COMPREHENSIVE DEFINITIONS OF EXPOSURE AND DOSE TO ENVIRONMENTAL POLLUTION

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COMPREHENSIVE DEFINITIONS OF EXPOSURE AND DOSE

TO ENVIRONMENTAL POLLUTION

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I. EPA BACKGROUND AND PERSPECTIVE

The many benefits of a modern, developing, industrial society are accompanied by certain hazards. Careful assessment of the relative risks of existing and new manmade environmental hazards is required for the establishment of effective regulatory policy. These regulations serve to enhance the quality of our environment in order to promote the public health and welfare and the productive capacity of our Nation's population.

The complexities of environmental problems originate in the interdependencies between the various physical, chemical, and biological segments of our natural and social world. Definitions of and solutions to these environmental problems requires an integrated program of research and development involving a number of scientific disciplines. The Office of Research and Development, U.S. EPA, conducts a coordinated environmental monitoring and health research program. The research focuses on entry, movement, fate, and effects of air pollutants, water pollutants, toxic substances, hazardous wastes, pesticides, and non-ionizing radiation. Wide ranges of chemical contaminants known or suspected to cause health problems are studied. Major emphasis is placed on development of new methods for environmental monitoring, health effects identification and design, analysis and interpretation of environmental data. The Office of Research and Development also develops and revises air and water criteria and health assessment documents on pollutants for which regulatory actions are being considered.
II. EPA RELEVANCE

Traditionally air pollutant exposure has usually meant exposure to ambient air. Environmental scientists have long recognized that measurements at outdoor monitoring sites provide a severely limited estimate of personal exposure. There is a rapidly growing awareness of the importance to exposure of enclosed locations, termed micro-environments, such as homes, offices, schools, shops and transportation vehicles such as automobiles, airplanes, or buses. Concerns about the adequacy of ambient measurements alone have been increased by recent information about the "tightness", i.e., lower air exchange rate, of newer homes, the large proportion of time that most individuals spend indoors, and the awareness of significant indoor sources of air pollution in many homes. Given the dramatic improvement in the ambient air concentrations for many pollutants, particularly the "criteria" pollutants, brought about by the environmental regulatory process, the focus of attention for exposure is shifting from outdoor to microenvironment locations.

Recent developments in the measurement technology (smaller, lighter, more portable instruments) of air pollution concentrations have created new opportunities for improving the estimates of personal exposures used in exposure assessment methodology and dose-response modeling. As the personal exposure capabilities develop, this research area is in need of consistent, rigorous definitions of key terminology such as exposure and dose in order that this area can continue to mature in an effective direction. In the present report by Duan, Dobbs, and Ott, a valuable framework is developed and discussed for the required definitions.
ABSTRACT

Exposure and dose are two of the most important and frequently used concepts in the environmental sciences. However, there is a lack of consistency and consensus about the exact meaning of those terms. Part of the ambiguity arises because both exposure and dose take on a variety of forms. In order to clarify the issues and help alleviate the ambiguity, we propose a set of definitions which are widely applicable, and have a consistent logical structure. Generically, exposure is the contact of a target with a pollutant. Dose is the presence of a pollutant inside a target. In order to obtain precise definitions of exposure and dose, we need to specify the time frame and five auxiliary parameters: the target, the pollutant, the medium, the route, and the exposure boundary.

This paper builds on the generic concepts described above, and proposes detailed definitions for various forms of exposures and doses, including instantaneous exposure, exposure profile, peak exposure, integrated exposure, average exposure, and analogous definitions for dose. We also discuss the relationship between exposure and dose.
1. INTRODUCTION

Exposure and dose are two of the most widely used concepts in the environmental sciences. They are used to describe the impact of environmental pollution on biological and ecological targets (both human and non-human). They are used to evaluate the success of environmental regulations: a successful regulatory action should lead to a general reduction in exposure and dose. They are also used to predict health effects, or as input for epidemiological models.

Despite the importance of the concepts exposure and dose, there is substantial ambiguity on the exact meaning of those concepts. Governmental officials, environmental scientists, and other specialists often intend different meanings when they use the terms exposure and dose for environmental pollutants.

Exposure as a general unqualified term has been used in many different ways when applied to environmental monitoring studies or human health effects assessments. Sometimes the term refers to a quantitative measure of the environmental pollutant. One example is that exposure is "the amount of a particular physical or chemical agent that reaches a receptor or target" (Gilpin, 1976). Another is that exposure is "normally measured as the concentration of pollutant in the ambient air, soil, food and water" (Moriarty, 1983). Sometimes the term is used as a qualitative measure of the severity of the environmental pollution. For example, the term is used to distinguish different types of toxicity tests such as acute and subacute exposures, lethal and sublethal exposures, etc. Sometimes the term is used as a qualitative indication for the presence of environmental pollution. An example is the
statement "children living in this neighborhood are exposed to lead in the paint." Similar inconsistency in the use of the term dose is also notable in the literature.

Although these uses have a common thread, when different shades of meaning are carried over into specific questions such as "What is the exposure of humans to lead?" or "What is the exposure of trees to sulfur dioxide?" disagreement and confusion can arise. The problems are especially severe when specialists from different fields -- such as air pollution, water pollution, ecology, and epidemiology -- try to communicate with each other.

Communication across different fields in the environmental sciences would be improved if uniform and precise definitions of these two concepts were available and used. Empirical studies which measure human exposure to environmental pollutants require that these concepts be defined rigorously so that they can be measured appropriately. Similarly, efforts to model human exposure and dose mathematically also require that these terms be defined precisely so they can be understood without ambiguity, and can be incorporated into computer algorithms. Despite the importance and wide use of the terms exposure and dose in the environmental sciences, no comprehensive definitions have been published to date that can be applied generally to all environmental fields.

Part of the source of ambiguity comes from the fact that neither exposure nor dose is a uniquely defined concept. Instead, they are two generic categories of a number of closely related concepts. They both depend on the time frame. For exposure, we need to distinguish among
instantaneous exposure, exposure profile, peak exposure, average exposure, etc. Furthermore, we need to specify a number of auxiliary parameters in defining an exposure, including the target, the pollutant, the medium, the route, and the exposure boundary. Similar distinctions and specifications are also required to define dose.

