Molecular dynamics simulation of cooling: Heat transfer from a photoexcited peptide to the solvent

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A systematic molecular dynamics (MD) simulation study of the photoinduced heat transfer from the model peptide N-methylacetamide (NMA) to various solvents is presented, which considers four types of solvent (water, dimethyl sulfoxide, chloroform, and carbon tetrachloride), and in total 24 different force field models for these solvents. To initiate nonstationary energy flow, an initial temperature jump of NMA is assumed and nonequilibrium MD simulations are performed. As expected from simple theoretical models of heat transfer, the cooling process is proportional to the heat capacity $C_V$ and—to some extent—to the viscosity $\eta$ of the solvent. The complex interplay of Coulomb and Lennard-Jones interactions is studied by scaling these interaction energies. The study reveals that realistic changes ($\leq 10\%$) of the Lennard-Jones and Coulomb parameters do not change the cooling time considerably. Including polarizability, on the other hand, appears to enhance the energy dissipation. Moreover, the solvent’s internal degrees of freedom may significantly participate in the heat transfer. This is less so for water, which possesses only three high-frequency vibrational modes, but certainly so for the larger solvent molecules dimethyl sulfoxide and chloroform, which possess several low-frequency vibrational modes. For water, the simulated cooling rate is in excellent agreement with experiment, while only qualitative agreement (up to a factor of 2) is found for the other considered solvents. The importance of the force field model and quantum-mechanical effects to correctly describe the cooling process is discussed in some detail. © 2009 American Institute of Physics. [doi:10.1063/1.3259971]

I. INTRODUCTION

Biomolecules such as proteins and nucleic acids function in narrow temperature ranges. Excess heat, e.g., due to a chemical reaction or photoexcitation, must therefore be dissipated rapidly and efficiently. Indeed, recent transient infrared spectroscopy experiments by Hamm and co-workers have shown that the cooling of photoexcited peptides occurs on a picosecond time scale. Employing a transient hot band in the amide I region as molecular thermometer, cooling times of 5–7 ps for water, 6 ps for dimethyl sulfoxide (DMSO), and 7 ps for chloroform (CHCl$_3$) were obtained. These results roughly coincide with earlier studies of organic dye molecules in various solvents, which indicates that the cooling time is mostly a solvent property and depends only little on the specific solute molecule.

On the theoretical side, various molecular dynamics (MD) simulations of vibrational cooling and vibrational energy redistribution processes in biomolecules have been reported. In particular, various groups have studied the cooling of photoexcited heme proteins. To model the experiments of Hamm and co-workers, we have developed various nonequilibrium MD techniques that are designed to mimic the experimental preparation by either a UV laser pulse triggering, a molecular photoswitch, or an infrared pumping of a local vibrational mode. While the simulations qualitatively reproduced the energy transfer to the solvent, the calculated energy transfer process was in general slower as observed in experiment. For example, the simulated cooling times of DMSO (Ref. 23) and chloroform were about a factor of 3 too long. These findings may be caused by a number of reasons, including the functional form and the parametrization of the solvent force field, the lack of polarizability of the solvent, and the usually assumed rigidity of the solvent molecules.

The aim of this work is to shed some light on the microscopic mechanism of cooling and to learn about the problems of its description through a standard force field. To this end, we perform a systematic MD simulation study of the photoinduced heat transfer from the model peptide N-methylacetamide (NMA) to various solvents. Because the photoinduced energy is rapidly converted via intramolecular vibrational relaxation into randomized vibrational energy, we assume an initial temperature jump of NMA in order to initiate nonstationary energy flow. The cooling process is studied for a number of potential-energy functions for water, including the “simple point charge” models SPC, SPC/E, and SPC/Fw, the “transferable intermolecular potential with three/four interaction sites” models TIP3P, TIP4P, and TIP3P/Fs, as well as the polarizable “shell water” model SW. We also consider three models for DMSO, two for chloroform, and one for carbon tetrachloride.
(CCL₄). Moreover, we vary the atom mass (to change the solvent viscosity) and the strength of the Lennard-Jones and Coulomb interactions, respectively. Augmented with simple theoretical models of heat transfer, the study aims to provide a microscopic understanding of the cooling process.

II. COMPUTATIONAL METHODS

A. Equilibrium simulations

All simulations were performed with the aid of the GROMACS (Ref. 44) software package (version 3.3.1). We employed the GROMOS96 forcefield, which treats the methyl groups of the solute molecule NMA (H₂C–CONH–CH₃) as united atoms. NMA was placed in a cubic box (edge length ≈3 nm), which was subsequently filled with either ≈870 water, 240 DMSO, 220 CHCl₃, or 220 CCL₄ molecules, respectively. As discussed below, we employed in total seven water solvent models, including SPC, SPC/E, and SPC/Fw, TIP3P, TIP4P, and TIP3P/Fs, as well as the polarizable model SW. For recent comparisons between modeling and experimental data of water, see Refs. 29, 46, and 47. Moreover, three models for DMSO, two for chloroform, and one for carbon tetrachloride were studied.

