

Final Technical Report

**Grant DE-FG02-87ER13714
“Fundamental Studies of Metastable Liquids”**

Covering the period June 1, 1987 through April 30, 2008

by

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Grant DE-FG02-87ER13714 supported fundamental work on the physical properties of metastable liquids from 6/1/87 to 4/30/08. Renewal proposals were submitted every three years (1990, 1993, 1996, 1999, 2002, 2005), and included, in every case, a detailed Final Technical Report on the previous three years. Accordingly, the bulk of this report covers the final 2-year period 5/1/06 to 4/30/08 of this grant, which is not covered in any of the previous Final Technical Reports. This is preceded by a brief overview of the main research objectives and principal accomplishments during these very fruitful and productive 21 years of DOE-funded research.

Objective. Materials that exist under thermodynamic conditions in which the stable state is in a different state of aggregation are said to be metastable. Examples include supercooled liquids (stable state: crystal), superheated liquids (stable state: vapor), and glasses (stable state: crystal). Metastable liquids and glasses play important roles in atmospheric phenomena (cloud formation), communications (optical fibers, which are made of amorphous silica), energy technology (solar cells made of amorphous silicon), and pharmaceutical technology (preservation of labile biochemicals in glassy matrices). In spite of the importance and ubiquity of metastable liquids and glasses, fundamental questions exist on the nature of the glassy state (is the glass transition kinetic or thermodynamic in nature? what is the microscopic origin of the extraordinary increase in relaxation times that gives rise to the glass transition?), and the physical properties of metastable liquids (does water possess a metastable critical point in the supercooled region? why do rotational and translational motions decouple in a supercooled liquid?). The goal of this project was to investigate the above fundamental questions through the use of molecular simulations and statistical mechanics.

Major Findings and Accomplishments. The major findings and accomplishments resulting from this research were:

- Discovery of the relationship between dynamics in supercooled liquids and their underlying potential energy landscape (Sastry, Debenedetti and Stillinger, *Nature*, 393, 554, **1998**; 459 citations).
- Discovery of the hierarchical pattern underlying structural, dynamic and thermodynamic anomalies in supercooled water (Errington and Debenedetti, *Nature*, 409, 618, **2001**; 213 citations).
- Invention of a computational algorithm that and allows the distinction between equilibrium and glassy states to be made using purely geometric means (Truskett, Torquato and Debenedetti, *Phys. Rev. E*, 62, 993, **2000**; 80 citations).
- Demonstration that random close packing of spheres is ill-defined (Torquato, Truskett and Debenedetti, *Phys. Rev. Lett.*, 84, 2064, **2000**; 287 citations).
- Formulation of one of the two widely accepted thermodynamic interpretations of the phase behavior of supercooled water (Sastry, Sciortino, Debenedetti and Stanley, *Phys. Rev. E*, 53, 6144, **1996**; 184 citations).
- Derivation of a new exact equation for the diffusion coefficient (Stillinger and Debenedetti, *J. Phys. Chem. B*, 109, 6604, **2005**).
- Introduction of a new algorithm for calculating the entropy in molecular simulations (Shell, Debenedetti and Panagiotopoulos, *J. Chem. Phys.* 119, 9406, **2003**; 41 citations).

This report summarizes the principal findings and accomplishments resulting from work carried out under grant DE-FG02-87ER13714, “Fundamental Studies of Metastable Liquids”, during the period May 1, 2006 through April 30, 2008.

The research addressed the following topics:

- Thermodynamics and dynamics of supercooled liquids and glasses.
- Thermodynamics of supercooled water and aqueous solutions.
- Statistical mechanics of liquids.
- Thermodynamics of protein solutions.

The work is described in detail in 12 publications, which are listed on pages 7-8 of this report.

Thermodynamics and dynamics of supercooled liquids and glasses

We used molecular dynamics simulations to investigate translational and rotational motion in a three-site model of the canonical fragile glass former, *ortho* terphenyl, over the temperature range $260 \leq T \leq 346\text{K}$ ($T_g = 243\text{K}$), at ambient pressure (Lombardo et al., 2006[§]).

