High resolution spectroscopic investigation of mono- and dimethylamines employing a cw cavity ringdown spectrometer

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OUTLINE

- **Introduction**
  - Trace gas sensing
  - Analysis of exhaled human breath
  - Methylamines

- **Experiments**
  - Near-IR combined direct absorption / CRD arrangement
  - Spectra of mono- and dimethylamines
  - Detection limits

- **Conclusions and outlook**
  - Preconcentration
  - Mid-IR studies

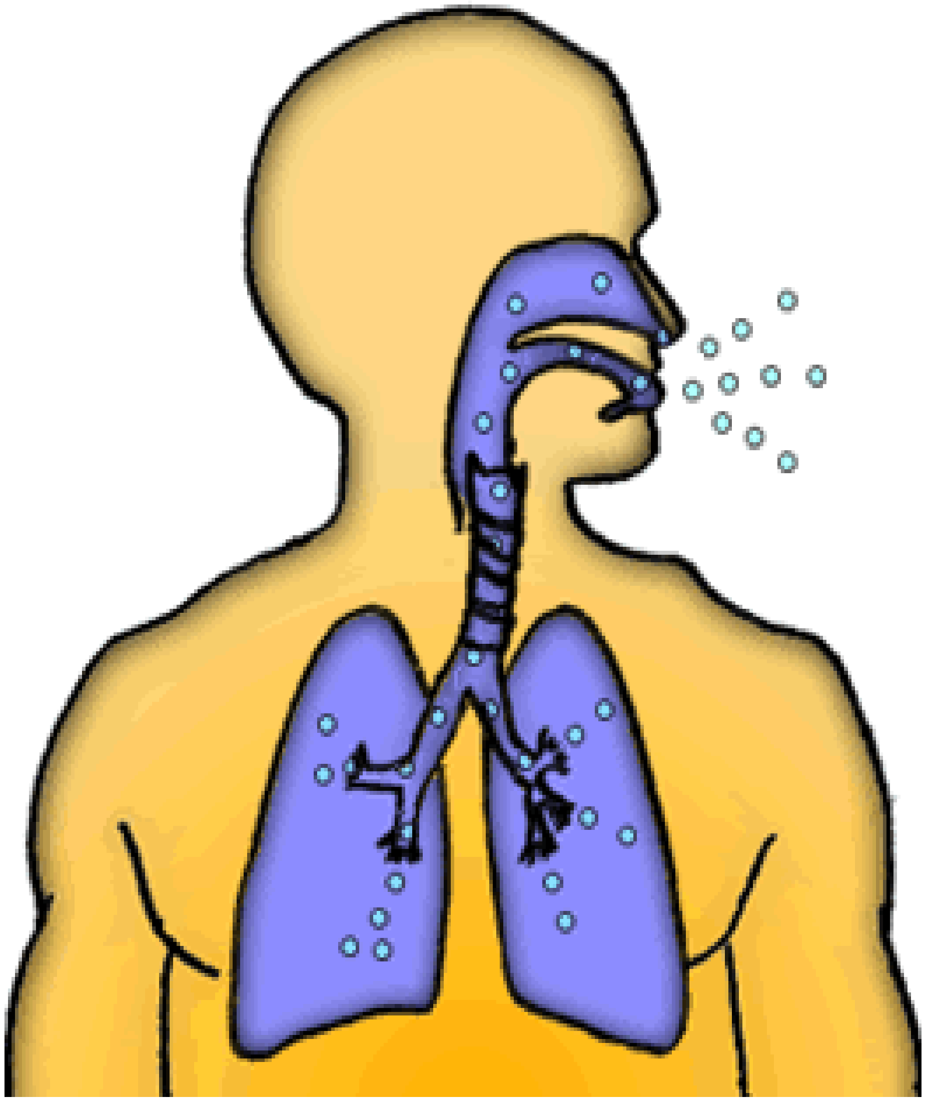
Trace gas analysis

- Ambient air monitoring
- Industrial environment and process monitoring
- Agricultural monitoring
- Noninvasive medical diagnostics

Trace-gas detection with *high sensitivity*, *high selectivity*, *multi-component*, *online*, and *in-situ measurement capability*

- Optical detection schemes
- Other detection schemes

Analysis of human breath air



Breath air

- N_2, O_2, CO_2, H_2O
- CO, NO, N_2O, H_2S, NH_3, CH_4, …
- Acetone, methanol, ethanol, isoprene, …

Composition of breath air

⇓

specific disease

Non-invasive medical diagnosis

Development of a novel medical diagnostic tool based on a laser-spectroscopic determination of specific trace compounds in breath air

- **Non-invasive method (neither blood nor urine sample)**
- **Fast gas analysis**
- **More than 1 gas compound**
- **High sensitivity und selectivity**

$\Rightarrow$

- screening method
- Diagnosis of selected diseases
- Observation of status of a disease (medication dosage)
- Diagnosis of intoxications

Physiological origins of some endogenous breath molecules

Compound	Physiological basis
Acetaldehyde	Ethanol metabolism
Acetone	Decarboxylation of acetoacetate
Ammonia	Protein metabolism
Carbon disulfide	Gut bacteria
Carbon monoxide	Production catalyzed by heme oxygenase
Carbonyl sulfide	Gut bacteria
Ethane	Lipid peroxidation
Ethanol	Gut bacteria
Ethylene	Lipid peroxidation
Hydrocarbons	Lipid peroxidation/metabolism
Hydrogen	Gut bacteria
Isoprene	Cholesterol biosynthesis
Methane	Gut bacteria
Methanethiol	Methionine metabolism
Methanol	Metabolism of fruit
Methylamine	Protein metabolism
Nitric oxide	Production catalyzed by nitric oxide synthase
Pentane	Lipid peroxidation

T.H. Risby, in *Breath Analysis* (World Scientific, 2005)

Clinical breath tests that are most developed

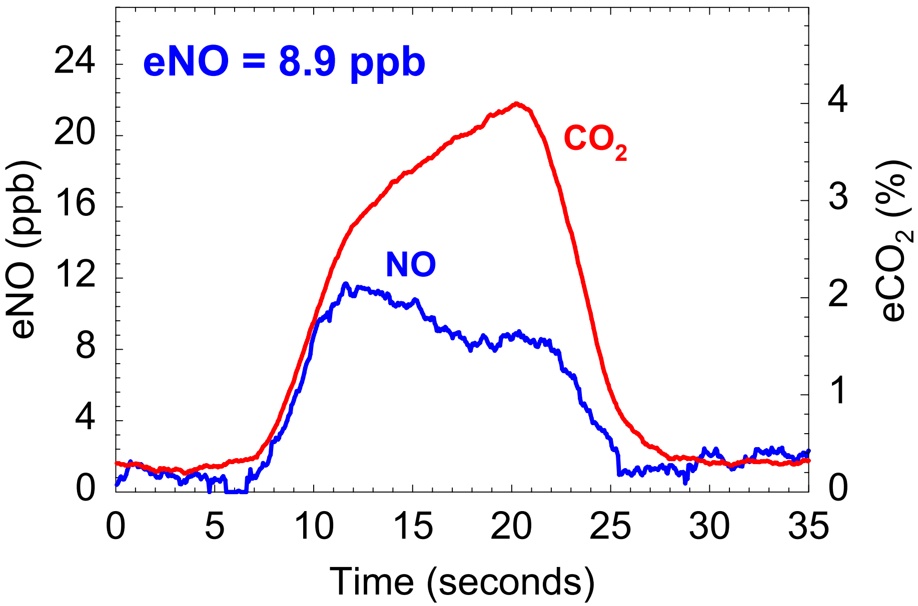
- Breath Carbon Dioxide Test for capnography
- Breath Carbon Monoxide Test for neonatal jaundice
- Breath Ethanol Test for blood ethanol (law enforcement)
- Breath Hydrogen Test to detect disaccharidase deficiency, gastro-intestinal transit time, bacterial overgrowth, intestinal statis
- Breath Nitric Oxide Test for asthma therapy
- Breath Test for detection of heart transplant rejection
- Urea Breath Test for detection of H. pylori infection

T.H. Risby, in *Breath Analysis* (World Scientific, 2005)