In this paper, we propose new and comprehensive definitions for exposure and dose. By providing the fundamental components for a uniform language of exposure and dose, we hope to reduce the potential for confusion about this topic and to facilitate communication in this important new field. Those definitions are comprehensive in that they are applicable to all chemical pollutants and to all organisms and other targets. The only limitation of those definitions is that we assume the pollutant of interest is in a substance form carried in a medium, such as air, water, food, soil, etc. This assumption excludes energy-form pollutions such as noise and radiation.

Our definitions are built upon earlier definitions in Ott (1982), Scientific Group on Methodologies for the Safety Evaluation of Chemicals (SGOMSEC, 1985), Committee on Biological Markers (1989), Lioy (1989), and Committee on Advances in Exposure Assessment to Airborne Contaminants (Committee on Exposure Assessment, 1990), and extends the earlier definitions. Our definitions emphasize the need to specify explicitly the parameters which determine the specific form of exposure and dose, including the time frame, and five auxiliary parameters: the target, the pollutant, the medium, the route, and the exposure boundary. A different set of parameters would define a different form of exposure and dose.
The rest of this paper is structured as follows. In Section 2, we review the earlier definitions for air pollution exposure. In Section 3, we review the auxiliary parameters. In Section 4, we propose definitions for exposure and dose based on specifying explicitly the time frame and the auxiliary parameters. In Section 5, we discuss the relationship between exposure and dose. Two examples are discussed in Section 6 to illustrate the underlying concepts.

2. EARLIER DEFINITIONS

Our proposed definitions are extensions of earlier work in this field, building upon earlier definitions, such as the air pollution exposure definitions in Ott (1982), SGOMSEC (1985), Committee on Biological Markers (1989), Lioy (1989), and Committee on Exposure Assessment (1990). The air pollution exposure definition in Ott (1982) conceived of an "exposure" to be the joint occurrence of two events: (1) the pollutant of concentration C was present at a particular location in space at a particular time, and (2) the person was present at the same time and location in space. For example, if a three-dimensional coordinate system is used to represent the location of the person at location \((x,y,z)\) in space at time \(t\), then an "exposure" to concentration C is said to occur when the following events occurred jointly:

\[
\{\text{Person is present at } \{\text{location } (x,y,z) \text{ at time } t\} \} \cap \{\text{Concentration C is present at } \{\text{location } (x,y,z) \text{ at time } t\} \}
\]
Similar definitions were given in SGOMSEC (1985), Committee on Biological Markers (1989), Lioy (1989), and Committee on Exposure Assessment (1990).

The above definition does not consider the detailed nature of the contact between the person and the pollutant. The target of the exposure is simplified as a single point in space. If the pollutant concentrations are spatially homogeneous, it might be irrelevant whether the person is indeed a single point in space or a body consisting of more than a single point. However, if the concentrations are not spatially homogeneous, it is not valid to simplify the person as a single point. For example, the pollutant concentration in a person's breathing zone (near his oral-nasal orifice) might be substantially different from the concentration in the person's alveolar space (Figure 1). For assessing the dose which enters through the lung epithelium and is internalized to the blood, it is more relevant to consider the pollutant concentration in the alveolar space, rather than the concentration near the oral-nasal orifice.\(^1\) Therefore, it is not valid to simplify the person as a single point: we should consider the detailed nature of the contact between the person and the pollutant.

This is discussed further in the next section.

\(^1\)The pollutant concentration in the alveolar space is difficult to measure. If an appropriate pharmacokinetic model is available, it might be possible to predict the alveolar concentration from the external concentration, ventilation rate, etc. It is, of course, necessary to consider the empirical validation of such a model.
3. AUXILIARY PARAMETERS

In order to define exposure and dose precisely, we need to specify explicitly a number of parameters which determine the specific form of exposure and dose. In particular, we need to specify "who is being exposed to what, when, where, and how." In this section, we discuss the auxiliary parameters which describe the target (who), the pollutant (what), the medium (how), the route (how), and the exposure boundary (where). The time frame (when) is discussed in the next section.

3.1. TARGET

To define an exposure, first it is necessary to specify the target of the exposure: who is being exposed. We propose to define a "target" as any biological or ecological entity occupying space. The target can be an organism, an organ of a creature, a cell, an ecosystem, etc. A target has an external surface that separates the target from the environment. The external surface can be interpreted as a conceptual boundary corresponding to the generally accepted interface between the target and the environment. For example, water that passes the lips is going inside the mouth, air entering nostrils is going inside the nose. Using this definition, organisms are exposed to chemicals in food and drink when the latter are presented for ingestion.

The distinction between a target and its environment is relative. Consider, for example, human exposure to airborne carbon monoxide (CO) via inhalation (Figure 1). We can take the whole body as the target, and treat the air mass outside the body as its environment.
Alternatively, we can take the lung as the target, and treat the air mass in the alveolar space as its environment. The environment in the latter example is part of the target in the former example. The two targets (and the two corresponding environments) define two different exposures.

3.2. POLLUTANT

Next we need to specify "to what the target is being exposed," i.e., the pollutant in the environment which might affect the target.\(^2\) As was noted earlier, we only consider substance-form pollutants.

The pollutant needs to be defined carefully. Many "pollutants," such as lead, can assume a variety of forms. Different forms of lead might have different penetration properties and result in different doses and different health effects. It might therefore be necessary to consider different forms of lead as different pollutants. However, this should not be pushed too far to the extreme. Usually, some compromise in the precise specification of the pollutant is necessary to take account of what is possible with available sampling and analytical methods. For example, in considering the exposure of organisms to chemicals in the air or water, a decision has to be made as to whether particles are considered as a part of that medium, and what size range of particles is to be included. The specification is usually determined

\(^2\)Strictly speaking, we can define exposure to any xenobiotic material, such as oxygen, which might not be a pollutant. Since our main interest is exposure to hazardous xenobiotic materials, we have restricted our consideration to pollutants, although the principles described in this paper can also be applied to nonhazardous xenobiotic materials.
by the observation used to take the sample, and is limited by the availability of measurement technologies.

