Signal analysis of NEMS sensors at the output of a chromatography column

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Abstract. This article introduces a joined Bayesian estimation of gas samples issued from a gas chromatography column (GC) coupled with a NEMS sensor based on Giddings Eyring microscopic molecular stochastic model. The posterior distribution is sampled using a Monte Carlo Markov Chain and Gibbs sampling. Parameters are estimated using the posterior mean. This estimation scheme is finally applied on simulated and real datasets using this molecular stochastic forward model.

INTRODUCTION

Gas study or gas separation is nowadays possible on nanoscopic systems. Working at this scale increases the sensitivity to analyze low concentration gas samples. Currently, Nano columns of Gas Chromatography (Nano-GC) have been developed and new sensors called Nano Electro Mechanical Systems (NEMS) have been designed. In this paper, a Nano-GC coupled with NEMS sensors has been used for gas mixture separation. This allows working with traces of gas. In this communication, we propose to estimate the concentration of each constituent of gas mixture. In the next section, we describe the GC-NEMS system. Then we introduce an inversion scheme to retrieve the concentration of each component of the mixture from this kind of NEMS signal. We are assuming that we know the number of constituents and the nature of each constituent. We are proposing to use an innovative stochastic forward model based on the random molecular walk as described by Giddings and Eyring [1]. We are presenting a Bayesian parameters estimation scheme. [2]

DESCRIPTION OF THE GC-NEMS

A gas chromatography column is used to separate the components of a gas mixture. This system is composed of an injector, a chromatography column and a sensor to acquire a signal. As illustrated on Figure 1, the injector pushes a gas mixture with carrier gas

into the column. The internal surface of the column is coated with a layer of SiOC
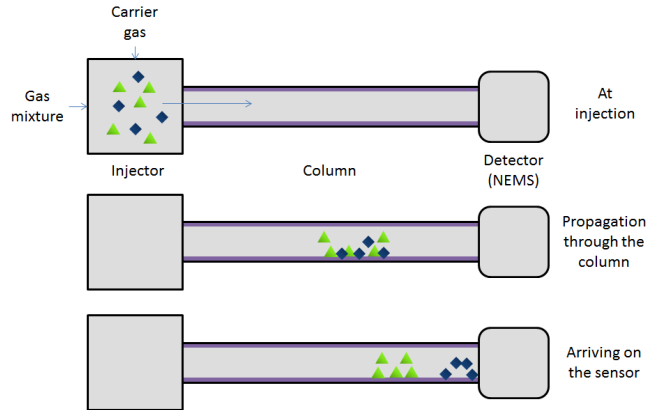
FIGURE 1.   Principle of the gas chromatography-NEMS

(the stationary phase) where molecules of organic compounds adsorb for a random time. The mobile phase must have no interaction with the stationary phase. That is why helium is generally used as carrier gas. So during its route, a molecule will adsorb and desorb many times depending on its own nature. The more the molecule is adsorbed on the stationary phase, the more the molecule spends time in the column. The total time spent by a molecule in the column before elution is called the retention time and will be noted t_R. The adjusted retention time, noted $t_{R'}$, defined as the total adsorbed time spent by a molecule, is also used. The affinity rate of the molecules with the stationary phase contributes to the separation power of the column.

At the exit of the column, a sensor converts this molecular flow into a digital signal. There are mainly three kinds of sensors used in output of chromatographic column [3, p.104]: the Flame Ionized Detector (FID), the Thermo Conductive Detector (TCD) and the Nano ElectroMechanical System (NEMS). This study is focused on the use of NEMS which is a gravimetric device. It is composed of vibrating cantilevers and coated with a SIOC chemical layer for molecular adsorption as shown on a microscopic view of one of those sensors in Figure 2.

The beam is a mechanical resonator of second order that has a resonance frequency [4]. The sensor contains an actuator which puts the beam in resonance. In order to measure the beam oscillations frequency, two gauges are linked to an electronic system that enslaves the actuator. It adjusts the frequency such that the shift phase between the actuator and the oscillations gauge remains equal to $\pi/2$. This phase tracking is called a Phase Locked Loop control. The most important property of NEMS sensors is that an adsorption of a molecule on the beam causes a shift of its resonance frequency. The frequency f of a second order resonator is indeed $\sqrt{\frac{k}{M}}$ where k is the spring constant and M is the vibrating mass. The frequency variation due to a mass variation dm on the beam is [5]:

$$\Delta f = -\frac{f}{2M}\,dm. \tag{1}$$

In the following, we note $\beta = \frac{f}{2M}$ the gain of the system. Then, we rewrite the equation (1):

