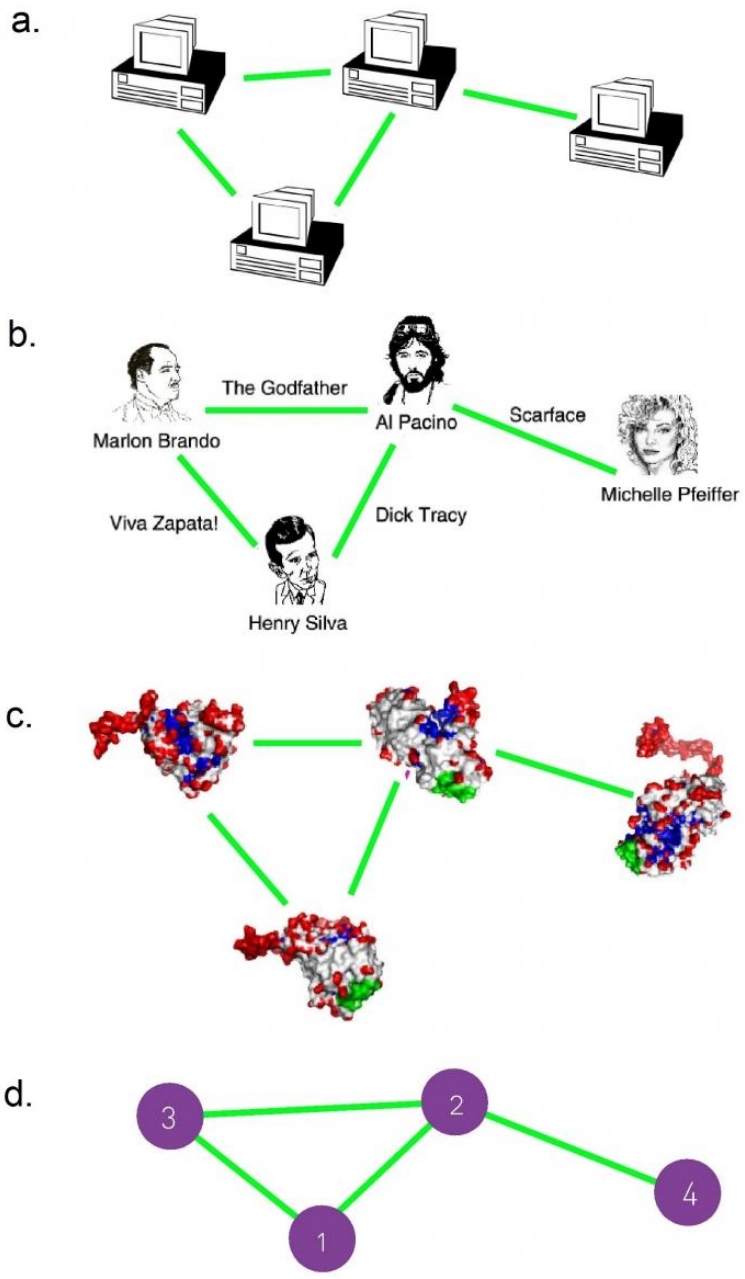
Molecular Networks

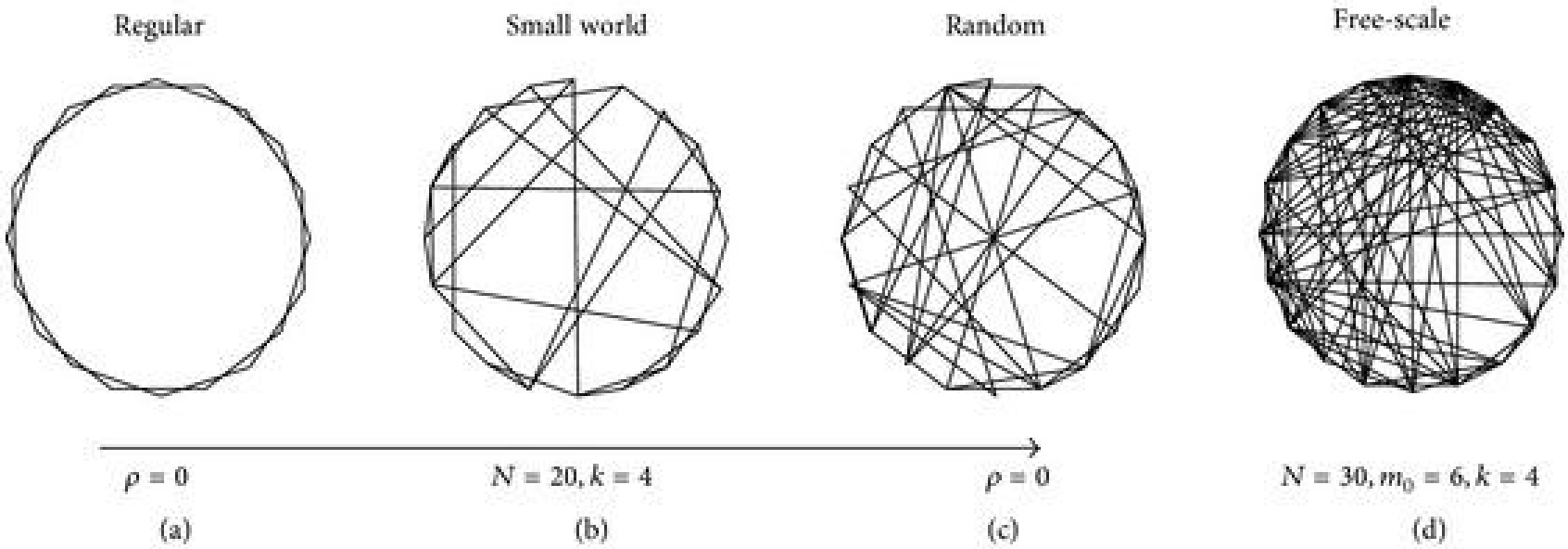
Networks

- Graph:
  - abstract mathematical representation, data structure
- Network
  - phenomenon modelled by graph

