

# Oral Contributions

## [MS7] Membrane Proteins

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### [MS7-01] Structure and mechanism of respiratory complex I, a giant molecular proton pump Leonid Sazanov

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NADH-ubiquinone oxidoreductase (complex I) is the first and largest enzyme in the respiratory chain of mitochondria and many bacteria. Mutations in complex I lead to most common human genetic disorders. It is an L-shaped assembly, with the hydrophobic arm embedded in the membrane and the hydrophilic arm protruding into the bacterial cytoplasm. We have determined all currently known atomic structures of complex I. Initially, we have solved the crystal structure of the hydrophilic domain of complex I from *Thermus thermophilus*, revealing the arrangement of NADH, flavin and nine Fe-S clusters in an electron transfer chain. Later structure of the hydrophilic domain reduced by NADH revealed significant conformational changes at the interface with the membrane domain. More recently, we have described the low-resolution architecture of the entire complex I from *T. thermophilus* and determined the crystal structure of the membrane domain of complex I from *E. coli*, showing unusual novel fold of antiporter-like subunits.

The mechanism of coupling between the electron transfer and proton translocation in complex I is not established, partially because the structure of the entire complex was not known. We have now solved the atomic structure of the intact complex from *T. thermophilus*. It includes the previously unresolved key subunit ND1/Nqo8/NuoH at the interface between the two main domains and the quinone-binding site. Many major mechanistic implications provided by the new structure will be discussed.