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# Stochastic Differential Equations With Applications to Biomedical Signal Processing

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## 1. Introduction

Dynamic behavior of biological systems is often governed by complex physiological processes that are inherently stochastic. Therefore most physiological signals belong to the group of stochastic signals for which it is impossible to predict an exact future value even if we know its entire past history. That is there is always an aspect of a signal that is inherently random i.e. unknown. Commonly used biomedical signal processing techniques often assume that observed parameters and variables are deterministic in nature and model randomness through so called observation errors which do not influence the stochastic nature of underlying processes (e.g., metabolism, molecular kinetics, etc.). An alternative approach would be based on the assumption that the governing mechanisms are subject to instantaneous changes on a certain time scale. As an example fluctuations in the respiratory rate and/or concentration of oxygen (or equivalently partial pressures) in various compartments is strongly affected by a metabolic rate, which is inherently stochastic and therefore is not a smooth process.

As a consequence one of the mathematical techniques that is quickly assuming an important role in modeling of biological signals is stochastic differential equations (SDE) modeling. These models are natural extensions of classic deterministic models and corresponding ordinary differential equations. In this chapter we will present computational framework necessary for successful application of SDE models to actual biomedical signals. To accomplish this task we will first start with mathematical theory behind SDE models. These models are used extensively in various fields such as financial engineering, population dynamics, hydrology, etc.

Unfortunately, most of the literature about stochastic differential equations seems to place a large emphasis on rigor and completeness using strict mathematical formalism that may look intimidating to non-experts. In this chapter we will attempt to present answer to the following questions: in what situations the stochastic differential models may be applicable, what are the essential characteristics of these models, and what are some possible tools that can be used in solving them. We will first introduce mathematical theory necessary for understanding SDEs.

Next, we will discuss both univariate and multivariate SDEs and discuss the corresponding computational issues. We will start with introducing the concept of stochastic integrals and illustrate the solution process using one univariate and one multivariate example. To address the computational complexity in realistic biomedical signal models we will further discuss the aforementioned biochemical transport model and derive the stochastic integral solution

for demonstration purposes. We will also present analytical solution based on Fokker-Planck equation, which establishes link between partial differential equation (PDE) and stochastic processes. Our most recent work includes results for realistic boundaries and will be presented in the context of drug delivery modeling i.e. biochemical transport and respiratory signal analysis and prediction in neonates.

Since in many clinical and academic applications researchers are interested in obtaining better estimates of physiological parameters using experimental data we will illustrate the inverse approach based on SDEs in which the unknown parameters are estimated. To address this issue we will present maximum likelihood estimator of the unknown parameters in our SDE models. Finally, in the last subsection of the chapter we will present SDE models for monitoring and predicting respiratory signals (oxygen partial pressures) using a data set of 200 patients obtained in Neonatal ICU, McMaster Hospital. We will illustrate the application of SDEs through the following steps: identification of physiological parameters, proposition of a suitable SDE model, solution of the corresponding SDE, and finally estimation of unknown parameters and respiratory signal prediction and tracking.

In many cases biomedical engineers are exposed to real-world problems while signal processors have abundance of signal processing techniques that are often not utilized in the most optimal way. In this chapter we hope to merge these two worlds and provide average reader from the biomedical engineering field with skills that will enable him to identify if the SDE models are truly applicable to real-world problems they are encountering.

## 2. Basic Mathematical Notions

In most cases stochastic differential equations can be viewed as a generalization of ordinary differential equations in which some coefficients of a differential equation are random in nature. Ordinary differential equations are commonly used tool for modeling biological systems as a relationship between a function of interest, say bacterial population size  $N(t)$  and its derivatives and a forcing, controlling function  $F(t)$  (drift, reaction, etc.). In that sense an ordinary differential equations can be viewed as model which relates the current value of  $N(t)$  by adding and/or subtracting current and past values of  $F(t)$  and current values of  $N(t)$ . In the simplest form the above statement can be represented mathematically as

$$\frac{dN(t)}{dt} \approx \frac{N(t) - N(t - \Delta t)}{\Delta t} = \alpha(t)N(t) + \beta(t)F(t) \quad N(0) = N_0 \quad (1)$$

where  $N(t)$  is the size of population,  $\alpha(t)$  is the relative rate of growth,  $\beta(t)$  is the damping coefficient, and  $F(t)$  is the reaction force.

In a general case it might happen that  $\alpha(t)$  is not completely known but subject to some random environmental effects (as well as  $\beta(t)$ ) in which case  $\alpha(t)$  is not completely known but is given by

$$\alpha(t) = r(t) + \text{noise} \quad (2)$$

where we do not know the exact value of the noise norm nor we can predict it using its probability distribution function (which is in general assumed to be either known or known up to a set of unknown parameters). The main question is then how do we solve it?

Before answering that question we first assert that the above equation can be applied in variety of applications. As an example an ordinary differential equation corresponding to RLC circuit

is given by

$$L * Q''(t) + RQ'(t) + \frac{1}{C}Q(t) = U(t) \quad (3)$$

where  $L$  is the inductance,  $R$  is resistance,  $C$  is capacitance,  $Q$  is the charge on capacitor, and  $U(t)$  is the voltage source connected in a circuit. In some cases the circuit elements may have both deterministic and random part, i.e., noise (e.g. due to temperature variations).

Finally, the most famous example of a stochastic process is Brownian motion observed for the first time by Scottish botanist Robert Brown in 1828. He observed that particles of pollen grain suspend in liquid performed an irregular motion consisting of somewhat "random" jumps i.e. suddenly changing positions. This motion was later explained by the random collisions of pollen with particles of liquid. The mathematical description of such process can be derived starting from

$$\frac{dX}{dt} = b(t, X_t)dt + \sigma(t, X_t)d\Omega_t \quad (4)$$

where  $X(t)$  is the stochastic process corresponding to the location of the particle,  $b$  is a drift and  $\sigma$  is the "variance" of the jumps. The locNote that (4) is completely equivalent to (1) except that in this case the stochastic process corresponds to the *location* and not to the population count. Based on many situations in engineering the desirable properties of random process  $\Omega_t$  are

- at different times  $t_i$  and  $t_j$  the random variables  $\Omega_i$  and  $\Omega_j$  are independent
- Stochastic process  $\Omega_t$  is stationary i.e., the joint probability density function of  $(\Omega_i, \Omega_{i+1}, \dots, \Omega_{i+k})$  does not depend on  $t_i$ .

