Module 1: Protein structure

Lecture 2: Biomolecules, history of structure

Lecture 3: Photosynthetic reaction centers

- Roderick Clayton: Purification of photosynthetic reaction center (1968)
- George Feher: Reaction center structure (1974)

Lecture 4: Energy landscape model of protein folding

- Peter Wolynes: to fold into that special native state, a protein molecule must be able to bypass a continuum of glassy states. (1974)
- Jose Onuchic, Ken Dill: folding funnel

Lecture 5: Future of protein folding

- Personal side (Ken Dill)
- AlphaFold
- Protein design

“Pop quiz”

- What is a protein structure?
- Why is it important to resolve protein structure?
- Name a property of amino acids which affects 3D folded structure.
- Name four main methods used to determine protein structure.
- How can proteins fold so much faster than a random search suggests?
- What is the “protein folding problem”?
- What might solving the “protein folding problem” enable?

Today’s agenda

Ken Dill, “Living Histories” (autobiographical)

Structure prediction (AlphaFold)

- Scientific American interview “One of the Biggest Problems in Biology Has Finally Been Solved” (journalistic, narrative)
- PNAS article “Protein folds vs. protein folding: Differing questions, different challenges” (journalistic, argumentative)
- Nature podcast interview (journalistic, narrative) *optional*

Protein design

- Science Magazine overview (journalistic, broad scientific audience)
- TED talk (David Baker)
- iBiology (David Baker)

Nobel Prize in Chemistry 2024

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David Baker

Prize share: 1/2

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Demis Hassabis

Prize share: 1/4

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John Jumper

Prize share: 1/4

The Nobel Prize in Chemistry 2024 was divided, one half awarded to David Baker "for computational protein design", the other half jointly to Demis Hassabis and John Jumper "for protein structure prediction"

Guiding questions

- What was the scientific breakthrough?
- Can you identify a key insight(s) needed for the breakthrough?
- How do the findings align with or challenge existing models?
- What are some potential implications of their findings?
- Pay attention to the sources, their attributes and “genre”

