Evanescent-wave and ambient chiral sensing by signal-reversing cavity ringdown polarimetry

Dimitris Sofikitis1,2*, Lykourgos Bougas1,2*, Georgios E. Katsoprinakis1,2, Alexandros K. Spiliotis1,2, Benoit Loppinet1 and T. Peter Rakitzis1,2

Detecting and quantifying chirality is important in fields ranging from analytical and biological chemistry to pharmacology and fundamental physics: it can aid drug design and synthesis, contribute to protein structure determination, and help detect parity violation of the weak force. Recent developments employ microwaves, femtosecond pulses, superchirality or photoionization to determine chirality, yet the most widely used methods remain the traditional methods of measuring circular dichroism and optical rotation. However, these signals are typically very weak against larger time-dependent backgrounds. Cavity-enhanced optical methods can be used to amplify weak signals by passing them repeatedly through an optical cavity, and two-mirror cavities achieving up to $10^4$ cavity passes have enabled absorption and birefringence measurements with record sensitivities. But chiral signals cancel when passing back and forth through a cavity, while the ubiquitous spurious linear birefringence background is enhanced. Even when intracavity optics overcome these problems, absolute chirality measurements remain difficult and sometimes impossible. Here we use a pulsed-laser bowtie cavity ringdown polarimeter with counter-propagating beams to enhance chiral signals by a factor equal to the number of cavity passes (typically $>10^4$); to suppress the effects of linear birefringence by means of a large induced intracavity Faraday rotation; and to effect rapid signal reversals by reversing the Faraday rotation and subtracting signals from the counter-propagating beams. These features allow absolute chiral signal measurements in environments where background subtraction is not feasible: we determine optical rotation from $\alpha$-pinene vapour in open air, and from maltodextrin and fructose solutions in the evanescent wave produced by total internal reflection at a prism surface. The limits of the present polarimeter, when using a continuous-wave laser locked to a stable, high-finesse cavity, should match the sensitivity of linear birefringence measurements ($3 \times 10^{-13}$ radians), which is several orders of magnitude more sensitive than current chiral detection limits and is expected to transform chiral sensing in many fields.

Our approach to the absolute measurement of chirality makes use of the development of a polarimeter based on a bowtie ring cavity, as proposed recently. Unlike a two-mirror cavity, a ring cavity can support two distinct, counter-propagating laser beams (Fig. 1), which we describe as ‘clockwise’ and ‘counter-clockwise’. The symmetry between the beams is broken by a longitudinal magnetic field $B$ applied to an intracavity magneto-optic window, which induces a Faraday rotation $\theta_B$. A chiral sample is introduced to only one arm of the cavity. Faraday and chiral optical rotation have different symmetries: $\theta_B$ is determined only by $B$, and has the same sign for both beams, whereas $\phi_C$ is determined only by the propagation direction and has opposite signs for the two beams (definitions are given for the laboratory frame; Fig. 1). Therefore, the total single-pass optical rotations for the clockwise and counterclockwise beams are given by the sum and the difference of $\theta_B$ and $\phi_C$, respectively: $\Theta_{\text{CW}} = \theta_B + \phi_C$ and $\Theta_{\text{CCW}} = \theta_B - \phi_C$.

As the beams traverse the cavity, their polarizations rotate with angular frequencies $\omega_{\text{CW}}(\pm B) = (\pm \theta_B + \phi_C)/L$ and $\omega_{\text{CCW}}(\pm B) = (\pm \theta_B - \phi_C)/L$, where the dependence of $\omega_{\text{CW}}$ and $\omega_{\text{CCW}}$ on the direction of the axial magnetic field $B$ is shown schematically (+$B$ and $-B$ refer to opposite directions of the magnetic field along one of the arms of the cavity, with $B = |B|$), and $L$ is the total round-trip cavity length. The difference $\Delta \omega(\pm B) = |\omega_{\text{CW}}(\pm B)| - |\omega_{\text{CCW}}(\pm B)|$ equals $\pm 2\phi_C/\omega L$. This key result