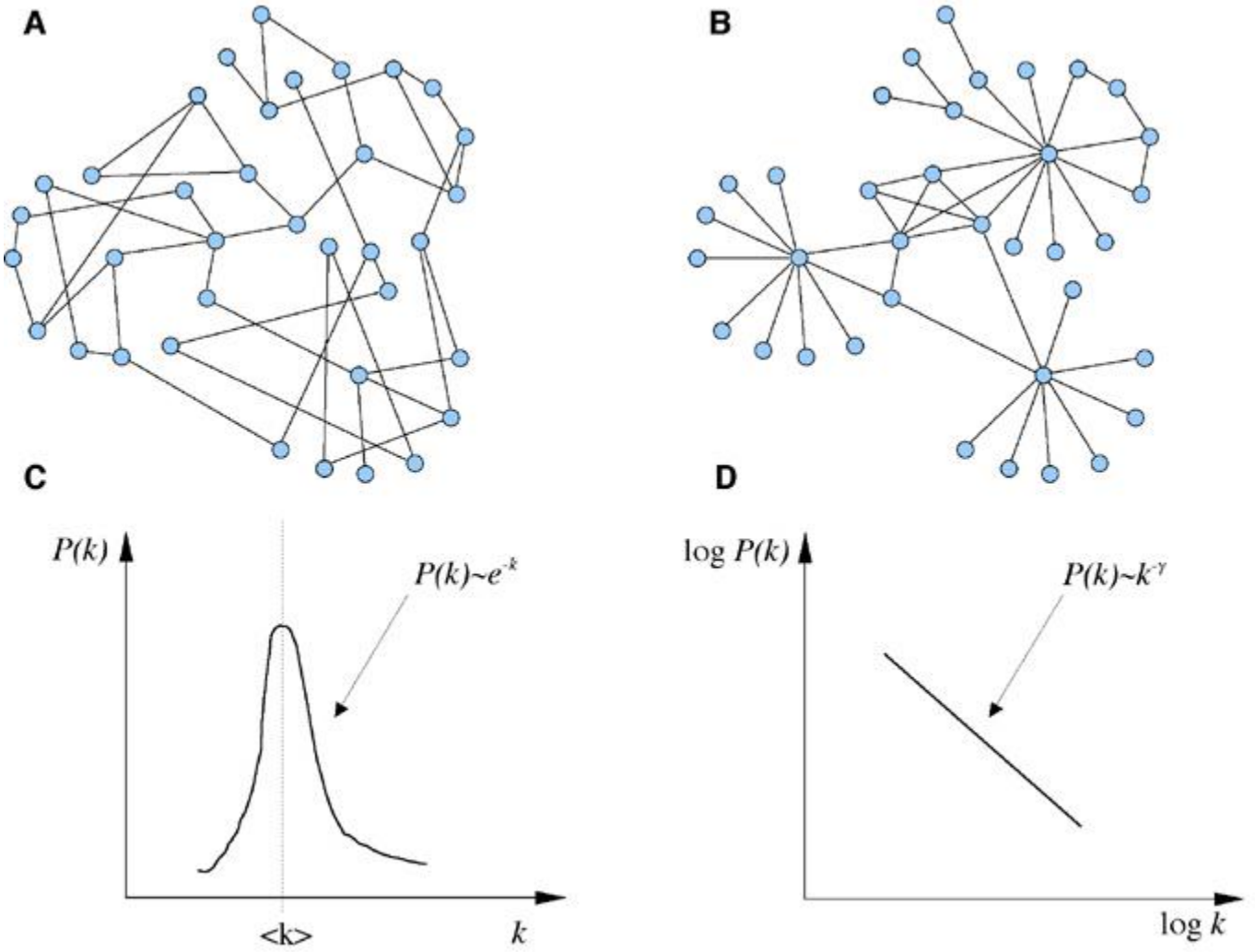


http://barabasi.com/networksciencebook/chapter/2

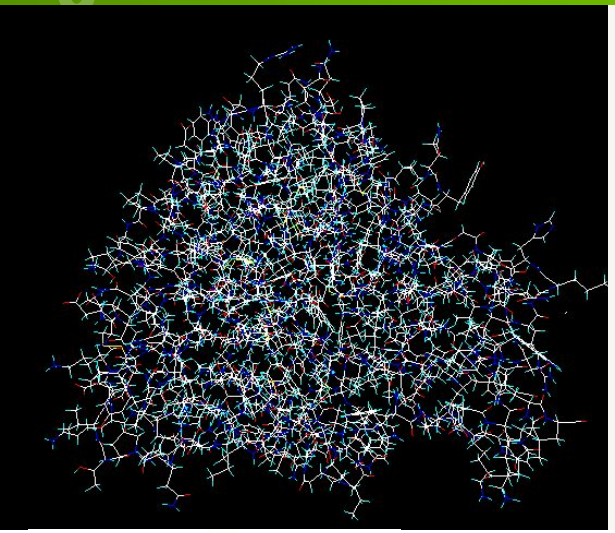
Network topology

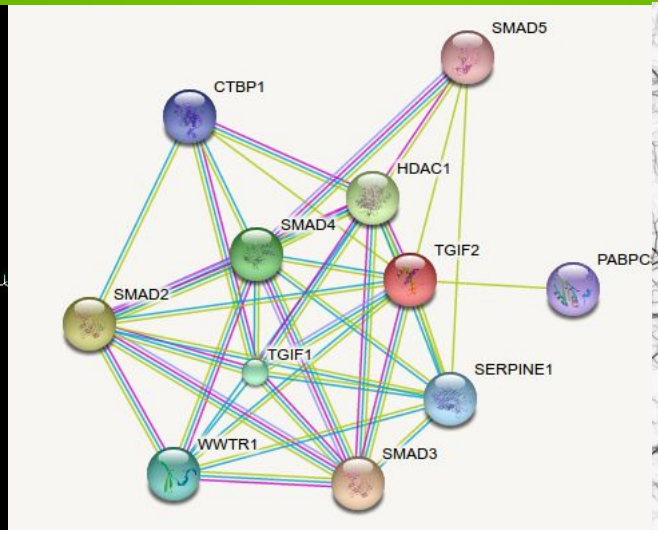


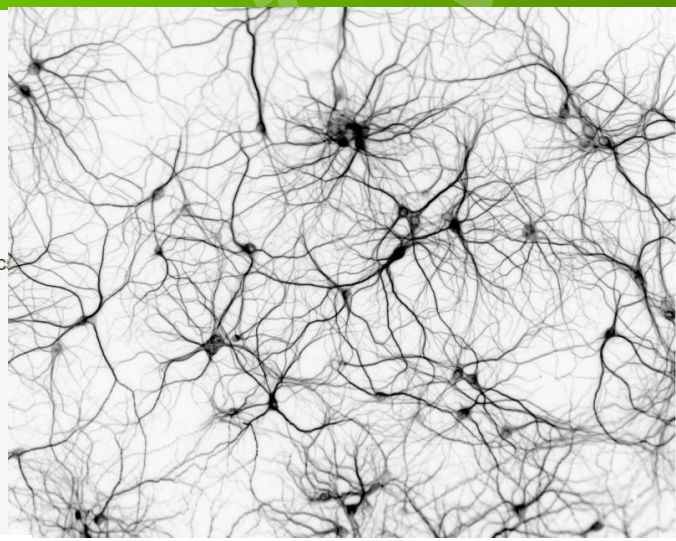
Network topology

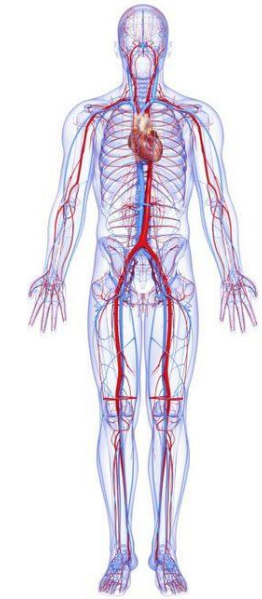


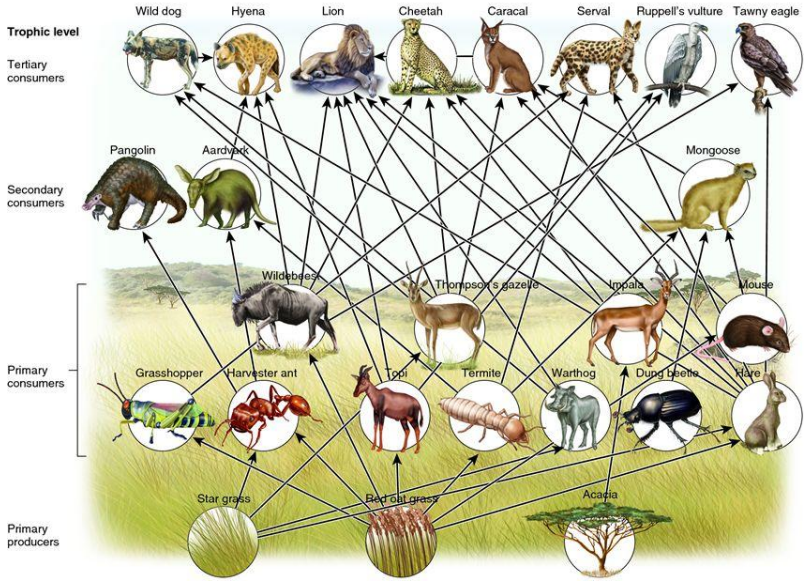
Networks in biology



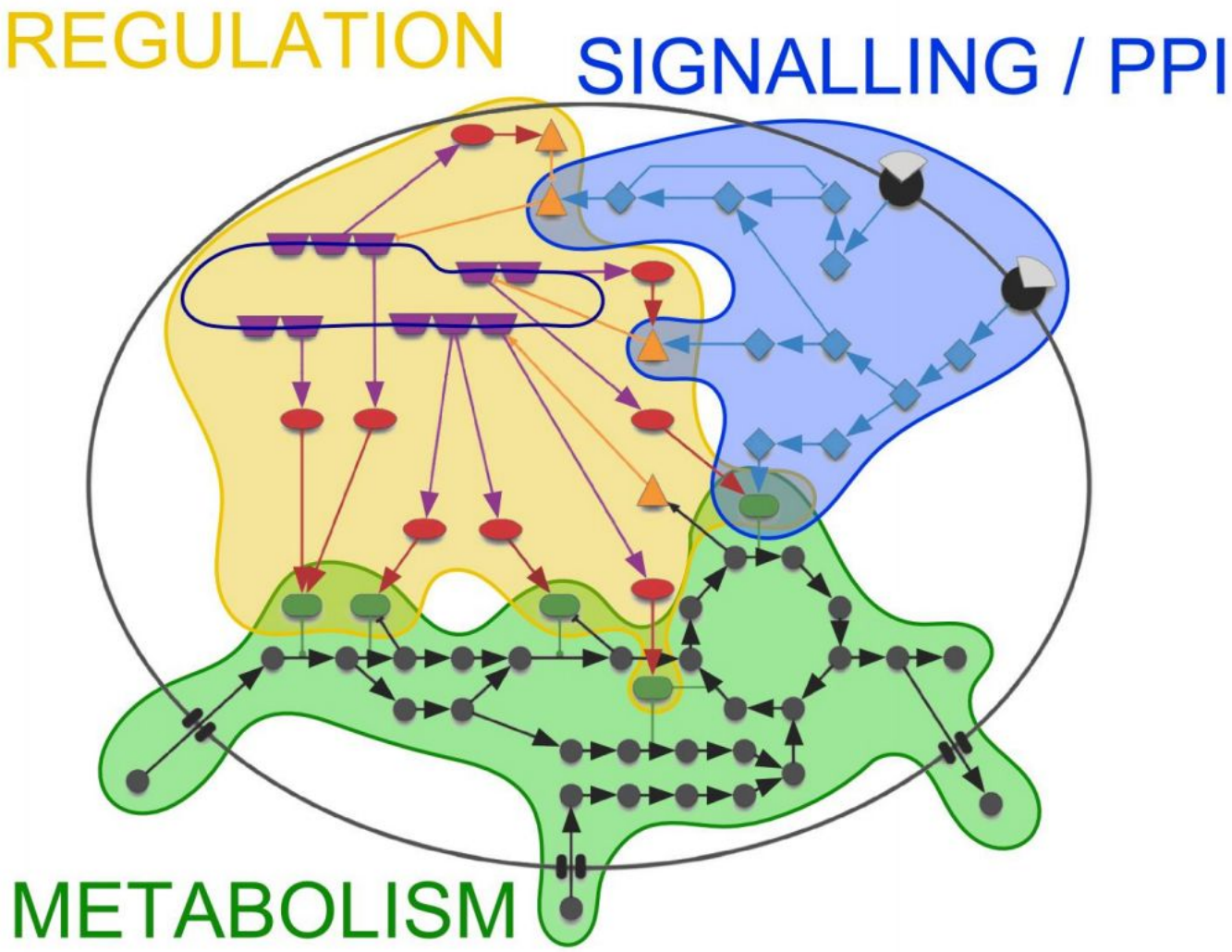








Molecular networks



Nodes and edges in molecular networks

- Nodes:
  - DNA: DNA region, gene
  - RNA: mRNA, non-coding RNA (miRNA, lncRNA)
  - Protein
  - Sub-protein: Domain, protein sequence region

- Edges:
  - DNA-DNA: sequence similarity
  - Protein-DNA: DNA binding
  - DNA-mRNA: transcription
  - miRNA-mRNA: RNA interference
  - mRNA-Protein: translation
  - Protein-Protein: physical interaction

Sources of Protein-Protein Interactions

- Small scale
  - Few interaction / publication
  - Could be directed
  - Many information / interaction
  - Individual errors
  - Local data
