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Chapter 4

Exposure assessment of air pollutants: a review on spatial heterogeneity and indoor/outdoor/personal exposure to suspended particulate matter, nitrogen dioxide and ozone

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Abstract

This review describes databases of small-scale spatial variations and indoor, outdoor and personal measurements of air pollutants with the main focus on suspended particulate matter, and to a lesser extent, nitrogen dioxide and photochemical pollutants. The basic definitions and concepts of an exposure measurement are introduced as well as some study design considerations and implications of imprecise exposure measurements. Suspended particulate matter is complex with respect to particle size distributions, the chemical composition and its sources. With respect to small-scale spatial variations in urban areas, largest variations occur in the ultrafine (< 0.1 μm) and the coarse mode ($PM_{10-2.5}$, resuspended dust). Secondary aerosols which contribute to the accumulation mode (0.1–2 μm) show quite homogenous spatial distribution. In general, small-scale spatial variations of $PM_{2.5}$ were described to be smaller than the spatial variations of PM_{10}. Recent studies in outdoor air show that ultrafine particle number counts have large spatial variations and that they are not well correlated to mass data. Sources of indoor particles are from outdoors and some specific indoor sources such as smoking and cooking for fine particles or moving of people (resuspension of dust) for coarse particles. The relationships between indoor, outdoor and personal levels are complex. The finer the particle size, the better becomes the correlation between indoor, outdoor and personal levels. Furthermore, correlations between these parameters are better in longitudinal analyses than in cross-sectional analyses. For NO_2 and O_3, the air chemistry is important. Both have considerable small-scale spatial variations within urban areas. In the absence of indoor sources such as gas appliances, NO_2 indoor/outdoor relationships are strong. For ozone, indoor levels are quite small. The study hypothesis largely determines the choice of a specific concept in exposure assessment,

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i.e. whether personal sampling is needed or if ambient monitoring is sufficient. Careful evaluation of the validity and improvements in precision of an exposure measure reduce error in the measurements and bias in the exposure–effect relationship.

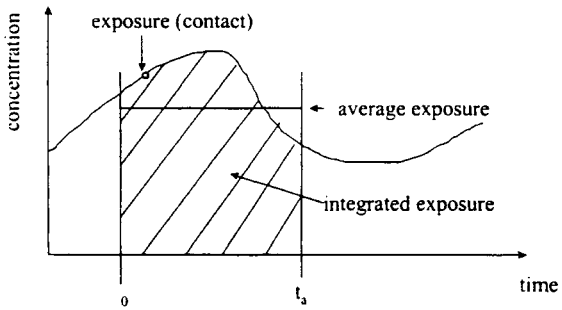
1. Introduction, definitions and concepts

1.1. Content and objective

The objective of this review is to describe exposure assessment techniques and to discuss databases of outdoor, indoor, and personal exposure levels of the following main air pollutants: suspended particulate matter (SPM), nitrogen dioxide (NO_2) and photochemical oxidants. The focus is on long-term exposure but also some important aspects of short-term exposure are addressed. Special emphasis is placed on suspended particulate matter because of its increasing significance in health-effect issues. A review on bioaerosols associated with particulates which may have a strong allergenic and inflammatory potential is also included. A short introduction outlines the definitions, concepts, some important aspects of study designs and the effects from errors in the measurements.

1.2. Definitions and concepts

The basic concepts used in exposure assessments were developed in the early 1980s by Duan (1982) and Ott (1982). Their introduction of the term "human exposure" (more simply exposure) emphasises that the human being is the most important receptor of pollutants in the environment. Ott (1982) elaborated a system of definitions for the term "exposure" and defined exposure as "an event that occurs when a person comes in contact with the pollutant". This is a definition of an instantaneous contact between a person i (or a group of persons) and a pollutant with concentration c, at a particular time t. This definition refers to a contact with a pollutant, but it is not necessary that the person inhales or ingests the pollutant. When the duration of exposure is also taken into consideration, the result is an "integrated exposure", calculated by integrating the concentration over time (t_a) (units: ppmh or $\mu g\,h\,m^{-3}$) (Fig. 1). These units, however, are uncommon and the calculation of such an integral is, in most cases, not possible. More easily understood is the term "average exposure"; it can be calculated by dividing the integrated exposure by the specified time and has the unit of mass in a volume of air (Fig. 1). In a pragmatic approach, average exposure is simply deduced by averaging the pollutant concentration over the specified period (e.g. expressed as annual mean). In air pollution epidemiology, the unit "concentration" is most commonly used. It refers to the



exposure (contact, in ambient media)	**dose** (in the body)
-integrated exposure:	-intake:
integral (t=0..t_a) $c_i(t)\,dt$ [e.g. ppbhr]	integrated exposure x ventilation rate [e.g ng]
-average exposure:	-average intake:
integr. exposure/time [e.g. ppb]	integrated uptake/time [e.g. ng day^{-1}]
	or: direct dose measurement of a biomarker [ng, or ng ml^{-1} body fluid]

Figure 1. Definitions of exposure and dose (Ott, 1982; Sexton and Ryan, 1988; NRC, 1991).

"average exposure" to which the population has been exposed over a specific time. Besides mean concentrations, the use of other statistical parameters (e.g. 95th percentiles, median, frequency of exceedance of a certain value) is also common.

The definitions of exposure described above refer to levels of pollutants in the ambient media. However, once the pollutant has crossed a physical boundary (e.g. skin, alveolar epithelial cells), the concept of "dose" is used (Ott, 1982). "Dose" is the amount of material absorbed or deposited in the body for an interval of time and is measured in units of mass (or mass per volume of body fluid in a biomarker measurement) (Fig. 1). Dose can be determined as internal dose or as a biologically effective dose (NRC, 1991). When data on exposure values are available, an "intake" (also called "potential dose" which assumes total absorption of the contaminant (NRC, 1991)), can be calculated by multiplying the integrated exposure with the volume of air exchanged in the lung per specified time (unit: mass). "Average intake" (in analogy to average exposure) or "dose rate" can be deduced by dividing intake by time (unit: mass $\times$ $time^{-1}$). In Section 2.1.2 the difficulties of relating ambient levels with levels of biomarkers will be addressed.

A comprehensive exposure assessment is part of a risk assessment that evaluates the relationship between the source of a pollutant and its health effect (Ott, 1990). The link between a pollutant emission and a particular target in the body consists of a sequence of events:

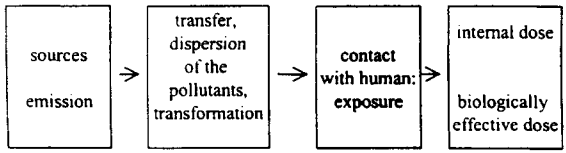


Figure 2. "Sequence of exposure" from source to biologically effective dose.

Fig. 2 shows a simplified version from Lioy (1990) and describes the route of a contaminant from its source into the body. In general, this scheme is valid for all environmental media (water, air, food). Air pollutants are dispersed ubiquitously, and contact between the target organ (airway system) of a human and the pollutant takes place continuously. In the comprehensive concept of "Total Exposure Assessment" (Ott, 1990; Lioy, 1990), all routes into the body have to be considered: contact with soil, water, food and air.

Conceptual approaches to measuring exposure can be classified according to their potential agreement with a "perfectly precise" personal exposure measurement. Table 1 depicts such a classification hierarchy based on the characterisation by Lioy (1995). Personal exposure measurement obviously reflects the individuals' exposure levels best, whereas qualitative methods provide less precise estimates.

Representative epidemiological studies have to include a large number of study individuals from the general population. Collecting exposure data from all these individuals is an expensive undertaking, so that a geographical clustering of the population is often used. In such studies, exposure data are collected

Table 1. Classification of exposure measurements with respect to true personal measurement

	Environmental study: examples	Occupational study: examples	Agreement with personal exposure
Direct/internal	Internal dose/biologically effective dose	Internal dose/biologically effective dose	Perfect
Direct/external	Personal measurement	Personal measurement	Very good
Indirect/external	Area measurement	Stationary measurement at workplace	Moderate–good
	Quantitative surrogate: e.g. distance to street	Quantitative surrogate: e.g. contact with chemicals	Moderate
	Qualitative data by questionnaire: e.g. high/medium/low pollution	Qualitative data by questionnaire: frequency of exposure, estimates high/low	Poor–moderate
	Qualitative data, categorical: polluted/unpolluted	Qualitative data: exposure: yes/no	Poor

by a central monitor and attributed to the residents of the cities in question. On the other hand, collecting exposure data on an individual level has the advantage of assessing frequency distributions in order to reveal whether part of the population is exposed to levels much higher or lower than the average level (Sexton and Ryan, 1988). Krzyzanowski (1997) stressed other key elements of exposure assessment, such as representative sampling, the control of confounding factors (factors which are related to the exposure and the health variable) and the appropriate averaging time. A further difficulty in an exposure assessment for air pollutants is related to the fact that pollutants are present as mixtures. Therefore assessment of exposure has to rely on measurements of markers in these mixtures (Leaderer et al., 1993). Markers, also called indicators, should be unique to the mixture's sources; they should be readily detectable in air at low concentrations and present in a consistent ratio to other components (Leaderer, 1993). Examples of such indicators are NO_2, O_3, airborne particles, metabolites in biological specimens, or variables obtained from questionnaires (e.g. contact to sources).

2. Methodology

Personal exposure measurements can be performed *directly* or *indirectly* (Ott, 1982). In the direct approach exposure levels are determined on an individual (by using a personal sampler or a biological marker); in the indirect approach exposure levels are either measured stationarily or determined by models (Ott, 1982; Lioy, 1995).

The evaluation of a method has to consider method-inherent criteria. These criteria are sensitivity, precision, accuracy, selectivity and detection limit. Besides these criteria, cost, and applicability are important factors in the choice of a particular method. WHO brochures summarise quality assurance (QA) and quality control (QC) protocols (Series GEMS/AIR handbook series, 1994), which are also important to warrant high-quality measurements. Table 2 lists the most important techniques used in air pollution studies. In addition the PAS sensor for PAH-loaded airborne fine particles is added (Burtscher and Siegmann, 1993, 1994). For the separation between gas- and particle-phase the so-called denuders have been developed (Koutrakis et al., 1988, 1989; Possanzini et al., 1983).

2.1. Direct measurements

2.1.1. Personal sampling

Passive samplers are the most widespread and easily used devices employed in personal sampling. They rely on the principle of the passive diffusion of

Table 2. Techniques for measuring air pollutants (note: continuous refers to a response signal within a few seconds to minutes) (Harrison and Perry, 1986; Finlayson-Pitts and Pitts, 1986; Williams, 1995; Willeke and Baron, 1993; Chow, 1995; Wijnand, 1996)

Pollutants	Measurement techniques	Time resolution
Gases: SO_2, NO_x, O_3, CO	Fluorescence, chemiluminescence photometry, non-dispersive infra red	Continuous, minutes
Particles, TSP, PM_{10}, $PM_{2.5}$	Gravimetry (size fraction: impaction, cyclone)	One day, hours
	Beta meter	Integrated, day, hours
	Tapered element	Continuous, minutes
	Nephelometer	Continuous, minutes
	Photoelectric aerosol sensor (PAS)	Continuous, minutes
Gases (personal)	Passive sampler (NO_2, O_3)	Integrated, days
	Electrochemical sensor (CO)	Continuous, minutes
Particles (personal)	Size fraction: impaction, cyclone gravimetry	Integrated: hours, one day
	Light scattering	Continuous, minutes
	Photo-emission sensor (PAS)	Continuous, minutes
Bioaerosols	Slit sampler	Integrated, minutes

a gas and the concentration in air can be calculated according to Fick's law of diffusion (Palmes et al., 1976). The samplers are straightforward for personal sampling as they are light, do not need electricity, and can be easily fixed to outer clothing. They exist as tubes or small personal badges. Passive samplers can also be used to take stationary measurements in outdoor and indoor settings. The most established method is the passive sampler for NO_2 (Palmes et al., 1976; Yanagisawa and Nishimura, 1982; Hangartner, 1990). The sampling time is usually from a few days up to one week, depending on concentration. Passive samplers also exist for CO, SO_2, VOC, O_3, formaldehyde and ammonia (Lee et al., 1992; McConnaughey et al., 1985; Shields and Weschler, 1987; Weschler et al., 1990; Koutrakis et al., 1993; Monn and Hangartner, 1990). Brown (1993) reviewed state-of-the art passive samplers for ambient monitoring. The precision of NO_2 tubes is quite good; the error is in the range of 5–10%. For example, in the Swiss Study on Air Pollution and Lung Diseases in Adults (SAPALDIA), the coefficient of determination between the continuous monitors and passive samplers ranged between 0.69 and 0.93. On average, concentrations of duplicates were within 5%. The problem for passive devices is, however, the lack of accuracy, i.e. the agreement with a reference method. The O_3 tube (Monn and Hangartner, 1990; Hangartner et al., 1996), for example, has acceptable precision (variation <5–10%) but the agreement with a continuous monitor is not always very good.

Real-time personal monitors for gases are also available, but the detection limit is often too high, so that their use is limited to occupational settings only. A personal monitor for CO has also been shown to be practical in ambient conditions (Ott et al., 1986; Jantunen, 1998). Personal monitors for particles exist with different cut-offs and size fractions, such as $PM_{2.5}$, PM_{10} or multistage samplers (analysis by gravimetry, collection of particles on filters). Real-time monitors, based on the principle of light scattering provide particle numbers in a volume of air (usually for particles with a $d_{ae} > 300$ nm). A real-time personal sampler also exists for the detection of combustion aerosols (coated with PAH), using the principle of a photoemission aerosol sensor (PAS) (Burtscher and Siegmann, 1993, 1994). The detection signal is related to levels of ultrafine combustion particles <1 μm.

2.1.2. Biological markers

Biological markers can be grouped into markers of exposure and markers of effects. A marker of an effect is generally a pre-clinical indicator of abnormalities which can also comprise a medical diagnosis (e.g. decreased lung function) (Grandjean, 1995). A marker of exposure reflects the concentration of the analyte which has passed a human boundary. According to Hulka and Wilcosky (1988) and Hulka (1990) biological markers have to fulfil the following purposes: elucidation of pathogenic mechanism, improvement in aetiological classification and the recognition of early effects. Grandjean (1995) further discussed the importance of "susceptibility-biomarkers" because the variability between individuals can be large due to heterogeneities of enzymes and genetic factors. Genetic polymorphism for enzymes will be an important factor in future epidemiological studies (e.g. for oxidative scavengers). Valid biological markers are those which have biological relevance, known pharmacokinetics, temporal relevance and defined background variability (Schulte and Talaska, 1995).

Biological markers can be collected from breath, urine, hair, nails, nasal lavage or, in a more difficult procedure, from blood or fluids from bronchoalveolar lavage. The use of biomarkers is most widespread in occupational studies with known specific exposures (e.g. solvents) (Lowry, 1995). The advantage of the use of a biological marker is that exposure is integrated over time and that all exposure pathways are included. This is, on the other hand, also a shortcoming as it is not possible to differentiate between exposure pathways anymore. For example, dermal exposure to pesticides (and some VOCs) can be very important, but little information on intake rates through the skin is available when looking only at the biological markers. Lioy (1990) described the parameters required to calculate and interpret internal dose relationships with ambient exposures. Data on kinetics, half-life, solubility, excretion and

metabolic transformation are needed. Models can be used to elucidate the relationship between concentration in air and level in the body. Such models rely on sophisticated pharmacokinetic data and are presently still in the stage of development (Georgopoulos et al., 1997).

