Revolutionary advances in biological and biomedical imaging over the last twenty years have brought about the development of improved methods for non-invasively imaging dynamic biological processes. Of particular significance have been optical (photonic) techniques that have allowed for the visualization and manipulation of molecular and cellular structures within living tissue with minimal perturbation. The importance of these approaches has led to the development of a new field, Biophotonics, the study of photon interaction with biological materials. A fertile area of Biophotonics research and development is in the area of optical instrumentation where collaborative efforts are needed to develop the next generation of optical instrumentation and computational approaches for visualizing and assaying key biological and biomedical phenomena. The efforts of the multidisciplinary UW-Madison Laboratory for Optical and Computational Instrumentation (LOCI), to develop optical and computational approaches for biological and biomedical studies will be presented. These efforts include signal processing approaches for multidimensional image analysis, image informatics, nonlinear optical and intrinsic fluorescence studies, optical histopathology, and adaptive optics for deep imaging of biological tissue.