

Applications of infrared laser spectroscopy to breath analysis

A thesis submitted for the degree of Doctor of Philosophy

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Balliol College, University of Oxford

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Abstract

The work presented in this thesis is concerned with development of spectroscopic detection methods based on absorption spectroscopy using semiconductor lasers, with particular reference to the field of medical diagnostics through breath analysis. The first part of this thesis deals with the design and testing of a prototype analyser for simultaneous monitoring of the exchange gases O_2 , CO_2 and H_2O in breath. The aim of this analyser is to provide information required to monitor respiration, with potential use in intensive care monitoring or during anaesthesia. The relatively high concentrations of these gases in breath and readily available diode laser sources make detection in the near-infrared (NIR) ideal. However, the relatively weakly absorbing A-band O_2 transitions at 760 nm require the application of a sensitive spectroscopic method, cavity enhanced absorption spectroscopy (CEAS). In contrast, CO_2 and H_2O are monitored using direct single pass absorption spectroscopy, with transitions arising from the $2\nu_1 + \nu_3$ band at 2 μm and $\nu_1 + \nu_3$ band at 1.3 μm , respectively. It has been demonstrated that these gases can be detected simultaneously over a short pathlength (2.74 - 4 cm) in the respiratory flow by combining various spectroscopic methodologies and real-time data analysis. This analyser is shown to offer a viable alternative for monitoring respiration, exhibiting absolute detection limits of changes of 0.26 % O_2 , 0.02 % CO_2 and 0.003 % H_2O with a 10 ms time resolution, which are comparable to current mass spectrometry based methods, but without their inherent delays.

Following this, investigations into the detection of the main gas constituents in breath in the NIR employing noise-reduction modulation based spectroscopic techniques, namely wavelength and frequency modulation (WMS and FMS respectively) are also reported. The described WMS studies on water at 1.37 μm provide a demonstration of conventional WMS detection, as well as a “proof-of-principle” example of a relatively new approach to calibrating the non-absolute information obtained from a WMS absorption signal. Typically WMS spectra are calibrated using mixtures of known gas concentrations or an absolute direct absorption spectrum where possible. In this work however, a self-calibrating method, the phasor decomposition method (PDM), is employed and the returned concentration from this calibration is compared to direct absorption measurement. From this, the calculated concentration using the PDM is found to differ by 9 % from the concentration value obtained by direct absorption, providing an alternative method of calibration for when direct

absorption measurements are not possible. The use of FMS in the NIR is also demonstrated as a potential alternative to CEAS for monitoring O₂ at 760 nm. FMS detection is performed on atmospherically broadened O₂ and a time-normalised $\alpha_{min}(t)$ of $2.45 \times 10^{-6} \text{ cm}^{-1} \text{ s}^{\frac{1}{2}}$ is obtained, which is two orders of magnitude less sensitive than the value of $\alpha_{min}(t) = 2.35 \times 10^{-8} \text{ cm}^{-1} \text{ s}^{\frac{1}{2}}$ obtained with CEAS. This combined with the experimental requirements of an FMS system, make its use for detection of O₂ a less practicable option compared to CEAS for real-time breath analysis.

The latter work in this thesis involves a change in focus to detection of trace gases in breath in the mid-infrared (MIR). The move of spectroscopic detection to the MIR exploits the larger absorption cross-sections available in this region, and to achieve this, a relatively new form of semiconductor laser, the quantum cascade laser (QCL) is used. The design of a continuous wave QCL spectrometer at 8 μm and its operating characteristics are demonstrated and improvements in its performances are also discussed. This QCL system is then utilised to demonstrate the potential of monitoring species in breath, namely the narrow-band absorber methane and the broadband absorber acetone, taking into consideration the potential interference from other absorbing species in breath and the different spectroscopic characteristics exhibited by these molecules.

Finally, the potential to further improve the sensitive detection of trace gases in breath in the MIR is also investigated with studies on the use of CEAS and multipass cells. In this work, the molecule of interest is the biomarker OCS, using transitions of the $2\nu_2$ band at 1031 cm^{-1} , that are probed using a 10 μm QCL. The application of CEAS in the MIR is not as well developed as in the NIR, and the experimental consequences of using optical cavities at these wavelengths, where equipment tends to be more limited, are investigated and sensitivities discussed in the context of other literature. The experimental procedure of optimising a cavity for CEAS using the off-axis alignment method is also studied in detail, as well as the addition of WMS to further improve the signal quality. An effective absorption pathlength of $\sim 100 \text{ m}$ was achieved in the cavity, with a bandwidth reduced $\alpha_{min}(BW)$ of $1.7 \times 10^{-7} \text{ cm}^{-1} \text{ Hz}^{-\frac{1}{2}}$ using WMS CEAS achieved. With the poorer quality optics and limitations in equipment in the MIR for CEAS experiments, the use of a multipass cell, a 238 m Herriott cell, is also investigated as an alternative to the use of an optical cavity at 10 μm . Detection of OCS using direct absorption and WMS is demonstrated in the Herriott cell, achieving $\alpha_{min}(BW) = 2.03 \times 10^{-8} \text{ cm}^{-1} \text{ Hz}^{-\frac{1}{2}}$ using WMS. This shows an improvement in sensitivity compared to WMS CEAS, and also shows the potential for future work on biomarker detection, as it approaches the $\sim \text{ppb}$ levels required for breath analysis.

*For Grandma and Grandad Newsham, and for
Grandma and Grandad Muir*

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To coming home, and new beginnings.

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Chapter 1

Introduction

1.1 Uses of laser absorption spectroscopy

Absorption spectroscopy enables the highly specific detection of atomic and molecular species, as well as the potential to study the various characteristics and behaviour they exhibit under changing experimental conditions. Absorption spectroscopy, the theory of which is discussed in more depth in section 1.3, has been used in a wide range of fields, from *in situ* monitoring of industrial processes and pollutants [1, 2] to atmospheric and environmental studies, leading to greater understanding of the processes that dominate atmospheric chemistry [3]. Other areas of interest range from atomic spectroscopy [4] to monitoring reaction dynamics [5], and with the continuing development of laser systems covering the near- and mid-infrared (NIR and MIR) [6, 7], these fields of research are likely to continue to grow [8, 9]. A relatively recent area of research utilising absorption spectroscopy is in medical diagnostics and is based upon analysing species in breath that are indicative of disease or physiological processes. These species, known as biomarkers, either occur naturally in breath or arise as products of interactions in the body with an ingested substance, which usually has some form of chemical labelling. The monitoring of species in breath is the area of research that is most relevant to the work in this thesis, although many of the spectroscopic techniques investigated are equally suitable for trace gas detection in other fields as well. Breath analysis using laser absorption spectroscopy in both the NIR, and more recently in the MIR [10], shows great potential for non-invasive and fast diagnosis, as there are hundreds of different species exhaled in breath [11], around 35 of which have already been well established as linked to various illnesses [12]. A classic example is the work on the urea breath test, where the measurement of $^{13}\text{CO}_2/^{12}\text{CO}_2$ ratio in breath can be used to ascertain the presence of the bacterium *helicobacter pylori* in the stomach, which in turn can lead to stomach ulcers and gastric cancers [13]. Further

studies on many other species indicative of disease have also been reported, for example on molecules such as NO, produced from lower airway inflammation in asthmatics [14], NH₃, which can be used for monitoring kidney dialysis [15] and acetone, which can potentially be used to monitor diabetes [16]. These examples name but a few of the possibilities for diagnosis via sampling breath, and with the range of molecules that can be detected with laser absorption spectroscopy, optical breath analysis is an exciting and promising area of research.

1.2 Laser sources

Lasers provide a coherent, monochromatic source of electromagnetic radiation that make them ideal for spectroscopic methods. The basis of any laser is induced emission of photons from an upper to a lower state ($n \rightarrow m$) in an active medium. For the level of induced emission to dominate the absorption process from m to n , there needs to be a population inversion between the two levels such that $N_m g_n > N_n g_m$, where N_i defines the population of the level and g_i describes any degeneracy in the levels. To achieve this population inversion, there must be some input of energy into the active laser medium, and for the medium to act as an amplifier such that induced emission occurs, a portion of the emitted photons must be re-injected into the laser medium. This is usually achieved via enclosing the active medium between two highly reflective surfaces, to form the laser cavity or resonator.

Whilst this description gives the basic theory behind a laser system, it is semiconductor lasers that are of specific interest to the work in this thesis, in particular the use of diode and quantum cascade lasers (QCL). The characteristics of the more conventional diode laser systems, which are used throughout Chapters 2 and 3, are discussed in more detail in the following section. The differing technology and operating principles behind QCL systems is reserved for later in this thesis.

1.2.1 Diode lasers

Diode lasers were first demonstrated in the 1960s [17–19] and fall under the category of solid state lasers. They are made from combining layers of insulating materials that have been doped with an impurity such that conduction occurs by the movement of extra electrons in the conduction band introduced from the dopant (an n-type semiconductor), or by electron vacancies, or holes (a p-type semiconductor).

When these two layers are combined, a p-n junction is formed, and at thermodynamic equilibrium across the junction, electrons fill up to the Fermi level. When a voltage is

applied across the junction, there is no longer equilibrium across it and the Fermi energies of the p- and n- type layers are now different, as illustrated by Figure 1.1. This produces the required population inversion between the valence and conduction band for lasing action, and the flow of electrons and holes in opposing directions as a voltage is applied results in photon emission as they recombine at the junction. The energy of the photons depends on the band-gap of the materials used and can, to some degree, be tuned by varying the temperature or the applied voltage. The combination of materials used in the construction of the p-n junction fall into several categories; a homojunction laser is one where both layers are from the same semi-conductor material, whereas a heterojunction laser is one where two different semiconductor materials form the layers.

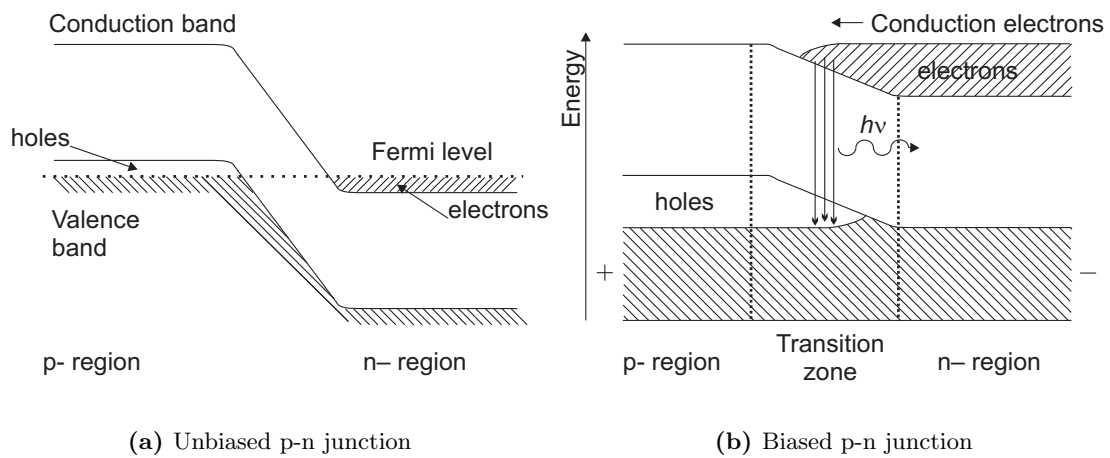


Figure 1.1: Illustration of the p-n junction of a diode laser: (a) shows the unbiased junction at thermodynamic equilibrium and (b) showing the system when a forward voltage is applied, resulting in a population inversion. Reproduced from [20].

To form the laser cavity itself, the simplest solution is to use the two end faces of a laser diode which can be highly polished, as illustrated in Figure 1.2a. To further reduce the possible resonant modes supported by the laser cavity, distributed Bragg reflectors (DBR) can also be integrated into the laser structure. A Bragg reflector consists of alternating layers of materials of differing refractive indices such that optimal reflection occurs for the desired operation wavelength of the laser. In a distributed Bragg reflector laser the Bragg reflectors are positioned at the surfaces of active medium, whereas in a distributed feedback (DFB) laser the variation of refractive indices is continued throughout the medium, further improving the single mode performance of the laser. The confinement of the operation wavelengths of the laser that results from the use of Bragg reflectors means that DBR and DFB lasers have a relatively small tuning range, but they have the advantage of being compact and robust systems that have been developed for the 635 to 2700 nm region of the electromagnetic spectrum [6]. These characteristics make DFB and DBR diode lasers of

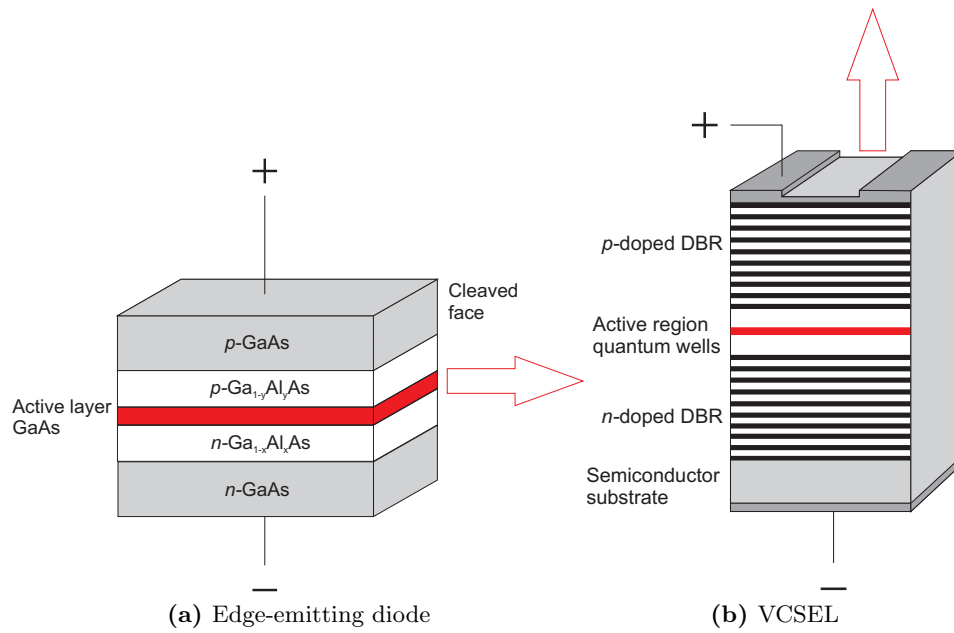


Figure 1.2: Figure (a) shows a simplified illustration of conventional edge-emitting diode laser consisting of, for example, doped GaAs. Figure (b) shows a VCSEL diode laser where the direction of light emission is normal to the surface. Reproduced from [25].

particular use in the development of spectrometers for gas detection, for example in breath analysis as is discussed in Chapter 2.

Another type of diode laser, first developed in the 1980s [21, 22], that is of relevance to this work is the vertical cavity surface emitting laser (VCSEL) where the direction of emission is perpendicular to the top surface, as opposed to the more traditional edge-emitting diode lasers already described. A summary of the differences in design is shown in Figure 1.2. In this figure, the VCSEL schematic illustrates the use of Bragg reflectors throughout the semiconductor material to form the resonator. The advantages of the VCSEL design are seen predominantly in the manufacture stage, as initial tests can be performed before cleaving individual chips, unlike in edge-emitting diodes where the emission surface is formed only after cleaving, hence tests can only be carried out on the final product. In terms of beam quality, VCSEL systems are also advantageous, since they emit a more circular and less divergent beam than the typical rectangular, highly divergent beam produced by edge-emitting diodes [23]. VCSELs also have the advantage of lower threshold currents and can be modulated to a greater extent, however, they have the disadvantage of lower power output than edge-emitting diodes [24]. Therefore careful consideration is required when selecting a laser type for a particular application.

Overall diode lasers are well developed, cheap, robust and tunable sources, making them ideal for use in spectroscopic studies in the NIR region of the electromagnetic spectrum.

However, for working in regions inaccessible to conventional diode laser technology, QCL based systems are typically used, as demonstrated and discussed in Chapters 4 and 5.

1.3 Absorption spectroscopy

Absorption spectroscopy provides an absolute and selective technique for detection of gaseous molecules or atoms, and in its most basic form, direct absorption spectroscopy is described by the attenuation of electromagnetic radiation as it passes through an absorbing medium. This transfer of energy occurs when the radiation is of an appropriate resonant frequency to interact with a dipole moment of, for example, a molecule as it oscillates through vibration or rotation. The reduction in intensity is observed as a frequency-dependent attenuation in the intensity of the light as the laser frequency is scanned over an absorption feature. This process is described by the Beer-Lambert law

$$I(\nu) = I_0(\nu)e^{-\alpha(\nu)l} \quad (1.1)$$

where $I_0(\nu)$ and $I(\nu)$ are the radiation intensities incident on and transmitted by the sample respectively, l is the pathlength through the sample, and $\alpha(\nu)$ is the frequency-dependent absorption coefficient described by $\alpha(\nu) = \sigma(\nu)c$, where c is the concentration of the absorption species and $\sigma(\nu)$ is its absorption cross-section. The absorption cross-section is unique to the medium of interest and its experimental conditions, making absorption spectroscopy a highly effective method for obtaining information about a sample. Since a transition between two states, as observed in absorption spectroscopy, is not seen as a sharp line of single frequency, but does in fact have a defined lineshape, it is more common to describe the absorption cross-section by its integrated value, σ_{INT} , with units $\text{cm}^2 \text{ cm}^{-1}$. This is the integral of the cross-section with respect to wavenumber across the transition, and is constant with respect to changes in the lineshape of the absorption profile. The lineshape itself is determined by several factors dictated by the properties of the sample studied, as well as experimental conditions. These factors can be divided into homogenous and non-homogeneous categories, i.e. contributions to the lineshape that affect every element present in the sample in an identical way, or contributions which arise from an average effect that is not identical to every element, respectively.

One example of a homogenous contribution to the the lineshape is natural broadening which arises from the natural lifetime, τ , of the upper state of the transition. From the Heisenberg uncertainty principle

$$\tau \Delta E \geq \hbar \quad (1.2)$$

it can be seen that the consequence of a finite lifetime of the upper state is an uncertainty in the corresponding energy and therefore, the state is described by a range of energies, ΔE . This contribution to the width of the absorption lineshape is relatively small however, and is normally dominated by other broadening contributions.

Another example of homogeneous broadening of the lineshape is collisional broadening or pressure broadening of the sample. When collisions in a gaseous sample of molecules occur, this effectively reduces the natural lifetime of the transition and according to Equation 1.2, correspondingly increases the uncertainty in the energy of the transition, i.e. there is a broadening of the lineshape. The extent of the lineshape broadening depends on the nature of the energy transfer during a collision, and of the natural lifetime of the transition compared to the frequency of collisions. Thus, as the pressure increases and the interval between collisional events is reduced, the extent of broadening of the lineshape is increased. This variation in the lineshape is described by a Lorentzian form

$$L(\nu) = \frac{\Delta\nu_L}{2\pi[(\Delta\nu_L/2)^2 + (\nu - \nu_0)^2]} \quad (1.3)$$

where $\Delta\nu_L$ is the Lorentzian linewidth given as a full width half maximum (FWHM) value and ν_0 is the line centre of the absorption profile.

Collisional broadening of the lineshape tends to dominate at higher pressures, but for low pressure systems, Doppler broadening, an example of inhomogeneous broadening, is the main contributor to the lineshape.

Doppler broadening results from the shift in the frequency of the absorbed radiation during a transition, and this shift is dependent on the relative velocity of the absorber with respect to the direction of propagation of the radiation. For a molecule that absorbs at a resonant frequency of ν_{res} when stationary, the actual frequency at which the transition is observed at is shifted to ν_a when the molecule travels with velocity, v , away from the radiation source, by

$$\nu_a = \frac{\nu_{res}}{(1 - v/c)} \quad (1.4)$$

where c is the speed of light. The distribution in velocities due to thermal motion of the molecules follows a Maxwellian distribution and the corresponding distribution in absorbed frequencies is described by a Gaussian lineshape

$$G(\nu) = \frac{2}{\Delta\nu_G} \sqrt{\frac{\ln 2}{\pi}} \exp \left[-\frac{4 \ln 2 (\nu - \nu_0)^2}{\Delta\nu_G^2} \right] \quad (1.5)$$

where $\Delta\nu_G$ is the FWHM Gaussian linewidth with temperature, T , dependence given by

$$\Delta\nu_G(T) = 2\nu_0 \sqrt{\frac{2 \ln 2 k T}{m c^2}} \quad (1.6)$$

where m is the molecular mass and k is the Boltzmann constant. For conditions where there are appreciable contributions from both Doppler broadening and collisional broadening, the lineshape takes a form that is a convolution of the Gaussian and Lorentzian components, namely a Voigt lineshape, that can be described by

$$V(\nu) = \frac{2}{\Delta\nu_G} \sqrt{\frac{\ln 2}{\pi}} \frac{y}{\pi} \int_{-\infty}^{+\infty} \frac{e^{-t^2}}{y^2 + (x - t)^2} dt \quad (1.7)$$

where x and y are given by

$$x = \sqrt{\ln 2} \frac{2(\nu - \nu_0)}{\Delta\nu_G} \quad y = \sqrt{\ln 2} \frac{\Delta\nu_L}{\Delta\nu_G} \quad (1.8)$$

Since the integral in Equation 1.7 cannot be fully resolved, approximations are normally used for evaluation of a Voigt profile.

Overall, the selectivity and specificity of direct absorption spectroscopy, due to the unique parameters of a species such as the absorption cross-section, and the range of information on the environment of the species that can be deduced from spectra, make absorption spectroscopy a valuable tool for gaseous detection. However, direct absorption spectroscopy, as a single-pass absorption technique, suffers from intrinsic low sensitivity due to the necessity of measuring a relatively small reduction in the radiation field compared to the measured background signal.

There are various techniques that can be utilised to improve the detection sensitivity of absorption spectroscopy such as those that increase the effective absorption pathlength. This can be achieved through the use of multipass cells or by the use of optical cavity based systems. Another option for improving the sensitivity is to employ various noise-reduction techniques such as wavelength and frequency modulation spectroscopy (WMS and FMS respectively). Both optical cavity based techniques and modulation spectroscopy are used throughout this thesis, and an overview of these methods is given in the following sections.

1.4 Optical cavity based sensitive detection systems

An optical cavity consists of two highly reflective mirrors that form a stable optical resonator aligned in such a fashion so that the light entering the cavity is repeatedly reflected between the mirrors. A small portion of the light, since the reflectivity, R , is not unity, leaks out of the exit mirror and this transmission can be detected and information extracted from it. Historically, the design and use of optical cavities arose due to progress in the manufacture of highly reflective dielectric coatings, and the purpose of the optical cavity was to accurately determine the reflectivity by trapping a pulse of light between two coated surfaces [26]. The rate of decay of the light as it escapes from between the surfaces can be directly related to the reflectivity, and this forms the basis of what has become spectroscopic detection using optical cavities. There have been many comprehensive descriptions written covering the theory behind cavity based spectroscopy and its experimental applications [27, 28], and a basic outline is given in the following sections.

1.4.1 Optical cavities

As radiation propagating through an optical cavity is tuned over a range of frequencies, conditions arise such that an integer number of half wavelengths equal the effective cavity length, resulting in constructive interference occurring. As the transmission from the exit mirror is monitored during this process, the resulting signal appears as a series of maxima. These maxima are cavity modes, occurring when the radiation is in resonance with the optical cavity. The transmission function of a cavity consists of modes with spacing defined by the free spectral range (FSR) of the cavity given by

$$\delta\nu_{FSR} = c/2L \quad (1.9)$$

where L is the cavity length. Another important parameter used to quantify a cavity is the cavity finesse, which describes the extent to which the resonance condition of the cavity is maintained when the system undergoes a slight perturbation in either laser frequency or cavity length, and is related to the reflectivity of the cavity mirrors. The higher the mirror reflectivity and therefore the higher the effective pathlength within the cavity, the larger the relative impact of a perturbation to the system. The result of this higher reflectivity is a smaller frequency region in which conditions for constructive interference are satisfied, and a narrowing of the cavity mode lineshape. Numerically, the cavity finesse, F , is related to the reflectivity through

$$F = \frac{\pi\sqrt{R}}{1-R} \quad (1.10)$$

Combined, the cavity finesse and FSR can be used to describe the cavity modes lineshape, which are Lorentzian in form and have a FWHM linewidth given by δ_{FSR}/F , the cavity bandwidth.

However, to obtain an optical cavity system where the light is trapped in a series of multiple reflections between the mirrors is not solely dependent on the reflectivity of the mirrors, but also on the optical stability of the cavity geometry itself. Light from a radiation source such as a laser tends to be a Gaussian shaped beam with a field amplitude in all directions perpendicular to the propagation axis, and as such the distribution of the decay of the field amplitude outward from the propagation axis follows a Gaussian form. The main restriction on the geometry of a cavity is choosing conditions so that diffraction losses of the beam are minimised and the radiation field is confined within the cavity for a workable number of passes.

For a cavity of length L consisting of two concave spherical mirrors with radii of curvature r_1 and r_2 , the stability condition to achieve confinement of the laser beam is

$$0 < g_1 g_2 < 1 \quad g_i = \frac{L}{r_i} \quad (1.11)$$

For the most commonly used systems where $r_1 = r_2 = r$ the condition is reduced to

$$0 < L < 2r \quad (1.12)$$

In a stable optical cavity the propagation of the electromagnetic field gives rise to cavity modes under certain resonance conditions as described above. For a cavity of geometry defined by g_1 and g_2 in Equation 1.11, the frequencies of the cavity modes are given by

$$\nu_{qmn} = \frac{c}{2L} \left(q + \frac{(n+m+1)}{\pi} \arccos \sqrt{g_1 g_2} \right) \quad (1.13)$$

Individual cavity modes and their frequency position are therefore defined by the q , m and n indices, where q indicates the gross frequency of the mode, or its longitudinal characteristics and m and n indicate the transverse characteristics. The transverse integers describe variation in the electric field plane perpendicular to the cavity axis and result in variation in the spatial intensity distribution of the mode. Longitudinal modes of differing q but the same m and n are spaced by the FSR of the cavity and the standard nomenclature

to describe transverse modes, i.e. those of the same q but different m and n is TEM_{nm} modes. The n and m integers themselves indicate the number of nodes in the intensity distribution in the plane perpendicular to the cavity axis and examples of how this appears for higher m and n values, also known as higher order modes, are shown in Chapter 5.

For the lowest order mode, namely TEM_{00} , which has a Gaussian profile, it can be useful to describe the cavity in terms of the beam waist that it forms in the cavity centre and the spot sizes on the two mirrors. This gives an indication of the mode volume within the cavity, the extent of the mirror surfaces that are used and can also be used for mode-matching. In a mode-matched setup, the input beam is tailored such that it matches the conditions of the light circulating within the cavity itself, i.e. the laser incident on the cavity is of a waist appropriate for the TEM_{00} mode, and therefore ideally only the TEM_{00} mode is resonant within the cavity. For the cavity geometry described above, the spot sizes on the mirrors, w_n , and the waist within the cavity, w_0 , are given by

$$w_{1,2} = \sqrt{\frac{L\lambda}{\pi}} \left[\frac{g_{1,2}}{g_{1,2}(1 - g_1g_2)} \right]^{\frac{1}{4}} \quad w_0 = \sqrt{\frac{L\lambda}{\pi}} \left[\frac{g_1g_2(1 - g_1g_2)}{(g_1 + g_2 - 2g_1g_2)^2} \right]^{\frac{1}{4}} \quad (1.14)$$

The conditions described so far give the requirements for obtaining a stable cavity system and describing the transmission resulting from the interaction of a laser source within the cavity. Experimentally, there are various methods that can be utilised to exploit the potential increase in detection sensitivity that an optical cavity offers. Originally, cavity ring-down spectroscopy (CRDS) was developed which is a temporal measurement of the decay of light exiting a cavity, and was soon followed by cavity enhanced absorption spectroscopy (CEAS), which measures the time-integrated output of the cavity.

1.4.2 Cavity ring-down spectroscopy

Early CRDS experiments for spectroscopic measurements were first reported in the 1980s by O’Keefe *et al.*, who worked with pulsed laser sources to measure atmospheric O_2 absorptions [29]. When a pulsed laser is coupled into a stable optical cavity to excite cavity modes, the termination of the pulse is followed by an exponential decay in the transmission of the cavity mode intensity as increasing losses occur incrementally with each pass through the cavity. Each cavity mode that is excited in the cavity will exhibit the same behaviour, resulting in a transmission consisting of information from many different modes.

More recent work has moved onto using continuous wave (cw) laser sources since they have the advantage of greater frequency resolution. In practice, the laser light coupled into the cavity is extinguished using a fast optical switch, for example an acousto-optic modulator

(AOM). The switch-off point is determined by monitoring the power build-up within the cavity that occurs when the cavity comes into resonance with a mode. This build-up is monitored with a detector that is connected electronically to the AOM such that when the cavity output reaches a certain level indicating a mode has been excited, a trigger is sent to the AOM to deflect the incident beam from the cavity, thus terminating the injection of light into the cavity, and the resulting decay is monitored. Ideally, the decay of a single mode is monitored and therefore the higher order modes are suppressed, for example through mode-matching, so that only the TEM₀₀ mode is excited and the decay of only this is monitored.

The form that the decay takes depends on the characteristics of the cavity and any absorbing medium present. When a laser is coupled into the cavity of length L , with an intensity I_{in} , and then extinguished, the losses of a single pass result in a detected signal modeled as

$$I_0 = T^2 e^{-\alpha d} I_{in} \quad (1.15)$$

where T is the transmittivity of each mirror, and α and d correspond to the absorption-coefficient and length of any absorbing medium present between the mirrors [28] of reflectivity R . For each consecutive round-trip of the light within the cavity, the intensity of the monitored decay decreases further and after n round-trips the detected signal can be described as

$$I_n = [R e^{-\alpha d}]^{2n} I_0 \quad (1.16)$$

The detected decay signal normally takes the form of a smoothed exponential reduction in intensity over time, and Equation 1.16 can therefore be rearranged in terms of time that the injected radiation has spent in the cavity, $t = 2Ln/c$, to give

$$I(t) = I_0 e^{-\frac{ct}{L}(-\ln R + \alpha d)} \quad (1.17)$$

From this, the decay time constant τ defined as the time taken for the intensity to decay to $1/e$ of its original value is given as

$$\tau = \frac{L}{c(-\ln R + \alpha d)} \quad (1.18)$$

For cavity systems where $R \rightarrow 1$ then $\ln R \approx -(1 - R)$ and so Equation 1.18 can be rewritten as

$$\tau = \frac{L}{c((1 - R) + \alpha d)} \quad (1.19)$$

When there is no absorbing medium present, then the decay time for an empty cavity, τ_0 is defined as

$$\tau_0 = \frac{L}{c(1 - R)} \quad (1.20)$$

These decay times, τ and τ_0 are described as the cavity ring-down times (RDTs) and together can be used to determine the concentration of an absorbing sample of known absorption cross-section, by recording both as functions of laser frequency and applying Equation 1.21

$$\alpha(\nu) = \sigma(\nu)c = \frac{\Delta\tau}{\tau_0\tau} \frac{L}{cd} \quad (1.21)$$

where $\Delta\tau = \tau_0 - \tau$.

Since the early work by O’Keefe using pulsed systems, the use of CRDS as a spectroscopic tool has rapidly grown [30]. The main advantage of CRDS is the potential to obtain absolute concentration information about a system, however, the experimental requirements of using fast optical switches and detectors as well as very high reflectivity mirrors are disadvantages, and can make cavity enhanced absorption techniques a more viable alternative.

1.4.3 Cavity enhanced absorption spectroscopy

Whereas CRDS utilises the measurement of the intensity decay with time from a single excited mode, CEAS relies on monitoring the time integrated-output of many different modes. The first use of CEAS was reported independently by Engeln *et al.* [31] and O’Keefe *et al.* [32], a decade after the first use of CRDS as a spectroscopic method. In practice, CEAS involves aligning the cavity such that many higher order modes are excited as the cavity is continuously injected with light. The laser is then repeatedly scanned over a range of frequencies that span an absorption feature. The resulting signal is a highly congested mode structure, and consecutive scans can be averaged out to obtain information about the absorption lineshape. If aligned effectively, the signal will have no dominant mode structure after averaging that will interfere with changes in the transmission attributable to the absorption. If alignment of the cavity is insufficient to reduce the residual mode structure then other techniques, such as slight mechanical dithering of the cavity mirrors, for example with a piezoelectric transducer (PZT), are employed. This induces changes in

the cavity length, and causes a shift in the mode central frequencies, further randomising the structure over the scans used to average the data. The different alignments required for CRDS and CEAS involve subtle changes in the system's optics, and a more thorough study of this is discussed in Chapter 5.

How the resulting averaged spectrum should be analysed to extract information about the absorber has been treated in several different ways [28]. The most commonly used method of analysis can be described from a similar start point as that used for CRDS in the previous section, where the signal can be defined in terms of the mirror transmittivity, or its reflectivity, since for an ideal mirror $T = (1 - R)$, and the single pass absorption from any medium present defined by Equation 1.1. For the most commonly used cavity where both mirrors are identical, and the entire length of which, L , can be occupied by an absorber, the output intensity from either mirror, I_{out} can be written in terms of the incident intensity, I_{in} , as

$$I_{out} = I_{in}(1 - R)^2(1 - A) \sum_{n=0}^{\infty} R^{2n}(1 - A)^{2n} \quad (1.22)$$

where A acts as a generic term to describe the reduction in intensity after each pass due to absorption. For the conditions of $R < 1$ and $A < 1$ then Equation 1.22 can be written as the sum of a geometrical progression

$$I_{out} = I_{in} \frac{(1 - R)^2(1 - A)}{1 - R^2(1 - A)^2} \quad (1.23)$$

Writing this in terms of the ratio of intensities for no absorption and when there is an absorber present, (I_{out}^0/I_{out}) , and describing the single pass absorption in terms of Equation 1.1 gives

$$\frac{I_{out}^0}{I_{out}} = \frac{1 - (Re^{-\alpha L})^2}{(1 - R^2)e^{-\alpha L}} \quad (1.24)$$

Assuming the conditions of $R \rightarrow 1$ and $\alpha \rightarrow 0$ then Equation 1.24 simplifies to

$$\frac{I_{out}^0}{I_{out}} = 1 + \frac{\alpha L}{1 - R} \quad (1.25)$$

which is the most commonly used model to analyse CEAS spectra. As can be seen from Equation 1.25 however, it is necessary to know the value of R to obtain absolute concentration information, and this non-absolutivity is one of the main drawbacks of CEAS.

To obtain R calibration mixtures of known concentration and absorption cross-section are typically used, or a CRDS experiment is performed on an empty cavity.

The theory described here gives an overview of cavity techniques and their development, in later chapters further practical and experimental considerations will be discussed where they become relevant as the applications of optical cavities are studied.

1.5 Modulation spectroscopy

Modulation spectroscopy aims to achieve a reduction of noise on the signal as opposed to an increase in the absorption pathlength. This is achieved by encoding the absorption information in a higher frequency regime, where $1/f$ noise sources, that are described in more detail in the following section, are reduced. Typically, modulation spectroscopy is based on superimposing a high frequency sine wave on top of the relatively low frequency scan over an absorption feature. The resulting signal which varies at the modulation frequency can be detected with frequency and phase sensitive electronics such as those provided by a lock-in amplifier. Modulation spectroscopy may result in improvements in the signal-to-noise ratio, but as with CEAS, it does have the disadvantage of being a non-absolute technique and therefore requires calibration.

Modulation techniques fall into two categories, differing in modulation amplitude and frequency characteristics. Wavelength modulation spectroscopy (WMS) typically operates in a low frequency regime (kHz-MHz) whereas frequency modulation spectroscopy (FMS) operates at much higher modulation frequencies ($\sim$ GHz). The two methods require different experimental considerations and requirements and a full discussion of the relevant theory, as well as experimental demonstrations of the two techniques is given in Chapter 3.

1.6 Sensitivity of spectroscopic methods

The sensitivity of a spectrometer is determined by the size of the absorption signal relative to any baseline noise. Generally, the approach to defining the sensitivity of a spectrometer is to assess the baseline noise of the signal, and determine for a specific technique what the noise equivalent absorption would be. This is defined as the minimum detectable absorbance for a system i.e. the $(\alpha l)_{min}$ value for which the signal-to-noise (S/N) is equal to one. There are various contributions to the noise that limit $(\alpha l)_{min}$ in an experimental setup and various ways of quoting the noise equivalent absorption of a system.

1.6.1 Noise sources

The contributions to the signal baseline noise have a variety of sources in a spectrometer. The detector itself will have an intrinsic level of noise due to shot noise which arises from the discrete nature of detection events, in this case the incidence of photons on the detector, and the fluctuations within these event occurrences [33]. Other intrinsic noise sources from the detector include what is referred to as white noise, the noise associated with thermal perturbations of the electrons within the detection system [25]. These noise levels are not necessarily the limiting factor in an experiment, and can be greatly reduced by moving detection to a higher frequency regime as they tend to scale with $1/f$ [33], but as well as the detector noise sources, other contributions from a laser absorption based setup need to be considered.

Noise sources outside the detection system can include, for example, power fluctuations in the laser, or etalons formed between reflective surfaces that can all introduce variations in the baseline that interfere with the absorption information. Noise sources that are inherent to the spectroscopic technique used are also possible, for example residual mode structure on CEAS signals as will be discussed in Chapter 5. In this thesis, these noise sources are quantified by taking the standard deviation (1σ) of a non-absorbing section of the baseline of an absorption spectrum, and this is defined as the noise of the system unless stated otherwise.

1.6.2 α_{min} values

There are many variations on quoting sensitivities, that include normalising to the acquisition time for the data or the bandwidth of any electronics in the detection process, however a level of consistency is required when comparing various techniques.

The simplest way of defining the sensitivity is using the noise equivalent absorption and defining it in terms of α_{min} with units of cm^{-1} . This defines the minimum detectable absorbance of a system, normalised to the experimental pathlength, but without taking into account the acquisition time of the experiment.

To compare similar experiments however, the acquisition time should be accounted for, and therefore a time-normalised value of $\alpha_{min}(t)$ can also be quoted. This is generally done by multiplying by $\sqrt{(n\tau)}$ where n is the number of averages and τ is the acquisition time. This gives a time-normalised $\alpha_{min}(t)$ in units of $\text{cm}^{-1} \text{ s}^{\frac{1}{2}}$.

Finally, it is possible to quote an $\alpha_{min}(BW)$ value, which is α_{min} normalised to the bandwidth of the detection electronics, such as in modulation spectroscopy where a lock-in

amplifier is used. In this case the bandwidth is defined as $1/\pi\tau$ where τ is the time constant set in, for example, the lock-in amplifier. The bandwidth reduced $\alpha_{min}(BW)$ is obtained by multiplying α_{min} by $\sqrt{(n\pi\tau)}$ to give a value normally quoted in units of $\text{cm}^{-1} \text{Hz}^{-\frac{1}{2}}$, to distinguish it from the time normalised $\alpha_{min}(t)$ quoted in $\text{cm}^{-1} \text{s}^{\frac{1}{2}}$ discussed previously. This value gives the minimum detectable absorption in terms of the theoretical minimum detectable change that can be observed in an α value averaged n times, within the time-resolution of the detection electronics.

How to quote an α_{min} value depends largely on what information about the setup one is trying to convey, but a consistent approach is required when comparing values between experimental systems. In this thesis, the α_{min} values that are quoted are those that have been defined above, depending on the setup, and comparisons will only be drawn between setups that have detection sensitivities that can be described in a equivalent manner.

1.7 Overview of this thesis

This thesis covers two very different fields of research, in terms of both the concentration of species monitored in breath and the region of the electromagnetic spectrum that this work has been performed in. The following two chapters focus mainly on the potential of monitoring the exchange gases found in breath during respiration, namely O_2 , CO_2 and H_2O , with both cavity and modulation based methods. This work has been performed using laser sources in the NIR, where the well developed laser sources and optics can be exploited. The exchange gases are found in relatively high concentrations in breath, and as such the challenge for the monitoring of changes in their concentration is in building a small, robust and fast measurement device that can monitor all gases simultaneously and accurately. This work is described in Chapter 2, with Chapter 3 focusing on potential alternative methods, WMS and FMS, that can be applied to breath analysis.

The final two chapters of this thesis involve a shift in focus to the potential detection of trace gases in breath, or biomarkers, and moving of the spectroscopic detection to the MIR to utilise the increase in absorption cross-sections typically available in this region. To achieve this, the use of QCLs is employed in these chapters, and a detailed description of the experimental considerations and requirements when building a QCL spectrometer is discussed in Chapter 4, as well as some preliminary studies on the monitoring of biomarkers at $8 \mu\text{m}$. Finally, the potential use of sensitive detection methods in the MIR is investigated in Chapter 5, with particular emphasis on using optical cavities for trace gas detection, and the implications that working in the MIR have on this methodology.

Chapter 2

Development of an analyser for monitoring respiration

The work in this chapter details the development stages for a laser based detection system for monitoring respiration. The concept of this detection system, or “breath analyser”, is a single device to simultaneously monitor changes in the three main exchange gases in breath: O_2 , CO_2 and H_2O . These changes will be measured in real-time, using techniques based on absorption spectroscopy.

2.1 Monitoring respiration

Respiration is the basic process in which O_2 is taken in by the body, and reacted with glucose to produce energy, in the form of adenosine-5'-triphosphate (ATP), with CO_2 and H_2O formed as by-products. During respiration, the main function of the lung is the transportation of O_2 into, and CO_2 and H_2O out of, the bloodstream via breathing.

The lung consists of a series of conducting airways that branch into increasingly shorter and narrower tubes, the function of which is to guide inspired air into the respiratory zone of the lung. The respiratory zone consists of areas of the lung where the walls are covered with alveoli, small air sacs about $\frac{1}{3}$ mm in diameter, and around which small blood vessels, or capillaries, are wrapped. It is at this blood-gas interface, which can in total span 85 m² [34], where gas exchange between the blood and the air occurs via diffusion.

Whilst it may appear at first to be a simple case of O_2 being inhaled, and CO_2 exhaled as respiration occurs, the complexity of the lung structure results in an added level of difficulty in monitoring gas exchange at the blood-gas interface. For example, the conducting airways are in effect an anatomic dead space where no gas exchange occurs due to the lack of alveoli,

and so a residual volume of ~ 150 ml of air takes no part in gas exchange. As well as this, different sections of the lung are also more efficiently ventilated, i.e. more gas reaches these areas per unit volume and finally, on exhalation, there will always remain a residual volume of gas in the lung. However, these complex workings of the lung can be modeled, and various CO_2 and O_2 exchange algorithms used to integrate the flow of CO_2 and O_2 along the airway, but to do this, accurate real-time measurements of the exchange gases in the respiratory air flow are needed [35].

The first rapid and continuous measurements of O_2 and CO_2 in breath began in the 1950s and 60s, where the method of analysis would involve extracting a sample from the flow of respired gas via a catheter. This “sidestream” sampling method for monitoring gases in breath has remained the conventional approach, however, for accurate breath-by-breath analysis it does have some disadvantages. The use of a catheter to sample the flow results in a delay between measurements of what is occurring at the mouth, and what is observed in the analyser, and can even result in variable delays between the gases themselves due to chromatographic effects of the tubing. These delays make it difficult to time-align the measurements of CO_2 and O_2 with the relatively instantaneous measurements of changes in flow that are normally taken in-line, i.e. in the main part of the breath stream. Therefore using conventional methods, the determination of breath-by-breath gas exchange is limited by delays due to the sampling method.

These conventional analysers were based on infrared absorption spectroscopy for CO_2 and either fuel cells or the paramagnetic effect for O_2 [36], with the analysis of O_2 tending to be slower and therefore introducing further delay in the measurements. Mass spectrometry has also been employed to monitor the gases, and can to some degree overcome these delays [37–39], but the equipment tends to be much more complex, expensive and difficult to maintain.

Overall, the high accuracy and time resolution available through the use of laser spectroscopic techniques, as well as designing an analyser that will be in-line as opposed to sidestream, would result in a much more effective means of monitoring breath-by-breath gas exchange.

2.2 Overall concept of the breath analyser

The concept behind this work is a small, robust measurement unit that could sit in the main respiratory stream and detect real-time, simultaneous changes in O_2 , CO_2 and H_2O . The potential uses for an instrument that accurately monitors breath-by-breath gas exchange range from sports testing to medical environments, particularly where the inspired gas

mixture is of an unknown and time-varying concentration, such as during oxygen therapy or when undergoing anesthesia. Furthermore, the analyser itself needs to be compatible with standard tubing and bacterial filters for breath measurements, therefore optical pathlengths ideally ≤ 4 cm are required.

Since O_2 and CO_2 are the two main exchange gases that need to be monitored in respiration, they have been dealt with initially, with measurements on H_2O introduced in later sections. As well as this, some initial studies on monitoring the respiratory flow and temperature are also reported. The various stages and design attempts are detailed throughout this chapter, as well as the improvements made from studies on the required optics, the mechanical design of the cell and the spectroscopy of the gases. A final prototype which is the culmination of this work is described in the final sections, and typical measurements from this are discussed. The final design of the prototype analyser and peripheral electronics needs to be such that it is comparable to, or an improvement on current methods. Therefore, to achieve comparable performance to these current methods, an ideal detection limit of an absolute change of 1 % for O_2 and CO_2 , with a measurement taken every 10 ms is required.

2.2.1 Detection of gases in the breath analyser

The actual measurement of O_2 , CO_2 and H_2O require the use of different techniques, and different practical considerations. For O_2 , cavity enhanced absorption spectroscopy (CEAS) on transitions around 760 nm is utilised. The work presented in this chapter utilises several models of ~ 760 nm lasers, and as such various O_2 transitions have been probed in this region, the specifics of which will be given when necessary in the text. The transitions used are all relatively weakly absorbing ($\sigma_{INT} \sim 10^{-24}$ cm² cm⁻¹ at 760 nm), hence the sensitive detection method CEAS is required. CEAS is not the only sensitive detection method available, however, it has been found to be the most appropriate one for monitoring O_2 in breath. A discussion of other methods not involving an optical cavity, such as modulation spectroscopy, and their potential in breath analysis is given in Chapter 3.

The detection of CO_2 was carried out at 2 μ m and is experimentally less complex, as the transitions that can be studied with readily available diode laser systems are relatively strong compared to those of O_2 . Therefore, single pass direct absorption spectroscopy is sufficient for monitoring changes in CO_2 levels in breath.

Finally, detection of H_2O was performed at 1.3 μ m where, as with CO_2 , direct absorption spectroscopy is also sufficient for monitoring concentration changes. The detection of H_2O is not as critical in monitoring respiration as O_2 and CO_2 , and at this stage is monitored in

a more qualitative manner, as will be discussed in later sections. A summary of the specific line parameters for the absorption features studied in this chapter is given in Table 2.1.

Gas	ν_0 / cm^{-1}	σ_{INT} / $\text{cm}^2 \text{ cm}^{-1}$	Assignment
H ₂ O	7306.75	1.80×10^{-20}	$\nu_1 + \nu_3, (3,1,3) \leftarrow (2,1,2)$
CO ₂	4991.26	1.26×10^{-21}	$2\nu_1 + \nu_3, \text{R18e}$
O ₂	$\sim 760 \text{ nm}$	$\sim \times 10^{-24}$	$b^1\Sigma_g^+ \leftarrow X^3\Sigma_g^-, \text{various } \Delta N N'' \Delta J J''$

Table 2.1: Line parameters for absorption features chosen for individual studies on CO₂ and H₂O in breath. Specific line positions and information will be given for O₂ where relevant. Data are taken from the HITRAN database [40].

The relevant spectroscopy that gives rise to the transitions, and a description of their nomenclature is given in the sections detailing measurements on the individual gases themselves.

2.2.2 Data acquisition and analysis

Another crucial consideration in the design of the breath analyser is the electronics and programming required for the acquisition of data and its analysis to give a gas concentration. This is what will determine the time resolution of the instrument and to some extent, its accuracy. Many aspects of the data handling can be used for monitoring both O₂ and CO₂, and are integral to the concept of the breath analyser. The process described in this section demonstrates the acquisition and analysis process in terms of monitoring a single gas, with a discussion of monitoring several gases reserved for when simultaneous measurements are performed, although the main principle remains the same.

For monitoring a single gas a computer running a LabVIEW Realtime operating system was equipped with data acquisition card with a single analogue-to-digital converter (ADC) [National instruments, DAQ-2010]. A specifically written LabVIEW program was used to run the experiment and collect and analyse data. This combination of electronics and programming will be described henceforth as the laser gas analyser (LGA). To run the experiment, the LGA provided the necessary triangular ramp to the laser injection current to scan over an absorption feature. The LGA could then collect the signal from the detector and either save individual scans, or could average together n consecutive scans as determined by the user. Averaging was normally employed to improve the signal-to-noise ratio on the data, especially for any CEAS data where residual mode noise is likely. The frequency of the scans, usually 1 kHz, combined with n determined the time resolution of the analyser, which was usually set to 10 ms. With averaged detector signal being collected every 10 ms, they could either be saved for later analysis, or the LGA itself could analyse them to give realtime variations in gas concentration.

For the LGA to process and analyse any data taken during a breathing cycle, and produce real-time gas concentrations, several steps were required. These steps are also illustrated with corresponding examples of CO₂ data in Figure 2.1.

