Exploring the Changes in the Structure of α-Helical Peptides Adsorbed onto Carbon and Boron Nitride based Nanomaterials

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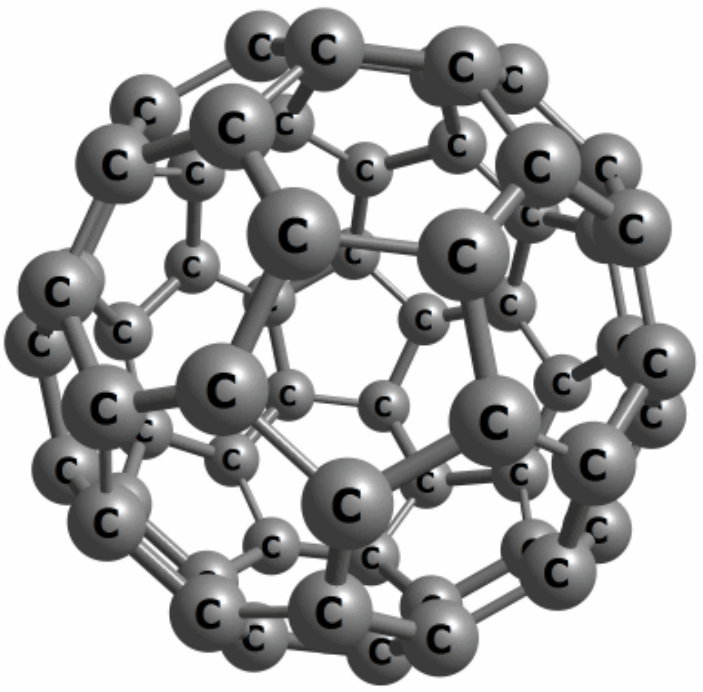
Outline

- Introduction
  - Carbon based Nanomaterials
  - Boron Nitride based Nanomaterials
- Interaction between α-Helical Peptides and Single Walled Carbon Nanotube
- Effect of Curvature on the Helix Breaking Tendency of Carbon Nanotube
- Length Dependent Stability of α-Helical Peptide upon Adsorption to Single Walled Carbon Nanotube
- Disruption of α-helix Folding by Carbon Nanomaterials
- Interaction of Polyalanine with Boron Nitride based Nanomaterials
- Future Plan

Fullerene

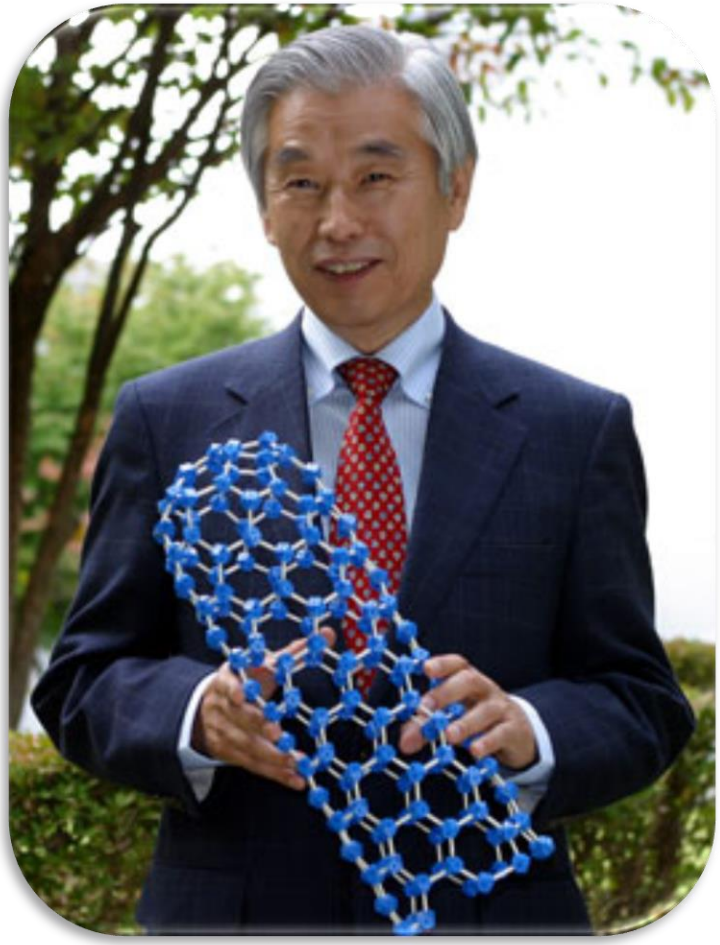


Prof. Kroto
Prof. Curl
Prof. Smalley

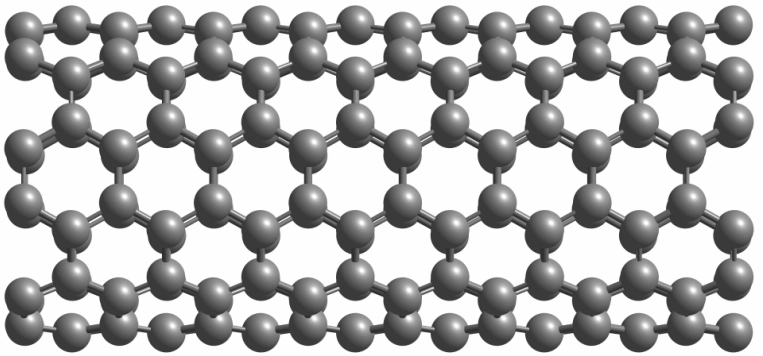
C_{60}

The Nobel Prize in Chemistry 1996

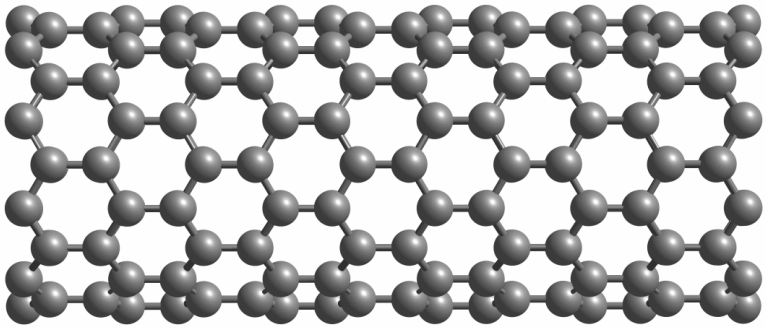
CNTs



Prof. Sumio Iijima



A-CNT



Z-CNT

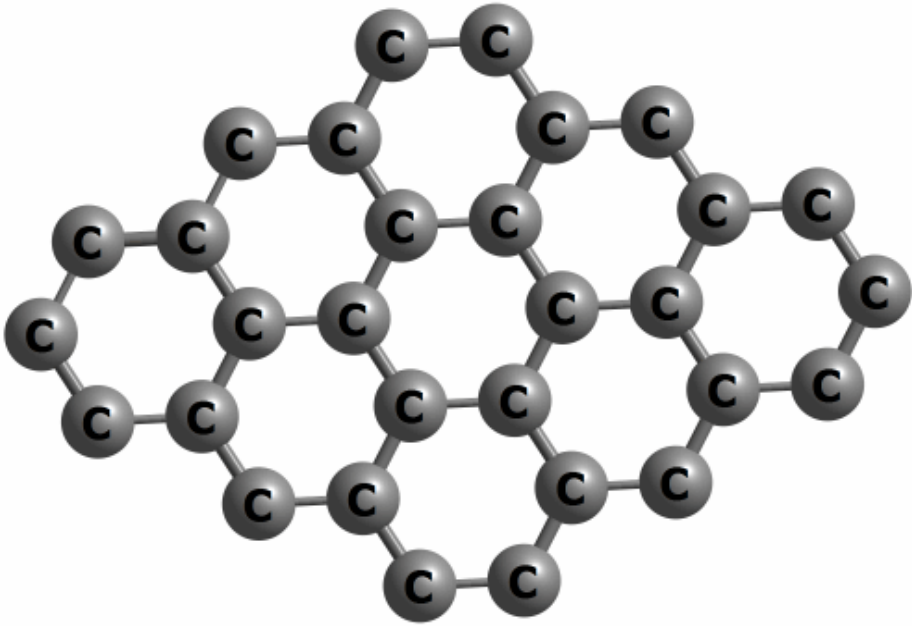
CNTs-Electronic Structure

(n, m) Nanotube

m = 0	m = n	m ≠ n
		
Zigzag (metallic)	**Armchair (metallic)**	**Chiral (Semi-conducting)**

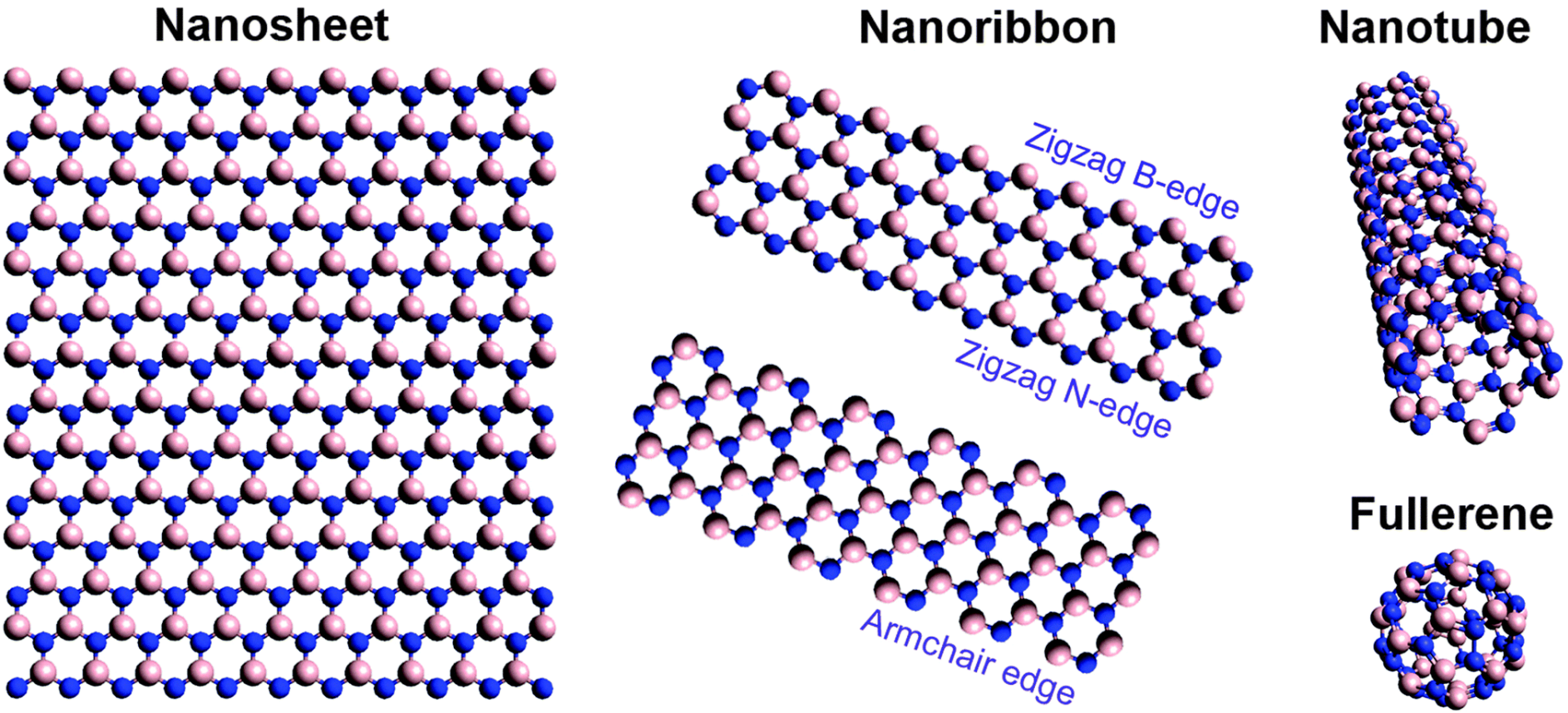
Graphene

Prof. Andre Geim
Prof. Konstantin Novoselov



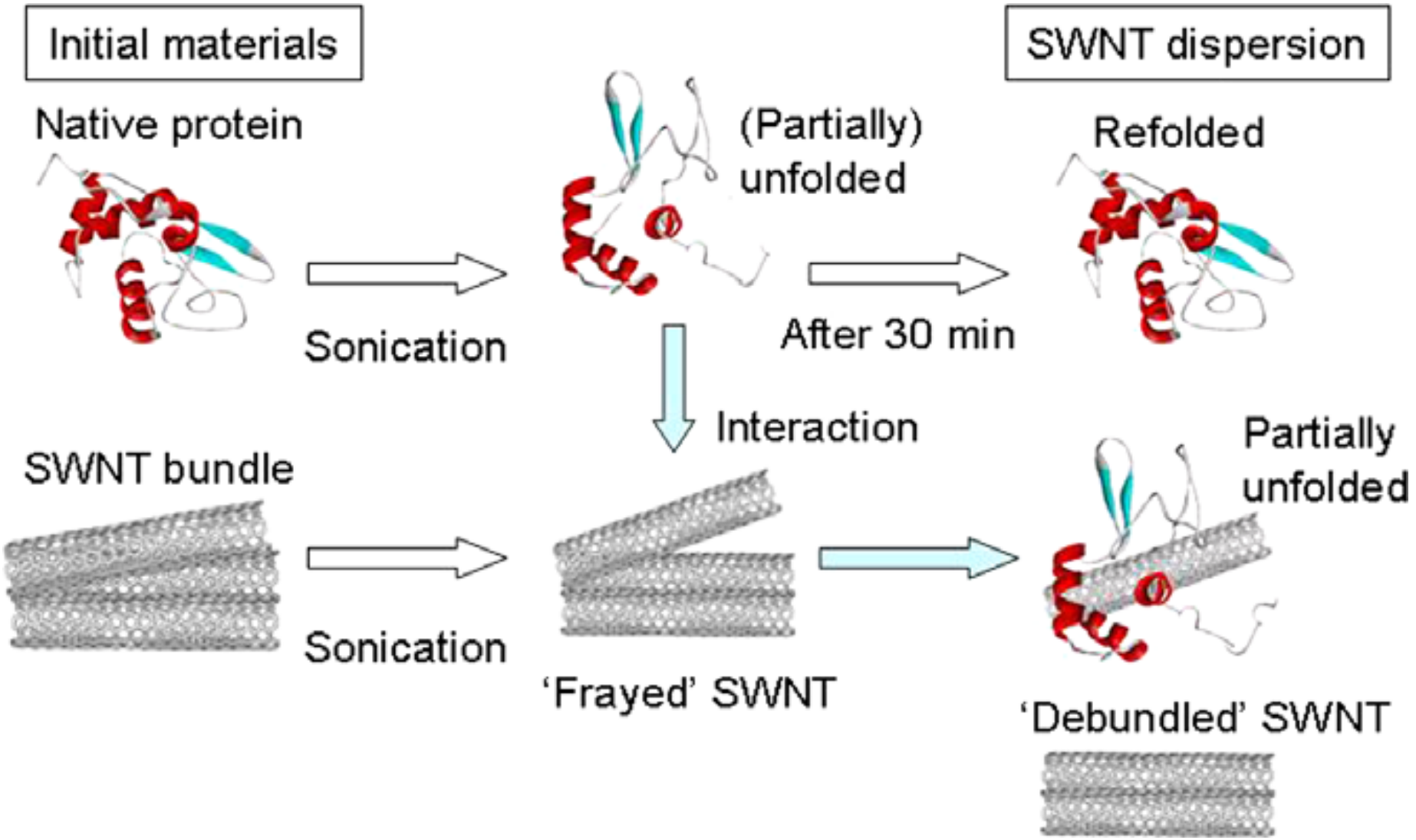
Graphene

BN Analogues of Graphene



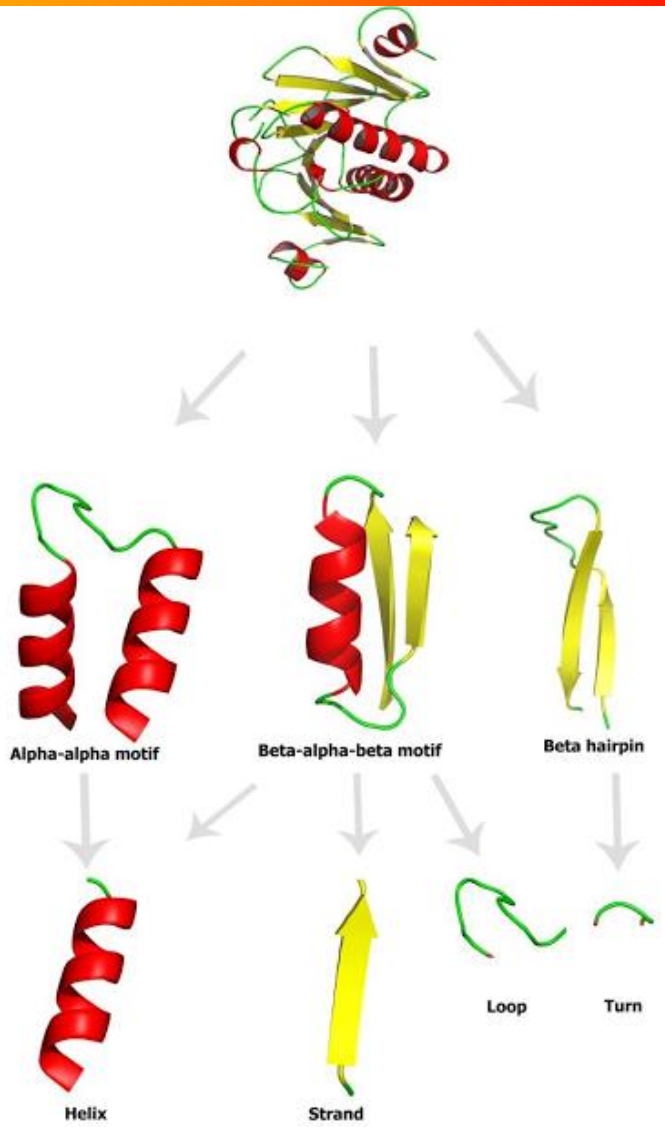
1. Blasé. et. al , Europhys. Lett., 1994, 28, 335–340. (Theoretical prediction)
2. N. G. Chopra et. al, Science, 1995, 269, 966–967. (Experimental Synthesis)

CNT Dispersion by Proteins



Matsuura, K.; Saito, T.; Okazaki, T.; Ohshima, S.; Yumura, M.; Iijima, S. Chem. Phys. Lett 2006, 429, 497–502.

