

## SIMPLE VERSUS SOPHISTICATED MODELS OF BREATH ALCOHOL EXHALATION PROFILES

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**Abstract** — For medicolegal purposes, breath alcohol content is typically determined from an end-expiratory sample. Measurements obtained by this method necessarily underestimate the alveolar breath alcohol content, and therefore underestimate the blood alcohol content. We suggest and analyse an improved paradigm which uses the entire time-series of breath alcohol measurements during exhalation, not simply the last recorded value. We present two mathematical models for the exhaling lung, and discuss the implications of each for more accurate and therefore more reliable breath alcohol measurement.

### INTRODUCTION

Breath alcohol measurement has a well-established protocol and a sizeable body of literature (for review, see Mason and Dubowski, 1976). The primary objective of breath alcohol measurement has historically been the reliable and rapid estimation of pulmonary blood alcohol concentration (BAC), though an increasing number of jurisdictions have statutes in terms of breath alcohol itself.

The analytical approach has typically been either to measure an end-expiratory breath sample or to acquire a time-series of breath alcohol data over the course of a single exhalation's three distinct phases (illustrated in Fig. 1), retaining only the peak recorded value of the time-series. Both of these approaches discard large amounts of information from the time-series, which, we will show, can be analysed appropriately to yield more accurate estimations of breath alcohol. Mathematical modelling offers a method for treating the entire exhalation time-series, while providing insight into both the analytical and biological dynamics of breath alcohol exhalation. Mathematical modelling has been applied successfully to problems in alcohol meta-

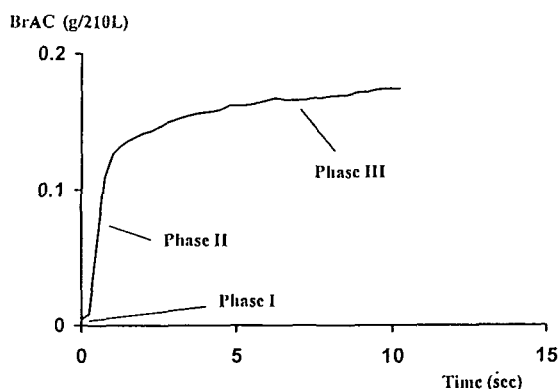


Fig. 1. Typical breath alcohol exhalation profile, illustrating its three distinct phases.

bolism (Smith *et al.*, 1993), and although mathematical treatment of breath alcohol data has been suggested elsewhere (Gullberg, 1990), appropriate and useful biologically justified models of breath alcohol data have not been previously identified.

Preliminary work has determined that the best fit to a breath alcohol exhalation profile is the sum of a decaying exponential and a linear term,

$$c = a(1 - e^{-\beta t}) + \gamma t \quad (1)$$

but to date no reasonable biological explanation

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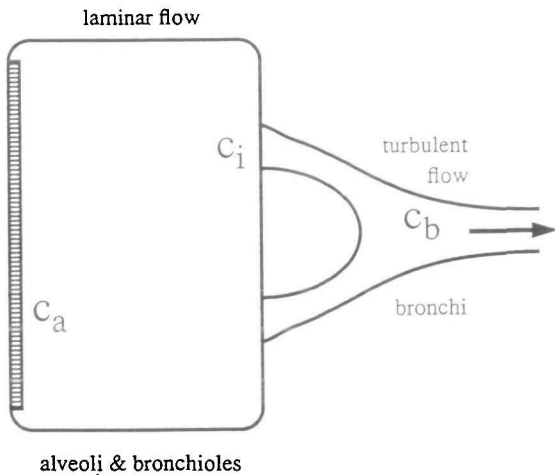


Fig. 2. Schematic lung modelled as two compartments.

(1) Alveoli and bronchioles, in which air flow is laminar, and (2) bronchi, in which flow is turbulent and fully mixed. We assume that at the deepest portion of compartment 1 the breath alcohol concentration (BrAC) is maintained at its 'true' level by constant blood flow, and that BrAC at the most rostral portions of compartment 1 depends on ventilation.

for the long linear portion (phase III) has been given. This paper describes a plausible model which can justify the use of this standard function for fitting breath alcohol exhalation data, as well as offering a physical/biological interpretation of the parameters.