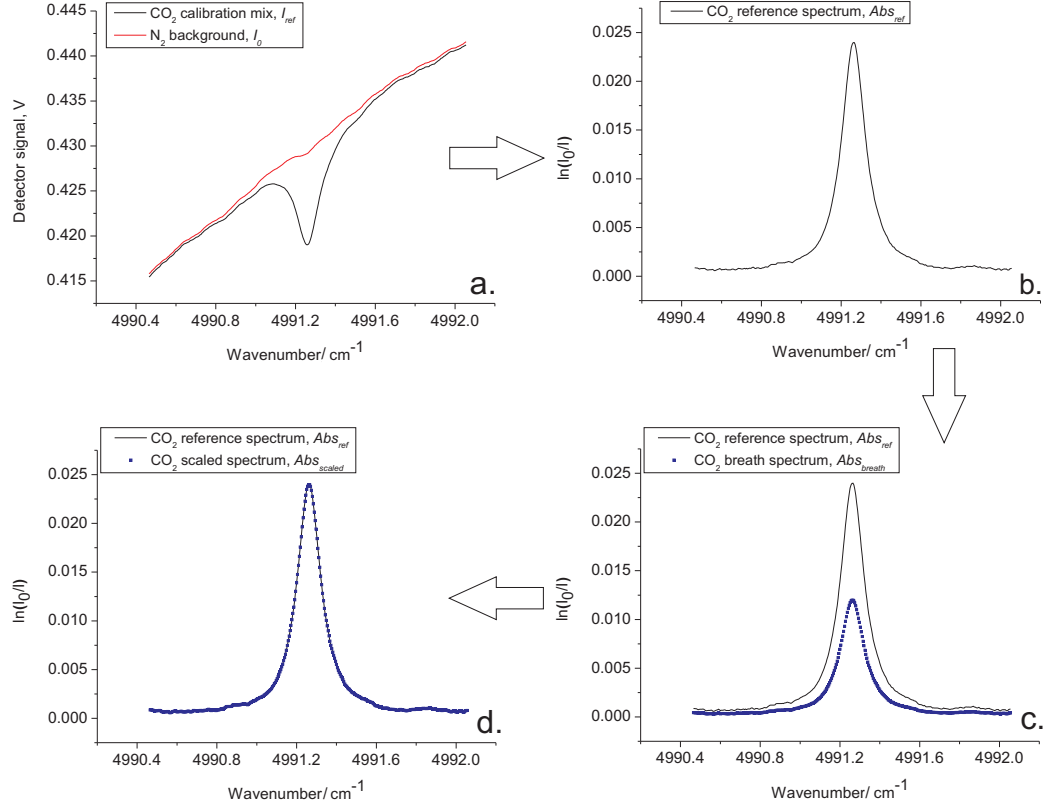


Figure 2.1: Illustration of data processing by the LGA for a CO₂ example: (a) shows the calibration steps to obtain I_0 (red) and I_{ref} (black). (b) shows the processed reference spectrum, Abs_{ref} corresponding to a known concentration of CO₂. (c) shows Abs_{ref} (black) compared to an absorption spectrum of an unknown CO₂ concentration Abs_{breath} (blue). (d) shows the scaling performed by the linear regression algorithm to match Abs_{breath} to Abs_{ref} .

Data acquisition and analysis procedure:

1. A baseline, I_0 , value is obtained by flushing the cell with N₂ for ~ 30 s and averaging the scans together to give a smooth baseline to be used in later processing.
2. Calibration of the setup was then performed by flowing a gas mixture of known concentration through the cell. As with I_0 , the LGA averages together spectra taken over ~ 30 s to give a smooth reference spectrum, I_{ref} . The two spectra, I_0 and I_{ref} , are then processed according to Equation 1.1 or 1.25 as required to give a reference absorption spectrum of a known gas concentration, Abs_{ref} .
3. A subject then breathes through the measurement cell for a set period, while the LGA records the detector output. The LGA produces an averaged breath spectrum every

10 ms, and each is processed with I_0 to give an absorption spectrum of an unknown concentration, Abs_{breath} .

4. These absorption spectra of unknown concentration are then compared to the reference spectrum using a linear regression algorithm to scale Abs_{breath} to match Abs_{ref} . The scaling factor required can then be interpreted as a percentage gas concentration and is returned by the LGA.

The advantage of analysing the data in this manner is that the calibration steps ensure absolute gas levels are returned and measurements are obtained very quickly. The linear regression algorithm provides a fast method of analysing the absorption feature, and whilst a full absorption profile analysis using a Voigt function is an option, the processing time was found to be too long for the 10 ms time resolution required.

So far, the general concept of the breath analyser and how data can be extracted from it have been described, however, to understand the experimental requirements of monitoring O_2 and CO_2 concentrations, each gas has initially been studied individually. The following sections detail the findings of analysing the gases separately, and any implications for combining the measurements in a single analyser.

2.3 CEAS studies on O_2

2.3.1 Spectroscopy of O_2

In the visible and NIR, O_2 has four bands corresponding to the $(0 \leftarrow 0)$, $(1 \leftarrow 0)$, $(2 \leftarrow 0)$ and $(3 \leftarrow 0)$ vibrational transitions of the $b^1\Sigma_g^+ \leftarrow X^3\Sigma_g^-$ electronic transition, as indicated in Figure 2.2. These four bands are labelled the A , B , γ and δ transitions, respectively, and it is the A band that was first analysed by Mulliken [41] and Van Vleck [42] centred at 762 nm, that is of most interest to this thesis. The $b^1\Sigma_g^+ \leftarrow X^3\Sigma_g^-$ electronic transition, however, is formally forbidden by the electric dipole moment selection rules for spin ($\Delta S = 0$), for symmetry ($+\leftrightarrow +$, $-\leftrightarrow -$) and parity ($u \leftrightarrow g$). The result of this is that the A band transitions occur only through magnetic dipole interactions, and are correspondingly weak.

Conventionally, the nomenclature for O_2 transitions between rotational levels is defined in terms of their rotational angular momentum quantum number, N and the total angular momentum quantum number, J , which is the sum of the rotational and spin angular momentum quantum numbers [44]. The upper and lower states are indicated by ' and ' ' respectively. The ground state, since it has a total spin of 1, is therefore split into three levels $J'' = N''$, $N'' + 1$ and $N'' - 1$ whilst the excited state has zero spin and is therefore

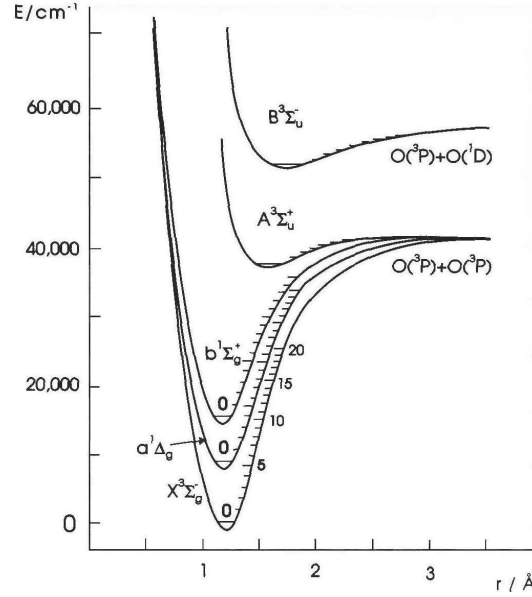


Figure 2.2: Diagram depicting the potential energy curves of O_2 electronic states. Taken from [43].

composed of singlet states for $J' = N'$. The allowed transitions between these levels can be written as $\Delta N \cdot \Delta J(N''J'')$ where $\Delta N \cdot \Delta J = PP$, PQ , RQ and RR , forming the P branch, which begins at 13120 cm^{-1} and extends to lower frequency, and the R branch, which spans $13125 - 13170 \text{ cm}^{-1}$, with a bandhead at 13165 cm^{-1} . The P branch itself consists of $PP(N'', J'' = N'')$ and $PQ(N'', J'' = N'' - 1)$ transitions, whereas the R branch consists of $RR(N'', J'' = N'')$ and $RQ(N'', J'' = N'' + 1)$ transitions. It is worth noting that occasionally slight variations in the nomenclature are used in literature, for example, $\Delta^N \Delta J(N''J'')$, $\Delta N N'' \Delta J J''$, and it is the latter of these variations that has been adopted in this thesis.

Another aspect of molecular oxygen spectroscopy is that, as O_2 is composed of two identical bosonic nuclei, rotational levels of the A band are subject to the Pauli principle, which states that when two identical bosons are interchanged, the overall wavefunction must remain unchanged. However, as the nuclei have spin $I = 0$ for ^{16}O there is only one symmetric nuclear spin wavefunction for O_2 with the result that only odd N'' values are allowed and the spectrum only shows alternate lines. As has already been discussed, various transitions from the O_2 A band are studied in this thesis, and will be defined where relevant using the nomenclature described.

2.3.2 Experimental details

For the detection of O_2 , the lasers used were DFB fiber-coupled models centred around $\sim 760 \text{ nm}$ [Eagleyard Photonics, e.g. EYP-CFB-0763-00010-1500-BFY02-0000] housed

in a temperature controlled mount [Thorlabs, LM14S2]. The laser was controlled by a laboratory-built current controller and a commercially available temperature controller [Thorlabs, TED 200C]. The fiber output was collimated using an AR-coated fiber-coupling lens system [Thorlabs, CfC-2X-BI] and directed through an optical isolator [Leysop, 560-800 nm]. The optical isolator was necessary as it minimises potentially damaging reflections that can feedback into the laser. The beam was then injected into the measurement cell containing the cavity mirrors of radius of curvature 1 m [Laseroptik]. Several variations of measurement cell of different length and design were used in these studies, depending on what was being investigated, and will be described in detail where relevant. The light exiting the measurement cell was focused onto an avalanche photodiode detector (APD) [Hamamatsu, C5460-01]. An interference filter [Thorlabs, FB760-10] was also placed in front of the detector surface which acted as a narrow-band filter to block out background light, as well as any amplified spontaneous emission (ASE) from the laser itself. A schematic of the experimental setup is shown in Figure 2.17.

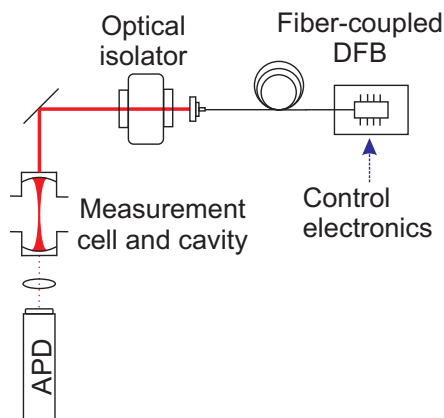


Figure 2.3: Schematic of the CEAS based setup for investigating the potential of monitoring O_2 in breath.

2.3.3 Studies on the cavity mirrors

Initially, the reflectivity of the mirrors needs to be measured so that unknown concentrations of O_2 in breath can be accurately determined. To achieve this, a measurement cell with the mirrors spaced 20 cm apart was used. The extra long cavity was utilised here to give a larger CEAS signal and thus improve the accuracy of the measurement of R . The cell consists of two Gimbal mounts to hold the mirrors, housed in vacuum mounts with Brewster angled windows. The housings for the mirrors are then joined using KF25 piping with appropriate gas inlets to give the required length. An example of a CEAS spectrum of O_2 in air taken at 900 Hz and averaged 100 times as obtained from this setup is shown in Figure 2.4. The transition studied was P5P5 at 13100.82 cm^{-1} with $\sigma_{INT} = 7.55 \times 10^{-24} \text{ cm}^2 \text{ cm}^{-1}$. The x-axis is calibrated from time to wavenumbers using a 2 GHz spectrum analyser [Melles

Griot, 135AE902]. Since air is an ideal calibration gas with a known level of O_2 (21 %), a value of R can be obtained and was found to be 99.831 ± 0.001 %.

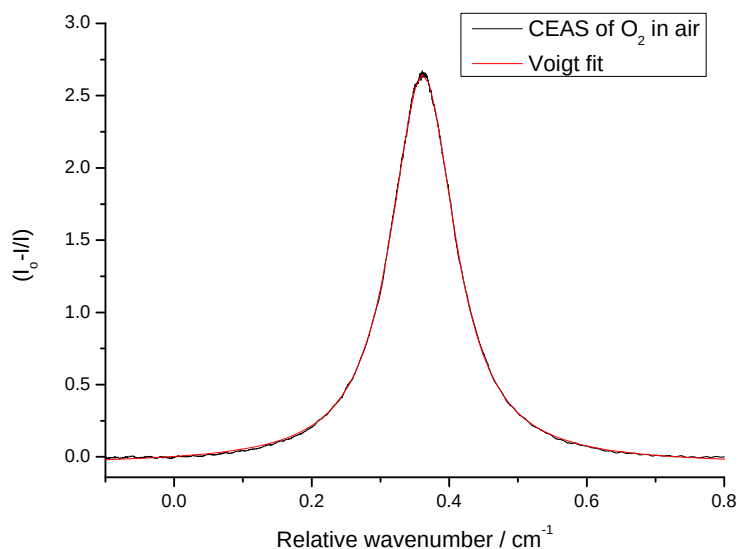


Figure 2.4: Example CEAS spectrum of O_2 transison P5P5 at 1300.82 cm^{-1} in air taken in a 20 cm cavity to determine R . Data were taken at 900 Hz and averaged 100 times and a corresponding Voigt fit is shown in red.

However, as well as taking spectra to calibrate the reflectivity, an unusual effect due to the presence of H_2O was also observed in this work. It was seen that as the level of H_2O in the measurement cell varied, the level of light exiting the cavity also varied. In fact, as the H_2O level increased, the transmission from the cavity appeared to increase as well, but with no apparent change to the value of R . This effect is demonstrated in Figure 2.5, which shows I as transmitted from the cavity at a series of different pressures of air. The first graph shows the variation in I when lab air is bled into the cell, therefore increasing the level of H_2O , and the second graph shows the same experiment but with dry cylinder air.

As can be seen in Figure 2.5, this is clearly an effect of adding H_2O and not simply a consequence of changing the overall pressure of gas in the cell. The consequence of this is that measuring O_2 in breath would result in large variations in baseline movement, as the content of H_2O in breath varies between ~ 1 to 5% between inhalation and exhalation.

An attempt at minimising this effect by heating the cavity mirrors was also investigated. To do this, a new cell design consisting of aluminium end pieces to hold the mirrors 4 cm apart was designed and built in-house. The metal end pieces could be heated using attached resistors, with a thermostat on the surface to control the temperature. The central body of the cell was plastic, so that the whole cell body did not require heating, and had an entry and exit port to flow gas perpendicular to the optical axis of the cavity. This is also the

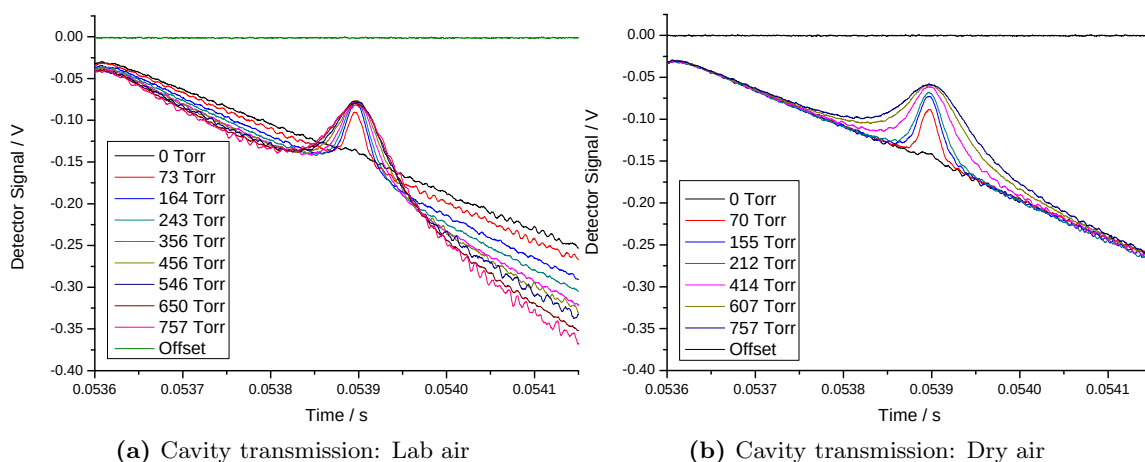


Figure 2.5: Graph (a) shows the effect on I by adding more lab air and therefore more H_2O to the cavity. Graph (b) shows a similar experiment carried out with dry cylinder air. Note that due to the use of the APD, the detected signals are inverted. O_2 transition P5P5 at 1300.82 cm^{-1} .

first cell design used for attempts at monitoring O_2 in breath and is therefore designated Mark I. A schematic of the design is given in Figure 2.6.

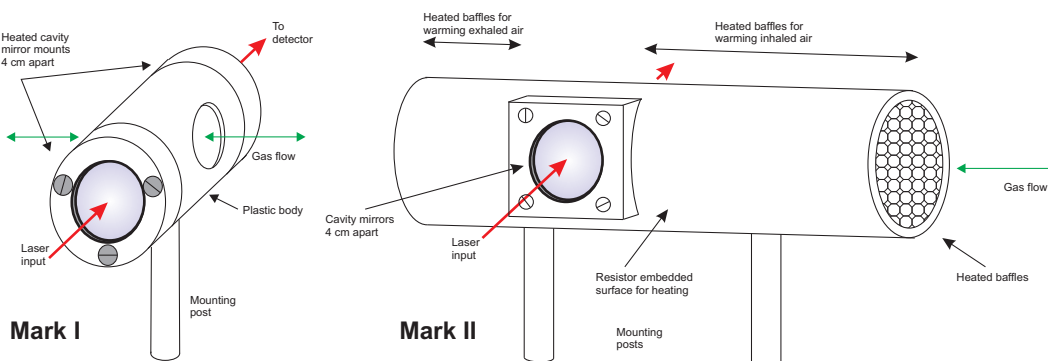


Figure 2.6: Schematic of breath analysis cells used in these studies. Mark I is the first attempt at using a heated cell (section 2.3.3) and Mark II is the first attempt at controlling both the temperature and flow (section 2.3.4). Mark II is also the first cell used in simultaneous measurements of O_2 , CO_2 and H_2O (section 2.5).

Overall, even though a level of heating of the cavity mirrors will be necessary for breath measurements to prevent condensation, it had no effect on the variation with cavity mirror transmission as the H_2O levels were changed, therefore this effect is not simply due to condensation on the mirror surfaces. However, a second set of mirrors purchased from a different company, *Layertec*, showed much more stable behaviour as shown in Figure 2.7. The data shown illustrate the response of the two mirror sets in the heated Mark I cell described above. The cells were heated for a length of time to allow the contained static air sample to heat up as well, such that the relative humidity would vary. The temperature of the gas sample was monitored using a calibrated thermocouple. The advantage of

this experiment as opposed to one simply monitoring different pressure of H_2O is that it simultaneously monitors any effect that heating the new Layertec cavity mirrors may have.

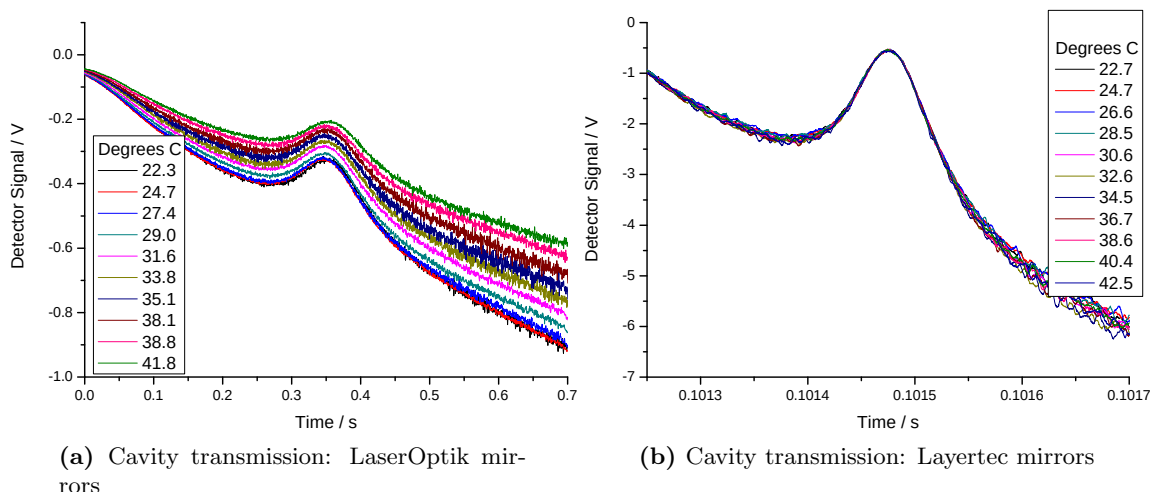


Figure 2.7: Graph (a) shows effect of varying the humidity in the cell by heating on the original LaserOptik mirrors (transition R15Q16) and graph (b) shows the equivalent data for the new Layertec mirrors (transition R11R11). The legends in each graph indicate the temperature in °C for each trace.

As can be seen from the two graphs, the new Layertec mirrors show a negligible response to variations in humidity and temperature compared to the previously used LaserOptik versions, which is ideal for breath measurements. Another advantage of the Layertec mirrors is a much higher reflectivity, calculated using a lab air sample as previously described, and which was found to be $99.979 \pm 0.001 \%$.

As information on mirror coatings and deposition techniques is usually considered a proprietary technology of the manufacturer, it is difficult to hypothesize what kind of surface interaction could occur between the mirror coatings and H_2O to result in such a large effect on the transmission. Coatings for mirrors in this region tend to be based on layered tantalum oxide or titanium oxide, but without further information on the layer deposition methods or structure, it is only possible to speculate on these observed effects.

With a measurement cell developed that was the required length (4 cm), and with mirrors that showed no adverse effects to humidity and heating, initial attempts at monitoring O_2 levels in breath via CEAS were attempted.

2.3.4 Studies on breath and air flow in the cavity

For determining real-time changes in O_2 concentrations in breath using CEAS, the LGA is initially calibrated with N_2 and air, and then spectra taken during the breath cycle are

compared to the air reference absorption spectrum using the linear regression algorithm, as described in section 2.2.2.

An example of a data set showing an early attempt to monitor O_2 levels in breath, with a value obtained every 100 ms is shown in Figure 2.8a.

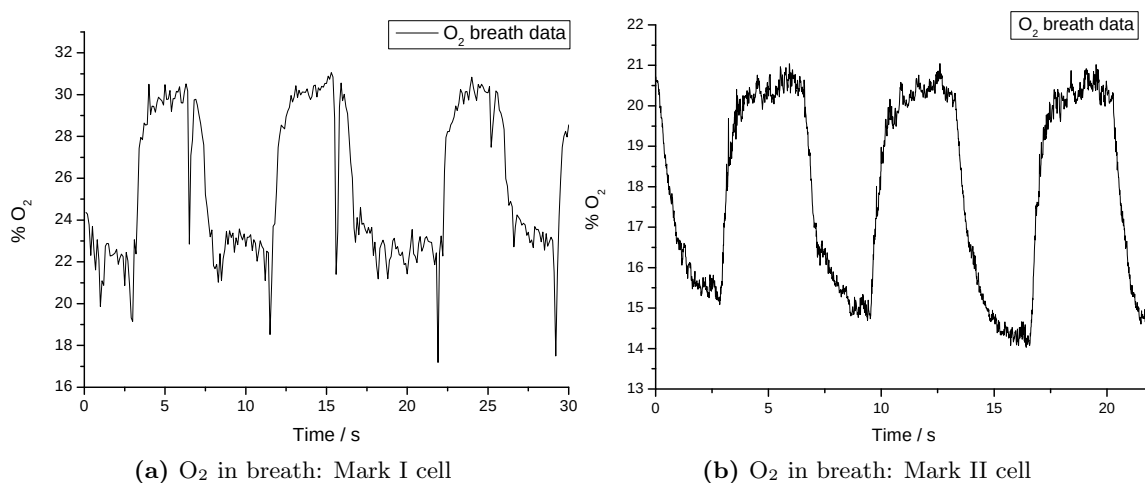


Figure 2.8: Graph (a) shows an example of the change in O_2 concentration in breath taken over 30 s, with a data point every 100 ms, in the Mark I cell. Graph (b) shows the improvement in signal-to-noise when using the new Mark II cell with heated baffles system, with a datapoint taken every 10 ms (transtion R15Q16).

These data show some of the first attempts at monitoring realtime changes in O_2 in breath using CEAS, however they also show large noise spikes in the measurements when there is a rapid change in direction of the gas flow. This can clearly be seen at the beginning of inhalation (for example, at 12 seconds in Figure 2.8a) and exhalation (for example, at 16 seconds in Figure 2.8a). This turbulence is most likely due to the cell design, which has areas of dead space and particular hot spots near the mirrors that all contribute to a chaotic flow in the cell. This in turn is causing a level of instability in the cavity that is enough to perturb the measurements. To overcome this, a second measurement cell was built to improve the flow dynamics and heating of the system.

A schematic of the new cell design, designated the Mark II, is shown in Figure 2.6. The cell is made entirely of aluminium with resistors embedded along its length for heating. A thermostat is also employed to keep the temperature constant. The cavity mirrors are placed 4 cm apart as previously. At the gas input and output of the cell, there are sections of heated aluminium baffles of density and length to keep the air flow regular and to keep the temperature of the sample constant. These lengths of baffles are designed taking into account the typical inspiratory flow rate and breath temperatures, and are 2.4 cm in length at the subject end and 7.2 cm at the exhaust end. Both are 3.5 cm in total diameter and the baffles themselves consist of coiled, corrugated aluminium foil resulting in a densely

packed series of tubes ~ 1 mm in diameter. Another important feature is that this design greatly reduces the dead space in the cell, and the ends have been adapted to connect to standard tubing and bacterial filters [*Intersurgical*].

This new design is not only an attempt to improve flow dynamics in the cell by minimising dead space, and channelling the flow through sections of baffles at a set temperature, but also takes into consideration the impact of changes in temperature on the absorption data itself. This is due to variations in temperature propagating through the populations of the rotational levels in the molecule as modeled by a Boltzmann distribution

$$\frac{N_J}{N} = \frac{(2J+1)\exp\left(-\frac{hcE_J}{k_B T}\right)}{q_R} \quad (2.1)$$

where k_B is the Boltzmann constant, h is Planck's constant, E_J and N_J are the energy and population associated with the lower level of the transition defined by the quantum number J , N is the overall population and q_R is the rotational partition function.

The population dependence on temperature translates as an effective change in the absorption cross-section of the molecule. Therefore, if unaccounted for, this will be misinterpreted as a variation in concentration since $\alpha(\nu) = \sigma(\nu)c$. To minimise errors such as these, the design of this new cell is such that the gas flow will be kept at a constant temperature and $\sigma(\nu)$ should be invariant.

The control of temperature and flow through the cell greatly improves the breath traces, as shown in Figure 2.8b. In fact, the overall improvement in noise is such that less averaging is required and the time resolution has been improved from 100 ms to 10 ms, the desired limit for this analyser.

The current setup has now been designed to such a level that real-time measurements of O_2 via CEAS with a 10 ms time resolution are possible. The studies described so far have highlighted potential interactions of H_2O with specific coatings on cavity mirrors; an effect that can be highly detrimental to breath analysis, and therefore careful selection of cavity mirrors is required. As well as this, the effects of flow and temperature in the measurement cell can impact greatly on the noise on the data, and as such the analyser requires careful design and construction to reduce these effects.

2.4 Direct absorption studies on CO₂

2.4.1 Spectroscopy of CO₂

CO₂ is a linear molecule with $D_{\infty h}$ symmetry with its spectroscopy governed by four fundamental vibrational modes: a symmetric stretch, an asymmetric stretch and a doubly degenerate pair of bends. A summary of these normal modes and their assignment is given in Table 2.2.

Mode	Description	Symmetry	Position / cm ⁻¹
ν_1	Symmetric stretch	Σ_g^+	1337
ν_2	Bend	Π_u	667
ν_3	Asymmetric stretch	Σ_u^+	2349

Table 2.2: Description of the fundamental vibrational modes of CO₂

As both the asymmetric stretch and bends bring about a change in the dipole moment of the molecule, these modes are infrared active. The asymmetric stretch alters the dipole moment parallel to the molecular axis, and so transitions involving ν_3 give rise to parallel bands in the spectrum, whereas the bends alter the dipole moment perpendicular to the molecular axis, giving rise to perpendicular bands. There is vibrational angular momentum associated with excitation of these degenerate bends and this gives rise to the appearance of a *PQR* branch structure, i.e., transitions $\Delta J = -1, 0, +1$, as opposed to the *PR* structure observed for the parallel bands.

The remaining ν_1 mode, which does not change the molecular dipole moment and is therefore infrared inactive is, however, Raman active. The spectrum of the ν_1 band actually consists of a pair of features at 1285 and 1388 cm⁻¹ due to an effect known as Fermi resonance. This describes the interaction between the ν_1 mode and the first overtone of the bending vibration, $2\nu_2$, which lies very close in energy to ν_1 at 1334 cm⁻¹. The similarity in energy of these two states of the same symmetry gives a new band structure that results from a linear combination of these two modes, resulting in a splitting of the spectrum.

The spectrum also only exhibits lines resulting from rotational levels of even J , which is a result of nuclear spin statistics resulting from the Pauli principle, in a similar manner that has already been described for the spectroscopy of O₂.

The conventional nomenclature for CO₂ follows the form $(\nu_1, \nu_2, l_2, \nu_3, r)$ where ν_n indicate the quantum number associated with each normal mode, l_2 gives the magnitude of the vibrational angular momentum associated with the bending mode ν_2 and r gives the ranking of the perturbation introduced by Fermi resonance. Transitions are described in terms of the branch, lower state and symmetry ($\Delta J J'' Sym''$) where the symmetry is either *e* or *f*

for ℓ -type doubling. For the work in these thesis, the R18e transition from the combination band $2\nu_1 + \nu_3$ is probed at 4991.23 cm^{-1} , with cross-section of $1.26 \times 10^{-21} \text{ cm}^2 \text{ cm}^{-1}$, which is ideal for sensitive detection.

2.4.2 Experimental details

As discussed previously, the detection of CO_2 is experimentally less complex than O_2 , since single pass direct absorption spectroscopy is sufficient. The laser used in these studies was a $2 \mu\text{m}$ VCSEL [Vertilas, VL-2004-1-SP-A5] controlled with a commercially available controller mount [Thorlabs, VITC002], with an AR coated 6.9 mm focal length lens [Altechna] placed to collimate the beam. Initially, CO_2 absorption was studied in an aluminium 4 cm cell with angled CaF_2 windows made in-house. The transmitted light was focused onto a long wavelength range type InGaAs PIN photodiode detector [Hamamatsu, G5852-01]. A schematic of the setup is illustrated in Figure 2.9.

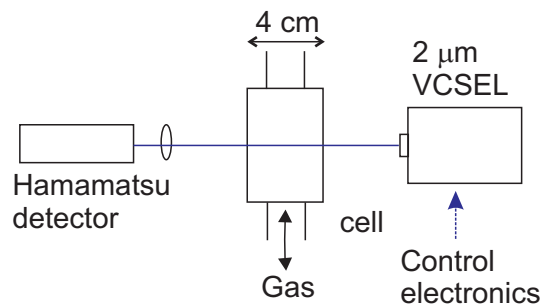


Figure 2.9: Schematic of the setup for investigating the potential of monitoring CO_2 in breath.

2.4.3 Studies on CO_2 in breath

When attempts at breathing through the cell were made, as with the O_2 measurements, heating of the windows is shown to be crucial as condensation causes a large reduction in the transmitted signal. Heating of the windows is achieved by attaching resistors to the aluminium holdings of the windows, in a similar manner to the O_2 measurements. The necessity of heating the cell windows for the CO_2 measurements is demonstrated in Figure 2.10.

Unlike with CEAS of O_2 , the CO_2 measurements were not as susceptible to issues with flow, since these minor instabilities do not impact as highly on a direct absorption system as they do on an optical cavity, where the extended pathlength is ~ 4 orders of magnitude larger.

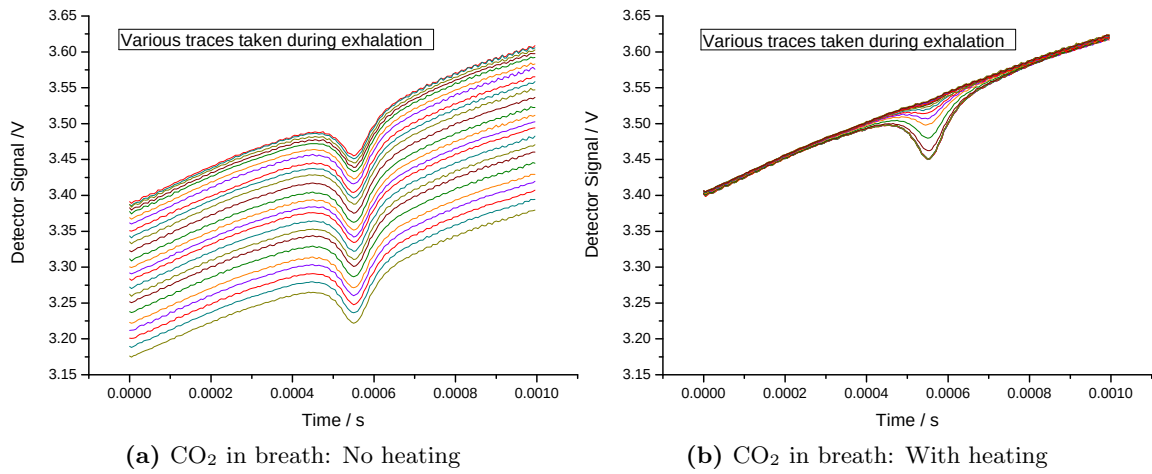


Figure 2.10: Graph (a) shows a selection of CO₂ absorption traces taken during exhalation exhibiting a decrease in overall signal as condensation occurs on the windows. Graph (b) shows similar traces taken with the windows gently warmed, exhibiting little variation in overall signal.

With variations in the baseline due to H₂O condensing on the windows reduced through heating, real-time breath CO₂ concentration measurements are possible using the LGA. The process of data acquisition and analysis is similar to what has been described already for O₂, however, a calibration gas with 5 % CO₂ is used instead of air to obtain I_{ref} and spectra are processed using Equation 1.1 as opposed to 1.25. An example of the processed breath traces obtained for a subject breathing for 30 s with a point every 20 ms is shown in Figure 2.11.

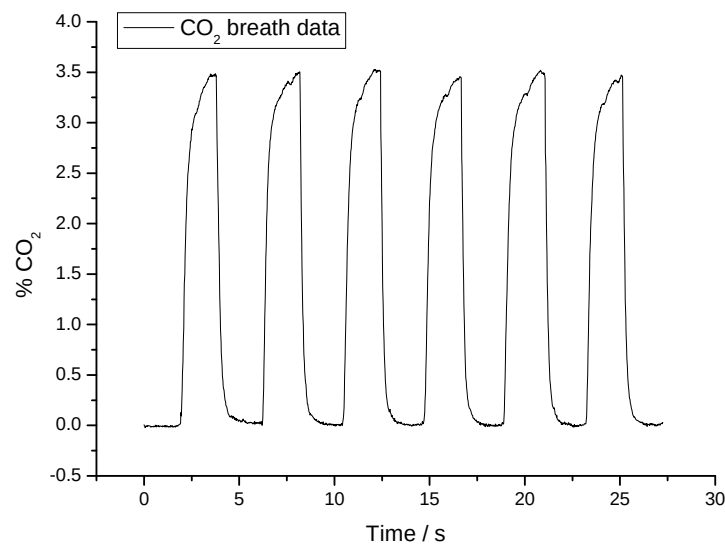


Figure 2.11: Data showing typical variations in CO₂ in breath as monitored by the LGA, with a data point taken every 20 ms.

As can be seen from this early attempt at monitoring CO₂ levels in breath using the LGA, the data exhibit very low noise levels and exhibits CO₂ levels consistent with inhaled air (0 %) and exhaled air (typically 3 - 4 % for this subject at rest).

At this stage, the monitoring of O₂ and CO₂ in breath in separate setups have been demonstrated, and issues with condensation, heating and flow dynamics have all been solved. The next stage was to combine these measurement systems in a single monitor to simultaneously detect O₂ and CO₂.

2.5 Monitoring respiration: Simultaneous measurements of O₂ and CO₂

To combine the O₂ and CO₂ measurements, a single device, the Mark II cell described in section 2.3.4 was used. Since the cavity mirrors used in this cell are only highly reflective in the 760 nm region, they can in effect act as windows for the 2 μ m radiation for the detection of CO₂, and the 1.3 μ m radiation for detection of H₂O as described in later sections. The lasers for monitoring each gas were then counter-propagated through the Mark II cell, as shown in a schematic of the setup in Figure 2.12.

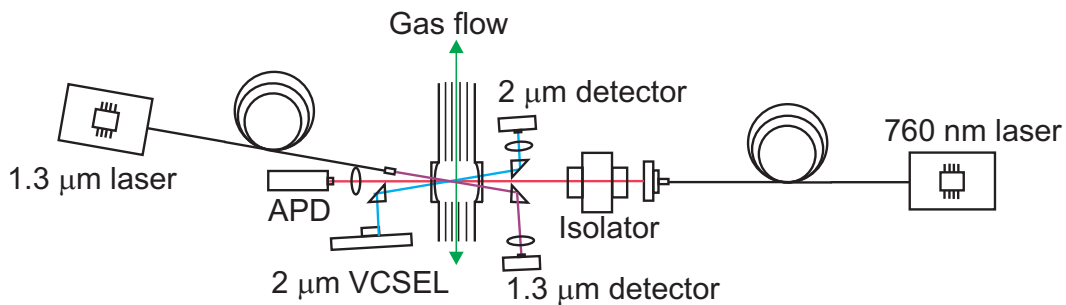


Figure 2.12: Schematic of combined setup using the Mark II cell. Detection paths are indicated for O₂ (red) and CO₂ (blue). The detection path used for H₂O detection (purple) in later studies (section 2.6) is also shown.

2.5.1 Comparisons with a Datex Normocap breath analyser

At this stage, the electronics are such that the full linear regression algorithm analysis can only be used on two gases simultaneously. Since measurements of O₂ and CO₂ are the more relevant in monitoring breath-by-breath gas exchange, the LGA was used to monitor these two gases in a comparison study with a commercially available breath analyser, a *Datex Normocap 200* breath analyser.

The Datex is a sidestream analyser using IR spectroscopy for detection of CO₂ and the paramagnetic effect for O₂, and is a typical example of the type of instrument found in

hospitals to monitor O_2 , CO_2 and N_2O , a common anaesthetic gas, in breath. The sample is drawn off from the main respiratory flow by a length of Nafion tubing, which is designed to bring exhaled air down to the daily atmospheric humidity level. This prevents condensation within the instrument itself, which is unable to monitor H_2O levels. In this comparison study, the subject breathed through the Mark II analyser and the O_2 and CO_2 levels were analysed using the LGA. At the same time, a sample was drawn off from a point near to the subject's mouth by the Datex catheter. The results from the LGA were then compared to the results from the Datex, and are shown in Figure 2.13.

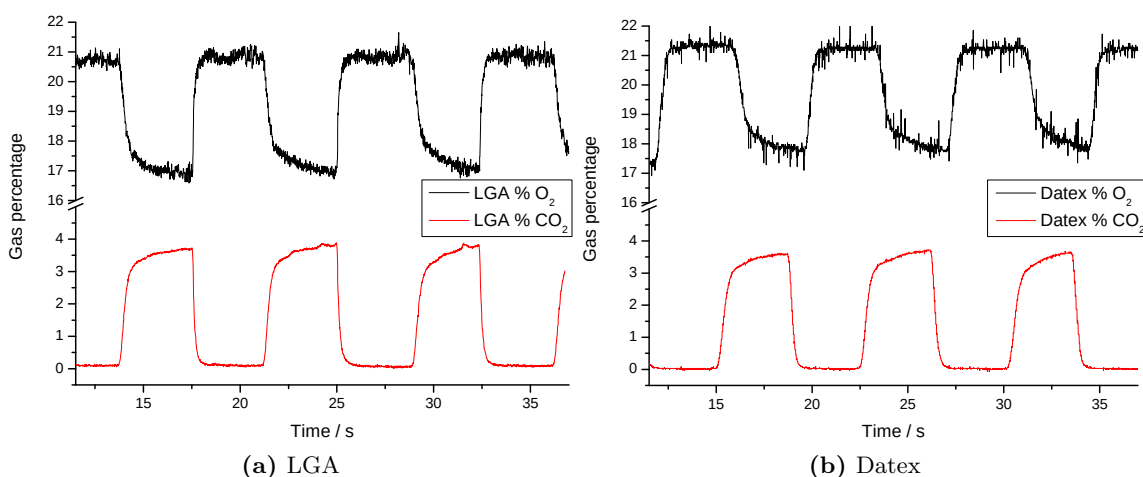


Figure 2.13: Graph (a) shows O_2 and CO_2 percentages as returned from the LGA and Mark II cell. Graph (b) shows equivalent values returned from the Datex, which was sampling the respiratory flow. In both graphs CO_2 levels are given in red and O_2 levels are given in black.

The data in Figure 2.13 show some of the first simultaneous measurements of O_2 and CO_2 by CEAS and direct absorption spectroscopy respectively, using the LGA linear regression algorithm to obtain concentration values. When comparing to the Datex, the data obtained by the LGA are comparable in absolute values and noise levels, however, the the LGA is producing a readout every 10 ms, whereas the Datex achieves a time resolution of only ~ 50 ms, and has a slower rise time as shown in Figure 2.14. In these data, a region of the breath curve showing the rapid increase in CO_2 during exhalation as recorded by the LGA and the Datex is shown, with the slower monitoring of the increase by the Datex indicated in red.

Another disadvantage of the Datex analyser compared to the experimental one developed in this work is the delays introduced by the use of different measurement techniques and the sidestream sampling approach, which can be more clearly seen in Figure 2.15.

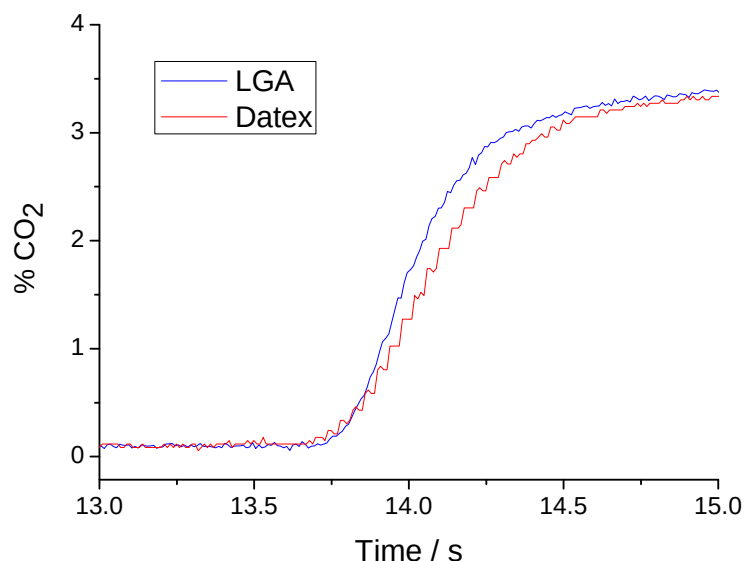


Figure 2.14: Data showing difference in response to rapid changes in CO_2 levels from the LGA breath analyser (blue) and the Datex analyser (red). Note that data have been time-aligned for ease of comparison.

Firstly, the data in Figure 2.15 show that the Datex records the start points of inhalation and exhalation ~ 2 s after the LGA analyser does. This is due to the delay introduced by the catheter sampling of the Datex as opposed to the in-line approach of the LGA setup. Secondly, in the Datex readouts, there is a delay in the start points of inhalation and exhalation between the O_2 and CO_2 measurements themselves. This delay is indicated in Figure 2.15 for an example exhalation, where the start point for O_2 is indicated with a blue dashed line, and can be seen to lag the start point for the CO_2 , shown with a green dashed line. This delay is due to the fact that the monitoring of the paramagnetic effect for O_2 detection is a slower method than IR spectroscopy used for CO_2 , and so the breath-by-breath measurements are offset from each other. In the results from the LGA analyser which utilise spectroscopic methods only, it can be seen that the O_2 and CO_2 turning points are perfectly aligned, and there are no such delays.

Other differences that can be seen between the Datex and LGA traces is in the absolute values obtained and this can be attributed to errors in the calibration of the analysers. In particular, the Datex shows an error in the O_2 measurements, as it reads above atmospheric O_2 concentration for inhalations. As well as this, the Datex requires the removal of some of the H_2O in breath to prevent condensation, which in itself can skew the effective percentages returned, as a partial pressure component to the overall gas mixture, the H_2O , is removed to different degrees throughout the breath.

Overall, compared to a commercially available instrument, the developed Mark II analyser

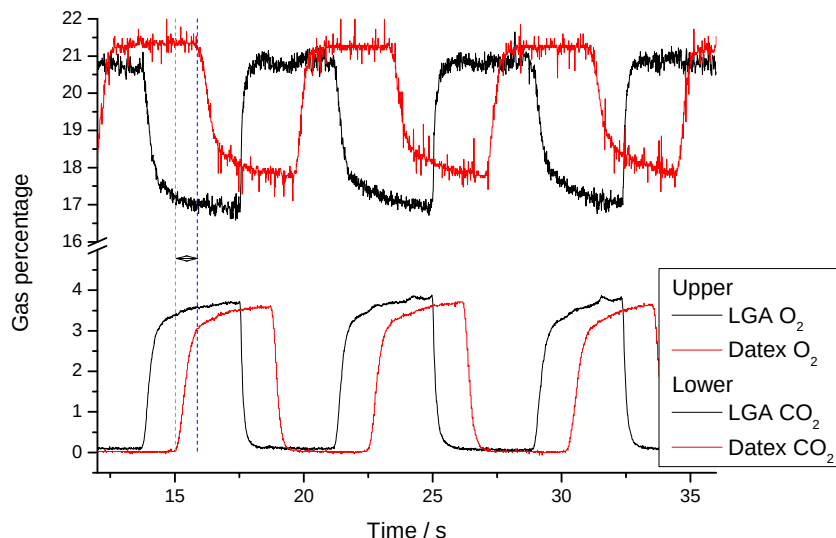


Figure 2.15: Comparison of simultaneous O₂ (upper traces) and CO₂ (lower traces) measurements taken by the experimental setup and analysed by the LGA (black) and the Datex (red). The indicated start point of exhalation for each gas measured by the Datex is indicated by dashed lines, with O₂ in blue and CO₂ in green.

and LGA based processing of the data show great improvements in removing delays in breath-by-breath gas exchange measurements of O₂ and CO₂. From the noise on the data given in Figure 2.15, absolute detection levels of 0.26 % O₂ and 0.04 % CO₂ are obtained with a time resolution of 10 ms. This is well within the required limits of the analyser as set out at the start of this work, which were an absolute detection limit of 1 % in 10 ms. The detection levels are also comparable to a commercially available mass spectrometer used in similar analysis [*Airspec, QP 9000*], which has detection limits of ~ 0.16 % O₂ and ~ 0.05 % CO₂.

2.6 Monitoring respiration: Towards measuring H₂O, flow and temperature

The detection of the third exchange gas, H₂O, would be beneficial to fully understanding breath-by-breath gas exchange. However, the breath analyser at this stage is currently designed to focus on O₂ and CO₂ and therefore is only capable of using the full linear algorithm analysis provided by the LGA on two gases simultaneously. However, an estimate of the H₂O levels can be obtained using a slightly more experimentally simplistic approach, made possible by the high stability of the 1.3 μm laser used for H₂O detection, and the high absorption cross-section of H₂O in this region.

2.6.1 Spectroscopy of H₂O

The H₂O molecule has C_{2v} symmetry with three normal modes, two of which are predominantly stretching modes and one which is mainly a bending mode. The details of the normal modes are given in Table 2.3.

Mode	Description (predominant motion)	Symmetry	Position / cm ⁻¹
ν_1	Symmetric stretch	A_1	3652
ν_2	Bend	A_1	1595
ν_3	Asymmetric stretch	B_2	3756

Table 2.3: Description of the fundamental vibrational modes of H₂O.

As all three modes result in a change in the dipole moment, they are all infrared active and as H₂O is not a centrosymmetric linear molecule, the exclusion rule that no modes can be both infrared and Raman active no longer applies, and all three normal modes are seen to be Raman active as well.

Transitions from a particular band denoted by (ν_1, ν_2, ν_3) in H₂O are conventionally assigned as $(J', K'_a, K'_c) \leftarrow (J'', K''_a, K''_c)$ where K_a and K_c give projections of J on the molecular rotational axis a and c . For the work in this chapter, the $(3, 1, 3) \leftarrow (2, 1, 2)$ transition at 7306.75 cm⁻¹ from the $\nu_1 + \nu_3$ band, with $\sigma_{INT} = 1.8 \times 10^{-20}$ cm² cm⁻¹ was studied.

2.6.2 Experimental details

Instead of determining the H₂O concentration by scanning the laser over an entire absorption feature, and fitting the whole spectrum, it is possible to monitor the change in peak absorbance only by simply positioning the laser at the central frequency of the absorption feature. The variation in the DC signal on the detector can then be interpreted as a variation in concentration. This method is referred to as single point analysis and doesn't require complicated electronics or computational power to scan the laser, or fit the resulting data.

Experimentally, the laser used for H₂O detection was a 1368 nm fiber-coupled diode laser [NTT Electronics, NLK1E5EAAA] housed in a temperature stabilised mount [Thorlabs, LM14S2], the output of which was collimated with an AR-coated fiber-coupling lens system [Thorlabs, F220FC-C]. The laser was controlled using commercially available temperature and current controllers [Thorlabs, TED200C and LDC205B respectively]. The laser was then aligned through the Mark II cell and onto a second long wavelength range Hamamatsu detector as has already been indicated in Figure 2.12. The voltage output from this detector as H₂O concentrations varied could then be monitored.

The monitoring of this voltage output gives the real-time changes required, when measured simultaneously with the O₂ and CO₂, however, some post processing of this signal is required to obtain an absolute value for the H₂O concentration. Firstly, a DC level of the background, I_0 is required, and is obtained by flushing the cell with N₂. The DC levels on the detector then obtained during a breath measurement are then converted into an absolute value using Equation 1.1, with the integrated cross-section, σ_{INT} , substituted by a peak cross-section, σ_{peak} . The disadvantage to monitoring the H₂O concentration in this way is that it is not possible to compensate for changes in σ_{peak} , due to variations in the absorption linewidth as the constituents in the gas mixture vary. Instead, an average value for σ_{peak} as modeled by using HITRAN data for different breath compositions was used to convert the detected signal into an H₂O concentration. Whilst a full analysis of the absorption feature utilising σ_{INT} would be ideal, as a first approximation, this approach enables the monitoring of changes in H₂O levels and the form that they follow during a breath.