The equations of motion were integrated via a leap-frog algorithm, using a time step of 2 and 0.5 fs for rigid and flexible solvent models, respectively. We used the SHAKE algorithm with a relative geometric tolerance of 0.0001 to constrain the internal degrees of freedom of all rigid solvent models as well as of the stretch motion of the hydrogen atom in NMA. We used a twin range cutoff (1 nm/1.4 nm) and updated the nonbonded pair list every 10 time steps. The long-range Coulomb interactions were treated by the particle mesh Ewald method. The system was first minimized using the steepest decent method, and subsequently relaxed for 1 ns at constant temperature (300 K) and pressure (1 atm), using the Berendsen coupling procedure with a coupling time of 0.1 and 0.5 ps, respectively. Then a 12 ns equilibrium simulation was carried out at constant volume and temperature. From the last 10 ns of this trajectory, 200 statistically independent configurations of the system were stored as initial conditions for the subsequent nonequilibrium simulations.

To relate the energy dissipation behavior of the solvent to its thermodynamic properties, the specific heat CV = (∂U/∂T)ₐ and the shear viscosity η of all considered solvent models were evaluated. To calculate CV we performed 1 ns NVT simulations at 290 and 310 K and computed CV via the finite difference method. The resulting values of CV listed in Tables I and 3 do not contain correction terms to account for quantum effects or the missing vibrational degrees of freedom in rigid models. Using 12 ns NVT simulations at 300 K, the shear viscosities η were calculated via the Einstein relation as implemented in GROMACS.

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Reference 51.
Reference 3.
Reference 52.

B. Nonequilibrium simulations

In a series of papers, we have recently developed several protocols of nonequilibrium MD simulations that are designed to mimic the experimental preparation by either a UV or an infrared laser pulse. Following subpicosecond intramolecular vibrational relaxation processes, in both cases the photoinduced energy is converted into randomized vibrational energy in the vicinity of the photoexcited moiety. For the sake of simplicity, we may therefore approximate the photoexcitation by an initial temperature jump (or more precisely by an initial jump in kinetic energy) of NMA. This procedure consists of three steps. First, 200 statistically independent configurations of the total system are generated from an equilibrium simulation. To heat the solute, we subsequently perform a short simulation where the solute is coupled to a heat bath at 500 K, while the solvent remains coupled to a 300 K heat bath. This way, the solute reaches the desired temperature of 500 K within ±2 ps. The resulting configurations are then used to perform nonequilibrium MD simulations at constant energy (NVE) conditions, which allow us to follow the cooling of the hot solute in the cold solvent.

To monitor this process, we calculate the mean kinetic energy $E(t)=1/2\Sigma_{i=1}^{N}m_i\langle v_i^2\rangle$ of the N atoms of NMA, where $\langle...\rangle$ denotes the ensemble average over all nonequilibrium trajectories. Employing the SPC model for water as a representative example, Fig. 1 shows the resulting time evolution of $E(t)$. Within 20 ps, the kinetic energy per atom decays from its initial value $E_0\approx5.9$ kJ/mol, corresponding to $m_i/2\dot{v}_i^2=1/2k_BT$ to a temperature of 500 K, to its final value $E_F\approx3.7$ kJ/mol, which approximately corresponds to the solvent temperature of 300 K. Evidently, the decay can be reasonably well fitted to the monoexponential expression,

$$E(t) = (E_0 - E_F)e^{-t/\tau} + E_F,$$

where $\tau=5.7$ ps represents the cooling time of SPC water. This result is in good agreement with the experimental finding of 5–7 ps. A biexponential model yields the decay times 0.07 ps (20%) and 7.7 ps, which leads to an improved fit for the first few picoseconds (data not shown). The additional
ultrafast (≤100 fs) time scale was found for virtually all models studied and is attributed to the initial ballistic motion of the molecule. Because of the well-known ambiguity of biexponential fits and since we are mainly interested in a simple and well-defined quantity to compare the overall cooling behavior of various systems, in this work we restrict the discussion to a single cooling time. The statistical error of the cooling time was checked by comparing to results obtained with 400 (instead of 200) nonequilibrium trajectories and turned out to be quite small (≤5%). Adding the fitting error (typically ≤2%), we estimate the overall error of the cooling time as ±0.5 ps.

As NVE simulations require a rather short time step of ≤0.5 fs to ensure energy conservation, it would be advantageous to resort to constant temperature simulations, which allow for a 2 fs time step. On the other hand, it is clear that strong coupling to a heat bath (i.e., with a short coupling time τT of the thermostat) would artificially accelerate the cooling process. As a compromise, we have performed NVT simulations in which the solvent is only weakly coupled (τT=5 ps) to the 300 K heat bath, while the NMA solute is uncoupled (τT=∞). Although the decay of the kinetic energy is somewhat faster, Fig. 1 reveals that the resulting NVT results for E(t) are in good agreement with the (computationally more expensive) NVE data. Hence we have used the described NVT protocol in all simulations reported in this paper.

III. THEORETICAL CONSIDERATIONS

As discussed by Zhang et al., the mechanism of molecular cooling may depend on various microscopic interactions between solute and solvent. This includes energy transfer via vibration-translation or vibration-rotation interactions, i.e., thermal collisions, which may be described by a diffusion-type equation. Furthermore, cooling can occur through hydrogen bonds and can be caused by direct vibration-vibration energy transfer, which may be described in a perturbative manner by a golden rule-type expression. To support the discussion of the computational findings below, it is therefore instructive to briefly consider these cases.

