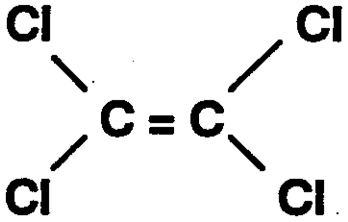
TECHNICAL SUPPORT DOCUMENT

PART A

PROPOSED IDENTIFICATION OF



PERCHLOROETHYLENE

AS A TOXIC AIR CONTAMINANT

AUGUST 1991

State of California
Air Resources Board

ACKNOWLEDGEMENTS

We wish to acknowledge the valuable assistance of the following Air Resources Board staff who contributed to the preparation and review of this document: Steve Brisby, Dora Chang, and Rich Miller.

This report has been reviewed and approved by the staff of the California Air Resources Board. The contents do not necessarily reflect the views and policies of the Air Resources Board, nor does mention of trade names or commercial products constitute endorsement or recommendation for use.

INITIAL STATEMENT OF REASONS FOR RULEMAKING

TECHNICAL SUPPORT DOCUMENT

PROPOSED IDENTIFICATION OF PERCHLOROETHYLENE AS A TOXIC AIR CONTAMINANT

PART A

REPORT TO THE AIR RESOURCES BOARD ON PERCHLOROETHYLENE

PUBLIC EXPOSURE TO, SOURCES, AND EMISSIONS OF PERCHLOROETHYLENE IN CALIFORNIA

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August 1991

PART A

PUBLIC EXPOSURE TO, SOURCES, AND EMISSIONS OF ATMOSPHERIC PERCHLOROETHYLENE IN CALIFORNIA

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I.

INTRODUCTION

According to section 39655 of the California Health and Safety Code, a toxic air contaminant (TAC) is "an air pollutant which may cause or contribute to an increase in mortality or an increase in serious illness, or which may pose a present or potential hazard to human health." This report, Part A of the Technical Support Document, "Proposed Identification of Perchloroethylene as a Toxic Air Contaminant" (prepared by the staff of the Air Resources Board), is an evaluation of the compound's emissions, ambient and indoor concentrations, statewide population exposure, and atmospheric persistence and fate. The Part B report prepared by the staff of the Department of Health Services (DHS) assesses the health effects of perchloroethylene. The Air Resources Board (ARB or "the Board") will consider the Part A and Part B reports, the findings of the Scientific Review Panel (SRP), written comments and public testimony to determine if perchloroethylene should be identified as a TAC.

A. SUMMARY OF CALIFORNIA HEALTH AND SAFETY CODE SECTIONS 39660-39662 (IDENTIFICATION OF TOXIC AIR CONTAMINANTS)

Section 39655 of the California Health and Safety Code requires the use of the following criteria for prioritizing compounds for evaluation as possible toxic air contaminants: 1) risk of harm to public health, 2) amount or potential amount of emissions, 3) manner of usage, 4) persistence in the atmosphere, and 5) ambient concentrations.

Once a compound is selected to enter the TAC identification process, the ARB requests relevant information from the public and a written evaluation of available health effects information (Part B) from the DHS. The DHS staff's evaluation is required to contain an estimate of the threshold exposure level above which the compound causes or contributes to adverse health effects. In the case where no threshold of significant adverse health effects can be determined, the DHS is required to state the range of risk to humans resulting from current or anticipated exposure.

Simultaneous with the preparation of the DHS health evaluation, the ARB staff prepares an exposure assessment (Part A) including information on the compound's usage, emissions or potential emissions, environmental persistence, and available ambient and indoor exposure levels.

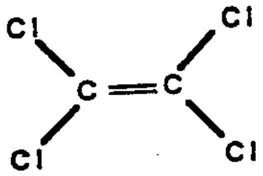
Following a public comment period, the Staff Report/Executive Summary and Parts A, B, and C are formally reviewed by the SRP at a public meeting. Upon reviewing the data, assessments, and conclusions of the report and ascertaining that appropriate scientific methods were used to gather and analyze the data presented, the SRP submits written findings to the ARB (the Board). At a public hearing, the Board decides whether or not the evidence in the document supports the identification of the compound as a toxic air contaminant and, if so, whether there is evidence of a threshold exposure below which adverse effects are not expected to occur. Once a compound is identified as a toxic air contaminant and listed in section 93000 of Title 17 of the California Code of Regulations, the ARB staff prepares a report on the need and appropriate degree of regulation pursuant to sections 39665-39668 of the Health and Safety Code.

B. PERCHLOROETHYLENE AS A CHEMICAL COMPOUND

Perchloroethylene is a chlorinated alkene: a chlorinated aliphatic hydrocarbon compound containing a double bond. Perchloroethylene is known by a variety of synonyms which include: perchloroethene, tetrachloroethene, 1,1,2,2-tetrachloroethene, tetrachloroethylene, PERC, PCE, ethylene tetrachloride, and perclene [Chemical Abstracts Service (CAS) Registry Number 127-18-4]. Perchloroethylene is not known to contribute to either global warming or depletion of the ozone layer. Perchloroethylene has the chemical formula C_2Cl_4 and the chemical structure shown in Figure I-1.

FIGURE I-1

Structure of Perchloroethylene



C. REASONS FOR EVALUATING PERCHLOROETHYELENE AS A POSSIBLE TOXIC AIR CONTAMINANT

Perchloroethylene is under evaluation as a possible TAC for the reasons described below.

1. Risk of Harm to Public Health

The International Agency for Research on Cancer (IARC) lists perchloroethylene as a Group 2B carcinogen (possibly carcinogenic to humans). In 1986, the Environmental Protection Agency's (EPA) Human Health Assessment Group (formerly Carcinogenic Assessment Group) proposed perchloroethylene as a probable carcinogen. At that time, the agency's Scientific Advisory Board (SAB) believed that perchloroethylene should be classified on a continuum between Group B2 (probable carcinogen, sufficient evidence of carcinogenicity in animals but inadequate evidence or no data in humans) and Group C (possible carcinogen, limited evidence of carcinogenicity in animals in the absence of human data). Until the controversy is resolved, the EPA's official posiition is that perchloroethylene is a Group C carcinogen.

2. Emissions in California

Perchloroethylene is widely used in California in a variety of processes and products including: dry cleaning, degreasing, paints and coatings, adhesives, aerosols, specialty chemical production, printing inks, silicones, rug shampoos, and laboratory solvents. In 1987, an estimated 17,000 tons of emissions resulted from these uses as well as from the production, distribution, recycling, and disposal of perchloroethylene.

3. Ambient Concentrations

Ambient concentrations of perchloroethylene ranging from 0.10 to 4.80 parts per billion by volume (ppbv) have been detected in California. The estimated mean annual population-weighted ambient concentration is 0.37 ppbv.

4. Atmospheric Persistence

The half-life of perchloroethylene in the atmosphere is approximately 100 days.

5. Federal Government Hazardous Air Pollutant

The Federal Clean Air Act Amendments of 1990 require the listing of perchloroethylene as a hazardous air pollutant in section 112(b) [section 7412, Title 42 (i.e. tetrachloroethylene), United States Code]. Therefore, pursuant to section 39655 of the California Health and Safety Code, perchloroethylene is required to be identified as a TAC.

In preparing Part A of the Technical Support Document, "Proposed Identification of Perchloroethylene as a Toxic Air Contaminant," the staff reviewed pertinent literature published through April 1989. As cited in the text of the report, the sources after April 1989 were selected pertinent reports and personal communications.

II.

PHYSICAL PROPERTIES OF PERCHLOROETHYLENE

At room temperature, perchloroethylene is a non-flammable, colorless, dense liquid with an ethereal odor. Perchloroethylene is relatively insoluble in water, but is miscible in alcohol, ether, chloroform, and benzene. Some of the other physical properties of perchloroethylene are shown in Table II-1 below.

TABLE II-1

Physical Properties of Perchloroethylene

Property	Value	Reference
Boiling Point (760 mm Hg)	121°C	Merck Index, 1983
Conversion (25°C, 760 mm Hg)	1 ppb = 6.78 ug/m^3	
	1 ug/m^3 = 0.15 ppbv	
Density, liquid (specific gravity) at 15°C	1.6311 gm/cm^3	Merck Index, 1983
at 20°C	1.6230 gm/cm^3	Merck Index, 1983
Molecular weight	165.85	Merck Index, 1983

TABLE II-1, Cont.

Property	Value	Reference
Partition coefficient		
1-octanol:water (25°C)	339-871:1, (409:1)	U.S. EPA, 1985; Barbari and King, 1982
undecane:water (25°C)	2700:1	Barbari and King, 1982
blood:water (99°F)	~ 31:1	U.S. EPA, 1985
Solubility, water (20°C)	150 mg/l	U.S. EPA, 1985
Vapor pressure (20°C)	14 torr	U.S. EPA, 1985
(25°C)	19 torr	U.S. EPA, 1985

References for Chapter II

Barbari, T. A.; C. J. King, 1982. "Equilibrium Distribution Coefficients for Extraction of Chlorinated Hydrocarbons and Aromatics from Water into Undecane," Environmental Science and Technology, 16(9), 624.

Merck Index, 1983. 10th Edition, Merck and Co., Inc., Rahway, New Jersey.

U. S. EPA, 1985. "Health Assessment Document for Tetrachloroethylene - Final Report," EPA-600/8-82/005F, July 1985.

III.

PRODUCTION, USES, AND EMISSIONS OF PERCHLOROETHYLENE

Perchloroethylene is one of the most widely-used chlorinated hydrocarbon solvents in industrial and consumer activities. Table III-1 shows that, based on available data, approximately 17,000 tons of perchloroethylene are released into California's atmosphere annually as a result of production, direct use, distribution, solvent reclamation, and disposal.

A. PRODUCTION OF PERCHLOROETHYLENE

In 1985, the EPA estimated that California's one perchloroethylene production facility had the capacity to produce an estimated 25,000 tons of the solvent annually (SRI International, 1990; U. S. EPA, 1985). During the production process, perchloroethylene was potentially emitted to the atmosphere from the facility's stack and from leaks in pumps, valves, flanges, and storage tanks. Based on independent estimates by the Environmental Protection Agency (EPA) and a private contractor, total annual emissions from this producer ranged from approximately 15 to 65 tons per year (TPY) (CMR, 1986; U. S. EPA, 1985). According to a company spokesman, this facility has ceased perchloroethylene production (Andersen, 1991).

B. USES AND EMISSIONS OF PERCHLOROETHYLENE

1. Uses

The Air Resources Board (ARB) staff conducted a survey of California's halogenated solvent distributors to estimate the amount and manner of

TABLE III-1

Sources and Emissions of Perchloroethylene in California

(All values are approximate)

Source Type		Emissions (Tons/Year)	Inventory Year or Reference
Production	25,000 tons produced	15-65	U.S.EPA, 1985a; CMR, 1986
Direct Uses	Tons Used[a]		
Dry Cleaning	13,000	11,000[b]	1987
Degreasing	3,300	3,000[c]	"
Paints, Coatings	1,300	1,300[d]	"
Adhesives	340	340[d]	"
Miscellaneous	1,600	1,600[e]	"
Distribution	19,000 tons distributed	5[f]	"
Solvent Reclamation	1,900 tons	5-20[g]	1985
Disposal	Unknown amount disposed		
POTWs		50	Chang et al., 1987
Landfills		Insufficient Data	
Groundwater Treatment		Insufficient Data	

Notes for Table III-1 follow on the next page.

Notes for Table III-1, <u>Sources and Emissions of Perchloroethylene in California</u>

a. Based on an ARB survey of California halogenated solvent distributors (ARB, 1989a).
b. Assumed 0.88 pounds of perchloroethylene were emitted for each pound used (Wolf and Myers, 1987).
c. Assumed 0.92 pounds of perchloroethylene were emitted for each pound used (U. S. EPA, 1985).
d. Assumed 100 percent of the perchloroethylene used was emitted.
e. Assumed 100 percent of the perchloroethylene used was emitted. Approximately 640 tons of perchloroethylene-usage in the miscellaneous category could not be identified. Some amounts of perchloroethylene in this category may have been used in dry cleaning, degreasing, paints and coatings, and adhesives.
f. Based on an EPA estimate of perchloroethylene emissions resulting from national distribution in 1984 (U. S. EPA, 1985).
g. Based on estimates by industry representatives that 0.0025 to 0.01 percent of the perchloroethylene received is emitted during reclamation (O'Morrow, 1986; Schneider, 1986a; Schneider, 1986b).

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perchloroethylene-usage in the 1987 inventory year. The survey did not distinguish between domestically-produced and imported perchloroethylene; therefore, data are unavailable on the amount of imported perchloroethylene used in California. In addition, the amount of domestic or imported perchloroethylene shipped directly to users was not included in the estimate.

Based on the staff's survey, an estimated 19,000 tons of perchloroethylene were used in California in the following processes and products: dry cleaning, degreasing, paints and coatings, adhesives, aerosols, specialty chemical production, printing inks, silicones, rug shampoos, and laboratory solvents. The direct uses section of Table III-1 shows that dry cleaning and degreasing operations consumed about 80 percent of the total perchloroethylene used in the state (ARB, 1989a)

In other areas of the United States, perchloroethylene is used as a substrate in the production of certain chlorofluorocarbons (CFCs), for example, CFC-113, CFC-114, CFC-115, and CFC-116 (EPA, 1989). Currently, these particular CFCs are not produced in California (SRI International, 1990).

2. Emissions

Emissions resulting from perchloroethylene production are estimated to be approximately 15 to 65 TPY (see Section III A, Production of Perchloroethylene). Other California source-categories of perchloroethylene emissions shown in Table III-1 are discussed below. Dry cleaning and degreasing operations contribute approximately 80 percent of the estimated 17,000 tons emitted into California's atmosphere from direct use. Emissions also result from the distribution, recycling, and disposal of perchloroethylene. Additional emissions may result from source types that have not been identified or for which data is not available (ARB, 1989a).

a. Emissions from the Direct Use of Perchloroethylene

1.) Dry Cleaners

Although perchloroethylene emissions from individual dry cleaning facilities are comparatively small, the combined releases from approximately 3,000 dry cleaners make this industry a major source in California (ARB, 1989a; BAAQMD, 1990; SCAQMD, 1987). Perchloroethylene is used by coin-operated, commercial, and industrial dry cleaners (U. S. EPA, 1985). According to a 1988 national survey by the industry, 79 percent of retail dry cleaners use perchloroethylene exclusively while another 9 percent use it in addition to another solvent (Fisher, 1990).

Most emissions from dry cleaning operations are from dryers and solvent recovery residues (U. S. EPA, 1985). During the drying cycle portion of the dry cleaning process, perchloroethylene is either vented to the atmosphere or recovered in a carbon adsorber or refrigerated condenser. Carbon adsorbers reduce vent emissions by about 95 percent while refrigerated condensers reduce vent emissions by about 70 percent (U. S. EPA, 1989).

When drying units are equipped with adsorbers and condensers, solvent recovery residues become more significant as a source of perchloroethylene emissions. In solvent recovery, used perchloroethylene is purified by filtration and distillation so that it can be reused. Perchloroethylene waste adsorbs on the filters and still-bottoms and then vaporizes into the atmosphere (Wolf and Myers, 1987). Enclosing the filtration and distillation equipment is expected to reduce emissions from this source.

Additional emissions may result from the disposal of waste, equipment leaks, and the transfer of clothes from washer to dryer (U. S. EPA, 1985). "Dry-to-dry" dry cleaning operations use and emit less perchloroethylene than "transfer" operations per pound of clothes cleaned. Most new dry cleaning establishments are dry-to-dry operations in which clothes are washed and dried in the same unit. Transfer operations are those in which clothes are manually transferred from washer to dryer (Lauman, 1986).

Wolf and Myers (1987) estimated that 0.88 pounds of perchloroethylene were emitted for each pound used in dry cleaning by subtracting the amount of waste generated in 1984 from the total amount of perchloroethylene used that year. For their study, Wolf and Myers considered the perchloroethylene use and waste generation by dry cleaners nationwide. They did not ascertain the percentage of dry cleaners using equipment to reduce emissions. Based on the Wolf and Myers emission factor, the use of approximately 13,000 tons of perchloroethylene by California dry cleaners in 1987 resulted in estimated emissions of about 11,000 tons (ARB, 1989a).

Currently, the overall average perchloroethylene emission factor for California dry cleaners may be lower than the 0.88 factor developed by Wolf and Myers using national data from 1984. In order to control perchloroethylene as an ozone-precursor, about 25 percent of California's air pollution control districts have adopted control measures specifying the installation of emission reduction devices (e.g., carbon adsorbers or refrigerated condensers) at larger dry cleaning facilities. The adoption of more stringent worker permissible exposure levels by the California Occupational Safety and Health Agency (Cal-OSHA) in 1990 may encourage the further use of control devices (Manchester, 1991). The DHS's hazardous waste regulations requiring the storage of filter and still-bottom waste in air-tight containers should simultaneously reduce emissions and increase the amount of perchloroethylene sent for reclamation (Gin, 1991). In addition, two industrial trends should result in declining emissions: the trend toward use of dry-to-dry rather than transfer equipment and the increasing use of soap and water solutions instead of perchloroethylene by large industrial cleaners (Devries, 1986; Lauman, 1986; Wolf, 1986)

2.) Degreasers

In California, the second major source of perchloroethylene emissions is degreasing operations. Degreasing is an integral part of many manufacturing industries including the following: automobile, electronic, furniture, appliance, textile, paper, plastic, and glass. PEI Associates estimate that there are several thousand cold cleaning, open-top vapor, and conveyor type degreasing units in operation in California (PEI, 1986). Many of these degreasing units are expected to use perchloroethylene as the solvent.

In the degreasing process, the part to be cleaned is placed in a degreasing tank or chamber and exposed to a liquid or vaporized solvent. In cold cleaners, dirty parts are manually sprayed clean and are then soaked in a tub. Open-top vapor degreasers clean as hot solvent vapor condenses on colder metal parts. Continuously-loaded conveyor degreasers use cold or vaporized solvent and are usually hooded or enclosed. After cleaning, the parts are either suspended over the tank to drain or placed on an external rack that directs solvent back into the tank (U. S. EPA, 1977; U. S. EPA, 1985).

Most perchloroethylene emissions attributed to degreasing result from solvent vapor escaping the tank by diffusion and convection and from solvent being carried out on cleaned parts. Other emissions result from handling, equipment and storage leaks, and disposal. The amount of perchloroethylene emissions from different degreasing operations varies with equipment and manner of operation. Open-top vapor degreasers are expected to emit more perchloroethylene than other types of degreasing units. Equipment may be added to reduce emissions, for example, freeboard chillers reduce diffusion and convection of solvent vapors and carbon adsorbers recover solvent vapors. Operating practices that reduce emissions include: keeping tanks covered, increasing freeboard area (the distance between the top of the degreaser and the solvent level), removing parts slowly, thoroughly draining parts on racks, and checking for leaks (ARB, 1989b).

The EPA used a materials balance approach to estimate that 0.92 pounds of perchloroethylene were emitted for every pound used in degreasing. In the study, the EPA did not ascertain the percentage of degreasing operations using equipment or procedures to reduce emissions. Based on the EPA estimate, the use of 3,300 tons of perchloroethylene by degreasers in California in 1987 resulted in estimated emissions of about 3,000 tons (ARB, 1989a; U. S. EPA, 1985).

3.) Paints and Coatings

Based on a survey of halogenated solvent distributors, approximately 1,300 tons of perchloroethylene were used by California's manufacturers of paints and architectural coatings in 1987. An estimated 1,300 tons of perchloroethylene were emitted from this source-category by assuming that 100 percent of the used perchloroethylene was released either during the manufacturing process or upon application of the paint or coating. This estimate does not include emissions from the application of paints and coatings manufactured outside of the state (ARB, 1989a).

4.) Adhesives

Based on a survey of halogenated solvent distributors, approximately 340 tons of perchloroethylene were used by California's adhesives manufacturers in 1987. An estimated 340 tons were emitted from this source-category by assuming that 100 percent of the used perchloroethylene was released either during the manufacturing process or upon application of the adhesive. This estimate does not include emissions from the application of adhesives manufactured outside of the state (ARB, 1989a).

5.) Miscellaneous

The ARB conducted a survey of halogenated solvent distributors to characterize perchloroethylene usage in California for the 1987 inventory year. Approximately 960 tons were used in the manufacture of the following products: aerosols (spray paints and cleaners), pharmaceuticals, textiles, printing inks, and dielectric fluid for power transformers. The distributors could not identify the product or process for approximately 640 tons of perchloroethylene distributed in 1987. Some of the 640 tons may have been used in the dry cleaning operations, degreasing operations, paints and coatings, and adhesives previously described (ARB, 1989a; HSIA, 1987). Also, some of the perchloroethylene with no identified use was probably used in the maskant operation of semi-conductor production.

There is insufficient data to estimate perchloroethylene emissions from each source in the miscellaneous category. However, an estimated 1,600 tons were emitted from this category based on the assumption that 100 percent of the perchloroethylene used was released to the atmosphere (ARB, 1989a).

b. Emissions from the Distribution and Recycling of Perchloroethylene

1.) Distribution

Based on a survey of approximately 65 California halogenated solvent distributors, an estimated 19,000 tons of perchloroethylene were sold in the state in 1987. EPA data on estimated emissions from national distribution were used to estimate emissions resulting from California distribution in the following manner:

$$\text{19,000 TPY distributed in California (1987)} \times \frac{\text{55 TPY emitted in U. S. (1984)}}{\text{178,000 TPY distributed in U. S. (1984)}} = \text{Approx. 5 TPY}$$

Most of the perchloroethylene emitted from California distribution facilities is due to vaporization of the solvent from large storage tanks (ARB, 1989a; U. S. EPA, 1985).

2.) Solvent Reclamation

An estimated 1,900 tons of perchloroethylene were sent to approximately 20 solvent reclaimers in California in 1985. This estimate is based on the 9,685 tons of halogenated solvent reported on hazardous waste manifests sent to recyclers and the estimated 20 percent of perchloroethylene contained in the halogenated solvents (CDHS, 1984; Schneider, 1986b). Industry representatives estimate emissions for a volatile solvent such as perchloroethylene to be 0.0025 to 0.01 percent of the amount received. Thus, an estimated 5 to 20 tons of perchloroethylene were emitted in California during 1985 as a result of solvent reclamation (Howle, 1986; O'Morrow, 1986; Schneider, 1986a; Schneider, 1986b).

The majority of emissions from solvent reclamation are from the storage and handling of waste and reclaimed solvents, although distillation condensers are expected to emit some perchloroethylene.

c. Emissions from the Disposal of Perchloroethylene

1.) Publicly-owned Treatment Works (POTWs)

Estimating emissions from POTWs (also known as municipal wastewater treatment facilities) is difficult because there are insufficient data on the amount of perchloroethylene discharged to them. However, limited studies have shown different perchloroethylene concentrations in the influent and effluent of individual POTWs. Chang, et al. (1987) used plant influent and effluent concentrations and flows to estimate POTW emissions. Assuming that no losses other than volatilization from plants occur, Chang, et al. estimate that approximately 50 TPY of perchloroethylene are emitted from California POTWs. Data are not available to estimate statewide emissions from pump stations and sewage lines along the routes of discharge to POTWs.

2.) Landfills

California's approximately 2,200 landfill sites are potential sources of perchloroethylene emissions. In 1987, section 41805.5 of the California Health and Safety Code required the testing of landfills (Landfill Gas Testing Program) for specified compounds including perchloroethylene. The data gathered in the Landfill Gas Testing Program will be used by air pollution control districts to provide a relative ranking of the sites based on the potential for exposure. The data showed perchloroethylene concentrations ranging from the detection limit (see Appendix C) of 10 ppbv to 45,000 ppbv in the internal gas of 241 out of the 340 landfills at which internal gas testing was conducted. In addition, 24-hour average ambient perchloroethylene concentrations ranged from the detection limit (see Appendix C) of 0.2 ppbv to 269 ppbv at 141 out of the 288 landfills tested for ambient concentrations. Perchloroethylene may be present in the ambient air at additional landfills but the three-day ambient testing period of the Landfill Gas Testing Program did not detect it. Since the limited testing conducted was designed for screening purposes only, there are insufficient data to estimate perchloroethylene emissions from landfills statewide (ARB, 1990).

