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A model for effective toxic load from fluctuating gas concentrations

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Abstract

At any receptor position in a dispersing gas plume there will be large fluctuations in concentration for the duration of the exposure. The non-linearity of acute toxicity with exposure concentration means that these fluctuations are important to evaluating the overall effect of a release. In this paper, an effective toxic load model with three receptor response parameters was proposed to provide a realistic model of toxicity when applied to a fluctuating concentration time series. The receptor response factors included were an uptake time constant, a recovery time constant, and a saturation concentration. The effective toxic load model was compared with the standard toxic load model using simulated time series produced by a stochastic model. For a realistic simulated hydrogen sulphide exposure, the effective toxic load was found to provide more realistic estimates of fatalities than the conventional exposure toxic load calculations.

Keywords: Toxic load; Concentration fluctuations; Receptor response; Toxic gas; Hydrogen sulphide

1. Introduction

The hazard posed by an acutely toxic gas release depends non-linearly upon exposure concentration and exposure duration. At a fixed receptor location in a dispersing gas

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plume, random turbulent dilution and dispersion processes cause wide fluctuations in the instantaneous concentrations from zero (background) levels to greater than 20 times the mean concentration. These large fluctuations coupled with the non-linearity of toxicity with exposure concentration can have a large effect on the toxic response from a release.

Acutely toxic chemicals cause effects ranging from annoyance caused by an offensive odor to fatality. All of these effects are important, but in practice only serious injury or fatalities can be reliably measured and reported. Less severe effects are necessarily subjective and difficult to quantify. Variability in individual susceptibility means that there are variable levels of response. At low doses only sensitive individuals respond while much higher doses are required to affect the resistant individuals. In some cases, the same sort of reactions leading to fatality may also cause the less severe effects so that dose levels that cause only a small fraction of population fatalities will cause less severe effects in the resistant individuals. In this study, the acute toxicity of a gas is evaluated in terms of the level of fatal response.

The limited information available for creating acute toxicity models consists mostly of experiments in which laboratory animals were exposed to constant concentrations for a fixed period of time and the number of fatalities were recorded. In these experiments, the only independent variables were the mean exposure concentration and the exposure duration.

In 1924, Haber reported experiments with various military poison gases and proposed that the appropriate parameter for describing fatal toxicity was $K = Ct$, where K is some constant value for a given level of fatalities, C is the mean exposure concentration, and t is the exposure duration, see Gelzleichter et al. [1]. Haber's law predicts the same level of response provided the product of concentration and time is the same. For example, doubling the exposure concentration would cause the same level of fatalities in half the exposure time. If Haber's law were true, concentration fluctuations would not affect the outcome of a gas release and the mean concentration would be sufficient to predict toxicity.

Busvine [2] proposed that the toxic response of insecticides was better fit by a non-linear parameter with the exposure concentration and time, $C^n t$, where C is the mean exposure concentration, t is the exposure duration, and n is an exponent that is constant for a particular chemical. This parameter is now more widely known as the toxic load $L = C^n t$. The exponent n in the toxic load relationship is typically found by analyzing experimental data using the probit method first proposed by Bliss [3,4]. A complete discussion of the probit method is given by Finney [5].

The toxic load concept and probit relationships have been applied in many studies of acutely toxic gases. Cremer and Warner [6] applied toxic load to the risk analysis of an industrial facility in Rijnmond, Holland. Withers and Lees [7–9] used toxic load to evaluate the effects of chlorine releases. The Center for Chemical Process Safety of the American Institute of Chemical Engineers [10] lists probit relationships to use for evaluating the hazard of many common industrial gases.

A thorough investigation of acutely toxic gas exposure experiments by ten Berge et al. [11] determined that the exponent n in the toxic load parameter is between 1.0 and 3.5 for a wide variety of industrial gases and the most common values of n are between 2 and 3. This non-linear relationship between the effects of concentration, duration and

toxic load means that doubling the exposure concentration has the same effect as increasing the exposure time by a factor of 4 to 8. In an atmospheric exposure to a point source plume with concentrations fluctuating between 0 and more than 20 times the mean concentration, this calculated non-linear effect on toxicity is very large.

There have been attempts to deal with the toxicity of fluctuating concentrations by simplifying the fluctuating time series. Griffiths and Megson [12], Griffiths and Harper [13] and Griffiths [14] modelled fluctuating concentrations as a series of constant peak level square concentration pulses and zero concentration intermittent periods. Ride [15] modelled the fluctuations as uniform spherical eddies of contaminated air suspended inside a cloud of clean air. The problem with both of these approaches is that they oversimplify the exposure concentration fluctuations and do not include physically realistic limitations on the receptor absorption rates or recovery from previous exposure.

Some recent work has incorporated receptor dependent factors into the toxicity calculations. Ride [16] notes that the uptake of toxic chemicals is not instantaneous and not all of the high frequency fluctuations are important for toxicity. Saltzman [17] does not specifically consider toxic load, but does examine the effect that a sine wave fluctuating concentration has on toxicity and notes that the important frequencies of fluctuations are related to the biological half-life of the chemical. However, receptor frequency response is only one of several interacting factors important to the toxic response.

In the present study, the exposure toxic load model is modified by accounting for three receptor response factors: an uptake time constant, a recovery time constant, and a saturation concentration. By applying these three factors, the exposure toxic load is converted to an effective toxic load. This effective toxic load model is used in conjunction with realistic simulated time series of concentration fluctuations in a point source plume. Ensemble averages for a wide range of the uptake, recovery, and saturation will be examined to determine their effect on the effective toxic load. A hydrogen sulphide exposure example is considered to examine the effects of realistic receptor response parameters on a realistic exposure. The objective of this study is to demonstrate that the definition of toxic load can be modified to produce more realistic estimates of fatal toxicity.

2. Exposure toxic load model

2.1. Probit method

The toxic load equation can be derived from experimental data that are fit using the probit method of Finney [5]. The probit method, first proposed by Bliss [3,4], is a way of linearizing a cumulative normal distribution of population response to some toxic exposure variable. One probit unit, Pr, is equal to one standard deviation of the normal distribution. The median or 50th percentile response was defined arbitrarily as $Pr = 5.0$ by Bliss. A probit value of $Pr = 4.0$ is one standard deviation below the median at a cumulative probability of 16%. That is, it is expected that 16% of the population responds to a toxic load that produces a probit value of 4.0. Similarly, 84% of the

population would be expected to respond to a toxic load that produces a probit of Pr = 6.0, one standard deviation above the mean. The fraction F of the population responding to a toxic exposure can be calculated from the probit value Pr using the following relationship

$$F = \frac{1}{2}\left(\mathrm{erf}\left(\frac{\mathrm{Pr}-5}{\sqrt{2}}\right)+1\right) \tag{1}$$

where erf is the error function.