A. Thermal conductivity

Although the cooling of a hot molecule in a solvent may be rather described in terms of vibrational energy redistribution than in terms of transport properties such as thermal conductivity and viscosity, it is nevertheless instructive to review some basic concepts of heat transfer by using simple well-established models for the solvent. Adopting the theory of thermal conduction, the heat transfer between the hot solute and the cold solvent is governed by Fourier's law,

\[ q = -\kappa \frac{\partial T}{\partial x}, \]  

where, for simplicity, a one-dimensional notation is adopted. Equation (2) relates the heat flux q (in units of energy per time and area) to the temperature gradient \( \partial T/\partial x \), where constant \( \kappa \) is the thermal conductivity of the solvent. Employing the continuity equation for the heat flux, we can derive a diffusion-type equation for the corresponding local heat \( Q \) (in units of energy),

\[ \frac{\partial Q}{\partial t} = \kappa \frac{\partial^2 T}{\partial x^2}, \]

which reveals that the rate of the energy transfer process is directly proportional to the thermal conductivity \( \kappa \). Hence, we expect that we can employ the thermal conductivity to explain the simulated cooling rate 1/\( \tau \).

As a simple model to discuss the overall behavior of the thermal conductivity, we first consider a dilute neutral gas with short-range interactions. Applying the linearized Boltzmann equation to this model, one may derive the relation,

\[ \kappa = \frac{5}{2m} C_V \eta, \]

which directly coincides with physical intuition that the thermal conductivity should be proportional to the heat capacity \( C_V \) and the shear viscosity \( \eta \). The heat capacity increases with the number of internal degrees of freedom of the system, which in turn provide more relaxation channels to dissipate the excess heat, therefore increasing \( \kappa \). The shear viscosity of a fluid is associated with the compensation of local deviations from the equilibrium momentum distribution and is therefore directly connected with the transport properties of the system. Assuming hard spheres of diameter \( d \), one obtains

\[ \eta = \frac{5}{16d^2} \sqrt{\frac{mk_b T}{\pi}}. \]

To test whether this simple model holds in the case of the cooling of NMA in SPC water, we have scaled the masses \( m \) of the solvent atoms by a factor \( \gamma_m \). By calculating \( \eta \) from these MD simulations (see Sec. II), we first checked that the relation \( \eta \propto \sqrt{m} \) [Eq. (5)] holds to a very good approximation (data not shown). Since \( \kappa \propto \eta/m \propto 1/\sqrt{m} \) [Eq. (4)], we expect for the ratio of cooling times,
Ref. 54

The free path of sound for the normal mode. As molecular photoexcited amide I mode to the bending mode of H2O scaled masses the solvent in harmonic approximation by calculating the solvent atoms. Compared are simulation results (crosses) and the theoretically predicted relation \( \tau_1/\tau_{\gamma M} = 1/\sqrt{\gamma_M} \) (dashed line).

\[
\frac{\tau_1}{\tau_{\gamma M}} = \frac{\kappa_M}{\kappa_1} = \frac{1}{\sqrt{\gamma_M}} \tag{6}
\]

Plotting this ratio for \( \gamma_M = 4, 8, 12, \) and 30, Fig. 2 clearly reconfirms this relation; thus demonstrating that the thermal conductivity of SPC water is indeed to a good approximation proportional to its viscosity. Furthermore, this indicates that the cooling time of NMA in D2O and H2O should be quite similar [unless resonant energy transfer occurs, e.g., from a photoexcited amide I mode to the bending mode of H2O (Ref. 54)]. We note in passing that the relation \( \kappa \approx 1/\sqrt{m} \) is also obtained from a harmonic description, if we associate the cooling time with the time scale of the harmonic model, that is, its vibrational period \( 2\pi/\omega_j \approx \sqrt{m} \).

### B. Normal mode description

Alternatively, one may describe the potential energy of the solvent in harmonic approximation by calculating the vibrational normal modes of the solvent. Within the Kubo formalism, the thermal conductivity is then given by 17,18,18

\[
\kappa = \sum_i C_i(\omega_i)D(\omega_i) = \int d\omega \rho(\omega)C_i(\omega)D(\omega), \tag{7}
\]

where \( \omega_i \) denotes the frequency of the \( i \)th normal mode, \( D(\omega_i) \) represents its energy diffusion coefficient, and \( \rho(\omega) \) is the density of states. For low-frequency modes, the diffusion coefficient can be approximated by \( D(\omega) = \frac{1}{2}c_s(\omega)l(\omega) \), where \( c_s(\omega) \) is the speed of sound and \( l(\omega) \) accounts for the mean free path of sound for the normal mode. 17 As molecular transport processes require that the “carrier” of the transport (i.e., the normal modes) extend over the length of at least several molecules, it is the low-frequency vibrational modes that are important for the energy flow in a molecular system.

To get an impression of the normal modes involved, Fig. 3(A) shows the density of states \( \rho(\omega) \) of the instantaneous normal modes56,57 of NMA and SPC water. As is well known, water exhibits a broad frequency band (\( \omega \approx 800 \text{ cm}^{-1} \)) reflecting its librational motion. This librational band overlaps well with low-frequency vibrational bands of NMA, thus facilitating efficient resonant energy transfer between solute and solvent. Including the three internal degrees of freedom of water within the flexible model SPC/Fw, the librational band becomes somewhat wider and shows an additional broad peak around 1500 cm\(^{-1}\), reflecting the bending modes of H2O (1670 cm\(^{-1}\) in experiment). Moreover, we find peaks of \( \rho(\omega) \) around 3500 cm\(^{-1}\), reflecting the well-separated stretching vibrations of H2O (not shown in Fig. 3).

