Université Paris Cité

Folding of a simplified protein model by Monte Carlo algorithm

Anis MERABET

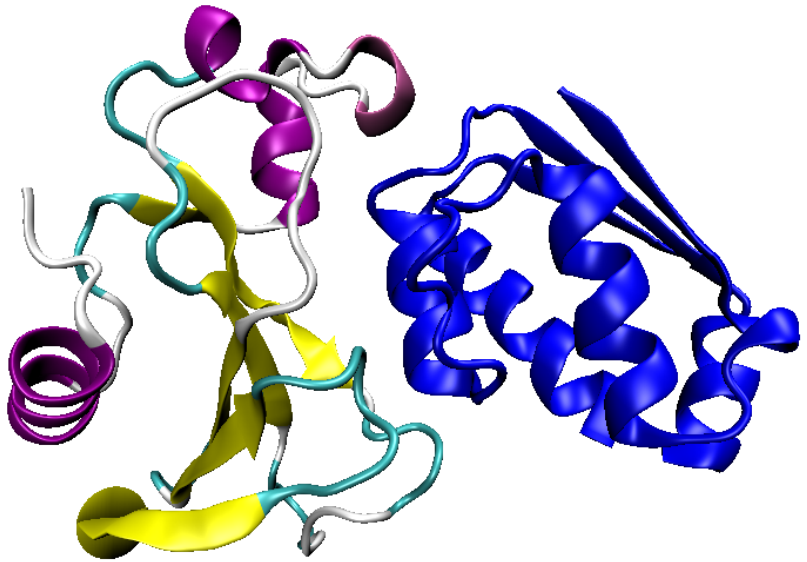
Master 2 Bio-informatique

Based on:

C. Thachuk, A. Shmygelska, and H. H. Hoos, “A replica exchange Monte Carlo algorithm for protein folding in the HP model,” BMC Bioinformatics, vol. 8, no. 1, p. 342, Sep. 2007, doi: 10.1186/1471-2105-8-342.