However it turns out that there does not exist reasonable stochastic process satisfying all the requirements (25). As a consequence the above model is often rewritten in a different form which allows proper construction. First we start with a finite difference version of (4) at times  $t_1, \dots, t_{k_1}, t_k, t_{k+1}, \dots$  yielding

$$X_{k+1} - X_k = b_k * \Delta t + \sigma_k \Omega_k * \Delta t \quad (5)$$

where

$$\begin{aligned} b_k &= b(t_k, X_k) \\ \sigma_k &= \sigma(t_k, X_k) \end{aligned} \quad (6)$$

We replace  $\Omega_k$  with  $\Delta W_k = \Omega_k \Delta t_k = W_{k+1} - W_k$  where  $W_k$  is a stochastic process with stationary independent increments with zero mean. It turns out that the only such process with continuous paths is Brownian motion in which the increments at arbitrary time  $t$  are zero-mean and independent (1). Using (2) we obtain the following solution

$$X_k = X_0 + \sum_{j=0}^{k-1} b_j \Delta t_j + \sum_{j=0}^{k-1} \sigma_j \Delta W_j \quad (7)$$

When  $\Delta t_j \rightarrow 0$  it can be shown (25) that the expression on the right hand side of (7) exists and thus the above equation can be written in its integral form as

$$X_t = X_0 + \int_0^t b(s, X_s)ds + \int_0^t \sigma(s, X_s)dW_s \quad (8)$$

Obviously the questionable part of such definition is existence of integral  $\int_0^t \sigma(s, X_s) dW_s$  which involves integration of a stochastic process. If the diffusion function is continuous and non-anticipative, i.e., does not depend on future, the above integral exists in a sense that finite sums

$$\sum_{l=0}^{n-1} \sigma_l [W_{i+1} - W_i] \quad (9)$$

converge in a mean square to "some" random variable that we call the Ito integral. For more detailed analysis of the properties a reader is referred to (25).

Now let us illustrate some possible solution of the stochastic differential equations using univariate and multivariate examples.

**Case 1 - Population Growth:** Consider again a population growth problem in which  $N_0$  subjects of interests are entered into an environment in which the growth of population occurs with rate  $\alpha(t)$  and let us assume that the rate can be modeled as

$$\alpha(t) = r(t) + aW_t \quad (10)$$

where  $W_t$  is zero-mean white noise and  $a$  is a constant. For illustrational purposes we will assume that the deterministic part of the growth rate is fixed i.e.,  $r(t) = r = \text{const}$ . The stochastic differential equation then becomes

$$dN(t) = rN(t) + aN(t)dW(t) \quad (11)$$

or

$$\frac{dN(t)}{N(t)} = rdt + adW(t) \quad (12)$$

Hence

$$\int_0^t \frac{dN(s)}{N(s)} = rt + aW_t \quad (\text{assuming } B_0 = 0) \quad (13)$$

The above integral represents an example of stochastic integral and in order to solve it we need to introduce the inverse operator i.e., stochastic (or Ito) differential. In order to do this we first assert that

$$\Delta(W_k^2) = W_k^2 + 1 - W_k^2 = (W_{k+1} - W_k)^2 + 2W_k(W_{k+1} - W_k) = (\Delta W_k)^2 + 2W_k\Delta W_k \quad (14)$$

and thus

$$\sum B_k \Delta W_k = \frac{1}{2} W_k^2 - \frac{1}{2} \sum (\Delta W_k)^2 \quad (15)$$

which yields under regularity conditions

$$\int_0^t W_s dW_s = \frac{1}{2} W_t^2 - \frac{1}{2} t \quad (16)$$

As a consequence the stochastic integrals do not behave like ordinary integrals and thus a special care has to be taken when evaluating integrals. Using (16) it can be shown (25) for a stochastic process  $X_t$  given by

$$dX_t = udt + vdW_t \quad (17)$$

and a twice continuously differentiable function  $g(t, x)$  a new process

$$Y_t = g(t, X_t) \quad (18)$$

is a stochastic process given by

$$dY_t = \frac{\partial g}{\partial t}(t, X_t)dt + \frac{\partial g}{\partial x}(t, X_t)dX_t + \frac{1}{2} \frac{\partial^2 g}{\partial x^2}(t, X_t) \cdot (dX_t)^2 \quad (19)$$

where  $(dX_t)^2 = (dX_t) \cdot (dX_t)$  is computed according to the rules

$$dt \cdot dt = dt \cdot dW_t = dW_t \cdot dt = 0, \quad dW_t \cdot dW_t = dt \quad (20)$$

The solution of our problem then simply becomes, using map  $g(x, t) = \ln x$

$$\frac{dN_t}{N_t} = d(\ln N_t) + \frac{1}{2} a^2 dt \quad (21)$$

or equivalently

$$N_t = N_0 \exp \left( \left( r - \frac{1}{2} a^2 \right) t + a W_t \right) \quad (22)$$

**Case 2 - Multivariate Case** Let us consider  $n$ -dimensional problem with following stochastic processes  $X_1, \dots, X_n$  given by

$$\begin{aligned} dX_1 &= u_1 dt + v_{11} dW_1 + \dots + v_{1m} dW_m \\ &\vdots \\ dX_n &= u_n dt + v_{n1} dW_1 + \dots + v_{nm} dW_m \end{aligned} \quad (23)$$

Following the proof for univariate case it can be shown (25) that for a  $n$ -dimensional stochastic process  $\vec{X}(t)$  and mapping function  $\vec{g}(t, \vec{x})$  a stochastic process  $\vec{Y}(t) = \vec{g}(t, \vec{X}(t))$  such that

$$d\vec{Y}_k = \frac{\partial g_k}{\partial t}(t, \vec{X})dt + \sum_i \frac{\partial g_k}{\partial x_i}(t, \vec{X})dX_i + \frac{1}{2} \sum_{i,j} \frac{\partial^2 g_k}{\partial x_i \partial x_j}(t, \vec{X})dX_i dX_j \quad (24)$$

In order to obtain the solution for the above process we first rewrite it in a matrix form

$$d\vec{X}_t = \vec{r}_t dt + V d\vec{B}_t \quad (25)$$

Following the same approach as in Case 1 it can be shown that

$$\vec{X}_t - \vec{X}_0 = \int_0^t \vec{r}(s) ds + \int_0^t V d\vec{B}_s \quad (26)$$

Consequently the solution is given by

$$\vec{X}(t) = \vec{X}(0) + V \vec{B}_t + \int_0^t [\vec{r}(s) + V \vec{B}(s)] ds \quad (27)$$

**Case 3 - Solving SDEs Using Fokker-Planck Equation:** Let  $X(t)$  be an on-dimensional stochastic process and let  $\dots > t_{i-1} > t_i > t_{i+1} > \dots$ . Let  $P(X_i, t_i; X_{i+1}, t_{i+1})$  denote a joint probability density function and let  $P(X_i, t_i | X_{i+1}, t_{i+1})$  denote conditional (or transitional) probability density function. Furthermore for a given SDE the process  $X(t)$  will be

Markov if the jumps are uncorrelated i.e.,  $W_i$  and  $W_{i+k}$  are uncorrelated. In this case the transitional density function depends only on the previous value i.e.

