Structure and dynamics of hydration shells (of proteins)

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Electrostatic potential at active sites

\[ \phi = \phi_w + \phi_p \]

\[ \Delta G_e/e = \langle \phi \rangle + e \frac{\langle (\delta \phi)^2 \rangle}{2k_B T} + \cdots \approx \frac{1}{2} \langle \phi \rangle \]

\[ \chi_G = - \frac{e\langle (\delta \phi)^2 \rangle}{2\langle \phi \rangle k_B T} \overset{\text{LRA}}{=} 1 \]

\[ \chi_G \gg 1 \]
Non-Gaussian electrostatics

Gaussian fluctuations:

$$\beta^{-1} \Delta q \left( \langle \phi \rangle_1 - \langle \phi \rangle_2 \right) = \Delta q^2 \langle (\delta \phi)^2 \rangle$$

Electrostatics become non-Gaussian above $T_D$
Distribution width: dynamical transition

Standard picture: \( \sigma(T)^2 = 2\lambda^\text{var} k_B T \propto T \)

Proteins: \( 2k_B T \lambda^\text{var} \propto T - T_0 \)
RMSD: Iron of the heme

The main contribution to RMSD above Td is electrostatics
Why is it important? Enzyme catalysis!

Fluctuations effectively lower the barrier
Potential fluctuations

Concerted protein-water fluctuations

Is water organized in polar domains?
Interfaces: Questions

**Density** and orientational structure of interfacial water

Weak dewetting vs density increase, 10-15% denser at the protein.

Dangling OH at the water-air interface, preferential in-plane orientation of the dipoles

Flipping of water dipoles by surface groups

**Slowing down** of interfacial water dynamics

PCCP 13 (2011) 19911
Minimum in the retardation factor of one-particle dynamics

Increasing local density with stronger hydrophilic character of the substrate

**Spatial extent** of interface: density vs orientational manifold

Intermediate band of 50-60 GHz is seen for solutions of sugars, assigned to hydration layer. Signal intensity correlates with the number of exposed OH groups, Fioretto and co-workers, JPCB 116 (2012) 14760.
Planar interfaces

FIG. 2. The dipole moment density, $P_z(z)$, for all studied liquids at the vapor-liquid interface. Dashed vertical lines represent the GDS of both interfaces for SPC/E.

$E \sim 10^9 V/cm$

$\mu_z = 1.87 \text{ D}$

$Q_{zz} = -0.13 \text{ D } \times \text{Å}$

$Q_{xx} - Q_{yy} = 5.13 \text{ D } \times \text{Å}$

“Dipolar wave” at the planar water interface! (Same for water-oil)
Hydrated NALMA dipeptide

Waters in the first shell are tilted toward the solute

Second shell loses most of the structure (no “dipolar wave” seen for planar surfaces)

Significant hydrophilic character of the first shell
Parameters and susceptibilities

**Orientational** order parameters of the hydration shell

\[ p_\ell = \langle P_\ell(\cos \theta_n) \rangle_{\text{shell}} \]

\[ \chi_{0s} \propto \langle \underbrace{M_0}_{\text{protein}} \cdot \underbrace{M_s(a)}_{\text{shell}} \rangle \]

\[ \chi_s \propto \langle \underbrace{M_s(a)}_{\text{shell}} \cdot \underbrace{M_s}_{\text{total}} \rangle \]

\( p_1 \) of the hydration shell of lysozyme
Hydration shells: questions

Origin of “intermediate” peaks in experimental loss spectra

Density vs. orientational structure of hydration shells

Depth of propagation into the bulk

Specific dynamics of hydration shells
DLS: Formalism

Sample polarizability:

\[
\Pi = \Pi^M + \Pi^I
\]

polarizability  molecular polarizabilities  induced polarizabilities

Dipole-induced-dipole polarizability (I-I):

\[
\Pi^I_s = \sum_{i \neq j}^{N_s} \alpha_i \cdot T_{ij} \cdot \alpha_j
\]

dipolar tensor

VH (DLS) time correlation function:

\[
C^{\Pi}(t) \propto \sum_{\alpha \neq \beta} \langle \delta \Pi_{\alpha \beta}(t) \delta \Pi_{\alpha \beta}(0) \rangle
\]

Kerr effect loss function:

\[
\chi(t) = -\beta \dot{C}^{\Pi}(t) \quad \chi''(\omega) = (\beta \omega / 2)C^{\Pi}(\omega)
\]

exp. DLS spectra
Depolarized light scattering of water

$$\chi''(\nu)$$

\[ \alpha_{xx} = 1.408, \quad \alpha_{yy} = 1.497, \quad \alpha_{zz} = 1.417 \text{Å}^3 \]

V-H Depolarized scattering of bulk water measures the dynamics of molecular translations through dipole-induced-dipole polarization anisotropy

Fukasawa et al, PRL 95, 197802 (2005)

A cooperative relaxation specific to hydrogen-bond liquids and arising from long range H-bond mediated dipole-dipole interactions gives the main contribution to the dielectric spectrum. This process is virtually not Raman active.
80 NALMA’s in 36,000 SPC/E waters

Searching for shell dynamics:

$$\phi(t) = A_1 \phi_s(t) + A_2 e^{-t/\tau_2} + A_3 e^{-t/\tau_3}$$

bulk water  dynamics of solutes

No shell dynamics could be identified!
Two low-frequency peaks

Slowest dynamics come from the density fluctuations of the solutes:

$$S_{00}(k, t) = N_0^{-1} \sum_{i, j=1}^{N_0} e^{i(r_{0i}(t) - r_{0j}(0)) \cdot k}$$

calculated at $k = 2\pi / \langle r \rangle$

single-particle rotational dynamics of the solutes

DLS response of the solution: solutes’ relaxation (two processes) + bulk water relaxation,

no specific dynamics of the hydration layer
DLS of lysozyme solution

\[ \phi^\Pi(t) = B_1 \phi_s^\Pi(t) + B_2 \phi_0^\Pi(t) + \phi_{\text{cross}}^\Pi(t) \]

