Concepts for Simplifying Automatic Blood-Gas Control during Extracorporeal Circulation

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Abstract— **To simplify and improve closed-loop control of the arterial oxygen partial pressure during extracorporeal circulation, three feed-forward control strategies are presented. These are deduced from some common indices of oxygenator performance. A simulation study revealed that these strategies react adequately in case of step-like blood-flow changes. Furthermore it could be shown, that two of the feed-forward strategies also react to changes of the venous conditions and the hemoglobin concentration.**

Keywords— **Extracorporeal circulation, oxygenator, closed-loop control, feed-forward control, oxygen partial pressure.**

I. Introduction

Extracorporeal circulation (ECC) can be described as a combination of several medical and technical interventions where blood is withdrawn from the patient in great quantities in order to treat it outside the body. Thereafter, the treated blood is recirculated to the body. A prime example is the cardiopulmonary bypass (CPB) or heart-lung machine (HLM), respectively.

A HLM is used during heart surgery (heart transplantation, bypass and valve surgery) when the heart beat is suppressed by applying paralyzing agents. The paralyzed heart permits precise and unhurried chirurgical interventions. Adequate perfusion of the body must then be provided by means of a HLM replacing temporarily the heart and the lung. Major components of a HLM are a blood pump, which drives the blood through the machine and the body, and an oxygenator (artifical lung), where a bidirectional gas-transfer between the circulating blood and a gas stream takes place.

Even though the HLM was continually enhanced and developed to a reliable and efficient device, its most important components (blood pump and oxygenator) must still be controlled manually in order to keep the related variables in physiological ranges. These tasks are carried out by well-trained personnel (perfusionist) who are acting on related control variables. Two tasks can be identified in which automatic control will be beneficial. The first one concerns the control of the blood pump and the second one the gas transfer in the oxygenator.

Another application of the system pump + oxygenator is the extracorporeal membrane oxygenation (ECMO), a treatment for patients who suffer from respiratory failure with a life threatening undersupply of the body with oxygen (hypoxemia). ECMO may be applied up to several weeks.

Strategies for automic pump control developed by the authors can be found in [1]. The focus of this paper is automatic blood gas control, especially the simplification of a recently published approach [2].

II. Control strategy

The automatic control strategy applied mimics the physiological regulation of blood gases, i.e. the maintenance of reasonable partial pressures for both oxygen and carbon dioxide (pO_2, pCO_2) in the arterial blood leaving the oxygenator. This most natural approach which is also often used for manual control guarantees appropriate O_2-supply and CO_2-removal For this, the gas mixture entering the oxygenator, which is made up of O_2, N_2, and sometimes CO_2, must be changed in order to set desired pO_2 and pCO_2. In this context, the control input for the arterial pO_2 is the O_2-fraction in the gas (FiO_2), and the control input for the arterial pCO_2 is primarily the total gas-flow rate q_g through the oxygenator, leaving the CO_2-fraction in the gas unchanged. Control reference values can be taken from CPB literature [3]. Suggested arterial values are pO_2 = 100…200 mmHg, pCO_2 = 35…45 mmHg, and a pH-value of 7.4.

III. Theoretical modelling

The process to be controlled consists of the gas mixing unit, the oxygenator, and the blood-gas analyzer.

The gas mixing unit is made up of electronic valves (GFC 17, Aalborg, Orangeburg, NY) which are actuated by the automatic controller's command signals total gas flow-rate q_g and oxygen fraction FiO_2. According to this signals, distinct gas flow-rates are taken from gas bottles containing pure gases (O_2 and N_2), so that the actual q_g and FiO_2 meet the controller's demand. This gas mixture is then fed to the oxygenator via a flexible tube. As the valves react very fast, the dynamics of the gas mixer can be described by a pure

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transport-(time)-delay which is due to the travel distance from the mixer to the oxygenator. This time-delay depends on the length and the diameter of the tube between the mixer and the oxygenator and, additionally, on the gas flow q_g. Hence, the time-delay is varying.

All blood-gas parameters are measured by means of a clinical blood-gas analyzer (CDI 500, Terumo, Japan) which is continuously supplied with small streams of arterial and venous blood. The blood-gas analyzer (BGA) continually measures the O_2- and CO_2-partial pressure as well as the pH-values. According to the BGA's specifications it was modelled as a first order system with time constant $T_{BGA} = 20$ s sampled with a sample time of 6 s. Additionally, a variable time-delay due to the transport of blood from the arterial line to the BGA must be considered. It depends on the tubing parameters (length and diameter) and on the blood flow q_b.