To assess the usability of a biological marker it is important to know its half-life in the body and its temporal variability. If the elimination rate of the contaminant is small and a biological marker is accumulated in the target tissue, then the measurement of the biological marker offers a significant advantage over external measurements (Rappaport et al., 1995). The key issue for the promotion of biological markers lies in the validation of the relationship between concentration in air and concentration of the marker in the body (Rappaport et al., 1995). A shortcoming is that biological markers reflect recent exposure only; therefore, they can only be used for prospective studies on acute effects.

Table 3 shows some examples of biological markers of effect and exposure. One example of an exposure marker is lead in blood. Pb is also retained in the bone marrow and has a rather long half-life in the body. Wallace et al. (1988, 1989) used VOCs in exhaled breath to assess personal exposure to VOCs. It corresponded well to previous exposure to VOCs. DNA- and protein-adducts can be used as markers for exposure to complex particle mixture which contain PAHs (diesel, tobacco smoke, coal emissions). Such adducts imply a carcinogenic and mutagenic potential (Mumford et al., 1996; Lewtas et al., 1993; Meyer and Bechtold, 1996). Yanagisawa et al. (1988) used hydroxy-proline as a biological marker for exposure to NO_2 and tobacco smoke in urinary samples. In urinary samples, secretion of creatinine is rather stable, so that the ratio between hydroxy-proline and creatinine can be used as a marker for exposure. This ratio mainly results from personal NO_2 exposure and smoking levels (active and passive). The ratio was also elevated in persons living near major roads. Nasal and bronchoalveolar lavage have been used in studies on effects of O_3 (Graham and Koren, 1990). Albumine, neutrophils, eosinophiles and cytokines can be used as markers of effects after exposure to pollutants.

Table 3. Examples of biological markers of exposure and effect (Lewtas et al., 1993; Wallace et al., 1988, 1989; Graham and Koren, 1990)

Type of marker	Examples of markers
Biological marker of exposure	Lead in blood, VOC in exhaled air, DNA/protein adducts, chemicals (DDT, PCBs) in mothers' milk, hydroxy-proline
Biological marker of effect	Chromosome aberration, lung function change mediators, cytokines

2.2. Indirect measurements

2.2.1. Ambient measurements

In many epidemiological studies exposure data are obtained from ambient monitoring networks. In these studies, people living in defined areas (e.g. in a particular city) are assigned to the same pollution concentration. In this type of study, the units of analysis are populations or groups of people rather than individuals (ecological analysis, according to Last, 1988). Ambient monitoring networks have been established all over Europe and the USA by national institutions or local councils. They are equipped with on-line monitors providing continuous data with sufficient time resolution (half-hourly values). The accuracy and precision of these monitors is generally good (within 5–10%). Running such a network is expensive, especially the implementation of quality assurance and quality control procedures. The quality control includes several steps from the calibration with independent standards to internal plausibility check, technical controls, and data acquisition control (EMPA, 1994). Ring calibration, where an external monitoring van moves around from site to site, is used to check the agreement between these sites.

2.2.2. The use of microenvironments (MEs)

An indirect way of assessing personal exposure is to use a microenvironmental model. In daily life, people move around and thus are exposed to various levels of pollutants in various locations. Duan (1982) introduced the term "microenvironments" (MEs), which is defined as a "chunk of air space with homogeneous pollutant concentration". Such microenvironments can either represent outdoor locations (e.g. in front of the home) or indoor locations (bedroom, kitchen, etc.). Mage (1985) defined MEs as a volume in space, during a specific time interval, during which the variance of concentration within the volume is significantly less than the variance between that ME and its surrounding MEs.

Selective measurements in MEs and a time-activity/time-budget questionnaire are used for the estimation of personally encountered pollution levels, calculated as integrated dose or concentration in a cubic meter of air. The total average exposure (X) can be defined as

$$X = \sum X_i t_i / \sum t_i,$$

where X_i is the total exposure in the ith ME, visited in sequence by the person for a time interval t_i (Mage, 1985).

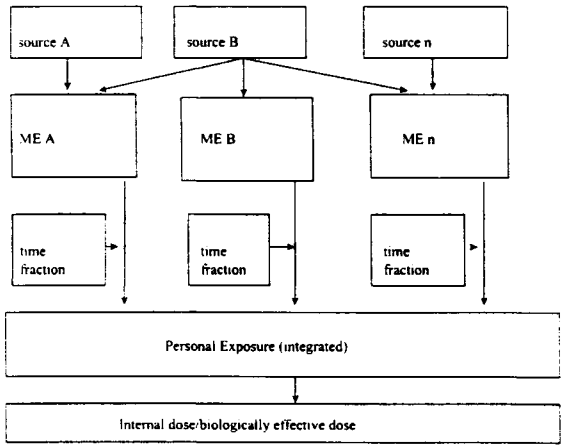


Figure 3. The concept of calculating personal exposure using time-activity data and pollutant levels in microenvironments (ME).

For J different microenvironments, integrated personal exposure can be calculated as follows:

$$X = \sum_{j=1}^{J} C_{iJ} T_{ij} / \sum t_{ij}.$$

C_{ij} is the concentration in microenvironment j in which the individual remains during period t_{ij}.

Fig. 3 shows the method for calculating personal exposure levels. Different emission sources contribute to pollution levels in different MEs. The time fraction spent in each ME allows calculation of integral personal exposure levels (= the sum from all MEs). Such approaches are based on easy-to-use and reliable time-activity diaries.

It is demanding and expensive to obtain refined data of dozens of MEs in large-scale epidemiological surveys. The most feasible approach is to use "group-MEs", where similar MEs are aggregated into ME types (e.g. indoor and outdoor MEs). Stock et al. (1985) used personal-activity profiles and household characteristics to partition the locations into seven broad microenvironments. Three of them were indoors, two outdoors and two in transportation modes. The following list shows the main microenvironments which cover most of the daily activities of adult persons. This list is similar to that of the EXPOLIS study (Jantunen et al., 1998):

- outdoor (at home, in study region),
- indoor home (kitchen, bedroom, living room),

- in transit (in car, train, bus, as pedestrian),
- others (shopping malls, restaurants, theatres, indoor sports),
- workplace.

2.2.3. Further models and the use of questionnaires

Models exist for a broad range of mathematical descriptions to predict the exposure of individuals or of populations. Generally, models can be grouped into physical (or deterministic) and statistical (or stochastic) models (Sexton and Ryan, 1988). Some models rely on both physical–chemical knowledge and incorporate statistical approaches (hybrid models). Physical models are based on mathematical equations, describing known physical/chemical mechanisms in the atmosphere. Statistical models are based on measured data and explanatory variables. For outdoor pollutants, sophisticated dispersion models (e.g. Gauss models) which incorporate meteorological variables and chemical processes, have been developed. They can be used to predict outdoor spatial and temporal behaviour of pollutants (Hanna et al., 1982). Their most important shortcoming is the need for detailed emission inventories, which are in most cases unavailable. Moreover, the application of dispersion models in epidemiology is sparse to date. Ihrig et al. (1998) demonstrated the usefulness of a combination of an atmospheric dispersion model with a geographical information system (GIS). In this approach, associations were detected between exposure to arsenic and stillbirths in Texas. In another study, McGraven et al. (1999) used a regional atmospheric transport model which incorporated spatially varying meteorology and environmental parameters for exposure calculations of beryllium in order to find association with lifetime cancer incidences. In these two examples, distinct air toxins with known sources were used. For air pollution mixtures with a variety of sources, the use of such models may be more difficult. Other models such as receptor models, based on mass conservation or with multivariate approaches, have found wide applications in source apportionment (Hopke, 1985).

Questionnaires are important tools for assessing exposure. They can be used to identify contact with emission sources and frequencies of contacts with potential sources (e.g. in a household) (Lebowitz et al., 1989). This is especially important for the identification of contacts to indoor sources which do not reflect the same mixtures than outdoor sources (e.g. NO_2 from gas cooking, $PM_{2.5}$ from tobacco smoke).

In microenvironmental models, questionnaires are used to obtain data on time-budget and time-activity patterns and they are essential in assessing long-term exposure to pollutants in retrospective studies (e.g. Künzli et al., 1997). Questionnaires can be used to assess the perception of traffic near the home, representing a surrogate for the traffic intensity and hence pollution levels in

air. The most important advantage of questionnaires is their low cost. However, as with all other methods, validation studies have to be performed to test reliability and validity.

3. Validity, errors, precision of exposure data and spatial variation

3.1. Validity

The validity of a measurement can be defined as "the degree to which a measurement measures what it purports to measure" (Seifert, 1995). The validity of an exposure measurement can also be defined as the capacity to measure the "true" personal exposure (Armstrong et al., 1992). Seifert (1995) defines three important aspects of validity:

- The "content-validity" implies that all important contacts which could cause the effect have to be considered. It further implies that all locations of potential contacts have to be incorporated into the exposure measurement (e.g. all microenvironments).
- The "criterion-validity" is the "extent to which the measurement correlates with the phenomenon under study". In practice, the criterion-validity can be determined by comparing personal exposure values with values obtained from surrogate measurements. The coefficient of determination ρ^2 (later called "validity coefficient") is a direct measure of the validity of the surrogate method.
- A further aspect is the "construct-validity", which is "the extent to which the measurement corresponds to the theoretical concepts concerning the phenomenon under study". This requires the evaluation of the biologically relevant exposure (which is often unknown) in relation to the type of measurements used.

For a critical review of a study, all three definitions have to be considered. In practice, however, only the criterion-validity can be quantified, for example by comparing the personal exposure measurement with a surrogate measurement.

Studies on long-term exposure to pollutants encounter further difficulties and potential lack of validity, as historical data on life-long exposure are scarce. Data from actual measurements (e.g. an annual mean) are often used as surrogates for long-term exposure. The only way to validate actual measurements reflecting a long-term trend is to use emission inventories. This information, however, is not easily accessible, and, most often, not very detailed in its geographical resolution. In addition, time-activity patterns over long-term periods may influence the exposure. Künzli et al. (1997) evaluated a more refined

method for assessing long-term exposures to ozone in California. Retrospective exposures to O_3 were estimated using available O_3 data and questionnaires on time-activity/budgets. From questions on the total time spent outdoors, the location of residence, and the monthly measured O_3 values at these sites, the integrated exposure over lifetime was calculated.

3.2. Types of measurement errors

Errors in measurement can occur as *systematic* or as *random* errors (Ahlbom and Norell, 1990). A systematic error can be defined as the mean of measured values minus the true value (Profos and Pfeifer, 1994). It occurs, for example, when a calibration procedure is based on a false standard. For exposure–effect relationships, a systematic error is not critical as it does not lead to a bias; it only shifts the regression line up or downwards. Moreover, if the systematic error is known, data can easily be corrected. Random errors are critical as they lead to a bias in the exposure–effect relationship, in most cases to an attenuation of the true effect (Armstrong et al., 1992). Random errors can occur at all stages of measurements (e.g. for particle measurements: during weighing, air flow variability, and erroneous use of exposure time). The extent of these errors are not predictable a priori; these errors can only be quantified from repeated measurements (e.g. by a Gaussian density curve).

These errors may occur as non-differential errors or as differential errors (Ahlbom and Norell, 1990). In the case of non-differential errors, the extent of the error is the same in the case and control group (in a case–control study), or does not vary over an entire range of exposure in a study using continuous exposure variables. In the case of differential errors, the errors deviate between the case and control group or are not the same over an entire exposure range in a study using continuous variables. Both differential and non-differential errors are critical as they distort the exposure–effect relationship (Armstrong et al., 1992). Theories on errors in measurements and their effects were published by Cochran (1968), Armstrong (1990), Armstrong et al. (1992) and Ahlbom and Steineck (1992). Most of the studies refer to biases occurring in case–control analysis. For environmental studies, analyses of dose–response relationships based on exposure data from individuals (or geographically clustered data) are more relevant.

3.3. Precision of exposure measurement and attenuation

For exposure assessment, precision of exposure measurement is related to the technical and analytical properties of the instrument and to the variation of the air pollutants in time and space (Armstrong et al., 1992). This is different from a "measurement error" in the narrow sense which is based on an error

in sampling and analysis only (Brunekreef et al., 1987). Precision and error discussed here are related to the error variance determined by sampling at different points in space and time. The variability of the pollutant concentration in time and space is often larger than the technically inherent precision of the instrument; an assessment of precision in this wider sense allows quantification of attenuation in an exposure–effect relationship.

3.3.1. Validity coefficient and attenuation

Armstrong et al. (1992) presented a model to quantify the extent of attenuation when multiple exposure values of individuals are available. This model refers to an exposure–effect model with only one exposure variable. The estimated (observed) β of an exposure–effect relationship is related to the true β_T by a factor ρ^2_{TX} [1] (Allen and Yen, 1979). ρ^2_{TX} is called the "validity coefficient"; in a "perfect" measurement ρ^2_{TX} reaches 1 and no attenuation is observed.

$$\beta = \rho^2_{TX}\beta_T, \tag{1}$$

where β is the expected (observed) effect estimate; β_T: true effect and ρ^2_{TX} the validity coefficient.

3.3.2. Calculation of the validity coefficient ρ^2_{TX}

ρ^2_{TX} is the coefficient of determination between the true (T) and the measured exposure value (X). When two data sets of exposure measurement in individuals are available, e.g. one from surrogate measurements (X) (e.g. indoor home levels) and another from personal ($\approx$"true") measurements (T), ρ^2_{TX} can be calculated by a regression analysis (coefficient of determination $= \rho^2_{TX}$).

In another case, where multiple exposure measurements from each individual are available, Cochran (1968), Allen and Yen (1979) and Armstrong et al. (1992) proposed a model which allows direct calculation of ρ^2_{TX}:

$$\rho^2_{TX} = 1 - \frac{\sigma^2_E}{\sigma^2_X} = \frac{\sigma^2_T}{\sigma^2_X}, \tag{2}$$

where σ^2_X is the total variance, σ^2_T the true error variance ("between-subject" variance) and σ^2_E the subject error variance (error component, "within-subject" variance).

In a study with multiple measurements from each individual, ρ^2_{TX} can be calculated using σ^2_E and σ^2_T:

$$\rho^2_{TX} = \frac{1}{1+\sigma^2_E/\sigma^2_T} = \frac{1}{1+\lambda}. \tag{3}$$

The ratio λ between the subject error variance σ^2_E and the true variance σ^2_T is defined as the variance ratio (λ) or the relative precision of a measurement, as it reflects the ratio between the variance of an individual relative to the variance of the true exposure in the study population. Having obtained a value for λ, the potential attenuation can be calculated. Table 4 shows some calculations for the expected attenuation with increasing variance ratios: when λ reaches unity, an attenuation of 50% has to be expected.

Examples of calculated λ from field measurements of NO_2 are shown in Table 5. Variance ratios from indoor, outdoor and personal values from the City of Basle are shown in the first three rows ($\approx$70 individuals, repetition: 3–4 times). The next three rows show variance ratios from different locations indoors from Holland (Brunekreef et al., 1987). The largest variability was found in NO_2 outdoor measurements.