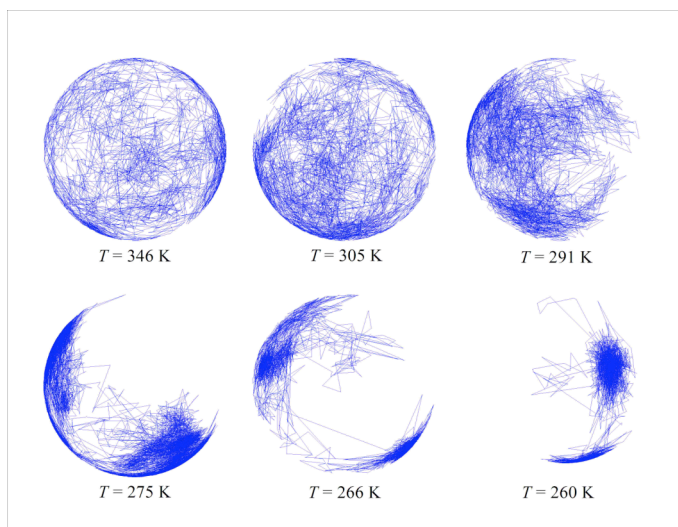


Fig. 1: Single-molecule rotational trajectory of a unit vector rigidly attached to a representative *ortho*-terphenyl molecule. Note evolution from high- T Debye behavior (short, uncorrelated displacements) to low-temperature regime characterized by infrequent large rotations (Lombardo et al., 2006).

We demonstrated breakdown of Debye behavior (whereby rotational motion occurs as a succession of small and uncorrelated rotations), upon supercooling. At sufficiently low temperature, we found instead that orientational relaxation occurs through large and infrequent rotations (Figure 1). We implemented an Einstein formalism for rotational motion, which supplements the traditional Debye approach. When applied to the analysis of decoupling between rotational and translational motion in the supercooled regime, we

found an enhancement of rotational motion relative to translation. This conclusion is opposite to trends seen when applying the conventional Debye approach. We also found that the model exhibits non-Gaussian behavior in the statistics of translational and

[§] See pp. 7-8 for a complete list of articles associated with this grant. Articles cited that are not associated with this grant are included as individual footnotes.

rotational displacements, which strengthens upon supercooling. Examination of particle mobility revealed spatially heterogeneous dynamics in translation and rotation, with strong spatial correlation between translationally and rotationally mobile particles.

We applied conformal solution theory and extended to binary mixtures (Shell et al., 2006) our energy landscape-based equation of state for glass-forming liquids (Shell et al., 2003[§]). The main result of the mixture theory is an equation for the glass transition of a binary mixture as a function of composition. The new equation is a cubic polynomial in composition, with coefficients being solely a function of pure component size and energy parameters (Shell et al., 2006). When applied to a binary Lennard-Jones mixture, the theory predicts a non-monotonic dependence of glass transition upon mixture composition. Simulation results for the composition dependence of species diffusivities were found to be consistent with the theoretical prediction.

Thermodynamics of supercooled water and aqueous solutions

The possibility that water may exhibit a liquid-liquid transition is the focus of much current experimental, theoretical and computational research (e.g., see review by Debenedetti, 2003[¶]). Because of the experimental difficulties associated with conducting measurements with deeply supercooled, hence metastable water, alternative approaches have been developed, including the experimental study of nano-confined water under conditions where nucleation is suppressed (e.g., Liu et al., 2007[‡]). From a theoretical perspective, an important knowledge gap is to understand the implications for mixture behavior that follow from the existence of a second critical point. This is not only of

