Supplemental Material: Short-Time Glassy Dynamics in Viscous Protein Solutions with Competing Interactions

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I. DETERMINING THE SELF-DIFFUSION COEFFICIENTS USING NEUTRON SPIN ECHO

Neutron spin echo (NSE) directly measures the intermediate scattering function (ISF), $I(q,t)$, over a range of length and time scales pertinent to protein solutions. In the short-time limit, the ISF can be fit with a single exponential decay function according to

$$\frac{I(q,t)}{I(q,0)} = \exp\left[-q^2 t D_c(q)\right] \tag{S1}$$

where $D_c(q)$ is the q-dependent collective diffusion coefficient. Examples of the ISF obtained by neutron spin echo are shown in Fig. S1 at a specific q-value at several solution conditions with the line of best fit using Equation S1. Each sample is measured over a range of q-values between about $0.04 - 0.17$ Å^{-1}. The diffusive time scale, t_D, determines the short-time limit,[1] which for lysozyme is about 25 ns. Therefore, the ISF is fit for $t < t_D$ by Eq. S1. The values of $D_c(q)$ are plotted in Fig. S2 as a function of q-value for each of the samples studied. The short-time self diffusion coefficient can be extracted by the value approached in the limit of large q-values according to the definition $D_S = \lim_{q\to\infty} D_C(q)$.

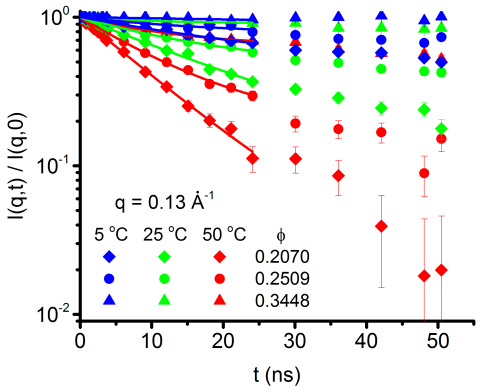

FIG. S1. Intermediate scattering functions (symbols) are plotted at $q = 0.13$ Å^{-1} for several lysozyme solution conditions along with best fits using a single exponential decay function. The fits produce a quantitative measure of the q-dependent collective diffusion, $D_c(q)$.

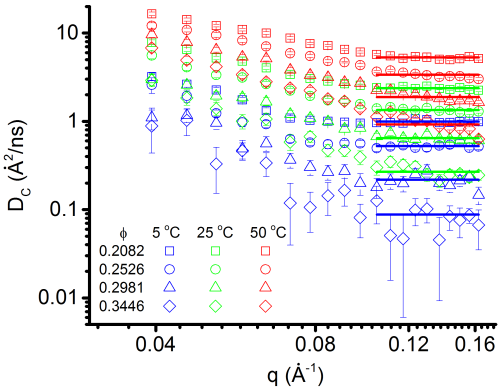

FIG. S2. Collective diffusion coefficients (open symbols) are plotted as a function of q-value for each of the high concentration lysozyme solutions. The solid lines represented the high-q asymptotic value calculated from the data to determine D_S.

II. THE COMPARISON OF THE SHORT-TIME AND LONG-TIME DIFFUSION BEHAVIOR

The long-time self diffusion coefficient, D_L, of concentrated lysozyme samples is difficult to determine experimentally due to its size and limitations of experimental techniques. However, D_L can be approximately estimated from either the zero-shear viscosity or a normalization of short-time self-diffusion using mode coupling theory (MCT). The first method is used in the main text to estimate the long-time mean squared displacement (MSD). Results estimated from both methods support our conclusion in the main text that at large concentrations and low temperatures, lysozyme proteins have localized glassy-like behavior

For the second method, according to MCT, the experimental values of D_S can be used to estimate D_L according to

$$\frac{D_L}{D_0} \approx \left(\frac{D_S}{D_0}\right) D_L^{MCT}, \tag{S2}$$

where D_L^{MCT} is a volume fraction dependent ratio of D_L/D_S determined by MCT.[2, 3] Note that D_L^{MCT} is originally determined using the MCT for hard sphere (HS) systems.[2, 3] However, there is no suitable theoretical framework yet to estimate D_L using MCT for a system with competing interactions. Therefore, as an rough approximation, we simply applied the theoretical results from the HS system to our lysozyme systems.

Despite the approximative manner of this approach, interestingly, we find that the results

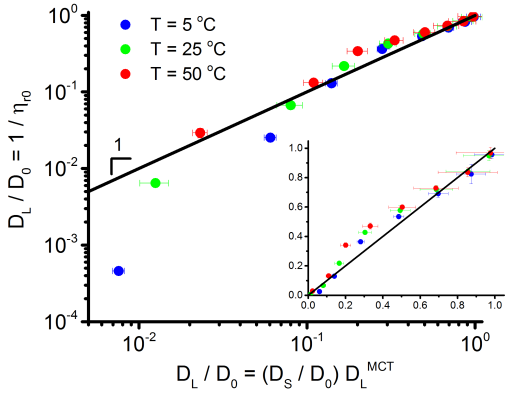

FIG. S3. Values of D_L/D_0 estimated from the viscosity $1/\eta_{r0}$ are plotted relative to estimates from MCT normalization of D_S/D_0 obtained from NSE. The solid line is the equivalence point and the inset provides a linear scale for clarity at large values of D_L/D_0.