The modelling of the blood-gas transfer in an oxygenator is based on a very comprehensive model of the respiratory system [4] which we extended to be used in the context here [5], [1]. The model consists of three basic compartments: gas, plasma and red blood cells. Volume balances are calculated in these compartments for the following state variables: pO_2, pCO_2, bicarbonate, carbamate, and hydrogenium. Variables influencing the gas transfer are the composition (gas fractions) of the gas, the total flow rate of gas and blood, the hemoglobin content, and the venous conditions. Due to the chemical binding of O_2 and CO_2 in blood, the model is non-linear.

To conclude this section, the entire process is non-linear and it has variable time-delays at the input and output of the oxygenator. As simulations revealed, the dynamics of the oxygenator can be neglected in comparison to the dominating time constant of the BGA ($T_{BGA} = 20$ s).

IV. A Brief Description of the First Version of the Control System

The control system for arterial pO_2 consists of an explicit input-output linearization of the process, which is embedded in a Smith-predictor structure. For both, explicit input-output linearization and Smith-predictor control, it was necessary to implement a model of the process (gas blender, oxygenator, BGA, gas- and blood-tubing systems) in the control system. This model was used to estimate some internal states of the process which can not be measured. Therefore, the whole system is somewhat complicated, but showed a good performance [1].

The control of the arterial pCO_2 is not so critical compared with the pO_2 control. For the pCO_2-process the static gain differs far less than in the pO_2 case and an input time-delay does not apply to the gas flow q_g. Therefore a PI-controller with controller gain scheduled to the blood flow q_b was designed [1].

For in-vitro evaluation of automatic blood-gas control, the conditions during a real cardiopulmonary bypass were reproduced with an artifical circulation system, where the patient was replaced by three oxygenators, which were operated in de-oxygenation mode. That means that their gas parameters were adjusted to achieve venous conditions at the blood outlet of the de-oxygenators. Furthermore, we used fresh porcine blood as a substitute for human blood as it has similar blood-gas transport properties.

Different tests were conducted: Switch-on tests, tests where the control reference was changed step-like, and disturbance rejection tests. For the latter, step-like blood-flow changes were invoked. The controllers showed a good performance and kept the process values in the predefined ranges (100-200 mmHg for pO_2 and 35-45 mmHg for pCO_2).

V. Symplification of O_2-Control: A Feasibility Study

A. Motivation

The potential users of the control system (perfusionists) may be confused because of the complexity of the pO_2-control system. This may lead to some aversion against its application. Therefore, we tried to develop a more simple system for pO_2-control which, additionally, implements basic knowledge of perfusionists by using some well-known performance indices of oxygenators.

B. Feed-forward control concepts based on oxygenator performance indices

The oxygen transfer slope (OTS) is the change in FiO_2 required for a given change in a patient's oxygen consumption $\dot{V}_{O2}$ or membrane O_2-transfer, respectively [6]. OTS is expressed by means of a linear correlation between the required FiO_2 for a certain oxygen consumption,

$$FiO_{2,req} = b + m \cdot \dot{V}_{O2} . \quad (1)$$

$\dot{V}_{O2}$ can be calculated by multiplying the concentration difference between arterial and venous blood (avD_{O2}) with the blood-flow rate,

$$\dot{V}_{O2} = avD_{O2} \cdot q_b = (c_a - c_v) \cdot q_b . \quad (2)$$

c_a and c_v are arterial and venous O_2-concentration, respectively. O_2-concentration in blood depends mainly on pO_2, but also on the pCO_2, the pH, the O_2-solubility in blood (α_{O2}

= 0.00003 $l_{O2}/(l_b \cdot mmHg)$), the Hüfner number *HN* (*HN* = 1.34 l_{O2}/kg_{Hb}), and the Hb-concentration c_{Hb} (in g_{Hb}/l_b). (Indices O2, b and Hb are oxygen, blood and hemoglobin). In case of arterial blood, it holds

$$c_a = \alpha_{O2} \cdot pO_{2,a} + HN \cdot c_{Hb} \cdot S(pO_{2,a}, pH_a, pCO_{2,a}) \cdot \quad (3)$$

S(·) is the oxygen saturation. It can be calculated by

$$S(x_x) = \frac{a_1 x + a_2 x^2 + a_3 x^3 + x^4}{a_4 + a_5 x + a_6 x^2 + a_7 x^3 + x^4}, \quad (4)$$

with

$$x = pO_2 \cdot 10^{0.024(37-T)+0.4(pH-7.4)+0.06\log(40/pCO_2)}, \quad (5)$$

where *T* is the blood temperature. Values for the a_i can be found in [1]. A feed-forward control law can now be obtained by combining equations (1)-(5) and setting $pO_{2,a}$ to the desired $pO_{2,a,set}$

$$FiO_{2,set}^{(1)} = b + m \cdot q_b \cdot avD_{O2}(pO_{2,a,set}) \cdot \quad (6)$$

