Inverting the diffusion-convection equation for gas desorption through an homogeneous membrane by Kalman filtering

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***Abstract*— This paper presents a dynamic transport model of a gaseous compound such as carbon dioxide based on the diffusion-convection through a three layered media composed of: a liquid medium (blood), a membrane (skin), a gaseous medium (air). The objective is to estimate the signal defined by the time variations in the concentration of the gaseous compound dissolved in the liquid medium based solely on the measurement signal defined by the time variations of the concentration of the gaseous compound in the gaseous medium. This dynamic model makes it possible to formulate the direct transport model in the form of a Markovian model with hidden states in order to generate synthetic data. We propose to implement a Kalman filter to calculate from the noisy observed variables, the hidden variables of the model, and in particular the concentration of the gaseous compound in the liquid medium. The challenge is to model the temporal evolution of a concentration profile as a function of time and depth taking into account the heterogeneity of the diffusion coefficients and the partition coefficients associated with the three media considered. The objective of this time recursive processing is to design an algorithm, which can be carried out on an embedded processor, taking into account the constraints of limited computing capacity. The application we are dealing with concerns the transcutaneous measurement of blood carbon dioxide in the forearm using an autonomous wristband-type worn device, in particular for monitoring respiratory diseases at home*[1],[2].

Keywords*— *inverse convection-diffusion problems, space-state models, Kalman filter, desorption phenomena, skin transport, carbon dioxide gas, wireless wristband

I. Introduction

One of the main functions of the skin is to protect the body against the action of various external agents. The resistance against mechanical or chemical factors is given by the keratin cells that form the stratum corneum on the surface of the skin. This layer represents the first barrier and it opposes the greatest resistance to the absorption or desorption of solutes through the skin.

The transport process through the skin has been studied extensively due to the possibility of drug administration using transdermal patches. The phenomenon of penetration of a solute through the epidermis and the dermis is often studied for the local and systemic administration of drugs from the patch through the epidermis [3],[4],[5]. Mathematical models have been developed in order to adjust the proper local and systemic administration of drugs. One mathematical approach used is the resolution of the transport equation in the Laplace domain that provides a steady-state solution for the transport equation. One of the drawbacks of this method is the difficulty to go from the expression of the solution in the Laplace domain back to the time domain.

In this paper, we will model the process of convection-diffusion of gas molecules from the blood medium, through the skin tissues to the surface with the ambient air. The changes that occur in the blood, and, consequently, the concentrations measured at the surface of the skin fluctuate over time as they depend on the correct or insufficient ventilation of the individual, his pathology, possible chronic diseases, etc. The gas transport is described by a system of differential equations. To get the numerical solution to this system of differential transport equations, we introduce a discretisation based on a centred finite difference scheme. These schemes are known to have higher flexibility regarding the boundary conditions than finite or boundary element methods[5]. In this work, we especially focus on the interface continuity equations and the boundary conditions in a one-dimensional simplification. The dynamic model is then converted into a discrete state-space model, which allows the processing of noisy observations using its associated Kalman filter. Moreover, this will allow to get a recursive implementation on an embedded microcontroller and to estimate unknown concentrations in close to real time, as soon as new data is available.

In the second section, we will set-up the system of differential equations related to gas desorption with the associated boundary and interface conditions. In the third section, we will establish the link between this system of continuous differential equations and their implementation in a discrete scheme. We will consider equally spaced points on a spatial grid for each compartment. Differences between of the explicit and implicit solution for a time integration schema will be presented to take into account the conditions of inversion stability. In the fourth section, we will present the results of the inference of the hidden variables using a Kalman filter. In order to reduce the memory requirement, we will study how to minimize the number of points necessary for the spatial discretisation path with respect to borders condition and Péclet number. In the fifth section, we will formulate some conclusions and give perspectives for the continuation of this work.