The concept of bioavailability should also be considered in this context. Information on the bioavailability (whether systemic or not) of different forms of a pollutant may be used to guide the selection of the species to be monitored in exposure assessment, so as to give dose estimates which are biologically relevant. For example, assume that for a given species of fish, particle-bound manganese are not bioavailable, in which case the study should focus on the exposure to dissolved manganese. Similarly, human exposure to fine particles in the air is usually more relevant than the exposure to total suspended particles.

3.3. MEDIUM

The pollutant of interest might be carried in several different media. For example, lead might be carried in air, water, soil, or food. The lead in different media might impact the target differently, therefore it is important to specify the medium in which the pollutant is carried when defining exposure and dose. More specifically, we need to distinguish the same pollutant carried in different media: lead in the air, lead in the water, lead in food, etc.

Our definitions of exposures and doses, to be given in the next section, define single-medium exposures and doses. Given a specific health effect of interest, it might be possible to define multimedia exposure and dose by summarizing the single-medium exposures and doses across the media of interest (see Section 5.2). Both acute and chronic effects should be considered; they might lead to different ways to summarize the single-medium exposures and doses.
3.4. ROUTE

The same pollutant carried by the same medium can impact the target via different routes. For example, ozone in the air can affect the human subject via inhalation and skin absorption. Since the impact of the same pollutant via different routes might be different, we need to specify the route in our definitions of exposure and dose.

3.5. EXPOSURE BOUNDARY

For a given target and a given route, we need to determine where the pollutant can penetrate into the target. We refer to the part of the external surface of the target where the penetration can occur as the exposure boundary. The exposure boundary depends on the route. For dermal exposure, the exposure boundary is the skin. For inhalation, the exposure boundary is the cross section of the oral-nasal orifice through which the subject inhales (see Figure 1, S1). The rest of the external surface where penetration cannot occur is not considered as part of the exposure boundary.

We shall assume that the pollutant concentration is homogeneous over the exposure boundary. If this condition is not satisfied, we should stratify the original exposure boundary into subregions with homogeneous pollutant concentrations, and consider each subregion as a separate exposure boundary. To be more specific, we define an exposure boundary to be a part of the external surface of a target where (1) pollutant can penetrate into the target, and (2) pollutant concentration is homogeneous. A target might have more than one exposure boundary.
In the next section, we define exposure and dose for one specific
exposure boundary. We will discuss in Section 5.2 the summarization of
exposures and doses across multiple exposure boundaries.

In order to illustrate the need to stratify the exposure boundary
according to pollutant concentration, consider a man with one foot in
boiling water and another foot in icy water. If we treat the two feet
together as one exposure boundary, and take the average of the
temperatures the two feet are exposed to, we would come to a rather
absurd conclusion about his exposure to temperature. It is natural in
this example to stratify the exposure boundary and consider each foot as
a separate exposure boundary.

We need to specify the target of interest before specifying the
appropriate exposure boundary. Consider the example discussed earlier
for human exposure to airborne CO via inhalation (Figure 1). If we
specify the whole body as the target, the appropriate exposure boundary
is the cross section of the oral-nasal orifice (S1). If we specify the
lung as the target, the appropriate exposure boundary is the alveolar
surface (S2). The two targets and the two corresponding exposure
boundaries define two different exposures.

4. DEFINITIONS OF EXPOSURE AND DOSE

As we discussed in Section 1, a number of parameters need to be
specified in order to arrive at a precise definition of exposure and
dose. The auxiliary parameters target, pollutant, medium, route, and
exposure boundary were introduced in the previous section. We assume
that the environmental scientist has considered the goal for the
exposure assessment, and has specified the auxiliary parameters. We now incorporate those parameters into a quantitative framework which also describes how exposure and dose depend on time.

4.1. DEFINITIONS OF EXPOSURE

Generically, we define exposure to be the contact between a target with a pollutant at an exposure boundary. We need to specify the time frame: when did the contact occur?

The smallest time frame is an instant of time. The instantaneous exposure is the environmental concentration of the pollutant near the exposure boundary at a given instant of time. It is measured with the same unit as the concentration, say, parts per million (ppm), or milligrams per liter (mg/l).

The instantaneous exposure is useful conceptually as the building block for other forms of exposures. We now consider the exposure during a time period which starts from \( t_0 \) and ends at \( t_1 \), denoted as \( (t_0,t_1) \).

INSERT FIGURE 2 APPROXIMATELY HERE

The exposure profile for the time period \( (t_0,t_1) \) is the collection of instantaneous exposures during this time period (Figure 2). It is a function of time: as time varies over the interval \( (t_0,t_1) \), the instantaneous exposure might also vary.

The exposure profile is highly informative when it is available. However, it might not be feasible to measure all the instantaneous exposures to derive the exposure profile. We might not have precise continuous instruments for this purpose. Furthermore, even if we have
precise continuous instruments, we might not want to record and analyze the entire exposure profile because it contains too much information. Therefore we need to summarize the exposure profile into simple quantities which are easier to measure, record, and analyze.

The choice of summary measures to be derived from the exposure profile needs to be determined both from the capability of the available instruments or models, and from the nature of the health effects of interest. Some relevant summaries include the average exposure, the peak exposure, and the integrated exposure. These are respectively the average, the peak, and the integral of the exposure profile over the time interval \((t_0,t_1)\). The average exposure and the integrated exposure are usually relevant for chronic health effects. The peak exposure is usually relevant for acute toxic effects.

The integrated exposure is measured with the unit "concentration-time," such as "ppm-hour" or "mg-hour/l." All other exposures mentioned above are measured in the same units as concentrations, such as ppm or mg/l.

In order to define an exposure, we need to specify the auxiliary parameters discussed in Section 2, and the time frame discussed above. We can then define an exposure, e.g., as the average exposure of Wayne Ott's whole body to airborne CO via inhalation at the exposure boundary \(S1\) (Figure 1), during the time period from 1 p.m., January 1, 1990, to 2 p.m., January 1, 1990. The exposure defined above can be measured as the average of environmental concentrations for CO near Wayne Ott's oral-nasal orifice during the specified time period.
If we change any of the parameters specified above, we would have defined a different exposure. For example, we can specify the peak exposure instead of the average exposure. Also, we can specify Wayne Ott's lung as the target and his alveolar surface S2 (Figure 1) as the exposure boundary. Since the alveolar CO concentration can be substantially different from the external CO concentration, the two definitions are likely to give different results.