Another common index for oxygenator performance is the diffusing capacity of oxygen (D_{O2}). It is defined as

$$D_{O2} = \frac{\dot{V}_{O2}}{P_{g,O2,in} - pO_{2,v}}, \quad (7)$$

where $P_{g,O2,in}$ is the O_2 partial pressure in the gas at the inlet of the oxygenator, and $pO_{2,v}$ is the venous partial pressure. Rearranging (7) for $P_{g,O2,in}$ and applying $FiO_2 = P_{g,O2,in} / P_{baro}$, where P_{baro} is the gas pressure in the oxygenator ($P_{baro} \approx 760$ mmHg), another potential blood flow sensitive feed-forward control law is obtained,

$$FiO_{2,set}^{(2)} = \frac{1}{P_{baro}}\left(pO_{2,v} + \frac{q_b}{D_{O2}} \cdot avD_{O2}(pO_{2,a,set})\right) \cdot \quad (8)$$

Finally, the blood flow related partial pressure gradient between gas inlet and arterial outlet (*ZGB*),

$$ZGB = \frac{P_{g,O2,in} - pO_{2,a}}{q_b}, \quad (9)$$

can be used for feed-forward control:

$$FiO_{2,set}^{(3)} = \frac{1}{P_{baro}}\left(pO_{2,a,set} + ZGB \cdot q_b\right) \cdot \quad (10)$$

Experimental data [6] for the oxygenator we used in our experiments (Quadrox, Jostra, Hirrlingen, Germany) are b = 0.14, m = 2.2 min/l_{O2}, D_{O2} = (0.48 ± 0.09)·10^{-3} $l_{O2}/(min \cdot mmHg)$, and *ZGB* = 54 ± 12 $mmHg/(l_{O2}/min)$. They had been measured during regular CPB with patients undergoing bypass surgery. Average blood flow was 4 l_b/min and Hemoglobin content c_{Hb} ranged between 80 and 100 g_{Hb}/l_b. As can be seen by the standard deviations, a pure feed-forward control would be imprecise. Therefore, an additional closed-loop control path is obligatory. Based on the given data one can calculate the dependency of the $FiO_{2,set}^{(j)}$ from blood flow q_b ,

$$\begin{aligned} \frac{\partial FiO_{2,set}^{(1)}}{\partial q_b} &= m \cdot avD_{O2}(pO_{2,a,set}) = 0.08 \\ \frac{\partial FiO_{2,set}^{(2)}}{\partial q_b} &= \frac{avD_{O2}(pO_{2,a,set})}{D_{O2} \cdot P_{baro}} = 0.10 \\ \frac{\partial FiO_{2,set}^{(3)}}{\partial q_b} &= \frac{ZGB}{P_{baro}} = 0.09 \end{aligned} \quad (11)$$

(Values are in min/l_b). In (11) avD_{O2} was estimated to 0.037 l_{O2}/l_{blood} assuming c_{Hb} = 90 g_{Hb}/l_b, T = 37°, $pO_{2,v}$ = 40 mmHg, $pCO_{2,v}$ = 44 mmHg, pH_v = 7.35, $pO_{2,a} = pO_{2,a,set}$ = 160 mmHg, $pCO_{2,a}$ = 40 mmHg, pH_a = 7.4. As can be seen the values in (11) differ to some extent as do the underlying performance indices. Note, that the feed-forward control-laws 2 and 3 have the potential to adjust automatically to changing conditions if avD_{O2} is updated with actual measurements of c_{Hb}, T and the venous conditions.

C. Simulation study

To evaluate the feasibility of the feed-forward path, a simulation study based on our process model was undertaken. The actual command signal was

$$FiO_{2,act}(i,k) = FiO_{2,set}^{(j)}(i) + K_c \cdot (e(k) + K_I \cdot \sum_{j=0}^{k} e(j)) \quad (12)$$

$FiO_{2,set}^{(j)}$ is any of the derived feed-forward control laws. It is operated at a sample time of 0.1 s, meaning that any change of q_b is directly prompted to the actual command signal. The rest is a simple ad hoc PI-controller: $e(k)$ is the control error, i.e. the difference between the desired $pO_{2,a,set}(k)$ and the actual value $pO_{2,a}(k)$ measured by the BGA. Controller parameters K_C and K_I had been tuned to obtain a rather slow closed-loop control, so that the influence of the feed-forward path could better be studied: K_C = 0.0005 $mmHg^{-1}$ and K_I = 0.5. Its sample time was 6 s which is the sample time forced by the BGA.