For acutely toxic gases it is observed that the logarithm of the toxic load L follows a normal distribution. This implies that the population response level follows a lognormal distribution with L. Toxic load $L = c^n t$ is the combination of two variables, the concentration c and the exposure duration t. To find the value of n for a particular chemical both variables must be considered using a two dimensional probit relationship:

$$\mathrm{Pr} = q + r \ln c + s \ln t \tag{2}$$

where q is the offset from zero, r is the coefficient of the logarithm of concentration, and s is the coefficient of the logarithm of time. The logarithms in Eq. (2) produce the required lognormal distribution of response with toxic load. For each experiment the probit of response is recorded along with the logarithm of the concentration c and the logarithm of exposure duration t. The linear two-dimensional relationship is solved to give the coefficients q, r, and s.

The toxic load relationship is obtained by combining the last two terms of Eq. (2):

$$\mathrm{Pr} = q + s \ln c^n t \tag{3}$$

where n is the toxic load exponent equal to r/s from Eq. (2) and the toxic load L is defined as

$$L = c^n t \tag{4}$$

In terms of the toxic load L, Eq. (3) can be rewritten as:

$$\mathrm{Pr} = q + s \ln L. \tag{5}$$

To determine the proportion of a population responding to a release, the toxic load L is calculated and then Eq. (5) is used to determine the probit value Pr. The percentage fatalities is obtained from the Pr value and Eq. (1).

2.2. Mean concentration toxic load

In animal experiments, the exposure is in controlled conditions at a constant concentration for a set period of time. In this case, there are no fluctuations in concentration and the instantaneous exposure concentration c is constant with time over the entire exposure duration t_e. With instantaneous concentration c equal to the mean concentration C the toxic load L_{mean} is

$$L_{mean} = C^n t_e. \tag{6}$$

Eq. (6) is the original definition of toxic load. Note that L_{mean} is not the mean toxic load, but rather is a representative toxic load based on the mean concentration C.

The toxic load of a fluctuating exposure concentration could also be calculated with the mean concentration C and the exposure duration t_e. If $n = 1$, the effect of concentration is linear and this is a reasonable approach, but it still does not take into account any uptake, recovery or saturation processes. For most chemicals, where $n > 1$, the mean concentration toxic load L_{mean} misses the important non-linear effects of the concentration fluctuations as well as any limitations on receptor response.

2.3. Instantaneous exposure toxic load

In the risk assessment literature, the definition of toxic load has been extended, without any toxicological justification, to include time varying exposure concentrations, see Ride [15] and ten Berge et al. [11]:

$$L = \int_0^{t_e} c^n \mathrm{d}t \tag{7}$$

where c is the exposure concentration as a function of time. This definition of the toxic load L is the total fluctuating exposure toxic load, and is the most useful toxic load for real exposure scenarios. If the toxic load exponent n is greater than 1 then the exposure toxic load L will be larger than the toxic load calculated with the mean exposure concentration L_{mean}.

The exposure toxic load does not take into account any physically realistic limitations on the fluctuations that will determines the effective toxic load that produces fatalities. In Eq. (7) it is implicitly assumed that the uptake of any exposure concentration is instantaneous; recovery does not occur, so toxic load increases indefinitely with time and repeated exposures; and saturation of biological uptake pathways does not occur. None of these assumptions are justifiable for real exposures and responses.

3. Effective toxic load

In this study, the problems with calculating the toxic load for fluctuating concentrations are addressed by adding three receptor response parameters. An effective toxic load is calculated using an uptake time constant τ_{up}; a recovery time constant τ_r; and a saturation concentration C_s.

3.1. Uptake time constant τ_{up}

The uptake rate of a toxic gas determines how much of the exposure concentration is available to cause damage. We define an effective concentration c_{eff} that is a function of the exposure concentration c and the uptake time constant τ_{up}.

Toxic gases have many possible absorption routes and mechanisms, so there are many possible models of uptake that can be considered. For example, if the gas is a contact irritant, it acts directly on the nose, throat and lung tissue and the relevant effective concentration is the concentration measured in the airways. If it is assumed that

each breath fills the lungs with a uniform well-mixed concentration then the effective concentration is the average concentration during the breath. If the toxic gas acts on internal organs it must first be absorbed into the bloodstream through the alveoli in the lungs and the effective concentration is the concentration in the bloodstream. This bloodstream concentration depends on absorption rates and transfer mechanisms between the lungs and the blood. Absorption of a toxic gas through the skin would involve different mechanisms and rates. The uptake process is complex and is gas specific.

In this study, we assume that all of the complex absorption processes that control the effective concentration can be approximated by a simple first order response function. Using the standard equation for a first order response:

$$\frac{\mathrm{d}c_{\mathrm{eff}}}{\mathrm{d}t} = \frac{c - c_{\mathrm{eff}}}{\tau_{\mathrm{up}}} \tag{8}$$

where c_{eff} is the effective concentration, c is the instantaneous exposure concentration, and τ_{up} is the uptake time constant.

The uptake time constant τ_{up} simply filters the exposure concentration fluctuation time series. Rapid changes in concentration are attenuated so c_{eff} fluctuates more slowly than the external exposure concentration. Fig. 1 illustrates the effect of an uptake time

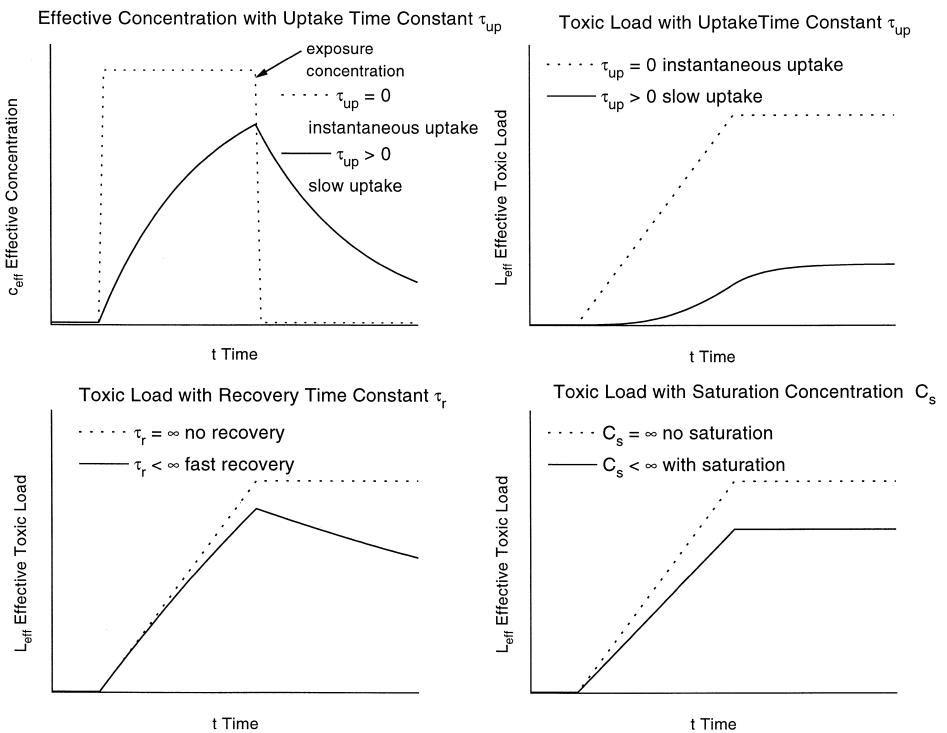

Fig. 1. Effects of uptake time constant τ_{up}, recovery time constant τ_{r} and saturation concentration C_{s} on the effective concentration and the calculated toxic load for a pulse of exposure concentration.

