Available online at www.sciencedirect.com

ScienceDirect

IFAC PapersOnLine 51-6 (2018) 42–47

Comparison of Mathematical and Controlled Mechanical Lung Simulation in Active Breathing and Ventilated State

Paštěka Richard [*,**] **Mathias Forjan** [*,***]
Andreas Drauschke [*]

[*] *University of Applied Sciences Technikum Wien, Department of Biomedical, health & Sports Engineering, Vienna, Austria (e-mail:richard.pasteka@technikum-wien.at) (e-mail: mathias.forjan@technikum-wien.at).*
[**] *Brno University of Technology, Department of Biomedical Engineering, Brno, Czech Republic*
[***] *Universidade de Tras-os-Montes e Alto Douro, School of Science and Technology, Vila Real, Portugal*

Abstract: Respiratory diseases are ubiquitous among European citizens and their prevalence is increasing steadily. Deeper insight into the respiratory process can be gained by modelling of the region of interest in the human body. The presented lung simulator xPULM bridges the gap between *in-silico* (mathematical), *in-vivo* (cell culture based) and mechanical models of the respiratory tract. By adopting selected mathematical models of the human respiratory tract two scenarios were simulated. The linear mathematical single compartment model was used for simulation of the human breathing pattern at rest. Higher complexity non-linear mathematical model reflecting diverse nature of the human respiratory tract was used as a basis for simulation of an artificially ventilated patient. The time-flow characteristics of the mathematical models have been implemented into the control software of the mechanical lung simulator - xPULM. The simulator was then configured to replicate these required breathing patterns employing feedback control loop. The airflow was measured over the course of breathing simulation. The results show high conformity of required and measured breathing patterns characteristic with steady frequency rate and minimal airflow variability. Furthermore, xPULM was capable of reproducing rapid changes of airflow occurring during simulation of artificially ventilated patient, showing high versatility and adaptability of the simulator. Future research will focus on reduction of flow fluctuations and implementation of new breathing patterns.

© 2018, IFAC (International Federation of Automatic Control) Hosting by Elsevier Ltd. All rights reserved.

Keywords: Breathing simulation, mathematical models, in-silico models, flow measurement, mechanical simulation, artificial ventilation, feedback control loop

1. INTRODUCTION

Respiratory diseases are ubiquitous among European citizens. The number of effected people is increasing steadily. A EU wide health survey of the OECD/EU (2016) has shown that 6.1% of the population in Europe aged 15 years or older suffer from asthma. Additionally, 4.0% of the same population group were reported to suffer from COPD. These numbers implicate that overall more than 10% of the population in the EU with an age of 15 years or older suffers from severe respiratory diseases. Deeper insight into the respiratory process might help to increase development potentials for respiratory care. Modelling of the region of interest in the human body is a state of the art method to increase knowledge and allow surveys for specific research questions. Over the course of time several fields of simulation like *in-vivo, in-vitro, in-silico* and mechanical models have been developed in the research field of respiratory science. The presented lung simulator, xPULM™, bridges the gap between *in-silico* (mathematical), *in-vivo* (cell culture based) and mechanical models.

1.1 In-Silico Models for Respiratory Processes

In-silico models of breathing processes have been developed under very different objectives. Many models rely on the morphological description of the human respiratory system by Weibel and Ewald (1963). The model assumes a symmetric setup of the lung. Due to the complexity of the organ, basic assumptions have to be regularly included in the intended in-silico models. Depending on the focus of research those models may also include the option of simulating particle deposition during breathing processes. Calay et al. (2002) published a numerical simulation, which uses a computational fluid dynamics (CFD) model as basis. The foundation of this model is a $3D$ asymmetrical bifurcation model, focusing on the human central airway. The performed simulations included breathing at rest and breathing under maximal exercise. A further CFD based simulation was published by Soni and Aliabadi (2013). This model simulates the airflow and even the particle deposition within the human airways. The basis of the simulation is a ten-generation geometry which is based

