

## Molecular Dynamics Folding Simulation of $\beta$ -hairpin Protein (1E0Q)

Nur Shima Fadhilah Mazlan<sup>1</sup> and Nurul Bahiyah Ahmad Khairudin<sup>1 +</sup>

<sup>1</sup>Faculty of Chemical Engineering, Universiti Teknologi Malaysia

<sup>2</sup>Malaysia Japan International Institute of Technology, Universiti Teknologi Malaysia International Campus,  
Jalan Semarak, 54100, Kuala Lumpur Malaysia

**Abstract.** The structure and trajectories of the mutant peptide of ubiquitin (PDB ID: 1E0Q) has been studied using Molecular Dynamics (MD) simulation. The investigation of protein folding pathway for protein 1E0Q had been carried out using MD Simulation for 50 ns at temperature 325 K. In this simulation, the protein 1E0Q has folded into its native  $\beta$ -hairpin structure within 5 ns. The RMSD value as compared to the NMR structure from the first residue to 17 residues is 2.17 Å. It has been observed that Gly 10 had been responsible to promote  $\beta$ -turn which caused the structure to turn into  $\beta$ -hairpin. In secondary structure analysis, it is shown that the residue from Thr 6 to Lys 11 has formed a bend in the structure. Two beta strands has also been found comprising residues Glu 2 to Lys 5 and Ile 13 to Glu 16.

**Keywords:** Molecular Dynamics, Protein folding,  $\beta$ -hairpin

### 1. Introduction

Protein folding is the physical process in which the polypeptide folded into a unique three-dimensional structure. It is known that proteins are fundamental components of all living cells. But, how exactly a protein folds from its linear chain into its native tertiary structure is yet to be solved. In fact, the folding process of proteins is known to be the biggest unsolved problems in science [1]. The protein folding process can be investigated using Molecular Dynamics (MD) simulation, which is the best method to describe the dynamics of protein molecules at atomic level [2].

### 2. Materials and Methods

This study focuses on simulating the folding of a small protein, a mutant peptide of ubiquitin (PDB code: 1E0Q), which consists of 17 residues using MD simulation. The simulation was performed using AMBER 11 [3] utilizing force field 99 [4] for 50 ns. The energy minimization was carried out using 500 cycles of steepest descent and another 500 cycles of conjugate gradient [5]. The simulations were performed in a periodic boundary condition [6] with the molecule immersed in a truncated octahedron water box filled with TIP3P water model [7]. Non-bonded interactions were truncated by using a 12 Å cut offs and PME, for Lennard Jones and coulumbic interactions respectively. The system was coupled to a temperature bath using Berendsen [8] thermostat to maintain the temperature at 325K.

### 3. Result and Discussion

All RMSD calculation was performed in order to make a quantitative comparison between the simulation structure and the native structure. The RMSD value to the NMR structure had been plotted versus the simulation time (Fig. 1). The RMSD was initially constant and then decreased to a value of around 4.5 Å at 4.5 ns to 5.5 ns. Then it increased up to 5 Å. It shows that the MD Simulation structure has the most similarity with NMR structure within 4.5 ns to 5.5 ns.

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<sup>+</sup> Corresponding author. Tel.: +60326154657; fax: +60326910342  
E-mail address: nurulbahiyah@ic.utm.my

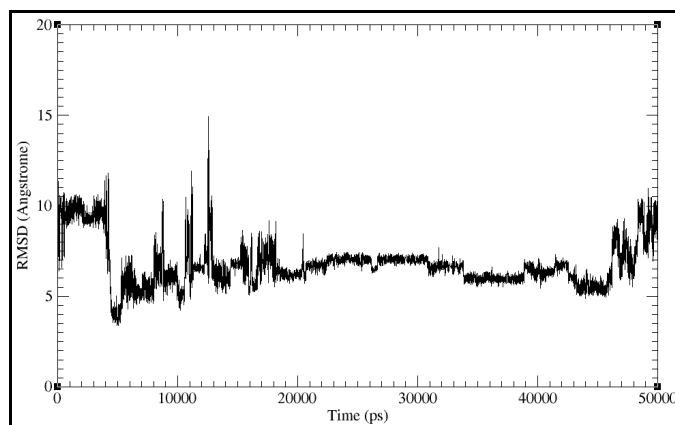


Fig. 1: Graph of RMSD to NMR Structure versus Time

From Fig. 1, the lowest RMSD value was located at 5 ns. The superimposed of the model with the native NMR (Fig. 2) gave RMSD value of 2.17 Å. The folding pathway can be observed through a series of snapshot starting from 0 ns to 10 ns as shown in Fig.3.

