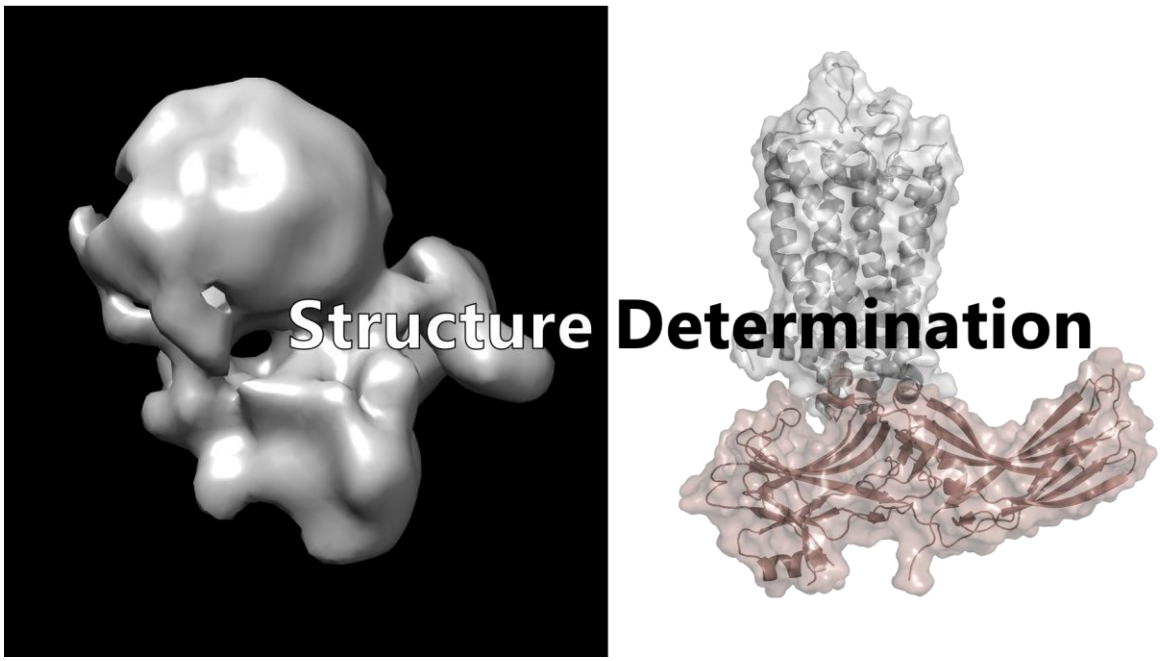
GPCR structural biology



G protein-arrestin complex cryo-EM image (left) and structure (right).

G protein-coupled receptors (GPCR) structures are invaluable for receptor function studies and for rational drug design. Technological advances in X-ray crystallography and cryogenic electron microscopy (cryo-EM) have led to an explosion of structures covering all major GPCR classes and diverse ligands (see latest statistics). However, there are still no structures for the vast majority of the 398 non-olfactory GPCRs and technological limitations remain that restrict which ligand complexes can be attained.

The GPCR structural biology combines the expertise of David Gloriam and Jette S. Kastrup – Professors in Computational Receptor Biology and Structure-based Drug Design, respectively. The projects aim to determine the structures of receptors and ligands, including in-house medicinal chemistry targets and biased ligands.

The Gloriam group maintains online tools to design receptor constructs and chose experimental reagents and conditions for structure determination (see Structure constructs in GPCRdb.org). The GPCRdb database also offers tools to analyse existing structures and, where lacking, structure models of all GPCRs in the inactive, active and intermediate states.

We collect data at the new state-of-the-art synchrotron MAX IV in Lund (X-ray crystallography), two national cryo-EM core facilities and a number of international resources. We are part of a structural biology network, ISBUC at the University of Copenhagen.