The CMIAG (Collaborative Medical Image Analysis on the Grid) project is a research programme designed to develop mathematical and computational methods for processing and analysing medical images for improved disease diagnosis, coordinated in the University of Nottingham as **Dr Li Bai** explains

The next level in advanced medical image analysis

Funded by the European Commission, the CMIAG project is an interdisciplinary project that recruits 12 Marie Curie Fellows to work on PhD projects in medical image analysis. MRI (Magnetic Resonance Imaging) is now a commonly used although recent (first used in the 70's) method to visualise the structure and function of the human body. It is advantageous to surgery as the technique is non-invasive – relying on non-ionising radiation, with a good resolution that defines soft tissues and can discriminate in any imaging plane.

Research into advancing MRI techniques for increasing accuracy in diagnosis of diseases is what drives the CMIAG project. Specific research themes can be further broken down into five areas:

- Diffusion-weighted MRI (DW-MRI)
- Functional MRI (fMRI)
- Advanced MRI techniques
- Magnetic Resonance Spectroscopy (MRS)
- Computational/mathematical methods for neuroimaging

Diffusion-weighted MRI (DW-MRI)

Diffusion weighted MR images utilise the motions of water molecules within tissue to provide anatomical information. DW-MRI analyses the scatter patterns of the water molecules to make inferences about the microstructure of the brain so to quantify changes of the brain during normal development or in disease. Another application of DW-MRI is brain connectivity mapping based on the fact that water molecules move along brain white matter tracts. From DW-MRI measurements, it is possible to estimate the white matter directions at every point in a 3D brain image. The analysis of these white matter directions can lead to the estimation of anatomical connectivity between different parts of the brain, as well as changes in brain structures induced by pathology.

The CMIAG project has developed new and effective methods based on Bayesian inference and graph theory for resolving crossing white matter directions and for reconstructing brain white matter tracts. The project has also developed new and effective indexes for quantifying anisotropy in DW images. Optimisation of diffusion-weighted MRI acquisition has been also tackled by exploring the effects of cardiac pulsation on the image quality.

> "We have also developed computational methods for pulse design, to improve the quality of MR images produced by the scanner"

Functional MRI (fMRI)

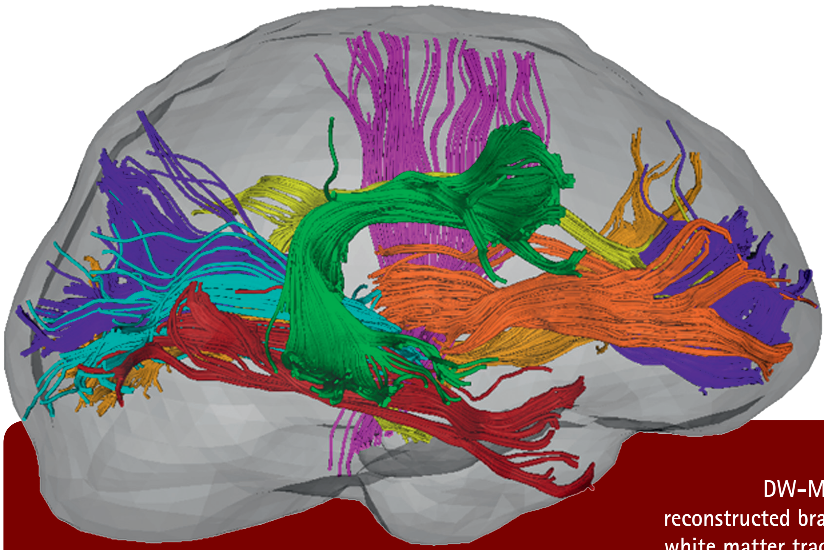
fMRI can be used to characterise the response of the brain to specific tasks and stimuli. It utilises blood flow changes in activated brain nuclei (groups of neuronal cell bodies that constitute the brain grey matter) to introduce contrast to images. These images are then analysed to identify regions with statistically significant blood flow changes in response to the presented stimulus.

