequency position. The aim of the work is to perform motion correction on multiple breathhold scans where the breathhold positions are similar enough to produce little cardiac deformation but have moved enough to be discarded by standard segmented k-space acquisitions. Given an undersampling factor $a$, KT-BLAST acquisitions are performed with incremental trigger delays to produce a fully sampled dataset. The DC images or volumes are registered together to provide motion correction parameters that are applied to each dataset. Reconstruction is then a straightforward IFFT.

3 Results and Further Work

3.1 Fourier Snakes
The algorithm was first tested on simulated images consisting of a bright blob in a dark background. A contour of excellent accuracy was produced with as few as two radial projections for an image of $64 \times 64$ samples, which would normally require over 64 radial projections ($64^2 \pi/2$) to be fully sampled. Next, a phantom consisting of an acrylic tank and tubes filled with Gadolinium chelate solutions was designed and built. This provided the flexibility in order to test the concept with real MRI data on images of varying simplicity, starting with a bright circle in a dark background and adding image features in a controlled manner. This demonstrated the limitations of the simple model. [1] Finally, real CMRI data were used. [2]

In ongoing work, the model is being improved with further parameterisations of image properties such as contrast both inside and outside the contour. The next stage is a paradigm shift in which the model will be altered to reconstruct dynamic scans, using prior information from the entire dataset, such as DC images (fully sampled but motion-blurred) and contours manually segmented from either DC images or sections of the data with little movement. A further possible extension is to 3D using spherical harmonics to model the object.

2.2 Motion Correction and Acquisition Strategies in KT-BLAST

Motion correction was applied successfully on 2D dynamic phantom simulations where the simulated inter-breathhold translations were known. It was then applied to fully sampled cardiac data by applying the appropriate under-sampling. This provided a test with real data and a gold standard of fully-sampled images for comparison.

Further work will include extension to 3D and investigation of further degrees of freedom in the registration. Another possible development is an alternative to the ‘multichunk’ acquisition scheme for dynamic volumes, in which several KT-BLAST volumes with different positions are aligned through the registration of DC images to provide fully sampled datasets.

Acknowledgements

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References

2. “Reconstruction of the Heart Boundary from Undersampled Cardiac MRI using Fourier Shape Descriptors and Local Basis Functions.” S R Arridge, I Kastanis, A M S Silver et al., ISBI 2004
Classification Improvement by Segmentation Refinement: Application to Contrast-Enhanced MR-Mammography

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1 Introduction

The development of computer aided diagnostic systems for MR mammography relies on the collection of ground truth information of the breast lesion’s image position and extent. Currently, a radiologist’s segmentation is the accepted gold standard for this definition. Manual segmentation is, however, very labour-intensive and prone to inaccuracies. We developed a segmentation refinement method to extract the most probable lesion for a user-provided crude manual segmentation. In this study we investigated whether this automatic refinement improves the discrimination of benign and malignant breast lesions.

2 Materials and Method

2.1 Data and Data-Preprocessing

We selected 10 benign and 16 malignant histologically proven lesions from the symptomatic database of the MARIBS study \cite{1}. The lesions were manually segmented by an experienced radiologist by defining contours on the coronal slices of a selected difference image.

For the segmentation refinement, the subtracted images (post- minus pre-contrast) were normalized to zero mean and unit variance for a rectangular 3D region of interest (ROI) extending the manual segmentation by 7mm. The probability distribution of the lesion or background was model-free estimated using Gaussian kernels. The dimensionality of the preprocessed data was reduced by principle component analysis to avoid sparse distributions.

2.2 Segmentation

The segmentation refinement aimed to extract the most probable connected lesion object of a 3D ROI for a given manual segmentation. Assuming equally likely image features $x$ and taking the prior class probability $P(C_k)$ for class $C_k$ into account, the most probable segmentation refinement is given by maximizing the a-posteriori probabilities, i.e. $\text{argmax}_x P(C_k|x) = P(x|C_k)P(C_k)$ where $P(x|C_k)$ was estimated from the manual segmentation. For a two class problem the discrimination function $y(x)$ can be written as

$$ y(x) = \frac{P(x|C_1)}{P(x|C_2)} \quad \text{with} \quad x \in \begin{cases} C_1 & \text{if } y(x) > \theta \\ C_2 & \text{otherwise} \end{cases} \quad \text{where} \quad \theta = \frac{P(C_2)}{P(C_1)}. \quad (1) $$

Eq. (1) emphasizes that the ratio of the prior probabilities act as a threshold ($\theta$) on the likelihood ratio. Instead of estimating $\theta$ from the number of lesion and background voxels in the manual segmentation, we propose to use $\theta$ for implicitly incorporating prior knowledge about the segmentation process. Assuming that one connected lesion was manually segmented per ROI we firstly extracted for a given $\theta$ the biggest connected object. Then we applied morphological closing and filling to model non-enhancing regions included in the manual segmentation.