Our proposed definitions are similar to those found in other scientific disciplines: we have distinguished the generic definition of the concept itself from the mathematical definitions that express its relation to measurements. For example, the physical concept of "voltage" refers to electrical potential. In order to implement this generic definition, we need to specify where the measurements should be taken. We need also specify the time frame for the measurements. We can find voltage expressed in a great variety of different mathematical forms: instantaneous voltage, average voltage, peak voltage, integrated voltage, and even root-mean-square (r.m.s.) voltage. All of these differ mathematically, but the underlying concept is the same.

Similarly, in our proposed definition, "exposure" is a concept meaning "physical contact of the pollutant with the target," but it can be expressed in a variety of different mathematical forms.
Choosing among Exposures

The environmental scientist engaged in an exposure assessment faces a nontrivial task choosing among a rich variety of different forms of exposures. Should he assess the exposure for the whole body, or should he assess the exposure for the lung? Should he assess the average exposure, or should he assess the peak exposure?

It is important to consider explicitly the specific form of exposure being assessed. A great deal of ambiguity and confusion can be avoided if all underlying parameters are specified explicitly.

The appropriate choice of the specific form of exposure depends on the goal of the study. We need to consider the implications for both dose assessment and the health effects of interest. For chronic health effects, if the dose-response relationship is cumulative and linear, we should consider the average exposure or the integrated exposure. For acute toxic effects, we should consider the peak exposure. The appropriate choice of the auxiliary parameters such as the target also depends on the site of health effect of interest. For eye irritation due to ozone exposure, we should take the eye epithelium as the target. For asthmatic attacks due to ozone exposure, we should ideally take the lung epithelium as the target. However, due to the difficulty in measuring/modeling the alveolar concentration, we might have to make a compromise and take the whole body as the target. We discuss in Section 5.1 the implication of dose assessment on the choice of the specific form of the exposure to be assessed.
We need also consider which exposures can be measured or modeled. If the best instrument available can only record twenty-four hour integrated exposure, we might not be able to assess the maximum one hour average exposure even though the latter is more relevant for the consideration of acute toxic effects. If appropriate models are available, we might be able to assess exposures which cannot be measured directly.

Qualitative Exposures

All the definitions given above can be interpreted as being either quantitative or qualitative. If we have the capability to measure the pollutant concentrations quantitatively, these measurements can be used to define the quantitative exposures, such as the quantitative instantaneous exposure, the quantitative exposure profile, the quantitative peak exposure, etc.

Sometimes we only have the capability to take qualitative measurements. These measurements can then be used to define qualitative exposures. The qualitative measurements can be either ordinal, say, high/medium/low/absent, or dichotomous: present/absent.\(^3\) We then have ordinal exposures such as "high instantaneous exposure at noon time on December 31, 1989," and dichotomous exposures such as "instantaneous exposure present at noon time on December 31, 1989." It might be difficult to summarize a qualitative exposure profile into an integrated exposure or an average exposure, because those summaries require

\(^3\)The dichotomy "present/absent" should be interpreted in terms of detectability, and might depend on the detection limit for the instruments.
quantitative measurements. We can still define a peak exposure qualitatively. We can also use qualitative summaries such as the frequency during which a qualitative exposure occurs, e.g., "exposure present more than half of the time during the time period \((t_0, t_1)\)."

For both qualitative and quantitative exposures, it is necessary to specify the time frame: we should not declare that a target is exposed (exposure is present) without specifying the time interval over which the statement refers to.

4.2. DEFINITIONS OF DOSE

Generically, we define dose to be the presence of the pollutant inside the target. We will consider four types of doses: (1) Intake dose, also known as potential dose, presented dose, or administered dose; (2) eliminated dose; (3) net dose; and (4) accumulated dose, also known as internal dose. Again, we assume that the environmental scientist has specified the auxiliary parameters discussed in Section 3. We discuss below the four types of doses, and the time frame: when the penetration occurs.

**Intake Dose**

The intake dose is the penetration of the pollutant into a target via an exposure boundary. It is also known as the potential dose, the presented dose, or the administered dose (Committee on Biological Markers 1989, Lioy 1989). The instantaneous intake dose is the rate (mass of pollutant per unit of time) at which the pollutant penetrates
into the target at a given instant of time. Its unit is mass per unit time, such as mg/hour. The intake dose profile over a time interval \((t_0, t_1)\) is the collection of the instantaneous intake doses during this time interval. Like the exposure profile, the intake dose profile is a function of time.

We usually summarize the intake dose profile into summary measures, such as the integrated intake dose, the total quantity of pollutant (mass) that has penetrated into the target via the exposure boundary during the time interval \((t_0, t_1)\). We can also define peak intake dose, average intake dose, etc., analogous to the corresponding exposures.

The unit for the integrated intake dose is mass, such as mg. The unit for all other doses mentioned above is mass per unit time, such as mg/hour.

**Eliminated Dose, Net Dose, and Accumulated Dose**

The pollutant might not stay inside the target. Some of it might be excreted back to the environment, say, by exhalation or urination. Some of it might be metabolized or neutralized by the body repair mechanism, therefore losing its potency for further health effects. We define the eliminated dose as the elimination of the pollutant which has penetrated into the target. The instantaneous eliminated dose is the rate at which the pollutant is eliminated. The eliminated dose profile is the collection of the instantaneous eliminated doses over the time interval \((t_0, t_1)\). We can summarize the eliminated dose profile into the integrated eliminated dose, the total quantity of pollutant eliminated during the time interval \((t_0, t_1)\). We can also summarize the eliminated dose profile into peak eliminated dose, average eliminated dose, etc.
The units for eliminated doses are the same as those for the corresponding intake doses.

The net dose is the net quantity of pollutant deposited inside the target and remaining potent during the time interval \((t_0, t_1)\). It is the difference between the intake dose and the eliminated dose. The net dose profile, the integrated net dose, the peak net dose, and the average net dose can be defined similarly, and have the same units as the corresponding intake doses.