In practice, not all the assumptions (no correlation between true value and error, the same magnitude of the error over the whole exposure range) of Armstrong's theory are fulfilled. At higher concentrations, the error is often proportional to the value. In addition, normal distributions for T and E cannot

Table 4. Attenuation for different variance ratios (according to Eq. (3))

λ	0.1	0.2	0.4	0.6	0.8	1
ρ^2_{TX}	0.91	0.83	0.71	0.63	0.55	0.5

Table 5. Estimates for lambda for NO_2 indoor, outdoor and personal values and also in indoor locations

	λ
Indoor NO_2, full year[a]	0.33
Outdoor NO_2, full year[a]	0.71
Personal NO_2, full year[a]	0.41
Kitchen, March–May[b]	0.18
Living room, March–May[b]	0.22
Bedroom, March–May[b]	0.41

[a]Monn et al. (1998).
[b]Brunekreef et al. (1987).

always be guaranteed. Despite that, Armstrong's theory provides a useful tool for estimating effects of measurement errors. A further shortcoming is that this concept applies to a regression model with a single variable only. In most cases, however, more than one exposure variable is included in a model, which again can be subject to errors. The correlation among the exposure variables and also errors in confounding variables will have an influence on the bias in the regression coefficients.

3.4. Grouped data (Berkson case) and the "ecological" analysis

In the previous section, a model for estimating attenuation was presented for random errors in exposure variables for individuals. In this case (so-called "classical random" errors), the model assumes independence between the error E_i and the observed value T_i (true value) and the bias can be quantified by the validity coefficient (Armstrong, 1990). The following cases need more detailed discussion: In the so-called Berkson case, group averages are used instead of individual values to estimate the regression coefficients (Table 6) (Armstrong, 1990). Cochran (1968) described the Berkson case as a case where measured values (X) are set at certain preassigned levels; with errors in the measurements present, the actual amount of the true values (T) will not be exactly equal to the pre-assigned levels but will vary about these values. It is assumed that the error term E' has a constant variance, a mean value of zero and is independent of the observed value $X_{\text{avg cat}}$.

The implication of the Berkson case is that random errors in the exposure variables do not lead to a bias in an exposure–effect model (Cochran, 1968; Armstrong, 1990). However, the confidence intervals become larger with increasing random errors. Lebret (1990) empirically tested effects of random errors in such cases and confirmed that no attenuation in the exposure–effect model occurs. In addition, he demonstrated that in multiple regression models the effect of errors in the measurement may not always produce an underestimation but may also produce an overestimation of the true effect. In multiple regression models with more than one exposure and confounding variable, the

Table 6. Description of types of errors and effects

	Description of random error	Effect
Individual data	Classical random error model: $X_I = T_i + E_i$	Bias, ρ^2_{TX}
Berkson case	$T_i = X_{\text{av cat}} + E'$	No bias
Ecological cases		
One stationary site	Random error model	Bias, ρ_{TX}
Group averages	Berkson case	No bias

extent of distortion was more pronounced in a variable with a strong exposure–effect relationship than in a variable with poor correlation with the effect variable. Another important finding was that an increase in the study size did not remove the bias in the exposure–effect relationship.

The so-called "ecological" studies in most cases, are designed as "semi-individual" studies (health variables are available from each study individual; exposure variables are available as average pollution levels over the city of residence) (Künzli and Tager, 1997). The following situations have to be distinguished (Table 6, last lines):

- Exposure data available from all study individuals (or from a representative sample): an average exposure level over each area can be calculated. The case refers to a Berkson case and no bias in the exposure–effect regression is to be expected.
- Data available from a single fixed site ambient monitor in each area only:
  - If the monitor reflects a population-based average level in each area, the case refers to the above-mentioned case and no bias is to be expected. This case, however, is not very realistic as fixed site monitors are mainly set up for the surveillance of air quality standards.
  - If the monitor does not reflect average population exposure, a bias is to be expected. Given a large number of study sites and an occurrence of these errors in a random fashion, the bias can be estimated according to Armstrong's model, if information on these errors is available. Given a small number of study sites, however, it is very likely that errors at the leverage points distort the exposure–effect relationship; the effect might be an under- or an overestimation. Brenner et al. (1992) pointed out that in ecological analysis based on dichotomous variables, the effect of non-differential misclassification is an overestimation of the exposure–effect association. A general discussion on ecological studies is out of the focus of this review, but it has to be noted that they need careful control of covariates and that an increase of the number of regions does not particularly cancel out biases in covariates' distributions (Greenland and Robins, 1992).

The latter cases show that information on the representativity of the fixed site monitor is needed in order to eliminate or reduce bias. Within-area spatial variability and the position of the monitor within the area have to be assessed. A study design using a combination of passive samplers (or spatial random samples with continuous monitors) with a fixed site monitor is most useful. The fixed site monitor assesses the temporal course (e.g. seasonal variation) of the pollutants and the passive samplers assess the spatial variability (during seasons).

3.5. *Study design considerations and cost efficiency*

When exposure data are related to health outcomes, effect estimates for health impacts are determined. An important goal of a study design is therefore to reduce the variance of the effect estimate (i.e. to obtain small confidence intervals). There are three factors which influence this variance: the range of exposure, the number of observations and the validity coefficient (statistically named the coefficient of determination) (Armstrong, 1990). Eq. (4) shows the relationship between the variance of the effect estimate (beta) and these three factors. For the reduction of the variance improvements can be made by increasing the number of study sites (or the number of study persons in an individual analysis), by choosing sites that reflect large pollution differences or by choosing an exposure measurement with good validity (ρ^2):

$$\text{var}(\beta) = \frac{\text{var(error)}}{N\rho^2\,\text{var(exp)}}, \tag{4}$$

where var(β) is the variance of the effect estimate, var(error) the variance of the exposure-health model, N the sampling size (e.g. number of subjects, number of sites, or number of days in a day-to-day analysis), ρ^2 the validity coefficient (coefficient of determination between "true" and "approximate" exposure) and var(exp) the variance of exposure (range of exposure concentrations between study sites).

3.6. *Introduction to spatial variations*

Most health-effects studies are based on exposure data from one "central" monitor. For uniformly distributed pollutants the choice of the site is uncritical, however, for most air pollutants considerable spatial variations in concentration levels occur.

An important factor for the spatial variation of a primary air pollutant is the geographical distribution and the type of the emission sources (e.g. line source, point source). After the emission takes place, inert pollutants (e.g. CO) simply disperse and a concentration gradient with increasing distance to the source develops (Seinfeld, 1986). For chemically reactive pollutants such as NO, a steeper concentration gradient than for inert pollutants develops (Seinfeld, 1986). In contrast, the formation of secondary pollutants (e.g. ammonium sulphate, ammonium nitrate, ozone) is a large-scale phenomenon and these pollutants have quite uniform spatial distributions (US-EPA, 1996a; Spengler et al., 1990). An exception to this occurs for the reactive gas ozone in the vicinity of other reactive species (e.g. depletion of O_3 by NO along traffic

arteries) (BUWAL, 1996). For primary suspended particulate matter, physical processes such as sedimentation and coagulation are the important factors for causing spatial heterogeneity (Hinds, 1982). Furthermore, diffusion and transport of pollutants are determined by atmospheric conditions such as wind speed, vertical temperature gradient, and solar radiation (Seinfeld, 1986). The time-scale of the small-scale spatial variation may also be important; the size of short-term (e.g. within minutes) spatial fluctuations is different from spatial fluctuations in annual means. Brimblecombe (1986) established the relationship between the half-life and the spatial coefficient of variation of several gases on a global scale: for highly reactive species (e.g. radicals) the biggest CVs were observed, for inert gases (e.g. O_2) the CVs were smallest. Table 7 shows estimates of spatial coefficients of variations at more than 25 rural and urban monitoring sites in Switzerland (based on annual means considered to represent long-term data). Data represent mid-range spatial variations of an area of about 200×100 km^2. An estimate for an OH radical, which has the largest spatial variation, is added (from Brimblecombe, 1986). NO, known as a reactive gas (Atkinson, 1990), had the highest CV of all gases. As this analysis was based on annual means, the reactive O_3 did not exhibit a stronger spatial variation than other gases, as it would do in a short-term analysis. Least spatial variation was observed for total suspended particles and for PM_{10}. The spatial variability of the inert gases CO_2 and O_2 is extremely small. All information in Table 7 is based on mid-scale spatial variation but may also be used for

Table 7. Spatial coefficients of variation, based on 25 sites in Switzerland in non-alpine regions in 1993 (PM_{10}, 15 sites only) (data from annual mean levels)

Species	Spatial CV[a]
OH radical[b]	10
NO	1.134
SO_2	0.608
CO	0.569
NO_2	0.525
O_3	0.432
TSP	0.336
PM_{10}	0.205
CO_2[b]	10^{-2}
O_2[b]	10^{-5}

[a]CV: coefficient of variation: standard deviation divided by mean level.

[b]Estimates for highly reactive and inert gases from Brimblecombe (1986).

small-scale spatial variation estimates: the magnitude might be different but the ranking between the pollutants might be similar.

4. Databases of exposure measurements

4.1. Airborne particles

Air pollution by suspended particulate matter has received much attention over the last decade due to its strong association with health parameters (e.g. Dockery et al., 1993; Schwartz, 1994).

Aerosols, by definition, comprise liquid or solid particles in a continuum of surrounding air molecules. Whitby and Sverdrup (1980) proposed the terms nucleation mode ($d_{ae} < 0.1$ μm), accumulation mode (0.08–1 μm) and coarse mode (>1.3 μm) for various size ranges. Size fractions usually refer to the aerodynamic diameter (d_{ae}) which is defined as the diameter of a sphere of unity density (1 g cm^{-3}) which has the same terminal settling velocity in air as the particle under consideration.

4.1.1. Size distribution

A bi-modal size distribution is very common in ambient urban aerosols (Hinds, 1982). The peak in the larger size range (8–15 μm) is derived from emissions from natural sources (e.g. from wind-blown dust); the peak in the lower size range (1–2 μm) originates from anthropogenic processes (fuel combustion emissions), gas-to-particle conversions and secondary formation of particles. The largest number of particles is found in the range less than 0.1 μm (Aitken particles in the nuclei mode). The greatest *surface area* is in the accumulation mode (0.08 to 1–2 μm). The highest *volume* (or mass) is found in the accumulation mode and also in the mode between 5 and 20 μm (Finlayson-Pitts and Pitts, 1986).

Over the last decade, measurements of total suspended particulates (TSP) have been replaced by total thoracic particles (particles smaller than 10 μm, PM_{10}) and also, more recently, by fine particles (particles smaller than 2.5 μm, $PM_{2.5}$) in the USA. Air quality standards for PM_{10} were implemented in the USA in the 1980s, and are now being set in Europe. A controversial discussion on these cut-points (10, 2.5 μm) took place in the USA as they were defined according to the available technology (US-EPA, 1996a). The choice of 2.5 μm is a technological compromise; it is good for the separation between anthropogenic and natural particles, but Wilson and Suh (1997) also stated that some natural particles also occur in the size range smaller than 2.5 μm. A further reduction of the cut-off is also in discussion (e.g. PM_1 or smaller for diesel particles).

The mass relationship between $PM_{2.5}$ and PM_{10} was determined in the PTEAM study (Clayton et al., 1993). $PM_{2.5}/PM_{10}$ ratios outdoors were around 0.49 during the day, and 0.55 during the night. In the Six City study (Dockery et al., 1993), the average ratio between fine ($PM_{2.5}$) and inhalable particles (PM_{10}) at the study sites was between 0.47 and 0.63. US-EPA (1996a) reviewed data on $PM_{2.5}/PM_{10}$ relationships for most of the US regions. These ratios varied between 0.71 (Philadelphia) and 0.29 (El Centro, CA), indicating a great spatial and seasonal variability. Ratios between fine and coarse particles are largely determined by the amount of coarse material, mainly by resuspended dust. Brook et al. (1997a, b) investigated the relationship between TSP, PM_{10}, $PM_{2.5}$ and inorganic constituents in Canada. The $PM_{2.5}$ fraction accounted for 49% of the PM_{10} mass and PM_{10} accounted for 44% of TSP. The variability between sites was high and the $PM_{2.5}/PM_{10}$ ratio varied between 0.36 and 0.65. The daily variability of the $PM_{2.5}$ mass correlated with the daily variation in the PM_{10} mass. At urban sites, which are influenced by heavy traffic and at the prairie site the fraction $PM_{10-2.5}$ dominated over the $PM_{2.5}$ fraction. Urban areas have higher PM_{10} concentrations than rural areas; the coarse size fraction ($PM_{10-2.5}$) has been identified as the cause of these differences.

The PM_{10}/TSP relationships were assessed on weekly means in the SAPALDIA study (Monn et al., 1995). TSP was collected with high-volume, PM_{10} with Harvard low-volume samplers (Marple et al., 1987). The average PM_{10}/TSP ratios for the whole year ranged from 0.57 to 0.74. PM_{10}/TSP ratios in the highly polluted urban regions (Geneva and Lugano) were found to be 0.75. Current measurements with high-volume PM_{10} devices indicate PM_{10}/TSP ratios around 0.75–0.9 (unpublished data). At rural and suburban sites, the ratios were between 0.57 and 0.62.

4.1.2. Small-scale spatial variation

The terminal settling velocity is an important factor for the spatial variation of suspended particulate matter (Hinds, 1982; Willeke and Baron, 1993). For very fine particles such as a particle of 1 μm d_{ae} the settling velocity is 8.65×10^{-5} cm s^{-1}, for a particle of 1 μm 3.48×10^{-3} and for a particle of 10 μm in size 3.06×10^{-1} cm s^{-1}. Primary particles (Aitken particles <0.1 μm) and large particles (e.g. >10 μm) are expected to have a bigger spatial variability than particles in the accumulation mode (0.1–1 μm). As mentioned above, coagulation (for very fine particles <0.01 μm) and gravitational settling (for particles >1 μm) are the underlying mechanisms which cause spatial heterogeneity (Hinds, 1982). Preliminary experimental field data, however, did not confirm the expected ranking between TSP, PM_{10} and $PM_{2.5}$. Interestingly, the variance in the PM_{10} concentration was smaller than in $PM_{2.5}$. The distrib-

ution of $PM_{2.5}$ might be uniform in situation where secondary formation is important; in cities, however, with large emissions from heavy duties (diesel exhaust), $PM_{2.5}$ can also exhibit significant spatial variation.

Spengler et al. (1981) published data from the Six City study on the within-area variability of $PM_{3.5}$. With the exception of one site (extreme pollution levels derived from a single source in Steubenville), the spatial variation within the study sites was found to be small. In the US-PTEAM study performed in Riverside CA, outdoor levels of $PM_{2.5}$ and PM_{10} at different homes were in good agreement with the central monitoring site, indicating a homogeneous spatial distribution (Clayton et al., 1993). Correlations between outdoor (i.e. back yard) levels of $PM_{2.5}$ and levels at the central monitor were very high (0.96 overnight and 0.92 during the day). For PM_{10}, the correlations were also found to be high (0.93 overnight and 0.9 during the day) (Clayton et al., 1993; Wallace, 1996).

Burton et al. (1996) assessed the spatial variation within Philadelphia. The spatial variation was small for $PM_{2.5}$ but larger for PM_{10}. Spatial correlations for $PM_{2.5}$ were found to be near 0.9–1 and around 0.8 for PM_{10}. In a study from Ito et al. (1995) in Chicago and Los Angeles, the spatial correlations for PM_{10} were around 0.7–0.8. Kingham et al. (2000) investigated small-area variations of pollutants within the area of Huddersfield, UK. Spatial variations of pollutants were only modest and there was no association to distance from roads. Absorbance measurements of fine particles provided the best general marker of traffic-related pollutants (diesel exhaust). Furthermore, the indoor/outdoor correlations were best for these absorbance measurements of fine particles, indicating that an outdoor measurement of the absorbance of fine particulates is a useful measure of exposure to traffic-related pollutants.