15 septembre 2023

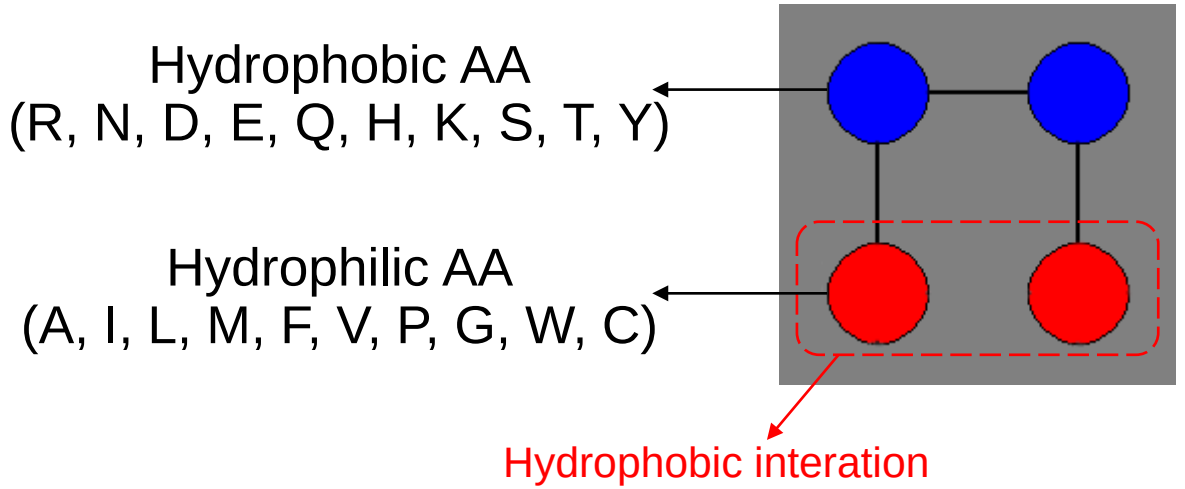
Introduction



Wikipedia

Real protein

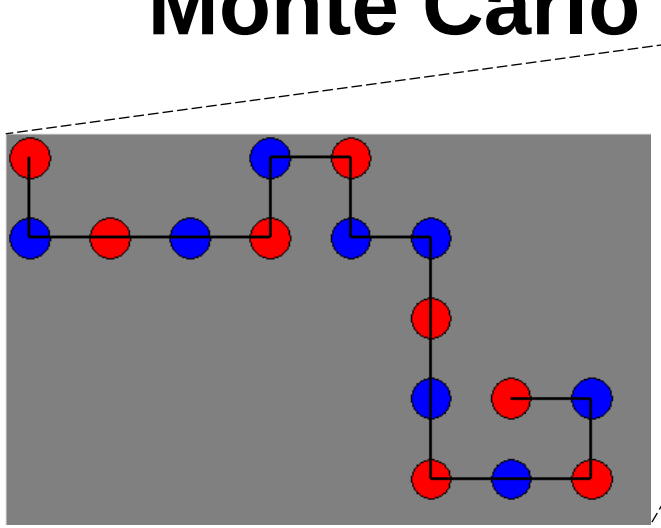
HP model

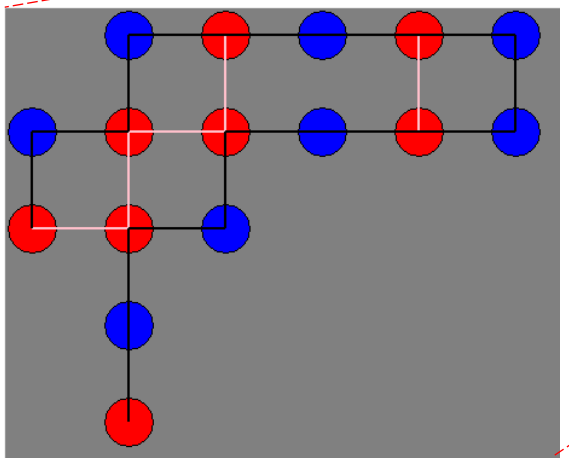


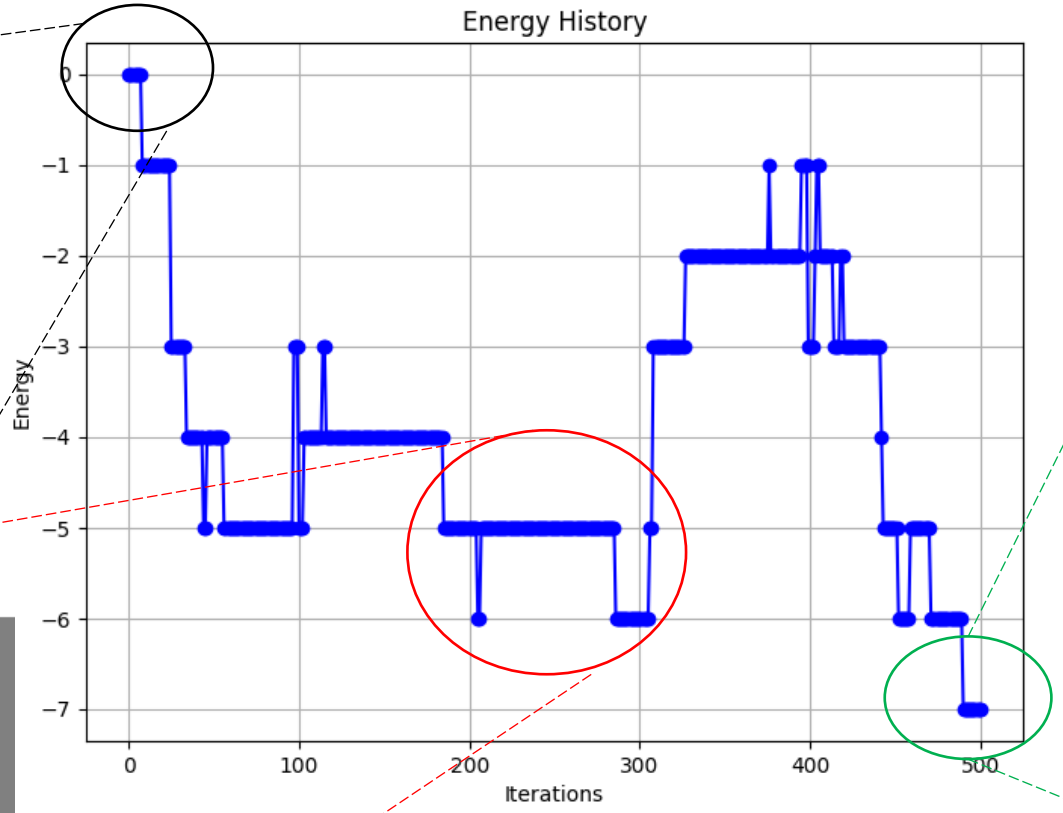
Study hydrophobic interations in 2D/3D

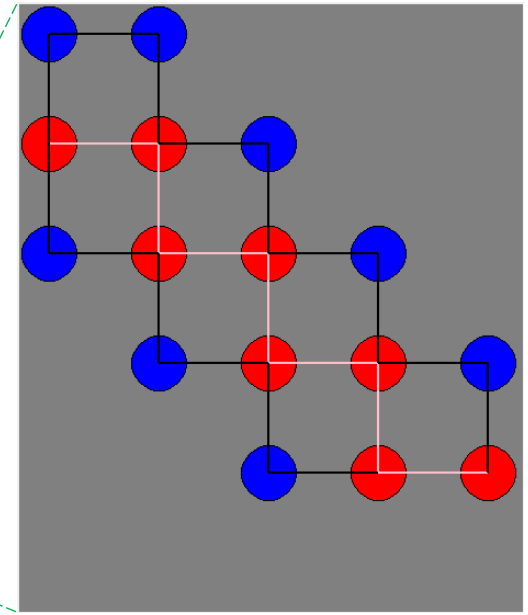
