Putting everything in perspective

EMBO Practical Course

Computational analysis of protein-protein interactions in cell function and disease

01 – 06 December 2019 | Bangalore, India

Topics of the course

PPIs and diseases
Protein families, functions
Sequence alignments
Networks (STRING)
Network visualization
Intrinsically disordered regions
Linear motifs
Protein structure (ChimeraX)
Tandem repeats and homorepeats
Modeling proteins and interaction interfaces

Synergies: Which different data types should be integrated to help the analysis of PPI function? e.g. sequence conservation with motif prediction

Opportunities: What should be the most useful goals of PPI comp analysis? e.g. designing new protein interactions, curing cancer

Limits (that we can address): What do we need to improve the methods of PPI comp. analysis? e.g. usability, more experimental data on PTM-dependent interactions

Limits (that we cannot address): Things PPI comp. analysis will never be able to do. E.g. predicting extremely transient interactions

Synergies

sequence conservation with motif prediction, large volume of masspec data, information about how PTMs affect PPIs (experimental and predicted information), curated database paths with PPI network, integration of docking tools in ChimeraXX, dynamics of gene expression changes in PPI network, consider expression transients, pathogenic vector bacteria database data, ncRNA database (expand PPI to Prot-RNAI network), consider alternative splicing variants, transcriptome variation, subcellular localization of proteins

Opportunities

designing new protein interactions, curing cancer, combine comp with experimental workflow (streamline mixed protocols), app for drug prediction (small molecules) in relation to PPIs (modify), understand the mechanisms of protein function, study of host-pathogen interactions, associate microbiome states to disease (tissue specific: skin, gut) (see before), perform covalent docking (focus on off-target effects, drug repurposing), molecular mimicry and auto-immunity (related to pathogens), multiple disease conditions (related proteins cause related diseases), understand relations genotype to phenotype, synthetic biology, study

Limits (soft) usability, more experimental data on PTM-dependent interactions, include feedback in the study of PPIs (integrating other levels of gene regulation), consider protein carbohydrate/lipid modifications, memory effect (in the protein folding), accurate motif prediction in highly ordered proteins, improve pred of effects of PTMs on structure, calculate linear motifs (degenerate) into affinities, simulation of phosphorylation (PTMs), structure of small peptides including mutations, better experimental readouts of PPIs, making docking of multiple proteins at once (e.g. complexes), improve protein purification and antibody quality/specificity

Limits (hard) predicting extremely transient interactions, no model is good enough to represent the physiology (exp always needed), exp validation necessary, protein prediction ab initio, predict patient response to drugs, how one protein affects the function of another protein, predicting the dynamics of large complexes, computational limits, dealing with different time-scales, prediction of structures and binding partners of IDPs.