

Respiratory Gas Analysis

CRFS

ANZSRS ASM, Brisbane 2010

David P. Johns PhD, CRFS, FANZSRS

Menzies Research Institute

University of Tasmania

Contents

☐ Introduction

- Barometric pressure, Partial pressure, Composition of air and alveolar gas, Effect of water vapour, Removal of water vapour and CO_2

☐ Analyser specifications

☐ Calibration and linearity

☐ Analyser response time

☐ Analysis of static gas samples

☐ Breath-by-breath gas analysis

☐ Common Gas Analysers and interfering gases

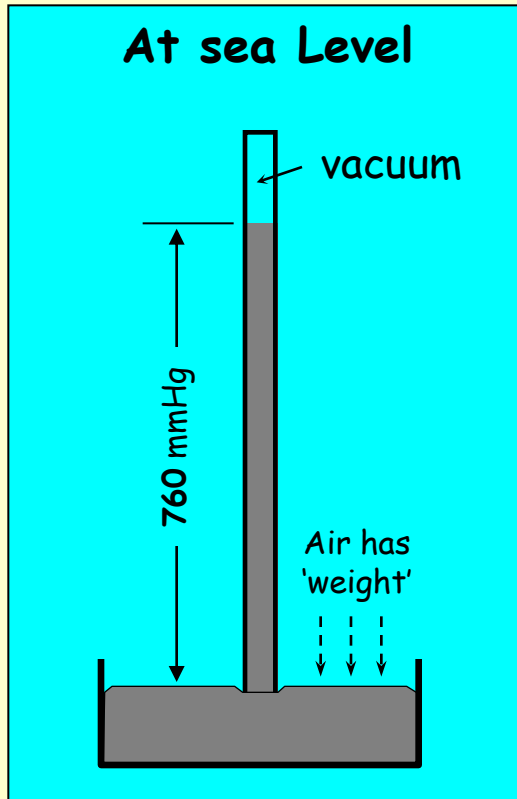
- Thermal conductivity, Gas chromatography, Paramagnetic, Infrared, Mass spectrometry

☐ Multiple choice questions

Introduction

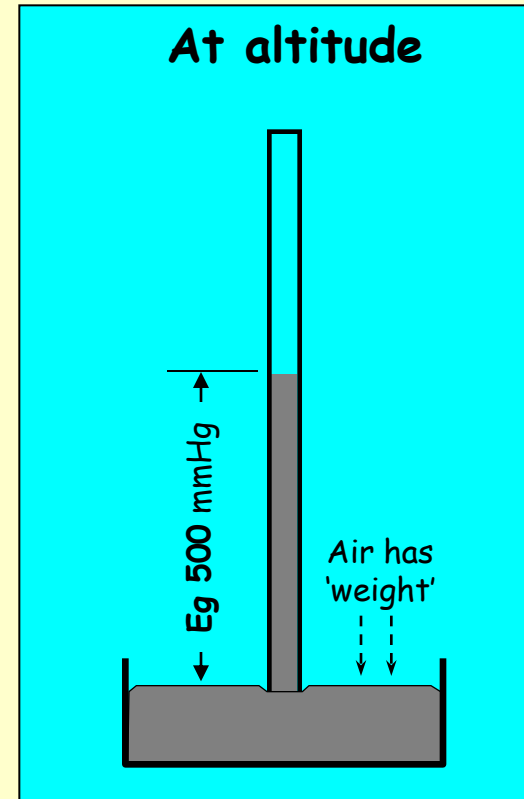
- ❑ Measurement of concentration or partial pressure of a gas based on:
 - Chemical analysis
 - Physical attributes
- ❑ Chemical Methods
 - Absorption of gas under study, especially CO_2 and O_2
 - Used up to 1970s.... now little used
 - Haldane and Lloyd-Haldane apparatus... developed initially for use in moving ships
- ❑ Physical Methods
 - Based on a physical property of the gas
 - e.g. Paramagnetism (O_2), infrared absorption (CO_2 , CO), thermal conductivity (He), mass/charge ratio (most), emission spectroscopy (N_2).....

Barometric Pressure



Overlying weight of atmosphere pushes the mercury up the tube.
Typical ambient pressure at sea level:

$$P_b = 760 \text{ mmHg}$$

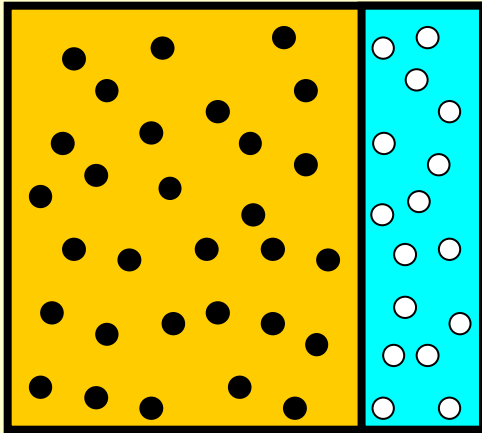


At altitude P_b falls ($< 760 \text{ mmHg}$)

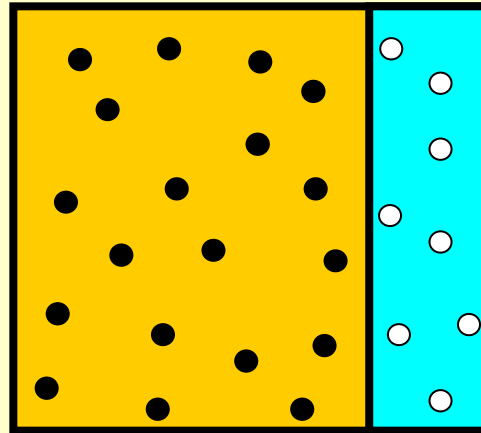
Note: Unlike other gases, the partial pressure of H_2O is not affected by gas pressure. Thus, in the lung at sea level and on Mt Everest the $P_{\text{H}_2\text{O}}$ is 47 mmHg

Partial Pressure and Concentration

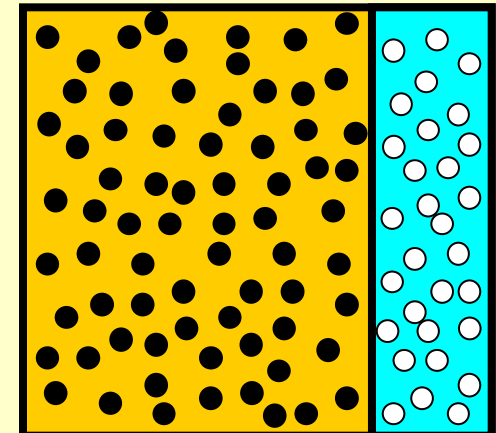
Sea level (Pb 760 mmHg)



Altitude (Pb 450 mmHg)



Depth (Pb 1500 mmHg)



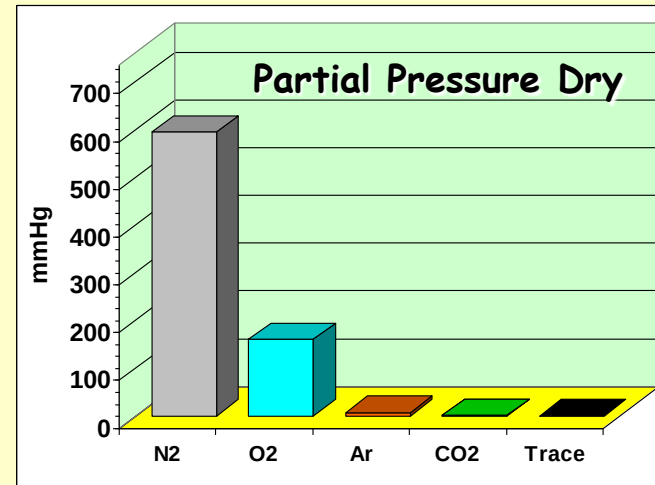
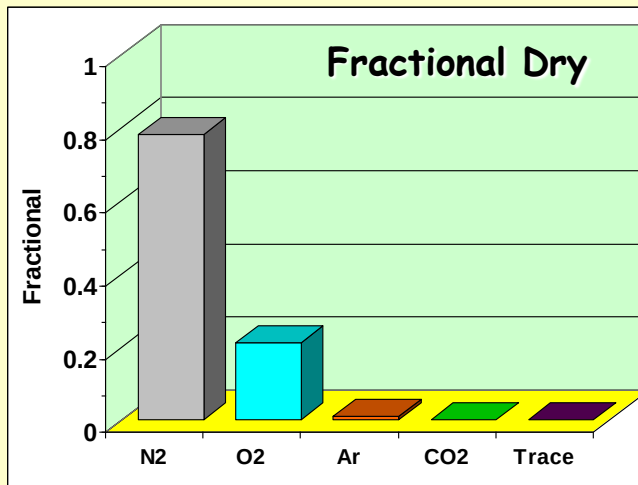
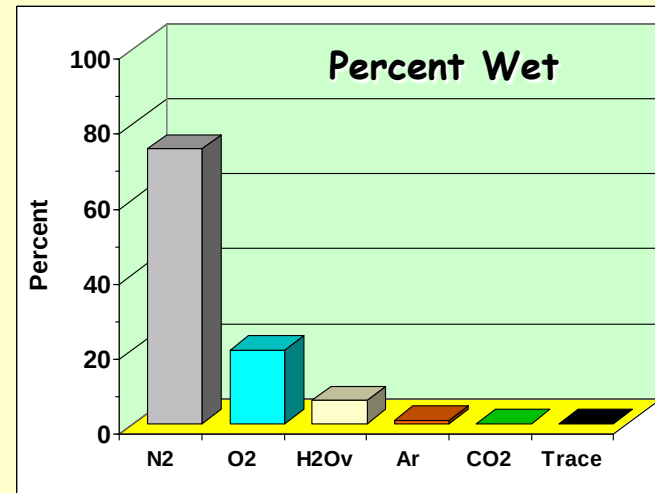
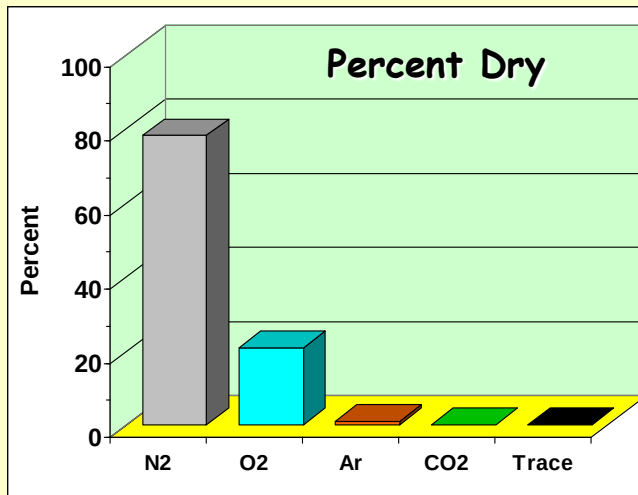
N₂ • O₂ •