3.) Ground Water Treatment

There is insufficient data to estimate statewide perchloroethylene emissions from the treatment of ground water by air stripping or aeration facilities. The quantity of emissions from different facilities is expected to vary depending on the concentration of perchloroethylene in the ground water, the water flow rate through the treatment process, and the hours of operation.

C. EMISSION TRENDS

The overall average perchloroethylene emissions from dry cleaning facilities are expected to decline as new commercial dry cleaners install dry-to-dry equipment and as industrial cleaners increasingly use water and detergent solutions instead of perchloroethylene (DeVries, 1986; Lauman, 1986; Wolf, 1986).

The use of perchloroethylene instead of polychlorinated biphenyls (PCBs) as a dielectric fluid in transformers is anticipated to increase, however, the resulting emissions are expected to be minimal (HSIA, 1987). A major use of perchloroethylene nationwide is as an intermediate in the production of CFC-113, CFC-114, CFC-115, and CFC-116. Currently, these particular chlorofluorocarbons are not produced in the state. Emissions from this source will depend on whether or not they are produced in California in the future (SRI International, 1990).

There is insufficient data to indicate potential changes in the emissions from perchloroethylene sources other than those mentioned above. However, many uses of perchloroethylene are related to population and the population in California is projected to increase approximately 20 percent from 1984 to 2000 (U.S. Department of Commerce Bureau of Census, 1985). Such an increase in population may result in increased perchloroethylene emissions providing other factors, such as control levels, remain the same.

D. INDOOR SOURCES OF PERCHLOROETHYLENE

Elevated indoor perchloroethylene concentrations may result from both indoor sources of perchloroethylene and from mechanisms by which outdoor perchloroethylene is concentrated indoors. Consumer products and dry-cleaned materials appear to be important indoor sources of perchloroethylene. However, the relative contributions from these two source categories cannot be quantified. Building materials and domestic water are expected to be minor indoor sources. Further research is needed to quantify the relative contributions of indoor sources and outdoor air to indoor perchloroethylene concentrations.

1. Building Materials and Consumer Products

The National Aeronautics and Space Administration (NASA), has been compiling emission data for volatile organic compounds since 1975. The database covers more than 5,000 materials used in the space program. Some of these materials are commercially available and are used in homes and offices. Based on their analysis of this data base, Ozkaynak et al. (1987) reported that perchloroethylene would be emitted from a number of common household products such as adhesives, foam, cosmetics and ink.

Recent emission tests conducted in chambers by different investigators found no perchloroethylene emissions from a variety of building materials such as caulks, adhesives, stains, paints, waxes and furniture polishes (Berglund et al., 1987; Knoppel and Schauenburg, 1987; Tichenor, 1987; Wallace et al., 1987b; Girman et al., 1986 and Molhave, 1982). As mentioned earlier in Section III B, perchloroethylene is used by California manufacturers for the formulation of paints and coatings and adhesives (ARB, 1989a). These products are expected to emit perchloroethylene during the manufacturing process and possibly during later use by the consumer. However, the ARB survey upon which this information is based was not designed to estimate emissions at the consumer level or to identify the locations where emissions occur. Further research is needed to estimate the contribution of these products to: 1.) indoor perchloroethylene emissions, 2.) the amount of perchloroethylene in these products, and 3.) their frequency of use in indoor environments.

In a national survey, the EPA (1987b) selected consumer products containing chlorinated solvents for chemical composition analysis. The samples were brand-name products selected randomly from six U. S. cities and represented 67 categories of household solvent products. The survey found perchloroethylene in products from 18 of the 67 categories. The three categories with the highest percentage of brand-name products containing some amount of perchloroethylene were: brake quieters/cleaners (58 percent), water repellents (25 percent) and fabric finishes (20 percent). Other categories with more than ten percent (11 percent to 17 percent) of perchloroethylene-containing products included: specialized aerosol cleaners, ignition wire driers, suede protectors, spot removers and spray cleaners. The concentration of perchloroethylene in individual products varied greatly. Some of the products contained as much as 90 percent perchloroethylene by weight.

2. Dry-Cleaned Materials and Dry Cleaning-Related Activities

Perchloroethylene is the primary solvent for dry cleaning clothing and fabrics. Freshly dry-cleaned garments probably serve as an emission source of indoor perchloroethylene, when brought home. According to an EPA (1987b) national survey of household solvent usage, the average frequency of household use of dry cleaning services is 0.96 times per month.

In reviewing all of the EPA's Total Exposure Assessment Methodology study results, Wallace and Clayton (1987a) concluded that perchloroethylene levels in air samples and breath samples were elevated for persons who were employed in or who had recently visited a dry cleaning shop. They also concluded that the main source of exposure appears to be wearing and storing dry-cleaned clothes. In following the personal activities of seven individuals, increased exposure of perchloroethylene was associated with visiting dry cleaning shops and laboratories using chemicals, and with using cleaning solvents (Wallace et al., 1987c).

3. Vaporization from Water Sources

Water can serve as a medium to carry pollutants from outdoor to indoor environments. Once in contact with indoor air, volatile and semi-volatile chemicals such as perchloroethylene can leave the water and enter the air. Human activities such as cooking, heating or showering with contaminated water can promote rapid vaporization of perchloroethylene from water. Industrial solvent-contaminated surface or ground water may, therefore, bring outdoor perchloroethylene indoors via the water supply.

Perchloroethylene has not been measured above the detection limit of 0.5 ppb(w/w) (the ratio of the weight of perchloroethylene in ppb to the total weight of the water) in California's surface water. In assessing ground water quality, the California Department of Health Services (CDHS, 1986) reported that only about 7 percent of large public water system wells and 0.6 percent of small public water system wells were contaminated with perchloroethylene. About half of these wells contained water concentrations of perchloroethylene below 2 ug/l [2 ppb(w/w)]. Water from wells with exceptionally high perchloroethylene concentrations are usually blended with water from wells with lower perchloroethylene concentrations to meet the water quality guideline of 4 ug/l [4 ppb(w/w)]. Based on the information supplied by Spath (1987), the concentration of perchloroethylene in most California domestic water supplies is essentially below 1 ug/l [1 ppb(w/w)].

Water may be contaminated with perchloroethylene when it is distributed in cement pipes lined with vinyl-toluene resin. The resin, dissolved in perchloroethylene, is sprayed on the inside of the pipes to form the lining and high levels of perchloroethylene have been found in water distribution systems using these pipes. (Larson et al., 1983). Although vinyl-toluene-lined pipes are used in some water distribution systems in the eastern United States, it is not known if they are used in California.

4. Perchloroethylene Sources Outside the Home that May Contribute to Indoor Concentrations

Homes built on or near landfills containing perchloroethylene or related chlorinated hydrocarbons may accumulate perchloroethylene indoors. The rate of accumulation varies, depending heavily on the soil permeability, source strength, air-exchange rate and structure of the house. Kliest et al. (1987) reported that houses built on contaminated soil had almost four times higher perchloroethylene levels in the crawl-space than houses on non-contaminated soil. The relationship between the concentration of a pollutant in the crawl space and its concentration in the living space is still under investigation.

Perchloroethylene from known emission sources may increase the indoor levels of nearby residential or commercial buildings. Of particular concern are small dry cleaning shops which usually locate in densely populated areas. In an EPA study of self-serve laundries with dry cleaning operations, similar perchloroethylene levels, around 10,000 mg/m^3 (1500 ppbv), were found in a laundry and in an occupied apartment directly above the laundry (Howie and Elfers, 1981).

Perchloroethylene is a registered pesticide in California for controlling wasps and hornets. However, the California Department of Food and Agriculture does not have any information on product types to indicate perchloroethylene use indoors (Formoli, 1987). Perchloroethylene was not detected in an EPA analysis of consumer products used as pesticides (Wallace et al., 1987b).

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IV.

EXPOSURE TO PERCHLOROETHYLENE

A. AMBIENT MONITORING FOR PERCHLOROETHYLENE

The perchloroethylene exposure assessment is based on ambient monitoring data collected at 19 ARB toxic air contaminant monitoring stations from July 1988 through June 1989. Figure IV-1 shows the location of each monitoring station and Table IV-1 shows the months for which data are available at each station and the number of samples per station (ranging from 15 samples at Merced to 23 samples at eight other sites). For this study, a total of 392 24-hour samples were collected in Tedlar bags and then analyzed by gas chromatography with an electron-capture detector. The perchloroethylene sampling and analytical procedures used by the ARB Monitoring and Laboratory Division are described in Appendix A.

During the one-year study period, only one of the 392 24-hour perchloroethylene samples was below the 0.01 parts per billion by volume (ppbv) limit of detection (LOD) (see Appendix B for the method used to determine the LOD). In order to avoid biasing the dataset's sample statistics and subsequent exposure estimates, Gleit's Method (see Appendix C) was used to estimate a replacement value of 0.006 ppbv for this observation below the LOD.

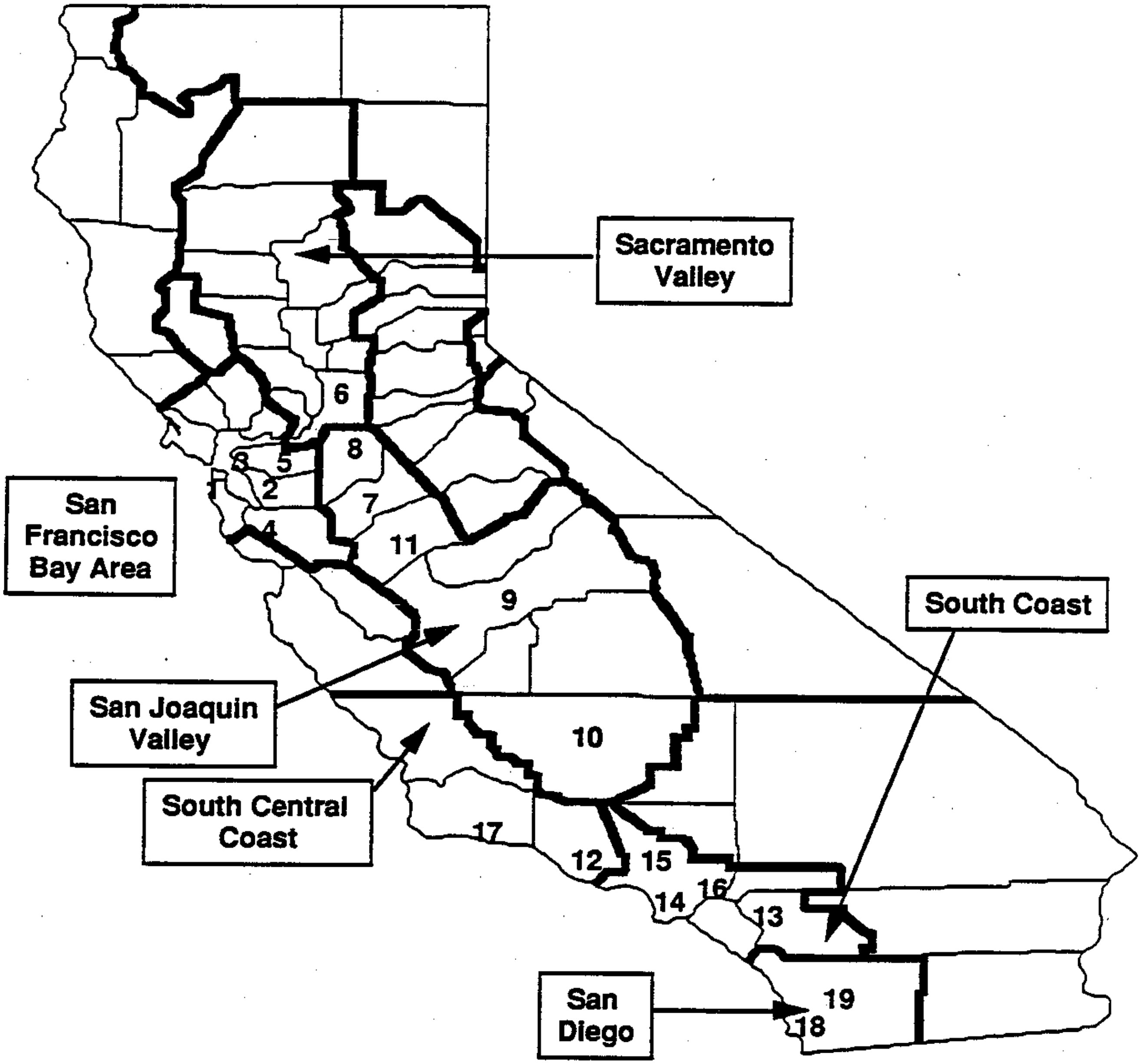
B. AMBIENT CONCENTRATIONS OF PERCHLOROETHYLENE

1. Site-specific

The minimum, maximum, median, and mean 24-hour ambient perchloroethylene concentrations for the 19 monitoring stations from

FIGURE IV-1

ARB Toxics Network Monitoring Sites



1. San Francisco
2. Fremont
3. Richmond
4. San Jose
5. Concord
6. Citrus Heights
7. Modesto
8. Stockton
9. Fresno
10. Bakersfield
11. Merced
12. Simi Valley
13. Rubidoux
14. Long Beach
15. Los Angeles
16. Upland
17. Santa Barbara
18. Chula Vista
19. El Cajon

TABLE IV-1

Months Where At Least One Sample Was Collected And Analyzed For Perchloroethylene[a]: July 1988 through June 1989

Site Location	J	A	S	O	N	D	J	F	M	A	M	J	Samples
South Coast Air Basin													
Long Beach	o	o	o	o	o	o	o	o	o		o	o	23
Los Angeles	o	o	o		o	o	o	o	o	o	o	o	18
Rubidoux	o	o	o	o	o	o	o	o	o		o	o	23
Upland	o	o	o	o	o	o	o	o	o	o	o	o	23
South Central Coast Air Basin													
Santa Barbara		o	o	o	o	o	o	o	o	o	o	o	17
Simi Valley	o			o	o	o	o	o	o	o	o	o	23
San Diego Air Basin													
El Cajon	o	o	o	o	o	o	o	o	o	o	o	o	22
Chula Vista	o	o	o	o	o	o	o	o	o		o	o	21
San Francisco Bay Area Air Basin													
Concord	o	o	o	o	o	o	o	o	o	o	o	o	21
Fremont	o	o	o	o	o	o	o	o	o	o	o	o	23
Richmond	o	o	o	o	o	o	o		o	o	o	o	23
San Francisco	o	o			o	o	o	o	o	o	o	o	16
San Jose		o	o	o	o	o	o	o	o	o	o	o	22
San Joaquin Valley Air Basin													
Bakersfield		o	o	o	o	o	o	o	o	o	o	o	18
Fresno	o	o	o	o	o	o	o	o	o	o	o	o	23
Merced	o	o	o	o	o	o		o	o				15
Modesto	o	o	o	o	o	o	o	o	o	o	o	o	23
Stockton		o	o	o	o	o	o	o	o	o	o	o	19
Sacramento Valley Air Basin													
Citrus Heights	o	o	o	o	o		o	o	o	o	o	o	19

a. A "o" indicates at least one sample was collected during the month.

July 1988 through June 1989 are shown in Table IV-2 and plotted in Figure IV-1. Standard deviations are included in Table IV-2 to indicate the degree of relative variability within the dataset. The 24-hour ambient minimum and maximum perchloroethylene concentrations ranged from below the LOD at San Jose to 4.80 ppbv (32 ug/m^3) at Simi Valley. Mean annual ambient perchloroethylene concentrations were calculated by averaging available monthly means. This was done so that the results from each monitoring site would be equally weighted for each month even though the number of samples per month varied. The mean annual ambient concentrations ranged from 0.10 ppbv (0.7 ug/m^3) at Citrus Heights to 0.70 ppbv (4.7 ug/m^3) at Concord.

The perchloroethylene data were tested for log-normality using the Shapero-Wilk test and found not to be log-normally distributed (Shapero and Wilk, 1965). Because a parametric distribution could not be identified for this set of data, a Bootstrap variability method (which does not depend on an identified distribution, see Appendix E) was used to estimate the relative error associated with mean annual concentrations. Table IV-3 shows the lower bound, mean, and upper bound estimates for each monitoring site using 95 per cent Bootstrap variability bounds. For example, Concord's mean annual ambient concentration of 0.70 ppbv (4.7 ug/m^3) has a lower bound of 0.45 ppbv (3.0 ug/m^3) and an upper bound of 1.04 ppbv (7.0 ug/m^3). The Bootstrap 95 per cent variability bounds should not be construed as absolute lower and upper bounds for perchloroethylene concentrations at Concord. Instead, the Bootstrap method indicates that a mean value between 0.45 ppbv (3.0 ug/m^3) and 1.04 ppbv (7.0 ug/m^3) would be expected from a separate, ARB-independent, perchloroethylene monitoring study conducted at Concord during the same time period (Efron, 1982).

High perchloroethylene concentrations were reported for Chula Vista during the study period: 13 ppbv (88 ug/m^3) on March 6, 1989 and 14 ppbv (95 ug/m^3) on April 4, 1989. With the exception of these two high values in the Spring of 1989, all Chula Vista station measurements from July 1988 through September 1990 are below 1 ppbv (6.78 ug/m^3) (data after June 1990 are preliminary). Analysis of the monitoring location showed that it was located within 50 feet of a print shop. Therefore, the high measurements

Table IV-2

Minimum, Maximum, Median and Mean of Perchloroethylene Samples Collected from July 1988 through June 1989

(ppbv)[a]

Air Basin Site Location	Minimum Conc.	Maximum Conc.	Median Conc.	Mean[b] Conc.	Standard[c] Deviation
South Coast Air Basin					
Long Beach	0.13	1.60	0.31	0.42	0.35
Los Angeles	0.21	1.90	0.51	0.57	0.38
Rubidoux	0.05	0.52	0.23	0.26	0.08
Upland	0.10	1.10	0.40	0.48	0.24
Basin Summary	0.05	1.90	0.35	0.43	0.29
South Central Coast Air Basin					
Santa Barbara	0.06	0.33	0.14	0.16	0.07
Simi Valley	0.07	4.80	0.17	0.39	0.47
Basin Summary	0.06	4.80	0.15	0.28	0.34
San Diego Air Basin					
Chula Vista	0.07	0.69	0.25	0.30	0.17
El Cajon	0.07	1.10	0.34	0.42	0.26
Basin Summary	0.07	1.10	0.27	0.36	0.22
San Francisco Bay Area Air Basin					
Concord	0.07	3.30	0.54	0.70	0.59
Fremont	0.06	0.73	0.26	0.27	0.13
Richmond	0.03	0.41	0.11	0.11	0.06
San Francisco	0.08	0.97	0.17	0.20	0.15
San Jose	<LOD[d]	0.87	0.15	0.23	0.17
Basin Summary	<LOD	3.30	0.15	0.30	0.29
San Joaquin Valley Air Basin					
Bakersfield	0.04	0.18	0.09	0.10	0.03
Fresno	0.05	0.68	0.12	0.18	0.14
Merced	0.06	0.39	0.15	0.19	0.06
Modesto	0.04	0.83	0.09	0.16	0.12
Stockton	0.04	0.26	0.11	0.12	0.05
Basin Summary	0.04	0.83	0.12	0.15	0.09
Sacramento Valley Air Basin					
Citrus Heights	0.03	0.21	0.08	0.10	0.05

---

a. 1 ppbv = 6.78 ug/m^3

b. Basin Means are the mean of the site means.

c. Basin Standard Deviations are pooled values of the standard deviations across sites within a basin.

d. LOD= 0.01 ppbv

FIGURE IV-2

MEAN ANNUAL PERCHLOROETHYLENE CONCENTRATION
PLOTTED USING EXTENDED BOX PLOTS
BASED ON JULY 1988–JUNE 1989 DATA

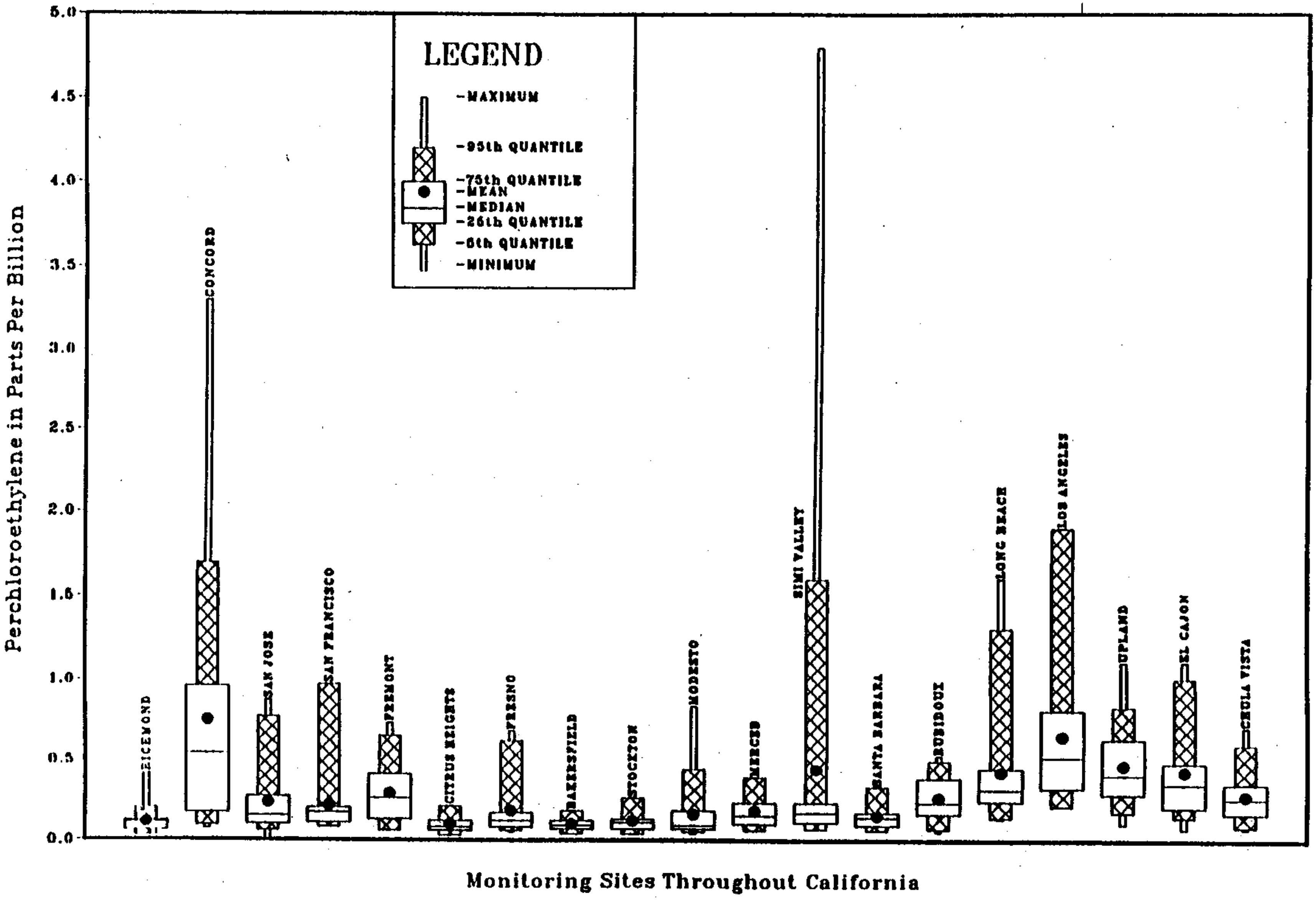


TABLE IV-3

Lower Bound, Mean and Upper Bound Perchloroethylene Concentrations for July 1988 through June 1989[a] (ppbv)[b]

Air Basin Site Location	Lower Bound	Site Mean	Upper Bound
South Coast Air Basin			
Long Beach	0.29	0.42	0.64
Los Angeles	0.40	0.60	0.84
Rubidoux	0.22	0.26	0.31
Upland	0.37	0.48	0.62
South Central Coast Air Basin			
Santa Barbara	0.12	0.16	0.19
Simi Valley	0.20	0.39	0.62
San Diego Air Basin			
Chula Vista	0.22	0.30	0.40
El Cajon	0.30	0.42	0.57
San Francisco Bay Area Air Basin			
Concord	0.45	0.70	1.04
Fremont	0.21	0.27	0.34
Richmond	0.08	0.11	0.14
San Francisco	0.13	0.20	0.30
San Jose[c]	0.15	0.23	0.34
San Joaquin Valley Air Basin			
Bakersfield	0.08	0.10	0.12
Fresno	0.12	0.18	0.27
Merced	0.16	0.19	0.23
Modesto	0.10	0.16	0.22
Stockton	0.09	0.12	0.15
Sacramento Valley Air Basin			
Citrus Heights	0.07	0.10	0.13

a. Upper and lower bounds represent 95 percent Bootstrap variability bounds (Efron, 1982) for each mean annual exposure estimate.

b. 1 ppbv = 6.78 ug/m^3.

c. One value below the LOD was reported for the San Jose site. The single observation was estimated to be .006 ppb. Using zero or the LOD as a replacement value, after rounding to two decimal places, gave the same annual mean exposure estimate for San Jose.

probably represented temporary influences from a nearby source and were not included in the dataset.