$$\Delta f = -\beta \, dm. \tag{2}$$

An example of a signal delivered by a NEMS is shown on Figure 2. It corresponds to an injection of a mixture of Toluene and Xylene.
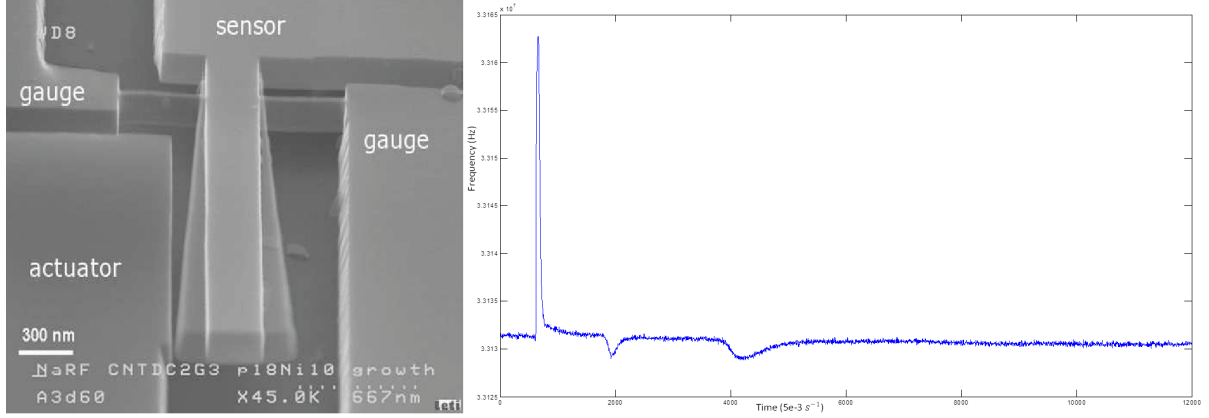

FIGURE 2. Microscopic view of a NEMS sensor (left picture), and an example of a chromatographic NEMS signal on a mixture of Toluene and Xylene (right picture).

The positive peak corresponds to the arrival of the mobile phase on the sensor. This frequency shift is due to a pressure shift. Each negative peak corresponds to the arrival of one chemical entity. The first one is the Toluene and the second one is the Xylene.

MODELING

Chemical equilibrium in the column

Considering one chemical entity S in the column with concentrations $[S_m]$ in the mobile phase and $[S_s]$ in the stationary phase ($[S] = [S_m] + [S_s]$), let's k_a and k_d be respectively the adsorption and desorption rates [6]. $k = \frac{k_a}{k_d}$ defines the kinetic constant of the equilibrium in the column also called retention factor. This equilibrium is described by the relationship:

$$S_m \underset{k_d}{\overset{k_a}{\rightleftharpoons}} S_s$$
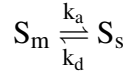
Molecular transport in the chromatography column based on a stochastic model

From equation (2), the output NEMS signal is written as:

$$y(t) = y_0(t) - \beta m(t) + \varepsilon(t), \tag{3}$$

where $m(t)$ is the mass adsorbed on the NEMS at time t and $\varepsilon(t)$ the noise of the system at time t.

In order to estimate this mass, we propose an approach based on a stochastic microscopic model. In this point of view, each molecule elutes with a random adjusted retention time $t_{R'}$ which probability density function is [1]:

$$p_{t_{R'}}(t, \eta_j) = \frac{\sqrt{4k_{a,j}k_{d,j}t_0t}}{2t} I_1\left(\sqrt{4k_{a,j}k_{d,j}t_0t}\right) e^{-k_{d,j}t - k_{a,j}t_0}, \tag{4}$$

where I_1 is the modified Bessel function of the first kind and first order, $\eta_j = (k_{a,j}, k_{d,j})$ the adsorption/desorption parameters vector and t_0 the time for carrier gas to elute without adsorption (dead time).
Assuming $\mu_j = t_0\frac{k_{a,j}}{k_{d,j}}$, $\sigma_j^2 = 2t_0\frac{k_{a,j}}{k_{d,j}^2}$ and $\theta_j = (\mu_j, \sigma_j^2)$, equation (4) becomes:

$$p_{t_{R'}}(t, \theta_j) = 2\frac{\mu_j\sqrt{\mu_j t}}{\sigma_j^2 t} I_1\left(\frac{\mu_j\sqrt{\mu_j t}}{\sigma_j^2}\right) e^{-2\frac{\mu_j}{\sigma_j^2}(t+\mu_j)}, \tag{5}$$

As described in [6], this model is more relevant than the classical Gaussian one for many physical reasons. The first is that $t_{R'}$ is defined on $\mathbb{R}^+$. The accuracy of this model is highlighted in the Results section.