The instantaneous normal modes of the models for DMSO (Ref. 36) and chloroform17,58 are shown in Fig. 3(B). Due to the larger mass, the librational band of these solvents extends only up to \( \approx 200 \text{ cm}^{-1} \). Allowing for the flexibility of the heavy atoms of DMSO (but treating the methyl groups as united atoms), we observe narrow peaks around 400 cm\(^{-1}\) (C–S–O bend), 700 cm\(^{-1}\) (C–S stretch), and 800 cm\(^{-1}\) (S–O stretch, 1150 cm\(^{-1}\) in experiment). In the case of chloroform, the (heavy-atom) internal degrees of freedom add three bands at around 300 cm\(^{-1}\) (Cl–C–Cl bend), 750 cm\(^{-1}\) (Cl–Cl stretch), and 1200 cm\(^{-1}\) (Cl–C–H bend). Apart from resonant energy transfer between solute and solvent in the librational band, there may be therefore additional relaxation channels involving specific intramolecular modes of the solvent (see Sec. IV D).

### C. Perturbative calculation of energy transfer

Besides the phenomenological description of cooling via the thermal conductivity, this process may also be described in terms of the energy transfer between the vibrations of the solute to the vibrations of the solvent. Adopting a system-bath approach in which the system includes the initially excited solute mode \( q \) with frequency \( \omega \) and the bath comprises all remaining vibrational modes \( q_j \) with frequency \( \omega_j \), the energy transfer is mediated by the system-bath interaction \( H_{SB} \), which couples the system and bath degrees of freedom. Quantum-mechanical time-dependent perturbation theory up to second order in \( H_{SB} \) leads to a golden-rule type expression for the energy transfer rate19,20 of the form (\( \hbar = 1 \)).
In the case of bilinear system-bath coupling $H_{SB} = -q \sum c_i^e q_j$, for example, we find

$$\Delta \omega = \omega - \omega_j,$$

$$f_j = n - n_j,$$

describing the resonance condition of the interaction ($\omega = \omega_j$) and the weighting factor $f_j$ of the relaxation channel, where $n$ and $n_j$ denote the initial mean occupation numbers of system and bath oscillators, respectively. Another case of practical importance represents cubic system-bath coupling $H_{SB} = -q \sum c_i^e c_j c_j q_j$, which gives rise to vibrational energy relaxation of the type $\omega \rightarrow \omega + \omega_j$. It leads to the energy transfer rate $1/\tau = \pi/2 \sum c_i^e c_j^2 f_j \delta(\Delta \omega)$, where now

$$\Delta \omega = \omega - \omega_i - \omega_j,$$

$$f_{ij} = n(1 + n_i)(1 + n_j) - (1 + n)n_i n_j.$$

As recently discussed, the perturbative approach to vibrational energy transfer is helpful to study the difference between classical and quantum descriptions. That is, by performing classical time-dependent perturbation theory, we obtain quite similar expressions for the energy transfer as in Eq. (8) with the only difference coming from the weighting factors $f_j$ or $f_{ij}$. In the case of bilinear coupling, we obtain even the same expression $f_{ij} = n - n_j$ for the classical weighting factor, however, the mean occupation numbers $n$ and $n_j$ are different in classical and quantum mechanics. Assuming thermal equilibrium, we obtain, for example,

$$n_j = \frac{k_B T}{\omega_j} \quad \text{versus} \quad n_j = \frac{1}{e^{\omega_j/k_B T} - 1}$$

in the classical and the quantum description, respectively. For nonlinear system-bath interactions, moreover, the form of the weighting factors changes. This difference between $f_j$ and $f_{ij}$ reflects the fact that the dynamics (i.e., the time evolution) of a nonlinear system differs in classical and quantum mechanics. By comparing both theories, we can define a quantum correction factor $Q = f_{ij}/f_{ij}^{CL}$ (that typically ranges between 1 and 5) by which the classical results need to be multiplied in order to obtain the correct quantum result.

IV. RESULTS AND DISCUSSION

A. Comparison of water models

To obtain a first impression, Table I lists the simulated cooling times of some widely used water models together with their heat capacity and viscosity. It is found that the cooling time of $\approx 5.7 \pm 0.5$ ps is virtually the same for the rigid water models SPC, SPC/E, TIP3P, and TIP4P. These results are in good agreement with the experimental finding of 5–7 ps. While the heat capacity varies only little (about 10%), we find significant changes (about 100%) of the viscosity of these models. It is interesting to contrast this finding with the prediction of the hard-sphere model, Eq. (4), stating that the cooling rate should be proportional to the heat capacity and the shear viscosity. According to this model, the cooling time of the SPC/E model should decrease by 50% because the viscosity of SPC/E is roughly twice as high as for the other models. This failure of the theory is caused by the fact that the viscosity of water also depends critically on long-range Coulomb interactions and the hydrogen bonding network. While changes of the viscosity due to a simple rescaling of the masses are well predicted by a hard-sphere model (see Sec. III A), the changes of the viscosity due to a different treatment of long-range Coulomb interactions can, of course, not be described by these models.