constant with an exposure pulse of concentration. The toxic load L_{eff} in this fluctuating exposure accumulates based on the effective concentration c_{eff} and not the external instantaneous exposure concentration c. The uptake time constant reduces the rate of change of concentration, and so reduces the rate of increase of effective toxic load as well as reducing the final effective toxic load accumulated as compared to the toxic load L calculated using an instantaneous uptake assumption as in Eq. (7).

3.2. Recovery time constant τ_r

By definition, no repair or recovery processes are accounted for in exposure toxic load. As a consequence, even a very small exposure concentration will produce a large toxic load if the exposure time is long. This is unrealistic because the atmosphere contains trace concentrations of many toxic gases, but no measurable effects occur in the general population. Even at much higher concentrations there are few or no measurable effects for many chemicals. For example, Young [18] discusses the case of the people of Rotorua, New Zealand who live in an area with a large amount of geothermal activity and who are routinely exposed to levels of 0.5 to 1.0 ppm of hydrogen sulphide without any apparent ill effects. A standard toxic load exposure calculation using Eq. (7) would predict that everyone in Rotorua would be dead.

As with uptake, recovery is a complex process involving a number of different biological mechanisms. One method of recovery is elimination of the toxic substance by excretion or metabolic reactions that convert it to a less toxic material. This type of recovery depends primarily on the internal concentration. Another recovery mechanism is the repair of damaged tissue, with recovery rate dependent on the type of tissue damaged and its repair mechanisms. Repair might occur at a constant rate or at a rate dependent on the amount of damage. If the recovery processes do not saturate, then first order recovery is a reasonable approximation, see Welling [19] and Gargas et al. [20]. First order recovery processes are also used by Hickey and Reist [21], Eide [22], and Saltzman [23] to adjust occupational exposure levels for unusual working schedules.

For our model, we chose a recovery rate dependent on the current effective toxic load. In effect, this assumes that the effective toxic load is linearly proportional to the internal concentration and the damage level. This assumption makes recovery a first order process with recovery time constant τ_{r}:

$$\frac{\mathrm{d}L_{\text{eff}}}{\mathrm{d}t} = c_{\text{eff}}^{n} - \frac{L_{\text{eff}}}{\tau_{\text{r}}}. \tag{9}$$

Eq. (9) produces an exponential decrease in the effective toxic load with time to simulate recovery. Because recovery is the most complex of the three receptor responses, alternative recovery models, such as a constant rate recovery independent of damage level, are equally plausible. The objective of this study was to include some recovery mechanism, because accounting for any recovery, even with a simplistic approximation, has a profound effect on estimated fatalities.

Fig. 1 shows the effect of the recovery time constant with a simple pulse of concentration. If $\tau_{\text{r}} < \infty$ there is some recovery from any toxic load accumulated. This

causes a reduction in the total toxic load accumulated and a gradual reduction in the toxic load during periods of zero concentration.

3.3. Saturation concentration C_s

Biological reactions are often limited by the availability of enzymes or reaction sites for the toxicant. To address this issue we propose a saturation concentration C_s that is incorporated into the effective toxic load model:

$$\frac{dL_{eff}}{dt} = \frac{c_{eff}^n}{1 + \frac{c_{eff}^n}{C_s^n}}. \tag{10}$$

This relationship follows the well-documented Michaelis–Menten enzyme reaction kinetics, see Pratt and Taylor [24].

The saturation concentration C_s simply clips off high concentration peaks and reduces the effective toxic load L_{eff} compared to having no saturation concentration. A simple example of a saturation concentration is shown in Fig. 1.

3.4. Effective toxic load model

The complete effective toxic load model for L_{eff} incorporates an uptake time constant τ_{up}, a recovery time constant τ_r and a saturation concentration C_s. The easiest way to present the model is with two differential equations. First, the uptake time constant τ_{up} is used to calculate the effective concentration c_{eff}

$$\frac{dc_{eff}}{dt} = \frac{c - c_{eff}}{\tau_{up}} \tag{11}$$

and then c_{eff}, τ_r and C_s are used to calculate the rate of increase of effective toxic load L_{eff}

$$\frac{dL_{eff}}{dt} = \left(\frac{c_{eff}^n}{1 + \frac{c_{eff}^n}{C_s^n}} \right) - \frac{L_{eff}}{\tau_r} \tag{12}$$

Eqs. (11) and (12) can be expressed numerically in time steps of Δt as:

$$c_{eff(n+1)} = c_{eff(n)} + \left(\frac{c - c_{eff(n)}}{\tau_{up}} \right) \Delta t \tag{13}$$

$$L_{eff(n+1)} = L_{eff(n)} + \Delta t \left(\frac{c_{eff(n+1)}^n}{1 + \frac{c_{eff(n+1)}^n}{C_s^n}} \right) - \frac{L_{eff(n)}}{\tau_r} \Delta t. \tag{14}$$

For the case of instantaneous uptake ($\tau_{up} = 0.0$), no recovery ($\tau_r = \infty$), and no saturation level ($C_s = \infty$) Eqs. (11) and (12) reduce to the original definition of exposure toxic load integrated with time over a fluctuating concentration time series as in Eq. (7).

$$\frac{dL_{eff}}{dt} = c^n = \frac{dL}{dt} \quad \text{if } \tau_{up} = 0,\ \tau_r = \infty,\ C_s = \infty. \tag{15}$$

The numerical toxic load model given by Eqs. (13) and (14) can be applied directly to experimental or numerically generated time series of concentration fluctuations.