Negative contribution of the cross term
DLS of water(!) in the lysozyme solution

\[ \phi^\Pi(t) = B_1 \phi^\Pi_s(t) + B_2 \phi^\Pi_0(t) + \phi^\Pi_{\text{cross}}(t) \]

\[ \Delta \chi''(\omega) = (\chi^{\text{sol}}_s)''(\omega) - \chi''(\omega) \]

Model Simulations
Stochastic model

Two bi-linearly coupled stochastic processes

\[ H = \frac{1}{2} k_0 (\delta X_0)^2 \quad + \frac{1}{2} k_s (\delta X_s)^2 + \gamma \delta X_0 \delta X_s \]

overdamped oscillator

\[ \zeta_0 \dot{x}_0 + \omega_0^2 x_0 = -\gamma_0 x_s + R_0 \]

random force

\[ \omega^{-1} = \sqrt{\frac{\tau_0^\text{sol}}{\tau_s}} \]

\[ \Delta \chi_s''(\tilde{\omega}) \propto \left(1 - \frac{\tau_0}{\tau_0^\text{sol}}\right) \text{Re} \left[ \frac{\tilde{\omega}}{(1 - i\tilde{\omega})(1 - i\alpha \tilde{\omega})} \right] \]
Orientational structure: NALMA

\[ g_{K}^{0s}(a) = \left( m_{0}m_{s} \sqrt{N_{s}(a)} \right)^{-1} \left\langle \delta m_{0} \cdot \delta M_{s}(a) \right\rangle \]

\[ \chi_{0s} \propto \left\langle \frac{M_{0}}{\text{protein}} \cdot M_{s}(a) \right\rangle \]

Long-range orientational perturbation of the interface extending ~ 5 water layers into the bulk.
Dipolar dynamics: NALMA

No significant change in the one-particle dynamics!

\[ C_2(t) = \langle P_2(\mathbf{u}(t)) \cdot \mathbf{u}(0) \rangle \]

\[ C_M(a, t) \propto \langle \delta \mathbf{M}_s(a, t) \cdot \delta \mathbf{M}_s(0) \rangle \]
Dipolar dynamics: lysozyme

The dynamics of the dipole moment of the solution is very different from the dynamics of the density fluctuations:

A separate shell dynamics!
Dipolar dynamics: water shells

NALMA:

\[ \chi_s \propto \langle M_s(a) \cdot M_s \rangle \]

Lysozyme:

These slow relaxation times do not appear in the correlation function of the sample dipole!
Nano-domains!
Lysozyme’s shell dipole: temperature dependence

\[ \chi_M \propto \left\langle \left( \overline{M_s(a)} \right)^2 \right\rangle \]

\[ \kappa \propto \frac{\left\langle (\delta N_s(a))^2 \right\rangle}{\left\langle N(a) \right\rangle} \]
Phenomenology of relaxor ferroelectrics

\[ \chi_M \propto \langle (\delta M_s(a))^2 \rangle \]\n
\[ \propto (1 - e^{-a/\Lambda}) \]

Samara, J.Phys.Cond.Mat.’03
Relaxor ferroelectrics: Maximum dispersion

glass-like transition temperature, $T_m$. The strong frequency dispersion in $\epsilon'(T)$ on the low-temperature side of $T_m$ is associated with the slowing down of dipolar fluctuations within the polar nanodomains. At sufficiently low temperature all dipolar motion freezes, and the dispersion vanishes. We should also note that relaxor behaviour is also manifested by a
Biological water?

- No specific structure in the density domain.

  1. Density dynamics reflects dynamical cross-correlations between solute diffusive rotations and water translations.
  2. No significant penetration into the bulk

- Specific orientational structure of the hydration shells

  1. Slow dynamics (10’s of ns)
  2. 3-5 hydration layers into the bulk

- Breaking of the hydration layers into nano-domains at lower temperatures
Dipolar correlations: lysozyme solution

\[
\chi_{0s} \propto \langle \overrightarrow{M}_0 \cdot \overrightarrow{M}_s(a) \rangle
\]

\begin{align*}
\Lambda &= 24 \text{ Å} \\
\Lambda &= 44 \text{ Å}
\end{align*}
Non-Gaussian electrostatics: How?

**Ferroelectric domains**

<table>
<thead>
<tr>
<th>Protein</th>
<th>( \langle (\delta M_p)^2 \rangle )</th>
<th>( \langle (\delta M_w)^2 \rangle )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ubiquitin</td>
<td>0.91</td>
<td>2.5</td>
</tr>
<tr>
<td>Lysozyme</td>
<td>1.44</td>
<td>1.4</td>
</tr>
<tr>
<td>Plastocyanin</td>
<td>24</td>
<td>438</td>
</tr>
<tr>
<td>Bact. RC</td>
<td>57</td>
<td>610</td>
</tr>
</tbody>
</table>

*Dipole variance in \( k(D)^2 \)*
THz absorption of sugars and amino acids (aq)

Rotations of a large solute are dynamically frozen on the THz time-scale, change in absorption mostly comes from hydration layers

Heyden et al, JACS 130 (2008) 5773
Structure of the water interface

This peak corresponds to the uncoupled OH stretch mode of water molecules that “straddle” the interface, with one OH (the “free OH”) oriented into the CCl$_4$ phase and the companion bond into the aqueous phase. These straddling water molecules tend to reside at the topmost interfacial layer. The VSF spectrum is dominated by weakly bonded water species, specifically the free OH and its companion modes.