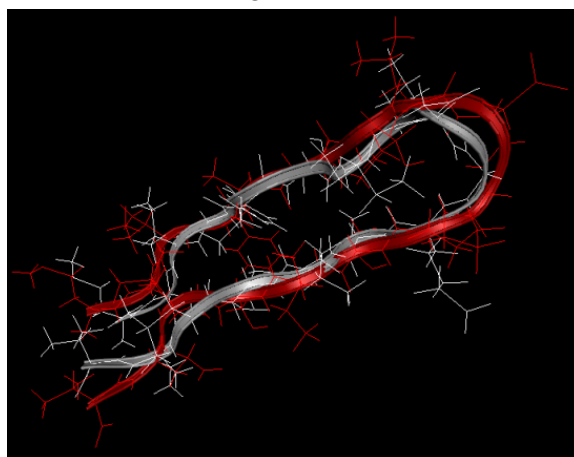
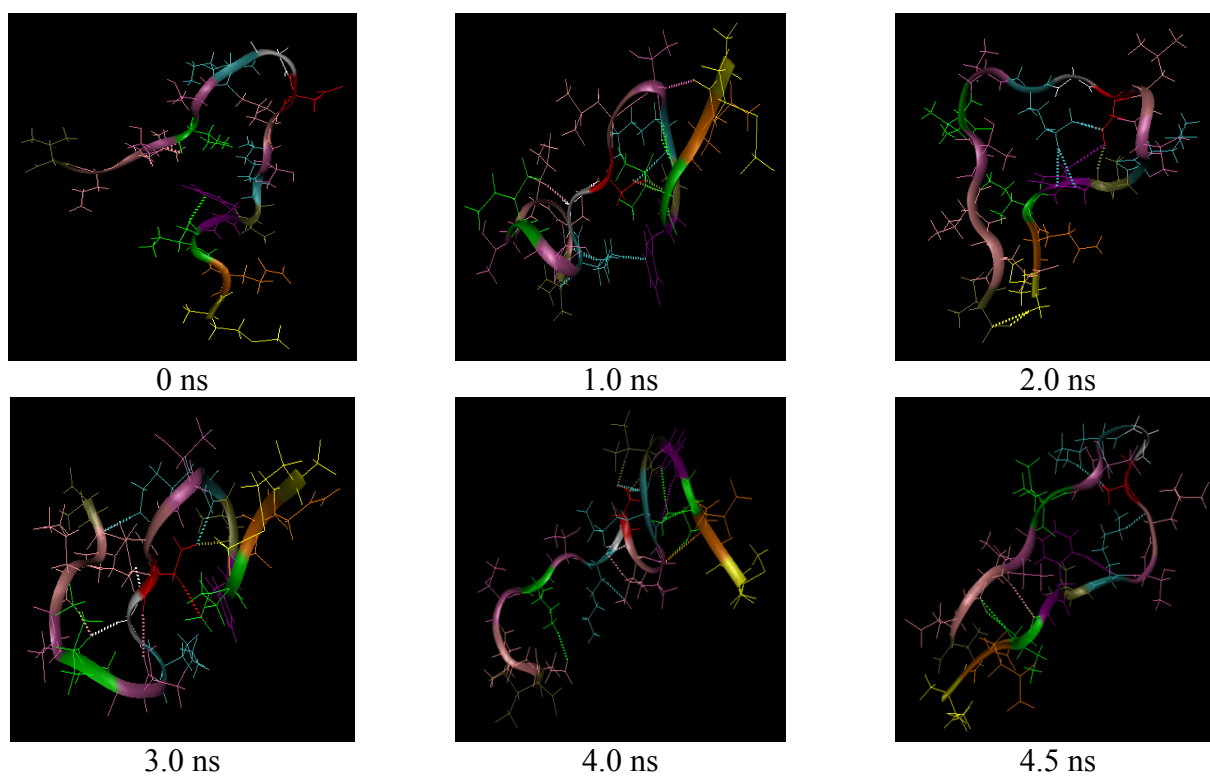


Fig. 2: Superimpose of model (White) to native NMR Structure (Red)