II. Transport model

We will use the following conventions for our notations: continuous scalar fields, vector fields, and constants will be denoted by lightface characters. The space-time variable will

appear as arguments between parentheses. Discrete representations will be given using arguments between brackets; these quantities will appear in boldface lowercase characters when regrouped into a vector or boldface uppercase characters when regrouped into a matrix (linear operator).

A. *Transport equation*

Desorption phenomenon for gas compounds involves two physical transport mechanisms: convection and diffusion. The diffusion process is related to the Brownian motion of the particles and is characterized by a diffusion constant, which describes how far the substance travels on a mean free path through the medium per unit time. Convection process models the mean velocity of the particles as a consequence of transport by another medium (convection). Table I resumes the principal parameters and their units.

Table I. Definition of physical parameters used in this manuscript

Abbreviation	Parameter	SI Units
D	diffusion coefficient	m^2/s
u	flow velocity	m/s
H	Henry's partition constant	$adim$
C	concentration	mol/m^3
P	pressure	$mmHg$

The diffusion process is characteristic for the transport of molecules and it is present in all three media. The diffusion process is the one that has the greatest impact on transdermal transport, the mean velocity of molecules at this level being zero. The convection process within the liquid phase is due to the blood flow that provides and removes concentration in the areas of exchange. In the gaseous phase, the convection is produced by an air flow induced by a mechanical ventilation in order to prevent the accumulation of carbon dioxide at the surface of the skin and to speed-up the time-response of the device.

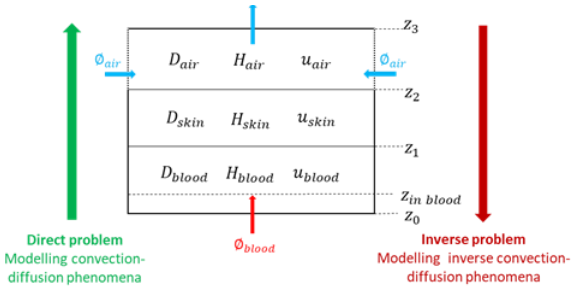

Fig.1. Direct and inverse transport model. The associated parameters for modelling transport phenomena through the three compartments are specified in Table I and their values in Table II.

Table II. Values of the physical parameters

	Blood	Skin	Air
D	$2.2 \cdot 10^{-5} cm^2/s$	$1.0 \cdot 10^{-7} cm^2/s$	$1.8 \cdot 10^{-1} cm^2/s$
H	$5.4 \cdot 10^{-1}$	1.6	1.0
u	$1.1 \cdot 10^{-1} cm/s$	0.0 cm/s	$1.0 \cdot 10^{-1} cm/s$
Δz	$3.0 \cdot 10^{-1}\ cm$	$1.6 \cdot 10^{-3}\ cm$	$3.0 \cdot 10^{-1}\ cm$
Δy	2.0 cm	2.0 cm	2.0 cm
Δx	5.0 cm	5.0 cm	5.0 cm

We consider the following convection-diffusion equation based on the mass conservation principle:

$$\frac{\partial C(z,t)}{\partial t} = -\frac{\partial}{\partial z}[u(z) \cdot C(z,t)] + \frac{\partial}{\partial z}\left[D(z) \cdot \frac{\partial}{\partial z} C(z,t)\right] \quad (1)$$

Where $C(z,t)$ is the solute concentration at position z and time t; $u(z)$ the velocity vector field of the solute; and $D(z)$ the scalar diffusion field.

Within the interior of each compartment, we assume the parameters u and D to be constant. Thus we derive from (1) the one-dimensional transport equation within the interior of each of the compartments of Fig. 1:

$$\frac{\partial C(z,t)}{\partial t} = -u\frac{\partial C(z,t)}{\partial z} + D\frac{\partial^2 C(z,t)}{\partial z^2} \quad (2)$$

B. *Boundary conditions*

To solve the transport equation Robin and Neumann boundary condition are imposed at the lower and upper boundary of the system as follows:

- Lower limit of the system: *zero flux*

$$uC(z,t) - D\frac{\partial C(z,t)}{\partial z}\Big|_{z=z_0} = 0 \quad (3)$$

For the transport direct model, the input CO_2concentration value $C_{CO_2}^{in\ blood} = 1.09\ mol/m^3$ is the average value (μ) of the concentration, which corresponds to a pressure $P_{CO_2}^{in\ blood} = 40\ mmHg$ in the blood. We consider here, there is neither convection, nor diffusion flux under $z = z_0$.