2405-8963 © 2018, IFAC (International Federation of Automatic Control) Hosting by Elsevier Ltd. All rights reserved.
Peer review under responsibility of International Federation of Automatic Control.
10.1016/j.ifacol.2018.07.127

on the modelled human bronchial tree generations $4 - 13$, which have been published by Weibel in Weibel and Ewald (1963). In order to simulate particle transport and flow, an inhalation at steady-state was assumed on the one hand, as well as an unsteady inhalation based on a sinusoidal wave-function on the other hand. Another approach is the algebraic model for deposition presented by Rudolf in Rudolf et al. (1990). The foundation of this model is a statistical analysis of experimental data performed prior to modelling. The presented model provides the option to differentiate between the deposition of particles at the bronchial and bronchiolar level. Due to its setup this model can be classified as a semi-empirical model on a regional compartment level. In Hofmann (2011) Hofmann has evaluated this model and identified the use of measured data from prior human experiments as its major advantage. On the contrary, the main disadvantage is given by the necessary assumptions made for modelling the local deposition. Further approaches in the field of *in-silico* models include the Langrangian and the Eulerian approach as modelling concepts.

1.2 Mechanical Models for Respiratory Processes

Over the last years multiple mechanical lung simulators have been presented. The main target of most of them are research and teaching purposes. The group of Chase et al. have presented a mechanically ventilated model which simulates a passively breathing lung in Yuta et al. (2006). The basic setup consists of six rubber bellows, with 200 ml volume each. The model therefore allows the simulation of six compartments. These compartments have variable resistances, which are implemented by valves, and are characterised by changeable compliance, which is realised by additional weights. The simulation options of the model of Chase et al. are limited by the provided breathing patterns, as they are depending on the used ventilator settings. The main purpose of this simulator is teaching. A further approach, published by Heili Frades et al. presents another, mechanically ventilated and therefore passively breathing lung model, which is focused on teaching, published in Heili-Frades et al. (2007). Their setup is characterised by a bag in a box system design. The inner bag of this models is ventilated by a ventilator. The pressure within the surrounding box can be observed and also adapted using a connected and calibrated syringe, which is characterised by a variable recoil. The setup of this model allows the simulation of typical characteristics occurring during restrictive and obstructive breathing. However, the actually simulated breathing patterns are again determined by the chosen ventilator settings. A different development of a mechanical lung simulator was published by Krueger-Ziolek et al. This model allows active moving, still being externally ventilated. The main components of the system are a motor, which is driving a cylinder piston system. Such a setup allows to neglect recoil forces, described in Krueger-Ziolek et al. (2013).

Other models, like the ones presented by Mesic et al. (2003) and He and Zhao (2011) combine mathematical approaches with mechanical setups. The model of Mesic et al. uses a motor driven cylinder piston system and an adjustable flow resistor as basic mechanical setup. The mathematical basis of the breathing generation system includes: non-linear static compliance, dynamic compliance and a model for the airway resistance. The complete model is realised in Simulink, including the real-time controller of the system. A similar approach was presented by He-Zhao. The components of the mechanical setup include a fixed volume vessel and two air connections, one with pressurised air and the other with a vacuum production unit. Flow is controlled via two valves, each connected to a proportional valve driver and the common PC interface. This presented model was implemented in Simulink using the respiratory muscle pressure as input signal and providing linear compliance and nonlinear resistance, which are varied by the flow. The produced signal is provided to a LabView program which is then connected to the peripheral mechanical equipment. This paper combines developed mathematical models which approximate breathing mechanisms of human respiratory system.

Selected models have been subsequently adapted from available literature and simulated *in-silico*. Resulting breathing patterns have been implemented into the mechanical lung simulator – xPULM control software. Furthermore, airflow measurements were conducted to compare similarities between required curved obtained from the mathematical models with measurements taken during mechanical simulations with xPULM. The overall aim was to increase versatility of the xPULM in order to further expand possible teaching as well as research applications.

