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Computer simulations of confined systems

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Principal Investigator: Rasaiah, Jayendran C.	**Award ID:** 0549187

Organization: University of Maine

Submitted By:

Rasaiah, Jayendran - Principal Investigator

Title:

Computer simulations of confined systems

Project Participants

Senior Personnel

>**Name:** Rasaiah, Jayendran
>
>**Worked for more than 160 Hours:**   Yes
>
>**Contribution to Project:**
>
>Jayendran C Rasaiah is the supervisor of the group and the desigener of all of the research projects. He is also involved in the carrying out some of the simulations, interpreting the data and writing up the work for publication.

Post-doc

>**Name:** Feng, Guogang
>
>**Worked for more than 160 Hours:**   Yes
>
>**Contribution to Project:**
>
>1: Developed a protocol to monitor the number of water molecules in
>a protein cavity.
>
>2: Implemented MD simulation on the largest protein cavity in tetrabrachion at 383K and 403 K for a long period time to check if water is still in the largest cavity to confirm the prediction of the recent published paper by the group.
>
>3:Developed and implemented quantum Oja-Shavitt-Singer (OSS2) potential for water clusters, and compared their results with Gaussian results.
>
>4. Currently working on water in the polar cavities of interleukin-1β.
>
>His work is supported by the current (CHE 0549187) NSF grant.
>
>5: Developed new method to determine upper and lower bounds for the chemical potential by computer simulation.
>
>6: Completed study of free energy of transfer of water into four cavities in interleukin-1β.

Graduate Student

>**Name:** Waghe, Aparna
>
>**Worked for more than 160 Hours:**   Yes
>
>**Contribution to Project:**
>
>Ms Aparna Waghe contributed to the project as part of her doctoral research on the 'Computer simulations of water and methanol in carbon nanotubes'. Her work was supported by the current (CHE 0549187) and previous (CHE 9981336) NSF grants. Ms Waghe investigated the free energy and kinetics of water filling narrow (8.1? diameter) carbon nanotubes(CNT) of two different lengths, and the extreme sensitivity of this filling to small changes in the nanotube-water interactions. From the temperature coefficient of the free energy, she showed that filling is driven by the energy and not the entropy of transfer. Ms Waghe also studied the thermodynamics filling CNT with methanol. Methanol readily enters into CNT of the same dimensions used in the study of water, suggesting their use in separating methanol/water mixtures. Ms Waghe received her doctorate in Chemistry from the University of Maine in May 2007.
>She is employed as an assistant professor at Plymouth State University in Plymouth, N.H. where she teaches freshman chemistry as well as physical chemistry.

Name: Yin, Hao

Worked for more than 160 Hours: Yes

Contribution to Project:

Hao Yin contributed investigated the structure and thermodynamics of water in nonpolar cavities and water in two protein cavities by computer simulation using the TIP3P model of water. He showed that water transfer into the nonpolar cavities of the fullerenes C140 and C180 leads to thermodynamically stable hydrogen bonded clusters similar to what is found in the gas phase. He then studied water in the relatively small central nonpolar cavity of interleukin-1β and found it is thermodynamically unstable showing that the cavity is mostly empty. His next project was on water in the largest nonpolar cavity of the right-handed coiled-coil stalk of tetrabrachion. He found that the cavity water was thermodynamically stable and existed as a hydrogen bonded cluster of 7-9 water molecules. Filling is driven by the energy rather than the entropy of transfer. Both energy and entropy only depended weakly on temperature. Drying of the cavity was predicted above 384K. Hao Yin was supported by the current the current (CHE 0549187) and previous (CHE 9981336) NSF grants.

He has completed all requirements for his PhD in Chemistry and will receive his doctorate from the University of Maine in August 2007.

Hao Yin received his doctorate from the University of Maine in August 2007 and was employed as a post-doctoral fellow in the Chemistry Department of the University of British Columbia, where he worked with

Professor G. Patey. He has recently returned to China, where he is working in private industry in the computational design of experiments.

Name: Samaratunga, Seneviratne

Worked for more than 160 Hours: Yes

Contribution to Project:

A second year graduate student Seneviratne Samaratunga carried out molecular dynamic simulations of peptides in carbon nanotubes. He studied the conditions under which alpha helix formation occurs in nanotubes when water is present.

Undergraduate Student

Name: Suvlu, Dylan

Worked for more than 160 Hours: Yes

Contribution to Project:

Dylan Suvlu is working on the structure and stability of polypeptides in
confined spaces such as carbon nanotubes in the presence of water.

Technician, Programmer

Name: Fortune, Stephen

Worked for more than 160 Hours: No

Contribution to Project:

Stephen Fortune maintained our work stations,printers and computer network connections. He is an excellent programmer and is expert in
maintaining computer hardware and installing software. He also contributed to our research studies of water in confined systems. He is now employed in the private sector in Portland, Maine.

Other Participant

Name: Silwal, Indira

Worked for more than 160 Hours: Yes

Contribution to Project:

Indira Silwal developed new ab-initio methods to calculate the proton affinity of a molecule from the potential energy surface for proton transfer between water and the other species.

Research Experience for Undergraduates

Organizational Partners

Other Collaborators or Contacts

Dr Gerhard Hummer, Chemical Physics Division, NIDDK, National Institutes of Health, Bethesda, MD
Professor. Jan. Miller, Department of Metallurgy, University of Utah, Salt Lake City, UT
Hao Du, Graduate student Department of Metallurgy, University of Utah, Salt Lake City, UT
Dr Jianjun Zhu, Research Associate, Department of Chemistry, State University of New York, Stony Brook, NY.
Dr Dev Thirumalai, I.P.S.T., University of Maryland, College Park, MD
Dr Song Hi Lee, Department of Chemistry, Kyung Sung University, Pusan, S.Korea.
Dr. Subramaniann Vatheewaran, Rensselaer Polytechnic Institute, Troy, NY
Dr. Marius Clore, Chemical Physics Division, NIDDK, National Institutes of Health, Bethesda, MD
Dr. Touradj Solouki, Dept of Chemistry, University of Maine
Dr. Jan Szulejko, Dept of Chemistry, University of Maine

Activities and Findings

Research and Education Activities: (See PDF version submitted by PI at the end of the report)
The research carried out during the second year of the current NSF grant (CHE 0549187) focused on five projects, all of which involved molecular dynamics(MD) simulations: (i) calculations of the energy and entropy of transfer as a function of temperature of water into nanotubes to determine the driving force for water occupancy. (ii)MD simulations of methanol occupancy of carbon nanotubes of different dimensions (iii)Studies of water occupancy of nonpolar cavities in two proteins (a) interleukin 1-β and (b)tetrabrachion using a combination of theory and molecular dynamics simulations.(iv) thermodynamics of water occupancy in the four polar cavities of interleukin 1-β. (v) Development of a new method to calculate the chemical potential of molecules, including water, in confined systems.

Two chemistry graduate students Aparna Waghe and Hao Yin worked on these projects. They completed all academic requirements for doctorates in chemistry with support from the Current NSF grant. Aparna Waghe received her PhD in May 2007 and Hao Yin received his PhD in August 2007.

A postdoctoral fellow, Dr. Guogang Feng also worked on Molecular dynamics and ab inito simulations of water in protein cavities, and the development of new methods to calculate the excess chemical potential in confined systems.

The PI (J.C.Rasaiah) collaborated with Professor Jan D.Miller and a graduate student Hao Du at the University of Utah on simulations of concentrated aqueous alkali halide solutions. The PI was on the doctoral thesis committee of Hao Du, who graduated in August 2007.

Dr Indira Silwal joined the group as a research fellow and is carrying out calculations of proton affinities of molecules from proton transfer energy profiles.

Dylan Suvlu, an undergraduate, is studying the structure of polypeptides in confined spaces (carbon nanotubes) in the presence of water.