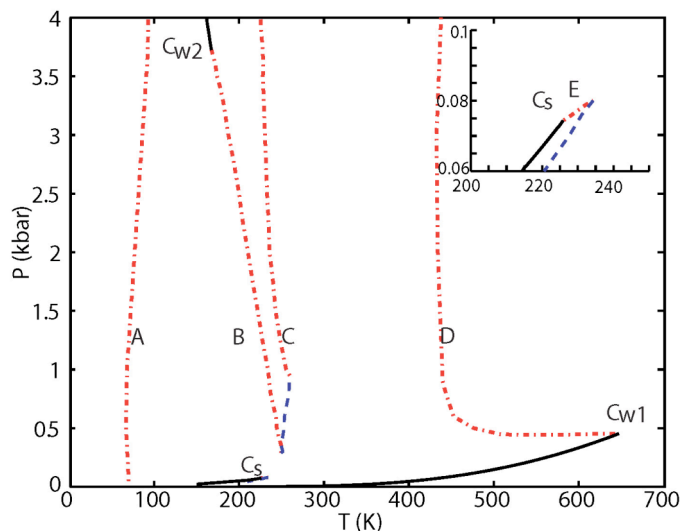


Fig. 2: P - T projection of fluid-phase behavior for a binary mixture of a van der Waals solute in water. Solid lines: pure component phase coexistence; red dot-dashed lines (A, B, C, D, E): binary mixture critical lines; blue dashed lines: triple point lines. Cw1 and Cw2 are the vapor-liquid and liquid-liquid critical points of water. Cs is the vapor-liquid critical point of the solute. (Chatterjee and Debenedetti, 2006).

intrinsic value in the theory of fluid mixtures, but could also result in the identification of mixture behavior that can unambiguously speak to the existence (or lack thereof) of a second critical point in water. This is the motivation behind our study of fluid-phase behavior in binary mixtures in which one component can have two critical points (Chatterjee and Debenedetti, 2006).

We investigated theoretically the binary fluid-phase behavior of mixtures in which one water-like component can have two critical points, by considering three

[§] M.S. Shell, P.G. Debenedetti, E. La Nave and F. Sciortino, **J. Chem. Phys.**, **118**, 8821, 2003.

[¶] P.G. Debenedetti, **J.Phys.: Condens. Matt.**, **15**, R1669, 2003.

[‡] D. Liu, Y. Zhang, C.-C. Chen, C.-Y. Mou, P.H. Poole and S.-H. Chen, **PNAS**, **104**, 9570, 2007.

equal-sized non-polar solutes differing in the strength of their dispersive interactions. Water was modeled with the statistical mechanical theory developed earlier by us (Truskett et al., 1999[†]). In each case, we compared the phase behavior predicted using two sets of parameters: one giving rise to a pure-component low-temperature liquid-liquid transition in water (e.g., Mishima and Stanley, 1998[¶]) terminating at a critical point (two-critical-point parameter set), and one in which no such second critical point exists (Sastry et al., 1996[‡]) (singularity-free parameter set). Regardless of the parameter set used, five mixture critical lines were identified (Figure 2). For the two-critical-point parameter set and for all three mixtures, we found a mixture critical line (B in Figure 2) emanating from water’s second critical point (Cw2 in Figure 2). For the mixtures involving solutes with the two smallest values of the dispersive energy, this mixture critical line extends to low pressures and high temperatures as the solute mole fraction is increased, and is closely related to the critical line originating at water’s ordinary vapor-liquid critical point: these lines are loci of upper and lower consolute points corresponding to the same liquid-liquid transition. In mixtures involving the solute with the intermediate value for the dispersion energy, the critical locus emanating from water’s second critical point is shifted to higher temperatures compared to those involving the solute with the smallest dispersive energy, and extends up to $T \sim 310\text{K}$ and moderate pressures (ca. 200 bars). *This suggests the possibility of an experimentally accessible manifestation of the existence of a second critical point in water.* For mixtures involving either of the two solutes with the lowest values of the dispersive energy, changing the water parameters from two critical points to singularity-free causes the disappearance of a lower consolute point at moderate pressures. For mixtures involving the more strongly interacting solute, the differences between the two-critical-point and singularity-free behaviors occur only in the experimentally difficult-to-probe low-temperature and high-pressure region.

Statistical mechanics of liquids

We developed an extension of the original Reiss-Frisch-Lebowitz scaled particle theory (Reiss et al., 1959[§]). The new approach serves as a predictive theory for the hard sphere radial distribution function $g(r)$ (Stillinger et al., 2006; Chatterjee et al., 2006). The theory’s key thermodynamic quantity, the reversible work of cavity creation, was formulated mathematically both for a single cavity (as in traditional scaled particle theory), and for a pair of identical spherical cavities, as a function of their separation. Knowledge of these quantities leads directly to $g(r)$, through the thermodynamic identity

$$g(r, \rho) = [2\beta W(\sigma, \rho) - \beta W_2(r, \sigma, \rho)] \quad (1)$$

[†] T.M. Truskett, P.G. Debenedetti, S. Sastry and S. Torquato, **J. Chem. Phys.**, **111**, 2647, 1999.