Examples of Asthma

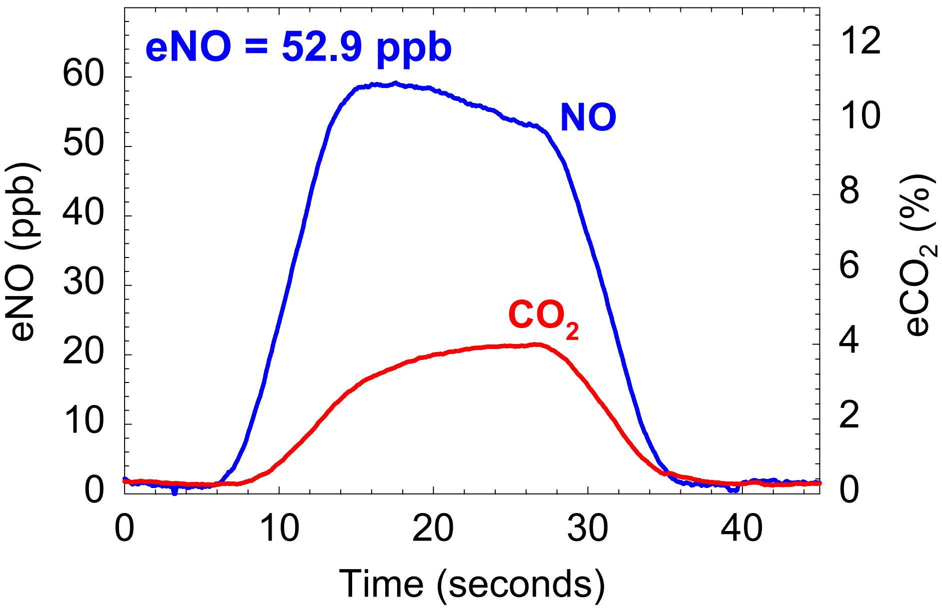
Age 5, Female, Mild-Persistent Corticosteriod Treated

Normal Airway



Age 14, Male, Mild-Persistent Non-Treated

Inflamed Airway



Concentrations of selected species in human breath

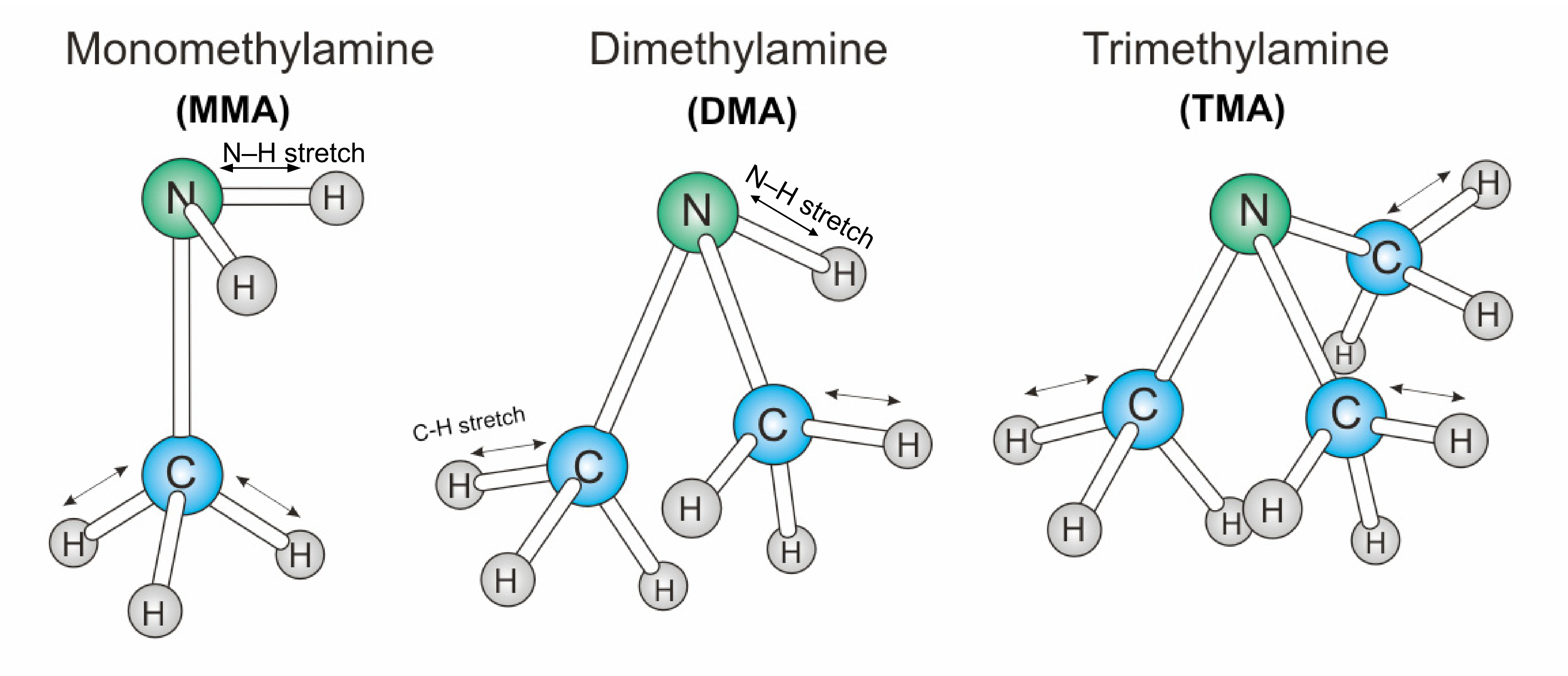
	Ammonia NH_3	TMA $N(CH_3)_3$	DMA $HN(CH_3)_2$	Isoprene C_5H_8
Healthy person	200 ppb	ppb range	ppb range	100 ppb
Renal disease	7x higher	2x higher	2x higher	controversial

Variation of average breath gas content of patient with renal disease (before/after haemodialysis)

	Ammonia NH_3	TMA $N(CH_3)_3$	Carbonyl sulfide COS	Dimehyl sulfide $S(CH_3)_2$
Healthy person	200 ppb	ppb range	50 ppb	0.35 mol/l
Liver disease	2x higher	higher	2x higher	5x higher

Increase of average breath gas content in patient with liver disease

Mono-, Di- and Tri-methylamines



Infrared absorption of methylamines

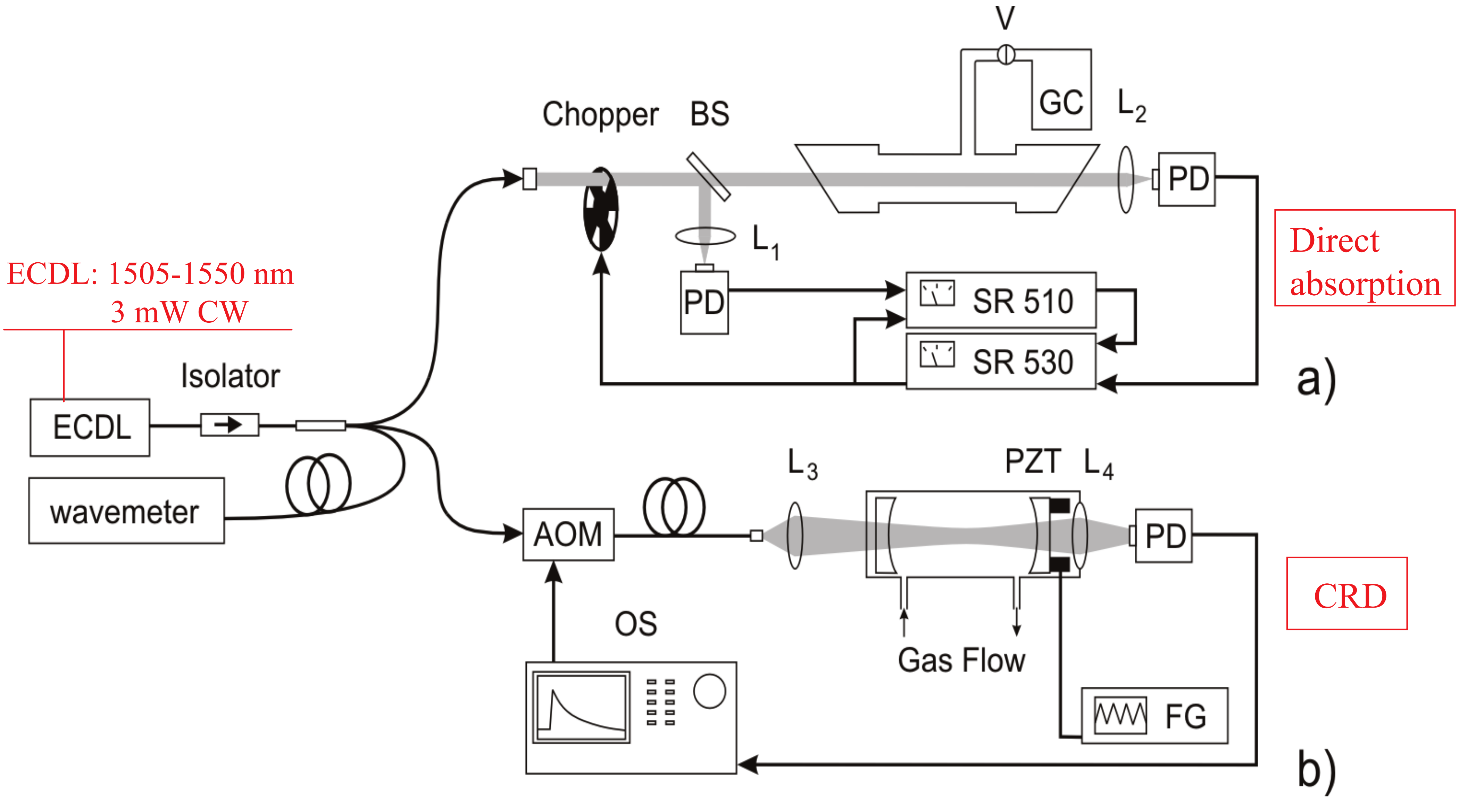
1st overtone of N-H stretch vibration in near-IR