The research carried out during the last year of the current NSF grant(CHE 0549187) focused on five projects, four of which involved molecular dynamics(MD)
Simulations. The projects are(i) alpha helix formation of peptides in carbon nanotubes(Dev Thirumalai, Dylan Suvlu and Seneiviratne Samaratunga (ii) Umbrella sampling studies of water occupancy of nonpolar and polar cavities in interleukin 1-β (with Gerhard Hummer)(iii)Upper and lower bounds for the chemical potential from particle insertion and removal from the bulk phase and confined geometries (with Gerhard Hummer and Guogang Feng))((iv)Mobility of the hydroxide ion in bulk water and carbon nanotubes using a new OSS2 potential(with Song Hi Lee) (v) Ab-initio calculations of the free energies of proton transfer from protonated water (H3O+) to halomethanes(with Indira Silwal). Two graduate student (Indira Silwal and Seneiviratne Samaratunga) and a senior undergraduate (Dylan Suvlu) worked on these projects.

The PI (J.C.Rasaiah) collaborated with Professor Dave Thirumalai at the University of Maryland on the studies of alpha helix formation of peptides in carbon nanotubes

and with Dr. Gerhard Hummer of the studies of water in interleukin 1- and on the upper and bounds for the excess chemical potential. The studies of helix formation of peptides in CNTs peptide was largely carried out by a senior undergraduate Dylan Suvlu and will be the main topic of his undergraduate thesis. A second year graduate student Seneviratne Samaratunga work on a different peptide in CNTs in and in doing so is learning how to do molecular dynamics simulations.

Findings: (See PDF version submitted by PI at the end of the report)

(a) Water flow through carbon nanotubes- Our studies under the current grant showed that the driving force for water to enter a carbon nanotube is the energy and not the entropy of transfer. The work was carried out by Aparna Waghe, a graduate student in chemistry, under the supervison of the PI.

(b)Methanol occupancy of carbon nanotubes. Although methanol is a larger molecule than water, we found that it easily enters a carbon nanotube. Methanol filled nanotubes do not empty as easily as water when the nanotube-water interaction is reduced. This may be useful in separating water-methanol mixtures. This investigation is complete and is being written up for publication.

(c) Water in the central nonpolar cavity of interleukin 1-β. By calculating the grand partition function term by term, we obtained the free energy of transfer of water into this cavity by MD simulation. The calculation shows that the cavity water may not be thermodynamically stable. This study helps resolve a controversy arising from x-ray scattering and NMR spectroscopy studies that claimed the presence or absence respectively of water in this cavity. The simulations were carried out by Hao Yin, a graduate student in chemistry, using the TIP3P model for water. Dr Guogang Feng, who joined the group in November last year as a postdoctoral fellow, extended the work to different water models . His study shows that the inclusion of polarizability in the water model may tip the free energy balance in favor of stable water clusters even in the nonpolar cavity. He also investigated the thermodynamics of transfer of water into four polar cavities in interleukin 1-β; which contain 1 or 2 molecules of water according to experimental X-ray studies. By showing that the water molecules in these cavities are thermodynamically stable we were able to validate the underlying theory and simulation methods developed by us to study the thermodynamics of water transfer into protein cavities. This research is being written up for publication.

(d)We have also carried out molecular dynamics (MD) simulations to investigate the structure and thermodynamics of water filling the largest cavity of the right-handed coiled-coil stalk of the thermostable protein tetrabrachion at 365 K (92oC), the temperature of optimal bacterial growth, and at room temperature (298 K). A hydrogen-bonded water cluster of seven to nine water molecules was found to be thermodynamically stable in this cavity at both temperatures, confirming the X-ray studies of this unusual protein. Water filling is driven by the energy of transfer, and opposed by the entropy, both depending only weakly on temperature. Our calculations suggest that cluster formation becomes unfavorable at ~384 K (110oC), signaling the onset of drying just slightly above the temperature of optimal growth. 'Drying' thus precedes protein denaturation. At room temperature, the second largest cavity in tetrabrachion accommodates a five water molecule cluster, as reported in the X-ray studies. However, the simulations show that at 365 K the cluster is unstable and breaks up. This work was carried out by Hao Yin under the supervision of the PI and in collaboration with Dr.Gerhard Hummer. This research was published in the Journal of the American Chemical Society.

(e)During the past two years, the PI has also worked with Dr. Jan Miller and graduate student Hao Du of the University of Utah on investigations of the structure and transport properties of concentrated alkali halides in water by computer simulation. We found that the chloride ion penetrates the hydration sheath of the lithium ion at high concentrations of lithium chloride. This work was published in the Journal of Physical Chemistry. It has led to collaboration with Dr. Alan Soper, who is at the Rutherford -Appleton laboratory in the United Kingdom. Beam time was approved and the structure of these solutions by Xray and neutron diffraction motivated by the simulations, was studied and the results are being analyzed.

(f) Dr.Guogang Feng, Dr. Hummer of NIH and the PI have developed a new method to calculate the chemical potential of molecules by combining both particle insertion and particle removal energy histograms obtained in computer simulations. This method is distinct from Bennett's method which is applied only to a narrow range of energies where the distribution functions overlap. The new method is extremely useful in studying water in confined systems and is being written up for publication. It was used in our recent study of water in the nonpolar cavity of interleukin 1-β.

(g)Hydration and confinement effects on alpha helix formation of peptides in carbon nanotubes.
Understanding the stability of peptides and proteins in confinement is important in a number of biological situations, including translocation through nanopores and the ribosome exit tunnel. We used MD simulations to study short peptides, ranging in length from 3 to 10 amino acid residues, in fully hydrated carbon nanotubes. We find that stability of peptide helices in carbon nanotubes depends on a number of factors such as the amino acid sequence, solvent conditions, the nanotube dimensions and the strength of the nanotube-peptide interactions.Our findings were presented by the PI at the last 2009 ACS National meeting in Washington DC.

(h) Water in the central nonpolar cavity of interleukin 1-β. By calculating the grand partition function term by term, we had previously obtained the free energy of transfer of water into this cavity by MD simulation. The calculation shows that the cavity water may not be thermodynamically stable. This study seemed to resolve a controversy arising from x-ray scattering and NMR spectroscopy studies that claimed the presence or absence respectively of water in this cavity. The previous work was done by Hao Yin a graduate student and DR. Guogang Feng a post doctoral fellow. We subsequently noticed that one or two water molecules in the nonpolar cavity tried to escape into the interior of the protein thus calling into question our free energy studies. We free enrgy calculations were redone using an umbrella potential to restrain the water molecules from leaving the cavity and then correcting for this. On balance the free energy of transfer is positive and unfavorable

but a modest change in the chemical potential of water could tip the balance in favor of filling. Our previous conclusions that the free energy of transfer for filling the four polar cavities is favorable remain unchanged. A manuscript describing this research is being written up for publication.

(i) Upper and lower bounds for the chemical potential. We have derived upper and lower bounds for the chemical potential of molecules in the bulk fluid as well as in confined systems from the probability distributions of the energies for insertion and removal respectively. By combining these two distributions we have been able to calculate the corrections to these bounds which provide the chemical potential in two ways that should coincide. We have applied to determining the chemical potentials of TIP3p and SPCE water and also the chemical potential of TIP3p water in the polar and nonpolar cavities of interleukin 1-β. The work was done in collaboration with Dr Guogang Feng and Dr. Hummer

(j) Mobility of the hydrogen and hydroxide ion in bulk water and in carbon nanotubes. We studied proton transfer between a hydroxide ion and water and a hydronium ion and water along a quasi-one dimensional chain of water molecules in narrow carbon nanotubes (CNT) of diameter 8.1Å by molecular dynamics (MD) simulations using a dissociating water model(OSS2 model of Ojame) based on ab initio calculations. Both the hydrogen and hydroxide ion have greatly enhanced mobilities due to proton transfer along the water wire of the carbon nanotube. The mobility of a hydrogen ion is about 3.4 times that of a hydroxide ion, which is almost twice the ratio in bulk water under ambient conditions. Unlike the hydrogen ion, the hydroxide ion moved easily out of the tube and into a water reservoir, suggesting an additional pathway for proton transport in biological channels. Details of the structural diffusion mechanism in proton transfer reactions involving a hydroxide ion in water and the structure of the solvated ions and transfer intermediates are in dispute. We elucidated the mechanism of proton transfer involving a hydroxide ion in water by molecular dynamics simulations using the OSS2 model. The hydroxide ion in bulk water was present as the four coordinated $OH^-(H_2O)_4$ complex which looses water molecule before a proton transfer occurs through the formation of a proton sharing intermediates in general agreement with the previously disputed first principles studies of small systems by Tuckermann et al.