- Upper limit of the system: *interfacing with the outer world*. The derivative on the upper boundary of the system is set to be zero

$$\frac{\partial}{\partial z} C(z,t)|_{z=z_3} = 0 \quad (4)$$

C. *Interface conditions*

The transport equation in gas dynamics corresponds to the conservation of mass between different media within the two boundaries of the physical system. At the two interfaces, we impose the condition of flow continuity since the quantity of CO_2 which leaves from one medium is entering in the next one. The mass transfer occurs gradually as the gas compound diffuses. The subscripts minus and plus refer to the parameter values before and after the interface, respectively. Two interfaces are identified in the model, one at $z = z_1$ and another at $z = z_2$.

$$\lim_{\delta z \to 0+} u_- C_-(z - \delta z_-, t) - D_- \frac{\partial C_-(z-\delta z_-,t)}{\partial z} = \lim_{\delta z \to 0+} u_+ C_+(z + \delta z_+, t) - D_+ \frac{\partial C_+(z+\delta z_+,t)}{\partial z} \quad (5)$$

The subscript "$-$" designs the medium before the interface and the subscript "+" represents the medium after the interface. The diffusion process occurs in the direction of the pressure gradient, from the compartment with high concentration towards the one with low concentration of molecules. In this simplified version of the model, we assume there are neither sources nor sinks. Thus, there is a conservation of the total carbon dioxide mass.

The partial pressure P and the concentration C of a gas compound in a liquid medium are linked by Ostwald's solubility coefficient $\beta = 0.0275\ mol\ m^{-3} mmHg^{-1}$

$$C = \beta P \quad (6)$$

The adimensional Henry partition coefficient H_i of CO_2 is defined by the ratio of the solubility coefficient $\beta_{CO_2}^i$ of CO_2 in

the media i with respect to the solubility $\beta_{CO_2}^{air}$ of CO_2 in the air.

$$H_i = \frac{\beta_{CO_2}^{i}}{\beta_{CO_2}^{air}} \qquad (7)$$

Thus, we formulate the second interface condition, which ensures pressure continuity, as:

$$\lim_{\delta z \to 0+} \frac{C_-(z-\delta z,t)}{H_-} = \lim_{\delta z \to 0+} \frac{C_+(z+\delta z,t)}{H_+} \stackrel{\text{def}}{=} C_{-|+} \qquad (8)$$

where $C_{-|+}$ defines the equivalent concentration in the air at the interface.

III. Numerical Approach

For a homogeneous medium with diffusion constant D and stationary convection u over a segment $z \in [0; L]$, we rewrite the diffusion equation with dimensionless parameters $\xi = \frac{z}{L}$ and the Péclet number defined as $P_e \stackrel{\text{def}}{=} \frac{uL}{D}$. For the blood media $P_{e\,blood} \gg 1$ reveals that convection is the principal transport mechanism compared to diffusion while in the ambient air, $P_{e\,air} < 1$, diffusion dominates convection.

In discretised time and space (uniform sampling), the transport equation within a homogeneous compartment and without source or sink can be written (after some manipulations and invoking the mean-value theorem) for some $\tau \in [t, t+\delta t]$ as

$$C[z,t+\delta t] - C[z,t] = D^{\delta}\left\{\left(1+\frac{P_e^{\delta}}{2}\right)C[z-\delta z,\tau] - 2C[z,\tau] + \left(1-\frac{P_e^{\delta}}{2}\right)C[z+\delta z,\tau]\right\} \qquad (9)$$

where we wrote $D^{\delta} \stackrel{\text{def}}{=} \frac{D\,\delta t}{(\delta z)^2}$ and $P_e^{\delta} \stackrel{\text{def}}{=} P_e \frac{\delta z}{L} = \frac{u\,\delta z}{D}$.