In the simulation scenario q_b was changed step-like by 1 l/min in the range from 1 – 5 l/min. $pO_{2,a,set}$ was 160 mmHg. The other conditions were c_{Hb} = 90 g_{Hb}/l_b, T = 37°, $pO_{2,v}$ = 40 mmHg, $pCO_{2,v}$ = 44 mmHg, and pH_v = 7.35. An example for $FiO_{2,set}^{(2)}$ is given in figure 1. As can be seen by the actual

FiO_2, the feed-forward control path tends to overcompensate, meaning that the initial rise in actual FiO_2 after a change in q_b is somewhat greater than the final steady-state value. If the performance of the model oxygenator is degraded, the situation changes to under-compensation (figure 2). Note, that this situation may occur in reality too. Comparable results had been obtained for the other feed-forward control laws. $FiO_{2,set}^{(2)}$ was further examined concerning its potential to react to changes of the venous conditions. Figure 3 shows an example where the venous pO_2 was changed step-like. Obviously, the feed-forward control path reacted adequately. The same holds true if the hemoglobin concentration is changed.

VI. Summary

Feed-forward control by one of the deduced laws can be used to simplify the control of the arterial pO_2 to a predefined value. Furthermore, the reaction to changes of the blood flow will be accelerated as adequate control reactions can be initiated much faster. This is due to the possibility to measure actual blood-flow rate with a high sample rate. Future work will concentrate on the implementation and test of these feed-forward concepts in a smith-predictor control system without explicit input-output linearization in order to eliminate the somewhat bulky process model as used in the initial control system.

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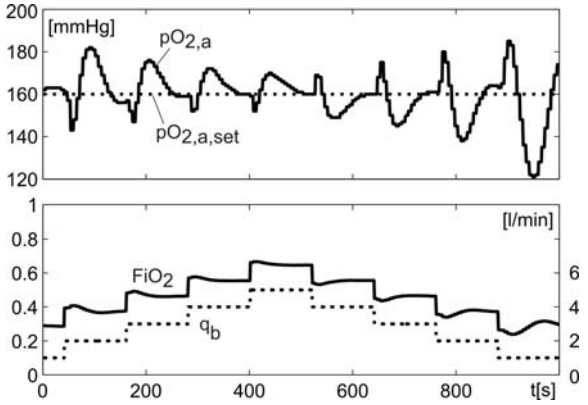

Fig. 1 Reaction to step-like changes of blood flow with nominal oxygenator performance.

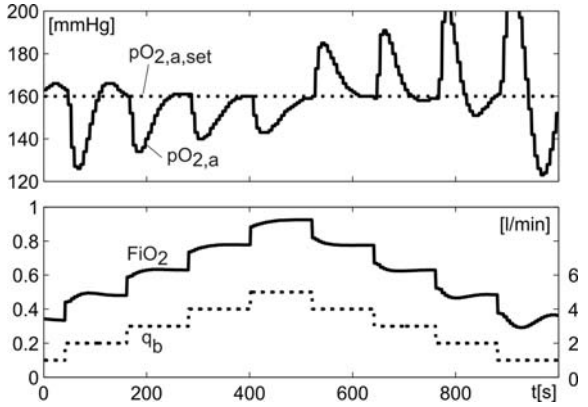

Fig. 2 Reaction to step-like changes of blood flow with degraded oxygenator performance.

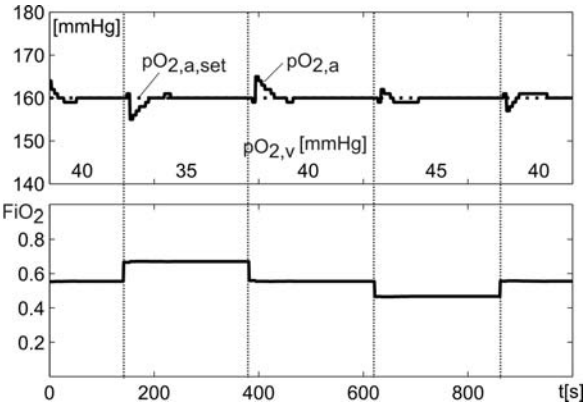

Fig. 3 Reaction to step-like changes of venous oxygen partial pressure $pO_{2,v}$ (nominal oxygenator performance, q_b = 4 l/min).