Surrogate for Debye–Waller Factors from Dynamic Stokes Shifts

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ABSTRACT: We show that the short-time behavior of time-resolved fluorescence Stokes shifts (TRSS) are similar to that of the intermediate scattering function obtained from neutron scattering at q near the peak in the static structure factor for glycerol. This allows us to extract a Debye–Waller (DW) factor analogue from TRSS data at times as short as 1 ps in a relatively simple way. Using the time domain relaxation data obtained by this method, we show that DW factors evaluated at times ≥ 40 ps can be directly influenced by α relaxation and thus should be used with caution when evaluating relationships between fast and slow dynamics in glass-forming systems.

SECTION: Kinetics, Spectroscopy

The Van Hove single-particle correlation function, \( G_r(t) \) gives the probability of finding a particle at a position r at time \( t \) relative to the position of that particle at time \( t = 0 \). Thus, this function and its Fourier space analogue, the incoherent intermediate scattering function, \( F_s(q,t) \), contain significant information about dynamics and thermodynamics of solids and glasses. A time-weighed average of \( F_s(q,t) \), the Debye–Waller (DW) factor, is commonly used for characterization of condensed matter systems.

The concept of a DW factor, originally defined as the mean-squared displacement \( \langle u^2 \rangle \) of atoms around equilibrium positions in a crystal, has been extended to a harmonic oscillator approximation of motion in amorphous materials and has emerged as an important parameter in theories of and experiments on supercooled liquids and glass. DW factors and changes in their behavior have been connected in one way or another to virtually all of the classical characteristics of these systems, including the Kauzmann temperature \( (T_K) \), crossover temperature \( (T_\alpha) \), glass transition temperature \( (T_g) \), viscosity, and fragility. This striking relationship between long-time and short-time dynamics seems also to be manifest in the relationship of DW factors to the dynamic coupling between proteins and solvent, between protein function and dynamics, and between host dynamics and stability of proteins encapsulated in sugar-based glass. This latter context is of considerable practical importance as protein instability accounts for significant losses in the biopharmaceutical industry. Both gaining a better fundamental understanding of this striking relationship and exploiting it for screening protein-stabilizing glasses require the ability to routinely and reliably measure DW factors without access to a nuclear reactor or need for Mossbauer-active elements in the sample. Until now, this has not been possible.

DW factors can be obtained from X-ray scattering, as well as from Mossbauer spectroscopy. Below, we show that one can also obtain a surrogate for DW factors in glasses through time-resolved fluorescence Stokes shifts (TRSS). Unlike X-ray, neutron, and Mossbauer scattering, Stokes shifts are not sensitive to oscillatory motion per se but respond to the same molecular rearrangements that cause decay of the correlation functions from which \( \langle u^2 \rangle \) values are derived.

The TRSS of a probe molecule senses changes in position and orientation of host molecules through their influence on the electric field at the probe. Upon \( S_1 \) → 0 photobleaching of a dye molecule, there can be a significant change in dipole moment. Concomitant with this change, nearby host molecules begin to reorganize to accommodate the new local electric field. As this occurs, the energy gap between the \( S_1 \) and \( S_0 \) states of the probe becomes smaller, resulting in a time-dependent red shift in the emitted fluorescence. The magnitude and time dependence of the red shift depend on the solvent relative permittivity \( (\varepsilon_r) \) and the time scale for relaxation in the material, respectively.

TRSS decays presented here were measured in the time domain subsequent to a sub-picosecond excitation pulse by spectrally dispersing fluorescence from rhodamine 6G (R6G) onto an eight-channel avalanche photodiode array (id150 Quantique). Detector output was digitized using a Becker and Hickl SPC 830 module. The convolved time resolution of the detector and digitizer was 54 ps. The 515 nm excitation light was generated by a cavity dumped 790 nm, 30 fs from a cavity dumped

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q = 1.4 Å

Figure 1. (a) Time-resolved Stokes shifts for R6G in glycerol at temperatures of (from top down) 169, 212, 234, 256, 278, 293, 300, and 322 K. (b) Φ(t) from Stokes shift data for R6G in glycerol (blue points) at the same temperatures. Solid black lines are stretched exponential fits to the TRSS data. Dashed red lines are F(t,q,t) at q = 1.4 Å⁻¹ from neutron scattering.