2. Basin-wide

Basin-wide mean annual ambient concentrations were calculated by averaging the site-specific means of all the sites within a basin. For the study period, the basin-wide mean annual ambient concentrations shown in Table IV-2 ranged from 0.15 ppbv (1.0 ug/m^3) in the San Joaquin Valley Air Basin to 0.43 ppbv (2.9 ug/m^3) in the South Coast Air Basin. The Sacramento Valley Air Basin was not included in the basin-wide evaluation because it has only one monitoring station.

C. POPULATION EXPOSURE ESTIMATES

The perchloroethylene population exposure estimates were made using 1985 population census data and mean annual ambient perchloroethylene concentrations calculated from 24-hour sample measurements for 19 monitoring stations from July 1988 through June 1989.

Census tract centroids were available for the more populous areas of the South Coast and Bay Area air basins. For these two air basins, exposure was estimated by interpolating mean annual station values to available census tract centroids. For the other air basins, the entire population of each monitored county in the basin was assumed to be exposed to the basin-wide mean concentration.

Table IV-4 shows the approximate population in each basin exposed to estimated mean annual ambient concentrations of perchloroethylene. The average population-weighted exposure for approximately 20 million Californians residing in the combined area monitored by the 19 stations is 0.37 ppbv (2.5 ug/m^3) perchloroethylene. The population-weighted mean annual estimate was approximately 22 percent higher than the overall

TABLE IV-4

Mean Perchloroethylene Exposure Estimates: July 1988 through June 1989

(ppbv)[a]

Air Basin	Estimated Mean	Population
South Coast	0.44[b]	10,092,133
South Central Coast	0.28[c]	925,822
San Diego	0.36[c]	2,135,872
San Francisco Bay Area	0.25[b]	4,394,374
San Joaquin Valley	0.15[c]	1,901,243
Sacramento Valley[d]	0.10[c]	889,806
Overall Population-Weighted Exposure	0.37	20,339,250

a. 1 ppbv = 6.78 ug/m^3.

b. Population-weighted exposure estimate

c. Mean for all sites within the basin

d. Exposure estimates are for Sacramento County residents only.

geographic mean annual concentration of 0.29 ppbv (1.9 ug/m^3) indicating that the highest perchloroethylene concentrations tend to be in areas of high population density.

D. EXPOSURE TO PERCHLOROETHYLENE NEAR EMISSION SOURCES

Emission and meteorological information were used in the Industrial Source Complex Short Term (ISCST) model to predict ambient annual average concentrations in the area immediately surrounding eight South Coast perchloroethylene-emitting facilities. Seven of the modeled facilities were degreasing operations and one was an industrial clothes cleaner. The modeled ambient annual concentrations were evaluated with forecasted 1985 census data to estimate exposure levels for the population residing near the eight facilities. Only the contributions the eight modeled sources made to perchloroethylene exposure were studied. In reality, other emission sources are expected to contribute to the total ambient perchloroethylene exposure for the modeled population.

Two 41-kilometer-square grids with 1 kilometer receptor scaling were used to model the eight facilities. The grid centered on the City of Industry contained five facilities with estimated combined emissions of 350 tons of perchloroethylene per year. Estimated emissions from each of the five individual facilities ranged from 23 to 214 tons per year. A second grid centered on Burbank contained three facilities with estimated combined emissions of 310 tons per year. Estimated emissions from each of the three individual facilities ranged from 41 to 227 tons per year. The modeling results indicated that there was minimal perchloroethylene exposure on the edges of the geographic areas where the grids slightly overlapped.

In the model, meteorological data for the City of Industry were obtained from 1978 Los Angeles Airport records. Meteorological data for Burbank were from 1964 Burbank Airport records. Both 1964 and 1978 were poor years in terms of pollutant dispersion in the South Coast Air Basin.

All of the following exposure estimates are based on the perchloroethylene contributed to ambient air by modeled facilities and do not include exposure to background perchloroethylene. According to the modeling results, the annual average population-weighted exposure to ambient perchloroethylene (above background perchloroethylene) for approximately 2.5 million people near the City of Industry is estimated to be 0.07 ppbv (0.5 ug/m^3). Approximately 2,000 people near the City of Industry are exposed to an estimated maximum annual average ambient (above background) concentration of 6 ppbv (41 ug/m^3). The annual average population-weighted exposure to ambient perchloroethylene (above background) for approximately three million people near Burbank is estimated to be 0.03 ppbv (0.2 ug/m^3) and approximately 600 people are exposed to an estimated maximum annual average ambient (above background) concentration of 3 ppbv (20 ug/m^3).

E. INDOOR AIR EXPOSURE TO PERCHLOROETHYLENE

Section 39660.5(d) of the Health and Safety Code states that "... the state board shall identify the relative contribution to total exposure to the contaminant from indoor concentrations, taking into account both ambient and indoor air environments." This section contains a review of the available literature on perchloroethylene personal exposure and indoor air concentration studies with special emphasis on studies conducted in California. The concentrations are presented in ug/m^3 (as they were originally reported) followed by the equivalent value in ppbv. The 24-hour average personal and indoor air concentrations were calculated using arithmetic means unless otherwise stated.

1. Personal Air Sampling Data

The best data for estimating indoor air exposure for perchloroethylene are from the Total Exposure Assessment Methodology (TEAM) studies conducted by the EPA during 1980-85 (referred to as TEAM 80/84 in this report; Wallace, 1987a; U.S. EPA, 1987a,b) and by the EPA and ARB during 1987 (referred to as TEAM 87 in this report; Pellizzari et al., 1989). The TEAM 80/84 studies provided personal and fixed-site outdoor sampling data whereas TEAM 87 provided personal and fixed-site indoor and outdoor sampling data.

The TEAM 80/84 studies monitored a total of 240 participants in the Los Angeles and Contra Costa areas (Wallace, 1987a; U.S.EPA, 1987b). Each participant carried a personal air sampler and was monitored for two consecutive 12-hour sampling periods. In the Los Angeles area, field studies were conducted in February 1984 and May 1984. In the February study, the 24-hour average personal air concentration of perchloroethylene was 16 ug/m^3 (2.40 ppbv). The personal air concentrations varied from 0.81 to 200 ug/m^3 (0.12 to 30 ppbv) during the 24-hour monitoring period. In the May study, the 24-hour average personal air concentration of perchloroethylene was 15 ug/m^3 (2.25 ppbv). The personal air concentrations ranged from 0.03 to 520 ug/m^3 (0.004 to 78 ppbv) during the 24-hour monitoring period.

The study in the Contra Costa area was conducted in June, 1984, and the 24-hour average personal air concentration was 5.6 ug/m^3 (0.84 ppbv). The personal air concentrations ranged from 0.03 to 200 ug/m^3 (0.004 to 30 ppbv) during the 24-hour monitoring period.

In Table IV-5, the median and maximum concentrations of the overnight Los Angeles and Contra Costa (12-hour) personal air samples are presented along with the median and maximum concentrations of concurrent and collocated outdoor ambient air samples (Pellizzari et al., 1986). The overnight personal sampler data provide a good estimate of residential indoor air exposure since most participants remained in their homes during the sampling period (6:00 PM to 6:00 AM). The data indicate that median and maximum indoor air levels were generally higher than median and maximum outdoor air levels. Overnight perchloroethylene concentrations as high as 96 ug/m^3 (14.1 ppbv) were detected in this study.

The TEAM 80/84 studies also included other geographical areas besides California. For example, studies were conducted during three seasons in New Jersey. The 12-hour weighted average overnight air concentrations for September through November 1981, July through August 1982, and January through February 1983 were 11, 9.0 and 13 ug/m^3 (1.65, 1.35 and 1.95 ppbv), respectively. The corresponding average outdoor air concentrations were

TABLE IV-5

Overnight Indoor and Outdoor Air Levels of Perchloroethylene in California (6:00 pm to 6:00 am) (ppbv)[a]

	Number of Matched Samples	Indoor[b]		Outdoor	
		Median	Maximum	Median	Maximum
Los Angeles (Feb./84)	25	1.34	14.1	1.1	5.1
Los Angeles (May/84)	23	0.26	8.4	0.2	0.72
Contra Costa (June/84)	10	0.32	1.32	0.04	0.84

---

a. Original data reported in ug/m^3; conversion factor: 1 ppbv = 6.78 ug/m^3

b. Overnight personal sampler data

Source: Pellizzari et al., 1986

3.7, 4.0, and 1.9 ug/m^3 (0.56, 0.60, and 0.29 ppbv), respectively (Wallace, 1987a; U.S.EPA, 1987a).

The TEAM 87 study (Pellizzari et al., 1989) was designed as a follow-up study of the TEAM 84 study for California. The same Los Angeles areas studied in 1984 were revisited and some of the original participants were included in the TEAM 87 study. A total of 51 and 43 persons participated in the January, 1987 and June, 1987 field studies, respectively. In the January study, the 24-hour average personal air concentration of perchloroethylene was approximately 12 ug/m^3 (1.80 ppbv). The personal air concentrations ranged from 0.02 to 146 ug/m^3 (0.003 to 22 ppbv) during the 24-hour monitoring period. In the June study, the 24-hour average personal air concentration of perchloroethylene was about 13 ug/m^3 (1.95 ppbv). The personal air concentrations ranged from 0.37 to 475 ug/m^3 (0.06 to 71 ppbv) during the 24-hour monitoring period. These two-season concentrations were very similar to those obtained in the TEAM 84 study for Los Angeles.

2. Fixed-site Air Sampling Data

The TEAM 87 study conducted in January 1987 and June 1987 provided fixed-site monitoring data on indoor air concentrations of perchloroethylene (Pellizzari et al., 1989). Indoor air samples were collected in the kitchens and living rooms of those people participating in the personal sampling program. Outdoor air samples were collected at the same time. January samples were assumed to represent perchloroethylene concentrations in the winter; June samples were assumed to represent concentrations in the summer.

Table IV-6 shows that indoor air concentrations of perchloroethylene were generally higher than outdoor concentrations during both sampling seasons. Table IV-6 also shows that indoor and outdoor air concentrations of perchloroethylene were generally higher during winter than summer and that the average concentrations in kitchens and living rooms were very similar. Only 10 percent of all the samples had concentrations higher than a 90th percentile concentration. The 24-hour average concentrations of perchloroethylene in the kitchen area were 6.72 ug/m^3 (1.01 ppbv) in winter

TABLE IV-6

24-Hour Concentrations of Perchloroethylene in Indoor and Outdoor Microenvironments

(ppbv)[a]

	INDOORS		OUTDOORS[b]
	Kitchen[b]	Living Area[c]	
Winter			
Mean	1.01	0.79	0.66
Median	0.66	0.66	0.53
90th Percentile	1.97	1.45	1.58
Summer			
Mean	0.34	0.41	0.26
Median	0.32	0.38	0.21
90th Percentile	0.61	0.86	0.54

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a. Original data reported in ug/m^3; conversion factor:
1 ppbv = 6.78 ug/m^3

b. Weighted averages of daytime and overnight 12-hour sample values

c. 12-hour daytime value only

Source: Pellizzari et al., 1989

and 2.27 ug/m^3 (0.34 ppbv) in summer. The 24-hour average concentrations at the 90th percentile in the kitchen area were 13.2 ug/m^3 (1.97 ppbv) in winter and 4.08 ug/m^3 (0.61 ppbv) in summer. The 12-hour average concentrations of perchloroethylene in the living area were 5.27 ug/m^3 (0.79 ppbv) in winter and 2.75 ug/m^3 (0.41 ppbv) in summer. The 12-hour average concentrations at the 90th percentile in the living area were 9.65 ug/m^3 (1.45 ppbv) in winter and 5.72 ug/m^3 (0.86 ppbv) in summer. The 24-hour outdoor average concentrations were 4.41 ug/m^3 (0.66 ppbv) in winter and 1.74 ug/m^3 (0.26 ppbv) in summer. The maximum 24-hour indoor concentration measured was 7.9 ppbv (53.4 ug/m^3).

In studies of indoor air quality in ten public-access buildings, Wallace et al. (1987b) reported that perchloroethylene was one of the 24 compounds most frequently found out of a total of over 200 identified organic compounds. The three-day mean concentrations of perchloroethylene in three newly completed buildings ranged from below the detection limit to 7 ug/m^3 (1.05 ppbv) while the three-day mean concentrations for seven old buildings (including a hospital, a school, two homes for the elderly, and several offices) ranged from 1 to 6 ug/m^3 (0.15 to 0.90 ppbv) (Sheldon et al., 1988 a, b).

Data are also available from several European studies. Although such data may not be representative of California indoor concentrations due to differences in consumer products and life styles, the European data nonetheless confirm the general presence of measurable levels of perchloroethylene in indoor environments. In a study of 14 homes and one office building in Italy, De Bortoli et al. (1986) detected indoor perchloroethylene concentrations ranging from 3 to 47 ug/m^3 (0.45 to 7.05 ppbv). Lebret et al. (1986) reported that 30 percent of 300 Dutch homes sampled had indoor air levels of perchloroethylene greater than the detection limit of 2 ug/m^3 (0.30 ppbv). However, the median perchloroethylene concentrations in the homes with different age-groups that Lebret et al. studied were below 2 ug/m^3 (0.30 ppbv). Krause et al. (1987) also reported preliminary results from a 500-home study in Germany. The observed indoor levels of perchloroethylene ranged from less than 1.0

ug/m^3 to 617 ug/m^3 (0.15 to 92.55 ppbv) with an average (geometric mean) concentration of 12 ug/m^3 (1.8 ppbv).

3. Summary of Indoor and Personal Air Exposure

Perchloroethylene is an ubiquitous indoor air pollutant. The indoor air concentrations of perchloroethylene are generally higher than outdoor air concentrations. TEAM studies conducted in California provide the most representative sampling data for assessing indoor air exposures for Californians. Based on the TEAM 87 data, average residential indoor air concentrations range from 2.27 to 6.72 ug/m^3 (0.34 to 1.01 ppbv). Based on personal air sampling data from the TEAM 87 and TEAM 80/84 data, average personal air exposure to perchloroethylene ranges from 5.6 to 16 ug/m^3 (0.84 to 2.40 ppbv).

4. Indoor Air Contribution to Total Exposure

Based upon available data and assuming Californians spend 86 percent of their time indoors (Jenkins et al., 1990), indoor inhalation may be the major route of exposure to perchloroethylene. A comparison of simultaneous indoor and outdoor perchloroethylene concentrations was conducted as part of the TEAM 80/84 study. The results of this comparison (Table IV-5) indicate that indoor perchloroethylene concentrations can be as much as 11 times greater than outdoor concentrations. However, this may not always be the case since indoor concentrations of perchloroethylene are dependent upon variable factors such as the use of dry cleaners and consumer products containing perchloroethylene (see Section III C, Potential Sources of Indoor Perchloroethylene).

F. OTHER ROUTES OF PERCHLOROETHYLENE EXPOSURE

1. Water Ingestion

California's drinking water supply is approximately 60 percent surface water and approximately 40 percent ground water (CDWR, 1987). Perchloroethylene has not been measured above the detection limit of 0.5

ppb(w/w) in the state's surface water. Although perchloroethylene is the most frequently found contaminant in ground water, the compound was detected in only seven percent of the state's large public water system wells. These large public water system wells potentially expose a population of about 461,000 persons to perchloroethylene (CDHS, 1986). Less than 0.6 percent of small public water system wells had detectable perchloroethylene levels (Spath, 1987).

Information on private well contamination is very limited. In limited testing of suspected private wells in Santa Clara County, about eight percent were contaminated with organic chemicals (Hinman et al., 1986). This percentage represents a high estimate since suspected, rather than random wells, were chosen for testing. In addition, the number of persons supplied by private wells is much less than those supplied by public water systems.

Based on available information about perchloroethylene in surface drinking water, public water systems, and private wells, perchloroethylene exposure through drinking water is expected to be minimal.

2. Food Ingestion

Perchloroethylene is not measured routinely in U.S. food products. Using a new technique for volatile organic compound analysis in food, Entz and Hollifield (1982) detected low levels of perchloroethylene in different fish from various U.S. waterways and in a variety of jellies and sauces from a food processor in Pennsylvania. These data do not provide quantitative estimates of perchloroethylene in food.

A more comprehensive analysis of different food groups was conducted in 1975 by British researchers. In general, they reported low perchloroethylene levels with the highest levels (7 ug/kg) in margarine and olive oil (McConnell et al., 1975). Based on these British data, Gilbert et al. (1982) estimated that perchloroethylene exposure in the United States via food ingestion was 1.2 ug/day.

In Europe, total daily intake of perchloroethylene via food consumption was estimated to range from 87.4 to 160 ug. These estimates resulted from market basket surveys in European countries as summarized in a Dutch criteria document (Ministerie van Volkshuisvesting, 1984). These high estimates of perchloroethylene in European food may not be applicable to California since food sources and food consumption patterns differ between Europeans and Californians.

3. Skin Absorption

Chlorinated hydrocarbons may be absorbed through the skin during bathing when a large portion of the body comes in contact with water containing such chemicals (Andelman, 1985). However, there is no single recognized method for calculating such absorbed dose. Because perchloroethylene levels in California water are generally low, the exposure to perchloroethylene through skin absorption is assumed to be negligible.

G. ESTIMATES OF TOTAL EXPOSURE FROM INDOOR AIR AND OTHER ROUTES

Estimates of the presented daily dose of perchloroethylene from different environmental media are provided in Table IV-7. The presented dose represents an amount of a chemical presented to an individual (host) without consideration of any subsequent biological interactions between the host and the chemical. The information below explains some of the factors considered in calculating the daily doses.

1. Indoor Air

TEAM data from the 24-hour air monitoring, including mean and 90th percentile concentrations, in the kitchen area were used to calculate the presented daily dose from residential indoor air exposure. In addition, 24-hour personal air monitoring data were used to estimate the total air exposures. Total air exposures include exposures through residential and non-residential indoor air, plus outdoor air. The estimates for presented

TABLE IV-7

Estimated Doses of Perchloroethylene from Exposure through Different Media

Media	Average Presented Daily Dose (inhaled or ingested)	References
AIR		
Residential Indoor Air	90 ug[a] (90th percentile, 172 ug[b])	Pellizzari et al., 1989
Personal Air Data	246 ug[c] (range, 0.4-10,400 ug)	Pellizzari et al., 1989; U.S. EPA, 1987b
FOOD		
British Data	1.2 ug	Gilbert et al., 1982; McConnell et al., 1975
European Food Market Survey	(87-160 ug)	Ministerie van Volkhuisvesting, 1984
WATER-FOR DRINKING PURPOSES		
Surface Water	Negligible	CDHS, 1986; Spath, 1987
Ground Water Supply Large public water system	0.6 ug	CDHS, 1986; Spath, 1987
Small public water system	Negligible	CDHS, 1986; Spath, 1987

Calculations:

(Assume an average person inhales 20 m^3 of air daily)

a. Let C1= the average (arithmetic mean) of 6.72 and 2.27 ug/m^3; the means of 24-hour kitchen air concentrations from the TEAM 87 winter and summer studies. When C1 = 4.5 ug/m^3, presented daily dose = C1 x 20 m^3 = 90 ug.

b. Let C2= the average (arithmetic mean) of 13.2 and 4.1 ug/m^3, the 90th percentile, 24-hour kitchen air concentrations from the TEAM 87 winter and summer studies. When C2 = 8.6 ug/m^3, presented daily dose = C2 x 20 m^3 = 172 ug.

Notes continued on the following page.

Notes for Table IV-7, Estimated Doses of Perchloroethylene from Exposure through Different Media (continued)

c. Let C2= the average of 16,15,13,12, and 5.6 ug/m^3, the means of 24-hour personal air concentrations from the TEAM 87 and TEAM 80/84 summer and winter studies. Personal air exposures include exposures through residential and non-residential indoor air, plus outdoor air. When C2= 12.32 ug/m^3, presented daily dose = C2 x 20 m^3 = 246 ug.

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daily dose by inhalation were calculated based on the assumption that an average person inhales 20 m^3 of air per day. The calculations and results are presented in Table IV-7.

2. Food

The estimated daily dose of perchloroethylene through food ingestion is highly uncertain since no California and little U.S. data are available. In addition, European data are not consistent and are not considered likely to represent food consumption habits in California. Therefore, the exposure through food ingestion shown in Table IV-7 may be overestimated.

3. Drinking Water

The relative contribution of drinking water to daily exposures of perchloroethylene appears to be minimal. The quality of data used for making the estimates is relatively good. The estimates for presented daily dose by ingestion were calculated based on the assumption that an average person ingests two liters of drinking water per day. The concentration of perchloroethylene in ground water for a large public water system is estimated to be 0.3 ug/l. Both the concentrations of perchloroethylene in surface water and in small public water system wells are considered negligible.

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V.

ATMOSPHERIC PERSISTENCE AND FATE OF PERCHLOROETHYLENE

The atmospheric persistence of a pollutant is its tendency to remain in the atmosphere in its original form. In analyzing human exposure to perchloroethylene (C_2Cl_4), its persistence is important for two reasons: 1) if the removal time is long compared to the time needed to advect (disperse by wind) the pollutant across an air basin, the concentration throughout the basin can be inferred from measurements at specific locations, and 2) if attenuation of concentration in the plume from a source occurs mostly by dispersion of the plume rather than by chemical or physical removal (i.e., if the pollutant is persistent), routine modeling procedures like Gaussian modeling can be used to estimate the local effect of the source. If removal is fast (i.e., if the pollutant is not persistent), much more complicated modeling may be needed to estimate local effects.

A. ATMOSPHERIC PERSISTENCE OF PERCHLOROETHYLENE

There are chemical and physical mechanisms that operate to remove pollutants from the troposphere (the lower part of our atmosphere). These mechanisms include: photolysis (degradation by solar radiation), photo-oxidation (reactions with reactive species found in polluted atmospheres), adsorption on particles that fall out of the air (dry deposition), and wash-out from interaction with fog or rain (wet deposition). Chemical mechanisms appear to be the dominant force responsible for removing perchloroethylene from the atmosphere.

