

Using data collected at the ESRF, we have determined the structures of two members of the Lrp/AsnC family of transcription regulatory DNA-binding proteins. The Lrp/AsnC family of transcriptional regulatory proteins is found in both archaea and bacteria. Members of the family have been shown to influence cellular metabolism in both a global (Lrp) and specific (AsnC) manner in response to exogenous amino acid effectors. *E.coli* Lrp regulates numerous operons encompassing a variety of processes such as transport, degradation and pili formation in pathogenic bacteria. The first structure determination was of the family archetype *E.coli* AsnC with bound asparagine. The asparagine acts as an effector molecule to modulate positively or negatively the gene regulatory activity of AsnC. Structure determination required a full MAD data collection on *E.coli* AsnC because molecular replacement efforts at the time using our previously determined structure of *P.furiosus* LrpA had been unsuccessful. Data was collected on a selenomethionine-incorporated form of the protein to a resolution of 3Å and the substructure solved using SHELXD. Selenium sites were refined and phases calculated using SHARP and a model fitted to the resulting map. Subsequently a 2.4Å data set was collected on a second crystal form and the model from the MAD phased maps used for successful molecular replacement with MOLREP, making this the highest resolution structure on a family member to date. The second structure determination was of *B. subtilis* LrpC, an unusual bacterial DNA architectural protein, which constrains positive supercoils in the DNA in addition to its gene regulatory role. Data was collected on this protein also to a resolution of 2.4Å and used for molecular replacement with the structure of *P.furiosus* LrpA as the search model.

Our asparagine-bound structure of AsnC is the first example of a family member with its effector clearly bound. The structure reveals AsnC to be an octameric disc, similar to that observed by us for *P.furiosus* LrpA. It identifies key residues involved in both ligand recognition and oligomer formation. The LrpC structure also reveals a stable octameric structure that is supportive of a topological role in DNA packaging. Taken together these structures confirm the Lrp/AsnC family's oligomerization states, the probable mode of action of the effector molecules and the basis of DNA binding. A manuscript is in preparation describing the details of both these structures and how they correlate with biochemical and genetic data.