Figure 1 | Cavity-enhanced polarimeter for chiral sensing. a. The layout of four mirrors (M1–M4), polarizers (P1, P2), photomultiplier tubes (PMT1, PMT2), the chiral sample, the Faraday medium and the counter-propagating laser beams (CW and CCW). b. The chiral sample gives opposite laboratory-frame optical rotations for CW and CCW ($\phi_C^\text{CW} = -\phi_C^\text{CCW}$). Measurements were performed on chiral samples in a gas cell, in open air and in an evanescent wave at a prism surface. c. The Faraday rotator gives the same optical rotation for CW and CCW ($\theta_B^\text{CW} = \theta_B^\text{CCW}$), controlled by the magnitude and sign of the applied magnetic field $B$. TGG, terbium gallium garnet crystal.
shows that reversing the sign of B inverts the sign of the measured angle \( \phi_C \) (Fig. 2). Using this signal reversal yields \( \Delta \alpha(+B) - \Delta \alpha(-B) = 4\phi_C(c/L) \).

For each subtraction, the chiral signal \( \phi_C(c/L) \), which is odd under reversal of the light propagation direction or of \( B \), doubles. In contrast, all background signals, which are even under either reversal, cancel.

These signal reversals are demonstrated in three different environments: (1) pressure-controlled chiral vapours, (2) open-air chiral vapours and (3) chiral solutions at a prism surface probed using evanescent waves. Experiment (1) demonstrates the full symmetry of the signal reversals in the absence of large noise, experiments (2) and (3) take advantage of these signal reversals to measure chiral optical rotation in high-noise environments.

For experiment (1), various pressures of \((+)-\) and \((-)-\)\(\alpha\)-pinene are introduced into an intracavity cell, and the four polarization frequencies \( \omega_{CW}^B, \omega_{CCW}^B, \omega_{CW}^B \) and \( \omega_{CCW}^B \) are measured (Fig. 2a). The angle \( \phi_C \) is determined for both \((+)-\) and \((-)-\)enantiomers, and for both \(+B\) and \(-B\), and is plotted versus pressure in Fig. 2b. The optical rotation \( \phi_C \) varies linearly with pressure, and the expected symmetry is obtained: \( \phi_C \) reverses sign for each inversion of enantiomer or \( B \). Notice how an inversion of \( B \) allows the determination of absolute optical rotation, without needing to change the gas pressure. We determined the specific rotation of \( (+)-\)\(\alpha\)-pinene and \( (-)-\alpha\)-pinene, as well as the frequency shift \( \delta \alpha \), for \(+B\) and \(-B\) signal pairs (insets). Measurements of optical rotations \( \phi_C \) and frequency shift \( \delta \alpha \), for \(+B\) and \(-B\) signal pairs, as functions of gas pressure. Each data point is the average of four data sets of difference signals \( (\omega_{CW}^B - \omega_{CCW}^B) \), each of 8,000 laser shots. Error bars are 2\(\sigma\) confidence intervals.

For experiment (2), we perform open-air measurements by inserting and removing a tray filled with liquid \((+)-\) or \((-)-\alpha\)-pinene, below one of the arms of the cavity, and measuring the optical rotation of the vapour that evaporates. The four measured frequencies \( \omega_{CW}^B, \omega_{CCW}^B, \omega_{CW}^B \) and \( \omega_{CCW}^B \) shown in Fig. 3a illustrate that each of the four traces separately yields correct results for the optical rotation, some even giving the wrong sign. This is because strong variations in the index of refraction of the vapour alter the alignment of the cavity, yielding spurious changes in the polarization beating frequencies, which are larger than those from the optical rotation. Also, a temperature drift causes a downward slope in all four channels. However, the result of the two signal reversals (Fig. 3b) yields a constant null signal (tray removed) and measurement of optical rotation of the open-air \((+)-\) and \((-)-\alpha\)-pinene vapours. By comparing Fig. 3b with Fig. 2b, we deduce that the partial pressure of the vapours was about 4 mbar, in agreement with the vapour pressure of \( \alpha\)-pinene.

