13. Simple fold composition and modular architecture of the nuclear pore complex

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Fold assignments of all the nucleoporins revealed simplicity in the composition and modularity in the architecture of the Nuclear Pore Complex (NPC). The small number of characteristic fold types in the NPC suggest that it has evolved through extensive motif and gene duplication from a simple set of precursors.

The nuclear pore complex (NPC) consists of multiple copies of ~30 different proteins (nups), forming a channel in the nuclear envelope that mediates macromolecular transport between the cytosol and the nucleus. With less than 5% of the nup residues currently available in crystallographic structures, little is known about the detailed structure of the NPC. Here, we use a combined computational and biochemical approach to assign folds for ~95% of the residues in the yeast, vertebrate, and Arabidopsis nups. These fold assignments exposed a simplicity in the composition and modularity in the architecture of the NPC. The simplicity of the composition is reflected in the presence of only 8 fold types, with the 3 most frequent folds accounting for ~85% of the residues. The modularity of the NPC architecture is reflected in its hierarchical and symmetrical organization that partitions the nup folds into 3 groups: the transmembrane group containing transmembrane helices and a cadherin fold, the central scaffold group containing b-propeller and a-solenoid folds, and the peripheral FG group containing predominantly the FG repeat and coiled-coil folds. Moreover, similarities between structures in coated vesicles and those in the NPC support our prior hypothesis for their common evolutionary origin in a progenitor proto-coatomer. The small number of fold types in the NPC and their internal symmetries suggest that the bulk of the NPC structure has evolved through extensive motif and gene duplication from a simple precursor set of only a few proteins.