The sensitivity of magnetic resonance imaging (MRI) to the diffusion of water in biological tissues offers the possibility of non-invasively discerning structural and physiological information about biological systems beyond what is capable by anatomical imaging methods. But the relationship between the signal effects and the underlying architecture and physiology is complex and elusive. The acquisition, analysis, and interpretation of diffusion tensor MRI (DT-MRI, or DTI) is thus a fascinating, but often frustrating, MRI method that offers unique challenges and promises unique information. In this lecture I will present a broad overview of the many technical components that are required to successfully utilize the DTI method, along with several of the applications that are driving its development, and set the stage for the more technical talks to follow. The history of diffusion measurements will provide an important backdrop to the development of current methods, as it is a history that is still unfolding as hardware advancements make increasingly sensitive measurement methods possible, and subsequently push the analysis to higher levels, and continue to open wider vistas of potential uses of DT-MRI for both clinical and research applications. I will set the stage for the more technical talks that follow by discussing the relationship between the experimental challenges, the information that can be obtained, and how this can be used in various applications.

The transport of water in biological systems is exceedingly complicated to describe because it is influenced by the local tissue architecture and physiology, which is complex in biological tissues such as the human brain. The MRI signal from excited water molecules (“spins”) is altered if these molecules are in motion, and this alteration depends upon the details of their motion. Unlike, for example, bulk flow of blood in vessels, the motion of water in confined, or restricted, spaces in tissues such as within nerve fibers, in intra- and extra-cellular spaces, etc is dominated by random motions driven by the local thermodynamics. The signal from a spin moving through a magnet field gradient depends upon the spins trajectory relative to the direction of that gradient. For randomly motions the signal must therefore be described in probabilistic terms, i.e., in terms of the distribution that characterizes the spins motion. Since the MRI signal from an imaging voxel is an average over the signal from all the spins contained within that voxel, this too is then described in statistical terms. In the talk by Dr Skare we will see how to describe the sensitivity of MRI to diffusion, and how to design pulse sequences to acquire diffusion sensitive data.

DTI acquisitions are intimately tied to the model we posit for the local diffusion characteristics, because it is necessary to collect enough data to fit the model. And the goal of fitting the diffusion data model is to be able to relate the signal characteristics to the structural and physiological tissue parameters that induce them. How rapid the spins diffuse is characterized by a local diffusion coefficient. The diffusion coefficient in an unconfined liquid is related to properties of the liquid, such as its viscosity and the molecular size, and to the thermodynamic properties of the surrounding environment, such as the temperature. But in biological tissue the situation is much more complicated as spins diffuse within complex geometric structures that impede their pathways. Moreover, there are a variety of ways in which
water can be transported in biological system. The local diffusion is not just dependent upon the local tissue geometry, but on the complicated biophysical processes that dictate the movement of water in biological tissues. These will be reviewed by Dr Ackerman. All of these factors conspire to produce measured signal changes that reflect apparent diffusion coefficients that can differ significantly from the diffusion coefficient of the free (unrestricted) liquid.

Within any given voxel the diffusion will interact with local geometry and thus be more or less impeded depending on which directions it diffuses. An important example is a voxel containing neural fibers, along whose principal axis water tends to diffuse. To capture this spatial dependence of the diffusion with its surroundings, the distribution of the spins can be characterized by a 3x3 matrix, called the diffusion tensor, that describes the diffusion along some combination of the 3 different spatial directions \{x,y,z\}. By taking diffusion measurements along different directions, called diffusion tensor imaging or DTI, it is possible to estimate this matrix, which then provides information on the local tissue structure. In the talk by Dr. Douaud, we will learn about the diffusion tensor and how it is used to investigate local tissue structure. DTI provides multiple measurement by which to construct the diffusion tensor in each voxel. But for extended structures, such as neural fibers, that traverse many voxels, one can use the local diffusion tensors to reconstruct the neural fiber pathways. This is the process of fiber tractography, which will be discussed in the talk by Dr. Campbell.

If the diffusion is influenced by the local tissue structure, why does a 3x3 suffice to describe the motion of spins, since one can imagine that this local tissue structure might be exceedingly complicated, for instance containing multiple fibers crossing within a voxel? In fact, it does not always suffice. For more complicated tissue structures, one can construct more complicated mathematical descriptions of the diffusion. This will be described in the talk by Dr Connelly. One cannot ultimately escape the information loss caused by the averaging of the signal over the voxel volume. If the tissue geometry varies on a spatial scale far smaller than the dimensions of a voxel, even more complicated models of the signal cannot recover much information on tissue microstructure. In this case new acquisition method (and associated analytical method) are required that are sensitive to tissue microstructure. These will be discussed by Dr Ozarslan.

Having summarized the interplay of experimental and theoretical issues involved in DTI, I will show some examples of important applications and discuss what I think are the critical issues in the use of DTI, and what I think the future holds for its future development.