4. Concentration fluctuations in plumes

The effective toxic load model L_{eff} is most useful when applied directly to a concentration time series. Fig. 2 shows two examples of typical intermittent exposure

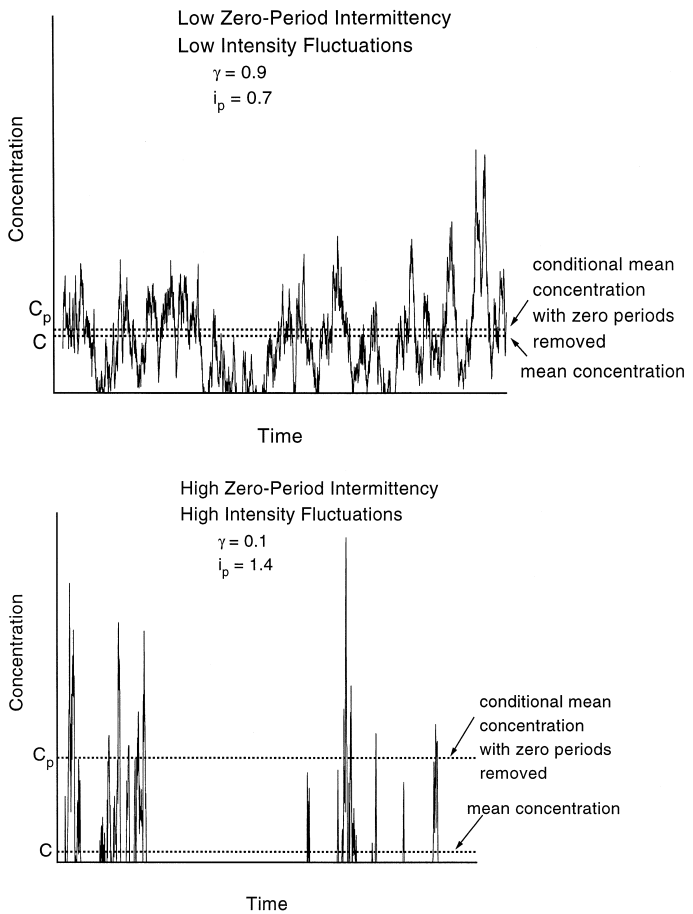

Fig. 2. Examples of typical intermittent concentration fluctuation time series.

concentration fluctuation time series. Highly intermittent plumes are characterized by short bursts of high concentration interspersed with long periods of zero concentration. Plumes with a low intermittency are characterized by much smaller fluctuations about the mean concentration. These time series can be described using four parameters: intermittency factor γ, mean concentration C, conditional fluctuation intensity i_p, and integral time scale of concentration fluctuations T_c.

4.1. Intermittency factor

The intermittency factor γ is defined as the fraction of the total exposure time t_e during which the concentration is greater than zero (background) concentration. In practice, the cutoff for zero concentration is set by the measurement instrument at some concentration slightly greater than zero or equal to the atmospheric background concentration of the particular chemical. For analysis purposes, all non-measurable or background concentrations in the fluctuating time series will be treated as zero concentrations.

With the intermittency concept, two different sets of statistics can be calculated for a given time series. Conditional (in-plume) statistics apply only to the non-zero measurable concentrations and are denoted by a subscript 'p'. The total statistics include all of the zero concentrations as well as the in-plume concentrations and have no subscript.

4.2. Mean concentration

The mean concentration C is the average concentration over the entire duration of the exposure, including the zero periods. A conditional mean concentration C_p is calculated by including only the non-zero (in-plume) concentrations where $C_p = C/\gamma$.

The total mean concentration C is the most sensible concentration to use for comparing two different fluctuation time series. It is the easiest concentration to measure because it is a long term average and is insensitive to the probe response time. Virtually all dispersion models are based on time averaged mass flux balances in a dispersing plume and they provide estimates of only the time or ensemble mean exposure concentration for a particular spatial position.

4.3. Fluctuation intensity

The conditional fluctuation intensity is $i_p = c'_p/C_p$ where c'_p is the conditional (in-plume) standard deviation of the concentration. The total fluctuation intensity $i = c'/C$ includes the zero concentrations where c' is the standard deviation including the zeroes.

The conditional fluctuation intensity i_p and the total fluctuation intensity i are related to each other through the intermittency factor γ by the exact equation:

$$\gamma = \frac{1 + i_p^2}{1 + i^2}. \tag{16}$$

A derivation of this relationship can be found in Wilson [25].

The conditional fluctuation intensity i_p is used as the parameter of interest because it is easier to interpret than the total fluctuation intensity and is much less sensitive to the intermittency factor γ. The conditional intensity gives an indication of how large the fluctuations are when measurable (non-zero) concentrations are present. If i_p increases, peak concentrations and exposure toxic load will both be higher.

The total time series fluctuation intensity i is less informative because it includes the intermittent periods of zero concentration. If i increases it could be due to either a smaller intermittency factor or an increase in the fluctuation intensity, so two pieces of information are required to decide if the peak concentrations increase.

Any combination of conditional fluctuation intensity i_p, fluctuation intensity i, and intermittency factor γ that satisfies Eq. (16) is possible, but it has been observed that in dispersing atmospheric plumes there is some relationship between i^2 and i_p^2. Wilson [25] suggests the following empirical equation determined from a variety of laboratory and full scale plumes:

$$i_p^2 \simeq \frac{2i^2}{2+i^2}. \tag{17}$$

4.4. Fluctuation time scale

The time scale T_c is the integral autocorrelation fluctuation time scale of the turbulent concentration fluctuations. The shorter the T_c, the faster the fluctuation process occurs. In the atmosphere, the fluctuation time scale varies depending on the wind speed, atmospheric turbulence, downstream position, height above the ground and distance from the centreline of the plume. Using an approximation for the fluctuation time scale near ground level given by Wilson [25], T_c is typically 10 to 100 s for receptor locations a few hundred meters downwind of a point source.

5. Parametric study

Each effective toxic load parameter τ_{up}, τ_r, and C_s was studied by applying the effective toxic load model calculation L_{eff} to an ensemble of random time series of intermittent concentration fluctuations generated with a stochastic simulation. Using the relationship between the conditional fluctuation intensity i_p and the intermittency factor γ from Eqs. (16) and (17), a realistic range of intermittency factors $\gamma = 0.1$, 0.5 and 0.9 and the corresponding conditional fluctuation intensities $i_p = 1.4$, 1.1 and 0.7 were tested with the toxic load exponents $n = 1$, 2 and 3. Ensembles of 100 random time series were generated for each intermittency factor γ and conditional fluctuation intensity i_p pair.

Large ensembles were required to find stable values for highly intermittent fluctuations. Even with 100 realizations there was still significant variability. The realization to realization variability is large therefore there can be a large difference between the ensemble average level of toxic response and the actual toxic response of a real release

that will have only a single realization. This has important implications for estimating the 'worst-case' scenario in a risk assessment.

The objective of this parametric study was to determine the range of τ_{up}, τ_r, and C_s that produced a significant effect on the effective toxic load. The effective toxic load L_{eff} calculated from Eqs. (11) and (12) should be significantly different from either the exposure toxic load L_{mean} calculated with the mean concentration as in Eq. (4) or the fluctuating exposure toxic load L calculated from the integrated instantaneous exposure concentration as in Eq. (7) depending on the value of the receptor response parameters.

