Probing the dynamics of biomolecules in liquid water by terahertz spectroscopy

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Spectroscopy probes structure and dynamics

Terahertz

Near infrared

UV-Visible

Microwave

Terahertz

Infrared

Ultraviolet

X-ray

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Terahertz: Conformational flexibility

Domain 1

Domain 2

T4 Lysozyme

http://molbio.info.nih.gov/cgi-bin/moldraw?1LZS
Theoretical calculations for Lysozyme

Normal mode analysis and Monte Carlo simulations

Hen Egg White Lysozyme

Normal Mode

Molecular Dynamics

Molecular Dynamics

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Limited Terahertz Absorption Measurements

Limited to Dry Protein Measurement

Markelz et al. (2002)

Previous work: Dry/Moist
Water absorption – Data collection from literature


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Water absorption: challenge

1mm water \( \sim 10^{18} \) attenuation

Precision Measurements

Terahertz absorption: previous data

Fundamental optical phenomena

A glass without and with water showing how light is refracted through water
Absorption and Refraction of water—Data collection from literature


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Related fundamental quantities

Complex index of refraction

\[ n_{\text{sol}}^*(\nu) = n(\nu) + iK(\nu) = \sqrt{\varepsilon_{\text{sol}}^*(\nu)} \]

Refractive index  Extinction coefficient  \[ K = \frac{c\alpha}{4\pi\nu} \]

Complex dielectric function

\[ \varepsilon_{\text{sol}}^*(\nu) = \varepsilon_{\text{sol}}'(\nu) + i\varepsilon_{\text{sol}}''(\nu) \]

\( \propto \) Energy stored per unit volume  \( \propto \) Energy dissipated per unit volume

\[ n(\nu), K(\nu) \Rightarrow \begin{cases} \varepsilon_{\text{sol}}'(\nu) = n^2(\nu) - K^2(\nu) \\ \varepsilon_{\text{sol}}''(\nu) = 2n(\nu) \cdot K(\nu) \end{cases} \]

\[ \begin{align*} \varepsilon'(\nu); \varepsilon''(\nu) &\Rightarrow \begin{cases} n(\nu) = \sqrt{\sqrt{\varepsilon'^2 + \varepsilon''^2} + \varepsilon'} / 2 \\ K(\nu) = \sqrt{\sqrt{\varepsilon'^2 + \varepsilon''^2} - \varepsilon'} / 2 \end{cases} \end{align*} \]
What can we learn from $\varepsilon^*(\nu)$?

- Charge dynamics
- Charge density
- Electronic relaxation times
- Frequencies of classical or quantum oscillations
- . . .
- Detailed comparison with microscopic theory
Outline

- GHz-THz spectroscopy setup
- Absorption of protein in liquid water
- Effective medium theory for the dynamics of biomolecules in liquid water
- Conclusions
UCSB 7-700 GHz vector spectroscopy

Frequency extenders (65-700 GHz)
(Virginia Diodes, Inc. + Thomas Keating, Ltd.)

Vector Network Analyzer (10 MHz-43 GHz)
Frequency multipliers, mixers, horns
RF source from VNA port 1

Mixer

eg: \( f_b = 360 \text{ GHz} \)

Sample

LO source from VNA port 3

Mixer

Freq. SOUR1 = \( \frac{1}{12} f_b \)

eg: \( f = 30 \text{ GHz} \)

Freq. SOUR3 = \( \frac{1}{12} f_b - \frac{1}{12} \times 0.279 \)

eg: \( 30 - 0.279/12 \text{ GHz} \)

REF

f = 279 MHz

to VNA

MEAS

f = 279 MHz

to VNA

<table>
<thead>
<tr>
<th>No.</th>
<th>Freq. band</th>
<th>Freq. Range (GHz)</th>
<th>Freq. factor</th>
<th>Horn dia. (mm)</th>
<th>Length (mm)</th>
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<tbody>
<tr>
<td>#1</td>
<td>WR10</td>
<td>75 – 110</td>
<td>x 3</td>
<td>40</td>
<td>234.12</td>
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<tr>
<td>#2</td>
<td>WR6.5</td>
<td>110 – 140</td>
<td>x 4</td>
<td>28</td>
<td>139.50</td>
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<tr>
<td>#3</td>
<td>WR5.1</td>
<td>140 – 220</td>
<td>x 6</td>
<td>20</td>
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<td>#4</td>
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<td>210 – 330</td>
<td>x 9</td>
<td>15</td>
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<tr>
<td>#5</td>
<td>WR2.2</td>
<td>280 – 440</td>
<td>x 12</td>
<td>12</td>
<td>54.20</td>
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<tr>
<td>#6</td>
<td>WR1.5</td>
<td>440 – 660</td>
<td>x 18</td>
<td>9</td>
<td>37.70</td>
</tr>
</tbody>
</table>

**Frequency extension**
Spectra – linear scale

![Spectra graph with different frequency bands and power levels]

- Power (mW) on the y-axis, Frequency (GHz) on the x-axis.
- Different frequency bands labeled: VNA / 10, WR10, WR6.5, WR5.1, WR3.4, WR2.2, WR1.5.
- Div 10 indicates a divide by 10 scale factor.
60-110 dB dynamic range

VNA

70 GHz to 700 GHz

Vapour (absorption line)

http://www.itst.ucsb.edu/vnavdi.html

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Variable path length sample cell

Precise measurement of attenuation and phase shift

Water, water, water

\[ I = I_0 e^{\alpha z} \]

\[ \Delta A = -\Delta (\ln(I_{transmitted})) \propto \alpha \cdot \Delta l \]

1mm water ~ $10^{18}$ attenuation

[Graph showing extinction vs. frequency]

Precision Measurements

- Opaque wall
- Transparent windows
- Translation stage

Variable Path Length Sample Cell

Following C. Schmuttenmaer
Liquid measurements

Absorption

Phase shift

Intensity (W)

Unwrapped phase (degree)

Path-length (mm)

Path-length (mm)
Complex dielectric constant - water

\[ \varepsilon^\prime_{\text{wat}} = n^2 - K^2 \]

\[ \varepsilon^\prime\prime_{\text{wat}} = 2nK \]
Complex dielectric constant - water

\[ \begin{align*}
\epsilon'_\text{wat} &= n^2 - K^2 \\
\epsilon''\text{wat} &= 2nK
\end{align*} \]
Conclusions

- Sensitive spectroscopy from 7 - 700 GHz
  High resolution and dynamic range up to 140 dB
  Large range of protein concentrations
  Real and imaginary response

- Use Bruggeman EMT to extract dielectric constant
  Dielectric spectroscopy of protein in water

- Water hydration level

- Dynamics of Lysozyme at 70-700 GHz
  Multiple harmonic oscillations,
  with a cut-off frequency of 300 GHz
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