Two commonly used measures of persistence are half-life ($t_{1/2}$) and lifetime (τ). Half-life is defined as the time required for the concentration of a reactant to fall to one-half of its initial value, whereas lifetime is defined as the time it takes for the reactant concentration to fall to 1/*e* of its initial value (where *e* = 2.718), or approximately 37 percent of its original value (Finlayson-Pitts and Pitts, 1986).

1. Chemical Removal Mechanisms

The atmospheric lifetime of perchloroethylene is related to the rate constant for the photo-chemical reactions that occur and the concentration of the reactants involved in the atmospheric reactions. For a second order reaction of perchloroethylene with atmospheric oxidants [e.g., hydroxyl (OH) radical, ozone (O_3), or nitrate (NO_3) radical], the following relationship holds:

$$\text{perchloroethylene} + \text{B} \xrightarrow{k_2} \text{products}, \quad \text{then} \quad \tau = 1/\,(k_2\,[\text{B}])$$

(where k_2 is the second order reaction rate constant, and [B] is the concentration of the atmospheric oxidant).

Of the chlorinated ethenes, perchloroethylene is the least reactive to electrophilic attack. This reduced reactivity is believed to be a consequence of the electron-inductive effect of the four chlorine atoms, which reduce the electron density about the double bond and, by doing so, reduce the reactivity of the double bond (U.S. EPA, 1985). The four chlorine atoms also provide steric protection to the double bond which would also decrease the reactivity of the double bond.

Howard (1976) reports that the effect of the four chlorine atoms may not completely account for the unusually low reactivity of perchloroethylene to electrophilic attack. Halogenated ethenes such as trifluorochloroethene (C_2F_3Cl) and trichlorofluoroethene (C_2FCl_3), and sterically hindered ethenes such as tetramethylethene [$(CH_3)_2C{=}C(CH_3)_2$] do not demonstrate the dramatic decrease in reactivity relative to other ethene derivatives as does perchloroethylene. Howard speculates that the bonding in perchloroethylene may differ from other ethenes. The electrons from the chlorine atoms in this planar symmetrical molecule could be involved in the pi electron system of the double bond, which could have a major effect on the nature of the bonding and the reactivity of the molecule.

There are three principal photo-chemical reactions that can affect the atmospheric persistence of perchloroethylene. These are: 1.) attack during daylight hours by hydroxyl radicals, 2.) attack at night by nitrate radicals, and 3.) attack by ozone (Finlayson-Pitts and Pitts, 1986).

a. Reaction with Hydroxyl Radicals

The principal mechanism for perchloroethylene removal from the atmosphere appears to involve reaction with hydroxyl radicals. The tropospheric lifetime of perchloroethylene as a consequence of this reaction (τ_{OH}) is inversely proportional to the atmospheric concentration of hydroxyl radicals and the reaction rate constant, k^{OH}. The reaction can be expressed as follows:

$$\tau_{OH} = 1/\ k^{OH}\ [OH] \quad \text{or} \quad (k^{OH}\ [OH])^{-1}\ .$$

Atkinson (1986) reviewed the work of several investigators studying the kinetics and mechanics of hydroxyl radical reactions. Based on this work

Atkinson produced a formula for calculating the k^{OH} for perchloroethylene:

$$k^{OH} = 9.64 \times 10^{-12} e^{-(1209)/T}$$

(where T is the absolute temperature in ^{o}K).

Using this formula, Atkinson estimated the rate constant for the reaction of perchloroethylene with hydroxyl radicals to be 1.67×10^{-13} cm^3 $molecule^{-1}$ $second^{-1}$ at 298^{o}K. Using a comparable rate constant of 1.7×10^{-13} cm^3 $molecule^{-1}$ $second^{-1}$ at 300^{o}K, Singh et al. (1981) calculated a lifetime for perchloroethylene in the troposphere of 68 days. This calculation was based on 12 hours per day of sunlight and a 24-hour average hydroxyl radical concentration of 1×10^6 molecules cm^{-3}, which has been reported as a reasonable estimate (Cupitt, 1983). The hydroxyl radical concentration may be somewhat lower during winter months. By using a seasonally averaged hydroxyl radical concentration of 4×10^5 molecules cm^{-3} Atkinson calculated a half-life of about 200 days (atmospheric lifetime of 292 days). Conversely, hydroxyl radical concentrations can be somewhat higher in heavily polluted atmospheres (i.e., higher criteria pollutant concentrations that are involved in hydroxyl radical formation). These results indicated that, depending on atmospheric conditions, the half-life of perchloroethylene, as a result of its reaction with hydroxyl radicals, may range from about one to eight months (atmospheric lifetime may range from slightly greater than two months to almost one year).

More recently, Prinn et al. (1987) estimated the 24-hour (diurnally and annually averaged) global tropospheric hydroxyl radical concentration at 7.7×10^5 molecules cm^{-3}. At the "average" tropospheric temperature of approximately 265^{o}K, $k^{OH} = 1.0 \times 10^{-13} cm^3$ $molecule^{-1}$ $second^{-1}$ and the resulting half-life of perchloroethylene is approximately 100 days (atmospheric lifetime is approximately 150 days).

b. Reactions with Nitrate Radicals and Ozone

The lifetime of perchloroethylene as a result of its reaction with nitrate radicals and ozone can be determined in the same manner as was done above with hydroxyl radicals, $\tau = 1/\ (k_2\ [B])$. Based on a nitrate reaction rate with perchloroethylene of less than 6 x 10^{-17} cm^3 $molecule^{-1}$ sec^{-1} and a 12-hour nighttime nitrate radical concentration of 10 ppt (2.4 x 10^8 molecule cm^{-3}), the calculated half-life of perchloroethylene with respect to reaction with nitrate radicals is greater than three years (atmospheric lifetime is greater than 4 years) (Atkinson, 1989).

Based on an ozone reaction rate with perchloroethylene of less than 2 x 10^{-23} cm^3 $molecule^{-1}$ sec^{-1} (Mathias et al., 1974) and a tropospheric ozone concentration of 1 x 10^{12} molecule cm^{-3} (Cupitt, 1980), the half-life of perchloroethylene as a consequence of its reaction with ozone is greater than 700 years (atmospheric lifetime is greater than 1,000 years) (Atkinson, 1989). Both nitrate radical and ozone chemical reaction removal processes are too long to compete with the hydroxyl radical reaction.

c. Other Reactions

Several chamber studies indicate perchloroethylene is more reactive than expected from calculations of its reactions with hydroxyl radicals (Dimitriades, et al., 1983). This has been studied by researchers interested in perchloroethylene's contribution to ozone/oxidant problems in the urban atmosphere. Dimitriades argues that the smog chamber reactions of perchloroethylene are dominated by chlorine atom substitution rather than hydroxyl radical attachment and that the chlorine atom reactions are the reason for the increased reactivity of perchloroethylene in the smog chambers. Although this reaction occurs under laboratory conditions, Dimitriades contends that this reaction does not occur at a high enough rate in the atmosphere to affect the reactivity of perchloroethylene. Other hydrocarbons present in the atmosphere will react much more rapidly with available chlorine atoms, effectively scavenging the atoms and preventing chlorine atom-initiated photo-oxidation from being a major degradation process. In addition, in real urban atmospheres, other organic gases are present at concentrations several hundred times as high as perchloroethylene. The source of the chlorine atoms in the chamber studies was not elucidated by Dimitriades.

2. Physical Removal Mechanisms

Dana et al. (1985) estimated that the perchloroethylene rain washout ratio (concentration in rain/concentration in air) at 298°K is approximately one. A washout ratio of this magnitude indicates that wet deposition is of negligible importance in the physical removal of perchloroethylene from the air. Data is not available on the rates for other types of physical removal of perchloroethylene from the atmosphere. However, Cupitt (1980), estimated the half-life of ethylene dichloride ($C_2H_2Cl_2$) under conditions of removal by rain washout, dry deposition, and adsorption on aerosols (that fall out) as about 270, 9, and 17 years respectively (atmospheric lifetime is 390 years, 13 years, and 25 years, respectively). Physical removal is dependent on several physical properties of a substance, including polarity (dipole moment), solubility in water, adsorptivity on particles (e.g., on carbon), and vapor pressure. Since perchloroethylene is comparable to ethylene dichloride in all of these properties, perchloroethylene is expected to have similarly long removal times for these removal processes. Therefore, chemical removal mechanisms will be the predominant factors influencing the persistence and fate of perchloroethylene.

B. FATE OF PERCHLOROETHYLENE IN THE ATMOSPHERE

The reaction of perchloroethylene with hydroxyl radicals is predicted to occur as shown below and is illustrated in Figure V-1 (Graedel, 1978).

$Cl_2C{:}CCl_2 + OH \text{ ------> } HOCCl_2CCl_2$

$HOCCl_2CCl_2 + O_2 \text{------> } HOCCl_2CCl_2O_2$

$HOCCl_2CCl_2O_2 + NO \text{ ------> } HOCCl_2CCl_2O + NO_2$

$HOCCl_2CCl_2O \text{ -------> } HOCCl_2 + COCl_2$

$HOCCl_2 + O_2 \text{ ------> } COCl_2 + HO_2$

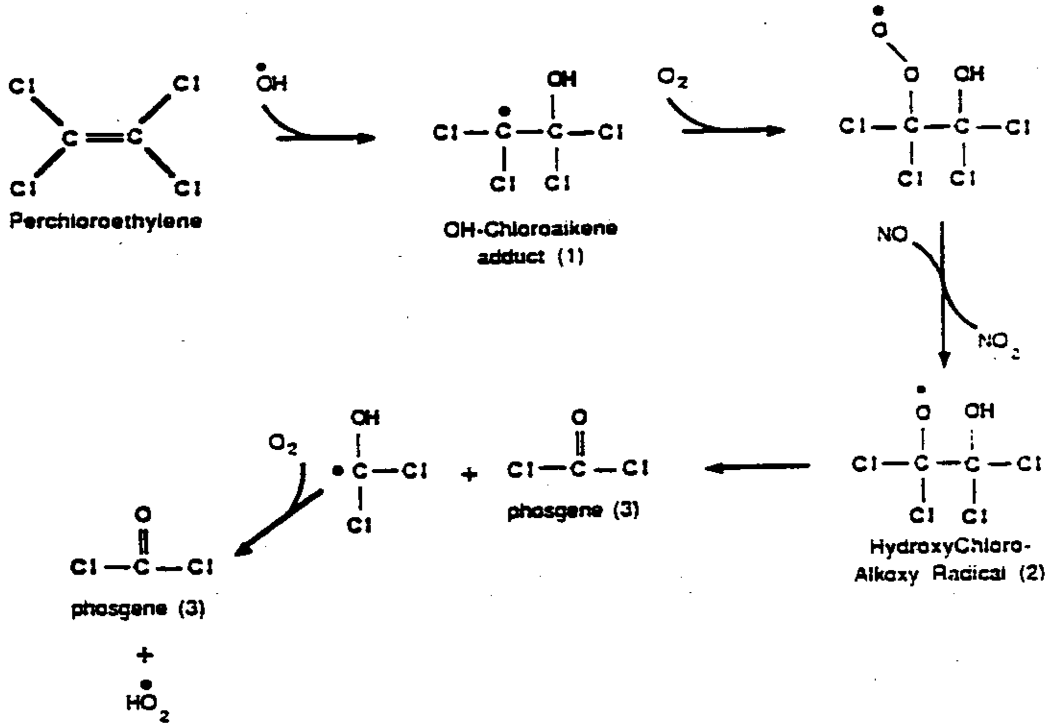
Lillian (1975) predicted that the decomposition of perchloroethylene should lead to the formation of large quantities of phosgene ($COCl_2$) in the atmosphere. Singh (1976) investigated the environmental significance of the production of phosgene from perchloroethylene in the atmosphere. Singh estimated that the photo-oxidation of perchloroethylene could result in phosgene levels in the low ppbv range in urban areas under adverse meteorological conditions. The low reactivity of perchloroethylene determined in smog chamber studies by Dimitriades (1983) suggested that only trace levels of phosgene were expected to be formed (U.S. EPA, 1985). More recently, Tuazon et al. (1988) showed that the reaction of the hydroxyl radical with perchloroethylene generated chlorine atoms and that the reaction pathway forming phosgene (see Figure V-1) occurred approximately 25 percent of the time. Thus, an estimated 0.5 moles of phosgene are formed per mole of perchloroethylene reacting with hydroxyl radicals.

In addition, the photo-oxidation of perchloroethylene is believed to lead to the production of potentially toxic compounds other than phosgene. Singh (1977) predicted that the major environmental impact of chloroethenes in general, and perchloroethylene in particular, is likely to be decomposition into highly toxic species. Chamber studies conducted by Gay (1976) found that the chlorinated photo-oxidation products of

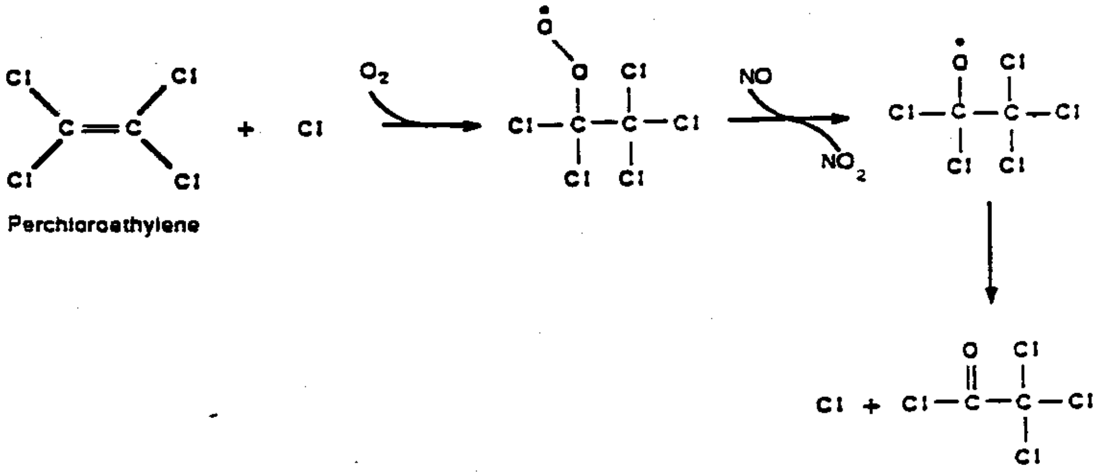
FIGURE V-1

FATE OF PERCHLOROETHYLENE

Reactions with OH Radicals



Reaction Products via Chlorine Substitution



perchloroethylene are hydrogen chloride (HCl) and trichloroacetyl chloride (Cl_3C_2OCl) as well as phosgene. Trichloroacetyl chloride can further decompose to carbon tetrachloride (CCl_4) (Singh, 1977). Singh estimated that as much as eight percent by weight of atmospheric perchloroethylene could eventually be converted into carbon tetrachloride. However, this reaction is believed to occur through a chlorine atom substitution process that is not likely to occur at a substantial rate in the atmosphere as opposed to a smog chamber. This chlorine substitution reaction is illustrated in Figure V-1.

Finally, a possible reaction pathway for the atmospheric oxidation of perchloroethylene to oxalyl chloride ($C_2Cl_2O_2$) has been suggested and is presented below (Howard, 1976):

$$OH + Cl_2C{:}CCl_2 \text{------>} CCl_2CCl_2OH$$

$$CCl_2CCl_2OH + O_2 \text{------>} O_2CCl_2CCl_2OH$$

$$O_2CCl_2CCl_2OH + NO \text{------>} COClCCl_2OH + NO_2 + Cl$$

$$OH + COClCCl_2OH \text{------->} COClCOCl + H_2O + Cl\ .$$

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APPENDIX A

STANDARD METHODS OF ANALYSIS FOR PERCHLOROETHYLENE

METHOD NO. ADDL002

STANDARD OPERATING PROCEDURE FOR THE DETERMINATION OF VOLATILE ORGANICS IN AMBIENT AIR USING TENAX TRAP PRECONCENTRATION GAS CHROMATOGRAPHY AND TANDEM PHOTOIONIZATION/ELECTRON CAPTURE DETECTORS

1.0 SCOPE

This document describes a procedure for the determination of volatile halogenated hydrocarbons and aromatics having a boiling point of less than 120°C. This procedure is based on documents received from the ARB Haagen-Smit Laboratory, El Monte, as well as EPA Method T01.

2.0 SUMMARY OF PROCEDURE

Ambient air is continuously sampled and collected in a Tedlar bag over a 24 hour period and immediately sent to the laboratory for analysis. A sample from the bag is drawn through a sampling valve attached to a Tekmar LSC-2 Tenax Sample Concentrator (see Figure I) with a vacuum pump at 50 cc/min for four minutes (total sample volume: 200 cc). The organic constituents are trapped on Tenax and when the collection is complete, the Tenax is purged with 40 cc of helium to remove any trapped moisture. The sample is then thermally desorbed onto the head of the GC column. The GC column is temperature programmed and component peaks eluting from the column are sequentially detected and quantified, first by a photoionization detector (PID) and then by an electron capture detector (ECD). The components are identified based on retention times. Positive identification or confirmation requires the use of an appropriately configured GC/MS.

3.0 INTERFERENCES/LIMITATIONS

a. Components having similar GC retention times will interfere, causing misidentification and/or faulty quantitation.

b. Because of the very low sample concentrations, extreme care must be taken to insure that the sample is not degraded or contaminated by the Tedlar sampling bag, sampling apparatus, or delayed delivery to the laboratory. Exposure of the Tedlar sampling bag to temperatures greater than 25°C should be minimized.

c. Only components of the sample which can be detected by PID/ECD detectors will be quantified.

4.0 APPARATUS

a. Varian Model 6000 Gas Chromatograph/PID/ECD system equipped with a Varian Vista 402 dual channel data system.

b. Tekmar LSC-2 Sample Concentrator equipped with Tenax trap and sampling valves as shown in Figure 1.

b. Primary Gas Standard (Scott Specialty Gases - Research Triangle Institute Certified Series 2)

Compound	Concentration (ppb)
1,2-Dichloroethane	101
1,1,1-Trichloroethane	98
Trichloroethene	100
1,2-Dibromoethane	102

c. Stock Gas Standard - Scott-Marrin Blend (assayed against primary cylinders)

Compound	Concentration (ppb)
Dichloromethane	4272
Chloroform	528
1,2-Dichloroethane	3104
1,1,1-Trichloroethane	424
Carbon tetrachloride	46
Trichloroethene	336
1,2-Dibromoethane	5
Perchloroethene	43
Vinyl chloride	4736
Benzene	388

c. Matheson Model 8240 Mass Flow Controller accurately calibrated in the 5-100 cc/min range.

d. Laboratory timer, accurate to within 0.1 minutes.

e. Gas tight microliter syringe, 50 ul.

f. GC column - 10' x 2 mm i.d. glass column packed with 1 percent SP-1000 on Carbopack B, 60/80 mesh.

5.0 REAGENTS

a. Primary Gas Standard (Scott Specialty Gases - Research Triangle Institute Certified Series 1)

Compound	Concentration (ppb)
Chloroform	107
Carbon tetrachloride	105
Perchloroethene	106
Vinyl chloride	104
Benzene	107

d. Control Gas Standard - Scott-Marrin Blend (assayed against primary cylinder)

Compound	Concentration (ppm)
Dichloromethane	6
Chloroform	0.2
1,2-Dichloroethane	0.2
1,1,1-Trichloroethane	3.6
Carbon tetrachloride	0.3
Trichloroethene	1.8
1,2-Dibromoethane	2.5
Perchloroethene	1.2
Vinyl chloride	3.3
Benzene	4.8

e. Surrogate Gas Standard (Scott-Marrin Blend)

Compound	Concentration (ppm)
Bromochloromethane	10
1,3-Bromochloropropane	33

6.0 PROCEDURES

a. Sample Trapping

1. The preconcentration system is shown in Figure 1.

2. The high concentration inlet is used for high concentration calibration standards and for other samples with concentrations higher than ambient levels. The sample is introduced through the high concentration inlet and 6 port valve into an appropriate size loop of known volume. The sample then passes through a 10 port valve, mass flow meter, and vacuum pump. Before an analysis, the system is leak checked by blocking the sample inlet port and observing that the mass flow meter reading drops to zero. The high concentration inlet then is connected to a Tedlar sample bag valve and the gas bag valve opened. The loop is then flushed with sample gas for three minutes. After three minutes of flushing, the 6 port valve is reset so that the sample contained in the loop is carried into the trap by the helium purge gas. This continues for three minutes to ensure that all of the contents of the loop are trapped.

3. Ambient samples are introduced from Tedlar bags as described above, except that the sample loop is bypassed and the sample goes directly to the 10 port valve. After flushing the system with sample for three minutes, the 10 port valve is reset so that 200 cc's of sample is trapped (50 cc/min. for four minutes). After sample trapping is complete, the Tenax trap is flushed with 40 cc of helium to remove water vapor and any nonadsorbed reactive gases.

4. In both ambient and high concentration cases, after the sample has been trapped, the Tekmar LSC-2 heats the Tenax trap to 180°C while the trap is swept with the G.C.'s internal carrier gas for four minutes. The contents of the trap are thus desorbed and collected on the head of the G.C. column. The trap is baked out after the end of the desorption cycle. In the bakeout cycle, the trap is flushed with helium purge gas for eight minutes while being held at 225°C in order to prepare the trap for the next cycle. After bakeout the trap is isolated from the system and ready for the next sample.

b. Analysis

1. The concentrated sample is separated under the chromatographic condition detailed below. The resulting chromatogram (see Figure II) is then integrated and quantified by reference to calibration standard gases.

2. Instrument Conditions:

GC: Column: 10' x 2 mm i.d. glass column, packed with 1 percent SP-1000 on Carbopack B 60/80 mesh

Temperatures: Injection: 200°C
Detector: 350°C
Oven: 45°C, hold for four minutes, 5°C/min ramp, to 210°C, hold for eight minutes

Flow Rates: Carrier: He, 20 c.c/min
ECD make up: N_2, 40 c.c/min

Detectors: ECD: Range X 10, Attenuation X 32
PID: Range X 1, Attenuation X 32, 10.2 ev lamp

Conc: Tekmar LSC-2: Purge: 4 minutes
Desorb: 4 minutes at 180°C
Bake: 8 minutes at 225°C

3. All blanks, standards, control samples, and ambient samples are spiked with surrogate compounds by injecting 50 microliters of the surrogate gas standard (5.e.) during sample trapping. The surrogate compounds, chosen such that they simulate the characteristics of the analytes of interest and are unlikely to occur in the environment, are added to insure that systematic errors or equipment failures will be noted and corrected promptly.

4. The first step in a calibration is to analyze a system blank. This is done by trapping and analyzing a 200 cc sample of auxiliary carrier gas. The system blank must be free of interfering peaks. A system blank must also be run after a high concentration sample is analyzed in order to detect any carry-over within the system.

5. A calibration is performed using a 1.25 cc loop of stock standard gas (5.c.). Two hundred cubic centimeters of helium gas is passed through the loop to carry the standard onto the trap. The calibration analysis is made as a normal analysis. The calculated concentration value for each component should be inspected to insure consistency with previous analyses. The stored chromatographic information may then be used to recalculate the response factors for the subsequent analyses. The G.C. data system will not accept updated response factors which are in excess of plus or minus 15 percent of historic data.

6. Following calibration, 200 cc of the control sample (5.d.) is concentrated on the trap and analyzed. The control sample data are plotted on control charts of the normal Shewhart type. Upper and lower warning limits are plus or minus two times the standard deviation. Any analysis which falls outside the upper and lower warning limits is repeated and the laboratory quality control officer is advised. Upper and lower control limits are plus or minus three times the standard deviation. If any analysis falls outside the upper or lower control limit, the method is discontinued until the out of control situation is remedied. The laboratory quality control officer is advised and provided with written documentation of the out of control condition and how it was remedied. All data generated prior to the out of control situation must be reviewed for possible decertification by laboratory management.