- Monomethylamine (MMA): expected at 6602 cm^{-1} (1515 nm)
- Dimethylamine (DMA): expected at 6574 cm^{-1} (1521 nm)
- Trimethylamine (TMA): no NH stretch vibration

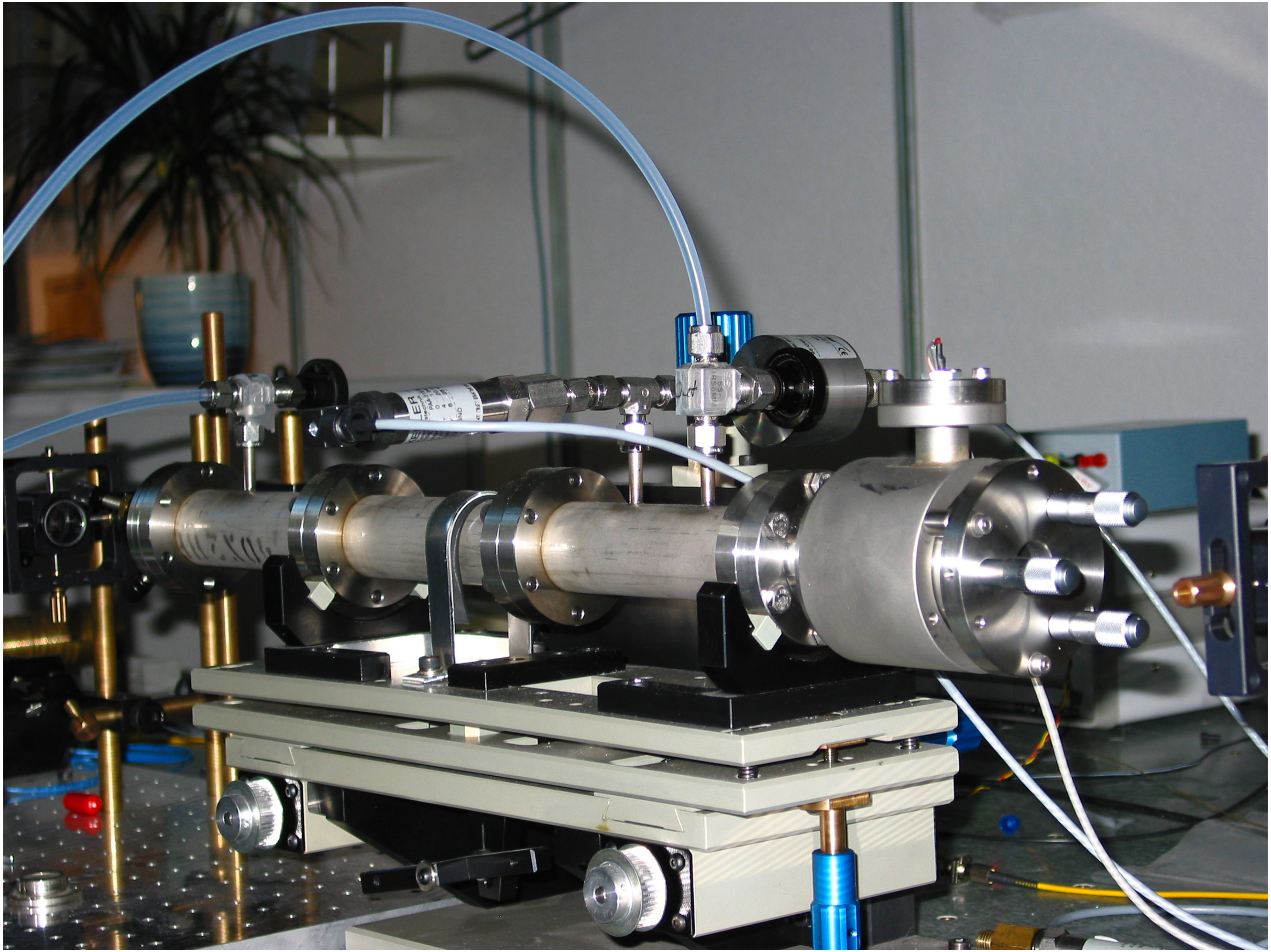
Mid-IR absorption

Mainly C-H stretch vibration around 2820 cm^{-1} (3.55 µm):
substantially stronger than in near-IR

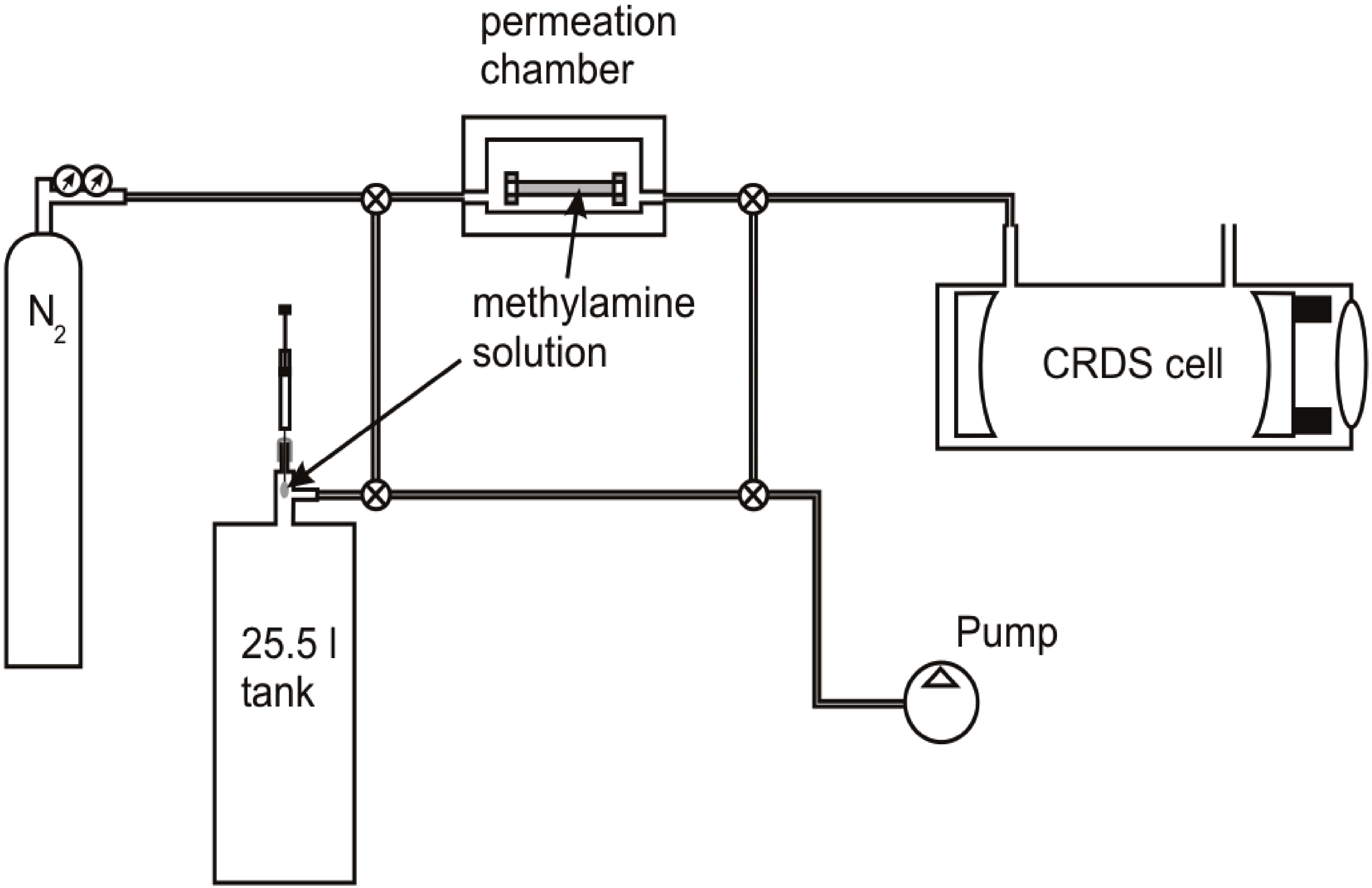
Near IR combined CRD / direct absorption set-up