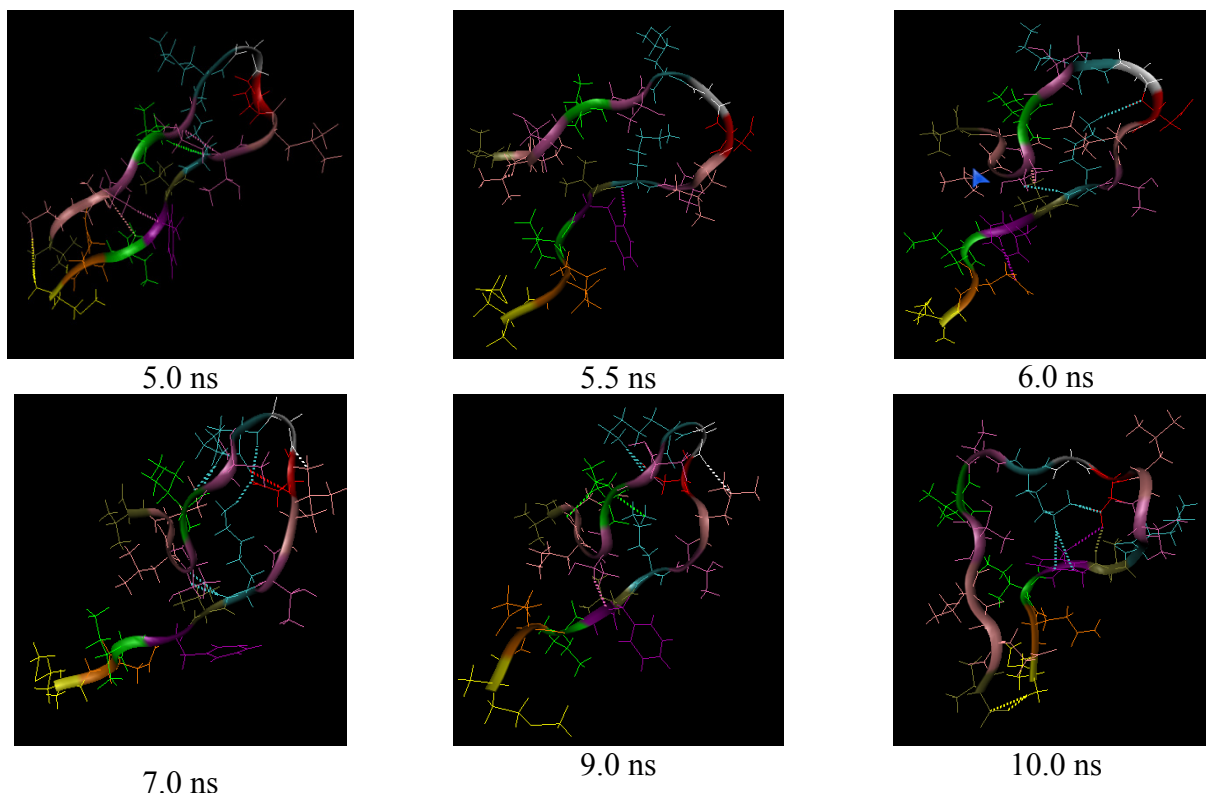


Figure 3: Folding pathways of protein 1E0Q for 10 ns

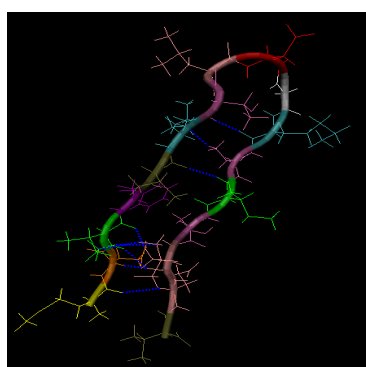


Fig. 4(a): NMR native with hydrogen bonds shown in blue line.

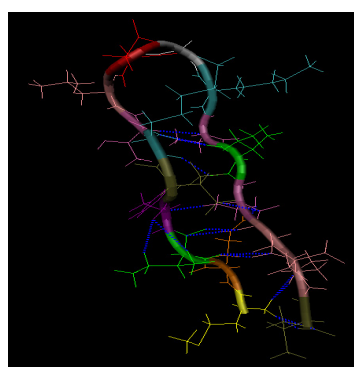


Fig. 4(b): Model structure with hydrogen bonds shown in blue line.

One of the major factors that contribute in the correct folding of proteins is the formation of hydrogen bonds. As shown in Fig. 4(a) and 4(b), there was a minor difference in the number of hydrogen bonds for both structures. It seemed that the model had more numbers of hydrogen bonds compared that of the native. The lists of the hydrogen bonds were tabulated in Table 1.

Table 1: Comparison of stable backbone hydrogen bonds between NMR Structure and the model structure

Donor (N) – Acceptor (O)	NMR Structure (Å)	MD Simulation Structure (Å)
VAL 17 (N) – MET 1 (O)	3.70	2.92
LEU 15 (N) – ILE 3 (O)	3.06	2.90
GLY 10 (N) – LEU 8 (O)	3.60	2.87
LYS 11 (N) – ASP 9 (O)	6.00	3.07
GLN 2 (N) – THR 14 (O)	5.70	2.88
ILE 3 (N) – LEU 15 (O)	3.30	2.84
MET 1 (N) – GLU 16 (O)	3.60	2.87
VAL 17 (N) – GLU 16 (O)	1.40	3.38
MET 1 (N) – VAL 17 (O)	3.70	2.91

## 4. Conclusion

In this study, the protein 1E0Q had folded into its native  $\beta$ -hairpin structure within 5 ns. The RMSD value as compared to the native structure was found to be 2.17 Å. Through observation on the folding pathway, it can be suggested that Gly 10 was responsible to promote  $\beta$ -turn which causes the protein structure to form  $\beta$ -hairpin.

## 5. Acknowledgements

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