Finally, for experiment (3) on solutions of maltodextrin, fructose and non-chiral glycerol as the reference sample, we insert a Dow prism into the beam such that the laser beams undergo total internal reflection with an angle of incidence \( \theta = 84° \) (Figs 1 and 4). Figure 4a shows \( \omega_{CW}^B, \omega_{CCW}^B, \omega_{CW}^B \) and \( \omega_{CCW}^B \). Time-dependent birefringent variations in the prism cause drifts in the polarization oscillations, which mask chiral optical rotation signals in any single trace. Figure 4b shows the chiral optical rotation signal obtained from the two reversals, which now show clear signal differences between the three solutions. Figure 4c shows the dependence of the maltodextrin and fructose signals on the solution refractive index \( n \), and emphasizes a strong increase as \( n \) approaches the critical index \( n_{\text{critical}} = n_{\text{water}} \sin(\theta) = 1.445 \).
(where \( n_p = 1.453 \) is the refractive index of the prism). An analytical expression is derived for the optical rotation from a chiral sample in an evanescent wave, \( \phi_{\text{EW}} \), according to the Drude–Condon model\(^{18} \) for Maxwell’s equations in isotropic optically active media, using the treatment developed in refs 19, 20:

\[
\phi_{\text{EW}} \approx \frac{\Delta n}{n} \frac{N}{1 - N^2} \frac{\cos (\theta)}{\sqrt{\sin^2 (\theta) - N^2}} \tag{1}
\]

Here \( \theta \) is the incidence angle, \( \Delta n = (n_+ - n_-) \), \( n = (n_+ + n_-)/2 \), \( n_+ \) and \( n_- \) are, respectively, the refractive indices of the chiral sample for left- and right-circularly polarized light, and \( N = (n/n_p) \). The data agree well with theoretical predictions, which are calculated from equation (1), using \( \Delta n_M = 4.25 \times 10^{-6} \) for maltodextrin and \( \Delta n_F = -2.28 \times 10^{-6} \) for fructose (determined from single-pass optical rotation measurements through a 10 cm cell), where \( c_F \) and \( c_M \) are the concentrations (in grams per cubic centimetre) of the maltodextrin and fructose solutions, respectively. We note that \( \phi_{\text{EW}} \) increases sharply near the critical angle (\( N \approx \sin (\theta) \)) and even more so as \( N \) approaches 1 (near index matching, when also \( \sin (\theta) \approx 1 \)). We approximate index matching closely with \( N = 1.1422 \), according to the Drude–Condon model\(^{21} \).

To better understand the physics behind equation (1), we express \( \phi_{\text{EW}} \) in terms of the Goos–Hänchen shift \( L_{\text{GH}} \) (where \( \phi_{\text{EW}} \approx \pi \Delta n / \lambda I_{\text{GH}} \)), where \( \phi_{\text{EW}} \) is the effective path length. Setting \( \phi_{\text{EW}} = \phi_{\text{GH}} \) yields \( I_{\text{GH}} = (\cos^2 (\theta) / \sin (\theta)) (1 - N^2) L_{\text{GH}} \). Away from the critical angle, \( I_{\text{GH}} < L_{\text{GH}} \). Near the critical angle and index matching (\( N \approx \sin (\theta) \approx 1 \)), \( I_{\text{GH}} \approx L_{\text{GH}} \), showing that in this case the Goos–Hänchen shift is the effective evanescent-wave optical rotation path length.

The cavity-enhanced polarimetric methods presented here can be extended to a continuous-wave laser locked to a stable, high-finesse cavity, which is much more sensitive\(^6 \) but also experimentally more complex. This should increase chiral sensitivities for conventional optical rotation and circular dichroism measurements by several orders of magnitude, and allow the routine analysis of subnanolitre volumes. Applications include the study of surface chirality (for which large effects have been recently shown\(^{22} \)), coupling of optical rotation and circular dichroism to gas and liquid chromatography for sensitive chiral analysis, monitoring of protein folding, and measurement of parity violation in atoms and molecules for which insufficient path lengths are otherwise available\(^{15,16} \).

**Online Content** Methods, along with any additional Extended Data display items and Source Data, are available in the online version of the paper; references unique to these sections appear only in the online paper.

Received 9 May; accepted 9 July 2014.

Published online 10 September 2014.