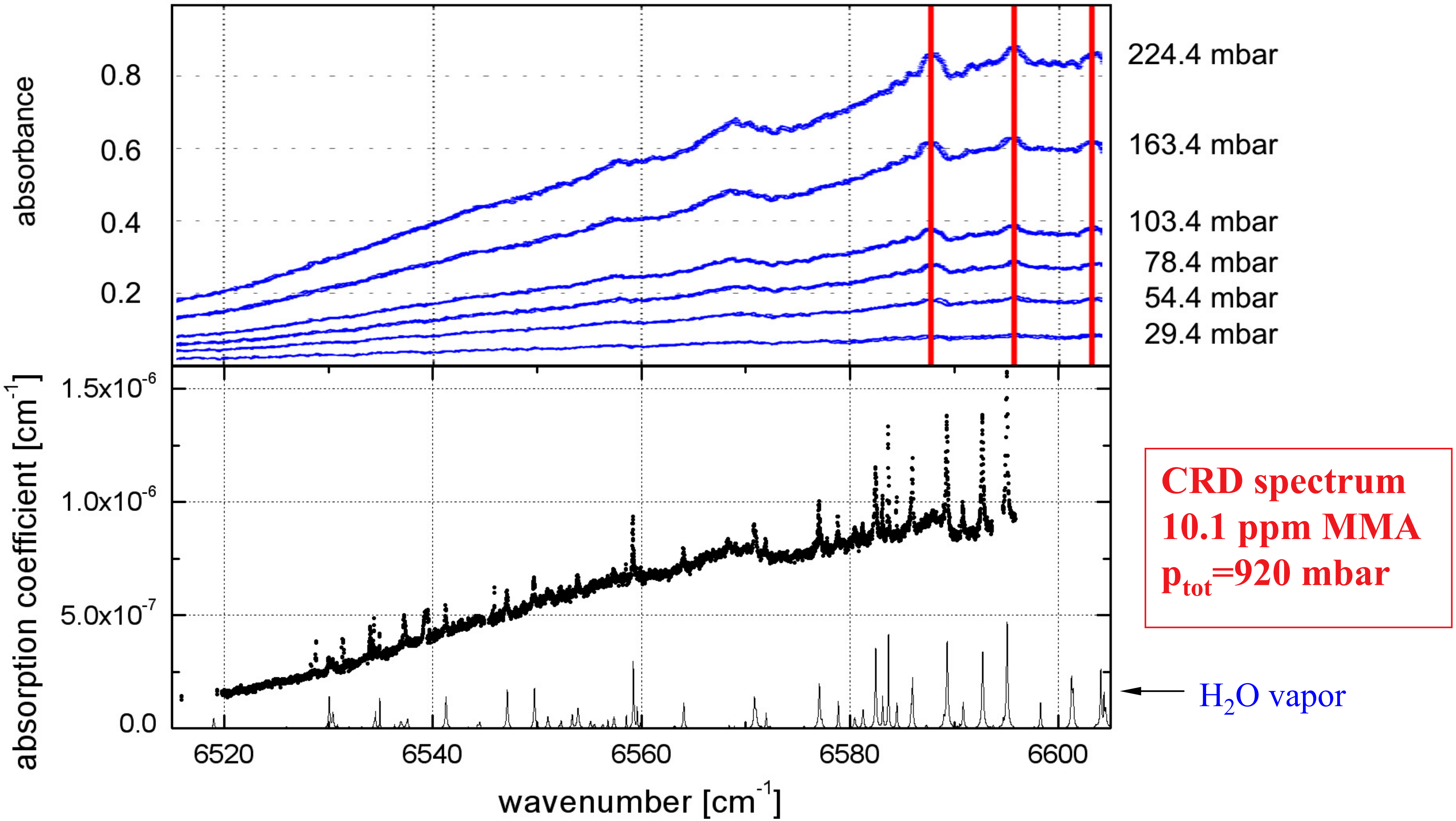
Cavity Ringdown Spectroscopy: Gas Cell



Gas handling system

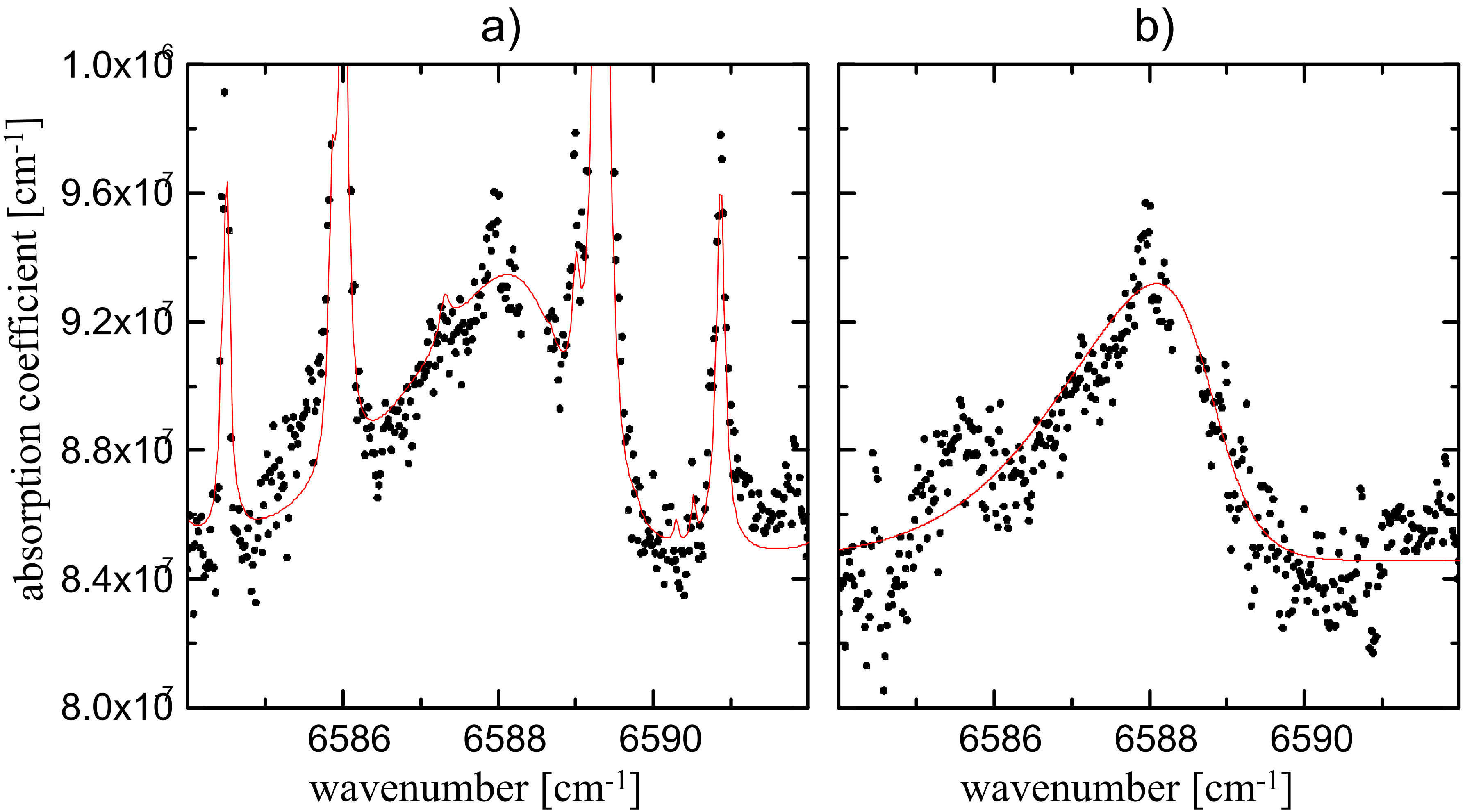


Monomethylamine (MMA) survey spectra

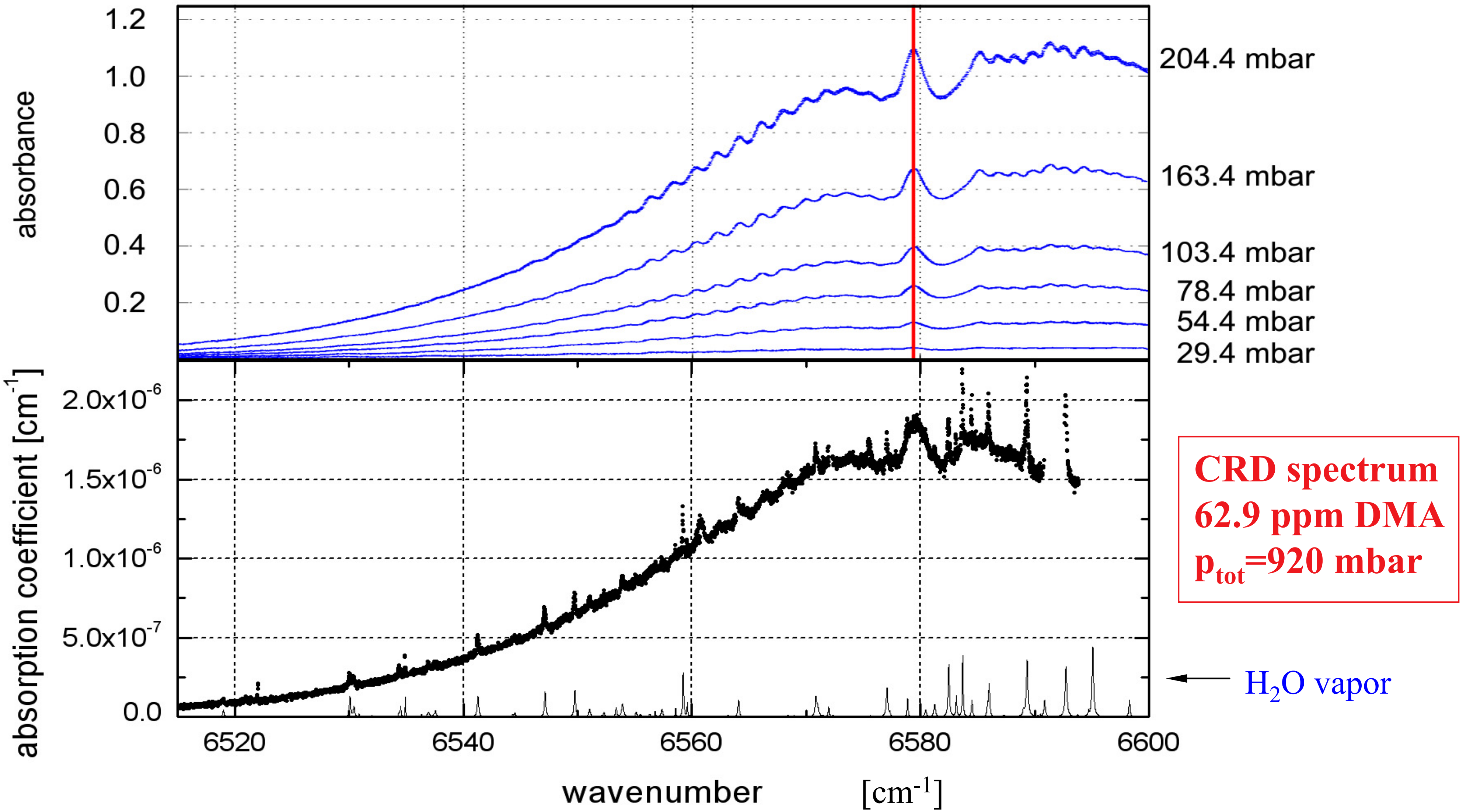


10.1 ppm MMA and 675 ppm H_2O in N_2

a) exp. data + fit   b) H_2O subtracted

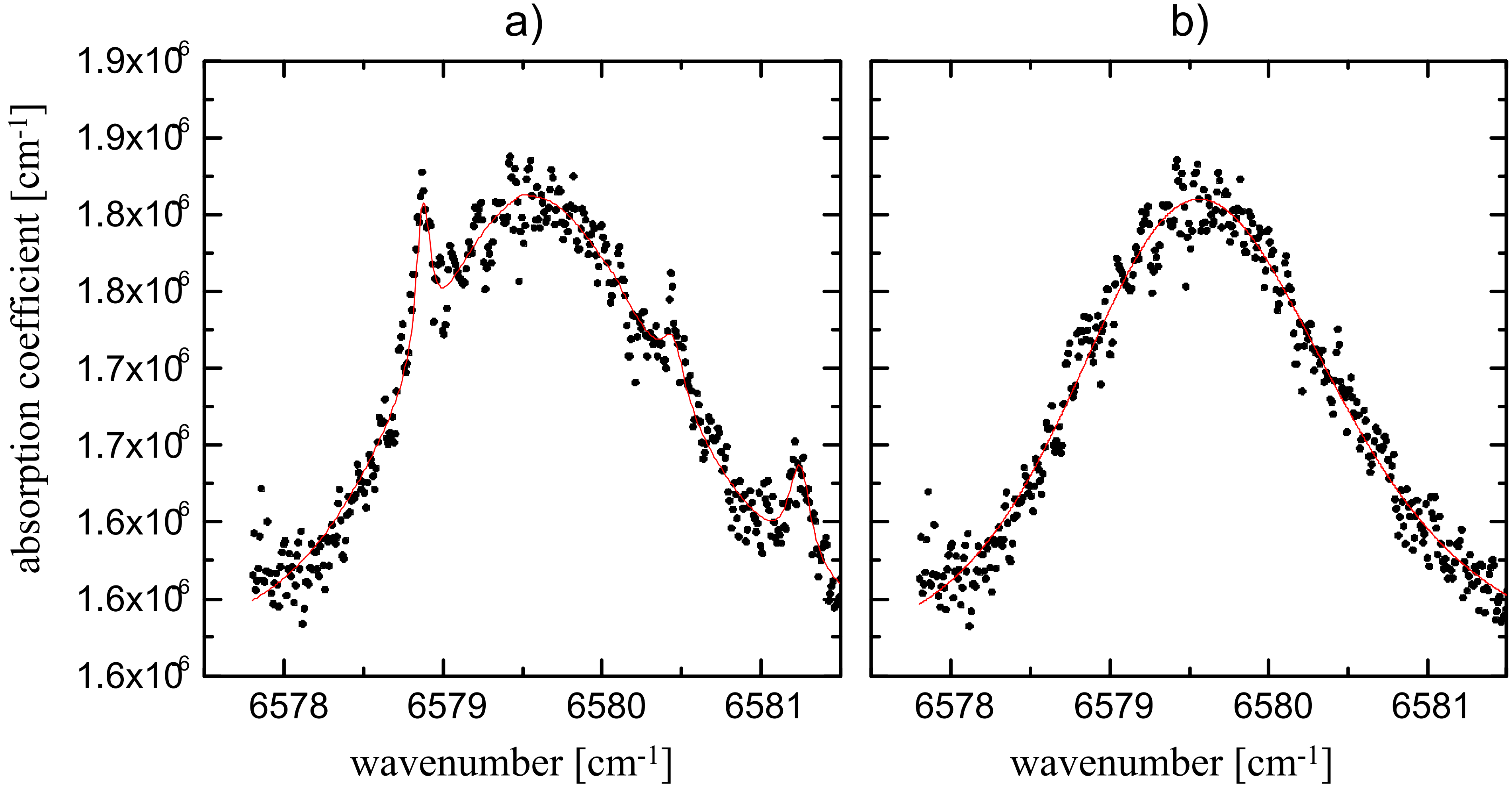


Dimethylamine (DMA) survey spectra



62.9 ppm DMA and 500 ppm H_2O in N_2

a) exp. data + fit   b) H_2O absorption subtracted



Near-IR CRD detection limits

- Ringdown time for cell filled with nitrogen: 38.6 ± 0.342 μs