		Oxygen		Nitrogen	
	Total Pb	Partial pressure	%	Partial pressure	%
Altitude	450	95	21	356	79
Sea Level	760	160	21	600	79
At Depth	1500	315	21	1185	79

Note: If H₂Ov is present then at 37°C it is always 47 mmHg i.e. occupies more of total available Pb at altitude and less at depth

Composition of Air

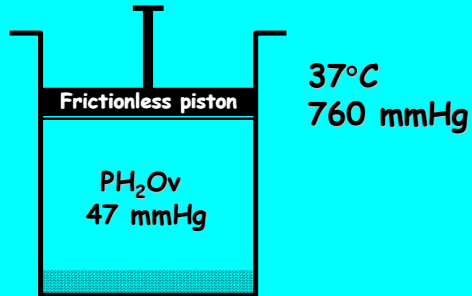
Percentage, fractional and partial pressure



Water Vapour

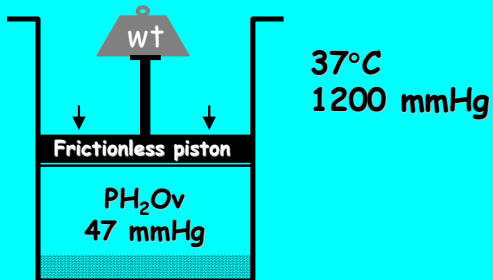
Effect of Pressure and temperature

ALVEOLAR GAS



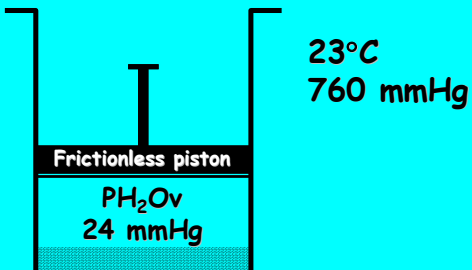
- ❑ Water vapour behaves differently from other gases because H₂O is present as gas and liquid
- ❑ The water vapour pressure of a wet gas mixture:
 - Does **NOT** vary with gas pressure
 - **Varies** with gas temperature
- ❑ At 37°C PH₂O is always 47 mmHg irrespective of barometric pressure

Effect of PRESSURE



- ❑ When the gas pressure of a mixture increases the partial pressure of each component increases proportionately... NOT SO for H₂Ov
- ❑ The increase in total gas pressure causes an increased rate of molecular collision... because they are closer together. Thus, some of the H₂Ov condenses.... until the PH₂O is restored.

Effect of TEMPERATURE



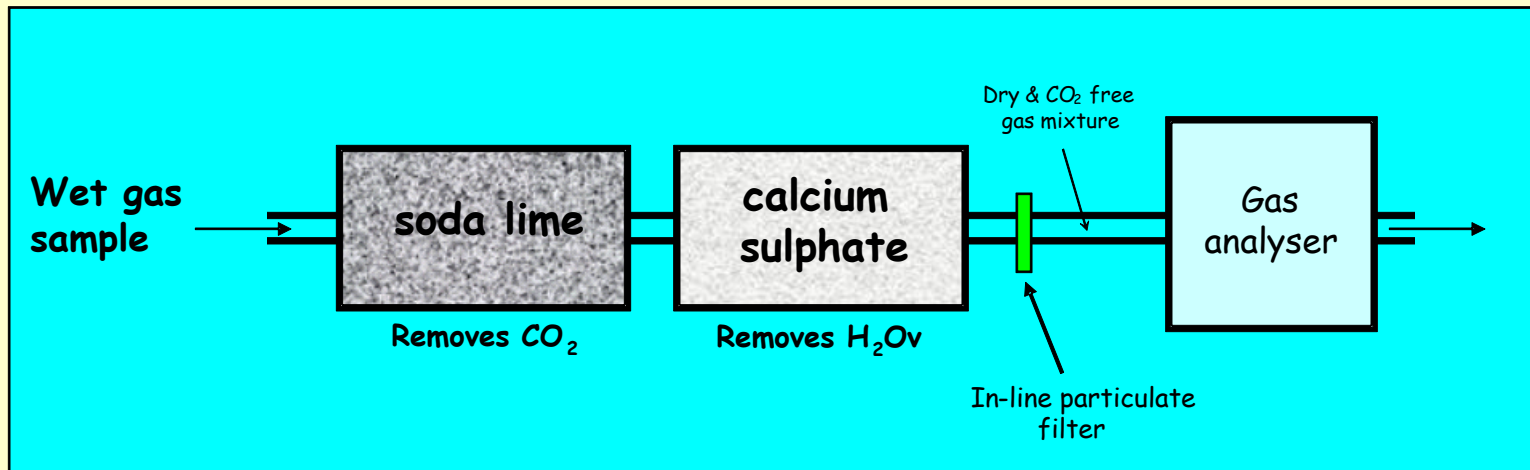
- ❑ Kinetic Energy = mass x (velocity)²
- ❑ It is the gases KE that causes molecular motion
- ❑ A decrease in gas temperature = a fall in KE
- ❑ Thus, at lower temperatures fewer H₂O molecules possess sufficient energy to remain in the gaseous state, this H₂Ov falls - Le Chatelier's Principle

Removal of Water Vapour and CO₂

- ❑ Presence of H₂Ov can interfere with analysis and will also dilute other gases
 - It can also condense within the sensor and compromise sensor function
- ❑ Therefore, need to either
 - Remove H₂Ov by passing gas through a desiccant e.g. silica gel
 - ✓ Then gas concentration/partial pressure will be for dry gas mixture
 - ✓ Need to take care to ensure even packing of desiccant and that there are no gas leaks
 - ✓ **Notes:** 1) desiccant will reduce response time of analyser and increase lag-time; 2) need to ensure dust does not reach sensor
 - Use a sampling tube which equilibrates sample PH₂Ov to ambient level (Perma Pure)
- ❑ Can correct for H₂Ov, but need to know temperature within sensor
 - Can usually assume that gas within sensor is fully saturated
 - ✓ e.g. if Pb = 760mmHg & sensor temperature is 37°C, then PH₂Ov = 47mmHg
 - ✓ Then the dry gas total pressure = 760-47 = 713 mmHg ... this pressure is the sum of the partial pressures of all gases other than water vapour present in the mixture
- ❑ The presence of CO₂ can also interfere with gas analysis (e.g. measurement of He using thermal conductivity) and is often removed using soda lime
 - **Note:** Water is produced when CO₂ is removed with soda lime
 - Therefore, a water absorber (desiccant) is usually required to remove it...