The number $n_j(t)$ of molecules of the entity j adsorbed on the beam at instant t is expressed as:
$$n_j(t) = \kappa C_j p_{t_{R'}}(t, \theta_j),$$
where κ is the total number of molecules in the sample and C_j the concentration of entity j.

The mass m on the beam at time t is:

$$m(t) = \kappa \sum_{j=1}^{N_e} mm_j C_j n_j(t) = \kappa N_j \sum_{j=1}^{N_e} mm_j C_j p_{t_{R'}}(t, \theta_j), \tag{6}$$

where mm_j is the molecular mass of constituent j, N_e the number of chemical entities in the sample. We denote $\alpha = \kappa\beta$.

Finally, combining (3) and (6), the final expression of the output signal is:

$$y(t) = y_0(t) - \alpha \sum_{j=1}^{N_e} C_j p_{t_{R'}}(t, \theta_j) + \varepsilon(t), \tag{7}$$

where $\varepsilon(t)$ is a zero mean gaussian noise. In the following, the ouput signal $y(t)$ is noted Y.

The peak shape density $p_{t_{R'}}$ in equation (4) is the forward model used for chromatographic peak. Its approximation is a Gaussian peak shape: $p_{t_{R'}}(t; \mu_j, \sigma_j) = \frac{1}{\sqrt{2\pi\sigma_j^2}} e^{-(t-\mu_j)^2/2\sigma_j^2}$.

Bayesian inversion

After having defined the forward model in a nano-system context, this section is focused on the Bayesian inversion of this model to simultaneously estimate the concentration C_j and the adsorption parameter θ_j of each molecule j, the gain α and the inverse variance of the noise γ of the system. In the following, we note $\Theta = [C, \theta_j, \alpha, \gamma]^T$.

Using Bayes' rule, we have $p(\Theta|Y) \propto p(\Theta)p(Y|\Theta)$. An estimator $\hat{\Theta}$ of Θ is the mean of this density, known as the posterior mean estimator:

$$\hat{\Theta} = \int_\Omega \Theta p(\Theta|Y) d\Theta, \tag{8}$$

where Ω is the domain of the possible values for the vector.

As computing this integral is impossible in an analytical way, a method of stochastic sampling of Θ is applied for estimating it. Having K samples of $\Theta^{(k)}$, this previous mean is easily computed with the following average sum:

$$\hat{\Theta} = \frac{1}{K} \sum_{k=K_0+1}^{K_0+K} \Theta^{(k)}, \tag{9}$$

where K_0 is the number of warming iterations.

Multidimensional sampling of Θ is quite difficult because its distribution is not standard. That is why a Gibbs sampler is used to generate K samples of Θ as described in Algorithm 1.

Algorithm 1 Gibbs sampling of the parameters.

Initialize $C^{(1)}, \alpha^{(1)}, \gamma^{(1)}, \theta_j^{(1)}$
for $i = 1$ to $K + K_0$ **do**
     Sample $\gamma^{(k+1)} \sim p\left(\gamma|Y, C^{(k)}, \alpha^{(k)}, \theta_j^{(k)}\right)$
     Sample $\alpha^{(k+1)} \sim p\left(\alpha|Y, C^{(k)}, \gamma^{(k+1)}, \theta_j^{(k)}\right)$
     Sample $C^{(k+1)} \sim p\left(C|Y, \alpha^{(k+1)}, \gamma^{(k+1)}, \theta_j^{(k)}\right)$
     Sample $\theta_j^{(k+1)} \sim p\left(\theta_j|Y, C^{(k+1)}, \alpha^{(k+1)}, \gamma^{(k+1)}\right), j = 1 : N_e$
end for

The likelihood of the data corresponds to our Gaussian assumption for modelling the noise which is normally distributed:

$$p(Y|\Theta) = \mathcal{N}\left(Y; g(t) - g_0 - \varepsilon(t), \gamma\right).$$

These parameters and hyper-parameters are hierarchically ordered as shown in Figure 3. According to [7], their prior information is translated with the following distribu-

tions, where $\mathscr{G}, \mathscr{N}, \mathscr{U}$ are respectively gamma, normal and uniform distributions:

$$
\begin{aligned}
p(\gamma) &= \mathscr{G}\left(\gamma; a_\gamma^{prior}, b_\gamma^{prior}\right) \\
p(\alpha) &= \mathscr{N}\left(\alpha; m_\alpha^{prior}, \Gamma_\alpha^{prior}\right) \\
p(C) &= \mathscr{N}\left(C; m_C^{prior}, \Gamma_C^{prior}\right) \\
p(\theta_j) &= \mathscr{N}\left(\theta_j; m_{\theta_j}^{prior}, \Gamma_{\theta_j}^{prior}\right) \quad \text{or} \quad \mathscr{U}\left(\theta_j; \theta_j^m, \theta_j^M\right)
\end{aligned}
$$