5.1. Toxic load ratio (TLR)

For the parametric study of the effective toxic load it is convenient to normalize by the mean concentration exposure toxic load L_{mean} calculated from Eq. (6). This toxic load ratio TLR is similar to that defined by Ride [15]. The TLR is:

$$\mathrm{TLR} = \frac{L_{eff}}{L_{mean}}. \tag{18}$$

The TLR can also be thought of as an amplification factor for the toxic load caused by the fluctuating concentration.

5.2. Fluctuating concentration exposure toxic load

Consider the case of instantaneous uptake ($\tau_{up} = 0$), no recovery ($\tau_r = \infty$) and no saturation level ($C_s = \infty$). The effective toxic load from Eqs. (11) and (12) reduces to the fluctuating exposure toxic load L from Eq. (7). Fig. 3 shows the toxic load ratio TLR_{fluct}

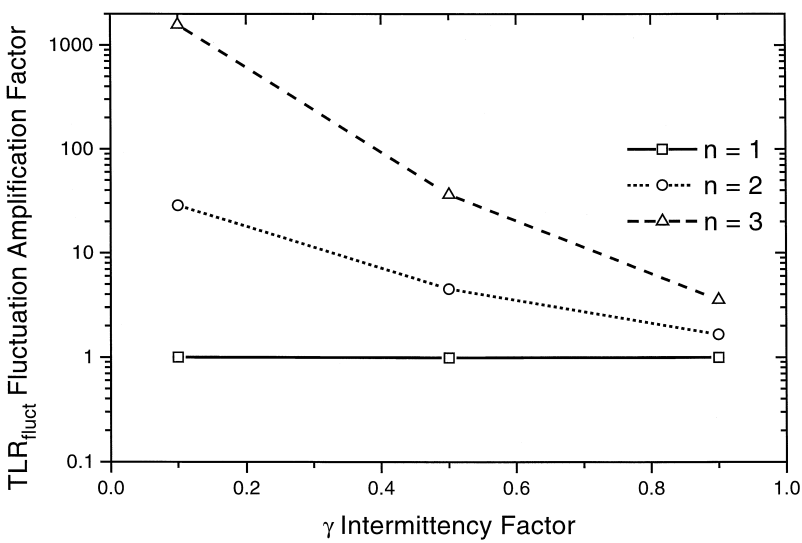

Fig. 3. Fluctuation amplification factor TLR_{fluct} for the fluctuating exposure toxic load L.

produced by calculating the exposure toxic load with no uptake time constant, no recovery and no saturation.

If the toxic load exponent $n = 1$, the effect of concentration is linear and the fluctuations have no effect on the exposure toxic load. The mean concentration toxic load L_{mean} is correct for this situation. If $n > 1$ the concentration has a non-linear effect and the fluctuations become very important. For example, if $n = 3$ and the intermittency factor is 0.1 with the corresponding fluctuation intensity of 1.4 the TLR_{fluct} amplification factor is about 1500. That is, the fluctuations cause an exposure toxic load 1500 times larger than the toxic load predicted from the mean concentration.

The additional time constants and saturation levels of the effective toxic load model L_{eff} will moderate these TLR_{fluct} amplification factors with realistic limitations on the uptake rate, recovery from the exposure, and a saturation level.

5.3. Uptake time constant

The uptake time constant τ_{up} was studied by setting the recovery time constant $\tau_r = \infty$ (no recovery) and the saturation concentration $C_s = \infty$ (no saturation). An uptake time constant has the effect of a low pass filter and simply reduces the fluctuation amplification factor TLR_{fluct} shown in Fig. 3. The toxic load ratio with an uptake time constant, $TLR_{\tau_{up}}$, grows quickly until it reaches a steady state value after approximately 5 τ_{up} has elapsed. If the uptake is very fast relative to the time scale of the concentration fluctuations, that is τ_{up} is less than 0.01 T_c, then very little of the fluctuation is removed by filtering and $TLR_{\tau_{up}}$ is approximately equal to the TLR_{fluct}. If τ_{up} is greater than 100 T_c then most of the fluctuations are removed by filtering, the mean concentration C is the only important concentration value, and the $TLR_{\tau_{up}} = 1$.

A typical exposure scenario can be considered to help interpret this information. In an atmospheric exposure near ground level a few hundred meters from the source, the time scale of the concentration fluctuations is $T_c \simeq 100$ s. If we assume that uptake rate is the only important factor and if the uptake rate for a human was $\tau_{up} \simeq 1$ s, after about 5 $\tau_{up} \simeq 5$ s, the $TLR_{\tau_{up}}$ will be near its steady state value. If the toxic load exponent is $n = 3$ and the fluctuations have a low intermittency factor, say $\gamma = 0.1$ with a fluctuation intensity of $i_p = 1.4$, then $TLR_{\tau_{up}} = 1500$ and the effective toxic load L_{eff} accumulated is about 1500 times larger than the mean concentration exposure toxic load L_{mean}. Even if the uptake rate of the gas were much slower, on the order of 100 s, $TLR_{\tau_{up}} \simeq 500$ and $L_{eff} \simeq 500\ L_{mean}$.

5.4. Recovery time constant

The recovery time constant τ_r was isolated by setting the saturation concentration $C_s = \infty$ (no saturation) and the uptake time constant $\tau_{up} = 0$ (instantaneous uptake). Recovery produces a gradual decay of the toxic load with exposure time. In Fig. 4 the toxic load ratio with some recovery time constant TLR_{τ_r} is normalized by the toxic load ratio that would be calculated with $\tau_r = \infty$ (no recovery). If there is no recovery the toxic load ratio is equal to the TLR_{fluct} as shown in Fig. 3.

