Applications of deep learning models in biology

projects week 3

Overview week 2

- Designed a deep learning model to predict protein stability change for mutations
- Optimized the model's architecure

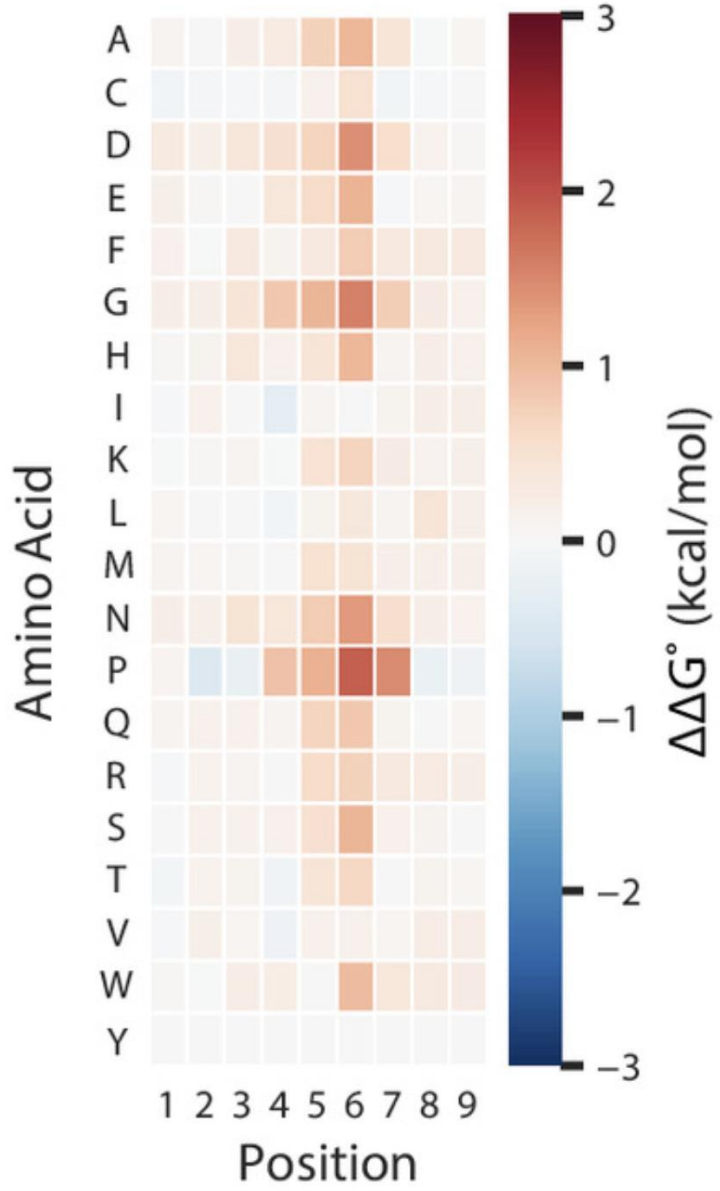
- For your presentations:
  - Explain architecture and design rationale
  - Compare with a minimal model following same architecture
    - Performance
    - Number of parameters

- Put results for validation set on the board – **this is not for your grade**
  - Performance (architecture, pearson correlation, number of parameters)

Biological application

Next – **apply the model for biology**

- Use the predictions in a biological setting
- What biological problem can the model address
- How can you validate the outcome?