  - No central database (publications)
  - Curation
- Large scale
  - Lot interaction / publication
  - Mostly undirected
  - Few information / interaction
  - Systematic errors
  - Global data
  - Few database
  - High-throughput – HTP methodes

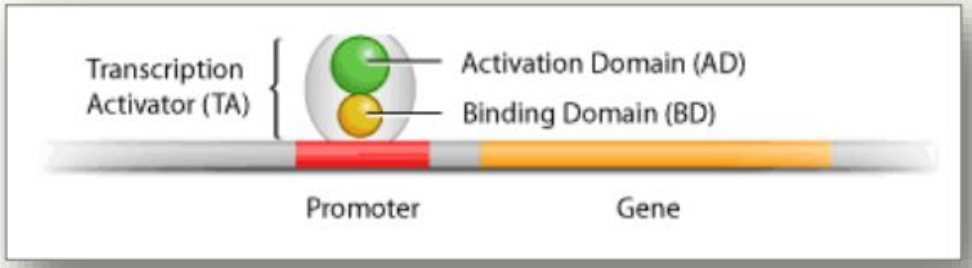
Collecting PPI data

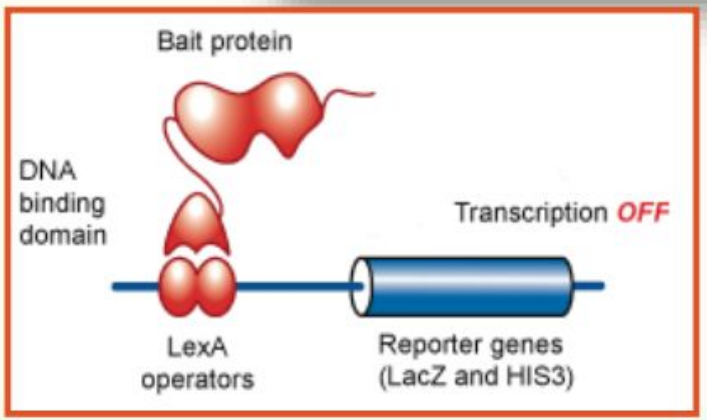
- Manual curation / literature mining
  - +: Small scale high precision data
  - -: Huge work, biased
- Prediction (homologous transfer)
  - +: Lot of data, low human/computer time
  - -: Quality of predicted data based on the quality of the original data
- Data integration
  - +: Wide scale of data
  - -: Systematic error

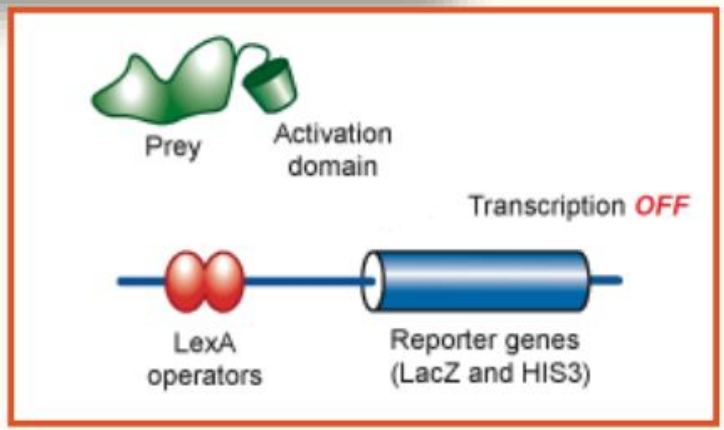
High-throughput methodes

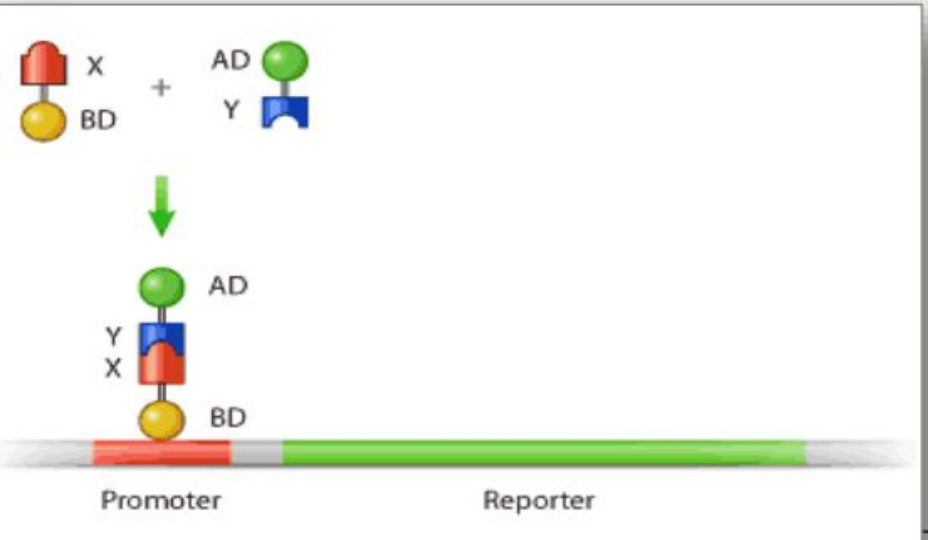
- Y2H: Two-hybrid screening
- AP-MS: Affinity purification-mass spectrometry
- Co-IP: Co-immunoprecipitation
- FRET (Fluorescence Resonance EnergyTransfer)
- biFC (Bimolecular Fluorescence Complementation):
- Protein-chip