Training and Development:
The following students and postdoctoral fellows were trained

(a) Aparna Waghe; Research Training in theoretical chemistry and computer simulations of water and methanol in carbon nanotubes. (doctorate in Chemistry awarded May 2007)

(b) Hao Yin; research training in Theoretical and computational studies of water in nonpolar cavities and proteins(doctoral candidate in Chemistry-graduation August 2007)

(c) Guogang Feng- postdoctoral fellow - studies of water in confined systems and development of new methods to determine the excess chemical potential of water in these systems.
Developed new methods to determine upper and lower bounds for the chemical potential of solutes by particle insertion and removal.

(d) Hao Du - University of Utah - computer simulation studies of alkali halide solutions at high concentrations(graduated in August 2007)

(e) Indira Silwal - graduate student in Chemistry, University of Maine
- ab-initio studies of proton affinity of solutes in water. (Graduated with PhD August 2008) She is currently continuing her work as a part time research fellow and teaching freshman Chemistry at the University of Maine.

(f) Dylan Suvlu - undergraduate Chemistry major, University of Maine
Working on stability and structure of polypeptides in carbon nanotubes in the presence of water.

The following students and postdoctoral fellows were trained

(g) Dylan Suvlu: Undergraduate Research training in computer simulation (molecular dynamics and Montecarlo simulations). Use of VMD and NAMD simulation packages and applications to studies of alphas helix formation of peptides in carbon nanotubes immersed in water
(h) Seneviratne Samartunga research training in Theoretical and computer simulation with applications to peptide conformations in confined systems.

(i) Indira Silwal- postdoctoral fellow ? ab initio studies of proton affinities and free energy of proton transfer reactions in the gas phase.

Outreach Activities:

We presented one paper and two posters on our work at the National American Chemical Society meeting in Boston August 19-23, 2007.

1. 'Water in nonpolar pores and protein cavities', G. Hummer, J.C.Rasaiah and Hao Yin. (Invited talk given by G. Hummer)
2. 'Metastable Water Clusters in the Nonpolar cavities of the Thermostable Protein Tetrabachion', H. Yin, G. Hummer and J.C. Rasaiah (Poster)
3. 'The mobility of the OH- ion in water and in carbon nanotubes', S.H. Lee and J.C. Rasaiah (Poster)

We presented two papers at the American Chemical Society on August 17-21, 2008 in Philadelphia, PA.
1. 'Water in protein cavities', G. Hummer, J.C.Rasaiah and G. Feng (invited talk given by G. Hummer)
2. 'Gas Chromatography/Fourier Transform Ion Cyclotron Resonance Mass Spectrometry and Ab-Initio Proton Affinity Calculations of Hydrocarbon Isomers in Petroleum', I. Silwal, J.C. Rasaiah, T. Solouki, Z. Luo

We presented a paper at the National American Chemical Society meeting in Washington DC August 19-23, 2009 and one paper at the forthcoming American Physical Society meeting in Portland Oregon. Both are invited papers.
1.Dylan Suvlu, S. Vaitheeswaran, Jayendran C. Rasaiah and D. Thirumalai 'Hydration effects on Peptide stability in Confinement' National meeting of the American Chemical Society meeting in Washington DC August 19-23, 2009.
2.Jayendran C.Rasaiah 'Water in the protein Interior' American Physical Society meeting March 15-19 2010.

Journal Publications

H.Du,J.C.Rasaiah and J.D.Miller, "Structural and dynamical properties of concentrated alkali halide solutions; a molecular dynamics study", J.Phys.Chem.B, p. 209, vol. 111, (2007). Published,

H.Yin,G.Hummer and J.C.Rasaiah, "Metastable water clusters in the nonpolar cavities of the thermostable protein tetrabrachion", J.Amer.Chem.Soc, p. 7369, vol. 129, (2007). Published,

Rasaiah, JC; Zhu, JJ, "Reaction coordinates for electron transfer reactions", JOURNAL OF CHEMICAL PHYSICS, p. , vol. 129, (2008). Published, 10.1063/1.302636

Rasaiah, JC; Garde, S; Hummer, G, "Water in nonpolar confinement: From nanotubes to proteins and beyond", ANNUAL REVIEW OF PHYSICAL CHEMISTRY, p. 713, vol. 59, (2008). Published, 10.1146/annurev.physchem.59.032607.09381

Lee, SH; Rasaiah, JC, "Local dynamics and structure of the solvated hydroxide ion in water", MOLECULAR SIMULATION, p. 69, vol. 36, (2010). Published, 10.1080/0892702090311525

Yin, H; Feng, GG; Clore, GM; Hummer, G; Rasaiah, JC, "Water in the Polar and Nonpolar Cavities of the Protein Interleukin-1 beta", JOURNAL OF PHYSICAL CHEMISTRY B, p. 16290, vol. 114, (2010). Published, 10.1021/jp108731

Silwal, IKC; Rasaiah, JC; Szulejko, JE; Solouki, T, "Proton transfer reactions of halogenated compounds: Using gas chromatography/Fourier transform ion cyclotron resonance mass spectrometry (GC/FT-ICR MS) and ab initio calculations", INTERNATIONAL JOURNAL OF MASS SPECTROMETRY, p. 1, vol. 293, (2010). Published, 10.1016/j.ijms.2010.03.00

Du, H; Rasaiah, JC; Miller, JD, "Structural and dynamic properties of concentrated alkali halide solutions: A molecular dynamics simulation study", JOURNAL OF PHYSICAL CHEMISTRY B, p. 209, vol. 111, (2007). Published, 10.1021/jp064659

Books or Other One-time Publications

G. Hummer, J.C.Rasaiah and Hao Yin, "Water in nonpolar pores and protein cavities", (2007). Poster, Published

Collection: American Chemical Society Meeting
Bibliography: Conference Proceeding

H.Yin, G.Hummer and J.C.Rasaiah, "Metastable Water Clusters in the Nonpolar cavities of the Thermostable Protein Tetrabrachion", (2007).
Poster, Published
Collection: American Chemical Society Meeting, Boston
Bibliography: Conference Proceeding

S. H. Lee and J.C.Rasaiah, "The mobility of the hydroxide (OH)- ion in water and in carbon nanotubes", (2007). Poster, Published
Collection: American Chemical Society Meeting, Boston
Bibliography: Conference Proceeding

I. Silwal, J.C.Rasaiah and T.Solouki,, "Multidimensional analysis of Environmental Samples Gas Chromatography/Fourier Transform Ion
Cyclotron Resonance Mass Spectrometry and ab-initio calculations", (2008). Talk, Published
Collection: 56 th ASMA Conference on Mass Spectrometry and Allied Topics, Denver Colorado
Bibliography: Conference Proceeding

Dylan Suvlu, S.Vaitheeswaran, J.C.Rasaiah and D.Thirumalai, "Hydration Effects on Peptide Stability in Confinement", (2009). Talk,
Published
Collection: American Chemical Society Meeting
Bibliography: Conference Proceeding

J.C. Rasaiah, "Water in Proteins", (2010). Talk, Published
Collection: American Physical Society Meeting, Portland, Oregon
Bibliography: Conference Proceeding

Jayendran C. Rasaiah, Guogang Feng and Gerhard Hummer, "Chemical potential from particle removal and insertion, Upper and power bounds
and accurate estimates from computer simulation", (2010). Poster, Published
Collection: American Chemical Society
Bibliography: Conference Proceeding

Seneviratne Samaratunga, Dylan Suvlu, Jayendran C. Rasaiah and Devarajan Thirumalai, "Hydration and confinement effects on helix
formation in a 23-residue polypeptide", (2010). Talk, Published
Collection: American Chemical Society
Bibliography: Conference Proceeding

Gerhard Hummer, Jayendran C. Rasaiah, Hao Yin and Guogang Feng, "Molecular dynamics studies of water protein interactions", (2010).
Talk, Published
Collection: American Chemical Society
Bibliography: Conference Proceeding

Song Hi Lee and Jayendran
C. Rasaiah
, "Structural and dynamic properties of revised OSS2 model", (2010). Poster, Published
Collection: American Chemical Society
Bibliography: Conference Proceeding

Web/Internet Site

URL(s):
http://chemistry.umeche.maine.edu/
Description:

Final Report: 0549187

Our research, eductational and outreach activities supported by NSF
are further described at this web site under the name of the PI - Jayendran Rasaiah

Other Specific Products

Contributions

Contributions within Discipline:

(a) Our computer simulation studies of the structural and dynamical properties of concentrated alkali halide solutions in collaboration with graduate student Hao Du and Dr.Jan Miller of the University of Utah have shown that cation size and the solvation shell structure have a significant effect on the viscosity of the solution. At high concentrations the solvation shell of the Li ion is penetrated by the chloride counterion to form a solvated dimer. This result has, to our knowledge, not been reported previously, and contributes to a better understanding of solution chemistry at high salt concentrations.