....removal of both CO_2 and water vapour

NOTE: 1st remove CO_2 then remove water vapour



Notes:

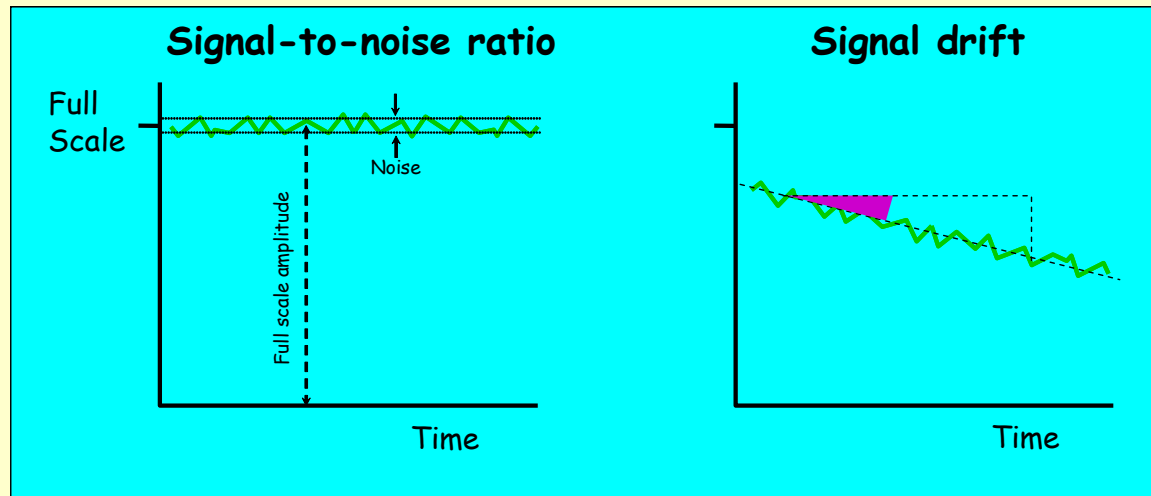
- ❑ Pack crystals evenly to prevent streaming and use filters to prevent dust from reaching the analyser - always carefully check for leaks
- ❑ H_2O is produced when CO_2 is absorbed by soda lime.... hence **MUST** put the water absorber DOWNSTREAM of the soda lime canister
- ❑ Replace crystals before they are spent

Analyser Specifications

- ❑ Measurement range
 - The measurement range must suit application
- ❑ Accuracy
 - Must be sufficiently accurate over measurement range used e.g. $\pm 0.02\%$ absolute
 - Calibration must remain stable during period of analysis
- ❑ Linearity
 - Most gas analysers have a linear response to changes in gas concentration (e.g. paramagnetic) either inherently or incorporate a linearising circuit (e.g. infrared) e.g. $\pm 1\%$ full-scale
- ❑ Specificity
 - Interference by other gases present in a mixture must be considered - remove if possible
- ❑ Response time and digital sampling rate
 - 90% rise time (defined as 0 - 90% or 5% - 95%); <200 ms for breath-by-breath
 - Digital sampling rate is an important consideration for breath-by-breath
- ❑ Sample flow
 - Most analysers incorporate a pump to draw the sample through the analysis cell

...Analyser Specifications, cont.

- ❑ Electrical output
 - Analogue, digital output or display only
- ❑ Signal drift
 - especially important when monitoring long-term
- ❑ Signal-to-noise ratio
 - e.g. <1% full-scale peak to peak
- ❑ Other features:
 - Pb compensation, materials in contact with sample, sampling tube dimensions



...Analyser Specifications, cont.

Examples

	He Analyser Thermal Conductivity	He Analyser Mass Spectrometer	CO Analyser Infrared	O ₂ Analyser Paramagnetic
Analysis Range	0 - 15%	0 - 100%	0 - 0.4%	0 - 100%
Accuracy (abs)	0.02%	1 mmHg	0.0003%	0.10%
Response time	20 sec	100 msec	120 msec	10 sec
Linearity	±1% full-scale	±0.5% full-scale	±1.5% full-scale	±2% full-scale
Sampling flow	300 ml/min	50 ml/min	80 - 200 ml/min	200 ml/min

Slow

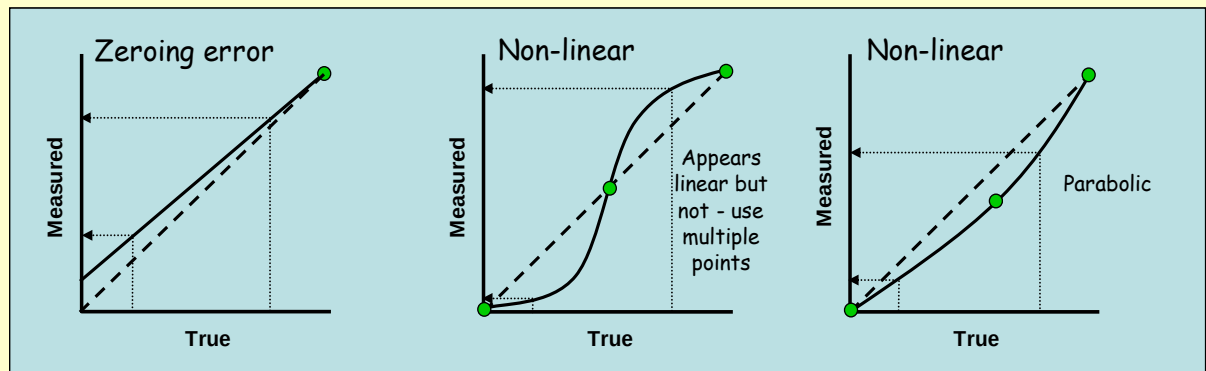
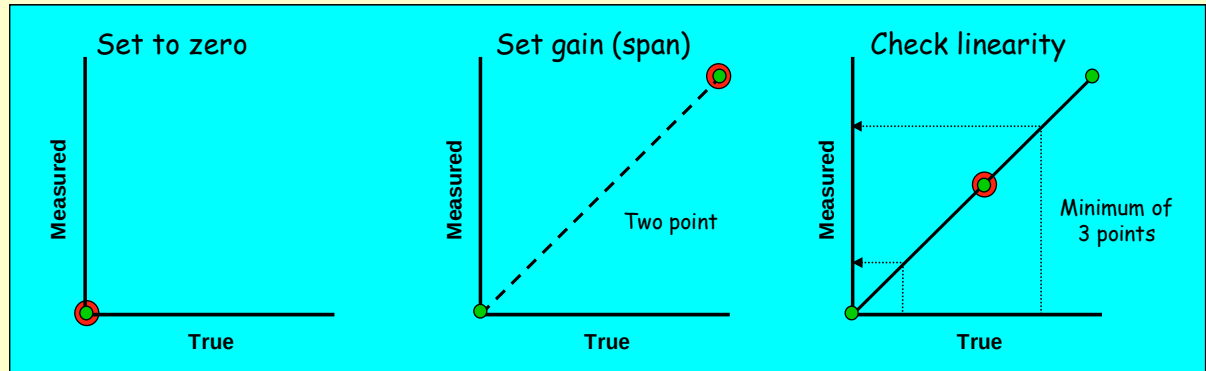
Fast

Fast

Slow

Calibration and Linearity

- ❑ Use appropriate calibration gases
 - Avoid mixtures containing interfering gases* and do not exceed measurement range
 - Calibrate over measurement range
 - Use certified mixtures (α or β stds)... or prepare your own e.g. serially dilute the span mixture
- ❑ Can use two-point calibration if analyser response is known to be linear
- ❑ Multiple points (at least 3) are required if response is non-linear
- ❑ Should re-check span and zero points after adjusting zero and gain settings

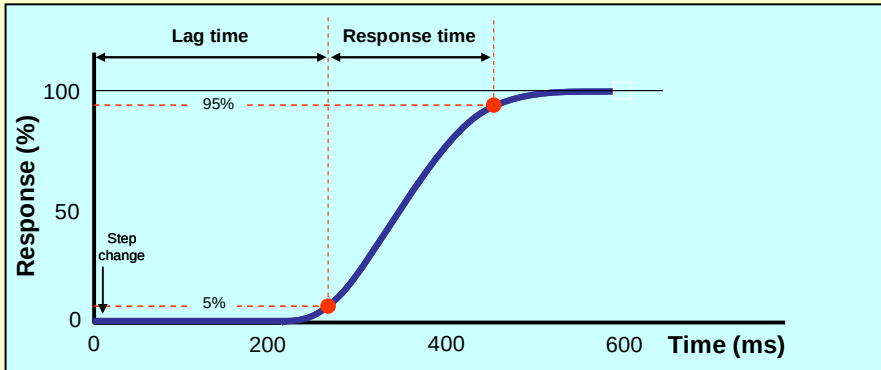


* There are exceptions... and in some instance we may deliberately use a calibration mixture containing an interfering gas if the gas is also present in the test mixture

Analyser Response Time

- ❑ How quickly an analyser responds to a sudden (step) change in gas concentration depends on:
 - Lag (or delay) time = time taken for the gas to arrive at the sensor
 - Response time = time required for sensor to measure gas signal
 - Defined as time to achieve eg 0 - 90% or 5% - 95% response
- ❑ Lag time mainly depends on:
 - Sampling flow, and
 - Diameter and length of sample tube from gas source to sensor
- ❑ Response time mainly depends on:
 - Physical properties and geometry of sensor
 - Sampling flow and sampling tube dimensions
- ❑ Response time is critical for breath-by-breath measurements
 - Usually require response time of <200 ms
 - Phase-shift relative to other signals (e.g. flow, volume) will occur unless gas measurements are temporally aligned
 - ✓ Need to correct for lag and response time