Roorda-Knape et al. (1998) measured pollution levels near motorways in Holland. Black smoke and NO_2 levels declined with distance from the roadside; for PM_{10}, $PM_{2.5}$ and benzene, however, no concentration gradient was observed. The contribution of the coarse particle fraction ($PM_{10-2.5}$) on PM_{10} can be important. In Holland, where the PM_{10} levels were described to be quite uniformly distributed, a recent study indicated that the coarse fraction has considerable influence on the PM_{10} levels and that it causes spatial variations in PM_{10} (Janssen et al., 1999).

Blanchard et al. (1999) studied the spatial variation of PM_{10} concentrations within the San Joaquin Valley in California. PM_{10} levels varied by 20% over distances from 4 to 14 km from the core sites. Local source influence was observed to affect sites over distances of less than 1 km, but primary particulate emissions were transported over urban and sub-regional scales of approximately 10–30 km, depending on season. Gas-phase precursors of secondary aerosols were transported over distances of more than 100 km. This indicates that primary particles affect local-scale areas whereas secondary particles af-

fect wide-range areas. Magliano et al. (1999) also found uniform spatial distributions of secondary ammonium nitrate (in fall and winter). Site-to-site variations were determined by differences in geological contributions in the autumn and due to carbonaceous sources in the winter.

Harrison and Deacon (1998) suggested that the number of monitors has to be large in order to cover the spatial variability in cities. With few monitors only, a quite general overview of the pollution climate can be obtained. As the correlations of the temporal concentrations profiles of different monitors are high, only a low-density network is needed for assessing short-term fluctuations.

An example of a study on small-scale spatial variations of PM_{10} is shown in Fig. 4. The spatial variability of PM_{10} (and NO_2) near a road in the city of Zürich was studied during one winter and one summer period in 1994/1995 (Monn et al., 1997a). PM_{10} and NO_2 levels were measured at different distances from the road. The measuring sites were positioned at 15 m (B), 50 m (C) and 80 m (D), and two meters above ground (m.a.g.) except for D: 6 m.a.g. During the summer period, an additional site was located at pedestrian level (1.8 m.a.g.) directly at the road (F). Because of the small difference between sites C and D during the winter period, site C was not used in summer. One site was installed on the roof of a house (20 m.a.g.) in order to investigate the vertical distribution. Fig. 4a shows the horizontal PM_{10} concentration profiles at the distances indicated. An almost parallel shift between the seasons was observed. The largest difference in concentrations occurred between the site closest to the road (A) and the first site at 15 m (B). The spatial variation at sites further away was very small indicating good horizontal mixing.

The vertical distribution (Fig. 4b) shows a similar pattern to that of the horizontal gradient. Levels during winter were higher than in the summer, and the

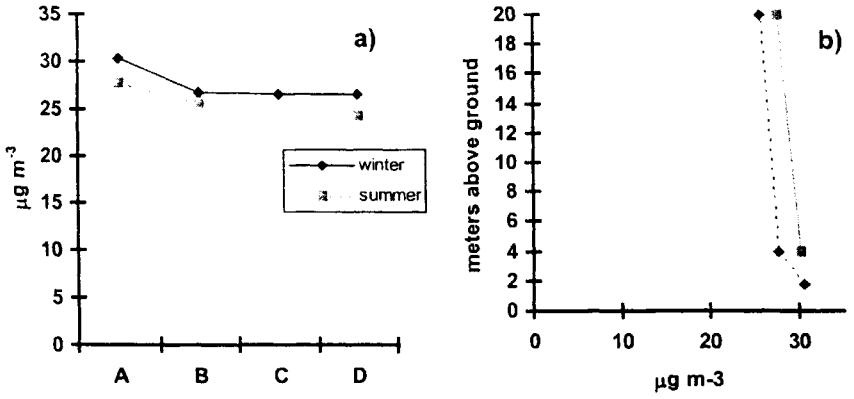


Figure 4. Horizontal (a) and vertical (b) distribution of PM_{10} in the vicinity of a road. (Monn et al., 1997a) (A = 2, B = 15, C = 50, D = 80 m from the road).

shift was almost parallel. The PM_{10} levels at the pedestrian level (F) were by far the highest of all sites. The levels at the upper vertical point 20 m.a.g., on the roof of the building, were similar to the levels 15 and 50 m away from the road, indicating urban "background" levels. Season, weekday and precipitation did not have a significant effect on the spatial CV in this study.

A similar investigation was made by Bullin et al. (1985), distinguishing between fine (<1 μm) and coarse particles (>1 μm). For fine particles, concentrations along the horizontal and vertical sites were almost the same. For coarse particles, increased traffic-related aerosols were detected near the road. These findings, however, are different from Roorda's (1998) findings, which did not observe a concentration gradient for PM_{10} and $PM_{2.5}$ with distance from the roadside. Chen and Mao (1998) observed large small-scale horizontal and vertical variations of PM_{10} in Taipei. The vertical profile showed a decrease in PM_{10} concentrations by 58% between the 2nd and 7th floor of a house, but no further decrease between the 7th and the 14th floor. Between a main and a side street in the city, large differences in PM_{10} levels were observed. Micallef and Colls (1998) and Colls and Micallef (1999) measured a vertical PM_{10} concentration profile over the first 3 m in a street canyon. At 0.8 m.a.g., PM_{10} levels were about 35% higher than at 2.8 m.a.g. For inhalable particles, this difference was 12%. Rubino et al. (1998) investigated a vertical profile of PM_{10} at a tower building and observed a decrease of PM_{10} concentrations by 20% between ground level and 80 m.a.g.

Kinney et al. (2000) investigated the small-area variation of $PM_{2.5}$, diesel exhaust particles (DPE) and elemental carbon (EC) in Harlem, New York. Site-to-site variations for $PM_{2.5}$ were only modest, however, EC contractions varied four-fold across sites. These spatial differences were associated with bus and truck counts. Local diesel sources created the spatial variation in sidewalk concentrations of DPE.

Recent studies investigated the distribution of ultrafine particles (<0.1 μm). Keywood et al. (1999) studied the distribution of $PM_{2.5}$, PM_{10} and ultrafine particles in six Australian cities. The $PM_{2.5}$ fraction dominated the variation in PM_{10}. PM_{10} and $PM_{2.5}$ correlated with each other but the correlation between the coarse fraction ($PM_{10-2.5}$) and PM_{10} was poor. An important finding was a lack of correlation between $PM_{2.5}$ and PM_{10} with ultrafine mass data as well with ultrafine particle number concentrations. This indicates that the former two cannot be used as surrogates for ultrafine particles. Junker et al. (2000) investigated the spatial and diurnal fluctuations of different parameters for particles within the urban area of Basle. Day profiles for ultrafine particle number concentrations, determined by a scanning mobility particle sizer (SMPS), were more closely related to the number of heavy-duty vehicles than to the number of light-duty vehicles. Diesel exhaust is a strong source of particles in the ultrafine mode, this fact is also reflected in the spatial variance of these particles: the

site exposed to heavy-duty traffic had two to four times higher particle number concentrations than a background urban site and a residential site, respectively. In a study from Harrison et al. (1999), the ratio between particle number concentrations and PM_{10} was higher at a traffic-influenced site than at a nearby background location. The particle size profile, determined by SMPS, showed a clear difference between roadside and background location with an additional mode in the roadside sample below 10 nm diameter. Measurement of particle number gave the clearest indication of road-traffic emissions and, in contrast to other studies, the correlations between particle numbers and PM_{10} were significant and moderate. The diurnal variation of PM_{10}, particle number counts and Fuchs surface area showed the same general patterns, however, particles number counts gave the clearest indication of road-traffic emissions.

4.1.3. Indoor, outdoor and personal exposure

The largest databases on indoor, outdoor and personal suspended particulates levels are from the Six City study (and related studies) and the PTEAM study (Dockery et al., 1993; Clayton et al., 1993). Not included here are studies related only to indoor air quality.

4.1.3.1. Relationship between indoor and outdoor levels and indoor sources. Earliest data on indoor/outdoor ratios of TSP were presented by Yocom (1982). Outdoor air has been identified as an important source of indoor particulates in homes without apparent indoor sources. In summer, indoor TSP levels were found to be higher than in winter indicating the importance of the ventilation rate. Indoor/outdoor ratios were observed to range between 0.2 and 3.5. In air-conditioned rooms with highly efficient dust filters, indoor/outdoor rates were much lower 0.1–0.3. In Yocom's (1982) review the importance of the difference in the chemical composition of indoor and outdoor particles was emphasised.

In all of the further studies, smoking has been identified as the most important source for indoor particle concentrations (Dockery and Spengler, 1981b; Sheldon et al., 1989; Leaderer, 1990; Santanam et al., 1990; Quackenboss et al., 1991; Neas et al., 1994; Leaderer et al., 1994). Neas et al. (1994) assessed a clear dose–response relationship between $PM_{2.5}$ levels in air and cigarettes smoked. Investigations of the influence of other sources were presented by Quackenboss et al. (1991), Sheldon et al. (1989), Santanam et al. (1990) and Özkaynak et al. (1996b). Gas cooking, vacuum cleaning, dusting and also wood burning were identified as important indoor sources. The influence of gas cooking and kerosene heaters, however, was not confirmed by Leaderer et al. (1994). In a study from Virginia, Leaderer et al. (1999) found strong con-

tribution of kerosene heaters to indoor $PM_{2.5}$, sulphates and acids (H^+) during the winter months.

In Wallace's review (1996) the importance of smoking and cooking was emphasised. Despite the strong effects of these indoor sources, the contribution of outdoor air to indoor PM levels remains significant. Infiltration of outdoor air into homes was estimated to contribute about 70% in naturally ventilated homes and 30% in air-conditioned homes to the indoor levels (Dockery and Spengler, 1981b). In homes without apparent indoor sources, outdoor particles contributed to about 75% of the indoor levels for $PM_{2.5}$ and 66% to the indoor PM_{10} levels in the PTEAM study (Özkaynak et al., 1996b). In homes with important indoor sources (smoking, cooking), outdoor air still contributed to about 55–60% to the indoor PM_{10} and $PM_{2.5}$ levels. Spengler et al. (1981) and Quackenboss et al. (1991) assessed the influence of season on indoor/outdoor relationships and stated that the differences between levels in homes with smokers compared to homes without smokers are stronger during winter than summer, due to reduced ventilation.

With respect to the correlations between indoor and outdoor levels, Dockery and Spengler (1981a), Ju and Spengler (1981) and Sexton et al. (1984) reported rather poor correlations. Indoor sources and differences in the ventilation rates were factors causing these inter-home differences. A further factor, which contributed to indoor PM levels, was that of human activity. Thatcher and Layton (1995) investigated deposition, resuspension and penetration of particles within a residence. The main finding was that the shell of a building did not provide any filtration of airborne particles. Differences in indoor/outdoor ratios in homes without major indoor sources for different size ranges are mainly explained by the difference in the deposition velocities of these particles. Concentrations of fine particles have a lower deposition velocity than coarse particulates. Light household activities such as walking around can increase levels of coarse particles. The resuspension rate increased with increasing particle size. Fine particles, therefore, undergo much less resuspension and deposition, which leads to indoor/outdoor ratios near unity, in the absence of other indoor sources. In a Swiss study investigations of the indoor/outdoor relationship for PM_{10} were performed in seven homes (Monn et al., 1997b). All homes had natural ventilation. The studies took place in the spring–summer periods. In each household, PM_{10} was measured for at least 3 periods for 48 h. Fig. 5 illustrates indoor/outdoor ratios for these homes. The highest indoor/outdoor ratios were found in the two homes with smokers (F, G). The indoor/outdoor ratios in homes with gas appliances were slightly higher than in homes without gas appliances. In the absence of smoking, the factor "activity" (people present in the home) influenced the indoor/outdoor ratios (home C versus A and B). Only in homes with inactive inhabitants did the indoor/outdoor ratio fall below unity (A + B). This figure confirms the importance of smoking and

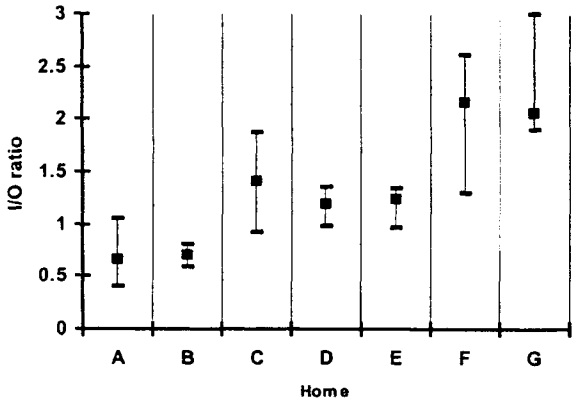


Figure 5. Indoor/outdoor (I/O) ratios for PM_{10} in homes with indoor sources and without obvious indoor source (A, B: no indoor sources, C: high activity of inhabitants; D, E: gas cooking, F, G: smokers) (dot: average, bars: minima and maxima) (Monn et al., 1997b). Reprinted with permission of Elsevier Science Ltd, previously published in *The Science of the Total Environment* 208, 15–21.

gas cooking but also shows the difficulty of the "human activity" factor when explaining indoor/outdoor ratios.

Abt et al. (2000) characterised indoor particle sources in Boston. Cooking, cleaning and the movement of people were identified as the most important indoor particle sources. Cooking (including broiling and baking, toasting and barbecuing) produced particles in a size range between 0.13 and 0.25 μm (volume diameter). Cleaning, moving of people and sautéing produced particles of a diameter between 3 and 4.3 μm. Frying was associated with both, fine and coarse particles.

Indoor/outdoor ratios in homes without apparent indoor sources can be estimated according to Wallace (1996). Indoor/outdoor ratios are a function of the air exchange and particle deposition rate, as the penetration rate is about unity and not different for fine ($PM_{2.5}$) and coarse particles ($PM_{10-2.5}$). Indoor/outdoor (I/O) ratios can be calculated using the equation

$$I/O = a/(a+k),$$

where a is the ventilation rate, and k is the deposition rate. Deposition rates for $PM_{2.5}$ were found to be between 0.4 and 1.0 h^{-1}. For a typical home with an air exchange rate of 0.75 h^{-1}, the indoor/outdoor ratio would be about 0.65 for fine particles and about 0.45 for coarse particles. In only a few homes, however, were such low indoor/outdoor ratios determined, indicating that most indoor environments are not free of indoor sources. In real situations, low in-

door/outdoor ratios around 0.2–0.5 were rarely observed; this again indicates the importance of non-apparent indoor sources (Wallace, 1996).