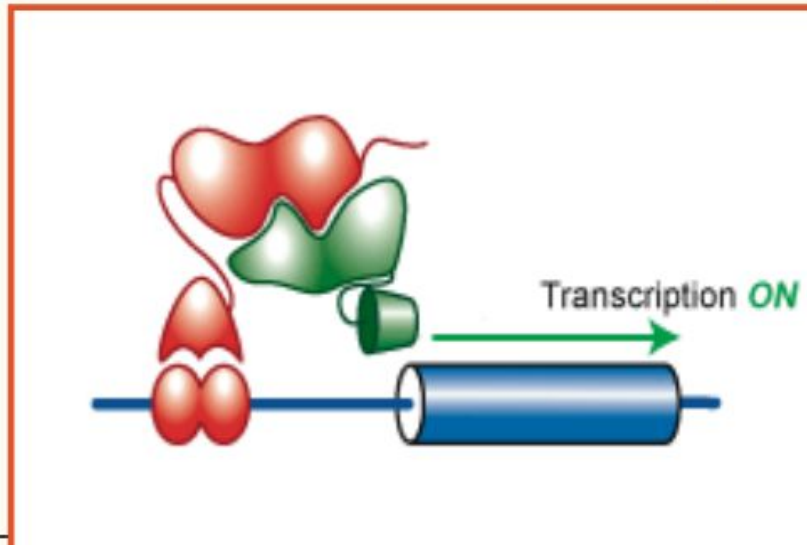
Two-hybrid screening











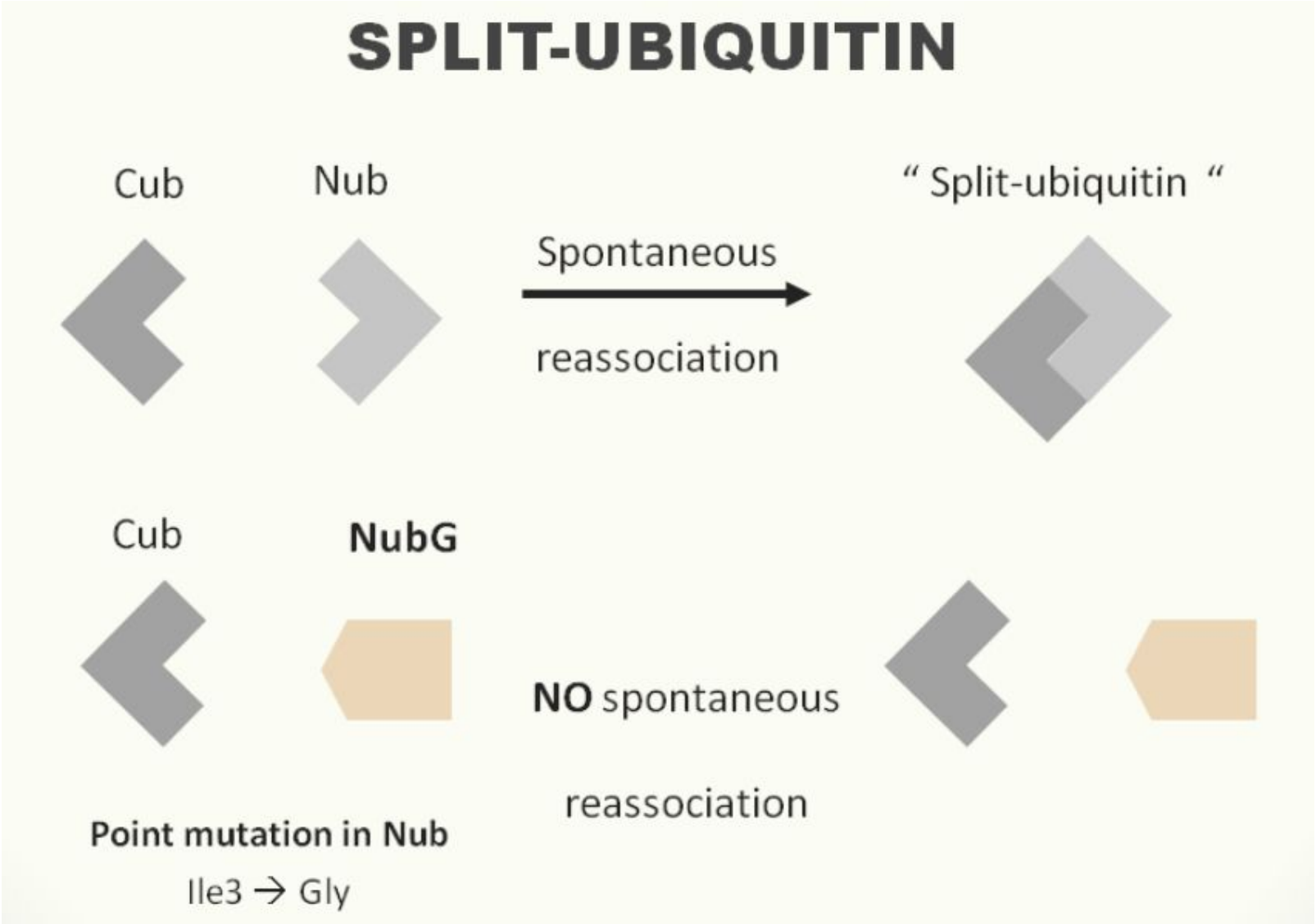
Limitations of two-hybrid screening

- Self activator bait
- Too big complex: can not enter to the nucleus

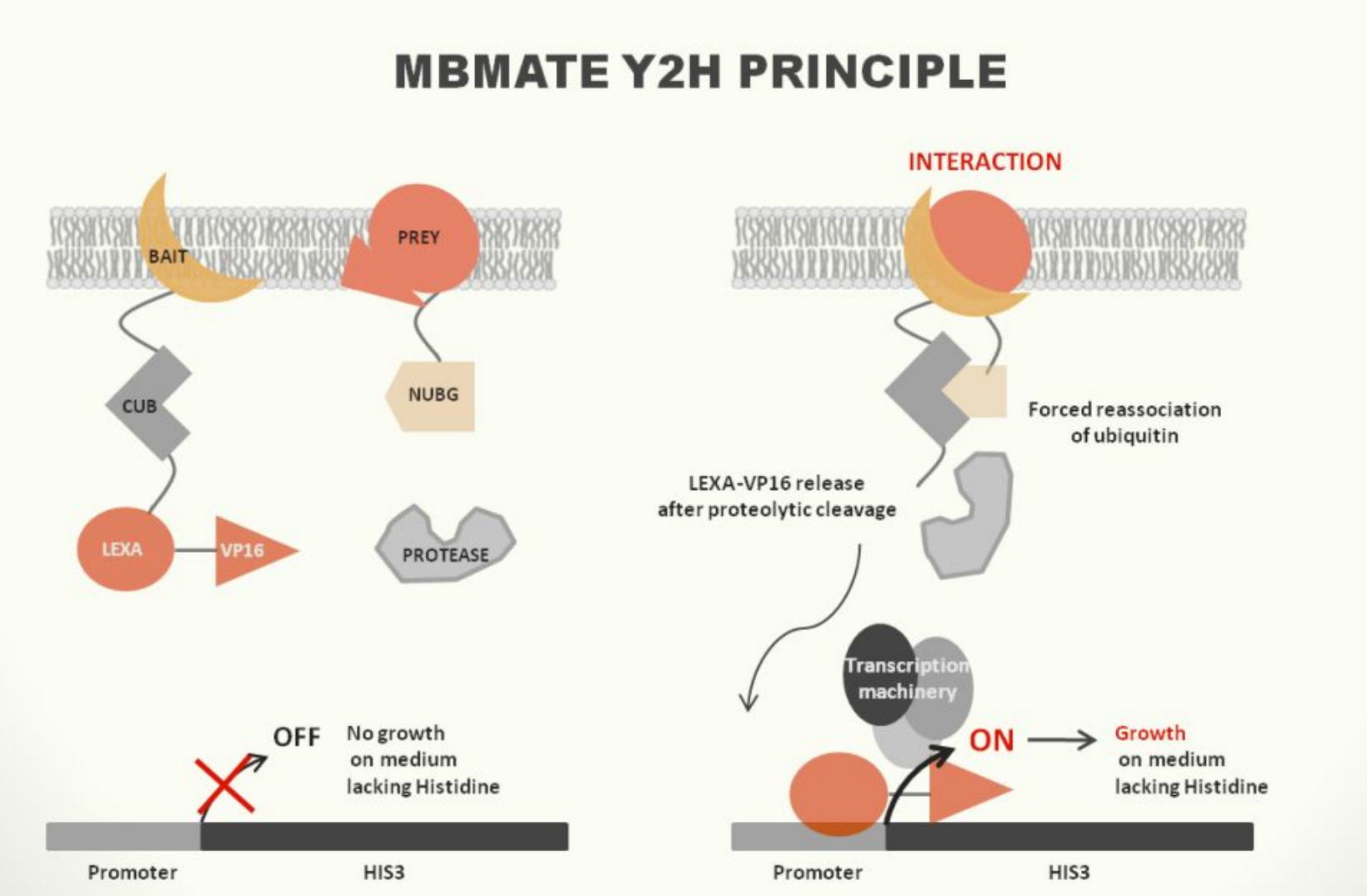
Excluded proteins:

- Membrane proteins
- Extra cellural proteins
- Transcription factors
- Proteins with acidic side chains