$$P(X_i, t_i | X_{i-1}, t_{i-1}; X_{i-2}, t_{i-2}; \dots, X_1, t_1) = P(X_i, t_i | X_{i-1}, t_{i-1}) \quad (28)$$

For a given stochastic differential equation

$$dX_t = b_t dt + \sigma_t dW_t \quad (29)$$

the transitional probabilities are given by stochastic integrals

$$P(X_{t+\Delta t}, t + \Delta t | X(t), t) = \Pr \left[ \int_t^{t+\Delta t} dX_s = X(t + \Delta t) - X(t) \right] \quad (30)$$

In (3) the authors derived the Fokker-Planck equation, a partial differential equation for the time evolution of the transition probability density function and showed that the time evolution of the probability density function is given by

### 3. Modeling Biochemical Transport Using Stochastic Differential Equations

In this section we illustrate an SDE model that can deal with arbitrary boundaries using stochastic models for diffusion of particles. Such models are becoming subject of considerable research interest in drug delivery applications (4). As a preliminary attempt, we focus on the nature of the boundaries (i.e. their reflective and absorbing properties). The extension to realistic geometry is straight forward since it can be dealt with using Finite Element Method. Absorbing and reflecting boundaries are often encountered in realistic problems such as drug delivery where the organ surfaces represent reflecting/absorbing boundaries for the dispersion of drug particles (11).

Let us assume that at arbitrary time  $t_0$  we introduce  $n_0$  (or equivalently concentration  $c_0$ ) particles in an open domain environment at location  $r_0$ . When the number of particles is large macroscopic approach corresponding to the Fick's law of diffusion is adequate for modeling the transport phenomena. However, to model the motion of the particles when their number is small a microscopic approach corresponding to stochastic differential equations (SDE) is required.

As before, the SDE process for the transport of particle in an open environment is given by

$$dX_t = \vec{b}(X_t, t)dt + \sigma(X_t, t)dW_t \quad (31)$$

where  $X_t$  is the location and  $W_t$  is a standard Wiener process. The function  $\mu(X_t, t)$  is referred to as the drift coefficient while  $\sigma()$  is called the diffusion coefficient such that in a small time interval of length  $dt$  the stochastic process  $X_t$  changes its value by an amount that is normally distributed with expectation  $\mu(X_t, t)dt$  and variance  $\sigma^2(X_t, t)dt$  and is independent of the past behavior of the process. In the presence of boundaries (absorbing and/or reflecting), the particle will be absorbed when hitting the absorbing boundary and its displacement remains constant (i.e.  $dX_t = 0$ ). On the other hand, when hitting a reflecting boundary the new displacement over a small time step  $\tau$ , assuming elastic collision, is given by

$$dX_t = dX_{t1} + |dX_{t2}| \cdot \hat{r}_R \quad (32)$$



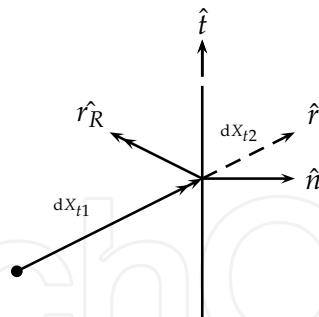


Fig. 1. Behavior of  $dX_t$  near a reflecting boundary.

where  $\hat{r}_R = -(\hat{r} \cdot \hat{n})\hat{n} + (\hat{r} \cdot \hat{t})\hat{t}$ ,  $dX_{t1}$  and  $dX_{t2}$  are shown in Fig. (1).

Assuming three-dimensional environment  $\mathbf{r} = (x_1, x_2, x_3)$ , the probability density function of one particle occupying space around  $\mathbf{r}$  at time  $t$  is given by solution to the Fokker-Planck equation (10)

$$\frac{\partial f(\mathbf{r}, t)}{\partial t} = \left[ - \sum_{i=1}^3 \frac{\partial}{\partial x_i} D_i^1(\mathbf{r}) + \sum_{i=1}^3 \sum_{j=1}^3 \frac{\partial^2}{\partial x_i \partial x_j} D_{ij}^2(\mathbf{r}) \right] f(\mathbf{r}, t) \quad (33)$$

where partial derivatives apply the multiplication of  $D$  and  $f(\mathbf{r}, t)$ ,  $D^1$  is the drift vector and  $D^2$  is the diffusion tensor given by

$$\begin{aligned} D_i^1 &= \mu \\ D_{ij}^2 &= \frac{1}{2} \sum_l \sigma_{il} \sigma_{lj}^T \end{aligned} \quad (34)$$

In the case of homogeneous and isotropic infinite two-dimensional (2D) space (i.e, the domain of interest is much larger than the diffusion velocity) with the absence of the drift, the solution of Eq. (33) along with the initial condition at  $t = t_0$  is given by

$$f(\mathbf{r}, t_0) = \delta(\mathbf{r} - \mathbf{r}_0) \quad (35)$$

$$f(\mathbf{r}, t) = \frac{1}{4\pi D(t - t_0)} e^{-\|\mathbf{r} - \mathbf{r}_0\|^2 / 4D(t - t_0)} \quad (36)$$

where  $D$  is the coefficient of diffusivity.

For the bounded domain, Eq. (33) can be easily solved numerically using a Finite Element Method with the initial condition in Eq. (35) and following boundary conditions (12)

$$f(\mathbf{r}, t) = 0 \quad \text{for absorbing boundaries} \quad (37)$$

$$\frac{\partial f(\mathbf{r}, t)}{\partial n} = 0 \quad \text{for reflecting boundaries} \quad (38)$$



where  $\hat{n}$  is the normal vector to the boundary.

To illustrate the time evolution of  $f(r, t)$  in the presence of absorbing/reflecting boundaries, we solve Eq. (33), using a FE package for a closed circular domain consists of a reflecting boundary (black segment) and an absorbing boundary (red segment of length  $l$ ) as in Fig. (2). As in Figs. (3 and 4), the effect of the absorbing boundary is idle since the flux of  $f(r, t)$  did not reach the boundary by then. In Fig. (5), a region of lower probability (density) appears around the absorbing boundary, since the probability of the particle to exist in this region is less than that for the other regions.

