Chapter 1

Introduction

1.1 Motivation

Magnetic resonance imaging (MRI) is an imaging technique that, since its beginnings in the 1970's, has become one of the most important tools in understanding how the human body works. Among its many applications in the biomedical sciences, MR imaging is used in studying the anatomy, pathology and, more recently, function of the brain. The development of this most recent MR imaging application, called Functional Magnetic Resonance Imaging (FMRI), has been driven in large measure by its potential to increase our understanding of how the human brain works, both in the normal and diseased states.

The aim of FMRI data analysis is to identify small, spatially localised changes in image intensity that are induced by the performance of some experimental task. This is normally accomplished by collecting a series of images covering part or all of the brain at intervals of a few seconds and analysing the resulting time-series obtained at each image voxel. The experimentally-associated intensity changes for each voxel are frequently only a few percent of the mean value at that spatial location and are embedded in a noisy signal contaminated by electronic and physiological artefacts. These are examples of significant imperfections in the

Figure 1.1: The 3T Varian/Siemens magnetic resonance imaging system installed at the Oxford Centre for Functional Magnetic Resonance Imaging of the Brain (FMRIB) where the research described in this report was carried out. It is designed specifically for ultra-fast imaging in brain functional magnetic resonance imaging studies and is equipped with both a body gradient coil and a fast head gradient coil insert.

FMRI method. Head motion is one further, and critically important, confound. Very small movements of the head, on a scale of less than a millimetre, can be a major source of error in FMRI analysis. This is particularly the case in situations when the motion is correlated with the task being carried out by the subject.

The imperfections due to artefacts in the FMRI method can not be resolved in a straightforward way. For a large number of artefacts, reduction or elimination is carried out before and during scanning by improving the scanning system, and choosing the appropriate parameters of the scanning process. However, for some of them (head motion, magnetic susceptibility induced magnetic field inhomogeneities, physiological changes in the body etc.) this is not possible. In the case of motion artefacts, the most common approach is to tell subjects not to move during scanning, and to repeat the scanning sequence if they do move appreciably. However, very often the subjects in the scanner are patients (as opposed to volunteers) or small children where movement is inevitable and scanning time limited and not repeatable.

In order for FMRI to become a reliable and widely used clinical tool, it is essential to have techniques and tools to recognise and eliminate, or at least minimise, artefacts that contaminate the signal. There has been a considerable amount of research effort directed at this issue. However, most of the artefact correction techniques that are developed are based on analyses of empirically acquired FMRI data. As a result, the ground truth is not known which makes it difficult to assess the precise accuracy of these methods. (e.g. see [32, 38, 25, 41, 36]).

In order to be able to measure the accuracy of existing techniques a computer simulation of the whole FMRI acquisition, starting from the first-principles of signal generation and detection has been developed in this thesis. This makes it possible to simulate various artefacts, such as head motion and B_0 inhomogeneities, in a controlled way. Understanding and quantifying the artefacts in this way enables a realistic ground truth for the signal to be established. Furthermore, with the simulator it is also possible to investigate the magnitude of the artefacts and their interactions, which can then lead to the development of new algorithms for their reduction, and ideally, removal.

Although the original motivation for this project came from its applications in artefact correction in FMRI, the simulator itself has many other exciting applications. These are in the fields of image acquisition, neuronal current imaging, eddy-current modelling as well as for educational purposes, to mention just a few examples. Some of these applications form a part of the research described in this thesis and they are set out in the Application section (Chapter 6). The precise scope and the objectives of this thesis are set out in the following section.

1.2 Scope and objectives

The aim of the research presented in this thesis is to develop and then consequently use a general computer simulation program for FMRI with the following properties:

- The ability to produce realistic anatomical simulated MR images of any brain (or any other object) for a variety of different scanning conditions;
- The ability to produce realistic time-dependent sequences of simulated MR images including the effects of physiological activations due to some external stimulus;
- The ability to model realistic image related artefacts (mainly due to rigid-body motion of the object and magnetic field inhomogeneities).