#### A SIMPLE MODEL OF ALCOHOL EXHALATION

Let us consider the lung to comprise two compartments, the rigid bronchi and the contracting alveoli. Let the concentration of alcohol in the air at the bottom of the alveoli be  $c_a$ , the concentration at the top of the alveoli be  $c_i$ , and the concentration in the bronchi be  $c_b$ . The latter is the air detected by the breath alcohol instrument. We reasonably consider the air flow in the bronchi to be turbulent, i.e. fully mixed, so that everywhere in the bronchi the concentration is  $c_b$ . On the other hand, the alveolar air flow is at low Reynolds number, not well mixed, with noticeable gradients from bottom to top (Pedley, 1977; Crawford *et al.*, 1991). Thus  $c_a > c_i$  in general (see Fig. 2).

The rate of change of the alcohol concentration in the exhaled air is taken to be

$$\frac{dc_b}{dt} = \phi(c_i - c_b) \quad (2)$$

where  $\phi$  is a parameter representing the volumetric flow rate divided by the volume of the bronchial compartment. The units of  $\phi$  are therefore in  $(\text{time})^{-1}$ . This states that the rate of change of alcohol concentration in the exhaled air is proportional to the difference between the bronchial and upper alveolar air alcohol concentrations, and also proportional to the rate at which these two mix (the exhalation rate). The general solution of (2) is

$$c_b = ae^{-\phi t} + \phi e^{-\phi t} \int^t e^{\phi \tau} c_i(\tau) d\tau \quad (3)$$

where  $a$  is a constant.

The simplest assumption we can make on  $c_i$  is that it is constant,  $c_i = c_a$ , for all time. This is equivalent to a one-compartment model, and, with the assumptions that  $c_b(t_0) = 0$ , and  $\lim_{t \rightarrow \infty} c_b = c_a$ , gives the familiar decaying exponential model

$$c_b = c_a(1 - e^{-\phi(t-t_0)}) \quad (4)$$

where  $t_0$  is the time exhalation commences. This function has a clear physical interpretation: the curve approaches an asymptote  $c_a$  for large time, which gives the alveolar alcohol concentration. Let us call (4) Model I.

The second simplest assumption we can make on the form of  $c_i$  is that it is linear in time, with some particular starting value. Let

$$c_i = c_0 + k(t - t_0) \quad (5)$$

where  $c_0$  can be physically interpreted as the alcohol concentration at the top of the alveoli at the beginning of exhalation and  $k$  is a constant to be determined as shown below. There can be a great deal of variation in the breath alcohol profile of the same individual, depending on exhalation style. An artificially low reading can come from a subject ventilating the lungs before giving a sample (a 'hyper' breath). Holding the breath for several seconds before exhalation (a 'hypo' breath) gives breath alcohol readings very close to alveolar alcohol concentration. We thus expect that a hypo breath will have a higher  $c_0$  than a hyper breath from the same person. But how can

we then interpret  $k$ ? Let us make the purely hypothetical assumption that a subject could empty the alveoli completely, exhaling a volume  $V_a$ . We find volumetric flow rates to be remarkably steady in breath tests, due to the high flow resistance of the narrow tube which first receives the breath. If the subject exhales at a constant volumetric flow rate  $R$ , and takes a time  $T$  to complete the exhalation, then  $k$  is given by

$$k = \frac{c_a - c_0}{T} = \frac{(c_a - c_0)R}{V_a} = \phi(c_a - c_0)\frac{V_b}{V_a} \quad (6)$$

Define  $\alpha = V_b/V_a$ , the ratio of bronchial to alveolar volume, effectively equivalent to FRC/VC, the ratio of functional residual capacity to vital capacity. Then  $\alpha$  is dimensionless, and should be constant for an individual. Next define  $c_0 = \lambda c_a$ , that is some fraction of the alcohol concentration at the bottom of the alveoli, where  $\lambda$  is between 0 and 1.