(b)Our molecular dynamics studies of the temperature coefficient of the free energy of transfer of water into carbon nanotubes carried out by graduate student Aparna Waghe showed that filling is extremely sensitive to the nanotube water interactions and that it is driven by the energy and not the entropy of transfer.This not only contributes to our understanding of how water fills nanopores but also raises the possibility of designing a water switch by chemical modification of nanotubes.

(c)Ms Waghe's studies showed that methanol readily enters into narrow carbon nanotubes. We are investigating the driving force for this process which unlike water does not form one dimensional chains in the nanotube.

(d)Our studies of the thermodynamics of water in nonpolar cavities of proteins(tetrabrachion and interleukin) are fundamental contributions to understanding the role of water in determining protein function and stability.

(e)Our studies of water in the four polar cavities of interleukin 1-β
are in complete agreement with the X-ray studies and validate our theoretical and computational methods used to study the thermodynamics of water transfer.

(f)The development of a new method to determine the excess chemical potential of water in confined systems will be important in future investigations of the thermodynamics of water transfer into confined systems.

(g)We have developed a new method to determine the proton affinity of a molecule by ab-initio methods involving the calculation of the potential energy surface for proton transfer from one molecule to another molecule of known proton affinity. The method distinguishes between proton affinities at different sites of the molecule and also provides information about molecular rearrangements after proton transfer occurs.

(h)A theoretical study of reaction coordinates for electron transfer reactions was published, in which a reaction coordinate was related to fluctuations in the polarization of the solvent molecules.

(i)A detailed invited review of water in non-polar confinement from 'Water in Nonpolar Confinement: From Nanotubes to Proteins and Beyond' was published in Annual Reviews of Physical Chemistry in May, 2008.

(j)Our studies of alpha-helix formation in carbon nanotubes with explicit solvent is an exciting and important approach to understanding the how protein helices are formed in the ribosome tunnel.

(k)Our work on the structure and dynamics of the hydroxide ion in water and carbon nanotubes is also of fundamental importance in understanding a different aspect of proton transfer in aqueous solutions.

Contributions to Other Disciplines:

(a)Our study of water in protein cavities would be useful in molecular biology and related disciplines in understanding the role that water plays in protein function and stability.Our work on water and methanol occupancy of carbon nanotubes may be useful in new technology to separate mixtures of water and methanol.Our studies of water in carbon nanotubes could be useful in the design of a water switch.

(b)Our calculations of the proton affinity of molecules by ab-initio methods have already provided a new dimension to the detection and characterization of molecules with the same mass-to-charge ratio by Fourier Transform Ion Cyclotron Resonance (FT-ICR) mass spectrometry through differences in the proton affinities of these compounds. Our development of methods to determine upper and lower bounds of the chemical potential by particle insertion and removal should be of value in determining the free energy of solutes in protein cavities and confined systems such as zeolites.

(c)Our work on alpha helixes in carbon nanotubes should help understand the role of the ribosome tunnel in enabling helix formation in proteins. The enhanced transport of the hydroxide in carbon nanotubes provides an additional mechanism for proton transport in biological channels.

Contributions to Human Resource Development:

The grant provided training for one postdoctoral fellow, Dr Guogang Feng, two graduate students, Aparna Waghe and Hao Yin who were doctoral candidates in my group.

Aparna Waghe recieved her PhD degree in May 2007 and Hao Yin received his PhD in August 2007.Ms Waghe is an Assistant Professor at

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Plymouth State University in New Hampshire where she teaches Physical and Freshman Chemistry. Hao Yin is a postdoctoral fellow in the Chemistry department of the University of British Columbia.

The PI has also trained a student and technician Stephen Fortune in molecular dynamics simulations. A new undergraduate student, Dylan Suvlu has joined the group and is being trained in molecular simulations and other aspects of computational chemistry.

The PI is continuing his research collaboration on water in protein cavities with Dr.Gerhard Hummer of the National Institutes of Health and with Professor Song Hi of Kyung Sung University in Korea on hydroxide ion and proton mobilty in aqueous solutions.

The PI is training two undergraduate students (Dylan Suvlu and Josh Gaylin) in to do large scale simulations of compounds of biological interest. A new graduate student Seneviratne Samartinga has joined our group and is being trained in computational and theoretical chemistry. The grant provided training for a postdoctoral fellow and students, at all levels. Graduate students S. Vaitheeswaran, A. Waghe, H. Yin, S. Samaratunga and an undergraduate, Dylan Suvlu, were members of the group at different times during the period of the grant and received partial or full support from the grant. A post doctoral fellow, Dr. Guogang Feng worked with full NSF support for two years. He left in 2009 to take a position at a company in Boston, Massachusetts.

Aparna Waghe completed her doctoral studies in Chemistry at the University of Maine in May 2008 and is an assistant Professor at Plymouth State University, Plymouth, New Hampshire.

Hao Yin completed his doctoral studies in Chemistry at the University of Maine ay 2007 and is now employed by the Henkel Company in Shanghai, China..

Indira Silwal completed his doctoral studies in Chemistry at the University of Maine in August 2008 and is now postdoctoral fellow at the Chemistry Department, United States Naval Academy, Annapolis, MD

Dylan Suvlu wrote his undergraduate thesis on 'Computer simulations of Confined Polypeptides' and is enrolled as a graduate student in my group at the University of Maine.

Guogang Feng was trained as a postdoctoral fellow (2008-2009)and is now working with in a company in Boston, Mass

Contributions to Resources for Research and Education:

Our simulation studies have led to introduction of hands on experience with molecular dynamics simulations in the graduate Statistical mechanics course(CHY673/PHY512) that I taught in the spring of 2007 to graduate students.
I taught the same course in the spring of 2009.
I am currently teaching (Spring 2010) a course in computer simulation methods CHY573 which includes Monte Carlo as well as molecular dynamics methods, calculations of free energy changes using umbrella sampling and multiple histograms, simulations of rare events and also phase transitions.
A course on Computer Simulation Methods (CHY 573), inspired and motivated by our research continues to be taught by me in the department. Graduate students from Physics and Chemistry, took the course when it was taught last time. I also teach 'Statistical Thermodynamics' (CHY 673) to graduate students in Chemistry and Physics department (I have a joint appointment with Physics) and introduced students to molecular dynamics simulations. This was a direct spin off of our research interest and support of computational studies by the NSF.

Contributions Beyond Science and Engineering:

Nothing yet to report.