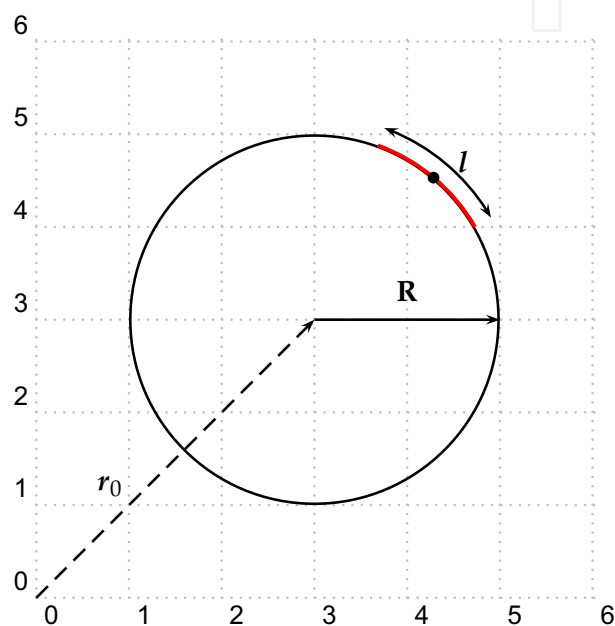


Fig. 2. Closed circular domain with reflecting and absorbing boundaries.

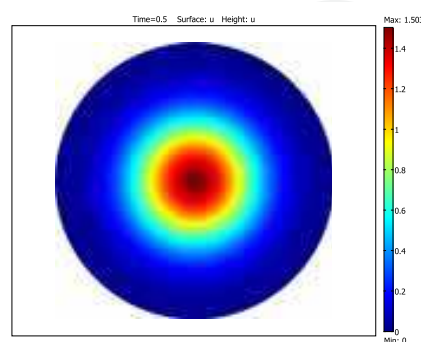


Fig. 3. Probability density function at time 5s after particle injection

Note that each of the above two solutions represents **the probability density function** of one particle occupying space around  $r$  at time  $t$  assuming it was released from location  $r_0$  at time

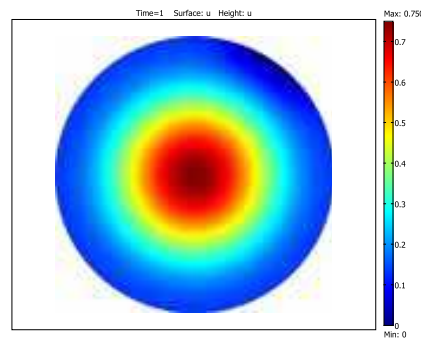


Fig. 4. Probability density function at time 10s after particle injection

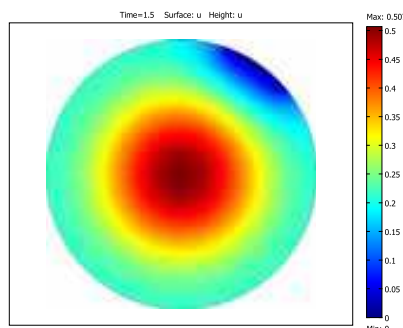


Fig. 5. Probability density function at time 15s after particle injection

$t_0$ . These results can potentially be incorporated in variety of biomedical signal processing applications: source localization, diffusivity estimation, transport prediction, etc.

#### 4. Estimation and prediction of respiratory signals using stochastic differential equations

Newborn intensive care is one of the great medical success of the last 20 years. Current emphasis is upon allowing infants to survive with the expectation of normal life without handicap. Clinical data from follow up studies of infants who received neonatal intensive care show high rates of long-term respiratory and neurodevelopmental morbidity. As a consequence, current research efforts are being focused on refinement of ventilated respiratory support given to infants during intensive care. The main task of the ventilated support is to maintain the concentration level of oxygen ( $O_2$ ) and carbon-dioxide ( $CO_2$ ) in the blood within the physiological range until the maturation of lungs occur. Failure to meet this objective can lead to various pathophysiological conditions. Most of the previous studies concentrated on the modeling of blood gases in adults (e.g., (14)). The forward mathematical modeling of the respiratory system has been addressed in (16) and (17). In (16) the authors developed a respiratory model with large number of unknown nonlinear parameters which therefore cannot be efficiently used for inverse models and signal prediction. In (17) the authors presented a simplified forward model which accounted for circulatory delays and shunting. However, the development of an adequate signal processing respiratory model has not been addressed in these studies.

So far most of the existing research (18) focused on developing a deterministic forward mathematical model of the  $CO_2$  partial pressure variations in the arterial blood of a ventilated neonate. We evaluated the applicability of the forward model using clinical data sets obtained from novel sensing technology, neonatal multi-parameter intra-arterial sensor which enables intra-arterial measurements of partial pressures. The respiratory physiological parameters were assumed to be known. However, to develop automated procedures for ventilator monitoring we need algorithms for estimating *unknown* respiratory parameters since infants have different respiratory parameters.

In this section we present a new stochastic differential model for the dynamics of the partial pressures of oxygen and carbon-dioxide. We focus on the stochastic differential equations (SDE) since deterministic models do not account for random variations of metabolism. In fact most deterministic models assume that the variation of partial pressures is due to measurement noise and that exchange of gasses is a smooth function. An alternative approach would result from the assumption that the underlying process is not smooth at feasible sampling rates (e.g., one minute). Physiologically, this would be equivalent to postulating, e.g., that the rate of glucose uptake by tissues varies randomly over time around some average level resulting in SDE models. Appropriate parameter values in these SDE models are crucial for description and prediction of respiratory processes. Unfortunately these parameters are often unknown and need to be estimated from resulting SDE models. In most case computationally expensive Monte-Carlo simulations are needed in order to calculate the corresponding probability density functions (pdfs) needed for parameter estimation. In Section 2 we propose two models: classical in which the gas exchange is modeled using ordinary differential equations, and stochastic in which the increments in gas numbers are modeled as stochastic processes resulting in stochastic differential equations. In Section 3 we present measurements model for both classical and stochastic techniques and discuss parameter estimation algorithms. In Section 4 we present experimental results obtained by applying our algorithms to real data set.

The schematic representation of an infant respiratory system is illustrated in Figure 1. The model consists of five compartments: the alveolar space, arterial blood, pulmonary blood, tissue, and venous blood respectively. The circulation of  $O_2$  and  $CO_2$  depends on two factors: diffusion of gas molecules in alveolar compartment and blood flow – arterial flow takes oxygen rich blood from pulmonary compartment to tissue and similarly, venous flow takes blood containing high levels of carbon-dioxide back to the pulmonary compartment. Furthermore, in infants there exists additional flow from right to left atria. In our model this shunting is accounted for in that a fraction  $\alpha$ , of the venous blood is assumed to bypass the pulmonary compartment and go directly in the arteries (illustrated by two horizontal lines in Figure 1).