For this 'second simplest' assumption on the form and interpretation of  $c_b$ , the exhaled breath will then fit the function

$$c_b = c_a[(\lambda - \alpha(1 - \lambda))(1 - e^{-\phi(t - t_0)}) + \alpha\phi(1 - \lambda)(t - t_0)] \quad (7)$$

which is proportional to the function

$$c = a(1 - e^{-\beta t}) + \gamma t \quad (8)$$

commonly used to consistently give the best fit to real breath alcohol data. Although (8) gives an excellent fit, it offers no physical interpretation, so it cannot be used to quantify a subject's alveolar alcohol concentration, or any other physical parameters. Let us call (7) Model II. We now have a function, to which data can be fitted, and which has some physical interpretation. It has the same shape as (8), but the ratio between the exponential and the linear parts tells us something physical about the breath — most importantly, the alveolar alcohol concentration  $c_a$ .

To review the physical interpretation of the terms in (7),

- $c_a$  is the alveolar alcohol concentration, in units of concentration.
- $\lambda$  is a dimensionless ratio between 0 and 1, characterizing how close the upper alveolar alcohol concentration is to the lower alveolar concentration. Hypo breaths will have  $\lambda$  close

to 1, and hyper breaths will have much lower  $\lambda$ .

- $\alpha$  is a dimensionless ratio, greater than zero, characterizing the ratio FRC/VC. It should be consistent within an individual, from breath to breath. From Weibel (1963), we estimate  $\alpha$  to be approximately 0.03.
- $\phi$  is a flow rate, the volumetric flow rate divided by the volume of the bronchi, i.e.  $R/V_b$ . It has units of  $(\text{time})^{-1}$ , and will be constant for a consistent flow rate.
- $t_0$  simply shifts the time for best fit.

## DATA FITTING

Experiments were carried out on human subjects with their informed consent and approval. Five subjects (two males, three females) were dosed with alcohol to a target BrAC of 0.10 g/210 l\*. The alcohol dose was administered over a period of 1 h, and the subjects were allowed an additional hour after consuming their last drink to ensure they were postabsorptive, before any breath measurements were made. Subjects were then asked to blow into an infrared breath test device (BAC Verifier DataMaster, NAPAS, Mansfield, OH, USA). They were instructed to take a deep breath and exhale until they ran out of breath. In addition to the breath alcohol measurement made by the DataMaster, the real-time analogue detector voltage signal was monitored using an analogue/digital convertor (MacLab) and a Macintosh Computer running MacLab Chart software. The voltage data was sampled at a rate of at least 0.4 Hz, and converted to breath alcohol concentration by comparison with known simulator standards. Breath alcohol exhalation profiles were reconstructed from these data, plotted and fitted to parameters using the S-Plus software package (Statistical Sciences, Inc.).

In order to introduce variability into the breath exhalation profiles, the subjects were asked to perform other breathing manoeuvres, including breath holding for 20 s (hypoventilation), and rapid breathing (hyperventilation) for 20 s immediately prior to exhaling.

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\*Corresponding to the legally defined limit for driving in many jurisdictions in the United States.