The derivatives in the boundary conditions are implemented by extending the spatial grid through reflection about $z = z_0$ and $z = z_3$ and solving for the unknown concentrations using the discretised differential equations given by the boundary conditions of section II.B. At the interfaces, one-sided differences are taken and slack variables $C_{blood|skin}$ and $C_{skin|col}$ are introduced according to (8). These two variables are then eliminated from the system through substitution, allowing to define the convection-diffusion continuity equations across the interface boundaries. The discretised spatial differential operators are then gathered in a matrix $\boldsymbol{F}$ acting on the concentration vector $\boldsymbol{c}[\tau]$.

The link with the temporal finite differences is done by using $\tau = t$ in (9) for an explicit Euler scheme, or $\tau = t + \delta t$ for the implicit scheme, yielding the matrix expression:

$$\boldsymbol{c}[t+\delta t] - \boldsymbol{c}[t] = \delta t\, \boldsymbol{F}\boldsymbol{c}[\tau] \qquad (10)$$

with δt the time between two successive sample points (sample period).$\boldsymbol{c}[t]$ is the state vector

$$[c(1,t), \ldots, c(i,t), \ldots, c(N,t)] \qquad (11)$$

where N is the total number of points considered to discretize the continuous spatial space and $c(i,t)$ is the concentration corresponding to the point i on the spatial mesh at time t. An important aspect when choosing one of Euler's integration schemes is inspecting the stability condition for the discrete-time model.

$$|1 + \lambda_F \cdot \delta t\,| \le 1 \Leftrightarrow -2 \le \lambda_F \cdot \delta t \le 0 \qquad (12)$$

Where λ_F are the eigenvalues of the discretised linear operator $\boldsymbol{F}$. Due to the fact that $|\lambda_{F,\max}| \cong 10^3$, it is required that $\delta t < 0.002$ to ensure convergence. This implies having a high sampling rate, around 500 samples/s (100 times more than the actual time step). For the implicit scheme the stability condition is:

$$|1 - \lambda_F \cdot \delta t\,|^{-1} \le 1 \qquad (13)$$

The above equation is always true, since for our operator $\lambda_F < 0$. Consequently, we choose the implicit scheme, which is unconditionally stable. Unfortunately, this comes with an additional computational load, since we need to solve a linear band-diagonal system for $\boldsymbol{c}[t+\delta t]$, i.e.,

$$(\boldsymbol{I} - \boldsymbol{F})\boldsymbol{c}[t+\delta t] = \boldsymbol{A}\,\boldsymbol{c}[t+\delta t] = \boldsymbol{c}[t] \qquad (14)$$

Where $\boldsymbol{I}$ represents the identity matrix of appropriate dimensions.

IV. Results

We are presenting here our stationary solution corresponding to an eigenvalue 1. This solution respects our conditions at the borders and for the two interfaces. Every solution to our convection-diffusion problem is supposed to be proportional to this solution when $t \to \infty$ in absence of any perturbation.