The Bayes' rule gives then the posterior distributions from which the parameters are sampled:

$$
\begin{aligned}
p(\gamma|Y, C^{(k)}, \alpha^{(k)}, \theta^{(k)}) &= \mathscr{G}(\gamma; \alpha_\gamma^{post}, b_\gamma^{post}) \\
p(\alpha|Y, C^{(k)}, \gamma^{(k+1)}, \theta^{(k)}) &= \mathscr{N}(\alpha; m_\alpha^{post}, \Gamma_\alpha^{post}) \\
p(C|Y, \alpha^{(k+1)}, \gamma^{(k+1)}, \theta^{(k)}) &= \mathscr{N}(C; m_C^{post}, \Gamma_C^{post}) \\
p(\theta_j|Y, C^{(k+1)}, \alpha^{(k+1)}, \gamma^{(k+1)}) &\propto p(\theta_j^{(k)}) \cdot p(Y|C^{(k+1)}, \alpha^{(k+1)}, \theta_j^{(k)}, \gamma^{(k+1)})
\end{aligned}
$$
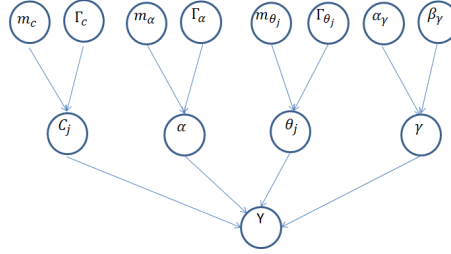
FIGURE 3. Hierarchical ordering of our model

The first three distributions are standard and easily generated with the following hyper-parameters deduced from the likelihood and the prior distributions:

$$
\begin{aligned}
\alpha_\gamma^{post} &= N/2 \\
\beta_\gamma^{post} &= 2/\|\varepsilon(t)\|^2 \\
m_\alpha^{(k+1)post} &= (\Gamma_\alpha^{(k+1)post})^{-1}(\Gamma_\alpha^{prior} m_\alpha^{prior} + \gamma^{(k+1)} \langle g(t) - g_0 | \Sigma_j C_j^{(k)} p_{t_{R'}}(t, \theta_j^{(k)}) \rangle_t^2) \\
\Gamma_\alpha^{(k+1)post} &= \Gamma_\alpha^{prior} + \gamma^{(k+1)} \| \Sigma C_j^{(k)} p_{t_{R'}}(t, \theta_j^{(k)}) \|_{t,2}^2 \\
m_C^{(k+1)post} &= (\Gamma_C^{(k+1)post})^{-1}(\Gamma_\alpha^{prior} m_\alpha^{prior} + \gamma^{(k+1)} \alpha^{(k+1)2} \langle p_{t_{R'}}(t, \theta_i^{(k)}) | g(t) \rangle_t) \\
\Gamma_C^{(k+1)post} &= \Gamma_C^{prior} + \gamma^{(k+1)} \alpha^{(k+1)2} \langle p_{t_{R'}}(t, \theta_i^{(k)}) | p_{t_{R'}}(t, \theta_j^{(k)}) \rangle_{i,j}
\end{aligned}
$$

At last, a Metropolis Hastings algorithm with a two-steps acceptance-rejection method is used to sample the non-standard a posteriori distribution $p(\theta_j|Y, C, \alpha, \gamma)$.

RESULTS

This section is focused on some applications of this Bayesian inversion on simulated and real datasets. All implementations have been written in Matlab.

TABLE 1. Parameters for simulated signal presented on figure 4, and estimated values

|	C_1	C_2	C_3	σ_1^2	σ_2^2	σ_3^2	μ_1	μ_2	μ_3
Prior	1	1	1	0.25	0.45	0.6	5	9.5	13.5
Truth	0.17	0.33	0.5	0.5	0.9	1.2	5	9.5	13.5
Estimated	0.17	0.45	0.38	1	3	1	5	10	14

A simulated dataset has been generated as a weighted mixture of three different distributions according to eq.(7) with true parameters $N_e = 3$, $\alpha = 50$, $\mu = [5; 9.5; 13.5]^T$, $\sigma = [0.5; 0.9; 1.2]^T$ and $C = [1/6, 1/3, 1/2]^T$. This simulated signal is shown on Figure 4. From initial prior values which are given in Table 1, parameters are drawn from Algorithm 1.