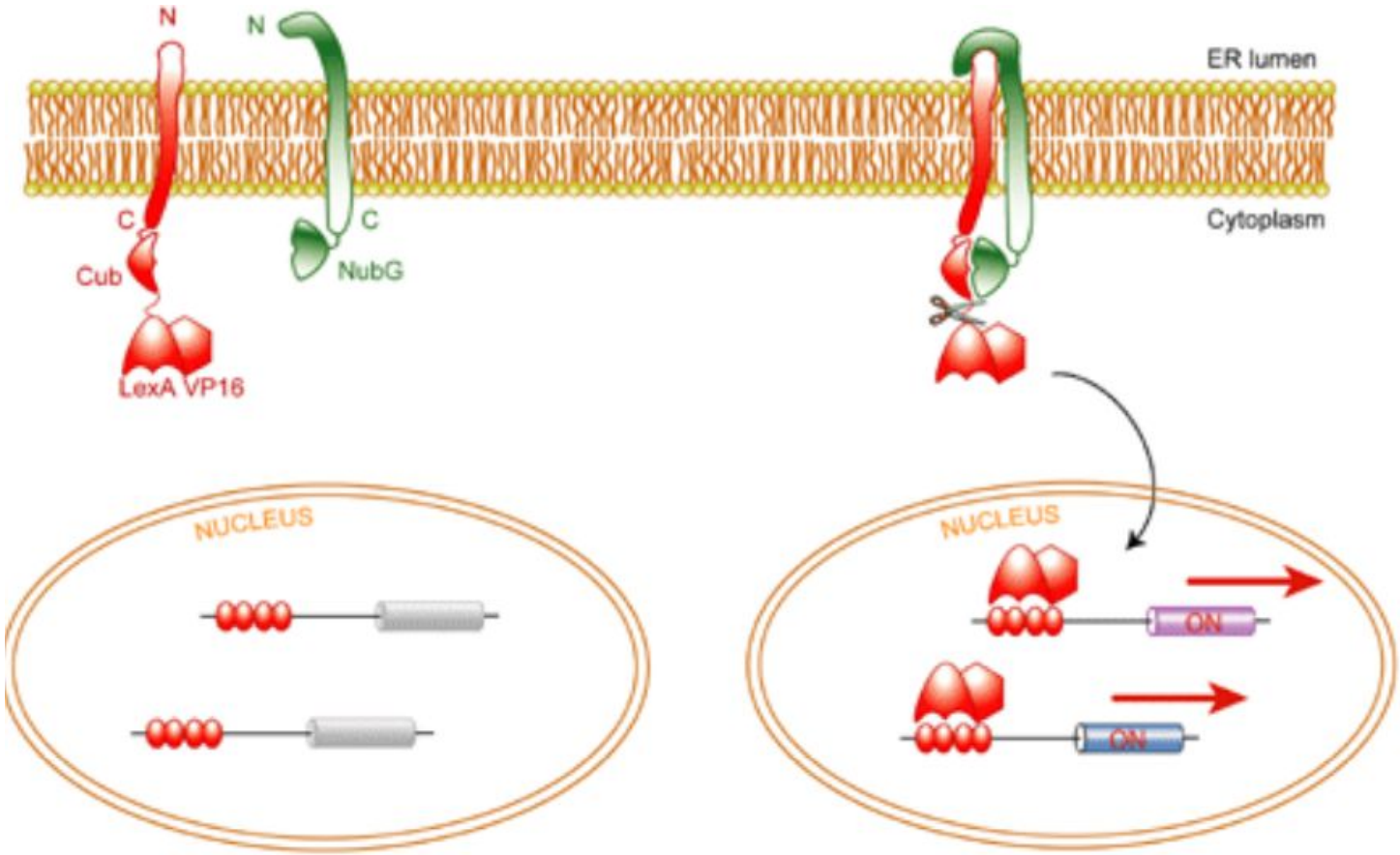
Modified Y2H system with split-ubiquitin system



Modified Y2H system with split-ubiquitin system



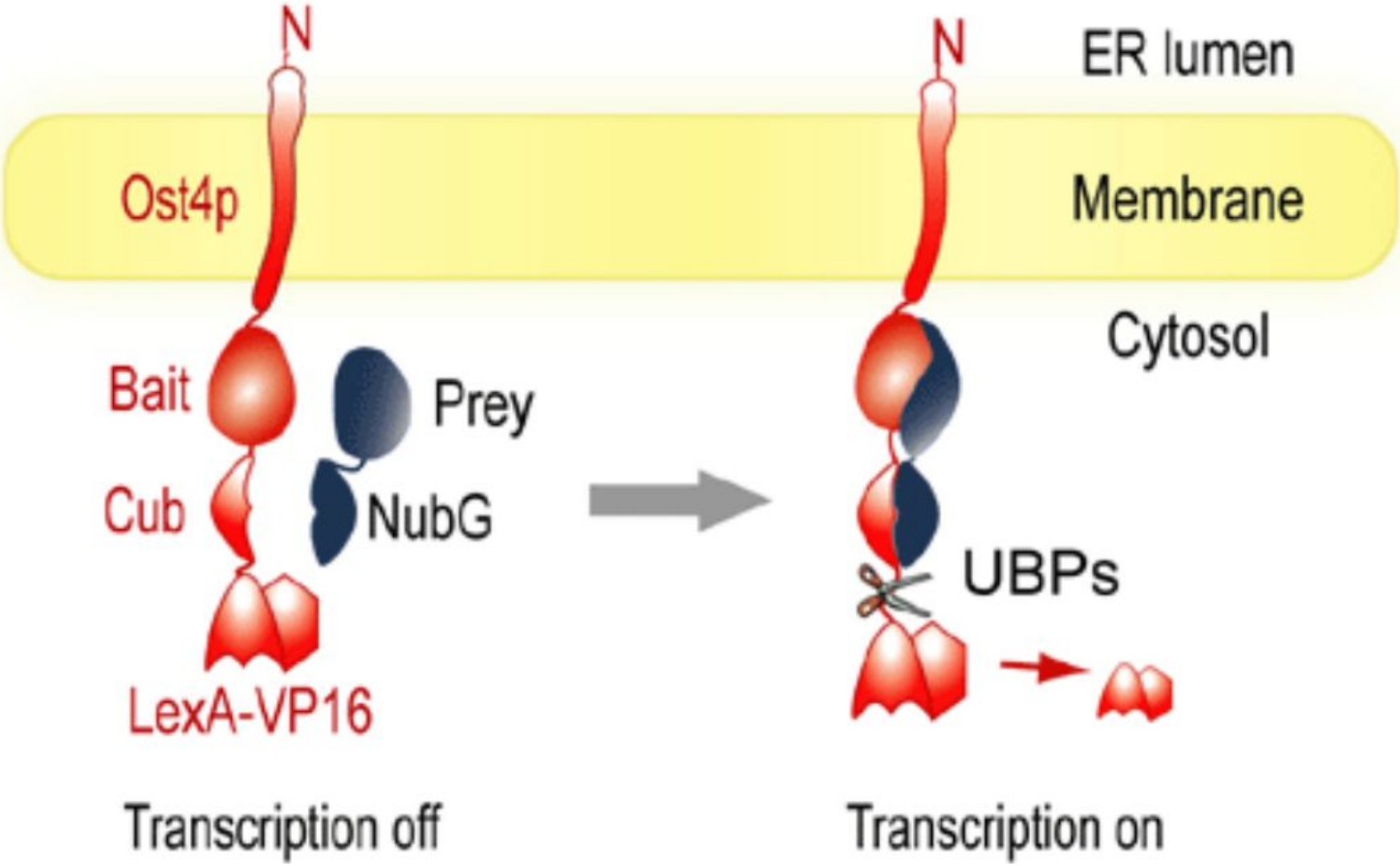
Study integral membrane proteins with split-ubiquitin-Y2H system