- Minimum detectable absorption coefficient: $\alpha_{min} = 1.55 \cdot 10^{-8}$ cm^{-1} (SNR = 1)
- With cavity modulation frequency of 20 Hz and averaging 100 CRD events:

  $\alpha_{min} = 5 \cdot 10^{-8}$ cm^{-1} Hz$^{-1/2}$

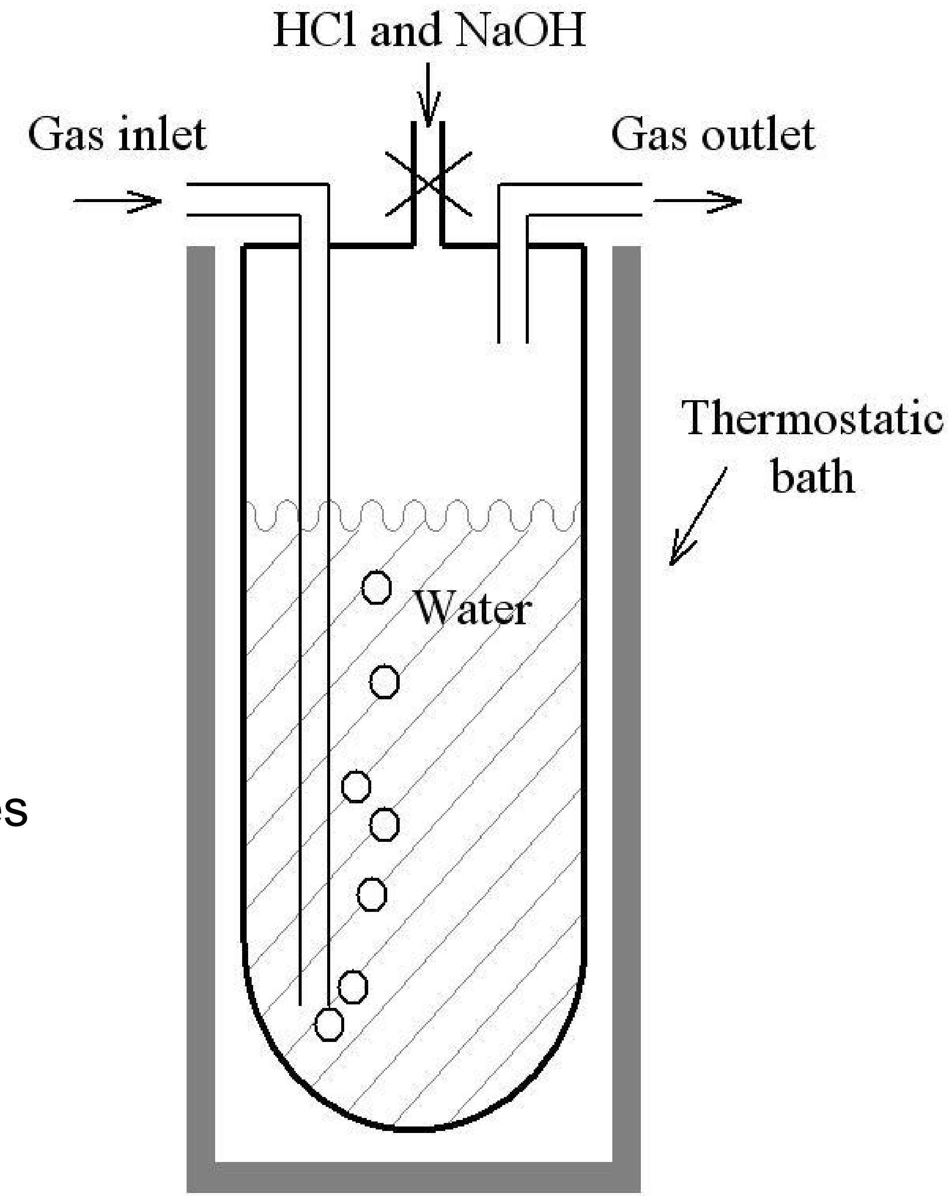
Species	Diluted in nonabsorbing gas mixtures	Diluted in absorbing gas mixtures
MMA	**350 ppb**	**2.3 ppm**
DMA	**1.6 ppm**	**10 ppm**

Problem: **Absorption interferences**, mainly by H_2O vapor (ca. 3% in human breath)

Approach I

Amines Preconcentration