7. Multipoint calibrations are conducted monthly. Each multipoint calibration includes a trap blank and three standard concentration levels to bracket the concentration ranges expected in ambient air. If subsequent data indicate that the resulting least squares analyses are consistently acceptable, less frequent multipoint calibrations may be made.

7.0 PERFORMANCE

a. All ambient field samples are analyzed in duplicate. The relative error between analyses must be less than 20 percent. Duplicate analyses having greater than 20 percent relative error must be decertified.

b. The percent recovery of the surrogate is recorded in the instrument laboratory workbook for each analysis. If this value is outside the 80% to 120% range, the sample analysis must be repeated.

8.0 METHOD SENSITIVITY, PRECISION AND ACCURACY

The method sensitivity, precision and accuracy are outlined in Table I. These data were produced with gaseous calibration standards, and using carrier gas as the sample matrix. The relative accuracy of the method, with the exception of dichloromethane, is based on reference to the Research Triangle Institute Certified Gas Standards (NBS traceable). Authoritative reference calibration standards for dichloromethane are under development at NBS but are not yet available. The concentration value of the present standard was assigned by the commercial manufacturer and found to be in good agreement with diluted pure dichloromethane prepared in our laboratory. The absolute accuracy of the method has not been determined by interlaboratory testing.

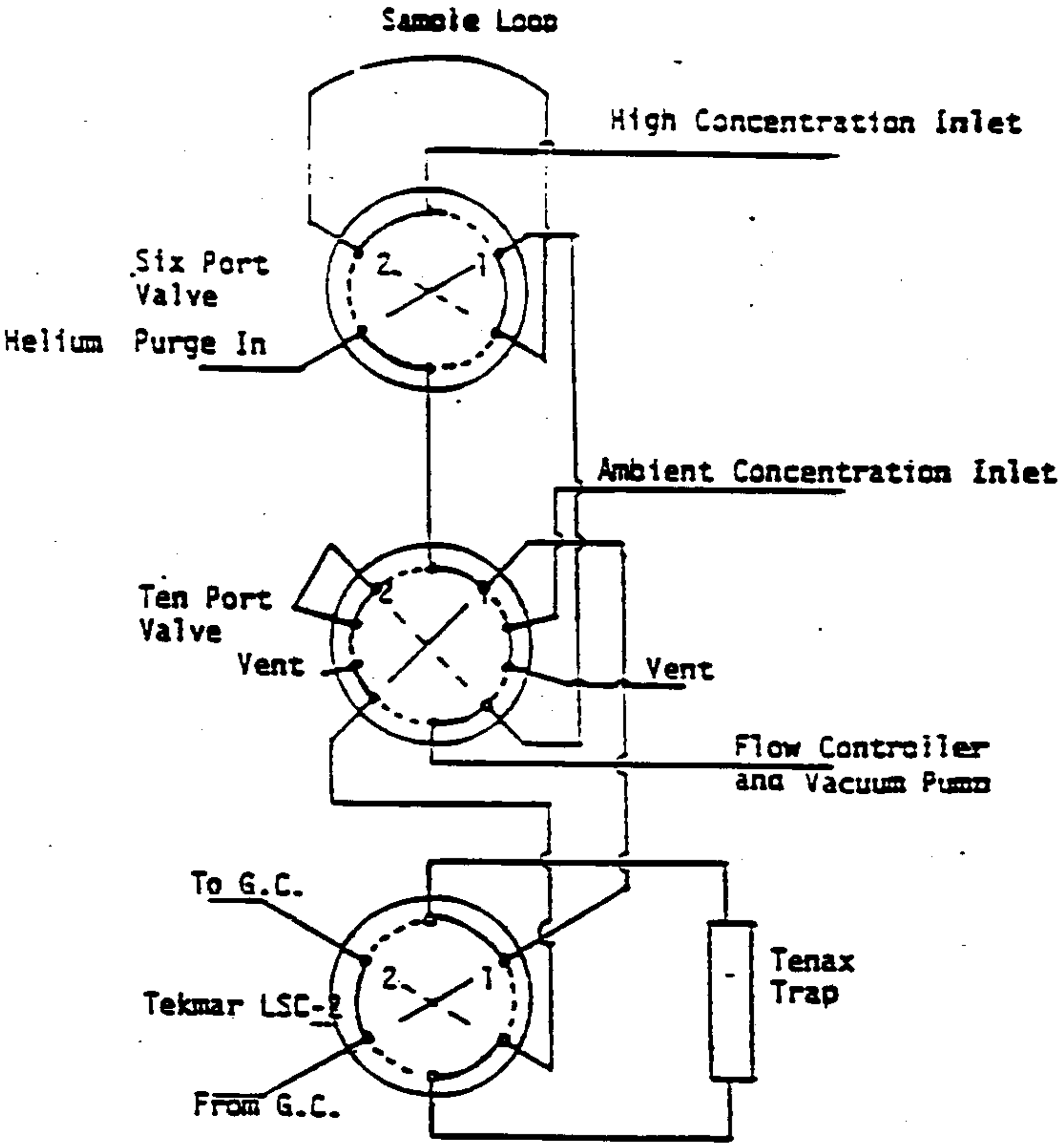
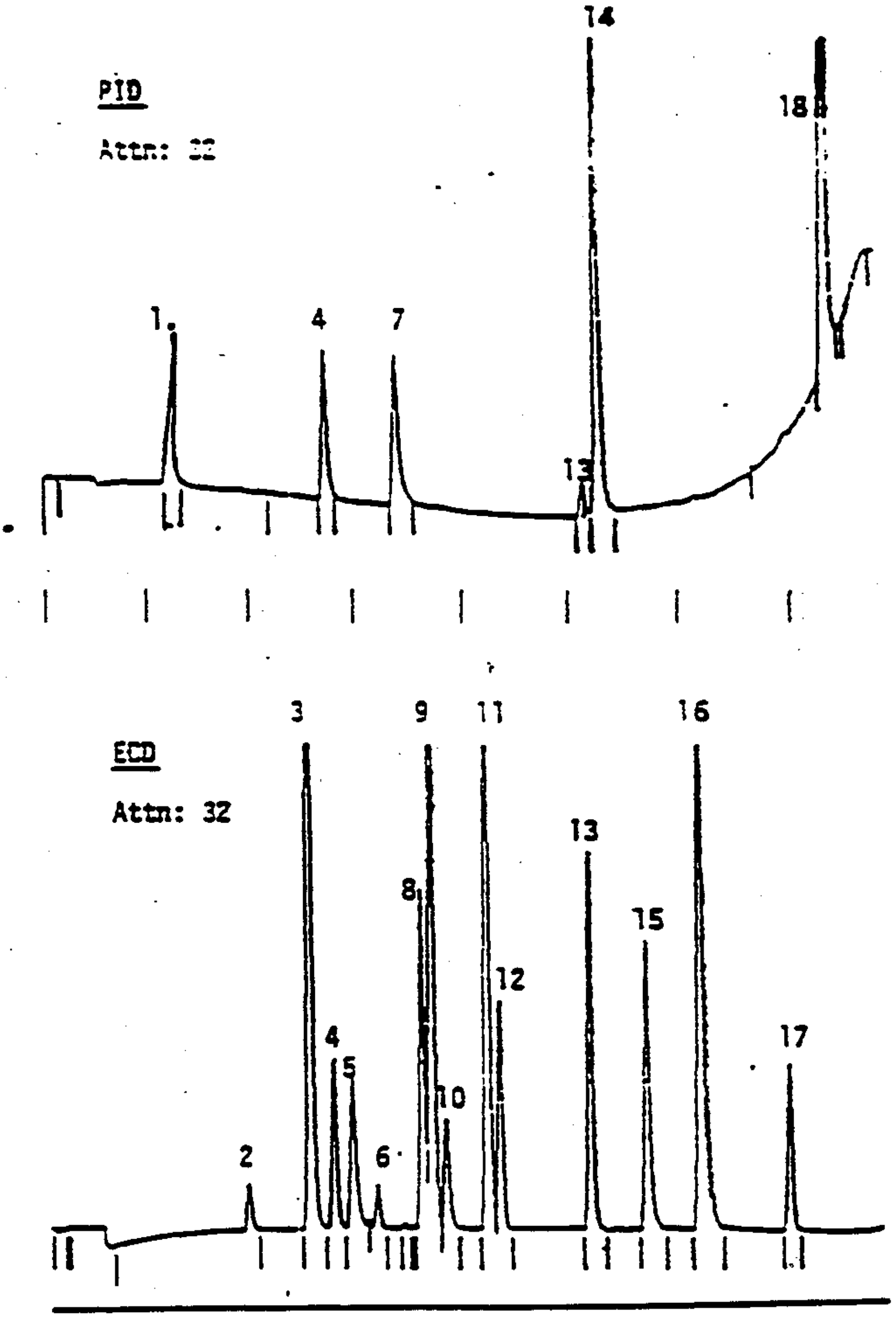


Figure 1. Schematic of concentrator system. Sampling Conditions are: 200 cc volume, purge at 40cc/min, 1 min., desorb at 180 C for 4 min., bake for 8 min. at 225 C.

SYSTEM GUIDE

Operational Step	Valve Position			
	6-Port	10-Port	LSC-2	Purge Gas
Loop Fill	1	1	1	Off
Loop Trap	2	1	1	On
Ambient Trap	1	2	1	Off
Trap Desorb	1	1	2	Off
Trap Bake Out	1	1	1	On



1. Vinyl Chloride
2. Dichloromethane
3. Trichlorofluoromethane
4. 1,1-Dichloroethylene
5. Bromochloromethane
6. 1,1-Dichloroethane
7. t-1,2-Dichloroethylene
8. Chloroform
9. Freon 113
10. 1,2-Dichloroethane
11. 1,1,1-Trichloroethane
12. Carbon Tetrachloride
13. Trichloroethylene
14. Benzene
15. 1,2-Dibromoethane
16. Bromochloropropane
17. Tetrachloroethylene
18. Toluene

Table I

Method Sensitivity and Precision

Compound	Correlation Coefficient	Slope	R.S.D* (Percent)	Detector	LOD ppbv
Vinyl Chloride	0.997	0.946	16	PID	0.8
Dichloromethane	0.999	0.975	5	ECD	0.6
1,1-Dichloroethylene	0.991	0.966	6	ECD	0.05
Chloroform	0.999	0.901	3	ECD	0.02
1,2-Dichloroethane	0.999	1.054	7	ECD	0.1
1,1,1-Trichloroethane	0.999	0.989	9	ECD	0.01
Carbon Tetrachloride	0.999	0.980	6	ECD	0.005
Trichloroethylene	0.999	0.992	6	ECD	0.02
Benzene	0.998	0.950	10	PID	0.5
1,2-Dibromoethane	0.974	1.067	9	ECD	0.005
Tetrachloroethylene	0.994	1.080	10	ECD	0.01

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* R.S.D. - Relative Standard Deviation at 5 x LOD, n = 5

APPENDIX B

THE AIR RESOURCES BOARD MONITORING AND LABORATORY DIVISION'S METHOD FOR DETERMINING THE LIMIT OF DETECTION

Analytical Limits of Detection (LOD) must be calculated. The LOD for each method must be calculated by the following equation (reference):

$$LOD = A + 3S$$

where

A is the least squares intercept calculated from the multipoint data (section 4.1.2).

S is the standard deviation of replicate determinations of the lowest standard. At least 3 replicates are required. The lowest standard must be run at 1 to 5 times the estimated detection limit. If data is not available in the concentration range near the detection limit, S may be estimated by:

$$S = RSD \times A$$

where RSD is the relative standard deviation of the lowest standard analyzed.

The equation as listed above was obtained from the Compendium of Methods for the Determination of Toxic Organics in Ambient Air. Research Triangle Park, North Carolina: U.S. Environmental Protection Agency; 1984 April: Method T)1. Publication No. EPA-600/4-84-041.

Note that the Laboratory Services Section policy is to report all analysis results above the analytical limits of detection. However, data errors may approach ± 100% at levels < 10 x LOD.-

All analysis methods must be written in detail as a Standard Operating Procedure to be used in the laboratory. Any subsequent revisions or improvements are documented. The procedures are reviewed yearly by laboratory management and the Quality Assurance Section to insure that they are being followed properly.

APPENDIX C

GLEIT'S METHOD

DESCRIPTION OF GLEIT'S METHOD

Gleit's method accounts for the concentrations below the LOD by setting them equal to the "below -LOD mean" μ_{BLOD}, the mean of the portion of the normal distribution below the LOD. Setting the unknown concentrations to their average value seems intuitively reasonable, and the simulations reported in Gleit's paper show that his method is more accurate than other commonly used approximations.

The below-LOD mean of a normal distribution of a variable with a limit of detection L is given, in terms of L and the mean μ and the standard deviation σ of the distribution, by equation 1:

$$\mu_{BLOD} = \mu - \sigma * [\, f((L-\mu)/\sigma) \,/\, F((L-\mu)/\sigma) \,] \qquad (1)$$

In equation (1), f and F are, respectively, the probability density function and cumulative distribution function of the standard normal distribution. The "Estimated Concentrations for Samples Below the LOD" reported in Table II-2 are the below-LOD means of the assumed lognormal distributions of the concentrations. These below-LOD means are computed from equation (2) in terms of parameters of the associated normal distribution: the LOD L, the mean concentration from Table II-2, and the estimated standard deviation (which is not tabulated).

$$\exp\,(\mu+0.5^{*}\,\sigma^{2})^{*}\; F((L-\mu-\sigma^{2})/\sigma) \,/\, F(L-\mu/\sigma) \qquad (2)$$

We now describe how Gleit's method estimates the mean and variance of the assumed normal distribution. The mean and variance cannot be estimated by merely substituting into standard formulas, if below-LOD concentrations are to be set to the below-LOD mean. On the one hand, the mean and variance must be known in order to calculate the below-LOD mean from (1); on the other hand, the below-LOD mean must be known if it is to be used in the calculation of the mean and variance. Statistical theory, by asserting that a "best -fitting " mean and variance for the distribution exist, provides a way out of this dilemma. Gleit uses a simple iterative procedure to compute these best-fitting parameters. Since his procedure can be simply described in words, a written description is given, supplemented where necessary by equations written in a notation more convenient than Gleit's.

Starting with initial guesses $\mu(0)$ and $\sigma^2(0)$ for the mean and variance, the procedure repeatedly generates new estimates of the mean and variance by the two-step computation described below until successive estimates of the mean and variance converge sufficiently (The K-th pair of estimates are denoted by $\mu(K)$ and $\sigma^2(K)$.). The two steps are:

(a) The K+1-st below-LOD mean $\mu_{BLOD}(K+1)$ is computed by substituting $\mu(K)$ and $\sigma(K)$ (the square root of $\sigma^2(K)$) into equation (1).

(b) The K+1-st estimate of the mean, $\mu(K+1)$, is computed in the usual way with $\mu_{BLOD}(K+1)$ substituted for the sample values below the LOD. The K+1-st estimate of the variance, $\sigma^2(K+1)$, is also computed in the usual way, with an analogous substitution for sample values below the LOD: the squared deviations from the mean of concentrations below the LOD are set equal to the average squared deviation from the mean of the below-LOD portion of the distribution.

Let the N sample items be $X(1),\ldots,X(N)$, and let p be the number of sample items below the LOD. $\mu(K+1)$ is computed by:

$$\mu(K+1) = (1/N)\ \Sigma\ Y(J), \text{ where } Y(J) = X(J) \text{ if } X(J) \geq L$$
$$\text{and } Y(J) = \mu_{BLOD}(K+1) \text{ otherwise.}$$

$\sigma^2(K+1)$ is computed by:

$$\sigma^2(K+1) = (1/N)\ \Sigma\ D^2(J), \quad \text{where } D^2(J) = (X(J) - \mu(K+1))^2$$
$$\text{if } X(J) \geq L, \text{ and } D^2(J) = \sigma^2_{BLOD}(K+1) \text{ otherwise.}$$

The quantity $\sigma^2_{BLOD}(K+1)$, the average squared deviation of the below-LOD portion of the distribution, is computed from the following equation:

$$\sigma^2_{BLOD}(K+1) = \sigma^2(K)^*[1 - Z(K)^* (f(Z(K)) / F(Z(K)))],$$

$$\text{where } Z(K) = ((L-\mu (K)) / \sigma(K)).$$

Gleit's method nearly always converges in a few steps unless there are only a few distinct values above the detection limit, in which case it may converge very slowly. Gleit's method and closely related methods appear to be the best available estimators of the mean when the sample includes values below the LOD, as is demonstrated by the simulations reported in Gleit's paper.

APPENDIX D

BOOTSTRAP VARIABILITY BOUNDS

Statistical Science
1986, Vol. 1, No. 1, 54–77

Bootstrap Methods for Standard Errors, Confidence Intervals, and Other Measures of Statistical Accuracy

B. Efron and R. Tibshirani

Abstract. This is a review of bootstrap methods, concentrating on basic ideas and applications rather than theoretical considerations. It begins with an exposition of the bootstrap estimate of standard error for one-sample situations. Several examples, some involving quite complicated statistical procedures, are given. The bootstrap is then extended to other measures of statistical accuracy such as bias and prediction error, and to complicated data structures such as time series, censored data, and regression models. Several more examples are presented illustrating these ideas. The last third of the paper deals mainly with bootstrap confidence intervals.

Key words: Bootstrap method, estimated standard errors, approximate confidence intervals, nonparametric methods.

1. INTRODUCTION

A typical problem in applied statistics involves the estimation of an unknown parameter θ. The two main questions asked are (1) what estimator $\hat\theta$ should be used? (2) Having chosen to use a particular $\hat\theta$, how accurate is it as an estimator of θ? The bootstrap is a general methodology for answering the second question. It is a computer-based method, which substitutes considerable amounts of computation in place of theoretical analysis. As we shall see, the bootstrap can routinely answer questions which are far too complicated for traditional statistical analysis. Even for relatively simple problems computer-intensive methods like the bootstrap are an increasingly good data analytic bargain in an era of exponentially declining computational costs.

This paper describes the basis of the bootstrap theory, which is very simple, and gives several examples of its use. Related ideas like the jackknife, the delta method, and Fisher's information bound are also discussed. Most of the proofs and technical details are omitted. These can be found in the references given, particularly Efron (1982a). Some of the discussion here is abridged from Efron and Gong (1983) and also from Efron (1984).

Before beginning the main exposition, we will describe how the bootstrap works in terms of a problem where it is not needed, assessing the accuracy of the sample mean. Suppose that our data consists of a random sample from an unknown probability distribution F on the real line,

$$X_1, X_2, \cdots, X_n \sim F. \tag{1.1}$$

Having observed $X_1 = x_1, X_2 = x_2, \cdots, X_n = x_n$, we compute the sample mean $\bar x = \sum_1^n x_i/n$, and wonder how accurate it is as an estimate of the true mean $\theta = E_F\{X\}$.

If the second central moment of F is $\mu_2(F) \equiv E_F X^2 - (E_F X)^2$, then the standard error $\sigma(F; n, \bar x)$, that is the standard deviation of $\bar x$ for a sample of size n from distribution F, is

$$\sigma(F) = [\mu_2(F)/n]^{1/2}. \tag{1.2}$$

The shortened notation $\sigma(F) \equiv \sigma(F; n, \bar x)$ is allowable because the sample size n and statistic of interest $\bar x$ are known, only F being unknown. The standard error is the traditional measure of $\bar x$'s accuracy. Unfortunately, we cannot actually use (1.2) to assess the accuracy of $\bar x$, since we do not know $\mu_2(F)$, but we can use the *estimated standard error*

$$\hat\sigma = [\hat\mu_2/n]^{1/2}. \tag{1.3}$$

where $\hat\mu_2 = \sum_{i=1}^n (x_i - \bar x)^2/(n-1)$, the unbiased estimate of $\mu_2(F)$.

There is a more obvious way to estimate $\sigma(F)$. Let

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$\hat{F}$ indicate the empirical probability distribution.

(1.4) $\hat{F}$: probability mass $1/n$ on $x_1, x_2, \cdots, x_n$.

Then we can simply replace F by $\hat{F}$ in (1.2), obtaining

$$\hat{\sigma} = \sigma(\hat{F}) = [\mu_2(\hat{F})/n]^{1/2}, \tag{1.5}$$

as the estimated standard error for $\bar{x}$. This is the *bootstrap estimate*. The reason for the name "bootstrap" will be apparent in Section 2, when we evaluate $\sigma(\hat{F})$ for statistics more complicated than $\bar{x}$. Since

$$\hat{\mu}_2 = \mu_2(\hat{F}) = \sum_{i=1}^{n} \frac{(x_i - \bar{x})^2}{n}, \tag{1.6}$$

$\hat{\sigma}$ is not quite the same as $\bar{\sigma}$, but the difference is too small to be important in most applications.

Of course we do not really need an alternative formula to (1.3) in this case. The trouble begins when we want a standard error for estimators more complicated than $\bar{x}$, for example, a median or a correlation or a slope coefficient from a robust regression. In most cases there is no equivalent to formula (1.2), which expresses the standard error $\sigma(F)$ as a simple function of the sampling distribution F. As a result, formulas like (1.3) do not exist for most statistics.

This is where the computer comes in. It turns out that we can always numerically evaluate the bootstrap estimate $\hat{\sigma} = \sigma(\hat{F})$, without knowing a simple expression for $\sigma(F)$. The evaluation of $\hat{\sigma}$ is a straightforward Monte Carlo exercise described in the next section. In a good computing environment, as described in the remarks in Section 2, the bootstrap effectively gives the statistician a simple formula like (1.3) for any statistic, no matter how complicated.

Standard errors are crude but useful measures of statistical accuracy. They are frequently used to give approximate confidence intervals for an unknown parameter θ

$$\theta \in \hat{\theta} \pm \hat{\sigma} z^{(\alpha)}, \tag{1.7}$$

where $z^{(\alpha)}$ is the $100 \cdot \alpha$ percentile point of a standard normal variate, e.g., $z^{(.95)} = 1.645$. Interval (1.7) is sometimes good, and sometimes not so good. Sections 7 and 8 discuss a more sophisticated use of the bootstrap, which gives better approximate confidence intervals than (1.7).

The standard interval (1.7) is based on taking literally the large sample normal approximation $(\hat{\theta} - \theta)/\hat{\sigma} \sim N(0, 1)$. Applied statisticians use a variety of tricks to improve this approximation. For instance if θ is the correlation coefficient and $\hat{\theta}$ the sample correlation, then the transformation $\phi = \tanh^{-1}(\theta)$, $\hat{\phi} = \tanh^{-1}(\hat{\theta})$ greatly improves the normal approximation, at least in those cases where the underlying sampling distribution is bivariate normal. The correct tactic then is to transform, compute the interval (1.7) for ϕ, and transform this interval back to the θ scale.

We will see that bootstrap confidence intervals can automatically incorporate tricks like this, without requiring the data analyst to produce special techniques, like the $\tanh^{-1}$ transformation, for each new situation. An important theme of what follows is the substitution of raw computing power for theoretical analysis. This is not an argument against theory, of course, only against unnecessary theory. Most common statistical methods were developed in the 1920s and 1930s, when computation was slow and expensive. Now that computation is fast and cheap we can hope for and expect changes in statistical methodology. This paper discusses one such potential change, Efron (1979b) discusses several others.

2. THE BOOTSTRAP ESTIMATE OF STANDARD ERROR

This section presents a more careful description of the bootstrap estimate of standard error. For now we will assume that the observed data $\mathbf{y} = (x_1, x_2, \cdots, x_n)$ consists of independent and identically distributed (iid) observations $X_1, X_2, \cdots, X_n \sim_{\text{iid}} F$, as in (1.1). Here F represents an unknown probability distribution on $\mathscr{X}$, the common sample space of the observations. We have a statistic of interest, say $\hat{\theta}(\mathbf{y})$, to which we wish to assign an estimated standard error.