So far the discussion has been restricted to rigid models, which constrain the intramolecular vibrations of water. Allowing for the flexibility of these three internal degrees of freedom, the force fields SPC/Fw and TIP3P/Fs (Ref. 32) are found to exhibit $\approx 60\%$ increase in the heat capacity compared to the respective rigid model (see Table I). Assuming that all classical degrees of freedom contribute equally to the heat capacity, this roughly corresponds to the expected linear increase in $C_v$ when going from 6 to 9 degrees of freedom. While the rigid models roughly reproduce the experimental heat capacity of water, the flexible models clearly overestimate the correct $C_v$. This reflects the well-known fact that in quantum mechanics the high-frequency vibrations contain zero-point energy, but—unlike to classical mechanics—are not thermally excited at room temperature, see Eq. (11). This problem represents one of the main reasons to prefer rigid solvent models in classical simulations.

Moreover, Table I reveals that the additional degrees of freedom lead to a speed-up of the cooling process, that is, the cooling times of the flexible models are shorter by 10%–20%. This modest increase in the thermal conductivity can be explained with the aid of the perturbation theory presented in Sec. III C and the instantaneous normal modes density shown in Fig. 3(A). While the additional vibrational modes lead to a wider librational band, the bending mode of water (and much more so the O–H stretch) is too high in frequency in order to majorly participate in the energy transfer [Eqs. (9) and (10)] caused by the initial temperature jump to 500 K.

B. Effects of electrostatic interactions and polarizibility

In the standard hard-sphere model, heat transfer is mediated through collisions. To investigate if this simple picture of balls bumping into each other still holds in the case of a polar solvent, it is instructive to study the relative importance of Coulomb and Lennard-Jones interactions for the cooling process. With this end in mind, we write the interaction energy between solute atom $i$ and solvent atom $j$ as

$$V_{ij} = \gamma^{CL} V_{ij}^{CL} + \gamma^{LJ} V_{ij}^{LJ},$$

where we have introduced the factors $\gamma^{CL}$ and $\gamma^{LJ}$, which allow us to scale the Coulomb term $V_{ij}^{CL}$ and the Lennard-Jones term $V_{ij}^{LJ}$ by some constant. Although the resulting force field may be rather unrealistic for rather small or large $\gamma$ factors, the numerical experiments nevertheless allow us to
study the main effects of these interactions. Figure 4 displays the resulting cooling curves of NMA in SPC water and Table II comprises the corresponding cooling times. Multiplication of the Coulomb interaction with \( \gamma_{\text{LJ}} = 0.1, 2, \) and 4 results in cooling times of 8.2, 3.4, and 2.1 ps, respectively (compared to 5.7 ps for \( \gamma_{\text{LJ}} = 1.0 \)). This significant dependence indicates that the electrostatic interaction is obviously important for the energy transfer. Nevertheless, it is clear that realistic differences (\( \leq 10\% \)) in the charge parametrizations of various force fields would not change the cooling time significantly.

On the other hand, we find that the cooling time is only little affected when the Lennard-Jones interactions are changed. Interestingly, the cooling process becomes even slower for larger Lennard-Jones interactions (e.g., 6.3 ps for \( \gamma_{\text{LJ}} = 20 \)) and faster for smaller Lennard-Jones interactions (e.g., 4.6 ps for \( \gamma_{\text{LJ}} = 0.1 \)). This behavior is readily explained by considering the radial distribution function \( g(r) \) between the center of mass of NMA and the center of mass of the solvent molecules (data not shown). When the Lennard-Jones interactions decrease, solute and solvent may get closer to each other, which in turn leads to stronger electrostatic interactions and therefore to faster energy transfer. That is, the Lennard-Jones interactions influence the cooling process only in an indirect manner because they affect the strength of the Coulomb interactions.

Since the energy transfer in a polar solvent is predominantly mediated via electrostatic interactions, an appropriate modeling of cooling clearly requires their appropriate description. As a first test along these lines, we have compared cooling simulations where the long-range Coulomb interactions are treated by the particle mesh Ewald method\(^{36} \) (our standard method) with simulations employing a simple cutoff of 1.4 nm. For NMA in SPC/E water, we obtained \( \approx 10\% \) increase in the cooling time for the cutoff treatment, indicating that also water molecules that are distant to the solute are important for the cooling process. Due to the strong electrostatic screening in water, though, the effect is relatively small.

Another much-debated issue concerning the proper treatment of electrostatic interactions is the lack of polarizability of most commonly used force fields. To study the effects of polarizability on the energy transfer properties of the solvent, we adopted the polarizable SW model introduced in Ref. 33. It utilizes a classical charged “shell” particle that is connected via a spring to a dummy particle located on the bisector of the water molecule. Moreover, we considered a nonpolarizable version of the SW model by fixing the position of the charge carrying shell particle. As listed in Table I, it is found that the cooling time of the nonpolarizable SW model (5.9 ps) is quite similar to the results obtained for the other rigid nonpolarizable water models such as SPC. Including polarizability, the cooling time decreases by 24% to 4.5 ps, that is, polarizability appears to enhance the energy dissipation, at least for the considered model. This finding is in line with the study of Morita and Kato,\(^{64} \) who showed that the vibrational energy relaxation rate of the azide ion in water may be enhanced by an order of magnitude when the charge polarization of the solute is taken into account.

### C. Comparison to DMSO, chloroform, and carbon tetrachloride

Due to its small size, high polarity (a dielectric constant \( \varepsilon = 80 \)), and outstanding hydrogen bonding properties, water represents a rather special case of a solvent. To put the above discussion on a somewhat broader basis, in the following we therefore want to consider also the widely used solvents DMSO (\( \text{H}_2\text{C}–\text{SO}–\text{CH}_3 \)), chloroform (CHCl\(_3\)), and carbon tetrachloride (CCl\(_4\)). These molecules are less polar and larger than water, i.e., DMSO has \( \varepsilon = 47 \) and 24 internal degrees of freedom, CHCl\(_3\) has \( \varepsilon = 4.8 \) and 9 internal degrees of freedom, and CCl\(_4\) is unpolar.

