Polarized hydration shells around proteins and the electrostatics of the protein-water interface

Dmitry Matyushov

Arizona State University,
Center for Biological Physics

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Photosynthetic reaction center with its first solvation layer
Electrostatics of redox proteins

Observables:

$\langle \phi \rangle$ (average potential)

$\langle (\delta \phi)^2 \rangle$ (potential variance)

Plastocyanin, electron carrier in photosynthetic systems of plants

Bacterial reaction center in a detergent micelle
Why electrostatics?

- Control enzymatic reactions
- Sensitive to the orientational structure of water around proteins
- Probed by optical (Stokes shift dynamics) and dielectric spectroscopies

**Gaussianity of fluctuations**

Water reorganization energy:

$$\lambda = -\frac{1}{2} q \langle \phi \rangle$$

Gaussian fluctuations:

$$\lambda^{\text{var}} = \frac{q^2 \langle (\delta \phi)^2 \rangle}{2kT}$$

Stokes-shift dynamics:

$$C(t) \propto \langle \phi(t) \phi(0) \rangle$$
Non-Gaussian electrostatics above the dynamical transition

Onset at about 160 K, methyl rotations

Exponential relaxation
Stokes-shift dynamics

Slaving of protein motions
Time-scale issues

Taking averages over parts of the trajectory

Average electrostatic potential is produced by fast water motions

~300-500 ps is the time-scale of developing non-Gaussianity
Non-Gaussianity: hydration shell dipole moment

Table 1: First and second moments of the dipole moment magnitude of proteins and their first hydration shells.

<table>
<thead>
<tr>
<th>Protein</th>
<th>$\langle M_p \rangle / D$</th>
<th>$\langle (\delta M_p)^2 \rangle / kD^2$</th>
<th>$M^I_s / D$</th>
<th>$\langle (\delta M^I_s)^2 \rangle$</th>
<th>$\kappa^I$</th>
<th>$R_{\text{eff}} / \text{Å}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ubiquitin</td>
<td>256</td>
<td>0.91</td>
<td>48</td>
<td>2.5</td>
<td>0.22</td>
<td>17.2</td>
</tr>
<tr>
<td>Lysozyme</td>
<td>150</td>
<td>1.44</td>
<td>77</td>
<td>1.4</td>
<td>0.23</td>
<td>20.0</td>
</tr>
<tr>
<td>Plastocyanin</td>
<td>249</td>
<td>24.0</td>
<td>582</td>
<td>438</td>
<td>0.20</td>
<td>18.2</td>
</tr>
<tr>
<td>Reaction center</td>
<td>996</td>
<td>56.9</td>
<td>705</td>
<td>609</td>
<td>1.19</td>
<td>50</td>
</tr>
</tbody>
</table>
Polar domains

For plastocyanin redox-active protein the first solvation layer breaks into two oppositely oriented polar domains.

For redox-inactive ubiquitin and lysozyme the distribution is close to Maxwellian.
Polarized ferroelectric domains in the hydration layer

Dielectric constant of the first hydration layer:

Lys.................... 23
Ubiq.................. 28
PC...................... $2.5 \times 10^3$

$$\varepsilon(r) = 1 + \frac{4\pi \langle (\delta M_s(r))^2 \rangle}{3V(r)}$$

10-15 Å, penetration into the bulk
How far does it go?

Small dipoles per water add up into large dipolar fluctuations!
Terahertz spectroscopy of protein solutions

Hydrated proteins: one needs a dramatic increase of an effective dipole of the protein to get experimental points.

Gruebele + Havenith, Protein polarizes water 20 Å away from its surface (PNAS’07)!
Not only proteins …

Kihara sphere in SPC/E water:

\[ \phi(r) = 4\varepsilon_{LJ} \left[ \left( \frac{\sigma}{r - r_{HS}} \right)^{12} - \left( \frac{\sigma}{r - r_{HS}} \right)^{6} \right] \]

High polarity layer penetrates the bulk to \( \sim \) the cavity radius!
Conclusions

Redox-active proteins, large polarity of the hydration shell (correlated with protein dipole's variance).

Non-Gaussian statistics of the electrostatic potential.

Statistics return to Gaussian below the temperature of dynamical transition, ~200-240 K.

Dynamics of ferroelectric domains are slow, hundreds of picoseconds.

The length-scale of polarized (ferroelectric) domains is 10-15 Å into the bulk.

Breaking into domains occurs as a weak first-order transition in a sub-ensemble of hydration layer.

\[
\langle (\delta M)^2 \rangle \gg Nm^2
\]

\[
\lambda_{\text{var}} \gg \lambda
\]

\[
T_{tr} \approx 200 - 240 \text{ K}
\]

\[
\tau_{rel} \approx 100 \text{ ps}
\]

\[
l \approx 10 - 15 \text{ Å}
\]
David LeBard

Allan Friesen

JPCB 2008, 112, 5218

JPCB 2008, 112, 10322

PRE 2008, 78, 061901.

JPCB 2009, 113, 12424.

JCP 2009, 130, 164522.

PRE 2010, 81, 021914.

$$ NSF, BES $$
Length-scale of fluctuations

Dependence of the first and second cumulants on the cutoff distance from the protein surface.

Different length-scales for the first and second cumulants!
Electron transport in molecular chains

\[ \lambda = \lambda_s = \lambda^{St} \]

\[ \lambda^{eff} = \frac{(\lambda^{St})^2}{\lambda_s} \]

Number of electron hops in the non-Gaussian paradigm per one hop in the Gaussian picture:

\[ \chi = \left( \frac{\lambda_s}{\lambda^{St}} \right)^2 \approx 10 \]

About 10 time higher energetic efficiency of biological machines in the picture of non-Gaussian electrostatic fluctuations!
Terahertz spectroscopy: Input from simulations

Protein+water dipole dynamics from simulations, plastocyanin

\( \Delta \alpha(\omega) / \alpha(\omega) \)

\( \lambda \)-repressor protein, Exp

volume fraction of protein
Gigantic reorganization energy: other studies


JACS 128, 13854 (2006)

JPCB 112, 14779 (2008) (CT in dendrimers)