Conference Proceedings

Hummer, G;Rasaiah, JC;Feng, GG, COMP 290-Free energy of hydration in the protein interior, "AUG 17-21, 2008", ABSTRACTS OF PAPERS OF THE AMERICAN CHEMICAL SOCIETY, 236: - 290-COMP AUG 17 2008

Silwal, IK;Luo, ZH;Rasaiah, JC;Solouki, T, PETR 79-Gas chromatography/Fourier transform ion cyclotron resonance mass spectrometry and ab initio proton affinity calculations of hydrocarbon isomers in petroleum, "AUG 17-21, 2008", ABSTRACTS OF PAPERS OF THE AMERICAN CHEMICAL SOCIETY, 236: - 79-PETR AUG 17 2008

Rasaiah, JC;Vaitheeswaran, S;Yin, H;Hummer, G, Water clusters in nonpolar cavities, "AUG 28-SEP 01, 2005", ABSTRACTS OF PAPERS OF THE AMERICAN CHEMICAL SOCIETY, 230: U2901-U2902 278-PHYS AUG 28 2005

Vaitheeswaran, S;Yin, H;Rasaiah, JC, Water between plates in the presence of an electric field, "AUG 28-SEP 01, 2005", ABSTRACTS OF PAPERS OF THE AMERICAN CHEMICAL SOCIETY, 230: U2904-U2904 283-PHYS AUG 28 2005

Categories for which nothing is reported:

Organizational Partners
Any Product

Activities

1. Research and educational activities.

The major research carried out during the period of this grant used computer simulation and theory to investigate (i) thermodynamics of water in confined spaces such as carbon nanotubes and protein cavities (ii) calculations of the chemical potential in comouter simulations of water in the bulk and in confined geometries (iii) Equilibrium structure, hydration and viscosity of concentrated electrolytes (iv) *ab-initio* calculations of proton transfer reactions in solution (iv) mobility of hydroxide ion (v) Helix formation of peptides in confined geometries (vi) rescaling the OSS2 dissociating model for water.

Specifically the problems studied were

(i)Thermodynamics of water and methanol occupancy of carbon nanotubes (A.Waghe and G.Hummer)

(ii) Structure and thermodynamics of water filling the largest nonpolar cavity of tetrabrachion (H. Yin and G. Hummer)

(iii)Water in the polar and nonpolar cavities of the protein interleukin 1-beta (H.Yin, G.Feng and G.Hummer)

(iv) Structure and transport properties of concentrated alkali halides in water by MD simulation (H. Du and Jan Miller)

(v) Upper and lower bounds for the excess chemical potential from particle removal and insertion in the bulk phase and in confined geometries (G. Feng and G Hummer)

(vi) *Ab-initio* calculations of the proton affinity from potential energy surfaces for prton transfer between water and other species(Indira Silwal, Jan Szulejko, Touradj Solouki)

(vii) Mobility of the hydroxide ion in bulk water and in carbon nanotube using the OSS2 potential (S.H.Lee)

(viii) preliminary studies of alpha helix formation of peptides in carbon nanotubes)D. Suvlu, S. Seneviratne and D. Thirumalai)

(ix) Rescaling the OSS22 model for water to study proton transfer reactions (S.H.Lee)

(x) Studies of proton transfer and the mobility of H^+ and OH^- ions(S.H.Lee)

Three graduate students (Aparna.Waghe, Hao. Yin, and Indira Silwal), an undergraduate (D.Suvlu) and a postdoctoral fellow (Guogang Feng) received training under this project.

We also collaborated with Dr. Gerhard Hummer of the National Institutes of Health MD,

Professor Devarajan Thirumalai of the University of Maryland, College Park, MD and Professor Song Hi Lee, Chemistry Department, Kyung Sung University, on some of the projects listed above.

Major findings resulting from these activities.

(a)Thermodynamics of water and methanol occupancy of carbon nanotubes

We have investigated the thermodynamics of filling of a short (6,6) open carbon nanotube solvated in water. Previously we had determined the free energy of transfer (Nature and Aparna JCP) from the bulk phase into the nanotube, with the nanotube-water interactions controlled by means of a switching parameter λ which modulates the nanotube –water interactions thereby mimicking chemical modification and changes in solvent osmolality. For $\lambda = 1$ the nanotube is always filled but it is mostly empty when $\lambda = 0.752$. For the intermediate value of $\lambda = 0.785$, the nanotube shows a nearly two state system oscillating between empty and filled states.
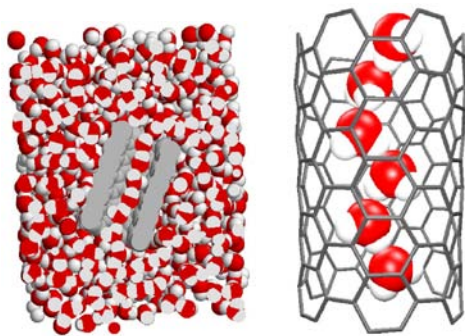
Figure 1 Nanotube filled with water. Slab view of the short nanotube filled with water molecules inside nanotube surrounded by water reservoir,
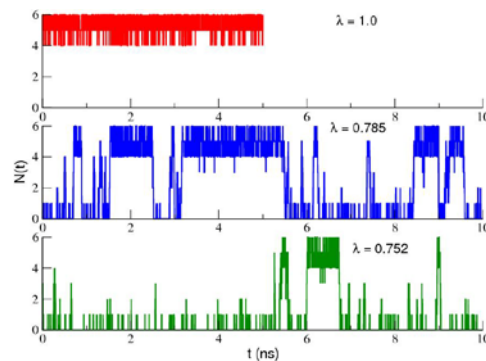
Figure 2 Sensitivity of water occupancy for different nanotube-water attractive interactions scaled by control parameter λ at 300K.

Under the current grant we determined the energy and entropy of transfer as a function of the water occupancy N from the corresponding free energy of transfer of as a function of temperature from 280K and 320K. The free energy barrier for filling decreases with the increasing λ corresponding to larger dispersion interaction between the nanotube and the water molecules in the nanotube.
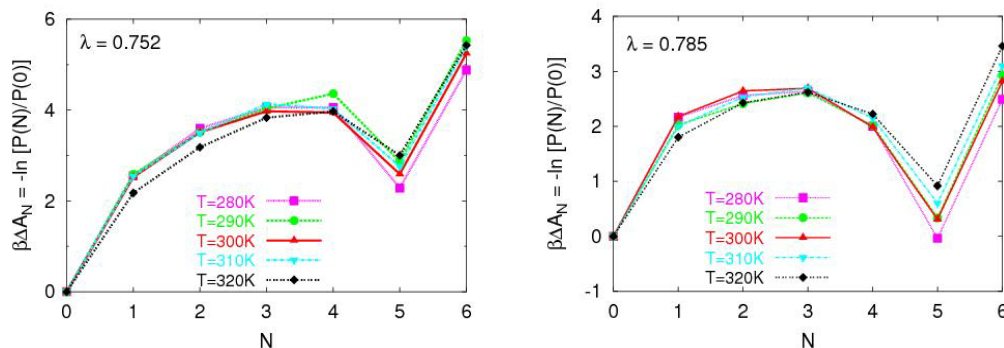

Figure 3 Free energies of transfer of water into a nanotube open to a reservoir as a function of number of water molecules transferred N for temperatures ranging between 280 K and 320 K for (a) $\lambda = 0.752$ and (b) $\lambda = 0.785$

The results were compared with our calculations for a periodically replicated nanotube in vacuum of same length and diameter containing different numbers of water molecules (Vaitheeswaran)
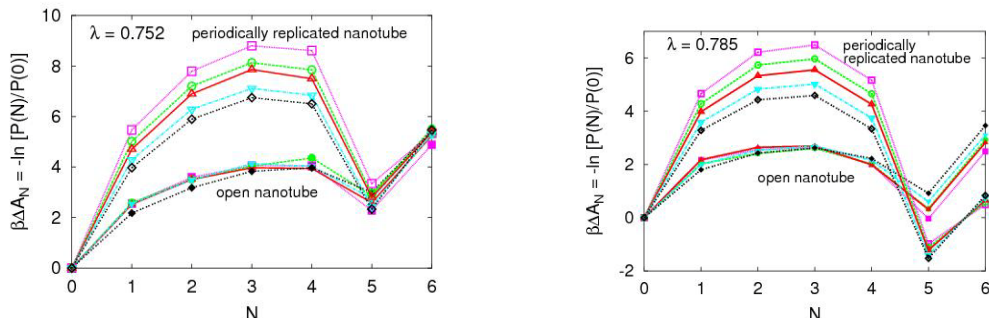

Figure 4 Free energies of transfer as a function of the number of water molecules transferred *N* at different temperatures for open nanotube (filled symbols) and periodically replicted nanotube[3,7] (open symbols) for (a) λ = 0.752 and (b) λ = 0.785.
[T= 280 K (■), T = 290 K (●), T =300 K (▲), T =310 K (▼) and T = 320 K (♦)].