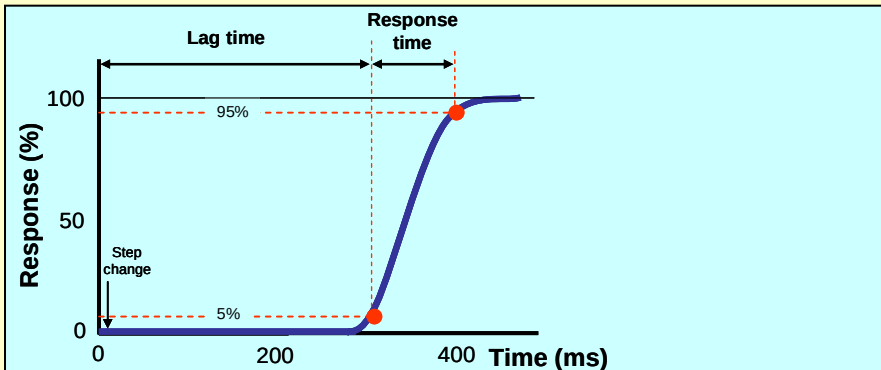
Analyser Response Time



□ Response Time = 200 ms

□ Lag Time = 280 ms

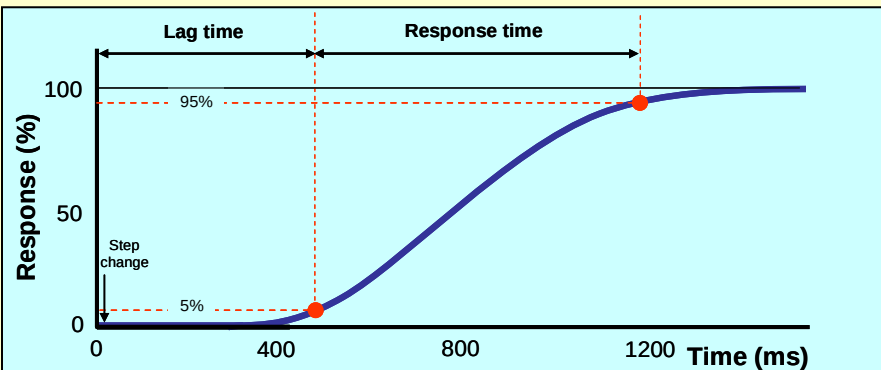
FAIRLY FAST



□ Response Time = 100 ms

□ Lag Time = 310 ms

Very FAST

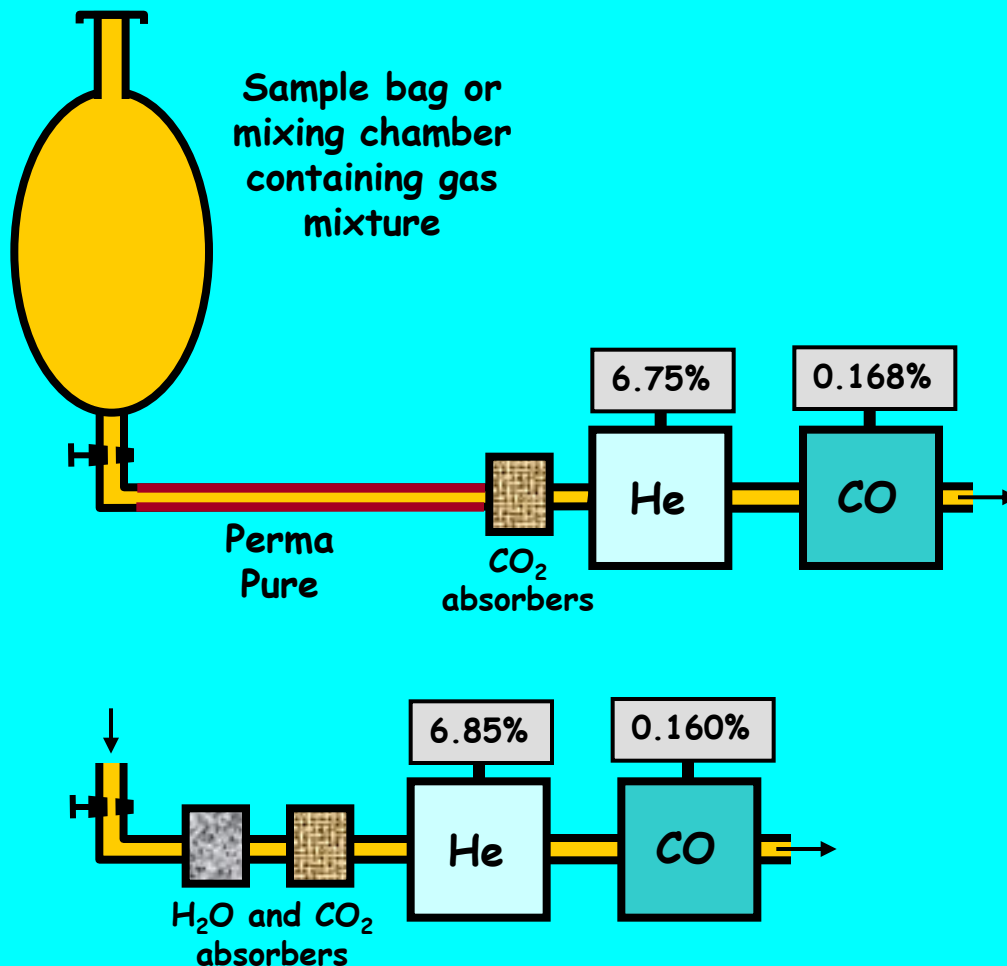


□ Response Time = 780 ms

□ Lag Time = 500 ms

SLOW

Static Gas Sample

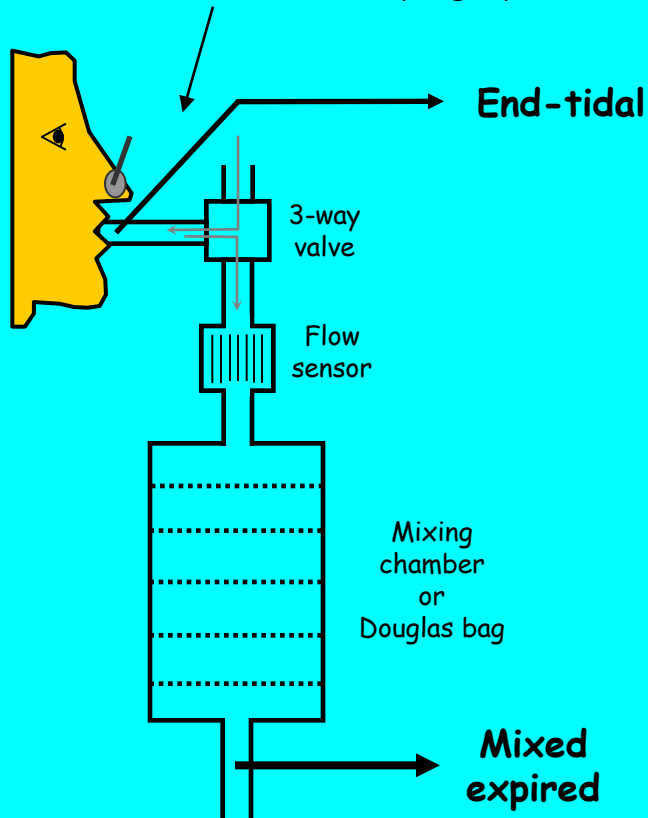


Perma Pure

- ❑ A teflon based co-polymer and therefore chemical-resistant. It has selective H₂O transport properties and dries the gas to ambient conditions without affecting other gases in the mixture
- ❑ Ionic sulphonic acid in the wall of the tube rapidly bonds with any H₂O present in the gas mixture
- ❑ H₂O molecules that are absorbed onto the surface of the tube are quickly passed on to underlying acid groups until the H₂O reaches the outside of the tube where they evaporate into the ambient air.
- ❑ This process continues until the partial pressure of H₂O within the Perma Pure tube equilibrates to ambient levels