2.6.3 Studies on O₂, CO₂ and H₂O in breath

To monitor the concentration levels of all three gases simultaneously, the percentage values of O₂ and CO₂ as returned by the LGA linear regression algorithm were converted into a voltage output from the DAQ-2010 cards. These, as well as the voltage from the 1.3 μm detector for H₂O were collected by a multichannel ADC [*National instruments, USB-6009*] and fed into a LabView display program for simultaneous monitoring on a PC. The returned voltages were then converted back into gas percentages. An example of typical traces for simultaneous, calibrated measurements of O₂, CO₂ and H₂O in breath is shown in Figure 2.16. The O₂ data are taken for transition R11Q12 at 760.445 nm.

Several conclusions from the measurements of the three exchange gases can be drawn from the data in Figure 2.16. Firstly, it can be seen the absolute H₂O levels are fairly low, ranging from ~ 1 % for atmospheric H₂O vapour level, to only ~ 2.5 % in breath. Typically, the level of H₂O measured in exhaled breath should be the saturated vapour pressure, P_s , of H₂O at body temperature, 37°, which can be described by the August-Roche-Magnus approximation [45]

$$P_s = 4.582 \exp\left(\frac{17.625T}{T + 243.04}\right) \quad (2.2)$$

This predicts a maximum H₂O level in exhaled air of 6.2 %, a level that has been confirmed by selected ion flow mass spectrometry measurements undertaken by Španěl *et al.* [46]. This predicted level is much higher than what is measured here, however, this can be

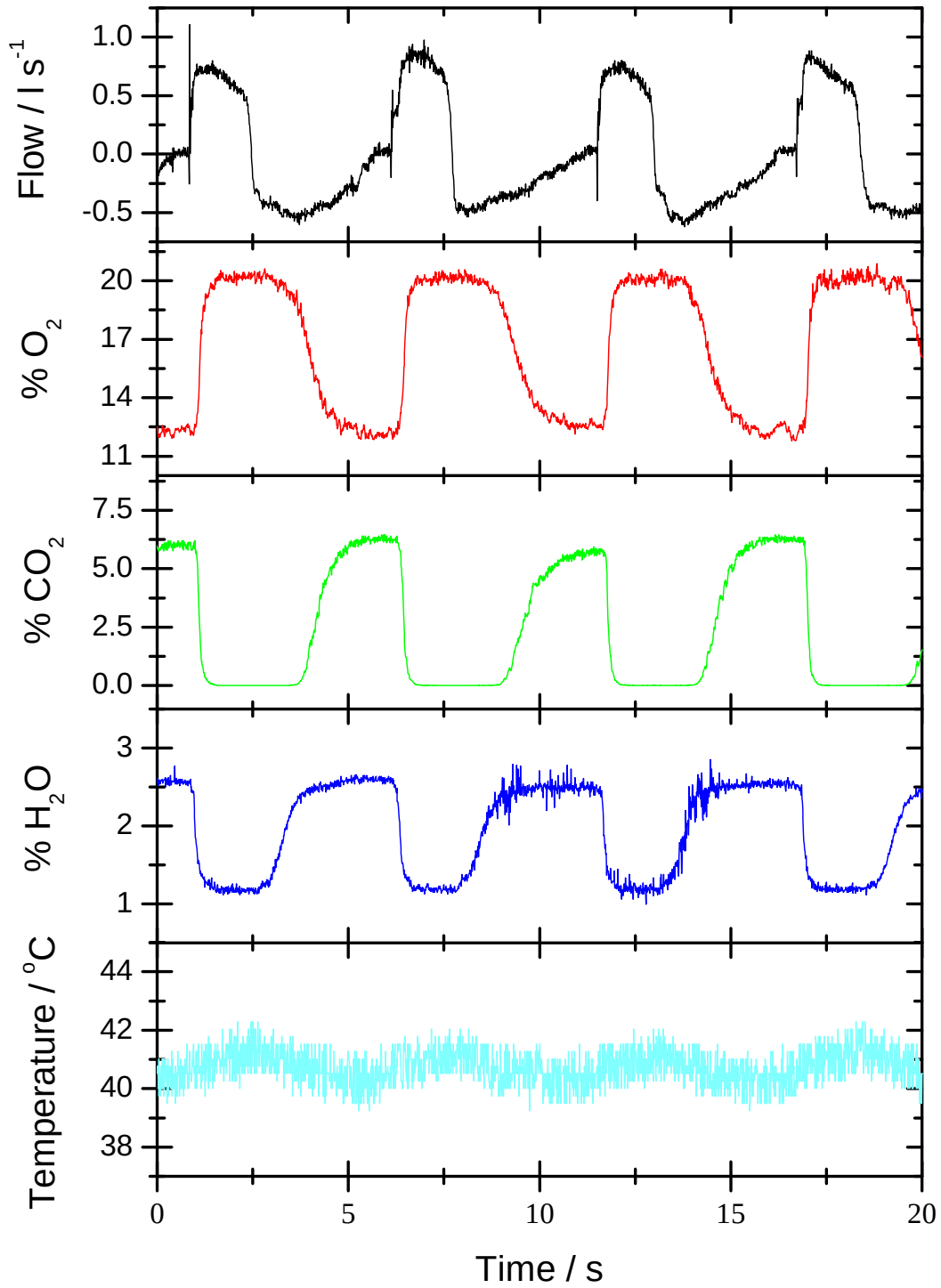


Figure 2.16: Examples of O₂, CO₂ and H₂O in breath with data taken every 10 ms. Initial measurements of flow and temperature are also shown.

attributed partly to an overestimation in σ_{peak} as discussed previously, but primarily to loss of H₂O in the experimental setup. This occurs through condensation in the length of tubing between the subject's mouth and the analyser, and in absorption in the bacterial filters.

Secondly, the measurements on the exchange gases display characteristics that show the impact of the anatomic dead space in the lung on this experiment. On exhalation, the initial sample pushed through the measurement cell is in fact the same O_2 and CO_2 composition as the last sample inhaled, as a volume of this will remain in the conducting airways of the lung, and in any tubing in the experiment, the volume of which can be estimated as ~ 200 ml. This initial exhaled sample will therefore appear similar to inhalation in terms of O_2 and CO_2 levels. However, this sample has also been in the dead space in the conducting airways of the lung, which are at $37^\circ C$. Therefore, the gas that is exhaled from the anatomic dead space, although identical to what was last inhaled in terms of O_2 and CO_2 concentrations, has taken on H_2O . This translates as a rise in H_2O content on exhalation, which slightly precedes the start of the O_2 decrease and CO_2 increase, and this exact behaviour is observed in the data shown in Figure 2.16.

The other measurements shown in Figure 2.16 are that of the temperature in the cell and the respiratory flow. The temperature measurements are obtained by inserting a calibrated thermocouple into the breath stream, and obtaining the response as a voltage via the USB-6009 ADC. The flow is monitored using a Fleisch head, which operates by monitoring the pressure differential across a length of baffles, and can be inserted into the subject end of the Mark II cell. The response of the Fleisch head pressure transducer can be read as a voltage output using the USB-6009 ADC and calibrated into a l/s flow rate.

Although the Fleisch head is correctly monitoring the form of the flow speed and direction, the electronics in the pressure transducer readout are too slow, hence there is a delay in the turning point in the flow (at 0 l/s) and the start point of inhalation and exhalation as indicated by O_2 and CO_2 concentrations. Therefore, a faster way of monitoring the flow is required to time align the flow data.

The temperature variations, however, are more promising. There are no dramatic change in the overall temperature of the sample, only small variations, $\sim 1^\circ$, between inhalation and exhalation. This shows the heated baffles are succeeding in keeping the gas temperature fairly consistent throughout the cell.

2.7 Conclusions from the Mark I and II breath analysers

Overall, the potential of using an all optical analyser for simultaneous measurements of the three exchange gases can clearly be seen from the data presented in Figure 2.16. The O_2 and CO_2 percentages themselves have been demonstrated to have detection limits comparable to mass spectrometry and within the aims of this work. The time resolution of the instrument is also an improvement on currently available instruments, such as the Datex analyser,

and delays in the system have been removed by the use of in-line measurements. As well as this, initial studies on H_2O using single-point analysis have already shown interesting physiological information. From these studies, the final improvements in terms of the setup electronics and data handling, the cell design itself and spectroscopic considerations can be incorporated into a final prototype, the Mark III.

2.8 Building the prototype breath analyser: Design considerations

In these final sections, the knowledge gained from the studies on the previous Mark I and II designs is combined into a final prototype, incorporating careful selection of the laser sources and cell design. As well as this, potential improvements in the measurements of the gas concentrations through a more thorough investigations into the spectroscopy of the transitions in O_2 , CO_2 and H_2O are discussed. Finally, improvements in the LGA processing are incorporated to monitor H_2O in a more quantitative manner than has been discussed previously.

2.8.1 Selection of laser sources

One of the main issues that has not been addressed in previous attempts to build a measurement cell is the necessity of enclosing all laser radiation as a safety precaution. The simplest and most elegant way to achieve this is to use fiber-coupled laser systems that can inject the radiation directly into the cell. The light then exiting the cell can then be monitored using detectors that have been designed into the measurements cell structure itself. Thus, all laser radiation is contained.

The previous setups have already utilised a single-mode (sm) fiber coupled NTT electronics $1.3\ \mu\text{m}$ laser for H_2O detection which is therefore ideal for the new cell design. A new $2\ \mu\text{m}$ VCSEL, identical to the previous model but with a sm-fiber coupled output was also obtained from Vertilas.

However, for O_2 detection, whilst the previously used Eagleyard DFB lasers were already fiber-coupled and therefore ideal in that respect, their unreliability proved problematic. The Eagleyard DFB lasers manufactured at this wavelength all exhibited degradation over several months, resulting in multimode behaviour and were therefore deemed unsuitable for the design of the prototype. Instead a new $\sim 760\ \text{nm}$ VCSEL [*ULM, ULM760-01-TN-S4LFZT*] was incorporated into the setup. The tuning of the VCSEL laser is only $\pm 1\ \text{nm}$, and so careful consideration was given to the central wavelength, since for O_2 , there are

many possible transitions around 760 nm that could be probed. These transitions display different absorption characteristics, and in particular different behaviour with changes in temperature.

Previously, the impact on the absorption cross-section that changes in temperature can have was discussed in section 2.3.4. This effect was minimised by heating the cell to a constant temperature, and as has been demonstrated with the Mark II design, only small fluctuations of $\sim 1^\circ$ were seen to perturb this consistency. However, a further way of reducing this temperature dependence is to select a transition, and therefore a laser operating wavelength, where the population of the lower J state of the transition exhibits minimal temperature dependence.

The populations of various J states can be modelled by the Boltzmann distribution given in Equation 2.1 and for O_2 follow the form shown in Figure 2.17a, where the case of $J'' = N''$ is illustrated. The impact of the temperature dependence on the observed peak absorption, (Abs), for O_2 in air at 760 nm can be modeled by examining the temperature dependence of the concentration of the sample, and of the populations as given by the Boltzmann distribution. Therefore, by then differentiating with respect to temperature, it is possible to see which J states will display the greatest variation in absorbance signal with changing temperature. This dependence is also illustrated in Figure 2.17b.

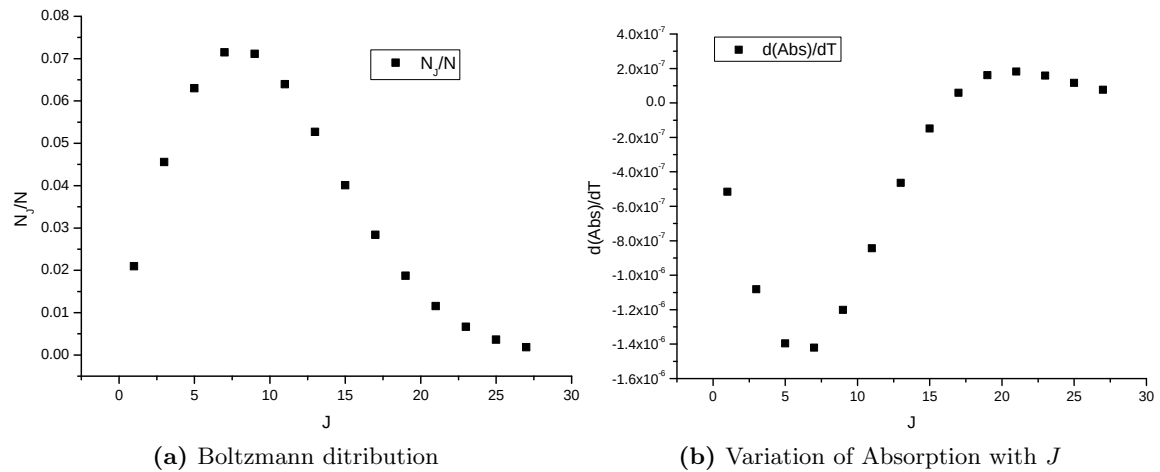


Figure 2.17: Graph (a) shows Boltzmann distribution for populations of various J states in O_2 and graph (b) shows dependence of observed peak absorbance on temperature for various J states.

So far for breath measurements on O_2 , $J = 11$ has been observed, and as can be seen from Figure 2.17b, moving to higher J states would reduce the temperature dependence slightly. Therefore, A VCSEL centred at 760.0 nm was selected so that a compromise was made between observing a transition with a higher $J = 13$ state, thus reducing the temperature

dependence by a factor of ~ 2 , and yet still having a relatively high absorption cross-section. The effects of various J levels described here are relatively small, with changes in temperature of 1 °C resulting in errors in the concentration measurements of less than 0.5 % at worst. However for optimal measurements of concentrations these small variations need to be taken into account or minimised.

The disadvantage of the ULM 760 nm VCSEL is that it was not fiber coupled by the manufacturer, and instead was coupled into a multi-mode (mm) fiber [Thorlabs, AF5105/125Y] with a standard fiber coupling lens system at the input and output [Thorlabs, F220FC-B]. The mm fiber for coupling the 760 nm radiation was employed to minimise power losses, as opposed to those for a single mode (sm) fiber, since the 760 nm VCSEL only emits < 1 mW.

2.8.2 Improving the cell design

With all three laser systems fiber-coupled, delivery into the measurement cell can now be considered. In this cell design, a description of which is given in Figure 2.18, the compatible measurement methods of both CO₂ and H₂O are used to advantage, by delivering the two lasers along the same path in the cell. This is achieved through combining the 1.3 μm and 2 μm radiation into a single fiber output using a 2×2 fiber coupler [Thorlabs, C-WD-AL-01-H-2210-35-AP/AP], which merges the two sources in a 90:10 ratio. In this case, the lower power 2 μm radiation is injected into the 90 % port. The combined output is then injected directly into the cell using a grin lens placed at an angle through an aperture on the top face of the cell. The grin lens is employed instead of a standard fiber coupler, as there is no free space path in the grin lens where H₂O could absorb. A small silver mirror at the base of the cell reflects the radiation back up to a second aperture where the detector is placed. Using this v-shaped path for the direct absorption measurements results in a ~ 5 cm path length, that can be measured accurately by flowing a CO₂ calibration mixture through the cell. The detector used in this case is a newer model of the Hamamatsu long wavelength range detector used for previous H₂O and CO₂ measurements, which has been adapted such that it inserts directly into the cell body [Hamamatsu, G8372-01]. This detector is used for measuring both CO₂ and H₂O absorption signals from the two lasers, by rapidly alternating which laser is on throughout the measurement, and then separating the two signals in the post-processing of the data.

For the O₂ measurements, the 760 nm radiation is coupled into the Layertec cavity mirrors on the side faces of the cell by mounting the output fiber coupler on a cage system suspended in front of the cavity input mirror. The cavity length is also reduced compared to the Mark II cell and is now 2.75 cm, to be of a more similar diameter to standard breathing tubing.

The detected output from the cavity is monitored using a commercially available large surface area (10×10 mm) silicon photodiode detector [Hamamatsu, S1337-1010BR]. This large detector covers the central portion of the exit cavity mirror volume, so that focusing of the cavity output is not required and the detector can be affixed directly onto the cell body. The main body of the cell itself is aluminium for heating, with two end pieces to attach to standard breathing tubes and filters. With the optical pathlength reduced to a size similar to the diameter of the breathing tubing, it is expected that flow issues and turbulence will be minimised.

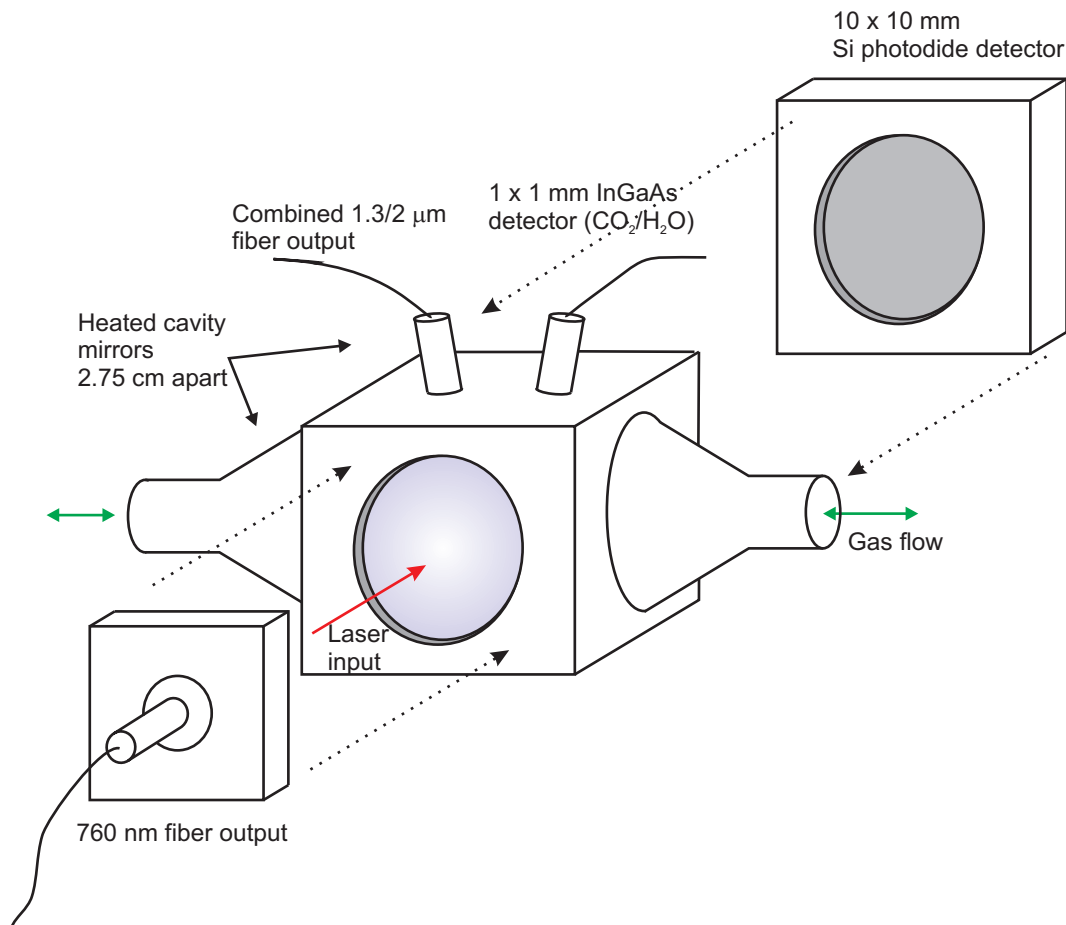


Figure 2.18: Schematic of the final prototype breath analyser, the Mark III. The diagram shows end sections that affix to faces housing the cavity mirrors to deliver and collect the 760 nm radiation.

Finally, the required hardware and programming was installed so that all three exchange gases, O_2 , CO_2 and H_2O could be monitored simultaneously using full spectrum analysis, and not the single point analysis that had previously been used for H_2O . With this new design, able to monitor the three exchange gases simultaneously and with the desired laser systems incorporated into the device, it is possible to investigate other issues that may impact on the accuracy of the measurements, namely the variation in the measured absorption lineshapes with changes in pressure broadening.

2.9 Building the prototype breath analyser: Spectroscopic considerations

One of the main considerations for analysing spectra taken from breath samples in the analyser is that they are at atmospheric pressure. As discussed in section 1.3, high pressure samples will be dominated by Lorentzian broadening of the feature, the extent of which depends on the unique interactions between a gas and any buffering species, and the partial pressures of the gases involved.

Currently, the linear regression algorithm performs a simple scaling of the data to a known concentration profile, and whilst this has proved successful in fitting sampled spectra at high speed, this form of linear regression does not compensate for any potential variations in the absorption feature width through a breath cycle. As the overall pressure remains at one atmosphere, these variations will occur as the partial pressures of O₂, CO₂, N₂ and H₂O change during inhalation and exhalation. To assess how big an impact on the absorption feature width these variations may have, and therefore how crucial they are to improving the fitting of the data, a series of pressure broadening studies was performed.

These studies were carried out on the absorption feature of interest for breath analysis using the prototype analyser, the line parameters of which are summarised in Table 2.4. The following sections describe the pressure broadening studies on CO₂ and O₂ by the main constituents in breath (N₂, O₂ and CO₂). The other measurements of interest include the broadening of these gases by H₂O, as well as the H₂O self-broadening which will become relevant as full peak analysis of the H₂O feature is incorporated into the analyser. The studies involving H₂O are described at the end of the section, as experimentally they necessarily differ from measurements involving simply N₂, O₂ and CO₂.

Gas	ν_0 / cm ⁻¹	σ_{INT} / cm ² cm ⁻¹	Assignment
H ₂ O	7306.75	1.80×10^{-20}	$\nu_1 + \nu_3, (3, 1, 3) \leftarrow (2, 1, 2)$
CO ₂	4991.26	1.26×10^{-21}	$2\nu_1 + \nu_3, R18e$
O ₂	13076.33	6.25×10^{-24}	$b^1\Sigma_g^+ \leftarrow X^3\Sigma_g^-, P13P13$

Table 2.4: Line parameters for absorption features chosen for analysis of O₂, CO₂ and H₂O in breath. Data are taken from the HITRAN database.

2.9.1 Pressure broadening of CO₂

The pressure broadening of CO₂ will be determined by the contributions from self-broadening and from the buffer gases N₂, O₂ and H₂O, with the dominant contributions likely to be from N₂ and O₂, as the level of both CO₂ and H₂O in breath rarely exceeds 5 %. In this section the contributions from self, N₂ and O₂ broadening are described.

To measure these contributions, the 2 μm VCSEL was aligned through an aluminium 4 cm cell already described for the CO_2 breath measurements in section 2.4.2. The cell has several ports so that samples of the required gases could be gradually bled in and monitored using either a 100 Torr or an atmospheric pressure gauge where appropriate [Leybold]. The light exiting the cell was focused onto the Hamamatsu detector as used in section 2.4.2. The measurements were taken using direct absorption spectroscopy, as is used in the breath analyser, to monitor the variation in the Lorentzian contribution, ν_L , to the Voigt lineshape of a sample of CO_2 as higher pressures of buffer gas were added. The increase in ν_L can then be interpreted as a pressure broadening coefficient, γ_{gas} , usually quoted in terms of the HWHM value in $\text{cm}^{-1} \text{ atm}^{-1}$.

A series of absorption profiles used to obtain, for example, γ_{self} , of CO_2 is shown in Figure 2.19. In these data, the x-axis has been calibrated using HITRAN line positions for $^{13}\text{CO}_2$ transitions observable in the low pressure data (up to ~ 100 Torr CO_2). As can be seen from Figure 2.19, there is the characteristic increase in the absorption width as the buffer gas pressure increases. Plotting the ν_L contributions extracted from the fit by setting the Doppler component of the width, ν_D , to its known value, against the pressure of the buffer gas gives the linear relationship shown in Figure 2.20. The errors for the individual ν_L measurements for the CO_2 absorption data are $\sim 1 \times 10^{-5} \text{ cm}^{-1}$ and are not shown on this graph, or on the following data for CO_2 broadening.

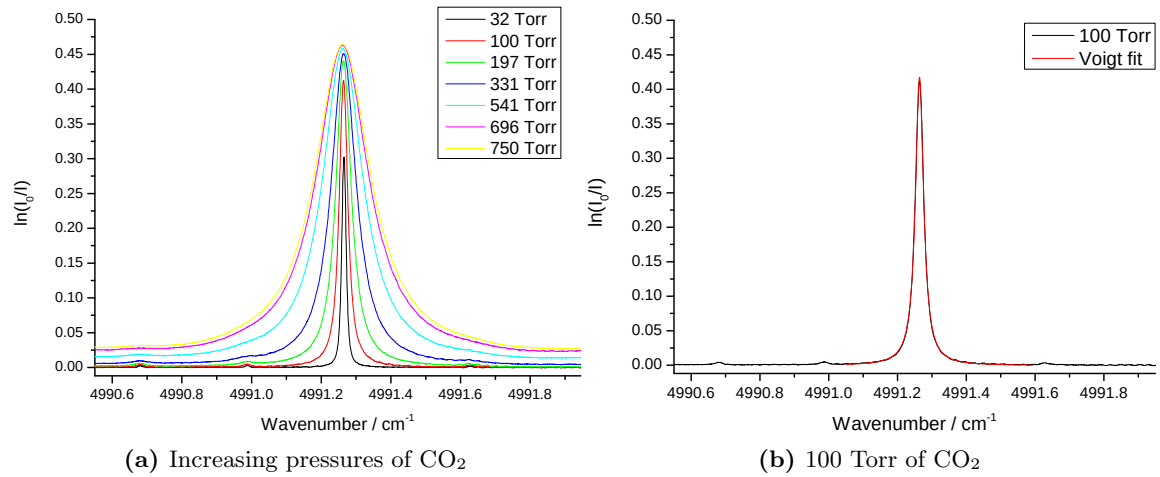


Figure 2.19: Graph (a) shows the direct absorption spectra of increasing pressures of CO_2 illustrating the increasing linewidth. Graph (b) shows an example spectrum of 100 Torr of pure CO_2 with corresponding Voigt fit in red.

From this, the value of $\gamma_{\text{self}} = 0.0953 \pm 0.0001 \text{ cm}^{-1} \text{ atm}^{-1}$, with an intercept of $5.41 \times 10^{-4} \text{ cm}^{-1}$ is calculated. The value of γ_{self} is in good agreement with that of the HITRAN database of 0.0987 cm^{-1} , and the intercept shows a small offset from the expected value

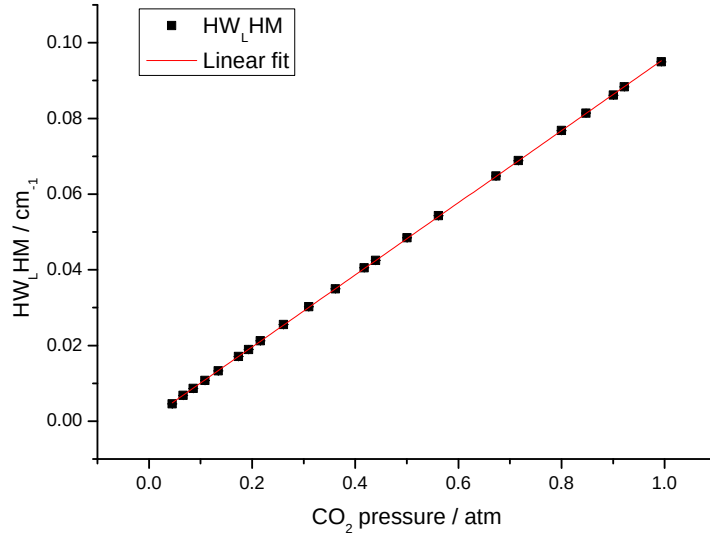


Figure 2.20: Data showing linear relationship between ν_L and pressure of CO_2 , the gradient of which gives γ_{self} .

of zero, which is likely to be due to a slight offset in the pressure gauge, or error in the calibration of the x-axis, however, it is negligible compared to the size of the linewidth.

Similar experiments were carried out to obtain values of γ_{N_2} , γ_{O_2} and γ_{air} . The measurement of γ_{air} is not strictly necessary for the fitting, as air is mostly comprised of O_2 and N_2 , however, it provides an effective way of confirming the measurements obtained for γ_{N_2} and γ_{O_2} . The linear fits of the data for ν_L vs. buffer gas pressure for these measurements is shown in Figure 2.21. A summary of the the γ values and intercepts is given in Table 2.5, as well as any HITRAN comparisons or expected values.

Gas	γ / $\text{cm}^{-1}\text{atm}^{-1}$	γ error / $\text{cm}^{-1}\text{atm}^{-1}$	$\gamma(\text{HITRAN})$ / $\text{cm}^{-1}\text{atm}^{-1}$	Intercept / cm^{-1}	Intercept (calc.) / cm^{-1}
CO_2	0.0953	0.0001	0.0987	0.0005	0
N_2	0.0735	0.0001	-	0.0044	0.0041
O_2	0.0618	0.0001	-	0.0047	0.0043
Air	0.0698	0.0002	0.0722	0.0047	0.0040

Table 2.5: Measured pressure broadening coefficients and errors for various buffer gases, with HITRAN values for comparison where applicable. Intercept values from linear fits are also given, as well, as an expected intercept value calculated as the self-broadening contribution to ν_L from the initial sample of CO_2 .

The measured values are in good agreement with the HITRAN data, which itself is quoted with an error range of 5 - 10 %, and are also comparable to measurements in this CO_2 band by Joly *et al.* [47], who reported γ_{self} and γ_{air} values for several lines and measured, for example, a $\gamma_{self} = 0.1009 \pm 0.0022 \text{ cm}^{-1} \text{ atm}^{-1}$ and a $\gamma_{air} = 0.0789 \pm 0.0004 \text{ cm}^{-1}$

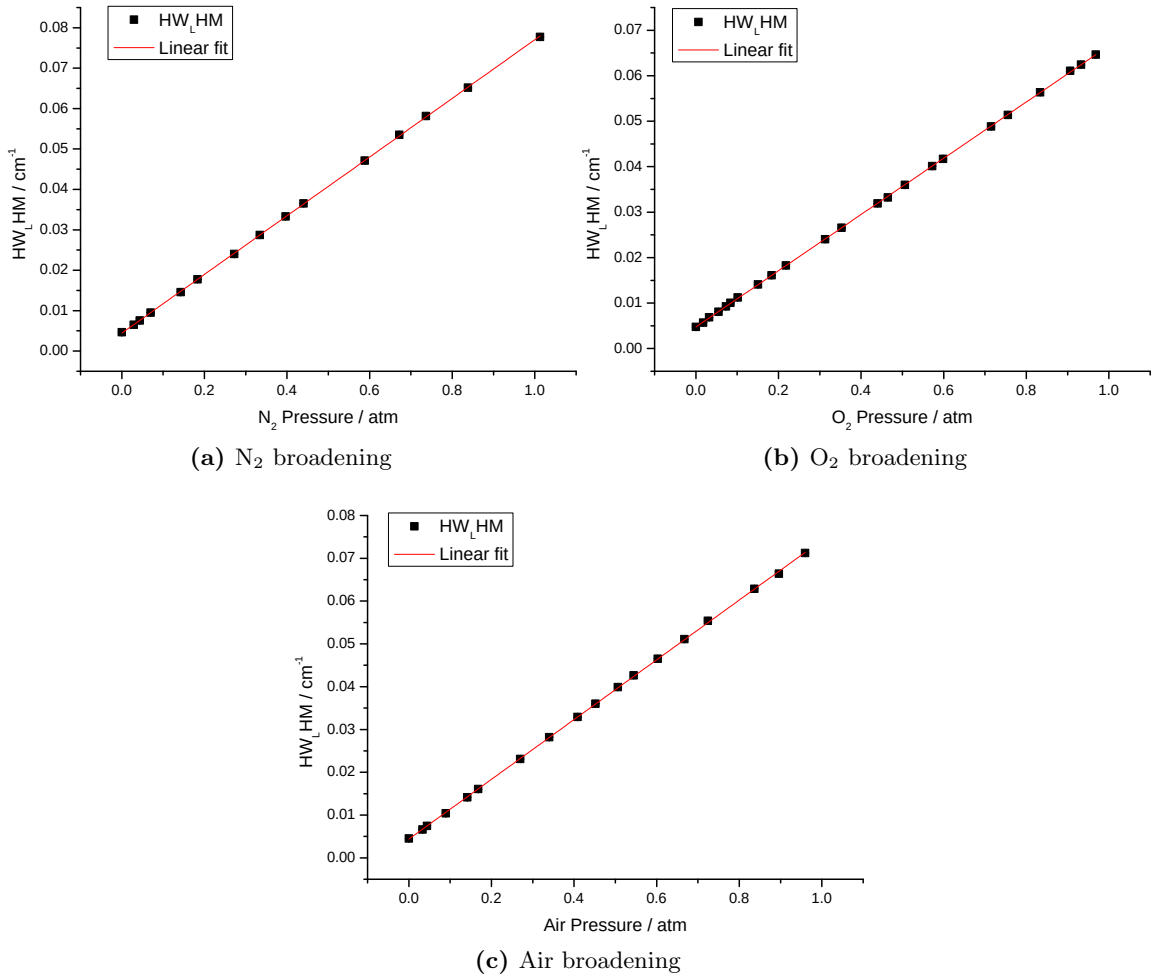


Figure 2.21: Data showing pressure broadening data for N₂, O₂ and air broadening of CO₂

atm⁻¹ for the (P12) line at 4843.99 cm⁻¹. The intercepts on the graphs indicate the contribution to ν_L from the original sample of CO₂ in the cell before the buffer gases are added. Those obtained from the linear fit are very similar to the expected values, which have been calculated using the measured self-broadening parameter for CO₂, and the initial pressure of the sample. The calculated values are slightly lower, but this is consistent with a slight offset in the pressure gauge or error in x-axis calibration. As well as this, combining the values for γ_{N_2} and γ_{O_2} in the ratio 79:21 as found in air gives a $\gamma_{air}(calc.)$ value of 0.0710 cm⁻¹ atm⁻¹, which is comparable to the measured value of 0.0698 cm⁻¹ atm⁻¹ and the HITRAN value of 0.0722 cm⁻¹ atm⁻¹. The absolute γ values themselves follow the trend of $\gamma_{self} > \gamma_{N_2} > \gamma_{O_2}$ and are determined by the intermolecular potential between the absorber and buffer gas. This in turn depends on the dominant multipole interaction between the molecules, which in this case are quadrupole-quadrupole interactions. Therefore, the interactions are dominated by the increasing quadrupole moments, Q_{gas} , reported as

$Q_{CO_2} = -4.1 \times 10^{-26}$ esu [48], $Q_{N_2} = -1.4 \times 10^{-26}$ esu [49] and $Q_{O_2} = -0.4 \times 10^{-26}$ esu [49].

2.9.2 Pressure broadening of O₂

Measuring the pressure broadening of O₂ by various gases is slightly more complex than that for CO₂. The contributions to ν_L will mainly arise from O₂ self and N₂ broadening, with smaller contributions from CO₂ and H₂O. The values that are measured in this section are the contributions from O₂, N₂ and CO₂.

Experimentally, the O₂ measurements require the optical cavity enhancement as used in the breath analyser. However, the prototype Mark III cell used, as described in section 2.8.2, is an open system where low pressure measurements are not possible. Instead, pressure broadening coefficients can be obtained by using gas mixtures resulting from different flow rates of constituent gases through the cell.

The broadening of O₂ by itself and by N₂ were measured simultaneously by varying the partial pressures of the gases, p_{gas} , through altering the ratio of O₂:N₂ in the mix and then assessing the contribution to ν_L from each gas. The level of O₂ was varied from $\sim 1\% - 90\%$ and the exact concentration value of O₂, and from this the exact concentration of N₂, could be obtained by analysing the CEAS signal. The absolute value was obtained by calibrating R with a sample of air (21 % O₂). Since p_{O_2} and p_{N_2} , were known, and ν_L could be measured from fitting the data, the contributions to ν_L from γ_{self} and γ_{N_2} could then be extrapolated by solving for all combinations of pairs of data and taking an average of the values.

The raw data signals from the cavity are shown in Figure 2.22 for the different mixtures. From these data, γ_{self} and γ_{N_2} were measured as $0.0549 \pm 0.0037 \text{ cm}^{-1} \text{ atm}^{-1}$ and $0.0524 \pm 0.0011 \text{ cm}^{-1} \text{ atm}^{-1}$. The errors on these values are given as the standard deviation of the values for γ_{self} and γ_{N_2} obtained from the solutions of all possible pairs of data sets.

The values obtained for γ_{self} and γ_{N_2} are comparable to the values measured by Brown and Plymate for the P13P13 line of $\gamma_{self} = 0.046 \pm 0.0011 \text{ cm}^{-1} \text{ atm}^{-1}$ and $\gamma_{N_2} = 0.0467 \pm 0.00008 \text{ cm}^{-1} \text{ atm}^{-1}$ [50], and the HITRAN values of $\gamma_{self} = 0.046 \text{ cm}^{-1} \text{ atm}^{-1}$ and $\gamma_{air} = 0.046 \text{ cm}^{-1} \text{ atm}^{-1}$ (with γ_{air} approximated to γ_{N_2} , and with quoted errors of $< 2\%$). The slight differences between the measured values and those of HITRAN is demonstrated in Figure 2.23. The lines indicate a simulation of the peak height of I for various mixtures of O₂ and N₂ calculated using the measured γ values (red) and the HITRAN γ values (blue). The data points are the measured peak heights from the data in

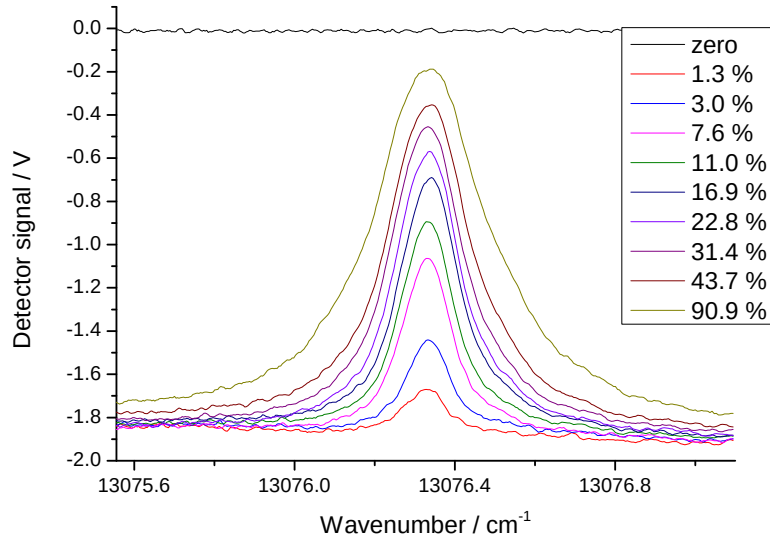


Figure 2.22: Data showing $I(\nu)$ signals from the cavity for different percentages of O_2 in N_2 .

Figure 2.22. From this, two conclusions can be drawn: that as the data points follow the model across the whole region, the methodology of determining average values of γ gives a valid measurement for various concentrations of O_2 and secondly, that the discrepancies from HITRAN are relatively small.

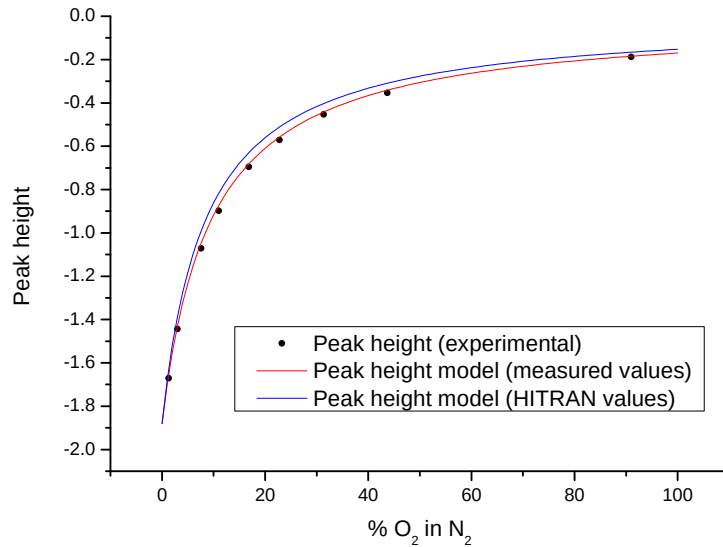


Figure 2.23: Data showing modelled peak heights for I for different mixtures of O_2 in N_2 , using both measured and HITRAN γ values. Peak heights measured in the experiment are shown as circles.

The other contribution to O_2 broadening will be from CO_2 . To measure this, mixtures of O_2 , CO_2 and N_2 were used, with the additional buffer of N_2 used to prevent the O_2 CEAS absorption level becoming too large, the impact of which will be discussed in section 2.10. Since the contributions from O_2 and N_2 are now known, the remaining broadening can therefore be attributed to CO_2 . Throughout this, the level of O_2 was kept approximately constant and the nitrogen level was varied such that a range of CO_2 concentrations could be measured whilst keeping the cell at 1 atm overall. The absolute concentrations of O_2 and CO_2 were measured simultaneously, such that the partial pressures of all three gases could be accurately monitored. A selection of the data for different $O_2:CO_2:N_2$ mixtures is shown in Figure 2.24 where the O_2 concentration can be seen to remain fairly constant, and CO_2 data is seen to vary between ~ 10 and 180 Torr are shown (mix 1 and mix 6 respectively).

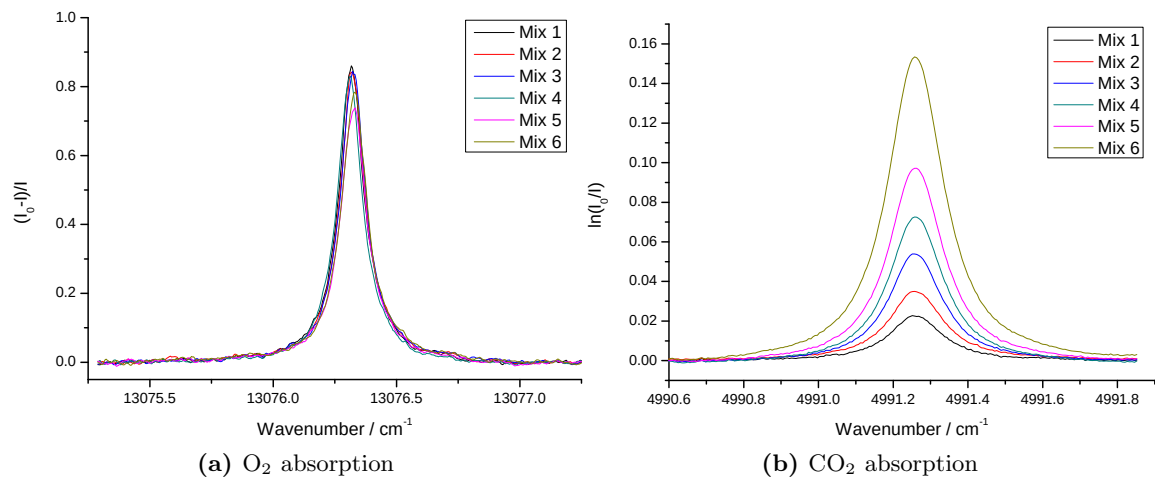


Figure 2.24: Graph (a) shows the O_2 absorption feature (P13P13) taken for various mixtures of O_2 , CO_2 and N_2 , with the concentration of O_2 held relatively constant. Graph (b) shows corresponding variations in CO_2 absorptions as the percentage CO_2 is increased.

By subtracting the contributions to ν_L from the O_2 self and N_2 broadening, the remaining increase in ν_L can be plotted as a function of CO_2 pressure and a value of γ_{CO_2} obtained. The data analysed in this fashion is shown in Figure 2.25.

Compared to the CO_2 absorption data, the O_2 spectra have a higher noise level and as such there is greater error in the Voigt fits. The value of $\gamma_{CO_2} = 0.0307 \pm 0.0011 \text{ cm}^{-1} \text{ atm}^{-1}$ is returned from the fit, with an intercept slightly offset from the expected zero value of $0.0031 \pm 0.0001 \text{ cm}^{-1}$. The error in the linear fit and the slight offset can be attributed to the poorer quality of the data when working with the cavity as well as errors introduced and amplified by having to interpret a three-gas system. As well as this, the change that CO_2 introduces to the width is relatively small that compared to the overall width, and such is

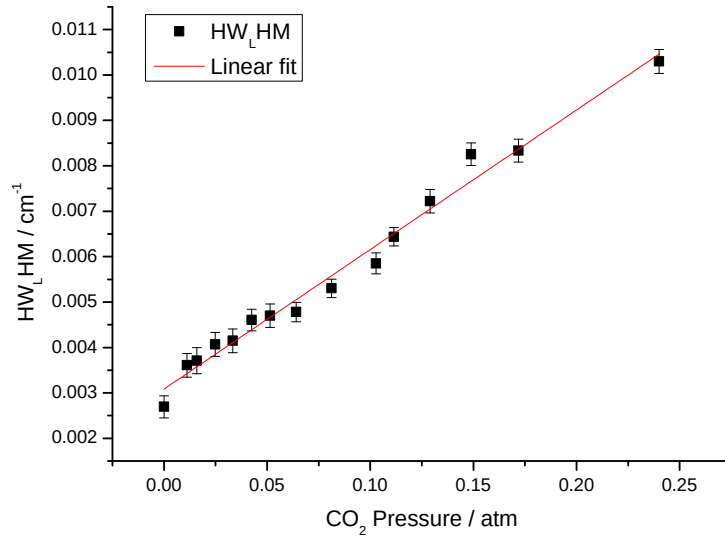


Figure 2.25: Data showing ν_L measured from the O₂ absorption as a function of added CO₂. A linear fit is shown in red.

susceptible to larger errors. However, the value obtained here shows that the contribution to the broadening of O₂ by CO₂ is fairly minimal.

2.9.3 Interactions of O₂, CO₂ and N₂ in breath

From these measurements, it is now possible to model the effects on the linewidth of a O₂ and CO₂ absorption during breathing and assess the impact this may have on the linear regression fitting routine. The impact of the pressure broadening variations of the gases O₂, N₂ and CO₂ can be demonstrated in Figure 2.26.

These simulations show CO₂ and O₂ absorptions under two extreme sets of conditions possible during a breath cycle. The Lorentzian widths have been simulated using the broadening parameters measured and described in the previous sections. As can be seen from these simulations, there is little change in the overall widths, in fact the O₂ Lorentzian widths which are typically 0.11 cm⁻¹ only vary by $\sim 10^{-3}$ cm⁻¹, and the CO₂ Lorentzian widths which are typically 0.14 cm⁻¹ vary by $\sim 10^{-4}$ cm⁻¹. So overall the interactions between O₂, CO₂ and N₂ during a breath cycle are fairly negligible and will not impact too dramatically on the accuracy of the linear regression algorithm. However, the contribution of H₂O to these absorption profiles also needs to be considered, and is discussed in the next section.

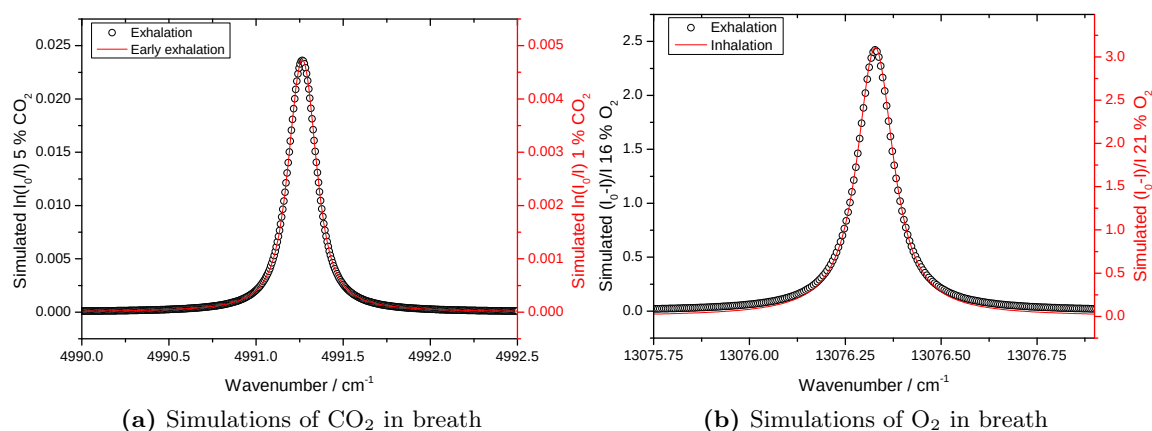


Figure 2.26: Simulations of Voigt profiles modeled on two conditions in a breath cycle for both CO₂ and O₂. Graph (a) illustrates the start (red) and end (black) of exhalation for CO₂ absorption and graph (b) illustrates exhalation (black) and inhalation (red) for the O₂ absorption.

2.9.4 Pressure broadening studies concerning H₂O

H₂O as the third exchange gas of interest to this study has so far been monitored using a single-point variation analysis as described in section 2.6.2. However, the contributions of H₂O broadening to CO₂ and O₂ need to be considered over the range of concentrations of H₂O typically found in breath (~ 1 to 5 %). As well as this, for future measurements involving measurement of H₂O by fitting of the full absorption feature, as is already performed for O₂ and CO₂, an estimate of at least the H₂O self-broadening would be required to assess how the absorption width may vary throughout a breath cycle.

Since H₂O is a notoriously difficult molecule to work with, as it is difficult to remove entirely from a system for background measurements and tends to stick to measurement cell walls, a similar approach to that used in the O₂ measurements described above was taken for estimating the self-broadening of H₂O. The data were taken by remaining at an overall pressure of 1 atm and varying the H₂O content to assess how the ν_L component of the width varies with H₂O partial pressure. The breath analyser cell described in section 2.8.2 was again utilised to monitor the H₂O absorption as various mixtures of N₂(dry) and N₂(wet) were flowed through the cell. The N₂(wet) was obtained by flowing cylinder N₂ through a H₂O bubbler to humidify it. The H₂O content could therefore be varied between nearly zero and a maximum level similar to the atmospheric humidity in the lab.