The free energy barrier for filling the periodically replicated nanotube is much larger than the corresponding barrier for the open nanotube. Furthermore, for a weak nanotube – water interaction (λ = 0.752) the free energy of the filled state with with occupancy N=5 is the same for the periodically replicated and open nanotubes but does not favor filling. For a slightly more attractive nanotube - water interaction with λ = 0.785, the periodically replicated nanotube is filled but the open nanotube oscillates between filled and empty states. This occurs despite the fact that the free energy barrier for filling the periodically replicated nanotube is much larger than the barrier for the open nanotube. The differences in behavior of the two types of nanotubes can be traced to the lower energy and entropy of transfer of water into the open nanotube which are finely balanced and the differences in the end effects. Water in the filled open nanotube is H-bonded to two distinct water molecules of the reservoir whereas in the periodically replicated nanotube the water molecules at the two ends are hydrogen bonded to each other.
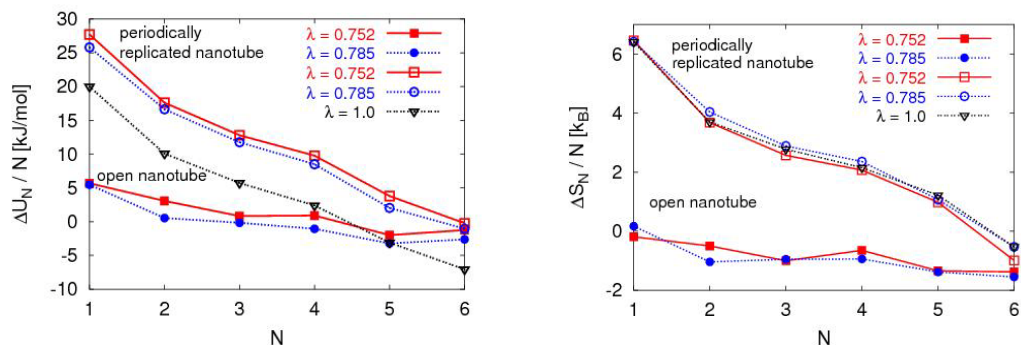

Figure 5 Comparison of internal energy per molecule and entropy of water inside nanotube open to reservoir and periodically replicated nanotube for λ = 0.752 and λ = 0.785.

Filling and emptying can also be discussed in terms of a simple model in which the energy of transfer is determined by the Lennard-Jones interactions and the hydrogen bonding between the water molecules as well as the energy required for removal of water from the bulk phase. This model explains the general trends in the thermodynamics of filling as a function of occupancy. This study and observations should be useful in the design of nanotubes to be selective in their behavior towards the adsorption and transport of water and other materials. (unpublished-mss in preparation)

(b) Structure and thermodynamics of water filling the largest nonpolar cavity of tetrabrachion (H. Yin and G.Hummer)

Water expulsion from the protein core is a key step in protein folding. Nevertheless, unusually large water clusters confined into the nonpolar cavities have been observed in the X-ray crystal structures of tetrabrachion, a bacterial protein that is thermostable up to at least 403 K (130 °C).
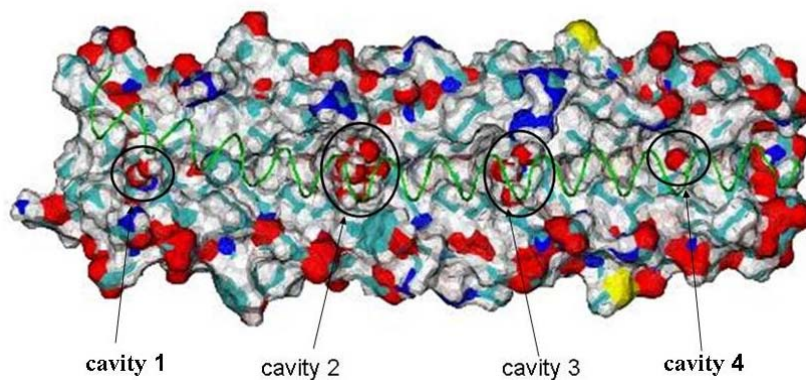

Figure 6: Structure of the tetrabrachion stalk segment after energy minimization of the crystal structure. Three of the four helices are shown as molecular surfaces, and the fourth one (on top) is indicated as a green backbone tube. Water molecules in the four cavities, numbered 1 to 4 from left to right along the central channel, are shown as VDW models (red and white; black circles). Solvent water molecules are not shown for clarity.

We used molecular dynamics (MD) simulations to investigate the structure and thermodynamics of water filling the largest cavity of the right-handed coiled-coil stalk of

tetrabrachion at 365 K (92 °C), the temperature of optimal bacterial growth, and at 298K.
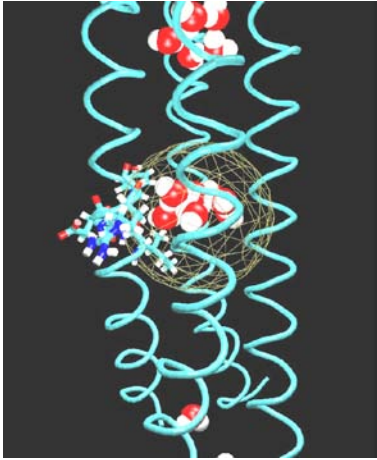

Fig. 7 Configuration of tetrabrachion shows largest cavity occupied by 9 water molecules after equilibration at 365 K.
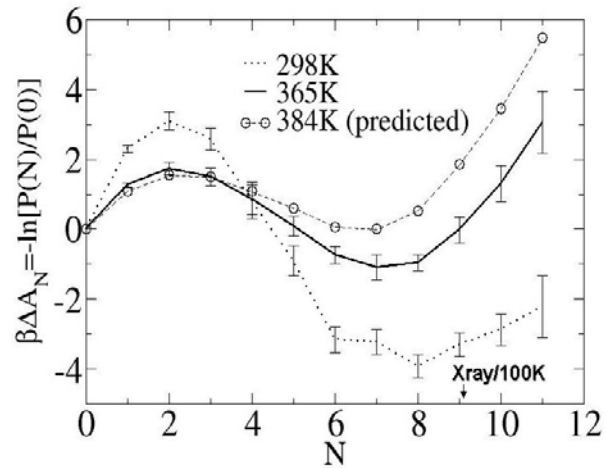

Fig.8. Free energy of transfer of water from the bulk into the interior of cavity 2 as function of the water occupancy N at 298,365, and 384K.

Hydrogen-bonded water clusters of seven to nine water molecules were found to be thermodynamically stable in this cavity at both temperatures, confirming the X-ray studies. Stability, as measured by the transfer free energy of the optimal size cluster, decreases with increasing temperature. Our calculations suggested that cluster formation becomes unfavorable at 384 K (110 °C), signaling the onset of drying just slightly above the temperature of optimal growth. "Drying" thus precedes protein denaturation. At room temperature, the second largest cavity in tetrabrachion accommodates a five water molecule cluster, as reported in the X-ray studies. The typical cluster at 365 K consists of seven water molecules, hydrogen bonded to each other and stabilized further through hydrogen bonds and weaker van der Waals interactions with the cavity walls. The filled and empty states are separated by a barrier of 2-3 $k_B T$, with the absolute barrier height increasing with temperature decreasing. The entropy of transfer per molecule of the thermodynamically most stable cluster of seven water molecules from the bulk into the cavity is approximately -25.8 J/mol at 365 K, and the energy of transfer per molecule is -9.9 kJ/mol. Filling is driven by the favorable transfer energy at this temperature and also at room temperature (298 K). The energy and entropy of transfer are found to depend only weakly on temperature, with the estimated entropy being slightly more negative at 298 K than at 365 K (Figure 8). A wider range of thermodynamically stable cluster sizes

(N) 6 to 9) of comparable free energy exist at 298 K than at 365 K. From our estimates of the entropy and energy of transfer, we predict that the transfer free energy of clusters with seven to nine water molecules would become unfavorable above temperatures of _384 K, signaling the onset of drying above. This result suggests that emptying occurs before denaturation (with the protein being stable at temperatures >400 K). In our simulations tetrabrachion is stable at 365 K even if the large cavity 2 is empty. Based on this and the experimental observation that the stalk and two proteases are stably bound even at 398 K, we suggest that a possible functional role of the largest nonpolar cavity (cavity 2) in tetrabrachion is to serve as the binding element for nonpolar anchors of its proteases.