The accumulated dose, also known as the internal dose,\(^4\) is the quantity of pollutant accumulated inside the target and remaining potent. The instantaneous accumulated dose is the quantity of pollutant inside the target at a given instant of time. Its unit is mass, such as mg. The accumulated dose profile is the collection of instantaneous accumulated doses during a time interval \((t_0, t_1)\). It is a function of time: as time goes on, the accumulated dose is increased by the intake dose and decreased by the eliminated dose. In considering the accumulated dose profile over a time period \((t_0, t_1)\), we need not only consider the intake and eliminated doses; we need also consider the initial accumulated dose, i.e., the instantaneous accumulated dose inside the target at the beginning of the time period.

\(^4\)If the target is the site of interest, the internal dose is also known as the biologically effective dose (Committee on Biological Markers 1989, Lioy 1989).
Accumulated dose is related to net dose as follows:

(1) \quad \text{Current accumulated dose} = \text{previous accumulated dose} + \text{integrated net dose.}

This can be expressed mathematically as follows:

\(1'\) \quad \text{ADP}(t_1) = \text{ADP}(t_0) + \text{IND}(t_0, t_1),\)

where \(\text{ADP}(t)\) denotes the accumulated dose profile at time \(t\), \(\text{IND}(t_0, t_1)\)
denotes the integrated net dose during the time period \((t_0, t_1)\).

Conversely, we have the relationship

(2) \quad \text{net dose} = \text{change in accumulated dose.}

This can be expressed mathematically as follows:

\(2'\) \quad \text{NDP}(t) = \text{ADP}'(t),\)

where \(\text{NDP}(t)\) denotes the net dose profile at time \(t\), and \(\text{ADP}'(t)\) denotes
the derivative of \(\text{ADP}(t)\).

We can also summarize the accumulated dose profile into summary
measures such as the peak accumulated dose, the average accumulated
dose, and the integrated accumulated dose. The unit for the integrated
accumulated dose is mass-time, such as mg-hour. The units for the other
accumulated doses mentioned above are mass, such as mg.

Choosing among Doses

The environmental scientist needs also choose the appropriate form
of dose to be assessed. Should he assess the dose for the whole body,
or should he assess the dose for the lung? Should he assess the average
net dose, or should he assess the peak net dose?
Again, the appropriate choice depends on the specific goal of the study. We need to consider the health effects of interest. We need also consider the feasibility of measuring a specific dose, or the feasibility of predicting a specific dose using a suitable model.

For both exposure and dose assessments, the ultimate goal is usually the prediction of health effects. We therefore suggest the guideline that we should consider the exposures or doses which can be measured or predicted, then choose the one which is the best predictor for the health effect of interest.

5. EXPOSURE AS A PREDICTOR FOR DOSE

For most purposes, knowledge of dose is more useful than knowledge of exposure. For the evaluation of environmental regulations, it is usually more relevant to know that a regulation leads to a reduction in the dose for the target, than to know that the regulation leads to a reduction in the exposure. If the reduction in the exposure occurs at the wrong time, e.g., when the subject is sleeping and has low ventilation rate, the resulting reduction in dose might be small, as compared to a reduction in the exposure occurring at the right time, e.g., when the subject is engaged in activities with high ventilation rates. Similarly, for epidemiological studies of health effects, dose is usually a more powerful predictor of health effects than exposure.

On the other hand, it is usually more difficult to measure dose than to measure exposure. It is usually possible to measure exposure passively without serious intrusions on the subject. It is usually
necessary to intrude on the subject actively to measure dose. Therefore, we frequently assess exposure rather than dose, and use exposure as a proxy for dose.

In order for exposure to serve as a useful proxy for dose, it is necessary for the two quantities to be related so that a high exposure can be seen as evidence for a high dose. We discuss below a useful relationship between exposure and dose.

We focus on the intake dose, and assume that the penetration of pollutant occurs in a matrix form, i.e., the pollutant is carried inside the target as part of the medium's matrix when the medium is taken inside the target. This includes inhalation and ingestion, and excludes penetrations which occur in a form of diffusion or osmosis, such as skin absorption.

For matrix-form penetration, dose depends on the amount of medium taken into the target. We therefore consider medium intake, the penetration of the medium into the target via a given exposure boundary. For air pollution exposure via inhalation, this is the ventilation. For food or drinking water, this is the ingestion.

The instantaneous medium intake is the rate (mass or volume per unit time) at which the medium is taken into the target. This is also known as the contact rate (Lioy 1989). For air pollution exposure via inhalation, the instantaneous medium intake is the ventilation rate. For food or drinking water, this is the amount of food or drinking water ingested per unit of time, say, each day.
The *medium intake profile* is the collection of instantaneous medium intakes during a given time interval. It is a function of time. We can summarize the medium intake profile into summary measures such as the *peak medium intake*, the *average medium intake*, and the *integrated medium intake*.

For matrix-form penetration, intake dose can be determined from exposure and medium intake as follows:

\[(3) \quad \text{intake dose} = \text{exposure} \times \text{medium intake}.\]

This can be expressed mathematically as follows:

\[(3') \quad \text{IDP}(t) = \text{EP}(t) \times \text{MIP}(t),\]

where IDP(t) denotes the intake dose profile at time t, EP(t) denotes the exposure profile at time t, and MIP(t) denotes the medium intake profile at time t.

If medium intake is (approximately) constant over time, a high exposure would indicate a high intake dose, therefore exposure serves as a useful proxy for dose when direct measurement of dose is difficult. However, the medium intake might vary substantially with the subject’s activities. For example, the ventilation rate is low during sleep, and high during active exercises. As a result, a high exposure during sleep might not lead to a high dose. Therefore, the relationship between exposure and dose should be considered in conjunction with activities.
5.1. CHOOSING AMONG EXPOSURES

We now consider an example to illustrate how to use dose assessment to guide the choice of a specific form of exposure. We assume that our goal is to estimate the average intake dose (AID) for a time period \((t_0, t_1)\). According to \((3')\), we have

\[
(5) \quad \text{AID} = \int \text{EP}(t) \times \text{MIP}(t) \, dt \bigg/ (t_1 - t_0),
\]

where the integration is taken over the time period \((t_0, t_1)\). If we observe both the exposure profile \(\text{EP}(t)\) and the medium intake profile \(\text{MIP}(t)\) for the time period \((t_0, t_1)\), we can use the right hand side of \((5)\) to determine AID. However, we might not observe both the exposure profile and the medium intake profile. Instead, we might only observe some summary measures such as the average exposure and the average medium intake. Are such summary measures adequate for assessing the dose of interest, AID?