Ti: Sapphire oscillator (Kapteyn-Murnane Laboratories Inc.). Fluorescence was collected in a 180° geometry and dispersed onto the detector as eight equally spaced emission bands in the range of 533–600 nm, covering the major fluorescence peak of R6G. The transmission efficiency of each spectral channel was calibrated against steady-state fluorescence of R6G in glycerol at 300 K. The instantaneous fluorescence energy was calculated as the first moment average of the signal from each detector channel, v(t) = Σi vi(t)/Σi ni(t), where n is the number of detector counts in time bin t, vi is the average energy of the light detected in each channel, and i runs from 1 to 8. Assuming a linear relationship between molecular relaxation and a change in fluorescence energy, a decay function, Φ(t), was defined in the usual way as

\[ Φ(t) = \frac{v(t) - v(∞)}{v(0) - v(∞)} \]

where v(∞) is obtained from the slightly temperature-dependent long-time values of v(t). In this work, v(∞) obtained at the lowest reliable temperature is used at all lower temperatures. The value of v(0) = 18100 cm⁻¹ is obtained from steady-state Stokes shifts in a series of solvents of decreasing polarity, as described in ref 17.

Figure 1a shows time-resolved Stokes shifts for R6G in glycerol at temperatures ranging from below Tg to above Tc and covering times from 13 ps to 20 ns. Dots in Figure 1b are Φ(t) values calculated from the TRSS data of Figure 1a. Solid lines fit to a stretched exponential function, Φ(t) = Φ₀ exp[−(t/τₐ)⁸], the fitting parameters for which are available as Supporting Information. The τ relaxation times (τₐ) that we obtain from these fits are similar to those from dielectric spectroscopy for T > 250 K. Consistent with observations of Richert et al. Dashed lines are F(t,q,t) from neutron scattering on glycerol. These neutron scattering data, obtained at q = 1.2 Å⁻¹, are slightly adjusted to q = q_max = 1.4 Å⁻¹, where q_max corresponds to the peak of the static structure factor. The data are also interpolated to match temperatures used in this study.

It is clear from Figure 1b that TRSS data from glycerol correspond to F(t,q,t) from neutron scattering extremely well at times on the order of 10 ps. In order to determine whether Φ(t) follows F(t,q,t) at longer times, we examine the correspondence between a quantity derived from F(t,q,t), the DW factor, and an analogous quantity derived from Φ. We use DW factors in this comparison for two reasons. One is that direct F(t,q,t) data as a function of time and temperature over the range needed for this comparison would be quite difficult to obtain by neutron scattering, whereas the DW factors can be obtained much more easily. The other is the DW factors themselves are of intrinsic interest, having become an important parameter in many theoretical and experimental studies of condensed matter systems.

DW factors can be obtained from neutron scattering under a harmonic oscillator approximation as the q² dependence of ln(S(q,ω)) where S(q,ω) is averaged over a range of ω corresponding to the width of the energy spread (σω) of the impinging neutron beam. DW factors can also be obtained from F(t,q,t), the Fourier transform of S(q,ω). The expression relating \( \langle u^2 \rangle \) and F(t,q,t) is

\[ \langle u^2 \rangle = -\frac{6}{q^2} \ln \left[ \frac{2\sigma_ω}{\pi} \int_0^{\infty} F(q,t)e^{-(t/\alpha_1)^2} dt \right] \]  \tag{2} \]

where the coherence time of the neutron beam, \( \alpha_1 \), is related to \( \sigma_ω \) by \( \alpha_1 = 0.44/\sigma_ω \) for a Gaussian energy distribution.

We calculate a surrogate for \( \langle u^2 \rangle \) from TRSS decays using an analogue of the expression in square brackets of eq 2

\[ \Phi(\alpha_1) = \sum_i \Phi_i e^{-(t/\alpha_1)^2} / e^{-b} \]  \tag{3} \]

The exponential term in the denominator accounts for logarithmic time sampling. Equation 3 contains no explicit length scale. In analogy to eq 2, we scale ln(Φ) by 6/\( q^2 \), using q at which the static structure factor has a maximum.

In Figure 2, we plot DW factors obtained from neutron scattering on several time scales along with values of ln(Φ) derived from TRSS data in glycerol. Annotation indicating the relevant energy resolution and time scales (\( \sigma_ω \) and \( \alpha_1 \)) is included in each panel. Because we do not have experimental TRSS data at 1 ps, we assign Φ(1 ps) = Φ₀ from fits to the TRSS data. The 1 ps values of \( \langle u^2 \rangle \) from neutron scattering are obtained through eq 2 using experimental F(t,q,t) data. Consistent with the treatment of time-of-flight (TOF) data in Figure 1, here we use \( q_{\text{max}} \) (q \( =1.4 \) Å⁻¹) to scale the TRSS data with no further fit parameters and obtain excellent agreement with the neutron scattering data, as shown in Figure 2.

