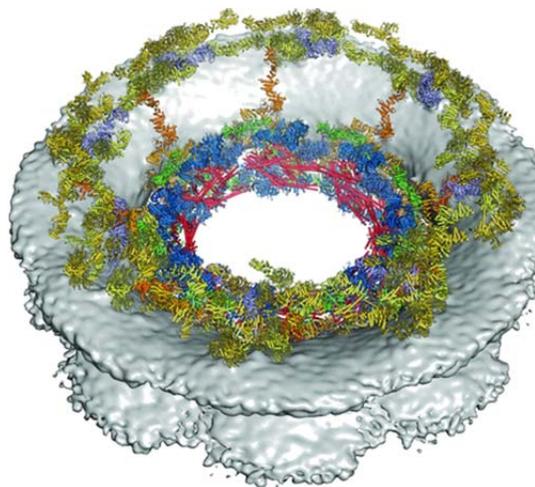


## Structure of the Cell's DNA Gatekeeper

The nuclear pore complex (NPC), a very large macromolecular machine embedded in the nuclear envelope, is the sole gateway for the bi-directional transport of macromolecules between the nucleus and cytoplasm<sup>1,2</sup>. The NPC is also involved in diverse cellular processes, including transcription, mRNA maturation, and genome organization. NPCs are composed of 34 different types of proteins (nucleoporins), which assemble into an eightfold-symmetric, ~1250 Å-diameter pore that fuses the inner and outer nuclear membranes. Despite progress in visualizing the overall shape of the NPC by means of cryo-electron tomography (cryo-ET) and in determining atomic-resolution crystal structures of individual nucleoporins or nucleoporin complexes, the molecular architecture of the assembled NPC has thus far remained elusive, hindering the design of mechanistic studies that could investigate its many roles in cell biology.



Overview of the composite structure of the NPC symmetric core.

Now, a group of researchers led by André Hoelz (Caltech) have biochemically reconstituted the protomers of the symmetric core of the NPC, determined the interactions between them, and fitted them into a tomographic reconstruction of the intact human NPC. They used crystallographic data sets collected from the synchrotron facilities at SSRL, APS and ALS to understand the molecular details of the interactions between nucleoporins. They found that flexible linker sequences, rather than interactions between the large structured nucleoporins, mediate the assembly of the inner ring complex and its attachment to the NPC coat.

By docking these structures into the cryo-electron tomographic reconstruction of the intact human NPC and validating their placement with the nucleoporin interactome, they built a near-atomic composite structure of the NPC symmetric core that contains ~320,000 residues and accounts for ~56 megadaltons of the NPC's structured mass.

Given their central role in cell biology, nucleoporins have been linked to a wide range of human diseases, including viral infection, cancer, and neurodegenerative disease. The structural and mechanistic details of the nuclear pore presented in this paper permits to begin structure-function investigation of the NPC.

### References

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