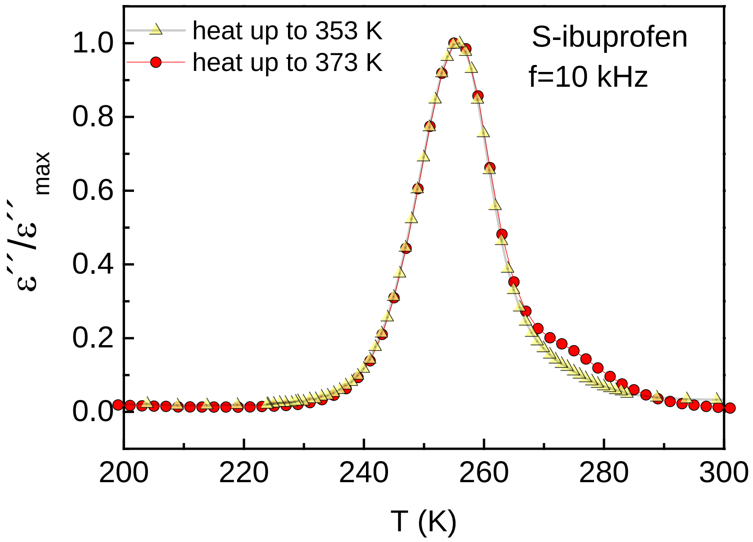
SUPPLEMENTARY MATERIALS

Impact of chirality on peculiar ibuprofen molecular dynamics: hydrogen bonding organizations and syn vs anti carboxylic group conformation

Martin Thierry Ottou Abe, Maria Teresa Viciosa, Natália T. Correia, Frédéric Affouard



Isochronal plot of normalized imaginary part, $\varepsilon''/\varepsilon''_{max}$, at 10 kHz, taken from isothermal data obtained on cooling a sample of molten S-ibuprofen at 353 K (yellow symbols) and another sample at 373 K (red symbols; data shown in Fig. 2b). The Debye relaxation is enhanced when S-ibuprofen is heated at the higher temperature.

Dipolar dynamics – comparison with DRS experiments

Dielectric properties obtained from DRS experiments are related to the total dipole moment $\vec{M}(t)$[1] (see eq. 3). The complex frequency dependent permittivity $\varepsilon^* = \varepsilon' - i \cdot \varepsilon''$ measured experimentally by DRS can be classically well approximated by the Fourier transform of the autocorrelation function $\Phi_\mathrm{M}(\mathrm{t}) = \langle \vec{M}(t).\vec{M}(0) \rangle$ of the total dipole moment. The macroscopic quantity $\Phi_\mathrm{M}(\mathrm{t})$ is usually challenging to compute from MD simulation because of poor statistics i.e. only one autocorrelation function is calculated for the whole system. The individual time-dependent correlation functions $\Phi_\mu(t) = \langle \vec{\mu}(t).\vec{\mu}(0) \rangle$ is often computed instead since it has advantage to be less noisy since an average is performed over the N molecules of the system. In the present study, we have calculated both $\Phi_\mathrm{M}(\mathrm{t})$ and $\Phi_\mu(t)$ functions for the two enantiomeric mixtures at the five different temperatures. In the following, we will only show the less noisy function $\Phi_\mu(t)$ since it behaves very similarly to $\Phi_\mathrm{M}(\mathrm{t})$. It should be mentioned that in the present case, $\Phi_\mu(t)$ is actually a very fair approximation of $\Phi_\mathrm{M}(\mathrm{t})$ since weak correlations between dipoles are present with calculated values of the Kirkwood factor close to 1 $G_k \approx 1$.[2] In case of strong dipolar correlations as observed in monohydroxy alcohols, $\Phi_\mu(t)$ and $\Phi_\mathrm{M}(\mathrm{t})$ would be significantly different as observed in monohydroxy alcohols.[3, 4]