Deconstruction of a Protein Structure



J. Venkatraman, S.C. Shankaramma , and P. Balaram Chem. Rev., 2001, 101 , pp 3131–3152

Let us Discuss…

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Interaction between α-Helical Peptides and Single Walled Carbon Nanotube

Objectives

- Understanding the interaction of CNT with α-helical model peptides based on alanine
- Validation of the results with respect to different force fields
- Interaction of long α-helical peptides derived from X-ray crystal structure with CNT
- Assessment of role of different interactions in the stabilization of CNT-peptide complex

K. Balamurugan, R. Gopalakrishnan, S. Sundar Raman, and V. Subramanian, J. Phys. Chem. B, 2010, 114, pp 14048–14058

Computational Details

- PA_{40} helix was build using the pymol package.
- CNT of chirality (6,6) and length 89.6Å was build using VMD.
- PA_{40} alone and PA_{40} at 8.5Å away from the surface of the CNT were solvated with TIP3P water molecule.
- Infinitely long CNT was simulated by extending the CNT on the Z-axis and the CNT was position restrained during the dynamics.
- In all the case CNT was modeled as uncharged Lenard Jones particle with rest of the Parameters of sp^2 aromatic carbon.
- The details of the simulated system are given in the fallowing table.
- *N*-ethylmaleimide sensitive factor attachment protein receptor (SNARE)

- Method: Molecular dynamics Package: Gromacs 4.0.3
- Ensemble: NPT
- Non-Bonded cutoff: 10Å
- Periodic Boundary conditions are applied
- Thermostat: V-rescale
- Barostat: Parrinello-Rahman
- Constraint: LINCS algorithm
- Temperature: 300K
- Equlibration:1ns
- Production time: 10ns.

K. Balamurugan, R. Gopalakrishnan, S. Sundar Raman, and V. Subramanian, J. Phys. Chem. B, 2010, 114, pp 14048–14058

Simulated Systems

System No	System Name	Forcefield	Description	Box size	No of Water
1	ALAALONEFF03	Amber FF03	PA40	6.0x6.0x8.0	9460
2	ALAALONEOPLS	OPLSAA	PA40	6.0x6.0x8.0	9460
3	CNTALALINFF03	Amber FF03	PA40 was aligned parallel to CNT at about 8.5Å distance	6.0x6.0x9.12	10347
4	CNTALALINOPLS	OPLSAA	PA40 was aligned parallel to CNT at about 8.5Å distance	6.0x6.0x9.12	10347
5	CNTALACROSSOPLS	OPLSAA	PA40 was aligned ~ 45° to the axis of the CNT at about 8.5Å distance	6.0x6.0x9.12	10363
6	CNTSNAREOPLS (PDBID:1scf CHAIN D 140-199)	OPLSAA	Snare Peptide was aligned parallel to CNT at about 12Å distance	6.0x6.0x12.46	14113

K. Balamurugan, R. Gopalakrishnan, S. Sundar Raman, and V. Subramanian, J. Phys. Chem. B, 2010, 114, pp 14048–14058

Simulated System-1

0 ns

FF03

10 ns

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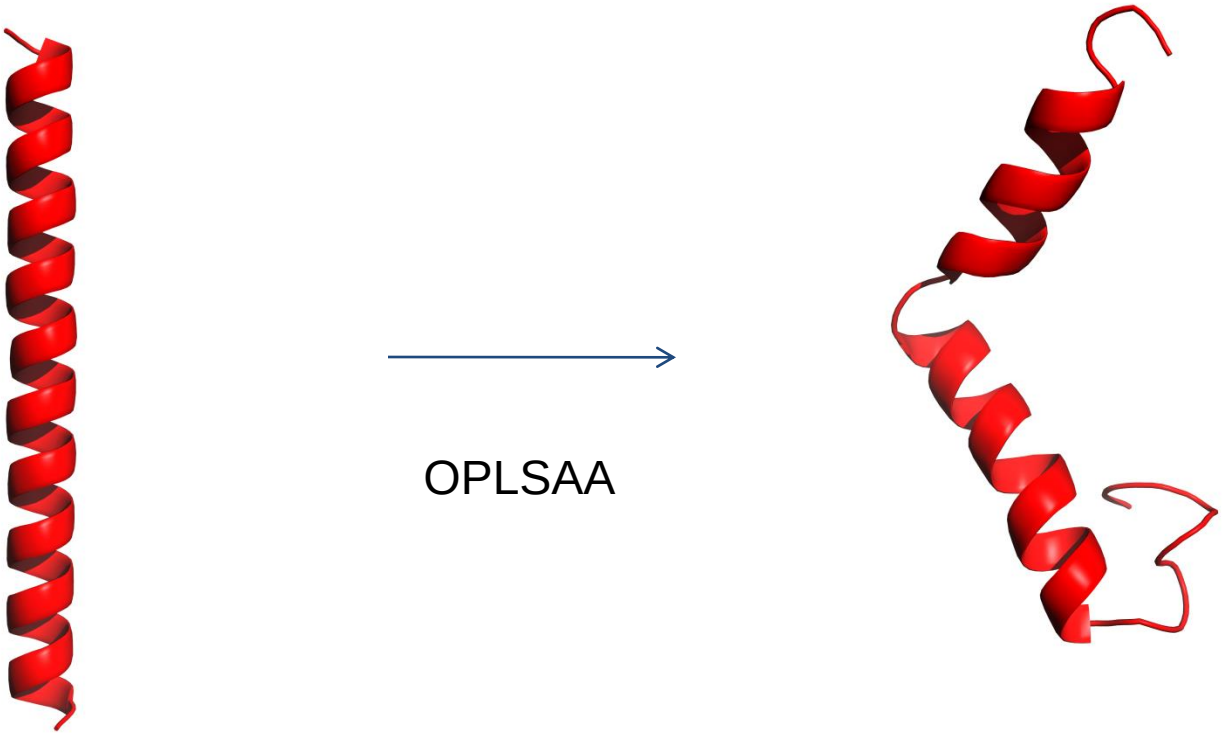
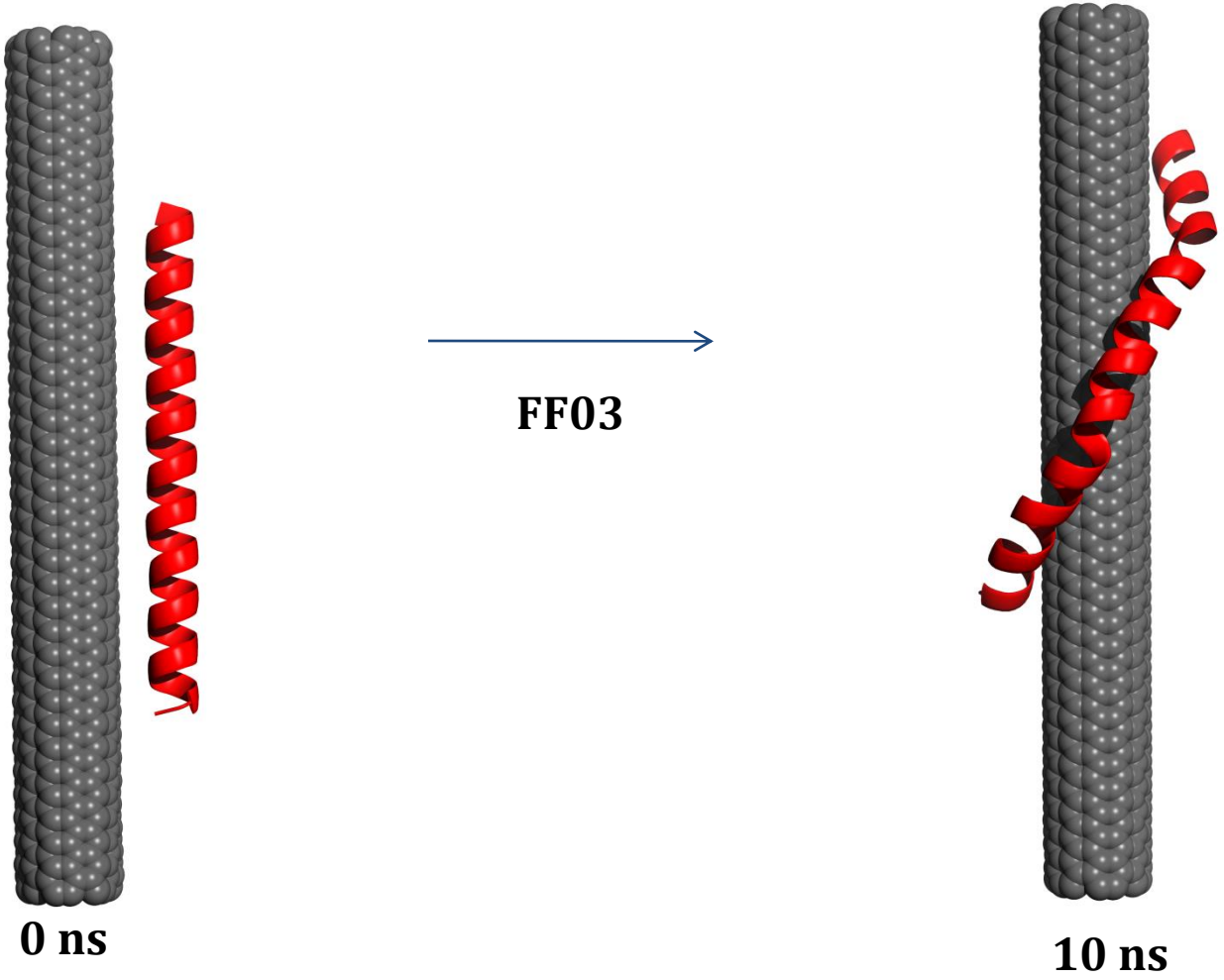
Simulated System-2



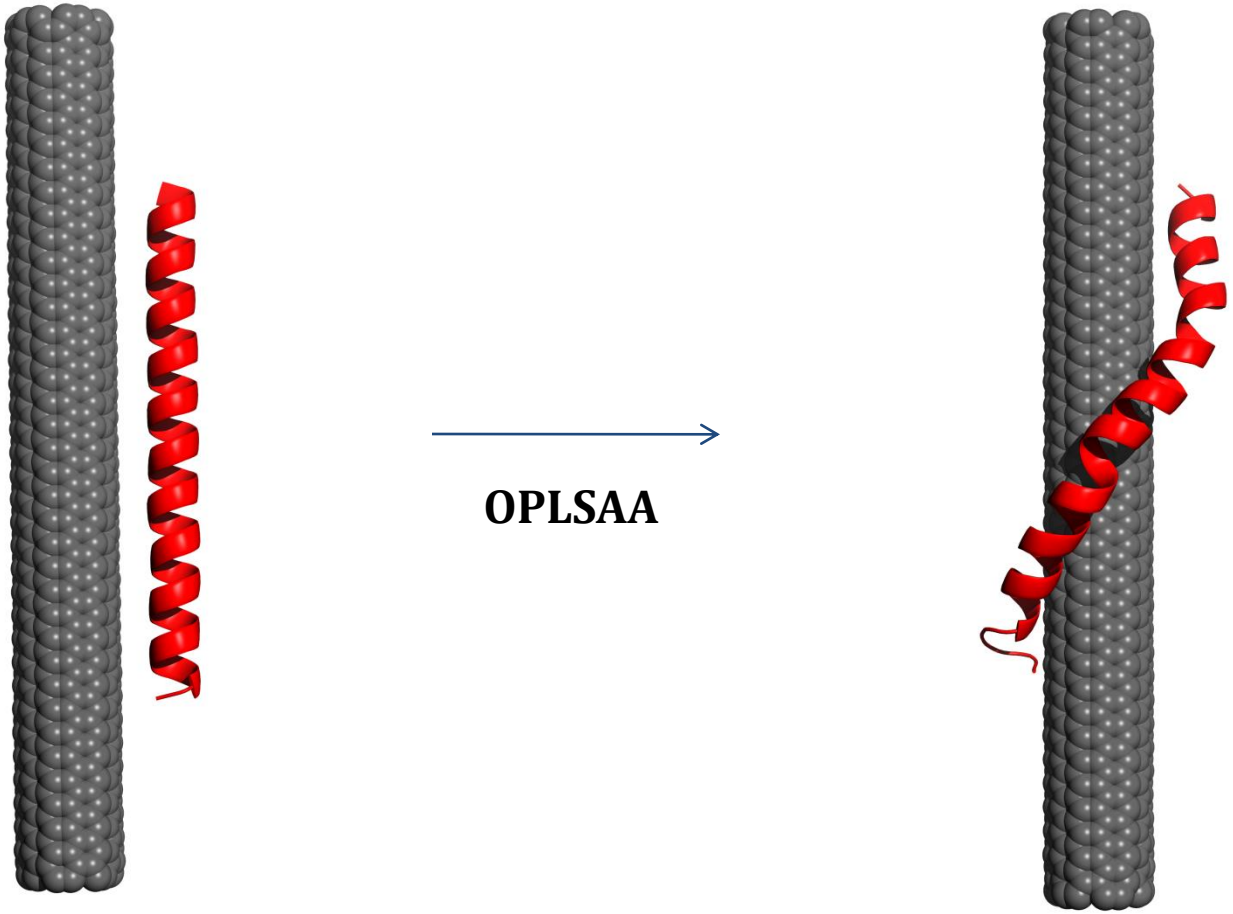
K. Balamurugan, R. Gopalakrishnan, S. Sundar Raman, and V. Subramanian, J. Phys. Chem. B, 2010, 114, pp 14048–14058

Simulated System-3



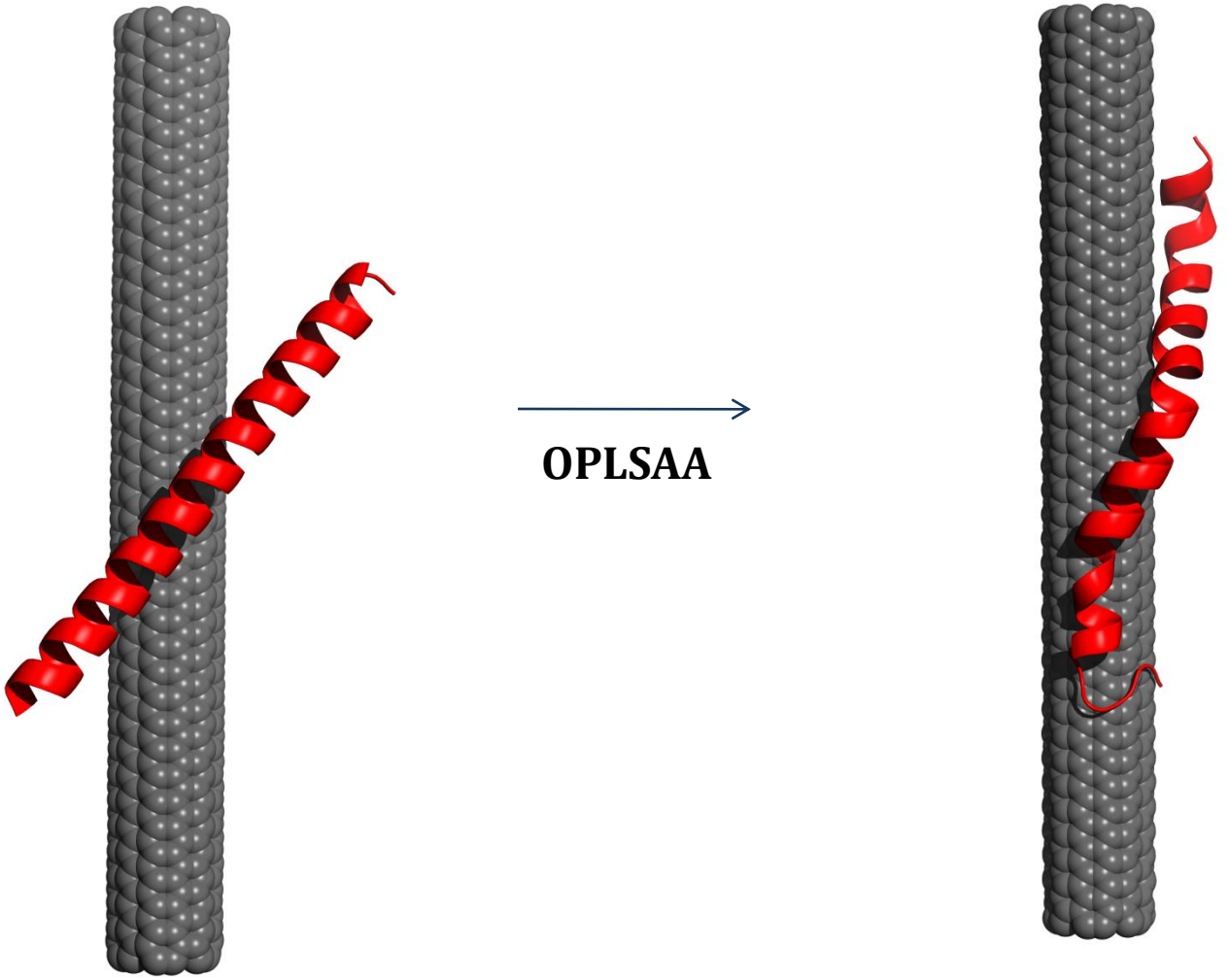
K. Balamurugan, R. Gopalakrishnan, S. Sundar Raman, and V. Subramanian, J. Phys. Chem. B, 2010, 114, pp 14048–14058