The plot of the ν_L variation with H₂O concentration is shown in Figure 2.27. The variation in ν_L is in fact a combination of the H₂O self and N₂ broadening, as N₂ has been used as a carrier gas. However, as the relative change in H₂O is much higher than the relative change

in N_2 , as a first approximation the increase in ν_L can be attributed to H_2O itself. The N_2 broadening also results in the non-zero offset of ν_L .

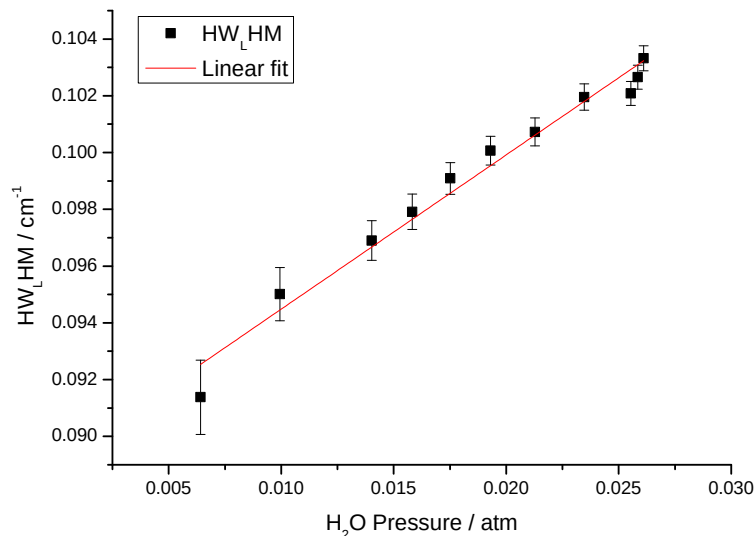


Figure 2.27: Data showing ν_L measured from the H_2O absorption as a function of increasing H_2O in N_2 . A linear fit is shown in red.

The value for γ_{self} for H_2O obtained from these data is $0.543 \pm 0.029 \text{ cm}^{-1} \text{ atm}^{-1}$. This, as a first estimate for the H_2O broadening, is comparable to the HITRAN quoted value of $0.510 \text{ cm}^{-1} \text{ atm}^{-1}$ (with a quoted error of $\geq 5 \%$, $< 10 \%$), and does show that the self-broadening of the H_2O feature will be more considerable than what has been observed for O_2 and CO_2 . An estimate of the impact on the width due to H_2O broadening is simulated in Figure 2.28, where mixtures of 1 % and 5 % H_2O in air have been simulated. The Lorentzian widths in this case have been modeled using the H_2O broadening coefficient measured in this work, and a value for $\gamma_{air} = 0.093 \text{ cm}^{-1} \text{ atm}^{-1}$ taken from HITRAN.

The Lorentzian component of the width in this case varies by nearly 20 % over the range of concentrations found in breath. Ideally, more accurate values for the broadening of H_2O by O_2 and N_2 would be needed to obtain a more thorough representation of the variation in ν_L during a breath cycle. However, as a first approximation, the value for γ_{self} for H_2O indicates that extra care will be needed when fitting H_2O absorption features, as the widths will vary far more substantially. This much higher level of self-broadening for H_2O compared to what has been observed for the other molecules is due to the introduction of dipole-dipole interactions [51], with the dipole moment of H_2O reported as $1.8549 \times 10^{-18} \text{ esu}$ [49].

The final contributions from H_2O that need to be considered are the broadening of O_2 and CO_2 by H_2O . These measurements are difficult to obtain, as with the H_2O self-broadening due to the reasons already discussed, but a more qualitative idea of the impact of H_2O

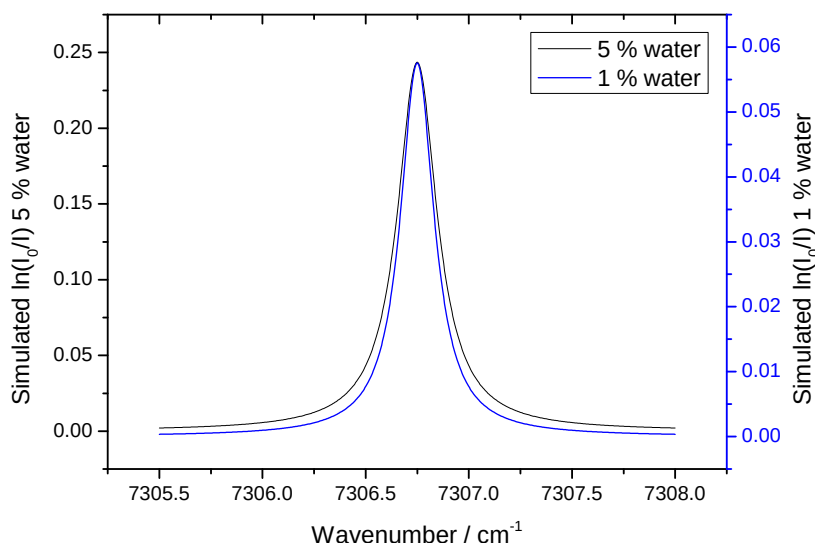


Figure 2.28: Simulations of H₂O absorption in breath during inhalation (blue) and exhalation (black).

on O₂ and CO₂ can be gained by monitoring absorption features taken during exhalation, where the H₂O content is highest, and then repeating the experiment with filters in place to remove as much H₂O as possible from the breath. As the data already described has shown that the change in broadening contributions to O₂ and CO₂ arising from the “dry” gases (O₂, CO₂ and N₂) is fairly negligible, any substantial differences in the width on drying a breath sample can be attributed to the influence of H₂O. An example series of spectra, taken from the maxima of an exhalation when the H₂O content is high, or has been artificially removed, are shown in Figure 2.29.

In Figure 2.29 the artificially dried data, shown on the right hand side for the three gases was obtained by placing a series of heat and moisture exchange filters in the respiratory flow. Whilst it is impossible to remove all the H₂O this way, a reduction by $\sim 50\%$ is observed and can therefore be approximated to represent the typical H₂O levels found in a breath cycle.

The slightly different CO₂ and O₂ concentrations between the “wet” and “dry” data sets result from natural variations in breathing, however, as shown above, these variations have minimal impact on the width of the feature. Overall, the percentage change in the widths of the lines that can be attributed to H₂O, is $\sim 5\%$ for O₂ and only $\sim 1\%$ for CO₂. The largest change in width is for the H₂O feature itself, with a variation of $\sim 6\%$ between the two measurements, due to the larger H₂O self-broadening coefficient that was measured experimentally.

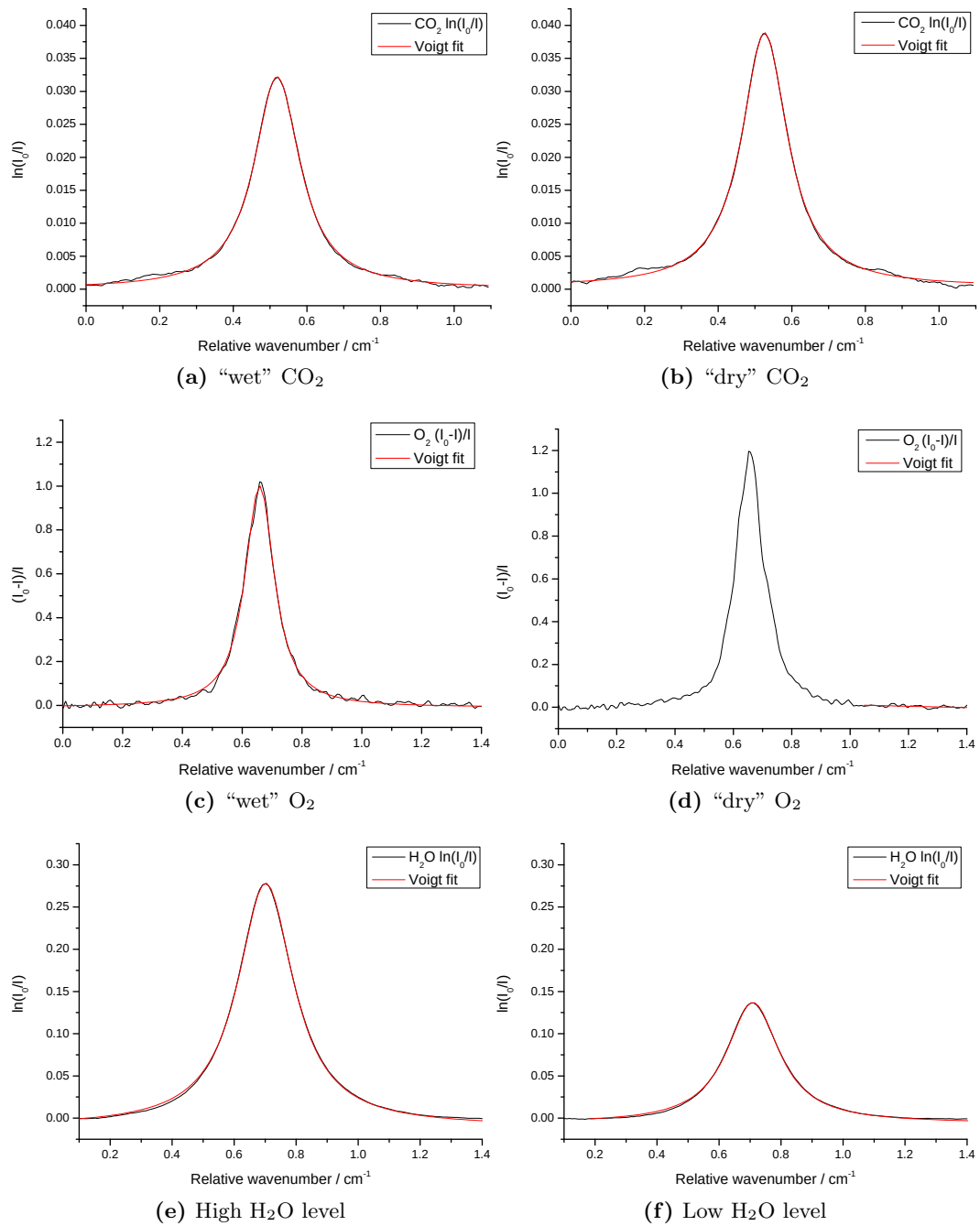


Figure 2.29: Data showing O_2 , CO_2 and H_2O absorptions taken at the maxima of exhalation. The data in on the left corresponds to absorptions when there is a high H_2O level in the exhaled air, and data on the right correspond to a low level of H_2O in the exhaled air. Corresponding Voigt fits on data are shown in red.

2.9.5 Implications of pressure broadening on data analysis

The interactions between O_2 and CO_2 have been shown to be fairly constant over the various gas mixtures occurring during respiration, as has the linewidth variation introduced by H_2O on these gases. However, the H_2O self-broadening contribution has been found to be more substantial. The overall implications of the change in widths of the absorption features is fairly minimal, but for more accurate measurements, should be accounted for in the fitting of the data.

To take the width variations into account, the LGA analysis programs were rewritten to compensate for changes in the lineshape as the gas mixtures vary, based on the self-broadening coefficients measured in this work and air broadening coefficients either reported here or taken from the HITRAN database when necessary for H_2O . The initialisation values for fitting the widths for each measurement were simulated using the concentration data from the previously measured spectrum in the breath cycle. From this, more accurate measurements, particularly for H_2O , could be obtained for all three exchange gases, using analysis of the full absorption lineshape.

2.10 First results from the prototype breath analyser

With the prototype analyser now improved in terms of design and data analysis, an example of a breath trace showing all three gases is shown in Figure 2.30. As can be seen from these data, which gives a gas concentration readout every 10 ms, the gas concentrations all vary between the expected levels found in breath on exhalation and in ambient air on inhalation. As with previous attempts at monitoring all three gases, it can be seen that the turning points of O_2 and CO_2 match very well, with the H_2O increase on exhalation slightly preceding the other two due to dead space in the conducting airways.

The H_2O and CO_2 data show very low noise, however the O_2 data exhibits a high frequency noise which is especially prominent on the inhalation, i.e., higher concentrations of O_2 . This is due to the CEAS absorption data approaching the detector zero line. Therefore, when the CEAS data is processed, the subtraction of the detector offset results in higher noise levels at the absorption maxima, which distorts the LGA fitting routine. This is not as significant a problem at the lower O_2 concentrations, hence the noise is lower on the inhalation data. This is an effect due to measuring a larger concentration with very high reflectivity mirrors and could be improved through using mirrors of slightly lower reflectivity.

The noise is such that, with a 10 ms time resolution, the minimum absolute change in percentage that can be measured for O_2 is 0.26 % (using inhalation data) which is identical to

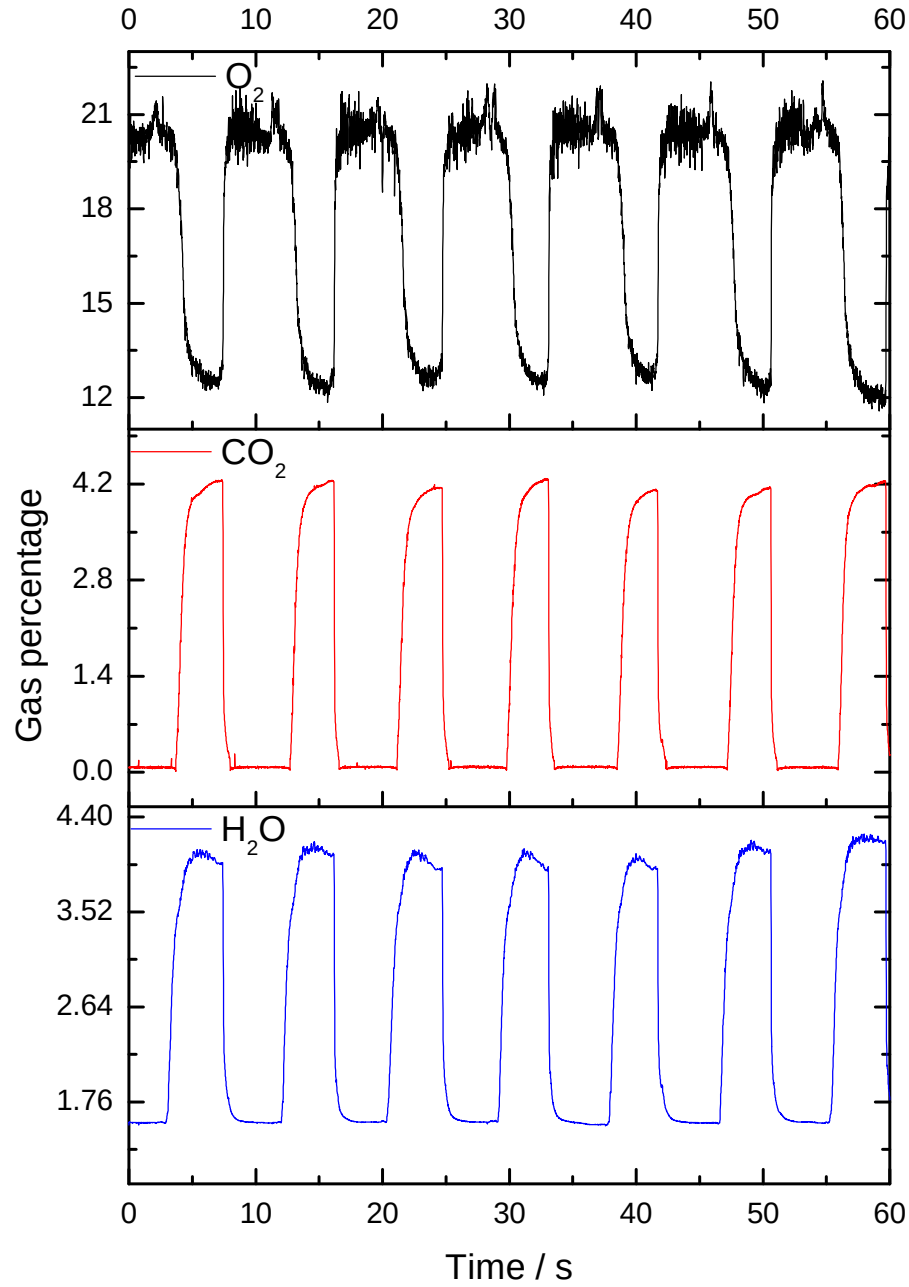


Figure 2.30: Simultaneous, real-time measurements of O₂, CO₂ and H₂O in breath using full absorption lineshape analysis and incorporating width variations into the LGA calculations.

what was achieved with the Mark II analyser, but has now been achieved over a pathlength of 2.75 cm as opposed to 4 cm. For the CO₂, the minimum absolute change detectable is now 0.02 %, as opposed to 0.04 % measured previously. The H₂O, which is a new addition to the prototype as it has never been measured using the full absorption peak analysis, exhibits a minimum detectable change of 0.003 %.

2.11 Conclusions and future work

This project has discussed the design implications of building a real-time respiration monitor for physiological studies. Both the mechanical and the optical requirements of the monitor have been met such that three gases can be measured with purely spectroscopic methods, including the challenging use of CEAS in this practical environment. Whilst the use of CEAS in the NIR is a well developed method, most experiments still tend to employ cell pathlengths ~ 1 m and longer acquisition times for further improvement of the signal to noise ratio on the CEAS signal. However, this type of experimental system can not be replicated here and the measurements have been performed in a cavity only 2.75 cm in length, and with an acquisition time of only 10 ms. This acquisition time is an achievement not only of the sensitive optical detection producing high quality data in a short period, but also in the data handling. The developed LGA system demonstrates a promising software design for running the analyser, collecting data and processing it to give real-time changes in gas concentrations. As well as this, further studies into the variations in the absorption features over a breath cycle due to pressure broadening have been undertaken and this information has been incorporated into the analysis of the data.

Whilst this will continue to be an ongoing project, the core essentials of the method have been demonstrated successfully in this work, with the final measurements reported here from the Mark III prototype all within the original aim of monitoring changes of 1 % in a 10 ms. The future development for this project will be in the engineering of the prototype itself to make it suitable for clinical trials. Steps have already been taken towards this with the use of optical fibers and including the detector modules in the analyser itself such that there are no open beam paths. However, further work however is required to make the analyser sturdy and lightweight enough to be mounted at the patient's mouth. Finally, the incorporation of fast flow measurements and temperature stabilisation are required, as this combined with the instantaneous O_2 and CO_2 concentration measurements will enable calculation of O_2 consumption and CO_2 production during a breath cycle.

An analyser such as the one that is envisioned for the future of this work has the potential for extensive use in medical and hospital environments, either for physiological studies for better understanding of the respiratory system or for patient monitoring. The concept that has been demonstrated here also has the potential for expansion to other important gaseous species in breath, such as anaesthetics, where real-time and accurate measurements would be ideal.

Chapter 3

Modulation techniques and their potential use in breath analysis

The work presented in this chapter details studies using other forms of sensitive spectroscopic detection methods, namely wavelength modulation spectroscopy (WMS) and frequency modulation spectroscopy (FMS), and their potential in the field of breath analysis. The possibilities of using WMS, and in particular a self-calibrating form of WMS in breath analysis are discussed, with a proof-of-principle example of the detection of H₂O. As well as this, the possibility of using FMS as an alternative to the CEAS method presented in chapter 2 for the detection of atmospheric O₂ is investigated.

3.1 Wavelength and frequency modulation spectroscopy

The improvement of detection sensitivity through pathlength enhancement by an optical cavity based system has already been discussed in Chapter 2. This type of enhancement is based on increasing the magnitude of the absorption signal, but improvements in the detection limit can also be achieved through reduction in the level of detected noise, and this is the basis of modulation spectroscopy. As has previously been discussed in Chapter 1 modulation spectroscopy can be separated into wavelength modulation and frequency modulation spectroscopy depending on the experimental parameters.

When laser light at frequency ω_0 is modulated with a sinusoidal function with modulation index M and frequency ω_m , the resultant optical electric field is given by

$$E(t) = E_0 \exp[i(\omega_0 t + M \sin \omega_m t)] \quad (3.1)$$

In WMS, modulations typically in the kHz range such that the modulation frequency is much smaller than the spectral feature width and modulation index $M \gg 1$ are utilised. In FMS, modulation frequencies that are in the MHz - GHz range and are greater than the absorption feature width and with $M \leq 1$ are typically used. The result of these high frequency modulations is the appearance of side bands on the carrier frequency, which in the case of WMS are a series of sidebands with relatively small spacing interacting with the absorption feature, whereas for FMS, due to the larger modulation frequency relative to the absorption width and the size of M , only one pair of sidebands is considered. The differences in the resulting sidebands for these two regimes are illustrated in Figure 3.1.

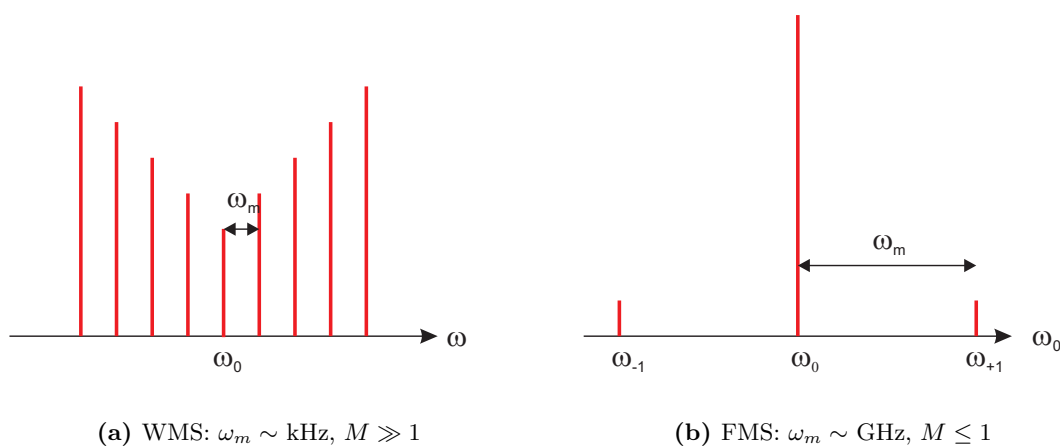


Figure 3.1: Figure (a) illustrates the theoretical sideband structure for a conventional WMS experiment and figure (b) illustrates the equivalent for a conventional FMS experiment.

Historically, WMS methods were implemented before FMS in the 1970s due to the available technology only being capable of providing modulations in the lower frequency regime [52, 53]. FMS studies soon followed and were first reported around a decade later [54]. Modulation spectroscopy of both types has been used in many fields involving trace gas detection, of which there are several reviews [55, 56]. These uses include atomic spectroscopy [57, 58], the measurement of atmospherically important species [59, 60] and, of more relevance to the work presented in this thesis, modulation techniques have been used to study potentially important biomarkers [61–63]. In the work reported here, this potential of modulation techniques for studying species in breath is investigated further. Initially however, a discussion on the theory behind modulation spectroscopy, which is utilised again in Chapter 4, and the importance of experimental parameters in these techniques is presented.

3.2 WMS studies on H₂O

WMS has been demonstrated as a practical sensitive detection method, but its main disadvantage is that it is non-absolute. Normally, WMS spectra are calibrated using a direct absorption spectrum taken of a known concentration. However, for weakly absorbing compounds or trace levels of strongly absorbing species such as those present in breath, a direct absorption spectrum is not always possible, and as such other forms of self-calibration of WMS signals are increasingly being investigated.

Various studies have been reported on self-calibrating WMS techniques that include algorithms to model the lineshape devised by Henningson *et. al* [64] or more commonly, attempts to normalise WMS signal using the intensity variations in lower harmonics of detection, as first proposed by Cassidy and Reid [59]. In the work presented here, a self-calibrating method, known as the phasor decomposition method (PDM) is discussed. This method was first illustrated by McGettrick *et al.* [65] for studies on methane in nitrogen, and relies on separating the residual amplitude modulation (RAM) and frequency amplitude modulation components of the WMS signal; a full description of the theory of which is given in later sections.

The results presented here include a demonstration of basic WMS theory with detection of H₂O at 935 nm, as well as a “proof-of-principle” study on self-calibrating WMS of H₂O at 1368 nm, using the PDM approach. In this spectral region, the integrated cross-sections of H₂O, the spectroscopy of which has already been discussed in Chapter 2, are $\sim 10^{-20}$ cm² cm⁻¹ and are therefore easily detectable by direct absorption spectroscopy over a path of a few cm. Whilst WMS is therefore not perhaps necessary for detecting H₂O in this region, it is necessary to have a large enough cross-section to obtain a direct absorption spectrum, as this is the only way to assess the accuracy of data that the PDM analysis gives.

In the following sections, the theory behind conventional WMS is discussed and demonstrated experimentally. The self-calibration PDM analysis is also described, and results comparing this form of calibration method to direct absorption are discussed.

3.2.1 Theory of wavelength modulation spectroscopy

The theory of WMS is most frequently described in a more intuitive manner, based on the instantaneous frequency of the laser when a time-dependent phase shift, i.e. a modulation, is applied [66]. The instantaneous frequency is the rate of change of phase with time, and since the phase is described by the argument of the complex exponential in Equation 3.1,

the instantaneous frequency, $\omega_i(t)$, can be written as the derivative of that phase term with respect to time

$$\omega_i(t) = \frac{d}{dt}(\omega_0 t + M \sin \omega_m t) = \omega_0 + \Delta F \cos \omega_m t \quad (3.2)$$

where $\Delta F = M\omega_m$. To describe the interaction of the instantaneous frequency of the laser with an absorbing medium, the light transmitted through the sample is modeled on the Beer-Lambert law (Equation 1.1) and described as $I_T(\omega) = I_0(\omega) \exp(-\alpha(\omega))$, with l set to 1 for this theoretical description. For small absorbance where $\alpha(\omega) \ll 1$ the transmitted intensity can be written as

$$I_T(\omega) \simeq I_0(\omega)[1 - \alpha(\omega)] \quad (3.3)$$

Expanding the absorbance $\alpha(\omega)$ as a Taylor series around the carrier frequency ω_0 , gives

$$\begin{aligned} I_T(\omega) = I_0 \left[1 - \alpha(\omega_0) - \left. \frac{d\alpha}{d\omega} \right|_{\omega_0} (\omega - \omega_0) \right. \\ \left. - \frac{1}{2!} \left. \frac{d^2\alpha}{d\omega^2} \right|_{\omega_0} (\omega - \omega_0)^2 \right. \\ \left. - \frac{1}{3!} \left. \frac{d^3\alpha}{d\omega^3} \right|_{\omega_0} \times (\omega - \omega_0)^3 - \dots \right] \end{aligned} \quad (3.4)$$

and substituting the instantaneous frequency term given in Equation 3.2, results in

$$\begin{aligned} I_T(\omega) = I_0 \left[1 - \alpha(\omega_0) - \left. \frac{d\alpha}{d\omega} \right|_{\omega_0} \times \Delta F \cos \omega_m t \right. \\ \left. - \frac{1}{2!} \left. \frac{d^2\alpha}{d\omega^2} \right|_{\omega_0} \times (\Delta F)^2 \frac{1}{2} (1 + \cos 2\omega_m t) \right. \\ \left. - \frac{1}{3!} \left. \frac{d^3\alpha}{d\omega^3} \right|_{\omega_0} \times (\Delta F)^3 \frac{1}{4} (3 \cos \omega_m t + \cos 3\omega_m t) - \dots \right] \end{aligned} \quad (3.5)$$

If the frequency deviation ΔF is relatively small compared to the absorption linewidth, then the higher order terms in Equation 3.5 can be disregarded and the intensity signal, I , that is detected at ω_m will resemble the n^{th} derivative when demodulated at the n^{th} (nf) harmonic

$$I \propto - \left. \frac{d^n \alpha}{d\omega^n} \right|_{\omega_0} (\Delta F)^n \quad (3.6)$$

Essentially, the intensity attenuation of the frequency component at ω_m as it is swept over an absorption feature is recorded, increasing in magnitude for steeper slopes on the absorption feature and changing phase at its maxima to give the derivative-type spectrum. A more qualitative illustration of this process is given in Figure 3.2.

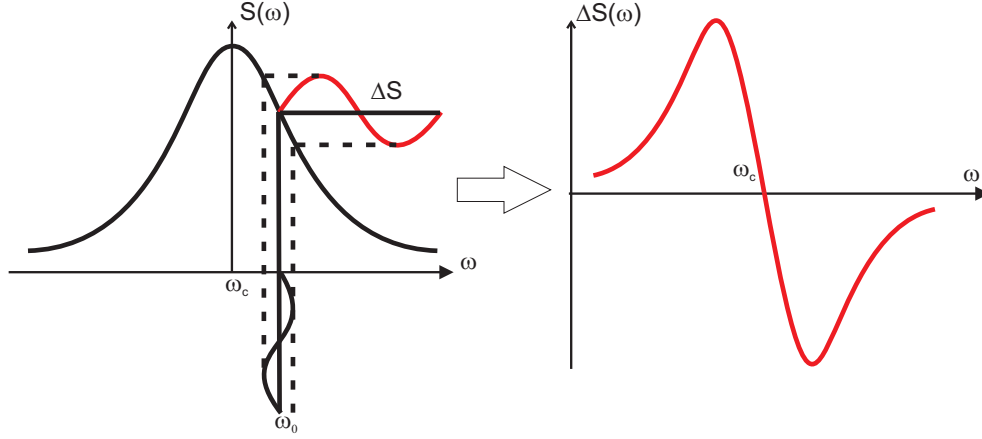


Figure 3.2: Illustration of generation of a WMS $1f$ signal by sweeping the modulated laser frequency across an absorption feature. Reproduced from [20].

3.2.2 WMS experimental considerations

When choosing parameters for experimental detection, the choice of which harmonic to demodulate at and what modulation parameters to employ depends largely on the absorption feature itself. Demodulation at higher harmonics results in an increasing drop in WM signal size as modeled by Cassidy *et al.* [59], hence demodulation at lower harmonics is usually preferable. However, demodulation at $1f$ is particularly sensitive to RAM and this can decrease the signal quality. RAM is a result of the power variation that occurs in diode lasers as the injection current and hence frequency is modulated, which translates itself as an amplitude modulation of the laser signal at frequency ω_m . This power modulation in a WMS signal manifests itself as background variation that can interfere with the absorption profile. However, as the WMS signals resemble the n^{th} derivative, much of this variation can be removed if the power variation is linear, by moving to $n = 2$ demodulation or, if it is non-linear, by moving to $n > 2$ demodulation. Typically, the best compromise between signal loss and adverse RAM effects is reached by demodulating at $2f$. It is worth noting however, that the presence of RAM in the signal can be used to advantage as this is the basis of the phasor decomposition method discussed in later sections.

To demonstrate the various harmonic lineshapes an experiment for WMS detection of H_2O was set up. In this, a 935 nm diode laser [*Eagleyard photonics, EYP-DFB-0935-00100-1500-TOC03-0000*] was housed in a commercial mount [*Thorlabs, TCLDM9*] and controlled with Thorlabs current and temperature controllers [*LDC205C and TEDC 200C, respectively*]. The laser was aligned through a 30 cm cell containing 3.06 Torr H_2O vapour. The signal was collected with a long-wavelength range InGaAs detector [*Hamamatsu, G5852-01*]. The necessary high frequency modulation for the WMS signals, and demodulation of the signal was provided by a lock-in amplifier [*Stanford research systems, SR830 DSP*]. Examples of the various obtained harmonics and their lineshapes are shown in Figure 3.3a, taken for a Doppler broadened H_2O absorption at $10667.763 \text{ cm}^{-1}$ ($2\nu_1 + \nu_3$, $(3, 1, 3) \leftarrow (2, 1, 2)$). As can be seen in these data, the lineshapes follow the characteristic derivative form, with a slight perturbation from a weaker transition at 10667.89 cm^{-1} ($3\nu_1$, $(4, 0, 4) \leftarrow (3, 1, 3)$).

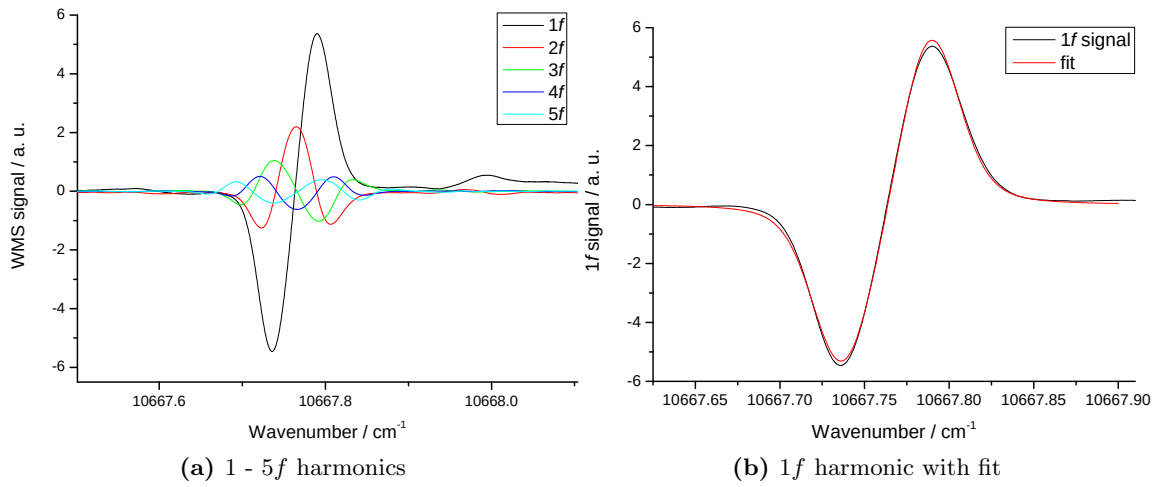


Figure 3.3: Graph (a) shows optimised 1 - 5f harmonics of H_2O absorption at $10667.763 \text{ cm}^{-1}$ ($2\nu_1 + \nu_3$, $(3, 1, 3) \leftarrow (2, 1, 2)$) with the 1f harmonic shown in more detail in graph (b), with a corresponding fit shown in red.

These data have been optimised to obtain the maximum signal height as determined by the magnitude of modulation amplitude, which is the maximum frequency excursion of ω and is defined as a . The possible magnitude of a falls into two regimes when compared to the halfwidth of the absorption feature $\nu_{1/2}$, and these are described as the derivative and non-derivative limit. The derivative limit, when $a \ll \nu_{1/2}$, results in signals that are proportional to the derivatives of the absorption feature, as demonstrated by Equation 3.6. However, this regime is rarely employed experimentally as larger signals can be obtained by optimising a for the particular absorption profile under investigation. This optimised limit where $a \approx \nu_{1/2}$ is the non-derivative limit, and whilst the form of the signal still resembles the various derivatives, a level of broadening to the signal occurs with larger modulation amplitudes, known as modulation broadening. This makes the resulting data more difficult to analyse, but with the advantage of larger signals.

The optimum value of a is normally defined in terms of the dimensionless quantity, b , given by

$$b = \frac{a}{\nu_{1/2}} \quad (3.7)$$

and the optimisation of b depends on the lineshape of the absorption feature studied and on the choice of demodulation harmonic. Various investigations into optimum b_{opt} values have been reported on Doppler, Lorentzian and Voigt lineshapes, [67–70], and confirmed experimentally [59, 71, 72]. Experimentally, b can be determined with knowledge of the applied injection current amplitude and the laser tuning characteristics, or by measuring the frequency excursion exhibited by the resonance peak of a Fabry-Perot etalon, or a spectrum analyser, of known FSR as the laser is scanned as shown in Figure 3.4.

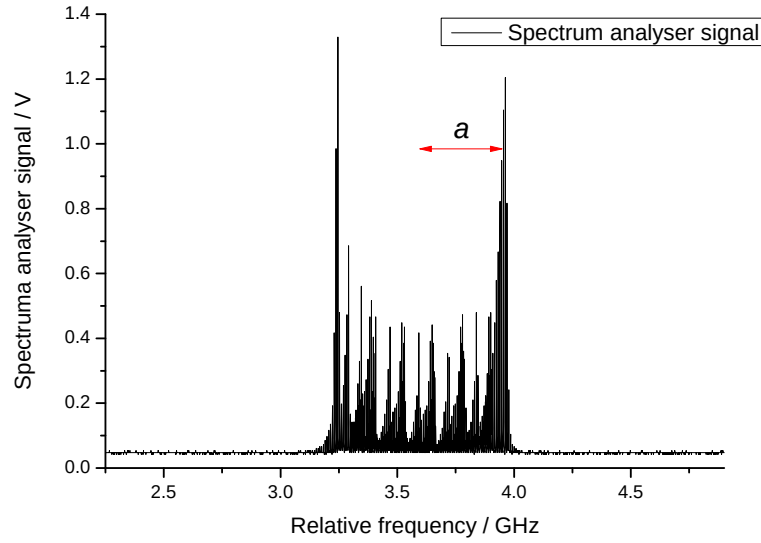


Figure 3.4: Example of a spectrum analyser trace showing the frequency envelope resulting from the amplitude modulation of the injection current, and therefore the modulation in frequency. In this case, a is defined as the excursion from the centre of the frequency envelope and is ~ 0.4 GHz. The data in this figure was taken using the setup for WMS detection of H_2O at 1368 nm, as described in the following sections.

To demonstrate the dependence of signal size on b and on the demodulation harmonic, WMS signals on a Doppler broadened sample of H_2O were taken experimentally as shown in Figure 3.5. These data show the expected trend of b_{opt} increasing in magnitude with higher harmonics, as predicted by Silver [69], and a comparison of these predicted values with the experimentally measured ones is also given. The slight deviations of the experimental values away from the predictions by Silver can be attributed to the broad turning points on the signal vs. b plots, resulting in ambiguity in the maxima.

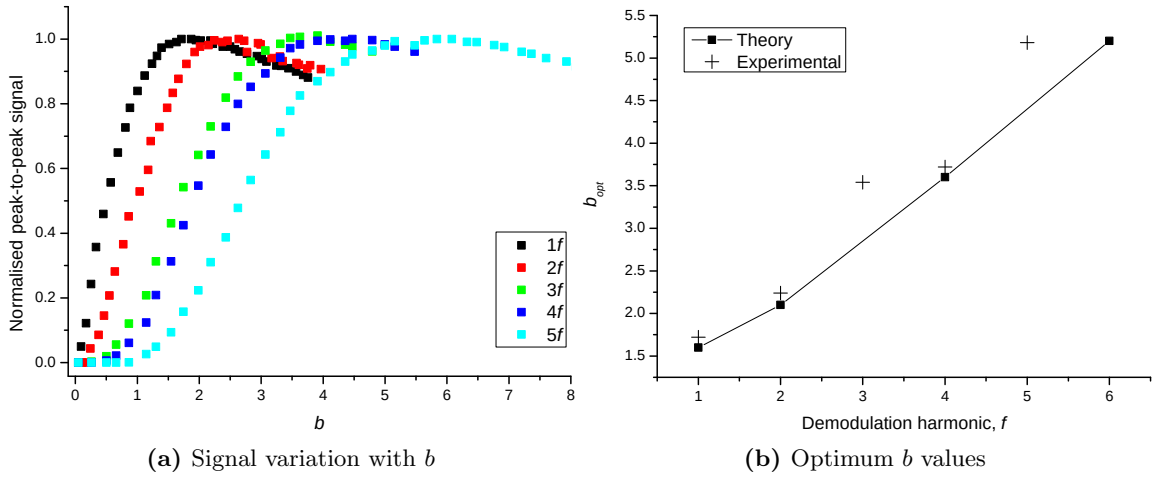


Figure 3.5: Graph (a) shows variation in WMS signal size with b for different harmonics for a Doppler broadened H_2O line ($2\nu_1 + \nu_3$, $(3, 1, 3) \leftarrow (2, 1, 2)$). Maximum peak heights have been normalised to one. Graph (b) shows comparison of b_{opt} values obtained experimentally with those predicted by Silver [69].

So far, the use of conventional WMS described has utilised the lock-in amplifier simply as a phase sensitive detector, however, for the use of PDM in a WMS experiment, a more thorough understanding of the workings of a lock-in amplifier and the forms of its outputs is required.

3.2.3 Lock-in amplifiers

A lock-in amplifier, in its most basic sense is a phase sensitive detection system that singles out only components of a signal at a specific frequency and phase. Frequently, the lock-in amplifier is also used to generate the high modulation frequency to apply to the laser as well. For the more general case, though, where the high frequency modulation is generated outside the lock-in, for example with a function generator, the demodulation process is described below with reference to Figure 3.6. In this figure, the top waveform represents the reference signal, for example a TTL pulse from the function generator at frequency ω_{ref} . This reference output is fed into the lock-in amplifier. The function generator is also used to modulate the experiment, typically with a sine waveform, and the resulting experimental signal is represented in red in Figure 3.6. This signal is modulated at ω_{ref} with a phase shift from the TTL reference of θ_{sig} , to give an overall signal described by $V_{sig} \sin(\omega_{ref}t + \theta_{sig})$. The lock-in amplifier generates its own sine wave, shown in blue in Figure 3.6, of the form $V_L \sin(\omega_L t + \theta_{ref})$.

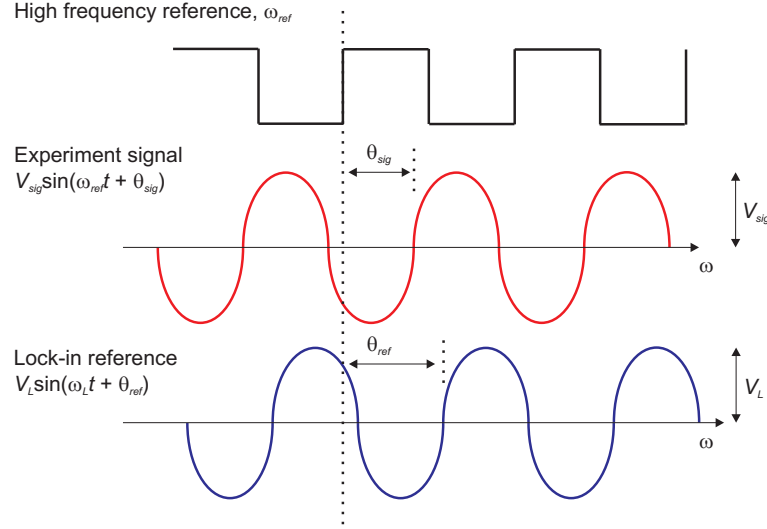


Figure 3.6: Illustration of signals involved in demodulation electronics in a lock-in amplifier. The black square pulse is a synced reference from the function generator driving the experiments. The red trace is the experimental signal and the blue trace is the lock-in amplifier's own generated reference.

The first step of the lock-in phase sensitive detection system (PSD) is to multiply the experimental signal by the lock-in reference. The resulting output of the PSD, V_{psd} , is therefore

$$\begin{aligned}
 V_{psd} &= V_{sig} V_L \sin(\omega_{ref} t + \theta_{sig}) \sin(\omega_L t + \theta_{ref}) \\
 &= \frac{1}{2} V_{sig} V_L \cos[(\omega_{ref} - \omega_L)t + \theta_{sig} - \theta_{ref}] - \\
 &\quad \frac{1}{2} V_{sig} V_L \cos[(\omega_{ref} + \omega_L)t + \theta_{sig} + \theta_{ref}]
 \end{aligned} \tag{3.8}$$

If this signal, which consists of two AC signals at $\omega_{ref} - \omega_L$ and $\omega_{ref} + \omega_L$, is passed through a low-pass filter then only the components where $\omega_{ref} = \omega_L$ will contribute to the resulting DC signal, which becomes

$$V_{psd} = \frac{1}{2} V_{sig} V_L \cos(\theta_{sig} - \theta_{ref}) \tag{3.9}$$

So far, this description represents the detection of an experimental signal simply at ω_{ref} , however, in reality the signal will have noise components at ω_{noise} . Since neither $\omega_{noise} \pm \omega_{ref}$ result in a DC signal from Equation 3.9, these signals are rejected by the low-pass filter. Only signals where ω_{noise} is very close to ω_{ref} will result in small contributions, and to what extent these are attenuated depends on the low pass filter bandwidth.

Having dealt with the selectivity and noise reduction processes, the different outputs given by a lock-in amplifier, which are crucial in using the phasor decomposition method, can be described. The PSD output in Equation 3.9 gives a signal that is proportional to $\cos \theta$ where the phase angle, θ , is equal to $\theta_{sig} - \theta_{ref}$. V_{sig} can therefore be measured, or set to zero, by altering the phase angle. Typically, a lock-in amplifier has a second PSD system which multiplies the experimental signal by the lock-in reference shifted by $\pi/2$, giving a second output proportional to $\sin \theta$. The two outputs therefore alternate in signal magnitude as the lock-in is cycled through values of θ , and are described by

$$X = V_{sig} \cos \theta \quad Y = V_{sig} \sin \theta \quad (3.10)$$

Typically, the X output is described as the in-phase (I) and Y as the quadrature (Q) components of the signal, and constitute the signal as vectors relative to the lock-in reference. The magnitude of the signal, R , can also be obtained from

$$R = (X^2 + Y^2)^{\frac{1}{2}} = V_{sig} \quad (3.11)$$

However, for the phasor decomposition method, it is the X and Y outputs that are of most interest.

3.2.4 The phasor decomposition method

The basis of the self-calibrating method for WMS was first demonstrated by Duffin *et al.* [65] who aimed at utilising the inherent phase lag between the amplitude modulation (AM) that occurs to the laser output power and the frequency modulation (FM) when the high frequency sine modulation is applied to a diode laser. They proposed that by singling out various components of the WMS signal separated by this phase lag, the absolute transmission function can be extracted. Their early approaches were based simply on RAM nulling but the high modulation frequencies required ($\sim$ MHz) were not always practical for diode laser systems. Instead, they developed the approach into the phasor decomposition method (PDM) that is independent of the modulation frequency [73, 74]. It is this approach that is discussed here, and demonstrated experimentally.

The advantage of the PDM calibration is that it removes the need of sometimes expensive gas mixtures, or provides a possible alternative to calibration by direct absorption when the signal levels are too low to detect in this manner. Its main disadvantage is that the theory begins to break down at modulation amplitudes where $b > 0.2$, where more complicated

correction factors are required to extract the absorption information. However, if adequate WMS signals can be obtained within the derivative limit, then this is not problematic.

The basis of PDM is that the FM signal phase lags the output power AM phase, which is aligned with the phase of the applied current modulation, by a phase angle, φ . This is due to the laser power modulation, and hence the RAM, being in phase with the applied current modulation, whereas the corresponding FM due to the current modulation is induced by a combination of fast carrier movement in the semiconductor material and slow thermal effects. The fast carrier injection, which varies the refractive index of the gain medium, is in phase with the current modulation, however, the thermal effect, which is the expansion and contraction of the DFB grating, is relatively slow. Hence the FM component arising from this is out of phase with the laser power modulation [75–77].

To represent the PDM theoretically, it is necessary to take into account the AM variation in intensity not only due to attenuation by an absorbing species, which has been represented in section 3.2.1, but also the AM component due to the power modulation of the laser. The spectral modulated intensity injected into the system, for a given frequency ω , can therefore be described to include this intensity AM component as

$$I_{in} = I(\omega) + \Delta I(\omega) \cos(\omega_m t) \quad (3.12)$$

where the pathlength, l , is again set to one. Therefore, the transmitted intensity $I_T(\omega)$, after interaction with an absorbing medium, as given by Equation 3.3, can be rewritten in terms of Equation 3.12:

$$I_T(\omega) = [I(\omega) + \Delta I(\omega) \cos(\omega_m t)](1 - \alpha(\omega)) \quad (3.13)$$

Following the same Taylor expansion as given by Equation 3.4, and in this case substituting in the modified $(\omega - \omega_0) = \delta\omega \cos(\omega_m t - \varphi)$, where $\delta\omega$ is the FM excursion of the laser output, and φ is the phase lag between the FM and laser power AM components, gives

$$\begin{aligned} I_T(\omega) = & [I(\omega) + \Delta I(\omega) \cos(\omega_m t)] \\ & \times \left[1 - \alpha(\omega) - \frac{d\alpha}{d\omega} \bigg|_{\omega_0} \delta\omega \cos(\omega_m t - \varphi) \right. \\ & \left. - \frac{1}{2!} \frac{d^2\alpha}{d\omega^2} \bigg|_{\omega_0} (\delta\omega)^2 \frac{1}{2} (1 + \cos 2(\omega_m t - \varphi)) - \dots \right] \end{aligned} \quad (3.14)$$

Finally, by disregarding the higher order terms and including only the terms dependent on the modulation frequency component, ω_m , Equation 3.14 simplifies to

$$I(\omega_m) = \Delta I(\omega_m) \cos(\omega_m t) - \Delta I(\omega_m) \alpha(\omega_m) \cos(\omega_m t) - I(\omega_m) \left. \frac{d\alpha}{d\omega} \right|_{\omega_0} \delta\omega \cos(\omega_m t - \varphi) \quad (3.15)$$

This representation of the intensity variation at ω_m now incorporates the background RAM signal, the absorption dependent RAM and the typical $1f$ signal resulting from the FM applied to the laser. The background RAM is the first term in the right hand side of Equation 3.15, and is independent of the gas concentration or intensity $I(\omega)$, but does depend on the intensity variation, $\Delta I(\omega)$, with ω . The component of the RAM that is absorption dependent is given by the second term. This term contains the absorption information, α , and its extraction from the experimental signal is the aim of this method. Finally, the derivative signal amplitude modulation due to the FM modulation, from here on called the FM/AM signal is given in the third term. This final term is typically of interest when extracting WMS signals. The first two terms defining the absorption dependent and independent RAM signals are in phase with the applied current modulation, however, as previously stated, there is a phase lag of φ on the FM/AM absorption signal information. It is this phase lag that enables the separate extraction of the overall RAM component, which contains the absolute absorption information required, and the FM/AM component.