The tested threshold variations were $\text{MAP}: \theta = V(C_2)/V(C_1)$ with volume $V(C_k)$ estimated from input segmentation; $\text{Tp}$: connected filled lesion that changed volume by less than $p\%$ while maximizing the average posterior probability, $p \in \{0, 10, 20\}$; $\text{ML}$: maximum likelihood decision $\theta = 0$. Crude segmentations (E) were simulated by approximating the manual segmentation by an ellipse on each 2D slice. The sensitivity to the size of the initial segmentation was assessed by changing the size by $s\%$, $s \in \{-33, -20, 0, 25, 50\}$. The overlap measure $O = V(A \cap B) / V(A \cup B)$ was employed to compare the segmented lesions $A$ and $B$ ($\cap$: intersection, $\cup$: union).

2.3 Feature Extraction

The size of our dataset limits the number of feature candidates that can reasonably be assessed. We therefore restricted ourselves to the 10 least correlated features of 27 previously reported 3D features \cite{2–4}. These were

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selected by hierarchical clustering the feature vectors derived from the radiologist’s segmentation according to their correlation. The 10 selected features consisted of 4 shape features (Irregularity, Eccentricity, Rectangularity, Entropy of Radial Length Distribution), 2 gross pattern of enhancement features (Maximum Intensity Time Ratio (MITR) Peripheral-Central Ratio, MITR Adjacent-Peripheral Ratio), 1 enhancement characteristic feature (Slope Factor) and 3 texture features (Correlation, Angular Second Moment, Difference Average).

2.4 Classification

To avoid overfitting, we combined at most two features using stepwise linear discriminate analysis. The classification performance was summarized by the area under the receiver operating characteristics (ROC) curve ($A_{ROC}$) for leave-one-out tests on a per-lesion basis. Statistical significance of ROC curves was tested using ROCKIT [5].

3 Results

![Figure 1](image-url) Example slices for three patients showing pre-contrast and difference images with overlaid contours of (top) initial segmentation (E-20), (middle) refinements of (top) by T₀, (bottom) radiologist’s segmentation.

On average, the largest overlaps between the refined crude initial segmentations (Eₙ) and the radiologist’s segmentation were achieved with T₀ (T₀: O within [56,66]% , T₂₀: [54,66]%, MAP: [37,59]%, ML: [38,52]%).

The best feature extracted from the radiologist’s segmentation was Correlation ($A_{ROC}$: 0.57). After segmentation refinement, it was generally MITR Peripheral-Central Ratio (average $A_{ROC}$: 0.65 (MAP), 0.70 (T₀), 0.75 (ML)). Stepwise linear discriminate analysis did not improve $A_{ROC}$ for features extracted from the radiologist’s segmentation. For the refined segmentations it provided $A_{ROC}$ values between 0.57 and 0.84. Best results were achieved with the ML refinement strategy ($A_{ROC}$: mean 0.77, range [0.70,0.84], statistically significantly better than manual segmentation for E-33 and E0 (ROCKIT, 5% level)). T₀ accomplished the second best results with a mean $A_{ROC}$ of 0.71 (range [0.68,0.71]) followed by MAP (mean 0.64, range [0.58,0.68]).

4 Conclusion

We have shown that the refinement of manual segmentations based on thresholding the likelihood ratio map can significantly improve the classification of contrast-enhanced MR breast lesions. Simplification of the lesion delineation and change of lesion size before refinement did not lead to inferior classification results. Similar classification approaches have been reported previously [2–4], with accuracies of 72%, 79% (no leave-one-out test) and 87%, respectively, when combining 2 features. Our results were on the lower end when based on features from manual segmentations (69%) but improved to 77% after maximum-likelihood segmentation refinement. This showed the importance of assessing the segmentation on the ultimate goal, in this case the classification performance.

Acknowledgements

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References

The quality of PET data has now reached a stage where it is limited by the effects of patient motion. Motion results in artefacts that can lead to misdiagnosis and often mimic disease. Existing methods of reducing motion artefacts involve either modifying the scanning protocols or modifying the reconstruction algorithm used to produce the images. The aim of this project is to develop methods of incorporating dynamic or gated MR and CT data into the reconstruction of PET images in order to correct for motion, with reference to the heart and lungs.

1 Introduction
Positron Emission Tomography (PET) is undergoing rapid expansion in its use as a functional imaging tool. The quality of PET data has now reached a stage where it is limited by the effects of patient motion, due to long scan times in PET (typically 20-30 minutes for whole body studies). Reconstruction algorithms, that are used to produce the final diagnostic images, operate on the assumption that the object being imaged has remained stationary throughout the data acquisition process, and hence any movement that occurs during the scan will produce artefacts in the final images. These motion artefacts degrade the quality, as well as affect the accuracy of the quantification of PET images. Image degradation is caused by the occurrence of artefacts, a decrease in the sensitivity (the ability to detect small lesions) and a decrease in the accuracy of quantification. Motion causes a decrease in the sensitivity of PET, causing small lesions to blur out.