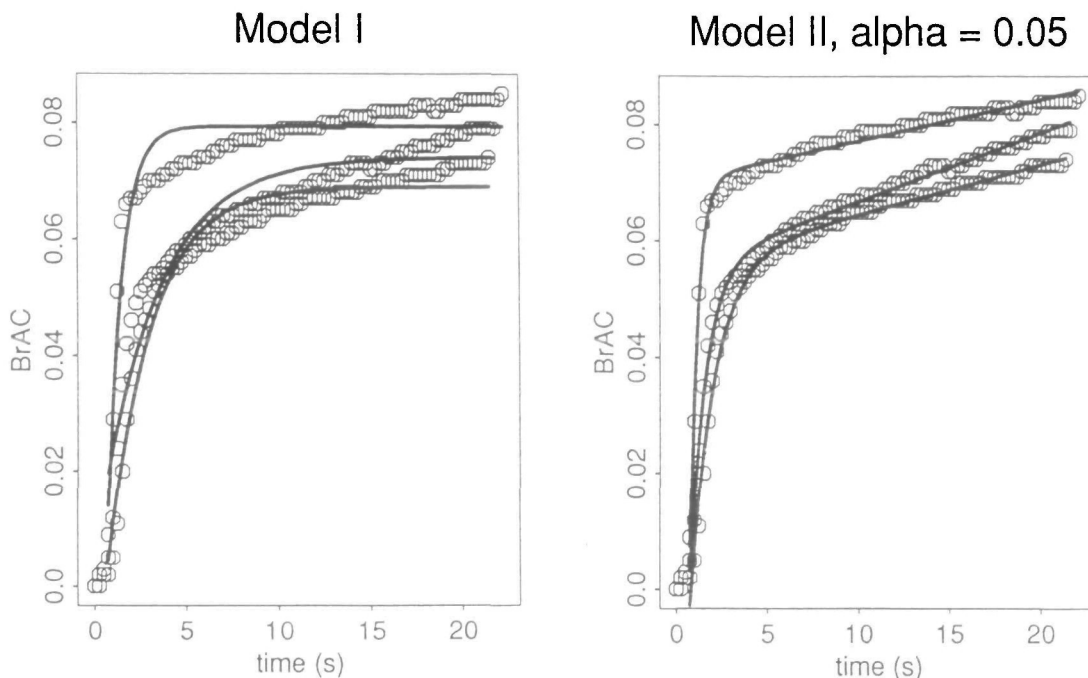


Fig. 3. Breath data and curve fits from a subject with BrAC of 0.085 g/210 l. The subject had been instructed to give normal, hyper, and hypo breaths. (left) Model I, (right) Model II.

Nonlinear regression was used to fit Models I and II to the breath data. Fixed values of 0.05 and 0.025 were used for  $\alpha$  in Model II, corresponding to anatomically-based estimates (Weibel, 1963). For the nonlinear regression, the initial transient upturn of the breath alcohol curve was excluded; it remains in Fig. 3. We consistently find that  $\lambda$  ranges from 0.5 to 1.0 and varies considerably from breath to breath.

A typical set of fits for one subject is shown in Fig. 3. Breath samples were taken in short succession, so we may assume the BAC is the same for all samples of an individual. If we consider the highest value recorded for an individual over all breath samples,  $M$ , to be the 'true' BrAC, then the subject of Fig. 3 is at  $M = 0.085$ . Model I gives, for the three samples, estimates of  $c_a$  of 0.0690, 0.0793 and 0.0740, and Model II gives 0.0797, 0.0772 and 0.0775. The residuals (sum of differences between data and data fit) are noticeably larger for Model I (mean standard error 0.0037 on mean 82 degrees of freedom) than for Model II (0.0012).

Similar fits were obtained for the other subjects.

The five subjects gave a total of 25 samples, which were fit to Models I and II ( $\alpha = 0.025$  and 0.05). Data are summarized in Table 1. In almost all cases, Model II gave a better fit to the breath time series than did Model I.

## DISCUSSION

We can ask two questions of Models I and II: which gives a better fit to the observed breath profiles, and which has greater value in indicating 'true' breath alcohol concentration, in the face of such complications as hypo and hyper exhalation patterns? Although the residuals are smaller with Model II, we must be careful when considering the predictive values of Models I and II.