[¶] O. Mishima and H.E. Stanley, **Nature**, **392**, 164, 1998.

[‡] S. Sastry, P.G. Debenedetti, F. Sciortino and H.E. Stanley, **Phys. Rev. E**, **53**, 6144, 1996.

[§] H. Reiss, H.L. Frisch and J.L. Lebowitz, **J. Chem. Phys.**, **31**, 369, 1959.

In the above expression, σ is the hard sphere diameter, ρ is the number density, $W(\sigma, \rho)$ is the reversible isothermal work that must be expended to expel all particle centers from a spherical region of radius σ , $\beta = 1/kT$, with k , Boltzmann's constant, and W_2 is the reversible isothermal work required to clear particle centers from the interior of a double cavity such that the cavity centers are separated by a distance r . Neither W nor W_2 are known exactly for large cavities, requiring the implementation of a numerical approach. To this end, we derived smooth connection conditions between the small-cavity situation, where the work can be expressed exactly in terms of $g(r)$, and the large-cavity regime, where macroscopic properties such as the interfacial tension become relevant. Closure

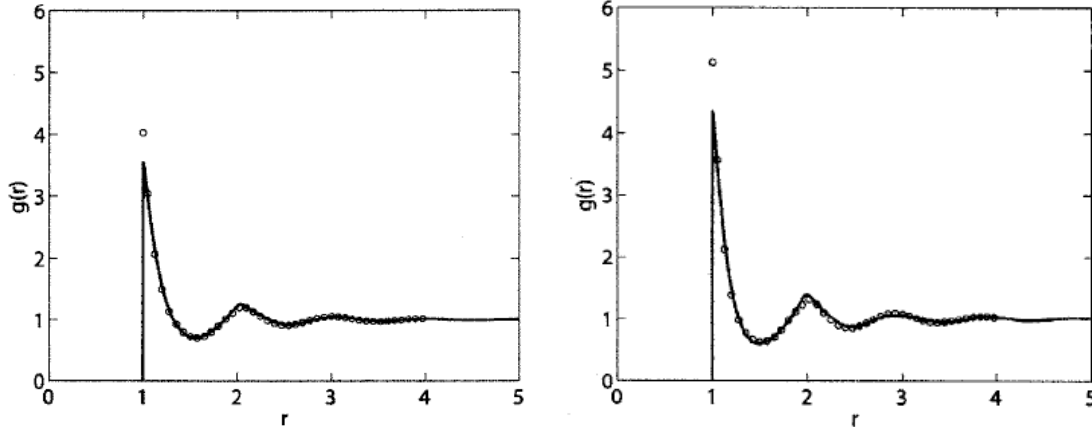


Fig. 3: The pair correlation function $g(r)$ obtained using the extended scaled particle theory (Stillinger et al., 2006) at densities $\rho\sigma^3 = 0.8$ (left) and 0.9 (right), with distance expressed in units of σ , the hard sphere diameter. The lines are numerical solutions of the governing integral equation. Open circles are molecular dynamics simulations (Labik and Malihevsky, 1981[‡]). The new theory reproduces fluid structure very well, but underestimates the pressure, as can be seen by the lower value of g at contact ($r = 1$) predicted by the theory with respect to simulations (Chatterjee et al., 2006).

conditions emerge that produce a nonlinear integral equation that must be satisfied by the pair correlation function. This integral equation has a structure that generates a solution in the form of a power series in density. The results of this series replicate the exact second and third virial coefficients for the hard sphere system, while the predicted fourth virial coefficient is approximately 0.6% lower than the exact value.

Numerical calculation of the pair correlation function over the density range $\rho\sigma^3 \leq 0.96$ reveals, upon comparison with computer simulation (Labik and Malihevsky, 1981[‡]), that the new theory is able to capture accurately the fluid's structure across the entire density range examined (Figure 3). The pressure predicted via the virial route is systematically lower than simulation results, while that obtained by the compressibility route is lower than the simulation predictions for $\rho\sigma^3 \leq 0.67$ and higher than simulation predictions for $\rho\sigma^3 \geq 0.67$.

