Theory of Headspace Sampling
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1 Basics

The Lonestar is a gas phase analyzer. It can be used to analyze liquid and solid substances by headspace sampling, as described here. The At-Line Sampling Module for the Lonestar is designed to make headspace sampling simple and reproducible. Figure 1 shows a cutaway diagram of the sample holder of the At-Line Sampling Module.

![Figure 1: Parameters of the At-Line Sampling Module that affect mass transfer into the headspace](image)

A glass bottle containing the sample is placed in the At-Line Sampling Module and held at a constant temperature. Chemicals from the sample evaporate and move into the headspace of the bottle. A constant flow of clean, dry air is passed through the headspace and then into the Lonestar, sweeping the analytes into the detector. As can readily be seen, only analytes that move from the sample into the headspace will enter the Lonestar and be detected. This means that the most important work in method development for Lonestar applications focuses on controlling the mass transfer of analytes into the headspace.

There are two types of headspace sampling: static and dynamic. These are described below.

2 Static headspace sampling

In static headspace sampling, the sample is left in a closed container until the headspace of the vessel is saturated with analyte vapour. The headspace is then swept into the Lonestar with a purge flow to be analysed.

Figure 2 shows a schematic of static headspace preconcentration, with the factors that influence the final headspace concentration. These are discussed more fully below.
2.1 Preconcentration time and volume
The build-up of vapour concentration in the headspace is a time-dependent process and also dependent on analytes vapour pressure and sample concentration and sample temperature. While it is still increasing, the volume of the headspace will be relevant. Once the headspace is saturated, however, the concentration will be the same for any volume.

2.2 Sample temperature
The At-Line Sampling Module can heat the sample bottle to a temperature of up to 60 °C, with a tolerance of ± 1 °C. Raising or lowering the sample temperature will increase/decrease the vapour pressure of all analytes leading to increasing /decreasing evaporation rates, and the time it takes to reach saturation, and more importantly it will increase/decrease the saturated concentration. Therefore changing the temperature is a direct way to affect sensitivity of the method and preconcentration timing. It will likely also affect analyte solubility (positively or negatively) and will increase /decrease humidity if the sample is a water solution.

2.3 Analyte vapor pressure
More volatile chemicals will evaporate more readily. Volatility of analytes can be compared by checking their vapor pressure: the pressure at which the gas phase of the analyte is in equilibrium with the liquid phase. A higher vapor pressure means higher volatility. The boiling point of a liquid is the temperature at which its vapour pressure is the same as the environmental pressure. If an analyte with low volatility is not being detected, increasing the sample temperature may help to increase the rate of evaporation.

2.4 Calculating the saturated headspace concentration
To calculate the saturated headspace concentration of an analyte, use the following equation:
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\[
\frac{V_p}{P} \times 10^6 = C
\]  

(1)

Where

- \( V_p \) is the vapour pressure of the analyte in mmHg at the sample temperature
- \( P \) is the pressure of the container (760 mmHg if at standard atmospheric pressure)
- \( C \) is the concentration of the analyte in the headspace, in ppm.

3 Dynamic headspace sampling

In dynamic headspace sampling, the headspace of the vessel is continuously swept into the Lonestar by a clean purge flow for analysis. Figure 3 shows a schematic of dynamic headspace sampling in the At-Line Sampling Module. The factors mentioned are discussed in more detail below.

![Figure 3: Dynamic headspace sampling](image)

3.1 Surface area

As all evaporation occurs at the surface of the sample, the surface area is a major factor in determining the mass transfer rate into the headspace. Using a wider sample bottle, which produces a larger surface area, may increase the amount of analyte moving into the detector and thus produce larger analyte peaks in the Lonestar DF matrices.

Keeping the surface area constant between samples is very important in ensuring consistent results. For this reason, solid samples should be melted or dissolved before sampling where possible. Alternatively, solids may be introduced in powder form. Sample volumes should be accurately measured and samples should always completely cover the bottom of the sample bottle.
3.2 Analyte surface concentration

Mass transfer into the headspace is a function of:

- the difference in concentration of the analyte between the liquid and headspace, at the surface of the liquid
- the concentration gradient between the surface of the liquid and the bulk of the liquid

Transport of analyte molecules from the bulk of the liquid to the surface layer is a diffusion-limited process and can be slow. This can in turn slow down the mass transfer from the surface into the headspace. Magnetic stirrers can be used to homogenize the sample during analysis, which will reduce this problem.

3.3 Purge flow rate

The purge flow sweeps analyte vapour from the sample headspace towards the Lonestar analyser. This reduces the concentration of the analyte in the headspace, increasing the rate of analyte mass transfer into the headspace. Thus the flow rate has a significant effect on the mass transfer rate.

A related factor is the distance between the purge flow inlet and the surface of the sample. This is illustrated in Figure 4. When a dip tube is used to reduce the inlet-surface distance, the flow travels through the entire depth of the headspace (A). Without a dip tube, the flow will take the shortest path to the outlet of the sample vessel (B). Analyte vapour from higher up in the headspace is taken to the Lonestar, while vapour from closer to the surface remains in the vessel. This causes the development of a boundary layer of higher-concentration air above the surface of the sample.