(published)

(iii)Water in the polar and nonpolar cavities of the protein interleukin 1-beta (H.Yin, G.Feng, G.Hummer and M.Clore)

Water in the protein interior serves important structural and functional roles and is also increasingly recognized as a relevant factor in drug binding. The nonpolar cavity in the protein interleukin-1β_ has been reported to be filled by water on the basis of some experiments and simulations and to be empty on the basis of others. Here we study the thermodynamics of filling the central nonpolar cavity and the four polar cavities of interleukin-1β_ by molecular dynamics simulation. We used different water models (TIP3P and SPC/E) and protein force fields (amber94 and amber03) to calculate the semigrand partition functions term by term that quantify the hydration equilibria. We consistently found that water in the central nonpolar cavity is thermodynamically unstable, independent of force field and water model.
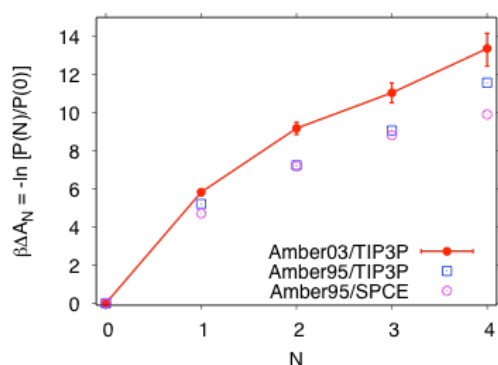
Figure 9. Free energy ΔA_N of transferring N water molecules from bulk into the nonpolar cavity of IL-1b, obtained from the logarithm of $P(N)/P(0)$. Results are shown for simulations using the amber03 force field with TIP3P water (filled circles), amber94 with TIP3P water (open squares), and amber94 with SPC/E water (open circles). Lines are guides to the eye.

The apparent reason is the relatively small size of the cavity, with a volume less than ~80 Å3.Our results are consistent with the most recent X-ray crystallographic and simulation studies but disagree with an earlier interpretation of nuclear magnetic resonance (NMR) experiments probing protein-water interactions. We show that, at least semi-quantitatively, the measured nuclear Overhauser effects indicating the proximity of water to the methyl groups lining the nonpolar cavity can, in all likelihood, be attributed to interactions with buried and surface water molecules near the cavity. The same methods applied to determine the occupancy of the polar cavities show that they are filled by the same number of water molecules observed in crystallography, thereby validating the theoretical and simulation methods used to study the water occupancy in the nonpolar protein cavity. We concluded from our molecular dynamics simulations and theoretical analysis that water molecules in the central cavityof IL-1 β _ are thermodynamically unstable. The transfer free energy from the bulk phase into the central cavity of IL-1β_ is positive and increases monotonically with the number N of water molecules in the cavity over the entire range, up to $N = 4$. This result is independent of the force field for protein and water used. The calculated free energy penalty for hydration is substantial. So while it is possible that the energetics could be altered by the inclusion of polarizability in the simulation force field, we do not expect such changes to be large enough to alter the main conclusion. Our finding of an empty nonpolar cavity in IL-1β_ is consistent with the experimental studies of Quillin et al. and is in qualitative agreement with simulations carried out independently by Yin26 and by Oikawa and Yonetani.

At least semi-quantitatively, we can also explain the observed NOE and ROE NMR couplings between the protons of nonpolar groups lining the cavity and water as arising from interactions with buried and surface water. Besides actual water penetration, additional contributions to the measured couplings[27] could arise from transient excursions of water molecules in the polar cavities of the protein. The apparent reason for the absence of water in the nonpolar cavity of IL-1β_ is its relatively small size of between 40 and 80 Å^3 in different X-ray structures, ~80 Å^3 in our simulations, and ~120 Å^3 in an NMR structure (Figure 1). Even the somewhat larger nonpolar cavity in T4 lysozyme, with a volume of ~170 Å^3, was previously found to be empty at ambient conditions by both experiment and simulation,[12,46] where filling with water was observed only at elevated hydrostatic pressures of >1 kbar. In small nonpolar cavities, the loss of interaction energy with bulk water cannot be fully offset by the gains in energy from water-cluster formation. We concluded from the simulations here of IL-1β_ and before of T4 lysozyme[12,46] and tetrabrachion[21] that nonpolar cavities in proteins are not stably hydrated if they can hold only about four water molecules. In contrast, the cavities of fullerenes, with their more densely packed carbon walls, were found to be stably hydrated by a four-water cluster.[28] Our results for the four polar cavities are also consistent with the experimental findings of Quillin et al.,[20] with one or two water molecules in each of them at equilibrium. Despite the large negative (unfavorable) entropy of transfer, filling is driven by the negative energy of transfer, which is an order of magnitude larger per water molecule than it is for water transferred into the nonpolar cavity and much greater than the unfavorable contribution from the entropy of transfer. (published)

(iv) Structure and transport properties of concentrated alkali halides in water by MD simulation (H. Du and Jan Miller)

We studied the structure and dynamics of concentrated LiCl, RbCl and CsI aqueous solutions by using molecular dynamics simulation from 0.22 to 3.97M. . It was found that a small ion such as Li+ has four water molecules in the hydration shell as shown in Fig.10 .
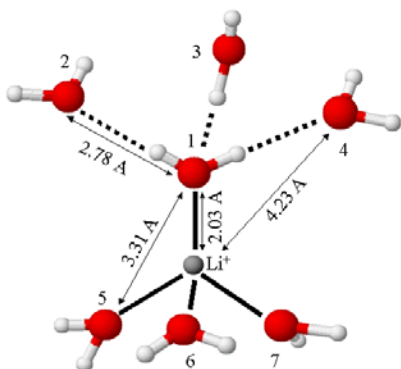
Figure 10. Schematic picture showing the hydration of Li$^+$. Water 5.6 sand 7 are within the primary shell of water 1.
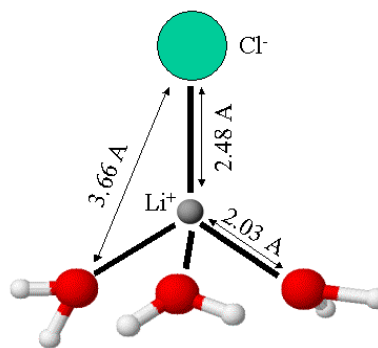

Figure 11. Schematic picture showing the replacement of one water molecle in a Li$^+$tetrahedral hydration with Cl$^-$ _

The higher the salt concentration, the denser the water molecules are packed as indicated by a monotonic increase of water/water coordination numbers as a function of salt concentration. On the other hand, large ions such as Rb+, Cs+, and I- form weak bonds with water molecules, and a loose hydrophobic hydration shell. Thus, the coordination between water molecules decreases with salt concentration. As the ion size increases, the ion/ water electrostatic interactions becomes less significant when compared to the hydrogen bonding interaction of water molecules.

Ion size influences the mobility of water molecules in solution. When small ions, such as Li$^+$ are present, the mobility of water molecules in the ion hydration shell and in bulk water decreases and the residence times increase with salt concentration. In contrast, for solutions containing large ions (CsI and RbCl), the weaker ion/water electrostatic interaction does not significantly immobilize water molecules in its hydration shell. Consequently, the residence times of water molecules do not show a substantial change with solution concentration. This is in accord with the self diffusion coefficients as a function of salt concentration, which show that when Li$^+$ ions are present, the diffusion coefficients of water molecules in the solution decrease significantly with salt concentration, but when Cs+ and I- ions are present, there is no significant change in the water diffusion coefficients with increase in salt concentration.

For anions, very interesting results were observed. Due to the asymmetry of water molecule, the hydration state of anions are different than that of cations of similar size . In LiCl solution, the hydration number for Cl$^-$ increases slightly with concentration

upto 3.97M. But when the cation is Rb^+, the hydration number of Cl^- ion decreases with the concentration. Thus the size of the cation has a substantial influence on the interaction between the anion and water molecules. In LiCl solutions, it is clear from Fig. 11 that, as the salt concentration increases, Cl- ions can replace some of the water molecules in the Li+ ion tetrahedral hydration shell.