If the medium intake profile is constant over time, the relationship \((5')\) simplifies to be

\[
(5') \quad \text{AID} = \text{AE} \times \text{AMI},
\]

where \(\text{AE}\) denotes the average exposure for the time period \((t_0, t_1)\), and \(\text{AMI}\) denotes the average medium intake. It is much easier to determine the dose of interest, AID, using the right hand side of \((5')\), rather than using the right hand side of \((5)\). For example, we need only measure the average environmental concentration to determine \(\text{AE}\), and measure the average ventilation rate to determine \(\text{AMI}\). We don't need to measure how the environmental concentration varies over time, nor do we need to measure how the ventilation rate varies over time.
The same simplified relationship \((5')\) holds if the medium intake profile is not constant, but the exposure profile is constant. Furthermore, when both the medium intake profile and the exposure profile vary over time, the simplified relationship \((5')\) would still hold if the medium intake is uncorrelated with exposure. In any of the three situations, we don't need to measure the exposure profile and the medium intake profile over time. We can simply measure the summaries AE and AMI, the use the right hand side of \((5')\) to assess AID.

The simplified relationship \((5')\) might not hold if the medium intake profile is correlated with exposure. The more general relationship \((5)\) can be written as

\[
(5'') \quad \text{AID} = \text{AE} \times \text{AMI} + \text{COV},
\]

where COV denotes the covariance between medium intake and exposure. If medium intake is correlated with exposure, it would be inappropriate to use the simplified relationship \((5')\): the right hand side of \((5')\) is a biased estimate for the dose of interest, AID, because it does not include the covariance term, COV.

We now give a biological example to illustrate the difference between \((5')\) and \((5'')\). We consider schoolchildren's exposure to ozone during a twenty-four hour period. Ozone concentration is usually higher during the day than at night. Children's activity levels are also higher during the day than at night. As a result, high medium intake (ventilation) occurs jointly with high exposure, i.e., medium intake is positively correlated with exposure, therefore the covariance term (COV) is positive. In this situation, it is inappropriate to use the right
hand side of (5') to determine the dose of interest, AID. We need to include COV in the expression (5'). In terms of measurements, we cannot just measure the average environmental concentration (AE) and the average ventilation rate (AMI). We have to measure how the environmental concentration and the ventilation rate vary over time in order to determine COV and AID.

When the covariance term (COV) in (5') is of concern, we cannot use AE and AMI to assess ADI. However, we might be able to eliminate the covariance term by using a microenvironment decomposition (Duan 1982): we stratify the subject's exposure (and the corresponding intake dose) according to his activities,

(6) \[ AID = \sum_k AID_k \cdot T_k \div (t_1 - t_0), \]

where AID\(_k\) denotes the average intake dose while the subject is in the \(k\)-th microenvironment, and \(T_k\) denotes the time spent in the \(k\)-th microenvironment. The summation is taken over a given list of microenvironments, \(k=1, \ldots, K\). Note that \(t_1 - t_0 = \sum_k T_k\).

We assume that the pollutant concentration and the medium intake are uncorrelated in a microenvironment. This assumption is satisfied if environmental concentration is constant in a microenvironment, if the medium intake is constant in a microenvironment, or if environmental concentration is uncorrelated with medium intake in a microenvironment. For the example considered earlier, the school children's ventilation rate might be correlated with his environmental concentration when we consider a twenty-four hour period. However, it is plausible that the correlation might vanish when we restrict to a single microenvironment.
For example, consider the microenvironment "exercising outdoor." The school child's ventilation rate might vary from time to time. The ozone concentration might also vary from time to time. It is probably reasonable to assume that while the subject is in the microenvironment "exercising outdoor," the ventilation rate is uncorrelated with the ozone concentration. Under this assumption, we have the expressions

\[(6') \quad \text{AID}_k = \text{AE}_k \times \text{AMI}_k,\]

\[(6'') \quad \text{AID} = \sum_k \text{AE}_k \times \text{AMI}_k \times T_k / (t_1 - t_0),\]

where \(\text{AE}_k\) and \(\text{AMI}_k\) denote the average exposure and the average medium intake in the \(k\)-th microenvironment. It follows that we should use the microenvironment-specific summary measures \((\text{AE}_1, \ldots, \text{AE}_K)\) and \((\text{AMI}_1, \ldots, \text{AMI}_K)\) to assess AID, instead of using the aggregate summaries AE and AMI.

5.2. COMBINING ACROSS EXPOSURE BOUNDARIES

As was discussed earlier, when the pollutant concentration is heterogeneous, we need to stratify the external surface and consider each homogeneous region as a separate exposure boundary. We now discuss how we can combine across multiple exposure boundaries for the same target.

Assume that the external surface is stratified into \(j=1, \ldots, J\) distinct exposure boundaries. Let \(\text{IDP}_j(t)\), \(\text{EP}_j(t)\), and \(\text{MIP}_j(t)\) denote the intake dose profile, the exposure profile, and the medium intake profile, respectively, for the \(j\)-th exposure boundary. The total intake dose profile \((\text{TIDP})\) summed over the \(J\) exposure boundaries is given by
(7) \( TIDP(t) = \sum_j IDP_j(t) = \sum_j EP_j(t) \times MIP_j(t) \),

where the summation is taken over the \( J \) exposure boundaries. We can further summarize the total intake dose profile into the total integrated intake dose, the total average intake dose, the total peak intake dose, etc.