Introduction

Monte Carlo









Escape local minima

Introduction

Monte Carlo

$$\begin{cases} 1 & \text{if } \Delta E < 0 \\ e^{\frac{-\Delta E}{T \times K_B}} & \text{else} \end{cases}$$

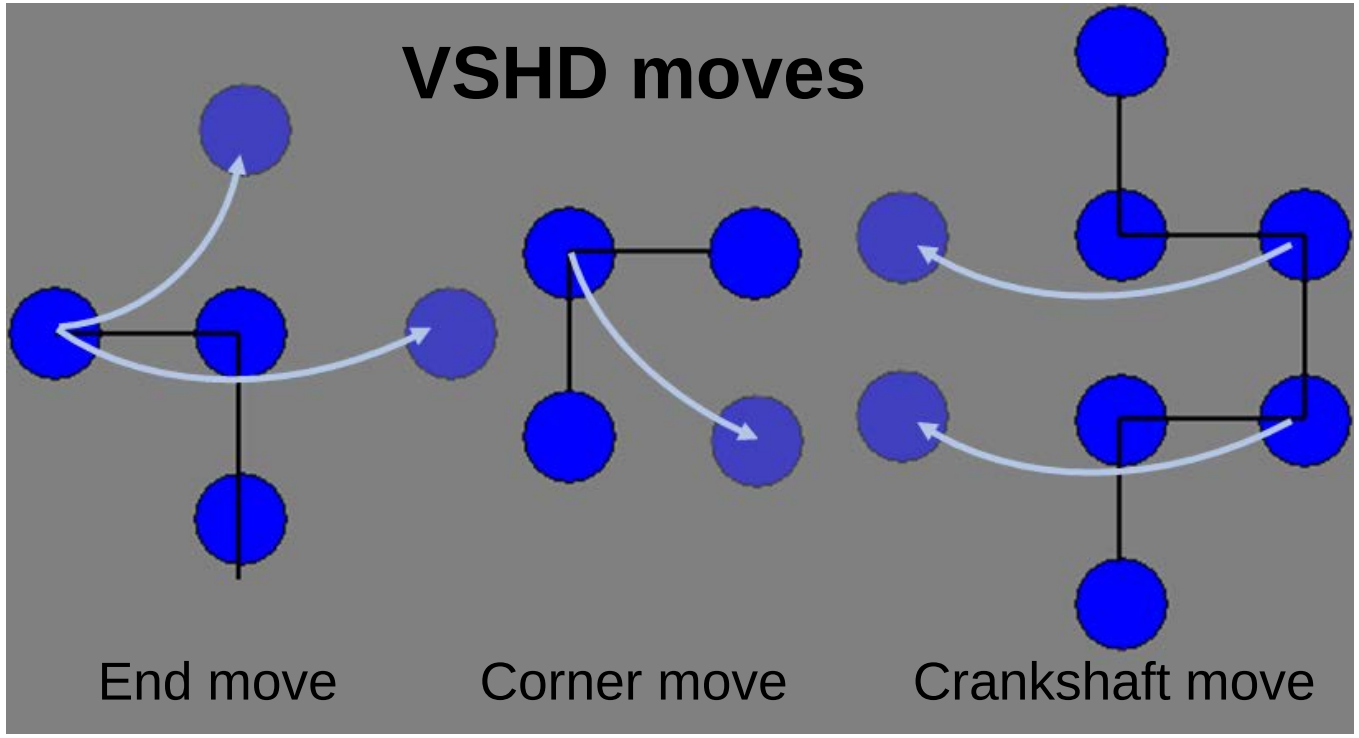
ΔE: energy difference between two conformations

