Protein Folding

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Overview

1. What is a protein?

2. Finding the structure of a protein

3. Why is this hard problem?
What is a protein?
1. What is a protein?

2. Finding the structure of a protein

3. Why is this problem hard?

- 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.

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

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

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Observations

- Energy is released during folding
- Transient states differ

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3. Why is this problem hard?
● Look at the energy landscape.

● Entropy will increase over time.

● Assume the landscape has the form of a funnel.

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● 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

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Why is this problem hard?
● Multidimensional energy landscape.

● Energy landscape is not always a funnel.

● Simulation will only give an approximation.

1. What is a protein?  
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3. Why is this problem hard?
• 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

1. What is a protein?  
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3. Why is this problem hard?
Computer game fold.it
Humans performed better than computers

Why?
- Intuition
- Used to 3D
- Cooperation

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3. Why is this problem hard?
Thank you for listening!