The study of resting state networks (RSN) reflecting spontaneous task-unrelated brain activities has attracted an increasing interest. The cardinal feature characterising RSN is low-frequency fluctuation (LFF) of blood oxygenation level dependant (BOLD) signals that are synchronised between spatially distinct, but functionally connected brain areas. This synchronisation is usually referred to as functional connectivity (FC).

Analysis of resting state holds promises for both basic neuroscience, for instance studying the biological underpinnings of consciousness or similarities and differences of large-scale brain function across animal species as well for applications in medicine, where many changes in RSN due to mental and neurological diseases are recently being reported. The analysis calls for development and application of suitable mathematical tools for both modelling and analysis of these data.

Advanced MRI techniques for production of high quality MR images

The Magnetic Resonance Imaging (MRI) signal is produced largely by protons situated on the water molecules, but this signal is influenced by the interaction of those protons with protons situated in other molecules including proteins, macromolecules, eg. lipids, and other components of cells. If the experiment is designed properly, these interactions can be measured. Factors such as the exact radio frequency (RF) field, the sensitivity



DW-MRI reconstructed brain white matter tracts

profile of the receiver coil, the receiver gain and the competing effects of different relaxation times, make all quantitative measures, including the relaxation time measure, a more reliable marker of tissue state than MRI signal intensities alone. The introduction of Ultra High Field Magnetic Resonance scanners has made it possible to increase the spatial resolution of MRI studies and to decrease the acquisition time in comparison to lower field strength scanners. However, high field scanners have their own problems, eg. field inhomogeneity (strength of the magnetic fields is not evenly distributed in the scanner, causing defects in the MR images produced).

The University of Nottingham is the only university in the UK that houses a high field 7T MR scanner, so part of CMIAG research is the design of radio frequency pulses for MR scanners. We have also developed computational methods for pulse design, to improve the quality of MR images produced by the scanner. Other areas of research include design and optimisation of imaging measurements of the brain at high field, more specifically the measurement of the longitudinal relaxation time T1, as well as the magnetisation transfer effects at 7T. This involves modelling the evolution of the MR signal during an imaging experiment, understanding how the image quality is affected by the encoding and the reconstruction process, and designing robust methods to measure the quantities of interest from the images. Measurement processes have been tested numerically via Monte-Carlo simulation, as well as physically on purposed-built phantoms, before being applied to human subjects. The obtained designed protocols yield reliable and inhomogeneity-free images, usable for neurological studies as well as for more specific clinical studies, such as the evolution of the white matter integrity in patients suffering from multiple sclerosis, both looking at quantitative parameters such as the T1 and the MT Ratio (MTR) at a fine resolution.

Magnetic Resonance Spectroscopy (MRS)

Instead of structural information, MRS is concerned with the analysis of chemical compositions of the brain and the detection of brain diseases eg. cancer and Alzheimer's, using the analysis.

Computational/mathematical methods for neuroimaging

Work in this area involves registering and segmenting brain structures (eg. the Hippocampus) and registering MR images for brain imaging. To make use of cellular level information, registration of histological images of the mouse brain has also been carried out to reconstruct 3D volumes.

The CMIAG project has achieved some excellent results in terms of research publications in high impact journals (Neuroimage, Magnetic Resonance in Medicine (MRM), Journal of Magnetic Resonance Imaging (JMRI), and the Brain etc.) and high impact conferences (MICCAI, SPIE, ISBI, MIUA, ISMRM, HBM etc.). ★

At a glance

Full Project Title

Collaborative Medical Image Analysis on the Grid (CMIAG)

Project Partners

The Fellows have been supervised by academic staff from different Schools within the University of Nottingham, including: the School of Computer Science, the School of Mathematical Sciences, Sir Peter Mansfield Magnetic Resonance Centre – and Medical Science, and the School of Medical and Surgical Science based in the Queens Medical Centre

Project Funding

European Commission Framework Programme 6
Human Resources and Mobility programme

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Dr Li Bai started her career as a mathematician before she received her PhD in Computer Science from the University of Nottingham, UK. Her research interests include the application of mathematics in Computer Vision, Pattern Recognition, and Medical Imaging.