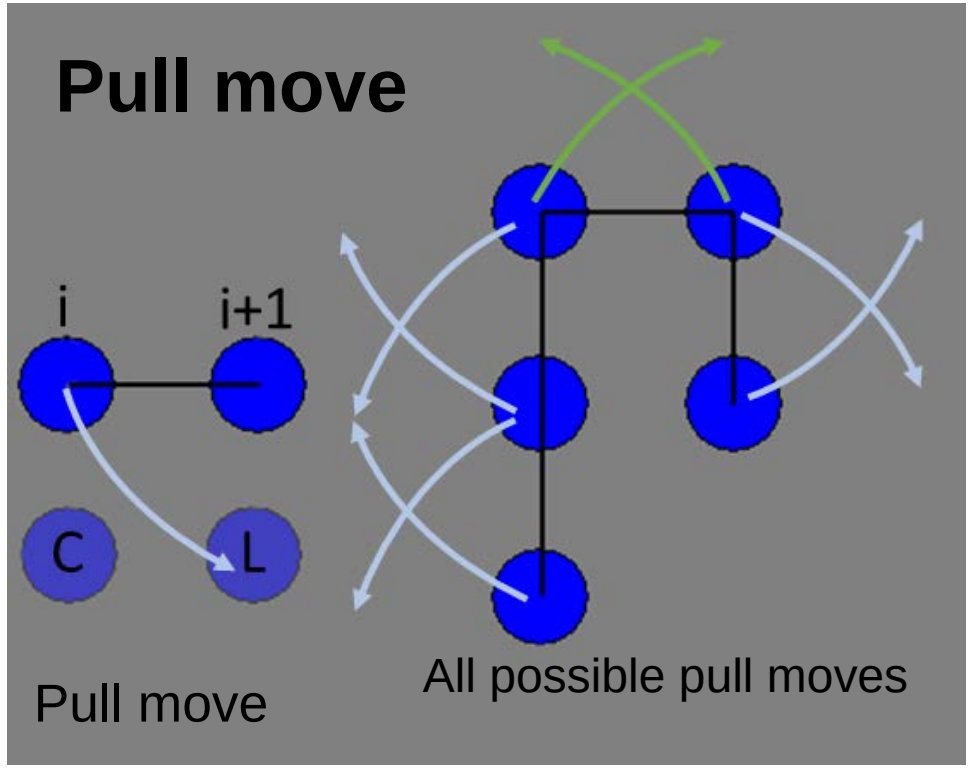
T: temperature

KB: Boltzmann's constant

Methods

