Calcium imaging has revolutionized the approaches for functional analyses in the living brain of animal experimental models. Changes in intracellular calcium concentration are strictly linked to the electrical activity in neurons and produce signals that are effectively detected by optical methods. Distinctive features of fluorescence-based calcium imaging are its high temporal resolution in the millisecond range and its high spatial resolution in the micrometer range. Recent progress includes the development of fluorometric calcium sensors, new approaches for targeted labeling with these sensors and the implementation of powerful imaging techniques, especially two-photon microscopy. An important and rapidly evolving field of current research is the use of calcium imaging for the analysis of in vivo mouse models for various brain diseases, such as Alzheimer's disease, stroke and epilepsy.