Breath-by-Breath Analysis

If barrier filter is used then must be downstream from sampling tip



End-tidal Sampling

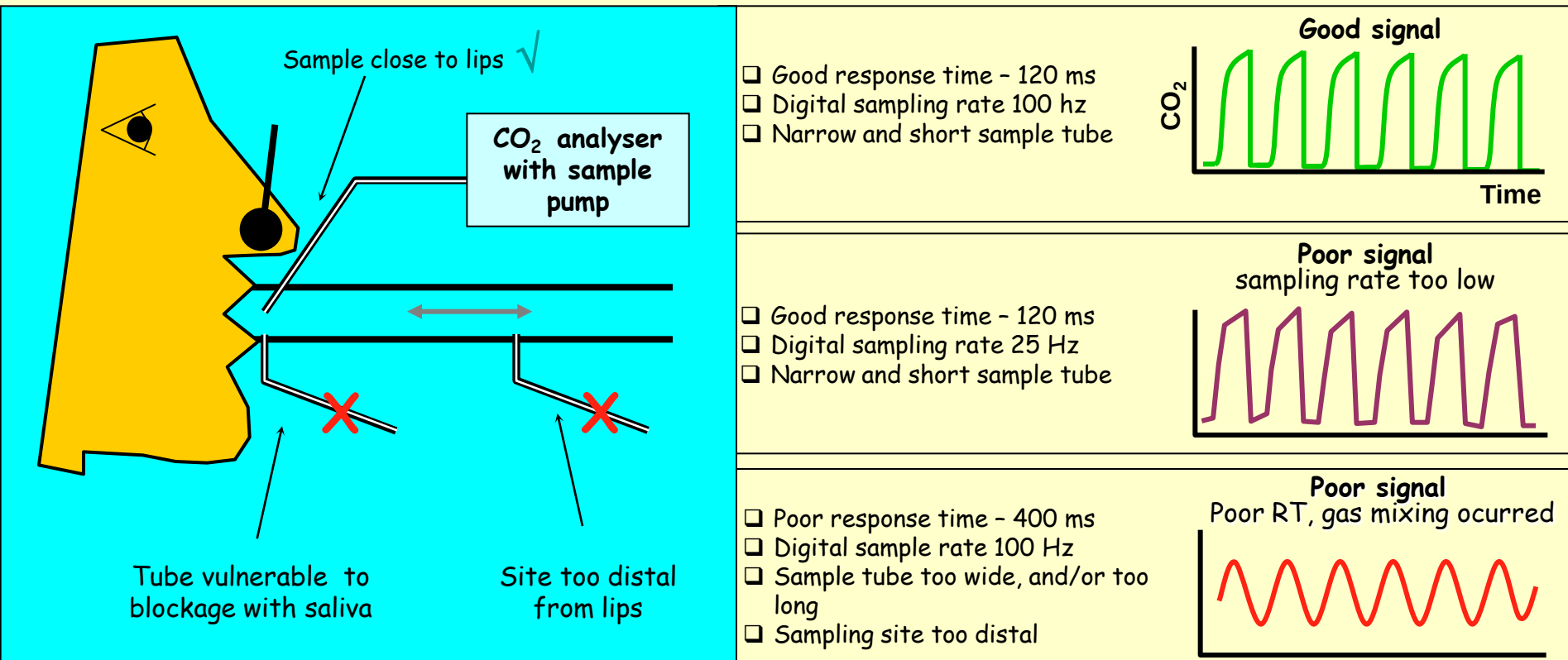
- ❑ Requires rapid response analyser(s) - <200 ms
- ❑ Position tip of sample tube centrally and close to mouth
- ❑ Consider tubing length and diameter - narrow and short are best.... BUT sampling pump has to cope with flow resistance
- ❑ Reduce H_2O_v to ambient levels using Perma Pure* - can't use desiccant as this reduces analyser response time
- ❑ Temporal alignment of each gas signal with flow signal
- ❑ Need to correct flows and volumes for sampling flow
- ❑ Sampling tubing can become very wet due to condensation

Mixed Expired

- ❑ Slow or rapid response analysers
- ❑ Tubing size and length not critical.... BUT must have sufficient sample volume for full scale response
- ❑ Provides average gas concentrations
- ❑ Gas signals should not show fluctuations
- ❑ Remove H_2O_v (use desiccant to fully dry the gas or reduce to ambient PH_2O_v using suitable length of Perma Pure)
- ❑ Less condensation in sampling tube as gas is now close to ambient temperature

Breath-by-Breath

Effect of response time and sampling rate



Sampling flow is usually constant and adjustable. Sampling flow may affect gas pressure within sensor - and hence change gas partial pressure; Note: sampling flow must be less than expired flow

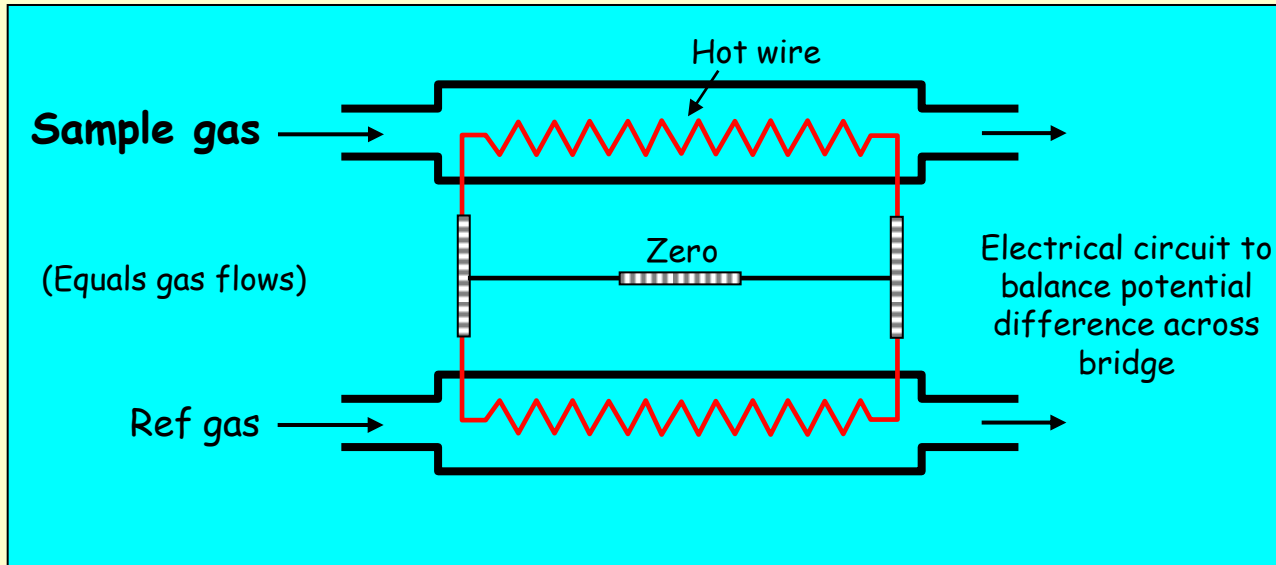
Narrow sampling tubes preserve the end-tidal waveform and can be up to 100 meter in length if diameter is 1 mm.... and also able to 'store end-tidal concentration profile for several minutes - BUT remember very narrow tubes have a high flow resistance

Common Gas Analysers

Types of Sensors & Interfering Gases

	Used to Measure	Interfering Gases
Chemiluminescence	NO	H ₂ Ov, CO ₂ , some hydrocarbons
Gas chromatography	CO, CO ₂ , Ne, CH ₄ , SF ₆ , etc	Carrier gas (e.g. He)
Infrared absorption	CO, CO ₂ , N ₂ O, CH ₄ , SF ₆	H ₂ Ov (mainly)
Mass spectrometry	Most - limited by m/e ratio	Limited by m/e ratio - cannot measure CO in presence of N ₂
Paramagnetic properties	O ₂ , NO	Fairly specific
Thermal conductivity	He, CO ₂ , N ₂ O, H ₂	O ₂ , H ₂ Ov, N ₂
Ultraviolet emission	N ₂	CO ₂ , H ₂ Ov, SF ₆

Thermal Conductivity (katharometer)



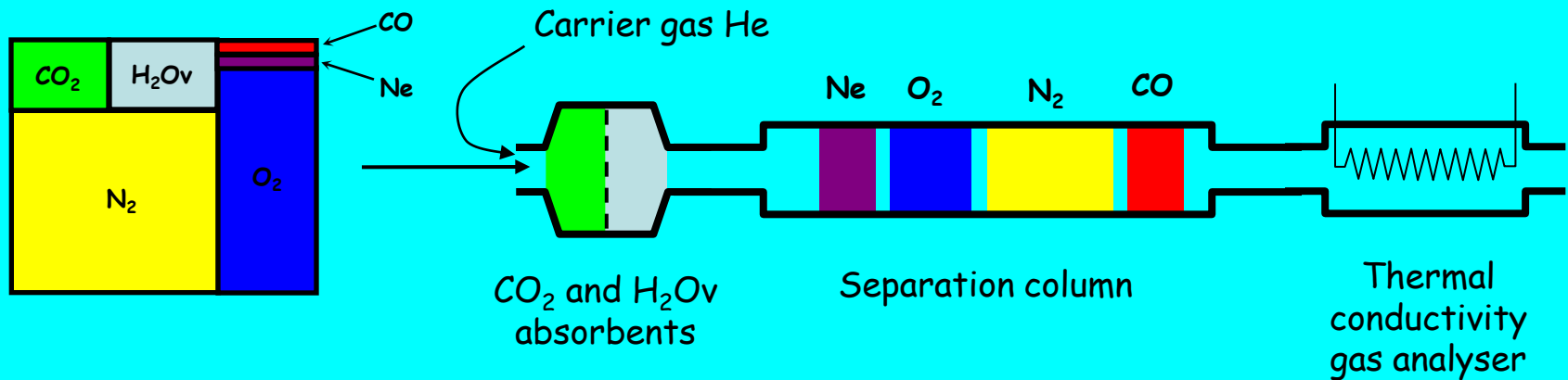
	Thermal Conductivity (air = 1.00)
H	6.90
He	5.55
N ₂	2.00
O ₂	1.01
H ₂ Ov	0.78
CO ₂	0.70
CO	0.96