Preconcentration technique allows storing the content of the gases of interest in an acidic solution.
Extraction after lowering the acidity of the solution increases the concentration of the methylamines.



Advantages

- Increases the concentrations of methyl-amines by 30 to 70 times
- Removes CO_2, H_2S, NO and other acidic gases

Drawbacks

- Requires preliminary investigation
- Extends measurement times

Approach II

Mid-infrared spectroscopy of methylamines

Advantages

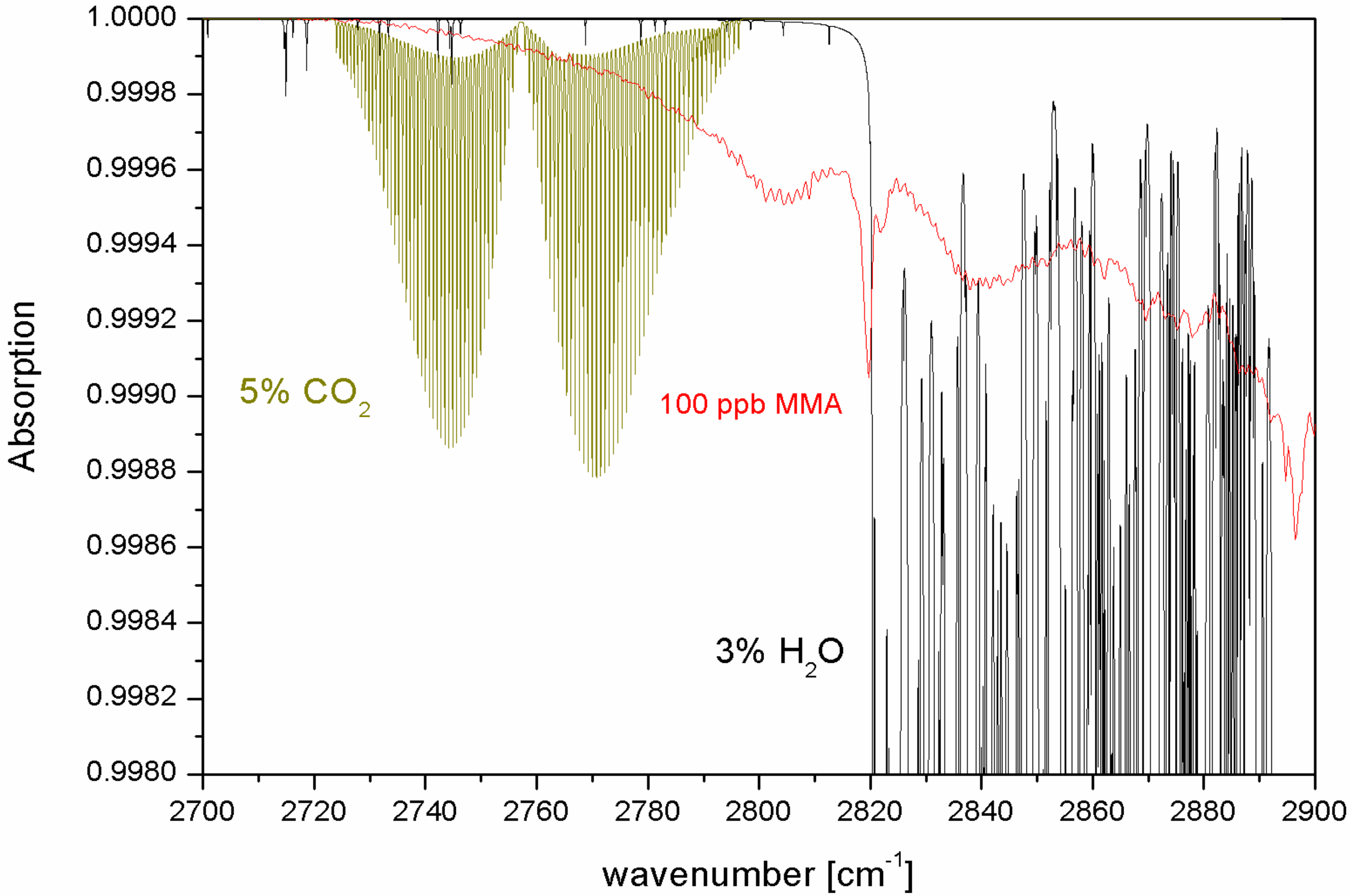
- Mid-IR: absorption cross sections increases substantially
- Much less interference by water vapor