The change of system viscosity with solution concentration, as determined from MD simulation in our study provides an in-depth understanding of the variation of viscosities with ion size and salt concentrations from a molecular perspective. For LiCl solutions, the system viscosity increases monotonically with salt concentration due to the strong ion/water interactions in the solution. For RbCl, hydrophobic hydration dominates and leads to negligible variation of system viscosity with salt concentration. Further increase in the ion size to Cs+ and I- reveals a noticeable decrease of system viscosity as a function of salt concentration. The agreement between the simulation results and the experimental results for the variation of viscosity with ion size and concentration is excellent and provides a molecular interpretation of the phenomenological behavior of alkali halide solutions.(published)

(v) Upper and lower bounds for the excess chemical potential from particle removal and insertion in the bulk phase and in confined geometries (G. Feng and G Hummer)
We have derived upper and lower bounds for the chemical potential of molecules in the bulk fluid as well as in confined systems from the probability distributions of the energies for insertion and removal respectively. By combining these two distributions we have been able to calculate the corrections to these bounds which provide the chemical potential in two ways that should coincide if the data and calculations are accurate. We have applied to determining the chemical potentials of TIP3p and SPCE water and also the chemical potential of TIP3p water in the polar and nonpolar cavities of interleukin 1-beta;.(unpublished- manuscript in preparation)
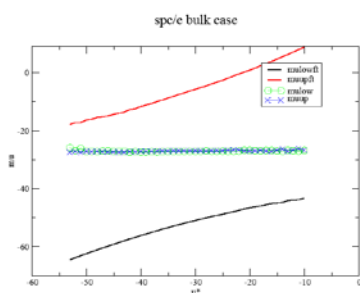
Figure 12. Upper and lower bounds for the excess chemical potential and corrections to the bounds.

(vi) *Ab-initio* calculations of the proton affinity from potential energy surfaces for proton transfer between water and other species. (Indira Silwal, Jan Szulejko, Touradj Solouki) We combined modern GC mass spectrometric techniques (GC/FT-ICR MS) and *ab-initio* molecular orbital calculations at G2, G3, and MP2/6-31+G** levels to characterize unknown disinfection byproducts (DBPs) present in treated drinking water samples. We presented an additional dimension to GC/MS analysis that utilizes theoretically calculated proton affinities (PAs) and gas-phase basicities (GBs) to elucidate reaction mechanisms. *The observed species at m/z = 100.9 (i.e., $CH_3OCl_2^+$) in our GC/MS experiments is an* ion-dipole complex ($CHCl_2^{+\cdots} H_2O$), formally corresponding to protonated dichloromethanol {G3 calculated $PA_{CH2OCl2} \sim 163.3$ kcal mol^{-1}}) produced in the gas phase either by the association of a water molecule with a $CHCl_2^+$ fragment ion from chloroform (present in the treated drinking water sample) or by the elimination of HCl in a condensation reaction between chloroform and protonated water. The calculated PA of chloroform at the G3 level ($PA_{CHCl3} \sim 157.8$ kcal mol^{-1}) as well as entropy considerations indicate that non-dissociative proton transfer (PT) reaction from H_3O^+ to $CHCl_3$ would be inefficient; however, the observed dissociative PT product ions (*e.g.*, $CHCl_2^+$) can be explained by considering the reaction entropy ($\Box S$). The overall dissociative PT reaction is unfavorable at 298 K and marginally exoergic ("entropy driven") under our experimental conditions at 360 K. Besides DBPs, we report the presence of the Zundel cation $H_5O_2^+$ in our mass spectrum. We observed that the Zundel cation is formed by multiple ion-molecule reactions involving water in the presence of helium carrier gas and GC eluting compounds. This combined exxpt and theory project strongly influenced our MD studies of proton transfer reactions described below (published)

(vii) Mobility of the hydroxide ion in bulk water and in carbon nanotube using the OSS2 potential (S.H.Lee)

Classical simulations using the OSS2 model potential derived from *ab initio* calculations were used to understand the mechanism of PT in bulk water. PT of the hydroxide ion in bulk water starts from the four-coordinated species and proceeds through a three-coordinated intermediate accompanied by specific solvent reorganization which must take
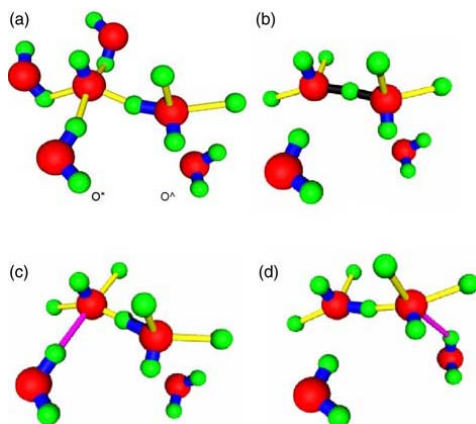

Figure 13. Representative configurations of OH2 ion showing the mechanism of PT leading to the transport of the hydroxide ion in a simulation of one OH^- ion in 31 water molecules using theOSS2 potential.

place for PT to occur. For hydrogen ions, the starting point is the Eigen complex and PT proceeds through a Zundel intermediate. These conclusions and the asymmetry in the transport mechanism of hydrogen and hydroxide ions in bulk water are in broad agreement with first principles AIMD simulations of H+ ions by Tuckerman et al. and of OH^- ions by Marx et al. Details of the structural diffusion mechanism in proton transfer (PT) reactions involving a hydroxide ion in water and the structure of the solvated ions and transfer intermediates are in dispute. We elucidated the mechanism of PT involving a hydroxide ion in water by molecular dynamics simulations using a dissociating water model based on *ab initio* calculations.We found that the hydroxide ion in bulk water is present as the four-coordinated $OH^-(H_2O)_4$ complex, which loses a water molecule before a PToccurs through the formation of proton sharing intermediates in general agreement with the previously disputed first principles studies of small systems.
 (published)

(viii) preliminary studies of alpha helix formation of peptides in carbon nanotubes.

D. Suvlu, S. Seneviratne and D. Thirumalai)

Confinement effects on the conformational preferences of proteins have important implications for our understanding of protein behavior in the biological environment. Consequently, several experiments have suggested that an α-helix forms in polypeptides inside the ribosome exit tunnel. In addition, many computational studies have elucidated some of the molecular interactions leading to helix stabilization, however, these simulations were not conducted in the presence of water which does not accurately represent the biological environment. We are carrying out all atom molecular dynamics simulations using a 23 residue polyalanine peptide confined to carbon nanotubes of various diameters open to a water reservoir to explore hydration and confinement effects on helix stability. Our results show that there is a critical range of radii that lead to helix stabilization which provides support for the entropic stabilization mechanism. These results are different from those reported by another group for the same polypeptide in a periodically replicated nanotube containing water, showing that the influence of solvent on helix formation is determined by whether the confined system is open or closed to an external reservoir. (unpublished)
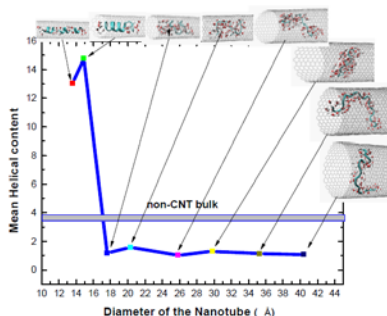

Figure 14. Helicity of polypeptide as a function of the diameter of the carbon nanotube.

(ix) Studies of proton transfer and the mobility of H^+ and OH^- ions using the rescaled (S.H.Lee)

Hydrogen H^+ and hydroxide OH^- ions in aqueous solution have anomalously large diffusion coefficients and the mobility of the H^+ ion is nearly twice that of the OH^- ion. The reasons for this significant difference in mobility are not fully understood. We are

using molecular dynamics (MD) simulations of a dissociating model for water based on scaling the interatomic potential for water developed by Ojamäe-Shavitt-Singer from *ab-initio* studies at the MP2 level to study proton transfer that occurs in the transport of hydrogen and hydroxide ions in acidic and basic solutions containing 215 water molecules. The model and methods described provide a novel approach to studies of liquid water, proton transfer and acid-base reactions in aqueous solutions, channels and interfaces. This work is ongoing (unpublished)