In Fig. 9a, the individual time-dependent correlation function $\Phi_\mu(t) = \langle \vec{\mu}(t).\vec{\mu}(0) \rangle$ is represented for RS- and S-ibuprofen at the temperature T = 380 K. Similar curves were also obtained for all other temperatures. The time decay of the $\Phi_\mu(\mathrm{t})$ functions can be well fitted with a stretched exponential law classically used for glass-forming liquids[5] $\exp\left[-\left(\mathrm{t}/\tau_\mu\right)^{\beta_\mu}\right]$, where τ_μ is the characteristic time associated with the long time decay and $0 < \beta_\mu \leq 1$ the non-exponential parameter. A stretching parameter $0.48 \leq \beta_\mu \leq 0.50$ allowed us to fit data for RS- and S-ibuprofen and all investigated temperatures. These values are in fair agreement with the experimental data $\beta_\mathrm{KWW} = 0.52$ reported for the α-relaxation from DRS.[6] From Fig. 9a, the comparison of the $\Phi_\mu(\mathrm{t})$ functions of the RS- and S- ibuprofen reveals no significance difference within computational accuracy. Note that the same behavior was also observed at 500, 450, 400 and 360 K (data not shown). This result is well in line with the DRS experiments for which no difference is observed as well.

Previous MD computations[1, 7] have shown the importance of the motion of the OH bond in the molecular frame of the —COOH carboxylic group (see Fig. 1 and inset in Fig. 8) and suggested that dynamics of this torsion could be at the origin of the Debye-like process seen from the DRS [6] (see Fig. 2 and 3). In addition to the computation of $\Phi_\mu(\mathrm{t})$, we have thus also performed calculation of the time-dependent function $\Phi_\mathrm{OH}(\mathrm{t}) = \langle \cos(\psi(\mathrm{t}) - \psi(0)) \rangle$, where $\psi(\mathrm{t})$ is the torsion angle of the considered —COOH carboxylic functional group at time t. The symbol < > indicates an average on both time and molecules. The function $\Phi_\mathrm{OH}(\mathrm{t})$ obtained for RS- and S-ibuprofen at the temperature T = 380 K is plotted in Fig. 9b. For both systems, $\Phi_\mathrm{OH}(\mathrm{t})$ can be well adjusted by means of a simple exponential law $\exp[-t/\tau_{OH}]$ well in line with the Debye-process observed in RS-ibuprofen[6, 8] and S-ibuprofen (see Fig. 2 and 3). Similar curves were also obtained for all other temperatures and these adjustments make it possible to estimate the characteristic time τ_{OH} as function of temperature for RS- and S-ibuprofen. At first glance, this figure does not reveal any marked differences but comparison is made difficult due to the noisy behavior that longer simulations could possibly improve. However, while the $\Phi_\mu(\mathrm{t})$ functions shown in Fig. 9a remain very close for the two enantiomeric concentrations, the $\Phi_\mathrm{OH}(\mathrm{t})$ functions from Fig. 9b seem to decay a bit longer for the RS-ibuprofen compared to the S-ibuprofen. Although no clear trend emerges from the scattering of the $\Phi_{OH}(t)$ functions, it may suggest more sensitivity of the Debye-process to the molecular chirality compared to the α-process. Interestingly, as previously shown, this small difference is well in line with the difference of polarity between RS- and S-ibuprofen.

The characteristic times τ_μ and τ_{OH} obtained for all analyzed mixtures are shown in Fig. 4. which allows us to compare simulation and experimental data for both RS- and S-ibuprofen. We can clearly see that the characteristic times τ_μ and τ_{OH} determined for RS- and S-ibuprofen from MD simulations are in very fair agreement with respectively the relaxation times of the α-process and the Debye-like process obtained from DRS experiments for RS- and S-ibuprofen. Overall, Fig. 4 clearly shows that all times τ_μ and τ_{OH} assigned to the α-process and Debye-like processes do not seem to be affected by the molecular chirality.