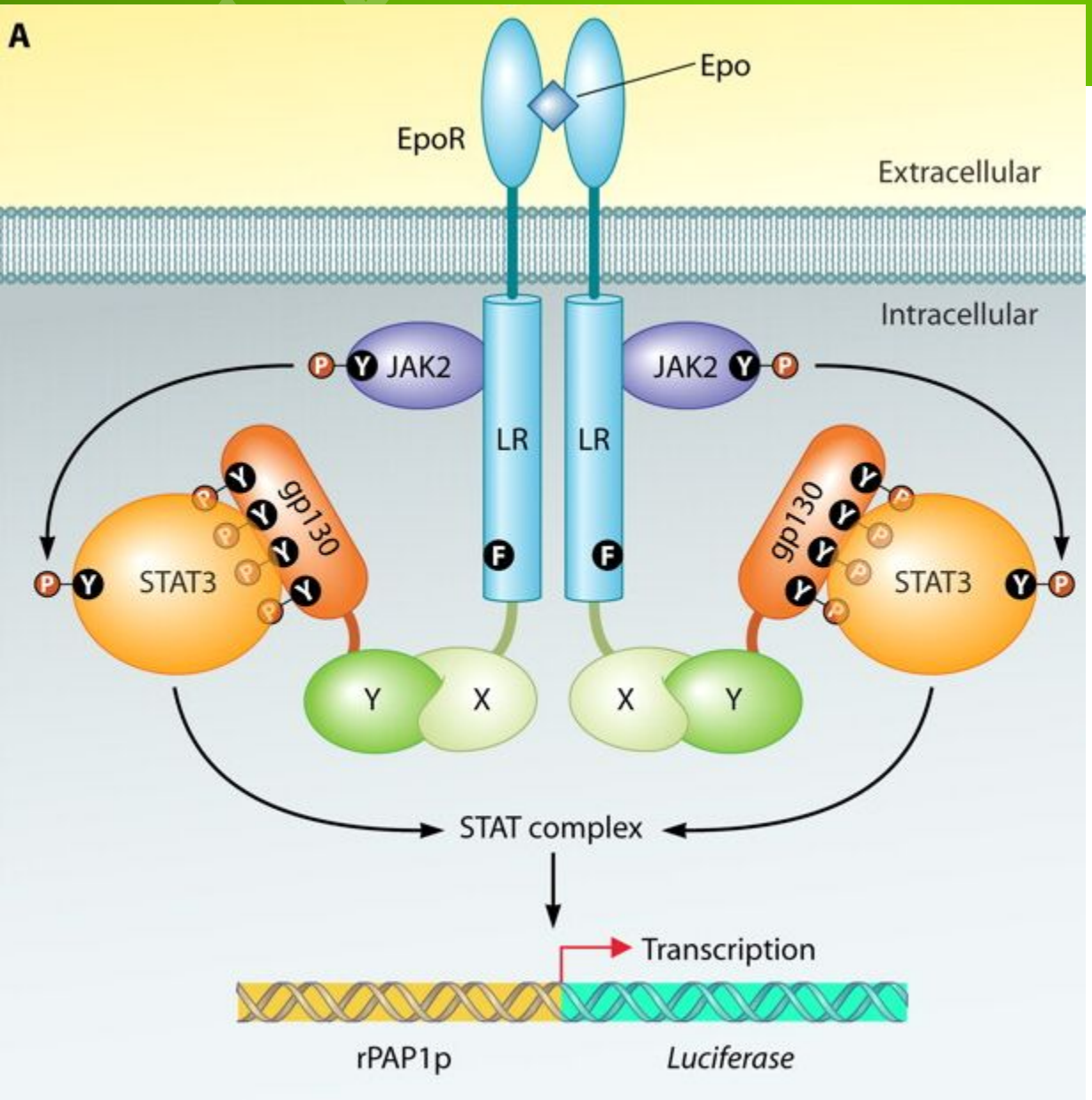
Growth on selective medium

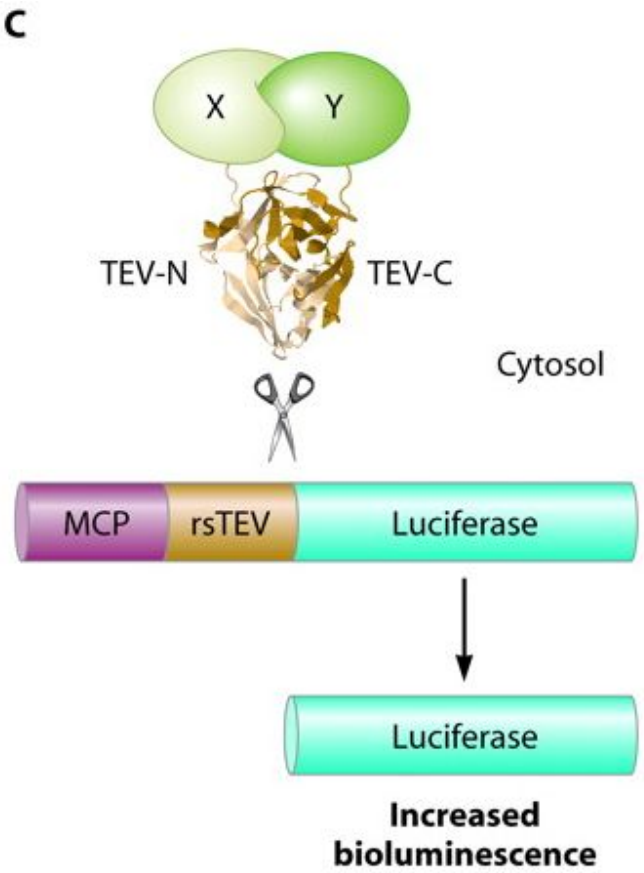
Blue coloration

Study transcription factors with split-ubiquitin-Y2H system

