

*Supporting Information for*  
**Stacking and Branching in Self-Aggregation of Caffeine in  
Aqueous Solution: From the Supramolecular to Atomic Scale  
Clustering**

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## Dynamic Light Scattering Data Analysis

Stretched exponential functions are used to describe a distribution of decay rates and, in turns, a distribution of diffusion constants. The  $n^{\text{th}}$  order momentum of the  $\tau$  distribution is:<sup>5</sup>

$$\langle \tau^n \rangle = \frac{\tau^n}{\beta} \Gamma\left(\frac{n}{\beta}\right). \quad (\text{SI.1})$$

The distribution polydispersity index  $\sigma$  is defined as the ratio  $s/\langle \tau \rangle$  between the standard deviation  $s$  and the mean value  $\langle \tau \rangle$ .

The individual decay constant  $\langle \tau(\theta) \rangle$  is directly related to the average apparent diffusion constant of the particles in solution:

$$D(\theta) = \frac{1}{\langle \tau(\theta) \rangle Q^2} \quad (\text{SI.2})$$

In general, in presence of large particles and polydispersed samples, the diffusion coefficient measured at a given  $\theta$  is an apparent diffusion constant. The zero-angle diffusion constant  $D_0$  was extracted from a linear extrapolation of  $\frac{1}{\langle \tau(Q) \rangle Q^2}$  vs.  $Q^2$  since

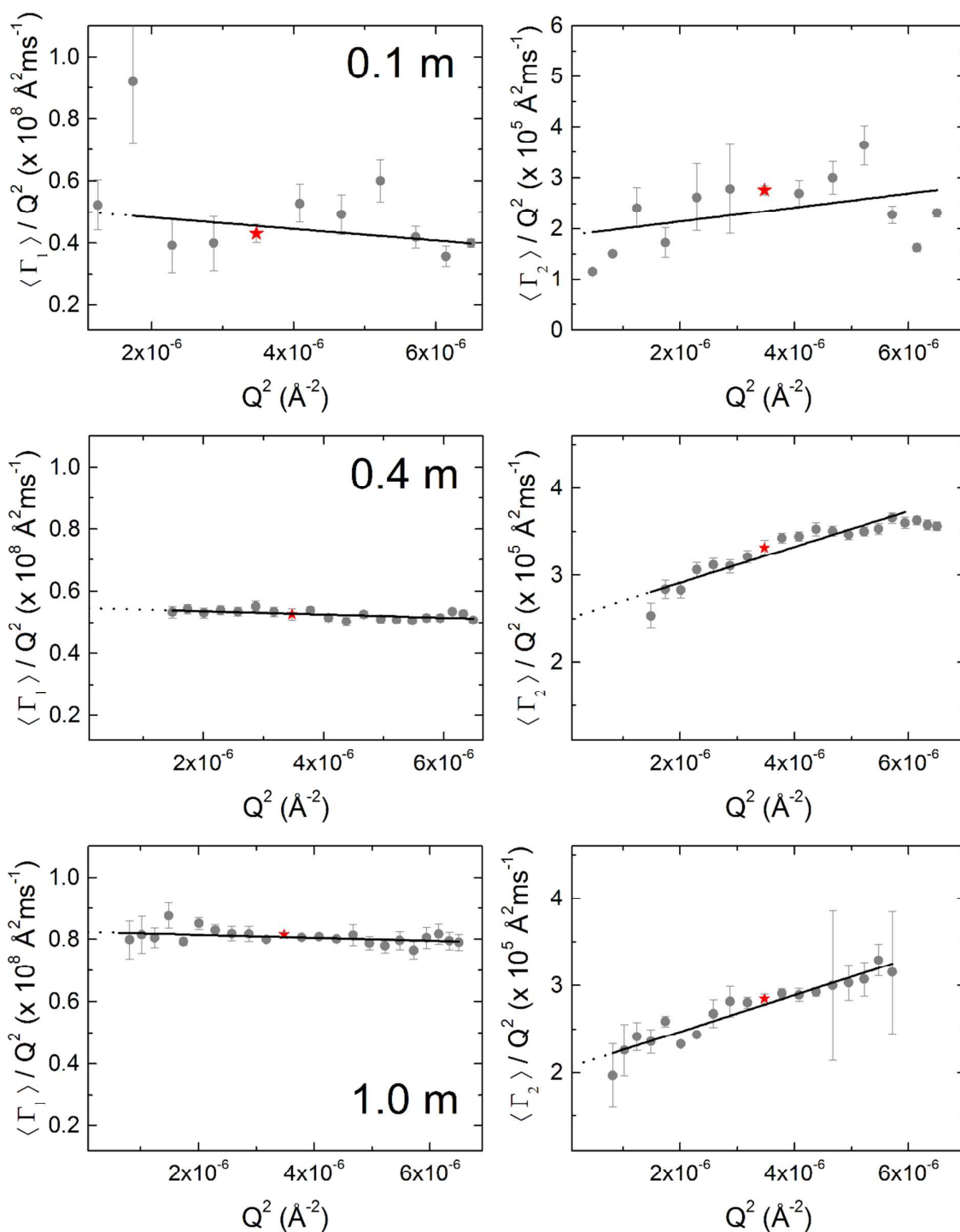
$$\frac{1}{\langle \tau(Q) \rangle Q^2} \approx D_0 + \kappa Q^2 \quad (\text{SI.3})$$

where  $\kappa$  is a sample dependent constant. The average hydrodynamic particle radii,  $\langle R_{h1} \rangle$  and  $\langle R_{h2} \rangle$ , were then obtained applying the well-known Stokes-Einstein relation as

$$\langle R_{h^i} \rangle = \frac{k_B T}{6\pi\eta(T)\langle D_0^i \rangle} \quad (\text{SI.4})$$

where  $k_B$  is the Boltzmann constant,  $T$  the absolute temperature and  $\eta(T)$  the solvent viscosity.