Simulated System-4



K. Balamurugan, R. Gopalakrishnan, S. Sundar Raman, and V. Subramanian, J. Phys. Chem. B, 2010, 114, pp 14048–14058

Simulated System-5



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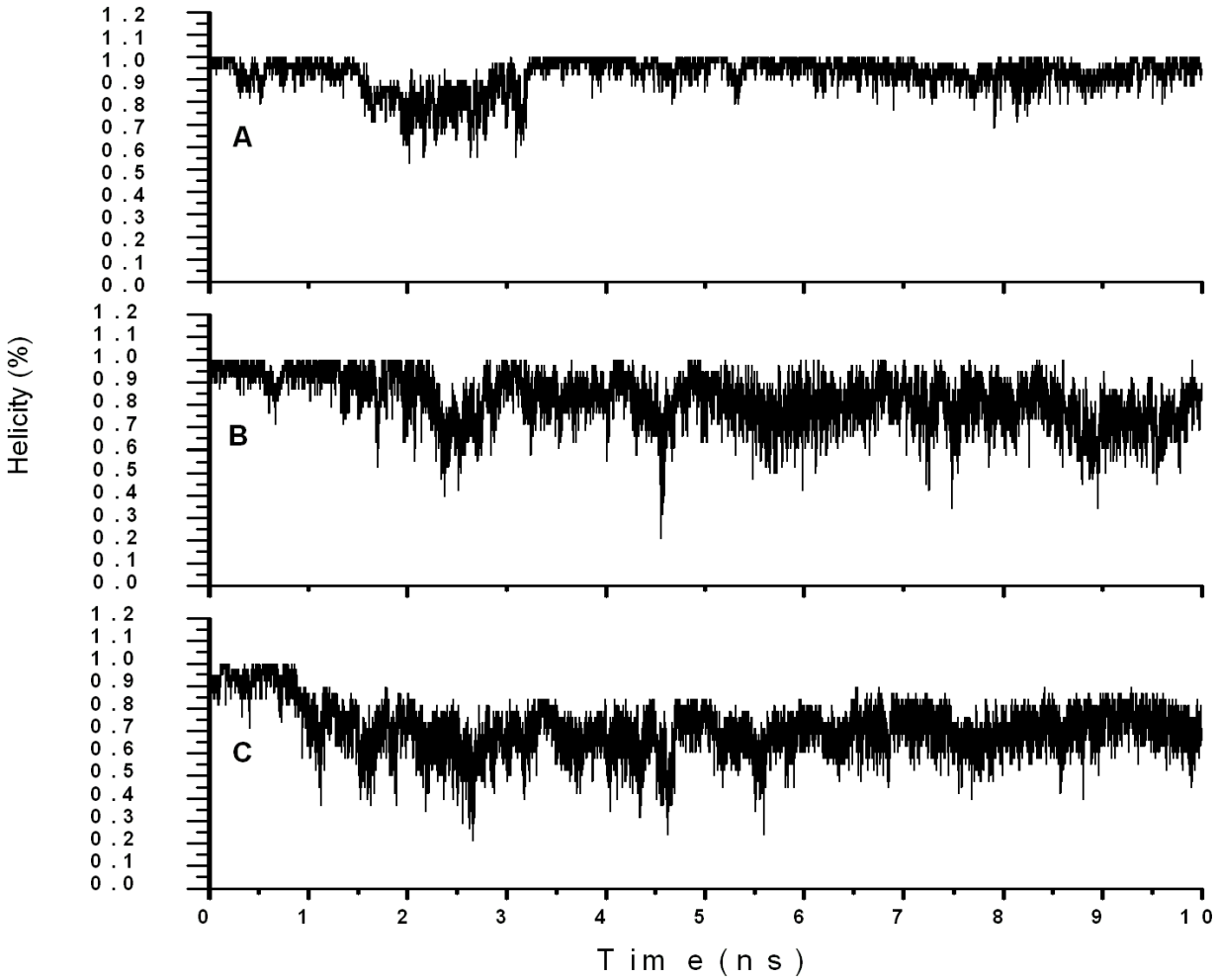
Helicity Change



Helical fraction of the SWCNT-PA40 systems as a function of time

(A) SWCNT-PA40(ff03) ,
(B) SWCNT-PA40(OPLS) and
(C)SWCNT- PA40Angular(OPLS)

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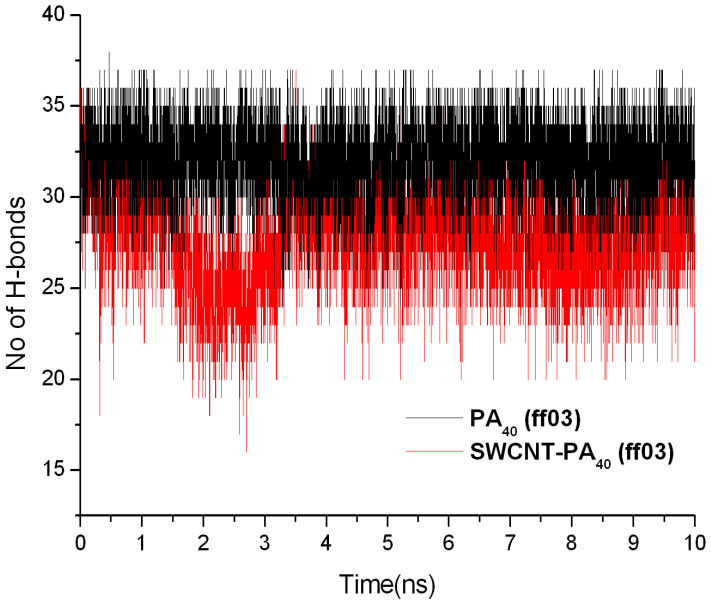
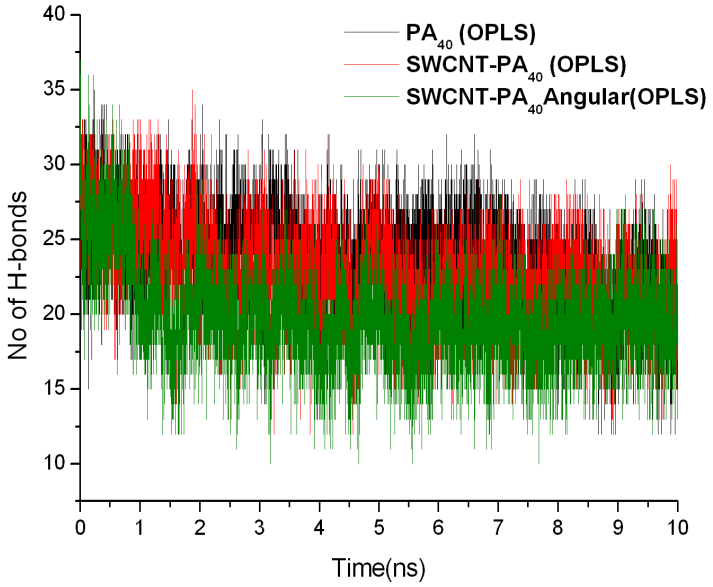
Number of H-bonds





Number of H-bonds present in the SWCNT-PA40 systems during the simulation time (A) PA40(ff03) and SWCNT-PA40(ff03) , (B) PA40(OPLS), SWCNT-PA40(OPLS) and SWCNT- PA40(OPLS)

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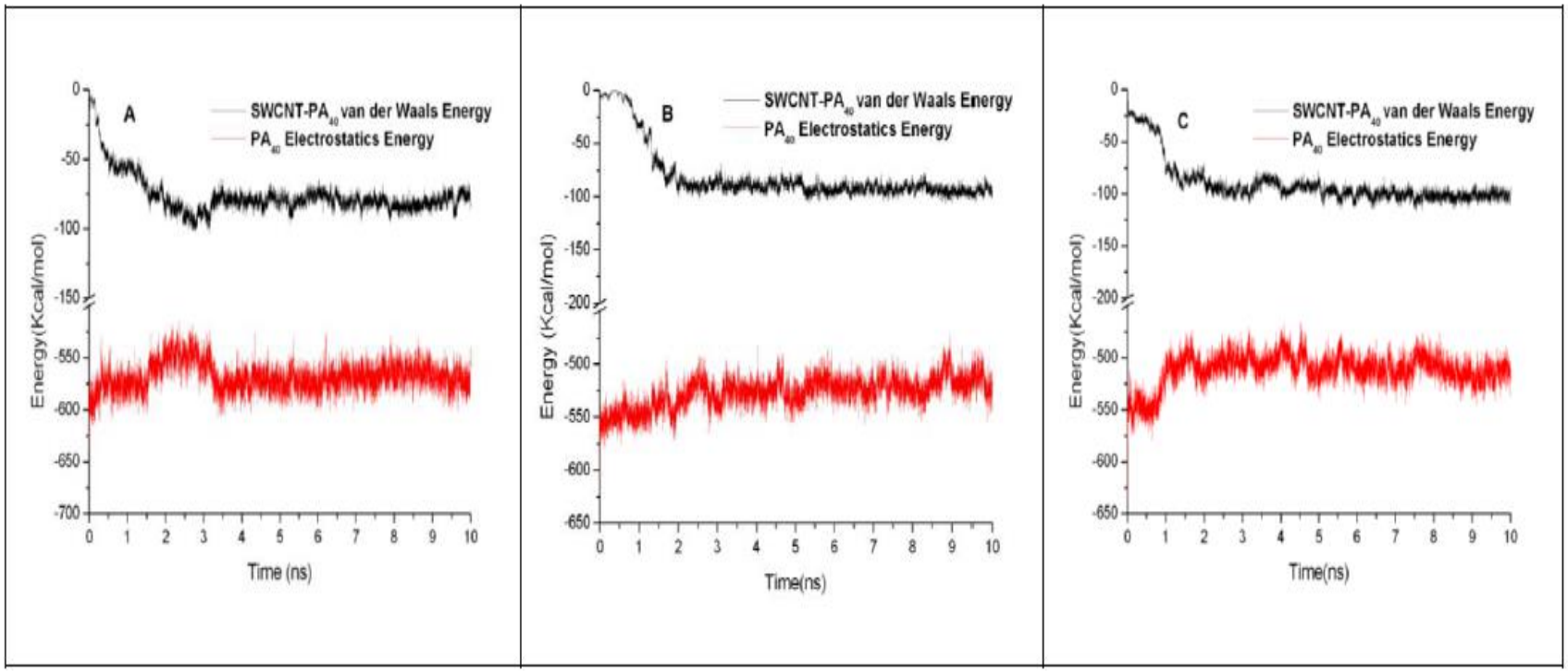
Origin of the Interaction



van der Walls interaction between SWCNT-PA40 system and Electrostatic interaction within PA40 during the simulation time are represented
(A)In SWCNT- PA40(ff03),
(B) SWCNT-PA40(OPLS) and
(C)SWCNT-PA40Angular(OPLS)

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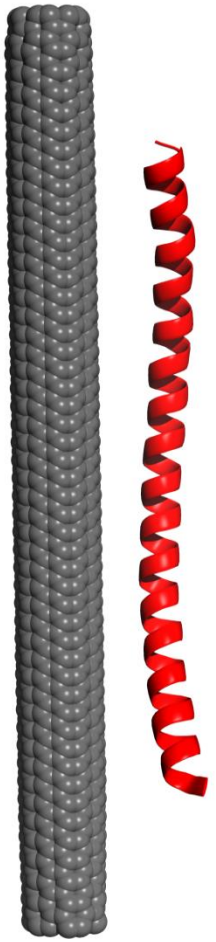
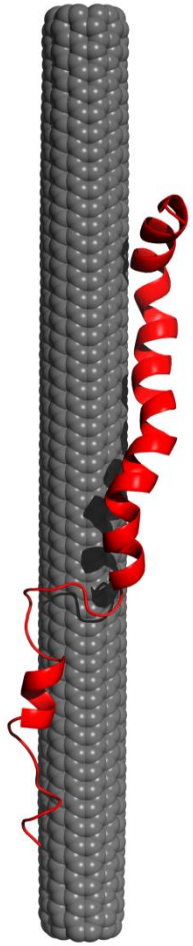
Simulated System-6



0 ns

OPLSAA



10 ns

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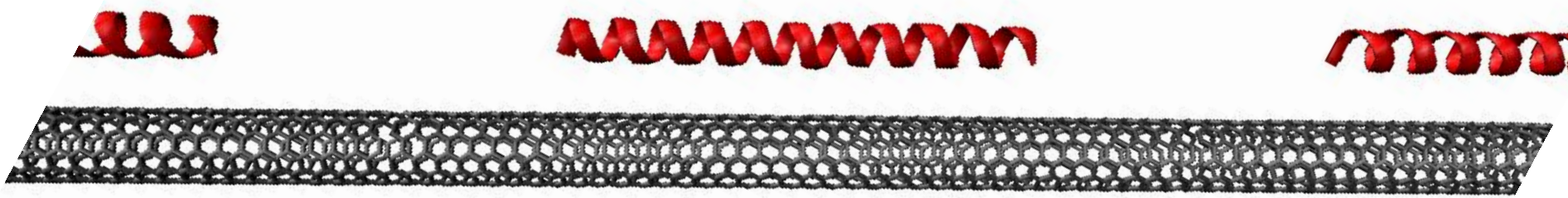
Dynamics of Interaction



Salient Observations

- ✓ Interaction of CNT with α-helical peptide causes helix breakage at some regular interval
- ✓ The abovementioned observation is verified by carrying out simulation in two different force fields.
- ✓ Irrespective of the starting geometry, the helix weakening and breaking can be observed.
- ✓ In the real life hetero polymeric sequence, the weaker regions of the helix are easily prone to breakage which is shown by the correlation between the helix breakage regions and amino acid helix propensity scale values on the CNTSNARE simulated systems.
- ✓ The interaction between the CNT and α-helix is driven by the hydrophobic interaction which is shown by the exponential increase in the surface area between the two systems.
- ✓ The stabilization of the complex formed by the simulated systems are shown using their saturated RMSD values and also by using the cluster analysis.

K. Balamurugan, R. Gopalakrishnan, S. Sundar Raman, and V. Subramanian, J. Phys. Chem. B, 2010, 114, pp 14048–14058

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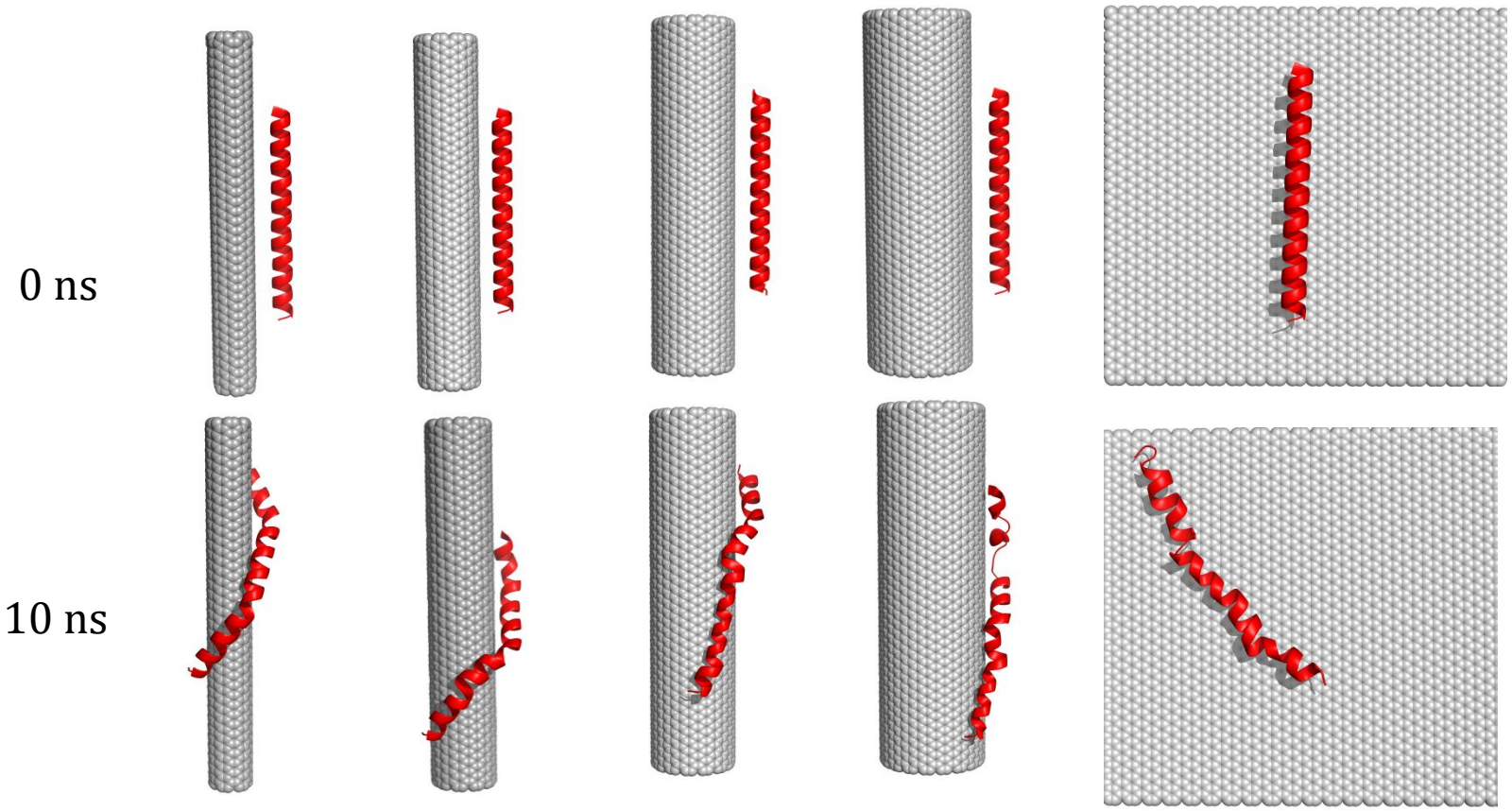
- Future Plan

Effect of Curvature on the Helix Breaking Tendency of Carbon Nanotube

K. Balamurugan, E. R. Azhagiya Singam, and V. Subramanian, J. Phys. Chem. C, 2011, 115, pp 8886–8892

Simulated Systems



K. Balamurugan, E. R. Azhagiya Singam, and V. Subramanian, J. Phys. Chem. C, 2011, 115, pp 8886–8892

Salient Observations

- ✓ Interaction of CNT with α-helical peptide causes helix breakage at some regular interval.
- ✓ The interaction between the CNT and α-helix is driven by the hydrophobic interaction which is shown by the exponential increase in the surface area between the two systems.
- ✓ The stabilization of the complex formed by the simulated systems are shown using their saturated RMSD values.
- ✓ The helix breakage caused by the Carbon nanomaterials increases exponentially with decrease in the curvature.
- ✓ Use of higher curvature CNTs for biological applications will have a less pronounced effect on the structure of the proteins present in the biological environment.