Fig. 1 shows an example. The sample space $\mathscr{X}$ is $\mathbb{R}^{2+}$, the positive quadrant of the plane. We have observed $n = 15$ bivariate data points, each corresponding to an American law school. Each point x_i consists of two summary statistics for the 1973 entering class at law school i

$$x_i = (\text{LSAT}_i, \text{GPA}_i); \tag{2.1}$$

LSAT_i is the class' average score on a nationwide exam called "LSAT"; GPA_i is the class' average undergraduate grades. The observed Pearson correlation

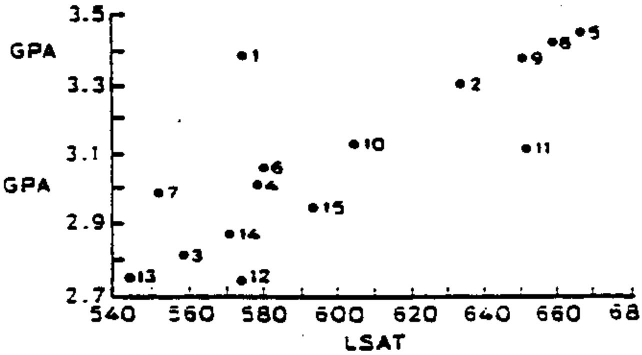

FIG. 1. *The law school data (Efron, 1979b). The data points, beginning with School 1, are* (576, 3.39), (635, 3.30), (558, 2.81), (578, 3.03), (666, 3.44), (580, 3.07), (555, 3.00), (661, 3.43), (651, 3.36), (605, 3.13), (653, 3.12), (575, 2.74), (545, 2.76), (572, 2.88), (594, 2.96).

coefficient for these 15 points is $\hat{\theta} = .776$. We wish to assign a standard error to this estimate.

Let $\sigma(F)$ indicate the standard error of $\hat{\theta}$, as a function of the unknown sampling distribution F,

$$\sigma(F) = [\mathrm{Var}_F\{\hat{\theta}(\mathbf{y})\}]^{1/2}. \tag{2.2}$$

Of course $\sigma(F)$ is also a function of the sample size n and the form of the statistic $\hat{\theta}(\mathbf{y})$, but since both of these are known they need not be indicated in the notation. The bootstrap estimate of standard error is

$$\hat{\sigma} = \sigma(\hat{F}), \tag{2.3}$$

where $\hat{F}$ is the empirical distribution (1.4), putting probability $1/n$ on each observed data point x_i. In the law school example, $\hat{F}$ is the distribution putting mass $1/15$ on each point in Fig. 1, and $\hat{\sigma}$ is the standard deviation of the correlation coefficient for 15 iid points drawn from $\hat{F}$.

In most cases, including that of the correlation coefficient, there is no simple expression for the function $\sigma(F)$ in (2.2). Nevertheless, it is easy to numerically evaluate $\hat{\sigma} = \sigma(\hat{F})$ by means of a Monte Carlo algorithm, which depends on the following notation: $\mathbf{y}^* = (x_1^*, x_2^*, \cdots, x_n^*)$ indicates n independent draws from $\hat{F}$, called a *bootstrap sample*. Because $\hat{F}$ is the empirical distribution of the data, a bootstrap sample turns out to be the same as a random sample of size n drawn *with replacement* from the actual sample $\{x_1, x_2, \cdots, x_n\}$.

The Monte Carlo algorithm proceeds in three steps: (i) using a random number generator, independently draw a large number of bootstrap samples, say $\mathbf{y}^*(1)$, $\mathbf{y}^*(2), \cdots, \mathbf{y}^*(B)$; (ii) for each bootstrap sample $\mathbf{y}^*(b)$, evaluate the statistic of interest, say $\hat{\theta}^*(b) = \hat{\theta}(\mathbf{y}^*(b))$, $b = 1, 2, \cdots, B$; and (iii) calculate the sample standard deviation of the $\hat{\theta}^*(b)$ values

$$\hat{\sigma}_B = \left(\frac{\sum_{b=1}^{B} \{\hat{\theta}^*(b) - \hat{\theta}^*(\cdot)\}^2}{B-1}\right)^{1/2}, \qquad \hat{\theta}^*(\cdot) = \frac{\sum_{b=1}^{B} \hat{\theta}^*(b)}{B}. \tag{2.4}$$

It is easy to see that as $B \to \infty$, $\hat{\sigma}_B$ will approach $\hat{\sigma} = \sigma(\hat{F})$, the bootstrap estimate of standard error. All we are doing is evaluating a standard deviation by Monte Carlo sampling. Later, in Section 9, we will discuss how large B need be taken. For most situations B in the range 50 to 200 is quite adequate. In what follows we will usually ignore the difference between $\hat{\sigma}_B$ and $\hat{\sigma}$, calling both simply "$\hat{\sigma}$."

Why is each bootstrap sample taken with the same sample size n as the original data set? Remember that $\sigma(F)$ is actually $\sigma(F, n, \hat{\theta})$, the standard error for the statistic $\hat{\theta}(\;)$ based on a random sample of size n from the unknown distribution F. The bootstrap estimate $\hat{\sigma}$ is actually $\sigma(F, n, \hat{\theta})$ evaluated at $F = \hat{F}$. The Monte Carlo algorithm will not converge to $\hat{\sigma}$ if the bootstrap sample size differs from the true n. Bickel and Freedman (1981) show how to correct the algorithm to give $\hat{\sigma}$ if in fact the bootstrap sample size is taken different than n, but so far there does not seem to be any practical advantage to be gained in this way.

Fig. 2 shows the histogram of $B = 1000$ bootstrap replications of the correlation coefficient from the law school data. For convenient reference the abscissa is plotted in terms of $\hat{\theta}^* - \hat{\theta} = \hat{\theta}^* - .776$. Formula (2.4) gives $\hat{\sigma} = .127$ as the bootstrap estimate of standard error. This can be compared with the usual normal theory estimate of standard error for $\hat{\theta}$,

$$\hat{\sigma}_{\mathrm{NORM}} = (1 - \hat{\theta}^2)/(n-3)^{1/2} = .115, \tag{2.5}$$

[Johnson and Kotz (1970, p. 229)].

REMARK. The Monte Carlo algorithm leading to $\hat{\sigma}_B$ (2.4) is simple to program. On the Stanford version of the statistical computing language S, Professor Arthur Owen has introduced a single command which bootstraps any statistic in the S catalog. For instance the bootstrap results in Fig. 2 are obtained simply by typing

```
tboot(lawdata, correlation, B = 1000).
```

The execution time is about a factor of B greater than that for the original computation.

There is another way to describe the bootstrap standard error: $\hat{F}$ is the nonparametric maximum likelihood estimate (MLE) of the unknown distribution F (Kiefer and Wolfowitz, 1956). This means that the bootstrap estimate $\hat{\sigma} = \sigma(\hat{F})$ is the nonparametric MLE of $\sigma(F)$, the true standard error.

In fact there is nothing which says that the bootstrap must be carried out nonparametrically. Suppose for instance that in the law school example we believe the true sampling distribution F must be bivariate normal. Then we could estimate F with its *parametric* MLE $\hat{F}_{\mathrm{NORM}}$, the bivariate normal distribution having the same mean vector and covariance matrix as the

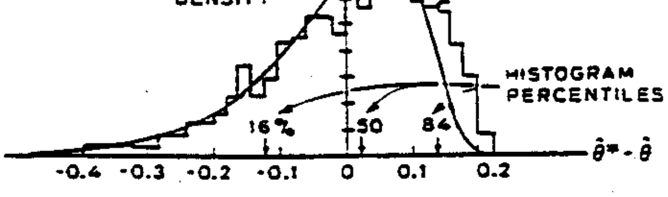

FIG. 2. *Histogram of $B = 1000$ bootstrap replications of $\hat{\theta}^*$ for the law school data. The normal theory density curve has a similar shape, but falls off more quickly at the upper tail.*

data. The bootstrap samples at step (i) of the algorithm could then be drawn from $\hat{F}_{\text{NORM}}$ instead of $\hat{F}$, and steps (ii) and (iii) carried out as before.

The smooth curve in Fig. 2 shows the results of carrying out this "normal theory bootstrap" on the law school data. Actually there is no need to do the bootstrap sampling in this case, because of Fisher's formula for the sampling density of a correlation coefficient in the bivariate normal situation (see Chapter 32 of Johnson and Kotz, 1970). This density can be thought of as the bootstrap distribution for $B = \infty$. Expression (2.5) is a close approximation to $\hat{\sigma}_{\text{NORM}} = \sigma(\hat{F}_{\text{NORM}})$, the parametric bootstrap estimate of standard error.

In considering the merits or demerits of the bootstrap, it is worth remembering that all of the usual formulas for estimating standard errors, like $\hat{\mathscr{I}}^{-1/2}$ where $\hat{\mathscr{I}}$ is the observed Fisher information, are essentially bootstrap estimates carried out in a parametric framework. This point is carefully explained in Section 5 of Efron (1982c). The straightforward nonparametric algorithm (i)–(iii) has the virtues of avoiding all parametric assumptions, all approximations (such as those involved with the Fisher information expression for the standard error of an MLE), and in fact all analytic difficulties of any kind. The data analyst is free to obtain standard errors for enormously complicated estimators, subject only to the constraints of computer time. Sections 3 and 6 discuss some interesting applied problems which are far too complicated for standard analyses.

TABLE 1

A sampling experiment comparing the bootstrap and jackknife estimates of standard error for the 25% trimmed mean, sample size $n = 15$

	F standard normal			F negative exponential		
	Ave	SD	CV	Ave	SD	CV
Bootstrap $\hat{\sigma}$ ($B = 200$)	.287	.071	.25	.242	.078	.32
Jackknife $\hat{\sigma}_J$	.280	.084	.30	.224	.085	.38
True (minimum CV)	.286		(.19)	.232		(.27)

How well does the bootstrap work? Table 1 shows the answer in one situation. Here $\mathscr{X}$ is the real line, $n = 15$, and the statistic $\hat{\theta}$ of interest is the 25% trimmed mean. If the true sampling distribution F is $N(0, 1)$, then the true standard error is $\sigma(F) = .286$. The bootstrap estimate $\hat{\sigma}$ is nearly unbiased, averaging .287 in a large sampling experiment. The standard deviation of the bootstrap estimate $\hat{\sigma}$ is itself .071 in this case, with coefficient of variation $.071/.287 = .25$. (Notice that there are two levels of Monte Carlo involved in Table 1: first drawing the actual samples $\mathbf{y} = (x_1, x_2, \cdots, x_{15})$ from F, and then drawing bootstrap samples $(x_1^*, x_2^*, \cdots, x_{15}^*)$ with $\mathbf{y}$ held fixed. The bootstrap samples evaluate $\hat{\sigma}$ for a fixed value of $\mathbf{y}$. The standard deviation .071 refers to the variability of $\hat{\sigma}$ due to the random choice of $\mathbf{y}$.)

The jackknife, another common method of assigning nonparametric standard errors, is discussed in Section 10. The jackknife estimate $\hat{\sigma}_J$ is also nearly unbiased for $\sigma(F)$, but has higher coefficient of variation (CV). The minimum possible CV for a scale-invariant estimate of $\sigma(F)$, assuming full knowledge of the parametric model, is shown in brackets. The nonparametric bootstrap is seen to be moderately efficient in both cases considered in Table 1.

Table 2 returns to the case of $\hat{\theta}$ the correlation coefficient. Instead of real data we have a sampling experiment in which the true F is bivariate normal, true correlation $\theta = .50$, sample size $n = 14$. Table 2 is abstracted from a larger table in Efron (1981b), in

TABLE 2

Estimates of standard error for the correlation coefficient $\hat{\theta}$ and for $\hat{\phi} = \tanh^{-1}\hat{\theta}$; sample size $n = 14$, distribution F bivariate normal with true correlation $\rho = .5$ (from a larger table in Efron, 1981b)

	Summary statistics for 200 trials							
	Standard error estimates for $\hat{\theta}$				Standard error estimates for $\hat{\phi}$			
	Ave	SD	CV	$\sqrt{\text{MSE}}$	Ave	SD	CV	$\sqrt{\text{MSE}}$
1. Bootstrap $B = 128$	.206	.066	.32	.067	.301	.065	.22	.065
2. Bootstrap $B = 512$	.206	.063	.31	.064	.301	.062	.21	.062
3. Normal smoothed bootstrap $B = 128$	.200	.060	.30	.063	.296	.041	.14	.041
4. Uniform smoothed bootstrap $B = 128$	.205	.061	.30	.062	.298	.058	.19	.058
5. Uniform smoothed bootstrap $B = 512$	.205	.059	.29	.060	.296	.052	.18	.052
6. Jackknife	.223	.085	.38	.085	.314	.090	.29	.091
7. Delta method (Infinitesimal jackknife)	.175	.058	.33	.072	.244	.052	.21	.076
8. Normal theory	.217	.056	.26	.056	.302	0	0	.003
True standard error	.218				.299			

which some of the methods for estimating a standard error required the sample size to be even.

The left side of Table 2 refers to $\hat{\theta}$, while the right side refers to $\hat{\phi} = \tanh^{-1}(\hat{\theta}) = .5 \log(1 + \hat{\theta})/(1 - \hat{\theta})$. For each estimator of standard error, the root mean squared error of estimation $[E(\hat{\sigma} - \sigma)^2]^{1/2}$ is given in the column headed $\sqrt{\text{MSE}}$.

The bootstrap was run with $B = 128$ and also with $B = 512$, the latter value yielding only slightly better estimates in accordance with the results of Section 9. Further increasing B would be pointless. It can be shown that $B = \infty$ gives $\sqrt{\text{MSE}} = .063$ for $\hat{\theta}$, only .001 less than $B = 512$. The normal theory estimate (2.5), which we know to be ideal for this sampling experiment, has $\sqrt{\text{MSE}} = .056$.

We can compromise between the totally nonparametric bootstrap estimate $\hat{\sigma}$ and the totally parametric bootstrap estimate $\hat{\sigma}_{\text{NORM}}$. This is done in lines 3, 4, and 5 of Table 2. Let $\hat{\Sigma} = \sum_{i=1}^{n} (x_i - \bar{x})(x_i - \bar{x})'/n$ be the sample covariance matrix of the observed data. The *normal smoothed bootstrap* draws the bootstrap sample from $\hat{F} \oplus N_2(0, .25\hat{\Sigma})$, $\oplus$ indicating convolution. This amounts to estimating F by an equal mixture of the n distributions $N_2(x_i, .25\hat{\Sigma})$, that is by a normal window estimate. Each point x_i^* in a smoothed bootstrap sample is the sum of a randomly selected original data point x_j, plus an independent bivariate normal point $z_j \sim N_2(0, .25\hat{\Sigma})$. Smoothing makes little difference on the left side of the table, but is spectacularly effective in the $\hat{\phi}$ case. The latter result is suspect since the true sampling distribution is bivariate normal, and the function $\hat{\phi} = \tanh^{-1}\hat{\theta}$ is specifically chosen to have nearly constant standard error in the bivariate normal family. The *uniform smoothed bootstrap* samples from $\hat{F} \oplus \mathfrak{U}(0, .25\hat{\Sigma})$, where $\mathfrak{U}(0, .25\hat{\Sigma})$ is the uniform distribution on a rhombus selected so $\mathfrak{U}$ has mean vector 0 and covariance matrix $.25\hat{\Sigma}$. It yields moderate reductions in $\sqrt{\text{MSE}}$ for both sides of the table.

Line 6 of Table 2 refers to the *delta method*, which is the most common method of assigning nonparametric standard error. Surprisingly enough, it is badly biased downward on both sides of the table. The delta method, also known as the method of statistical differentials, the Taylor series method, and the infinitesimal jackknife, is discussed in Section 10.

3. EXAMPLES

Example 1. Cox's Proportional Hazards Model

In this section we apply bootstrap standard error estimation to some complicated statistics.

The data for this example come from a study of leukemia remission times in mice, taken from Cox (1972). They consist of measurements of remission time (y) in weeks for two groups, treatment ($x = 0$) and control ($x = 1$), and a 0–1 variable (δ_i) indicating whether or not the remission time is censored (0) or complete (1). There are 21 mice in each group.

The standard regression model for censored data is Cox's proportional hazards model (Cox, 1972). It assumes that the hazard function $h(t \mid x)$, the probability of going into remission in next instant given no remission up to time t for a mouse with covariate x, is of the form

$$h(t \mid x) = h_0(t)e^{\beta x}. \tag{3.1}$$

Here $h_0(t)$ is an arbitrary unspecified function. Since x here is a group indicator, this means simply that the hazard for the control group is e^{β} times the hazard for the treatment group. The regression parameter β is estimated independently of $h_0(t)$ through maximization of the so called "partial likelihood"

$$\text{PL} = \prod_{i \in D} \frac{e^{\beta x_i}}{\sum_{j \in R_i} e^{\beta x_j}}, \tag{3.2}$$

where D is the set of indices of the failure times and R_i is the set of indices of those at risk at time y_i. This maximization requires an iterative computer search.

The estimate $\hat{\beta}$ for these data turns out to be 1.51. Taken literally, this says that the hazard rate is $e^{1.51} = 4.33$ times higher in the control group than in the treatment group, so the treatment is very effective. What is the standard error of $\hat{\beta}$? The usual asymptotic maximum likelihood theory, one over the square root of the observed Fisher information, gives an estimate of .41. Despite the complicated nature of the estimation procedure, we can also estimate the standard error using the bootstrap. We sample with replacement from the triples $\{(y_1, x_1, \delta_1), \cdots, (y_{42}, x_{42}, \delta_{42})\}$. For each bootstrap sample $\{(y_1^*, x_1^*, \delta_1^*), \cdots, (y_{42}^*, x_{42}^*, \delta_{42}^*)\}$ we form the partial likelihood and numerically maximize it to produce the bootstrap estimate $\hat{\beta}^*$. A histogram of 1000 bootstrap values is shown in Fig. 3.

The bootstrap estimate of the standard error of $\hat{\beta}$ based on these 1000 numbers is .42. Although the bootstrap and standard estimates agree, it is interesting to note that the bootstrap distribution is skewed to the right. This leads us to ask: is there other information that we can extract from the bootstrap distribution other than a standard error estimate? The answer is yes—in particular, the bootstrap distribution can be used to form a confidence interval for β, as we will see in Section 9. The shape of the bootstrap distributiion will help determine the shape of the confidence interval.

In this example our resampling unit was the triple (y_i, x_i, δ_i), and we ignored the unique elements of the problem, i.e., the censoring, and the particular model being used. In fact, there are other ways to bootstrap

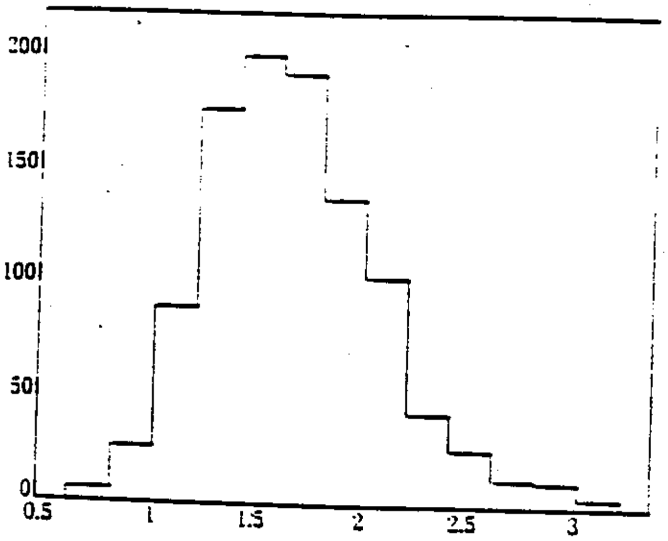

FIG. 3. *Histogram of 1000 bootstrap replications for the mouse leukemia data.*

this problem. We will see this when we discuss bootstrapping censored data in Section 5.

Example 2: Linear and Projection Pursuit Regression

We illustrate an application of the bootstrap to standard linear least squares regression as well as to a nonparametric regression technique.

Consider the standard regression setup. We have n observations on a response Y and covariates $(X_1, X_2, \cdots, X_p)$. Denote the ith observed vector of covariates by $x_i = (x_{i1}, x_{i2}, \cdots, x_{ip})'$. The usual linear regression model assumes

$$E(Y_i) = \alpha + \sum_{j=1}^{p} \beta_j x_{ij}. \tag{3.3}$$

Friedman and Stuetzle (1981) introduced a more general model, the *projection pursuit* regression model

$$E(Y_i) = \sum_{j=1}^{m} s_j(a_j \cdot x_i). \tag{3.4}$$

The p vectors a_j are unit vectors ("directions"), and the functions $s_j(\cdot)$ are unspecified.

Estimation of $\{a_1, s_1(\cdot)\}, \cdots, \{a_m, s_m(\cdot)\}$ is performed in a forward stepwise manner as follows. Consider $\{a_1, s_1(\cdot)\}$. Given a direction a_1, $s_1(\cdot)$ is estimated by a nonparametric smoother (e.g., running mean) of y on $a_1 \cdot x$. The projection pursuit regression algorithm searches over all unit directions to find the direction $\hat{a}_1$ and associated function $\hat{s}_1(\cdot)$ that minimize $\sum_1^n (y_i - \hat{s}_1(\hat{a} \cdot x_i))^2$. Then residuals are taken and the next direction and function are determined. This process is continued until no additional term significantly reduces the residual sum of squares.

Notice the relation of the projection pursuit regression model to the standard linear regression model. When the function $s_1(\cdot)$ is forced to be linear and is estimated by the usual least squares method, a one-term projection pursuit model is exactly the same as the standard linear regression model. That is to say, the fitted model $\hat{s}_1(\hat{a}_1 \cdot x_i)$ exactly equals the least squares fit $\hat{\alpha} + \sum_{j=1}^{p} \hat{\beta}_j x_{ij}$. This is because the least squares fit, by definition, finds the best direction and the best linear function of that direction. Note also that adding another linear term $\hat{s}_2(\hat{a}_2 \cdot x_2)$ would not change the fitted model since the sum of two linear functions is another linear function.