Notes:

- ❑ Hot wire - electrical resistance is higher at higher temperatures
- ❑ When the gas sample flows past the hot wire its temperature falls depending on the thermal conductivity of the gas mixture
- ❑ All gases conduct heat, but especially helium and hydrogen, thus non-specific
- ❑ Thus, have to take care to account (or reduce) the effect of background gases
 - Usually remove water vapour and CO₂
 - He is then measured against background of O₂ and N₂ - ratio kept fairly constant
- ❑ These analysers are robust and have a very long life but usually slow response
- ❑ Ideal sensor to measure the concentration of individual gas components after separation by gas chromatography... i.e. no interference by other gases

Gas Chromatography

Most gases



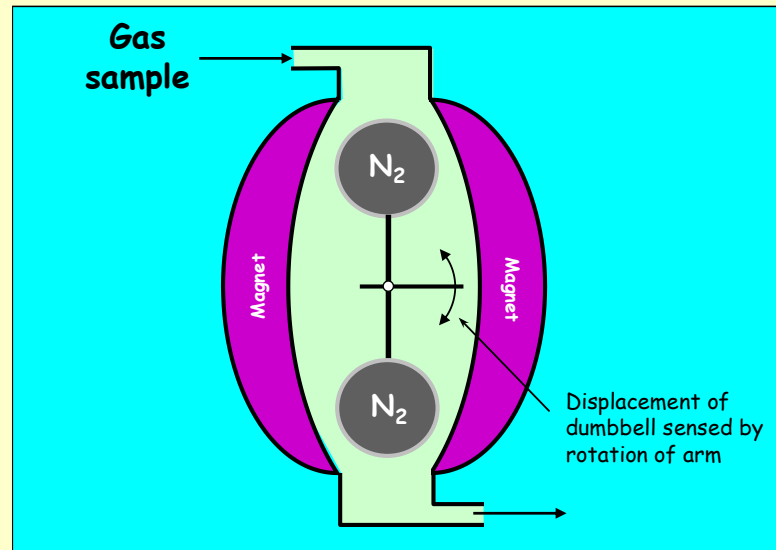
Notes:

- ☐ Column containing heat activated diatomaceous material that adsorbs gases according to their molecular size.
- ☐ Gas mixture is carried through column by a carrier gas, usually helium.
- ☐ CO_2 and H_2Ov will not elute and eventually contaminate column.

Paramagnetism

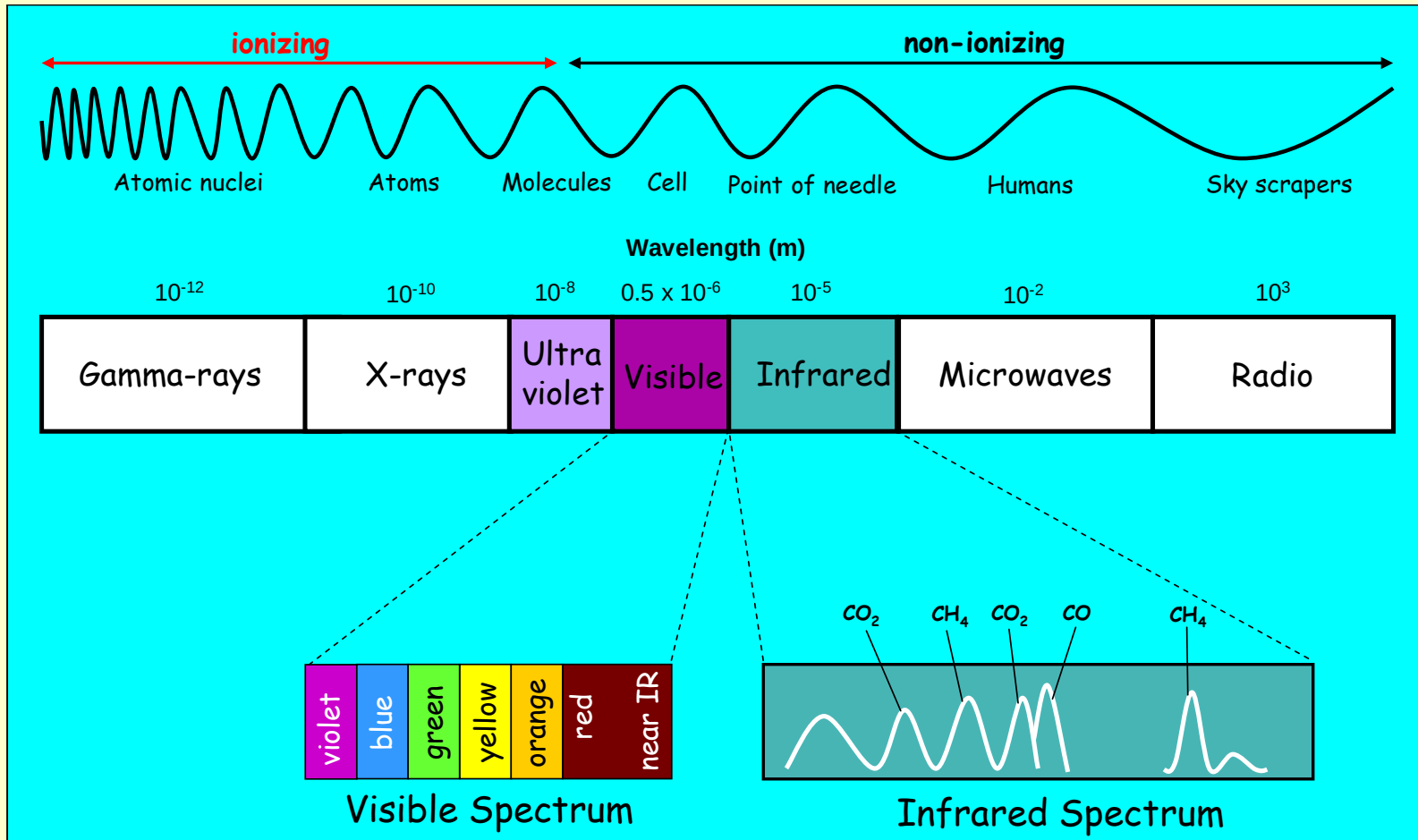
O_2

- ❑ Oxygen is only common gas which will influence an magnetic field
- ❑ It affects a magnetic field in direct proportion to its PO_2
- ❑ There is little interference by other gases
- ❑ Early paramagnetic analysers were cumbersome, delicate and slow response
- ❑ The dumbbell (or magneto-dynamic) type is the most common
- ❑ A N_2 filled dumbbell shaped glass suspended freely in the sample chamber on a quartz or platinum fiber near a permanent magnetic field
- ❑ The dumbbell is displaced in the presence of oxygen - degree of displacement proportional to PO_2 .



Electromagnetic Spectrum

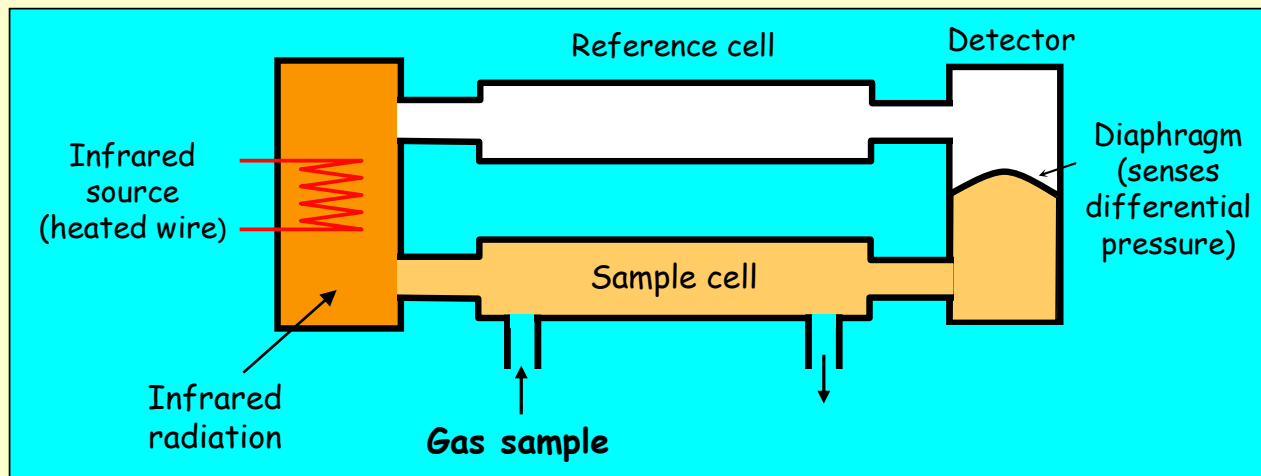
Infrared and Ultra-violet



Infrared Absorption

e.g. CO , CO_2 , CH_4

- ❑ Most hetero-atomic gases absorb infrared radiation at specific wavelengths
 - The intensity of the IR emerging from the sample cell will fall depending on the concentration of the gas in the sample cell. The intensity of emerging IR is measured and from Beer's law is related to the concentration of gas under study
 - Errors may arise due to overlap of absorption bands and collision broadening between different gases (e.g. H_2O , CO and CO_2 overlap). These are best overcome by removing unwanted gases or by using thin filters
- ❑ Widely used for breath-by-breath measurements
 - Capnography is the measurement of CO_2 in each breath (called end-tidal CO_2)
- ❑ Solid state instruments are available which are very robust, accurate and stable