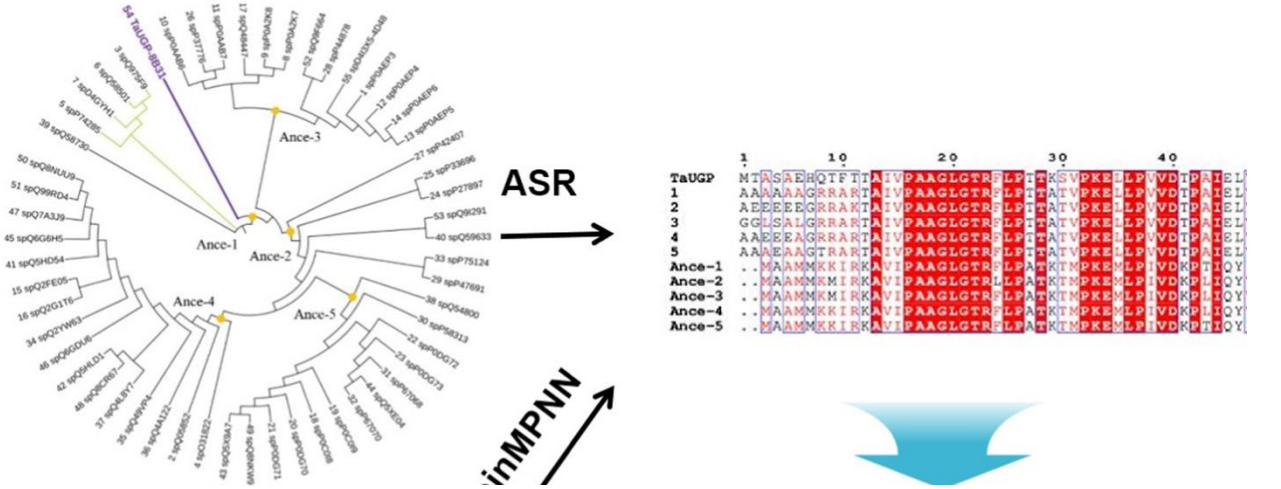
https://www.pnas.org/doi/10.1073/pnas.2314853121

Example: protein engineering

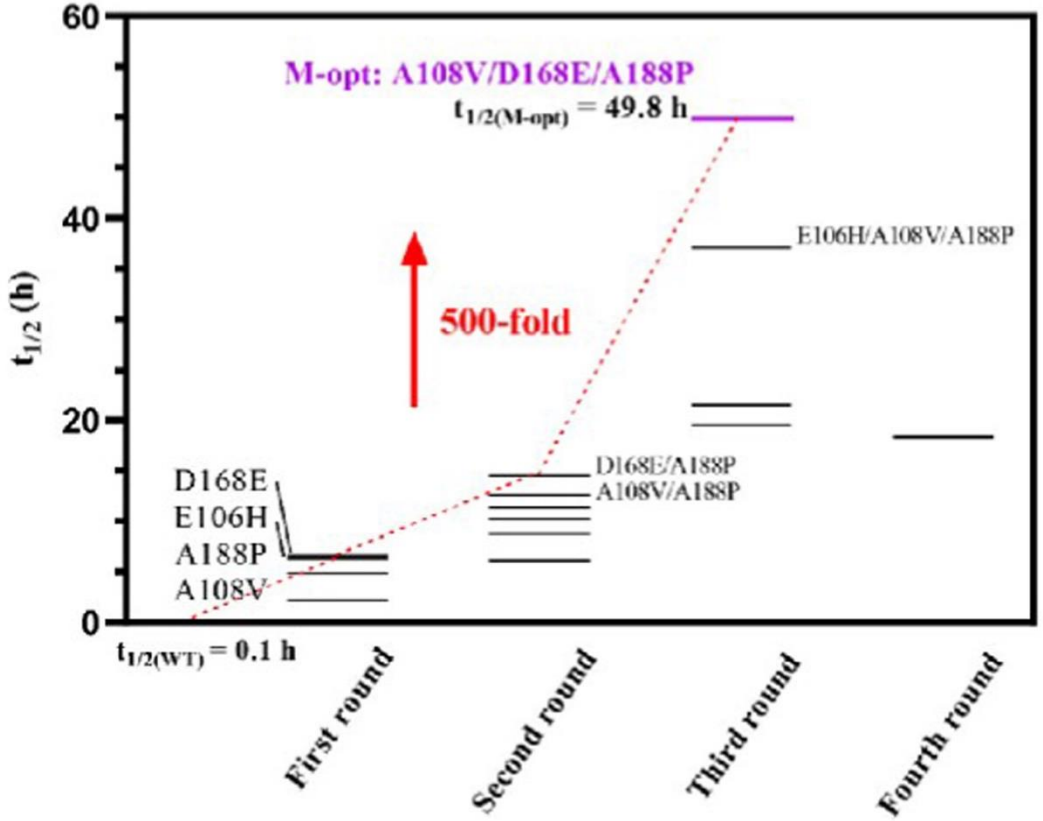
- Industrial applications - improved stability can improve:
  - Efficiency/yield
  - Resistance to temperature (thermostability)
- Sequentially mutate sequence and experimentally measure result
- Idea:

Apply predictions of model
for engineering a more stable protein

Example: PETase

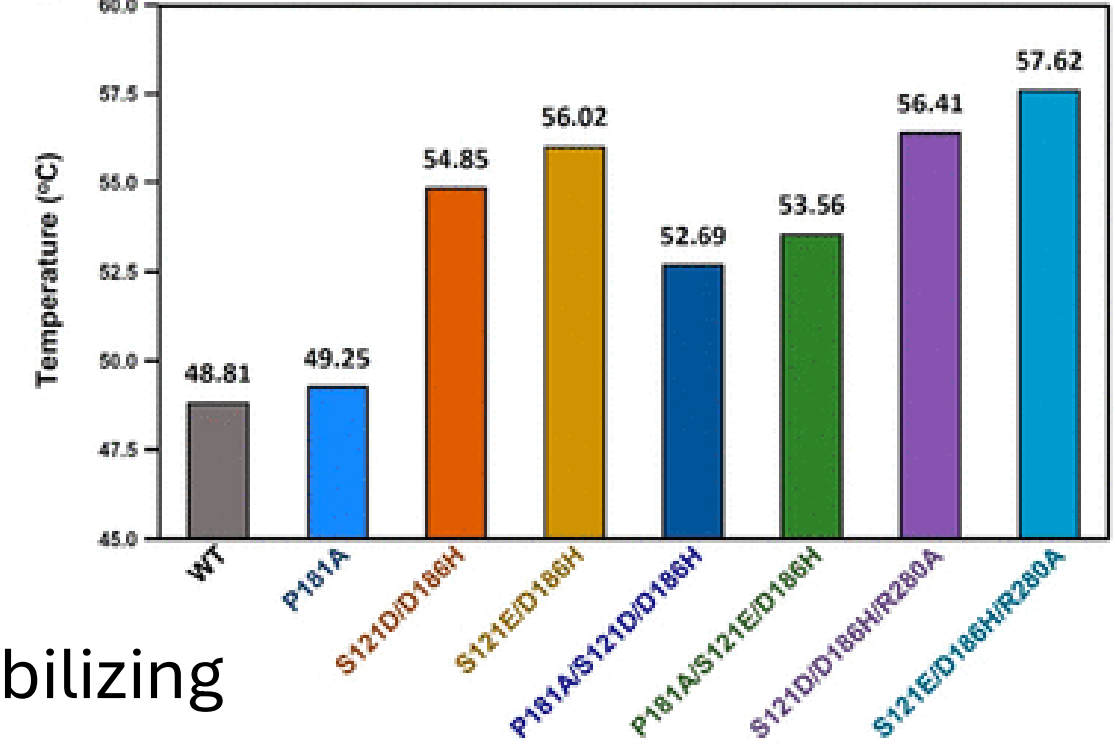


- Enzyme for degrading plastics
- Favor higher temperatures
- Compound/sequential mutations to improve thermostability
- **Stability != function**



https://doi.org/10.1016/j.bidere.2025.100005
https://pubs.acs.org/doi/10.1021/acscatal.9b00568

Example: PETase



- Predict stabilizing mutations
- Check with experimentally known stabilizing mutations
- e.g. S121E -> D186H -> R280A
- Questions to address:
  - Is each step predicted to be stable?
  - More stable than other mutations at the same sites?
  - Does compounding mutations work with the model?

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Biological application of models

- Think of your own ideas, e.g.,
  - Genetic variants for (rare) disease
  - Protein engineering
  - Identifying functional regions
  - Structural effects
  - etc
- Discuss with us

If the idea does not work its fine, we care about the idea, approach, implementation and takeaways