As described in section 3.2.3, the use of a lock-in amplifier results in two outputs X and Y that are $\pi/2$ out of phase, and it is this phase difference that is used to extract the necessary signals. To better understand how this is achieved, the cosine terms in Equation 3.15 are represented as phasors relative to the lock-in X and Y axis, as shown in Figure 3.7.

In Figure 3.7, the total RAM component given by the first two terms in Equation 3.15 is represented in red. The FM/AM component given by the third term, and which differs in orientation to the total RAM component by the phase lag angle φ , is shown in blue. The FM/AM component is represented here as two phasors in anti-phase, as the signal undergoes a π phase change as it goes through the absorption line center.

Experimentally, the lock-in amplifier settings are adjusted such that the total RAM is aligned with the lock-in X -axis, and correspondingly nulled on the Y -axis, as shown in Figure 3.7. What this means in practice, is that the lock-in phase angle is changed until a point is reached where the Y output shows no RAM signal components, i.e., there are no characteristic baseline variations due to RAM, and the baseline signal runs through zero.

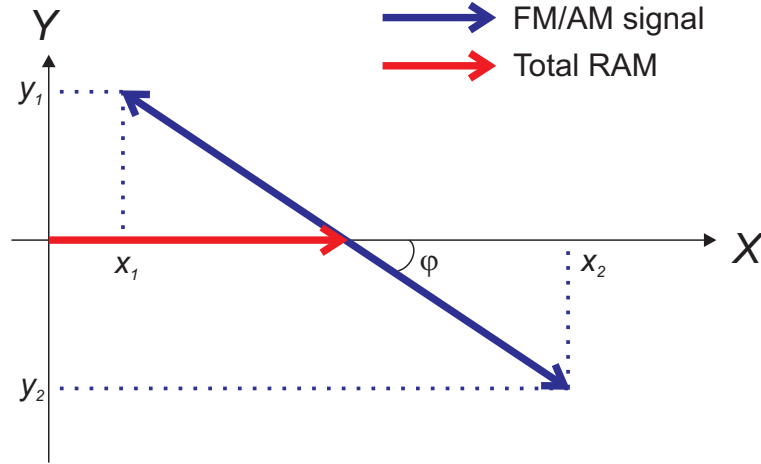


Figure 3.7: Phasor diagram representing the total RAM component, $\Delta I(1 - \alpha)$, in red and the FM/AM signal in blue. Note that these phasors are out of phase by the lag angle φ . The lock-in X and Y axes, which are $\pi/2$ out of phase are also shown, along with the relevant projections of the FM/AM component onto these axes.

Therefore, any signal components of the total RAM can be monitored on the X -output, as it is $\pi/2$ out of phase. Experimental examples of the X and Y outputs aligned this way are given in the next section, in Figure 3.9.

The Y -output itself, now that it has been set to be out of phase with the RAM components, simply measures the projection of the FM/AM signal, given by the third term in Equation 3.15, onto the Y -axis. The result of these manipulations is that the X -axis now measures, at a given frequency, ω , the total RAM, which contains the absorption profile information, and the FM/AM projection on to the X -axis, given by

$$RAM_{total} = x_{1,2}(\omega) + \frac{y_{1,2}}{\tan(\varphi)} \quad (3.16)$$

where $x_{1,2}$ and $y_{1,2}$ are indicated on Figure 3.7. If the line measured is symmetric and the RAM contribution is linear across the region, then $x_1 = x_2 = x$ and $y_1 = y_2 = y$. Therefore, by applying Equation 3.16 point-by-point along the range of ω values, the pure RAM signal can be obtained. This, however, does require the measurement of φ which can be calculated, assuming the same symmetry conditions mentioned, from the trigonometric manipulation

$$\tan \varphi = \frac{|y_1| + |y_2|}{x_2 - x_1} \quad (3.17)$$

With the pure RAM signal obtained, it needs to be normalised to the background RAM variation which is absorption independent. This can either be obtained by monitoring the variation when no absorber is present, or by applying a polynomial fit of the baseline section

where there is no absorption. After this normalisation, the resulting data gives the absolute absorption line transmission function.

3.2.5 WMS and PDM calibration of atmospheric H₂O: Experimental

The experimental setup is indicated in Figure 3.8. The laser used is the 1368 nm diode laser described in Chapter 2 [NTT Electronics, NLK1E5EAAA], and is mounted and controlled in the same manner as described previously. The line probed in this work was at 7406.737 cm^{-1} from the $\nu_1 + \nu_3$ band, $((3, 1, 3) \leftarrow (2, 1, 2))$, and with $\sigma_{INT} = 1.8 \times 10^{-20} \text{ cm}^2 \text{ cm}^{-1}$. The beam path was aligned through air to detect H₂O at atmospheric conditions. To prevent too high a signal overloading the lock-in amplifier, reflections from beam splitters were used to cut down the incident power on the detector, which resulted in an overall pathlength of 12 cm through lab air. The detector used was an amplified photodiode detector [Thorlabs, PDA255]. The X and Y outputs of the lock-in amplifier [Stanford research systems, SR830 DSP], were recorded simultaneously using an oscilloscope [LeCroy 93114M] after 100 averages to improve the signal-to-noise. A spectrum analyser [Melles Griot, 13SAE048] was also used to monitor the modulation amplitude.

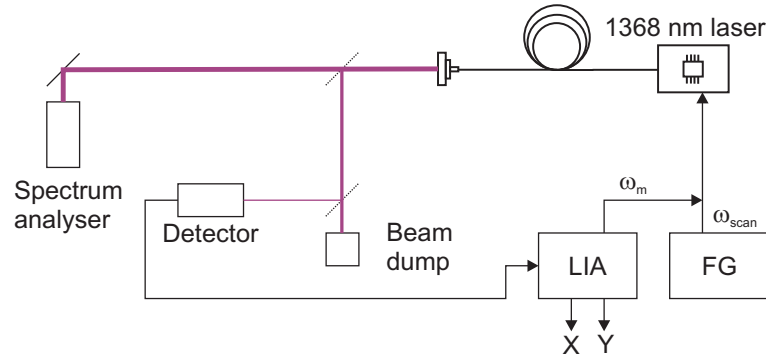


Figure 3.8: Schematic of the experimental setup used for WMS on atmospheric H₂O at 7306.737 cm^{-1} . In this figure, beam splitters are represented by dashed lines and the key electronics providing modulation to the laser, the lock-in amplifier (LIA) and the function generator (FG) are indicated.

For obtaining WMS signals of H₂O absorption to be used for PDM calibration, the experimental parameters were set to optimise signal-to-noise on the absorption feature but without exceeding $b = 0.2$, as dictated by the theory, which was kept at 0.19, by applying a 0.116 V modulation amplitude at 30 kHz to the laser, using the lock-in amplifier as the waveform generator.

3.2.6 WMS and PDM calibration of atmospheric H₂O: Results

Typical examples of the X and Y outputs obtained after nulling the RAM contribution on the Y -axis, by setting the lock-in phase angle to -15.82° , are shown in Figure 3.9.

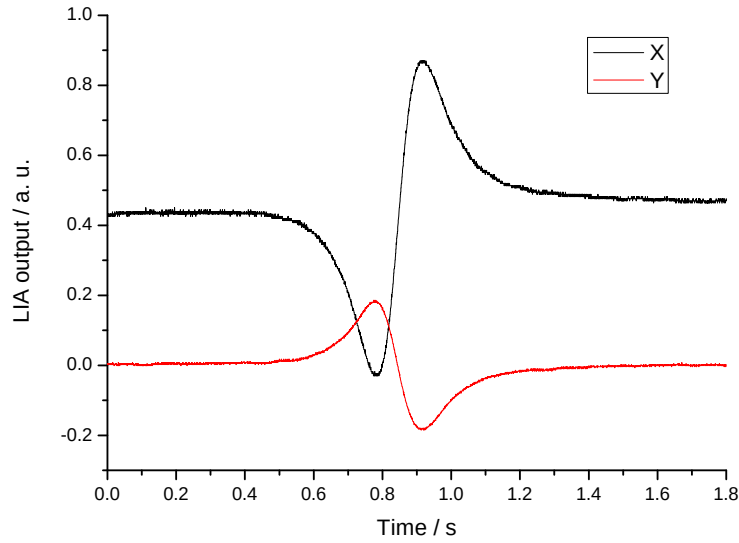


Figure 3.9: Examples of data from the X and Y outputs of the lock-in amplifier after aligning the RAM component to the X -axis.

After applying the required manipulation to the X and Y data as described previously, and obtaining a phase lag angle of $\varphi = 31.0^\circ$, the absolute absorption information can be retrieved in the form of a transmission function, and is shown in Figure 3.10a.

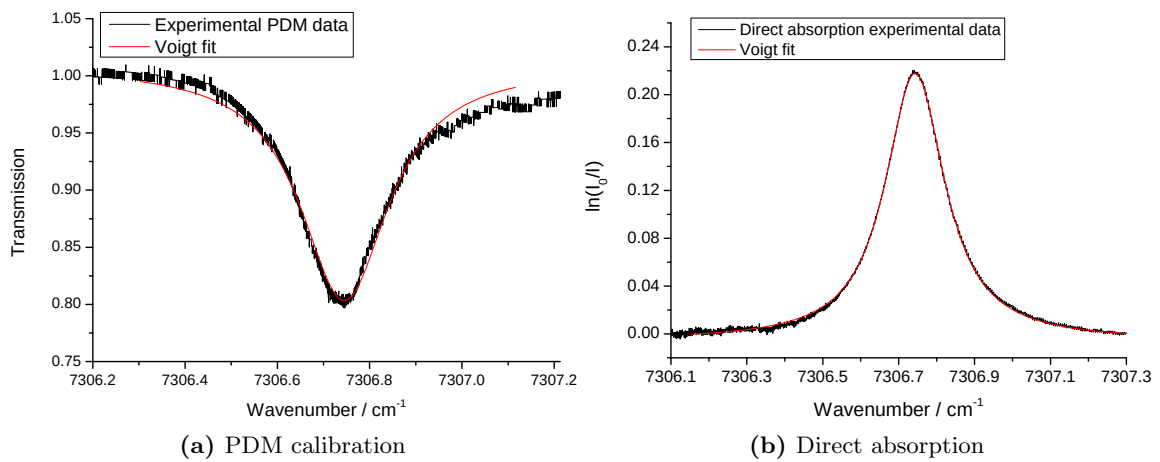


Figure 3.10: Graph (a) shows the absolute transmission function in black obtained from the PDM analysis of the X and Y outputs of the lock-in when the RAM component is aligned to the X -axis. The equivalent direct absorption spectrum taken over the same pathlength is shown in graph (b). Both data sets show corresponding Voigt fits in red.

The main issue with the data returned from the PDM analysis is the noise level on the data, as the digitization limit of the signal has been reached. However, this is to be expected with such large X and Y output signals, as shown in Figure 3.9, with comparatively low baseline noise. This could further be improved by use of a higher resolution data acquisition setup, or when using this method with lower absorption levels, where the WMS signals will not be limited by digitization. The slight variation in the baseline when compared to the fit is attributable to inadequate normalisation to the background RAM signal. Ideally, this would be obtained with no absorber present, but as this is not an option for H_2O in air, an estimate has been made for the form of the background RAM.

3.2.7 WMS and PDM calibration of atmospheric H_2O : Conclusions

Whilst the main aim of this thesis has been focused towards breath analysis, it is important to emphasize that many of the techniques demonstrated apply equally well in other sensitive detection fields as well. This is particularly true for the WMS studies on H_2O , which have successfully utilised the phasor decomposition method as a self-calibrating form of WMS detection. The calibration via PDM was not strictly necessary on such a strong absorption, but this line was chosen such that a direct absorption measurement could be used for comparison and the use of PDM on atmospherically broadened H_2O as a “proof-of-principle” study shows great potential for calibrating WMS absorption signals in a more realistic breath analysis environment, i.e. where concentrations are lower, but absorption features are atmospherically broadened.

The returned concentrations of H_2O from the PDM calibration and the direct absorption calibration differed by 9 % with a ~ 15 % difference in the Lorentzian widths, which is most likely due to poor subtraction of the RAM background variation. Further improvements could be made to reduce the level of digitisation noise on the spectra, but this is unlikely to be the limiting factor in a more practical application of the PDM method, where the signal sizes are likely to be lower for weaker absorption levels. Therefore, further investigation using this method on trace species in breath, or even in atmospheric samples would be of interest.

Overall, the data shown here demonstrate that calibration by the PDM shows great potential in fields such as breath analysis, where low concentrations of species make direct absorption studies difficult, and where this convenient and robust approach would therefore be invaluable.

3.3 FMS studies on O₂

In this section, the use of frequency modulation spectroscopy for the detection of atmospheric O₂ is investigated, as a potential alternative to the CEAS method described in Chapter 2. The use of FMS would potentially have some advantages over an optical cavity method, as it does not rely on the use of high quality cavity mirrors, however, it does produce more complex signals that require a higher level of post processing. The work presented here is a discussion of whether the sensitivity and experimental practicalities would make FMS a viable alternative for real-time breath analysis.

3.3.1 Theory of frequency modulation spectroscopy

FMS, like WMS, is a non-absolute technique and the theory presented here describes the form of the resulting signals. As previously stated, FMS operates at much higher values of ω_m and lower values of M compared to WMS. For discussing the theory of a frequency modulated laser source interacting with an absorbing medium, it is more convenient to work in terms of the spectrally modulated optical field as given by Equation 3.1 [66, 78]. This can be re-written in terms of the individual frequency components as follows

$$\begin{aligned} E(t) &= E_0 \exp[i(\omega_0 t + M \sin \omega_m t)] \\ &= E_0 \exp(i\omega_0 t) \sum_{n=-\infty}^{+\infty} J_n(M) \exp(in\omega_m t) \end{aligned} \quad (3.18)$$

where the probe spectrum is characterised by the expansion in a series of n^{th} order Bessel functions, J_n . For FMS where M is typically small, the resulting probe spectrum consists of the main carrier frequency component, ω_0 , and two sidebands at $\omega_{\pm 1} = \omega_0 \pm \omega_m$. These sidebands can be detected using a spectrum analyser, an example of which is shown in Figure 3.11.

The interaction of the components ω_n with an absorbing medium can be described in terms of the complex transmission function

$$T(\omega_n) = \exp(-\delta_n - i\phi_n) \quad (3.19)$$

where δ_n is the field amplitude attenuation due to the absorber and ϕ_n is the optical phase shift. The transmitted optical field is therefore described by

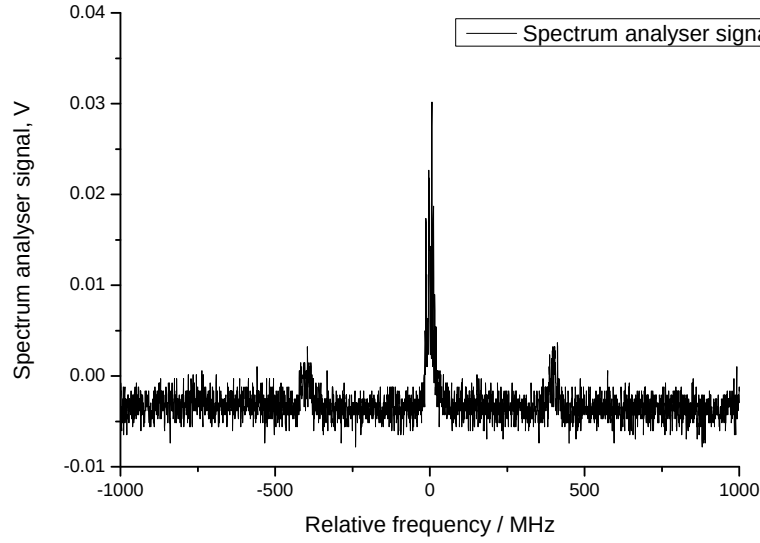


Figure 3.11: Example of a spectrum analyser trace showing the sidebands at $\omega_{\pm 1} = \omega_0 \pm \omega_m$. In this case $\omega_m = 400$ MHz. The data in this figure was taken using the setup for FMS detection of O_2 at 760 nm, as described in the following sections.

$$E(t) = E_0 \exp(i\omega_0 t) \sum_{n=-\infty}^{+\infty} T(\omega_n) J_n(M) \exp(in\omega_m t) \quad (3.20)$$

When using a “square law” photodetector, changes in δ and ϕ due to the absorption result in a time varying intensity, $I_T(t)$, that is proportional to the square modulus of the transmitted optical field $|E^2(t)|$. Assuming the difference in absorption and dispersion between the two sidebands at $\omega_{\pm 1} = \omega_0 \pm \omega_m$ are small, as well as the overall absorption and dispersion associated with the absorption being weak, $|E^2(t)|$ can be written as

$$\begin{aligned} |E^2(t)| = & E_0^2 \exp(-2\delta_0) \left[1 + 2 \cos \omega_m t \sum_{n=0}^{\infty} J_n J_{n+1} \right. \\ & \times (\delta_{-n-1} - \delta_{n+1} + \delta_{-1} - \delta_n) + 2 \sin \omega_m t \\ & \left. \times \sum_{n=0}^{\infty} J_n J_{n+1} (\phi_{-n-1} - \phi_{n+1} + \phi_{-1} - \phi_n) \right] \end{aligned} \quad (3.21)$$

Equation 3.21 describes the detected signal form when the spectrally modulated probe light interacts with the absorbing medium, assuming there is no amplitude modulation. The signal is made up of a DC component and the time-varying absorption and phase components that can be detected separately with phase sensitive electronics.

In typical FM experiments, as previously stated, only one pair of sidebands are considered because M is small, and therefore the amplitude of higher order sidebands dictated by $J(M)$ are negligible. With this assumption made, and since $J_0(M) \approx 1$ and $J_1(M) \approx M/2$, Equation 3.21 simplifies to

$$|E^2(t)| = E_0^2 \exp(-2\delta_0) [1 + M(\delta_{-1} - \delta_1) \cos \omega_m t + M(\phi_{-1} + \phi_1 - 2\phi_0) \sin \omega_m t] \quad (3.22)$$

In essence, during an FMS experiment, the three components ω_0 and $\omega_{\pm 1}$ are attenuated/phase-shifted by the absorption profile as the carrier frequency, ω_0 , is scanned across the feature. The resulting FMS absorption signal takes a form resembling the relative difference in attenuation of the side bands compared to ω_0 as a function of frequency, and the dispersion signal, the difference in $\phi_{\pm 1}$ relative to ϕ_0 . The production of these signal forms, for example for absorption, is represented schematically in Figure 3.12.

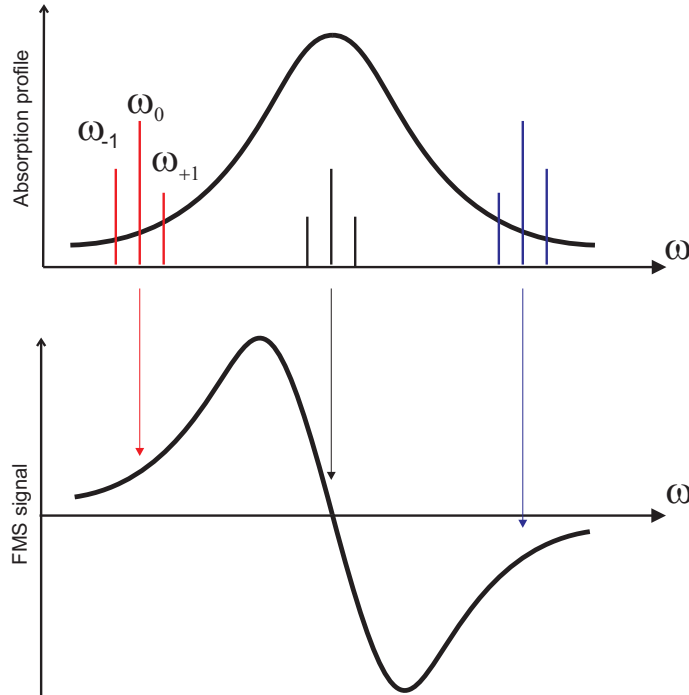


Figure 3.12: Illustration of generation of an FMS differential signal by sweeping the laser carrier frequency and sidebands across an absorption feature, and monitoring the relative attenuation.

Extracting this signal information requires certain demodulation electronics and settings, to separate out the information pertaining to the absorption signals (the cosine component of Equation 3.22) and the dispersion signal (the sine component). The experimental implications of this are discussed in the following section.

3.3.2 FMS experimental considerations

An FMS experiment requires the means to generate a high frequency modulation, usually through use of an rf generator which can then be applied to the laser output. This can be achieved by directly modulating the laser current [79] or by the use of an electro optic modulator (EOM) in the beam path. The advantage of using an EOM, is that if aligned carefully, the result is only pure frequency modulation of the signal as has been described so far theoretically. Conversely, when using direct modulation of the laser current, the resulting RAM also introduces a background intensity variation, as discussed for WMS, which needs to be accounted for. For the work in this thesis, modulation via an EOM has been utilised. The resulting FM signal is detected and requires demodulation to analyse the absorption and dispersion components, a description of which is now given.

For ease of analysis, by viewing only the time-varying components, i.e., the absorption and dispersion components of Equation 3.22, the intensity of the FMS signal can be written as

$$I_{FMS}(t) = E_0^2 \exp(-2\delta_0) [M(\delta_{-1} - \delta_1) \cos \omega_m t + M(\phi_{-1} + \phi_1 - 2\phi_0) \sin \omega_m t] \quad (3.23)$$

or more simply,

$$I_{FMS}(t) = A_{FM}(\omega) \cos \omega_m t + D_{FM}(\omega) \sin \omega_m t \quad (3.24)$$

The cosine term in this form, containing the absorption information, is denoted A_{FM} and the sine term is correspondingly denoted D_{FM} . The A_{FM} and D_{FM} components are obtained by mixing I_{FMS} with the rf reference at the modulation frequency and using an I/Q demodulator to extract the signal. The I/Q demodulator works on a similar principle to the lock-in amplifier described in section 3.2.3. The demodulator itself does not return the separate absorption and dispersion signals themselves. Instead, in a similar manner to the lock-in amplifier, it provides an in-phase and quadrature component of the signal with a fixed phase shift of $\pi/2$ between them.

The resulting signals I and Q signals are related to A_{FM} and D_{FM} through a phase angle, θ .

$$I(\omega) = c_I [A_{FM}(\omega) \cos \theta + D_{FM}(\omega) \sin \theta] \quad (3.25)$$

$$Q(\omega) = c_Q [A_{FM}(\omega) \sin \theta + D_{FM}(\omega) \cos \theta] \quad (3.26)$$

where c_I and c_Q are constants of proportionality. In this definition, the phase angle θ is essentially the phase difference between the reference signal and the detected signal, and can be altered by applying an added voltage to the electronics to introduce a further phase shift. By assuming that the signal magnitudes are equal, i.e., $c_I = c_Q = c$, the absorption and dispersion components can be calculated from

$$A_{FM} = \cos \theta I(\omega) + \sin \theta Q(\omega) \quad (3.27)$$

$$D_{FM} = \sin \theta I(\omega) - \cos \theta Q(\omega) \quad (3.28)$$

The use of this equation however, implies that the phase angle θ is known, the calculation of which will be discussed in the results section.

3.3.3 FMS of atmospheric O₂: Experimental

A schematic of the setup, plus the relevant electronics used for FMS detection of O₂ is illustrated in Figure 3.13.

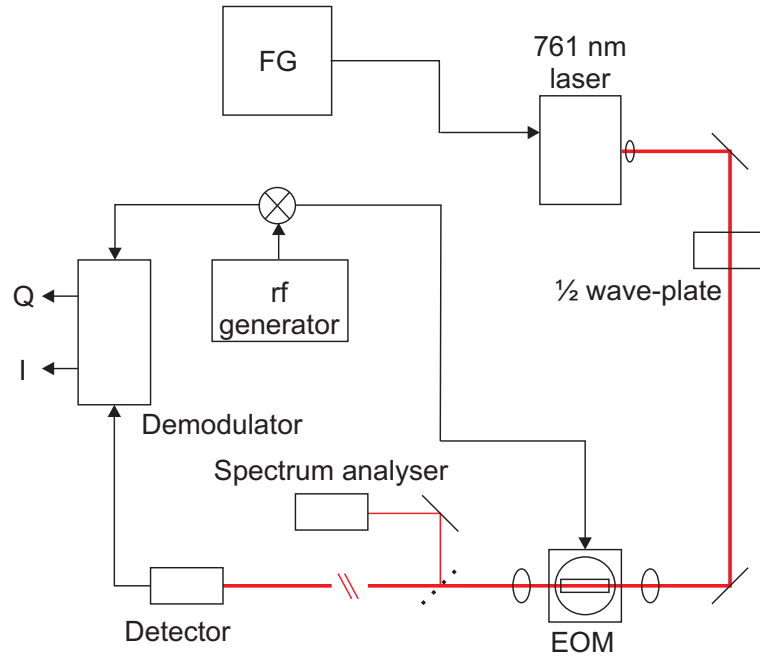


Figure 3.13: Schematic of experimental setup for FMS of atmospheric O₂ setup showing optical components and relevant electronics.

The laser used was a 761 nm DFB diode laser [Sarnoff, SAR-761-DFB] mounted in a temperature controlled mount [Thorlabs, TCLDM9] and controlled by commercially available current and temperature controllers [Thorlabs, LDC205 C and TEDC 200C respectively]. The laser was aligned through a $\frac{1}{2}$ -wave plate to rotate the polarisation to optimise the

output of the EOM [New Focus, 9071]. The beam was focused entering and exiting the EOM using a pair of lenses. The EOM itself was modulated using an rf generator [Marconi Instruments, 202]. A reflection from a beam splitter was then taken off to monitor with a spectrum analyser [Thorlabs, SA200-6A] and the main part of the beam monitored using a photodiode detector [New Focus, 1601 1GHz]. To improve the sensitivity of the system in these investigations, a relatively long pathlength through the air of 136 cm was used.

3.3.4 FMS of atmospheric O₂: Results

Obtaining the maximum A_{FM} or D_{FM} component from either the I or the Q channel signal can be achieved by setting the phase to $n\pi$ or $n\pi/2$, where the two signals are independent due to their opposing sine and cosine dependence on the I and Q channels.

To set the phase angle, a phase-shifter is introduced into the electronics as previously mentioned, however, an accurate way of determining its value is also required. To obtain θ the I and Q signals given by Equations 3.26 are simultaneously fit using an optimisation routine to vary θ and the Lorentzian width of the feature, with the Doppler width set at its calculated value. The fit is based on the Voigt absorption lineshape as discussed in section 1.3, as the O₂ sample in air is atmospherically broadened. In this modeling of the lineshapes, the dispersion profile is related to the absorption profile through the Kramers-Krönig relations and the fitting of a Voigt profile, which has no analytical solution [80], is carried out using the Hilbert transform [81].

Some typical examples of the I and Q outputs for various phase angles are shown in Figure 3.14. The fits to the I and Q outputs to obtain θ are also shown. These data have been averaged 200 times and were taken with a 1 kHz scan rate over the feature, and with the rf generator set to produce a 400 MHz frequency modulation. As can be seen from these examples, as θ cycles through 0 to $n\pi$ the relative magnitudes of the I and Q outputs also cycle as either the A_{FM} or D_{FM} components are minimised.

With determination of θ now possible, the phase shift was set as close to $n\pi$ as possible to maximise the absorption and dispersion components in each of the two output channels. An example of the absorption and dispersion signals obtained is shown in Figure 3.15.

However, since the aim of these investigations is to obtain a measurement system with a maximum signal to noise to improve the sensitivity of detection of O₂, a full separation of absorption and dispersion lineshapes is not necessarily required. Instead, by maximising one of the outputs of the demodulator, the optimum signal-to-noise ratio can be obtained, and the sensitivity of this compared with what is necessary for breath analysis, and with the CEAS experiments in Chapter 2. An example maximised Q signal taken using FMS

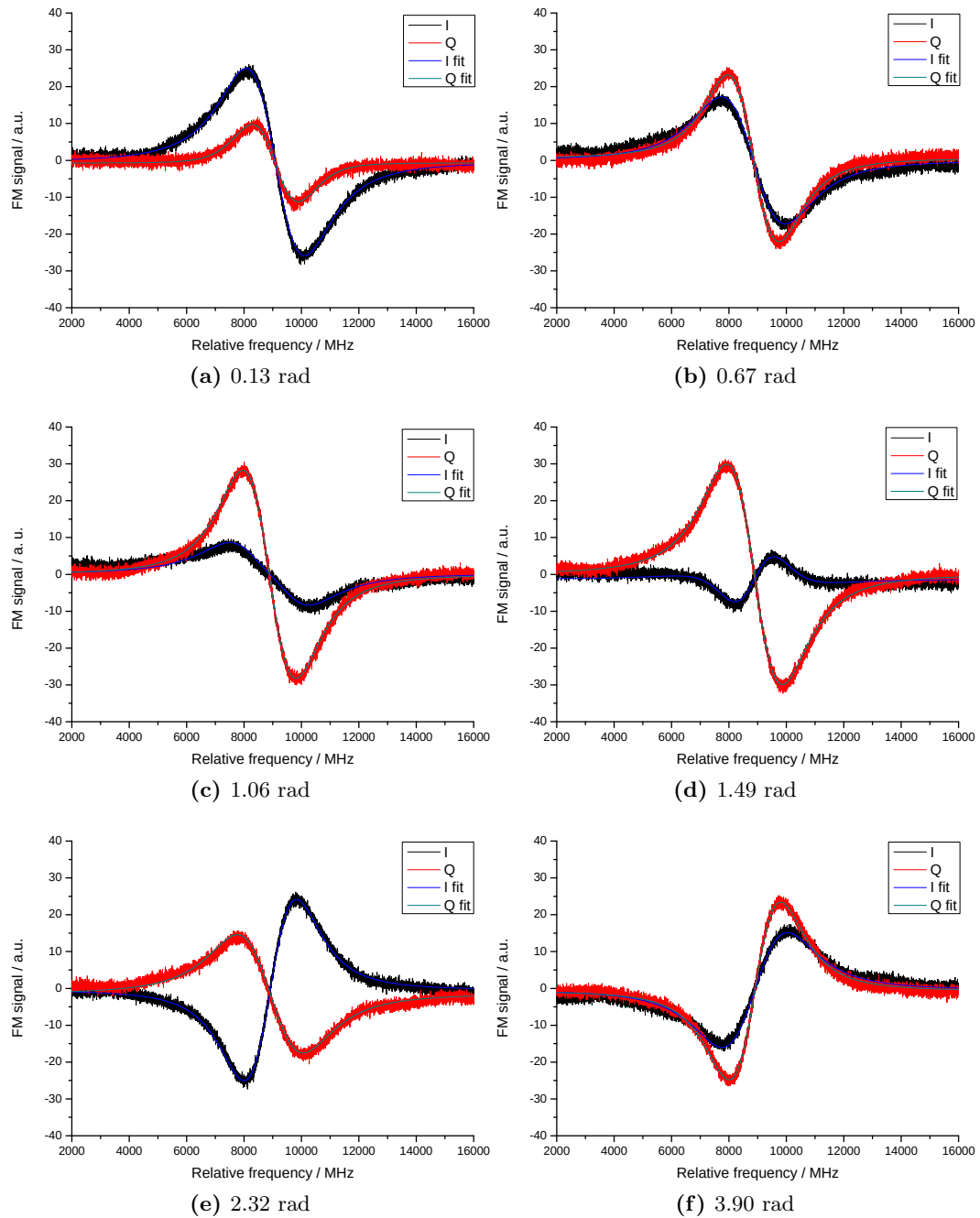


Figure 3.14: Examples of I and Q outputs for different phase shift settings and their corresponding fits to obtain θ .

over 10 ms is shown in Figure 3.16, as well as a typical CEAS trace obtained from the setup described in Chapter 2, also with an acquisition time of 10 ms. However, the data shown here has for FMS has been taken over a relatively long pathlength (136 cm) compared to that which has been achieved with CEAS measurements of O_2 (2.75 cm), and so this needs to be taken into account when comparing sensitivities.

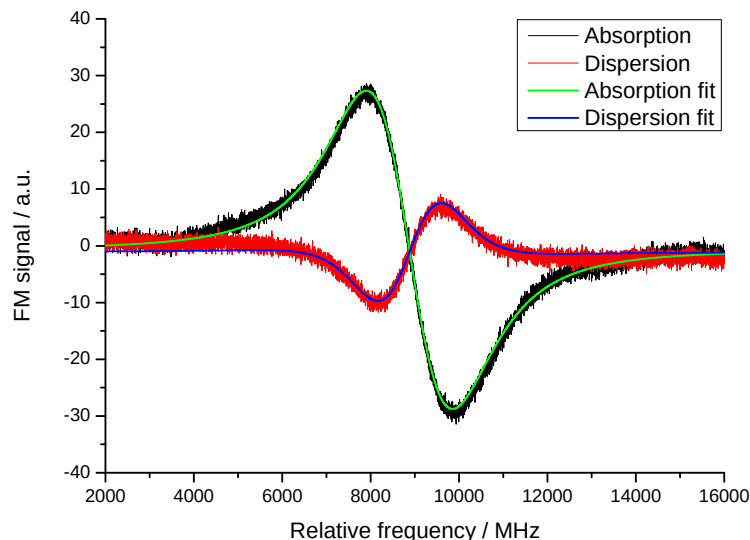


Figure 3.15: Example of absorption (black) and dispersion (red) traces, with respective fits shown in green and blue, of atmospheric O_2 at 760.954 nm, R11R11 taken over 136 cm and with an acquisition time of 200 ms.

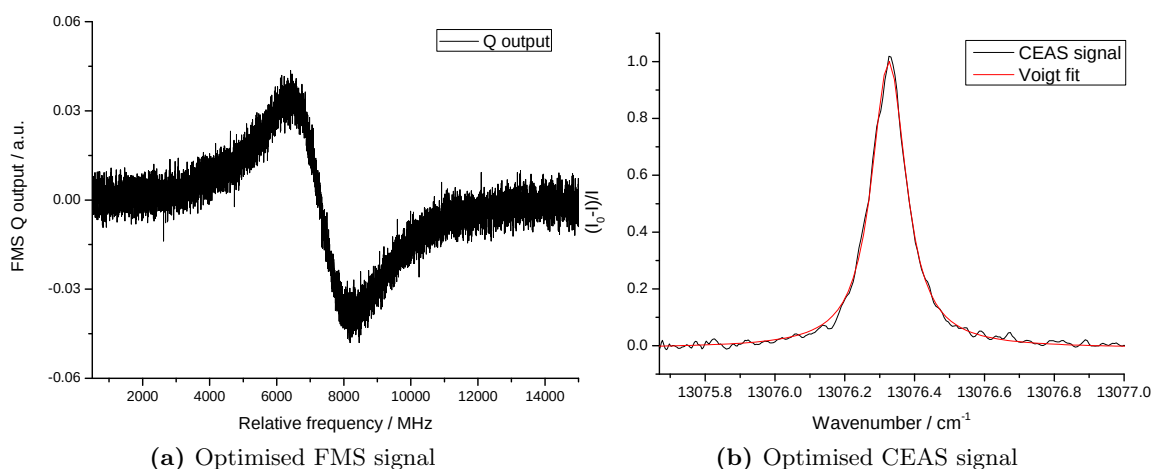


Figure 3.16: Graph (a) shows example of a maximised Q output from FMS of atmospheric O_2 R11R11 over 136 cm, taken over 10 ms. Graph (b) shows a CEAS spectrum of atmospheric O_2 P13P13 for comparison, taken over 2.75 cm and with an acquisition time of 10 ms.

One way of comparing the FMS and CEAS measurements is through their α_{min} values, although, this only accounts for noise levels on an instantaneous measurement of a particular concentration, since it relies simply on the baseline noise level on an individual spectrum. Therefore, it does not take into account other possible noise sources that occur during a typical breathing experiments such as turbulence, temperature gradients or mechanical

movement in the system. However, for comparing the two techniques in terms of their absolute sensitivity, α_{min} values can be very informative.

The lowest time normalised $\alpha_{min}(t)$ value obtained for the O₂ CEAS spectra obtained using the Mark III prototype analyser in Chapter 2 was $2.35 \times 10^{-8} \text{ cm}^{-1} \text{ s}^{\frac{1}{2}}$. For the FMS data reported here, the equivalent measurement for a maximised Q output signal was $2.45 \times 10^{-6} \text{ cm}^{-1} \text{ s}^{\frac{1}{2}}$, which is obtained by assessing the data's signal-to-noise, i.e., the signal height divided by the standard deviation of the baseline, normalised to the peak absorbance for this transition.

As can be seen, when the systems are compared and differences in acquisition time and pathlength accounted for, the sensitivity of the FMS is ~ 2 orders of magnitude worse than the data acquired by the CEAS system described in Chapter 2. This could potentially be further improved by moving to an even higher modulation frequency regime, however, the difficulty this presents is in either driving an EOM or the laser injection current itself at such high modulation frequencies. As well as this, it is unlikely that the improvement would be such as to compare with the sensitivity obtained by using CEAS.

3.3.5 FMS of atmospheric O₂: Conclusions

An FMS based detection system of atmospheric O₂ has been demonstrated at 761 nm, as a potential method for monitoring O₂ levels in breath. Whilst the FMS measurements display a high detection sensitivity, the pathlength and acquisition time demands of a breath analysis system mean that the technique is not yet as sensitive as the alternative CEAS method that has been utilised instead for real-time breath analysis. Further to this, when considering the practical elements of the two techniques, the experimental complexity and expense introduced by the use of an EOM could be considered a less favourable alternative to cavity mirrors, which can be relatively inexpensive when ordered in bulk.

However, whilst FMS is presented here as a potential alternative to the use of an optical cavity, it is another detection methodology with a wide range of applications. Although the use of FMS was not found to be comparable to CEAS in the context of real-time breath analysis, its use as a effectual tool for sensitive detection of atmospherically broadened species has been demonstrated, and it has great potential for analysis of other biomarkers, where the pathlength and time constraints may not be as stringent. It is also a much more likely alternative for situations where the use of an optical cavity is not ideal, for example when the species of interest can contaminate the mirror coatings or when working in spectral regions where the cost and quality of cavity mirrors outweighs potential gain in sensitivity.

Chapter 4

Spectroscopy in the MIR using QCLs: The potential for breath analysis

So far, the work in this thesis has considered the sensitive detection of the main respiratory gases by working in the NIR. With such high concentrations of these gases in breath, working in the NIR, where there tend to be relatively weak absorption cross-sections but more readily available equipment, is still a practical option. However for trace gas detection, for example of biomarkers in breath or for atmospheric trace gases with concentrations of $\sim$ ppb, working with these smaller cross-sections becomes increasingly difficult.

An alternative is to move to the MIR, where the fingerprint region around 3 to 25 μm contains fundamental absorptions from most molecular species, allowing the exploitation of these stronger cross-sections. However, this region of the electromagnetic spectrum is not accessible with conventional diode lasers and instead other means of generating MIR radiation need to be employed. This chapter outlines the moving of trace gas detection to the MIR and in particular the use of quantum cascade lasers (QCLs) for potential breath analysis studies. QCL systems for trace gas detection involve relatively new technology and in this work, a single mode continuous wave (cw) QCL has been utilised. As the underlying principles behind QCL technology differ significantly from conventional semiconductor laser systems, the relevant theory behind their operation is described. As well as this, the experimental practicalities and requirements when setting up an 8 μm QCL spectrometer are also detailed, with particular focus on improving the control electronics and characterising the laser output for spectroscopic studies. Finally, some preliminary studies showing the potential for MIR detection of biomarkers at 8 μm , specifically acetone and methane, are described.

4.1 Moving trace gas detection to the MIR

The main advantage of moving spectroscopic detection to the MIR region is access to the strongly absorbing fundamental bands of a variety of molecules, as opposed to their weaker overtone and combination bands that are more commonly probed in the visible and NIR region. For example, for biomarkers and atmospherically important species such as OCS and CO the increase can be 2 orders of magnitude by simply moving from 2.5 to 5 μm . Examples of the absorption cross-sections for a wide range of absorbers in the MIR for different medically and atmospherically important species are shown in Figure 4.1.

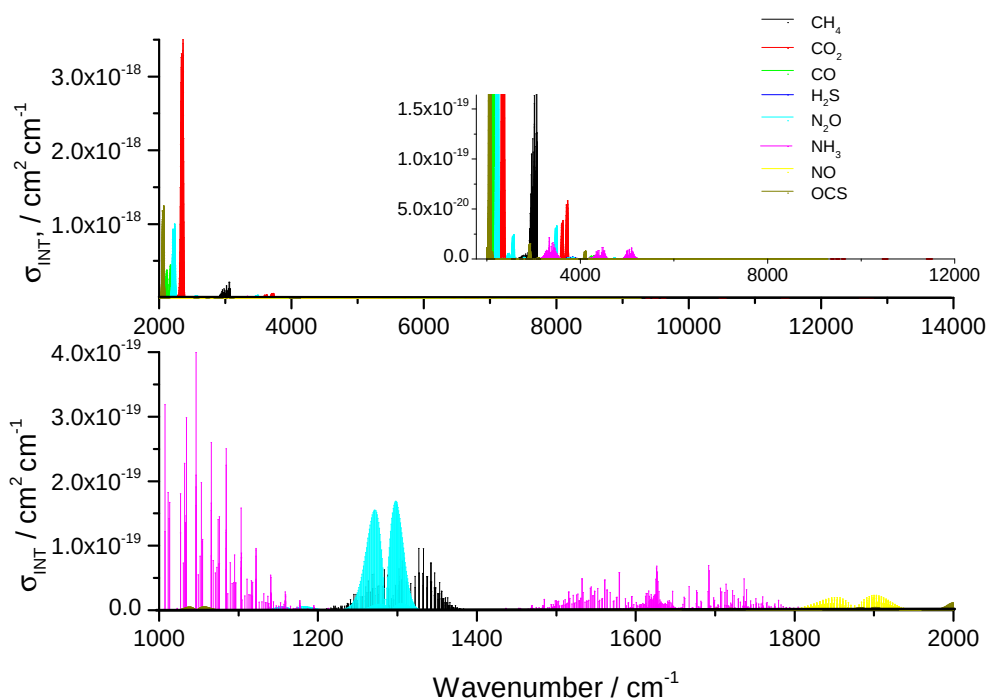


Figure 4.1: Integrated cross-section values for a selection of atmospherically and medically important species sourced from the HITRAN database [40].

Working in the MIR can be achieved through various means. Many solid state laser sources already exist that cover regions within the MIR [7], for example cryogenically cooled semiconductor lead-salt lasers have been developed in the ~ 3 up to $30 \mu\text{m}$ region, but typically exhibit low power outputs in cw mode and poor beam quality. However, even with these disadvantages, the use of lead-salt lasers for sensitive detection has been widely reported, for example, the airborne atmospheric sensing of formaldehyde has been demonstrated by Fried *et al.* [82], where special attention was required to maintain temperature stability of the system to minimise alterations in the laser tuning. Other direct laser sources include the CO and CO_2 lasers, however, for trace gas detection these lasers are limited by the relatively small regions in the MIR that they can access and the large footprint of the laser systems themselves.

Alternatively, other systems that rely instead on the generation of MIR radiation and not on obtaining MIR wavelengths directly from a single laser source are also showing promise for sensitive detection in the MIR. For example, difference frequency generation (DFG) provides a way of producing radiation by combining two other sources. This is achieved using a non-linear material, such as a periodically poled lithium niobate (PPLN) crystal to combine two input optical fields of frequencies ω_1 and ω_2 to produce $\omega_1 - \omega_2 = \omega_3$. A more detailed description of DFG theory and other non-linear systems can be found in ref. [83]. In general, DFG setups have the advantage of relatively large tunability, as both sources can be tuned, but with the disadvantage of low conversion efficiency and corresponding low power output, due to the strict experimental requirements to phase-match the sources. Another option is to employ optical parametric oscillator (OPO) systems, which also utilise a non-linear crystal, but unlike DFG is placed inside a cavity and is used to generate two new frequencies from a single pump beam. Whilst OPO systems are also seeing further progress, especially as pulsed sources, their use in cw experiments is still underdeveloped. Furthermore, DFG and OPO systems are used most frequently in the 2 - 5 μm window due to the commercial availability of the non-linear optics, and spectrometers using non-linear optics have already successfully been described in the detection of atmospherically important species in this region such as acetylene [84], formaldehyde [85] and in the field of breath analysis [86]. However, for work above 5 μm or when higher power outputs are required, a relatively new type of laser, QCLs, are a more efficient alternative.

4.1.1 Quantum cascade lasers

The concept behind QCL lasing action was first proposed in the 1970s [87] but the first demonstration of a viable QCL system was only reported by Faist *et.al.* in 1994 [88], who utilized molecular beam epitaxy to grow layered semiconductor structures. Although still a semiconductor laser, a QCL is not based on the radiative recombination of electron-hole pairs, but instead relies only on the transitions of electrons between discrete conduction band states within quantum wells that are formed by carefully engineering the relative thickness of the semiconductor layers in the structure. A schematic of this type of structure is shown in Figure 4.2, illustrating two stages of the QCL cascade. Each of these stages contains an electron injector and active region, with quantum confinement resulting in a 3-level laser system in the active region where radiative transitions occur from the upper excited state (3) to the lower excited state (2). The electron then relaxes to the ground state (1) and is able to tunnel to the next quantum well in the structure. The layering of materials results in the characteristic energy staircase structure in the conduction bands, when an appropriate voltage is applied. Due to this, an electron tunneling from the ground level in a quantum well is injected into the upper excited state (3) of the next quantum well.

This cascade process results in the recycling of an electron and is responsible for the high output powers that are common among QCLs (10 - 100 mW). The layers are constructed in such a manner that the resulting energy difference between states (2) and (1) is about equal to that of an optical phonon, thus, the relaxation from states (2) to (1) and the tunneling between wells is relatively fast compared to the radiative transition, therefore the necessary population inversion between states (3) and (2) is maintained.

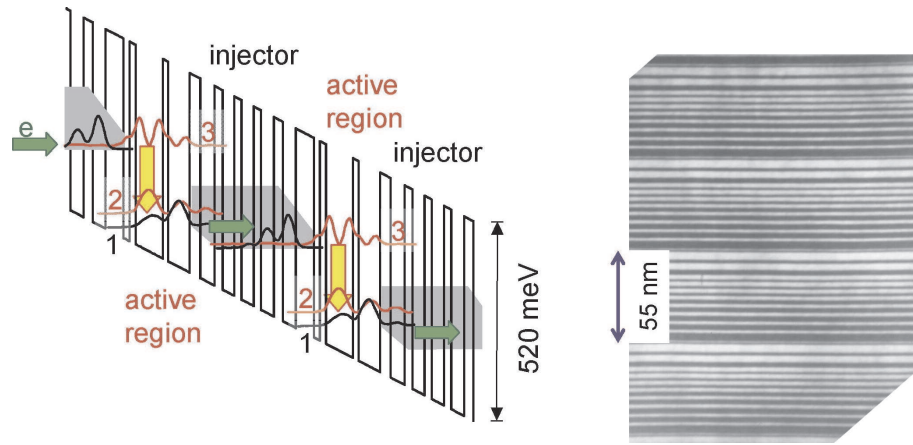


Figure 4.2: Left hand image shows schematic of the QCL energy diagram for two stages, with probability distributions obtained from solving Schrödinger's equation. Right hand image shows a transmission electron microscope picture of the layered structure of a 7.5 μm AlInAs/GaInAs QCL. Both reproduced from ref. [89].

In the early stages of QCL development, the laser cavity reflective surfaces were formed by the cleaving of the laser chip. Since the 1990s, QCL technology has advanced to include Bragg reflectors, as with other semiconductor lasers, that are etched onto the surface of the laser ridge above the active region to improve single mode selection within the laser. Overall, the main principle of selecting the radiative wavelength by engineering of the structure layers as opposed to the intrinsic band-gap properties of more traditional semiconductor lasers, means that a much wider range of emission wavelengths (3.5 μm to 19 μm) is available at higher operating powers. The other main advantage of the QCL structure as opposed to a diode laser is the reduction in laser linewidth due to the absence of spontaneous emission contributing to the laser output. In diode lasers spontaneous emission is the main source of frequency noise, but in a QCL energy level system, the non-radiative relaxation rate from the upper level is faster than the spontaneous emission rate, therefore the contribution to the laser linewidth from spontaneous emission is negligible [90].

Further progress of QCL technology has led to the development of widely tunable broadband sources constructed by stacking active regions corresponding to different optical energies, and emitting multiple wavelengths [91], or by forming arrays of DFB-QCLs that can in total span $\sim 100 \text{ cm}^{-1}$ in single mode operation [92, 93]. These systems are still undergoing more

development and whilst they show promising possibilities for future broadband detection, they are only beginning to enter mainstream use [94].

In the work described in this chapter an *Alpes Lasers* 8 μm cw DFB-QCL that can be current and temperature tuned over a quoted $\sim 10\text{ cm}^{-1}$ is used. An image of the 8 μm QCL chip showing typical dimensions and the conventional mounting of the QCL chip on a gold submount and its connectors is shown in Figure 4.3.

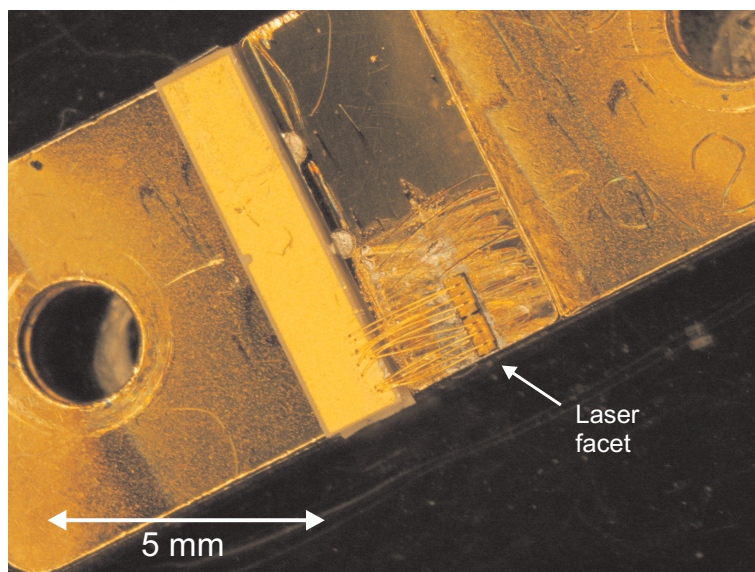


Figure 4.3: Image of the 8 μm QCL chip used in this work. The laser facet and gold contact threads on the submount are clearly visible.