4.1.3.2. Personal exposure. In 1981, Dockery and Spengler (1981a) reported that indoor $PM_{3.5}$ levels were better correlated with personal exposure levels than outdoor levels. The best correlation was observed between indoor sulphate (representing fine particles <1 μm) and personal exposure levels. One of the largest databases on indoor, outdoor and personal particle exposure levels is available from the PTEAM study. From the pilot study, Clayton et al. (1991) concluded that people living in the same household tended to be exposed to similar personal PM levels. In the PTEAM pilot study, the correlations of the concentrations between different rooms of one household were found to be quite high, suggesting that one measuring site per household is adequate. In the PTEAM study, more than 178 non-smoking people participated in a study on indoor, outdoor and personal sampling of PM_{10} and $PM_{2.5}$ (indoor and outdoor only) (Clayton et al., 1993). An important finding was that the personal PM_{10} levels in the daytime sample were higher than the corresponding indoor and outdoor levels. The nighttime personal levels were lower than the daytime personal values. The average personal exposure levels lay between those measured indoors and outdoors. Indoor PM_{10} nighttime values were lower than outdoor values, whereas during the daytime indoor levels were similar to outdoor levels. The correlations for PM_{10} between fixed site monitor levels and outdoor home levels ($r = 0.61$) were higher than for fixed site versus indoor levels ($r = 0.51$) and fixed site versus personal levels ($r = 0.37$). At night all these correlations were higher than during the day ($r = 0.93$, 0.59 and 0.54, respectively). For $PM_{2.5}$, the outdoor home levels during the day were similar to the values at night. The correlations between outdoor fixed site $PM_{2.5}$ levels and residential outdoor levels were good and slightly better at night than during the day. At night the indoor levels were lower than the outdoor levels. The increase in the daytime personal PM_{10} levels was explained by personal activities, mainly by indoor activities such as smoking, vacuuming, dusting, carpeting, cooking, using cloths drier, and spraying. The elemental analysis indicated that the coarse fraction (>2.5 μm) might be responsible for the elevated personal levels. Resuspension of house dust (which comes partly from outdoors) and dust from clothing may largely contribute to the so-called "personal cloud" (Özkaynak et al., 1996b). For personal monitoring Clayton et al. (1993) ruled out a possible sampling bias (in the personal monitor) and skin flakes as a possible source. Özkaynak et al. (1996b) concluded that all elements were elevated in the daytime personal sample, suggesting that both outdoor and indoor particles contributed to the elevated personal levels. With regard to the size range mainly the coarse fraction (>2.5 μm) and only a minor proportion of the fine fraction (<2.5 μm) contributed to the "personal cloud". This find-

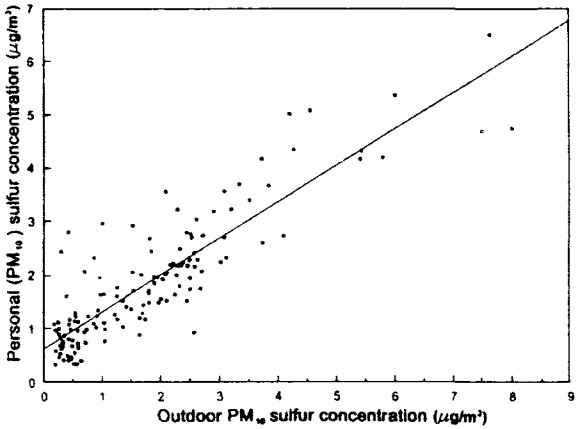


Figure 6. Personal exposure versus outdoor concentrations for sulphur ($R^2 = 0.77$) (Özkaynak et al., 1996b). Reprinted with permission from Nature Publishing Group. First published in *Journal of Exposure Analysis and Environmental Epidemiology* 6, 57–78.

ing was supported by observations of the sulphur levels, mainly found in the fraction below 1 μm, which were not elevated in the personal exposure values compared to those of fixed site monitors. Furthermore, the correlation between outdoor and personal levels for sulphur (representing fine, secondary particles) was good (Fig. 6).

Tamura and Matsumoto (1996) performed a study on personal exposures to PM_2 and PM_{10} in seven elderly non-smoking individuals in Tokyo. Indoor, outdoor and personal measurements were made for eleven 48 h periods. The correlations between the ambient and the personal levels in a cross-sectional analysis were quite high ($r > 0.8$), as was the correlation between the ambient and the indoor levels ($r > 0.8$). This study differed from the American studies with respect to indoor sources; smokers were not present and the reed-mat flooring and habits such as taking shoes off reduced the resuspension of particles. This study confirmed that in the absence of indoor sources the correlation between ambient and personal levels are good, and also that in clean homes without carpets the generation and resuspension of particles is low.

Janssen et al. (1995, 1998) presented results of personal PM_{10} monitoring from non-smoking adults in Amsterdam and from children in Wageningen. Median individual regressions between personal and ambient levels were fairly good (r around 0.6). For the children, parental smoking explained 35% of the variance between the personal and ambient levels. For the adults, dwelling "near a busy road", time spent in traffic and the exposure to ETS explained 75% of the variance between personal and ambient levels. This study confirmed that measurements of outdoor levels are appropriate for estimates of personal levels

Table 8. Potential factors in PM which influence human health

Physical properties[a]	Size mode, number, volume
	Hydrophobicity/philicity
	Electrostatic forces
Chemical composition[b]	Ionic compounds (nitrate, sulphates, acidity)
	Transition metals (e.g. Fe, V, Cr)
	Carbonaceous material (PAH; elemental carbon)
Biological species[c]	Allergens (pollen, fungal spores, glucans)
	Bacterial and bacterial structures (endotoxin)

[a]Yeh et al. (1976), Oberdörster (1995) and Peters et al. (1997).
[b]Spengler et al. (1990), Pritchard et al. (1996) and Lewtas et al. (1993).
[c]Wüthrich et al. (1995) and Rylander (1998).

in follow-up investigations but also that in a cross-sectional analysis the relationship between personal and outdoor levels is poorer. Aggregation of personal exposure levels to daily averages in the study areas, regressed against the daily outdoor averages, also increased the personal–outdoor correlations (Mage and Buckley, 1995; Wallace, 1996). The finer the particles, the better the correlation between the personal and outdoor levels; the best correlation was found for sulphur, representing particles smaller than 1 μm (Wilson and Spengler, 1996).

4.1.3.3. Other potential factors, relevant in an SPM exposure assessment. The particle size is an important factor, as it determines the site of deposition in the respiratory tract (Yeh et al., 1976). Associations between exposure and health are expected to be stronger for fine particles (<2.5 μm) than for coarse particles (>2.5 μm) (Schwartz and Neas, 1996). It is, however, unclear whether the mass load itself, some other physical factors such as the number of particles, the total surface area, or electrostatic factors, or the chemical and biological composition are the causative parameters. In a study from Peters et al. (1997), health effects from fine (0.1–2.5 μm) and ultrafine particles (0.01–0.1 μm) were more strongly attributed to the number of ultrafine particle than to the mass. This single example, while not conclusive, may be a first step in identifying the mechanisms of health effects.

Table 8 summarises parameters of PM which might potentially influence respiratory health and mortality.

4.1.4. Summary

- The spatial distribution of fine particles (<2.5 μm) is relatively uniform; therefore a central monitor for $PM_{2.5}$ may collect a sample representative for a study area. In vicinity to emission sources (e.g. diesel exhaust), however,

the $PM_{2.5}$ levels larger than the urban "background" may be observed. For larger particles (the coarse fraction of PM_{10} and TSP) the spatial variation is larger than for fine particles and the collection of representative samples is more critical.

- Ultrafine particle numbers do not strongly correlate with PM_{10} (and $PM_{2.5}$) mass concentrations. Primary traffic-related emissions are not well reflected by mass measurements.
- The fine (<2.5 μm) and the coarse (>2.5 μm) modes represent two different sets of pollutants with different emission sources, different chemical composition and different spatial and temporal behaviour.
- For indoor PM levels, outdoor air is the most important source besides smoking, which is the most important indoor source. The size range influenced by smoking is the fine mode (<1 μm), while other human activities influenced mainly the coarse mode (>2.5 μm).
- Indoor/outdoor ratios of PM_{10} and $PM_{2.5}$ in homes without smokers reach about unity; in homes with smokers, the ratios are larger.
- Indoor PM levels are not well correlated with the corresponding outdoor levels in cross-sectional studies. In follow-up, i.e. day-to-day studies, the correlation between indoor and outdoor concentrations becomes much better.
- The finer the particles, the better the correlation between the personal and outdoor levels.
- Personal PM_{10} levels were generally higher than the corresponding indoor and outdoor levels. The chemical composition of the personal PM_{10} mass mainly indicated contributions from the coarse mode (>2.5 μm).
- The personal, indoor and outdoor sample of PM_{10} have different chemical compositions. A personal sample can even be described as a "confounding factor" in investigations dealing with effects of outdoor particles.
- Up to date, adverse health effects were associated with the measured *mass* concentrations of particles in air. But surface area or number counts may also be relevant. The chemical constituents and biological materials also have to be considered.
- A move towards source-related markers of particles has to be made in order to understand their specific health effects and to develop efficient emission-reduction strategies.

4.2. Bioaerosols and allergens in ambient air

Biological material is present in all ambient aerosols. The biological material consists of proteins, lipids, carbohydrates (starch, cellulose), DNA, and RNA and all these components can be used as unique markers for particles of biological origin (Matthias-Maser, 1998). However, data on the amount of biological material in aerosols are sparse. In studies from Matthias-Maser (1998), the

content of primary biological aerosol particles (PBAP) accounted for 10–13% of urban and rural fine aerosol particles, determined by particle counting. The amount of protein accounted for about 2% of the total mass in urban and rural aerosols (Schäppi et al., 1996). In a study from Miguel et al. (1996) biological particles were found to be abundant in paved road dust and in air samples in California. Pollen, pollen fragments, animal dander and moulds were detected in resuspended dust from roads. About 5–12% of the allergenicity of TSP and PM_{10} were attributed to resuspended road dust. In contrast to on-line measurements used for air pollutants, the methods for measuring bioaerosols are more time consuming and difficult. Therefore, large databases on small-scale variations of bioaerosols do not exist. It has to be assumed that the spatial variations are large as local sources of pollen, bacteria and spores strongly influence receptor sites. On the other hand, in a study on personal exposure to pollen, the correlation between personal exposure and fixed site samples was significant with respect to day-to-day variations for people within a city (Riediker et al., 2000).

4.2.1. Natural constituents of the atmosphere

4.2.1.1. Pollen. Pollen is produced by vascular flowering plants and is the main source of allergens in the atmosphere. The most frequent pollen-induced allergies are caused by grasses (*Poacea, Phleum, Lolium*), ragweed (*Ambrosia*), birch (*Betula*), olive (*Olea*), pellitoria (*Parietaria*), mugwort (*Artemisia*) and cedar pollen (in Japan) (Spieksma, 1995; Wüthrich et al., 1995; Ishizaki et al., 1987). All these pollen are from wind-pollinating plants. The size of pollen is around 15–40 μm and larger. The aerodynamic shape enables the pollen to remain airborne over long distances. In most European countries and the USA, pollen grains are counted routinely within pollen survey networks (Lewis et al., 1983; Emberlin, 1997). The usual instrument for collecting pollen is the Burkard Pollen trap, a volumetric method in which pollen is deposited on a sticky film. The pollen grains are differentiated into species and counted microscopically. Results are given as numbers of pollen grains per cubic meter of air. The time resolution for routine measurement is hours to daily means.

4.2.1.2. Fungi, spores. The major structures of fungi are filaments and spores. Spores are the main biological airborne material, with a size range from 2 to 10 μm. Fungal spores can be found in large quantities in the atmosphere during summer and autumn with levels up to more than ten thousand spores per m^3 of air (Spieksma, 1995). In outdoor air, *Alternaria* and *Cladosporium* are the most abundant genera in mid-Europe (Flückiger et al., 1998). Spores can be collected by volumetric methods where they are deposited on a culture dish

by impaction. The sampling time is short (about 5–15 min) and provides information on a short-term basis. The culture dishes are incubated for 2–5 d (at 20–35° C) and the number of spores is then counted. The results are given as colony forming units (CFU) per m^3 of air. The non-viability of many spores is a drawback of this method. Direct microscopical counting yields a higher number of spores than the use of culture dishes for viable spores (Burge, 1995). It is especially important to determine the allergen content, e.g. with an ELISA test (enzyme-linked-immuno-sorbent assay) as dead spores may still contain active allergenic components (Flückiger et al., 1999). In addition to allergens, fungi also contain antibiotics and mycotoxins. Cell wall components such as D-glucans are also known to induce irritative effects (Fogelmark et al., 1994).

4.2.1.3. Bacterial aerosols. Environmental bacteria in soil and water can be released into the atmosphere by wind, splashing rains and mechanical disturbances. The particle sizes vary from 1 to 50 μm. In indoor settings, the concentration of bacteria in air is mainly due to the presence of humans; most of these bacteria are non-infectious (COST, 1993). To determine the bacteria content in air, techniques similar to those used for fungal spores are employed: a volume of air is drawn through an impactor and particles are deposited on culture dishes. The results are given in CFUs per m^3 of air. The sampling time is between a few and 15 min, providing short-term data. A major distinction is made among Gram-negative, Gram-positive bacteria and actinomycetes. Relevant for human health is the presence of bacterial toxins. Allergenic material can be determined by ELISA and the quantification of toxins is obtained by analytical chemistry.

4.2.1.4. Endotoxins, lipopolysaccharides. Endotoxins are cytoskeletal molecules of the cell wall of Gram-negative bacteria. Lipopolysaccharides (LPS) are the most important and the biologically active component of endotoxins. In occupational studies (e.g. farming and waste industry) exposure to LPS causes inflammation, airway constriction, chest tightness, and induction of nitric oxide reactions (Fogelmark et al., 1994). In indoor settings, e.g. in the sick building syndrome (SBS), inflammation was often related to endotoxins in the air (COST, 1993). Endotoxins were also detected in ambient air particles, where they were responsible for causing pro-inflammatory reactions in macrophages (Becker et al., 1996; Monn and Becker, 1999).

4.2.1.5. Further biological material in aerosols. Latex is a natural rubber from the plant *Hevea braziliensis*. A variety of allergens have been identified recently in latex (Muguerza et al., 1996). Exposure to latex particles is common in certain occupations (dentistry, medicine, etc.) and the increased use of latex devices as a protective barrier against viral infections in the general population

raised the incidence of sensitisation observed during the last decade (Vandenplas et al., 1995). Besides dermal contact, the intake of latex particles through the airways may be important (e.g. inhalation of latex dust from gloves) (Baur, 1995).

Latex has also been detected in ambient air particles (Miguel et al., 1996). Automobile tyre production is the largest application for natural rubber. The fabrication method has changed recently and a higher content of natural rubber is now used. Latex particles have been identified in airborne and deposited particulates in the near vicinity of roads in California (Miguel et al., 1996). For people living near roads with heavy traffic this might constitute a further sources of contact with latex particles. In a study in Switzerland, latex allergens have been identified in ambient coarse (2.5–10 μm) but not in ambient fine (<2.5 μm) particles (Monn and Tenzer, 2000).

In some occupational settings, for example in the handling and storing industry of farm products such as hay, grain, etc., a large amount of allergenic material can be released into the atmosphere (Lacey and Dutkiewicz, 1994).

Excretions from house dust mites, cats, dogs, birds, insects and cockroaches are important sources of indoor allergens in homes (COST, 1993).

Table 9 depicts some of the most important biological species in ambient air. Major allergens from pollen, e.g. from birch trees (Bet V 1), timothy grass (Phl p 5) and rye grass (Lol p 1), and allergenic fungal spores from *Cladosporium* (Cla h 1) and *Alternaria* (Alt a 1) may be responsible for some acute allergic reactions. The peptide sequence of pollen allergens shares similarities with some enzymes, recognition structures, and bacterial defence or stress-related proteins (Knox and Suphioglu, 1996a; Swoboda et al., 1994). To date, only a few of the hundreds of potential fungal allergens have been characterised. Also relevant to health effects are cell components such as D-glucans, antibiotics from fungi and endotoxins from Gram-negative bacteria. Ambient air

Table 9. Summary of important aerosols of biological origin found in ambient air and some examples of associated inflammatory and allergenic material

Biological species	Content	Examples of inflammatory and allergenic species
Plant: pollen grains, leaves	Proteins, lipids, starch, cellulose, carbohydrates	Bet v 1, Phl p 5, Lol p 1
Fungi: spores, mycel	Proteins, lipids, toxins, glucans, antibiotics	Alt a 1, Cla h 1, D-glucans
Bacteria: Gram-negative	Proteins, lipids, toxins, lipopolysaccharides	Endotoxins
Rubber from tires	Protein, latex	Hev b 1

samples collected near roads may contain a major allergen from the airborne latex rubber (Hev b 1) resulting from tyre abrasion.

