Hardware-in-the-loop test bench for artificial lungs

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Abstract. Extracorporeal lung assist therapy is a life saving treatment for acute lung failure patients. While developing such systems current technology requires extensive testing in animal experiments. These are complex, time consuming, lack repeatability and are subject to ethical considerations. We propose the development of a hardware-in-the-loop test bench to overcome these limitations. In such a test bench the device under test can be operated under the same conditions as in a live experiment while at the same time providing exact controllability. This can be achieved by providing physiological media conditions at the interface of the machine (blood in- and outlets). The reference values for these are provided by an integrated mathematical model of patient physiology. Test show that this enables realistic testing of interaction with physiological conditions.

INTRODUCTION

Acute respiratory failure is a syndrome requiring treatment of the underlying disease as well as application of supporting therapies ensuring sufficient gas exchange. Standard therapy is the use of an artificial ventilator applying protective ventilation schemes. In case of severe progression of the disease (e.g. an Acute Respiratory Distress Syndrome (ARDS)), artificial ventilation might not be sufficient any more or has to be set to unphysiological high pressures/volumes so that further lung injury (VILI) may result.

Extracorporeal Lung Assist (ECLA) or Extracorporeal Membrane Oxygenation (ECMO) were established as ultima ratio therapy for most severe forms. Different configurations of extracorporeal circulation are available. A typical veno-venous ECMO withdraws Oxygen depleted blood using a cannula in the femoral veins. After that, it is pumped through an oxygenator for gas exchange and returned centrally to the venous system.

Currently duration of ECMO Treatment is typically limited to 30 days, however even applications of more than 100 days have been reported until a lung transplant was available. On the road to long-term or even permanent lung support, many challenges have to be met. Apart from biocompatibility issues, such systems would require fully automatic control of operating parameters in patient oriented control loops. At the moment, laboratory testing is mainly focusing on determining static transfer characteristics and endurance of the oxygenator. Further testing, especially investigations on interaction with physiology requires animal experiments, which are complicated, require ethical consideration and often lack reproducibility. In order to overcome this shortcoming and enabling higher functionality testing of ECMO designs and physiological controllers we propose a Hardware-in-the-loop setup to mimic physiological interaction for long-term laboratory experiments.

MATERIALS AND METHODS

The idea of a HIL simulator is based on the concept that the device under test is connected to a hardware interface, which provides the same physical quantities as the real process. This way, the device operates under the same conditions as if connected to the real process. Set values for the hardware interface are generated by a software process model, which represents the biological system.

In our case the device interface is defined by the in- and outflow of blood to the ECMO, where fluid with defined gas concentration is connected. We measure the output concentrations and feed this value to a software simulation model of physiology. This in turn computes the effect of e.g. increased oxygen content on venous concentration. The simulation provides set values for the control loop of the fluid conditioning hardware-interface in the HIL, where we use an “inverse” ECMO system to withdraw oxygen and to add CO2. For this we use three Xenios Hilite 7000 adult oxygenators which are connected in series. This larger transfer capacity is required as the available partial pressure
difference for de-oxygenation is far less as compared to oxygenation. An electronic gas mixer provides a freely defined mixture of Oxygen, Nitrogen and CO2 from 0.5 to 10 l/min. Figure 1 shows the system components:

![Figure 1. Concept of the HIL test bench.](image)

Partial pressures of in- and outflowing blood are continuously measured with the CDI500 Blood gas measurement system. Circulation through the system is provided by the blood-pump integrated into the ECMO device under test. Process control and real time computation of the patient model is implemented using a dSpace MicroAutoBox2 system, which can be directly programmed using Matlab. Figure 2 shows the realization of our HIL system in the laboratory.

