

Observation of phonon modes in DNA

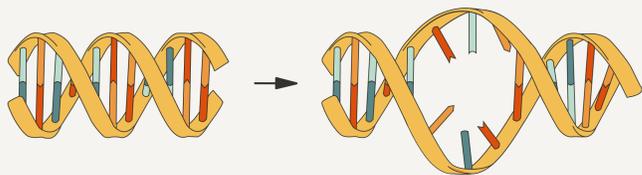
Mario González Jiménez, Gopakumar Ramakrishnan, Thomas Harwood*, Adrian J. Laphorn, Sharon M. Kelly, Elizabeth M. Ellis* & Klaas Wynne

School of Chemistry, WestCHEM, University of Glasgow, UK

*Institute of Pharmacy and Biomedical Sciences, University of Strathclyde, Glasgow, UK

Introduction

DNA replication, transcription, denaturation, and molecular intercalation processes all start with the breaking of the hydrogen bonds between the bases of the nucleic acid. Driven by the torsional stress of the molecule, the destabilization of weak bonds leads to the splitting of a section of the double helix of DNA into single strands, forming a gap in the nucleic acid known as a transcriptional bubble. In this process, low-frequency phonon-like modes that propagate along the length of the molecule play a key role, expanding and contracting the space between the bases without unstacking them.



Formation of a DNA bubble

Despite their importance, the study of these phonon-like modes has been limited by the strong absorption of infrared radiation by water in the terahertz region and only indirect evidence of their existence have been obtained measuring unnatural solid DNA preparations (humidified films, fibers, etc.) with techniques like inelastic x-ray and neutron scattering. [1]

Experimental technique

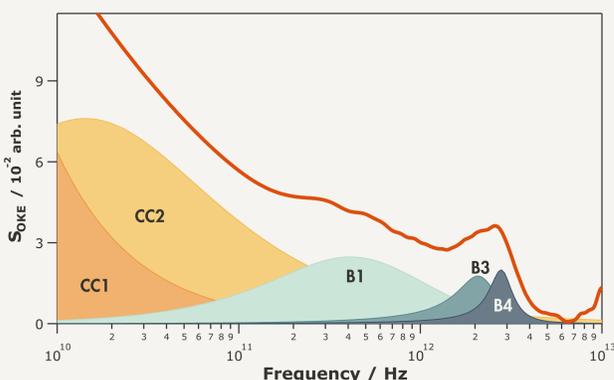
We have employed ultrafast optical Kerr-effect (OKE) spectroscopy, a technique that measures the depolarized Raman spectrum in the time domain and depends on the anisotropic part of the polarizability tensor: [2]

$$S_{OKE}(t) \propto (k_B T)^{-1} \frac{d}{dt} \langle \Pi_{xy}(t) \Pi_{xy}(0) \rangle$$

OKE spectroscopy is much less sensitive to scattering from water, allowing us to characterize the low-frequency vibrational modes in DNA in solution.

Solvated DNA spectrum

We have measured the OKE spectrum of an adenine-thymine double stranded DNA 20-mer in potassium phosphate buffer solution at 298 K.



OKE spectrum and fitting for our DNA oligomer

To obtain the contribution of the solvated nucleic acid, we have subtracted the solvent spectrum from the OKE spectrum of the oligomer solution. This difference spectrum was fit using a combination of two Cole-Cole functions and four Brownian oscillators.

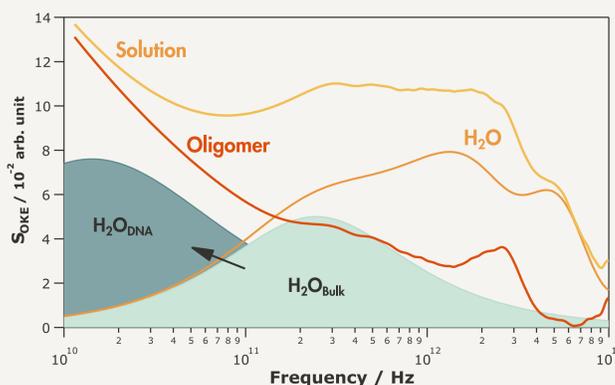
Cole-Cole function (CC)

$$S_{CC}(\omega) = \epsilon_{\infty} + \frac{\epsilon - \epsilon_{\infty}}{1 + (i\omega\tau)^{\beta}}$$

Brownian oscillator (B)

