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Supplementary information

Three decades of protein-fragment complementation

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Three decades of protein-fragment complementation

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Supplementary information

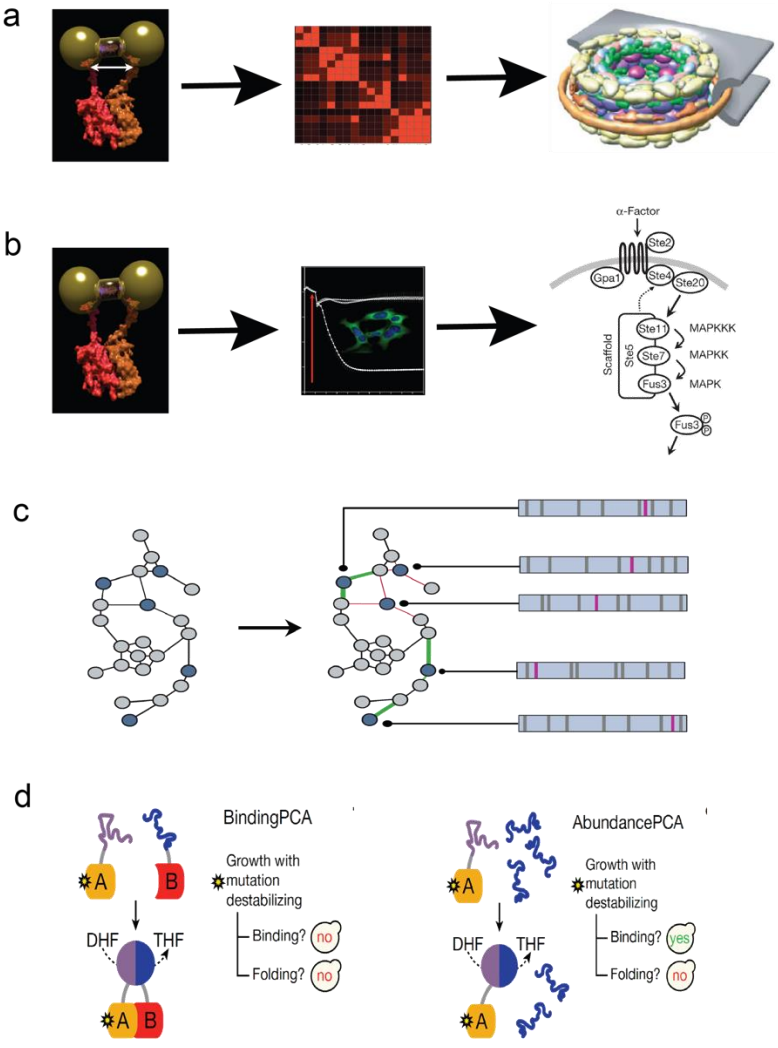

Figure 1. PCA maps topologies, and spatial and temporal perturbations of protein-protein interaction networks, and amino acid sequences of proteins
a, Topology of protein complexes can be deduced based on distance constraints on PCA determined by the lengths of linker peptides between binding proteins (gold spheres, left) and PCA fragments (red, orange). (middle) PPI contact map for a nuclear pore complex determined by PCA, is consistent with a structural model (right) (reprinted from ref. 28, Springer Nature Limited). **b,** signaling pathway dynamics can be deduced

from changes in PPIs caused by a stimulus, here a decrease in the number of complexes (middle) following the stimulus (red arrow) and order of interactions in time and space (inset) can be mapped (right) (reprinted from ref. 29, Springer Nature Limited). **c,** network perturbations (arrow) can manifest as increases (green) or decreases (red) in PPIs (middle). Equally, genomic variations in coding and non-coding sequences can have similar effects on PPI, permitting quantitative trait loci identification for gene *cis* and *trans* effects. **d,** Two PCAs for deducing free energies of binding (left) and stability (right) of a library of single and double mutants of a protein (A*). In BindingPCA, A* is fused to one fragment and biding partner B, to complementary fragment of methotrexate resistant DHFR. If A* binds to B, DHFR is reconstituted and can convert Dihydrofolate (DHF) to Tetrahydrofolate (THF) in the presence of methotrexate, permitting cells to divide. In AbundancePCA, A*-fragment 1 fusion is expressed with high levels of complementary fragment alone, resulting in spontaneous reconstitution of DHFR and growth of cells is then proportional to the abundance of A* and therefore its stability (reprinted from ref. 22, Springer Nature Limited).

Further reading:

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