We considered three models for DMSO, which all treat the methyl groups as united atoms and use the same point charges. Introduced as an advancement of the model of Rao and Singh\(^{34} \) (RS), the rigid model of van Gunsteren (vG) and co-workers\(^{35} \) has been shown to successfully reproduce a number of thermodynamic and transport properties.\(^{65} \) Both models yield virtually the same cooling time of \( \approx 16 \) ps (Table III). The flexible model by Benjamin\(^{36} \) (BJ\(_{\text{flex}}\)) adds six internal degrees of freedom (see the discussion of Fig. 3). This results in a further reduction of the cooling time to 11 ps and a doubling of the specific heat. A further inclusion of the 6 \( \times \) 3 = 18 internal degrees of freedom due to the hydrogen

![Image](https://example.com/image.png)

**FIG. 4.** Cooling curves of NMA in SPC water, assuming that (top panel) the Coulomb interactions between the solute and the solvent atoms were scaled by a factor of \( \gamma_{\text{C}} = 0.1, 2, \) and 4, and (bottom panel) the Lennard-Jones interactions were scaled by a factor of \( \gamma_{\text{LJ}} = 0.1, 2, \) and 20.

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<td>CCl(_4)(vG)</td>
<td>28</td>
<td>38</td>
<td>19</td>
<td>30</td>
<td>29</td>
<td></td>
</tr>
</tbody>
</table>

*Table II. Effects of the Coulomb and Lennard-Jones interactions on the cooling process, studied by varying these interactions through the scaling with \( \gamma_{\text{LJ}} = 0.1, 2, \) and \( \gamma_{\text{C}} = 0.1, 2 \) [see Eq. (12)]. Shown are cooling times (in picoseconds) of NMA in various solvents.*
atoms would result in a further speed-up of the cooling, however, also in a significant overestimation of the specific heat.

For chloroform we used the rigid united-atoms models of Dietz and Heinzinger,37,38 (DH) and of Kovacs et al. (KV),39 which have been compared in Ref. 40. The models are based on the same geometry, but use different charges. Furthermore, we considered a flexible version of the DH model (DHflex), which uses the harmonic force constants of Ref. 58 and constrained the C–H stretch motion, thus resulting in eight internal degrees of freedom. Both rigid models show similar cooling times of 23 ps, the flexible model gives a 35% faster decay ($\tau \approx 14$ ps). While it overestimates the experimental specific heat by about 50%, the flexible model still seems to underestimate the experimental cooling rate.5 That is, the measured cooling process is quite fast, although one would expect that the energy transfer is less efficient in CHCl$_3$ due to its low polarity ($\epsilon = 4.8$). To further investigate this issue, we also considered the CCl$_4$ model of Tironi et al.41 (Ti) as a typical example of an unpolar solvent. The resulting cooling time of $\approx 27$ ps is similar to the calculated result for rigid CHCl$_3$ and also in qualitative agreement with the experimental value of 40 $\pm$ 10 ps.8

As the above solvents are significantly less polar than water, it is instructive to again study the relative effects of Coulomb and Lennard-Jones interactions on the cooling process.66,67 Varying these interactions through the scaling with $\gamma^{LJ} = 0.1, 2$ and $\gamma^{Coul} = 0.1, 2$ [see Eq. (12)], we expect a decreasing importance of the Coulomb interactions compared to the Lennard-Jones interactions, when we go from polar (DMSO) via weakly polar (CHCl$_3$) to unpolar (CCl$_4$) solvents. Indeed, we find that the cooling time of CCl$_4$ hardly changes when the Coulomb interaction is varied, while it decreases to 19 ps (65% of its original value) when the Lennard-Jones interactions are doubled ($\gamma^{LJ} = 2$). The situation is similar for CHCl$_3$, where the cooling time also decreases to 65% of its original value for $\gamma^{LJ} = 2$. In this case, though, the cooling time is at least somewhat sensitive to the Coulomb interactions, as it increases by 20% for $\gamma^{Coul} = 0.1$, but remains the same for $\gamma^{Coul} = 2$. The situation is less clear for DMSO, which is less polar than water but significantly more polar than chloroform. As a consequence, the cooling time reflects a delicate balance between Coulomb and Lennard-Jones interactions. It decreases by 20% for both $\gamma^{LJ} = 0.1$ and 2, and it increases by 50% and 25% for $\gamma^{Coul} = 0.1$ and 2, respectively. These findings are supported by the ratio of the mean Lennard-Jones interactions and the mean Coulomb interactions obtained for the various solvents,68 which yields 0.6 for H$_2$O, 1.4 for DMSO, and 5.2 for CHCl$_3$.