1. Berova, N., Polavarapu, P. L., Nakashima, K. & Woody, W. (eds) Comprehensive Chiroptical Spectroscopy Vols 1, 2 (Wiley, 2012).
2. Bouchiat, M. A. & Bouchiat, C. Parity violation in atoms. Rep. Prog. Phys. 60, 1351–1396 (1997).
3. Patterson, D., Schnell, M. & Doyle, J. M. Enantiomer-specific detection of chiral molecules via microwave spectroscopy. Nature 497, 477–487 (2013).
4. Rhee, H. J. et al. Femtosecond characterization of vibrational optical activity of chiral molecules. Nature 450, 191–194 (2007).
5. Tang, Y. Q. & Cohen, A. E. Enhanced enantioselectivity in excitation of chiral molecules by supercritical light. Science 322, 333–336 (2011).
6. Janssen, M. H. M. & Puisis, I. Detecting chirality in molecules by imaging photocell electro-optic chiroptical signal. Phys. Chem. Chem. Phys. 16, 856–871 (2014).
7. Busch, K. W. & Busch, M. A. (eds) Chiral Analysis (Elsevier, 2006).
8. Durand, M., Morville, J. & Romanini, D. Shot-noise-limited measurement of sub-parts-per-trillion birefringence phase shift in a high-finesse cavity. Phys. Rev. A 82, 031803 (2010).
9. Berden, G., Peeters, R. & Meijer, G. Cavity enhanced absorption and circular dichroism measurements by several orders of magnitude, and allow the routine analysis of subnanolitre volumes. Applications include the study of surface chirality (for which large effects have been recently shown\(^{22} \)), coupling of optical rotation and circular dichroism to gas and liquid chromatography for sensitive chiral analysis, monitoring of protein folding, and measurement of parity violation in atoms and molecules for which insufficient path lengths are otherwise available\(^{15,16} \).

![Figure 4](image-url) | Evanescent-wave optical rotation. a. The four polarization frequencies \( \omega_{\mathrm{CW}}, \omega_{\mathrm{CCW}}, \omega_{\mathrm{CCW}} \), and \( \omega_{\mathrm{CW}} \) are shown for evanescent-wave measurements of maltodextrin, glycerol (a non-chiral reference sample with zero optical rotation) and fructose solutions, all with refractive index \( n = 1.442 \). The solutions are changed with a flow cell every 10 min. Each data point is the average of 4,000 laser shots. b. Subtractions of the polarization signals give the optical rotations of the samples in the evanescent wave. c. Measurements for solutions with \( n = 1.417–1.442 \). Error bars are 2\( \sigma \) confidence intervals determined from the 15 points in b. The theoretical curves are generated using equation (1). d. Goos–Hänchen shift \( L_{\text{GH}} \) of the evanescent wave.
16. Bougas, B., Katsoprinakis, G. E., von Klitzing, W., Sapirstein, J. & Rakitzis, T. P. Cavity-enhanced parity-nonconserving optical rotation in metastable Xe and Hg. *Phys. Rev. Lett.* **108**, 210801 (2012).

17. Bougas, B., Katsoprinakis, G. E., von Klitzing, W. & Rakitzis, T. P. Fundamentals of cavity-enhanced polarimetry for parity-nonconserving optical rotation measurements: application to Xe, Hg and I. *Phys. Rev. A* **89**, 052127 (2014).

18. Condon, E. U. Theories of optical rotatory power. *Rev. Mod. Phys.* **9**, 432–457 (1937).

19. Silverman, M. P. Reflection and refraction at the surface of a chiral medium: comparison of gyrotropic constitutive relations invariant or noninvariant under a duality transformation. *J. Opt. Soc. Am. A* **3**, 830–837 (1986).

20. Lekner, J. Optical properties of isotropic chiral media. *Pure Appl. Opt.* **5**, 417–443 (1996).

21. Goos, F. & Hänchen, H. Ein neuer und fundamentaler Versuch zur Totalreflexion. *Ann. Phys.* **436**, 333–346 (1947).

22. Emile, J. et al. Giant optical activity of sugar in thin soap films. *J. Coll. Inter. Sci.* **408**, 113–116 (2013).

**Acknowledgements** This research was supported by the ERC grant TRICEPS (grant no. 207542), and the FP7 IAPP Programme SOFORT (PIAPGA-2009-251598). B.L. acknowledges the FP7 Infrastructure programme ESMI (CP&CSA-2010-262348) for partial support. We thank P. Tzallas for access to the Attosecond labs at IESL-FORTH.