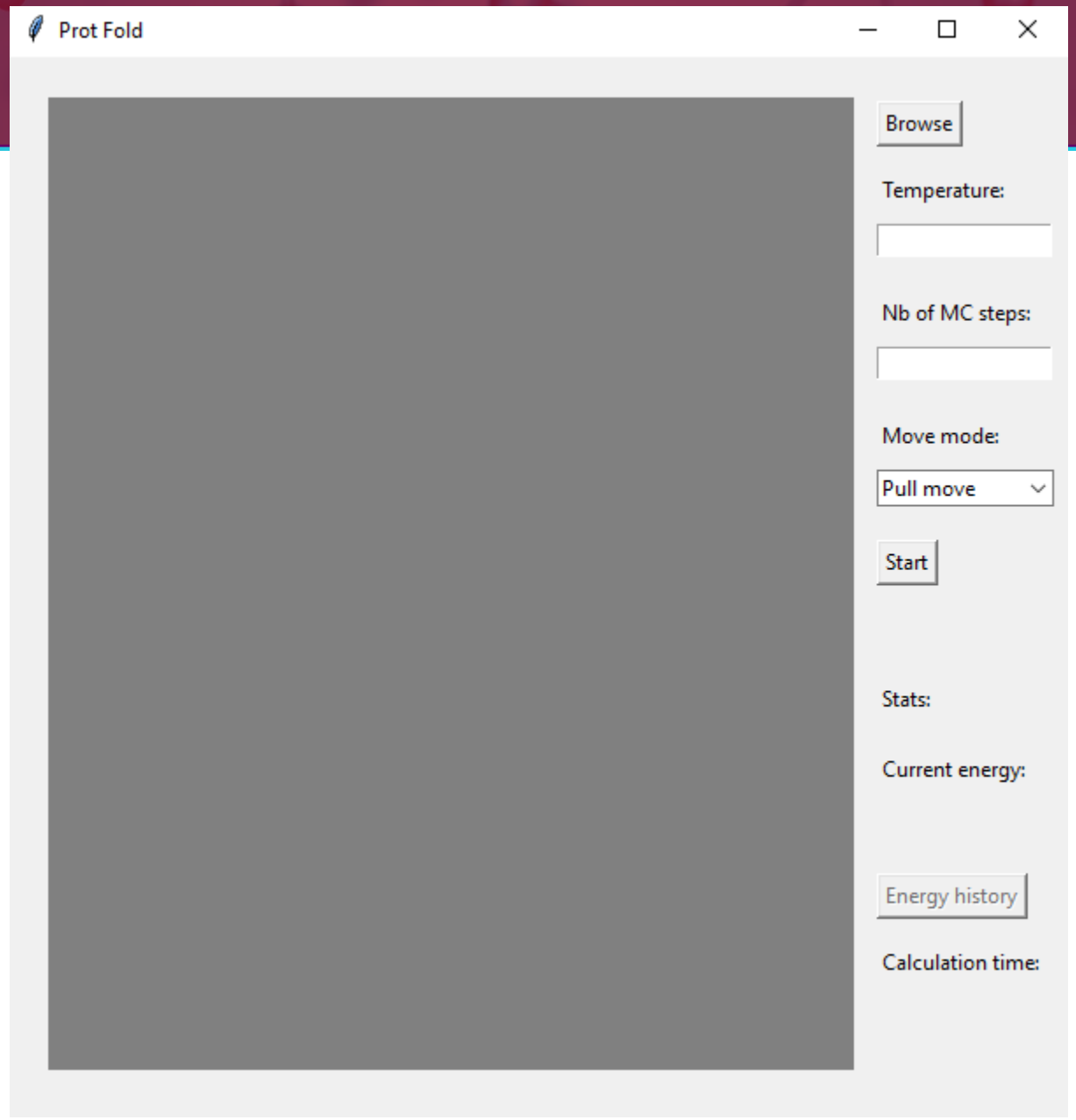
Move modes





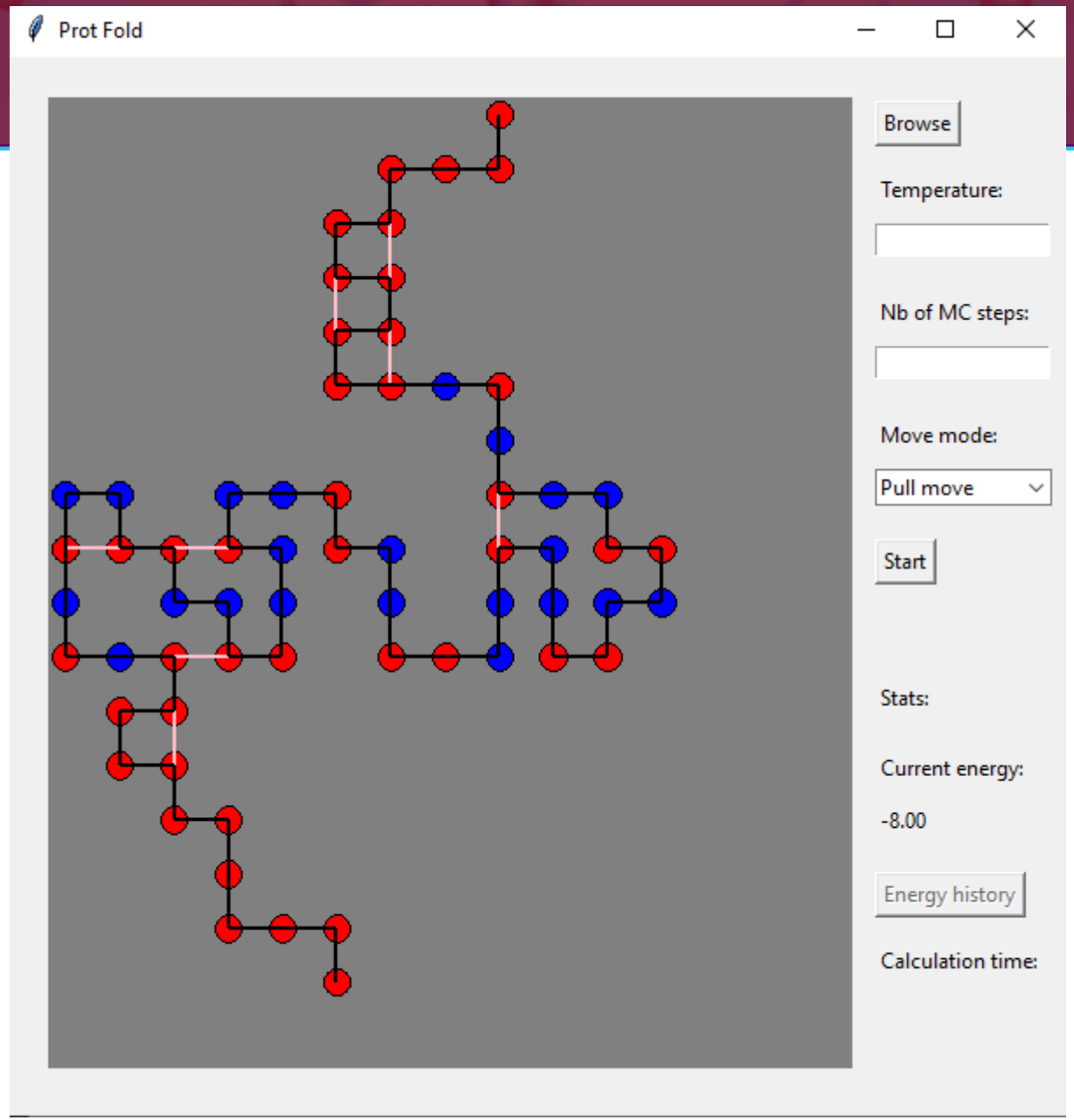
Methods