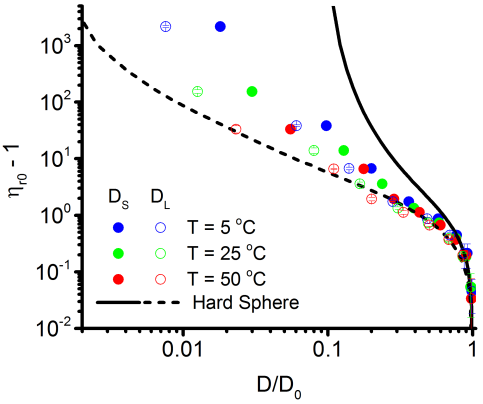

FIG. S4. The specific viscosity of lysozyme is plotted as a function of D_S (filled symbols) and D_L (open symbols) relative to calculations for HS fluids (solid line and dotted line, respectively).

agree with those obtained from the zero-shear viscosity reasonably well over a fairly large range of protein concentrations and temperatures as shown in Fig. S3. The detailed reason is still under investigation.

As mentioned in the main text, the long-time self-diffusion of concentrated lysozyme samples is faster than a particle in a HS system with an equivalent viscosity. Figure S4 shows the estimated D_L for lysozyme (open circles) and the HS systems (dashed line) using the MCT theory. As a comparison, the results from short-time behavior (solid line and solid symbols) are also kept in the same figure. The smaller volume fractions of the lysozyme

system relative to a HS system result in a less significant shift in diffusivity from short to long time scales. Therefore, qualitatively, lysozyme samples have a smaller D_S and larger D_L compared to a HS system, indicating enhanced mobility at short length scales at long time scales in the presence of intermediate range order.

Distinguishing the disparate short and long time scales in concentrated lysozyme samples ($\phi > 0.3$) was also accomplished using dynamic light scattering (DLS). Two distinct relaxation times were observed at all temperatures, which were fully reversible over three temperature sweeps between $5°C$ and $50°C$.

III. INTER-PROTEIN INTERACTION POTENTIAL PARAMETERS OBTAINED BY THE SANS FITTING

The inter-protein interaction parameters between lysozyme can be obtained from 1-D SANS profiles using the HSDY potential. By holding the inverse range of attraction, z_1, constant at a value of 10, as determined from previous studies to be representative for lysozyme samples,[4] the remaining four parameters (ϕ_{fit}, K_1, K_2, z_2) could be extracted from the best fit to the data. The results are compiled in Table III. The strength of the short-range attraction ranges from $4k_BT$ to 6_BT for our lysozyme samples, which is signficanlty smaller than the attraction strength between large PMMA colloidal particles reported in ref[5], which is about $15k_BT$. This difference of the attraction strength has dramatic effects on the solution structure of the systems as the weaker attraction places the lysozyme state points different from those of the PMMA systems from in the generalized phase diagram.[6]

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TABLE I. A compilation of parameters determined from fits to the SANS data over a range of lysozyme solution conditions.

$T = 5°C$				
ϕ_{fit}	K_1	K_2	z_2	τ_B
0.0398	6.1837	4.031	1.2238	0.7627
0.0773	7.2	4.0715	1.9061	0.2454
0.1263	6.5301	3.3148	2.5337	0.1901
0.1432	6.4666	3.2868	2.7839	0.1918
0.2017	6.3	3.0811	3.6117	0.1665
0.2388	6.05	3.0033	4.1718	0.1842
$T = 25°C$				
ϕ_{fit}	K_1	K_2	z_2	τ_B
0.0398	6.0291	4.2743	1.2473	1.3479
0.0765	5.7	3.8857	1.8616	1.0865
0.1286	5.8446	3.525	2.6287	0.4994
0.1472	5.8511	3.5588	2.9338	0.5030
0.2099	5.743	3.3574	3.8785	0.3955
0.24	5.587	3.3283	4.3792	0.4284
$T = 50°C$				
ϕ_{fit}	K_1	K_2	z_2	τ_B
0.0401	6.0136	4.4161	1.2656	1.7420
0.074	5.206	3.9707	1.8335	2.7741
0.1262	5.4706	3.8298	2.6729	1.2629
0.1551	6.1753	4.3252	3.3055	0.9561
0.2091	5.2251	3.7215	4.0331	1.2886
0.2437	4.61	3.2208	4.3814	1.3278