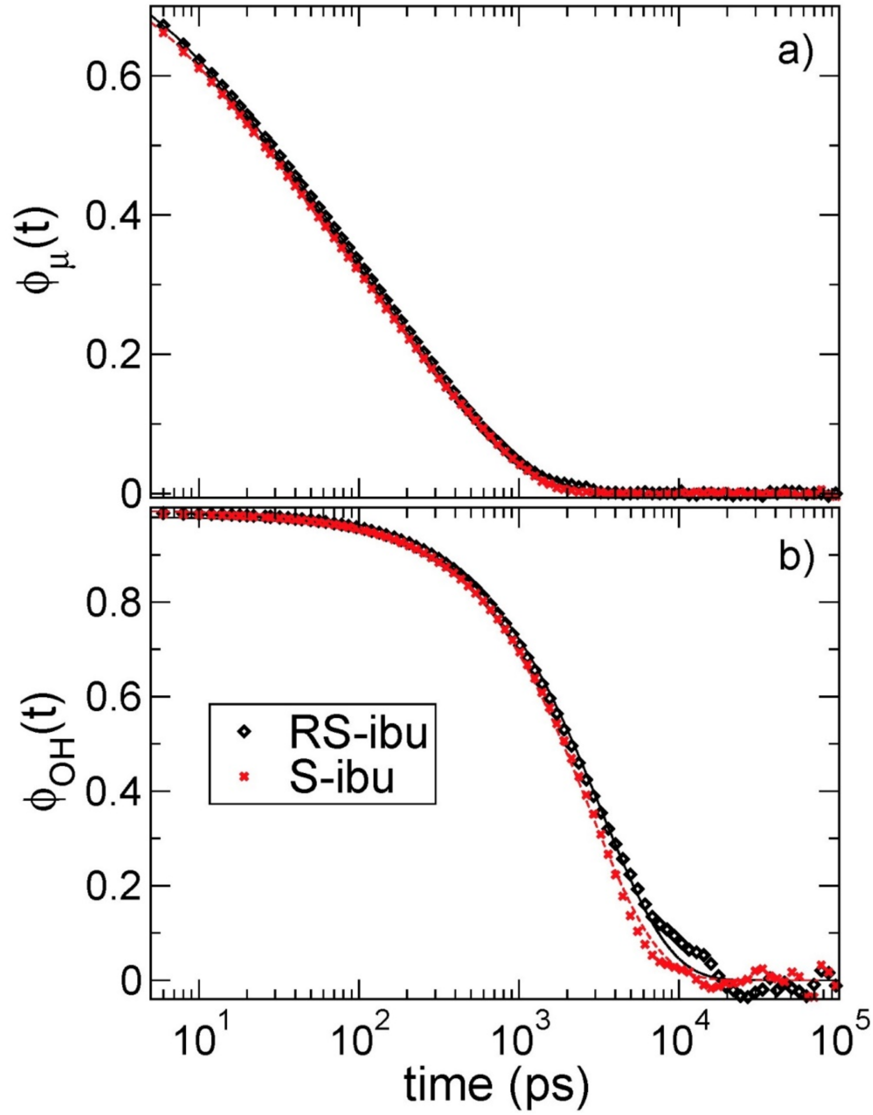


Fig. 9. (a) Time-dependent correlation functions $\Phi_\mu(t)$ (a) and $\Phi_{OH}(t)$ (b) at 380 K for the RS- and S-ibuprofen calculated from MD simulations. Similar curves are obtained for the other temperatures. Solid and dashed lines indicate fits for the RS- and S-ibuprofen respectively. $\Phi_\mu(t)$ and $\Phi_{OH}(t)$ data have been fitted using stretched exponential function $\exp\left[-\left(t/\tau_\mu\right)^{\beta_\mu}\right]$ and single exponential law $\exp[-t/\tau_{OH}]$ respectively (see text).

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