Prot Fold



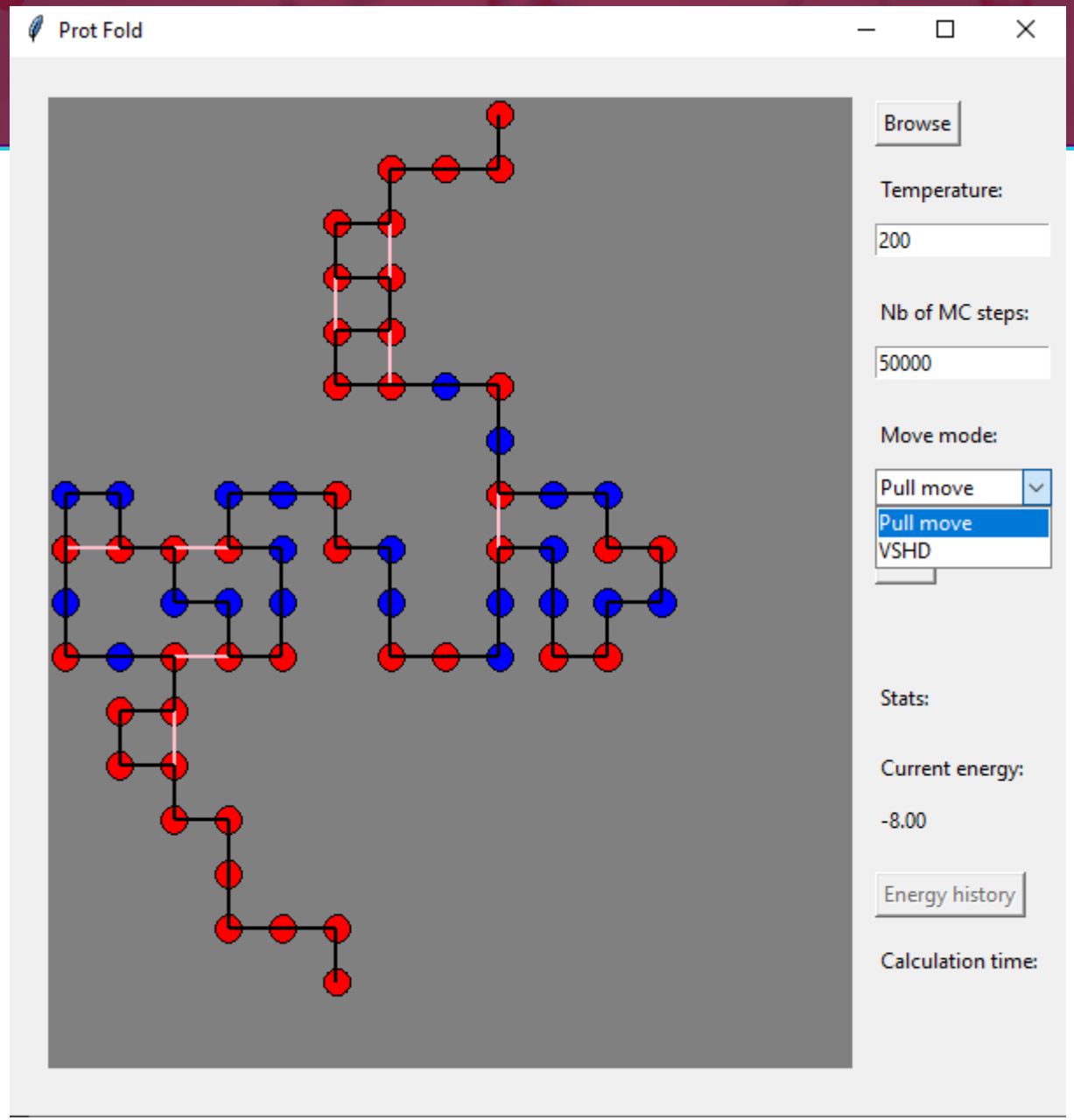
Methods

Prot Fold



Methods

Prot Fold