At 8 μm , the QCL can be used to detect a multitude of different molecules, however it is those that are potential biomarkers in human breath that are of most interest to this work, an overview of which is given in the following section.

4.1.2 Breath analysis in the MIR using QCL systems

In recent years, the number of reported works detailing the detection of potential biomarkers in the MIR has increased as QCL technologies enabling the generation of MIR radiation have progressed [10]. The basis of using species in breath as diagnostic tools requires a molecule, or group of molecules, that can be attributed to a particular process or physiology to show an appreciable deviation away from a defined normal profile. This difference also needs to be measurable using the spectroscopic method of interest and more work is required in this field in building up a “normal” profile of biomarkers found in breath as a benchmark for diagnostic limits, by sampling large numbers of subjects and conditions. However, there are many biomarkers whose origin and levels have already been identified, and work towards detecting them spectroscopically using QCLs has been reported [10, 12]. A selection of examples is given in Table 4.1.

Species	Absorption / μm	Physiological source	level	Ref.
Ethane	3.4	Lipid peroxidation	1 ppb	[95]
Acetone	8.4	Diabetes	1 ppm	[96]
NO	5.4	COPD ¹	10 ppb	[97]
NH ₃	10.3	Renal disease	100 ppb	[98]
OCS	4.9	Liver disease	0.5 ppb	[99]
CO	4.6	Lung inflammation	1 ppm	[100]

Table 4.1: Examples of biomarkers found in breath that have been monitored spectroscopically with QCLs. Details of their physiological sources and order of magnitude of the levels found in breath from healthy subjects are also given. ¹Chronic obstructive pulmonary disease.

Overall, breath analysis in the MIR using QCLs is an area of increasing interest for medical diagnostics, and when combined with other sensitive detection methods has the potential to be a powerful medical tool. The work presented here describes the construction of a QCL spectrometer for potential detection of the biomarkers at 8 μm , with the main focus on the future detection of acetone in breath. Acetone itself is found naturally in breath with ~ 0.5 –1 ppm levels. It is produced by liver cells when there is excess acetyl CoA, an intermediate molecule formed during energy production, along with other ketones. Acetone diffuses into the blood stream and therefore is continually present in breath at low levels, however these levels can increase under stress, diet or exercise or in subjects with diabetes mellitus or chronic alcoholism. The potential for monitoring acetone concentrations in breath as a management tool for diabetes was first introduced in the 1960s by Barnett *et al.* [16] and since then various studies on the potential of monitoring acetone in breath have been reported working in the UV [101] and NIR [102], however, little work towards detecting acetone in the MIR using QCLs has been attempted, although some works have been reported using QCLs combined with photoacoustic spectroscopy [96, 103]. In this work, whilst the 8 μm region chosen for acetone detection does not have the strongest acetone absorption cross-sections, which are located around 6 μm , it is however the optimum region in terms of minimising interferences from CO₂ and H₂O absorptions, as well as in terms of availability of QCLs.

As well as the detection of acetone, the detection of methane, which is another biomarker, is also discussed. Methane is produced by colonic bacteria metabolising carbohydrates that were not absorbed in the small bowel and therefore excess methane levels can be an indicator of carbohydrate malabsorption [104]. Whilst methane is a biomarker in its own right, the detection of it here serves several purposes. Firstly, its well-characterised absorption spectrum in the MIR makes it ideal for wavelength calibration, and to demonstrate the sensitivity of the QCL system on a narrowband absorber. Secondly, it is important to assess how the methane absorptions may interfere with the acetone detection, since both molecules are found in breath at similar concentrations and as such a region relatively free

from methane is desirable. As with acetone, studies on detecting methane in the NIR have been reported [102, 105] and there have also been some studies in the MIR using FTIR [106] and DFG/OPO systems [107], and as well as this, some studies on the use of QCLs for methane detection have also been reported [108–110].

4.2 Building the QCL detection system

As QCLs are a less mature technology than conventional diode lasers, the practicalities and characteristics of setting up a QCL spectrometer are discussed in more detail in this section, particularly the controlling electronics and the characterisation of the laser output.

4.2.1 The QCL operating parameters

Running a QCL requires several key components, many of which are becoming more readily available from commercial sources, however it is often more efficient to tailor the components to a specific laser system and design and build them in-house. In this work, the mount for the QCL and the control electronics have all been designed and built in-house, and are described in this section.

The QCL mount design is shown in Figure 4.4. The laser submount is positioned on a copper heat sink, with thermal contact improved using a small amount of *Apiezon N* contact grease. The copper heat sink forms the back plate of the mount, and is constructed with cavities to allow cooling via water circulation. The central section of the mount containing the QCL chip itself is kept under vacuum using a dry pump [*KNF, N 84.3 ANE*], to prevent condensation or crystallisation of any water that might otherwise be present when the laser is cooled. The laser facet itself is positioned as close as possible to the front face, containing a polished BaF₂ window (diameter 6.85 mm, thickness 0.5 mm), to minimise the divergence of the beam before the collimation optics.

The temperature of the QCL chip is controlled using a thermoelectrically cooled (TEC) controller positioned at the back of the heat sink, and the temperature is monitored using a calibrated thermocouple positioned on the copper block itself. The current supplied to the TEC is provided by a home-made temperature controller designed to cool to -30°C. The injection current for the laser in this work is provided initially by a commercially available controller [*ILX lightwave, LDX 3232*], with the replacement by an improved, homemade current controller discussed in later sections. Electrical contact between the DB-9 connector for the current controller and the laser submount is made using spring loaded contacts that were positioned once the laser chip was secured in the mount.

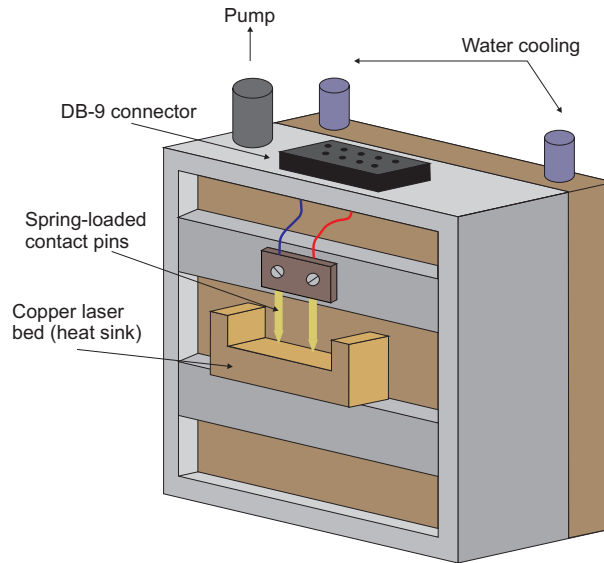


Figure 4.4: Schematic of custom-built QCL mount, with front face removed. The copper heat sink and water cooling are illustrated, as is the laser bed and positioning of contact pins for supplying the injection current.

When testing a new QCL system, the first requirement is to ensure that the voltage, V , measured across the laser increases in the expected manner as given in the manufacturers specifications, as the current, I , increases, as this is usually the first indication of a fault. These readings are given as an output from the ILX current controller and an example of the $I - V$ curve compared to the manufacturers specifications is shown in Figure 4.5a. As can be seen from the data in Figure 4.5a, the voltage increase shows the characteristic rapid rise before leveling off as indicated by the specifications, indicating normal operating parameters.

Another characteristic of the laser output that requires confirmation is the power variation with current at different temperature settings. This also gives the threshold currents, I_T , where lasing action occurs. The measured power variation of the laser as compared to the specifications for various temperatures is shown in Figure 4.5b. The data clearly indicate that not only is the laser output lower in power than expected, but the values for I_T are also clearly higher than the specifications. This could be due to several reasons; firstly the method of monitoring the temperature on the the copper block, which, while necessary, naturally does not give the true temperature of the laser and results in a discrepancy between the temperature that is measured and what is expected from the manufacturer. Secondly, another issue may be that the laser is not cooling as effectively as hoped. This is supported by the fact that the threshold currents are not at the values expected, implying that the laser is not at the temperature indicated by the thermocouple on the heat sink. This difference in the heat removal in laser systems is one of the main reasons for deviations from manufacturer specifications, especially with an Alpes laser, where the tested chip is either glued or soldered onto a heat sink, and materials with high thermal conductivity

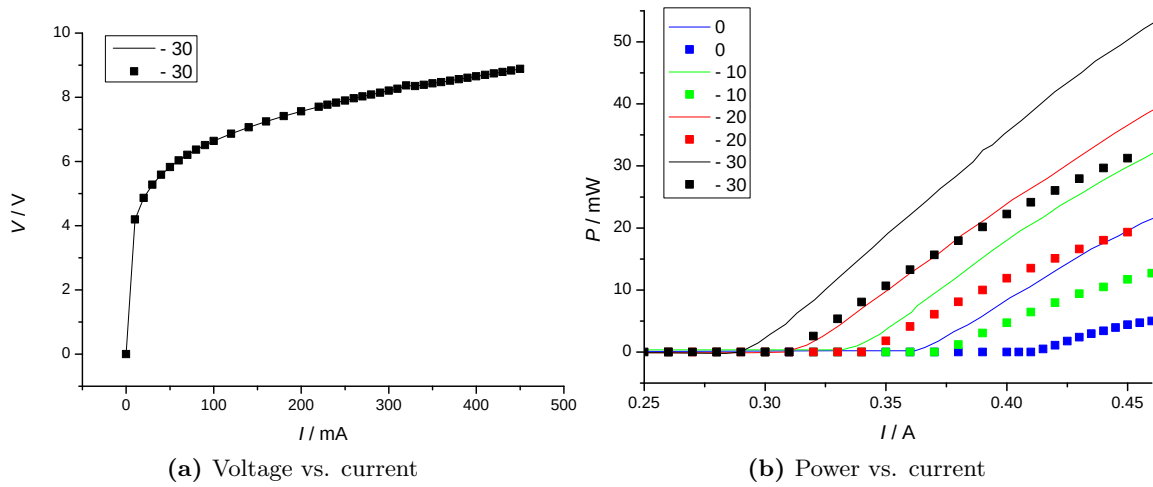


Figure 4.5: Graph (a) shows a typical example of the measured voltage across the laser (squares) compared to the specifications (line) for -30°C . As the V vs. I plots are all fairly similar for different temperatures, only one is shown here. Graph (b) shows the measured power output (squares) compared to the specifications (line) for various temperatures as the current is increased.

such as indium are used to aid better thermal contact. In fact, the thermal conductivity of indium is $81.8 \text{ W m}^{-1} \text{ K}^{-1}$ compared to $0.19 \text{ W m}^{-1} \text{ K}^{-1}$ for the Apiezon N grease used here, and whilst soldering the laser into the mount may result in an improvement, it does risk damage to the laser or the mount for future use. The upshot of this is that a laser chip must be characterised in terms of output power and tuning characteristics for the specific mount and control electronics that it is housed in.

4.2.2 Improving the control electronics of the QCL system

Whilst the ILX lightwave current controller is adequate for monitoring the PIV outputs of the QCL, initial attempts to use it to scan the laser over an absorption feature showed variations in the behaviour of the laser, resulting in consecutive scans of the injection current being non-reproducible. This, coupled with other noise sources on the current output from the ILX gives rise to a spread in the central frequency of the laser during an experiment when multiple scans are averaged. The broadening of the “effective laser linewidth” during an experiment will be the limiting factor in the spectral resolution of the experiment, since, as has already been discussed, the natural laser linewidth of a QCL is inherently small, and is estimated to be as small as $\sim 100 \text{ Hz}$ [111]. The fluctuations on the injection current when using the ILX controller are clearly going to reduce the accuracy of the experiment, and as such a custom designed controller built in-house was developed to improve the noise on the system. This new design has been named the ILX- β .

The design of the ILX- β is based upon low-noise high-speed diode laser current controllers designed by Libbrecht and Hall [112]. The main advantage of designing a custom controller is that, whilst the commercial equivalent is designed for versatility, the ILX- β can be tailored for the QCL system described here. As well as this, the tendency in commercial controllers to use smaller but higher noise components can also be avoided to some extent. The main benefits of the design of the ILX- β is the use of linear power supply as opposed to the higher noise switchmode counterpart, which tends to be used in commercial systems as it is smaller and requires less cooling. As well as this, electronic pick-up is minimised by directly soldering the cable used to provide the injection current to the laser mount into the ILX- β electronics board, as opposed to using BNC connectors. The use of the circuit design to modulate the injection current developed by Libbrecht and Hall also enables a larger range of modulation inputs on the injection current, and the absolute value of the injection current required has been tailored to this specific QCL. The differences in the parameters most relevant to this work are summarised in Table 4.2.

Parameter	ILX lightwave LDX 3232	ILX β
Current range	0-4000 mA	0-1000 mA
Bandwidth	DC to 250 kHz	DC to 2 MHz
Baseline noise	60 μ App	0.7 μ App

Table 4.2: Comparison of the essential parameters of the commercially available ILX lightwave LDX3232 current controller and the custom built ILX- β . Note that the ILX lightwave data is quoted for the full current range available and the bandwidth given is the upper limit when operating in high bandwidth mode. The noise levels were monitored across a 25 Ω load for 10 Hz to 100 kHz operation.

The most crucial improvement for this work is the reduction in noise on the current output, and in the system's reproducibility when it is repetitively scanned, resulting in the reduction in the spread of the effective laser linewidth when using the ILX- β . To demonstrate this, a direct absorption experiment was set up to monitor the deviation in the central frequency of a CH₄ absorption (~ 2 Torr CH₄ in a 10 cm glass cell at 1217.63 cm⁻¹) over consecutive scans. The experimental setup details and spectroscopy of methane are described in more detail in section 4.3. This deviation can then be described as an effective laser linewidth, if the laser scans are fast enough to minimise the impact of long term drifts in the system.

The spread of the line centres taken from 100 scans over the feature taken at a scan rate of 5 kHz using both the ILX and the ILX- β are shown in Figure 4.6. From these data, it can be seen that the use of the ILX- β results in a dramatic improvement in the effective laser linewidth, which from the fit is calculated as 7.2 MHz (2.4×10^{-4} cm⁻¹) (FWHM) as opposed to the spread of ~ 70 MHz from the original ILX. This small effective laser linewidth is ideal for monitoring transitions at low pressure which, for example for methane in this region, have a Doppler width of ~ 110 MHz ($\sim 3.7 \times 10^{-3}$ cm⁻¹).

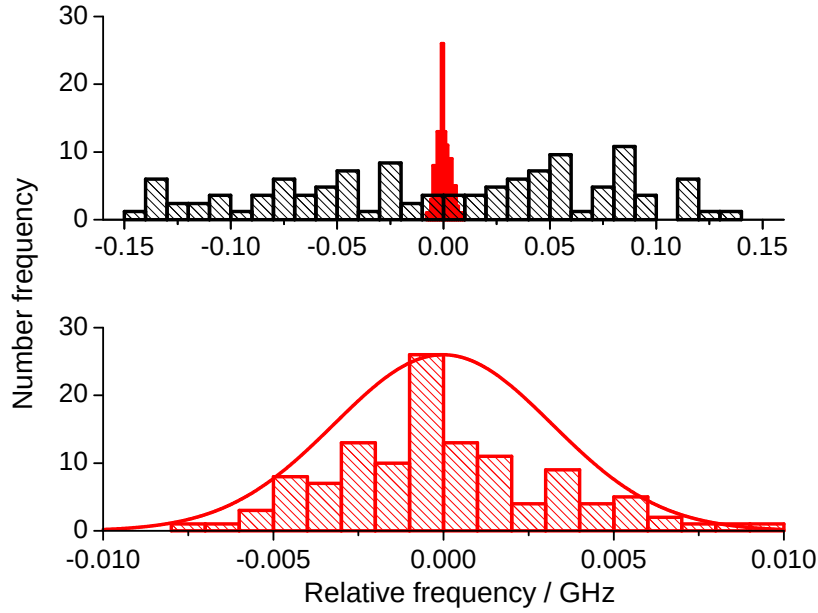


Figure 4.6: Distribution of line centres recorded using the ILX, shown in black in the upper graph, and the ILX- β , shown in red. The lower graph shows the ILX- β data with greater resolution, as well as a Gaussian fit to the distribution.

4.2.3 Characterising the laser output

With the improved control electronics by incorporating the ILX- β into the setup, it is possible to begin to assess the output wavelength of the laser under various conditions. With the differences from the specifications already indicated from the *PIV* curves, it is probable that the wavelength output will also differ. Therefore it is necessary to measure the tuning characteristics of the laser setup, such that accurate wavelength calibration is possible.

To achieve this, the laser output was collimated using a 4 mm focal length lens [*Thorlabs, C036TME-F*] positioned in front of the laser facet on an x, y translation mount. The laser itself was also mounted on an x, y, z translation stage [*Thorlabs, MBT602/M*] for fine adjustment of the lens positioning relative to the laser. The output was monitored with an infrared micro-bolometer camera array [*Les Ulis Sofradir, Micro 384E-BB*], and the lens adjusted until a beam collimated over several metres was achieved. An example image of the QCL beam profile taken 50 cm away from the facet is shown in Figure 4.7, demonstrating the near Gaussian intensity output of the beam. From this, the diameter of the beam (defined as the cut off point where the relative intensity is above 13.5 %) is measured as 1.79 mm.

The output of the laser was then aligned through a Fourier transform infrared (FTIR) spectrometer [*Perkin Elmer, Spectrum 100 FT-IR spectrometer*]. The basis of an FTIR spectrometer in this instance is to monitor the emission of the laser over a wide range of

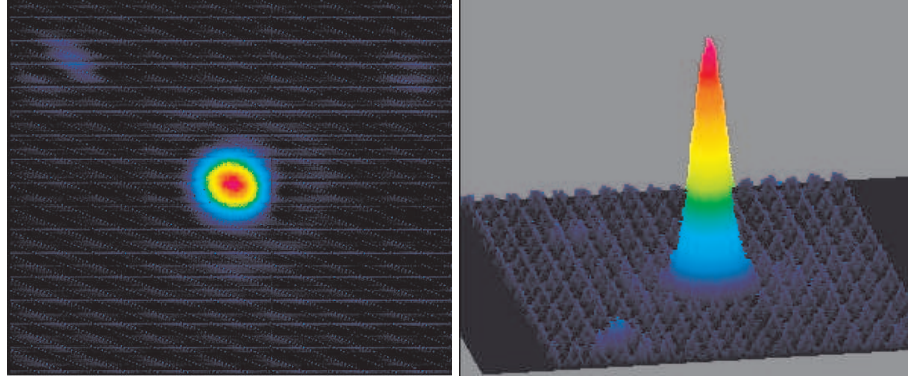


Figure 4.7: Intensity output of the 8 μm QCL as imaged on the camera. The camera used for this was a 2-16 μm IR camera [DataRay, WinCamD FIR-2-16 μm].

wavelengths using a Michelson interferometer. The resolution of the spectrometer depends largely on the construction of the arms in the interferometer, and for this instrument is 0.5 cm^{-1} . A more thorough description of FTIR spectroscopy and the data processing required can be found in refs. [113] and [114].

The laser was tuned over various current settings at temperatures monitored at the heat sink ranging from -30 to $0\text{ }^{\circ}\text{C}$. An example of the laser emission at -30°C for various current settings is shown in Figure 4.8a. The tuning gradients of the different temperature settings as compared to the manufacturers specifications are also shown in Figure 4.8b.

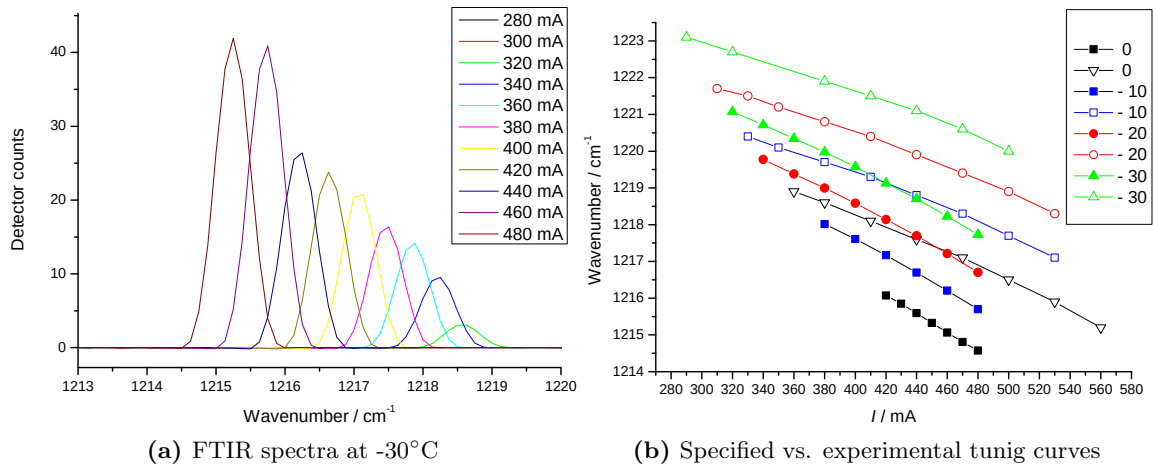


Figure 4.8: Graph (a) shows a typical example of emission from laser at -30°C for various currents, taken with the FTIR spectrometer. Graph (b) shows the measured tuning rates with current for various temperature settings ($^{\circ}\text{C}$) of the laser. The solid symbols indicate the recorded FTIR data and the open symbols indicate the manufacturer specified tuning characteristics.

As can be seen from the data in Figure 4.8, the laser is showing a single-mode output within the resolution of the spectrometer, but this data also indicates that the chip appears to be running at a different temperature from the value indicated by the thermocouple,

as can be seen in the offset in the measured data from the specified data. As well as this, the measured data exhibit steeper gradients, due to poorer heat extraction at the higher current settings. Whilst these deviations from the specifications are not necessarily detrimental to the use of the laser in spectroscopic measurements, it does highlight the variability in behaviour dependent on the housing conditions of the chip, and the need to characterise the laser wavelength output before use. From this tuning data, the laser tuning with current and temperature can be given as $\Delta\nu/\Delta I = -2.53 \times 10^{-2} \text{cm}^{-1} \text{mA}^{-1}$ and $\Delta\nu/\Delta T = -1.03 \times 10^{-1} \text{cm}^{-1} \text{K}^{-1}$.

4.3 Methane detection

Whilst methane is a biomarker in its own right, its detection in this work also aids to characterise the setup and to demonstrate detection sensitivities of a narrowband absorber as opposed to the broadband absorber, acetone, discussed in later sections. The detection of methane using direct absorption at $8 \mu\text{m}$ is demonstrated in both long and short pathlengths, and its detection in the context of breath analysis is also discussed.

4.3.1 Spectroscopy of methane

Methane is a spherical rotor belonging to the T_d symmetry group. The four normal modes are summarised in Table 4.3.

Mode	Description(predominant motion)	Symmetry	Position / cm^{-1}
ν_1	Symmetric stretch	A_1	2917
ν_2	Degenerate deform	E	1534
ν_3	Degenerate stretch	T_2	3019
ν_4	Degenerate deform	T_2	1306

Table 4.3: Description of the fundamental vibrational modes of methane, CH_4

The motions of the normal modes are such that the ν_3 and ν_4 modes are infrared active, and all are Raman active. In this work, the nomenclature for methane transitions is defined by the band, which is the ν_4 band around 1220cm^{-1} , and in terms of the rotational quantum number J and the symmetry C i.e., $(J', C') \leftarrow (J'', C'')$.

4.3.2 Methane detection: Experimental

For methane detection, measurements were taken in both a relatively short absorption pathlength single pass cell, as well as in a long path multipass cell. Multipass cells typically fall into two classes; Herriott [115] and White [116] cells, both of which are based on spatially

separated passes between mirrored surfaces to increase the path length. A White cell is the simpler of the two and typically utilises three mirrors of equal radius of curvature to multipass the light back and forth within the cell. The input and output beams also enter and exit the cell at different points. A Herriott cell uses two, normally astigmatic mirrors with an aperture in the centre of one. This aperture is the point at which the light enters, and exits the cell. The use of astigmatic mirrors tends to lead to a greater number of passes, however, the disadvantage is that the Herriott cell has more strict criteria for alignment. In the experiments described here, the multipass cell used is a White cell [*Specac, Tornado 20 m*] with a maximum pathlength of 20 m.

The laser radiation was aligned through either the short pathlength 20 cm cell or the White cell using an overlapped visible diode, and focused onto the detector [*Vigo, PVMI-3TE-10.6*] using a using a 2 " focal length off-axis paraboloid (OAP). Schematics of the two setups are shown in Figure 4.9. The White cell itself was aligned using the positioning of the visible diode spots incident on the three mirrors, such that the total number of passes could be calculated.

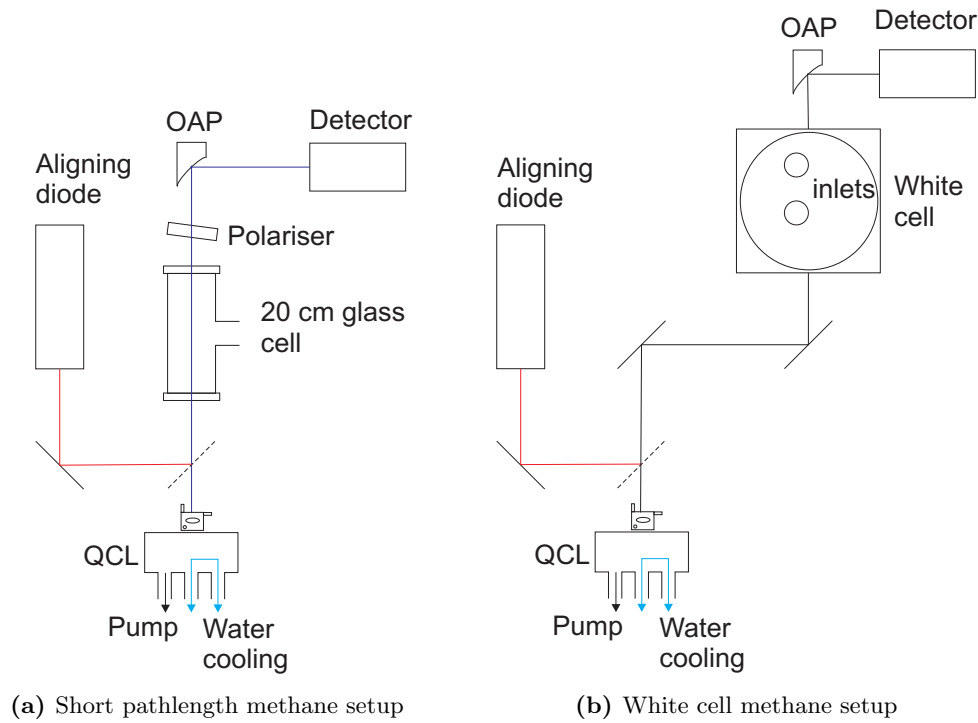


Figure 4.9: Schematic of experimental setups used for methane detection.

4.3.3 Methane detection: Results and discussion

Initially, direct absorption experiments of methane through the White cell were performed to confirm the wavelength tuning of the laser at various temperature and current settings, and to identify any interfering water absorptions. The use of the White cell is necessary such that weaker lines can be resolved at low concentrations, i.e., as close to the Doppler broadened limit as possible. Examples of absorption spectra and the corresponding HITRAN peak positions are shown in Figure 4.10 for ~ 2 Torr methane in the White cell, with the x-axis calibrated using a 500 MHz germanium etalon. The spectra in this figure show the different regions accessible through temperature tuning of the laser, as well as current tuning.

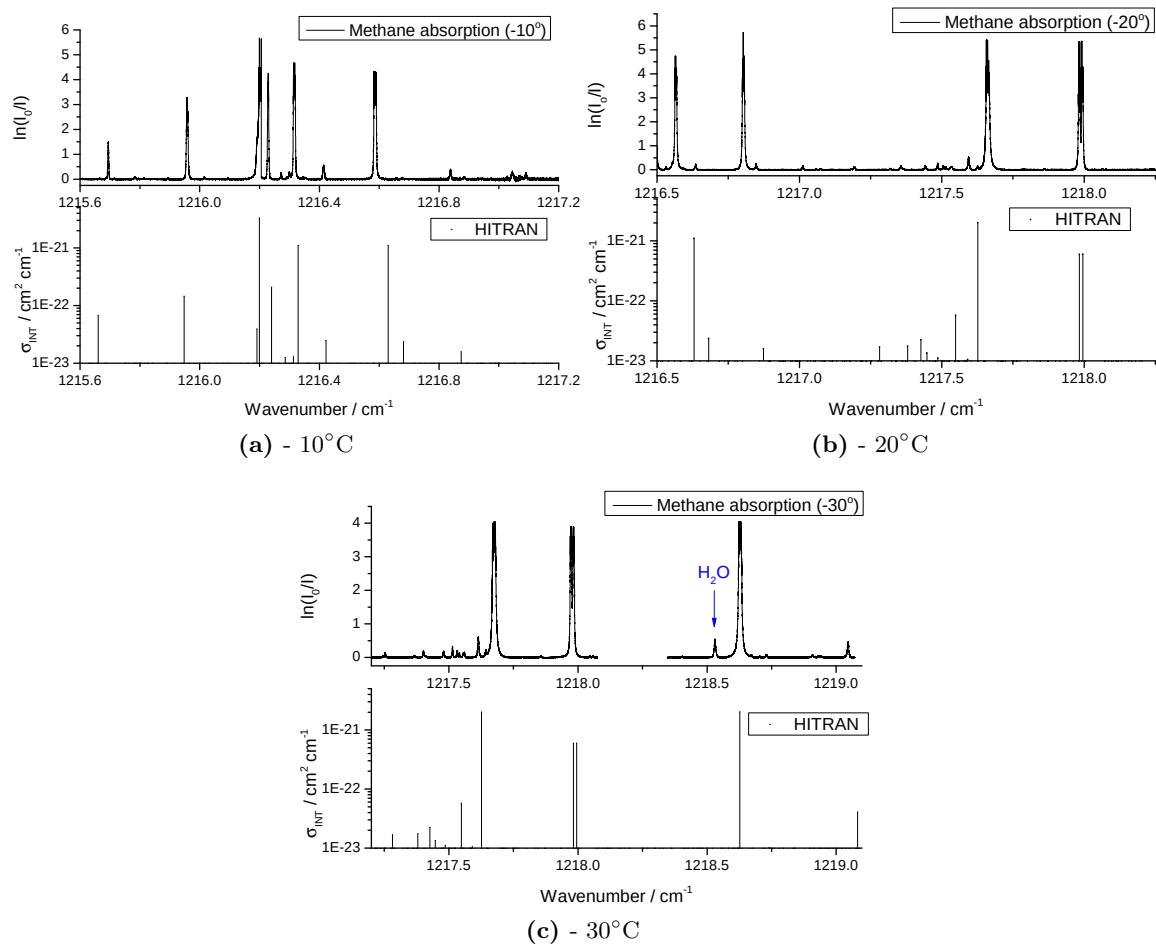


Figure 4.10: Examples of methane absorption features accessible at -10°C , -20°C and -30°C . The peak positions are shown compared to the HITRAN database values for methane line positions. Each spectrum is the result of combining ~ 10 scans of the laser. An additional water feature is also indicated at 1218.5 cm^{-1} (ν_2 , $(6, 1, 5) \leftarrow (7, 4, 4)$).

The survey spectra of these regions consist of up to 10 individual spectra being combined together, hence slight inaccuracies in the peak positioning relative to the HITRAN database.

However, there are enough distinctive features and overlap with the HITRAN data for accurate line assignment to be possible. Comparing the expected wavelength output from the FTIR data taken in section 4.2.3 to the HITRAN line position for various features confirm that the tuning calibration obtained from the FTIR data is accurate to within 0.5 cm^{-1} , the resolution of the spectrometer. With confident assignment of absorption lines, it is possible to characterise the detection sensitivity of the setup. These data also indicate the presence of a water absorption near 1218.5 cm^{-1} , as indicated in Figure 4.10c, therefore highlighting a region that would be unsuitable to future measurements on biomarkers.

Whilst the use of a White cell with a 20 m pathlength is ideal for simply obtaining relative peak positions as shown in Figure 4.10 it was, however, found to be inadequate for more detailed absorption spectroscopy, such as obtaining accurate concentration values or linewidths. This was due to the high level of mechanical instability of the laser beam over the 20 m pathlength, coupled with instabilities of the White cell itself, resulting in large variation in the detected signal and changes in the absorption pathlength with time. Although the White cell is not suitable for accurate methane experiments, there are several strongly absorbing lines that can be easily detected over a shorter pathlength using the more stable 20 cm glass cell. From these measurements, it is possible to demonstrate the detection sensitivity of the QCL setup for narrowband absorbers.

An example of a CH_4 absorption for the $(12, F_2) \leftarrow (13, F_1)$ line at 1218.63 cm^{-1} with an integrated cross-section of $2.02 \times 10^{-21} \text{ cm}^2 \text{ cm}^{-1}$ is shown in Figure 4.11. The sample consisted of 4.1 Torr of pure methane and the data were taken at a scan rate of 20 kHz and averaged 500 times. The x-axis was calibrated using a 500 MHz germanium etalon as before.

The fit shown in the data corresponds to a Voigt profile with the Gaussian width set to 112.6 MHz, the calculated Doppler width value for this line. The Lorentzian width is returned as $30.1 \pm 0.2 \text{ MHz}$, which is in good agreement with the calculated value of 23.8 MHz for the self broadening contribution of this line, as taken from the HITRAN database, with slight discrepancies likely due to the small contribution from the effective laser linewidth.

The noise on the baseline is mostly due to etalons in the system, and correspond to an $\alpha_{\min} = 2.18 \times 10^{-4} \text{ cm}^{-1}$, or a time-normalised $\alpha_{\min}(t)$ of $2.44 \times 10^{-5} \text{ cm}^{-1} \text{ s}^{\frac{1}{2}}$. Theoretically, if the pathlength could be extended to a full 20 m without increasing the noise this could be further reduced to $\alpha_{\min} = 5.45 \times 10^{-7} \text{ cm}^{-1}$, however, this would require a much more stable multipass cell arrangement than is currently available in this work. In terms of atmospherically broadened methane, as would be found in breath, this noise level corresponds to a minimum detectable methane concentration of 0.34 Torr over 5 cm

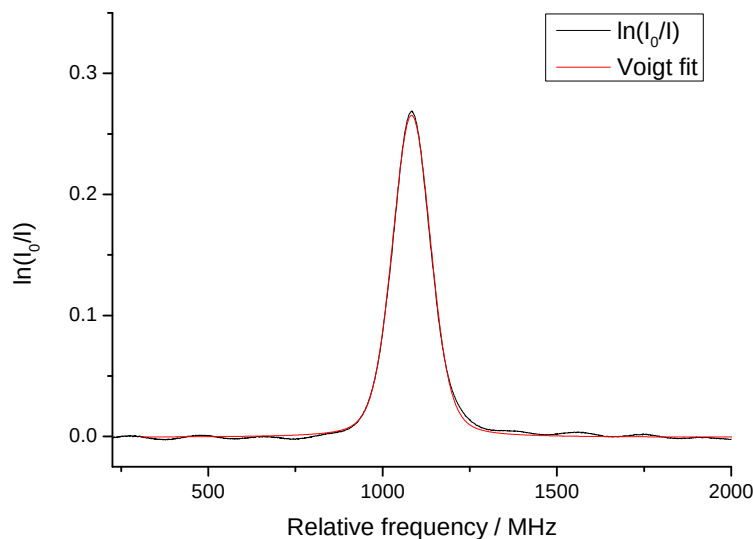


Figure 4.11: Direct absorption spectrum of 4.1 Torr methane at 1218.63 cm^{-1} and corresponding Voigt fit shown in red.

or a theoretical 1.1 ppm limit over 20 m for this particular transition, and is therefore approaching the levels that would be sufficient for detection of atmospheric methane, which is typically at 1.6 ppm concentration, or for methane in breath which also tends to be at the ppm levels. This detection sensitivity could also be further improved by moving to an area of the MIR ($\sim 1290 \text{ cm}^{-1}$) where methane absorbs more strongly, and integrated cross-sections are up to 25 times larger than those accessible in this region. Overall, the detection of methane in this work illustrates the potential of sensitive detection of biomarkers using QCL spectrometers, which, with an increase in sensitivity from an extended pathlength, would be a practical option for detection in the $\sim$ ppm levels.

Whilst methane itself is a relatively small molecule resulting in a spectrum of well defined, narrowband absorptions, some biomarkers such as acetone have a much more complicated absorption spectrum and therefore require a different approach. In the following sections, the potential for using the $8 \mu\text{m}$ QCL system for detecting the broadband absorber acetone is explored, as its potential use as a biomarker for diabetes, coupled with the larger cross-sections available in the MIR, makes its detection in this region worth investigating.

4.4 Towards monitoring acetone in breath

4.4.1 Spectroscopy of acetone

Acetone, $(\text{CH}_3)_2\text{CO}$, has C_{2v} symmetry with a much more complex series of vibrational modes than the molecules studied so far, a full summary of which can be found in the NIST database [117]. The complexity of the acetone spectra results in broadband absorptions that span a much larger wavelength range ($\sim 100 \text{ cm}^{-1}$), unlike the discrete, narrow lines that have been studied so far that tend to have widths that are $\sim 0.1 \text{ cm}^{-1}$. The absorption spectrum for acetone in the IR taken from the PNNL database [118] is shown in Figure 4.12. These data show the equivalent absorption for 1 ppm acetone in 1 atm N_2 over a path of 1 m, and are a composite spectrum taken from FTIR scans (resolution of 0.112 cm^{-1}) of different acetone concentrations.

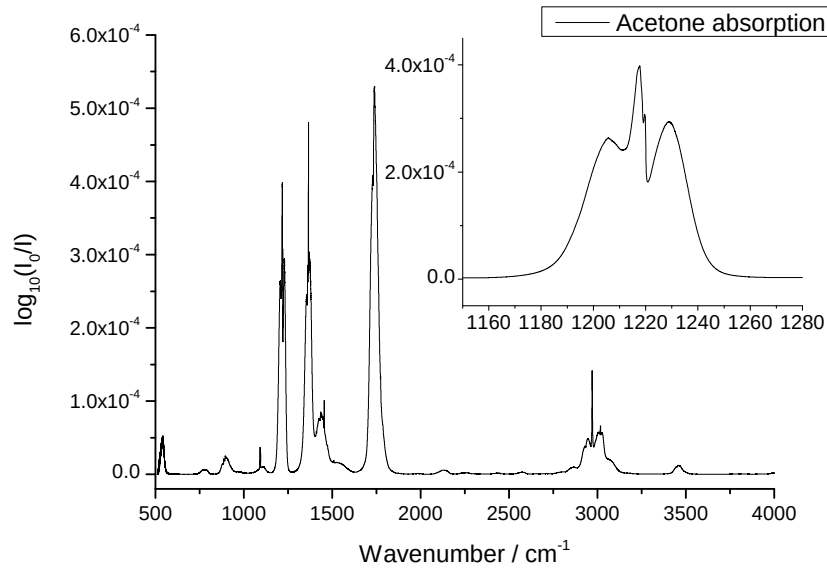


Figure 4.12: IR absorptions of acetone at 25°C taken from the PNNL database [118]. Insert shows the feature of interest for this work.

As acetone is a broadband absorber, conventional spectroscopic techniques of scanning a laser over a feature resulting from a single, well defined transition and fitting the data to a Gaussian or Voigt lineshape where appropriate are no longer applicable. This can clearly be seen in Figure 4.13, which shows simulations of the acetone absorption feature that can be probed using the $8 \mu\text{m}$ QCL, compared to the narrowband absorber methane.

Although the spectral region covered in Figure 4.13 encompasses the full tuning range of the laser, practically only $\sim 0.2 \text{ cm}^{-1}$ can be scanned by applying a ramp to the injection current at a given temperature. This is therefore not a large enough range to distinguish any distinctive feature in the acetone spectrum. Instead, concentrations of acetone were

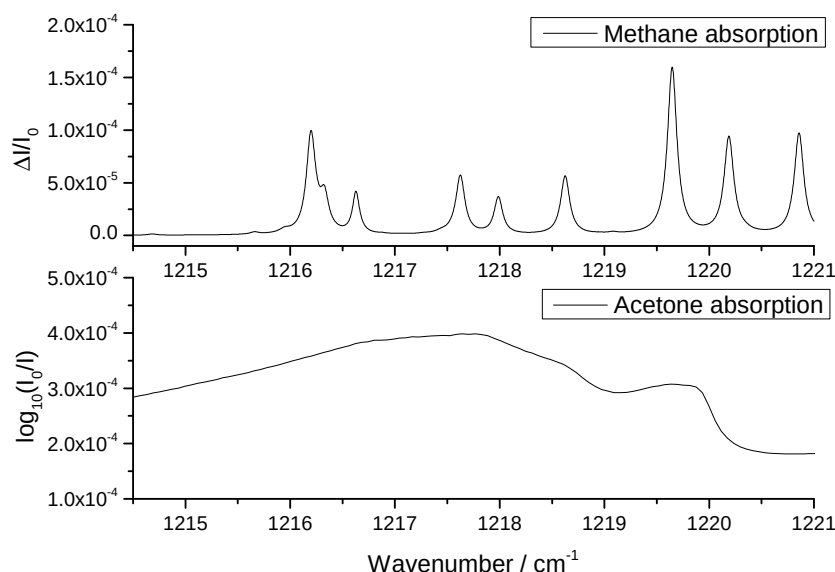


Figure 4.13: Illustration of absorption feature for methane (upper graph) and acetone (lower graph) that can be accessed using full current and temperature tuning of the QCL. The methane data are a HITRAN simulation for atmospheric methane over 1 m, whereas the acetone data correspond to the PNNL database equivalent of 1 ppm in 1 atm over 1 m, calculated from a range of acetone pressures ($\sim 1 - 65$ Torr) broadened up to 760 Torr.

measured by setting the laser to a known wavelength, and monitoring the variation in the DC output of the detector as the level of acetone was increased, as described in the following section.

4.4.2 Acetone detection: Results and discussion

For the detection of acetone, a setup similar to that shown in Figure 4.9a was used, except that a 5 cm glass cell replaced the 20 cm cell, as the absorption cross-section of acetone is ~ 10 times larger than that of methane.

To assess the potential for determining acetone concentrations, a measured value of $\sigma(\nu)$ was extracted by feeding known concentrations of pure acetone into the cell using calibrated 10 and 100 Torr pressure gauges. I_0 was obtained from the empty cell, and $\ln(I_0/I)$ vs. pressure was plotted for the different concentrations. The value of $\sigma(\nu)$ could then be extracted from the gradient. At this stage, the laser was set to the temperature and current settings corresponding to the position of a distinctive methane feature, a doublet of lines at 1217.98 cm^{-1} as determined in section 4.3.3. This was done so that ν was confidently known.

Some typical plots of $\ln(I_0/I)$ vs. pressure of acetone recorded in the described manner are shown in Figure 4.14. As can be seen from these data, there is the expected linear

relationship, corresponding to a gradient of $\sigma(\nu)l$. The error measurements on these data are the equivalent error in the absorption corresponding to random fluctuations in the detector signal over the time required to take the data, taken by monitoring the detector signal fluctuations on an empty cell. These fluctuations are due to slight variations in the laser power, or mechanical vibrations of the system slightly altering the focusing of the radiation onto the detector surface. Therefore, the nature of these variations means the signal-to-noise is not improved through conventional noise reduction techniques, such as mechanically chopping of the beam and demodulating the signal at a set frequency.

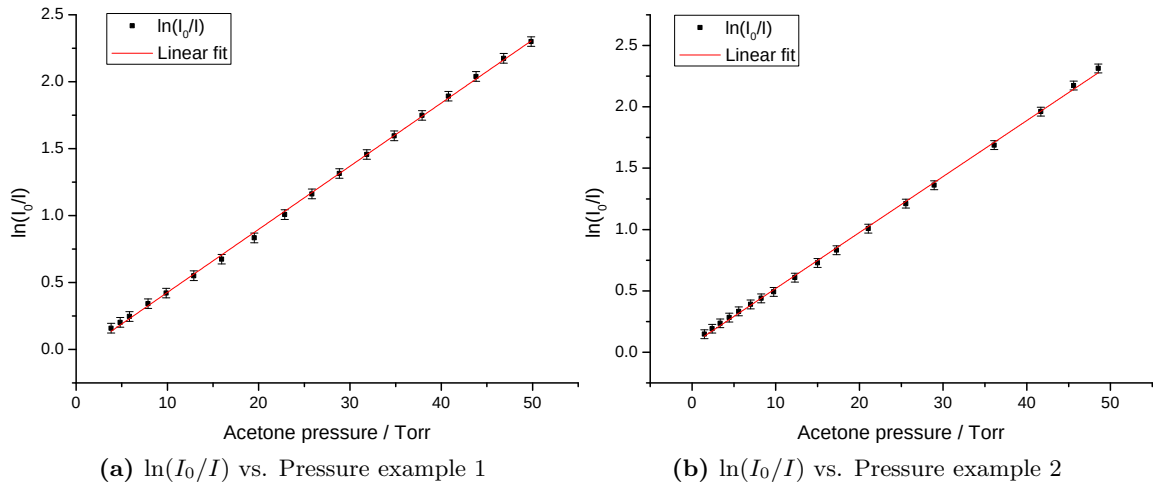


Figure 4.14: Two repeat examples of plots of $\ln(I_0/I)$ vs. acetone pressure with linear fit used to determine $\sigma(\nu)$ shown in red.

The data shown in Figure 4.14 return an average peak cross-section of $\sigma(1217.98 \text{ cm}^{-1}) = 2.85 \pm 0.1 \times 10^{-19} \text{ cm}^2$ and the data show a linear relationship as expected from Equation 1.1. The absolute value of $\sigma(\nu)$ returned is considerably below the value of $3.58 \times 10^{-19} \text{ cm}^2$ from the PNNL database, and the source of the discrepancy between the measurements remains unknown. Errors in the pressure measurements recorded in this work can also contribute to errors in the measured value of $\sigma(\nu)$ and seem likely, as there is an inconsistent non-zero y-intercept on the data. However, these concentration errors will be relatively small. Impurities in the acetone can also result in errors in the concentration readings, but the use of HPLC grade acetone and freezing of the sample to remove water should minimise these impurities, and has little effect on the data.

Although the method for measuring acetone concentration by observing the variation in the detector DC output at a single wavelength shows promise, the discrepancy in the published and experimental measurements needs further investigation. Ideally, for monitoring acetone in breath, an optimum operating wavelength would need to be chosen, and would require a balance between working in a region relatively free from interferences from other species in breath (CO_2 , H_2O , CH_4) and a region with a relatively high acetone cross-section.

For this laser system, the ideal wavelength of 1216.92 cm^{-1} , with a σ_{peak} taken from the PNNL database of $3.42 \times 10^{-19}\text{ cm}^2$, is proposed by examining the interfering absorption features from methane and H_2O discussed in section 4.3.3, and from the relatively weak CO_2 absorptions in this region. By extrapolation from the noise level on absolute absorption measurements that was determined previously by monitoring the fluctuations on the DC signal from the detector on an empty cell, it is possible to estimate a minimum detectable change in acetone concentration at 1217.78 cm^{-1} of 0.63 Torr over 5 cm. Therefore, to obtain detection limits adequate for breath analysis a longer pathlength would be required, for example, a stable 20 m White cell would bring this minimum detection level down to ~ 2 ppm in an atmosphere, which is comparable to what is required for breath analysis. However, this noise level, and therefore minimum detectable absorbance, is determined by the long term stability of the system and if the mechanical instabilities that contribute to these fluctuations in the DC signal could be removed, the the minimum detectable absorption would be determined by the noise on the detector signal itself, further improving the detection sensitivity.

The results presented here show the potential of acetone detection in breath using QCLs and direct absorption spectroscopy in the MIR, by simply monitoring the change in absorption at a single wavelength, a methodology that can easily be applied to other broadband absorbers in the MIR and one that will become more practical with longer absorption pathlengths and if a more stable system can be achieved. The data also indicate an ideal region to work in for acetone detection, free from other absorbing species found in breath and with a relatively strong acetone cross-section.

4.5 QCL spectroscopy of biomarkers in the MIR: Conclusions

The work presented in this chapter has illustrated the practical and experimental considerations in building a QCL spectrometer at $8\text{ }\mu\text{m}$ and improvements in the control electronics to further reduce the noise on the effective laser linewidth have been demonstrated. The laser system itself has been characterised, taking into account the importance of considering variations in laser mount design and how these impact on the laser output through variations in temperature. Preliminary studies on the detection of a narrowband absorber, methane, and a broadband absorber, acetone, both of which are important biomarkers found in breath have also been described. The results from these studies highlight the potential for analysis of these molecules in breath samples particularly if stable, longer pathlengths can be achieved. Whilst this can in theory be achieved with multipass cells, for example the White cell discussed in this work, multipass cells can have the disadvantage

of errors resulting from mechanical instability of the mirrors, and are also typically quite high in volume, which is not necessarily practical for breath analysis.

There is however another potential option for increasing the effective optical pathlength, without increasing the cell volume significantly, and that is the use of an optical cavity. The use of CEAS has already been demonstrated in the NIR in Chapter 2 for the detection of O₂ in breath, and it is the potential for utilising CEAS detection in the MIR that is the focus of the following chapter.