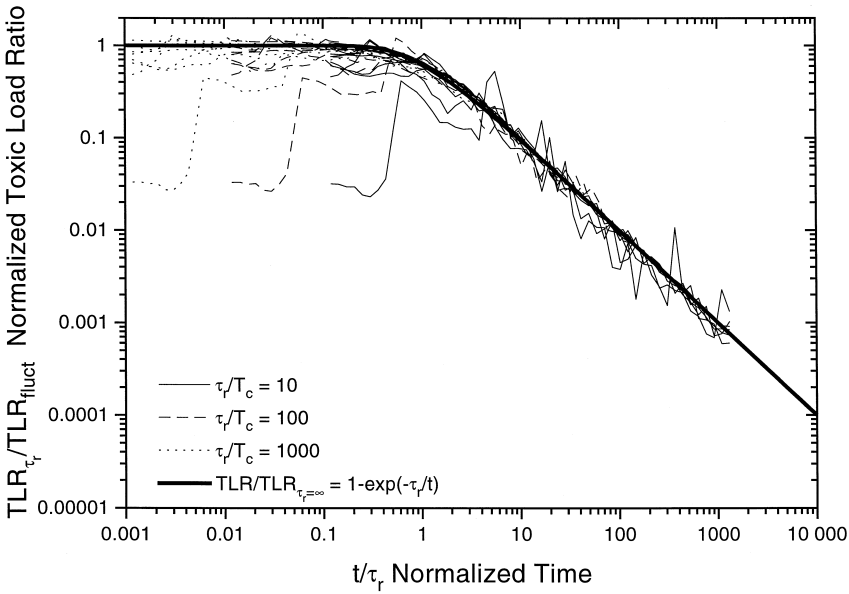

Fig. 4. Ratio of $\mathrm{TLR}_{\tau_r}/\mathrm{TLR}_{\mathrm{fluct}}$ for three recovery time constants τ_r/T_c at time t/τ_r. For each time constant value three different intermittency factor γ and conditional fluctuation intensity i_p combinations were tested (1) $\gamma = 0.1$ and $i_p = 1.4$ (2) $\gamma = 0.5$ and $i_p = 1.1$ (3) $\gamma = 0.9$ and $i_p = 0.7$. Each line is the ensemble average of 100 realizations with one combination of recovery time constant, intermittency factor and fluctuation intensity.

Fig. 4 shows the decay of the toxic load with time. This decay rate is independent of γ, i_p, and n and is only a function of the elapsed time. After about 10 τ_r the TLR_{τ_r} is less than 10% of the $\mathrm{TLR}_{\mathrm{fluct}}$ with no recovery. This relationship can be well approximated by:

$$\frac{\mathrm{TLR}_{\tau_r}}{\mathrm{TLR}_{\mathrm{fluct}}} = 1 - \exp\left(-\frac{\tau_r}{t}\right). \tag{19}$$

The recovery time constant always makes the effective toxic load L_{eff} less than the fluctuating exposure toxic load L calculated from Eq. (7). If the total exposure time is long enough the TLR_{τ_r} amplification factor can be less than 1.0.

For a typical example, consider the hydrogen sulphide biological half life of 20 min from Saltzman [17]. This corresponds to a recovery time constant τ_r of about 30 min. The toxic load exponent n for hydrogen sulphide is about 2.5. Assume that the exposure is in a moderately intermittent point source plume with $\gamma = 0.5$ and $i_p = 1.1$. If the total exposure time is less than 30 min, the recovery time constant has no effect, and $\mathrm{TLR}_{\tau_r}/\mathrm{TLR}_{\mathrm{fluct}}$ is approximately unity so $L_{\mathrm{eff}} \simeq L \simeq 10\ L_{\mathrm{mean}}$. If the exposure goes on for longer than 300 min or 5 h $L_{\mathrm{eff}} < L_{\mathrm{mean}}$ with significant recovery occurring during the exposure.

5.5. Saturation concentration

The saturation concentration C_s was isolated by setting $\tau_{up} = 0.0$ (instantaneous uptake) and $\tau_r = \infty$ (no recovery). Unlike uptake and recovery, saturation is not a time dependent process. The saturation concentration simply cuts off peak concentrations and has a constant effect throughout the exposure. Because concentration controls the rate of increase of the toxic load, C_s also limits the maximum uptake rate.

If the saturation concentration is very high, that is greater than 100 times the mean concentration $C_s > 100C$, then it has little effect and the TLR_{C_s} amplification factor is approximately equal to the fluctuating exposure toxic load ratio TLR_{fluct}. As C_s becomes small, more of the high concentration peaks are cut off. If the saturation concentration is approximately equal to the mean concentration then the fluctuation peaks are all removed and the TLR_{C_s} is very small. Unfortunately, values of the saturation concentration for toxic gases are difficult to find in the literature.

Consider an exposure to an average concentration of 10 ppm of hydrogen sulphide where $n \simeq 2.5$. If the saturation levels are low, on the order of 100 ppm, then the TLR_{C_s} is about 5 for the highly intermittent case with $\gamma = 0.1$. This means that the fluctuations would only amplify the toxic load of the mean concentration by about a factor of 5. The conservative assumption is that the saturation level is very high and therefore the saturation concentration does little to reduce the effects of high peak concentrations.

6. Example for hydrogen sulfide exposure

The effective toxic load model is intended to be used by applying it directly to a realistic fluctuating concentration time series. The limited parametric study in Section 5 demonstrated the effects of each individual factor τ_{up}, τ_r and C_s, but it is not clear how these receptor response factors interact in a realistic exposure. To demonstrate that these factors are significant two hydrogen sulphide gas exposure scenarios were simulated and the results are shown in Figs. 5 and 6.

For the simulated exposures the mean concentration was set to $C = 10$ ppm to match the 8 h average concentration allowed for occupational exposure in Alberta [26]. Two intermittency factor and fluctuation intensity pairs were used to simulate a wide range of exposure conditions. An exposure near the plume centreline was simulated with $\gamma = 0.9$ and $i_p = 0.7$. An exposure to the highly intermittent edges of the plume had $\gamma = 0.1$ and $i_p = 1.4$. The fluctuation time scale was set to $T_c = 100$ s which is a typical time scale for concentration fluctuations in the atmosphere.

The fatal toxic load for the simulated exposures was calculated from the probit model given by Rogers [27] for predicting fatalities for human exposures in Alberta. The probit equation is:

$$\mathrm{Pr} = -36.2 + 2.366 \ln c^{2.5} t \tag{20}$$

where Pr is the probit value, c is the concentration in ppm, and t is the time in seconds. The toxic load equation from this probit relationship is $L = c^{2.5} t$. Using Eq. (20) the exposure toxic load required to produce a certain level of fatalities can be calculated. At

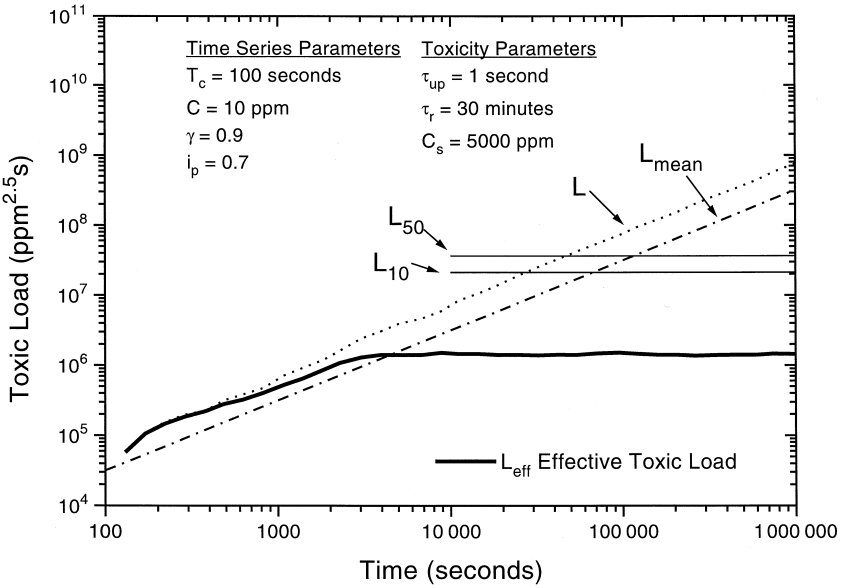

Fig. 5. Example of the effective toxic load L_{eff} predicted for a hydrogen sulphide exposure with a high intermittency factor $\gamma = 0.9$ and the corresponding low fluctuation intensity $i_p = 0.7$. The L_{10} level is the toxic load predicted to cause 10% fatalities in the population and the L_{50} level is the toxic load predicted to cause 50% fatalities according to Rogers [27]. L is the fluctuating exposure toxic load and L_{mean} is the exposure toxic load calculated using the mean concentration. Each L_{eff}, L_{mean}, and L line is the smoothed through ensemble average of 10 realizations.