#### *Classical Model*

Let  $c_w$  denote the concentration of a gas ( $O_2$  or  $CO_2$ ) in a compartment  $w$  where  $w \in \{p, A, a, ts, v\}$  denotes pulmonary, alveolar, arterial, tissue, and venous compartments respectively. Using the conservation of mass principle the concentrations are given by the following

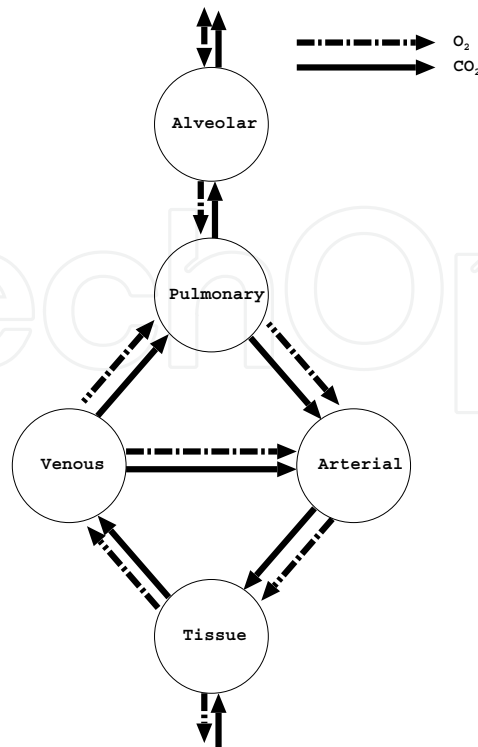


Fig. 6. Graphical layout of the model.

set of equations (18)

$$\begin{aligned}
 V_A \frac{dc_A}{dt} &= D(c_P - c_A) - ec_A \\
 V_P \frac{dc_P}{dt} &= -D(c_P - c_A) + Q(1 - \alpha)c_V - Q(1 - \alpha)c_P \\
 V_a \frac{dc_a}{dt} &= Q(1 - \alpha)c_P + \alpha Qc_V - Qc_a \\
 V_{ts} \frac{dc_{ts}}{dt} &= Qc_a - Qc_{ts} + r \\
 V_v \frac{dc_v}{dt} &= Qc_{ts} - Qc_v
 \end{aligned} \tag{39}$$

where  $e$  is the expiratory flow rate,  $D$  is the corresponding diffusion coefficient,  $Q$  is the blood flow rate, and  $r$  is the metabolic consumption term (determining the amount of oxygen consumed by the tissue).

#### Stochastic Model

In the above classical model we assumed that the metabolic rate  $r$  is known function of time. In general, the metabolic rate is unknown and time-dependent and thus needs to be estimated at *every time instance*. In order to make the parameters identifiable we propose the constrain the solution by assuming that the metabolic rate is a Gaussian random process with known

mean. In that case the gas exchange can be modeled using

$$\begin{aligned}
 \frac{dn_A}{dt} &= D \left( \frac{n_p}{V_p} - \frac{n_A}{V_A} \right) - e \frac{n_A}{V_A} \\
 \frac{dn_p}{dt} &= -D \left( \frac{n_p}{V_p} - \frac{n_A}{V_A} \right) + Q(1-\alpha) \frac{n_v}{V_v} - Q(1-\alpha) \frac{n_p}{V_p} \\
 \frac{dn_a}{dt} &= Q(1-\alpha) \frac{n_p}{V_p} + \alpha Q \frac{n_v}{V_v} - Q \frac{n_a}{V_a} \\
 \frac{dn_{ts}}{dt} &= Q \frac{n_a}{V_a} - Q \frac{n_{ts}}{V_{ts}} + r \\
 \frac{dn_v}{dt} &= Q \frac{n_{ts}}{V_v} - Q \frac{n_p}{V_p}
 \end{aligned} \tag{40}$$

where we use  $n$  to denote number of molecules in a particular compartment. Note that we deliberately omit the time dependence in order to simplify notation.

Let us introduce  $\mathbf{n} = [n_A, n_p, n_a, n_{ts}, n_v]^T$  and

$$A = \begin{bmatrix} -\frac{D+e}{V_A} & \frac{D}{V_p} & 0 & 0 & 0 \\ \frac{D}{V_A} & -\frac{D+Q(1-\alpha)}{V_p} & 0 & 0 & \frac{Q(1-\alpha)}{V_v} \\ 0 & \frac{Q(1-\alpha)}{V_p} & -\frac{Q}{V_a} & 0 & \frac{\alpha Q}{V_v} \\ 0 & 0 & \frac{Q}{V_a} & -\frac{Q}{V_{ts}} & 0 \\ 0 & -\frac{Q}{V_p} & 0 & \frac{Q}{V_{ts}} & 0 \end{bmatrix}$$

Using the above substitutions the above the SDE model becomes

$$d\mathbf{n} = A\mathbf{n}dt + \boldsymbol{\sigma}d\mathbf{r} \tag{41}$$

where  $\boldsymbol{\sigma} = [0, 0, 0, 1, 0]^T$ .

In this section we derive signal processing algorithms for estimating the unknown parameters for both classical and stochastic models.

#### Classical Model

Using recent technology advancement we were able to obtain intra-arterial pressure measurements of partially dissolved  $O_2$  and  $CO_2$  in ten ventilated neonates. It has been shown (15) that intra-arterial partial pressures are linearly related to the  $O_2$  and  $CO_2$  concentrations in arteries i.e., can be modeled as

$$\begin{aligned}
 c_a^{CO_2}(t) &= \gamma p_p^{CO_2}(t) \\
 c_a^{O_2}(t) &= \gamma p_p^{O_2}(t) + c^h
 \end{aligned}$$

where  $\gamma = 0.016\text{mmHg}$  and  $c^h$  is the concentration of hemoglobin. Since the concentration of the hemoglobin and blood flow were measured, in the remainder of the section we will treat

$c^h$  and  $Q$  as known constants. Let  $n_p$  be the total number of ventilated neonates and  $n_s$  the total number of samples obtained for each patient

$$\begin{aligned} \mathbf{y}_{ij}^w &= [c_{A,i}^w(t_j), c_{P,i}^w, c_{a,i}^w, c_{v,i}^w, c_{t,i}^w]^T \\ \mathbf{y}_{ij} &= [\mathbf{y}_{CO_2}(t), \mathbf{y}_{O_2}(t)]^T \\ i &= 1, \dots, n_p; j = 1, \dots, n_s; w = O_2, CO_2. \end{aligned}$$