Chapter 5

Spectroscopy in the MIR using QCLs: Sensitive absorption techniques

The work described in this chapter utilises sensitive detection methods based upon cavity enhanced absorption spectroscopy (CEAS) and long pathlength techniques. This work has been performed in the mid infra-red (MIR) with a quantum cascade laser (QCL) as the light source. CEAS experiments using diode lasers are currently very well developed in the visible and near infra-red (NIR), due to the available technologies resulting from the growth of the telecommunications industry. However, work in the MIR region, which has recently become more accessible due to the advent of QCL systems, is relatively under developed. In this chapter the potential of CEAS, as well as other sensitive detection methods, at $10\text{ }\mu\text{m}$ is explored, and the advantages and disadvantages of working with an optical cavity in this region are discussed.

The molecule of interest in this region is OCS, and the detection of OCS has dual purpose in this experiment; firstly, it is an appropriate molecule for the study of the detection limits of a MIR CEAS system, as it has a range of transitions with large absorption cross-sections in this region. Secondly, OCS has also been shown in some early studies to be a potential biomarker in breath. OCS is present in the atmosphere at ppt levels [119], and has been shown to be produced at elevated levels (ppb) in patients with liver disease and organ transplant rejection [120]. Several studies on the detection of OCS as a biomarker have been reported [99, 121–123] and most involve the use of multipass cells. In this work, the development of a sensitive OCS detection system in the MIR using CEAS is investigated.

5.1 CEAS in the MIR

The advantages of moving sensitive detection to the MIR have already been discussed in Chapter 4, however there are some disadvantages that, as will be demonstrated in this chapter, are more relevant when working with optical cavities. The main difficulty is the underdeveloped and low availability of equipment when working in the MIR compared to the NIR, particularly in terms of optics and detectors. However, even with the lower availability of equipment, there have been some successful studies using QCL cavity based systems reported in the MIR, particularly around $5\text{ }\mu\text{m}$, and these studies range from breath analysis on biomarkers such as NO [97], NH_3 and ethylene [124] to atmospheric studies [125]. What these studies have in common, however, is that to achieve the best sensitivities possible from a CEAS system, careful alignment of the cavity is required. This is normally achieved through what is described as the off-axis approach, which is an aligning methodology based on the input beam orientation with respect to the cavity optical axis, and is designed to give as dense a mode structure as possible. This is an alternative to another common approach of increasing the mode structure through slight misalignment of the cavity mirrors themselves, which is commonly used successfully in the NIR, for example in Chapter 2. It is this off-axis CEAS (OA-CEAS) approach that has been utilised in the work reported here to gain the maximum possible sensitivity from the setup. Initially, however, the characteristics of the QCL system that will be eventually used for OA-CEAS are investigated, using direct absorption spectroscopy.

5.2 Direct absorption and laser characterisation

The following studies detail the initial steps in setting up the $10\text{ }\mu\text{m}$ QCL-CEAS system. These involve determining QCL characteristics such as tuning parameters and linewidth, such that appropriate OCS transitions within the working range of the laser are selected and the relevant experimental parameters can be determined.

5.2.1 Spectroscopy of OCS

Carbonyl sulphide, OCS, is a linear triatomic molecule with $C_{\infty v}$ symmetry, and in many ways the spectroscopy is described in a similar manner to CO_2 . OCS also has four fundamental modes, the two stretches and a pair of degenerate bends, summarised in Table 5.1. The nomenclature for OCS is defined in terms of $(\nu_1, \nu_2, l_2, \nu_3)$ where ν_n gives the quantum number associated with each mode and l_2 gives the absolute sum of the vibrational angular momentum quantum number in ν_2 . Unlike CO_2 , there is no Fermi resonance term, as there

is no similar match in energy. Transitions are described by the branch, Br , lower state J'' and the symmetry for ℓ -type doubling, in terms of (Br, J'', sym) . In this work, the main focus is on transitions from the $2\nu_2$ overtone band around 1031 cm^{-1} .

Mode	Description	Symmetry	Position / cm^{-1}
ν_1	CO stretch	Σ^+	2062
ν_2	Bend	Π	520
ν_3	CS stretch	Σ^+	859

Table 5.1: Description of the fundamental vibrational modes of OCS.

5.2.2 Experimental details and laser characterisation

The work in this chapter was part of a collaboration with the Science and Technology Facilities Council and the experimental work was performed at the Rutherford Appleton Laboratory, Harwell. The basic experimental setup used throughout this work is shown schematically in Figure 5.1, and any later additions or variations will be highlighted where relevant. The laser used in this work was a cw-DFB-QCL centered at 1031 cm^{-1} [Hamamatsu, L10195-9700] with power output $\sim 10\text{ mW}$. The QCL was housed in a temperature controlled mount [ILX Lightwave, Bozeman MT 59715] and the laser injection current and temperature were controlled with commercially available controllers [ILX Lightwave, LDX-3232 and LDT-5545B, respectively]. The laser output was collimated using a 4.8 mm focal length anti-reflection coated lens [Hamamatsu, A11331-01] mounted on an x, y, z adjustable stage. A polariser was then placed in the beam path so that the power could be reduced when using an infrared micro-bolometer camera array [Les Ulis Sofradir, Micro 384E-BB] for alignment. A beam size reduction system, to aid effective coupling into the cavity, was then aligned in the setup, consisting of 6.35 mm and 1.87 mm focal length lenses [Hamamatsu]. The beam was then directed into the gas chamber which consisted of an aluminium box made in-house with two possible paths accessible via angled BaF_2 windows. The main path was directed through the cavity which consisted of two mirrors [Tayside Optics] with radii of curvature of 1 m, and diameter of 2.54 cm. These were placed 38 cm apart and initially aligned on-axis using a visible diode overlapped with the QCL beam. As the crucial feature of the off-axis alignment process is the correct orientation of the injected beam, the input turning mirror that steers the beam into the cavity was mounted so that translation in the x -direction, and adjustments in both θ_x and θ_y were possible (see Figure 5.9). The secondary path, 64.5 cm in length, could be accessed using a flip mirror and was used for taking direct absorption measurements to determine absolute gas concentration levels. The output of the cavity, or the direct absorption path, was collected using a 25.4 mm focal length off-axis paraboloid (OAP) and monitored using either the camera or a detector. In this work, two detectors were used for the direct and CEAS measurements,

a thermoelectrically cooled (TEC) IR photovoltaic detector [Vigo, *PDI-ZTE-10.6/VPOC-D.11*] and a LN₂ cooled HgCdTe (MCT) detector [Bruker, *D316/2-M*], respectively, the advantages of which will be discussed in later sections. The detector signals were recorded using an oscilloscope [LeCroy, *Wavesurfer 424*].

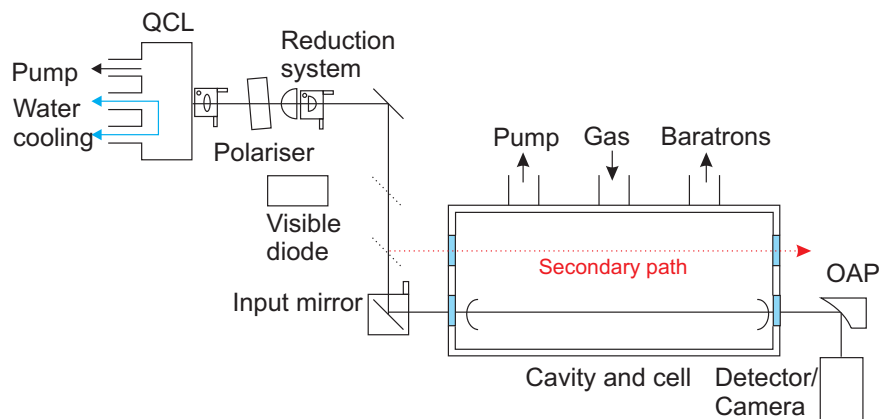


Figure 5.1: Experimental setup for the detection of OCS at 10 μm , using direct absorption and CEAS.

Initially the setup was used to confirm the tuning characteristics of the laser, such that any absorption features could be assigned confidently. The tuning characteristics of this laser with current, I , and temperature, T , have been previously measured for work presented by Weidmann *et al.* using a wavemeter [Bristol, *721B-XIR*] [126]. These coefficients were found to be $\Delta\nu/\Delta I = -4.55 \times 10^{-3} \text{cm}^{-1} \text{mA}^{-1}$ and $\Delta\nu/\Delta T = -8.68 \times 10^{-2} \text{cm}^{-1} \text{K}^{-1}$. To measure these characteristics for this specific laser chip in a new experimental system, which differs in terms of the laser housing and mounting, direct spectra over a region containing several well characterised and relatively strong transition of 0.69 Torr OCS were taken and ~ 4 scans over the spectral region under different setting were compiled to give a survey spectrum as shown in Figure 5.2a. The x-axis was calibrated into wavenumbers using a germanium etalon, with FSR of 0.0485cm^{-1} . A section of the spectrum is also shown in more detail, showing the Gaussian nature of the absorption lines.

As can be seen in Figure 5.2a, the line positions match fairly well with those given by the HITRAN database except at the extremes of the survey spectrum where inaccuracies in the etalon calibration over such a large wavelength range become more pronounced, and errors in overlapping the multiple spectra become apparent. From this, however, the line assignments and therefore their wavelength position can be confidently described, and the current and temperature conditions corresponding to these line positions give tuning coefficients of $\Delta\nu/\Delta I = -3.4 \times 10^{-3} \text{cm}^{-1} \text{mA}^{-1}$ and $\Delta\nu/\Delta T = -8.4 \times 10^{-2} \text{cm}^{-1} \text{K}^{-1}$. These values are similar to those previously measured for this laser, with slight differences

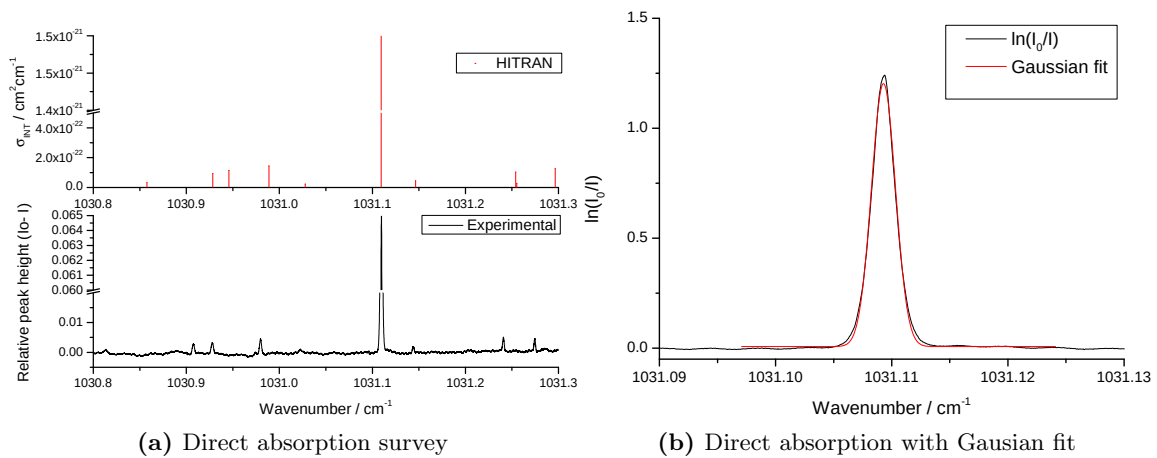


Figure 5.2: Graph (a) shows OCS experimental spectrum (black) with corresponding HITRAN line positions and integrated cross-sections (red). For better resolution of the weaker transitions, the scales have been adjusted on the y-axis. Graph (b) shows a section of the absorption spectrum (P42 transition) with corresponding Gaussian fit shown in red.

arising from using a different laser chip, and the impact of differing housing and temperature monitoring of the laser, as has been discussed in Chapter 4.

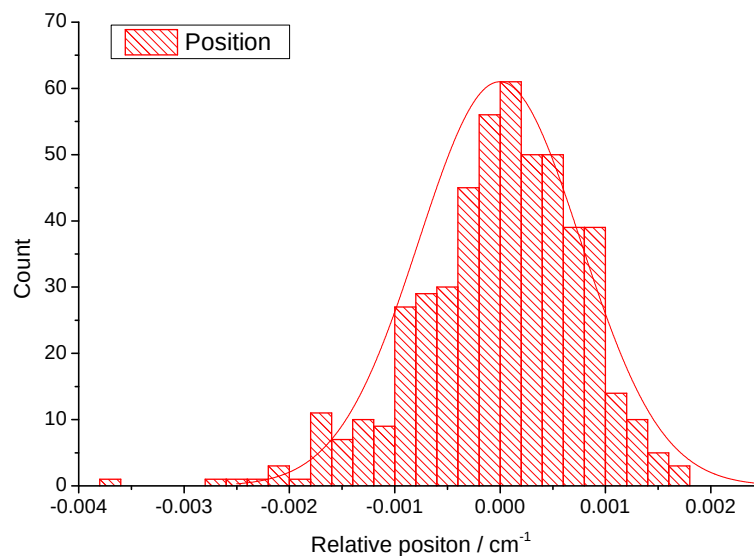


Figure 5.3: Distribution of line centre values taken from 500 consecutive direct absorption spectra of 0.738 Torr OCS on the P42 transition at 1031.109 cm⁻¹. A Gaussian fit to the data is also shown.

Another feature inherent to a laser system that is worth quantifying is the contributions from any frequency noise sources in the current controller, or any instability in the behaviour of the laser as it is scanned as described in Chapter 4. To monitor the impact on the laser central frequency spread, a similar experiment to determine the experimental “effective

linewidth” as for the 8 μm QCL in the previous chapter was undertaken. In this work, the laser was scanned over the absorption feature of 0.738 Torr OCS at 1031.109 cm^{-1} (P42) using the direct absorption path, and 500 consecutive spectra were taken at a 100 Hz scan rate. The distribution of the line centre values was then obtained to assess the spread of the laser frequency output, the results of which are shown in Figure 5.3. The measured width from a single shot of this Doppler broadened line is $1.5 \times 10^{-3}\text{ cm}^{-1}$ and from the Gaussian fit of the data in Figure 5.3, the spread in line centres over multiple scans, and therefore the contribution to the “effective FWHM laser linewidth” is estimated as $1.81 \times 10^{-3}\text{ cm}^{-1}$ over an experiment. The result of this is that the effective broadening that this will introduce to a low pressure absorption feature should be taken into account when analysing averaged spectra, as it is of the order of the measured width of this transition .

5.3 Off-axis CEAS studies

With the QCL system characterised, a comprehensive study into aligning the cavity off-axis was conducted. The following sections describe the process involved in aligning the cavity as predicted by simulations, and how this impacts on the CEAS signal in terms of both the spatial intensity distribution of the rays incident on the cavity mirrors and the transmitted mode structure.

5.3.1 The off-axis approach

Firstly, in describing the off-axis approach, it is important to clarify the differences in alignments that are necessary for various cavity based systems. So far the description for alignment requirements as discussed in section 1.4 states that, for an ideal CRDS experiment, the alignment is such that only a single intense mode, generally the TEM_{00} mode, is brought into resonance. This is achieved by carefully aligning the input laser beam along the optical axis of the cavity, and potentially even mode-matching the input beam waist to a similar size as given by Equation 1.14. This type of alignment is often referred to as on-axis or on-resonance.

However, for a CEAS alignment, a different approach is required to obtain a high detection sensitivity. An alignment is required that results in a higher mode density compared to CRDS, such that no single mode dominates the signal as the frequency of the laser is scanned, and therefore the time-integrated output averages to give a smooth baseline resulting in a good signal-to-noise ratio. This can be achieved by adjusting the cavity mirrors themselves slightly, so that this slight misalignment brings higher order transverse modes into resonance. This increases the overall mode density and improves the averaging of the

signal. A slightly different approach is to align the setup so that the cavity is off-axis or off-resonance. To achieve this, the input beam has to be oriented at a specific displacement and angle relative to the optical axis of the cavity, such that the beam undergoes multiple round-trips in the cavity before re-tracing its path.

Studies on off-axis geometries and their potential uses were first carried out by Herriott *et al.* [115, 127] who investigated the ray tracing paths indicated by the pattern of spots formed on the mirrors of an interferometer. Herriott stated that, when the following condition is satisfied

$$2n\theta = 2\pi \quad (5.1)$$

where θ is the angle between two consecutive spots, as indicated in Figure 5.4, and n is an integer, the beam is re-entrant; the ray returns to its entrance point (x_0, y_0) after n round-trips. The ray then re-traces its original path between the mirrors. This is described as a closed system, many variations of which are possible for a stable cavity, and for which the exact value of θ and n depend on the resonator length and focal length of the mirrors. These off-axis alignments, when imaged onto a camera, show a characteristic elliptical or circular pattern of spots on the mirror surface. As the number of passes increases before the ray returns to its start point, the increasing number of incidences on the mirror surface result in a blending of the spot pattern into a ring.

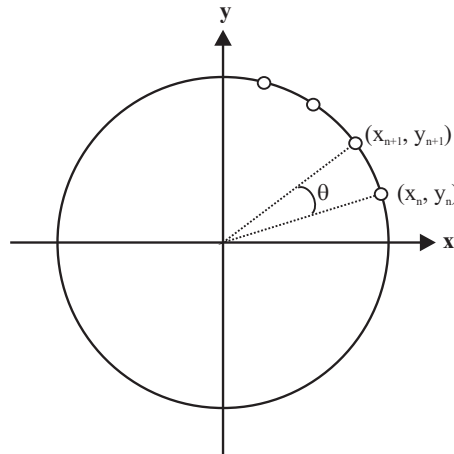


Figure 5.4: Schematic of a cavity mirror indicating spot position relative to the optical axis, which runs through the figure origin.

The result of these roundtrips is that the cavity begins to display characteristics similar to those of a cavity that is actually n times longer, the most crucial of these characteristics being the change in the effective FSR. As the number of passes increases and re-entrant condition lengthens, the effective FSR is reduced, and the cavity transmission shows a

higher density of excited modes for a given wavelength range compared to that of an on-axis alignment. This can be illustrated by simulating the transmitted modes of a theoretical cavity of length $L = 1$, and of a cavity 5 times as long, as modeled by an Airy function

$$\frac{I_T}{I_0} = \frac{1}{1 + \frac{4R}{(1-R)^2} \sin^2 \frac{\delta}{2}} \quad (5.2)$$

where it is assumed that the transmission of the cavity mirrors is $(1 - R)$, and the phase difference between successive transmitted waves is $\delta = 2kL \cos \theta + 2\eta$ where $k = 2\pi/\lambda$, θ is the angle of incidence and η is any contribution to the phase change on reflection. Overall, the cavity finesse remains constant and the cavity mode width narrows concurrently with this reduction in effective FSR, as demonstrated in Figure 5.5. In this illustration, the impact on mode width with varying R can also be seen.

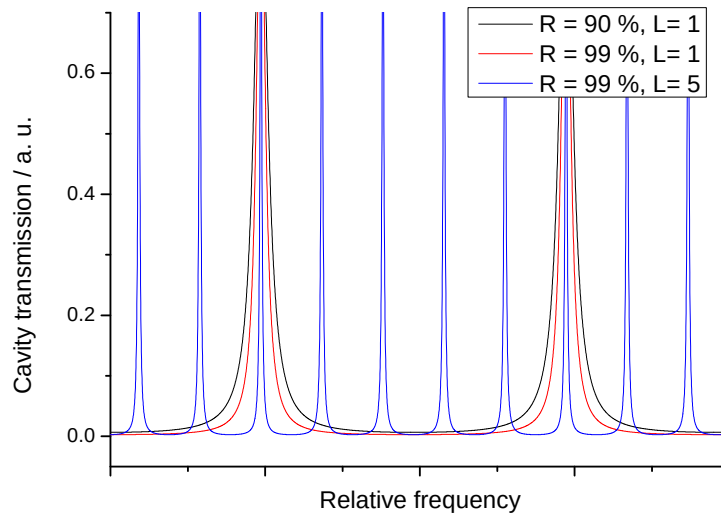


Figure 5.5: Illustration of cavity transmission based on an Airy function. The black transmission function illustrates the increase in cavity mode width with decreasing reflectivity, 90 %, as opposed to the 99 % shown in the red transmission function. The blue transmission is for a cavity still with reflectivity of 99 %, but now in effect 5 times longer, illustrating a reduction in the FSR by a factor of five.

Ultimately, as the number of round-trips approaches infinity, the system reaches a point where the cavity mode intensity begins to fall in order to conserve energy as more modes are excited per unit wavelength [128]. Eventually, the modes are suppressed and the transmission becomes frequency independent - this is the ideal case for a CEAS alignment. In reality, the system will be limited by its overall stability and the quality of the mirrors, and there is typically a level of residual mode structure which is normally minimised through averaging and/or dithering of the cavity.

Experimentally, an off-axis setup requires a level of control over the input beam so that the laser position relative to the optical axis can be adjusted appropriately. Another consideration is the detection of the light exiting the cavity. Since each incidence of the laser beam on the cavity mirror falls on a ellipse or ring and not on the optical axis, and the output from the cavity mirror itself will be divergent, the cavity output occupies a larger volume than that of an on-axis cavity. Therefore, special care must be taken to collect all the transmitted light to reduce losses, as will be discussed in later sections. However, one advantage of the divergent nature of an off-axis cavity output is that it removes the requirement for an optical isolator, as feedback from the cavity along the optical axis is eliminated [129].

Early CEAS work using an alignment specifically chosen to trace an off-axis path in the cavity has been demonstrated by Paul *et. al.* [128] for the detection of molecular oxygen, achieving noise-equivalent absorption levels of $6.5 \times 10^{-10} \text{ cm}^{-1} \text{ Hz}^{-\frac{1}{2}}$, an order of magnitude improvement on previously reported CEAS work [31, 32]. Since this study, the use of off-axis alignments has been reported in works including detection of atmospherically important species [130], biomarkers [124] and detection of broadband absorbers [129], amongst many others. In this work, OA-CEAS is applied in the MIR and the implications and advantages of this are discussed.

5.3.2 Off-axis alignment procedure: Imaging the spatial intensity output

In practice, the off-axis approach is implemented by injecting the input beam at a specific orientation relative to the optical axis of the cavity. To do this, there are four parameters that can be altered; the translation in the x - and y - directions and changes in the angles θ_x and θ_y , all relative to the optical axis defined as the line perpendicular to two parallel cavity mirrors and connecting their centres. However, to obtain the necessary alignment to give the characteristic ellipse pattern, only three of these parameters need to be varied [131], which in this case were the x -translation, θ_x and θ_y , as defined by the adjustable mount of the input mirror.

The level of translation was monitored using the translation stage scale and the input angles were adjusted using the tilt adjustment on the input mirror mount. Some research groups working with off-axis alignments in the MIR have set experimental parameters to obtain geometries fulfilling a specific, predetermined re-entrant condition for a cavity length [131], however in this work, a level of flexibility in the setup was desirable such that various input geometries could be examined.

Initially, the various stages in aligning the cavity were simulated using a LabView based program modelling the ray propagation of a Gaussian beam between two curved mirrors,

after it has been injected into the cavity under defined x -translation, θ_x and θ_y conditions. These simulations predict the spot pattern formed on the mirror after multiple passes. It was observed in these simulations that the optimum sequence of adjustments was to apply angles to the input beam such that $\theta_x \sim -\theta_y$, where the magnitude of θ_n increases as the level of translation in the x -direction increases. Simulations of this set of input criteria, as well as the outcomes of other, less favourable possible geometries for this setup are shown in Figure 5.6 for comparison. As can be seen in the less favourable alignments, too high a mismatch between the input angles and x -translation results in a less circular shape and more uneven intensity distributions.

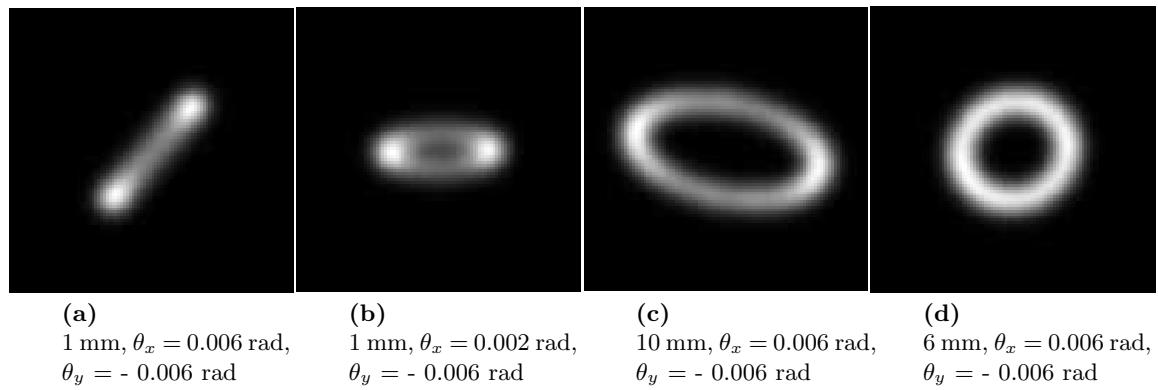


Figure 5.6: Simulations of possible cavity alignments with various x -translation and θ_x and θ_y values: (a) illustrates input angles that are too large relative to translation. In (b) the angles are too dissimilar to each other. In (c) the translation is too large relative to input angles and finally the optimal is shown in (d) where input angles are of similar magnitude and appropriate for level of translation.

Once the appropriate input conditions had been simulated, the necessary alignment steps were then attempted using the cavity, and the affects on the cavity signal monitored using the camera. The starting point is with the cavity aligned on-axis, as it would be used for a CRDS experiment to excite the TEM_{00} mode. This is achieved by using the overlapping visible diode and pinholes over the mirrors that have been carefully aligned parallel to each other and perpendicular to the direction of the input beam. Final adjustments are made using the camera to align to the TEM_{00} mode. However, monitoring the cavity output at this stage shows that there are enough instabilities in the setup, most likely mechanical vibration or electronic noise in the current source slightly altering the output of the laser, so that the system does not remain aligned to TEM_{00} but also shows transitory higher order modes as well. A selection of camera images obtained from this setup, showing the spatial intensity distribution of some of these higher order modes as well as the characteristic TEM_{00} are shown in Figure 5.7. Whilst this lack of stability would be problematic for a CRDS experiment, it poses less of a problem here and will actually help to average out the CEAS signal in a similar manner to mechanical or current dithering.

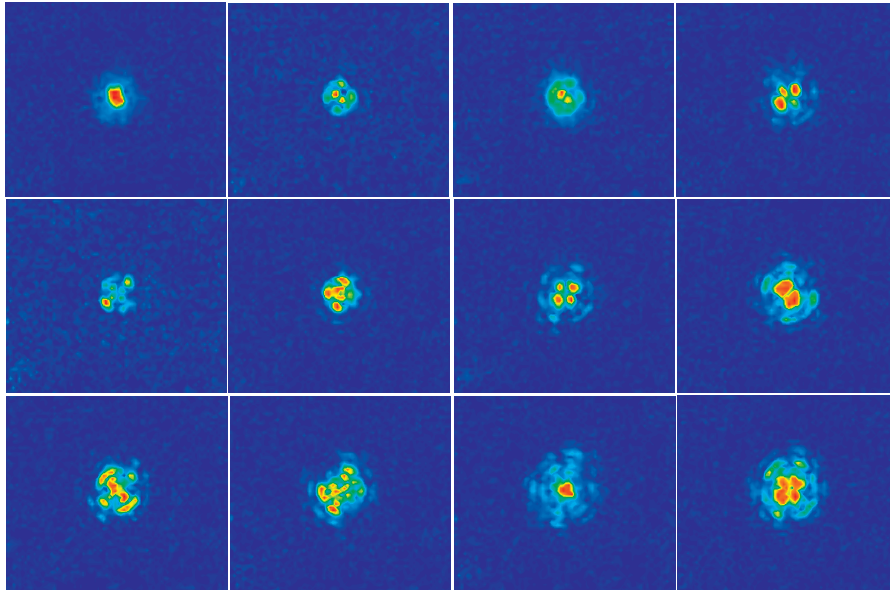


Figure 5.7: Images from the camera showing the output of an on-axis cavity. The expected TEM_{00} spatial intensity distribution can be seen in the top left, as well as examples of higher order TEM_{nm} modes.

From this “on-axis” position, the alignment steps required to achieve the conventional ring image are demonstrated in Figure 5.8. In this figure, an illustration of the change in the input beam geometry is given on the left hand side, with the corresponding LabView ray-tracing simulations given for each step in the central panel. The experimental equivalent, as imaged on the camera, is shown on the right hand side. From this, it can be clearly seen that the alignment steps and the pattern produced on the mirrors follows the predicted model as described by the simulations.

The data so far show the alignment procedure in terms of imaging the light incident on the cavity mirrors. However, the crucial aspect that the theory of aligning the cavity off-axis predicts is the increase in mode density and corresponding decrease in mode intensity, such that the signal averages out more effectively. This can be best studied by monitoring the effect alignment has on the mode structure as the laser is scanned over an absorption feature.

5.3.3 Off-axis alignment procedure: Detecting the cavity modes

One of the main issues that needs to be addressed when aligning a cavity off-axis is the difficulty in detecting all the light exiting the cavity, since the signal diverges on exiting the cavity and, unlike an on-axis cavity, the area of the transmitted signal is much larger. Ideally, focusing of the signal onto a large surface area detector maximises the level of

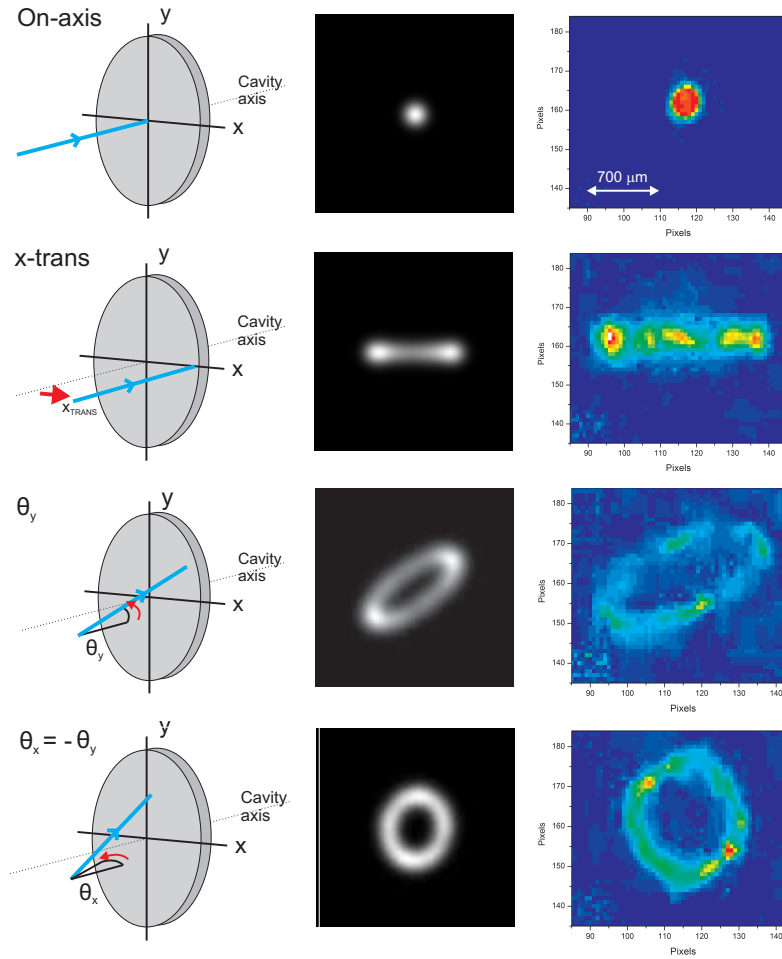


Figure 5.8: Left hand panel shows schematic of off-axis aligning steps with injected beam path shown in blue. The central panel shows corresponding ray tracing simulations on cavity mirrors and the right hand panel shows camera contour images taken from the cavity output for the corresponding steps.

light collected. Therefore, first attempts at monitoring the cavity output were made using the 1 x 1 mm TE cooled Vigo detector that has been used to monitor signals from the direct absorption pathway, but this was found to have too low a sensitivity for detection of the cavity output. This was mainly due to the extremely low intensity transmitted by the cavity, and therefore a correspondingly low signal-to-noise on the detected signal. Another issue was that the Vigo detector exhibited variations in signal level independent of the incident radiation, which are likely due to thermal variations in the lab environment, resulting in drifts in the signal on a time scale comparable to that required to take the data. Due to the low sensitivity and instabilities of the Vigo detector, a more sensitive and stable detection system using an AC coupled LN₂ cooled MCT detector was employed. To extract the signal and improve the overall signal to noise, a mechanical chopper placed in the beam path and lock-in amplifier were utilised. Although use of the MCT has the advantage of higher sensitivity and stability, it has the disadvantage of a smaller detector

surface area, $600 \times 600 \mu\text{m}$, the implications of which will be seen in later sections.

With the MCT detection system in place, the variation in mode structure as the alignment was moved from on-axis to off-axis could be studied. To compare the theory with the experimental data, a series of single shot and averaged spectra, acquired over 25 s, were taken of a 0.66 Torr sample of OCS at different alignments steps, the results of which are shown in Figure 5.9. The data in this figure are the first examples of detection of OCS at $10 \mu\text{m}$ using OA-CEAS.

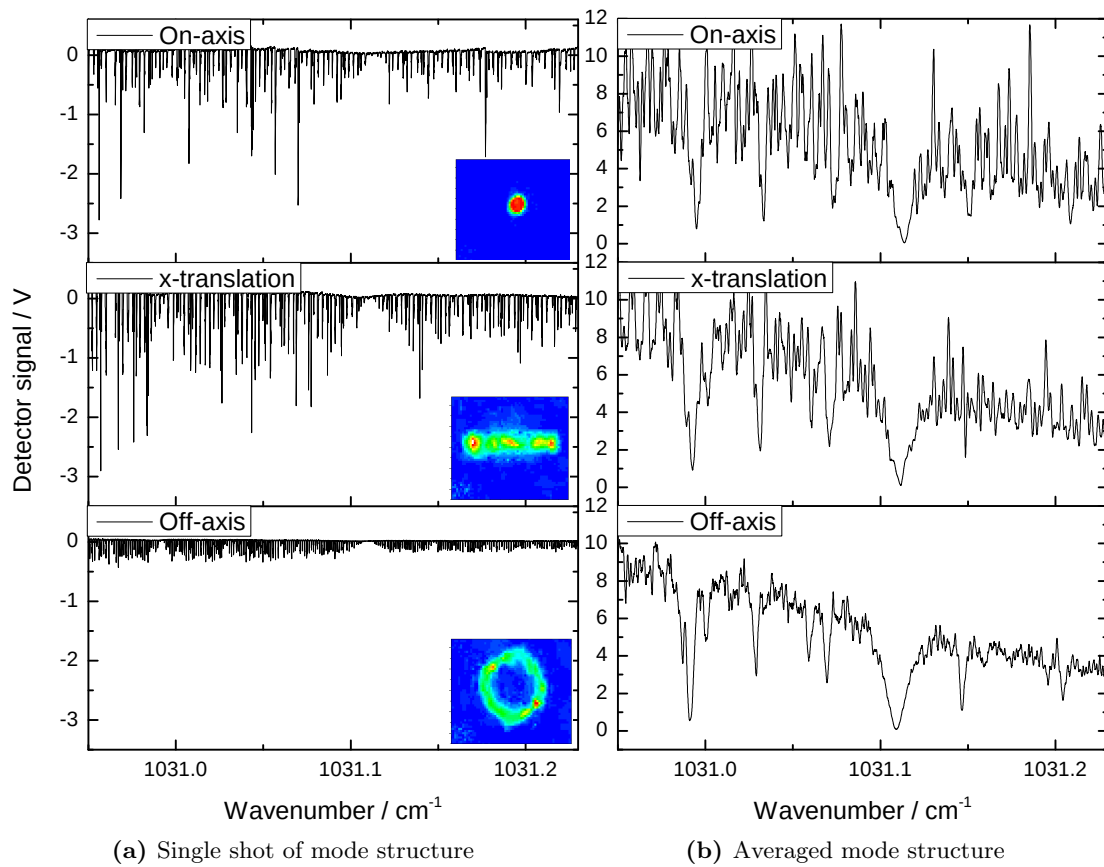


Figure 5.9: Panel (a) shows single shot spectra of cavity mode structure for alignments progressing towards off-axis, shown as inserts. Panel (b) show the equivalent averaged data. Averaged data have been amplitude modulated at 16 kHz and demodulated using the lock-in amplifier.

Several conclusions can be drawn from the mode structure observed in these alignment steps. Firstly, when aligned on-axis, the transitory high order modes introduced by instabilities in the setup as have previously been observed with the camera, are now seen on the detected signal, since the cavity does not display a characteristic uniform mode pattern of TEM_{00} modes spaced by the FSR. Secondly, when progressing the alignment towards off-axis, it is also apparent that the signal follows the predicted trend in that there is a decrease in mode intensity and increase in mode density, with the the OCS absorption

superimposed on top. This effect is in turn seen in the improvement in signal-to-noise on the averaged spectra, with less residual mode structure.

A final observation from these data made possible by the improved sensitivity of CEAS is that there are more transitions in this region than the data from the HITRAN database predict and that are detectable through direct absorption spectroscopy. HITRAN data lists no other species that absorb at these line positions, and the level of absorbance of these lines scales with increasing OCS in the cell, and are not present when the cell is simply filled with lab air. Therefore the conclusion from this data is that the unknown absorption features are either unassigned lines due to OCS, which is possible as the unknown transition exhibit similar widths, or an impurity in the gas, that is outside the scope of the HITRAN database. These unassigned features can be more clearly seen in Figure 5.10, which shows the cavity transmission ($I(\nu)$), the x-axis of which has been calibrated using an etalon, compared to the line positions from the HITRAN database. The cavity data show several very strongly absorbing transitions where $I(\nu)$ tends to zero. In particular the line at 1031.109 cm^{-1} (P42) that has an integrated cross-section a order of magnitude larger than the other transitions in this region shows a highly broadened lineshape at such high absorption levels. This type of signal where $I(\nu)$ approaches zero is particularly difficult to process using Equation 1.25 as it results in an increase in noise at the maximum of the absorption. This has already been demonstrated in Chapter 2, where the higher concentration of O_2 on inhalation, 21 %, results in errors in the measured O_2 level in breath, as opposed to on exhalation where the O_2 concentraion is $\sim 16\%$ and the noise level is correspondingly lower.

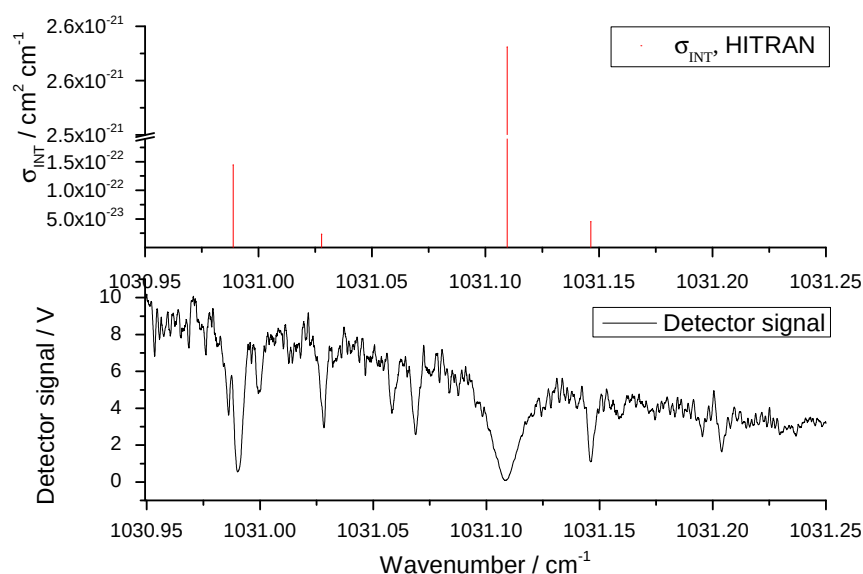


Figure 5.10: Data showing detected absorption features using the CEAS system shown in black, relative to those in the HITRAN database, shown in red. As can be seen there are several unassigned lines in this spectral region.

Overall, the experimental output of the cavity matches the predicted behaviour for aligning a cavity off-axis as opposed to on-axis in both the spot pattern formed on the mirrors and the improvement in the averaging of the detected signal. Already, improvements in the sensitivity using CEAS over direct absorption have enabled detection of weaker unassigned transitions that were unresolvable in the short pathlength. However, the possibility of improving the CEAS sensitivity further through alignment has also been investigated, as the data shown here is for just one of many possible alignments that could lead to improvements in the signal.

5.3.4 Optimising the off-axis alignment

One way of optimising the cavity is to gradually alter the input parameters, to gradually use more of the mirror surface, therefore increasing the ring size and, ideally, the number of discrete passes before the re-entrant condition is satisfied. Experimentally this was attempted through incrementally increasing the magnitude of the x -translation on the input mirror, and then adjusting the input angles to return to an ellipse or ring shape, such that more of the mirror surface is used. The resulting outputs are monitored using the camera and the detector to investigate the optimum conditions in terms of mode structure. A series of different rings, increasing in size, are shown in Figure 5.11. The corresponding single shot spectra for each alignment are also shown.

From these data, several important conclusions can be drawn. Firstly, considering the first three rings and associated spectra (moving from 2 mm to 6 mm x -translation), it does appear that there is an increasing mode density and decrease in intensity as expected, which is desirable for a CEAS alignment. However, the ring at 8 mm does not follow this trend. Instead it shows that an unfavourable set of input conditions has been reached where the re-entrant condition is satisfied after fewer passes, hence discrete spots are visible on the mirror surface and the mode structure is less dense relative to that obtained for the 6 mm ring. Finally, the ring at 10 mm shows another interesting aspect of this setup and indeed of working in the MIR: as the ring has been increased in size, there has come a point where the image is too weak to be picked up by the camera, and the mode structure is much less intense. This loss in intensity could be due to a variety of reasons. Firstly, a more optimal alignment may have been reached where the number of passes has increased to such a point that the energy exiting the cavity per mode is much reduced. This is because, as the beam undergoes more and more reflections, the output mode intensity decreases as the effective FSR decreases. Secondly, as more and more of the mirror surface is used, other losses in signal such as diffraction losses will increase, resulting in a reduced signal, and the particular relevance of these types of losses when working in the MIR will be discussed in later sections.

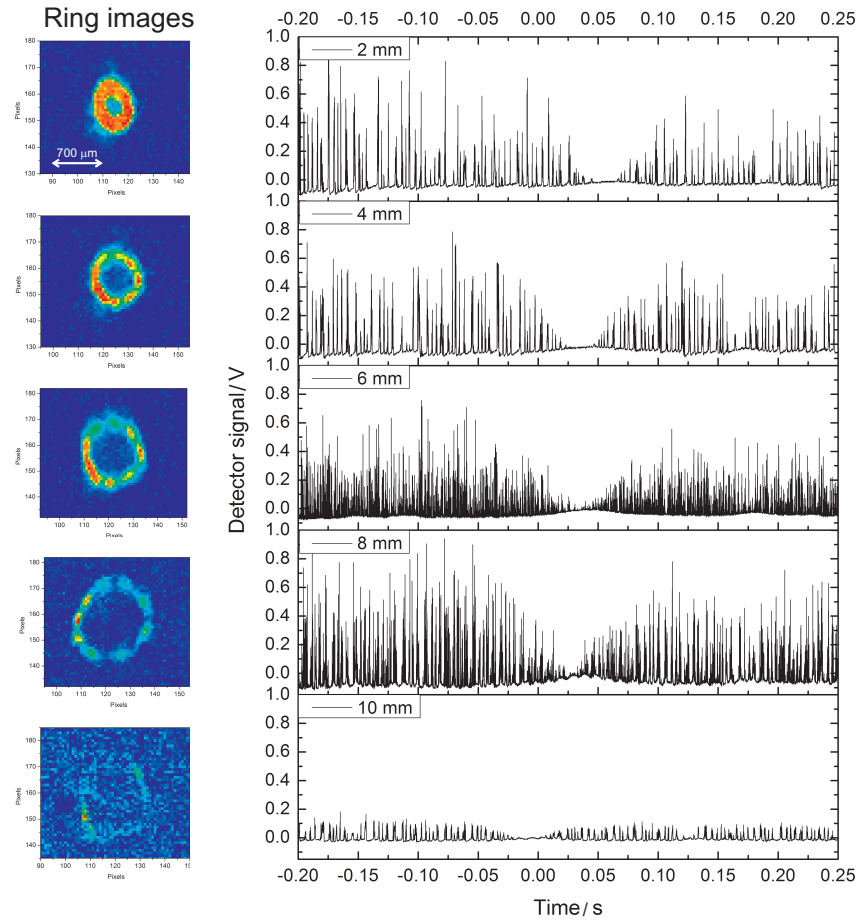


Figure 5.11: Comparison of single shot mode structure for various cavity alignments, shown as a function of time as the laser injection current is scanned.

Finally, this reduction in intensity as observed in the cavity modes could be due to the detection system. Another result of working in the MIR is that there is the added disadvantage of having inferior detectors, in both size and detectivity, for example, a silicon based NIR detector can have a detectivity of ~ 3 orders of magnitude larger than an MCT MIR detector. This means that the spatial output of the cavity has possibly reached a point where it is too large to be focused onto the detector in its entirety and there is a large reduction in signal, and loss of information about the mode structure. Therefore, at this stage it is difficult to assess the true density of the mode structure for such a large ring, or to definitely assign reductions in intensity to improved alignment, or losses from the detector.

What these data do show, however, is that in terms of optimising an off-axis alignment in the MIR, the limited quality and size of detectors is an important practical consideration. As the output of the off-axis cavity covers a much larger area than a CRDS alignment, the

limitations in the detection end of a setup need to be considered when trying to reach an optimum balance between improving the off-axis alignment, and maintaining a workable signal-to-noise level on the detector. Taking these considerations into account, the cavity was aligned with as large a ring as possible before losses on the detector became unworkable, and with an even intensity distribution, indicating a high number of passes within the cavity.

5.3.5 Optimised OA-CEAS and fitting the results

The work reported so far describes many considerations that need to be taken into account for optimising an OA-CEAS experiment, such as alignment, detector size and signal to noise ratio. However, it is possible to further improve the detected signal by applying a slight frequency dither to the laser. The majority of reported works describing OA-CEAS in the MIR also report that a level of dithering is required to smooth the residual mode structure further [131–134], however, this is normally achieved using mechanical dithering of a cavity mirror through use of a PZT. As dithering the mirrors themselves was not possible in a closed system such as this, another approach was investigated, namely, current dithering. As the injection current is scanned over an absorption feature, usually with a triangular ramp function, it is possible to superimpose a comparably small current dither or “noise” in the form of a high frequency sine wave. This slight dither on the laser wavelength slightly alters the coupling conditions between the laser and the cavity over the scans that are averaged together, resulting in a smoothing of the mode structure. An example of the improvement due to current dithering is shown Figure 5.12, which shows a the spectral region of interest of a sample of 0.807 Torr of pure OCS with various levels of averaging and with a current dithering sine wave at 2 kHz per scan and with a peak-to-peak amplitude of 10 mV ($\sim 6 \times 10^{-3} \text{ cm}^{-1}$).

With the cavity alignment and detected signal optimised, it is possible to assess the effective pathlength enhancement that can be obtained by fitting the resulting data from a CEAS absorption of a known concentration of OCS. In this work a fitting routine utilising line-by-line HITRAN data written in IDL and developed by Weidmann *et al.* [135] was utilised. The advantages of this fitting algorithm include using information from multiple absorption features to assess the pathlength enhancement resulting from the cavity, and allows the inclusion of instrumental parameters such as effective laser linewidth in the fitting process. A brief overview of the fitting routine, henceforth described as the IDL fitting algorithm is now given, with a more thorough description of the IDL algorithm, including how it is solved, given in references [135] and [136].

The fitting algorithm is based on building a forward model described by $F(\mathbf{x})$ where $\mathbf{x}$ represents the state vector which are the unknown variables that the user wishes to extract

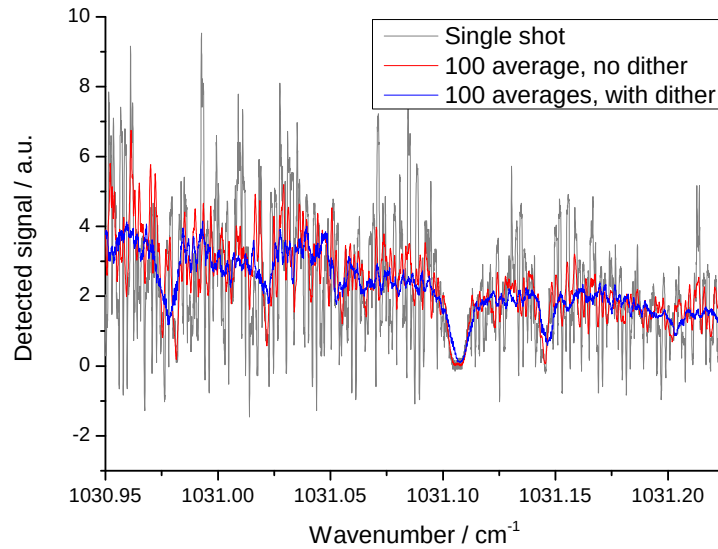


Figure 5.12: Example of reduction in residual mode structure with a current dither applied to the laser. Grey trace shows residual modes with no averaging, red shows the same signal averaged 100 times, and blue shows an averaged signal with the superimposed current dither as well.

from the fitting routine, for example, an unknown pathlength or I_0 baseline. The forward model itself is constructed from various known experimental parameters for example pressure, concentration, instrumental broadening, etc. and includes the relevant HITRAN lineshape information such as line position, broadening and temperature dependence. $F(\mathbf{x})$ is described mathematically by

$$\mathbf{y} = F(\mathbf{x}) + \epsilon \quad (5.3)$$

where $\mathbf{y}$ is the measurement vector, i.e. the measured experimental information such as the spectra shown in Figure 5.12 with ϵ the error associated with the measurements. The retrieval of information required, $\mathbf{x}$, such that the forward model accurately describes the experimental data, $\mathbf{y}$, is achieved by using an optimal estimation method to minimise the function χ^2

$$\chi^2 = (\mathbf{y} - F(\mathbf{x}_n))\mathbf{S}_\epsilon^{-1}(\mathbf{y} - F(\mathbf{x}_n))^T + (\mathbf{x}_a - \mathbf{x}_n)\mathbf{S}_a^{-1}(\mathbf{x}_a - \mathbf{x}_n)^T \quad (5.4)$$

This optimisation is an iterative process for various solutions $\mathbf{x}_n$ where each iterative step locally linearises the outcome and converges to a point where χ^2 reaches a minimum. This is achieved by reducing the quadratic spread between the measured values, $\mathbf{y}$, and the forward model with solutions $\mathbf{x}_n$ weighted by the errors $\mathbf{S}_\epsilon$, as given in the first term of Equation

5.4. This is further constrained by minimising the difference between the solutions $\mathbf{x}_n$ and a set of *a priori* values $\mathbf{x}_a$, weighted by the errors on these *a priori* values, $\mathbf{S}_a$, that are in put into the fitting routine. This optimisation method works within the assumption that the uncertainty in the parameters have a normal distribution and was first developed by Rodgers [137].