4.2.2. Interactions between air pollutants and pollen

Intact pollen grains have a size larger than 10 μm and should, therefore, be found only in sizes larger than 10 μm. However, allergens from pollen were detected in fine particles (<2.5 μm) (Solomon et al., 1983; Rantio-Lehtimaeki et al., 1994; Spieksma, 1990; Spieksma et al., 1995; Schäppi et al., 1996).

How might these allergen-loaded fine particles be produced? A plausible mechanism was suggested by Knox and Suphioglu (1996a). After contact with water, grass pollen undergo osmotic rupturing. This leads to a release of hundreds of small Lol p 5 containing starch-granules (0.6–2.5 μm) in *Lolium perenne* pollen. Cytosolic allergens (such as Lol p 1) are also released into the atmosphere and are free to react with water droplets and other atmospheric particles. Molecular characterisation of these pollen allergens reveals that they are homologous to recognition proteins. Such cysteine-rich molecules tend to bind to other molecules such as carbohydrates, proteins and lipids (Knox and Suphioglu, 1996b). Lol p 1 has been shown to interact with diesel soot particles (Knox et al., 1997). The release of orbiscules of small size (<0.1 μm) may also be a factor (Ong et al., 1995); allergens may also originate from organs other than pollen. Size-fraction allergen studies revealed that antigens were found in periods outside the pollen season (e.g. for Bet v 1) (Schäppi et al., 1996). Antigens transferred to fine particles may have a different half-life in the atmosphere and may remain in the atmosphere longer than larger particles. Bet v 1 was also found in fine particles before pollen counts were positive, indicating either production of Bet v 1 from other plant organs than pollen or lack of sensitivity in the pollen-counting procedure. Schäppi et al. (1997) suggested a mechanism for the production of fine particles containing Bet v 1 which, in contrast to grass pollen, do not show humidity rupturing. Birch pollen grains were seen to sediment on leaves. After a rain-shower, a germination tunnel grew through which allergen-loaded starch particles of small size were released into the atmosphere. Therefore, according to Schäppi's observation, the content of Bet v 1 in fine particles was higher after a rainy period than before.

There are two important mechanisms in the interaction between air pollutants and pollen allergens: air pollutants can induce stress-related allergens in the pollen antheres and air pollutants can modify the surface of pollen and increase the bioavailability of allergens. Breitender and Scheiner (1990) provided evidence for a higher content of Bet v 1 in birch pollen exposed to traffic compared to that of trees in rural areas. Induction of Bet v 2, which is homologous to the stress-related allergen profilin, has also been observed in birch trees

exposed to stress (e.g. bacterial infections, drought, pollution, etc.). The direct effects of ozone on the content of Phl p 5 in *Lolium perenne* in Germany were investigated in open-top and closed-top chambers (Masuch et al., 1997). Elevated ozone levels were associated with an elevated allergen content in grass pollen. The effect was dose dependent, but O_3 peak levels were less important than long-term O_3 averages.

In polluted urban areas, pollen surfaces are contaminated by fine particles (Kainka-Staenicke et al., 1988; Behrendt et al., 1992; Schinko et al., 1994). The modification of the pollen surface may alter the availability of allergens although the outer wall of pollen (exine, made of sporopollinin) and the inner wall (intine, made of polysaccharides) are rather inert. For gases, the germinal pore may offer a site of reaction. Behrendt et al. (1997) investigated interactions between pollen and air pollutants in a floating chamber under controlled conditions. Pollen exposed to particles underwent structural changes and increased allergen release was observed. Exposure to SO_2, but not to NO_2, resulted in a reduction of allergen release. Behrendt concludes that air pollutants may modulate the bioavailablity of grass pollen allergens.

The role of these fine particles in promoting allergic symptoms and sensitisation is, however, unknown. It has been suggested that allergen-loaded fine particles affect lower-airway symptoms (e.g. allergic asthma), whereas intact pollen grains cause upper-airway allergic symptoms such as hay fever (Wilson et al., 1973; Suphioglu et al., 1992). During a thunderstorm in Australia, a large number of people suffered from allergic symptoms. It has been suggested (but not measured) that such fine particles may have played an important role in this case (Bellomo et al., 1992). For a similar event in England, a potential influence of a high allergen content in air and of allergen-loaded fine particles has been discussed (Celenza et al., 1996).

Emberlin (1995a, b) reviewed the literature on the interactions between air pollutants and aeroallergens. She concluded that there was a need for more research on aeroallergens and air pollution. This interdisciplinary field requires collaboration between biologists, air pollution scientists, plant physiologists, physiologists and epidemiologists. Her review focused mainly on outdoor conditions, but she pointed out that compounds of biological origin also play an important role in indoor settings.

4.2.3. Summary

- Both, the coarse (>2.5 μm) and the fine fraction of particles (<2.5 μm) contain material of biological origin (bacteria, pollen, fungal spores), but the major part of intact bioaerosols (pollen, bacteria, spores) occurs in the coarse mode.

- In deposited and resuspended dust, particles of biological origin may be abundant. Furthermore, the allergenicity of suspended particles is largely influenced by deposited dust.
- Pollen allergens present in fine particles (<2.5 μm) offer a potential route of entry into the small airways, whereas the target organ of intact pollen (>10 μm) are the mucous membranes of the nose and mouth.
- In addition to pollen allergens, other compounds of biological origin, such as endotoxins, mycotoxins, spores, allergens from pets and mites (both indoors) may significantly affect human health.
- Interactions between anthropogenic pollutants and biological material are not well understood. Gases (e.g. O_3, NO_2) may increase the allergen content in pollen (e.g. by induction of stress-related proteins). Airborne fine particles may adhere to pollen surfaces and modify the bioavailability of allergens. On the other hand, pollen allergens may also adhere to fine particles and produce allergenic fine particles with a potential to penetrate into the alveoli.

4.3. Nitrogen dioxide

4.3.1. Small-scale spatial variation

A large database on small-scale spatial variations of NO_2 was established in SAPALDIA (Martin et al., 1997; Monn et al., 1998). Data on the spatial variability of NO_2 were collected in two phases; in the cross-sectional study (1991) NO_2 was measured stationarily and in the follow-up study (1992–1993) population-based at home with passive samplers. Examples from this study ill be used to show spatial outdoor differences and an approach to deduce a multiple regression model.

An example of stationary measurements at two sites is shown in Fig. 7. Monitoring took place during four weeks in each season. During spring and summer, large spatial variations in NO_2 concentrations were observed, whereas in the autumn and winter periods, the variation was small. During winter, inversion layers prevail on the Swiss Plateau; this situation favours a homogeneous mixing of the pollutants within this layer. The conversion of the primary pollutant NO to NO_2 is slow during winter (Atkinson, 1990); in spring and summer, however, the conversion from NO to NO_2 is much faster. Higher ozone levels and photochemical reactions favour the oxidation of NO. Therefore, a steeper concentration gradient is expected in summer compared with winter periods. In fact, observed levels at the most polluted sites in spring were higher than in winter, although the regional NO_2 levels were higher during winter than during summer. In 1992–1993, a population-based outdoor and indoor/personal monitoring study was performed during a full year period in SAPALDIA. Overall,

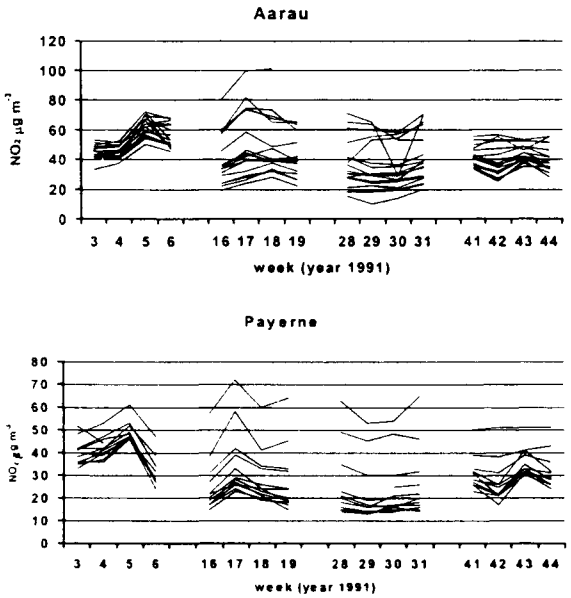


Figure 7. Temporal and spatial concentration profile of NO_2 at Aarau (suburban, 17 sites) and Payerne (village, rural, 12 sites) measured at fixed sites with passive samplers (Hegner, 1994).

about 50 individuals, a random sample of the SAPALDIA population, participated three times during four consecutive weeks in each region. In contrast to the cross-sectional study (1991) a larger number of measurements were obtained and the pollution levels represent randomly population-based outdoor home levels. On the other hand, the number of (temporal) parallel measurement periods was smaller than in 1991 because of the measuring scheme.

Fig. 8 compares the regional (population-based) outdoor annual mean averages (measured with passive samplers) with the annual means of the continuous monitors. At the urban sites, the levels of the central monitors were slightly higher than the population-based outdoor average. This observation is plausible, as in large cities part of the population lives in residential areas outside the city centres (where the central monitors were installed). At the rural sites Payerne and Wald and the Alpine site Montana, the central monitor underestimated the population-based values. At these three sites, the central monitor was located outside the villages and the measured values reflect this fact. A comparison between the technical error (between passive sampler and monitor) and the error due to a "non-representative" sampling shows that the latter can be larger. Such errors in non-representative sampling with respect to population exposures may introduce errors in the exposure-health effect rela-

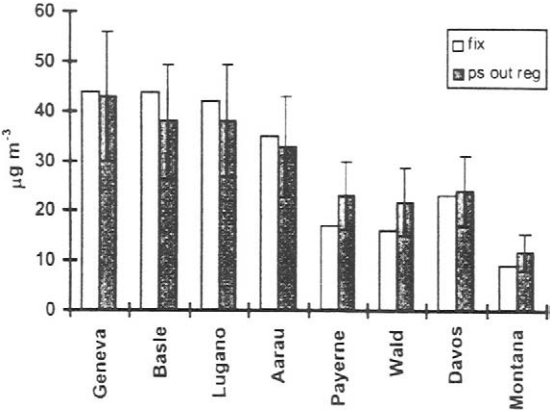


Figure 8. Comparison between ambient NO_2 annual means measured with the fixed site monitors (fix) and the averages obtained from passive sampling measurements outdoors (ps out reg) during 1993 (columns: mean values; bars: average standard deviation of the spatial variation).

tionship. The shown example highlights the need for a careful selection of the central monitors or the use of passive sampler to evaluate the representativity of the central monitor. Based on these results, improved exposure estimates were used in the health-effect analyses of SAPALDIA (Ackermann-Liebrich et al., 1997; Schindler et al., 1998). Based on the spatially refined NO_2 data, Schindler et al. (1998) revealed health effects due to exposure to NO_2 which were hidden in an aggregated analysis.

4.3.2. Indoor/outdoor and personal exposure

Yocom (1982) reviewed indoor/outdoor relationships of NO_2 from early studies. Some of the referred data are from Portage, WI, Boston, Southern California, Holland, Los Angeles and Switzerland (Quackenboss et al., 1986; Leaderer et al., 1986; Drye et al., 1989; Billick, 1990; Noy et al., 1990; Spengler et al., 1994; Monn et al., 1998).

An important study on personal exposures to nitrogen dioxide based on more than 700 individuals in Los Angeles was published by Spengler et al. (1994). The purpose of the "Nitrogen Dioxide Exposure Study" was to quantify the relative contributions of indoor and outdoor sources, as well as factors relating daily activity patterns and human exposure to NO_2. In the main study, which included more than 700 individuals, NO_2 was measured over a 48-h period. In a sub-sample, a microenvironmental study was performed. In addition, these individuals participated more than once in order to quantify the variability between season and within subjects. All the monitoring took place in the

bedroom, in outdoor air and on a personal level. Personal levels were higher in homes with gas ranges and pilot lights than in homes with gas ranges only and in homes with electric stoves. Season had a great influence on the outdoor levels, but the influence on the bedroom levels was not substantial. About 40% of the variation in bedroom concentration was explained by outdoor levels. Regression between indoor and outdoor levels yielded slopes of 0.4–0.5 with higher slopes in summer and lower slopes in winter. 60% of the variation in personal exposure levels was explained by the variation in the bedroom level. 51% of the variation in personal exposure could be explained by the outdoor levels. In the SAPALDIA study, outdoor levels explained 33% of the variation in personal levels, and indoor levels about 51% of the personal levels (Monn et al., 1998). The personal exposure showed seasonal and spatial variation. Personal exposure levels were highest during winter months. The spatial patterns in exposure reflected the location of an individual home with respect to the distribution of ambient levels and the intra-urban distribution (zones) of housing characteristics (type of range, pilot light, etc.). The parameters determined to explain personal levels were type of range, season, ambient NO_2 zone, and day of the week. The within-household variation (in some households more than one person was participating) for bedroom or outdoor levels was small. Within-household variation of personal exposure, however, was three times that of the stationary measurement. This suggests that some other factors (such as differences in time-activity pattern) also largely determine the personal exposure levels.

The main findings of these studies, namely that gas stoves, outdoor air and season (ventilation) are the most important parameters for the indoor NO_2 levels, were confirmed in all other studies. Indoor levels were generally better predictors for personal NO_2 exposure levels than outdoor levels. Indoor/outdoor ratios in homes without indoor sources were around 0.4–0.8; and in homes with gas appliances about three times higher (Yocom, 1982; Quackenboss et al., 1986; Leaderer et al., 1986; Ryan et al., 1988a, b; Drye et al., 1989; Billick, 1990; Brunekreef et al., 1990; Schwab et al., 1994; Monn et al., 1998). In homes with gas appliances, attention has to be paid to other compounds, such as HNO_2, which is produced indoors (Brauer et al., 1991). The NO_2-concentration gradient within a household was small in homes using electric appliances but was significant in homes with gas appliances (Ryan et al., 1988a, b; Billick, 1990; Neas et al., 1991). Noy et al. (1990) observed that the correlation between weekly averages and peak levels for personal or stationary indoor measurements was poor. The ratio between the peak and the mean levels was about five. In most of the presented studies, NO_2 levels have been determined with passive samplers exposed for periods lasting from two days up to weeks. This indicates that important information could be lost with this device.

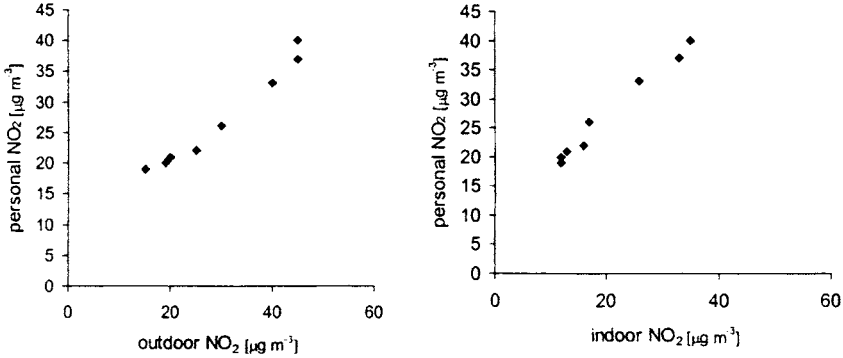


Figure 9. Scatterplot for outdoor/personal ($R^2 = 0.965$ and indoor/personal ($R^2 = 0.983$) NO_2 ratios of aggregated data (annual mean estimates) N: indoor = 1501, N: outdoor = 1544, N: personal data = 1494 (Monn et al., 1998).