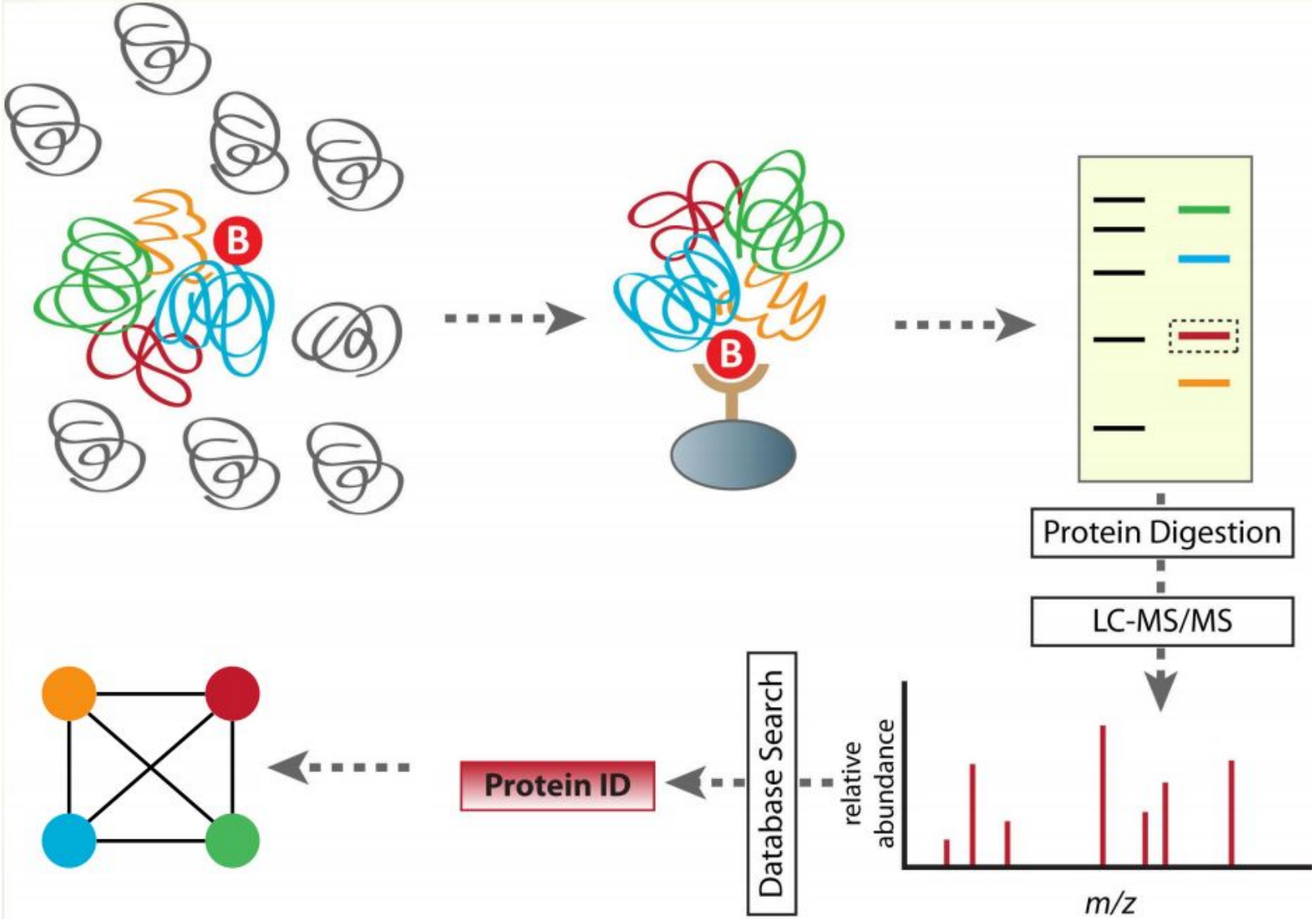


MAPPIT - mammalian protein protein interaction trap

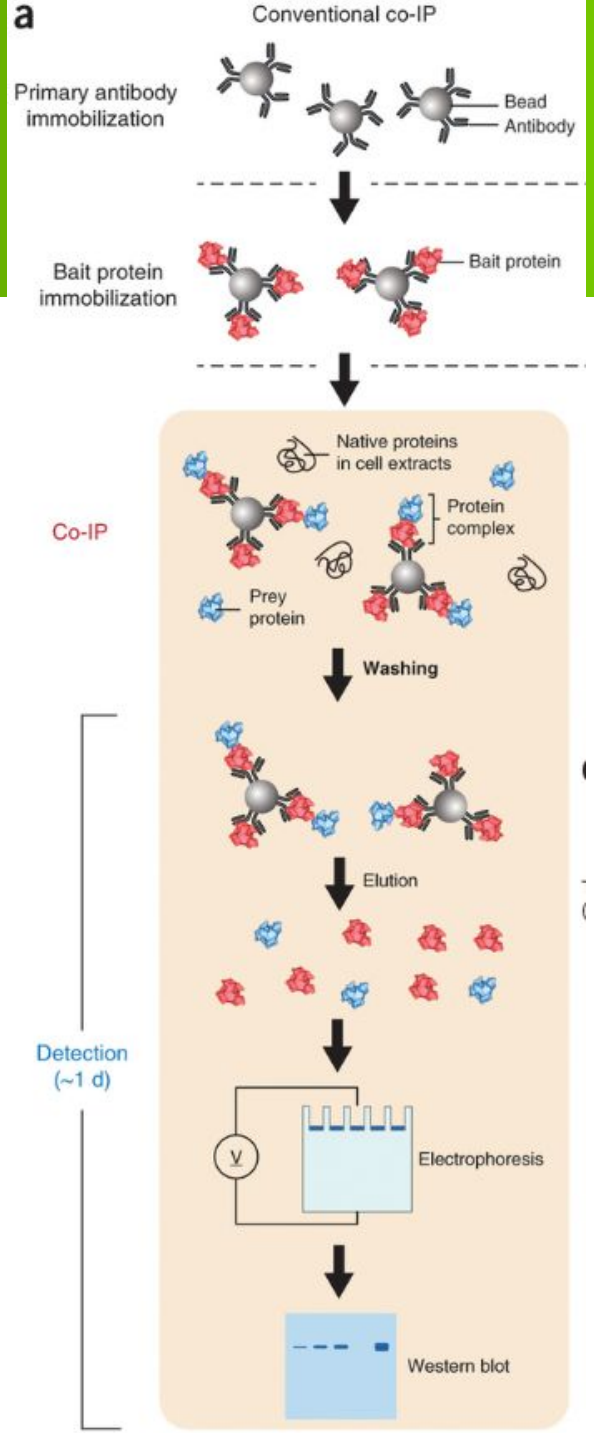




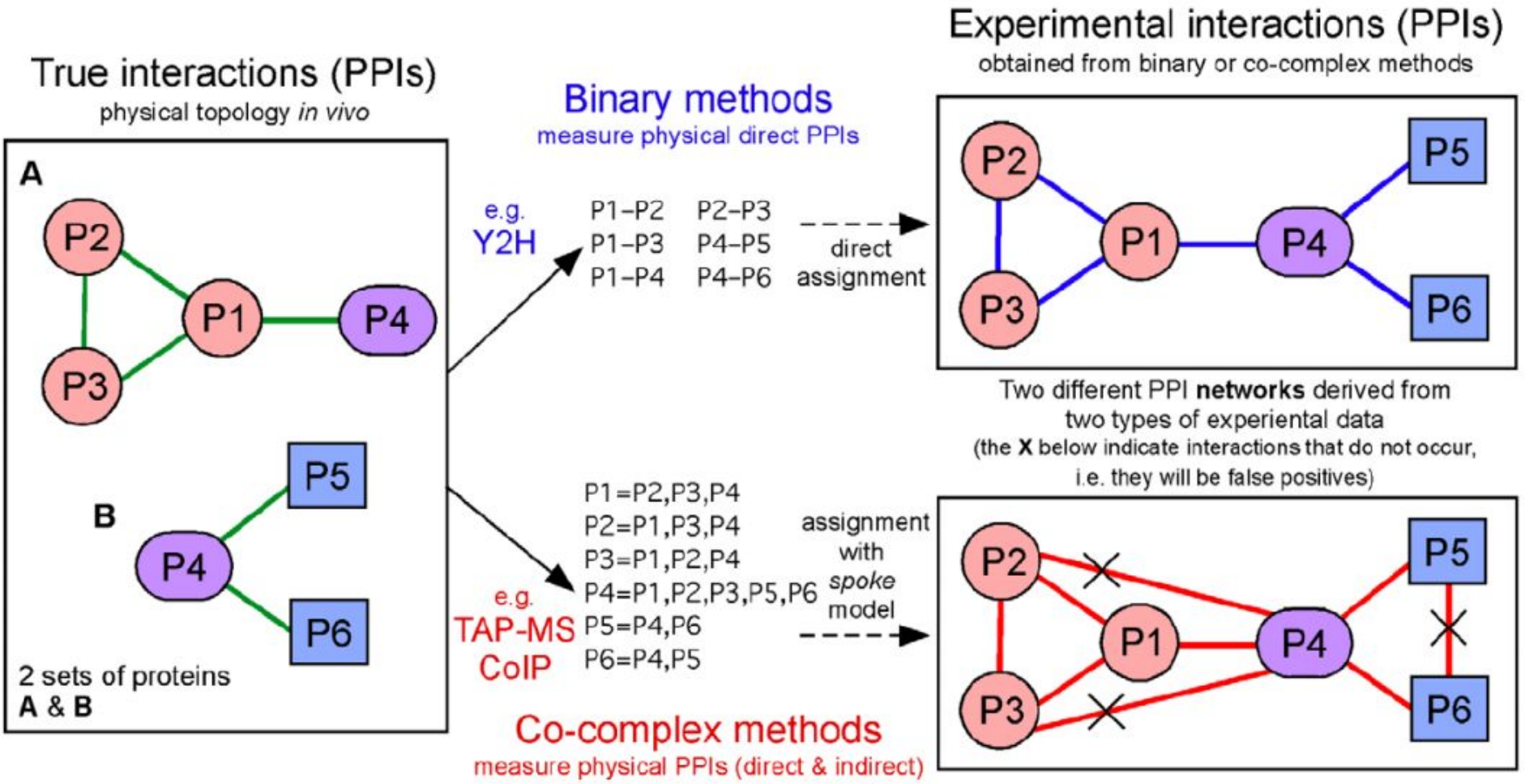
Affinity Purification - Mass Spectrometry