K. Balamurugan, E. R. Azhagiya Singam, and V. Subramanian, J. Phys. Chem. C, 2011, 115, pp 8886–8892

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Length dependent stability of α-helical peptide upon adsorption to single walled carbon nanotube

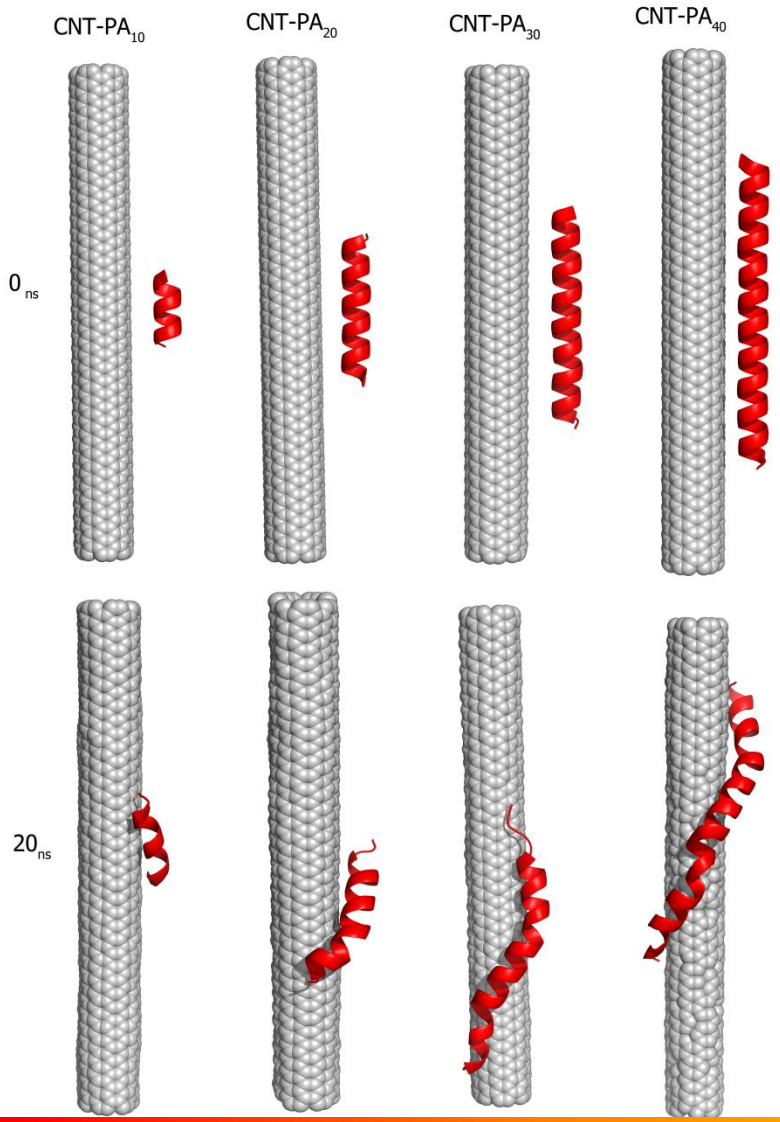
K. Balamurugan, and V. Subramanian, Biopolymers, 2013, 99, pp 357–369

Objectives

- Understanding the interaction of the CNTs with α-helical model peptides of different length.
- Observation of the conformational changes in the α-helical peptide
- Confirmation of the results obtained by studying physical and energy parameters which is responsible for the interaction pattern
- Assessing the role of hydrophobic interaction in the stabilization of CNT-peptide complex

K. Balamurugan, and V. Subramanian, Biopolymers, 2013, 99, pp 357–369

Simulated Systems



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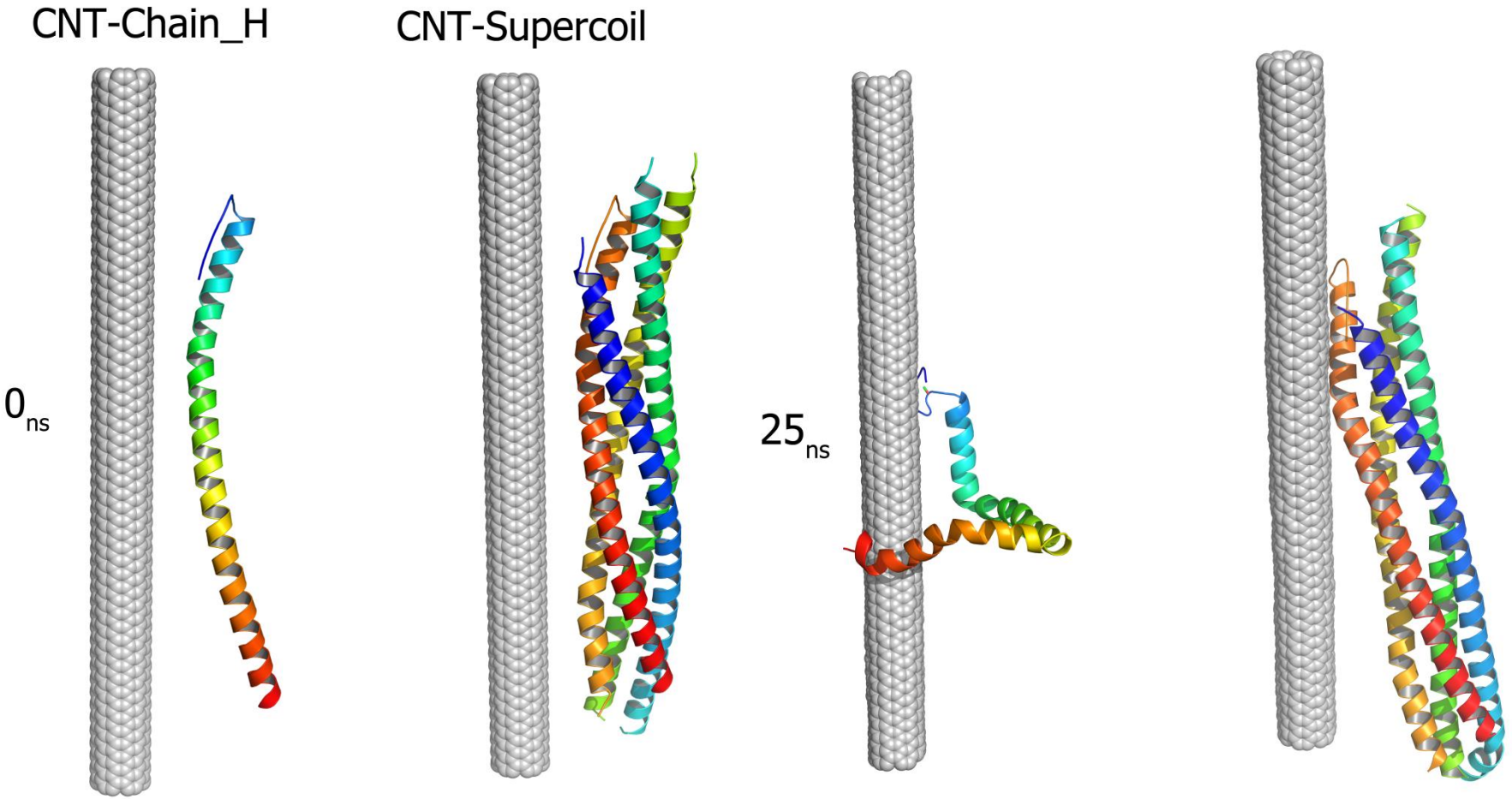

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Salient Observations

- ✓ In general, it has been shown with the help of both experimental and theoretical studies that the stability of the α-helix increases when the length of the helix increases.
- ✓ In stark contrast to the above-mentioned observation, the shorter helical peptides are structurally more stable on interaction with CNT whereas longer helical peptide undergoes considerable structural changes upon interaction with CNT.
- ✓ Thus small globular proteins having smaller helices may be less affected whereas proteins having longer helices may be considerably disturbed by the introduction of CNT into the biological systems.
- ✓ MD simulation of CNT-ChainH and CNTSupercoil systems reveal that structural perturbations in the isolated helical fragment are higher than those in supercoiled helix. It is interesting to note that structure (helicity) of helical chain in supercoiled bundle does not change appreciably upon interaction with CNT
- ✓ Both the length of the helical peptide and the inherent structural stability of the helical unit in the supercoiled helix influence the interaction pattern with the CNT

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Disruption of α-helix Folding by Carbon Nanomaterials

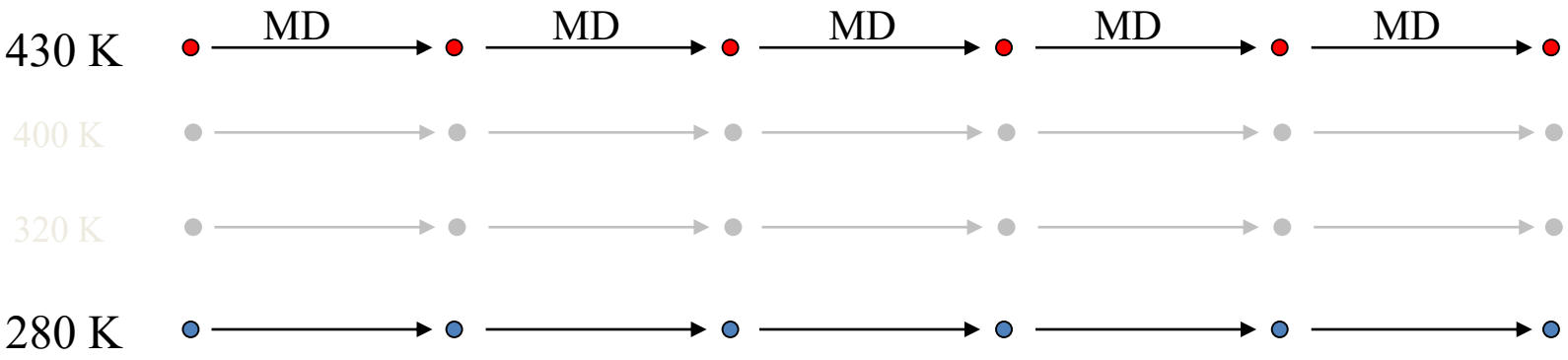
Objectives

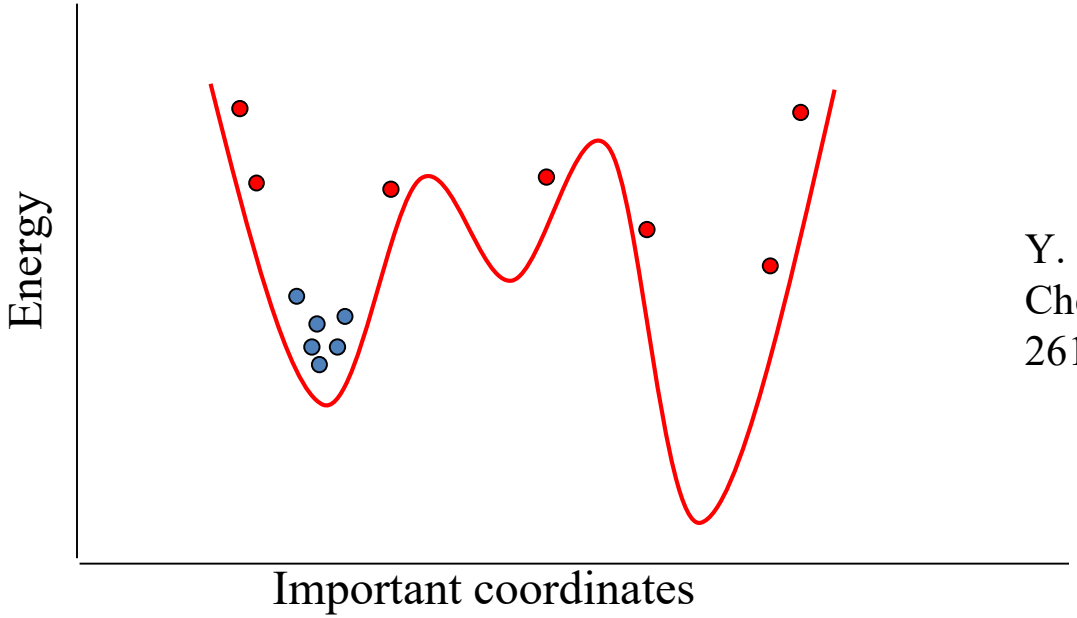
- To understand the effect of single walled carbon nanotube and graphene on the folding of α-helical peptide.
- To predict the structural perturbations and associated energy changes in the folding of α-helical peptide in the vicinity of carbon nanomaterials.

Computational Details

- PA_{12} in extended conformation was build using the Pymol package.
- The SWCNT of chirality (6,6) and length 6.15 nm consisting of 732 carbon atoms and graphene sheet of dimension 6.65 nm X 6.80 nm with 1860 carbon atoms are built using the Nanotube Builder in the VMD
- PA_{12} alone and PA_{12} at 10Å away from the surface of the SWCNT and Graphene were solvated with SPC water molecule.
- Infinitely long carbon nanomaterials were simulated by extending the appropriate axis through periodic boundary conditions.
- In all the cases carbon nanomaterials were modeled as uncharged Lennard Jones particle with rest of the parameters of sp^2 aromatic carbon
- Replica Exchange Molecular Dynamics (REMD)
- GROMACS 4.6.5 package
- Total of 49, 63 and 62 replicas were utilized for PA_{12}, SWCNT-PA_{12} and Graphene-PA_{12} systems respectively where temperatures are exponentially distributed between 280 to 430 K
- NPT ensemble
- Production time of 100 ns for each replica