Note that we use superscript  $w$  to distinguish between different vapors. Using the transient model (1) the vapor concentration can be written as

$$\mathbf{y}_{ij} = \mathbf{f}_0 e^{B(\boldsymbol{\theta}_i)t_j} \mathbf{i}_a + \mathbf{e}_i(t_j)$$

where  $B$  is the state transition matrix obtained from model (1)

$$B(\boldsymbol{\theta}) = \begin{bmatrix} \frac{-D+e}{V_A} & \frac{D}{V_A} & 0 & 0 & 0 \\ \frac{D}{V_P} & -\frac{D+Q(1-\alpha)}{V_P} & 0 & 0 & \frac{Q(1-\alpha)}{V_P} \\ 0 & \frac{Q(1-\alpha)}{V_a} & -Q & 0 & \frac{\alpha Q}{V_a} \\ 0 & 0 & \frac{Q}{V_{ts}} & -\frac{Q}{V_{ts}} & 0 \\ 0 & -\frac{Q}{V_v} & 0 & \frac{Q}{V_v} & 0 \end{bmatrix}$$

and

$$\boldsymbol{\theta} = [V_A, V_P, V_a, V_t, V_v, r] \quad (42)$$

is the vector of respiratory parameters for a particular neonate, and  $\mathbf{e}(t)$  is the measurement noise. Observe that we use subscript  $i$  to denote that parameters are patient dependent. We also assumed that the metabolic rate is changing slowly with time and thus can be considered as time invariant, and  $\mathbf{i}_a = [0 \ 0 \ 1 \ 0 \ 0 \ 0 \ 1 \ 0 \ 0]^T$  is the index vector defined so that the intra-arterial measurements of both  $O_2$  and  $CO_2$  are extracted from the state vector containing all the concentrations. Note that the expiratory rate can be measured and thus will be treated as known variable.

In the case of deterministic respiratory parameters and time-independent covariance the ML estimation reduces to a problem of non-linear least squares. To simplify the notation we first rewrite the model in the following form

$$\begin{aligned} \mathbf{y}_{ij} &= \mathbf{f}_{ij} + \mathbf{e}_{ij} \\ \mathbf{f}_{ij} &= e^{\{A(\boldsymbol{\theta}_i)t_j\}} \end{aligned}$$

The likelihood function is then given by

$$L(\mathbf{y}|\boldsymbol{\theta}, \sigma^2) = \frac{1}{\sigma^2} \sum_{i=1}^n \sum_{j=1}^n (\mathbf{y}_{ij} - \mathbf{f}_{ij})^T (\mathbf{y}_{ij} - \mathbf{f}_{ij})$$

The ML estimate can then be computed from the following set of nonlinear equations

$$\begin{aligned}\hat{\boldsymbol{\theta}}_{\text{ML}} &= \arg \min_{\boldsymbol{\theta}} \sum_{i=1}^n \sum_{j=1}^n (\mathbf{y}_{ij} - \mathbf{f}(\boldsymbol{\theta}_i))^T (\mathbf{y}_{ij} - \mathbf{f}(\boldsymbol{\theta}_i)) \\ \hat{\sigma}_{\text{ML}}^2 &= \frac{1}{n_p n_s} \sum_{i=1}^n \sum_{j=1}^n (\mathbf{y}_{ij} - \hat{\mathbf{f}}_{ij})^T (\mathbf{y}_{ij} - \hat{\mathbf{f}}_{ij}) \\ \hat{\mathbf{f}}_{ij} &= \mathbf{f}_0 e^{B(\hat{\boldsymbol{\theta}}_i) t_j}\end{aligned}$$

The above estimates can be computed using an iterative procedure (19). Observe that we implicitly assume that the initial model predicted measurement vector  $\mathbf{f}_0$  is known. In principle our estimation algorithm is applied at an arbitrary time  $t_0$  and thus we assume  $\mathbf{f}_0 = \mathbf{y}_{i0}$ .

#### Stochastic Model

In their most general form SDEs need to be solved using Monte-Carlo simulations since the corresponding probability density functions (PDFs) cannot be obtained analytically. However if the corresponding generator of Ito diffusion corresponding to an SDE can be constructed then the problem can be written in a form of partial differential equation (PDE) whose solution then is the probability density function corresponding to the random process. In our case, the generator function for our model 41 is given by

$$A p_{\mathbf{n}}(\mathbf{n}, t) = (\mathbf{n} - \boldsymbol{\mu}_r)^T \cdot \frac{\partial p_{\mathbf{n}}(\mathbf{n}, t)}{\partial \mathbf{n}} + \frac{1}{2} \partial p_{\mathbf{n}}(\mathbf{n}, t)^T \sigma \sigma^T \partial p_{\mathbf{n}}(\mathbf{n}, t) \quad (43)$$

where

$$\boldsymbol{\mu}_r = [0, 0, 0, \mu_r, 0]^T \quad (44)$$

where  $\mu_r$  is the mean of metabolic rate.

Then according to Kolmogorov forward equation (25) the PDF is given as a solution to the following PDE

$$\frac{\partial p_{\mathbf{n}}(\mathbf{n}, t)}{\partial t} = A p_{\mathbf{n}}(\mathbf{n}, t) \quad (45)$$

In our previous work (26) we have shown that the solution to the above equation is given by

$$\begin{aligned}p_{\mathbf{n}}(\mathbf{n}, t) &= \frac{1}{(2\sqrt{\pi})^5 (t - t_0)^{\frac{5}{2}}} e^{-\frac{1}{2\sqrt{t-t_0}} \mathbf{z}^T (\sigma \sigma^T)^{-} \mathbf{z}} \\ \mathbf{z} &= \mathbf{n} - \boldsymbol{\mu}_r t - \mathbf{n}(t_0)\end{aligned} \quad (46)$$

where  $-$  denotes Moore-Penrose matrix inverse.

Note that the above solution represents the joint probability density of number of oxygen molecules in five compartments of our compartmental model assuming that the initial number of molecules (at time  $t_0$ ) is  $\mathbf{n}(t_0)$ . Since in our case we can measure only intra-arterial concentration (number of particles) we need to compute the marginal density  $p_{n_a}(n_a)$  given by

$$p_{n_a}(n_a, t) = \int \cdots \int p_{\mathbf{n}}(\mathbf{n}, t) d n_A d n_V d n_P d n_{TS}. \quad (47)$$



Once the marginal density is computed we can apply the maximum likelihood in order to estimate the unknown parameters

$$\hat{\theta}_i = \arg \max_{\theta} \prod_{j=1}^m p_{n_a}(n_a, t_j) \quad (48)$$

where we use  $t_j$  to denote time samples used for estimation and  $m$  is the number of time samples (window size). These estimates can then be used in order to construct the desired confidence intervals as will be discussed in the following section. To examine the applicability of the proposed algorithms we apply them to the data set obtained in the Neonatal Unit at St. James's University Hospital. The data set consists of intra-arterial partial pressure measurements obtained from twenty ventilated neonates. The sampling time was set to 10s and the expiratory rate was set to 1 breathe per second. In order to compare the classical and stochastic approach we first estimate the unknown parameters using both methods. In all examples we set the size of estimation window to  $m = 100$  samples. Since the actual parameters are not known we evaluate the performance by calculating the 95% confidence interval for one-step prediction for both methods. In classical method, we use the parameter estimates to calculate the distribution of the measurement vector at the next time step, and in stochastic estimation we numerically evaluate the confidence intervals by substituting the parameter estimates into (36).