In practice, since the forward model is based on HITRAN data, particular consideration is required when selecting a spectral region to fit, as the unassigned lines described in section 5.3.3 are likely to interfere with the fitting routine. Therefore a region with as few as possible unassigned lines was chosen around the (P42) and weaker (R34) transition, centred at 1031.109 cm^{-1} and 1031.146 cm^{-1} with integrated cross-sections of $2.58 \times 10^{-21} \text{ cm}^{-1}$ and $4.52 \times 10^{-23} \text{ cm}^{-1}$, respectively. This region is ideal as it has transitions with large absorption cross-sections and only two relatively small unassigned peaks so that there should be minimal interference with the fitting routine.

An example of the data and its corresponding fit obtained with the cavity aligned off-axis and with current dithering to further smooth the signal is shown in Figure 5.13.

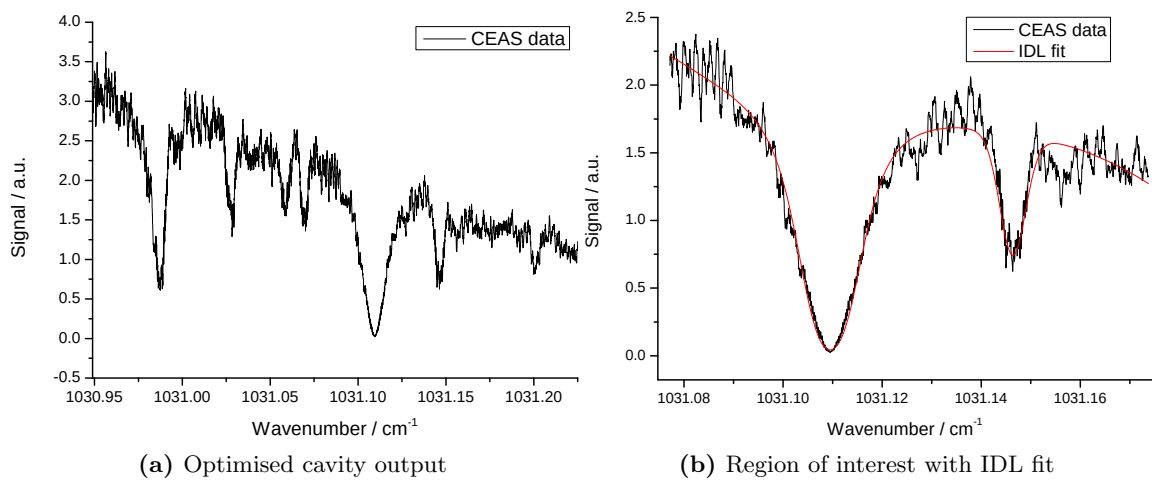


Figure 5.13: Optimum CEAS spectrum using improvements in detection sensitivity and alignment. Graph (a) shows entire scanned region of OCS absorption spectrum and graph (b) shows the region selected for fitting, with the IDL algorithm fit shown in red.

The fit from this optimised CEAS data in Figure 5.13b returns an effective pathlength of $108 \pm 3.5 \text{ m}$, with a corresponding effective mirror reflectivity of 99.56%. The 108 m pathlength was the largest achieved from alignments in this cavity, which tended to range from 70 - 100 m. The sensitivity of the setup in terms of minimum detectable absorbance is therefore $\alpha_{min} = 7.7 \times 10^{-6} \text{ cm}^{-1}$ or $\alpha_{min}(t) = 3.8 \times 10^{-5} \text{ cm}^{-1} \text{ s}^{\frac{1}{2}}$ when normalised to the acquisition time. This pathlength enhancement and corresponding sensitivity are relatively low when compared to what is commonly achieved in the NIR, where pathlength enhancements of $\sim \text{km}$ and $\alpha_{min} \sim \times 10^{-8} \text{ cm}^{-1}$ are frequently obtained. To understand

these variations in setups, it is important to investigate the differences between working in the NIR and MIR, some of which have been highlighted experimentally already, and to discuss these differences in the context of this and other works reported on CEAS in the MIR.

5.3.6 OA-CEAS in the MIR: Conclusions

The work reported here has demonstrated the improvement in signal-to-noise with a more rigorous approach to aligning the cavity off-axis. In this study, the alignment of the cavity from on-axis to off-axis was shown to match the predicted theory and simulations in terms of both the intensity spatial output and the reduction of residual mode structure. However, compared to the NIR, a relatively low pathlength enhancement has been obtained and the limitations in sensitivity of the CEAS spectrometer described in this work essentially stem from this. This low effective pathlength, or effective reflectivity, results in a lower absorption signal, and a correspondingly high level of residual mode noise. This poor coupling of the light into the cavity compared to what is observed when working in the NIR can be attributed to several factors.

The interaction of light with the cavity optics at 10 μm varies in terms of both the divergence of the beam and in diffraction losses. The divergence of the beam, θ_D , scales as

$$\theta_D = \frac{\lambda}{\pi w_0} \quad (5.5)$$

which results in a larger spread in mode volume within the cavity, such that more of the optic surface is utilised in a cavity at longer wavelength compared to one of comparable dimensions at a shorter wavelength. The diffraction losses for optics in the setup also increase, as diffraction scales with wavelength. For example, for a plane mirror cavity system the dominant mode diffraction losses, δ_D , scale via

$$\delta_D = 0.207 \left(\frac{L\lambda}{a^2} \right)^{1.4} \quad (5.6)$$

Equation 5.6 illustrates the increase in diffraction losses with wavelength, as well as with decreasing mirror size, a . Whilst this equation, proposed by Li *et al.* [138], only models the diffraction loss dependence with λ of planar resonator systems, similar diffraction trends with wavelength and optic size are observed with confocal resonators, although typically an order of magnitude less in size [139]. Overall, these losses scaling with wavelength, without an equivalent rescaling in the optics used, means that the off-axis alignment used for CEAS in a MIR cavity is very restricted and indeed limited by the mirror size, and

the point at which the beam “walks-off” the mirror, or reaches the outer edges where the coating tends to degrade. The losses in the signal are also much higher, and therefore the signal is harder to detect on exiting the cavity. The result is that the optimal alignment as described in section 5.3, where the mode structure is essentially suppressed and there is a long effective pathlength within the cavity, is much harder to achieve, hence the lower pathlength enhancement and corresponding high baseline noise levels due to this residual mode structure.

Another issue that has been observed experimentally in the data presented in this work, is limitations in available equipment when working at $10\ \mu\text{m}$. This results in the use of poorer quality optics, for example more highly absorbing substrates such as ZnSe and coatings on cavity mirrors that tend to be less reflective than their NIR counterparts. Limitations in detector size and quality in the MIR, coupled with the necessarily larger mode volume of an off-axis aligned cavity, results in signal losses when monitoring the output signal, as was demonstrated in section 5.3.4.

These difficulties with working in CEAS in the MIR have also been demonstrated at other wavelengths, and a summary of effective pathlengths achieved by other researchers, as well as other relevant experimental information is given in Table 5.2.

Reference	λ / μm	L_{cavity} / cm	Mirror diameter / cm	L_{eff} / m	R_{eff} %
Miller [134]	3.5	50	5	83	99.4
Menzel [140]	5.2	35.5	2.5	670	99.942
Bakhirkin [131]	5.2	2.75	5.08	75	99.96
Bakhirkin [132]	5.45	50	5.08	700	99.928
McCurdy [97]	5.47	50	5.08	500	99.9
Moyer [125]	6.7	90	10.16	4200	99.988
<i>This work</i>	<i>10</i>	<i>38</i>	<i>2.5</i>	<i>108</i>	<i>99.56</i>
Silva* [133]	5.2	50	2.54	1500	99.966
Manne* [124]	10.3	53	2.54	76	99.3

Table 5.2: Comparison of pathlength enhancements and corresponding effective reflectivities obtained by research groups working on OA-CEAS in the MIR. Data marked with * indicates pulsed OA-CEAS as opposed to cw measurements.

As can be seen from the values reported in Table 5.2, typical enhancements tend to range from ~ 10 -100 m as opposed to the typical km observed in the NIR. Work carried out by Manne *et al.* [124] using a pulsed QCL system, is the only OA-CEAS setup at a similar wavelength region to the work reported here, and exhibits a comparable pathlength enhancement of 76 m. Only work by Moyer *et al.* [125] has achieved anything approaching the enhancements observed in the NIR, with an effective pathlength of 4200 m. However, one of the main distinctions in the work presented by Moyer is that specially designed 4" (10.16 cm) cavity mirrors were used, therefore dramatically aiding the off-axis alignment

in the cavity. As well as this, the resulting signal from these much larger mirrors, which would be impossible to collect with conventional 1 or 2 " focusing optics and available detectors, was focused using a specially made 4 " ZnSe lens and a custom built 3 x 3 mm MCT detector. However, even with these costly measures, only an estimated 50 % of the cavity output light was captured.

The effective pathlength reported here of 108 m is comparable to what has been achieved by other researchers, however, it has been achieved here at a longer wavelength, therefore incurring greater losses, and with relatively small cavity mirrors (2.5 cm) and detector surface (600 x 600 μm). The potential for this technique has clearly been demonstrated and further improvements such as the current trend of moving towards larger optics, where the full realisation of the benefits of aligning a cavity off-axis could be achieved, would make OA-CEAS in the MIR a practical detection method for trace gases.

One final route towards improving the detection limit that is possible in this CEAS system, has been demonstrated by Bakhirkin *et al.* [132] and involves reducing the noise level on the signal by the addition of WMS, enabling the shifting of the absorption information to a higher frequency regime as discussed in Chapter 3. In their work on detection of NO at 5.45 μm using OA-CEAS, Bakhirkin *et al.* achieved a minimum detectable level of 3 ppb NO using OA-CEAS alone, but managed to reduce this level to 0.7 ppb with the use of WMS as well. The improvements to the signal that have been achieved in this work are discussed in the next section.

5.3.7 Improving the signal further with WMS CEAS

Whilst a large contribution to the noise in the CEAS work described above is from the residual mode noise, other sources can potentially be removed using WMS, as described in Chapter 3. This attempt at noise reduction, as it is only adding an extra layer to the electronics of the experiment, is an efficient way of improving a setup's detection capabilities and as such is worth pursuing. The required changes to the setup are simply the addition of a second function generator and using the lock-in amplifier [*EG and G, Signal Recovery 7265*] to provide the extra high frequency modulation required, and to demodulate the signal. The chopper that has been used to aid signal extraction from the AC coupled MCT detector was also removed as it unnecessary for WMS demodulation.

The WMS signals were obtained by optimising the modulation depth as described in Chapter 3, and choosing appropriate scan rates and time constant such that baseline noise is reduced without losing information pertinent to the absorption feature. An example of a 1f signal compared to an equivalent CEAS signal is shown in Figure 5.14a

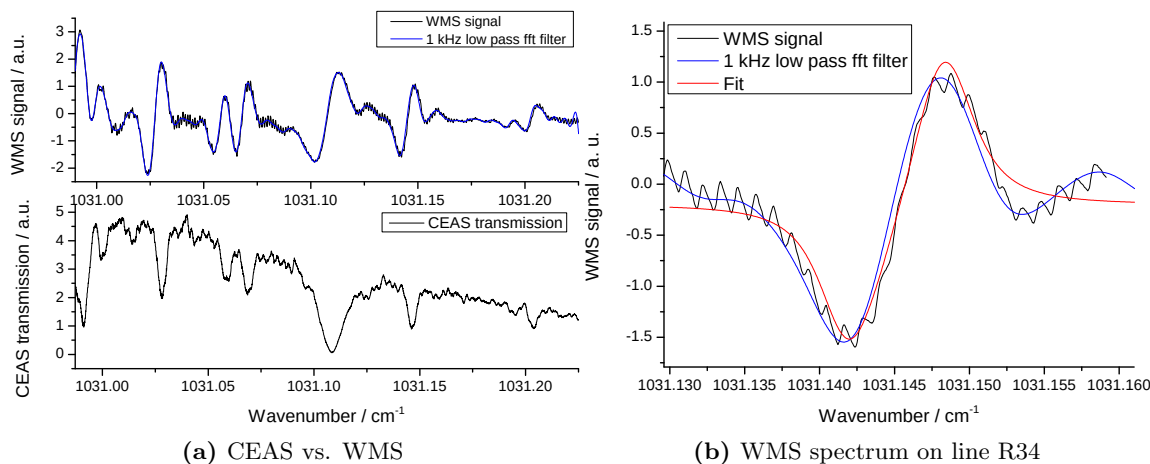


Figure 5.14: Data showing a comparison of the CEAS signal and its equivalent WMS CEAS signal, both taken over 100 averages. The WMS CEAS signal was obtained with a scan rate of 10 Hz over the absorption feature with a 16 kHz fast modulation imposed on top. The lock-in time constant was set to 640 μ s. The WMS data also shows an filtered equivalent (1 kHz low pass fft) in blue. A single WMS feature and a corresponding simulation are also shown in Graph b, highlighting the high-frequency noise component.

As can be seen when comparing the WMS CEAS signal to pure CEAS, there appears to be an overall reduction in the baseline noise. There is, however, a high frequency component to the WMS noise, clearly seen in Figure 5.14b, that cannot be removed by varying the experimental parameters, and is likely to be due to a slight frequency mis-match in the demodulation process of the lock-in itself. The high frequency component can be filtered out computationally with a low-pass filter as shown in blue in Figure 5.14. The result in this is α_{min} values of $3.8 \times 10^{-7} \text{ cm}^{-1}$ and a hypothetical value of $3.6 \times 10^{-7} \text{ cm}^{-1}$ for the filtered data. This is a further improvement on the CEAS data by a factor of ~ 10 in terms of α_{min} .

In fact, the additional sensitivity gained from the use of WMS allows the detection of a much lower sample pressure of OCS, using the transition at 1031.109 cm^{-1} (P42), of a 50 ppm OCS in air mixture. A total pressure of 50 Torr was bled into the cell as this is the partial pressure condition at which σ_{peak} is still at its optimum value before pressure broadening begins to broaden the absorption feature too substantially, as shown in the simulations using HITRAN data in Figure 5.15.

The resulting WMS-CEAS spectrum of a 50 Torr sample of a 50 ppm OCS mixture in air, which is unobservable using CEAS alone, is shown in Figure 5.16 at 50 Torr. Whilst this data is not yet demonstrating the detection levels that would be required for monitoring OCS in breath, as this tends to be at ppb level and at atmospheric pressure, it does show the potential of using modulation spectroscopy to further improve the detection capabilities of a CEAS spectrometer, which could be utilised in future studies on trace gas detection. The

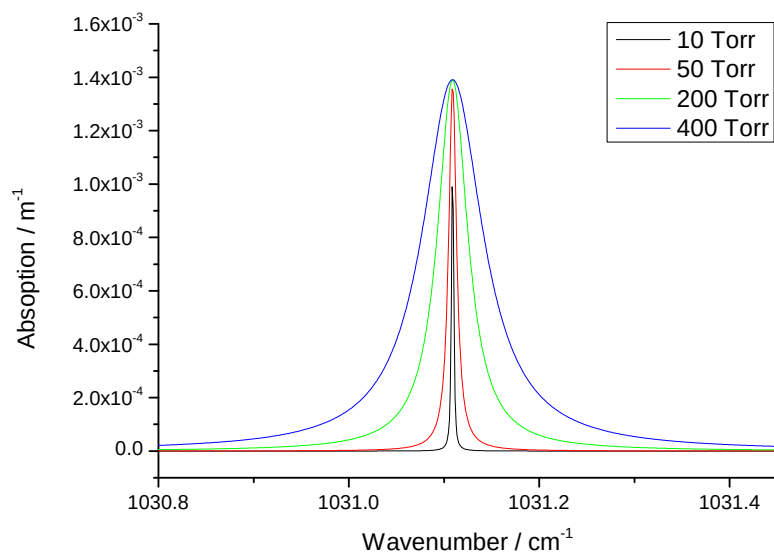


Figure 5.15: Data showing simulations of absorption over 1 m from a 50 ppm OCS in air sample at various total pressures OCS.

detection of OCS in breath would also become more practicable if the stronger fundamental bands were probed, in particular the ν_1 band centred around 2062 cm^{-1} , which is up to ~ 250 times stronger than the overtone band probed here.

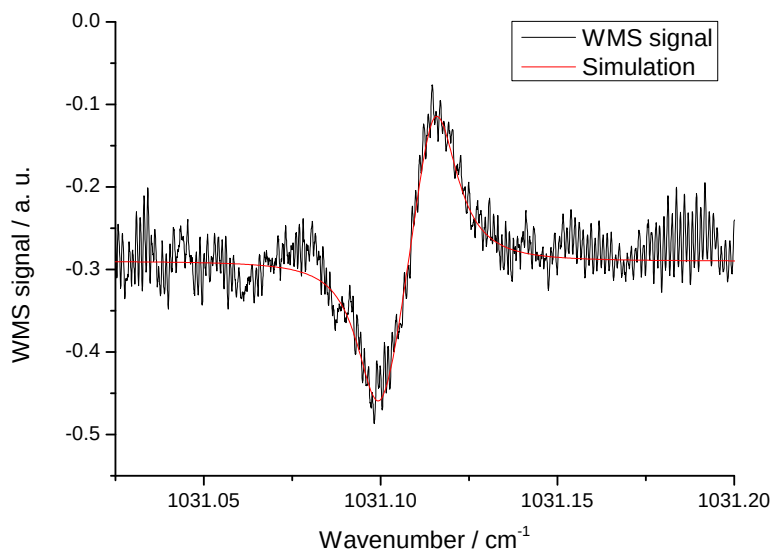


Figure 5.16: Data showing WMS CEAS trace and fit of a 50 Torr sample of a 50 ppm OCS in air mixture. Data has been averaged for $t_{acq} = 5\text{ s}$.

The sensitivity of the CEAS system and any improvements from the addition of WMS are summarised in Table 5.3. The α_{min} values in Table 5.3 highlight the successive improvements from moving from direct absorption, to OA-CEAS and then finally to OA-CEAS

with WMS, with optimum sensitivities $\sim \times 10^{-7} \text{ cm}^{-1}$ achieved. However, the dominant noise source is still the residual mode noise from the cavity, which is a direct result on the restrictions on the cavity alignment imposed by limitations in the available equipment.

Method	α_{min}	$\alpha_{min}(t)$			$\alpha_{min}(BW_{eff})$		
	α / cm^{-1}	n	τ / s	α / $\text{cm}^{-1} \text{ s}^{\frac{1}{2}}$	n	τ_c / μs	α / $\text{cm}^{-1} \text{ Hz}^{-\frac{1}{2}}$
Direct	5.3×10^{-5}	100	0.5	4.1×10^{-5}	-	-	-
CEAS	7.7×10^{-6}	100	25	3.8×10^{-5}	100	640	3.4×10^{-6}
CEAS WMS	3.8×10^{-7}	100	5	8.6×10^{-7}	100	640	1.7×10^{-7}
CEAS WMS (fft1kHz)	3.6×10^{-7}	100	5	7.9×10^{-7}	100	640	1.6×10^{-7}

Table 5.3: Minimum detectable absorption levels for detection of OCS at $10 \mu\text{m}$. α_{min} values are given as time-normalised and bandwidth normalised values where appropriate. n indicates the number of averages for the data. τ indicates the acquisition time and τ_c gives the time constant of the lock-in amplifier for experiments where demodulation of the signal has been used.

5.4 Long pathlength and WMS studies on the detection of OCS at $10 \mu\text{m}$

An alternative possibility for sensitive detection in the MIR, is to use a multipass cell instead of an optical cavity to achieve an extended pathlength. Multipass cells are not normally preferred over an optical cavity when working in the NIR, since typical pathlengths obtainable are normally only $\sim 100 \text{ m}$ compared to $\sim \text{km}$ with a cavity. As well as this, the volume of a multipass cell tends to be larger, since it relies on spatially separated reflections between the mirrors, therefore contributing to the overall footprint of the experiment. However, with the relatively low pathlength enhancements obtainable via CEAS when working in the MIR, coupled with the high residual mode noise, the use of a multipass cell is potentially a practical alternative.

The following studies describe the detection of OCS using a multipass cell using both direct absorption spectroscopy, and the more sensitive WMS, to compare with the CEAS work already discussed.

5.4.1 Experimental setup

The use of multipass cells to increase the absorption pathlength has already been discussed in Chapter 4 where a White cell was used to measure methane absorptions. In the experiments described here, a highly stable Herriott cell [*Aerodyne Research Inc., AMAC-200*] with a maximum pathlength of 238 m is used instead, along with many of the same components as the CEAS work.

The $10\ \mu\text{m}$ QCL and collimation lens, as well as the appropriate controllers, used previously were again employed, with the polariser also used to reduce the signal level if required, since almost the full laser power ($\sim 10\ \text{mW}$) will be incident on the detector or camera. The beam was directed into the multipass cell using an in-house constructed mount for D-mirrors, setting them at the appropriate angle and height to guide the input beam on the correct input geometry, and to retrieve the output beam. As well as this, the alignment of the Herriott cell ideally requires that the beam waist forms at the midpoint of the cell, and so the beam is focused to the correct point using a $100\ \text{cm}$ focal length lens. A schematic of the setup is shown in Figure 5.17.

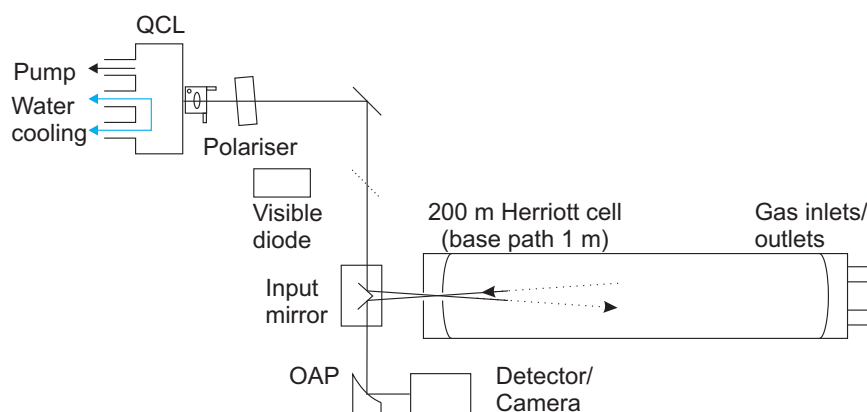


Figure 5.17: Experimental setup diagram for multipass detection of OCS at $10\ \mu\text{m}$.

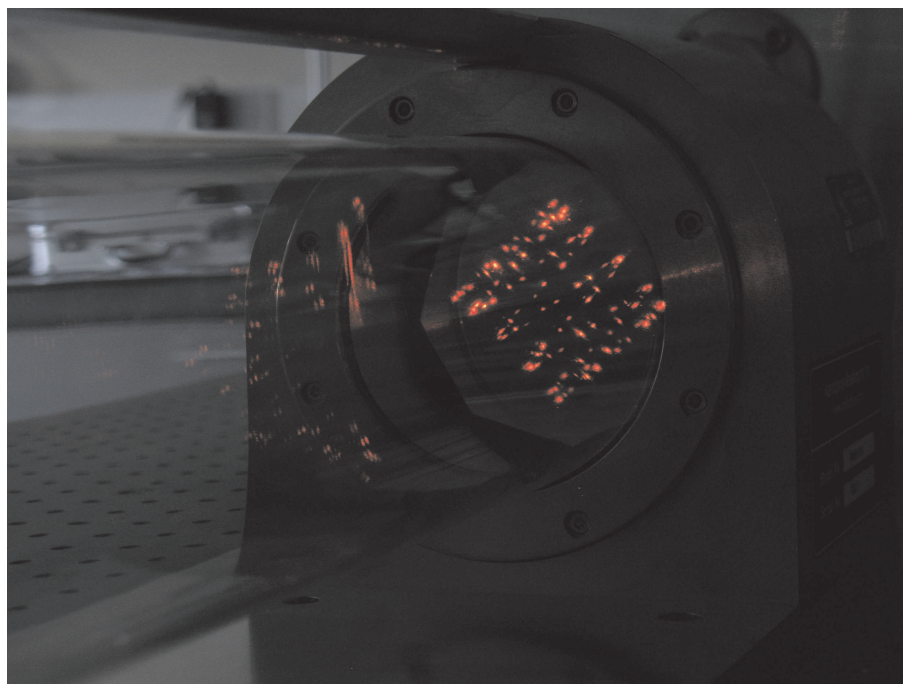


Figure 5.18: Image showing the Lissajous pattern of spots formed in the Herriott cell by the aligning diode.

The Herriott cell is aligned using the overlapping visible diode beam until the spot pattern displayed on the mirrors is that of the characteristic Lissajous pattern consistent with the 238 m pathlength. The pattern observed is shown in Figure 5.18, where the two perpendicular sinusoidal arrays of spots forming the Lissajous pattern are clearly visible.

5.4.2 Direct absorption studies: Results

The first measurements taken with the aligned Herriott cell were direct absorption measurements to confirm the overlap of the QCL with the visible diode, and hence the pathlength enhancement. Figure 5.19 shows an example of a direct absorption spectrum taken at 10 Hz and averaged 100 times, of the same region around 1031.1 cm^{-1} as examined using CEAS. Also shown is an example fit of the (R34) line.

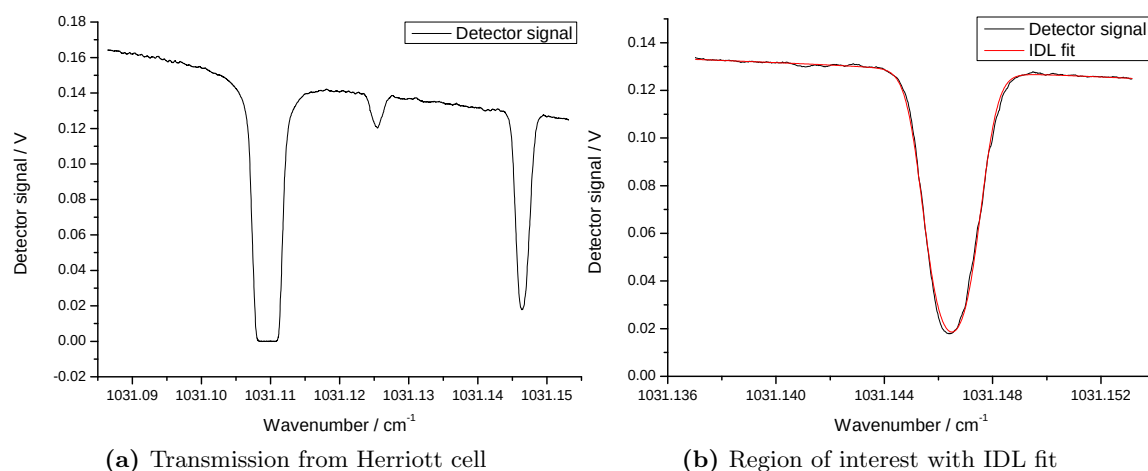


Figure 5.19: Graph (a) shows an example direct absorption spectrum of 0.114 Torr pure OCS taken over 5 s using the Herriott cell. Graph (b) shows the line at 1031.146 cm^{-1} (R34) and an IDL fit to measure the pathlength enhancement.

Taking similar data at several pressures and averaging the resulting pathlengths returned from the fit gives an average pathlength of 213 m. The discrepancy between this and the expected 238 m is likely due to errors in the pressure gauge at such low pressures, and therefore it is assumed that the pathlength in total is that expected from the Lissajous pattern exhibited by the visible diode.

As can also be seen from this data, there is already a marked improvement between the direct absorption taken over 238 m and the CEAS data taken over an effective pathlength of $\sim 100 \text{ m}$. The sensitivity of this direct measurement is in fact $\alpha_{min} = 2.7 \times 10^{-7} \text{ cm}^{-1} \text{ s}^{\frac{1}{2}}$, which is already 2 orders of magnitude better than the equivalent acquisition time normalised CEAS data. This is to be expected since there is not only a longer pathlength enhancement with the Herriott cell, but also no issues with residual mode noise as seen

when using an optical cavity in the MIR. As well as this, there are fewer losses in intensity with a laser propagating through the Herriott cell as opposed to an off-axis cavity, and therefore there is a much higher intensity on the detector. However, to improve the sensitivity of the system further and to investigate whether detection limits suitable for breath analysis are possible, WMS can also be employed in the setup.

5.4.3 WMS studies: Results

WMS measurements were taken by the inclusion of the Stanford research systems lock-in amplifier used in section 5.3.7 to provide the high frequency modulation and demodulate the resulting signals. Typical examples of 1 to 3 f demodulation are shown in Figure 5.20.

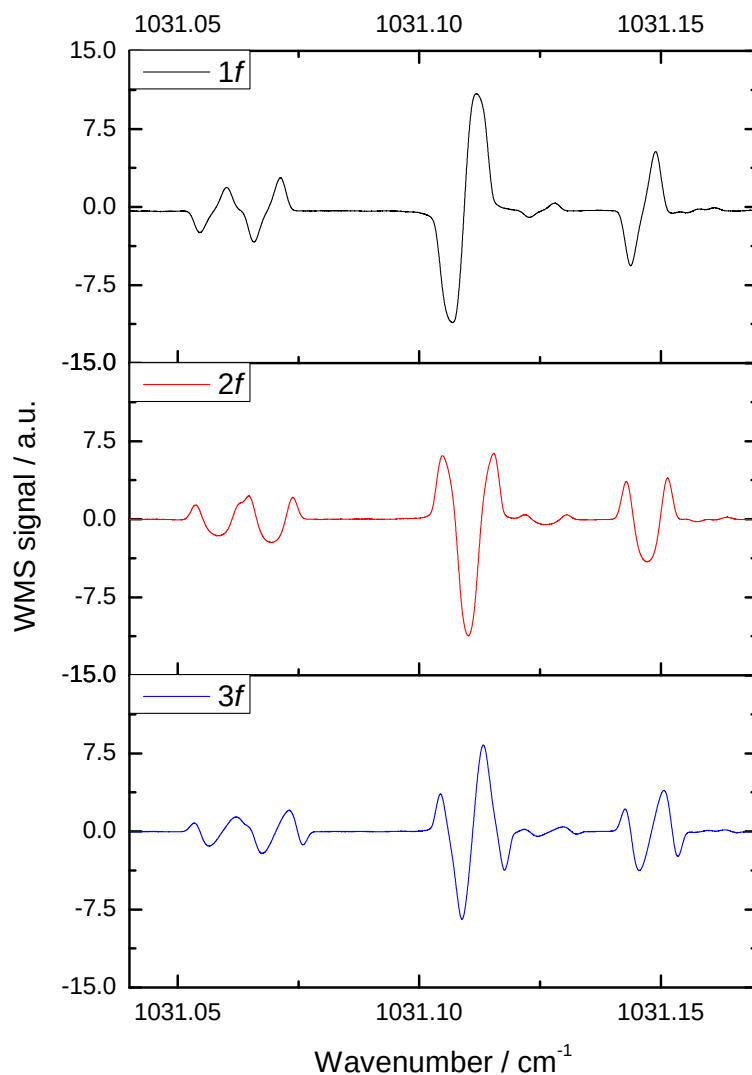


Figure 5.20: Examples of 1 - 3 f harmonics of 0.074 Torr pure OCS taken through Herriott cell with an acquisition time of 10 s.

The data in figure 5.20 demonstrate the increasing complexity of the signal structure on moving to higher harmonics. The data were taken with an overall acquisition time of 10 s and the lock-in provided a modulation frequency of 15 kHz, with a time constant set to 640 μ s. The spectra shown in Figure 5.20 were optimised to the maximum signal size setting b to the appropriate value for each harmonic, as has been described in Chapter 3. This optimisation is clearly demonstrated in a series of $1f$ spectra taken at various b values in Figure 5.21. These data demonstrate the increase in signal as $b \rightarrow b_{opt} = 2.1$, as well as the increase in modulation broadening as the experimental parameters move further from the derivative limit.

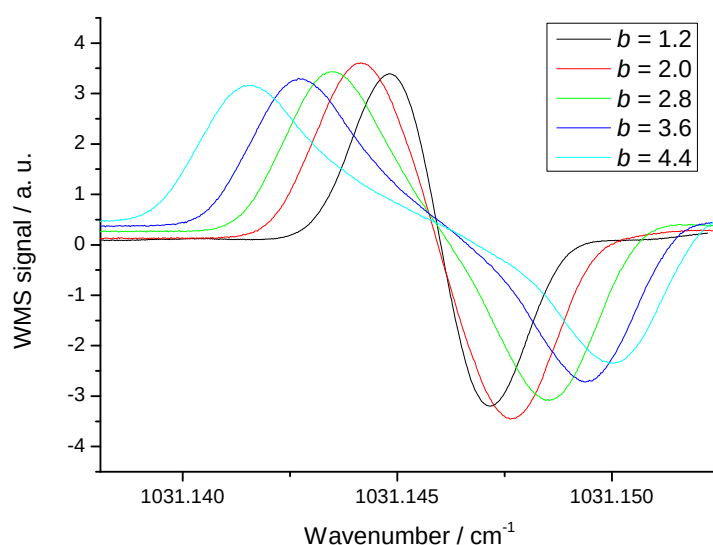


Figure 5.21: Examples of $1f$ spectra of 0.079 Torr pure OCS taken through the Herriott cell with an acquisition time of 10 s. Data show variation in spectra for increasing values of b , all taken at a modulation frequency of 15 kHz.

Examples of the optimised WMS absorptions for $1f$ and $3f$ harmonics are also shown in more detail in Figure 5.22, where a specifically written MATLAB routine to model the detected harmonic signal has been used to fit the data.

The average Gaussian width returned from these fits is $2.31 \times 10^{-3} \text{ cm}^{-1}$ (FWHM) which is comparable to the predicted convolution of the absorption Doppler width and the effective laser linewidth measured in section 5.2.2, which give a width of $2.42 \times 10^{-3} \text{ cm}^{-1}$ (FWHM).

The WMS data here show very high signal-to-noise, for example the $1f$ data exhibits a signal-to-noise ratio of 782, and the sensitivities are an improvement on both the CEAS and the direct absorption through the Herriott cell data described previously. In fact, the time normalised $\alpha_{min}(t)$ value is $\alpha_{min}(t) = 1.43 \times 10^{-7} \text{ cm}^{-1} \text{ s}^{\frac{1}{2}}$, which is only ~ 2 times more sensitive than direct absorption alone. This is likely due to the fact that, whilst WMS

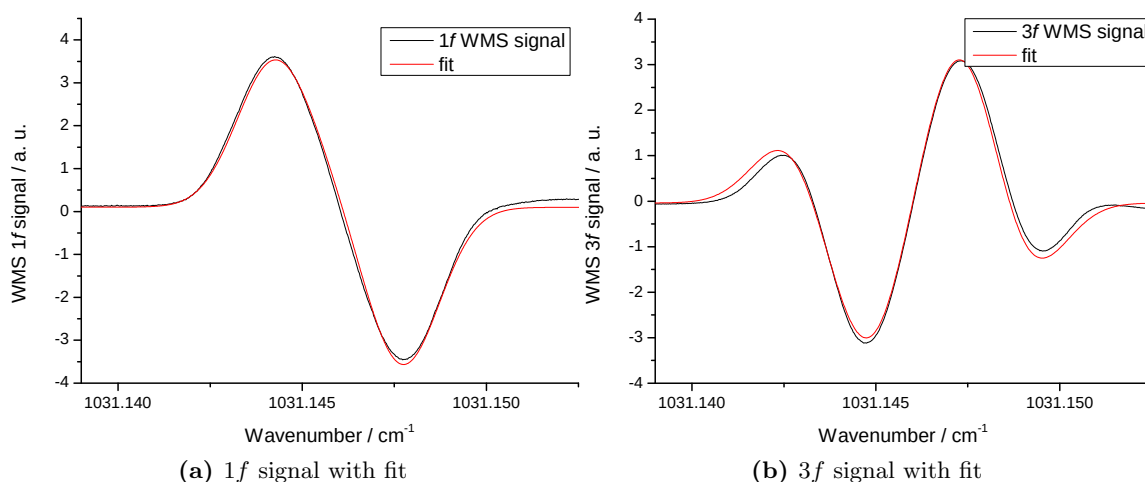


Figure 5.22: Graph (a) shows an example 1f spectrum of pure OCS on the R34 line as well as the returned fit shown in red. Graph (b) shows an equivalent spectrum demodulated at the 3f harmonic. Both data sets were taken over 10 seconds with a modulation frequency of 15 kHz.

improves the signal through removing spurious noise sources, the dominant improvement in this system is the 238 m pathlength, and the absence of high noise sources such as the residual cavity mode structure seen in the CEAS work. Theoretically however, if the detection sensitivity is normalised to the lock-in amplifier bandwidth instead of the acquisition time, this gives a bandwidth reduced value of $\alpha_{min}(BW) = 2.03 \times 10^{-8} \text{ cm}^{-1} \text{ Hz}^{-\frac{1}{2}}$, and so the theoretical detection limit is in fact much lower, as is expected from WMS.

The extended pathlength increases the sensitivity to such a degree that it is easily possible to see low pressure samples (~ 7 Torr) of the 50 ppm OCS in air mixture. Absorption due to OCS can be observed when probing the (P42) line with WMS, or even direct absorption, as shown in Figure 5.23, however the weaker lines in the same region are still unresolved. This is an improvement on the measurements on the 50 ppm mixture using CEAS WMS, where absorption was only visible at higher concentrations (~ 50 Torr).

The data returned from the fits to the 50 ppm data are similar to those measured for the pure OCS samples and are comparable to the expected $2.42 \times 10^{-3} \text{ cm}^{-1}$ (FWHM). The Gaussian fit of the direct absorption returns a width of $2.89 \times 10^{-3} \text{ cm}^{-1}$ (FWHM), although with the difficulty in baseline fitting this error is not unexpected. The fit from the WMS 1f data returns a width of $3.34 \times 10^{-3} \text{ cm}^{-1}$ (FWHM), which is higher than the expected value, and likely due to the poorer fit on the absorption feature wings. Overall, the analysis shows that the spectroscopic information that can be obtained from use of the Herriott cell is in good agreement with the expected values.

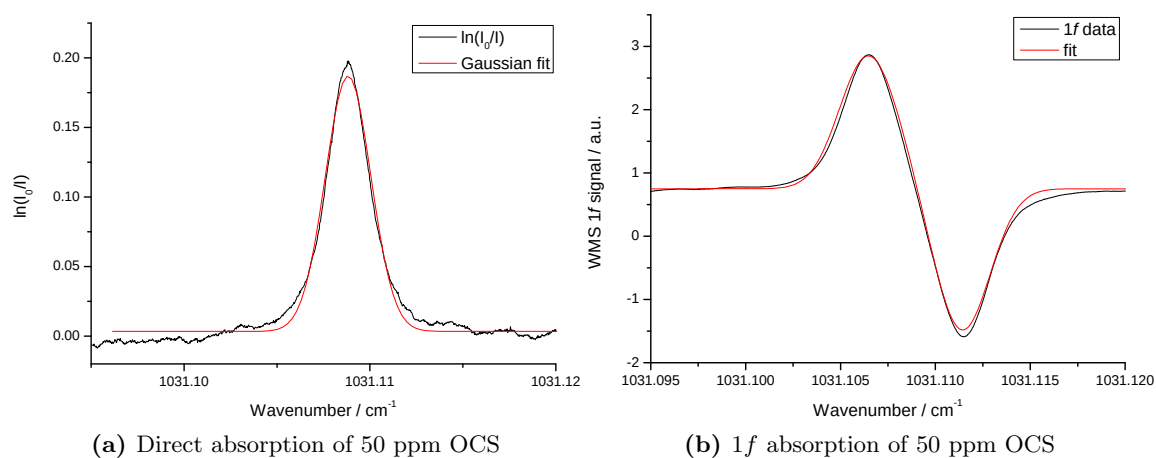


Figure 5.23: Spectra showing absorption of the P42 line of a sample of 7.60 Torr 50 ppm OCS in air mixture. Graph (a) shows the direct absorption spectrum and Gaussian fit in red, and graph (b) shows the corresponding WMS 1f signal and fit on the same sample.

5.5 Multipass cell vs. OA-CEAS in the MIR: Conclusions

The data obtained from the use of the Herriott cell displays a higher detection sensitivity than that obtained from OA-CEAS when using both direct absorption spectroscopy and WMS, as expected from the greater pathlength enhancement in the Herriott cell compared to the cavity, coupled with lower noise levels and orders of magnitude loss in the transmitted light intensity. The optimum bandwidth reduced $\alpha_{min}(BW)$ value measured for WMS in the Herriott cell was $2.03 \times 10^{-8} \text{ cm}^{-1} \text{ Hz}^{-\frac{1}{2}}$ compared to $1.7 \times 10^{-7} \text{ cm}^{-1} \text{ Hz}^{-\frac{1}{2}}$ for CEAS WMS. In terms of the potential for MIR detection of the biomarker OCS, only the sensitivity achieved from using WMS in the Herriott cell approaches what is required, with the optimum $\alpha_{min}(BW)$ corresponding to a minimum detectable atmospheric level of 47 ppb OCS. Whilst this is approaching $\sim$ ppb levels required for breath analysis, further gains in sensitivity are required, perhaps through probing stronger transitions for OCS in the ν_1 band, before measurements of OCS in breath can be viable.

However, the main conclusions that can be drawn from this work are from the investigation into using sensitive detection methods in the MIR, in particular CEAS, and the implications on experimental considerations and detection limits. In this work, the improvements in signal-to-noise from aligning a cavity off-axis have been demonstrated, as has the impact of restrictions in equipment and increasing losses at longer wavelengths on the sensitivity of CEAS. However, even with these disadvantages, a pathlength enhancement comparable to other reported works in the MIR has been achieved. In light of the experimental restrictions for CEAS in the MIR demonstrated in this work, another alternative for future work is the investigation of CRDS, as the alignment required for this form of cavity work is likely to incur fewer losses than what has been observed for CEAS. Whilst CRDS requires a more

complex level of electronics, as well as higher quality mirrors than CEAS, it is potentially worth investigating as an alternative sensitive detection method. Overall, in its current state, CEAS in the MIR is unable to perform at the same level of sensitivity as WMS in an astigmatic Herriott cell, without significant investment in custom optics and detectors.

Chapter 6

Conclusions and future directions

The work presented in this thesis has described novel approaches to breath analysis using spectroscopic methods. The methods used, including direct absorption spectroscopy, cavity enhanced absorption spectroscopy (CEAS) and wavelength and frequency modulation spectroscopy (WMS and FMS), have all either been applied directly to the detection of species in breath, or their potential in this field has been discussed. In terms of the species studied, this too has varied widely from the monitoring of high concentration species such as O_2 and CO_2 during respiration, to the detection of trace gas species ($\sim$ ppb levels) that are potential biomarkers. In this final chapter, a general overview of the conclusions from this thesis as a whole are given, and ideas for further improvements and areas for investigation are discussed.

The task of monitoring respiration in a medical environment by accurate, simultaneous detection of O_2 , CO_2 and H_2O has been presented in this work with the design and construction of a small robust analyser. The analyser is a culmination of various studies on the molecules of interest, in terms of what experimental practicalities are required, and studies on the impact that variations in pressure broadening have on the absorption features which in turn have been incorporated into the data analysis. The studies on CO_2 and H_2O were performed using direct absorption over a pathlength of ~ 5 cm, however, spectroscopically, the most challenging aspect of this analyser has been the use of an optical cavity for measuring the weak O_2 absorptions. In this work the measurements have been performed in a cavity only 2.75 cm in length, and with data acquisition times of only 10 ms, which is comparable to currently used mass spectrometry based methods. The detection limits achieved within this time resolution are also comparable to current methods and are within the limits outlined for the overall concept of the analyser. The continuation of this work will involve further miniaturising of the design and making it robust enough for clinical

trials, as well as incorporating additional measurements such as flow and temperature so that physiological information can be obtained from studies on breath.

As well as the use of an optical cavity to enhance absorption signal-to-noise ratios, modulation techniques have also been utilised throughout this thesis, and their potential in the field of breath analysis discussed. Conventional WMS detection of water has been demonstrated, and the use of a recently developed self-calibrating WMS detection method, the phasor decomposition method (PDM), has been investigated. The PDM technique exploits the inherent phase lags present in a WMS experiment to overcome one of modulation spectroscopy's main disadvantages: its non absolutivity. In this thesis, the PDM has been demonstrated on atmospherically broadened water, as would be found in breath, and the resulting calibration differed by 9 % compared to an equivalent direct absorption measurement. This difference is most likely due to the difficulty in obtaining a baseline when working with water, however, the results do show that PDM is a promising method that is worth investigating. In particular, future work utilising this methodology with lower concentration biomarkers in breath would be beneficial, as it is often difficult to calibrate WMS signals with direct absorption spectra in these environments. Another form of modulation spectroscopy that has been implemented in this work is FMS, and the potential gains in sensitivity compared to what was achieved with CEAS for the detection of O_2 , with the eventual focus being the detection of O_2 in breath. Whilst FMS was shown to be an effectual detection methodology, it was, however, not comparable to the detection sensitivity achieved with CEAS, which was two orders of magnitude lower and therefore more practical over the short pathlength and acquisition times required for breath analysis.

This thesis has also discussed the monitoring of trace gases in breath, by shifting spectroscopic detection to the mid-infrared (MIR) using QCL based spectrometers. The characterisation of an 8 μm QCL has been demonstrated in this work and new control electronics designed and built in-house to minimise the frequency spread of the effective laser linewidth, a limiting factor in spectroscopic resolution. The 8 μm QCL has been used in some preliminary studies for detection of two important biomarkers, methane and acetone. These studies, whilst successfully demonstrating the spectrometer's ability to monitor changes in gas concentration, highlight the need for added sensitivity if the levels of these biomarkers in breath are to be detected. A likely way to achieve this is through extending the optical pathlength by use of CEAS, as for near-infrared (NIR) O_2 detection in the breath analyser prototype, or using multipass cells. The use of extended pathlengths in the MIR is therefore the final section of work discussed in this thesis.

The use of an optical cavity in the MIR in this work has been demonstrated for the detection of OCS at 10 μm . In many ways, the work presented here on CEAS has investigated features inherent to working with cavities in the MIR, as well as attempting to use them

for detecting the biomarker OCS. CEAS in the MIR has been shown to be more challenging to achieve experimentally than its NIR counterpart, with restrictions on equipment and the scaling with wavelength of losses in a cavity contributing greatly to the reduced sensitivity. Even with these disadvantages the setup has been used to demonstrate the improvement in signal-to-noise when combined with a more rigorous approach to aligning the cavity off-axis, achieving a pathlength enhancement comparable to other reported values for CEAS in the MIR. In this study, the alignment of the cavity from on-axis to off-axis was shown to match the predicted theory and simulations in terms of both the intensity spatial output and the reduction of residual mode structure. Future work that would therefore be of interest for CEAS in the MIR would be custom designing an optical cavity with larger mirrors, focusing optics and detector surface. This would allow an even more thorough investigation into the potential sensitivity of CEAS in the MIR, and enable the full realisation of the benefits of aligning a cavity off-axis. In terms of specific detection of OCS in breath, when combining CEAS with WMS the work here returns calculated minimum detectable concentration of $\sim$ ppm as opposed to the $\sim$ ppb levels required, highlighting the need for an even longer extended pathlength and improvement in noise levels. If a higher sensitivity could be achieved with a new design of cavity, further work on reducing the measurement cell volume to make it practical for breath samples, and studies on atmospherically broadened OCS could be performed.

The alternative to CEAS to increase the experimental pathlength is the use of multipass cells, which, as the optical cavity enhancement at $10\text{ }\mu\text{m}$ in this work was typically found to be $\sim 100\text{ m}$, become a more viable alternative. The use of White cells has been briefly demonstrated for detection of methane at $8\text{ }\mu\text{m}$ in this work, but it also exhibits characteristic experimental difficulties when working with multi-pass experimental setups, in that instabilities result in uncertainties in the pathlength. The use of a much more stable Herriott cell based system for the work on OCS at $10\text{ }\mu\text{m}$ was much more successful, achieving a pathlength of 238 m that was used in direct absorption and WMS measurements. With the improved pathlength enhancement and low noise with the use of WMS, the minimum detectable absorption for atmospheric OCS was calculated as approaching what is required for breath analysis, at 47 ppb . This is a very encouraging result not only for the detection of OCS using multipass cells, but also for CEAS as well: if optical cavities in the MIR with pathlength enhancements similar to that in the NIR can be achieved ($\sim\text{ km}$), then the detection of OCS in breath via CEAS should be a distinct possibility. With continuing progress in improvement in optics in the MIR, in particular the highly reflective coatings for cavity mirrors, it is likely that the use of optical cavities can also be extended to build on the work shown here for the detection of methane and acetone as well.

Overall, this thesis presents the use of several spectroscopic methods based on absorption spectroscopy, and has applied them to a range of important areas of breath analysis. These

methods have been used across the NIR, and extended to the MIR where the importance of the work presented is not only in terms of detecting biomarkers, but also in better understanding the use of sensitive detection methods when applied to a new spectral region.

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