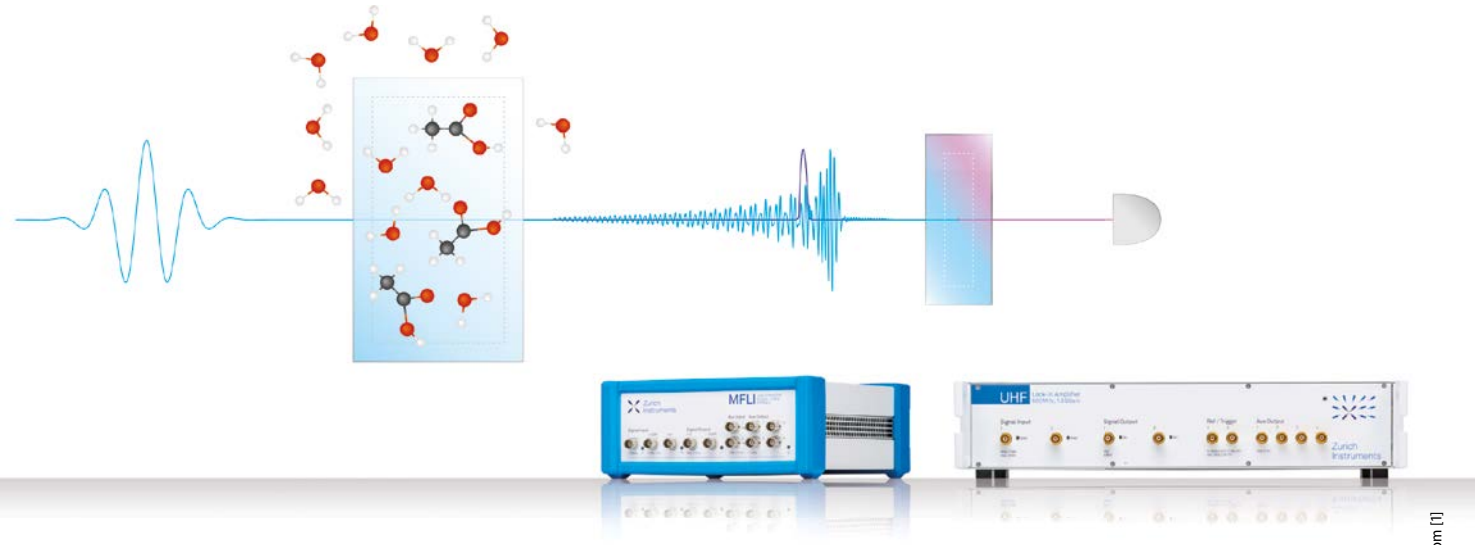

Fig. 1 Illustration of the measurement technique for detection of small concentrations of water

adapted from [1]

Fast and precise detection of molecules

Zurich Lock-in Amplifiers ensure the highest signal-to-noise ratio in field-resolved spectroscopy.

Anchit Srivastava, Kilian Scheffter, Hanieh Fattahi, and Heidi Potts

Recent advances in ultrafast lasers enable high-sensitivity, label-free detection of molecular responses in liquids at near-petahertz frequencies, improving measurement sensitivity and speed in spectroscopy.

High-sensitivity spectroscopic measurements of molecular samples in liquid and gas phases are crucial for applications in aqueous biology and chemistry. Conventional near-infrared spectroscopy often faces sensitivity limitations due to background noise, restricting its effectiveness in detecting weak molecular signals.

Recent advances in ultrafast lasers have enabled the ambient air detection of the electric field of ultrashort pulses. At the Max Planck Institute of the Science of Light, we have utilized these advancements for field-resolved, label-free detection of the molecular response of liquid samples at near-petahertz frequencies. This technique, known as "fieldoscopy" allows access to the response of matter interacting with ultrashort pulses in the sub-cycle regime and offers high detection sensitivity, dynamic range, and access to phase information [1].