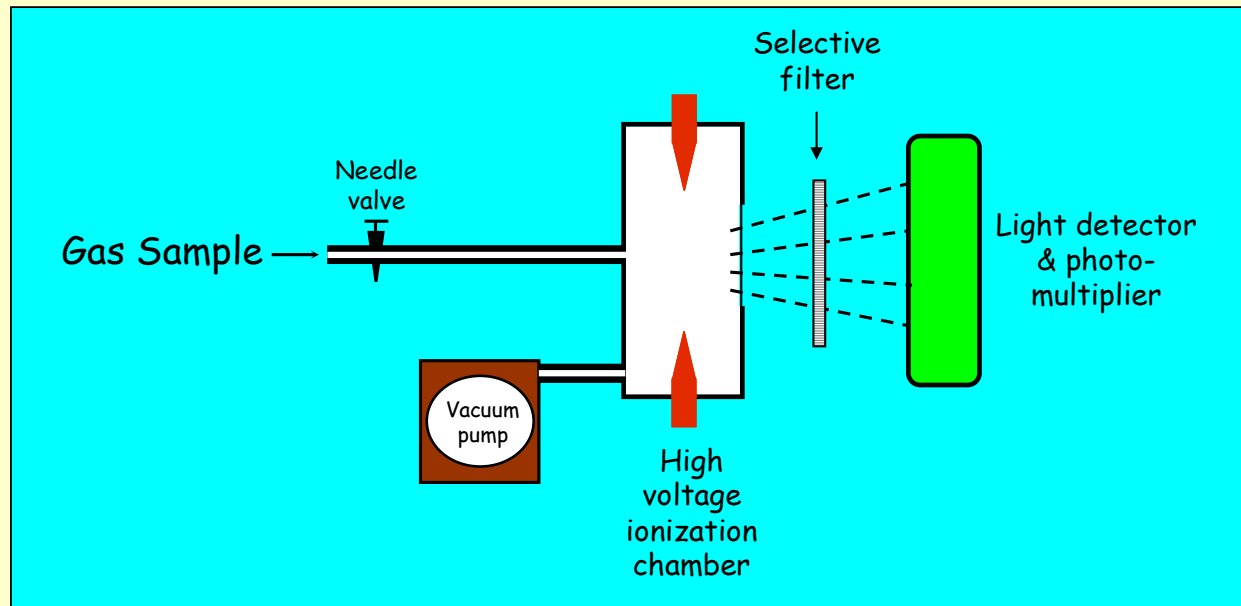


IR radiation is often delivered in pulses to reduce thermal changes

Ultraviolet Emission Spectroscopy

N_2

- ❑ Ultraviolet light is emitted (300-480nm) when N_2 (low pressure) is exposed to high voltage
- ❑ The intensity of light is related to the concentration of N_2 (non-linear) - linearising circuit used
- ❑ Unwanted emissions from other wavelengths (e.g. CO_2 and H_2O) removed by selective filters
- ❑ Rapid response time (often 50-80 ms)
- ❑ Measurement range 0 - 100% nitrogen: calibration is required
- ❑ **NB:** some systems estimate N_2 by difference (i.e. N_2 in dry gas = $P_b - P_{CO_2} - P_{O_2}$)



Mass Spectrometry

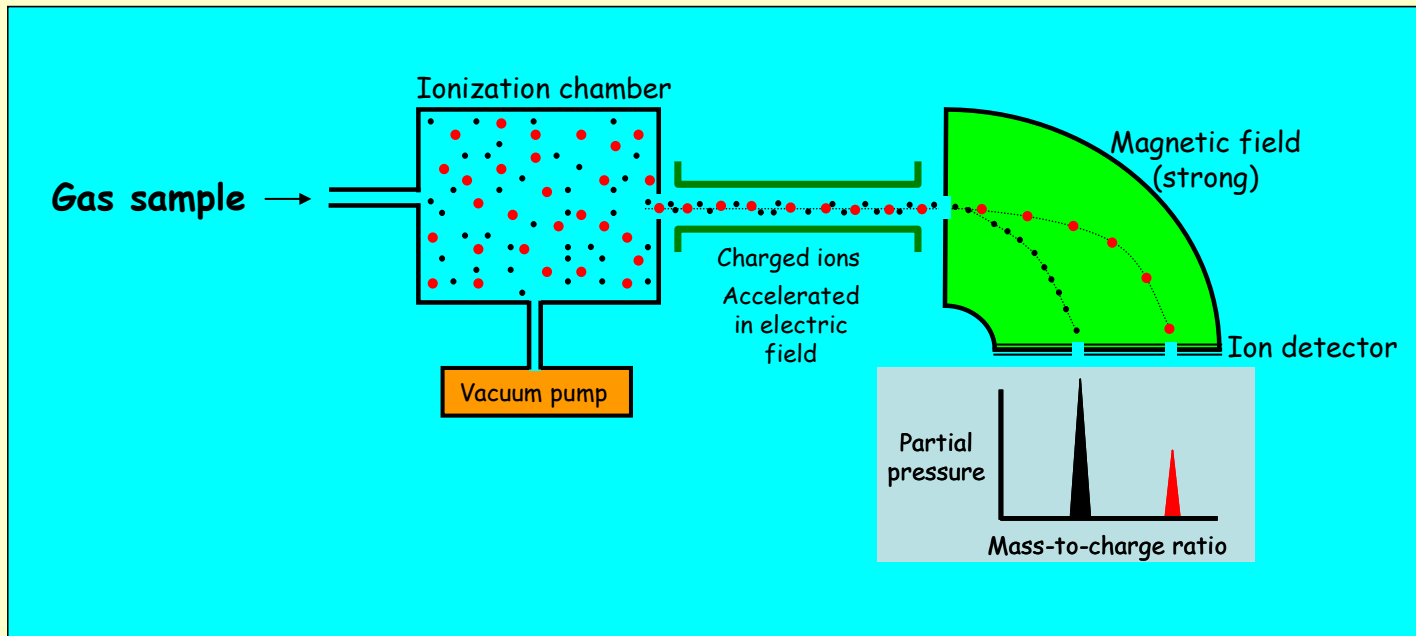
(most gases)

- ❑ **Magnetic sector** and **Quadrupole**
- ❑ Provide continuous and simultaneous measurement of more than one gas
 - Fast response, low sampling flow, linear output proportional to concentration
 - Range of gases detected limited by mass/charge ratios
- ❑ Measurement: four main stages
 - Sampling pump draws gas sample via a narrow heated tube (250 μm capillary)
 - Gas molecules are ionized by impacting them with electrons. Most gases acquire a unique mass/charge ratio (some acquire more than one charge)
 - Charged gases (ions) are separated according to their mass/charge ratio
 - Output voltage generated proportional to the concentration of each ion
- ❑ An electronic circuit corrects for presence of H_2O by ensuring that the sum of the partial pressure of dry component gases = $(P_b - P_{\text{H}_2\text{O}})$
- ❑ CO and N_2 cannot be resolved - have same mass/charge ratio of 28
- ❑ Up to 0.6% of CO_2 can be reduced to CO and can effect N_2 analysis

