SYSC-5104

Methodologies for Discrete-Event Modelling and Simulation

Protein Folding in a two dimensional Hydrophobic Polar Model

(Assignment 2)

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Introduction:

Building models of any biological phenomenon usually consists of finding a certain abstraction of some type. Models can be used to understand a problem from a certain point of view. Since proteins are complex molecules, there are many simplified models or simple exact models (SEMs) of proteins. The most commonly used SEM is the HP model where amino acids are classified to be either a hydrophobic amino acid or a polar amino acid.

This model represents the hydrophobic-polar protein folding model. The paper that this model was based on is entitled "Protein Folding in the Two dimensional Hydrophobic Polar Model based on Cellular Automata and Local Rules" [1] and is written by Alia Madain , Abdel Latif Abu Dalhoum , and Azzam Sleit from The University of Jordan, Amman.

Model Definition:

The CA proposed is a two-dimensional one with a homogeneous regular grid. The CA states can be one of the following: Hydrophobic amino acid (H), Polar amino acid (P), or empty cell state. The neighbourhood assumed is an extended Moore neighbourhood, which includes the diagonals of a core cell. The boundary of the cell space is null, meaning the boundary is not wrapped.

We simply assume that the amino acids of the primary sequence are located at (x=0) in the initial configuration of the CA, and we assume that the row located at (x=0) corresponds to the core of the folded protein. So assuming that water is surrounding the protein (as it is in nature) then polar amino acids will surround the hydrophobic core. This is the first rule: If it is a polar amino acid then it should surround the hydrophobic core and the hydrophobic amino acids stay in place. If the polar amino acid move in the direction from the core of the protein to the water environment, the sequence will move accordingly since the protein is a connected chain of amino acids. In other words, if the cell in the cellular automata is in state P, and P is going to move over the 2D grid, then all cells to the right are going to move in a cascade or a recursive manner. Assuming x on the vertical axis and y on the horizontal axis, and one cell is going to move, the following rules apply:

1. If the moving cell is (P) and the state in the cell to the right is empty and the state in the next cell to the right is (P) then it will move over y axis. If the next cell is occupied, then it will move over x axis also.
2. If the moving cell is (P) and the state in the next cell to the right is (H), then it will move over both dimensions (x and y).

3. If the moving cell is (H) and the cell to the right has an (H) state, it will move over the y axis only. If the position is occupied then the H state stay in place until there is a free space on the right.

4. If there are any spaces or empty cells between any two cells, a compactness rule applies. Also if there is more (P) cells on the bottom of the amino acid (H) core, they will go to the top for compactness.

	(-2,-2)	(-2,-1)	(-2,0)	(-2,1)	(-2,2)	
	(-1,-2)	(-1,-1)	(-1,0)	(-1,1)	(-1,2)	
(0,-3)	(0,-2)	(0,-1)	(0,0)	(0,1)	(0,2)	(0,3)
	(1,-2)	(1,-1)	(1,0)	(1,1)	(1,2)	
	(2,-2)	(2,-1)	(2,0)	(2,1)	(2,2)	

Figure 1: Model Neighbourhood

Cell-DEVS Formal Specification:

- M = <Xlist, Ylist, I, X, Y, d, N, {r,c}, C, B, Z, SELECT>
- Xlist = { Ø };
- Ylist = { Ø };
- I = { Ø };
- X = Y = {0,1,2};
    - 0 means an empty cell
    - 1 means a Polar amino acid (P)
    - 2 means a Hydrophobic amino acid (H)

d = 100;

N = (-2,-2), (-2,-1), (-2,0), (-2,1), (-2,2), (-1,-2), (-1,-1), (-1,0), (-1,1), (-1,2), (0,-3), (0,-2), (0,-1), (0,0), (0,1), (0,2), (0,3), (1,-2), (1,-1), 1,0), (1,1), (1,2), (2,-2), (2,-1), (2,0), (2,1), (2,2)};

r = 30; c = 12;

C = {Cij | i ϵ [0,11], j ϵ [0,29]};

B = {Ø};

Z = Inverse neighbourhood of N

SELECT = { (-1,0), (0,1), (0,0), (0,-1), (1, 0)}

Simulation Results:

Sequence Tested: $PHP_2(HP)_3PH(HP)_2PHP_2HP$

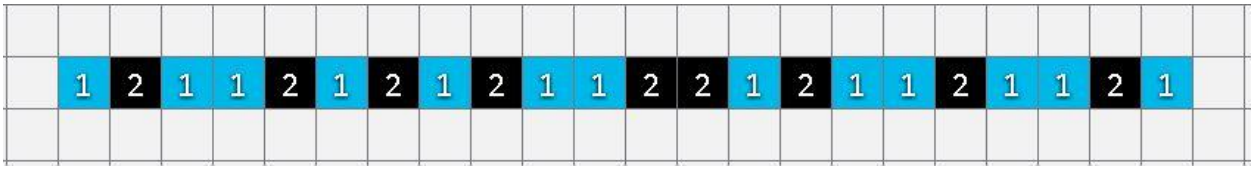

Figure 2a: sequence starting orientation

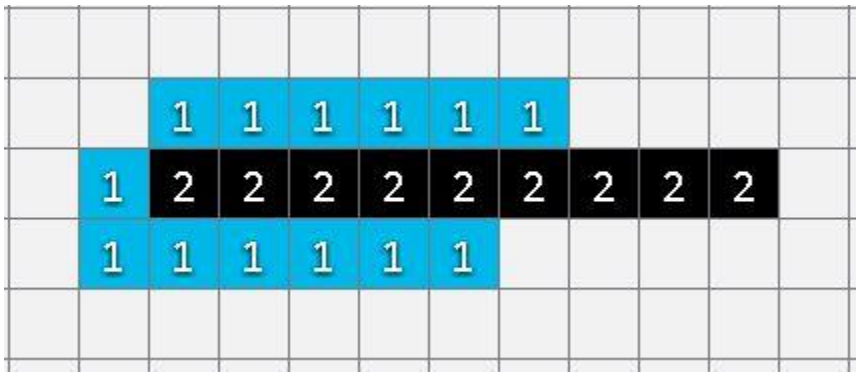

Figure 2b: sequence ending orientation

The final orientation of the sequence shows that the Hydrophobic amino acids moved towards each other to form a hydrophobic core and that the Polar amino acids moved to surround the hydrophobic core.

Sequence Tested: $H_2P_2(HP_2)_6$

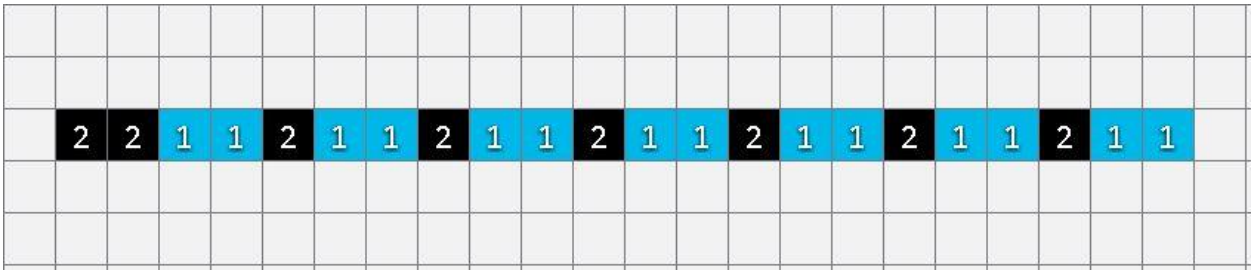

Figure 3a: sequence starting orientation

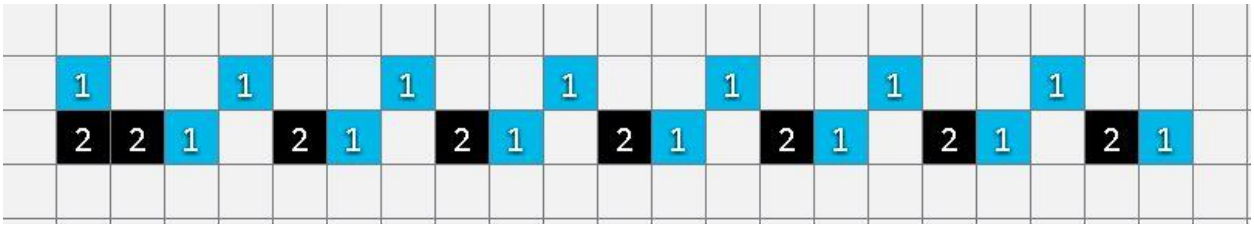

Figure 3b: sequence 3rd position

We can see here in figure 3b that rule one was enacted since P moved over x axis when cell to the right is occupied with a P cell.

