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Studying large (>400 kDa) macromolecular complexes

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Abstract content
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Proteins are nanoscale molecular machines that use chemical potential energy to shift chemical and mechanical processes away from equilibrium. These include components such as motors, chemical catalysts and switches with an average size of ~2000 atoms (30 kDa). These "modules" self-assemble to form large complexes that perform tasks such as reading and writing data, recycling, chemical manufacturing and data transfer. Over 80% of proteins physically associate with at least one other protein in the living cell, but crystallographic studies usually target only those that function in isolation, creating a bias in our understanding of biological function. Single-particle cryo-electron microscopy (Nature Method of the Year 2015) is used to study large macromolecular structures at close-to-atomic resolution in their native state. We have used this technology to understand the mechanism of large biological catalysts with potential biotechnology applications.

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