Cytochrome c oxidase (CcO) is the terminal enzyme in the electron transfer chain of essentially all organisms that utilize oxygen to generate energy. It reduces oxygen to water and harnesses the energy to pump protons across the membrane where it resides. The latest understanding of the oxygen reduction mechanism will be discussed. Despite extensive studies, the mechanism by which the redox reaction is coupled to proton translocation remains unresolved, owing to the difficulty of visualizing proton movement within the massive protein matrix during the turnover of the enzyme. With a novel H/D exchange resonance Raman spectroscopic method, a proton gate and a proton loading site have been identified, which are regulated by the redox state of heme a. These data support a new molecular mechanism by which unidirectional proton translocation along the H-channel is coupled to the electron transfer from heme a to heme a₃ associated with the redox chemistry.