Equations SI.1 to SI.4 were used for the calculation of the zero-scattering angle hydrodynamic radius. The last step of the extrapolation is reported in Figure SI.1.

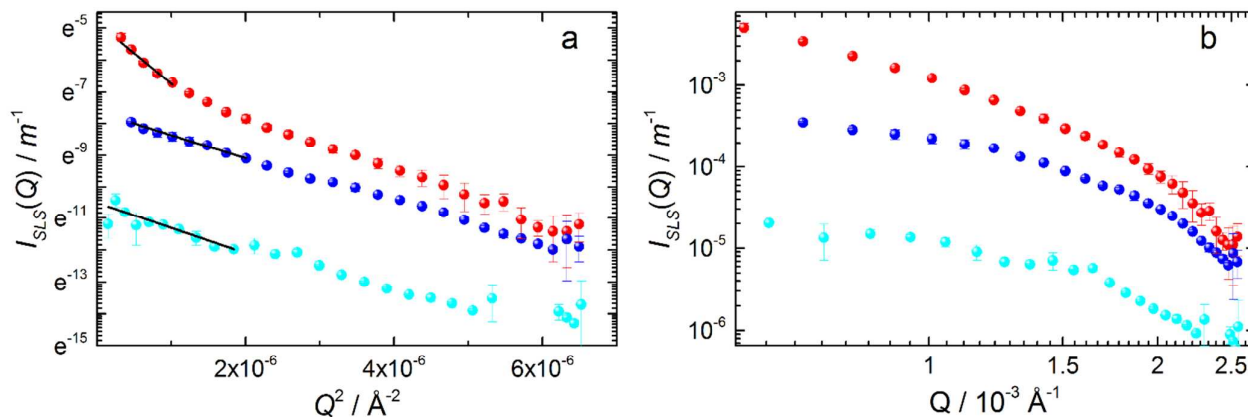


**Figure SI.1.** Angular dependence of the apparent diffusion constants  $D_i(\theta) = \frac{\langle \Gamma_i(\theta) \rangle}{Q^2}$  obtained from the analysis of the intensity auto-correlation functions for the 0.1 m, 0.4 m and 1.0 m caffeine samples measured in D<sub>2</sub>O at the 25°C, 43°C and 80°C respectively. The apparent diffusion constants measured at 90° scattering angle are indicated by red symbols (stars). Significant differences were present especially in the case of  $D_2(90^\circ)$  vs.  $D_2(0^\circ)$  values. Average hydrodynamic radii reported in the manuscript were always derived from

the extrapolated  $D_i(0^\circ)$  values.

## Guinier Analysis of SLS data

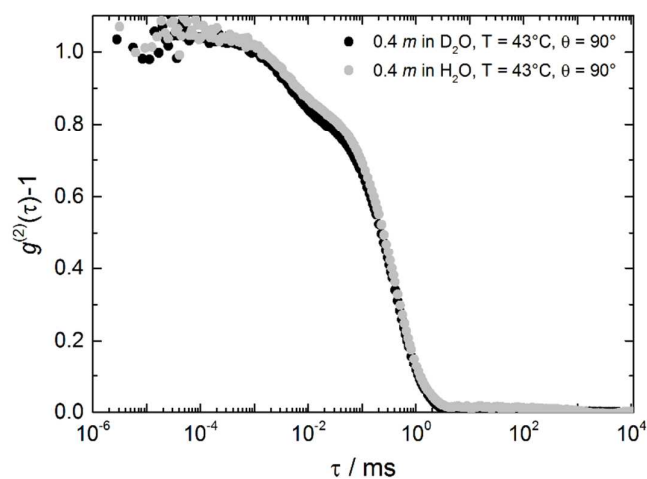
Static light scattering data were analyzed in terms of Equation (1). The fits, in the  $Q$ -range where the Guinier approximation is valid, are reported in Figure SI.2.



**Figure SI.2.** **a)** Guinier plots for the SLS data for 0.1 *m* (cyan), 0.4 *m* (blue) and 1.0 *m* (red) caffeine samples measured in D<sub>2</sub>O. The more concentrated sample was characterized by the presence of larger aggregates (higher slope at low  $Q$ ) as already indicated by DLS data. Fits according to Equation (1) of the manuscript are reported as solid lines. **b)** SLS data in the classical  $I(Q)$  vs.  $Q$  representation. The Guinier region is clearly visible.

## Isotopic Effect

In order to reduce the background incoherent scattering coming from  $^1\text{H}$  atoms and to enhance the scattering intensity SANS measurements were performed in D<sub>2</sub>O. Light scattering measurements were performed on the same solutions as used for SANS but they were also repeated in H<sub>2</sub>O to investigate any possible effect induced by the isotopic substitution. As shown here by the intensity auto-correlation functions reported in Figure SI.3, exchange of H<sub>2</sub>O for D<sub>2</sub>O does not affect the self-aggregation processes. The small differences visible could be induced by differences in the overall caffeine concentration.



**Figure SI.3.** Comparison between the intensity auto-correlation functions for 0.4 *m* caffeine samples in  $\text{H}_2\text{O}$  (gray) and in  $\text{D}_2\text{O}$  (black). Time-axis values for the  $\text{D}_2\text{O}$  sample were corrected by a factor 1.118 in order to account for viscosity differences (at  $45^\circ\text{C}$   $\eta_{\text{D}_2\text{O}} = 0.671$  cP and  $\eta_{\text{H}_2\text{O}} = 0.600$  cP). No substantial differences are visible.