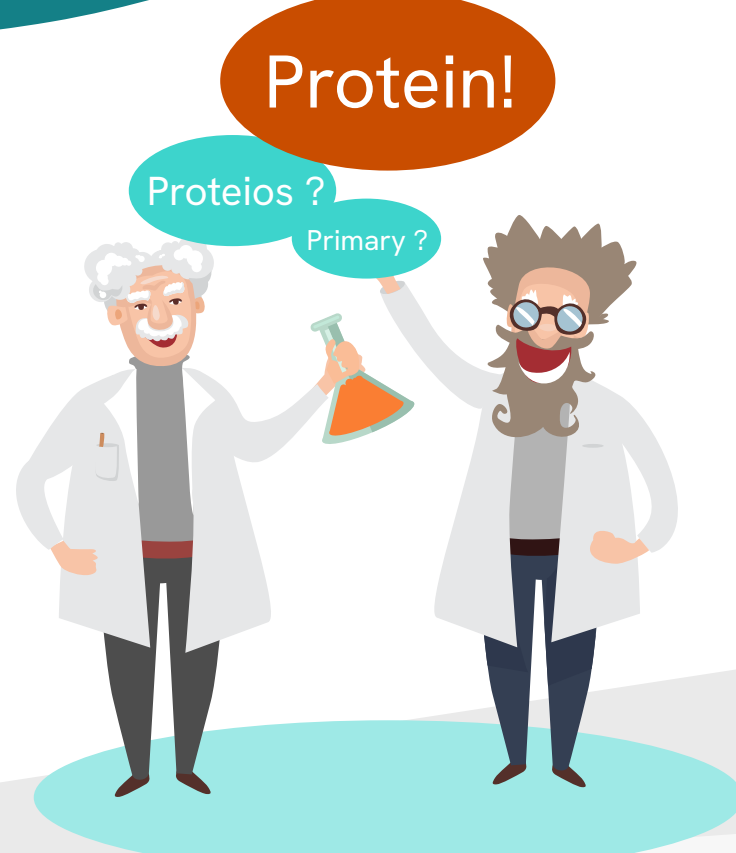


# A brief history of protein-protein interactions

## 1835-1838

**Berzelius** and **Mulder** were confronted with organic material shared by plants and animals, and proposed to call them "proteins", from the Greek word for "primary", proteios.



Biologists and chemists deciphered biology slowly. Key findings advanced knowledge about proteins and led to better understanding of the inner life of cells by the 1950s and 1960s.

1891

Ab/Ag interactions are revealed. Ab have yet to be identified.

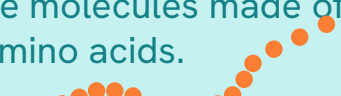


1906

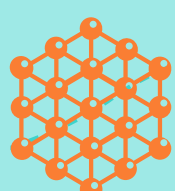
Trypsin and its inhibitor are the first formerly identified PPIs.

1920

Proteins are shown to be molecules made of amino acids.



Late 1950s



X-ray crystallography resolves the structure of proteins starting with carchalot myoglobin.



J. Cowdery Kendren and M. Perutz

1955

Insulin is the first sequenced protein.



F. Sanger

1940

Physical motion is explained by the interaction of myosin and actin.



## 1960s and 1970s

The rise of bioinformatics resulted in the first networks and shined the light on the importance of protein interactions. Key discoveries about proteins made them the center of interest in biology.



1965

The expression of genes is shown to be regulated through proteins interacting with DNA and each other (notion of "operons" and "promoters").

J. Monod and F. Jacob

1968

Protein Kinase A is discovered and leads to the very first transduction signal cascade.

H. Fischer and Edwin G. Krebs



1970

Computer innovations trigger the rise of bioinformatics and first biologic networks.

1971

Most proteins are assumed to be composed of interacting subunits. Interactions become a key part of cellular biology.

## 1970s and 1980s

The growing interest in proteins and their interactions triggered the development of ever-more numerous tools and technologies to study them.

FRET techniques theorized and modeled by T. Förster in 1946 are eventually adapted to the study of PPIs.



1970s

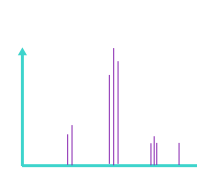
Atomic Force Microscopy.

G. Binnig and H. Rohrer



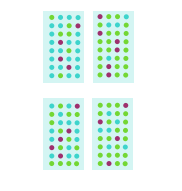
Early 1980s

MALDI and ESI innovations in mass spectrometry allows for macromolecule and protein characterization.



1980s

Microarray technology evolves from DNA chips to protein chips.



1990s

1975

2D gel electrophoresis.

O'Farrell and Klose

1983

Surface plasmon resonance detects biomolecule interactions.

Nylander and Liedberg

1985

Phage display.

G.P. Smith

1989

Yeast two-hybrid approach to PPI studies.

Stanley Fields and Ok-Kyu

## 1990s and 2000s

A new analytical arsenal enabled the astronomical collection of data on proteins. Paired with advances in bioinformatics, this data was transformed into interaction networks of increasing importance and relevance. Interactions are now so critical to the understanding of biology that the terms "genome", "proteome", and "interactome" were invented to cover them.

1990s

Proteomics rises as a discipline of its own.

late 1990s

PPI interactions are shown to depend on critical "hot spots" rather than all interfacing residues.

1999

First use of "Interactome"

Bernard Jacq et al

2000s

More than 40 PPIs are successfully targeted by the end of the decade.

## Recent years

PPIs have become a potential source of new therapies and are being investigated increasingly in pharmaceutical research. Most are still unknown.

2016 ▶ 36 PPI inhibitors have already reached clinical development.

2023 ▶ 20% of PPIs investigated <5% of PPIs structurally characterized

LOADING ...

Who knows how many miracle cures are yet to be discovered?!

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