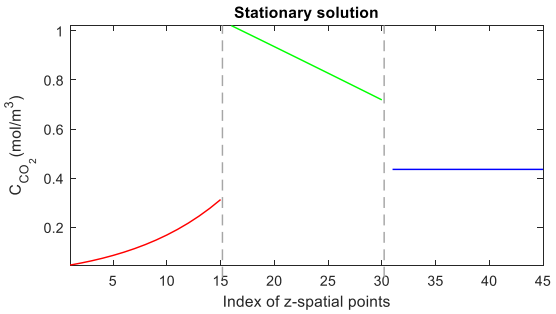

Fig.2. Stationary solution for 45 z-spatial points considered for the direct transport problem, space is not proportional to the sample distances from one medium to another (red: blood, green: skin, blue: air)

A. Numerical protocol for direct transport process

Synthetic data is generated using a signal model based on a recursive relation between a sample at instant $t + \delta t$ an the previous sample at time t.

$$\boldsymbol{A}\boldsymbol{c}[t+\delta t] = \boldsymbol{c}[t] + \boldsymbol{G}\boldsymbol{q}[t+\delta t] \qquad (15)$$

$\boldsymbol{A}$ is the implicit transition matrix (incorporating the boundary conditions), that is defined as indicated in (16):

$$\boldsymbol{A} = \boldsymbol{I} - \boldsymbol{F} \cdot \delta t \qquad (16)$$

The state vector$\boldsymbol{c}$ is initialized with the stationary solution.

$\boldsymbol{G}$ the control matrix and $\boldsymbol{q}$ the vector containing the exogenous input (boundary conditions or known concentration rate).

The term $\boldsymbol{G}\boldsymbol{q}$ contains the initial vector concentration in the liquid phase that is injected in the system. This term portrays the variations around the average value of CO_2 concentration (μ) in the liquid phase: a level of hypercapnia and hypocapnia ($\mu \pm 0.27\ mol/m^{-3}$). It represents a compensatory source by keeping in the chosen point the same value of concentration than the one provided by the blood flow.

In the framework of Markov model, one attempts to explain the behaviour of the physical system using just the previous sample in order to predict the actual one for each of the hierarchical layers determined by the spatial sampling. As we suppose a completely known signal model, we generate noiseless data. In order to simulate real recordings of transcutaneous pressure of CO_2, we are going to add a quantity of white Gaussian noise to the observed output. This will be used as the noisy input for the inversion of the transport model. We have to make sure that adding the magnitude of a random variable to the signal of interest the concentration will remain positive.

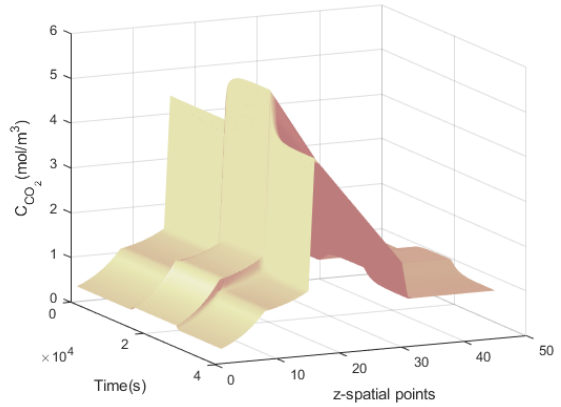

Fig.3. Synthetic data generated with 45 spatial points for the direct transport model. Temporal sampling at 1 point every 10 seconds.

We simulate from 0 to 15000 s and for 25000 s to 40000 s a normocapnia level corresponding to a concentration of 1.09 mol/m^3 and from 15000 s to 25000 s an hypercapnia level of 1.36 mol/m^3. We are discretising the spatial space using 45 sample points in total: 15 equispaced points per medium.

To reduce the computational load for the inversion of the transport process, we will choose our spatial sampling points to be the most parsimonious possible, yielding a good approximate solution.