Agreement between TRSS and DW data is quite good, particularly at low temperatures and short times. This suggests that TRSS might be used as a reliable surrogate for DW factors from neutron scattering on the 1 ps time scale, which are currently obtained by TOF methods and quite costly to measure compared to DW factors on longer time scales. Disagreement between TRSS and DW data at 322 K in the bottom panel is probably due to significant τ relaxation that occurs at this temperature before our measurement time window starts, impairing
The quality of \( \Phi_0 \) estimation in the fit. This is likely not a fundamental limitation; if our detectors were of higher temporal resolution, we would catch the earlier decay and better estimate \( \Phi_0 \). On the other hand, the slight disagreement between TRSS and DW data in the top panels of Figure 2, particularly at higher temperatures, seems more likely to arise from fundamental differences between the two measurements. Neutron backscattering data are sensitive to dynamics over the range of \( 0.36 \leq \xi \leq 1 \) nm, and the DW factors in the top panels of Figure 2 are derived from \( q^2 \) dependence of scattering intensity over this range, where \( \xi = 2\pi/q \). In contrast, analysis of the TRSS signal under a continuum approximation suggests that motions on all length scales contribute to the signal, including significant contribution from \( \xi > 1 \) nm. Given that \( \alpha \) relaxation associated with a longer length scale (lower \( q \)) occurs more slowly, one expects the results observed in the top two panels of Figure 2, that TRSS underestimates the degree of relaxation relative to neutron scattering at long times and high temperatures.

In light of the discrepancy in length scales probed, it may seem surprising that the short-time and low-temperature TRSS data agree so well with the TOF scattering data. There are two possible reasons for the agreement. One possibility is that, in contrast to \( \alpha \) relaxation, the fast \( \beta \) relaxation being probed at 1 ps is scale-invariant, at least on short and intermediate length scales. This does not seem too unreasonable as it is single-particle motion that we are interested in, and only local relaxation should occur on these short time scales. This potential explanation is consistent with \( q \)-dependent neutron scattering results for glycerol. It is also possible that the TRSS response is not entirely scale-invariant in highly viscous media and that motions on an intermediate length scale may be sensed preferentially. We see from the long-time behavior discussed above that if motions on some length scale are sensed preferentially, this length scale must be \( \xi > 1 \) nm for glycerol. It is left for future work to determine the underlying reasons for the striking correspondence between TRSS and neutron scattering at short times and low temperatures.

Having time domain data that reproduces the short-time behavior of the intermediate scattering function, we are in a position to comment on recent treatments of the relationship between short-time and long-time dynamics in glass-forming liquids. During the past couple of decades, several lines of investigation have led to a number of proposed relationships between DW factors obtained on the ps time scale and \( \alpha \) relaxation that occurs on much longer times. Typically, the functional forms used are variations on a proportionality proposed by Hall and Wolynes (HW), as \( \ln(\tau_\alpha) \propto a^2(\xi^2)^{-1} \). This relation holds if \( \alpha \) relaxation is assumed to progress along a potential energy landscape where the energy wells are parabolic and uniformly separated by a distance \( a \). This formalism considers \( \langle u^2 \rangle \) for the system within the potential wells; therefore, DW factors used in these relationships must be measured in a narrow time window where both the ballistic and the relaxation effects are not present. This time window starts at roughly 1 ps.

The HW relation assumes uniform separation of potential energy minima and thus a dynamically homogeneous system. On the other hand, dynamics in supercooled liquids and glasses are known to be spatially heterogeneous. Larini et al. have proposed that dynamic heterogeneity can be represented in the HW formalism by a distribution of potential energy minima spacings and thus have added a quadratic term. They have suggest that this form can universally fit rescaled DW data from the high-temperature regime down through \( T_g \).

Here, we use our time-resolved resolution data to comment on conditions under which this expanded HW relationship might be valid. We evaluate the relationship in terms of an absolute (rather than rescaled) fit for glycerol. To do so requires only that we add a term to the relation of Larini et al. to account for \( \alpha \) relaxation time in the high-temperature limit (\( \tau_\alpha \to \infty \))

\[
\tau_\alpha = \tau_{\alpha,\infty} \exp \left[ \frac{a^2}{2\langle u^2 \rangle} + \frac{\sigma_{u^2}^2}{8\langle u^2 \rangle^2} \right]
\]

where \( a^2 \) and \( \sigma_{u^2}^2 \) are the average and variance in the square of a molecular displacement required for local structural relaxation.

