A Parameter Identification Approach towards Analyzing Hemodynamics based on Capnography

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Abstract

During cardiopulmonary resuscitation (CPR), end-tidal CO_2 ($etCO_2$) is often used as a surrogate parameter for systemic blood flow and a sudden rise in $etCO_2$ is regularly associated with a return of spontaneous circulation (ROSC). We model this transportation of metabolic CO_2 from the tissues via systemic perfusion to the lungs, and its exhalation through the alveoli, in a simple compartment-based ODE model. The aim is to determine a slowly time-dependent scalar describing the level of systemic perfusion based on tidal flow, airway pressure and capnography data in a multishooting parameter identification approach.

We test our model on synthetically generated data as well as on data from a porcine model of cardiac arrest. In the porcine model, we compare the estimated level of systemic perfusion with invasively measured mean arterial blood pressure as a surrogate of blood flow.

First experiments on both synthetic and real-world data show good identifiability for the level of systemic perfusion based on the capnography data.

A validated simple ODE model for CO_2-extraction during CPR could help to quantify the effects of tidal volumes and ventilation rates on $etCO_2$ and furthermore assist physicians to detect a ROSC more reliably during out-of-hospital cardiac arrest.

1. Introduction

Rapid and reliable detection of return of spontaneous circulation (ROSC) during cardiopulmonary resuscitation (CPR) is an important, but difficult task. While manual pulse palpation is time-consuming and poorly specific, a sudden rise in end-tidal CO_2 ($etCO_2$) is regularly associated with ROSC [1, 2] . Additionally, $etCO_2$ is commonly used as a surrogate parameter for systemic blood flow during clinical CPR, as metabolic CO_2 from the tissues is transported by the blood to the lungs and exhaled through the alveoli. Thus, increasing $etCO_2$ levels during CPR could indicate improved systemic perfusion, while decreasing $etCO_2$ levels might be caused by deteriorating of systemic perfusion [3]. But a number of variables such as tidal volume and ventilation rates, but also artefacts from chest compressions complicate the interpretation of measured $etCO_2$ [4]. Similarly, taking certain $etCO_2$ levels as ROSC predictor does not lead to consistent threshold values [5]. Moreover, to identify rising or falling $etCO_2$ levels, a trend in CO2 must be observed, which is possible only after at least some ventilations, allocating highly valuable time during a resuscitation attempt.

Lately, many research groups tried to investigate the capnogram during CPR with respect to chest compression artifacts and e.g. varying ventilation rates, on a phenomenological level [4,6]. In this work, we model CO_2 extraction during ventilation in a simple compartment based ODE model in order to account for the ventilation related confounding factors and to maximize the gain of information about the level of systemic blood flow given in the capnogram signal.

2. Methods and Models

2.1. Data Aquiration

Continuous experimental data was recorded in a porcine model of cardiac arrest. The experiment was approved by the Austrian Federal Ministry of Education, Science and Research. Ventilation pressure and tidal flow were recorded with 200 Hz sampling frequency , while capnography was recorded with 40 Hz sampling frequency. Invasive arterial, central venous and intracranial blood pressures were recorded with 50 Hz sample frequency. Af-

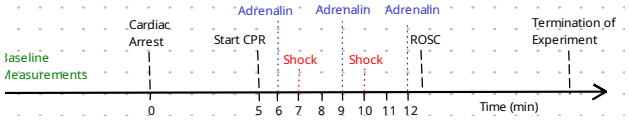

Figure 1. Schematical experimental design

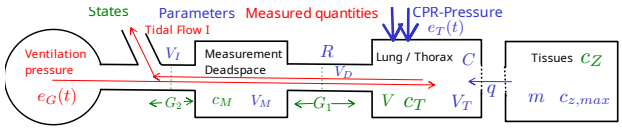

Figure 2. Schematic illustration of model structure.

ter baseline measurements and 5 minutes of cardiac arrest, chest compressions were performed using a mechanical compression device (LUCAS, Stryker Medical, Kalamazoo, MI) until a ROSC was achieved or CPR was terminated. The timestamps of the chest compressions were recorded by the compression device. Simultaneously to chest compressions, epinephrine and shocks were delivered in 3-minute intervals. Over the total span of the experiment mechanical ventilation was performed. The design of the experiment is also shown in Figure 1.