In Figures (7 – 11) we illustrate the confidence intervals for five randomly chosen patients. Observe that in the case of classical estimation we estimate the metabolic rate and assume that it is time-independent i.e., does not change during  $m$  samples. On the other hand for stochastic estimation, we use the estimation history to build pdf corresponding to  $r(t)$  and approximate it with Gaussian distribution. Note that for the first several windows we can use density estimation obtained from the patient population which can be viewed as a training set. As expected the MLE estimates obtained using classical method provide larger confidence interval i.e., larger uncertainty mainly because the classical method assumes that the measurement noise is uncorrelated. However due to modeling error there may exist large correlation between the samples resulting in larger variance estimate.

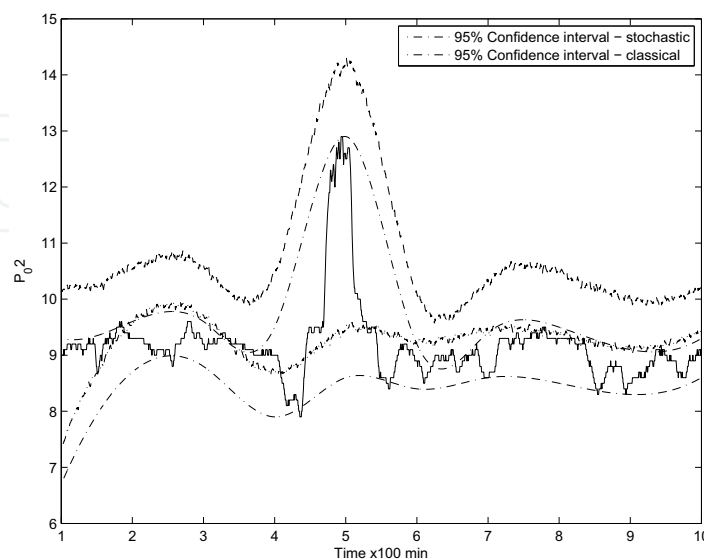


Fig. 7. Partial pressure measurements.

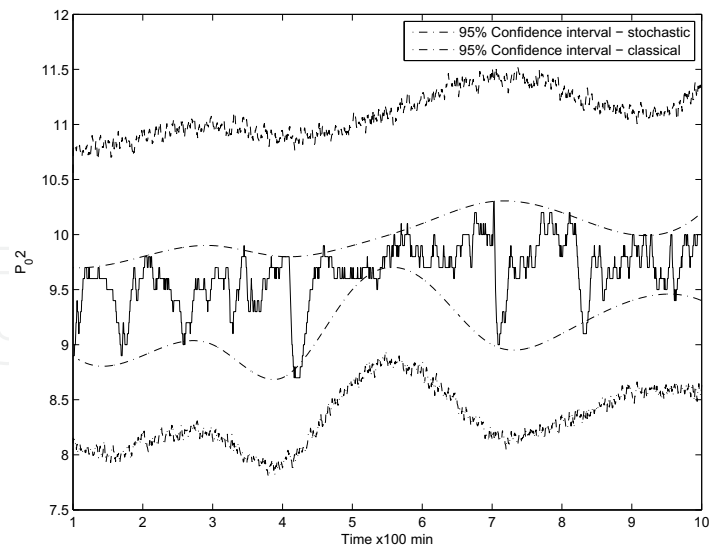


Fig. 8. Partial pressure measurements.

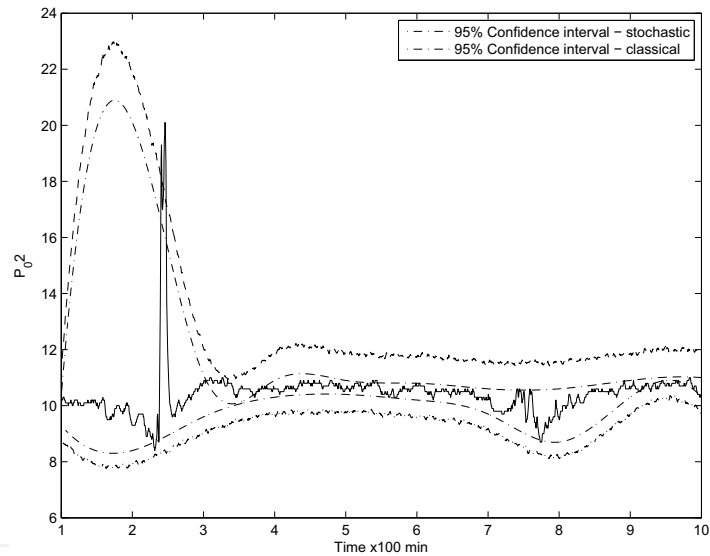


Fig. 9. Partial pressure measurements.

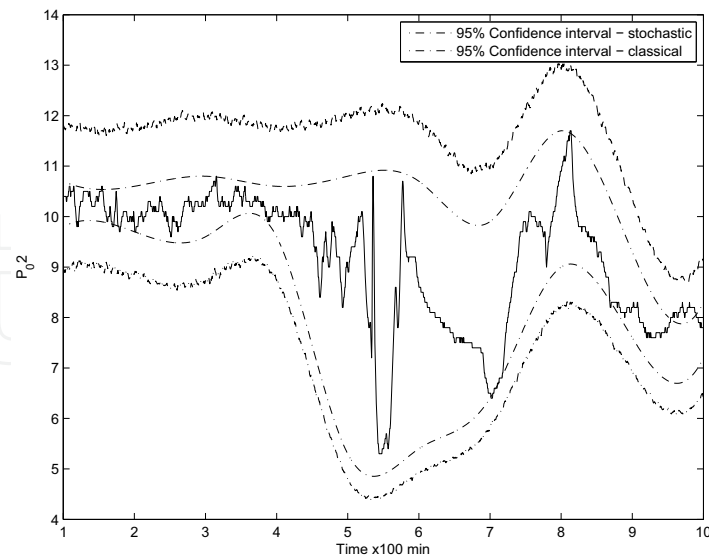


Fig. 10. Partial pressure measurements.

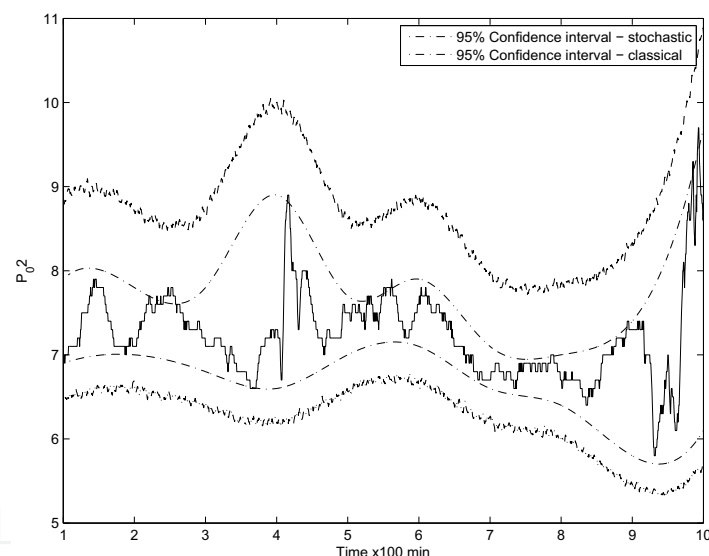


Fig. 11. Partial pressure measurements.