Drawbacks

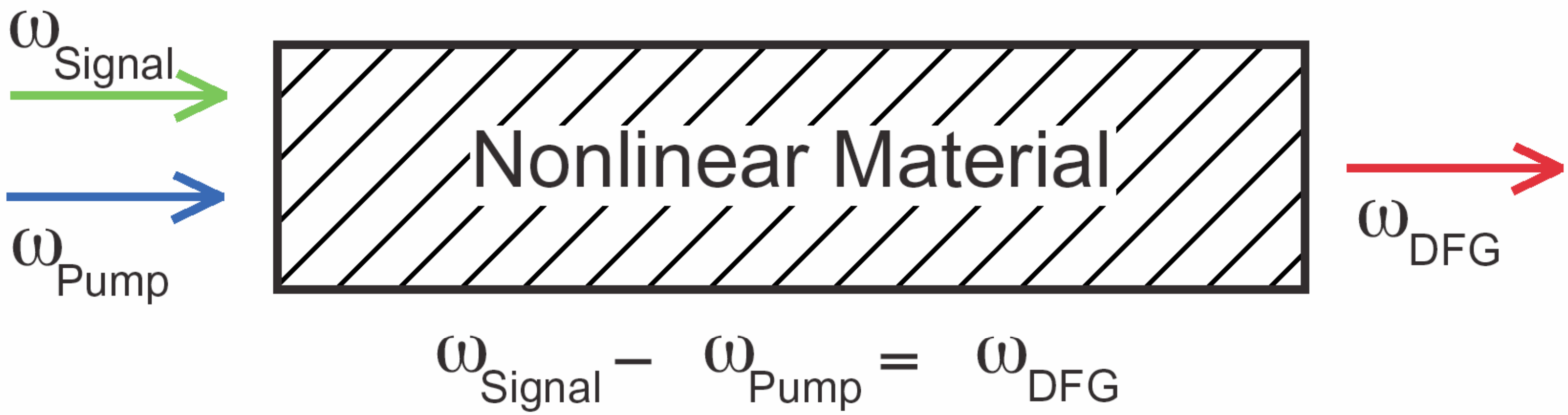
- More complex laser source
- Detection scheme less sensitive:
  Low laser power (μW) → CRD becomes difficult
  → Multi-pass absorption spectroscopy

Mid-IR spectrum of monomethylamine (MMA) in human breath

(in presence of 5% CO_2, 3% H_2O vapor, 36 m optical pathlength)



Difference Frequency Generation (DFG) in PPLN



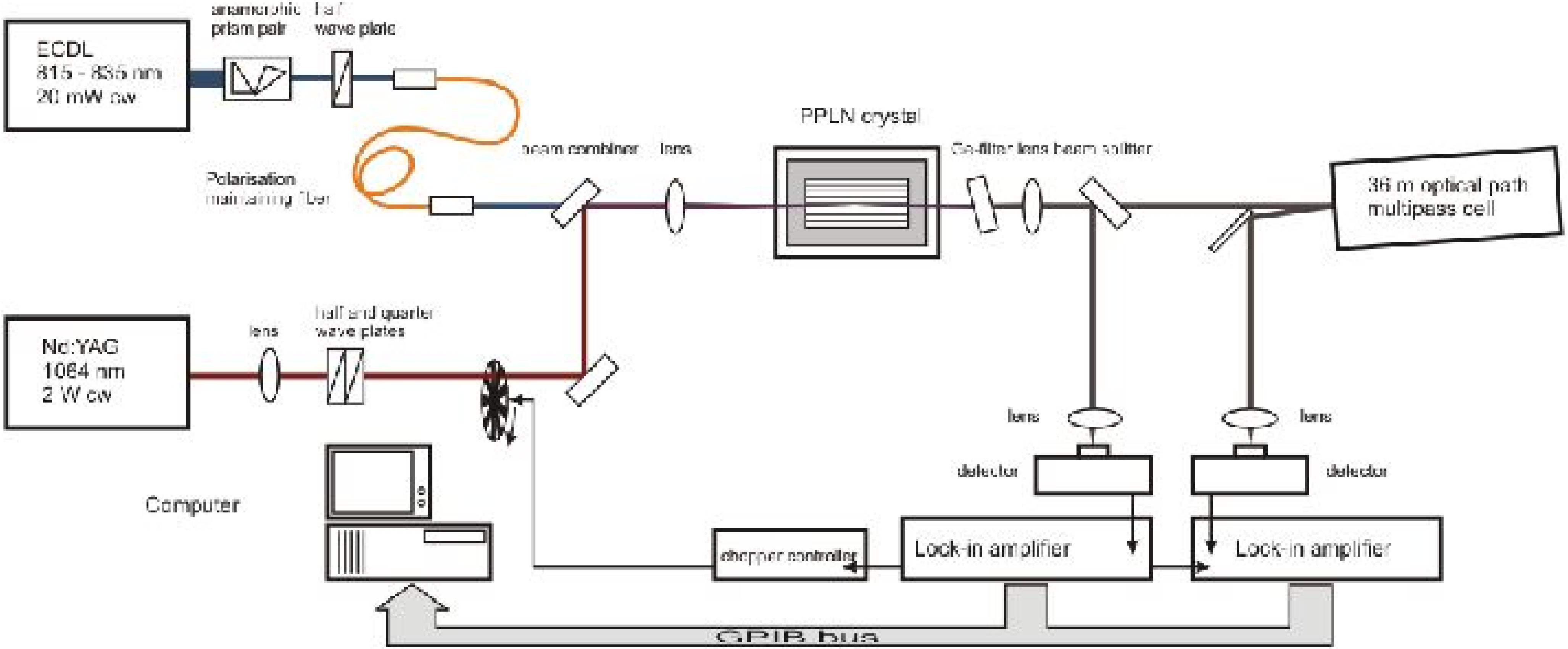
Energy conservation:

$$\omega_{DFG} = \omega_{Pump} - \omega_{Signal}$$

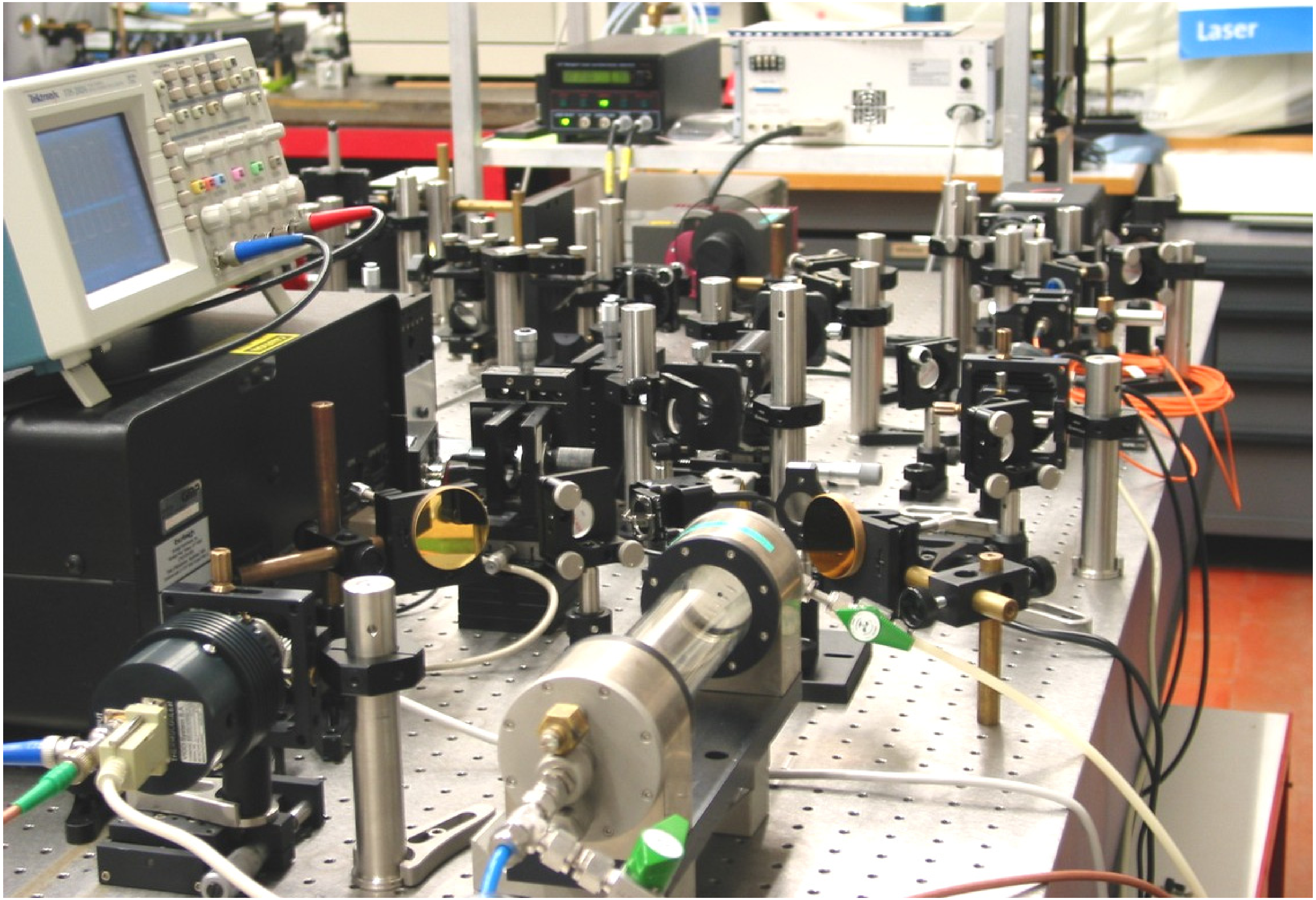
Momentum conservation:

$$k_{DFG} = \omega_{DFG}\left(\frac{c}{n_{DFG}}\right) = k_{Pump} - k_{Signal} - \frac{1}{\Lambda}$$

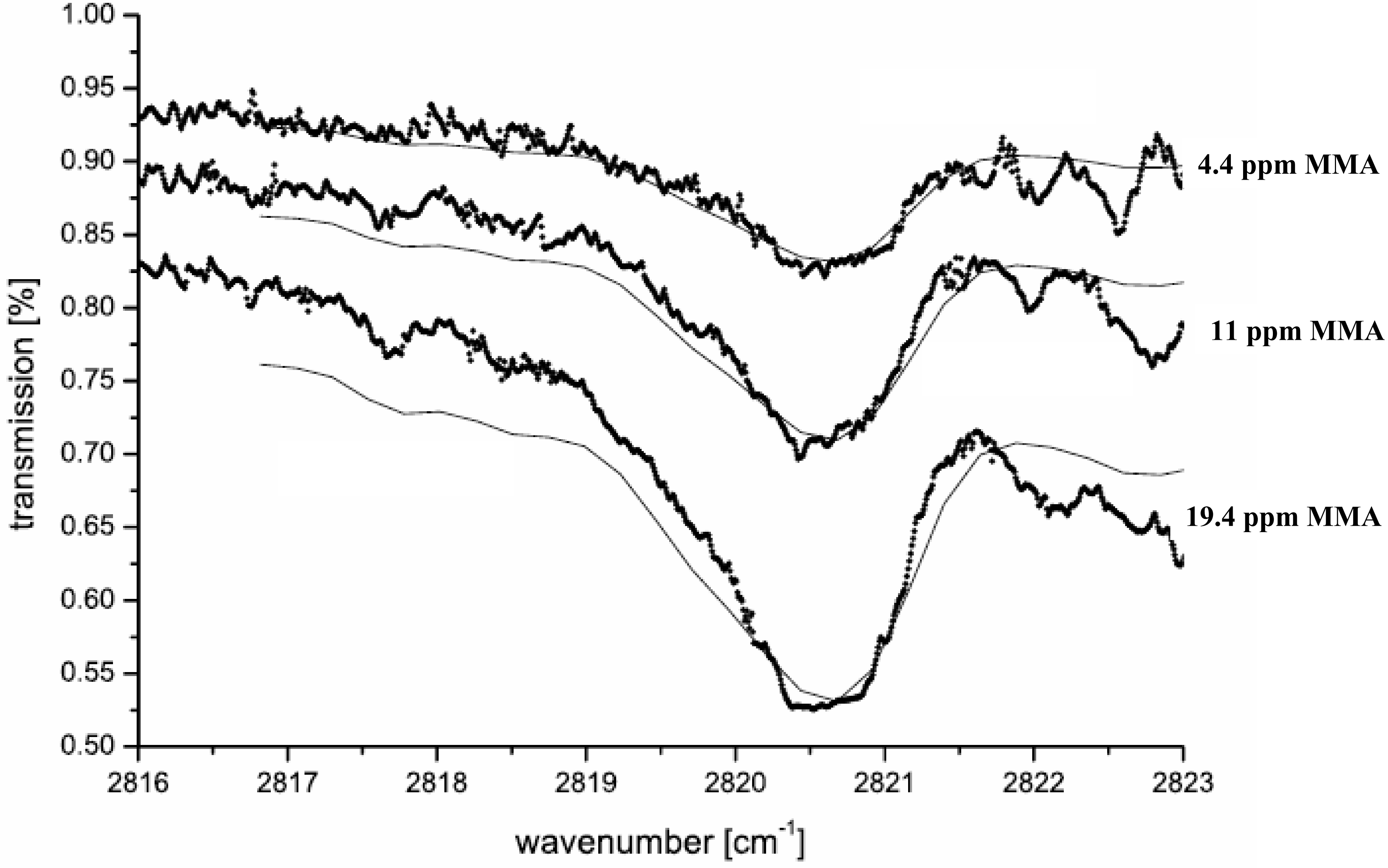
CW DFG setup for breath analysis



CW-DFG laser spectrometer for breath analysis



Monomethylamine (MMA) in ambient air recorded with CW-DFG multipass absorption spectrometer



Conclusions

- **Breath analysis**

  Goal: non-invasive medical diagnostic tool

  Methylamines

- **Experimental arrangements**

  Near-IR tunable diode laser

  Combined direct absorption / cavity ring-down

  Mid-IR DFG laser multi-pass absorption system

- **Results**

- Near-IR CRD-spectra of mono- and di-methylamines
  Detection limits:
  350 ppb for MMA, 1.6 ppm for DMA (interference-free)
  Problem: H_2O vapor interference

- Mid-IR multi-pass absorption spectra
  Detection limits (dilution in ambient air):
  550 ppb for MMA, 340 ppb for DMA, 170 ppb for TMA

Outlook

Target: Improve detection limits

- **Pre-concentration of methylamines**
- **Mid-IR CRD ?**

Use $LiNbO_3$ ridge waveguide as nonlinear medium for DFG

→ 100x higher conversion efficiency

→ **mW** power of mid-IR tunable laser radiation