A number of methods for correcting motion have been investigated. These include (i) modifying the reconstruction algorithm itself [1,2]; (ii) correcting individual lines of response [8]; (iii) acquiring data into a new frame when a significant amount of motion has been detected [9]; (iv) realigning estimated projections with measured projections (limited to translational motion only [6]); and (v) acquiring the data in smaller time frames (gates) so motion within each frame is minimised. The frames are then registered back to a common reference frame [10], or motion-corrupted frames are rejected [7].

2 Methods
Two approaches will be investigated to correct for motion in gated PET data: (i) to use anatomical images from MR/CT and a motion model to correct the functional PET images for motion following the reconstruction of individual gated images, (ii) to incorporate transformations directly into the PET reconstruction algorithm. The position gated PET data will be acquired by tracking or will be derived directly from List Mode PET. The methods will then be verified by first running some simulations using a complete PET simulation (NCAT/SIMSET), and then moving on to clinical patient data.

2.1. Use of Gated CT with image registration and a motion model to correct for Gated PET
Two specific problems are associated with using gated CT to motion-correct gated PET data. (i) The CT and PET images may not be sampled at the same points in the respiratory cycle, and thus the registration transformation from one CT image, maybe used to transform the wrong corresponding PET image. (ii) The number of CT frames that can be acquired in a patient study is limited by the CT radiation dose. There is a trade-off between CT radiation dose and image quality. The question that needs to be investigated is: for a given CT dose what is the optimum number of CT images to take e.g. 10 low quality (for 10 PET gates) or 2 good quality (one at inspiration and one at expiration). To avoid problems associated with data being acquired at different times, and dose vs. image quality, a motion model could be used. We intend to use the lung motion model developed by Jane Blackall, Guys Hospital [5]. The following steps were taken to develop this motion model: (i) A rapid sequence of free-breathing MR images were first acquired, (ii) Motion was parameterised according to the position of the diaphragm in the superior-inferior direction. Images were then selected exhale to inhale, (iii) A high quality breath hold image was then acquired at exhale position and used as a reference image (as is the most reproducible), (iv) Automatic image registration was then used to co-register the reference MR image to each of the images in the free breathing sequence and the resulting transformations were obtained, (v) These transformations were then used to transfer a set of surface landmark positions from the reference image to the corresponding positions over the breathing cycle, (vi) Linear Interpolation was then used between the corresponding points in these data sets to create a model that allowed the user to estimate the organ motion and deformation at any point in the breathing cycle. B-spline interpolations were done between the images.
2.2. The Different Methods for Incorporating the Motion Correction Transformations into the Reconstruction

There are two ways that these identified transformations can be incorporated into the reconstruction algorithms, these are either (i) post-reconstruction – apply inverse transformation to individual gated reconstructed images, and then sum all images to obtain an image of better statistical quality or (ii) prior to reconstruction (e.g. rigid list mode methods such as Crawford 1996 [1]); or incorporated into the reconstruction (e.g. Jacobson and Fessler [2]) – apply transformations at sinogram level and then reconstruct giving one estimate of the object. One of the aims of this study is to evaluate the statistical gains of incorporating the motion correction into the reconstruction both post-reconstruction, and pre-reconstruction. These methods will be implemented using the filtered back projection (FBP) and MLEM reconstruction algorithms. The proposed methods must then be evaluated and proven for simple controlled situations, in which the basic anatomy and whereabouts of any abnormalities (e.g. a lesion etc) is known, to verify image quality and quantification. For this we have a setup complete PET simulation. The advantages of running simulations are that the whereabouts of any introduced lesions are known and complex data corrections (e.g. attenuation, scatter, randoms and normalisation etc) do not have to be included in the reconstruction, making the reconstruction problem a whole lot simpler. When looking at real clinical data, these data corrections will need to be incorporated into the algorithm.

3 Simulations

The PET simulation consists of two parts: NCAT and SIMSET. NCAT or NURBS (Non Uniform Rational B Splines) based CAT (Cardiac Torso Phantom) [3] simulates both respiratory and cardiac motion. NURBS is a bi-directional parametric representation of an object. All points of the object can be altered easily via affine and other transformations to model anatomical variations or patient motions. NCAT is used to simulate both the distribution and the attenuation map in the object. SimSET (Simulation System for Emission Tomography) models the physical processes and PET scanner itself using Monte Carlo techniques [4], and produces sinogram data that can be reconstructed using standard algorithms. Figure 1 shows the type of images obtained from the simulation. We estimated standard FDG activity concentrations for NCAT Phantom and some standard count rates/acquisition times for SimSET - based on the GE discovery ST scanner on which human studies will be performed. Datasets were then created for the chest : (i) Total counts - no motion, (ii) Same total counts but now divided up into 16 frames with motion, (iii) Same total counts and frames with motion but summed.

4 Preliminary results and Future Work

Dividing the total number of counts into 16 frames, gives each frame of lower statistical quality, on summing these frames we obtain a single frame with motion. The single frame with no motion was of better image quality than the single frame including motion, as expected. The next step is to include lesions into the phantom and then incorporate the motion model and register each frame back to the reference frame.

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References