B. Inverse transport process.

By contrast with the direct deterministic model, we are choosing for the inverse transport process a probabilistic framework in order to study the system dynamics. We propose to use a discrete state space model, since we have a set of time-varying variables that are embedded in noise. Our objective is to infer recursively the CO_2 concentration in the liquid phase, as the measurements in the gaseous phase are progressively recorded. Except for the observations, all concentrations corresponding to the points on the spatial mesh are hidden variables of the system. In this context, a suitable tool is the Kalman filter to estimate the state variables. We consider the vector state equation derived from the physical system laws and the scalar observation equation:

$$\boldsymbol{Ac}[t+\delta t] = \boldsymbol{c}[t] + \boldsymbol{Gq}[t+\delta t] + w[t+\delta t] \qquad (17)$$

$$\tilde{c}[t] = \boldsymbol{h^t} c[t] + v[t] \qquad (18)$$

where $w[t+\delta t] \sim \mathcal{N}(0, \delta t\, \sigma_w^2)$ is the noise process that integrates the errors related to the model and $v[t] \sim \mathcal{N}(0, \delta t\, \sigma_v^2)$ describes the inaccuracies of sensor outputs as measurements are taken. We assume that w and v are independent. $\boldsymbol{h^t} = [0,0,\ldots,1]$ is the observation vector collecting measurements in the gaseous phase. The state vector $\boldsymbol{c}[t]$ contains the corresponding concentrations for different locations, as defined in equation (11). The state vector is initialized with the stationary solution given by the eigenvector of the operator $\boldsymbol{F}$ of which all entries have the same sign (corresponding to the largest eigenvalue, i.e., ideally $\lambda_{\boldsymbol{F},i} = 0$) [6],[7].

As input, we will take the measurement signal generated in the way described in the previous section: 15 equispaced spatial points within a medium – 45 sample points in total – for the direct transport model. To get a concentration signal that is closer to what we obtain in the reality we will add a noise variance $\sigma^2{}_{meas} = 10^{-3}\ (mol/m^{-3})^2$ (light blue signal in figure 4).

For the inference problem, we choose a noise variance equivalent to $\sigma_w^2 = 10^{-10}\,(mol/m^{-3})^2$ for the model noise and $\sigma_v^2 = 10^{-8}(mol/m^{-3})^2$ for the measurement noise.

We are interested in choosing a number of points for spatial sampling as small as possible to reduce the computation on the microprocessor of the device. As such, we select a number of 15 points allocating 5 points to each media. Each concentration signal in the figure 5 corresponds to the concentration in a point chosen within one of three media.

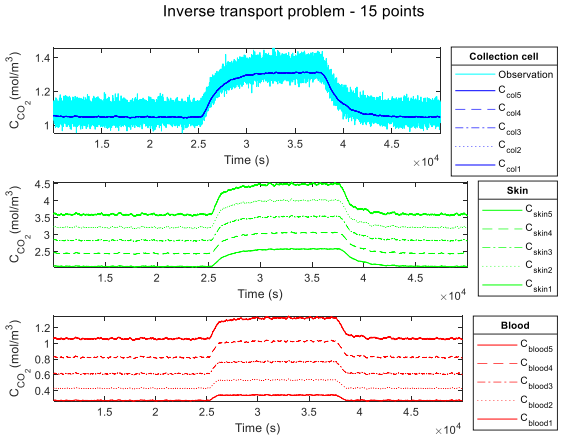

Fig.5. Inferring blood concentration starting from the noisy observation generated by the direct transport model using a grid of 15 samples points

The root mean square error $RMSE$ between the true and estimated blood concentration is 0.0041 mol/m^3. The $RMSE$ is calculated from $10^{4\text{th}}$ sample point to avoid disturbances due to filter adjustment. The hypercapnia level of estimated concentration $\tilde{C}_{blood\ 1}$: $\tilde{\mu}_{hypercapnia} = 0.3378\ mol/m^3$.

V. Discussion

We are studying the impact of the model process noise on the $RMSE$, keeping the same value for the measurement process noise. The $RMSE$ is computed between the variation in concentration obtained for the direct problem (using 45 spatial points) and the one estimated by the Kalman filter (using 9 spatial points). We maintain the variance of the measurement process noise to $10^{-8}\,(mol/m^3)^2$ - a mean absolute amplitude of $10^{-4}\ (mol/m^3)^2$ (we recall that this noise is considered in equation (17) and gives the measurement noise covariance matrix used for the algorithm

implementation of Kalman filter) and we are varying the variance of model noise between $[10^{-10}, 10^{0}]$ $(mol/m^3)^2$.

