# 1. Introduction

The aims of this lab are:

- Understand the physiological background of ventilation distribution of the lungs.
- Have an insight of how to measure the degree of inhomogeneous ventilation.
- Study parameters that characterize the ventilation distribution of the lung.

You will start the lab by implementing a model that can be used to study lung ventilation (Exercise 1). Then, you will measure the volume of trapped gas on an example of a real measurement (Exercise 2 and 3). As last task, you will analyse the graphs and values obtained from a ventilation assessment of one subject (Exercise 4). The exercises are done in pairs. After each exercise you are required to make a thorough presentation of your results. This discussion is the examination, and it will be extensive. To pass you need to be thoroughly prepared.

In the following sections you will find the preparatory questions you will have to submit beforehand, additional theoretical background information and the instruction on how to get ready to run the lab.

## 1.1 Preparatory questions

Read the information in the section "*Determination of volume of trapped gas*". In that paragraph a method to examine the degree of inhomogeneous ventilation is described. Study also the enclosed data printout (**Appendix 2**) from such an examination. You need to understand how to calculate the relevant parameters in Exercise 3.

<u>Answer the questions and submit them in Lisam not later than **four working days** before your lab session.</u>

1- The measurement system used in Exercise 2 is a pneumotachograph. Describe the working principle of the pneumotachograph and how to compute the volume from the flow measurement. What are some of the precautions that need to be made to obtain an accurate measurement from such device?
2- Bronchial obstruction can be caused, for example, by asthma. Give another example of pulmonary disease that causes bronchial obstruction and how this disease affects the gas flow into the lungs.
3- Focus on Eq. (1) and (2). Describe these two equations with your own words.
4- In Exercise 1 the lungs are modelled as two balloons which volumes receive pure $O_2$ at each inspiration. In this model was omitted the influence of the volume of the common airways. Try to describe how the inclusion of the common airways volume will influence the model (focus of what happens to the oxygen concentration in the two lungs).

## 1.2 Determination of trapped gas

To understand this session, you might need to check the notes from the lectures on washout volume, especially the part on *nitrogen washout volume*. Chapter 4 in Blom (refer to the course literature in lisam: *FlowSensors_Blom_Monitoring_of_respiration_and_circulation.pdf*) and the lecture notes give a good description of this lab.

During normal respiration the inhaled air (tidal volume) is mixed with the already present air in the lungs. Certain lung diseases, such as asthma, cause bronchial obstruction which result in certain parts of the lungs being less ventilated than others due to increased resistance in the air flow. Therefore, the efficiency of the lungs decreases. If the obstruction is extensive some parts of the lung may be cut off entirely and not participate in the gas exchange during normal respiration at all. The combined volume of these parts is called the lungs volume of trapped gas (VTG). In the ideal case the VTG is small, but it is not zero, not even for healthy subjects.

An inhomogeneous ventilation in the lung means that it takes longer time to reach the nitrogen washout volume. The degree of inhomogeneity can be used as a diagnostic tool by measuring the necessary time to reduce the $N_2$-level of the lungs, usually from 80% to 2%, a dilution of 40:1.

However, the necessary time will be dependent on the breathing rate. A better tool to measure inhomogeneous ventilation is to measure the total volume of exhaled gas during the washout phase (WoV= washout volume). The disadvantage of this method is that the result of a given volume of breath is dependent on the size of the lungs. One way of creating a normative standard is to divide WoV with the functional residual capacity (FRC). We then get the so-called lung clearance index (LCI=WoV/FRC)

To establish VTG one can complement the nitrogen washout with a period of respiration at inspiratory vital capacity (VC). Only the ventilated volume of the lungs has been cleared from $N_2$ during the wash-out, while the trapped parts have its original gas left. When breathing with deep breaths the lungs are dilated thoroughly, the trapped parts are opened, and the trapped gas released. If you measure the amount of $N_2$ in the exhalation air and assume balance of mass, you can calculate VTG (see equations below). This method has been developed by the Departments of Paediatrics and Clinical Physiology, Faculty of Health Sciences; University Hospital in Linköping by Gustafsson, Johansson et al. (1994). A more detailed description of the procedure follows below.