Hastie and Tibshirani (1984) applied the bootstrap to the linear and projection pursuit regression models to assess the variability of the coefficients in each. The data they considered are taken from Breiman and Friedman (1985). The response Y is Upland atmospheric ozone concentration (ppm); the covariates X_1 = Sandburg Air Force base temperature (C°), X_2 = inversion base height (ft), X_3 = Daggot pressure gradient (mm Hg), X_4 = visibility (miles), and X_5 = day of the year. There are 330 observations. The number of terms (m) in the model (3.4) is taken to be two. The projection pursuit algorithm chose directions $\hat{a}_1 = (.80, -.38, .37, -.24, -.14)'$ and $\hat{a}_2 = (.07, .16, .04, -.05, -.98)'$. These directions consist mostly of Sandburg Air Force temperature and day of the year, respec-

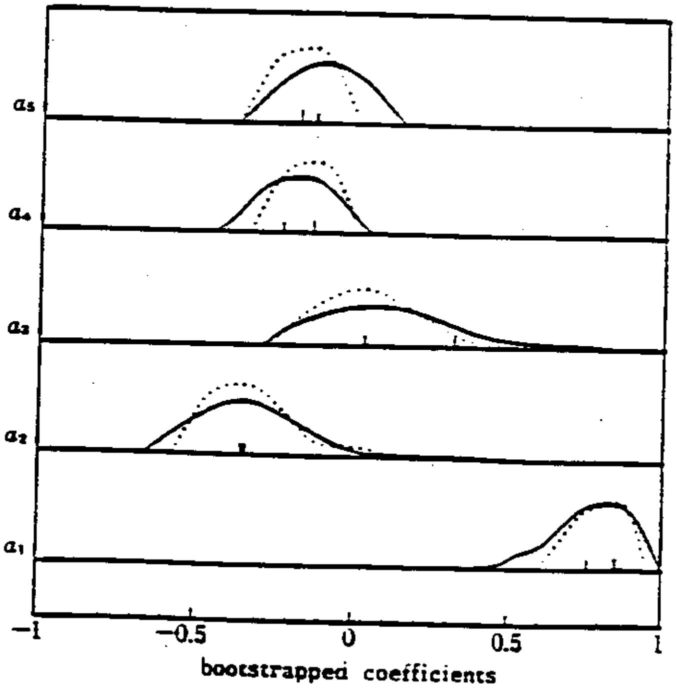

FIG. 4. *Smoothed histograms of the bootstrapped coefficients for the first term in the projection pursuit regression model. Solid histograms are for the usual projection pursuit model; the dotted histograms are for linear $s_1(\cdot)$.*

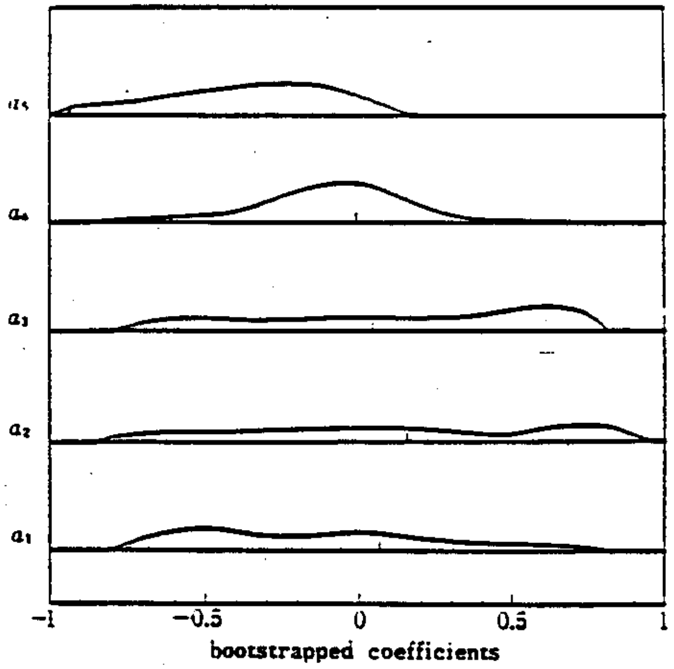

FIG. 5. *Smoothed histograms of the bootstrapped coefficients for the second term in the projection pursuit model.*

tively. (We do not show graphs of the estimated functions $\hat{s}_1(\cdot)$ and $\hat{s}_2(\cdot)$ although in a full analysis of the data they would also be of interest.) Forcing $\hat{s}_1(\cdot)$ to be linear results in the direction $\hat{a}_1 = (.90, -.37, .03, -.14, -.19)'$. These are just the usual least squares estimates $\hat{\beta}_1, \cdots, \hat{\beta}_p$ scaled so that $\sum_1^p \beta_j^2 = 1$.

To assess the variability of the directions, a bootstrap sample is drawn with replacement from $(y_1, x_{11}, \cdots, x_{15}), \cdots, (y_{330}, x_{330\,1}, \cdots, x_{330\,5})$ and the projection pursuit algorithm is applied. Figs. 4 and 5 show histograms of the directions $\hat{a}_1^*$ and $\hat{a}_2^*$ for 200 bootstrap replications. Also shown in Fig. 4 (broken histogram) are the bootstrap replications of $\hat{a}_1$ with $\hat{s}_1(\cdot)$ forced to be linear.

The first direction of the projection pursuit model is quite stable and only slightly more variable than the corresponding linear regression direction. But the second direction is extremely unstable! It is clearly unwise to put any faith in the second direction of the original projection pursuit model.

Example 3: Cox's Model and Local Likelihood Estimation

In this example, we return to Cox's proportional hazards model described in Example 1, but with a few added twists.

The data that we will discuss come from the Stanford heart transplant program and are given in Miller and Halpern (1982). The response y is survival time in weeks after a heart transplant, the covariate x is age at transplant, and the 0–1 variable δ indicates whether the survival time is censored (0) or complete (1). There are measurements on 157 patients. A proportional hazards model was fit to these data, with a quadratic term, i.e. $h(t \mid x) = h_0(t)e^{\beta_1 x + \beta_2 x^2}$. Both $\hat{\beta}_1$ and $\hat{\beta}_2$ are highly significant; the broken curve in Fig. 6 is $\hat{\beta}_1 x + \hat{\beta}_2 x^2$ as a function of x.

For comparison, Fig. 6 shows (solid line) another estimate. This was computed using *local likelihood estimation* (Tibshirani and Hastie, 1984). Given a general proportional hazards model of the form $h(t \mid x) = h_0(t)e^{s(x)}$, the local likelihood technique assumes nothing about the parametric form of $s(x)$; instead it estimates $s(x)$ nonparametrically using a kind of local averaging. The algorithm is very computationally intensive, and standard maximum likelihood theory cannot be applied.

A comparison of the two functions reveals an important qualitative difference: the parametric estimate suggests that the hazard decreases sharply up to age 34, then rises; the local likelihood estimate stays approximately constant up to age 45 then rises. Has the forced fitting of a quadratic function produced a misleading result? To answer this question, we can bootstrap the local likelihood estimate. We sample with replacement from the triples $\{(y_1, x_1, \delta_1) \cdots (y_{157}, x_{157}, \delta_{157})\}$ and apply the local likelihood algorithm to each bootstrap sample. Fig. 7 shows estimated curves from 20 bootstrap samples.

Some of the curves are flat up to age 45, others are decreasing. Hence the original local likelihood estimate is highly variable in this region and on the basis of these data we cannot determine the true behavior of the function there. A look back at the original data shows that while half of the patients were under 45, only 13% of the patients were under 30. Fig. 7 also shows that the estimate is stable near the middle ages but unstable for the older patients.

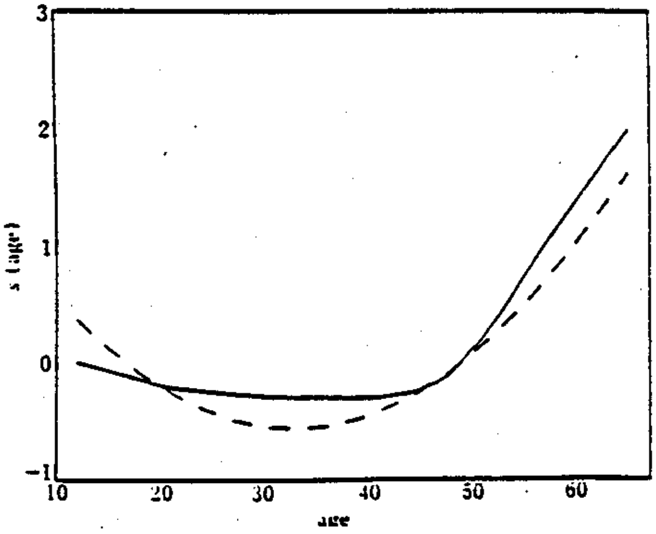

FIG. 6. *Estimates of log relative risk for the Stanford heart transplant data. Broken curve: parametric estimate. Solid curve: local likelihood estimate.*

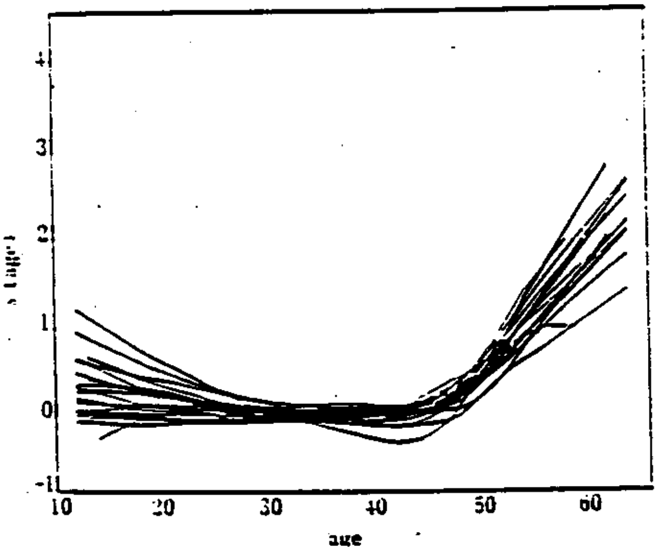

FIG. 7. 20 bootstraps of the local likelihood estimate for the Stanford heart transplant data.

TABLE 3

βHCG blood serum levels for 54 patients having metasticized breast cancer in ascending order

0.1,	0.1,	0.2,	0.4,	0.4,	0.6,	0.8,	0.8,	0.9,	0.9,	1.3,	1.3,	1.4,	1.5,	1.6,
1.6,	1.7,	1.7,	1.7,	1.8,	2.0,	2.0,	2.2,	2.2,	2.2,	2.3,	2.3,	2.4,	2.4,	2.4,
2.4,	2.4,	2.4,	2.5,	2.5,	2.5,	2.7,	2.7,	2.8,	2.9,	2.9,	2.9,	3.0,	3.1,	3.1,
3.2,	3.2,	3.3,	3.3,	3.5,	4.4,	4.5,	6.4,	9.4						

4. OTHER MEASURES OF STATISTICAL ERROR

So far we have discussed statistical error, or accuracy, in terms of the standard error. It is easy to assess other measures of statistical error, such as bias or prediction error, using the bootstrap.

Consider the estimation of bias. For a given statistic $\hat{\theta}(\mathbf{y})$, and a given parameter $\mu(F)$, let

$$R(\mathbf{y}, F) = \hat{\theta}(\mathbf{y}) - \mu(F). \tag{4.1}$$

(It will help keep our notation clear to call the parameter of interest μ rather than θ.) For example, μ might be the mean of the distribution F, assuming the sample space $\mathcal{X}$ is the real line, and $\hat{\theta}$ the 25% trimmed mean. The bias of $\hat{\theta}$ for estimating μ is

$$\beta(F) = E_F R(\mathbf{y}, F) = E_F\{\hat{\theta}(\mathbf{y})\} - \mu(F). \tag{4.2}$$

The notation E_F indicates expectation with respect to the probability mechanism appropriate to F, in this case $\mathbf{y} = (x_1, x_2, \cdots, x_n)$ a random sample from F.

The bootstrap estimate of bias is

$$\hat{\beta} = \beta(\hat{F}) = E_{\hat{F}} R(\mathbf{y}^*, \hat{F}) = E_{\hat{F}}\{\hat{\theta}(\mathbf{y}^*)\} - \mu(\hat{F}). \tag{4.3}$$

As in Section 2, $\mathbf{y}^*$ denotes a random sample $(x_1^*, x_2^*, \cdots, x_n^*)$ from $\hat{F}$, i.e., a bootstrap sample. To numerically evaluate $\hat{\beta}$, all we do is change step (iii) of the bootstrap algorithm in Section 2 to

$$\begin{aligned} \hat{\beta}_B &= \frac{1}{B} \sum_{b=1}^{B} R(\mathbf{y}^*(b), \hat{F}). \\ &= \frac{\sum_{b=1}^{B} \hat{\theta}^*(b)}{B} - \mu(\hat{F}). \\ &= \hat{\theta}^*(\cdot) - \hat{\mu}(F). \end{aligned} \tag{4.4}$$

As $B \rightarrow \infty$, $\hat{\beta}_B$ goes to $\hat{\beta}$ (4.3).

As an example consider the blood serum data of Table 3. Suppose we wish to estimate the true mean $\mu = E_F\{X\}$ of this population using $\hat{\theta}$, the 25% trimmed mean. We calculate $\hat{\mu} = \mu(\hat{F}) = 2.32$, the sample mean of the 54 observations, and $\hat{\theta} = 2.24$, the trimmed mean. The trimmed mean is lower because it discounts the effect of the large observations 6.4 and 9.4. It looks like the trimmed mean might be more robust for this type of data, and as a matter of fact a bootstrap analysis, $B = 1000$, gave estimated standard error $\hat{\sigma} = .16$ for $\hat{\theta}$, compared to .21 for the sample mean. But what about bias?

The same 1000 bootstrap replications which gave $\hat{\sigma} = .16$ also gave $\hat{\theta}^*(\cdot) = 2.29$, so

$$\hat{\beta} = 2.29 - 2.32 = -0.03. \tag{4.5}$$

according to (4.4). (The estimated standard deviation of $\hat{\beta}_B - \hat{\beta}$ due to the limitations of having $B = 1000$ bootstraps is only 0.005 in this case, so we can ignore the difference between $\hat{\beta}_B$ and $\hat{\beta}$.) Whether or not a bias of magnitude -0.03 is too large depends on the context of the problem. If we attempt to remove the bias by subtraction, we get $\hat{\theta} - \hat{\beta} = 2.24 - (-0.03) = 2.27$. Removing bias in this way is frequently a bad idea (see Hinkley, 1978), but at least the bootstrap analysis has given us a reasonable picture of the bias and standard error of $\hat{\theta}$.

Here is another measure of statistical accuracy, different from either bias or standard error. Let $\hat{\theta}(\mathbf{y})$ be the 25% trimmed mean and $\mu(F)$ be the mean of F, as in the serum example, and also let $\hat{i}(\mathbf{y})$ be the interquartile range, the distance between the 25th and 75th percentiles of the sample $\mathbf{y} = (x_1, x_2, \cdots, x_n)$. Define

$$R(\mathbf{y}, F) = \frac{\hat{\theta}(\mathbf{y}) - \mu(F)}{\hat{i}(\mathbf{y})}. \tag{4.6}$$

R is like a Student's t statistic, except that we have substituted the 25% trimmed mean for the sample mean and the interquartile range for the standard deviation.

Suppose we know the 5th and 95th percentiles of $R(\mathbf{y}, F)$, say $\rho^{(.05)}(F)$ and $\rho^{(.95)}(F)$, where the definition of $\rho^{(.05)}(F)$ is

$$\text{Prob}_F\{R(\mathbf{y}, F) < \rho^{(.05)}(F)\} = .05, \tag{4.7}$$

and similarly for $\rho^{(.95)}(F)$. The relationship $\text{Prob}_F\{\rho^{(.05)} \leq R < \rho^{(.95)}\} = .90$ combines with definition (4.6) to give a central 90% "t interval" for the mean $\mu(F)$,

$$\mu \in [\hat{\theta} - \hat{i}\rho^{(.95)}, \hat{\theta} - \hat{i}\rho^{(.05)}]. \tag{4.8}$$

Of course we do not know $\rho^{(.05)}(F)$ and $\rho^{(.95)}(F)$, but we can approximate them by their bootstrap estimates $\rho^{(.05)}(\hat{F})$ and $\rho^{(.95)}(\hat{F})$. A bootstrap sample $\mathbf{y}^*$ gives a bootstrap value of (4.6), $R(\mathbf{y}^*, \hat{F}) = (\hat{\theta}(\mathbf{y}^*) - \mu(\hat{F}))/\hat{i}(\mathbf{y}^*)$, where $\hat{i}(\mathbf{y}^*)$ is the interquartile range of the bootstrap data $x_1^*, x_2^*, \cdots, x_n^*$. For any fixed number ρ, the bootstrap estimate of $\text{Prob}_F\{R < \rho\}$ based on B bootstrap samples is

$$\#\{R(\mathbf{y}^*(b), \hat{F}) < \rho\}/B. \tag{4.9}$$

By keeping track of the empirical distribution of $R(\mathbf{y}^*(b), \hat{F})$, we can pick off the values of ρ which make (4.9) equal .05 and .95. These approach $\rho^{(.05)}(\hat{F})$ and $\rho^{(.95)}(\hat{F})$ as $B \to \infty$.

For the serum data, $B = 1000$ bootstrap replications gave $\rho^{(.05)}(\hat{F}) = -.303$ and $\rho^{(.95)}(\hat{F}) = .078$. Substituting these values into (4.9), and using the observed estimates $\hat{\theta} = 2.24$, $\hat{i} = 1.40$, gives

$$\mu \in [2.13, 2.66] \tag{4.10}$$

as a central 90% "bootstrap t interval" for the true mean $\mu(F)$. This is considerably shorter than the standard t interval for μ based on 53 degrees of freedom, $\bar{x} \pm 1.67\hat{\sigma} = [1.97, 2.67]$. Here $\hat{\sigma} = .21$ is the usual estimate of standard error (1.3).

Bootstrap confidence intervals are discussed further in Sections 7 and 8. They require more bootstrap replications than do bootstrap standard errors, on the order of $B = 1000$ rather than $B = 50$ or 100. This point is discussed briefly in Section 9.

By now it should be clear that we can use any random variable $R(\mathbf{y}, F)$ to measure accuracy, not just (4.1) or (4.6), and then estimate $E_F\{R(\mathbf{y}, F)\}$ by its bootstrap value $E_{\hat{F}}\{R(\mathbf{y}^*, \hat{F})\} \doteq \sum_{b=1}^{B} R(\mathbf{y}^*(b), \hat{F})/B$. Similarly we can estimate $E_F R(y, F)^2$ by $E_{\hat{F}} R(\mathbf{y}^*, \hat{F})^2$, etc. Efron (1983) considers the prediction problem, in which a training set of data is used to construct a prediction rule. A naive estimate of the prediction rule's accuracy is the proportion of correct guesses it makes on its own training set, but this can be greatly over optimistic since the prediction rule is explicitly constructed to minimize errors on the training set. In this case, a natural choice of $R(\mathbf{y}, F)$ is the over optimism, the difference between the naive estimate and the actual success rate of the prediction rule for new data. Efron (1983) gives the bootstrap estimate of over optimism, and shows that it is closely related to cross-validation, the usual method of estimating over optimism. The paper goes on to show that some modifications of the bootstrap estimate greatly out perform both cross-validation and the bootstrap.

5. MORE COMPLICATED DATA SETS

The bootstrap is not restricted to situations where the data is a simple random sample from a single distribution. Suppose for instance that the data consists of two independent random samples,

$$\begin{aligned} &U_1, U_2, \cdots, U_m \sim F \quad \text{and} \\ &V_1, V_2, \cdots, V_n \sim G, \end{aligned} \tag{5.1}$$

where F and G are possibly different distributions on the real line. Suppose also that the statistic of interest is the Hodges–Lehmann shift estimate

$$\begin{aligned} \hat{\theta} = \\ &\text{median}\{V_j - U_i, i = 1, 2, \cdots, m, j = 1, 2, \cdots, n\}. \end{aligned} \tag{5.2}$$

Having observed $U_1 = u_1$, $U_2 = u_2, \cdots, V_n = v_n$, we desire an estimate for $\sigma(F, G)$, the standard error of $\hat{\theta}$.

The bootstrap estimate of $\sigma(F, G)$ is $\hat{\sigma} = \sigma(\hat{F}, \hat{G})$, where $\hat{F}$ is the empirical distribution of $u_1, u_2, \cdots, u_m$, and $\hat{G}$ is the empirical distribution of $v_1, v_2, \cdots, v_n$. It is easy to modify the Monte Carlo algorithm of Section 2 to numerically evaluate $\hat{\sigma}$. Let $\mathbf{y} = (u_1, u_2, \cdots, v_n)$ be the observed data vector. A bootstrap sample $\mathbf{y}^* = (u_1^*, u_2^*, \cdots, u_m^*, v_1^*, v_2^*, \cdots, v_n^*)$ consists of a random sample $U_1^*, \cdots, U_m^*$ from $\hat{F}$ and an independent random sample $V_1^*, \cdots, V_n^*$ from $\hat{G}$. With only this modification, steps (i) through (iii) of the Monte Carlo algorithm produce $\hat{\sigma}_B$, (2.4), approaching $\hat{\sigma}$ as $B \to \infty$.

Table 4 reports on a simulation experiment investigating how well the bootstrap works on this problem. 100 trials of situation (5.1) were run, with $m = 6$, $n = 9$, F and G both Uniform $[0, 1]$. For each trial, both $B = 100$ and $B = 200$ bootstrap replications were generated. The bootstrap estimate $\hat{\sigma}_B$ was nearly unbiased for the true standard error $\sigma(F, G) = .167$ for either $B = 100$ or $B = 200$, with a quite small standard deviation from trial to trial. The improvement in going from $B = 100$ to $B = 200$ is too small to show up in this experiment.

In practice, statisticians must often consider quite complicated data structures: time series models, mul-

TABLE 4

Bootstrap estimate of standard error for the Hodges–Lehmann two-sample shift estimate: 100 trials

	Summary statistics for $\hat{\sigma}_B$		
	Ave	SD	CV
$B = 100$	.165	.030	.18
$B = 200$	.166	.031	.19
True σ	.167		

Note: $m = 6$, $n = 9$; true distributions F and G both uniform $[0, 1]$.

tifactor layouts, sequential sampling, censored and missing data, etc. Fig. 8 illustrates how the bootstrap estimation process proceeds in a general situation. The actual probability mechanism P which generates the observed data $\mathbf{y}$ belongs to some family $\mathbf{P}$ of possible probability mechanism. In the Hodges–Lehmann example, $P = (F, G)$, a pair of distributions on the real line, $\mathbf{P}$ equals the family of all such pairs, and $\mathbf{y} = (u_1, u_2, \cdots, u_m, v_1, v_2, \cdots, v_n)$ is generated by random sampling m times from F and n times from G.

We have a random variable of interest $R(\mathbf{y}, P)$, which depends on both $\mathbf{y}$ and the unknown model P, and we wish to estimate some aspect of the distribution of R. In the Hodges–Lehmann example, $R(\mathbf{y}, P) = \hat\theta(\mathbf{y}) - E_P\{\hat\theta\}$, and we estimated $\sigma(P) = \{E_P R(\mathbf{y}, P)^2\}^{1/2}$, the standard error of $\hat\theta$. As before, the notation E_P indicates expectation when $\mathbf{y}$ is generated according to mechanism P.

We assume that we have some way of estimating the entire probability model P from the data $\mathbf{y}$, producing the estimate called $\hat P$ in Fig. 8. (In the two-sample problem, $\hat P = (\hat F, \hat G)$, the pair of empirical distributions.) *This is the crucial step for the bootstrap.* It can be carried out either parametrically or nonparametrically, by maximum likelihood or by some other estimation technique.

Once we have $\hat P$, we can use Monte Carlo methods to generate bootstrap data sets $\mathbf{y}^*$, according to the same rules by which $\mathbf{y}$ is generated from P. The bootstrap random variable $R(\mathbf{y}^*, \hat P)$ is observable, since we know $\hat P$ as well as $\mathbf{y}^*$, so the distribution of $R(\mathbf{y}^*, \hat P)$ can be found by Monte Carlo sampling. The bootstrap estimate of $E_P R(\mathbf{y}, P)$ is then $E_{\hat P} R(\mathbf{y}^*, \hat P)$, and likewise for estimating any other aspect of $R(\mathbf{y}, P)$'s distribution.

A regression model is a familiar example of a complicated data structure. We observe $\mathbf{y} = (y_1, y_2, \cdots, y_n)$, where

$$y_i = g(\beta, t_i) + \varepsilon_i \quad i = 1, 2, \cdots, n. \tag{5.3}$$

Here β is a vector of unknown parameters we wish to estimate; for each i, t_i is an observed vector of covariates; and g is a known function of β and t_i, for instance $e^{\beta' t_i}$. The ε_i are an iid sample from some unknown distribution F on the real line,

$$\varepsilon_1, \varepsilon_2, \cdots, \varepsilon_n \sim F, \tag{5.4}$$

where F is usually assumed to be centered at 0 in some sense, perhaps $E\{\varepsilon\} = 0$ or $\text{Prob}\{\varepsilon < 0\} = .5$. The probability model is $P = (\beta, F)$; (5.3) and (5.4) describe the step $P \to \mathbf{y}$ in Fig. 8. The covariates $t_1, t_2, \cdots, t_n$, like the sample size n in the simple problem (1.1), are considered fixed at their observed values.

