PL04

Chemical microscopy: at the frontier of proteomics

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Accurately modelling the structures of proteins and their complexes using artificial intelligence is revolutionizing molecular biology. Remaining challenges result from the limited information available on specific protein states including protein-protein interactions. We present how proteomics data enable systematically modelling novel protein assemblies and how proteomics data can inject information about in-cell states of proteins into the modelling workflow. Taking a decisively in-cell approach allows discovering aspects of biology that are lost when lysing cells. Indeed, we propose novel structural models of 153 dimeric and 14 trimeric protein assemblies in the model organism *Bacillus subtilis*. We report and validate novel interactors of central cellular machineries that include the ribosome, RNA polymerase, and pyruvate dehydrogenase, assigning function to several uncharacterized proteins. Our approach uncovers protein-protein interactions inside intact cells, provides structural insight into their interaction interfaces, and is applicable to genetically intractable organisms, including pathogenic bacteria. Facile generation of pseudo-atomic models of PPIs provides a plausible shortcut to the improved functional understanding of the many currently uncharacterised proteins.