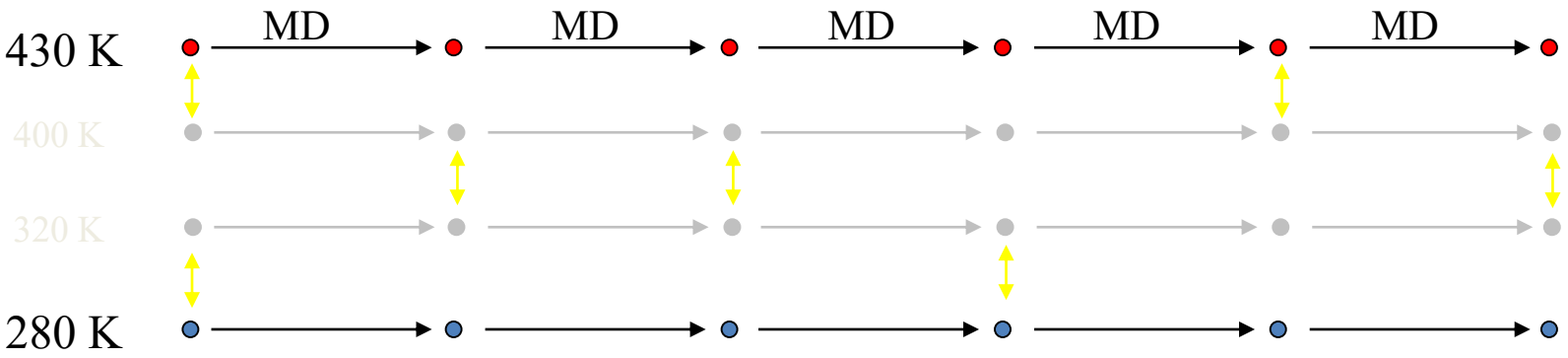
Replica Exchange Molecular Dynamics

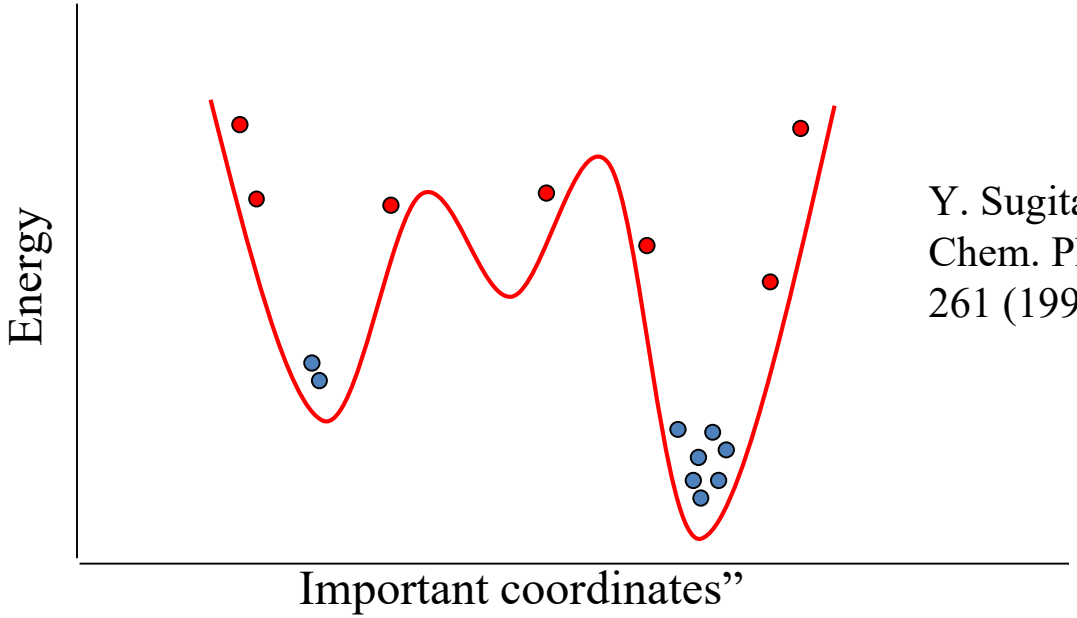




Y. Sugita, Y. Okamoto
Chem. Phys. Let., 314,
261 (1999)

Replica Exchange Molecular Dynamics





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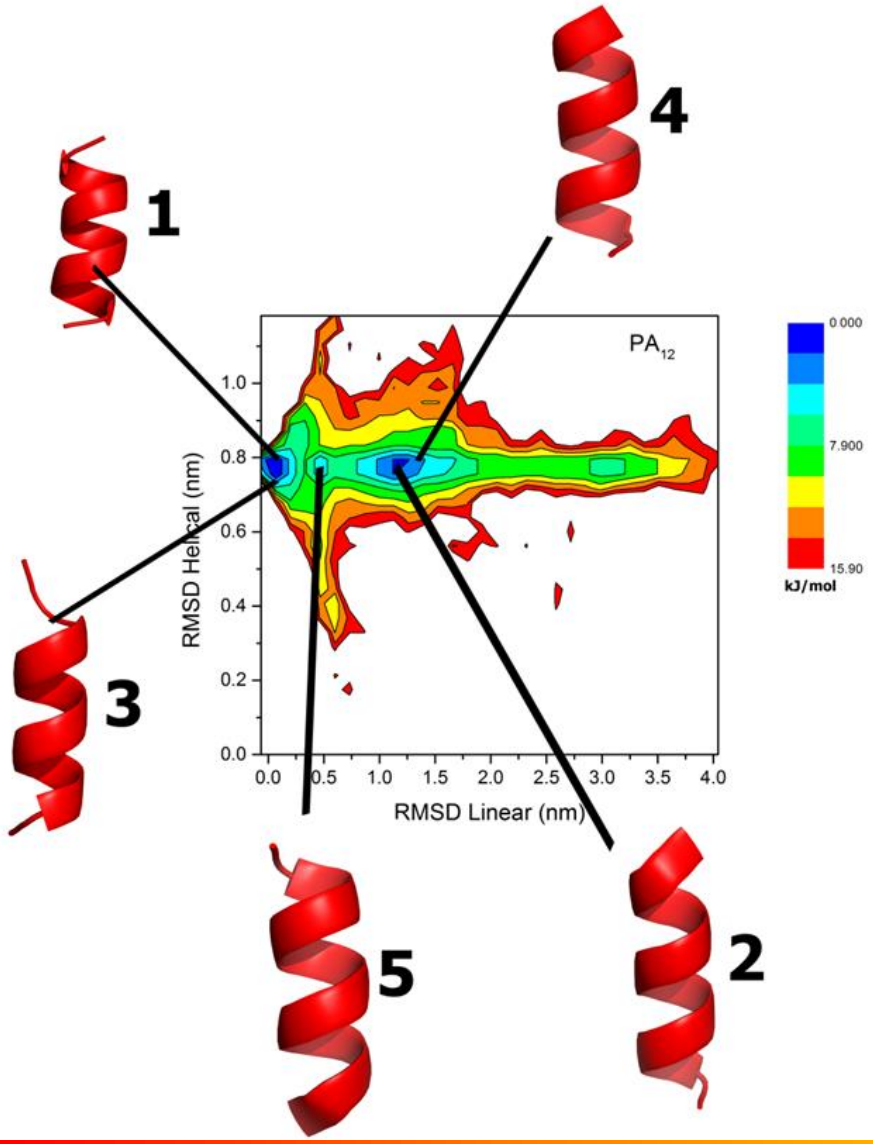
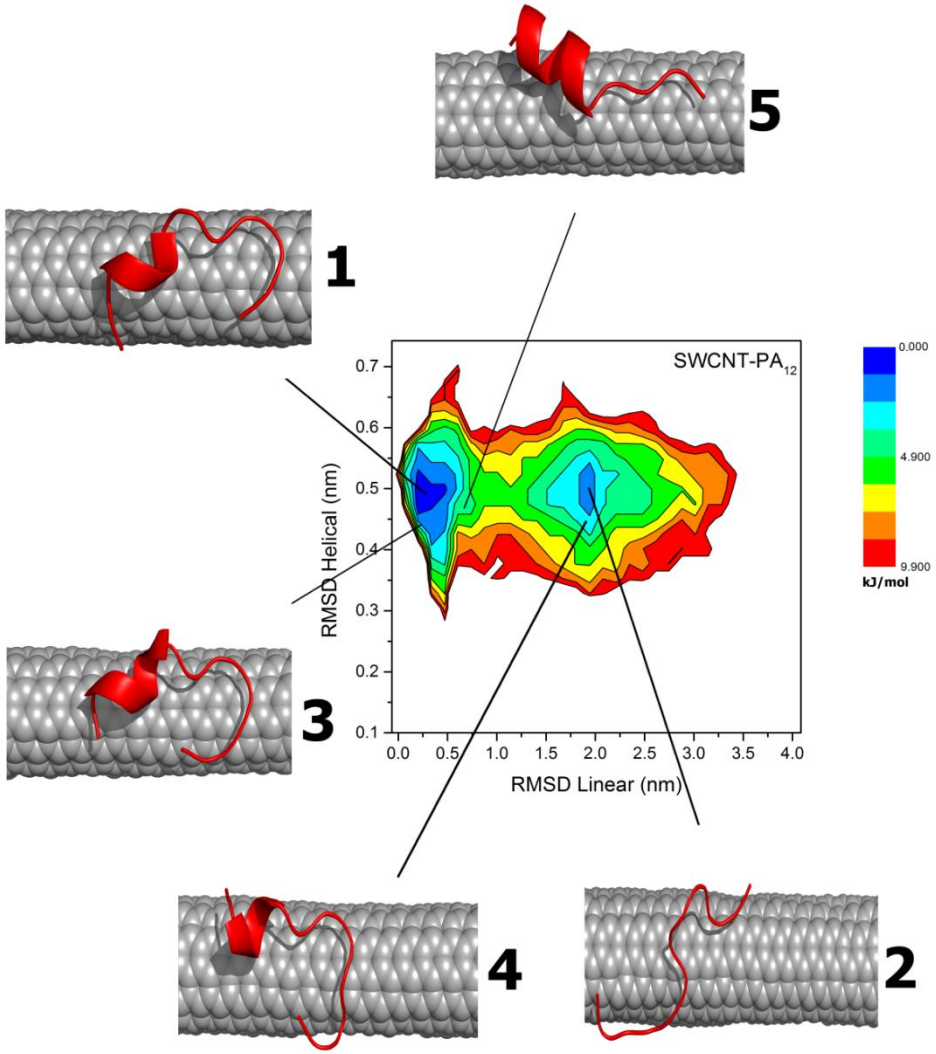
Chem. Phys. Let., 314,
261 (1999)

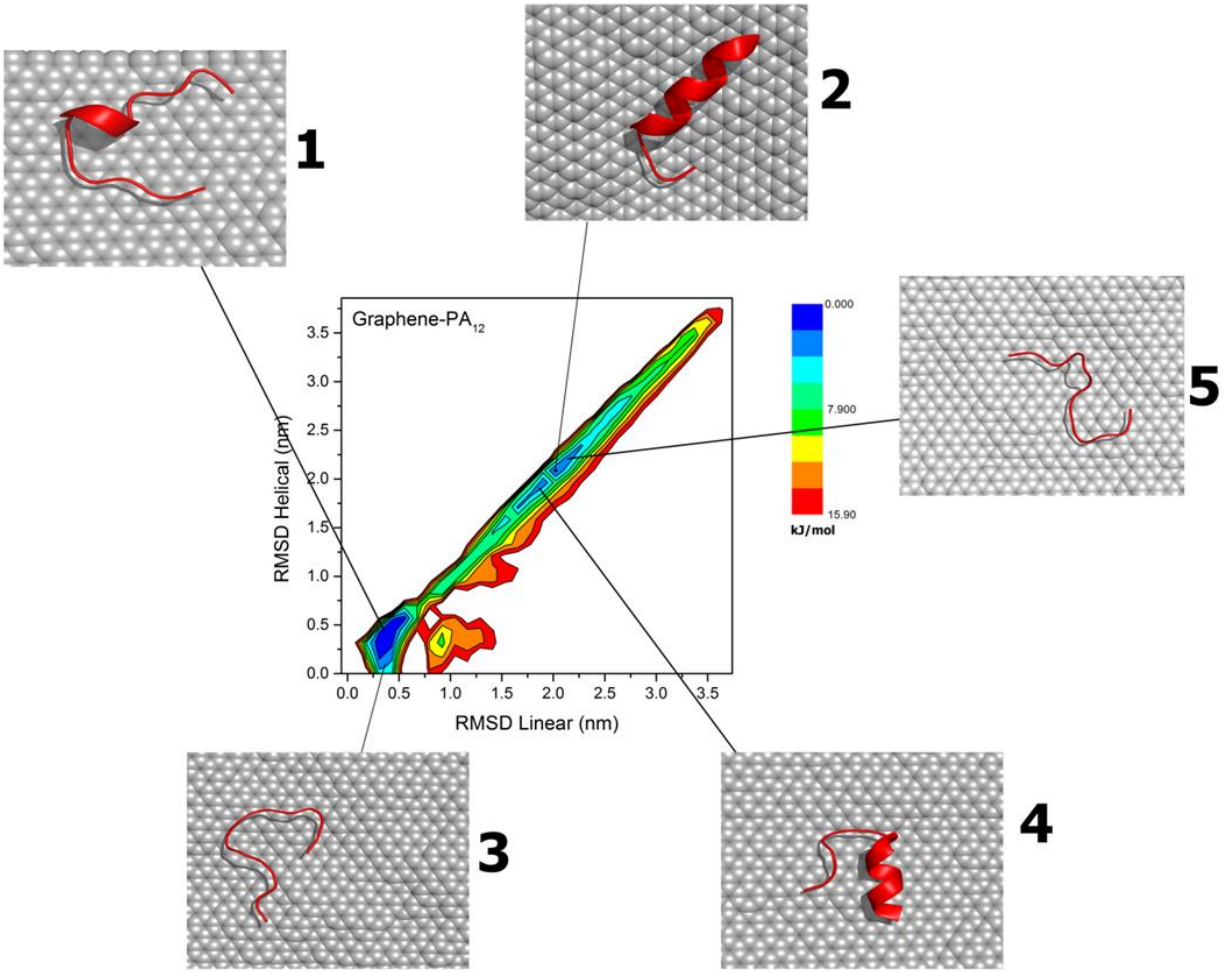
Free Energy Landscape of PA12



Free Energy Landscape of SWCNT-PA12



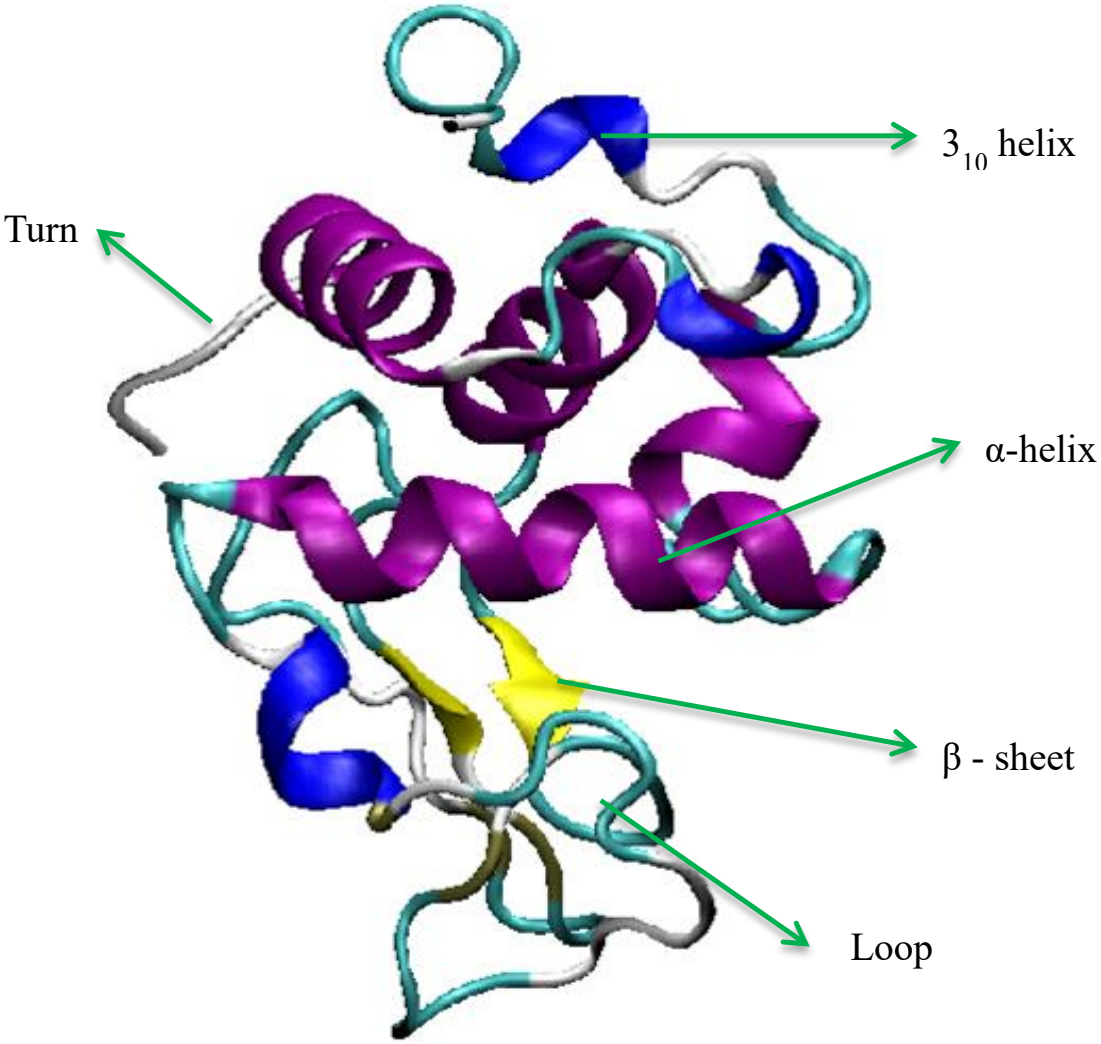
Free Energy Landscape of Graphene-PA12



Salient Findings

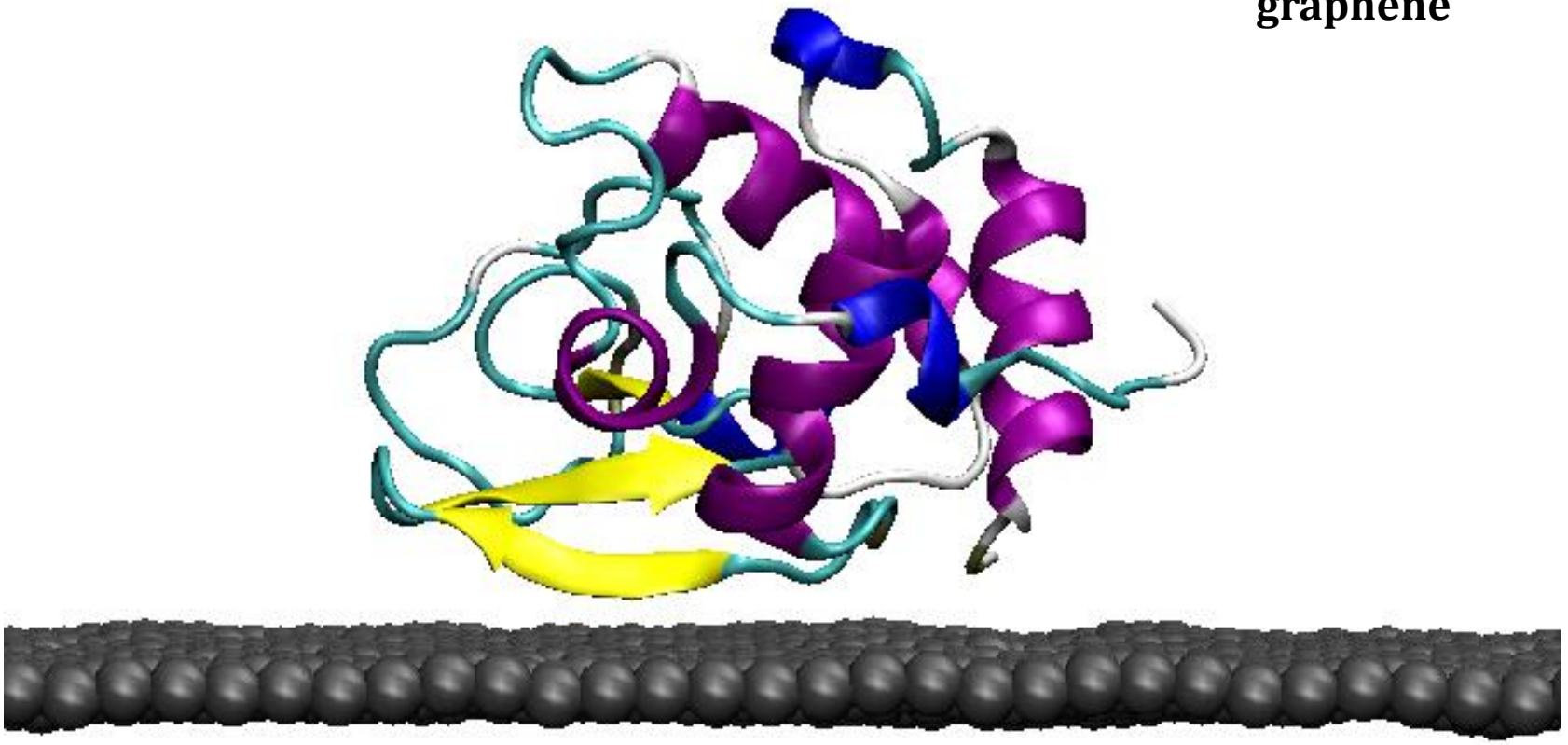
- ✓ The folding of α-helix is disrupted in the presence of carbon nanomaterials such as SWCNT and Graphene.
- ✓ The adhesion of peptide onto the surface of the hydrophobic SWCNT and Graphene restricts the conformational flexibility of the peptide to undergo folding.
- ✓ The hydrophobic association of the peptide with the carbon nano-surfaces also reduces the interaction of water molecules with the peptide which in turn reduces the solvent assisted folding.