The relationship (7) can be rewritten as follows:

(7') \( TIDP(t) = \overline{EP}(t) \times TMIP(t) \),

where TMIP denotes the total medium intake summed over the \( J \) exposure boundaries,

(8) \( TMIP(t) = \sum_j MIP_j(t) \),

and \( \overline{EP}(t) \) denotes the average of the exposure profiles,

(9) \( \overline{EP}(t) = \sum_j EP_j(t) \times MIP_j(t) / TMIP(t) \),

where the average is weighted by the share of the medium intake for each exposure boundary.

The relationship (7') for multiple exposure boundaries can be interpreted as a generalization of the earlier relationship (3) which was given for a single exposure boundary. When considering multiple exposure boundaries, we need to average the exposure profiles over the individual exposure boundaries.

We can also use the relationship (7') for combining exposures and doses across different media and routes. We need to sum the medium intake profiles, and average the exposure profiles, across the exposure boundaries for the various media and routes.
6. EXAMPLES

We now discuss several important examples to illustrate the application of the theoretical concepts described above.

6.1. HUMAN EXPOSURE TO AIRBORNE CO

For human exposure to air pollution, we can take the whole body as the target of interest. We take the pollutant to be carbon monoxide (CO). The medium is air. The route of exposure is inhalation. An appropriate exposure boundary is the cross section of the oral-nasal orifice (S1 in Figure 1). The instantaneous exposure is the environmental concentration in the breathing zone.

Alternatively, we might be interested in the exposure for the lung. In this case, the exposure boundary is the alveolar surface of the lung (S2 in Figure 1). The instantaneous exposure is the alveolar concentration.

The alveolar concentration might be substantially different from the concentration in the ambient air. The dose for the whole body can also be substantially different from the dose for the lung. The exposures for the whole body are determined by environmental factors. The exposure for the lung are also affected by biological factors such as the ventilation rate.

A human exposure field study measured the air exposure of the human population to carbon monoxide (CO) in 1982-1983 (Aklend, et al. 1985). This study took a random sample of more than 1200 persons in two U.S. metropolitan areas, equipped them with small personal exposure monitors
(PEM) which the individuals carried for 24 or 48 hours in their normal activities.

**INSERT FIGURE 3 APPROXIMATELY HERE**

The exposures for a 36-year old female homemaker from Denver, Colorado are plotted in Figure 3 to illustrate the concepts and definitions presented in this paper. The observed CO exposure (dark line) is the average exposure over short intervals (one hour or less) measured for the homemaker during the day. The codes at the top of the figure show the activities in which the person was engaged, grouped into the categories "indoor chores," "sleeping," and "shopping."

The instantaneous CO exposure was not available in this case because the PEMs did not store the instantaneous readings. The observed CO exposure is the best measurement we have for the exposure profile over the twenty-four hour period.

The peak exposure (33 ppm) occurred about 2:40 p.m. (14:40) when the homemaker drove her car to go shopping. Also plotted in the diagram are the 8-hour moving average CO exposures (light solid line). Comparison of the observed CO exposure and the 8-hour moving average shows the striking impact of averaging time.

The observed carboxyhemoglobin (COHb) estimated from the CO concentration in the subject’s forced expiration at the end of the monitoring day is plotted at 17:00. The observed COHb can be interpreted as a proxy or a biological marker for the subject’s accumulated dose at that time. The blood COHb (dotted line) computed by a pharmacokinetic model (Wallace, et al. 1988) estimates the accumulated
dose profile as a function of time. The changes in the blood COHb measures the net dose profile.

6.2. SWIMMER'S DERMAL EXPOSURE TO WATER-BORNE CHLOROFORM

We now consider a swimmer's dermal exposure to water-borne chloroform. Assume that the swimmer just came out of a shower and was sitting by the pool, paddling in the pool water. Later, the swimmer jumps into the pool and his entire body is immersed in the pool water.

INSERT FIGURE 4 APPROXIMATELY HERE

Assume the target of interest is the swimmer's whole body. In the first phase of the scenario, the environmental concentration for the body surface is heterogeneous: part of the body surface (his feet) is exposed to the chloroform concentration in the pool water, the rest of his body surface is exposed to the chloroform concentration in the residual show water. Since the two chloroform concentrations might be substantially different, we should stratify the body surface, and consider the two parts as two separate exposure boundaries. Therefore, the swimmer has two distinct exposure profiles, and two distinct dose profiles.

In the second phase of the scenario, when the swimmer changes his activity from paddling by the pool to swimming in the pool, his entire body surface is in contact with the chloroform concentration in the pool water. Assuming that the chloroform concentration in the pool water is homogeneous, we should now consider his entire body surface as one exposure boundary. He now has only one exposure profile and one dose profile.
It is useful to compare the swimmer's exposures and doses under the two activities. Assume that the chloroform concentration in the pool water is homogeneous over time. The swimmer's chloroform exposure from the pool water is the same before and after he jumps into the pool. However, the corresponding intake dose profile is very different before and after the jump. The swimmer has a larger surface area for penetration after the jump, therefore the intake dose profile is higher after the jump. It should be noted that exposure depends only on the environmental concentration and does not depend on the surface area, while dose depends on both.

7. SUMMARY

The definitions of exposure and dose proposed in this paper, along with the related concepts introduced, are summarized in Tables 1.1 -- 1.4. We believe that a uniform set of definitions, such as the ones proposed in this paper, is essential to facilitate effective communication in the environmental sciences. We also believe that rigorous definitions are necessary if environmental researchers and practitioners are to develop valid mathematical exposure models or to undertake field studies attempting to measure the exposures of populations of humans, animals, or ecosystems. We urge the environmental community to consider adopting the concepts presented in this paper as the basis for a uniform language of exposure and dose assessments.
8. ACKNOWLEDGEMENTS

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Breath CO, CO Exposure, and Coburn Model Predictions in the U.S. EPA
S1: Exposure boundary for whole body exposure
S2: Exposure boundary for lung exposure