![Figure 2. Realisation of the HIL test bench](image)

The Patient model used in the HIL simulator is described in [1]. Model parameters were adapted to fit recent measured datasets. The basic idea is, that the physiological system can be represented in few compartments covering the main time constants, gas exchange as well as transport delays, see Fig.3.
The whole circulation is subdivided in two main compartments (Lung and Capillaries) which can be described by balance equations following our previously published model[1]. The storage of oxygen in the lung (gas fraction $F_a$ and volume $V_a$ of the alveoli) can be described by balancing both ventilation (minute volume $MV$, inspiratory and expiratory gas fraction $FIO2$, $FE02$) and gas transport by circulation (bloodflow $Q_b$, pulmonary arterial and venous concentrations $C_{vmx}$, $C_a$), eq. (1):

$$\dot{F}_AV_a = MV(F_{I}O_2-F_{E}O_2)+\frac{863}{(P_{bar}-P_{H_2O})}\dot{Q}_b(C_{vmx}-C_a)$$  

(1)

Gas transfer in the lung between ventilation and circulation is described by a diffusion process, eq. (2):

$$P_{aO2} = P_{A02}-AaD_{O2} = (P_{bar}-P_{H_2O}) \cdot F_A-AaD_{O2}$$  

(2)

The balance equation for the capillaries can be formulated similarly computing tissue concentration $C_{Ti}$ from effective Tissue Volume $V_{Ti}$ metabolic rate $MR$ and from circulation gas transport ($Q_b$, arterial and venous concentrations $C_a$, $C_v$), eq. (3):

$$\dot{C}_{Ti} = \frac{1}{V_{Ti}} \cdot [MR + \dot{Q}_b \cdot (C_a - C_v)]$$  

(3)

Blood transport in the circulation is dominated by the transport process caused by volume flow. These can be described by a lag time element, eq. (4):

$$G_{bl}(s) = e^{-\frac{V_b}{Q_b}}$$  

(4)

After passage through the capillaries some of the blood is collected by the ecmo, the rest bypasses where it is then subsequently mixed with the oxygenated blood returning from the ecmo. The mixture is described by eq. (5):

$$C_{vmix} = \frac{1}{Q_b}(\delta \cdot C_{T} \cdot (\dot{Q}_b - \dot{Q}_{ecmo}) - C_{ecmo} \cdot \dot{Q}_{ecmo})$$  

(5)

Parameterization is performed by numerical optimization fitting the data to experimental data accounting for inter-individual changes of subjects.
RESULTS AND DISCUSSION

A standard ECMO was connected to our HIL Simulator as device under test (DUT). To prove feasibility, we chose to reproduce a longer measurement episode from our previous clinical recordings. We chose the specific sequence as it displays relatively extensive dynamic changes in the process variables while at the same time providing a physiological realistic scenario.

![Graphs showing oxygen and CO2 partial pressures in HIL Simulator](image)

**Figure 3.** Measurement in the HIL Simulator (a) Oxygen partial pressures and (b) CO2 partial pressures

Figure 4 shows the time course of the process values simulated in the HIL test bench. $P_{\text{HILout}}$ Measurements are the output concentrations of the HIL which replay the clinical concentrations entering into the ECMO. $P_{\text{HILin}}$ are the return concentrations from the ECMO which correspond to the concentrations in Blood being returned to the patient. $P_{\text{mv}}$ Measurements refer to the physiological patient measurements being made in the pulmonary vein after mixing of ECMO return blood with venous blood. The time dynamics of the dynamic changes of the gas partial pressures of O2 and CO2 can be exactly reproduced and the ECMO device under test is subject to the same conditions as in the real experiment. This impressively demonstrates the performance of the HIL test bench.

CONCLUSION

Hardware-in-the-loop technology can provide testing environments in the laboratory which re-creates complex physiological conditions. This is especially beneficial for development of higher functionality like closed loop control or validation on system level. Using the presented approach we could show that we can provide physiological coherent blood gas behavior which we did prove in replaying actual clinical data which we recorded during clinical experiments. Further work will focus on integrating fluid dynamics to simulate the hydraulic interface of the ECMO as well.

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REFERENCES