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.¹²
- 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 confinement³; however, MD simulations with water show the opposite effect with the α-helix destabilized upon confinement.⁴

Objectives

- Our group has performed MD simulations of non-polar (Alanine₁₃) and polar (Serine₁₃) polypeptides inserted into carbon nanotubes (CNT) open to a water bath.
- 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 1: Summary of experimental studies on the ribosome tunnel (picture left).²
Figure 2: Average number of helical residues from MD simulations of polyalanine in periodically replicated CNTs with water.⁴
Figure 3: Representative conformations of Alα₁₃ in CNT of diameters D=12.2, 13.6, 14.9, 16.3, 20.4, and 35.3 Å from the CHARMM36 force field.
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 A for the CNT.

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
- Polyelectrolyte does not form 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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