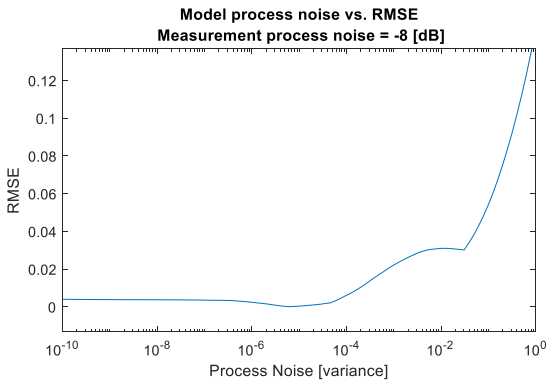

Fig.4 Root mean square error function of the quantity of noise injected on the model given the power of measurement noise process

Figure 4 shows: a minimum of RMSE around $10^{-5}(mol/m^3)^2$ and for a variance higher than 10^{-4} $(mol/m^3)^2$ an increase in the $RMSE$ estimated between the input concentration in the direct transport model and the related signal concentration in the inverse problem. Even if the $RMSE$ around 10^{-5} $(mol/m^3)^2$ is minimized, the inversion of transport process does not permit an accurate estimation of the blood concentration. The signal to be estimated is hidden within the noise and it is impossible to track variations in blood concentration. Within the interval $[10^{-10}, 10^{-8}]$ $(mol/m^3)^2$ the variations of CO_2 blood concentration can be tracked.

Keeping the same values for noise processes, we are still searching to diminish the number of spatial points on the z-grid as follows:

Table III. Performance parameters ($\tilde{\mu}_{hypercapnia}$ and $RMSE$) for the estimation of CO_2 blood concentration for a different number of z – spatial points

Number of z-spatial points			$\tilde{\mu}_{hypercapnia}$ (mol/m^3)	$RMSE$ (mol/m^3)
Blood	Skin	Air		
5	5	4	0.3387	0.0041
5	4	4	0.3388	0.0041
4	4	4	0.3762	0.0040
4	4	3	0.3782	0.0040
4	3	3	0.3784	0.0040
3	3	3	0.3789	0.0039

We can observe that when a smaller number of points for the inversion problem is used than for the direct problem, the level of estimated concentration $\tilde{C}_{blood\,1}$ is smaller than the level introduced for the direct problem.

VI. Conclusions and Perspectives

In this paper, we have presented a method for the inversion of convection-diffusion equation using the algorithm proposed by Kalman. In this innovative model, we take care of both the convection associated with the blood flow in the blood compartment and with the convective air flow in the air compartment, and the diffusion phenomena in each compartment. The synthetic data were generated using a Markovian model, the system being completely described by the physical laws. The continuous system of equations is discretised using a centred difference method. A Kalman filter was proposed in order to estimate the hidden variables and infer blood concentration of the gas compound. We have shown that the quantity of noise on the model has an impact upon the estimation: a smaller variance for the model noise does permit to follow the measurement. Contrary, if the model noise value would be higher or zero, the inference would completely depend on our model and the variations recorded at the skin surface are no longer followed. Regarding the bias between real levels and those estimated, there is a compromise between noise variance and signal variance introduced by the algorithm of Kalman proposed for the inversion of the problem. Also there is a compromise between choosing a small number of points to reduce the computational time and the precision on the amount of concentration estimated. A transcutaneous device for the measurement of a gas compound pursue the variations in concentration. The method proposed here is adequate to track that type of changes, even if a quantitative estimator was not obtained so far.

In the near future, we attempt to develop a more accurate transport model derived for the 2D transport convection-diffusion equation. This model is supposed to better describe the physics for gas desorption phenomena . A validation of this method is expected to be performed on the experimental data.

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