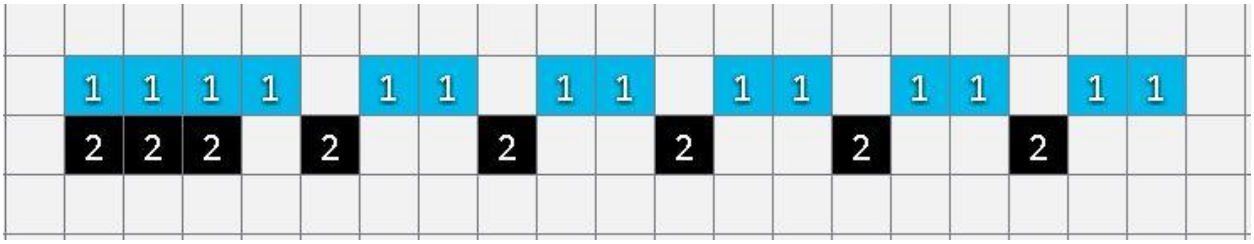

Figure 3c: sequence 5th position

Here we see in figure 3c that rule two was enacted since P moved over x and y axis when cell to the right is occupied with an H cell.

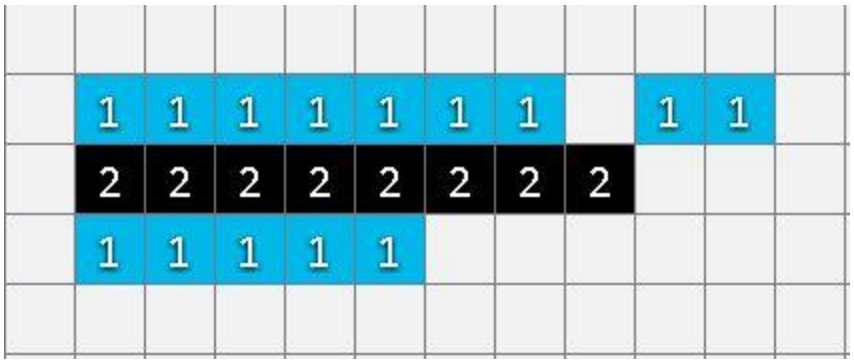

Figure 3d: sequence 15th position

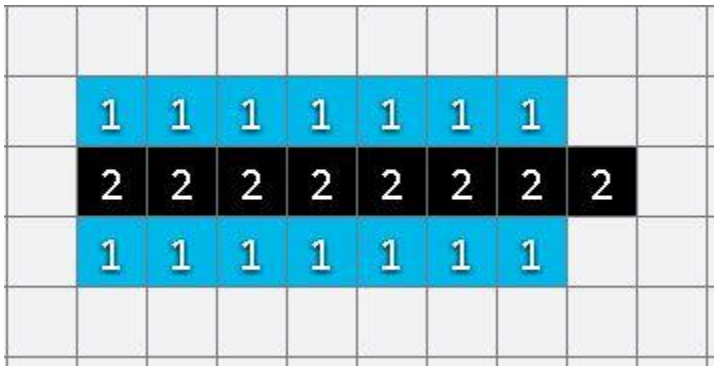

Figure 3e: sequence ending orientation

In Figure 3e we see that the compactness rule was enacted when the upper surface had more P cell than the bottom surface.