2.2. Model Development

We employ a simple compartment-based ODE-system to model the respiratory system and the CO_2-transport. This model does not aim to describe all processes occurring during CO_2 extraction in high detail, but to reflect the main qualities of the system in order to identify the level of systemic perfusion. Other physiological parameter like airway resistance or compliance are estimated simultaneously as well. The model consists of measurement compartment, a thorax compartment and a tissue compartment, and describes tidal flow and $CO2$ transport separately. It is schematically illustrated in Figure 2.

We model the airflow from the ventilation machine through measurement compartment to the thorax, influenced by ventilation pressure $e_g(t)$, compression pressure $e_t(t)$ as well as airway resistance R and lung compliance C by assuming laminar flow. The change of volume in thorax compartment $V(t) = V_T + \tilde{V}(t)$ is given by

$$\dot{\tilde{V}}(t) = \frac{\Delta p(t)}{R_t}, \text{ with } \Delta p(t) = \left(e_g(t) - e_T(t) - \tilde{V}(t)/C\right), \tag{1}$$

where we have decomposed the alveolar volume V in a constant part V_T and a variable part $\tilde{V}$. Since we assume the volume of the measurement compartment V_M constant, it does not contribute to this equation. While the airway pressure is included by interpolating measurements, the CPR pressure $e_T(t)$ will be modeled as a convolution of a unknown function p_{CPR} with delta-peaks at the recorded time of the compression instances. The unknown function p_{CPR} will be estimated based on the flow and CO_2 during the parameter identification process.

For modeling the CO_2 concentration in measurement, thorax and tissue compartment (c_M, c_T, and c_Z, respectively), we assume that CO_2 is generated at some rate m in the tissue by a factor $m(c_{z,max} - c_Z)$, where $c_{z,max}$ is a maximal possible CO_2 concentration. The CO_2 is transported to the alveoli by blood modeled by a term $q_t(c_Z - c_T)$, with q_t is the possibly slowly time varying level of systemic blood flow. For the alveolar and measurement compartment we model the CO_2 transport by assuming perfect mixing in each compartment and mass conservation for the CO_2 exchange. We include the anatomical and the instrumental deadspaces not via separate compartments, but model them as a fixed volume V_D and V_I with a movable concentration difference layer at position $G \in [0, 1]$, where $G = 0$ / $G = 1$ means that the deadspace is totally filled with air from the inner/outer compartment respectively. The total compartment volume is the sum of the proper compartment volume and the contributions from the adjacent deadspaces. The position of this layer in the deadspace moves with the direction of the tidal flow. Two smooth auxiliary functions $H_\pm : [0, 1] \mapsto [0, 1]$, for inflow $(+)$ and outflow $(-)$ which fulfill $H_+(1) = 1$ and $H_-(0) = 0$ describe the permeability of the layer for inward/outward flow respectively. This formulation of the deadspaces is capable to explain delays between a change in flow and a change in concentrations as well as CO_2 patterns during reversed airflow under the presence of chest compressions. In total, the concentration model is given by

$$\begin{aligned}
\dot{G}_1(t) =& \frac{1}{V_D R_t}\left(I_+(\Delta p)(1 - H_+(G_1)) - \right. \\
& \left. I_+(-\Delta p)(1 - H_-(G_1))\right) \\
\dot{G}_2(t) =& \frac{1}{V_I R_t}\left(I_+(\Delta p)(1 - H_+(G_2)) - \right. \\
& \left. I_+(-\Delta p)(1 - H_-(G_2))\right) \\
\dot{c}_M(t) =& \frac{-I_+(\Delta p)H_+(G_2)c_M(t)}{R_t\left(V_M + G_1 V_D + (1 - G_2)V_I\right)} + \\
& \frac{I_+(-\Delta p)H_-(G_1)(c_T(t) - c_M(t))}{R_t\left(V_M + G_1 V_D + (1 - G_2)V_I\right)} \\
\dot{c}_T(t) =& \frac{I_+(\Delta p)H_+(G_1)\left(c_M(t) - c_T(t)\right)}{R_t(V_T + \tilde{V}(t) + (1 - G_1)V_D)} + \\
& q_t(c_Z(t) - c_T(t)) \\
\dot{c}_Z(t) =& q_T\left(c_T(t) - c_Z(t)\right) + m\left(c_{z,max} - c_Z(t)\right),
\end{aligned} \tag{2}$$

with $I_+(x) = \max(0, x)$.