Model II, for  $\alpha = 0.05$ , gives a fit of  $c_a$  that is, on average, very close to the 'true'  $c_a$ ,  $M$ , with a mean error of  $-0.00064$ . The values of  $c_a$  predicted by Model II, with  $\alpha = 0.025$ , and Model I differ from the actual value by an equivalent amount, the former overestimating by 0.0093, and the latter underestimating by 0.0105 (Table 2). One could use an appropriate scaling factor to

Table 1. Alveolar alcohol fits for models

Subject	Peak	I		II, $\alpha = 0.05$		II, $\alpha = 0.025$	
		$c_a$	$M - \bar{c}_a$	$c_a$	$M - \bar{c}_a$	$c_a$	$M - \bar{c}_a$
A ( $M = 0.102$ )	0.094	0.0887	0.0114	0.0889	0.0118	0.0963	0.0056
	0.102	0.0984		0.0978		0.103	
	0.091	0.0847		0.0830		0.0899	
B ( $M = 0.102$ )	0.086	0.0864	0.0132	0.0862	0.0191	0.0861	-0.0159
	0.102	0.0963		0.0916		0.0934	
	0.084	0.0838		0.0708		0.0778	
C ( $M = 0.085$ )	0.074	0.0690	0.0109	0.0797	0.0069	0.103	-0.0103
	0.085	0.0793		0.0772		0.0837	
	0.079	0.0740		0.0775		0.0991	
D ( $M = 0.129$ )	0.127	0.126	0.006	0.142	-0.055	0.170	-0.017
	0.119	0.115		0.118		0.136	
	0.129	0.126		0.137		0.166	
	0.126	0.125		0.148		0.186	
	0.126	0.127		0.158		0.207	
	0.123	0.126		0.168		0.227	
	0.124	0.125		0.156		0.199	
	0.118	0.117		0.142		0.187	
	0.120	0.118		0.117		0.137	
	0.123	0.122		0.150		0.188	
0.124	0.126		0.166		0.225		
E ( $M = 0.082$ )	0.070	0.0660	0.0109	0.0777	0.0070	0.0981	-0.0089
	0.082	0.0809		0.0815		0.0823	
	0.070	0.0674		0.0664		0.0800	
	0.075	0.0746		0.0758		0.0989	
	0.071	0.0665		0.0737		0.0951	

For five subjects at various peak-exhalation breath-alcohol levels  $M$ , the corresponding model fits for  $c_a$ , alveolar alcohol concentration, for Models I and II. Each subject has presented multiple exhalations. Units for all quantities except  $\alpha$  are g/210l;  $\alpha$  is dimensionless.

compensate for this flaw of Model I and Model II ( $\alpha = 0.025$ ), to eliminate the overestimate or underestimate, or use Model II ( $\alpha = 0.05$ ) to determine  $c_a$ ; the latter will be very accurate, on average.

At this point, however, we must closely examine the variance of the  $c_a$  fits of each model: the variance of  $(M - \bar{c}_a)$  is considerably higher for Model II than for Model I, and is worst in the case with the least error, Model II ( $\alpha = 0.05$ ) (see Table 2.) We must also note the inherent variance in the exhalation peaks, which are used in the field to determine breath alcohol content. The variance of the breath peaks is found to be  $3.9 \times 10^{-5}$ , whereas the variance of the Model I fits for  $c_a$  is  $7.1 \times 10^{-6}$ , roughly 5.5 times less than the natural variance in the breath peaks. Thus although Model I fits the breath profiles rather poorly in shape and has an inherent bias (an underestimate of  $c_a$  of 0.0105), it is far more useful for inter-

Table 2. Comparison of models vs peak readings

Model	$M - \bar{c}_a$	
	Mean	Variance
I	0.0105	$7.1e - 6$
II, $\alpha = 0.05$	-0.00064	$9.6e - 4$
II, $\alpha = 0.025$	-0.0093	$8.2e - 5$

Mean variance of individuals' peaks:  $3.9e - 5$ .

Mean and variance over all subjects of the gap between  $M$ , the peak breath alcohol reading, and  $c_a$ , the best data fit from each model of alveolar air alcohol concentration. We see that the best fit corresponds with the highest variance (Model II,  $\alpha = 0.05$ ) and the worst fit with the lowest variance (Model I). Thus where consistency may be important, a poor fit which underestimates BrAC by a consistent amount may be most reliable.

preting the breath data with the primary aim of determining  $M$  in conditions of uncertain ventilation style — where subjects may be hypo-

ventilating or hyperventilating, unknown to the examiner.