Additionally, in a similar experiment at terahertz frequencies, we have demonstrated that compressed sensing can be used to accelerate measurement time by reducing the number of required sampling points beyond the Nyquist criterion [2]. Both schemes highlight the effective use of field-resolved detection techniques to probe weak molecular features, using Zurich Instruments Lock-in Amplifiers to ensure the highest signal-to-noise ratio (**Fig. 1**).

Fieldoscopy of liquids

The experimental setup for fieldoscopy of liquids at near-petahertz frequencies is shown in **Fig. 2**. A crucial part of the experiment is the generation of near-single-cycle pulses, which is described in more detail in [1]. The resulting pulses have a pulse duration of 4.8 fs, centered at 315 THz with a spectrum spanning over 300 THz. Ninety-five percent of the energy of these pulses is used to generate 15 fs excitation pulses centered at 150 THz via intrapulse difference frequency generation with carrier to envelope phase stability. The remaining five percent energy serves as a probe for electric field detection.

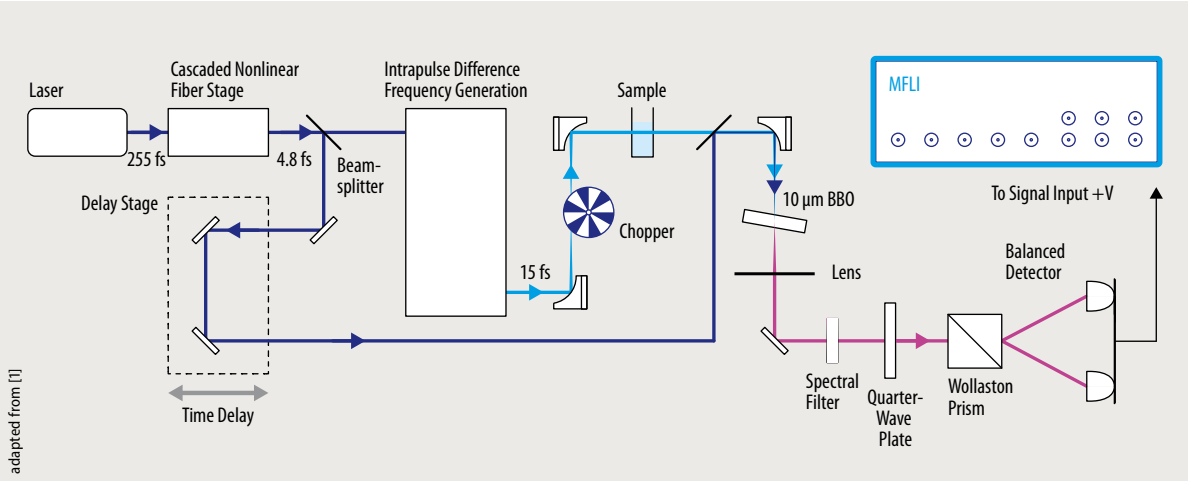

Fig. 2 This simplified schematic of the experimental setup consists of the non-linear fibre stages, the intrapulse difference frequency generation, and the field detection.

The generated excitation pulses are amplitude modulated via a chopper and propagate through a sample. The transmitted excitation pulses which carry the coherent response of the sample are focused into a thin Beta Barium Borate (BBO) crystal along with the probe pulses for field detection. In the crystal, a sum-frequency signal between the probe and excitation pulses is generated, which has an orthogonal polarization relative to the probe pulses. Due to the high spectral bandwidth of the interacting pulses, sum frequency and probe spectra overlap partially. This spectral region is filtered out and detected via ellipsometric detection at various temporal delays between the excitation and probe pulses to resolve the electric field of the waveform.

Due to the high detection sensitivity, we can resolve molecular vibrations of the liquid sample at both their fundamental and combination resonances, as well as detect contributions from atmospheric molecules along the beam path. Excitation pulses are limited in time to 15 fs, and therefore temporally separated from the molecular responses of the sample and surrounding air. The response of the liquid sample remains distinct from that of ambient air due to the faster dephasing dynamics in the liquid phase.