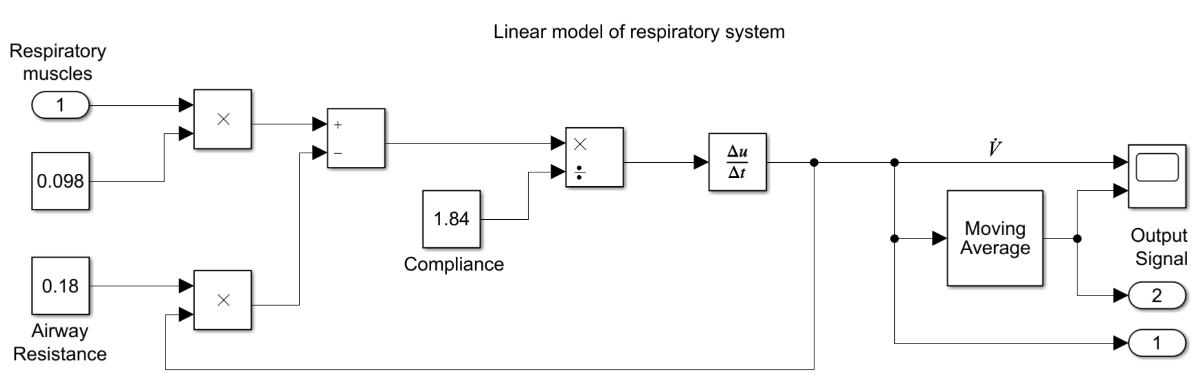

Figure 1. Linear single compartment model of the respiratory system (based on He and Zhao (2011))

2. MATERIALS AND METHODS

Two mathematical models approximating human breathing processes have been selected from literature, each focusing on different aspects of respiration. The first, linear single compartment model is a simple yet effective way of simulating spontaneously breathing human. The second non-linear single compartment model takes into consideration the complex structure of a human respiratory tract by introducing variable airway resistance and static/dynamic lung compliance. For modelling purposes MATLAB and Simulink software have been used. The combination of textual and graphical programming mediates implementation of a respiratory system models in a simulation environment.

2.1 xPULM Simulator for Respiratory Processes

The presented xPULM simulator combines the approaches of *in-silico* and mechanical simulation. The simulator is equipped with a thoracic chamber as a core element, which allows simulations with various lung equivalents, like latex or silicone bags. Artificial lung equivalents of various volumes are mainly used for calibration purposes as they do not have any inner structure. In addition the primed porcine lungs can be also placed into the thoracic chamber and used during breathing simulations. The porcine lungs are a suitable choice for aerosol deposition measurement due to the tissue properties and complex inner structure. The morphology of the lower human respiratory tract effecting the transport of airborne particles is therefore approximated well. This characteristic allows simulations with different focus and research questions, due to the interchangeable geometry of the modelled lung as shown in Paštěka and Forjan (2017b). The thoracic chamber is connected to a bellows system, driven by a DC motor, which evacuates the chamber leading to a pressure drop inside and inflation of the used lung equivalent. The motor movements, thereby the breathing flow simulation, are controlled using a National Instruments cRIO FPGA real time processing unit running LabVIEW based control software. A PI controller based on the flow information of two unidirectional Honeywell (AWM720P1) flow sensors is regulating the motor movements in order to concord with the required input signal as described in Paštěka and Forjan (2017a).

2.2 Linear Single Compartment Model - Breathing at Rest

A simplified model of a human respiratory system capable of describing flow dependencies at rest is a simple linear model, depicted in Fig. 1. The airway resistance (R) over the whole length of a respiratory tract together with lung compliance (C) is assumed to be constant and also unchangeable in the course of the entire time of simulation. This well-known single-compartment model is described with following equation:

$$P_{mus}(t) = \frac{1}{C}V(t) + R\dot{V}(t) \tag{1}$$

Where: P_{mus} is a respiratory pressure generated by respiratory muscles, C is a lung's compliance R is an airway resistance, $V(t)$ is an air volume breathed in lungs and $\dot{V}(t)$ is a respiration air flow, model adapted from He and Zhao (2011). The performed simulation was run with following physiological values $R = 0.18\ Pa \cdot s/l$ and $C = 1.84\ l/kPa$ originally taken from Tang et al. (1995).