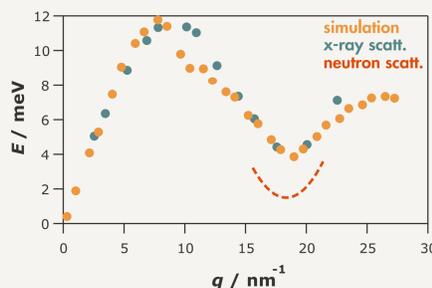
$$S_{BO}(\omega) = \frac{A_{BO} \omega_0^2}{\omega_0^2 - \omega(\omega + i\gamma)}$$

CC1 fits the molecular orientational diffusion of the oligomer. Because of the size of the molecule, this process has a timescale on the order of microseconds and we can see only the high-frequency wing of these bands. The CC2 band is interpreted as the translational dynamics of water molecules in the solvation shell of the biomolecule. At this temperature, it shows a slowdown of the dynamics of water by a factor of 17, which is inconsistent with the predictions made by the jump model of water diffusion.



Slowdown of water dynamics

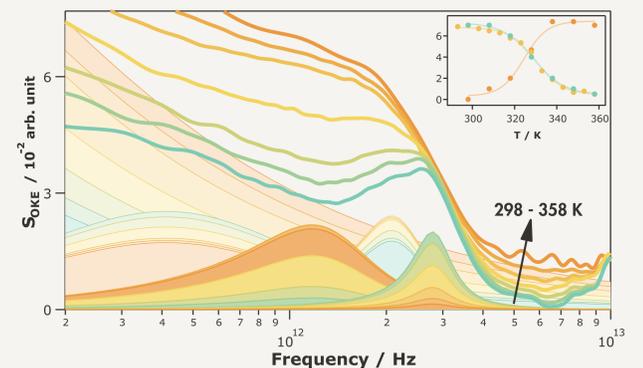
The pronounced peak at 2.83 THz was fit using an underdamped oscillator ($\gamma = 1.8$ THz). This band coincides with the reported frequency for base-pair opening phonons in double-stranded nucleic acids (2.9 THz \approx 12 meV). [3]



Dispersion curve for DNA oligomers [3]

Effect of temperature

The influence of temperature on the oligomer spectra is consistent with our interpretation. Increasing the temperature shifts the molecular orientational diffusion and water translational dynamics bands to higher frequencies. The most interesting features are the changes that appear in the high-frequency part of the OKE spectra (> 200 GHz). B1 and B3 barely change, but as the temperature increases, the intensity of B4 decreases, while a new band (B2) appears and increases in intensity.



Influence of temperature on the spectra. Inset: intensity of B2 and B4 compared with the melting curve of the oligomer

The comparison of the intensity of these bands with the proportion of denatured oligomer at each temperature measured by circular dichroism strongly suggests that B2 and B4 are associated with the single- and double-stranded conformation of the oligomer, respectively.

Influence of annealing

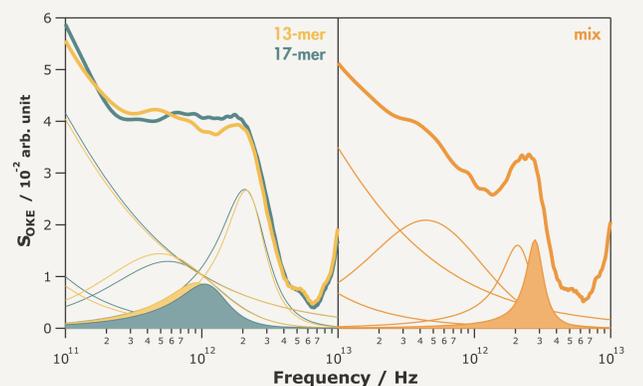
To confirm the relationship between the bands and the conformation of the nucleic acid we designed two different oligomers with sequences that only allow forming a double helix if they are dissolved together.

13-mer
CGAAAAATGTGAT
TAGTGTAAAAAGC

17-mer
CTAGATCACATTTTTCG
GCTTTTACACTAGATC

mix
CGAAAAATGTGATCTAGATCACATTTTTCG
GCTTTTACACTAGATCTAGTGTAAAAAGC

We have measured their OKE spectra in solution separately and together, showing that the band B4 only appeared in the spectrum for the solution of both oligomers together and B2 in the spectra for the solutions of each oligomer solved separately.



Spectra and fittings for 13-, 17-mer, and mixed solution of both

Conclusion

All these experiments show for the first time the existence of phonon-like modes in the double helix of DNA.

References

- [1] C. Choi et al. DNA dynamically directs its own transcription initiation. *Nucleic Acids Res.* 32, 1584, 2004
 - [2] M. González-Jiménez et al. Observation of coherent delocalised phonon-like modes in DNA under physiological conditions. *Nature Commun.* 7, 11799, 2016
 - [3] F. Merzel et al. Atomistic model of DNA: Phonons and base-pair opening. *Phys. Rev. E* 76, 031917 2007
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