Methods

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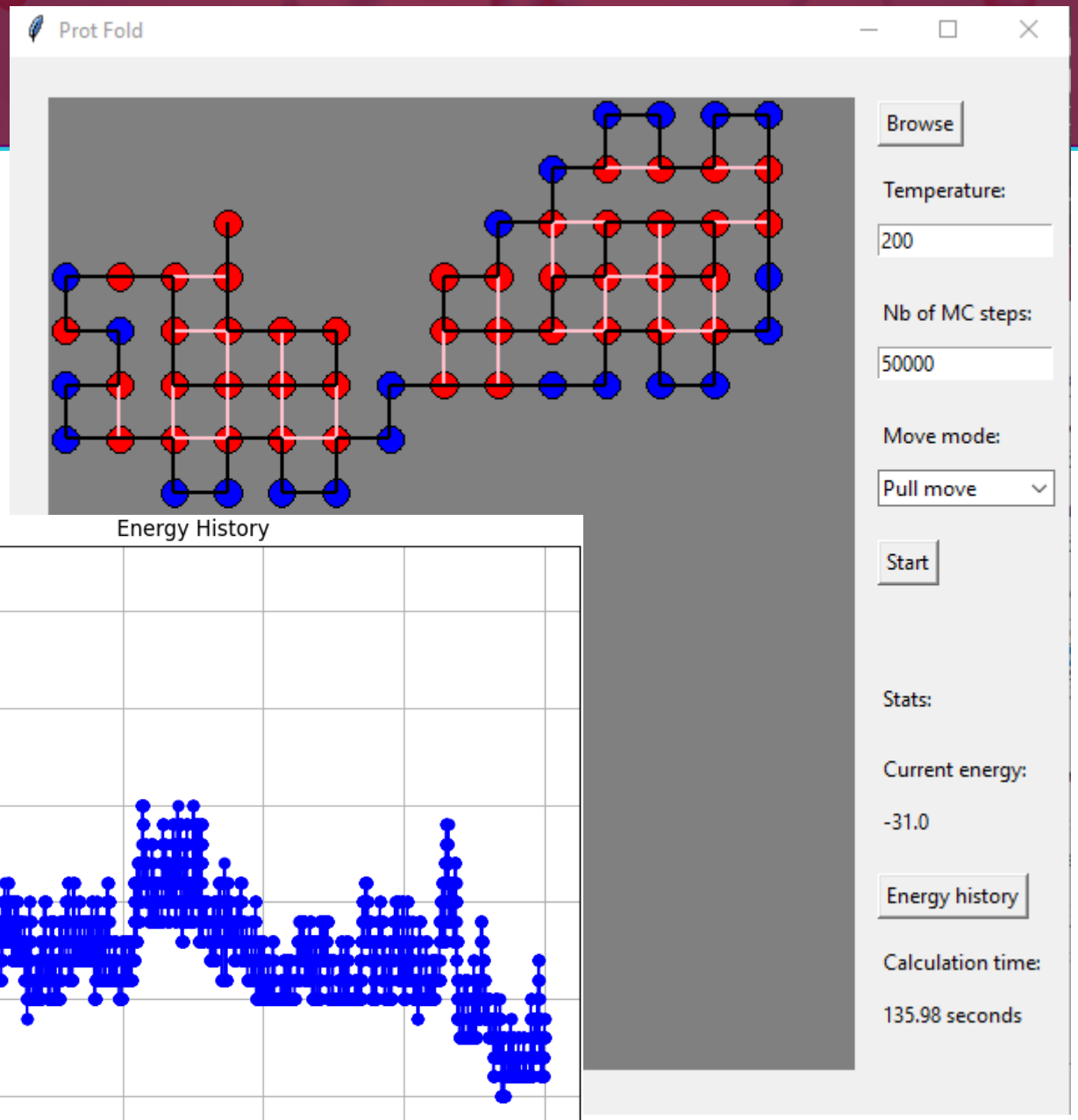