2.3. Parameter identification

We interpret the ODE-model (1), (2) as a function $\mathcal{G} : \mathbb{R}^{n_p+n_{States}} \mapsto \mathcal{C}^1([T_{start}, T_{end}], \mathbb{R}^6), \mathcal{G}(\theta, x_0) = x$ which maps a set of parameters θ and initial conditions x_0 to the solution of the ODE x on an interval $[T_{start}, T_{end}]$. Additionally, we define a measurement operator $\mathcal{M} : \mathcal{C}^1([T_{start}, T_{end}], \mathbb{R}^6), \mathcal{C}([T_{start}, T_{end}], \mathbb{R}^2)$,

$$\mathcal{M}\left(\left(V, G, G_2, c_M, c_T, c_Z\right)^T(t)\right) = \left(\frac{d}{dt}V(t), c_M(t)\right)^T$$

which describes the mapping from the states to the measured quantities flow and concentration in the measurement compartment. We choose the parameters q_t and R_t to be slowly varying in our model by describing them as a linear interpolation between grid points with distance 2 or 6 seconds, respectively. Thus, for given data d, we are looking for a vector of parameters θ and initial conditions x_0 which minimizes a functional $\mathcal{R}(\theta, x_0)$ consisting of the residua of Flow and concentration data, $\begin{pmatrix} r_{Flow} \\ r_{Conc} \end{pmatrix} = \mathcal{M}\mathcal{G}(\theta, x_0) - d$, between model output and data for flow and concentration measurement respectively, as well as regularization terms for q_t and R_t with regularization weights α_R, α_q and a weight α_C for the concentration term:

$$\begin{aligned}\mathcal{R}(\theta, x_0) =& ||r_{Flow}||_2^2 + \alpha_c||r_{Conc}||_2^2 + \\ & \alpha_q||\frac{d}{dt}q_t||_2^2 + \alpha_R||\frac{d}{dt}R_t||_2^2. \end{aligned} \tag{3}$$

We use a multishooting approach [7, 8] to identify the parameters. Thus, we solve the ODE system independently on several subintervals and try to estimate parameters and freely chooseable initial conditions for each subinterval. In order to ensure continuity of the total solution at the boundaries of the subintervals we add constraints to our functional $\mathcal{R}$ via augmented Lagrangian formulation. This leads to

$$\begin{aligned}\tilde{\mathcal{R}}(\theta, x_0) = & ||r_{Flow}||_2^2 + \alpha_c||r_{Conc}||_2^2 + \alpha_q||\frac{d}{dt}q_t||_2^2 + \\ & \alpha_R||\frac{d}{dt}R_t||_2^2 + \sum_{k=1}^{N_i}\sum_{j=1}^{n_{States}} \lambda_{jk}c(x_{jk}) + \mu c^2(x_{jk}) \end{aligned} \tag{4}$$

where $c(x_{jk}) = x_{j,k}^{(0)} - x_{j,k-1}^{(-1)}$ is the difference between initial condition of the j-th state in the k-th sub-interval and the estimated value of the j-th state in the $(k-1)$-th sub-interval at the same time.

We solve the minimization problem $\min_{\theta,x_0} \tilde{\mathcal{R}}(\theta, x_0)$ for given values of λ_{kj} and μ_{kj} via Levenberg-Marquardt Methods, where we compute the necessary Jacobians $\frac{\partial x}{\partial \theta}$ and $\frac{\partial x}{\partial x_0}$ by solving the adjoint equation. After having obtained an approximate minimizer, we update λ_{kj} and μ_{kj} according to [9].

Since a short sensitivity analysis shows that V_T, V_M and m are hardly identifiable in this problem, we set them to fixed values based on literature values or grid search. Thus, we estimate the following parameters: N_R parameters for R_t, C, V_D, V_I, $c_{z.max}$, N_q parameters for q_t, N_{CPR} parameters describing p_{CPR} and the initial conditions for each subinterval.

3. Results

We test our model on synthetically generated data of tidal flow, capnography, and ventilation pressure as well as on data from a porcine model of cardiac arrest. In the porcine model, we compare the estimated level of systemic perfusion with invasively measured mean arterial pressure, while on the synthetic data, the parameter estimation is compared to the known ground truth.