### D. Comparison to experiment

To facilitate the comparison of our computational results to experimental work, we first try to estimate the validity of the assumptions underlying both the theoretical and experimental approach. To begin with our calculations, we have assumed that the cooling time is mostly a solvent property, meaning that the cooling times of NMA and other peptides should be similar. Furthermore, we have assumed that the photoinduced energy is rapidly converted into randomized vibrational energy, such that we may approximate the photoexcitation by an initial temperature jump of NMA. As a test of these assumptions, we compare the above calculations to the results of previously performed nonequilibrium MD simulations, which mimicked the experimental preparation of peptides by a UV or infrared laser pulse.5,22,24,25,69 Despite the explicit simulation of the photoexcitation and the fact that bicyclic or linear peptides with eight amino acids (instead of NMA) were considered, the resulting cooling times are found to be quite similar as in the case of temperature-jump induced cooling of NMA. Specifically, we find 7 and 16 ps for photoexcited bicyclic azobenzene octapeptide in water69 and DMSO,22 which is virtually identical to the results reported in Tables I and III. Simulations of the UV and infrared-induced cooling of a short Aib$_3$10 helix in chloroform gave a cooling time of 18 ps,25 which is somewhat shorter than the 22 ps obtained for NMA. Moreover, we have performed nonequilibrium MD simulations of the vibrational energy relaxation of the amide I mode of NMA in flexible SPC water,24 which gave a cooling time of $\approx 4$ ps in good agreement with the results presented here. From these findings, we conclude that the main two assumptions made in our study—NMA represents a generic example and the photoexcitation is well approximated by an initial temperature jump to 500 K—are at least qualitatively valid. It should be stressed, however, that the consistency of the two computational descriptions does not necessarily mean that they represent an appropriate modeling of the experimental laser-induced preparation of the system.

In the experiments of Hamm and co-workers, the main assumption is that the transient bleaching of a vibrational hot
band of a high-frequency mode can be directly related to the temperature of the molecule.\textsuperscript{4,5,25,26} Although this assumption has been successfully tested by spectral simulations for azobenzene using simple models,\textsuperscript{6} it is difficult to prove whether this—essentially linear—model holds in general. Furthermore, we note that somewhat longer cooling times were estimated from previous experiments that monitored the temperature-dependent change of the $S_0-S_1$ absorption edge of vibrationally hot molecules.\textsuperscript{3} For example, studies of azulene in chloroform and coumarin in 6 chloroform reported cooling times of $35 \pm 10$ ps (Ref. 8) and $11 \pm 2$ ps,\textsuperscript{3} respectively, which are longer than the 7 ps found in Ref. 5 for chloroform.

Having pointed out these inherent uncertainties of theory and experiment, the virtually perfect agreement of calculated (6 ps) and experimental (5–7 ps) cooling times in water (see Table I) appears almost surprising. As already standard rigid water models such as SPC and TIP3P reproduce well the correct heat capacity and cooling time, the flexible models SPC/Fw and TIP3P/Fs were found to overestimate the correct $C_V$ and cooling rate. This reflects the fact that in quantum mechanics the high-frequency vibrations contain zero-point energy, but—unlike to classical mechanics—are not thermally excited at room temperature.

The situation is different for the larger solvent molecules DMSO and CHCl$_3$, which possess 6 and 8 low-frequency vibrational modes (including mostly heavy atoms) as well as 18 and 1 high-frequency vibrational modes (including mostly hydrogen atoms), respectively. Standard rigid models of these solvent were found to significantly underestimate the experimental heat capacity, see Table III. Inclusion of the low-frequency vibrations leads to a better agreement, while the additional inclusion of the high-frequency vibrations overestimates the true heat capacity. Using a flexible model for the low-frequency vibrations yields 30% and 36% reductions of the cooling time of DMSO and CHCl$_3$, respectively. Nevertheless, the resulting cooling times of 11.5 ps (DMSO) and 14.5 ps (CHCl$_3$) are about twice as long as measured in the experiments of Hamm and co-workers.

Apart from the inherent uncertainties of theory and experiment discussed above, there may be two more reasons for this finding. First, it is well known that standard biomolecular force fields significantly underestimate the correct anharmonicity of the solvent vibrational modes, because—besides the overall Lennard-Jones and Coulomb interactions—typically no cross-terms (e.g., $\propto \omega_i \omega_j$) or anharmonic couplings (e.g., $\propto \omega_i^2 \omega_j$ or $\propto \omega_i \omega_j^2$) are included. Second, and probably more important, there may be additional relaxation channels not considered in the present study. For example, consider the vibrational energy transfer from NMA to chloroform. By assuming an initial temperature jump of NMA to 500 K (corresponding to $k_B T \approx 330$ cm$^{-1}$), this relaxation is expected to take mostly place through resonant energy transfer [Eq. (9)] between solute and solvent in the librational band ($\approx 200$ cm$^{-1}$) and the Cl–C–Cl bend band ($\approx 300$ cm$^{-1}$) of chloroform.

However, in an experiment employing, e.g., an impulsive excitation of the amide I mode ($\omega = 1650$ cm$^{-1}$), there could also be the possibility of the relaxation of the type $\omega \rightarrow \omega_i + \omega_j$ [Eq. (1)], where $\omega_i$ and $\omega_j$ may be any mode of the solute or the solvent. For example, by visual inspection of the instantaneous normal mode densities shown in Fig. 3(B), one could imagine a relaxation channel of 1650(NMA) $\rightarrow$ 1350(NMA) $+ 300$(CHCl$_3$). Adopting the perturbative approach outlined above, this example leads to a quantum correction factor $q \approx 1.8$, that is, the classical rate is only about half of the quantum rate. Hence, the experimental excitation of the solute molecule by a UV or infrared laser pulse may render relaxation channels of the type $\omega \rightarrow \omega_i + \omega_j$ important, the rate of which are typically underestimated in a classical description. We note that this relaxation process may also occur in water, but is expected to be of less importance because of the many competing relaxation channels involving the broad librational band of water.