Lysozyme

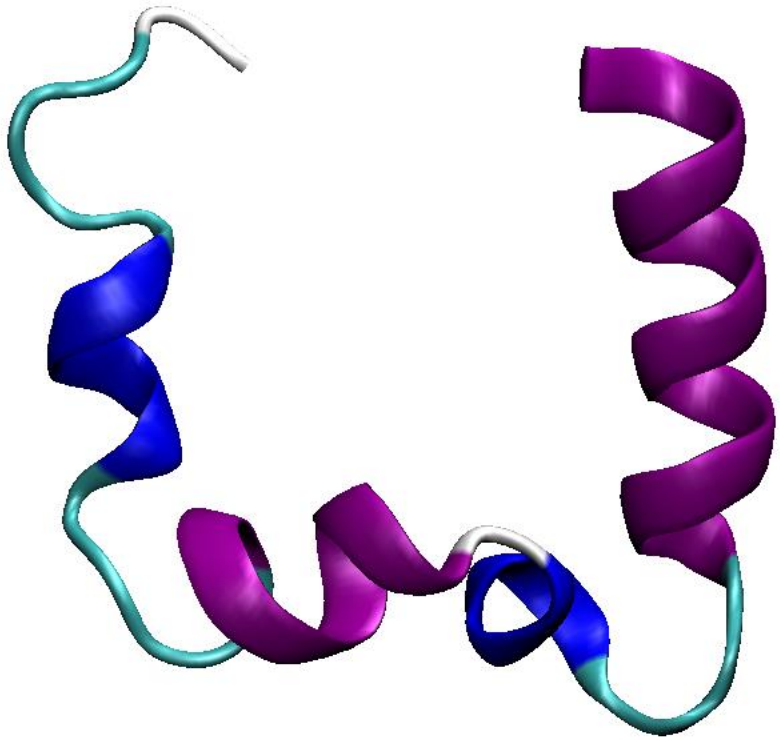


Interaction of Lysozyme with Graphene

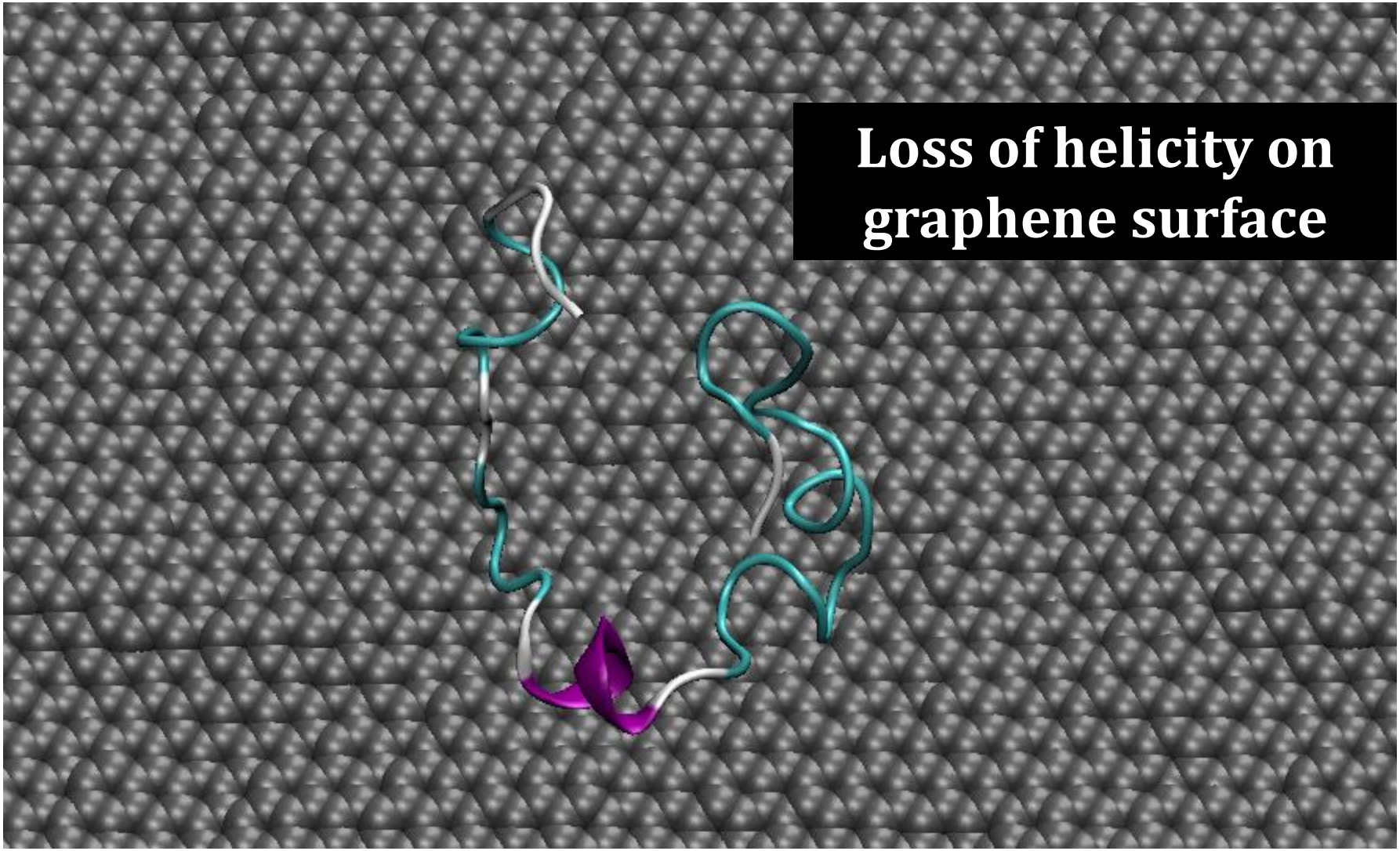
Structure of α-helix and β-sheet is retained the on surface of graphene



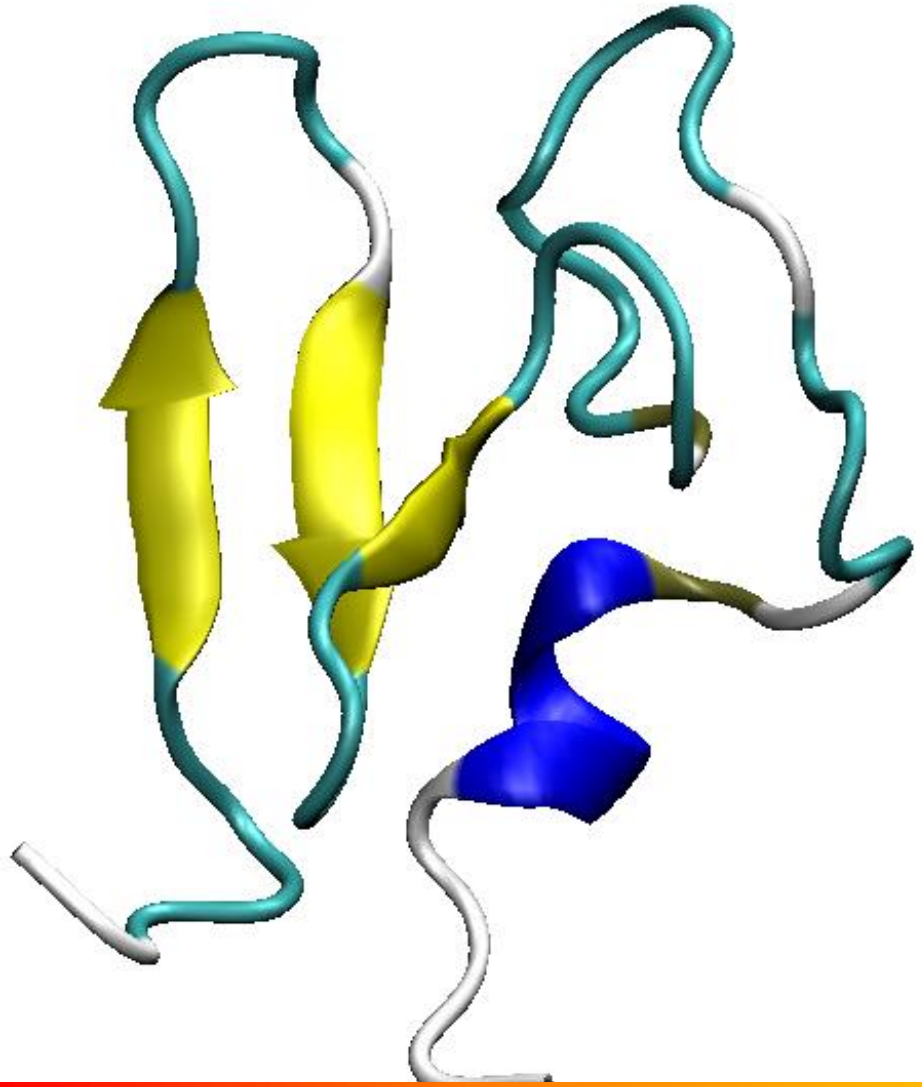
Structure of One of the α – Helix in Lysozyme



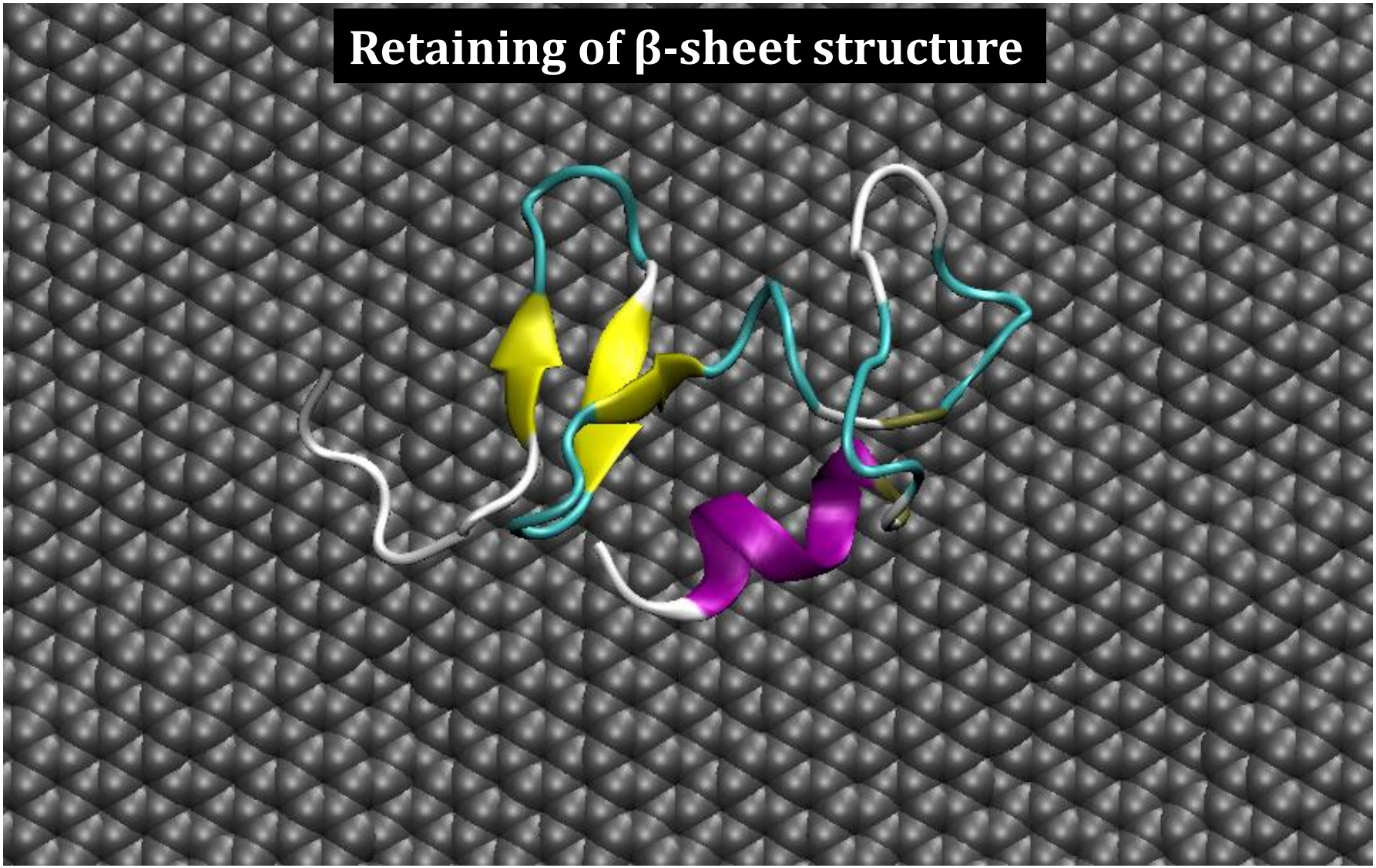
Interaction of α-helix with Graphene



Structure of β - Sheet of Lysozyme



Interaction of β-sheet with Graphene



Let us Discuss…

- Introduction
  - Carbon based Nanomaterials
  - Boron Nitride based Nanomaterials
- Interaction between α-Helical Peptides and Single Walled Carbon Nanotube
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- Disruption of α-helix Folding by Carbon Nanomaterials
- **Interaction of Polyalanine with Boron Nitride based Nanomaterials**
- Future Plan

Interaction of Polyalanine with Boron Nitride based Nanomaterials

S. K. Mudedla, K. Balamurugan, and V. Subramanian, J. Phys. Chem. C, 2016, 120, pp 28246–28260

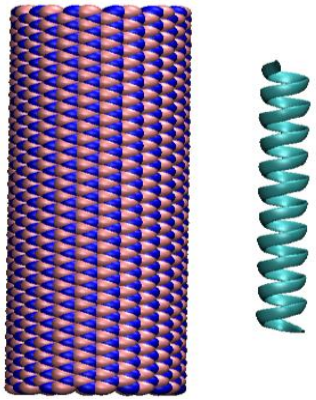
Introduction

- Boron nitride based nanomaterials structurally similar to carbon based nanomaterial
- Boron nitride based nanomaterials have superior prosperities than carbon based nanomaterials
- Boron nitride materials are used in drug delivery, boron neutron capture therapy and electroporation therapy
- These are used in the delivery of DNA into the interior of cells
- Exposure of boron nitride nanomaterials will increase in future
- Understanding of secondary structure of biomolecules upon interaction with boron nitride based nanomaterials in important

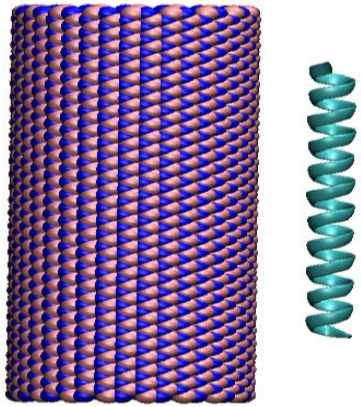
S. K. Mudedla, K. Balamurugan, and V. Subramanian, J. Phys. Chem. C, 2016, 120, pp 28246–28260

Simulated Systems

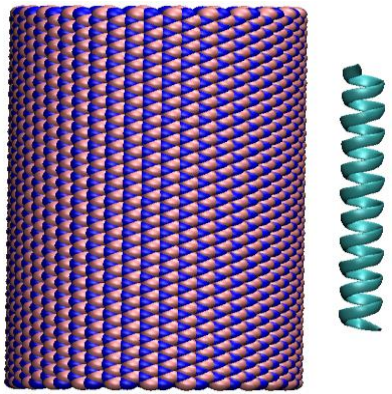
At 0 ns



(12, 12)

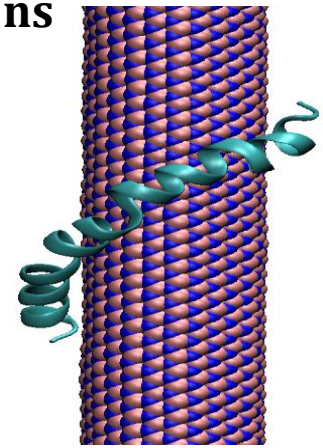


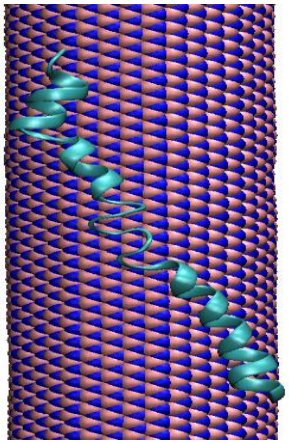
(18, 18)

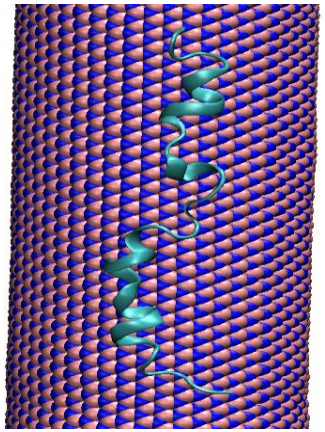


(24, 24)