$\text{Pr} = 3.72$ we expect 10% fatalities in the population, $L_{10} = 2.1 \times 10^7$ ppm$^{2.5}$ s. At $\text{Pr} = 5$ we expect 50% fatalities and $L_{50} = 3.7 \times 10^7$ ppm$^{2.5}$ s.

The receptor response parameters were set based on limited available data and some reasonable assumptions. An uptake time constant τ_{up} was determined by making the conservative assumption that the uptake rate is governed primarily by the inhalation rate. It is estimated that τ_{up} is about 1 s. Given that the uptake is treated as a first order process this means that the effective concentration c_{eff} would reach 95% of the external concentration c after 3 time constants or 3 s (approximately the time for a deep breath). The recovery time constant τ_r was based on the biological half life of hydrogen sulphide given by Saltzman [17] of 'less than 20 min'. This corresponds to a recovery time constant of $\tau_r \simeq 30$ min. The saturation concentration C_s has not been documented in the literature. A conservative assumption of $C_s = 5000$ ppm was used for this simulated hydrogen sulphide exposure.

6.1. Simulated exposure results

For each intermittency and fluctuation intensity pair 10 separate random realizations were created with a stochastic model and the average effective toxic load L_{eff} was calculated using Eqs. (13) and (14). Figs. 5 and 6 show the results of these calculations.

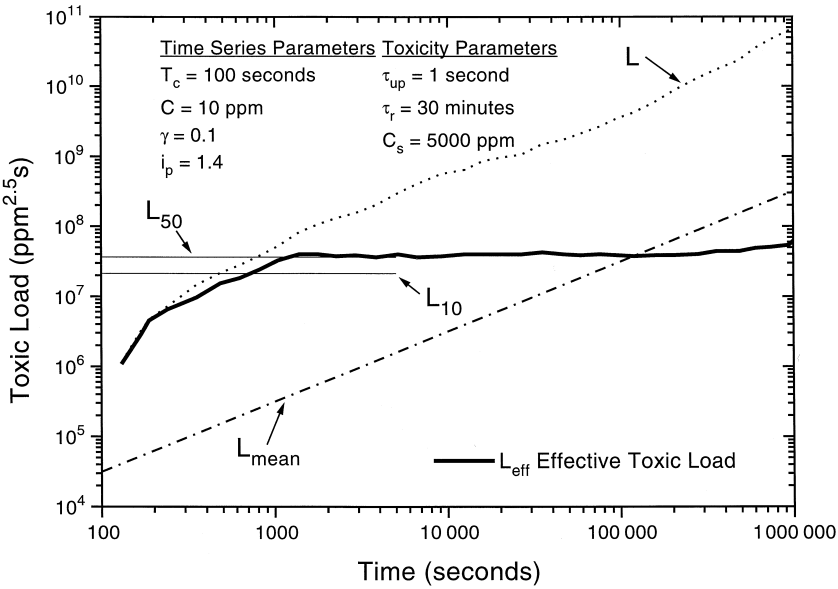

Fig. 6. Example of the effective toxic load L_{eff} predicted for a hydrogen sulphide exposure with a low intermittency factor $\gamma = 0.1$ and the corresponding high fluctuation intensity $i_p = 1.4$. The L_{10} level is the toxic load predicted to cause 10% fatalities in the population and the L_{50} level is the toxic load predicted to cause 50% fatalities according to Rogers [27]. L is the fluctuating exposure toxic load and L_{mean} is the exposure toxic load calculated using the mean concentration. Each L_{eff}, L_{mean}, and L line is the smoothed through ensemble average of 10 realizations.

For comparison, L_{mean} from Eq. (6) calculated using the mean exposure concentration of 10 ppm and the fluctuating exposure toxic load L from Eq. (7) are also plotted. The L_{10} and L_{50} lines indicate the toxic load necessary to cause 10% and 50% fatalities according to Rogers [27]. In these examples only the average toxic loads have been considered, with curves smoothed through variations caused by the small ensemble of 10 realizations. Worst case scenarios could be evaluated by considering a number of random realizations and finding the time at which the toxic load first exceeds a dangerous level.

If the total exposure time is short, $t < 600$ s, then the effective load L_{eff} is approximately equal to the fluctuating exposure toxic load L. The additional parameters of the effective toxic load model have little effect for very short duration exposures. At longer times it is apparent that the exposure toxic load calculated from the mean concentration L_{mean} and the fluctuating exposure toxic load L without any receptor response parameters both increase steadily with time while L_{eff} levels off after approximately 2000 s or 30 min when the effect of the increasing toxic load caused by uptake is balanced by the recovery process.

6.2. Accuracy of the toxic load model

It is difficult to determine the accuracy of any of the methods of calculating the toxic load because there is no direct experimental data available for human or animal

exposures to fluctuating concentrations. However, more general information on the toxicity of hydrogen sulphide can be used to estimate which of the toxic load calculation approaches is more realistic.

Fig. 5 has a mean concentration of 10 ppm, an intermittency factor of $\gamma = 0.9$ and fluctuation intensity $i_p = 0.7$. This relatively constant exposure with small fluctuations about the mean meets the requirements of a safe occupational exposure level according to Alberta Health [26]. The toxic load calculated with the effective toxic load model L_{eff} indicates that not even 10% fatalities would occur with this type of exposure and the toxic load would level off at a relatively safe level. Calculation of the mean concentration exposure toxic load L_{mean} and the fluctuating concentration exposure toxic load L indicate at least 10% fatalities after 30 000 to 60 000 s or 8 to 16 h of exposure. It is inconceivable that the allowable occupational exposure limit would be set at a level that would produce fatalities, so in this particular case we conclude that the effective toxic load L_{eff} is a more realistic estimation of the actual effects of the release.