2.3 Non-linear Single Compartment Model - Artificially Ventilated Patient

A simulation of an artificially ventilated patient suffering with cystic fibrosis is based on the non-linear single compartment mathematical model of the human respiratory system developed by Mesic et al. (2003). The presented model further expands simple linear single compartment model by taking into account dynamic, nonlinear and nonstationary character of the human respiratory system. The properties of the respiratory system are described by non-linear static and dynamic compliance and nonlinear flow-resistance. Resulting transfer functions describing two components of the lung compliance are:

$$G_{V1}(s) = \frac{1}{\tau_1 s + 1} \qquad G_{V2}(s) = \frac{1}{\tau_2 s + 1}. \tag{2}$$

Where: time constants represent the fast change in the lung volume due to lung elasticity $\tau_1 s$ or slow change due to viscosity $\tau_2 s$. Furthermore, the upper-airways resistance is considered to be flow depended, the lower-airways resistance modelled as volume dependent and the resistance of small airways is taken as a constant.

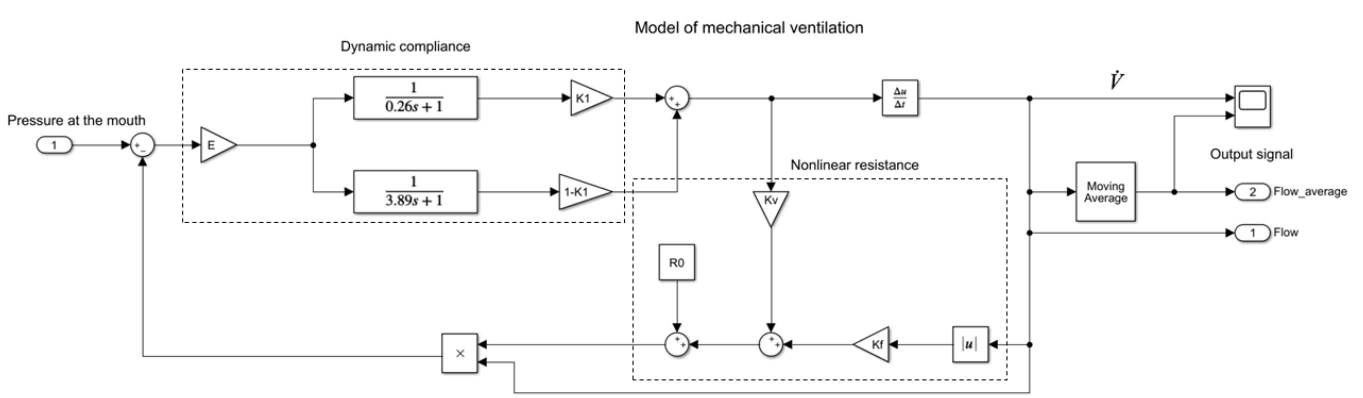

Figure 2. Complete non-linear single compartment mathematical model of the respiratory system (based on Mesic et al. (2003))