At 60 ns







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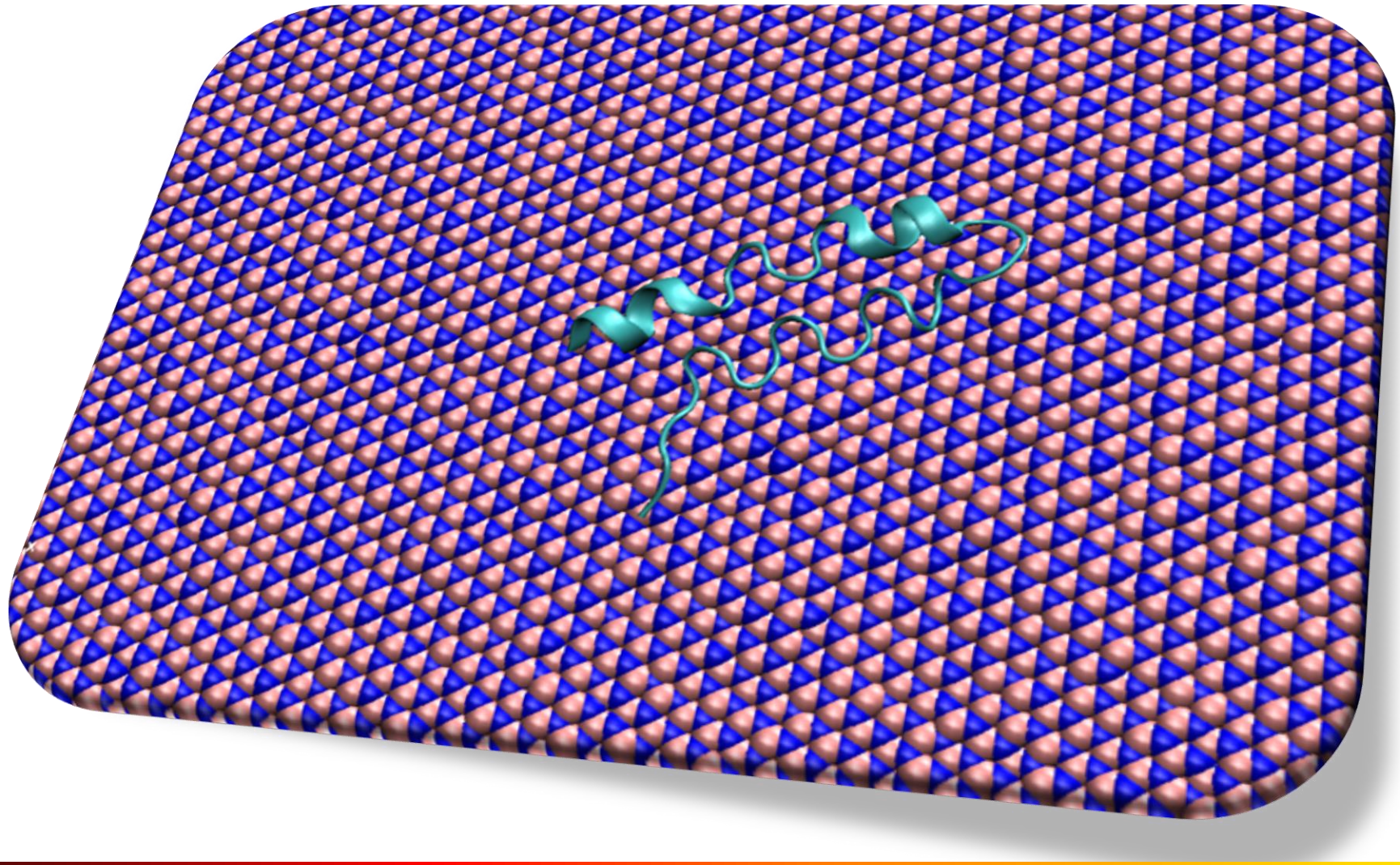
BN Sheet with Peptide



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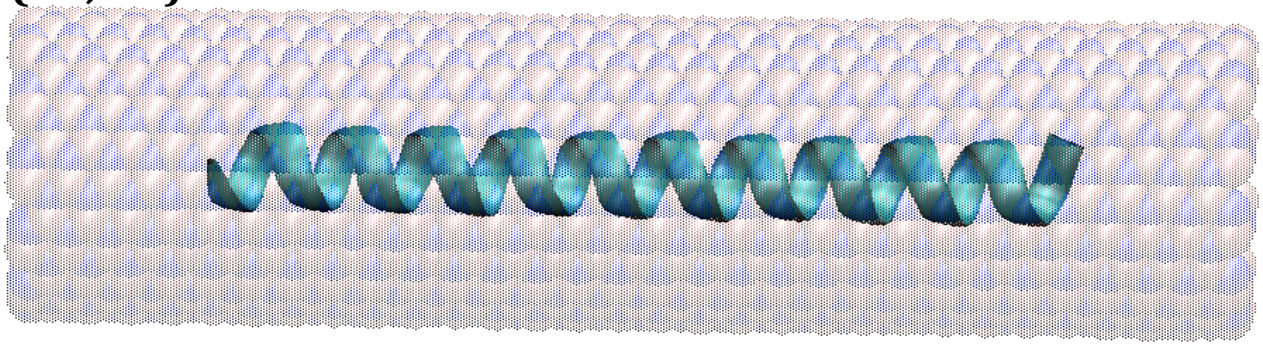
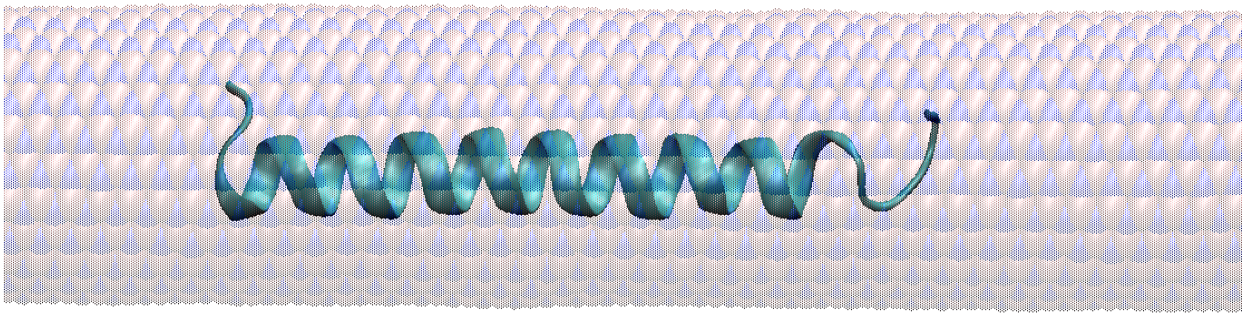
Simulated Systems: Inside - BNNT

(12, 12) at 0 ns



(12, 12) at 60 ns



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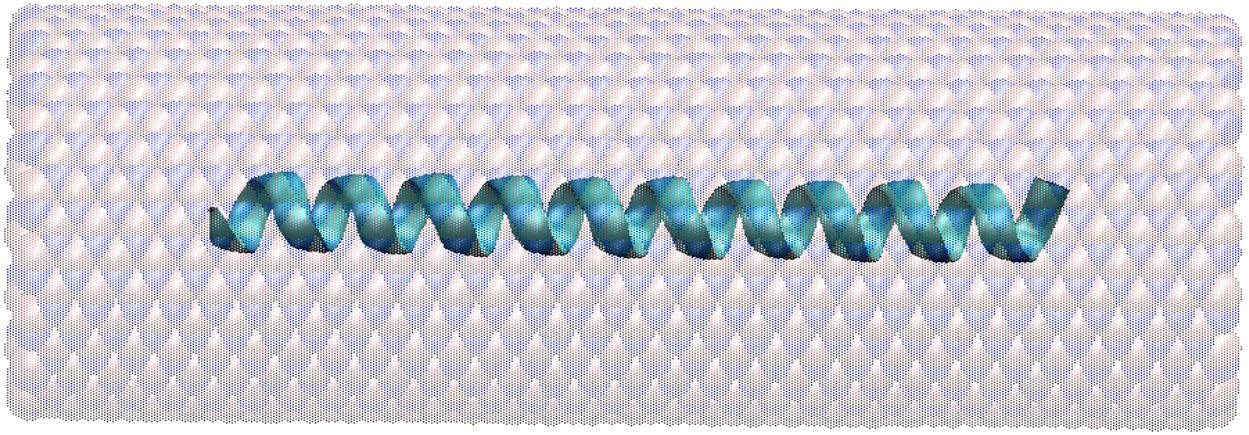
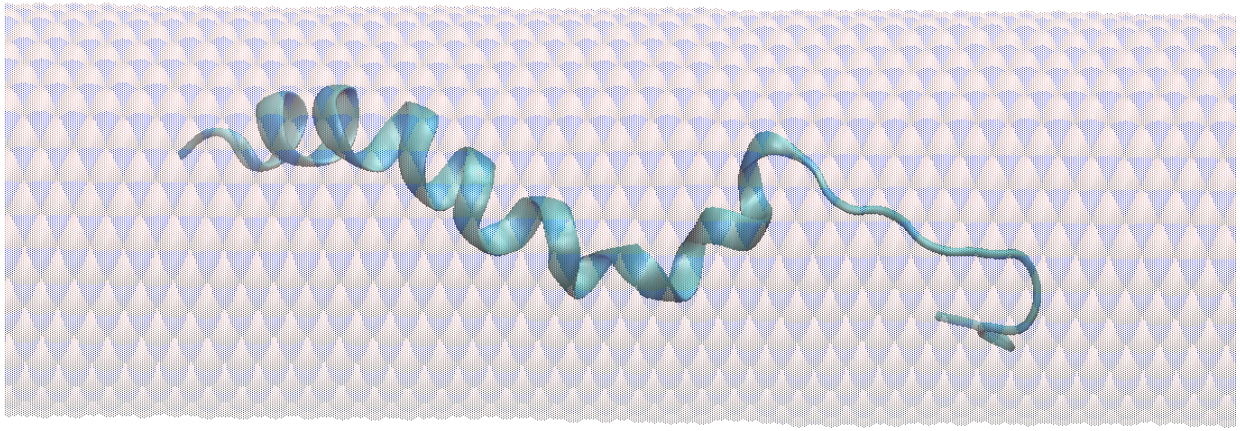
Simulated Systems: Inside - BNNT

(18, 18) at 0 ns



(18, 18) at 60 ns



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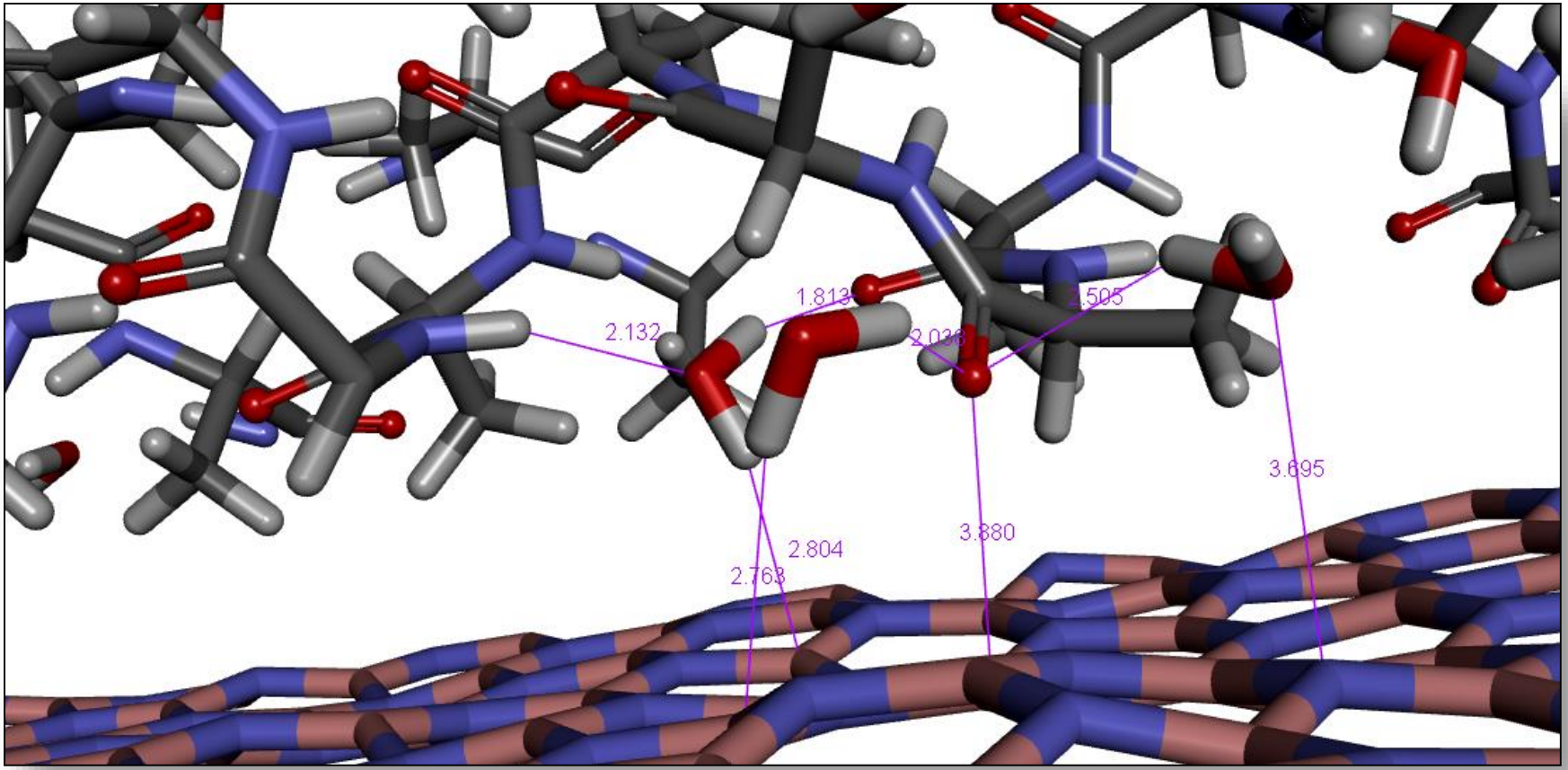
Encapsulated water molecules in concave surface



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Salient Findings

- ✓ Secondary structural changes in helical peptide increases with decrease in the curvature of boron nitride based nanomaterials
- ✓ Water molecules plays important role in the stabilization of peptide conformation in the case of concave surface
- ✓ Boron nitride sheet induces large structural changes in peptide when compared to graphene
- ✓ High interaction energy of peptide with Boron nitride sheet causes more variations in peptide compared to graphene

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Interaction of Amphiphilic Peptide with Boron Nitride Sheet

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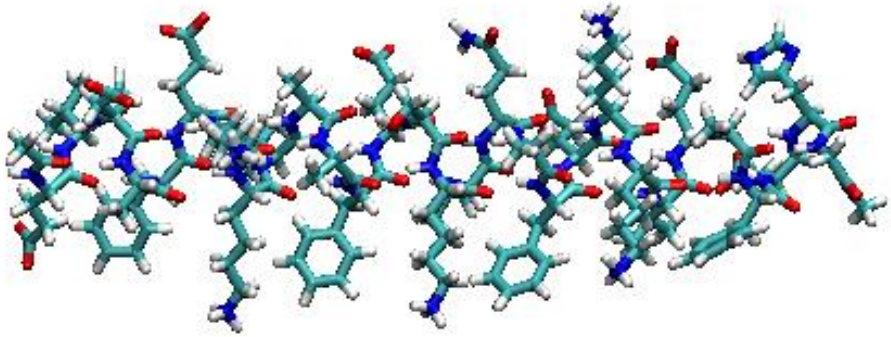
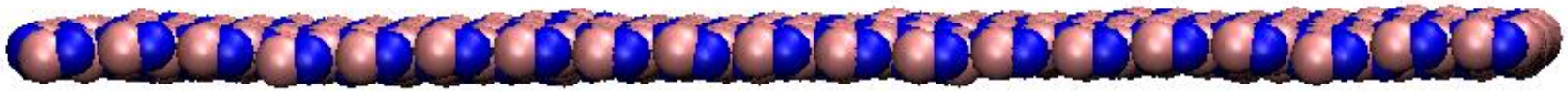
Model

