Confinement and hydration effects on helix formation of polyalanine in open nanotubes

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Introduction

- Experiments indicate that large proteins fold to their native structure faster in the cell than in dilute solution.[1]
- Studies suggest the ribosome may play a role in this process by allowing proteins to form α-helices inside its tunnel during protein synthesis but experiments indicate this process is sequence dependent.[1,2]

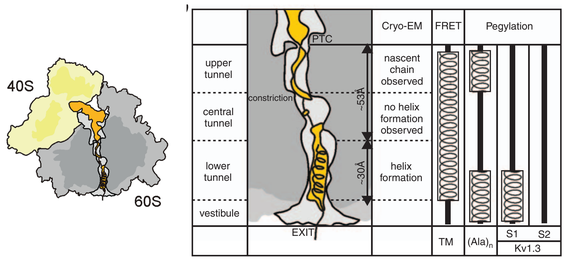


Figure 1: Summary of experimental studies on the ribosome tunnel (picture left).[2]

- Molecular dynamics (MD) simulations of model systems relevant to these experiments display conflicting behavior. Simulations without water reveal α-helix stabilization due to a dramatic reduction of entropy of the coiled state upon confinement[3], however, MD simulations with water show the opposite effect with the α-helix destabilized upon confinement.[4]

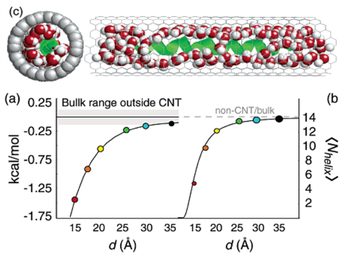
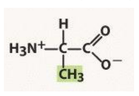
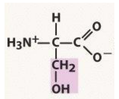


Figure 2: Average number of helical residues from MD simulations of polyalanine in periodically replicated CNTs with water.[4]

Objectives

- Our group has performed MD simulations of non-polar ($Alanine_{23}$) and polar ($Serine_{23}$) polypeptides inserted into carbon nanotubes (CNT) open to a water bath.

Alanine  Serine 

- We would like to elucidate water's crucial role in determining the preferred conformation of proteins in these confining geometries.
- We also would like to determine the thermodynamics of the α-helix-coil transition inside nanoscale confinement.
- We hope this will inform future studies on the ribosome tunnel.

Methods

Replica Exchange Molecular Dynamics (REMD):

- 62-88 replicas spanning the temperature range 280-500 K simulated in the NPT ensemble using GROMACS 5.1.1
- Langevin dynamics to control the temperature.
- Berendsen pressure coupling
- CHARMM36 and AMBER99SB*-ILDN force fields
- Bulk water and D = 12.2, 13.6, 14.9, 16.3, 20.4 and 35.3 Å CNTs

Results

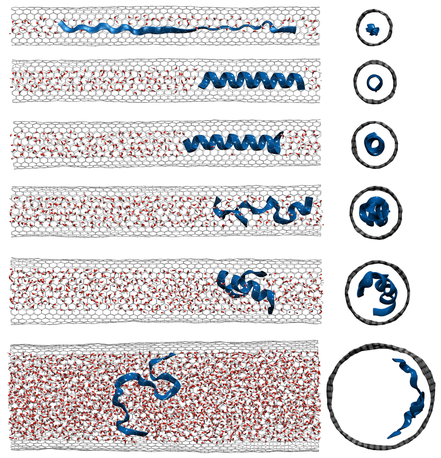
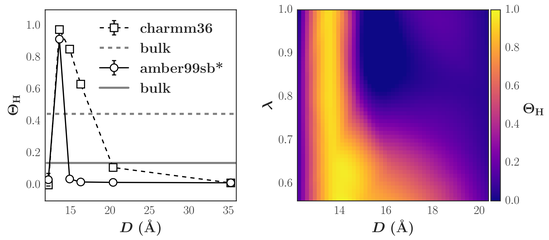


Figure 3: Representative conformations of Ala_{23} in CNT of diameters D=12.2, 13.6, 14.9, 16.3, 20.4, and 35.3 Å from the CHARMM36 force field.