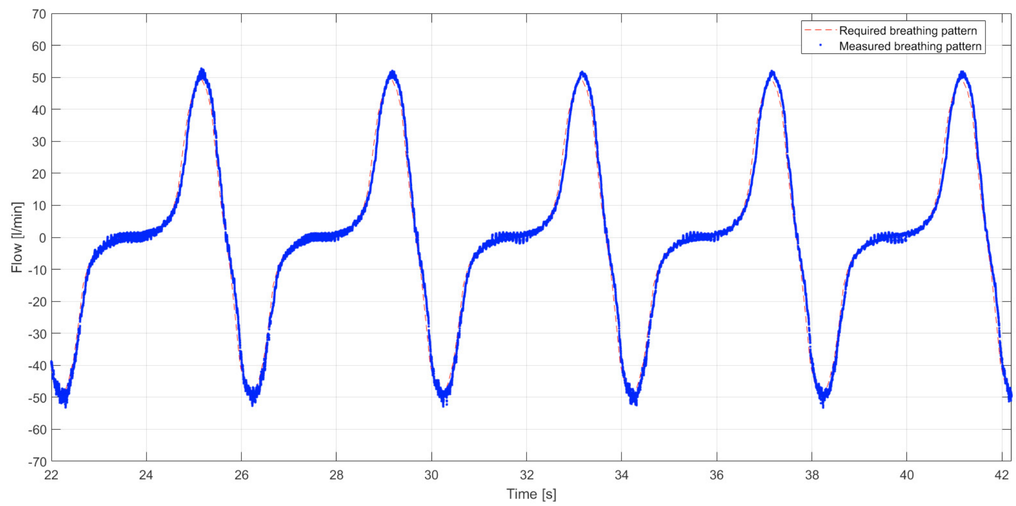

Figure 3. Linear single compartment model - breathing at rest: 1) Red dashed line - required curved defined as an output of a mathematical model 2) Blue dotted line - xPULM flow measurements

These considerations result in equation (3) describing the airways resistance:

$$R = R_0 + K_V V + K_F |V|. \tag{3}$$

Where: R_0 is the resistance of small airways, K_V is the resistances of upper airways and K_F is the resistance of lower airways Mesic et al. (2003). The adapted model used for simulating artificially ventilated patient can be seen in Fig. 2. The final values of parameters estimated by Mesic were used during simulations and verified prior using model parameter estimation tool of Simulink. The model input signal is a pressure at the mouth recorded from ventilated patient suffering with cystic fibrosis by Mesic et al. (2003).

2.4 Measurement Procedure

All measurements have been conducted under laboratory conditions at a temperature of 25 °C and relative humidity 45%. The xPULM was configured to reproduce the breathing curve which was defined as an output of the mathematical simulations of:

- Linear Single Compartment Model - Breathing at Rest
- Non-linear Single compartment model - Artificially Ventilated Patient

Implementation of new breathing patterns into the xPULM simulator was preceded by signal preprocessing. The outputs of mathematical simulations were smoothened using a moving average filter with window size $n = 2$. The filter was applied due to the abrupt changes occurring in the original flow output signals of both mathematical models. This preprocessing step eliminated necessity for rapid movement of the motor and bellow system during xPULM breathing simulations which could potentially overload and damage simulator components.

Overall four measurements trials were conducted, two for each breathing pattern with a duration of 60 s for each trial. Two 2.3 l latex bags (connected via a Y-connector with the simulated trachea) were used as a lung equivalents. The airflow during the simulation process was recorded using the two unidirectional Honeywell (AWM720P1) flow sensors.

3. RESULTS

3.1 Breathing at Rest

The lung simulator was configured to reproduce human respiratory breathing pattern at rest during this measurement trial. The output of the single compartment mathematical model was set as a required breathing pattern. Movement of the bellow system was adjusted by the feedback control algorithm based on the measurements from the airflow sensors. In each iteration of a control loop the algorithm compares difference between measured and required flow curves. In case of discrepancy, the software calculates required change in motor movement, subsequently reducing variations between signals to minimum. In order to examine the process of the mechanical simulation, five consecutive breathing cycles were extracted from a full 60 s measurement trial, depicted on Fig. 3. The peak flow measured during inhalation and exhalation is 50 l/min. The measured curve shows good concordance with the required breathing pattern. The inspiration to expiration ratio (I:E) is close to the physiological value of 1:2. Variation between cycles is minimal and lies within the range of millilitres.

3.2 Artificial Ventilation

During this measurement trial the output of the non-linear single compartment mathematical model simulating artificially ventilated patient suffering with cystic fibrosis was taken as a required ventilation curve. The feedback control algorithm was also incorporated during this measurement. The comparison between the measured flow curves of mathematical model (required) and xPULM (physically simulated) is shown in Fig. 4. The results of