### 1.2.1 Measurement equipment

The patient breaths into a mouthpiece of an instrument consisting of a flow meter (pneumotachograph) and a $N_2$- analyser (Fig. 1). The flow meter is built on the principle of measuring the decrease in air pressure over a flow resistor while the $N_2$- analyser is based on emission spectrophotometry ($N_2$-gas is ionized, and then emits light of a specific wavelength which intensity is recorded). Both signals are sampled and registered on a computer. The instrument also contains channels and regulators for distribution of inhalator gas (air from the room or pure $O_2$) and for release of exhalatory gas.

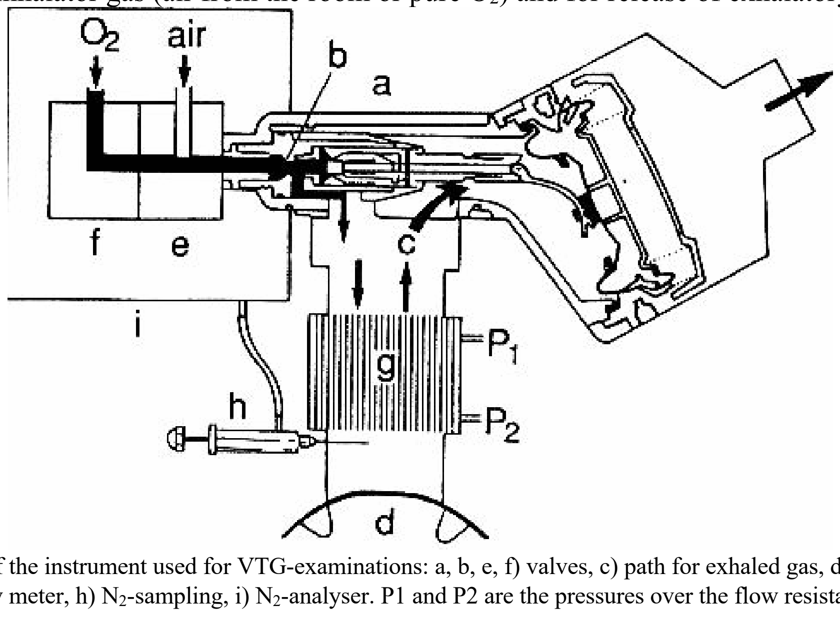


Fig. 1. Sketch of the instrument used for VTG-examinations: a, b, e, f) valves, c) path for exhaled gas, d) mouthpiece, g) flow meter, h) $N_2$-sampling, i) $N_2$-analyser. P1 and P2 are the pressures over the flow resistance.

### 1.2.2 Method of measurement

The subject breaths regularly through a mouthpiece wearing a nose clip to make sure that all inspiratory gas passes the instrument. When the patient is breathing regularly the inspiratory inlet is switched to pure $O_2$. This marks the start of the so called $N_2$ washout phase (*wo* in Fig. 2). The subject continues with tidal volume breathing until the instrument readings has reached a nitrogen gas fraction ($FN_2$) of 0.02 (2%). Here the maximum ventilation phase starts (*mv*) and the patient is instructed to take five slow maximum inspirations of $O_2$ and to exhale slowly. The four first breaths end at the residual volume, and the fifth at normal resting expiration level, *i.e.* at functional residual capacity (FRC).

### 1.2.3 Calculations

The calculation of VTG is based on mass balance regarding the $N_2$ volume. The volume of $N_2$ in the lungs after the wo-phase is the same as the exhaled volume during the mv-phase plus the residue in the lungs after the mv-phase:

$$FRC \cdot F_{N_2\,ewo} + VTG \cdot F_{N_2\,air} = V_{N_2\,mv} + (FRC + VTG) \cdot F_{N_2\,emw} \tag{1}$$

On the left-hand side, the $N_2$ volume in the lungs after the washout phase is presented. The first term is the $N_2$-volume in the open part of the lungs (FRC), where the $N_2$-fraction is measured at the end of the washout phase (*ewo* = end washout phase). The other term is $N_2$ in the VTG where the air remains. On the right-hand side we have the volume of $N_2$ that has disappeared (been exhaled through the instrument) during the mv-phase and what is left in the lungs after the mv-phase (*emv*=end maximum ventilation phase). The open and trapped parts of the lungs can be added in the last term, since one can assume that VTG is fully opened.

