Protein Folding

CSS Presentation by Niclas Ståhl

Paper: Theory of protein folding by Onuchic and Wolynes (2004)

Overview

1. What is a protein?

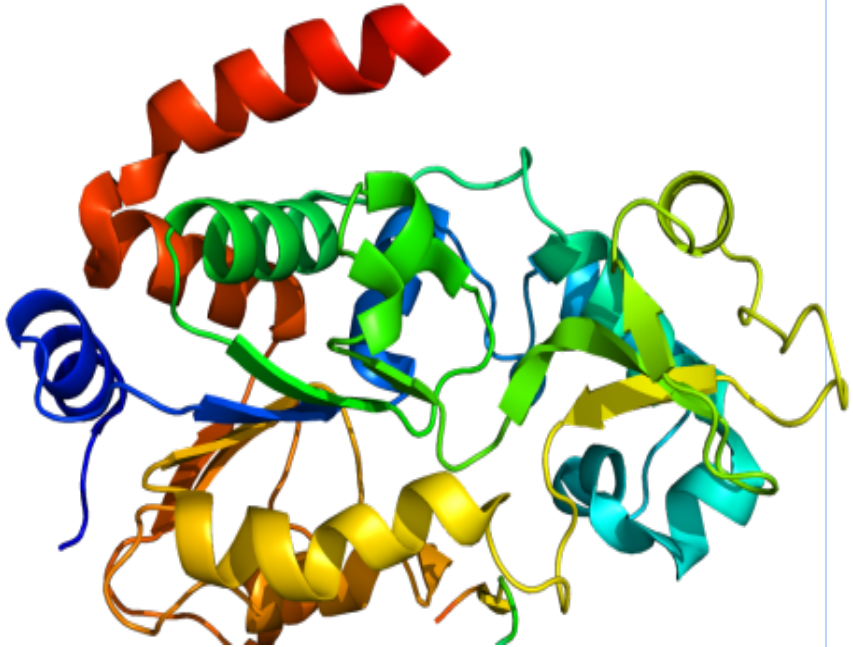
2. Finding the structure of a protein

3. Why is this hard problem?

1. What is a protein? 2. Finding the structure of a protein 3. Why is this problem hard?

What is a protein?

- Huge Molecules
- Long chain of amino acids
- DNA is the blueprint for proteins



- Proteins control reactions and is one of the main building blocks in the body.

- The function of the protein is dependent on its folded state.

- Alzheimers and ALS are just a few diseases due to protein misfolding.

- Takes less than a microsecond for a protein to fold.
- Still a mystery how this happens.
- Reliable process.

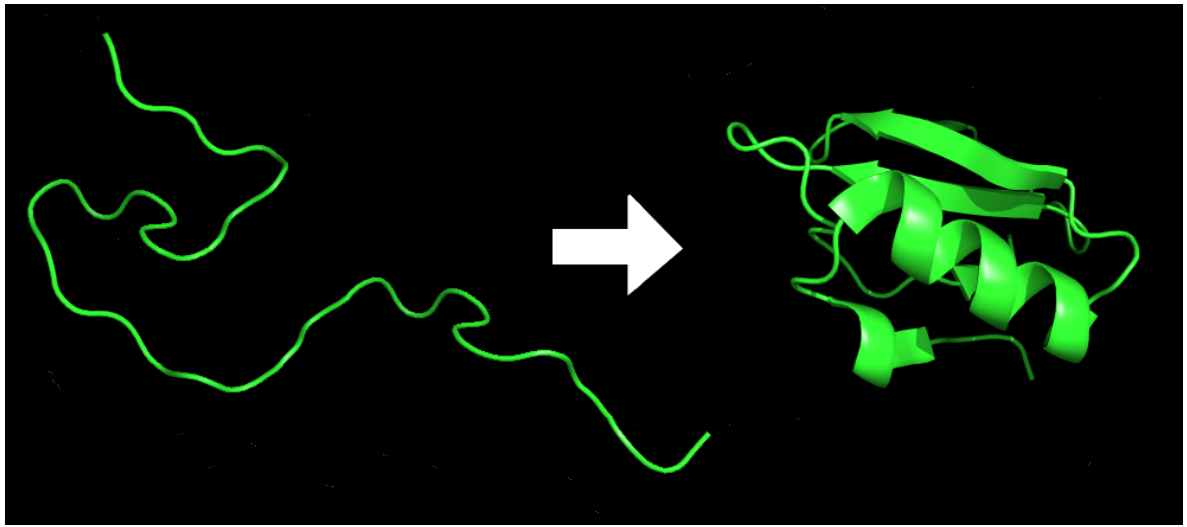
Finding the structure of the protein

The structure of proteins
can be found by X-ray crystallography.