## 5. Conclusions

One of the most important tasks that affect both long- and short-term outcomes of neonatal intensive care is maintaining proper ventilation support. To this purpose in this paper we develop signal processing algorithms for estimating respiratory parameters using intra-arterial partial pressure measurements and stochastic differential equations. Stochastic differential equations are particularly amenable to biomedical signal processing due to its ability to account for internal variability. In the respiratory modeling in addition to breathing the main source of variability is randomness of the metabolic rate. As a consequence ordinary differential equations usually fail to capture dynamic nature of biomedical systems. In this paper we first model the respiratory system using five compartments and model the gas exchange

between these compartments assuming that differential increments are random processes. We derive the corresponding probability density function describing the number of gas molecules in each compartment and use maximum likelihood to estimate the unknown parameters. To address the problem of prediction/tracking the respiratory signals we implement algorithms for calculating the corresponding confidence interval. Using the real data set we illustrate the applicability of our algorithms. In order to properly evaluate the performance of the proposed algorithms an effort should be made to investigate the possibility of developing real-time implementing the proposed algorithms. In addition we will investigate the effect of the window size on estimation/prediction accuracy as well.

## 6. References

- [1] F. B. (1963). Random walks and a sojourn density process of Brownian motion. Trans. Amer. Math. Soc. 109 5686.
- [2] Milshtein G. N.: Approximate Integration of Stochastic Differential Equations, Theory Prob. App. 19 (1974), 557.
- [3] W. T. Coffey, Yu P. Kalmykov, and J. T. Waldron, The Langevin Equation, With Applications to Stochastic Problems in Physics, Chemistry and Electrical Engineering (Second Edition), World Scientific Series in Contemporary Chemical Physics - Vol 14.
- [4] H. Terayama, K. Okumura, K. Sakai, K. Torigoe, and K. Esumi, "Aqueous dispersion behavior of drug particles by addition of surfactant and polymer," Colloids and Surfaces B: Biointerfaces, vol. 20, no. 1, pp. 73-77, 2001.
- [5] A. Nehorai, B. Porat, and E. Paldi, "Detection and localization of vapor emitting sources," IEEE Trans. on Signal Processing, vol. SP-43, no.1, pp. 243-253, Jun 1995.
- [6] B. Porat and A. Nehorai, "Localizing vapor-emitting sources by moving sensors," IEEE Trans. on Signal Processing, vol. 44, no. 4, pp. 1018-1021, Apr. 1996.
- [7] A. Jeremić and A. Nehorai, "Design of chemical sensor arrays for monitoring disposal sites on the ocean floor," IEEE J. of Oceanic Engineering, vol. 23, no. 4, pp. 334-343, Oct. 1998.
- [8] A. Jeremić and A. Nehorai, "Landmine detection and localization using chemical sensor array processing," IEEE Trans. on Signal Processing, vol. 48, no.5 pp. 1295-1305, May 2000.
- [9] M. Ortner, A. Nehorai, and A. Jeremic, "Biochemical Transport Modeling and Bayesian Source Estimation in Realistic Environments," IEEE Trans. on Signal Processing, vol. 55, no. 6, June 2007.
- [10] Hannes Risken, *The Fokker-Planck Equation: Methods of Solutions and Applications*, 2nd edition, Springer, New York, 1989.
- [11] H. Terayama, K. Okumura, K. Sakai, K. Torigoe, and K. Esumi, "Aqueous Dispersion Behavior of Drug Particles by Addition of Surfactant and Polymer", Colloids and Surfaces B: Biointerfaces, Vol. 20, No. 1, pp. 73-77, January 2001.
- [12] J. Reif and R. Barakat, "Numerical Solution of Fokker-Planck Equation via Chebyshev Polynomial Approximations with Reference to First Passage Time", Journal of Computational Physics, Vol. 23, No. 4, pp. 425-445, April 1977.
- [13] A. Atalla and A. Jeremić, "Localization of Chemical sources Using Stochastic Differential Equations", IEEE International Conference on Acoustics, Speech and Signal Processing ICASSP 2008, pp.2573-2576, March 31 2008-April 4 2008.
- [14] G. Longobardo *et al.*, "Effects of neural drives and breathing stability on breathing in the awake state in humans," *Respir. Physiol.* Vol. 129, pp 317-333, 2002.

- [15] M. Revoew *et al*, "A model of the maturation of respiratory control in the newborn infant," *IEEE Trans. Biomed. Eng.*, Vol. 36, pp. 414–423, 1989.
- [16] F. T. Tehrani, "Mathematical analysis and computer simulation of the respiratory system in the newborn infant," *IEEE Trans. on Biomed. Eng.*, Vol. 40, pp. 475–481, 1993.
- [17] S. T. Nugent, "Respiratory modeling in infants," *Proc. IEEE Eng. Med. Soc.*, pp. 1811–1812, 1988.
- [18] C. J. Evans *et al.*, "A mathematical model of CO<sub>2</sub> variation in the ventilated neonate," *Physi. Meas.*, Vol. 24, pp. 703–715, 2003.
- [19] R. Gallant, *Nonlinear Statistical Models*, John Wiley & Sons, New York, 1987.
- [20] P. Goddard *et al* "Use of continuously recording intravascular electrode in the newborn," *Arch. Dis. Child.*, Vol. 49, pp. 853–860, 1974.
- [21] E. F. Vonesh and V. M. Chinchilli, *Linear and Nonlinear Models for the Analysis of Repeated Measurements*, New York, Marcel Dekker, 1997.
- [22] K. J. Friston, "Bayesian Estimation of Dynamical Systems: An Application to fMRI," *NeuroImage*, Vol. 16, pp. 513–530, 2002.
- [23] A. D. Harville, "Maximum likelihood approaches to variance component estimation and to related problems," *J. Am. Stat. Assoc.*, Vol. 72, pp. 320–338, 1977.
- [24] R. M. Neal and G. E. Hinton, In *Learning in Graphical Models*, Ed: M. I. Jordan, pp. 355–368, Kluwer, Dordrecht, 1998.
- [25] B. Oksendal, *Stochastic Differential Equations*, Springer, New York, 1998.
- [26] A. Atalla and A. Jeremic, "Localization of Chemical Sources Using Stochastic Differential Equations," ICASSP 2008, Las Vegas, April 2008.

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