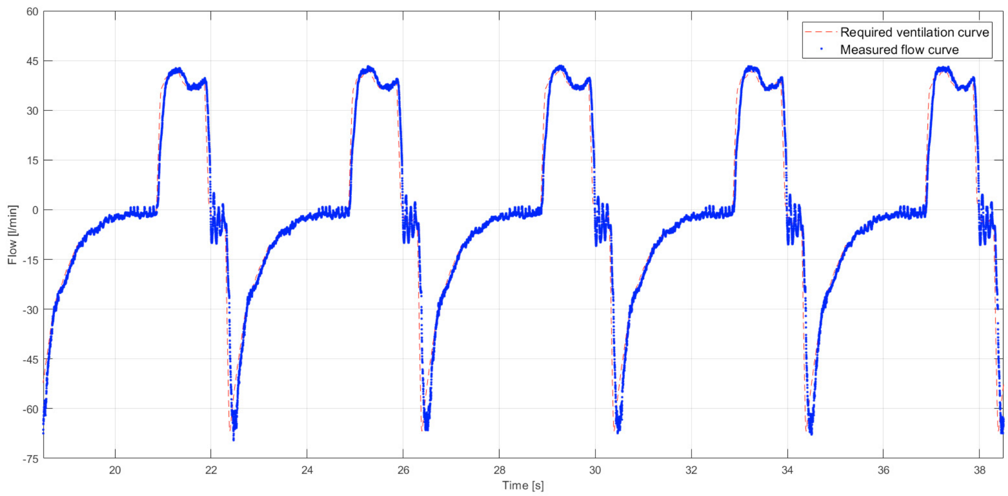

Figure 4. Non-linear single compartment model artificially ventilated patient: 1) Red dashed line - required curved defined as an output of a mathematical model 2) Blue dotted line - xPULM flow measurements

5 consecutive curve measurements represent simulation of mechanically ventilated patient extracted form 60 s measurement trial. The measured flow during inhalation was in average 38 l/min and measured flow during exhalation was −62 l/min. The steep and rapid transitions during alternating phases of the artificial ventilation are reproduced well.

4. DISCUSSION

The presented paper shows the potential capabilities of the xPULM simulator to mimic various flow patterns encountered in everyday life and in the clinical environment. Two breathing patterns, based on the selected mathematical models of the respiratory system, were chosen for testing: a) resting human breathing b) artificially ventilated patient.

The linear single compartment mathematical model has proven to be sufficient for physical simulations of breathing at rest. The measurements show good cycle-to-cycle reproducibility. Flow during both inhalation and exhalation reaches stable peak value of 50 l/min over all measurement cycles. Physiological value of I:E ration (1:2) is also retained. The non-linear single compartment mathematical model was used as a basis for physical measurements of simulating artificially ventilated patient. The flow patterns during artificial ventilation are characterised by rapid changes of flow placing high demands on the system trying to replicate them. Overcoming these constrains the measurements with xPULM show good correlation with required curve and flow variance in order of millilitres. Respiratory pause following the end of inspiration is also clearly distinguishable even though small oscillations in the region of zero flow are present. In summary, both input signals were reproduced in an acceptable range of variance.

It has to be mentioned, that the fast changes of the signal during artificial ventilation lead to high demands to the mechanical system. Especially the rotational speed of the motor and the inertia of the system components lead to small fluctuations of the system's response. Nevertheless, these fluctuations are within an acceptable range and do not significantly influence the main flow output of the simulator. Further development steps will include implementation of various breathing patterns, fine tuning of the integrated controller and the motor driver settings to allow even faster responses in changing signals. The additional negative pressure within the thoracic chamber, which was implemented to keep the used lung equivalent inflated, was held at a steady state, even when the induced pressure changes based on the intended breathing signal, lead to very fast changes of the pressure within the chamber. This allows the conclusion that the xPULM simulator can also be used with such fast changing input signals in the case of a more complex and inert lung equivalent like a porcine lung.

ACKNOWLEDGEMENTS

The authors want to thank the Austrian Workers Compensation Board (AUVA), National Instruments and Palas GmbH for their supportive efforts. Moreover, sincere gratitude goes to our colleagues from Brno University of Technology and College of Polytechnics Jihlava.

REFERENCES

R.K. Calay, J. Kurujareon, and A.E. Holdo. Numerical simulation of respiratory flow patterns within human lung. *Respiratory Physiology & Neurobiology*, 130(2):201 – 221, 2002. ISSN 1569-9048. doi: 10.1016/S0034-5687(01)00337-1. URL `https://doi.org/10.1016/S0034-5687(01)00337-1`.