By introducing amplitude modulation with a chopper and utilizing the Zurich Instruments MFLI 500 kHz Lock-in Amplifier, the signal-to-noise ratio of the measurement can be further enhanced, significantly improving measurement sensitivity. **Fig. 3a** presents the fieldoscopy measurements of two different concentrations of liquid water dissolved in 4.81 µL of acetic acid, with pure acetic acid serving as a reference. The temporal electric field between 0.3 and 1 picoseconds is selected to isolate the response of the liquid phase

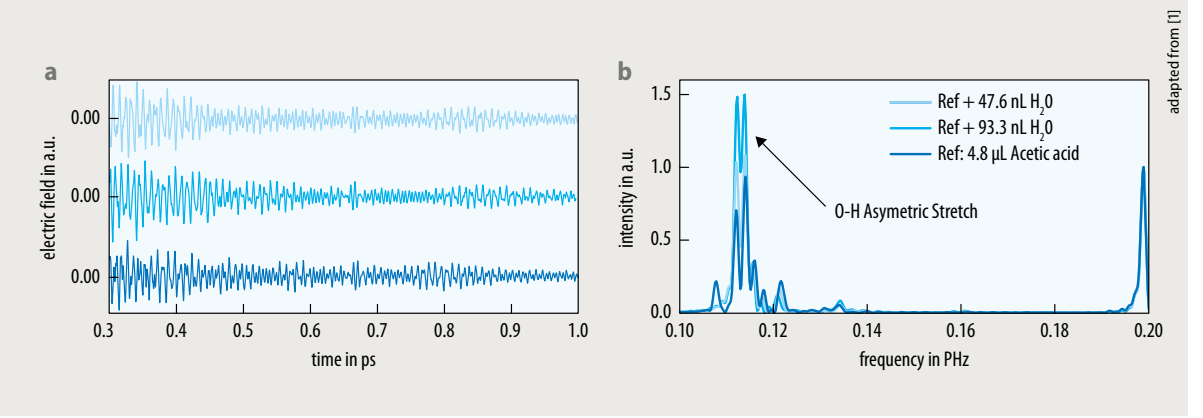

Fig. 3 Liquid water molecules with a volume of 47.6 nL (light blue), 93.3 nL (blue) in 4.8 µL of acetic acid, which is also measured as a reference measurement (dark blue). Electric field and Fourier analysis are shown in (a) and (b) respectively.

from the atmospheric response. The gated Fourier transformed spectra of the temporally isolated regions are shown in **Fig. 3b** presenting the quantitative analysis of the sample with a minimum detectable water concentration of 47.6 nL.

Measurements in real time

In a similar experiment at terahertz frequencies, it is shown that real-time measurements can be performed by accelerating the measurement time using compressed sensing combined with an acousto-optical delay line. The acousto-optical delay line allows for shot-to-shot changes of the temporal overlap between the terahertz waveform and a probe pulse at kilohertz rates, enabling randomly sampled waveforms (a detailed description can be found in [2]). As every probe pulse overlaps with a random value of the electric field amplitude within the waveform, it is crucial that the detected signal of one pulse contains no information from the previous pulse. Capturing the full information from every individual pulse is achieved using the UHFLI 600 MHz Lock-in Amplifier with the UHF-BOX Boxcar Averager option.

By employing compressed sensing on the randomly sampled waveform, it is possible to reconstruct multiple absorption lines of atmospheric water beyond the Nyquist criterion, which limits conventional sampling techniques. Employing this technique led to a three-fold improvement in measurement time compared to a standard sampling scheme [2].

Conclusion

Assessing transient optical fields is crucial for both comprehending ultrafast phenomena and quantitatively detecting diverse molecular species within a sample. The two studies presented in this article advance field-resolved spectroscopy to new regimes, paving the way for innovative label-free microscopy techniques.

[1] *A. Srivastava* et al., Nat. Photon. **18**, 1320 (2024)
[2] *K. Scheffter* et al., Ultrafast Sci. **4**, 0062 (2024)

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