In contrast, Fig. 6 shows a highly intermittent exposure with $\gamma = 0.1$ and $i_p = 1.4$. The time averaged concentration is still 10 ppm, so these fluctuations would meet the Alberta occupational exposure limits. Other exposure limits for hydrogen sulphide have been defined in an attempt to cover some fluctuating situations. For example, the immediate danger to life and health limit (IDLH) is 300 ppm set by the National Institute for Occupational Safety and Health (NIOSH) in the USA, see Environmental Protection Service [28]. There is no time factor given with this value. The exposures in Fig. 6 do exceed 300 ppm for times as long as 1 $T_c = 100$ s despite the fact the average concentration is only 10 ppm.

In Fig. 6, the fluctuating exposure toxic load L produces 50% fatalities in about 10 min, the effective toxic load L_{eff} indicates up to 50% fatalities within about 30 min and the toxic load calculated with the mean concentration L_{mean} predicts 50% fatalities after approximately 28 h. The fatalities would be caused by exceeding the high concentration levels long enough to cause adverse effects. With large fluctuations it seems reasonable that this could occur relatively quickly. The 28 h estimate of L_{mean} is probably too long, while the 30 min estimate of L_{eff} is more reasonable.

With these two simple example release scenarios it seems that the effective toxic load L_{eff} is a more consistently realistic estimation of the fatal response from a hydrogen sulphide release than the mean exposure toxic load L_{mean} or the fluctuating exposure toxic load L_{fluct}.

7. Conclusions

The effective toxic load model presented in this study adds three additional receptor response parameters to the standard toxic load model: an uptake time constant τ_{up}, a recovery time constant τ_r, and a saturation concentration C_s. These additional parameters are used to correct the exposure toxic load model which is based on constant concentration and fixed duration exposures to laboratory animals. Real exposure scenarios are much different than these experimental exposures and include large fluctuations about the mean concentration and intermittent periods of zero concentration clean air.

The parametric study demonstrated that the receptor parameters make a significant difference to the toxic load that is calculated for a fluctuating exposure. The simple methods of calculating exposure toxic load using the mean exposure concentration, or even using the instantaneous fluctuating concentration, produce different toxic load levels than those calculated with the effective toxic load model.

Two realistic example hydrogen sulphide exposures were considered to determine the accuracy of the effective toxic load model. There is no direct data available for human exposures to fluctuating concentrations, but some simple concentration exposure standards were used to determine which toxic load model is more realistic. For a low intermittency low fluctuation intensity plume the effective toxic load model agreed with the Alberta occupational exposure limits while the exposure toxic loads predicted unrealistically high fatalities. For a highly intermittent high fluctuation intensity exposure which would exceed the immediate danger to life and health level, all toxic load models predict fatalities, but the effective toxic load model predicted up to 50% fatalities within 30 min while the mean concentration exposure toxic load model required 28 h to cause fatality. The effective toxic load model provides more consistently realistic estimates of toxicity for a wide range of intermittent fluctuating exposures.

The effective toxic load model is a significant advancement over the standard exposure toxic load calculations because it incorporates some simple receptor response parameters and produces more realistic estimates of fatalities from a fluctuating exposure. Although the ideal toxicity model would be a complete physiologically based pharmacokinetic model of the human body for each specific toxic gas, at the present time this is not technically feasible. The effective toxic load model provides a method of accounting for some of the most important receptor response factors and improving the hazard assessment of toxic releases.

The weakest link in the present effective toxic load model is the simplified recovery process which is difficult to justify in toxicological terms. Future work should test alternative models for recovery and applying the effective toxic load model to toxic gases other than hydrogen sulphide.

References

[1] T.R. Gelzleichter, H. Witchi, J.A. Last, Toxicol. Appl. Pharmacol. 112 (1992) 73–80.
[2] J.R. Busvine, Ann. Appl. Biol. 25 (1938) 605–632.
[3] C.I. Bliss, Science 79 (1934) 38–39.
[4] C.I. Bliss, Science 79 (1934) 409–410.
[5] D.J. Finney, Probit Analysis, 3rd edn., Cambridge Univ. Press, 1971.
[6] Cremer and Warner, Risk Analysis of Six Potentially Hazardous Industrial Objects in the Rijnmond Area, a Pilot Study, Reidel, Dordrecht, Holland, 1982.
[7] R.M.J. Withers, F.P. Lees, J. Hazard. Mater. 12 (1985) 231–282.
[8] R.M.J. Withers, F.P. Lees, J. Hazard. Mater. 12 (1985) 283–302.
[9] R.M.J. Withers, F.P. Lees, J. Hazard. Mater. 15 (1987) 301–342.
[10] Guidelines for Chemical Process Quantitative Risk Analysis, Center for Chemical Process Safety of the American Institute of Chemical Engineers, 1989.
[11] W.F. ten Berge, A. Zwart, L.M. Appelman, J. Hazard. Mater. 13 (1986) 301–309.
[12] R.F. Griffiths, L.C. Megson, Atmos. Environ. 18 (1984) 1195–1206.
[13] R.F. Griffiths, A.S. Harper, J. Hazard. Mater. 11 (1985) 369–372.

[14] R.F. Griffiths, J. Loss Prevent. Process Ind. 4 (1991) 49–57.
[15] D.J. Ride, J. Hazard. Mater. 9 (1984) 235–240.
[16] D.J. Ride, Environmetrics 6 (1995) 643–650.
[17] B.E. Saltzman, J. Air Waste Manage. Assoc. 46 (1996) 1022–1034.
[18] M.R. Young, Study trip to Rotorua, New Zealand, Technical report, Amoco Canada Petroleum, 1983.
[19] P.G. Welling, Pharmacokinetics, Chap. 16, American Chemical Society, 1986.
[20] M.L. Gargas, M.A. Medinsky, M.E. Andersen, Crit. Rev. Toxicol. 25 (1995) 237–254.
[21] J.L.S. Hickey, P.C. Reist, Am. Ind. Hyg. Assoc. J. 38 (1977) 613–621.
[22] I. Eide, Ann. Occup. Hyg. 34 (1990) 13–17.
[23] B.E. Saltzman, Am. Ind. Hyg. Assoc. J. 49 (1988) 213–225.
[24] W.B. Pratt, P. Taylor, Principles of Drug Action, 3rd edn., Churchill Livingstone, 1990.
[25] D.J. Wilson, Concentration Fluctuations and Averaging Time in Vapor Clouds, Center for Chemical Process Safety of the American Institute of Chemical Engineers, 1995.
[26] Report on H_2S toxicity, Alberta Health, 1988, 65 pp.
[27] R.E. Rogers, Toxicological justification of the triple shifted Rijnmond equation, in: Risk Approach: An Approach for Estimating Risk to Public Safety from Uncontrolled Sour Gas Releases, Appendix B, Vol. 7, Technical report, Alberta Energy Resources Conservation Board, 1990.
[28] Hydrogen sulphide, Technical Services Branch, Environmental Protection Programs Directorate, Ottawa, Ontario, July 1984.