From a practical point of view, therefore, the uncertainty of a subject's alveolar alcohol concentration is considerably less if, instead of simply using the peak recorded value of a given profile, one uses the best fit for  $c_a$  from Model I, and adds 0.0105 to that fit. This is our main result.

Model II, which gives a better fit to  $c_a$  than Model I, is based on the assumption of a linear shape of  $c_i$ , which was the second-simplest assumption on its form. One could develop increasingly more sophisticated models, and for instance include the known fluid dynamics and lung anatomy (Chang and Farhi 1973; Davidson 1975, 1977; Tsu *et al.*, 1988), but this would introduce many more parameters into the model. It is a consistent phenomenon in modelling that too many parameters make good data fitting very difficult. Too few parameters give bad fits, but too many parameters give inconsistent fits. It is important for practical purposes to use the simplest model which will give a good fit to data and have predictive value, neither of which will be found in a ventilation model with more parameters.

The process by which alcohol appears on the breath is undoubtedly complex, involving alveolar gas exchange, deposition of alcohol into the cooler airway mucosa during expiration, and some net flux of alcohol into the breath from the mucosa during inspiration (Ralph *et al.*, 1986). The breath profile is therefore undoubtedly affected by other factors such as body and ambient air temperatures. We have not attempted here to identify the specific biological origin of the ethanol submitted to an instrument for detection. Although this has been investigated elsewhere (Ralph *et al.*, 1986; Tsu *et al.*, 1988; George *et al.*, 1993), it is unimportant from a medicolegal perspective, in that breath presented to a breath alcohol instrument has originated from within the subject's respiratory system, and cannot have a breath alcohol concentration higher than that of the residual alveolar air.

Ralph *et al.* (1986) described three phases of the breath ethanol exhalation profile with phases I and II nonlinear, and the linear phase III being reached after the expiration of about 1.2 l (see Fig. 1). Their value for the phase III slope at an exhalation rate of 0.5 l/s, 0.055 g/210 l/s, is

substantially larger than our third-phase slope, 0.002 g/210 l/s, measured under conditions which more closely resemble those of field testing.

In related work, George *et al.* (1993) evaluated a model for soluble gas exchange in the mucosa. Their phase III slopes agree more closely with ours. They concluded that ethanol, like other soluble gases, displays a reduced diffusion coefficient in the airway mucosa, resulting in the positive slope of phase III. However, their model consistently overestimates the end-expiratory concentration since there is a net deposition of alcohol from the breath into the airway mucosa during expiration. Their model suggests that the end-expiratory breath of a subject can underestimate the alveolar alcohol concentration by as much as 28%, and is never likely to result in an overestimate.

The forensic application of breath alcohol analyses faces many challenges with regard to both analytical and biological issues, including, for example, radio frequency interference (RFI), mouth alcohol bias, abnormal pre-exhalation breathing pattern, and interfering substances. Application of an appropriate model having biologically relevant parameters may assist in evaluating for the presence of these concerns in the exhalation profiles of those arrested for driving while intoxicated. Abnormal profile characteristics can be identified through data retention and appropriate model analysis, where they could not in the case of simple end-expiratory sampling. In addition, self-contained micro-processor-based instruments can employ these algorithms in the field for detection and analysis of abnormal profiles. Moreover, knowledge of a biologically appropriate model could assist in instrument development and evaluation through the use of simulated breath data.

The statutory language of most jurisdictions prohibits driving a motor vehicle with a breath alcohol concentration above some threshold. An important legal question is, 'What is breath?' That is, at what point in a continuous exhalation does the sample's alcohol concentration constitute the statutory breath alcohol concentration? Direct sampling of alveolar air is impossible, yet is theoretically the best correlate of pulmonary blood alcohol. Data retention and mathematical modelling could assist in establishing a firmer legal definition of 'breath' which correlates more closely

with alveolar and blood alcohol levels.

The appropriate forensic protocol is to obtain at least duplicate breath samples. Modelling and parameter determination of duplicate breaths could further verify the analytical and biological reproducibility of breath alcohol measurements and bolster forensic confidence in court.

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