Figure 1. Human Inhalation Exposure
Figure 2. Hypothetical Exposure Profile: Pollutant exposure as a function of time for a human subject.
<table>
<thead>
<tr>
<th>Term</th>
<th>Symbol</th>
<th>Units</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exposure</td>
<td></td>
<td></td>
<td>The contact between a target and a pollutant on an exposure boundary.</td>
</tr>
<tr>
<td>Instantaneous</td>
<td></td>
<td>mg/m³, ppm</td>
<td>The pollutant concentration in the medium in contact with the target on the exposure boundary at a given instant of time.</td>
</tr>
<tr>
<td>Exposure Profile</td>
<td>EP(t)</td>
<td>mg/m³, ppm</td>
<td>Record of instantaneous exposures over a time period; a function of time.</td>
</tr>
<tr>
<td>Average Exposure</td>
<td>AE(t₀, t₁)</td>
<td>mg/m³, ppm</td>
<td>The instantaneous exposures averaged over a time period.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>AE(t₀, t₁) = \frac{1}{t₁ - t₀} \int_{t₀}^{t₁} EP(t)dt</td>
</tr>
<tr>
<td>Peak Exposure</td>
<td>PE(t₀, t₁)</td>
<td>mg/m³, ppm</td>
<td>The maximum of the instantaneous exposures over a time period.</td>
</tr>
<tr>
<td>Integrated Exposure</td>
<td>IE(t₀, t₁)</td>
<td>mg-hr/m³, ppm-hr</td>
<td>The integral of the instantaneous exposures over a time period.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>IE(t₀, t₁) = \int_{t₀}^{t₁} EP(t)dt</td>
</tr>
<tr>
<td>Term</td>
<td>Symbol</td>
<td>Units</td>
<td>Definition</td>
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</tr>
<tr>
<td><strong>Dose</strong></td>
<td></td>
<td></td>
<td>Presence of pollutant inside a target.</td>
</tr>
<tr>
<td><strong>Intake Dose</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Instantaneous Intake Dose</td>
<td></td>
<td>mg/hr</td>
<td>Penetration of pollutant into the target via an exposure boundary.</td>
</tr>
<tr>
<td>Intake Dose Profile</td>
<td>IDP(t)</td>
<td>mg/hr</td>
<td>Rate of pollutant entering the target via an exposure boundary at a given instant of time.</td>
</tr>
<tr>
<td>Average Intake Dose</td>
<td>AID(t₀,t₁)</td>
<td>mg/hr</td>
<td>Record of instantaneous intake doses over a time period; a function of time.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>The instantaneous intake doses averaged over a time period.</td>
</tr>
<tr>
<td></td>
<td>AID(t₀,t₁)</td>
<td></td>
<td>[ AID(t₀,t₁) = \frac{1}{t₁ - t₀} \int_{t₀}^{t₁} IPD(t)dt ]</td>
</tr>
<tr>
<td>Peak Intake Dose</td>
<td>PID(t₀,t₁)</td>
<td>mg/hr</td>
<td>The maximum of the instantaneous intake doses over a time period.</td>
</tr>
<tr>
<td></td>
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<td></td>
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</tr>
<tr>
<td>Integrated Intake Dose</td>
<td>IID(t₀,t₁)</td>
<td>mg</td>
<td>The amount of pollutant entering the target via an exposure boundary during a time period.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>[ IID(t₀,t₁) = \int_{t₀}^{t₁} IPD(t)dt ]</td>
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<tr>
<td>Term</td>
<td>Symbol</td>
<td>Units</td>
<td>Definition</td>
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<tr>
<td><strong>Eliminated Dose</strong></td>
<td></td>
<td></td>
<td>Elimination of pollutant from a target.</td>
</tr>
<tr>
<td><strong>Net Dose</strong></td>
<td></td>
<td></td>
<td>Intake dose minus eliminated dose.</td>
</tr>
<tr>
<td><strong>Accumulated Dose</strong></td>
<td></td>
<td></td>
<td>Amount of pollutant accumulated inside a target.</td>
</tr>
<tr>
<td>Instantaneous Accumulated</td>
<td>ADP(t)</td>
<td>mg</td>
<td>Amount of pollutant accumulated inside a target at a given instant of time.</td>
</tr>
<tr>
<td>Dose</td>
<td></td>
<td></td>
<td>Record of instantaneous accumulated doses over a time period; a function of time.</td>
</tr>
<tr>
<td>Accumulated Dose Profile</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average Accumulated Dose</td>
<td>AAD(t₀, t₁)</td>
<td>mg</td>
<td>The instantaneous accumulated dose averaged over a time period.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>AAD(t₀, t₁) = \frac{1}{t₁ - t₀} \int_{t₀}^{t₁} ADP(t)dt</td>
</tr>
<tr>
<td>Peak Accumulated Dose</td>
<td>PAD(t₀, t₁)</td>
<td>mg</td>
<td>The maximum of the instantaneous accumulated dose over a time period.</td>
</tr>
<tr>
<td>Integrated Accumulated Dose</td>
<td>IAD(t₀, t₁)</td>
<td>mg-hr</td>
<td>The integral of the instantaneous accumulated doses over a time period.</td>
</tr>
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<td>IAD(t₀, t₁) = \int_{t₀}^{t₁} ADP(t)dt</td>
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<tr>
<td><strong>Medium Intake</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Instantaneous Medium Intake</td>
<td></td>
<td>m³/hr</td>
<td>Rate of medium entering the target via an exposure boundary at a given instant of time.</td>
</tr>
<tr>
<td>Medium Intake Profile</td>
<td>MIP(t)</td>
<td>m³/hr</td>
<td>Record of the instantaneous medium intake over a time period; a function of time.</td>
</tr>
<tr>
<td>Average Medium Intake</td>
<td>AMI(t₀,t₁)</td>
<td>m³/hr</td>
<td>The instantaneous medium intake averaged over some time period.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>$\text{AMI}(t₀,t₁) = \frac{1}{t₁ - t₀} \int_{t₀}^{t₁} \text{MIP}(t) , dt$</td>
</tr>
<tr>
<td>Peak Medium Intake</td>
<td>PMI(t₀,t₁)</td>
<td>m³/hr</td>
<td>The maximum of the instantaneous medium intake over a time period.</td>
</tr>
<tr>
<td>Integrated Medium Intake</td>
<td>IMI(t₀,t₁)</td>
<td>m³</td>
<td>The integral of the instantaneous medium intake over a time period.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>$\text{IMI}(t₀,t₁) = \int_{t₀}^{t₁} \text{MIP}(t) , dt$</td>
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