First experiments on both synthetic and real-world data show good identifiability for the level of systemic perfusion based on the capnography data. An exemplary result can be found in Figure 3. The other relevant parameters were identified to $C \approx 23.8\ \frac{\text{ml}}{\text{hPa}}$, $R_t \approx 18\frac{\text{hPa}}{\text{l/s}}$, $V_D = 99$ ml, $V_I \approx 10$ ml.

4. Discussion

Our proposed method uses the information contained in the capnogram and tidal flow signal to quantitatively determine changes in systemic blood flow without delays. It is able to predict the overall trend of MAP and cardiac output during an ongoing resuscitation attempt and also provides information on other respiratory parameters (dead spaces, resistance, compliance). However, there are some issues in the model and experimental design that need to be discussed.

First, the experimental setup and data we used are not able to fully illustrate the potential of this technique because ventilation rates and tidal volumes were nearly constant over large periods of time. However, in the real world, ventilation rates and tidal volumes are not necessarily constant, especially during manual ventilation, and could strongly influence the end-tidal CO2 concentration. The proposed method should work well in principle even under these conditions, but further experimental data are needed to demonstrate this. In addition, repeated administration of epinephrine during resuscitation in the current experimental setup affects vascular resistance and thus MAP but not necessarily cardiac output and systemic blood flow. Therefore, we may see deviations from our estimated level of systemic perfusion to MAP that may be

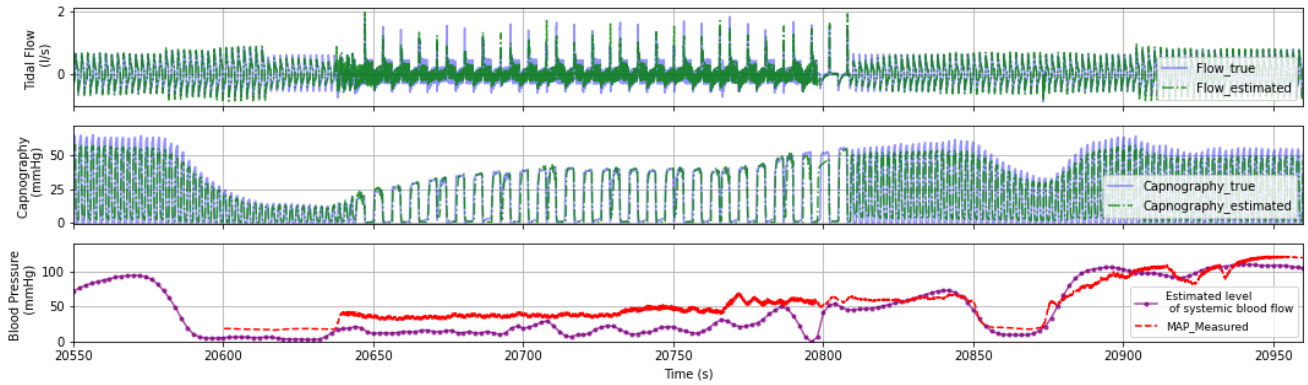

Figure 3. Exemplary situaion of systemic perfusion estimation. The level of systemic perfusion is scaled to the same scale as the measured arterial blood pressure.

explained by the documented epinephrine medication.

Furthermore, like any method purely based on capnography data, our model is not capbale to capture the influence of shunts and functional deadspaces exhaled CO_2, because the observed exhaled CO2 origins from parts of the lung which are perfused and ventilated. In presence of deadspaces and shunts, our estimated parameter q might be a bad surrogate for cardiac output. The comparison of the CO_2-concentration in the tissue-compartment c_Z with the arterial CO_2 pressure form blood gas analysis could help improve our model and subsequently, assist to monitor arterial CO_2 concentrations and identify shunts and deadspaces during a resuscitation attempt as well.

Finally, the knowledge of the tidal flow data and airway pressure is necessary to perform the proposed analysis, but these data could be recorded by new devices to monitor ventilation.

5. Conclusion

A validated simple ODE model for CO_2-extraction during CPR could help to quantify the effects of tidal volumes and ventilation rates on etCO_2 and furthermore assist physicians to detect a ROSC more reliably during out-of-hospital cardiac arrest. Further investigations are necessary to verify the proposed method.

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