Thermodynamics of protein solutions

We investigated the effect of temperature and pressure on polypeptide conformational stability, using a two-dimensional lattice model in which water is represented explicitly

[‡] S. Labik and A. Malihevsky, *Mol. Phys.*, **42**, 739, 1981.

(Patel et al., 2007a). The model captures many aspects of water thermodynamics,

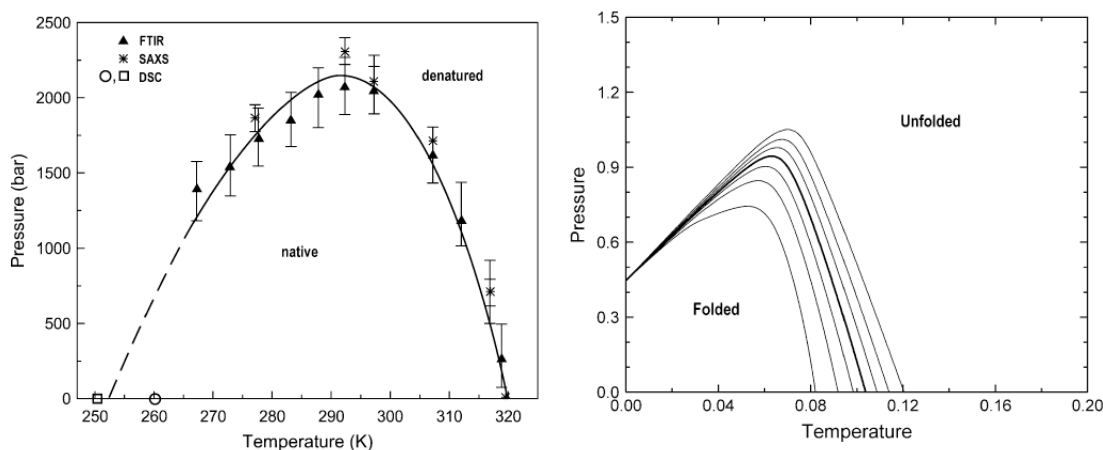


Fig. 4: Experimental (left) and calculated (right) phase diagram for proteins in water. Experiments are for Staphylococcal nuclease, using Fourier transform infra-red spectroscopy (FTIR), small angle x-ray scattering (SAXS) and differential scanning calorimetry (DSC) (Ravindra and Winter, 2003[¶]). Calculations are for a 17-mer hydrophobic homopolymer, with pressure scaled by the ratio of the energy of a hydrogen bond to the volume of a water molecule, and the temperature scaled by the ratio of the hydrogen bond strength to Boltzmann's constant. The lines demarcate the regions within which the probabilities of observing the folded state are $\geq 87.5\%$, 75% , 62.5% , 50% (bold), 37.5% , 25% and 12.5% (outermost). Note that the protein can be destabilized by pressure, heat, and cold. (Patel et al., 2007a).

including the existence of density anomalies. An explicit treatment of hydrophobic hydration applied to a hydrophobic homopolymer is sufficient to produce the experimentally-observed (e.g., Ravindra and Winter, 2003[¶]) pressure and temperature-dependence of cold, pressure, and thermal denaturation (Figure 4). We subsequently refined the model so as to account for hydrophobic and polar residues along the heteropolymer's backbone (Patel et al., 2008). As experimentally observed, model heteropolymer sequences were found to fold into stable native states characterized by a hydrophobic core, to avoid unfavorable interactions with water. The native states undergo cold, pressure, and thermal denaturation in distinct configurations for each type of unfolding transition. However, the heteropolymer sequence was found to be important, as not all polymer sequences fold into stable native states at positive pressures. Simulation of a large collection of sequences indicates that these fall into two general groups, those exhibiting highly stable native structures and those that do not. Statistical analysis of important patterns in sequences showed a strong tendency for observing long blocks of hydrophobic or polar monomers in the most stable sequences. Statistical analysis also shows that alternation of hydrophobic and polar monomers appears infrequently among the most stable sequences. These observations, however, were found not to be absolute design rules and, in practice, are not sufficient to rationally design very stable heteropolymers. We also studied the effect of mutations on improving the stability of the model proteins, and demonstrated that it is possible to obtain a very stable heteropolymer from directed evolution of an initially unstable heteropolymer.

[¶] R. Ravindra and R. Winter, *ChemPhysChem*, **4**, 359, 2003.

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