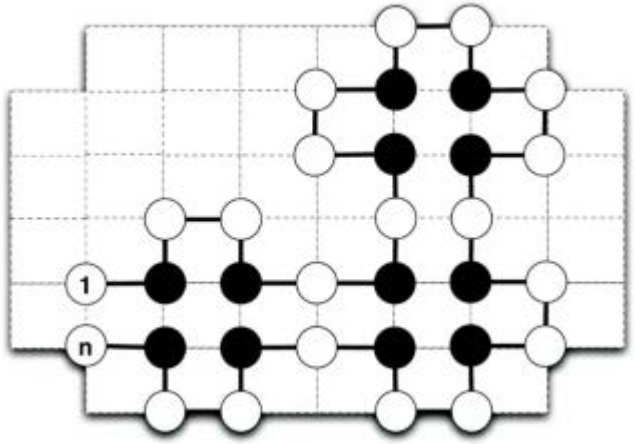
Results

Study the impact of the temperature

$$\begin{cases} 1 & \text{if } \Delta E < 0 \\ e^{\frac{-\Delta E}{T \times K_B}} & \text{else} \end{cases}$$

Benchmark protein 1

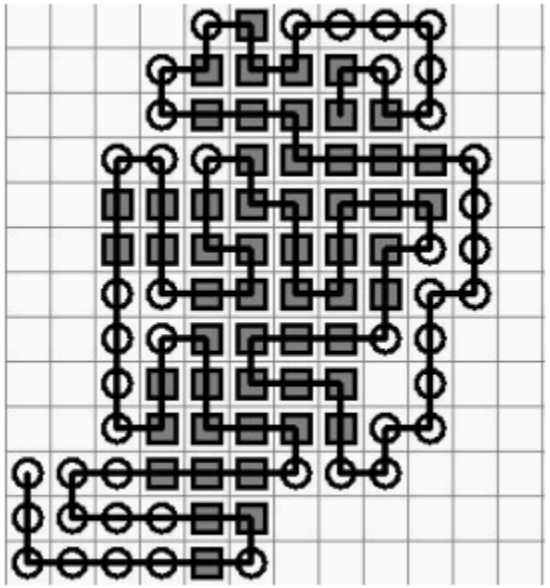
- 32 AA
- Optimal energy: -12



Thachuk, Shmygelska, and Hoos 2007

Benchmark protein 2

- 100 AA
- Optimal energy: -48



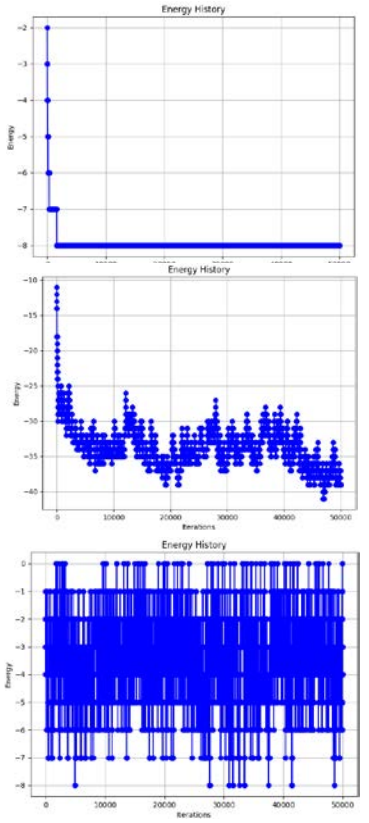
Lesh, Mitzenmacher, and Whitesides 2003

Results

Study the impact of the temperature

- Number of steps: 50000
- Move mode: Pull move

Temperature	Benchmark protein 1	Benchmark protein 2
40	-8	-33
120	**-9**	-37
190	-8	**-39**
300	-4	-27



- Low temperature decrease escaping local minima and high temperature decrease conformation stability.
- The optimal temperature might depend on protein size

Results

Compare our Monte Carlo simulation to REMC form Thachuk *et al*

- Number of MC steps: 50000
- Temperature: 190

	Thachuk *et al*		Our MC simulation	
Benchmark	REMC (vshd)	REMC (pm)	With vshd	With pm
S1-8 (65 AA)	-35	-42	-24	-33
S1-9 (85 AA)	-50	-53	-30	-40
S1-10 (100 AA)	-46	-50	-31	-37
S1-11 (100 AA)	-46	-48	-30	-35

- Pull moves provide better results than VSHD moves.

Results

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- Pull moves provide better results than VSHD moves.
- REMC performed better than our MC simulation.

Conclusion and perspective

- **Pull moves** performed better than **VSHD moves** probably because they offer a larger conformation reachability.
- **REMC** performed better than our **MC simulation** probably because it considers a wide range of temperature.

- Upgrade our algorithm to REMC.
- Perform computationel assessment to obtain reproducible results.

Thank you for your attention