It is important to note that this simulator is aimed at modelling the artefacts that are one possible cause of errors in investigating the functional response. Physiological aspects of that functional response are modelled via changes in physical parameters (mainly T_2^*) but the relations between the various physiological variables (such as the blood volume or the blood flow) are not modelled. This is why the main attention of the thesis is on generation of images and image artefacts. Less detail is given to the description of the physiology of the functional response in the brain.

Throughout this thesis this simulation program will be referred to as "the simulator" or "POSSUM" (Physics Oriented Simulated Scanner Utility for MRI). The outline of the work done in this thesis is described in the following section.

1.3 The outline of the thesis

The material in this thesis is organised as follows:

Chapter 2 (The background) describes the physical and physiological principles of FMRI. Its main focus, and the majority of the chapter, is dedicated to the theory of MRI which is the main tool exploited by FMRI. The simulator is ultimately a scanner simulator and therefore relies on the main concepts of MRI. MRI physics is given in necessary details, covering each step of the image formation, which are essential for the research work described in this thesis. Description of the commonly used pulse sequences (specifically Echo Planar Imaging - EPI) is also given together with the generation of image contrast, and various scanning parameters.

In the second part of the chapter, the physiological principles of FMRI are described. The nature and interpretation of the BOLD (blood oxygen level dependent) signal, and the spatial and temporal resolution of the signal are discussed. Finally, common FMRI artefacts (namely: motion and the magnetic field inhomogeneities) are discussed.

Chapter 3 (Simulator model) describes the development of the theoretical model which is used by the simulator. The main engine of the simulator is based on solving the Bloch equations. This chapter starts from the basic form of the Bloch equations and then discusses solving them when magnetic field inhomogeneities are present and the object is moving. In addition, a few other important parts of the simulator are discussed and these are: the eddy current artefact, RF inhomogeneities and thermal noise.

Chapter 4 (Simulator implementation) builds on where the previous chapter stopped. It describes the way the model was implemented in software. An overview of all component parts of the software is given. One of the main issues with the software has been improving its speed and therefore the main focus in this chapter is on the work devoted to reducing computational time. The chapter concludes with a presentation of the parallelisation technique implemented into the software and the relevant results.

Chapter 5 (Simulator validation) is the last step in the development process of the simulator. It is concerned with the quantitative evaluation of the software against both theoretical and experimental results. In addition, qualitative results which demonstrate the possibility of simulation of images impacted by realistic B_0 inhomogeneities, chemical shift, ghosting, eddy currents and within-scan motion are also presented.

Chapter 6 (Simulator applications) consists of five different applications of the simulator. Firstly, application of the simulator in evaluating a motion correction algorithm is presented. The accuracy of the algorithm is discussed under various scanning (simulated) conditions: with a few different types of motion paradigms, with or without the magnetic field inhomogeneities and with and without noise. Different cost functions, interpolation techniques and tolerance levels of the algorithm were compared.

The second application of the simulator was an investigation of the performance of Independent Component Analysis (ICA) as a tool for quantifying motion-related artefacts. An artefact-rich simulated data set when a) the object is not moving; b) the object is moving a minimal amount; c) the object is moving with an average amount of motion; d) the object is moving with a large amount of motion; is analysed using an ICA method. A number of conclusions were drawn from these results.

The third application of the simulator was quantitative evaluation of the impact of stimulus correlated motion (SCM) artefacts in FMRI data. Two groups of simulated data sets, with SCM and without SCM, are presented. Both groups contained simulated data with various levels of realistic “patient” extracted motion. Data was processed using a General Linear Model (GLM) based tool for functional analysis. The influence of the magnetic field inhomogeneities on the analysis is also discussed.

The fourth application of the simulator was concerned with the eddy current effects. Two different pulse sequences were looked at: standard and optimised sequence. The simulations for both of these pulse sequences were carried out, and the respective results compared in order to choose the sequence which minimises the eddy current effects. In addition, the ability to correct for the effect of eddy currents using an affine registration method is analysed.

The fifth, and last application concerns neuronal current imaging. Various pulse sequence parameters were considered in order to investigate the magnitude of the signal change due to the neuronal currents. The results were compared to the results obtained experimentally.

Chapter 7 (Conclusions) presents a summary of the previous chapters and results, and discusses the contributions of this thesis. In addition, further developments of the simulator, together with suggestions for some interesting applications of the simulator in the future are also discussed.