In spite of rapidly improving magnetic resonance imaging (MRI) acquisition sequences for neuroimaging applications, there are, of course, inherent limitations with respect to our ability to visualize or analyze MRI data at cyto-, myelo-, chemo-, and genoarchitectonic levels. In this sense, many groups have used histological and MRI data in tandem to answer different complex preclinical and translational research questions. The pairing of these different modalities have been used in order to understand the relationships between these rich sources of mutually complementary biological information at multiple levels of resolution that span the mesoscopic to the microscopic to the molecular.

However, there are several technical challenges involved in using histological and MRI data in this fashion. Unlike MRI, the lack of uniform histological data acquisition paradigm makes it challenging to build a three dimensional spatial homology between modalities. The details of any specific histological data acquisition protocol vary with respect to a myriad of points within the experimental design protocol; these decision points may impact the choice of staining and counter staining methods, the angle of the acquisition plane, sampling density (ie: the spatial distance between slices of serial histological sections), and the resolution at which individual slices are imaged. Further, the data acquisition process may induce nonlinear stretching, local tears, and staining and lighting inhomogeneities that further complicate the development of methodologies that enable the establishment of an accurate spatial correspondence between histological and MRI data. Finally, even before post mortem specimens are processed, they also undergo non-uniform shrinkage due to fixation in addition to several other structural changes (such as collapsing of the lateral ventricles) that need to be accounted for regardless of the species that are being analyzed. A common strategy for overcoming these limitations includes the development of a reconstruction pipelines that utilizes blockface imaging (optical images of the specimen block taken during sectioning), MRI, and linear and nonlinear registration techniques in order to develop three-dimensional reconstructions that permit the development of a spatial homology between serial two-dimensional histological specimens and volumetric MRI data.

In this talk we will cover several reconstruction pipelines that have been used in order account for these challenges in order to create morphologically contiguous three-dimensional representations derived from serial histological data that were then warped to fit volumetric MRI data. The goal of this talk will be to cover several methodologies through the use of specific applications in both preclinical and translational settings. These applications include:

- The use of histological and immunohistochemistry data in preclinical research involving mice and rats in order to build correspondences with MRI data;

- Using histologically-based digital atlases to enhance visualization of structures that are often targeted in functional neurosurgical procedures using standard and emerging MRI acquisition sequences;

- The use of histologically derived measures to infer finer-grain neuroanatomical localization than currently possible with standard acquisition techniques for group-level morphometric and fMRI analyses;

- Validation of emerging high-resolution structural imaging methodologies that are currently being used to define various architectural subdivisions of neuroanatomical structures (such as the human hippocampus).

Participants of this sunrise educational course will learn about state-of-the-art techniques for histological reconstruction and 3D warping methodologies for fitting reconstructions to MRI data. The emphasis of this talk will be on how these types of reconstruction pipelines can be used in translational research applications in both preclinical and clinical settings and used for validation of image contrast features that are used to infer the localization of neuroanatomical substructures.