Membrane proteins are bilayer-embedded nanomachines that fulfill key functions such as energy conversion, solute transport, secretion, and signal transduction. The lack of structural information is related to the instability of membrane proteins in a detergent-solubilized state, making the growth of three-dimensional (3-D) crystals difficult. Two-dimensional (2-D) crystals of purified membrane proteins reconstituted in the presence of lipids provide a close to native environment and allow the structure and function of membrane proteins to be assessed. To this end, electron crystallography is used, and provides 3-D information at the atomic level. Membrane protein surfaces are studied by atomic force microscopy at sub-nanometer resolution and in buffer solution, providing information about their conformational variability at the single molecule level that cannot be assessed by crystallographic methods. In addition, atomic force microscopy allows the molecular arrangements of proteins in native membranes to be assessed. Recent application of these methods to study rhodopsin, different aquaporins and large bacterial outer membrane complexes will be discussed.