Comparison of methods

Method	Advantages	Disadvantages
X-ray crystallography	- Broad range of molecular weights - Soluble proteins, membrane proteins as well as macromolecular complexes (e.g. DNA/RNA and protein complexes) - High resolution (< 3Å)	- The protein of interest must be crystallized and crystals must diffract to the required resolution - The 3D structure represents a static form of the target protein
Cryo-EM	- Allows the structure determination of samples that are unamenable to crystallization (e.g. proteins with flexible regions, membrane proteins and large complexes) - Vitrification of the sample maintains it in a closer-to-native state than crystallization - Very low material consumption (about 0.1 mg) - No need for extensive protein engineering to improve the likelihood of crystallization	- Relatively low resolution (mostly > 3Å) compared to X-ray crystallography - Applicable to target proteins and complexes with high molecular weights
NMR	- 3D structure of target protein can be measured directly in its natural state in solution - It can provide unique information about dynamics and intermolecular interactions	- The NMR spectrum of biomolecules with large molecular weight (> 40 kDa) is complicated and difficult to interpret - It is necessary to have large amounts of labelled protein (and it might be necessary to have differently labelled protein, if the spectra needs to be assigned)