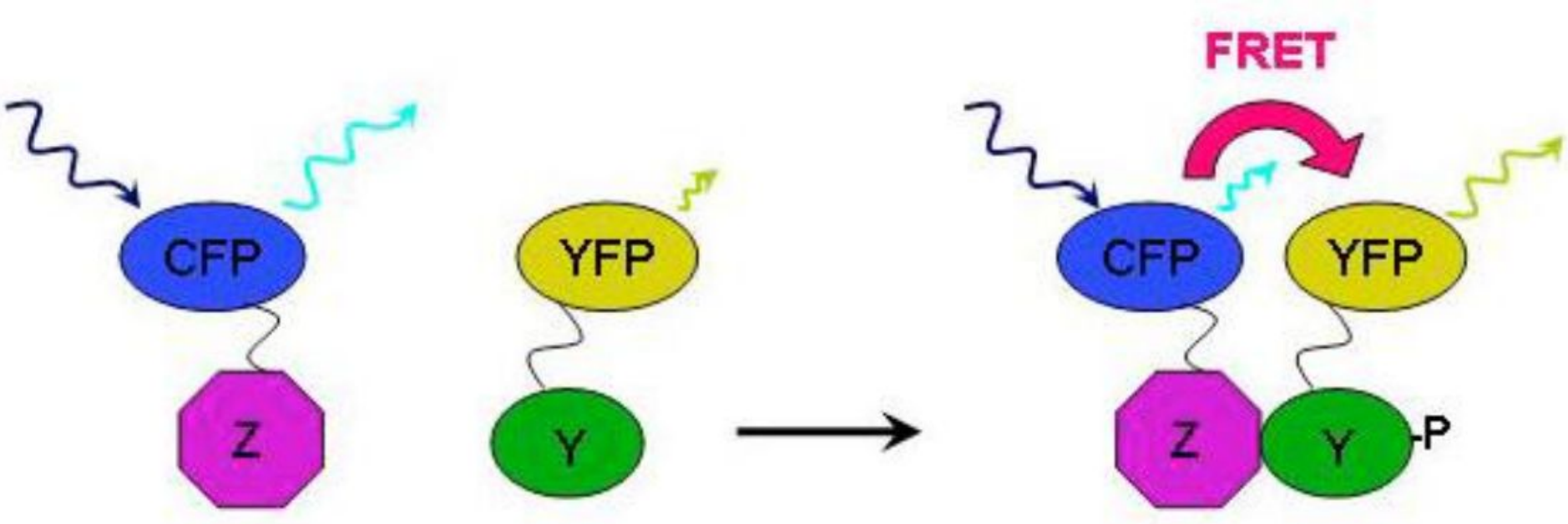
Co-immunoprecipitation



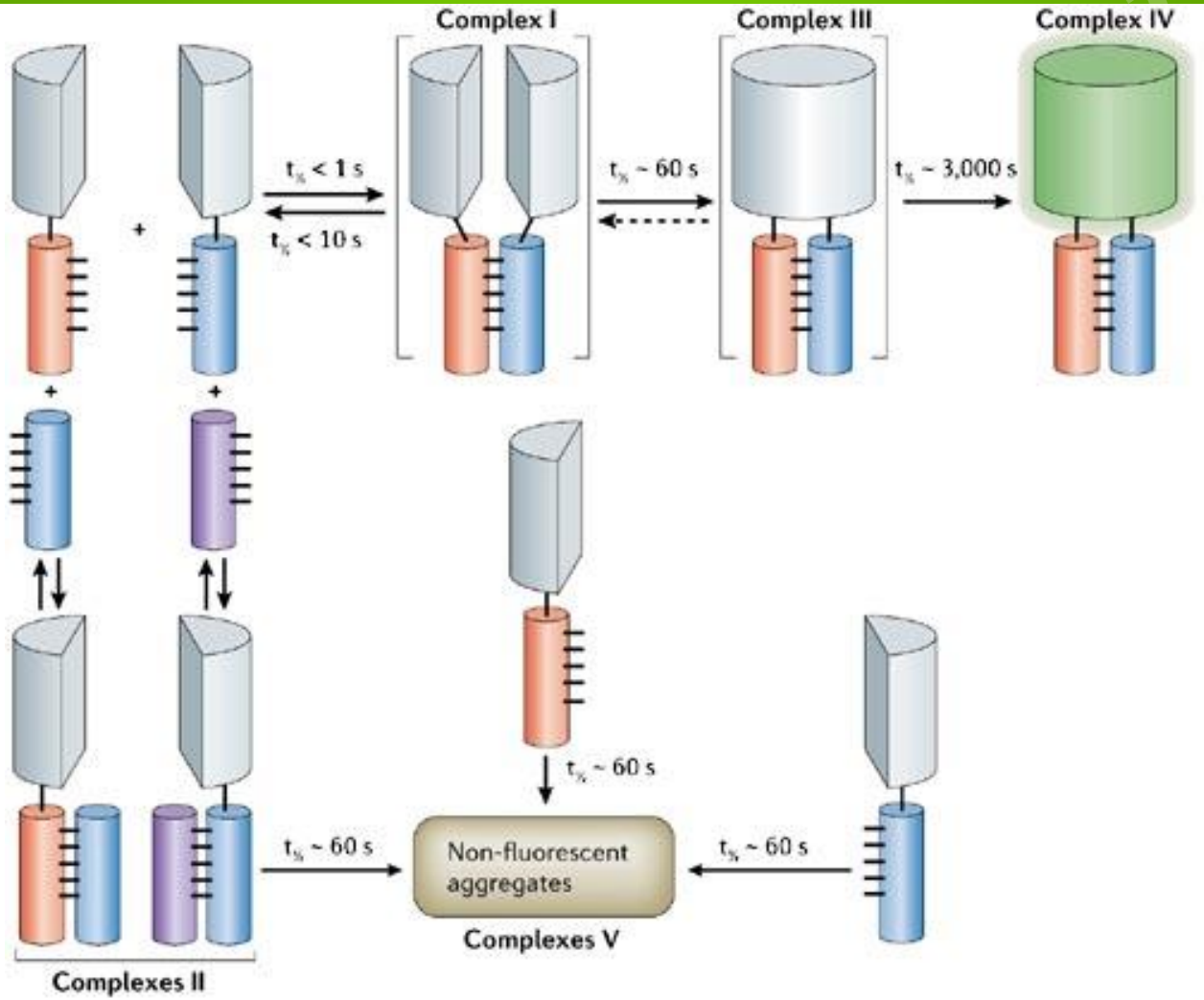
Y2H vs. TAP-MS / CoIP



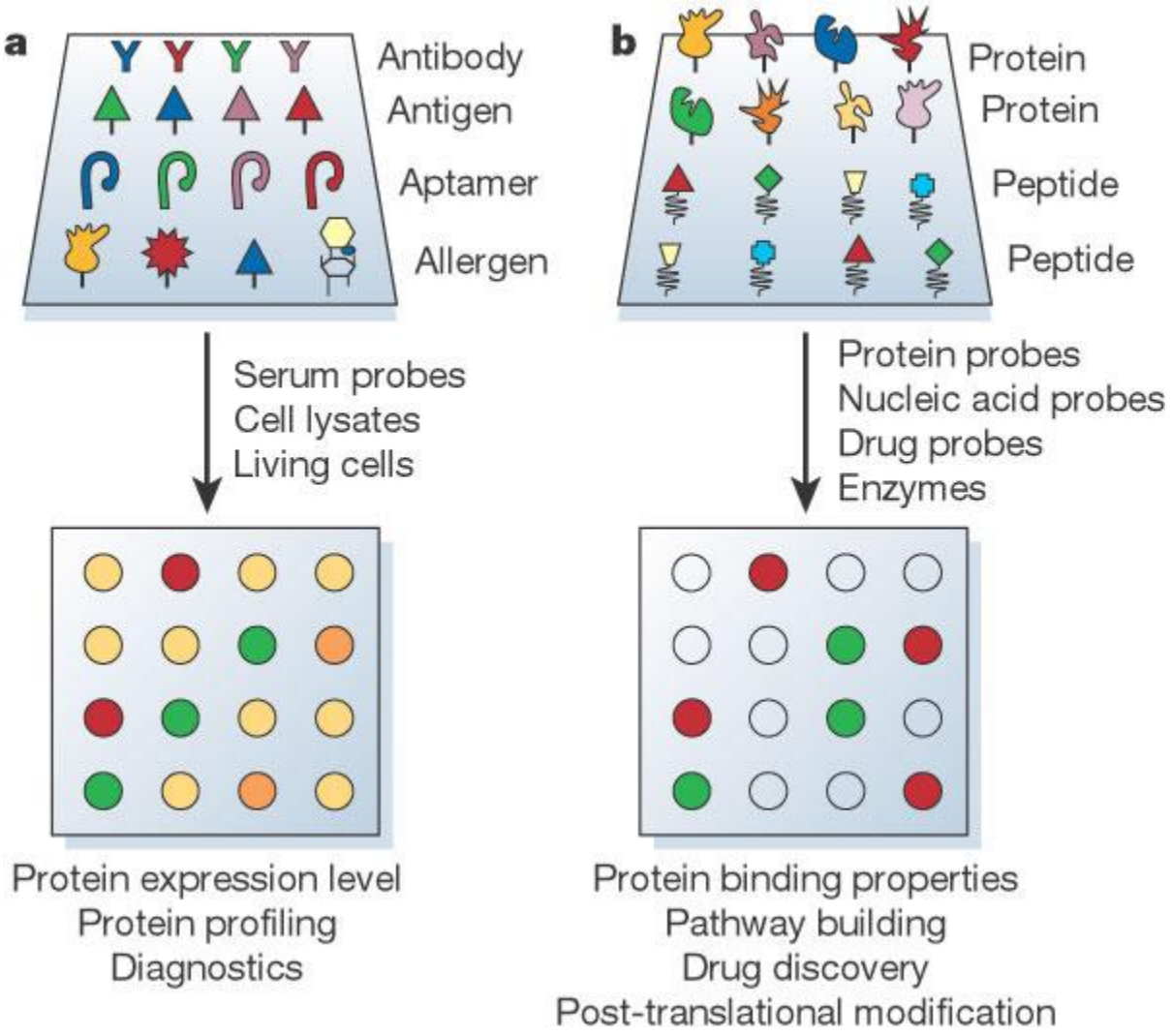
FRET
Fluorescence Resonance Energy Transfer



biFC
Bimolecular Fluorescence Complementation



Protein chip



PPI prediction

- Homologous transfer
- Enzyme biondig motif search
- Based domine-domine interaction
- 3D docking

- Literature mining
- Co-expression