In Figure 3, we plot \( \log(\tau_\alpha) \) from glycerol against \( \langle u^2 \rangle^{-1} \) obtained from neutron scattering on time scales of 2.2 ns, 40 ps, and 1 ps (triangles). Neutron scattering data is from refs 14 or measured on NG2 and NCNR, and viscosity data are from refs 21 and 33.
or 1 ps, as indicated. These data are fitted to eq 4, and fit parameters are shown in Table 1. We note that the data clearly fit better to a quadratic form than a linear one at all time scales but that the fit values for \( \alpha = 40 \) ps and 2.2 ns data are unphysical. Inspection of the time domain data in Figure 1b gives us the reason for the unphysical fit parameters. \( F_0(q_{\text{max}},t) \) and, thus, DW factors derived from it are directly influenced by slow relaxation processes at almost all temperatures for the 2.2 ns data and at the highest temperatures for the 40 ps data. DW factors obtained in these regimes become artificially high to an increasing extent as the temperature is raised, leading to excessive curvature at low values of \( (\alpha^2)^{-1} \). In this vein, Ottochan et al.\(^{34,35} \) have suggested that DW factors acquired on time scales of 5 ns may not be used in eq 4 to obtain universal fits. Our results are consistent with theirs, although we show that one obtains reasonable fit values to absolute (rather than rescaled) data only when DW factors on the shortest time scales are considered. We also see that DW factors acquired at times as short as 40 ps can have significant influence due to \( \alpha \) relaxation at elevated temperatures and suggest that these should be used with care, even in a rescaled fit. Within the model of Larini et al.,\(^{29} \) the positive value of \( \sigma_{\alpha} \) indicates the presence of heterogeneity, and while we clearly obtain a positive, nonzero value for \( \sigma_{\alpha}^2 \), we note that such curvature could arise independent of heterogeneity if, as proposed by Martinez and Angell,\(^{36} \) the glass formers explore potential surfaces of increasing curvature as they are cooled.

We have shown that TRSS data can be used as a surrogate for DW factors in glycerol. We expect this result to be general to the extent that that fast (~1 ps) dynamics are intrinsically local. Further exploration of the correspondence between TRSS and \( F_0(q_{\text{max}},t) \) at these short times is expected to shed further light on the behavior of supercooled and glassy systems and perhaps provide insight into the TRSS response. As evidenced by the work presented here, we expect that the ability to extract DW-like factors from TRSS data will facilitate a better understanding of the relationships between \( (\alpha^2) \) and long-time phenomena. We also expect that it could form the basis for more widespread and routine use of DW factors in characterization of glasses, such as routine and rapid prediction of protein stability in sugar glasses.\(^{10} \)

## REFERENCES

15. Certain commercial equipment, instruments, or materials are identified in this paper in order to specify the experimental procedure adequately. Such identification is not intended to imply recommendation or endorsement by the National Institute of Standards and Technology nor is it intended to imply that the materials or equipment identified are necessarily the best available for the purpose.

## Supporting Information

**Supporting Information.** Fit parameters for Figure 1. This material is available free of charge via the Internet at http://pubs.acs.org.

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### Table 1. Fit Parameters for Data in Figure 3 to Equation 4

<table>
<thead>
<tr>
<th>( \alpha )</th>
<th>( \log(t_{\text{on}}) )</th>
<th>( \sigma^2(q_{\text{max}}/2\pi)^2 )</th>
<th>( \sigma^2(q_{\text{max}}/2\pi)^2 )</th>
</tr>
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<tbody>
<tr>
<td>1 ps</td>
<td>–11 ± 0.5</td>
<td>0.4 ± 0.05</td>
<td>1.0 ± 0.1</td>
</tr>
<tr>
<td>40 ps</td>
<td>–8.5 ± 0.6</td>
<td>1.3 ± 0.2</td>
<td>1.8 ± 0.2</td>
</tr>
<tr>
<td>2.2 ns</td>
<td>–7.2 ± 0.4</td>
<td>–0.7 ± 0.2</td>
<td>4.0 ± 0.4</td>
</tr>
</tbody>
</table>


(34) Ottochian, A.; Leporini, D. Scaling between Structural Relaxation and Caged Dynamics in Ca0.4K0.6(NO3)1.4 and Glycerol: Free Volume, Time-Scales and Implications for Pressure—Energy Correlations. Philos. Mag. 2011, 91, 1786–1795.