Z. He and Y. Zhao. *Modeling in Respiratory Movement Using LabVIEW and Simulink, Modeling, Programming and Simulations Using LabVIEW Software.* InTech, 2011. ISBN 978-953-307-521-1.

S. Heili-Frades, G. Peces-Barba, and M.J. Rodriguez-Nieto. Design of a lung simulator for teaching lung mechanics in mechanical ventilation. *Arch Bronconeumol.*, 43(12):674–679, December 2007. doi: 10.1157/13112966. URL `https://doi.org/10.1157/13112966`.

W. Hofmann. Modelling inhaled particle deposition in the human lung - a review. *Journal of Aerosol Science*, 42(10):693 – 724, 2011. ISSN 0021-8502. doi: 10.1016/j.jaerosci.2011.05.007. URL https://doi.org/10.1016/j.jaerosci.2011.05.007.

S. Krueger-Ziolek, C. Knoebel, C. Schranz, and K. Moeller. Combination of engineering and medical education using an active mechanical lung simulator. In *Proceedings of the 26th IEEE International Symposium on Computer-Based Medical Systems*, pages 542–543, June 2013. doi: 10.1109/CBMS.2013.6627868. URL https://doi.org/10.1109/CBMS.2013.6627868.

S. Mesic, R. Babuska, H.C. Hoogsteden, and A.F.M. Verbraak. Computer-controlled mechanical simulation of the artificially ventilated human respiratory system. *IEEE Transactions on Biomedical Engineering*, 50(6):731–743, June 2003. ISSN 0018-9294. doi: 10.1109/TBME.2003.812166. URL https://doi.org/10.1109/TBME.2003.812166.

OECD/EU. *Health at a Glance: Europe 2016: State of Health in the EU Cycle*. Health at a Glance: Europe. OECD Publishing, Paris, November 2016. doi: 10.1787/9789264265592-en.

R. Paštěka and M. Forjan. Actively Breathing Mechanical Lung Simulator Development and Preliminary Measurements. In *IFMBE Proceedings*, volume 65, pages 751–754. Springer Singapore, 2017a. ISBN 978-981-10-5122-7. doi: 10.1007/978-981-10-5122-7188. URL http://link.springer.com/10.1007/978-981-10-5122-7_188.

R. Paštěka and M. Forjan. Evaluation of an Active Lung Simulator for Aerosol Inhalation Test Replacement. In *Alternatives and Animal Use in the Life Sciences: 3Rs in Action*, pages 47–48, Seattle, 2017b. ALTEX. URL http://www.altex.ch/altex-proceedings/wc-10-seattle.

G. Rudolf, R. Kobrich, and W. Stahlhofen. Modelling and algebraic formulation of regional aerosol deposition in man. *Journal of Aerosol Science*, 21 (Supplement 1):S403 – S406, 1990. ISSN 0021-8502. doi: 10.1016/0021-8502(90)90266-Z. URL https://doi.org/10.1016/0021-8502(90)90266-Z. Proceedings of the 1990 European Aerosol Conference.

B. Soni and S. Aliabadi. Large-scale cfd simulations of airflow and particle deposition in lung airway. *Computers & Fluids*, 88:804–812, December 2013. ISSN 0045-7930. doi: 10.1016/j.compfluid.2013.06.015. URL https://doi.org/10.1016/j.compfluid.2013.06.015.

Y. Tang, X. Zhang, and D. Han. Human body medical parameters and concepts, 1995.

E. Weibel and R. Ewald. *Morphometry of the Human Lung*. Academic Press Inc., Publishers, 1 edition, 1963. doi: ISBN: 978-1-4832-0076-7.

J.G. Chaseand T. Yuta, K.J. Mulligan, G.M. Shaw, and B. Horn. A novel mechanical lung model of pulmonary diseases to assist with teaching and training. *BMC Pulmonary Medicine*, 6(21):11, August 2006. ISSN 1471-2466. doi: 10.1186/1471-2466-6-21.