$$\Theta_H = \frac{\sum_{\phi,\psi} H^{\phi} H^{\psi}}{N^{\phi,\psi}} \qquad \begin{matrix} \psi_0 = -47^\circ \\ \phi_0 = -57^\circ \\ a = 30^\circ \end{matrix}$$

$$H^{\phi} = \begin{cases} 1 \text{ if } |\phi - \phi_0| \le a \\ 0 \text{ if } |\phi - \phi_0| > a \end{cases}$$

$$V = 4\varepsilon\lambda\left[(\sigma/r)^{12} - (\sigma/r)^{6}\right] \qquad 0 < \lambda \le 1$$

Figure 4: (Left) Definition of helicity and a plot of helicity vs D. (Right) A phase diagram of helicity in the (D, λ) plane with an expression for the Lennard-Jones potential scaled by λ for the CNT.

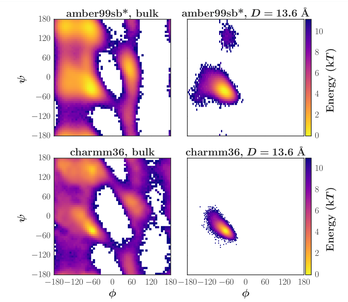


Figure 5: Ramachandran potentials of mean force for Ala_{23} in bulk water and in the D=13.6 Å CNT for both force fields.

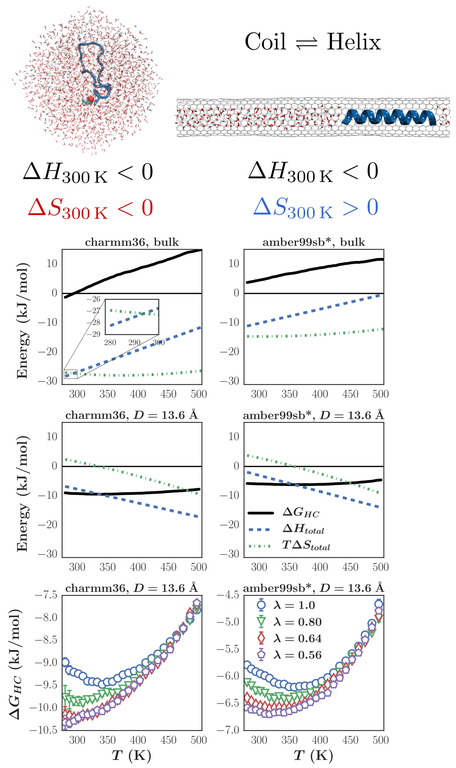


Figure 6: Thermodynamics of the coil-helix transition for Ala_{23} in bulk water and in the D=13.6 Å CNT for different λ.

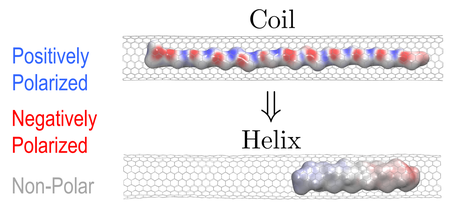


Figure 7: Electrostatic potential for Ala_{23} as a coil and as a helix. The polar surface of the coil experiences a solvent mediated repulsion from the CNT while the non-polar surface of the helix experiences a solvent mediated attraction. This drives helix formation in the CNT.[5]

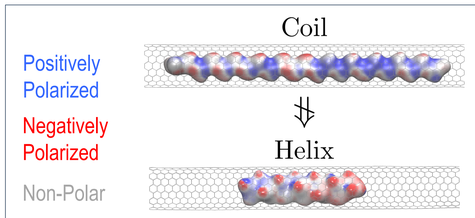


Figure 8: Electrostatic potential for Ser_{23} as a coil and as a helix. The polar surface of the coil experiences a solvent mediated repulsion from the CNT but so does the polar surface of the helix. This opposes helix formation in the CNT.[5]

Conclusions

- Our extensive atomically detailed MD simulations with open CNTs highlight the importance of water in determining the conformation of polymers in nanoscale confinement.
- Polyalanine forms a thermodynamically stable α-helix inside the open CNT which is different from previous studies using periodically replicated CNTs.[4]
- Polyserine does not from an α-helix inside the CNT. We attribute this to the solvent mediated repulsion between the surface of the helix and the CNT.
- We intend to extend our results to surfaces with mixed polarity. We also intend to further characterize water in these systems.

References

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