

## Cytochrome c2 - reaction center transient complex: dissociation studies and evolutionary implications

Type c cytochromes play a central role as the small water-soluble redox proteins in connecting major bioenergetic membrane protein complexes in both cyclic photosynthesis and respiration. In the photosynthesis cycle, cyt c2 in its reduced form, transiently docks to the reaction center (RC), undergoes electron transfer, and exits in its oxidized form for the cytochrome bc1 complex. Translations of the cyt c2 about the RC-cyt c2 docking interface and surrounding membrane reveal a probable exit pathway. Using a full-atom steered molecular dynamics (SMD) simulation of the RC-cyt c2 complex from *Rhodobacter sphaeroides* with an extensive bioinformatics analysis of the structures and sequences of cyt c we analyze this pathway. The structure-based phylogenetic trees allow more reliable cyt c multiple sequence alignments. The patterns of evolutionary variation obtained from the phylogenetic analysis of both docking partners of cyt c2 revealed conservation of key residues involved in the interaction interface. We report the evolutionary changes of cyt c1 that differentiate it from its docking partner, cyt c2. Additionally, using the MM/PBSA method we calculate binding free energies of RC-cyt c2 complex for both redox states of cyt c2. The all atom details of molecular dynamics simulation with explicit water molecules in combination with evolutionary analysis and free energy calculations provide a descriptive picture of this important transient complex.