To be able to solve VTG from equation (1) it is necessary to know the FRC. This can be determined from the wo-phase:

$$FRC \cdot F_{N_2 air} = V_{N_2 wo} + FRC \cdot F_{N_2 ewo} \tag{2}$$

In the same manner we have on the left-hand side the $N_2$ volume in the lungs at the start of the washout phase. The right side is the $N_2$ volume that has disappeared during the wo-phase and what is left in the lungs after the wo-phase. A correction of Eq. $FRC \cdot F_{N_2 air} = V_{N_2 wo} + FRC \cdot F_{N_2 ewo}$
(2) is necessary to get the correct FRC. Since the duration of the washout phase is several minutes, one cannot assume a complete balance of mass. $N_2$ is added from the body (mainly from the blood) to the expired gas during the measurement. How to solve this is part of an exercise described below. In Eq. $FRC \cdot F_{N_2\,ewo} + VTG \cdot F_{N_2\,air} = V_{N_2\,mv} + (FRC + VTG) \cdot F_{N_2\,emw}$
(1) the added $N_2$ is negligible since the mv-phase is comparatively short.

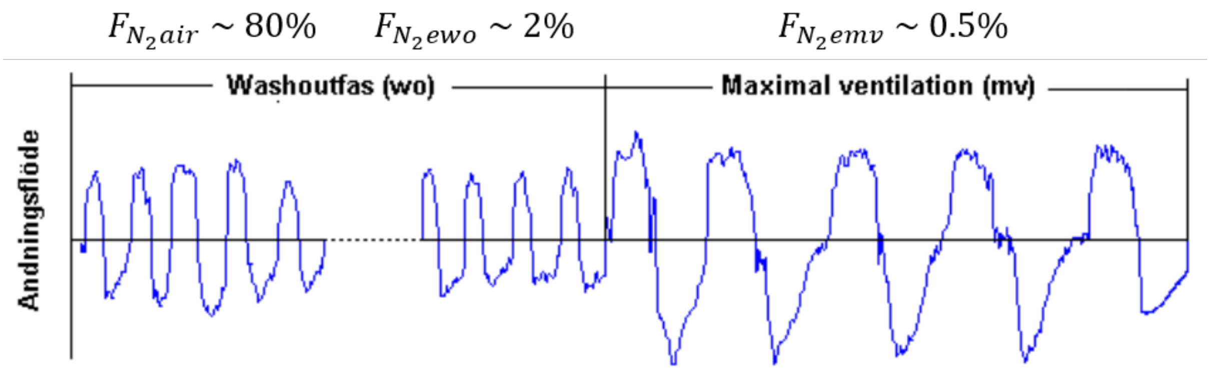


Fig. 2. The phase during a VTG-determination and typical values of the nitrogen gas fraction.

## 1.3 Set up

Wherever you are using your own computer or you are connected remotely, download the zip file available in the Lisam course page (Course documents > LaboratoryExercises > RespirationLab > RespirationLab.zip). This contains the following:

| *File* | *Description* |
|---|---|
| *Exercise_1_N2WO.m* | MATLAB script used in Exercise 1&5 |
| *Exercise_2_calc_V.m* | MATLAB script used in Exercise 2a |
| *Exercise_2_calc_VN2.m* | MATLAB script used in Exercise 2b |
| *Exercise_2_flow.txt* | Registrations used in Exercise 2b |
| *Exercise_2_FN2.txt* | Registrations used in Exercise 2b |
| *Exercise_2_pneum_flow.txt* | Registrations for Exercise 2a |
| *Exercise_3_measurement.xls* | Clinical registrations used in Exercise 3 |

# Exercise 1

As described in the theory section above, it takes longer to ventilate the nitrogen in the lungs if they are inhomogeneously ventilated. To start with, we will demonstrate this by a simulation. The program models the lungs as two balloons with volumes V1 and V2 with initially 80% $N_2$. We want to study the situation when these two balloons are inhomogeneously ventilated. During the ongoing nitrogen washout each inhalation is divided in the volumes DV1 and DV2 of pure oxygen to each balloon, and the concentration of nitrogen in each balloon is diluted.