Mass Spectrometry, con't

Magnetic sector

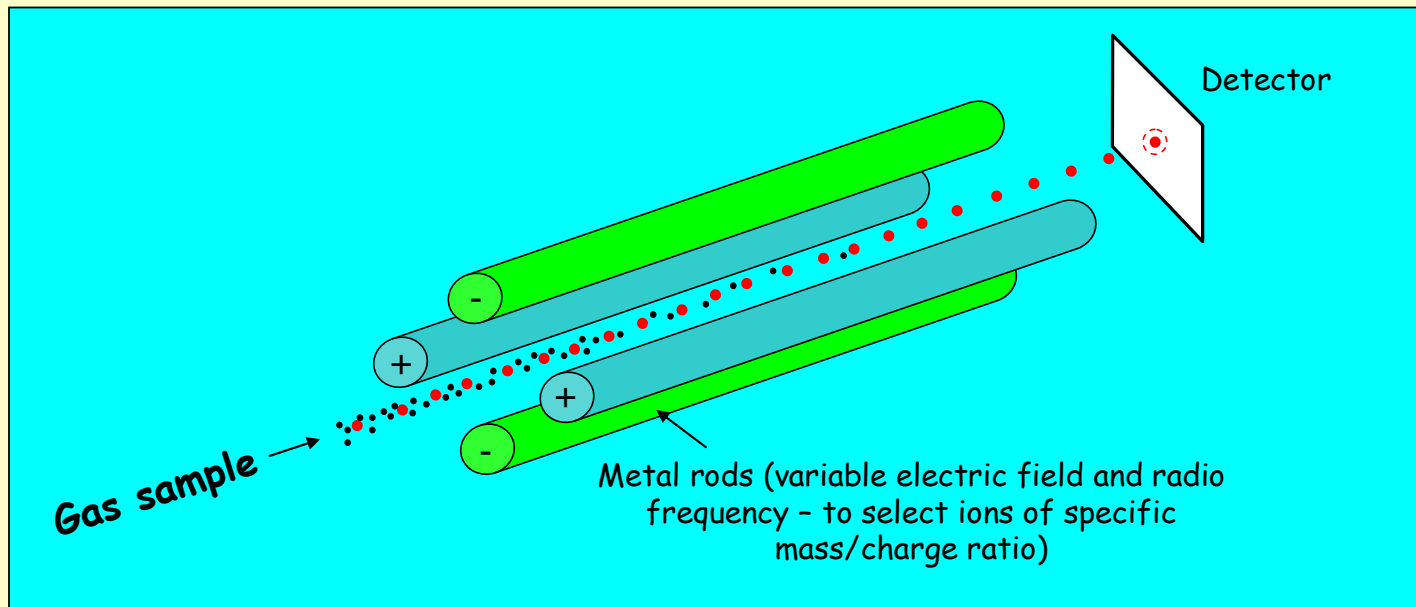
The ionized components of the gas mixture are accelerated by an electric field into a curved magnetic field where the ionized gases are separated according to their mass/charge ratio



Mass Spectrometry, con't

Quadrupole (mass filter)

- ❑ The ionized components of the gas mixture are accelerated by an electric field between four metal rods which are charged with a combined oscillating electric field and radio frequency (quadrupole field)
- ❑ The oscillating electric field and radio frequency impose forces on the ions according to their mass/charge ratio with only selected ions passing through the rods to the ion collectors
- ❑ Scanning at different frequencies allows simultaneous measurement of several gases



Multiple Choice Questions

Always read the question very carefully
Then read the question again
Eliminate incorrect answers
If in doubt read the question again
There are no trick questions

Q1

Infrared analysers used to determine CO concentrations actually measure:

- A - CO paramagnetic properties
- B - CO infrared production
- C - CO infrared absorption
- D - electrical activity of the CO molecules

Answer = C

Hetero-atomic molecules such as CO acquire energy by absorbing infrared radiation of a specific wavelength

Q2

The data on the right were obtained when serial dilutions of 9.55% He are analysed for quality assurance of a He analyser:

Based on these data the respiratory scientist should conclude which of the following?

A - the data are acceptable with no further testing needed

B - the He analyser is linear at all points

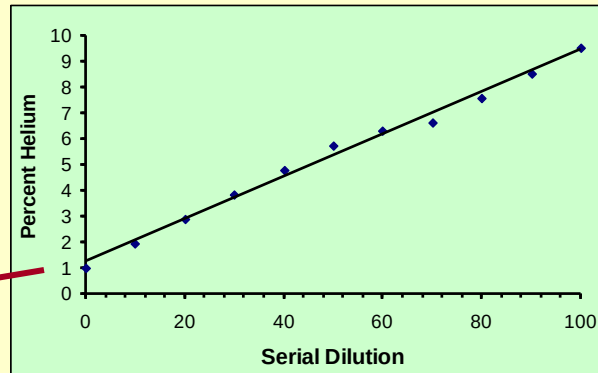
C - the zero of the analyser is offset

D - the span should be reduced and testing repeated

% Test Gas	% He Reading
100	9.55
90	8.55
80	7.60
70	6.65
60	6.30
50	5.75
40	4.80
30	3.85
20	2.91
10	1.95
0	1.00

Answer = C

*Calibration line
does not pass
through zero*

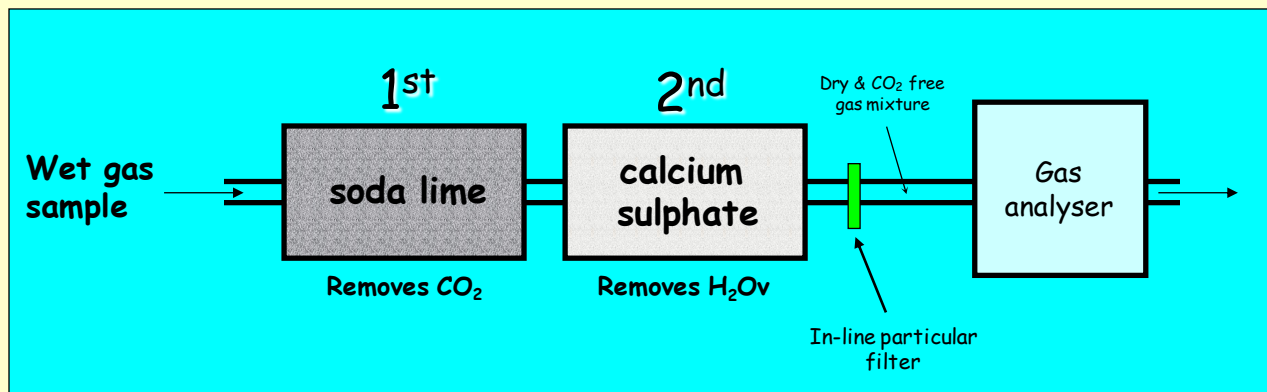


Q3

When setting up gas and water absorbers for a single breath TLCO using infrared CO and thermal conductivity He analysers, which of the following is the correct order of the absorbers?

- A - Order not important
- B - Soda lime first, then CaSO_4 (Drierite)
- C - CaSO_4 (Drierite) first, then soda lime
- D - Silica gel first, then CaSO_4 (Drierite)

Answer = B



Q4

A CO_2 analyser, to be used for expired breath analysis, is calibrated using a 5.00% CO_2 mixture with a water vapour absorber in the sample line. If the barometric pressure is 747 mm Hg and the analyser is set to read partial pressure, the analyser should be adjusted to read which of the following?

- A - 40 mmHg
- B - 37 mmHg
- C - 35 mmHg
- D - 31 mmHg

Answer = C

$$\text{Partial pressure of 5\% CO}_2 = (747 - 47) \times 5/100 = 35 \text{ mmHg}$$

$\nearrow$
 P_b

$\nearrow$
 $P_{\text{H}_2\text{O}}$

$\nearrow$
5% CO_2
as fraction

Q5

With respect to saturated water vapour pressure which of the following statements is incorrect?

- A - the partial pressure of water vapour varies with temperature
- B - at 37 °C, saturated water vapour pressure is always 47 mmHg
- C - the partial pressure of water vapour varies with pressure
- D - at altitude the partial pressure of water vapour in the lung is 47 mmHg

Answer = C

Water vapour pressure is independent of gas pressure because at ambient conditions water exists as both a liquid and gas and an equilibrium exists between these two states that is dependent on Kinetic Energy which is only temperature dependent. An increase in gas pressure causes a proportional increase in the partial pressure of all gases except H₂O because the increase in pressure causes water to condense to an extent that returns the vapour pressure back to its original pressure (Le Chatelier's Principle)

Summary

- ❑ Chemical methods of gas analysis are rarely used today
- ❑ Gas concentrations are now measured based on their physical properties and by removing or correcting for interfering gases
- ❑ Gas analysers need to be calibrated using mixtures of known composition - at least 3 points to check linearity
- ❑ Slow responding instruments are only suitable for analysis of discrete or static gas samples
- ❑ Rapidly-responding analysers are suitable for breath-by-breath analysis but signals may need to be temporally aligned
- ❑ Always consider circuit design, including site of sampling, sampling flow, instrument measurement range, etc.
- ❑ Knowledge of the influence of interfering gases likely to be present in the mixture is important - remove if possible
- ❑ CO_2 and H_2O are often removed prior to analysis and the effect of removing them may need to be taken into account - remember correct order of absorbers

BEST WISHES FOR SUCCESS IN THE
CRFS EXAMINATION

NEVER GIVE UP

READ WIDELY AND ASK LOTS OF
QUESTIONS

Learn the basic principles... they are the key