An example from the SAPALDIA study illustrates indoor/outdoor/personal exposure relationships based on aggregated data. Highly significant correlations ($R^2 > 0.9$) were found for an outdoor versus personal and an indoor versus personal exposure analysis (Fig. 9). The three areas with the highest NO_2 outdoor levels (urban) also are the sites with the highest percentage (>31%) of gas users. This might be the reason why the three upper sites do not follow a strict linear line in the outdoor/personal exposure plot. In an analysis of individual single data, however, these correlations were much weaker (indoor/outdoor 0.5, indoor/personal, personal/outdoor <0.3) (Monn et al., 1998).

4.3.3. Summary

- Outdoor small-scale spatial variations of NO_2 were observed to be significant, especially during periods of elevated photochemical activity.
- A well-established passive device is available for measuring NO_2. The time resolution of the sampler ranges from about one day up to two weeks.
- Indoors, gas stoves are the major emission source of NO_2. In homes without indoor sources, outdoor NO_2 levels were the strongest source of indoor levels.
- Personal exposure levels for NO_2 were better correlated with indoor home levels than with outdoor levels.
- One difficulty in the use of personal and indoor NO_2 levels as an indicator is the difference of the pollutant mixture generated indoor and outdoors: outdoor combustion mixtures are different from the mixture of gas stove emissions.

Table 10. Photochemical pollutants and acids

Parameter	Precursor, reaction partner	I/O ratios approx.[a]
O_3	NO_2, VOC	0.2–0.8
H_2SO_4	SO_2; $HO_2^{\cdot}$	0.86–0.96 (SO_4^{2-})
HNO_3	NO_2; $OH^{\cdot}$	0.1–0.47
HNO_2	NO, $OH^{\cdot}$; heterogeneous	>1–5 (with gas appliance)
H^+	In acids	0.35–0.48
PAN	NO_2, VOC, radicals	Not determined

[a]I/O: estimates for indoor/outdoor ratios, from Brauer et al. (1991, 1995), Yocom (1982), Moschandreas (1981), Lustenberger et al. (1990) and Weschler et al. (1989).

4.4. Photochemical pollutants

4.4.1. Ozone and related photochemical pollutants in the atmosphere

Important photochemical constituents, such as sulphuric acid (H_2SO_4), nitric acid (HNO_3), and peroxy-acetyl-nitrate (PAN) are produced in outdoor air (Atkinson, 1990; Carter et al., 1995; Table 10). Nitrous acid (HNO_2) is an important constituent in ambient air during the night but is also produced by heterogeneous reactions in homes with gas stoves (Brauer et al., 1991). Table 10 shows rough estimates for indoor/outdoor ratios. Indoor levels for O_3, HNO_3, and H^+ were observed to be considerably lower than the corresponding outdoor levels. For H_2SO_4 (determined as SO_4^{2-}), indoor/outdoor ratios reached unity.

Ozone concentrations undergo distinct seasonal and diurnal variations; peak levels are observed on afternoons with intense sunshine in spring and summer (BUWAL, 1996). The photochemical production of O_3 in the troposphere depends on NO_x and VOC emissions (Atkinson, 1990); therefore, highest O_3 levels in rural areas are observed downwind of urban plumes (Altshuller, 1988). The small-scale variation within a study region is dependant on the vicinity of the site to NO emissions: in urban areas, reduced O_3 levels are observed in the vicinity of traffic arteries; in rural areas, O_3 levels are observed to be more or less uniformly distributed (BUWAL, 1996).

Peak values of O_3 were considered to be more relevant for causing adverse health effects than long-term exposures (Lippmann, 1989; Tager, 1993). In considering these findings, air quality standards for O_3 rely on peak values such as 1-h values and 8-h daytime values in the USA and WHO guidelines. In an ecological approach, where the average exposure concentration and also the ranking of the exposure levels between the study sites were important, an inconsistency in the use of different statistical parameters for the description of long-term exposure to O_3 were observed at the SAPALDIA sites (Monn

et al., 1999). For SO_2, PM and NO_2, the ranking between the study sites remained the same if percentiles (e.g. 95th or 98th percentiles of $\frac{1}{2}$ values) or annual means were used. For O_3, however, this was not the case. Alpine sites exhibited highest averages but were only in the mid-range for peak values. The reason for these findings can be explained by the fact that two different pathways contribute to O_3 concentration levels in the troposphere: the photochemical reactions, mainly during spring and summer, and the influx of O_3 from the free troposphere, which mainly affects elevated sites (above 1000 m.s.l.) (BUWAL, 1996). A comparison of photochemically produced HNO_3 also revealed that HNO_3 occurred in much lower quantities in the Alps than at urban sites.

Improvements of the assessment of long-term O_3 exposure measures were performed by Künzli et al. (1997). A questionnaire was designed to ask for time activity, time budgets (especially time spent outdoors) and physical activity in the past. Based on measured O_3 levels in two study sites in California, the method enabled a better calculation of life-long exposures than the use of outdoor data only.

4.4.2. Acids

Spengler et al. (1990) reviewed data on acidic compounds in outdoor air and stated that after a change in emission patterns, whereby SO_2 is now largely emitted by high stack power plants, acid sulphates can be transported over large distances. Increasing emissions of NO_x by vehicular traffic has increased the levels of HNO_3 in large urban areas. Acidic aerosols and gases can be neutralised by ammonia, yielding ammonium salts. In the atmospheric surface layer where the amount of NH_3 is higher than in the upper atmosphere, the quantities can be sufficient to neutralise acids. The diurnal variation of acids shows generally higher daytime levels than at night and higher levels during the summer than in winter. Because of higher NH_3 emissions in urban areas (related to the population density) compared to rural areas, the excess of acidity is larger in rural than in urban areas. Acidity can be determined by measuring the strong acids (H^+), H_2SO_4, and HNO_3. Sulphate measurements were also used as surrogates for aerosol acidity, but the two measurements were sometimes weakly correlated. Waldman et al. (1990) found a strong correlation between three sites in the Toronto metropolitan area for aerosols consisting of H^+, NO_3^-, SO_4^{2-}. While for sulphates the peak levels were quite uniformly distributed, strong acidity varied considerably between the sites. Downtown areas had lower aerosol acidity levels than suburban areas. Sulphates and H^+ levels were correlated over time, but considerable differences in the spatial behaviour of these two components were observed (Waldman et al., 1990). Brook and Spengler (1995), Spengler et al. (1996) and Özkaynak et al. (1996a) pre-

sented data on ozone and strong acidity in 24 North American communities. Strong acidity was mainly detected in areas close to high sulphur emission areas (western Pennsylvania, eastern Ohio, West Virginia). Low particle strong acidity was found in regions without high sulphur emission (western and midwestern cities). Substantial concentrations of nitric acids were detected in two Californian sites and many sites in the northeast. Suh et al. (1997) studied the distribution of photochemical pollutants in Washington DC. A strong correlation among particulate measurements (PM_{10}, $PM_{2.5}$) with SO_4^{2-} and H^+ was found. H^+ was found to be uniformly distributed across the study area, and a larger spatial variation was observed for coarse particles and NH_3 than for H^+. While sulphur-related acidity is an important problem in parts of the USA, nitrogen species are dominating in Western Europe. In Switzerland and also in other parts of eastern Europe for example, H_2SO_4 levels were found to be negligible (<2 ppb) (Alean-Kirkpatrick, 1993; Brauer et al., 1995; Monn et al., 1998). In western Europe, NO_2-driven chemistry and neutralisation by NH_3 was found to be important. Although SO_2 levels were high in eastern Europe, the conversion to SO_4^{2-} was too slow to produce high amounts of acids. Within a photochemical pollutant mixture, the production of aerosols (<2.5 μm) (e.g. ammonium sulphate) is also an important source of elevated particulate levels (US-EPA, 1996b).

4.4.3. Indoor and personal exposure to photochemical pollutants

Measurements of personal exposure to O_3 and acids have not yet been carried out extensively. Studies from Europe and from the USA (Monn et al., 1993; Brauer and Brook, 1997; Liu et al., 1993; Liu et al., 1997) indicated weak to moderate correlations between outdoor and personal O_3 levels, and also between indoor and personal O_3 levels. However, the correlation coefficients increased for special groups such as children in summer camps or farmers, who spent most of the time outdoors. In such cases, ambient measurements described personal exposure levels much better than in the general working population. Suh et al. (1993) published data on levels of personal exposures to sulphates and aerosol strong acidity. Personal levels of sulphate exposures for children were consistently lower than the measured outdoor values. The same finding was obtained for personal strong acidity levels (H^+). A model was computed in order to calculate personal exposure values by using stationary outdoor sulphate data and information on time spent indoors and outdoors. Indoor levels were modelled using the outdoor levels and a loss-rate for indoor levels (different in air-conditioned than in non-air-conditioned homes). For the calculation of an H^+ concentration model, data on personal NH_3 exposure values were needed, including the reaction rate accounting for a loss due to NH_3 neutralisation. A good model could be computed by using stationary H^+ lev-

els from outdoor air, personal NH_3 levels and time-activity data (time spent indoors and outdoors). However, the accuracy and the precision of this model predicting H^+ personal levels was much lower than for the sulphate model. This is an indication of the large variability in H^+ and NH_3 concentrations. In the validation study it was demonstrated that the interpersonal variability can be very high. It is noteworthy that this model was applied to estimate children's exposure. Children may have a better-defined time-activity pattern with fewer microenvironments than adults, such that the model may not be as accurate and precise for adults. Liu et al. (1997) investigated personal exposures to O_3. Personal exposure levels were not well predicted by outdoor concentrations. An improved model was computed using elevation, distance to stationary monitor and traffic. The low predictive power was due to spatial variability of outdoor O_3 (which is very important in regions with high traffic sources) and also because of errors in time-activity records and in the measurements. Brauer and Brook (1997) studied personal exposures to O_3 and health effects for selected groups (people working indoors, people spending more time outdoors than indoors, such as farm workers). Differences between these groups' exposures to O_3 were associated with time spent outdoors. Leaderer et al. (1999) investigated acids, ammonia and particles in more than 58 homes in Virginia. The contribution of kerosene heaters to increased $PM_{2.5}$, sulphates and acids (H^+) concentrations has already been mentioned. Indoors, nitrous acid levels were higher than outdoors and higher in homes with unvented combustion sources. As ammonia levels are higher indoors than outdoors, the particle acidity was lower indoors than outdoors.

4.4.4. Summary

- The small-scale variation of O_3 within an urban and rural area is dependant on the proximity to NO emissions (e.g. traffic arteries).
- In the assessments of exposure to O_3, short-term parameters are considered to be more important than long-term parameters.
- Besides O_3, a number of other constituents are produced in photochemical reactions such as acids (e.g. H_2SO_4, H^+, HNO_3), radicals and aerosols with different spatial distributions.
- The use of O_3 alone as an indicator of such a mixture is not always adequate, as its spatial and temporal variation differs from that of other species.
- Acidity levels are strongly determined by levels of ammonia, which acts as a neutralising agent.
- Indoor O_3 levels were significantly lower than the corresponding outdoor levels.
- For sulphates, indoor/outdoor ratios reached almost unity.

- Personal exposures to acids showed large interpersonal variations for H^+ and NH_3.

5. Final discussion

In this review, several methods of assessing exposure to air pollutants were reviewed. The main focus was on the small-scale spatial variation of pollutants and the relationship between indoor, outdoor and personal exposure patterns.

Individual personal exposures can be measured directly or indirectly. The direct methods require air pollution measurements on the person (e.g. by carrying a monitoring device), or analyses of biological markers from body fluids (Leaderer et al., 1993). Direct measurements clearly reflect individual personal exposure levels best. With the exception of passive sampling (e.g. for NO_2), measurements of personal exposure are expensive, time consuming and difficult to apply to large study populations. It is important to note that a personal measurement does not a priori provide more valid data than a stationary outdoor measurement, i.e. a personal sample in a study investigating effects from outdoor combustion pollutants is often influenced by sources other than outdoor sources and may thus confound the exposure–effect outcome. Internal dose measurements of biological markers provide the best measurements of personal exposure as they refer directly to the amount of material which has crossed the physical boundary of the body. Understanding of pharmacokinetics is necessary in order to relate the measured biomarkers to ambient pollutant levels. Analysis of most biomarkers is expensive and difficult to carry out in large-scale surveys. In occupational studies, where investigations focus on specific air toxins with known sources, such applications are very useful. In environmental studies on complex mixtures, however, such applications are usually difficult.

An approach to indirect personal exposure measurements is the use of microenvironmental (ME) modelling (Duan, 1982). This approach requires data from selected MEs (e.g. outdoor home, indoor such as bedroom or kitchen, in transit) and the time-activity budgets of the people (Duan, 1982; Duan and Mage, 1997). It is, however, difficult to take all MEs of a persona or population into account; a simpler approach uses data from the most significant MEs only (e.g. outdoor and indoor home levels). A further simplification is to model indoor levels from outdoor levels by incorporating the penetration, ventilation and deposition rates (for particles) and a chemical reaction term (Wallace, 1996; Weschler et al., 1991). In addition to time budgets, people's habits (e.g. smoking, staying outdoors) and their exposure at work have to be taken into account in detailed personal exposure models. The ME method is promising but costly, as the validation of the models, which requires personal

measurements, is time consuming. The best application for such ME models will probably lie in risk assessment studies.

In epidemiological studies on air pollutants, indirect measurements are most commonly used and exposure data are collected with fixed site ambient monitors. Measured concentrations derived from these monitors are assigned to people living in these areas. Although, in this "aggregated design", a bias in the exposure–effect outcome may be minimised, an evaluation of the representativity of these "central monitors" has to be preformed. Spatial variations in pollution concentrations within a city may be significant and are most critical for NO_2 and O_3, less critical for PM_{10} and $PM_{2.5}$, but critical again for ultrafine particles (<0.1 μm). The monitors' readings may be influenced by these small-area climates. An assessment of people's average exposure compared to the monitors data is especially important in areas representing "leverage points". Existing deviations between measured fixed site data and average peoples' exposure do not fulfil a Berkson-case and over- or underestimation of effect estimates has to be expected.