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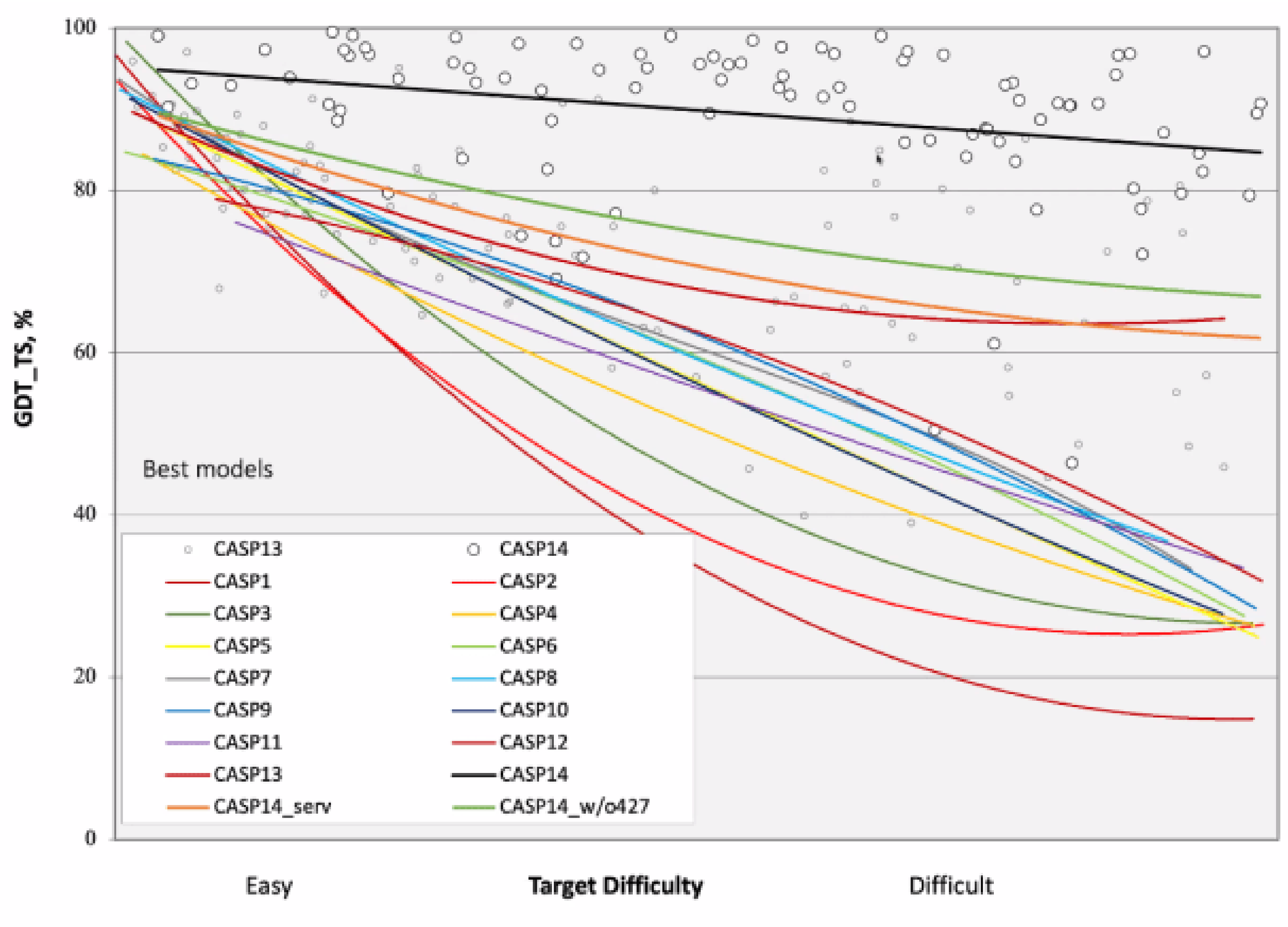
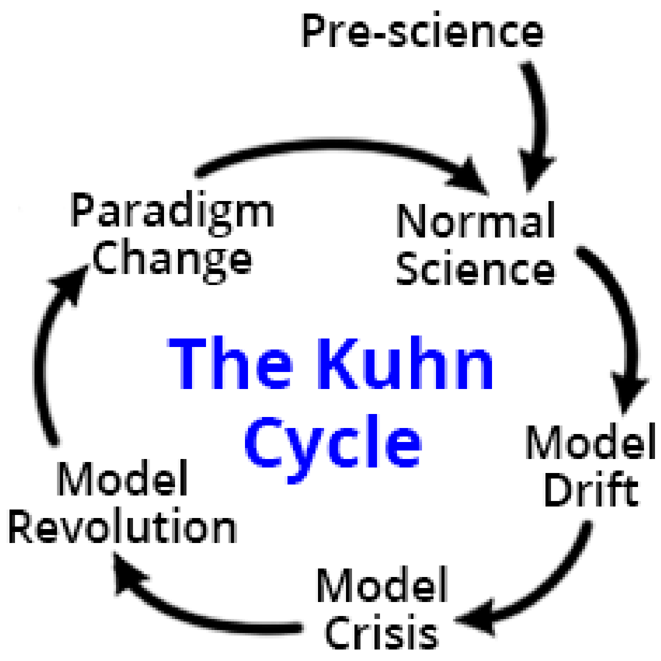
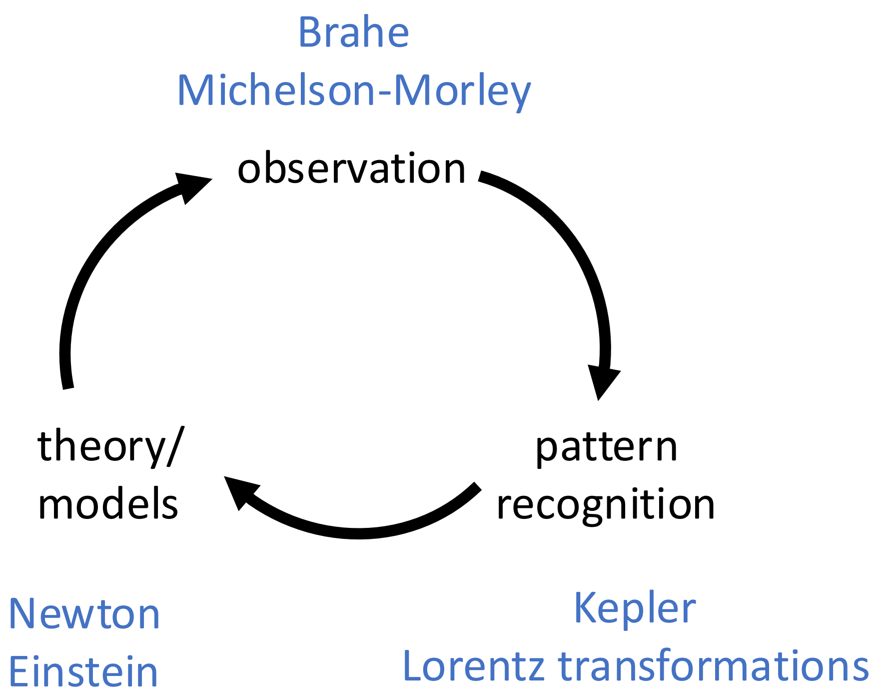
Critical Assessment of Structural Prediction competition



https://www.blopig.com/blog/2020/12/casp14-what-google-deepminds-alphafold-2-really-achieved-and-what-it-means-for-protein-folding-biology-and-bioinformatics/

Protein folds vs. protein folding:
Differing questions, different challenges





Brahe
Michelson-Morley

observation

theory/
models

pattern
recognition

Newton
Einstein

Kepler
Lorentz transformations

Others, including us, feel that solving the protein-folding problem means making accurate predictions of structures from amino acid sequences starting from first principles based on the underlying physics and chemistry -Moore et al.

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