**Author Contributions** L.B. constructed the experiment, performed the gas-cell and open-air experiments, and analysed the data. D.S. performed the evanescent-wave experiments and analysed the data. G.E.K. and A.K.S. developed the data acquisition and analysis software, and assisted in the experiments. G.E.K. prepared the figures. B.L. derived the evanescent-wave optical rotation equations. T.P.R. had the idea for and directed the experiments, and wrote the manuscript. All authors provided important suggestions for the experiments, discussed the results and contributed to the manuscript.

**Author Information** Reprints and permissions information is available at www.nature.com/reprints. The authors declare no competing financial interests. Readers are welcome to comment on the online version of the paper. Correspondence and requests for materials should be addressed to T.P.R. (ptr@iesl.forth.gr).
A 1.3 mJ, 800 nm, 35 fs laser pulse was split and the resulting beams sent in different directions (‘clockwise’ and ‘counterclockwise’). We note that the laser half-width at half-maximum bandwidth of 20 nm did not significantly affect the measurement of chiral optical rotation at the central wavelength of 800 nm for molecular spectra without sharp optical rotation features, such as those studied here. For the study of sharp optical rotation spectra, our cavity ringdown polarimeter is fully compatible with narrow-bandwidth pulsed lasers that are typically used in cavity ringdown spectroscopy\textsuperscript{9,10,14,15}. Note that no temperature stabilization or vibration isolation was employed. The mirrors had reflectivity $R < 99.7\%$ and the cavity length was $L = 3.6$ m. All intracavity optics were antireflection coated for 800 nm, with reflectivities below 0.01\% (ATF Boulder). The gas cell and the open-air tray were both of length $l = 0.75$ m. The 70$°$ fused-silica prism had dimensions 80 $\times$ 25 $\times$ 25 mm. The time-dependent intensity of the output light decayed exponentially\textsuperscript{13} as $I(t) = I_0 \frac{e^{-t/t_0}}{1 - R^4}$, where the photon lifetime $t_0 = Lc(1 - R^4) = 1$ $\mu$s (Fig. 2a). Faraday rotation $\theta_F = 2.5 - 4$ $\mu$ was generated by applying a 0.2–0.3 T magnetic field to a 3 mm-thick terbium gallium garnet crystal. Using a polarizer at the output, the optical rotation appears in the clockwise signal $I_{CW}$ as an oscillation with frequency $\omega_{CW}$, $I_{CW} = I_0 e^{-t/t_0} \cos^2 (\omega_{CW}t) + \beta$, and in the counterclockwise signal with frequency $\omega_{CCW}$: $I_{CCW} = I_0 e^{-t/t_0} \cos^2 (\omega_{CCW}t) + \beta$, where $I_0$ is the output intensity at $t = 0$ (Fig. 2a) and $\beta$ is a fit parameter that accounts for reduced amplitude modulation\textsuperscript{14,15} (caused by imperfections, such as imperfect polarization alignment, birefringence and detector saturation) and is typically less than 0.1. The laser repetition rate was 1 kHz; however, the data acquisition rate was 100 ringdown traces per second, limited by the digital oscilloscope. The magnetic field reversal rate was between 0.02 and 0.045 Hz. The data traces were fitted with the $I_{CW}$ and $I_{CCW}$ fit functions, and $\omega_{CW}$ and $\omega_{CCW}$ are determined using a nonlinear regression analysis. The magnetic field was reversed between each data point.

Enantiopure (+)- and (−)-α-pinene (Sigma Aldrich) were used. Maltodextrin and fructose were bought commercially. Maltodextrin and fructose solutions (with concentrations between 50 and 60\%) and glycerol–water solutions are prepared with refractive indices $n$ ranging from 1.417 to 1.442 (at 0.005 intervals). For the evanescent-wave set-up (Fig. 1b, (iii)), a magnesium fluoride compensator was inserted to reduce the birefringence $\delta$ of the prism (typically 10–20 $\mu$m) to about 0.5 $\mu$m for both beams (the large, position-sensitive birefringence in the prism and imperfect beam alignment precluded better compensation). Modelling the depolarization effects of birefringence on the measurement of $\alpha_{CW}$ and $\alpha_{CCW}$ (refs 16, 17), the ratio $\delta/\theta_F < 0.2$ yields a correction coefficient $q^2 > 0.99$, so that the effect of birefringence is less than 1\%.