

Magnetic Resonance Imaging (MRI) is an extremely powerful, non-invasive method that revolutionized medical diagnostics. The principle of MRI is based on differences in a quantity referred to as ^1H spin-lattice relaxation time (or its reciprocal value – a relaxation rate) between normal and pathological tissues. The quantity depends on structural and dynamical properties of the investigated tissues. From the perspective of molecular science one can distinguish two fractions in tissues: the first one is formed by water molecules, while the second one from proteins and other structural molecules. The macromolecular fraction forms fibers, vesicles, vessels, *etc.* with entrapped (confined) water molecules and the arrangement is affected by diseases. The arrangement of the macromolecules also influences the water mobility. Thus, alterations in the arrangement of the macromolecules can be detected directly or via changing the timescales of translational and rotational dynamics of water molecules and creating geometrical obstacles for free movement of water.

Standard Nuclear Magnetic Resonance (NMR) experiments (MRI, spectroscopy, relaxation experiments) are performed at a single, high magnetic field – in other words, at a high resonance frequency, as the resonance frequency is proportional to the applied magnetic field. Not going into details of relaxation processes (this is a complex physical phenomenon), the dominating contribution to the relaxation process at a given frequency is associated with molecular motion occurring on a time scale matching the reciprocal frequency. Consequently, at a high magnetic field one can probe only fast dynamical processes (of the order of nanoseconds or faster). This is a serious limitation of NMR relaxation studies and MRI. Fast Field Cycling (FFC) technology enables changing of the magnetic field in a remarkably broad range, encompassing five orders of magnitude: from about $30\mu\text{T}$ to 3T (this corresponds to ^1H resonance frequency from about 1kHz to 120MHz). This development was greeted with enthusiasm by the scientific community as it opens the possibility of investigating dynamical processes in macromolecular systems. This implies that by varying the magnetic field one can probe dynamical processes occurring on the time scale from milliseconds to nanoseconds. Moreover, frequency dependent relaxation studies possess the exceptional potential to reveal the underlying mechanisms of molecular motion (not only the time scale). In other words one can, for instance, trace diffusion paths of water molecules entrapped in a macromolecular matrix and enquire into whether the movement occurs freely in all possible direction (3D diffusion) or whether it is restricted to two – or even one (2D, 1D) dimension.

Frequency (magnetic field) dependent NMR relaxation studies are referred to as NMR relaxometry. This method has been exploited to investigate dynamical properties molecular and ionic systems of various complexity, from liquids, via proteins and polymers, to solids providing unique information, not available by other methods. As far as tissues are concerned, it has turned out that differences between relaxation rates for tissues are most pronounced at low magnetic fields – in this range the relaxation data for pathological and normal tissues are visible even without any contrast agents. Alterations in molecular arrangements caused by diseases affect more significantly slow dynamics of large objects, while dynamics of water molecules weakly (especially bounded to the macromolecular matrix) is affected to a lesser degree. This has given rise to combining the FFC and MRI technologies. As a result of the IDentIFY H2020 project (<https://cordis.europa.eu/project/id/668119/en>) fully functional prototypes of FFC-MRI scanner (operating at a varying magnetic field) have been built at the Aberdeen University.

The aim of the present project is to assess the potential of NMR relaxometry for medical diagnostics and provide means for identifying pathological changes in tissues on the basis of NMR relaxometry data. We shall also use NMR relaxometry to reveal the influence of pathological changes in tissues on their dynamics and structure on the molecular level for the purpose of getting insight into the mechanisms of the formation of the pathology. For this purpose it is necessary to combine an advanced theoretical framework linking dynamical and structural properties of tissues with their relaxation features, validate the approach against data for model systems and then apply it to a large NMR relaxometry data sets for tissues with the ultimate goal of establishing characteristic relaxation markers of specific diseases. The markers must be verified against other diagnostic techniques (roentgenography, standard MRI, ultrasonography, elastography) and histopathology reports. The markers should indicate the state of the tissue not resorting to a full analysis of NMR relaxometry data and could straightforwardly be used as indicators of pathological changes on the basis of a small number of experimental points (in the most favorable case, the relaxation rates could be measured only at a few magnetic fields). From the perspective of the very successful outcome of NMR relaxometry studies of dynamics in porous, structured and confined systems, it is expected that NMR relaxometry can give valuable insight into the state of tissues affected by osteoporosis, osteoarthritis and sarcopenia and the mechanism of tumor formation and evolution.