To date, the strongest associations between health parameters and air pollution have been observed for mass measurements of small particles below 10 μm (PM_{10}) and particles below 2.5 μm ($PM_{2.5}$) (Dockery et al., 1993). The size and shape of the particles, as well as their physico-chemical properties, determine the depth of inhalation, the extent of exhalation, and the deposition rate in the airways (Yeh et al., 1976). These mass measurements (in $\mu g\, m^{-3}$) of ambient or personal exposure represent a complex mixture which comprises ions, PAHs, salts, acids, metals and also some compounds of biological origin (e.g. pollen, endotoxins). However, the causative agents and mechanism of the observed health effects are not known. For transition metals, PAHs and some compounds of biological origin (e.g. endotoxin) toxicological data are available; possible biochemical pathways for the effects have been proposed but their relationship to ambient pollution is difficult to assess (Lewtas et al., 1993; Pritchard et al., 1996; Becker et al., 1996). It is also well known that allergic symptoms can be attributed to biological particles (pollen, fungal spores, etc.) (Wüthrich et al., 1995). It has been suggested that interactions between anthropogenic air pollutants and natural particles can modify the allergen profiles and promote the formation of allergen-loaded fine particles (Behrendt et al., 1997; Knox et al., 1997). All these findings highlight the complexity of the particles' composition and the difficulties in investigating the causative agents. With respect to exposure parameters it is important to note that personal exposure concentrations for particulate matter do not correlate well with outdoor ambient concentrations (in cross-sectional analyses), and that personal levels were found to be higher than the corresponding outdoor and indoor levels in cross-sectional studies (Clayton et al., 1993). However, when personal levels in a study area were aggregated, the correlation between personal and outdoor

values was stronger. This suggests that the variation in personal exposure levels between study persons within a study area was responsible for the poor correlation. In follow-up studies (where multiple samples are collected over time), the correlations between outdoor and personal values were also stronger than in cross-sectional studies (Janssen et al., 1997). For elemental markers of ultrafine particles (traffic-related primary particles, such as Pb and Br), the correlation between personal and outdoor levels is weaker than for markers of secondary particles (e.g. S). This indicates that for the homogenously distributed secondary aerosols, an outdoor measurement is a good approximation to personal exposures and that for the personal ultrafine particle exposure, individual activity pattern and vicinity to sources are important in the short-term analyses (Oglesby et al., 2000). Despite some lack of correlation between personal (PM_{10}) and outdoor values, outdoor fine particle concentrations were strongly associated with mortality and morbidity indicating that outdoor sources (e.g. vehicular emission) emit the toxic entity (Dockery et al., 1993; Schwartz and Neas, 1996).

The complexity of the discussion on the validity of outdoor, indoor or personal exposure markers shows that there is no general recommendation on the use of specific exposure measurements. Depending on the design of the study (e.g. cross-section, longitudinal study, long-term or day-to-day study) and the underlying hypotheses, different approaches have to be chosen.

For a comprehensive risk assessment, the move towards source-attributed particulate concentrations is promising. The type of sources, chemical composition, size and their health effects have to be evaluated in order to take the correct strategy to minimise health risks. In the exposure to pollutants in European cities (EXPOLIS) study such strategies are implemented (Jantunen et al., 1998). The primary goals are to establish a database on microenvironmental concentrations (indoor home, outdoor and occupational), on personal exposure distributions, and on time-activity patterns for a random population in different European cities. In the second step (EXPOLIS-EAS) (Mathys et al., 1999), source identification will be performed based on elemental analyses in order to relate source specific emissions to personal exposures. Such a database will then be used to determine the health risk of specific particulates and their sources and for modelling population exposure distributions and effects of reduction strategies.

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Appendix

1. Introduction and methods

The purpose of this Appendix is to present some aspects of the results of the recently completed BRISKA- (Basle Risk Assessment Study of Ambient Air Pollutants) and EXPOLIS-study (Air Pollution Exposure in European Cities) (Braun-Fahrländer et al., 1999; Jantunen et al., 1998). The first study focussed on spatial variations of air pollutants in an urban environment and the latter on the relationships between indoor, outdoor, workplace and personal exposures to $PM_{2.5}$, CO and VOCs. In the BRISKA-study, suspended particulate matter (TSP, PM_{10}, $PM_{2.5}$) and gaseous air pollutants were measured at six sites within the urban area of Basle. In the EXPOLIS-Study, 50 (at one site 250) study persons participated in six cities in a 48-hour measurement of indoor, outdoor, workplace and personal exposures.

The objective of the BRISKA-project was to obtain small-scale, spatially resolved air pollution data within the urban area of Basle. In a second step, cancer risks of the population in Basle were estimated based on the spatial gradients of the pollutants in a unit-risk model. Measurements of air pollutants were performed during a one-year period in 1997. A mobile container, equipped with measuring devices for air pollutants was installed at six sites reflecting differences in pollutant patterns (traffic, residence, etc.). As the measurements did not cover a full year at each site, a model calculation was made in order to consider the temporal variation of the pollutants over the year and the meteorological conditions. The model incorporated air pollution data from an additional stationary or fixed site survey and meteorological data (Braun-Fahrländer et al., 1999; Röösli et al., 2000a,b). Of the meteorological variables, daily average temperature, relative humidity, sum of the precipitation, global radiation, wind speed, temperature gradient between 250 and 493 m (at day and night) and

wind direction were included in the model. Based on the resulting multiple regression model, annual average levels were estimated for each site. The coefficients of determination (R^2) in the models were very good and ranged between 0.945–0.989. After gravimetric analyses, the filters were further analysed for their content of elements. Estimates for annual averages at each site for the chemicals were calculated based upon a model described in Braun-Fahrländer et al. (1999) and Röösli et al. (2000a). In the EXPOLIS-study, each participant measured personal exposure levels during 48 hours (study period: autumn 1996– winter 97/98). In addition, pollutant levels were measured in the bedroom, outdoors of the home and at the workplace (Koistinen et al., 1999).

2. Results and discussion

The estimates of the annual averages of the particle levels in BRISKA are shown in Fig. 10a. Within the class of suspended particulate matter, TSP had the largest spatial variation of the concentration, followed by $PM_{2.5}$ and PM_{10}. The difference in the ranking between $PM_{2.5}$ and PM_{10} was not significant. For the elements, largest spatial variation was found for Pb, elemental carbon (EC) and nitrate and least spatial variation for ammonium and sulphate. Secondary pollutants (sulphate, ammonium, organic matter) were more homogeneously distributed. The big coefficient of variation for NO_3^- was due some uncertainties in the model. For the gases (Fig. 10b), the spatial variation was largest for NO, followed by SO_2 and NO_2. Smallest spatial variations were observed

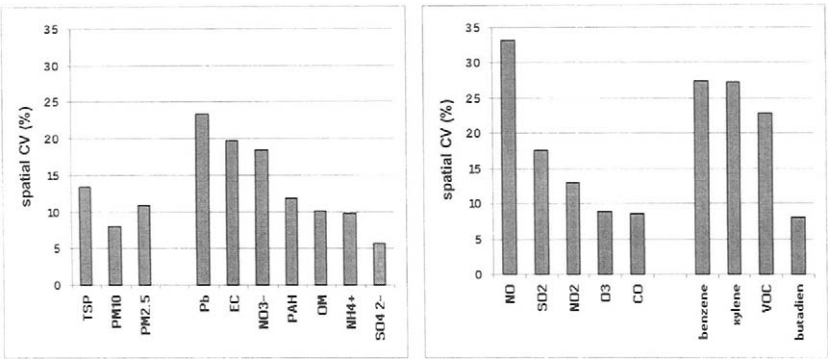

Figure 10. Spatial coefficient of variation (CV: standard deviation divided by average value) for suspended particulate matter (TSP: total suspended particulate matter, PM_{10}, $PM_{2.5}$: particles <10, 2.5 μm) and elements (lead (Pb), elemental carbon (EC), nitrate (NO_3^-), polyaromatic hydrocarbons (PAH), ammonium (NH_4^+), organic matter (OM) and sulphate (SO_4^{2-})) (10a) and for gases (10b). (Data from Braun-Fahlränder et al., 1999.)

for CO and O_3. In the group of the VOCs, the aromatic hydrocarbons, benzene and xylene had largest variations, almost in the range of that of NO. The spatial variance of butadiene was about one third of that of the aromatics.

In conclusion, these results confirmed the spatial heterogeneity of traffic markers of primary emissions (Pb, EC) and the spatial homogeneity of secondary pollutants SO_4^{2-} and O_3. Some other results of the BRISKA-study (Junker et al., 2000) showed that for the ultrafine and fine particle mass and number (concentrations) the spatial non-homogeneity increased with decreasing particle size. This is due the direct emission of the ultrafine particles (e.g. from diesel sources) which undergo coagulation resulting in a more homogeneous distribution over an area than the primary emitted particles.

While the BRISKA-project focussed on health risks of ambient air pollutants, the EXPOLIS study aimed to assess the relationships between personal exposures and stationary measurements (home outdoor, indoor, workplace). In the data analysis from Oglesby et al. (2000a) the relationship between ambient levels of $PM_{2.5}$, sulphur and potassium, lead and calcium was determined. These elements were chosen, as they are distinct markers of certain emission sources. Lead and bromine stem for traffic related particulates, calcium is a soil derived crustal element, sulphur and potassium reflect regional air pollution. Table 11 shows the Spearman rank correlations between the personal measurements and the home outdoor levels of the $PM_{2.5}$ mass and some elements. Data was only available for the city of Basel. The strongest correlations were observed between personal and outdoor sulphur levels. Note that in the calculations smokers and homes with indoor activity such as indoor combustion or grilling were excluded. Weak to moderate correlations were found for the traffic-related elements Pb and Br. No correlation was observed for the ubiquitous element Ca. This analysis showed that the correlation between personal exposures to particles and outdoor measurements differs strongly between different particle parameters. For secondary pollutants (e.g. sulphur), reflecting particles in the accumulation mode and regional air pollution, the correlation

Table 11. Spearman rank correlation for $PM_{2.5}$ parameters between personal and home outdoor levels. (**: $p < 0.001$, *: $p < 0.05$). (Data from Oglesby et al., 2000)

	Spearman rank correlation (r)
mass	0.21
sulphur	0.85**
potassium	0.79**
lead	0.53*
bromine	0.49*
calcium	0.14

is good. For markers of primary traffic emissions (Pb), the correlation becomes weaker. Differences in time activity patterns (e.g. spending time near sources) and the strong spatial inhomogeneity of the ultrafine (traffic) primary particles are two important factors which bias the relationship.

In studies on long-term exposure and effects using the so-called semi-individual study design, where health parameters exist for all individuals and where exposure data is assigned to a group of people (living in a well-defined area) spatially aggregated data are used. Fig. 11 compares aggregated (non-weighted) geometric mean values of indoor and outdoor data from the cities Athens, Basle, Helsinki and Prague. Despite some potential interference of indoor smoking, a large R^2 (= 0.9137) was obtained. The personal $PM_{2.5}$ exposures were measured as night-time (private) and daytime (workday) samples. The personal night-time values correlated strongly with the home indoor values $R^2 = 0.92$ (figure not shown), indicating that the outdoor sample is a good surrogate for personal (private) exposure. In Fig. 12, the personal workday values are plotted against the workplace and the outdoor home values. For Basle, and Helsinki, the geometric means of the workplace levels corresponded with the home outdoor levels. For Milan and Athens, the workplace levels were much higher than the home outdoor levels. For both relationships the coefficients of variation were above 0.9, indicating good agreement. In conclusion, all these analyses based on aggregated city data showed that, on average, personal exposures are quite well reflected by outdoor (or workplace) measurements. A look

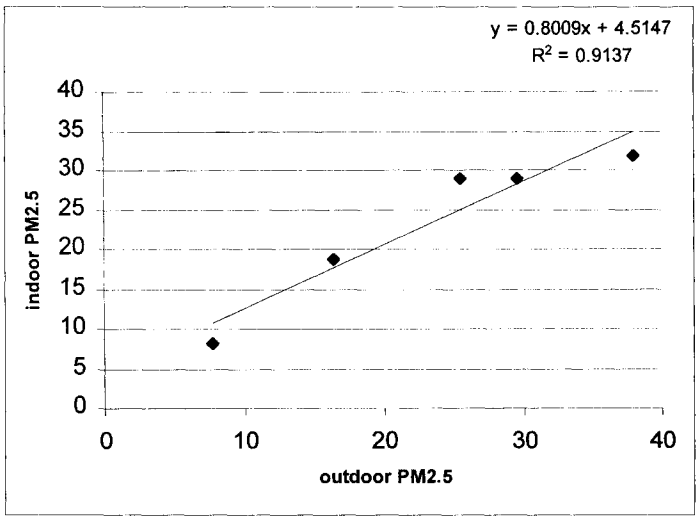

Figure 11. Outdoor vs. indoor $PM_{2.5}$ levels (in $\mu g\, m^{-3}$) for the EXPOLIS sites Athens, Basle, Helsinki, Milan and Prague. (Data from Jantunen, 1999).

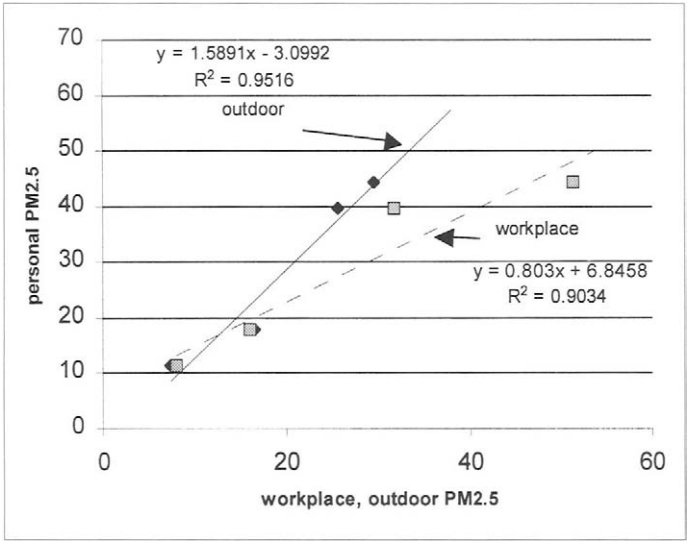

Figure 12. Workplace and outdoor home $PM_{2.5}$ levels vs. personal workday levels (in $\mu g\,m^{-3}$) for the EXPOLIS sites Athens, Basle, Helsinki and Prague. (Data from Jantunen, 1999).

at the absolute average levels of personal exposures and outdoor levels shows that the personal (workday) levels were about 40% higher than the outdoor levels. This finding corresponds to previous findings (Wallace, 1996). This difference also shows that careful attention has to be paid when calculating health effect-estimates based on outdoor levels.

3. Conclusion

In studies using aggregated data of air pollutants, ambient outdoor measurements are good surrogates of personal exposures. The difference in absolute terms between outdoor and personal levels has to be considered in order to reduce bias in the effect-estimate. Moreover, the "aggregate" has to reflect average population-exposure levels. This is not always guaranteed when exposure assignments are based on a single fixed site monitor. For pollutants with large spatial variation such as markers of primary traffic or NO_2 this can be critical. As it is not practical to perform measurements at each home some alternatives have to be evaluated. As an example, Oglesby et al. (2000b) evaluated a questionnaire based on an annoyance score. Annoyance due to traffic correlated well with measured PM_{10} and NO_2 levels when regressing average annoy-

ance levels against measured values (between-area analysis). The validity of the method, however, is restricted.

In studies on long-term exposures, the loss of study persons due to moving is a problem. Moreover, data from ambient monitors are often restricted to short time periods (e.g. a few years). This shows that there is a need for spatially resolved long-term data. In order to solve the first problem, multiple regression models were calculated for the estimation of annual mean PM_{10} values in grids of 1 km^2 over the three countries Switzerland, Austria and France (Filliger et al., 1999). These values can be assigned to the population living in distinct square grids. Such an approach of multiple regression modelling (e.g. for NO_2, PM_{10} and $PM_{2.5}$) for spatially resolved pollution data helps to assign the exposure of people who moved away from the original study site. Furthermore, emission trends can be considered and data can be calculated in a retrospective manner for an estimation of long-term exposures. It is clear that these approaches need strong validations as the static multiple regression model may be restricted to a limited geographical area. Moreover, people are exposed to a mixture of pollutants and the single pollutant approach can be misleading. The exposure-effect relationship will show if the new approach reduces bias.

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