Let $C_1(j)$ and $C_2(j)$ be the $N_2$-concentration in balloon 1 and 2, respectively, during exhalation number $j$. After each respiration the $N_2$ volumes are $V_1 \cdot C_1(j)$ and $V_2 \cdot C_2(j)$ in respective balloon. After the next respiration the volumes of the lungs are $V_1 + DV_1$ and $V_2 + DV_2$.

The gas has after mixing (assumed to be instantaneous) the $N_2$-concentration $C_1(j+1)$ and $C_2(j+1)$, which are calculated through mass balance according to the volume of nitrogen:

$$V_1 \cdot C_1(j) = (V_1 + DV_1) \cdot C_1(j+1)$$
$$V_2 \cdot C_2(j) = (V_2 + DV_2) \cdot C_2(j+1)$$

Insert the correct expression for $C_1$, $C_2$ and $C_{et}$ in the Matlab code. $C_{et}$ (et = end tidal) is the $N_2$-concentration in the expired air which is a weighted mean of the $N_2$-concentration of each balloon. Calculate how many respirations are necessary for the $N_2$-concentration of the expired gas to decrease from 80% to 2%. Each balloon has a volume of 2 liters and each respiration is 0.5 liters. The air is distributed in the balloons as follows:

a) (0.2, 0.3)     b) (0.1, 0.4)     c) (0.05, 0.45)

If you have made the correct calculations, you will see that the number of respirations, and thereby the washout time, is higher when the lungs are inhomogeneously ventilated. As described in the theory, the washout time is presented as either WoV or LCI in a clinical investigation.

# Exercise 2

It is often desirable to estimate the volume of trapped gas in the lungs (VTG). To do this, the nitrogen washout measurement is supplemented with a period of respiration at vital capacity. During the whole session continuous signals are recorded to measure the total gas flow and the N2-level in it. These signals are then used to establish the expired volume of nitrogen in each phase. How to use this information to establish VTG is described in the theory part.

a) Time to recreate the calculation of total gas volume made during a VTG-investigation. The same kind of pneumotachograph used in a VTG-examination is described in the video available in the course Microsoft Stream group (*Flowmeter_description_TBMT09.mp4)*. Data from a couple of breaths at tidal volume and at vital capacity were recorded and the available in the *Exercise_2_pneum_flow.txt* file.
b) Start from the MATLAB script *Exercise_2_calc_V.m* and add the code to calculate TV and VC. In this exercise you only have to identify one respiration cycle in the graph for each calculation. The signal is sampled with 100 Hz.
c) Since Eq. $FRC \cdot F_{N_2\,ewo} + VTG \cdot F_{N_2\,air} = V_{N_2\,mv} + (FRC + VTG) \cdot F_{N_2\,emw}$ (1) and $FRC \cdot F_{N_2air} = V_{N_2wo} + FRC \cdot F_{N_2ewo}$ (2) are based on nitrogen gas volume and not total gas volume you need to establish the volume of the nitrogen gas exhaled during the wo-phase and mv-phase. The equipment available does not contain a nitrogen gas analyser so you have to derived it from the provided recorded signals. Run the MATLAB script *calc_VN2.m* and you will find examples on a complete VTG-examination plotted with signals both from a pneumotachograph and a nitrogen gas analyser. Complete the code with the calculation of the nitrogen gas volume exhaled during the wo-phase and mv-phases respectively and plot the nitrogen gas flow. The signals are sampled at 100 Hz. You do not need to calculate VTG and FRC in this exercise.