Figure 4: (A) Schematic of sample holder with dip tube in place. (B) Schematic of sample holder without dip tube, showing increased boundary layer

To limit the formation of a boundary layer, either a dip tube or a higher purge flow rate is necessary.
Increasing the purge flow rate will increase its penetration into the sample vessel and increase
the rate of headspace replacement for the system.

This value can be calculated as shown:

\[ N = \frac{f}{b - s} \]  

where:

- \( N \) is number of headspace replacements per minute
- \( f \) is the sample flow rate, in ml/min
- \( b \) is the bottle volume (120 ml for the standard bottles supplied by Owlstone)
- \( s \) is the sample volume in ml

### 3.4 Calculating the headspace concentration in dynamic sampling

The concentration of the analyte in the headspace may be calculated using the following equa-
tion:

\[ \frac{MT}{F_{\text{purge}}} = C \]

where:

- \( MT \) is the mass transfer rate in ng / min
- \( F_{\text{purge}} \) is the purge flow rate in ml / min
- \( C \) is the concentration of the sample flow into the Lonestar, in ng / ml

### 4 Other factors influencing mass transfer into the headspace

The solubility of a chemical measures its propensity to form a homogeneous solution in a solvent
by mixing at a molecular level. An analyte will have a different solubility in each solvent.

When analysing solutions with the Lonestar, the solubility of an analyte in the matrix plays a
key role in determining its mass transfer into the headspace. The greater the solubility, the less
likely the analyte is to leave the sample solution. Some factors affecting solubility are described
below.

#### 4.1 Polar vs. nonpolar solvent and solution

In general, polar molecules will have greater solubility in polar solvents (e.g. water, ethanol)
than in nonpolar ones (e.g. hexane) and vice versa. In polar solutions, ionic compounds will
dissolve by dissociating into positive and negative ions. The positive ions are attracted to the
negative charge on the polar solvent molecules and the negative ions are attracted to the positive
charge. Ionic compounds will have very low solubility in nonpolar solvents.
4.2 Temperature
The solubility of analytes may increase or decrease with temperature. Solubility profiles for many compounds in water are useful and publicly available.

4.3 pH
The pH of the solvent can affect the solubility of an analyte that reversibly dissociates in solution, losing a proton, as shown here:

$$M \leftrightarrow M^- + H^+$$

In this case, making the solution more acidic (adding more protons, decreasing the pH) will shift the equilibrium of this process away from the dissociation. More of the analyte will be in the M form and less in the M- form. Only the analyte molecule, M, will evaporate out of the solution, not the ion M-, so this will increase mass transfer into the headspace.

In the case of an analyte molecule that tends to pick up a proton and become positively charged, the reverse will apply.

$$M + H^+ \leftrightarrow M^+ \quad (4)$$

Making the solution more alkaline (adding more OH- ions, increasing the pH) will help here. The extra OH- ions will form H$_2$O molecules with H$^+$ ions, decreasing the amount that are available to form the M$^+$ ion. There will be more of the molecular form of the analyte, M, to evaporate and the mass transfer rate will increase. In the case of amphoteric analytes, which can show either acidic or alkaline behaviour, careful adjustment of the pH level is required to maximise the mass transfer rate into the headspace.

The pKa value of a chemical is $-\log_{10}(K_a)$, where $K_a$ is the acid dissociation constant of the chemical. This is a reflection of the degree to which the chemical dissociates when in solution. If the pH of the sample solution is equal to the pKa of the analyte of interest, 50% of the analyte molecules will be dissociated ($M^- + H^+$) and 50% will be in the molecular form ($M$). Adjusting the pH of the solution to 2 greater or less than the pKa of the analyte will be enough to shift towards 100% dissociated or molecular form. Whether the pH should be greater or less than the analyte pKa depends on the acidity of the analyte, but it is only necessary to examine the pH range pKa(analyte) $\pm$ 2.

4.4 Salting
An analyte may be salted out of a solution - that is, made less soluble by adding salt to the solution.

If the solute molecules are nonpolar and have not dissociated, the main forces holding them into the solution are the intermolecular forces between solute molecules and polar water molecules (e.g. hydrogen bonds). The salt dissociates into ions on dissolving. These ions are more attractive to the polar H$_2$O molecules than the nonpolar solute molecules, which reduces the intermolecular forces holding them into the solution. The solubility of the analyte, and any other organic/nonpolar molecules, is reduced. Adding salt to a sample solution can also have the beneficial result of reducing humidity. As above, the extra ions from the salt attract the water molecules in the solution, making them less likely to evaporate out into the headspace.
If the Lonestar’s sensitivity to an analyte is reduced with higher humidity, adding salt can be very useful. There are tables available online comparing humidity at various temperatures for saturated solutions of various salts.