A costly and time consuming task

- More than a week and 100000$ per protein.
- Around 50000 different proteins in the human body.

Find a “function” that maps a given amino acid sequence to the corresponding protein structure



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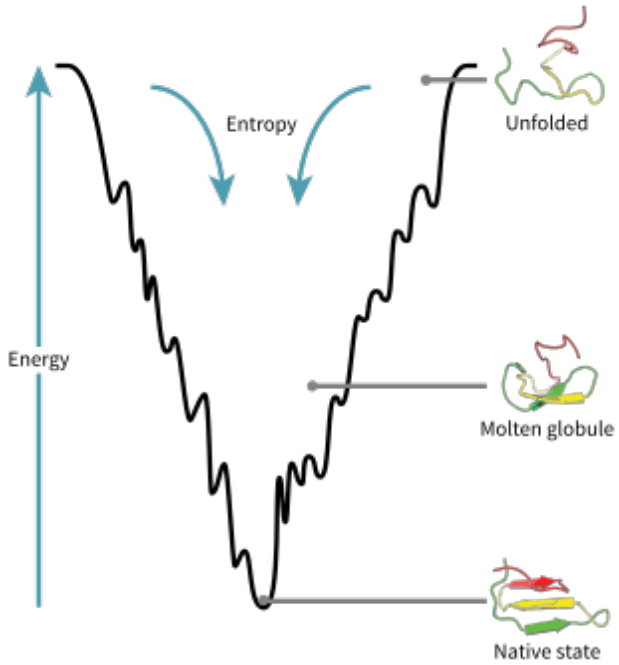
Random search?

- Over 3^{300} configurations
- Tells us that protein folding can’t be a random process in nature (*The Levinthal paradox*)

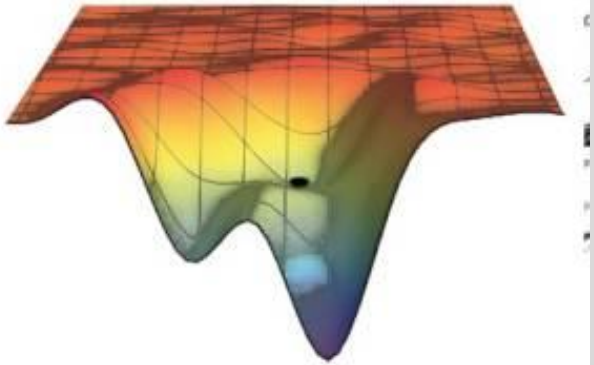
Observations

- Energy is released during folding
- Transient states differ

- Look at the energy landscape.
- Entropy will increase over time.
- Assume the landscape has the form of a funnel.



- This behavior can be simulated with an simulated annealing algorithm.
- May get stuck in local optima.



- Atomic level (agent based) simulations
- Computationally heavy
- fold@home

Why is this problem hard?

- Multidimensional energy landscape.
- Energy landscape is not always a funnel.
- Simulation will only give an approximation.

- Computationally heavy
- May be compared with the Ising model in 3D and moving magnets.

Depend on a lot more than just the sequence of amino acids.

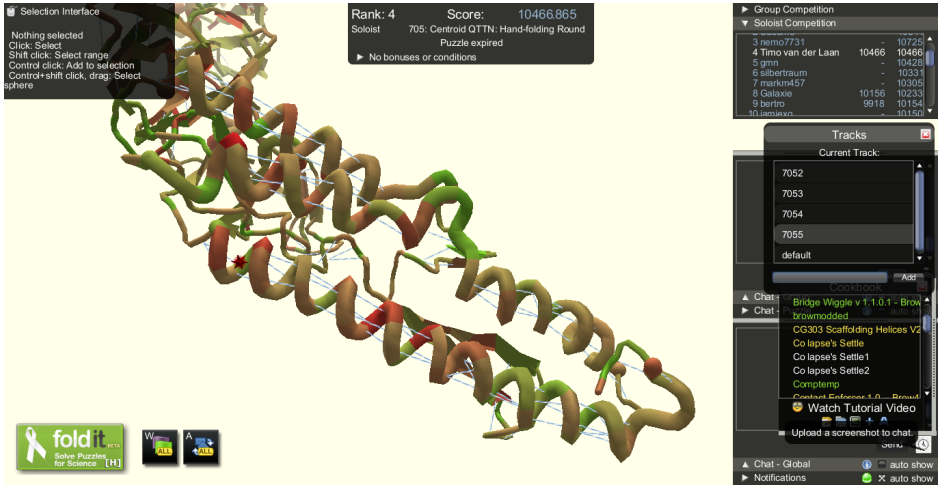
- pH
- Temperature
- Reaction solution

Computer game fold.it

Humans performed better than computers

Why?

- Intuition
- Used to 3D
- Cooperation



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Thank you for listening!