Project 1

Protein residue interaction networks as *in silico* tool for functional, evolutionary, and design applications

Synopsis/Abstract (max 800 words)
Proteins play a central role in biological processes, and understanding their structure and dynamics is essential to determine their functional mechanisms as well as for fields ranging from evolutionary biology to protein engineering. Residue Interaction Networks (RINs) are an innovative way to summarize protein structural information as graphs, with residues as nodes and non-covalent interactions as edges connecting them. This facilitates visual analytics and highlights significant interactions present in conformational ensembles of protein complexes. The RING software has been developed to harness the power of RINs for non-expert users, providing a rich description of different non-covalent interaction types integrated with advanced analysis tools. Recent updates have made the tool more versatile and accessible, but its application remains limited to theoretical or demonstrative cases. However, the full potential of RING has yet to be explored across a range of different use cases. This project aims to fill this gap, demonstrating the effectiveness of RINs through relevant examples in functional, evolutionary, and protein design studies, including the analysis of functionally relevant conformational ensembles.
The Project aims are: (1) Functional protein studies, identifying use cases of proteins where RINs can be used to understand complex functional mechanisms, such as signal transmission or allosteric modulation; (2) Applying RINs to compare homologous proteins or evolutionary variants, highlighting key changes in residue interactions linked to functional adaptation; (3) Using RINs to support protein engineering strategies, identifying mutations that stabilize or modify protein function; (4) Developing methods to analyze ensembles of structurally relevant conformations through RINs, enhancing the understanding of conformational dynamics. (5) Developing guidelines for standard protocols applying RINs in functional, evolutionary, and design studies.
The use cases for RINs will be drawn from protein systems under study by different partners of the ArchiFun consortium, providing novel in silico tools to complement experimental studies being carried out in the consortium. The project will significantly enhance our understanding of proteins in a multidisciplinary context, creating new research opportunities and technological applications.

Collaborations:
The project involves collaboration with laboratories specializing in structural, evolutionary, and computational biology, ensuring interdisciplinary synergy for achieving the objectives.

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Proposed collaboration within ArchiFun network (not mandatory at this stage):
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Proposed list of secondments (not mandatory, but recommended if known already):
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Main ArchiFun theme involved:

Host-pathogen interactions;
Mechanisms of bacterial resistance and cancer onsets;
Translational research in prevalent diseases.