V. CONCLUSIONS

We have performed a systematic MD simulation study of the photoinduced heat transfer from a small peptide to various solvents. Assuming that the cooling time is mostly a solvent property and depends only little on the specific solute molecule, we have restricted us to a single model peptide, NMA, and considered four types of the solvent (water, DMSO, chloroform, and CCL$_4$), 14 different force field models, and in total ten parameter modifications of these models. To initiate nonstationary energy flow, we have assumed an initial temperature jump of NMA and performed nonequilibrium MD simulations using 200 statistically independent trajectories for each case. The underlying assumptions of the computational approach—the cooling time is mostly a solvent property and the photoexcitation is well approximated by an initial temperature jump—were tested by comparing the present study to nonequilibrium MD simulations of photoswitchable octapeptides, which gave quite similar results.

According to simple theoretical models of heat transfer [see Eqs. (4)–(7)], the cooling process is governed by the thermal conductivity, which is expected to be proportional to the heat capacity $C_V$ and viscosity $\eta$ of the solvent. When $C_V$ and $\eta$ were varied by changing the number of degrees of freedom (Tables I and III) and the atom masses (Fig. 2), respectively, our simulations have largely confirmed this picture. However, it has also been shown that realistic force fields for polar solvents may exhibit a much more complex behavior than expected from simple hard-sphere models. This becomes evident when the interplay of Coulomb and Lennard-Jones interactions is studied. The situation is fairly clear in the limiting cases of highly polar water and unpolar CCL$_4$, in which the cooling is predominantly mediated through electrostatic and Lennard-Jones interactions, respectively. In the intermediate cases DMSO and CHCl$_3$, however, we find that the cooling time reflects a delicate balance between Coulomb and Lennard-Jones interactions.

Concerning the applicability of standard biomolecular force fields to describe cooling, the study revealed that realistic changes (5%–10%) of the Lennard-Jones and Coulomb parameters do not change the cooling time significantly. Moreover, only relatively small effects (5%–10%) on the cooling time of water were found for an approximate evaluation
of the Coulomb interactions, i.e., by employing a simple cutoff of 1.4 nm instead of the particle mesh Ewald method. Including polarizability within the SW model, on the other hand, the cooling time was found to decrease by ≈20% compared to the corresponding nonpolarizable model, that is, polarizability appears to enhance the energy dissipation. However, the excellent agreement of calculated (6 ps) and experimental (5–7 ps) cooling times in water indicates that the standard practice of approximately accounting for the effects of polarizability via the charge parameters might be sufficient to describe cooling.

A significant effect on both the heat capacity and the cooling time may be caused by the internal degrees of the solvent. In the case of water, we have considered two flexible models, SPC/Fw and TIP3P/Fs, which were found to overestimate the correct $C_V$ and cooling rate by 10%–20%, see Table I. The situation is different for the larger solvent molecules DMSO and CHCl₃, which possess several low-frequency vibrational modes. Standard rigid models of these solvent were found to significantly underestimate the experimental heat capacity and cooling rate, see Table III. Using a flexible model for the low-frequency vibrations yields 30% and 36% reductions of the cooling time of DMSO and CHCl₃, respectively. However, the resulting cooling times of 11.5 ps (DMSO) and 14.5 ps (CHCl₃) are about twice as long as measured in the experiments of Hamm and co-workers.

Apart from the inherent uncertainties of theory and experiment discussed above, this discrepancy may be associated with the general question of the applicability of classical mechanics to describe cooling and associated quantum-mechanical energy transfer processes. There are two main aspects in which quantum mechanics matters. First, quantum statistics gives the correct occupation number of a vibrational mode. As a consequence, this means that in quantum mechanics the high-frequency vibrations contain zero-point energy, but—unlike to classical mechanics—are not thermally excited at room temperature. This failure of classical mechanics may explain, for example, that flexible water models overestimate the correct heat capacity and cooling rate. Furthermore, it gives rise to well-known problems associated with the spurious transfer of zero-point energy in nonequilibrium MD simulations.²⁴,7⁰ Second, it should be kept in mind that—apart from the statistics—also the dynamics may differ significantly in classical and quantum mechanics. As is already clear from Ehrenfest’s theorem, this effect occurs whenever the potentials and interactions are nonlinear. A comparison of classical and quantum-mechanical perturbation theory suggests that this effect may lead a factor of 2 correction to the classical cooling rate.

To conclude, we have found that force-field issues (including Lennard-Jones and Coulomb parameters and polarizability) have only a relatively small impact on the cooling behavior of a solvent model. An important point, on the other hand, is the classical approximation of quantum statistics and dynamics, which was shown to deteriorate if internal degrees of freedom of the solvent participate in the cooling process. Furthermore, the approximate computational description of the laser-induced excitation and the interpretation of the experimental signals represent inherent uncertainties. Put together, an agreement of calculated and experimental cooling time within a factor of 2 appears quite reasonable.

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3. J. Bredebenck, J. Helbing, J. R. Kumita, G. A. Woolley, and P. Hamm, Proc. Natl. Acad. Sci. U.S.A. 102, 2379 (2005); P. Hamm, (personal communication). The cooling time of 5.7 ps can be estimated from Fig. 2.