# Exercise 3

Now when you have understood how a VRG-examination is performed and how the volumes of gas are calculated from the recorded signals, it is time to establish these values for a real patient. In *Exercise_3_measurement.xls* you find the results from a complete VTG-examination (patient: 820700-0000). Read the whole instruction and then perform the following calculations in the Excel file:

### Comment to data printouts

| *Parameter* | *Description* |
|---|---|
| BreathNr | Respiration number |
| Vexhair | Measured total gas volume in exhalation |
| VexhN2 | Measured volume $N_2$ in the exhalation |
| FN2 | The end expiration fraction of $N_2$ in each exhalation |
| Time | Time of measurement |

In the FCR calculation it is necessary to compensate for the nitrogen added by the body. Use Table 1 below. Moreover, in the LCI calculation it is necessary to compensate for the dead space of the instrument, that is, the volume in the mouthpiece outside the mouth cavity that is re-inhaled at the start of the washout, *i.e.* the first inhalation of pure $O_2$. Approximately 200 ml air is present in the inhalator part of the equipment. In the following respirations pure $O_2$ will be present, and the dead space will be much smaller for the rest of the inhalations (60 ml). If the washout lasts for N respirations, the volume $0.2 + 0.060 \cdot (N - 1)$ l should be withdrawn.

Table 1: Volume $N_2$ from the body that is added to the exhalation as a function of the washout time (Gustafsson, Johansson et al. 1994)

| **Washout time [min]** | **Volume $N_2$ [ml]** | **Washout time [min]** | **Volume $N_2$ [ml]** | **Washout time [min]** | **Volume $N_2$ [ml]** |
|---|---|---|---|---|---|
| 1 | 50 | 6 | 180 | 11 | 280 |
| 1.5 | 70 | 6.5 | 190 | 11.5 | 290 |
| 2 | 90 | 7 | 200 | 12 | 300 |
| 2.5 | 110 | 7.5 | 220 | 12.5 | 310 |
| 3 | 120 | 8 | 220 | 13 | 320 |
| 3.5 | 130 | 8.5 | 230 | 13.5 | 320 |
| 4 | 150 | 9 | 240 | 14 | 340 |
| 4.5 | 160 | 9.5 | 250 | 14.5 | 350 |
| 5 | 170 | 10 | 260 | 15 | 360 |
| 5.5 | 175 | 10.5 | 270 | | |

If your calculations are correct, you should obtain the following values:

| *Parameter* | *Expected value* |
|---|---|
| FRC (corrected for the nitrogen added from the body) | 4513.24 ml |
| VTG | 136.57 ml |
| VTG/VC | 1.94 % |
| WoV | 44484.42 ml |
| LCI (corrected fo the dead space of the instrument) | 9.07 |

# Exercise 4

To establish whether the patient has a pathological condition or not, it is necessary to have normal values to compare with. The normal values for the parameters we have studied here have been established statistically through measurements on healthy and pathologic individuals. The limit for LCI is approximately 9 and for VTG/VC approximately 2.4% (Gustafsson, Johansson et al. 1994). The result from two VTG examinations of an asthmatic is found in **Appendix 2**. One is a basal measurement and the other is performed after a light asthma attack had been provoked. Motivate which is which based on the normal values.

# Exercise 5

**Do this exercise only if you have time left.** In Exercise 1 you developed a model which shows that it takes longer to ventilate the lungs if they are inhomogeneously ventilated. In the model you made the assumption that each inhalation consisted of pure oxygen ($O_2$). This is only true if the volumes of common airways are zero. A more realistic model includes the dead space ($V_{daw}$= airway dead space, see Fig. 3). Complete the program you wrote and take $V_{daw}$ into consideration and repeat the calculations in Exercise 1 for:

a) $V_{daw}$ = 0.1 liters

b) $V_{daw}$ = 0.2 liters

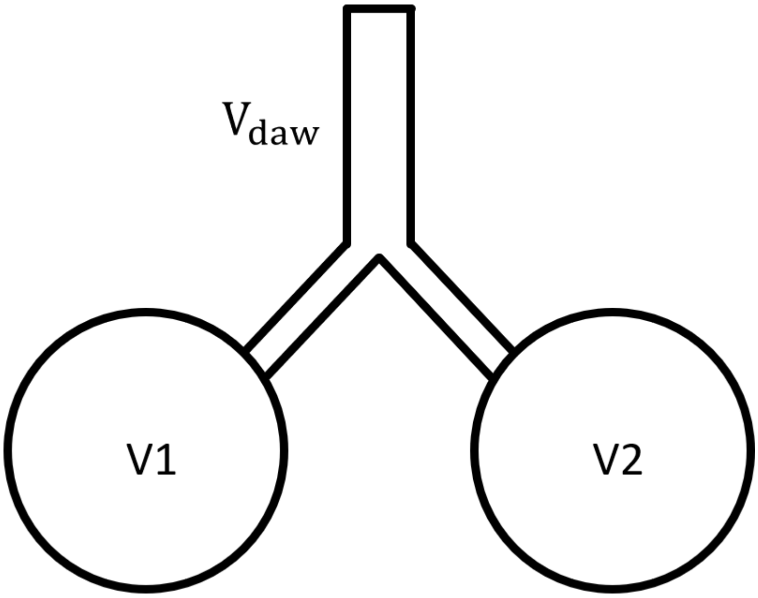


Fig. 3. Lung model for Exercise 1 and 5

# References

[1] Gustafsson, P. M., et al. (1994). "Pneumotachographic nitrogen washout method for measurement of the volume of trapped gas in the lungs." **17**(4): 258-268.

# Appendix 1

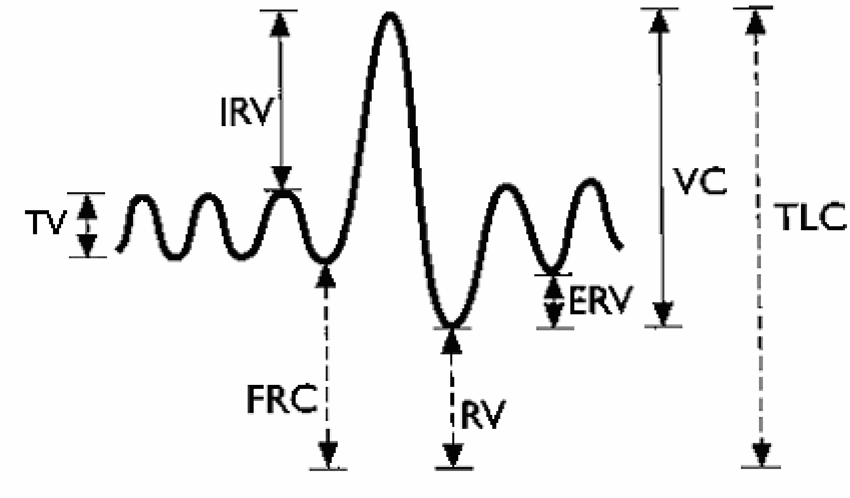


Fig. 4. Lung volumes at inhalation and exhalation

| | | |
|---|---|---|
| **VC** | *Vital capacity* | The volume of gas that can be expelled from the lungs from a position of full inspiration. |
| **FRC** | *Functional residual capacity* | The volume of air remaining in the lungs at the end of a normal, quiet expiration. |
| **ERV** | *Expiratory reserve volume* | The maximal volume of air, usually about 1000 millilitres, that can be expelled from the lungs after normal expiration |
| **RV** | *Residual volume* | The volume of air remaining in the lungs at the end of a maximal expiration |
| **VT** | *Tidal volume* | The volume of air inspired or expired during each normal, quiet respiratory cycle |
| **IRV** | *Inspiratory reserve volume* | The extra volume of air that can be inspired with maximal effort after reaching the end of a normal, quiet inspiration. |
| **TLC** | *Total lung capacity* | The volume of air contained in the lungs at the end of a maximal inspiration |

Normal gas distribution

| | **Atmosphere** | **Alveola** |
|---|---|---|
| **$N_2$** | 78% | 75% |
| **$O_2$** | 21% | 14% |
| **$CO_2$** | 0.04% | 5% |
| **$H_2O$** | 0.5% | 6% |

## ***Appendix 2 –VTG-examination (patient 990928-0000)***