PfamAlyzer paves way for an augmented understanding of protein domain architectures. It utilises the wealth of protein domain families present in the Pfam database and enables easy-to-use access to complex domain architectures as well as providing means for the study of their evolution.

**Domain query**

PfamAlyzer enables comprehensive study of domain architectures. Using a powerful, user-friendly graphical query language, arbitrary domains may be freely combined on the screen. PfamAlyzer uses Drag & Drop functionality as an intuitive approach for query formulation. Specific domains can be excluded from the search, in addition tolerated gaps between domains may be specified as domains or amino acids.

The manually curated Pfam-A domains are displayed as ovals, whereas automatically curated Pfam-B domains are shown as rectangles. Additional information for Pfam-A domains is available through context menus as well as links to other resources.

**Homology search**

PfamAlyzer provides innovative homology searching. So far, the identification of homologues has been conducted by direct sequence comparison. This is appropriate if sequences are not very distant. However, for distantly related proteins the search for homologues is difficult. Domain querying allows a new tool for finding such homologues.

PfamAlyzer introduces a domain-centric homology search based on Pfam domains. In a first step, Pfam domains are predicted from the sequence. This is achieved using the hmmer package which is also applied for generating Pfam full alignments from curated seeds. Subsequently, SwissProt/TrEMBL is queried for the obtained domain architecture. This type of domain-centric homology analysis provides a means to identify relationships that are distant yet possess a conserved domain architecture.