Sequence Tested: $P_2HP_2(H_2P_4)_3$

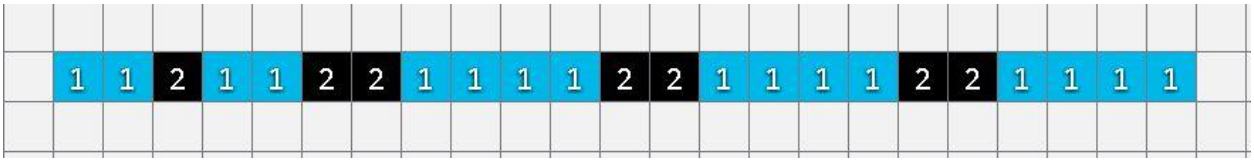

Figure 4a: sequence starting orientation

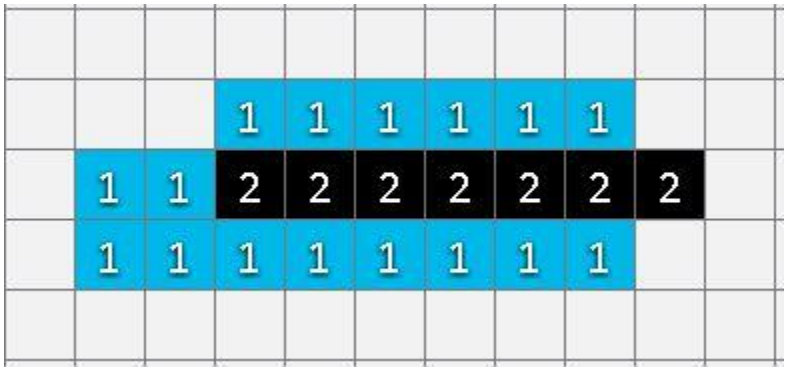

Figure 4b: sequence ending orientation

The final orientation of the sequence shows that the Hydrophobic amino acids moved towards each other to form a hydrophobic core and that the Polar amino acids moved to surround the hydrophobic core.

Sequence Tested: $(HP)_2PH(HP)_2(PH)_2HP(PH)_2$

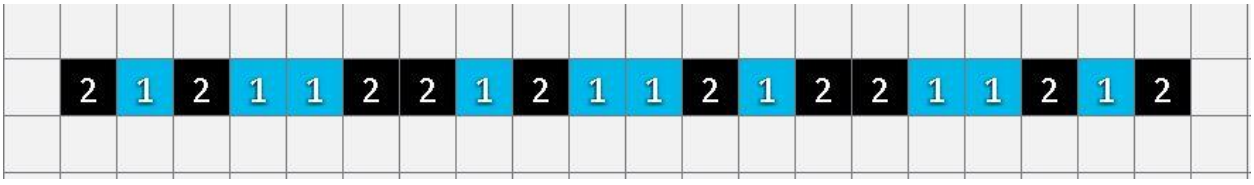

Figure 5a: sequence starting orientation

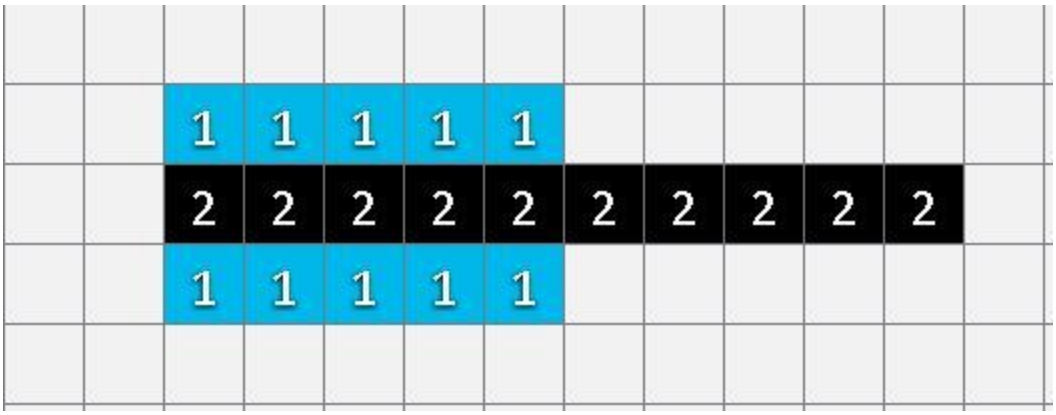

Figure 5b: sequence ending orientation

The final orientation of the sequence shows that the Hydrophobic amino acids moved towards each other to form a hydrophobic core and that the Polar amino acids moved to surround the hydrophobic core.

Conclusion:

To conclude, this rule set behaves very well. Multiple simulations were performed, and there were no polar amino acids stuck in the hydrophobic core. The compactness rule worked to keep the polar cells balanced across the surface of the hydrophobic core of the protein. Overall this model was successful.

References:

[1] Alia Madain, A. Dalhoum, Azzam Sleit. “Protein Folding in the Two dimensional Hydrophobic Polar Model based on Cellular Automata and Local Rules”, 2016.