Sequence of peptide : EVEAFEKKVAAFESKVQAFEKKVEAFEHG





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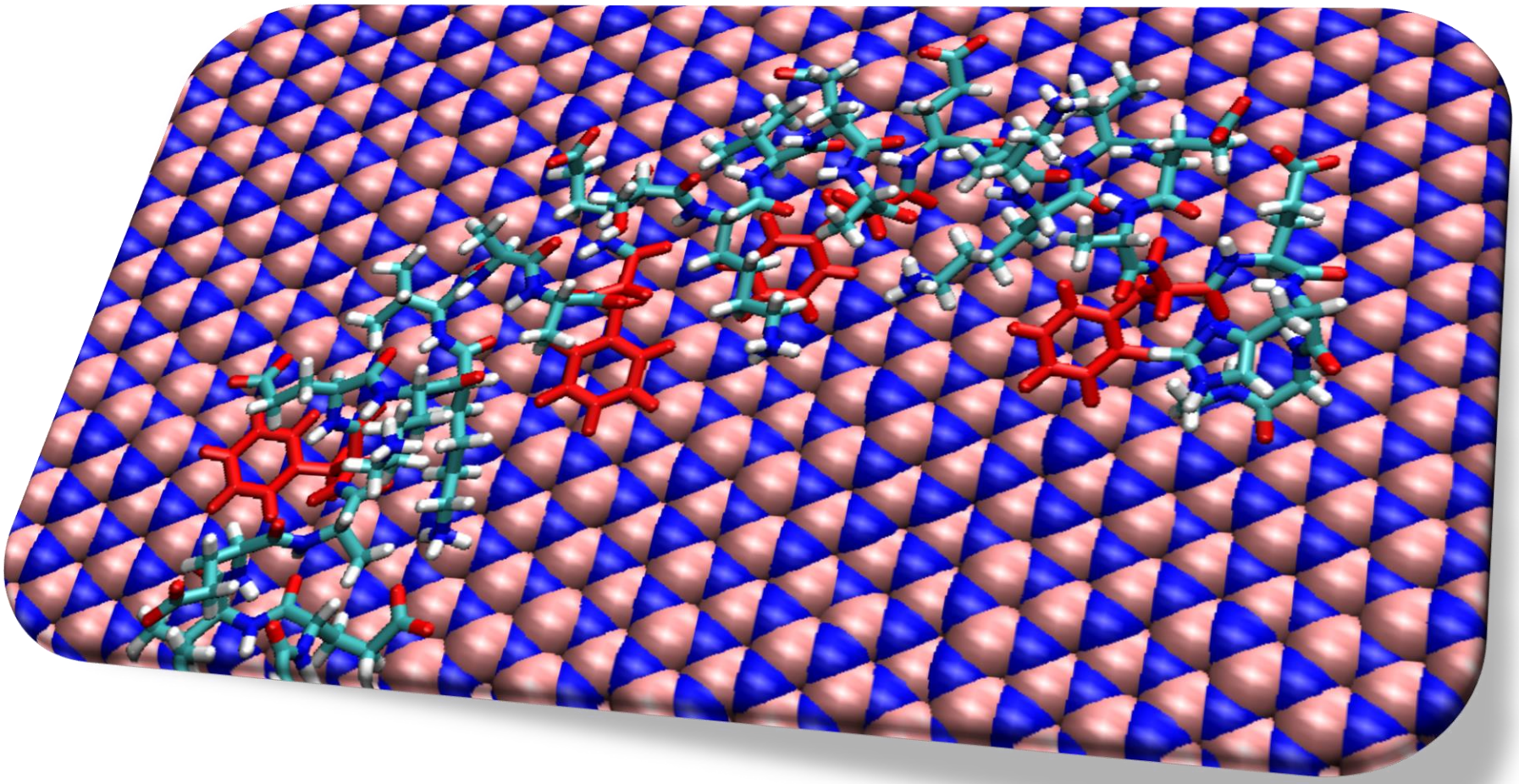
Simulated System



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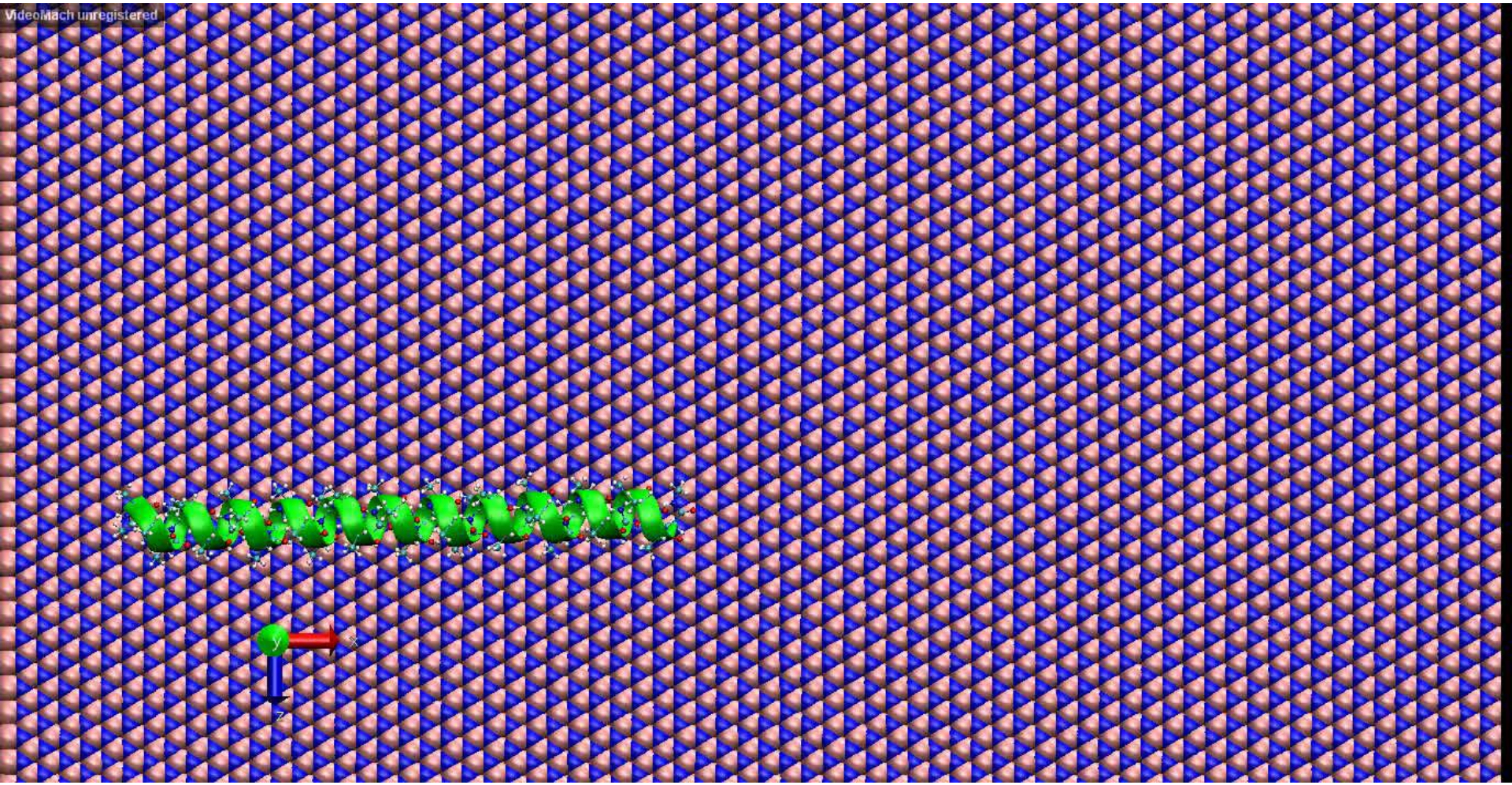

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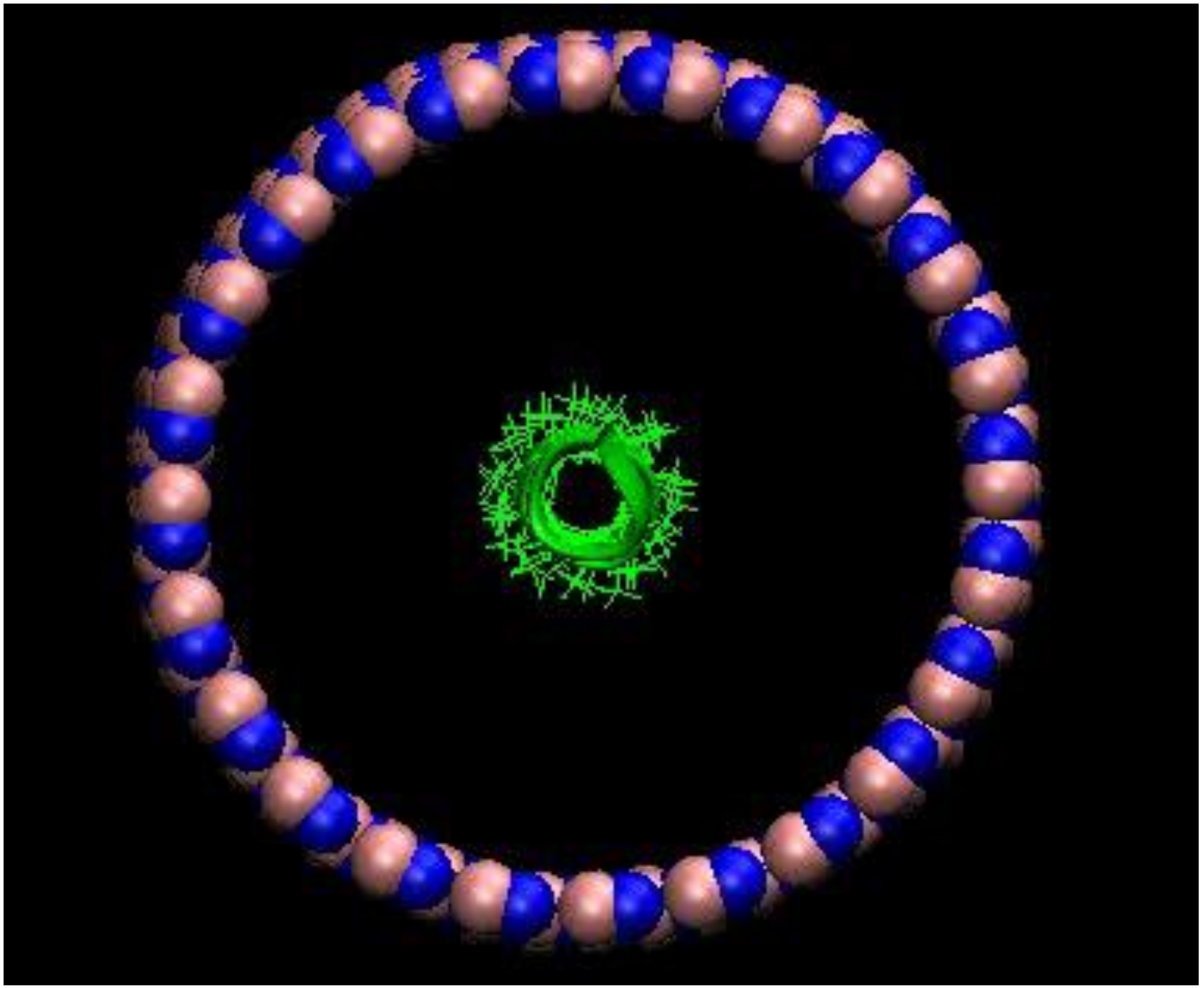

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Salient Findings

- ✓ Amphiphilic peptide interacts through π-π stacking
- ✓ Amphiphilic peptide become hydrophilic in nature after adsorption
- ✓ Aromatic amino acids are important for the adsorption process
- ✓ Acidic and basic residues are not involved in the adsorption process and they are stabilized by water molecules

S. K. Mudedla, K. Balamurugan, and V. Subramanian, J. Phys. Chem. C, 2016, 120, pp 28246–28260

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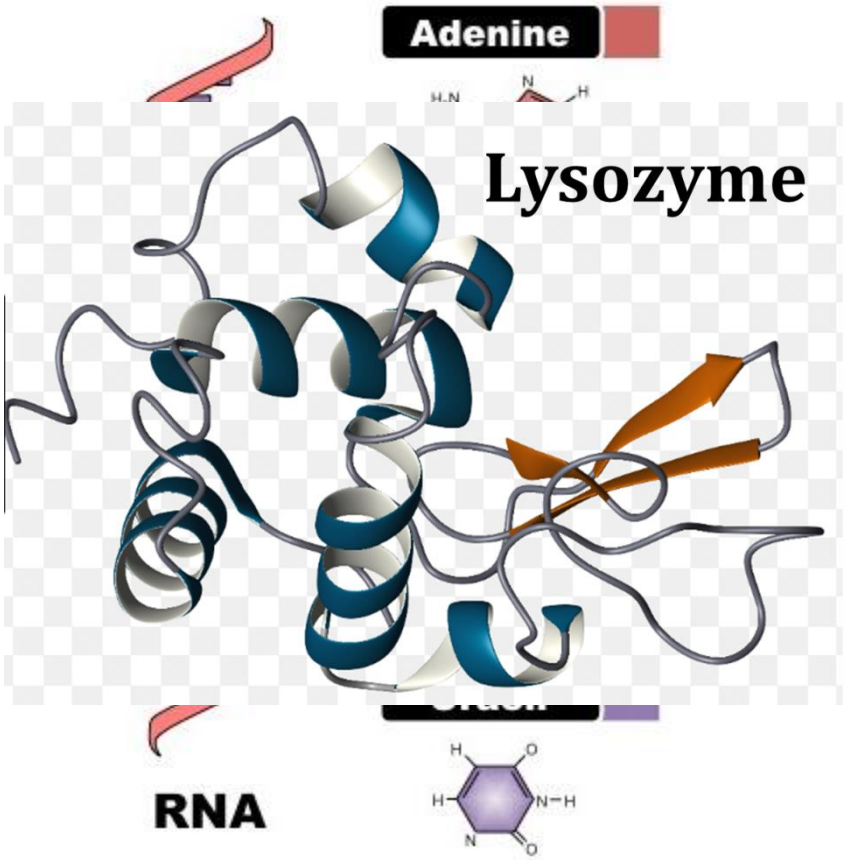
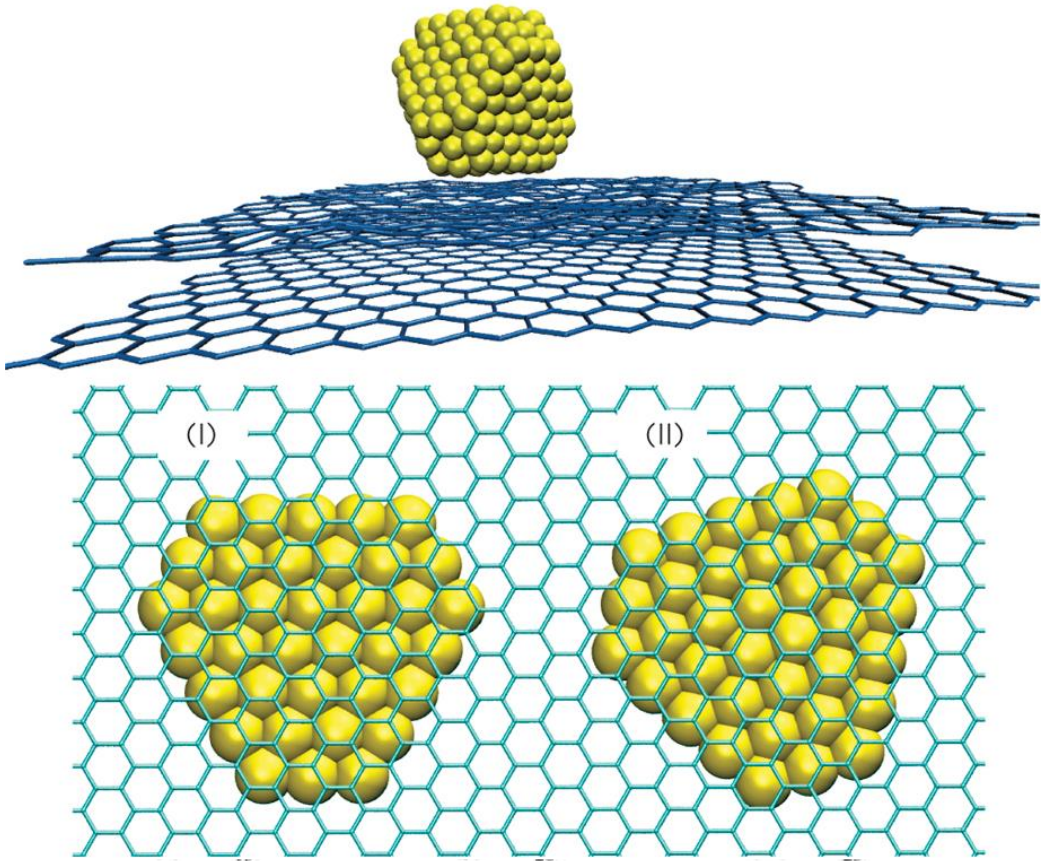
Future Plan





I thank my teachers and mentors for their support and encouragement

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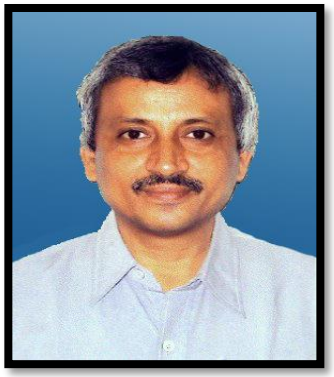
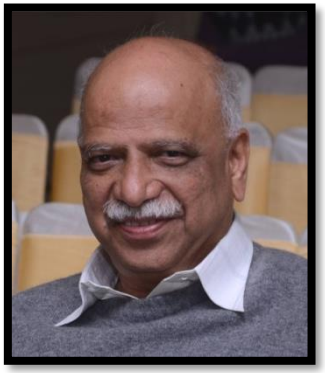
Prof. N. Sathyamurthy



Prof. P. K. Chattaraj



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MD Simulation of the Carbon Nanotube–α-Helix Complex Reveals the Breakage of Hydrogen Bonds in the α-Helix (see page 6A)
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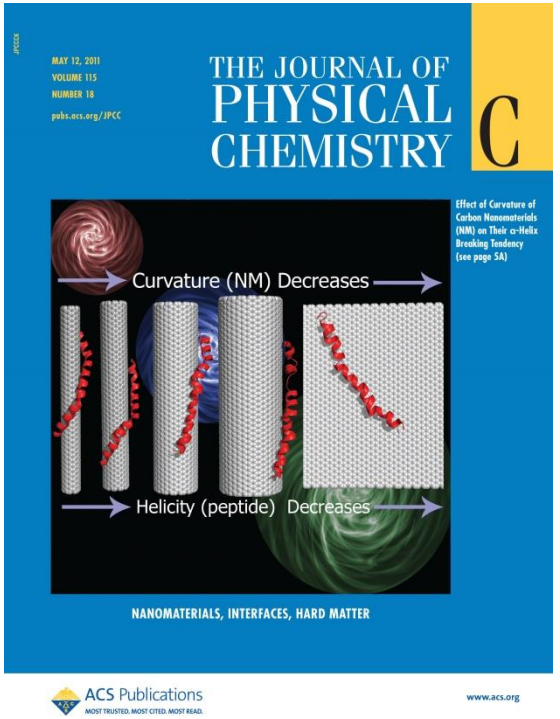
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Effect of Curvature of Carbon Nanomaterials (NM) on Their α-Helix Breaking Tendency (see page 5A)
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