Figure 4 shows the evolution of the relative error with the index. The final estimation of parameters are computed from samples generated beyond iteration #150 where the Gibbs sampler has converged. The final estimated signal is shown in Figure 4 and after 1000 iterations. The sum of relative errors on the concentrations is less than 9.5%. The final estimated values are also in Table 1.

Some preliminary results are presented here for some NEMS signals recorded from a mixture of two gases. As these signals are quite new, we present here only some qualitative results to highlight the potential of future Bayesian inversion. The estimations are presented after warming iteration $K_0 = 150$. Some signal pre-processing has been computed to remove the baseline and reduce the noise. Noise filtering has been performed by averaging the signal on a sliding window on five samples in order to obtain a signal to noise ratio lower than 7. The baseline corresponding to g_0 in the equation (7) is removed by the algorithm developed by Vincent Mazet [8].
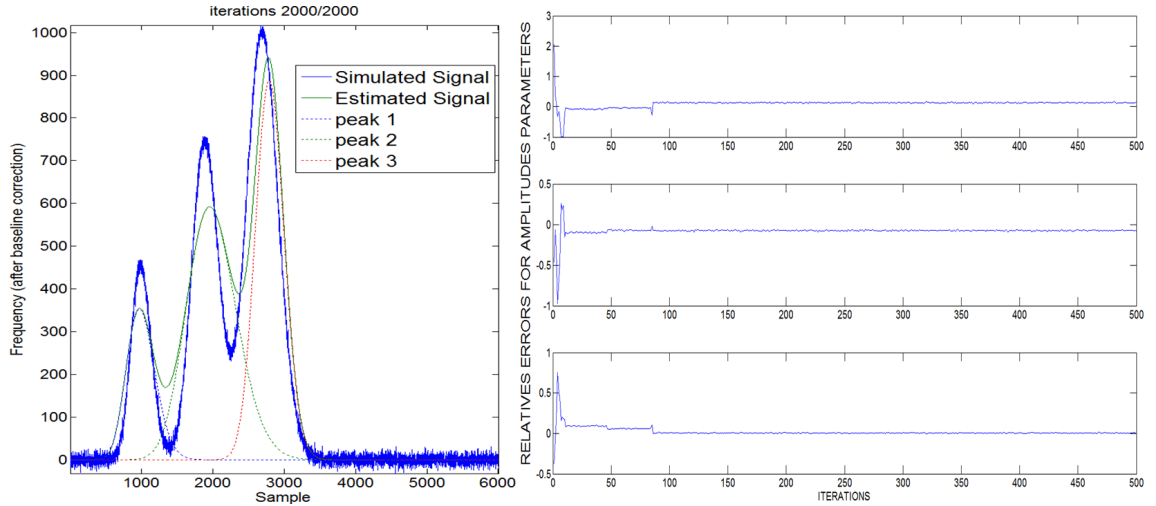
FIGURE 4. Convergence of the algorithm on simulated data. Fit of estimated signal to simulated signal (left) and relative errors of 3 amplitude parameters versus the iteration index in the MCMC chains (right)
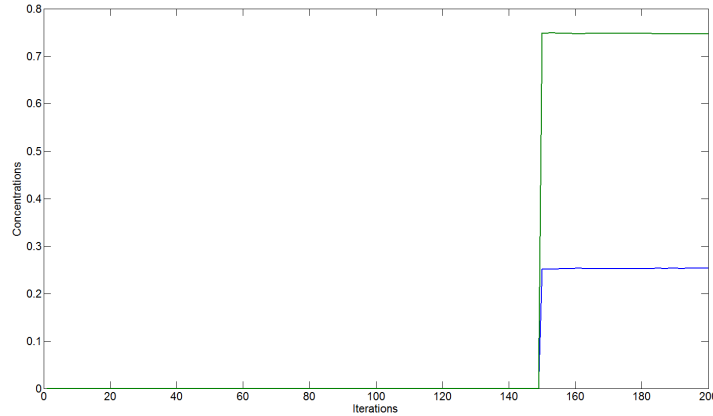
FIGURE 5.   Convergence of the algorithm on real data

CONCLUSION

To sum up we have presented a Gas chromatography system coupled with a NEMS sensor that separates gas of a mixture. We have proposed a forward model taking into account the physic of the column and the sensor. We have introduced a new molecular and stochastic model developed by Giddings and Eyring to estimate the concentrations of constituents. After implementing a Bayesian inversion method, we have analyzed the convergence of this model. We have observed that it is converging rapidly.

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