For every choice of β we have a vector $\mathbf{g}(\beta) = (g(\beta, t_1), g(\beta, t_2), \cdots, g(\beta, t_n))$ of predicted values for $\mathbf{y}$. Having observed $\mathbf{y}$, we estimate β by minimizing some measure of distance between $\mathbf{g}(\beta)$ and $\mathbf{y}$,

$$\hat\beta: \min_{\beta} D(\mathbf{y}, \mathbf{g}(\beta)). \tag{5.5}$$

The most common choice of D is $D(\mathbf{y}, \mathbf{g}) = \sum_{i=1}^n \{y_i - g(\beta, t_i)\}^2$.

How accurate is $\hat\beta$ as an estimate of β? Let $R(\mathbf{y}, P)$ equal the vector $\hat\beta - \beta$. A familiar measure of accuracy is the mean square error matrix

$$\begin{aligned} \Sigma(P) &= E_P(\hat\beta - \beta)(\hat\beta - \beta)' \\ &= E_P R(\mathbf{y}, P) R(\mathbf{y}, P)'. \end{aligned} \tag{5.6}$$

The bootstrap estimate of accuracy $\hat\Sigma = \Sigma(\hat P)$ is obtained by following through Fig. 8.

There is an obvious choice for $\hat P = (\hat\beta, \hat F)$ in this case. The estimate $\hat\beta$ is obtained from (5.5). Then $\hat F$ is the empirical distribution of the residuals,

$$\hat F: \text{mass}(1/n) \quad \text{on} \quad \hat\varepsilon_i = y_i - g(\hat\beta, t_i), \qquad i = 1, \cdots, n. \tag{5.7}$$

A bootstrap sample $\mathbf{y}^*$ is obtained by following rules (5.3) and (5.4),

$$y_i^* = g(\hat\beta, t_i) + \varepsilon_i^*, \quad i = 1, 2, \cdots, n, \tag{5.8}$$

where $\varepsilon_1^*, \varepsilon_2^*, \cdots, \varepsilon_n^*$ is an iid sample from $\hat F$. Notice that the ε_i^* are independent bootstrap variates, even though the $\hat\varepsilon_i$ are not independent variates in the usual sense.

Each bootstrap sample $\mathbf{y}^*(b)$ gives a bootstrap value $\hat\beta^*(b)$,

$$\hat\beta^*(b): \min_{\beta} D(\mathbf{y}^*(b), \mathbf{g}(\beta)), \tag{5.9}$$

as in (5.5). The estimate

$$\hat\Sigma_B = \frac{\sum_{b=1}^B \{\hat\beta^*(b) - \hat\beta^*(\cdot)\}\{\hat\beta^*(b) - \hat\beta^*(\cdot)\}'}{B} \tag{5.10}$$

approaches the bootstrap estimate $\hat\Sigma$ as $B \to \infty$. (We could just as well divide by $B - 1$ in (5.10).)

In the case of ordinary least squares regression, where $g(\beta, t_i) = \beta' t_i$ and $D(\mathbf{y}, \mathbf{g}) = \sum_{i=1}^n (y_i - g_i)^2$,

FIG. 8. *A schematic illustration of the bootstrap process for a general probability model P. The expectation of $R(\mathbf{y}, P)$ is estimated by the bootstrap expectation of $R(\mathbf{y}^*, \hat P)$. The double arrow indicates the crucial step in applying the bootstrap.*

Section 7 of Efron (1979a) shows that the bootstrap estimate, $B = \infty$, can be calculated without Monte Carlo sampling, and is

$$\hat{\Sigma} = \hat{\sigma}^2\left(\sum_{i=1}^{n} t_i t_i'\right)^{-1} \quad \left[\hat{\sigma}^2 = \sum_{1}^{n} \frac{\hat{\varepsilon}_i^2}{n}\right]. \tag{5.11}$$

This is the usual Gauss–Markov answer, except for the divisor n in the definition of $\hat{\sigma}^2$.

There is another, simpler way to bootstrap a regression problem. We can consider each covariate-response pair $x_i = (t_i, y_i)$ to be a single data point obtained by simple random sampling from a distribution F. If the covariate vector t_i is p-dimensional, F is a distribution on $p + 1$ dimensions. Then we apply the bootstrap as described originally in Section 2 to the data set $x_1, x_2, \cdots, x_n \sim_{\text{iid}} F$.

The two bootstrap methods for the regression problem are asymptotically equivalent, but can perform quite differently in small sample situations. The class of possible probability models P is different for the two methods. The simple method, described last, takes less advantage of the special structure of the regression problem. It does *not* give answer (5.11) in the case of ordinary least squares. On the other hand the simple method gives a trustworthy estimate of $\hat{\beta}$'s variability *even if the regression model* (5.3) *is not correct*. The bootstrap, as outlined in Fig. 5, is very general, but because of this generality there will often be more than one bootstrap solution for a given problem.

As the final example of this section, we discuss *censored data*. The ages of 97 men at a California retirement center, Channing House, were observed either at death (an uncensored observation) or at the time the study ended (a censored observation). The data set $\mathbf{y} = \{(x_1, d_1), (x_2, d_2), \cdots, (x_{97}, d_{97})\}$, where x_i was the age of the ith man observed, and

$$d_i = \begin{cases} 1 & \text{if } x_i \text{ uncensored} \\ 0 & \text{if } x_i \text{ censored.} \end{cases}$$

Thus (777, 1) represents a Channing House man observed to die at age 777 months, while (843, 0) represents a man 843 months old when the study ended. His observation could be written as "843+," and in fact d_i is just an indicator for the absence or presence of "+." A full description of the Channing House data appears in Hyde (1980).

A typical data point (X_i, D_i) can be thought of as generated in the following way: a real lifetime X_i^0 is selected randomly according to a survival curve

$$S^0(t) = \text{Prob}\{X_i^0 > t\}, \quad (0 \le t < \infty) \tag{5.12}$$

and a censoring time W_i is independently selected according to another survival curve

$$R(t) = \text{Prob}\{W_i > t\}, \quad (0 \le t < \infty). \tag{5.13}$$

The statistician gets to observe

$$X_i = \min\{X_i^0, W_i\} \tag{5.14}$$

and

$$D_i = \begin{cases} 1 & \text{if } X_i = X_i^0 \\ 0 & \text{if } X_i = W_i. \end{cases} \tag{5.15}$$

Note: $1 - S^0(t)$ and $1 - R(t)$ are the cumulative distribution functions (cdf) for X_i^0 and W_i, respectively; with censored data it is more convenient to consider survival curves than cdf.

Under assumptions (5.12)–(5.15) there is a simple formula for the nonparametric MLE of $S^0(t)$, called the *Kaplan–Meier estimator* (Kaplan and Meier, 1958). For convenience suppose $x_1 < x_2 < x_3 < \cdots < x_n$, $n = 97$. Then the Kaplan–Meier estimate is

$$\hat{S}^0(t) = \prod_{i=1}^{k_t} \left(\frac{n-i}{n-i+1}\right)^{d_i}, \tag{5.16}$$

where k_t is the value of k such that $t \in [x_k, x_{k+1})$. In the case of no censoring, $\hat{S}^0(t)$ is equivalent to the observed empirical distribution of $x_1, x_2, \cdots, x_n$, but otherwise (5.16) corrects the empirical distribution to account for censoring. Likewise

$$\hat{R}(t) = \prod_{i=1}^{k_t} \left(\frac{n-i}{n-i+1}\right)^{1-d_i} \tag{5.17}$$

is the Kaplan–Meier estimate of the censoring curve $R(t)$.

Fig. 9 shows $\hat{S}^0(t)$ for the Channing House men. It crosses the 50% survival level at $\hat{\theta} = 1044$ months. Call this value the observed median lifetime. We can use the bootstrap to assign a standard error to the observed median.

The probability mechanism is $P = (S^0, R)$; P produces (X_i^0, D_i) according to (5.12)–(5.15), and $\mathbf{y} = \{(x_1, d_1), \cdots, (x_n, d_n)\}$ by $n = 97$ independent repetitions of this process. An obvious choice of the estimate $\hat{P}$ in Fig. 8 is $(\hat{S}^0, \hat{R})$, (5.14), (5.15). The rest of

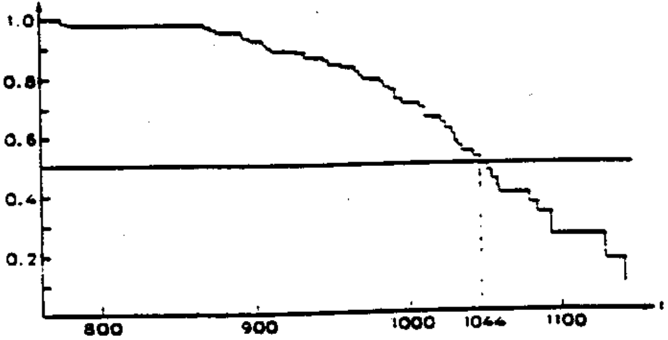

FIG. 9. *Kaplan–Meier estimated survival curve for the Channing House men; t = age in months. The median survival age is estimated to be 1044 months (87 years).*

bootstrap process is automatic: $\hat{S}^0$ and $\hat{R}$ replace S^0 and R in (5.12) and (5.13); n pairs (X_i^*, D_i^*) are independently generated according to rules (5.12)–(5.15), giving the bootstrap data set $\mathbf{y}^* = \{x_1^*, d_1^*, \cdots, (x_n^*, d_n^*)\}$; and finally the bootstrap Kaplan–Meier curve $\hat{S}^{0*}$ is constructed according to formula (5.16), and the bootstrap observed median $\hat{\theta}^*$ calculated. For the Channing House data, $B = 1600$ bootstrap replications of $\hat{\theta}^*$ gave estimated standard error $\hat{\sigma} = 14.0$ months for $\hat{\theta}$. An estimated bias of 4.1 months was calculated as at (4.4). Efron (1981b) gives a fuller description.

Once again there is a simpler way to apply to bootstrap. Consider each pair $y_i = (x_i, d_i)$ as an observed point obtained by simple random sampling from a bivariate distribution F, and apply the bootstrap as described in Section 2 to the data set $y_1, y_2, \cdots, y_n \sim_{\text{iid}} F$. This method makes no use of the special structure (5.12)–(5.15). Surprisingly, it gives *exactly the same answers* as the more complicated bootstrap method described earlier (Efron, 1981a). This leads to a surprising conclusion: bootstrap estimates of variability for the Kaplan–Meier curve give correct standard errors even when the usual assumptions about the censoring mechanism, (5.12)–(5.15), fail.

6. EXAMPLES WITH MORE COMPLICATED DATA STRUCTURES

Example 1: Autoregressive Time Series Model

This example illustrates an application of the bootstrap to a famous time series.

The data are the Wolfer annual sunspot numbers for the years 1770–1889 (taken from Anderson, 1975). Let the count for the ith year be z_i. After centering the data (replacing z_i by $z_i - \bar{z}_i$), we fit a first-order autoregressive model

$$z_i = \phi z_{i-1} + \varepsilon_i \tag{6.1}$$

where $\varepsilon_i \sim$ iid $N(0, \sigma^2)$. The estimate $\hat{\phi}$ turned out to be .815 with an estimated standard error, one over the square root of the Fisher information, of .053.

A bootstrap estimate of the standard error of $\hat{\phi}$ can be obtained as follows. Define the residuals $\hat{\varepsilon}_i = z_i - \hat{\phi} z_{i-1}$ for $i = 2, 3, \cdots, 120$. A bootstrap sample $z_1^*, z_2^*, \cdots, z_{120}^*$ is created by sampling $\hat{\varepsilon}_2^*, \hat{\varepsilon}_3^*, \cdots, \hat{\varepsilon}_{120}^*$ with replacement from the residuals, then letting $z_1^* = z_1$, and $z_i^* = \hat{\phi} z_{i-1}^* + \hat{\varepsilon}_i^*$, $i = 2, \cdots, 120$. Finally, after centering the time series $z_1^*, z_2^*, \cdots, z_{120}^*$, $\hat{\phi}^*$ is the estimate of the autoregressive parameter for this new time series. (We could, if we wished, sample the $\hat{\varepsilon}_i^*$ from a fitted normal distribution.)

A histogram of 1000 such bootstrap values $\hat{\phi}_1^*, \hat{\phi}_2^*, \cdots, \hat{\phi}_{1000}^*$ is shown in Fig. 10.

The bootstrap estimate of standard error was .055, agreeing nicely with the usual formula. Note however that the distribution is skewed to the left, so a confidence interval for ϕ might be asymmetric about $\hat{\phi}$ as discussed in Sections 8 and 9.

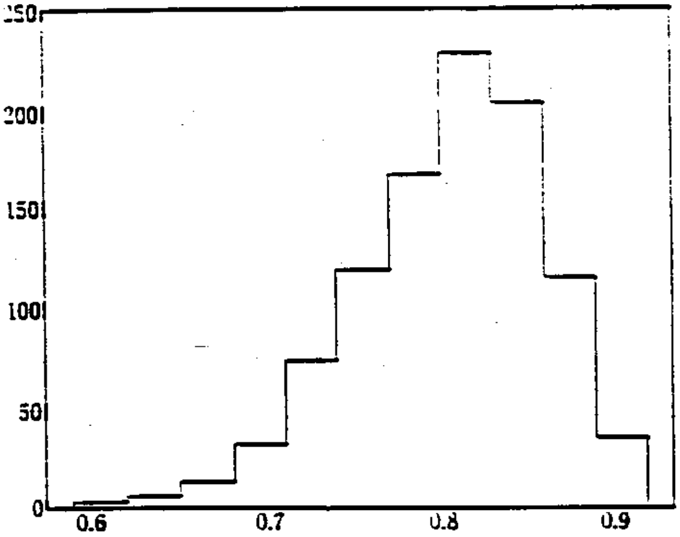

FIG. 10. *Bootstrap histogram of $\hat{\phi}_1^*, \cdots, \hat{\phi}_{1000}^*$ for the Wolfer sunspot data, model* (6.1).

In bootstrapping the residuals, we have assumed that the first-order autoregressive model is correct. (Recall the discussion of regression models in Section 5.) In fact, the first-order autoregressive model is far from adequate for this data. A fit of second-order autoregressive model

$$z_i = \alpha z_{i-1} + \theta z_{i-2} + \varepsilon_i \tag{6.2}$$

gave estimates $\hat{\alpha} = 1.37$, $\hat{\theta} = -.677$, both with an estimated standard error of .067, based on Fisher information calculations. We applied the bootstrap to this model, producing the histograms for $\alpha_1^*, \cdots, \alpha_{1000}^*$ and $\theta_1^*, \cdots, \theta_{1000}^*$ shown in Figs. 11 and 12, respectively.

The bootstrap standard errors were .070 and .068, respectively, both close to the usual value. Note that the additional term has reduced the skewness of the first coefficient.

Example 2: Estimating a Response Transformation in Regression

Box and Cox (1964) introduced a parametric family for estimating a transformation of the response in a regression. Given regression data $\{(x_1, y_1), \cdots, (x_n, y_n)\}$, their model takes the form

$$z_i(\lambda) = x_i \cdot \beta + \varepsilon_i \tag{6.3}$$

where $z_i(\lambda) = (y_i^\lambda - 1)/\lambda$ for $\lambda \neq 0$ and $\log y_i$ for $\lambda = 0$, and $\varepsilon_i \sim$ iid $N(0, \sigma^2)$. Estimates of λ and β are found by minimizing $\sum_1^n (z_i - x_i \cdot \beta)^2$.

Breiman and Friedman (1985) proposed a nonparametric solution for this problem. Their so called ACE

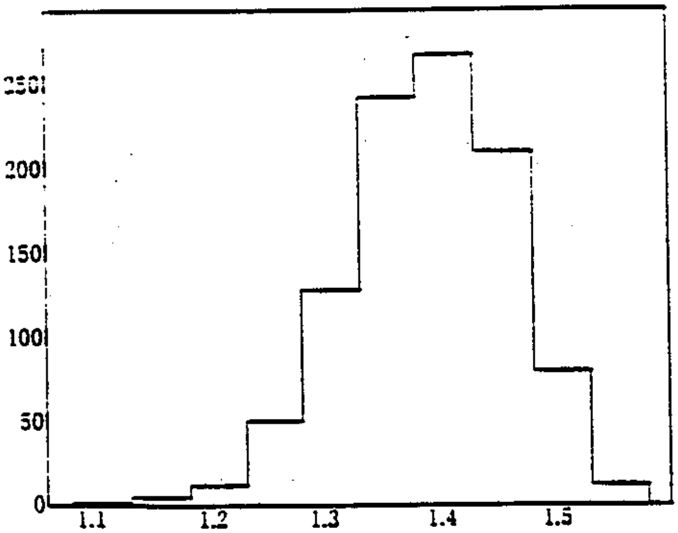

FIG. 11. *Bootstrap histogram of* $\hat{\alpha}^*_1, \cdots, \hat{\alpha}^*_{1000}$ *for the Wolfer sunspot data, model* (6.2).

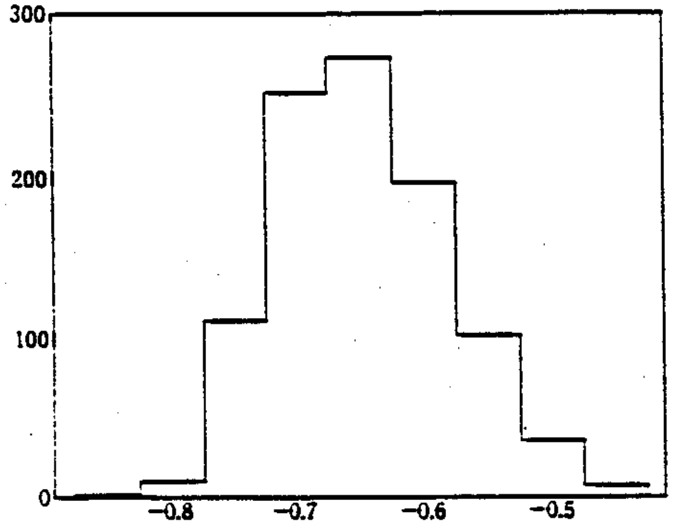

FIG. 12. *Bootstrap histogram of* $\hat{\theta}^*_1, \cdots, \hat{\theta}^*_{1000}$ *for the Wolfer sunspot data, model* (6.2).

(alternating conditional expectation) model generalizes (6.3) to

$$s(y_i) = x_i \cdot \beta + \varepsilon_i, \tag{6.4}$$

where $s(\cdot)$ is an unspecified smooth function. (In its most general form, ACE allows for transformations of the covariates as well.) The function $s(\cdot)$ and parameter β are estimated in an alternating fashion, utilizing a nonparametric smoother to estimate $s(\cdot)$.

In the following example, taken from Friedman and Tibshirani (1984), we compare the Box and Cox procedure to ACE and use the bootstrap to assess the variability of ACE.

The data from Box and Cox (1964) consist of a 3 × 3 × 3 experiment on the strength of yarns, the response Y being number of cycles to failure, and the factors length of test specimen (X_1) (250, 300, and 350 mm), amplitude of loading cycle (X_2) (8, 9, or 10 mm), and load (X_3) (40, 45, or 50 g). As in Box and Cox, we treat the factors as quantitive and allow only a linear term for each. Box and Cox found that a logarithmic transformation was appropriate, with their procedure producing a value of −.06 for $\hat{\lambda}$ with an estimated 95% confidence interval of (−.18, .06).

Fig. 13 shows the transformation selected by the ACE algorithm. For comparison, the log function is plotted (normalized) on the same figure.

The similarity is truly remarkable! In order to assess the variability of the ACE curve, we can apply the bootstrap. Since the X matrix in this problem is fixed by design, we resampled from the residuals instead of from the (x_i, y_i) pairs. The bootstrap procedure was the following:

```
Calculate residuals   $\hat{\varepsilon}_i = \hat{s}(y_i) - x_i \cdot \hat{\beta}$,   $i = 1, 2, \cdots, n$.
Repeat $B$ times
    Choose a sample   $\hat{\varepsilon}^*_1, \cdots, \hat{\varepsilon}^*_n$
                      with replacement from   $\hat{\varepsilon}_1, \cdots, \hat{\varepsilon}_n$
    Calculate   $y^*_i = \hat{s}^{-1}(x_i \cdot \hat{\beta} + \hat{\varepsilon}^*_i)$,   $i = 1, 2, \cdots, n$
    Compute   $\hat{s}^*(\cdot)$ = result of ACE algorithm
                      applied to   $(x_1, y^*_1), \cdots, (x_n, y^*_n)$
End
```

The number of bootstrap replications B was 20. Note that the residuals are computed on the $s(\cdot)$ scale, not the y scale, because it is on the $s(\cdot)$ scale that the true residuals are assumed to be approximately iid. The 20 estimated transformations, $\hat{s}^*_1(\cdot), \cdots, \hat{s}^*_{20}(\cdot)$ are shown in Fig. 14.

The tight clustering of the smooths indicates that the original estimate $\hat{s}(\cdot)$ has low variability, especially for smaller values of Y. This agrees qualitatively with

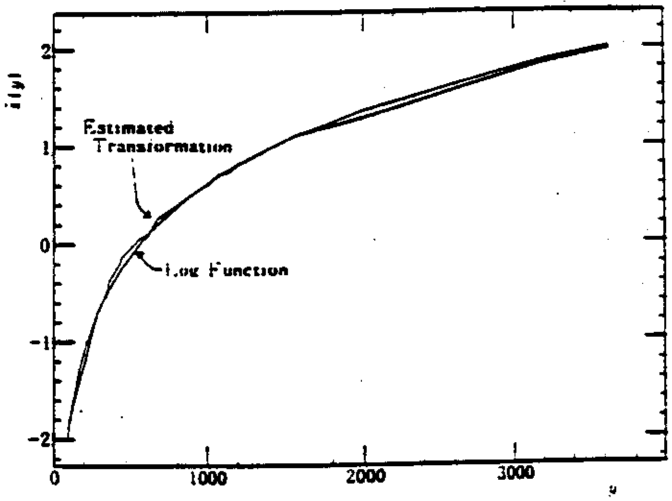

FIG. 13. *Estimated transformation from ACE and the log function for Box and Cox example.*

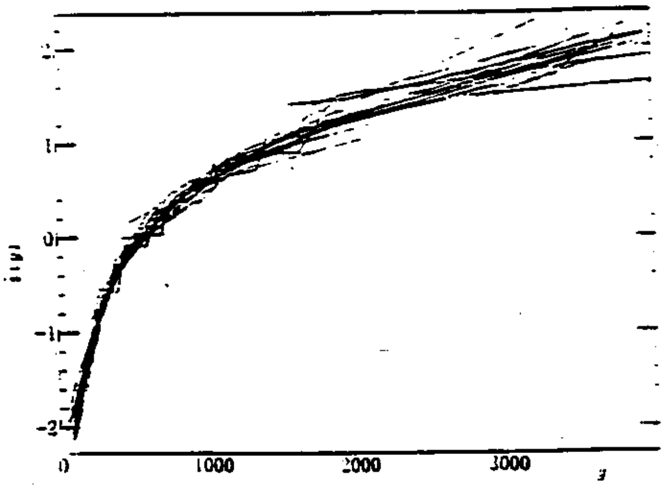

FIG. 14. *Bootstrap replications of ACE transformations for Box and Cox example.*

the short confidence interval for λ in the Box and Cox analysis.

7. BOOTSTRAP CONFIDENCE INTERVALS

This section presents three closely related methods of using the bootstrap to set confidence intervals. The discussion is in terms of simple parametric models, where the logical basis of the bootstrap methods is easiest to see. Section 8 extends the methods to multiparameter and nonparametric models.

We have discussed obtaining $\hat{\sigma}$, the estimated standard error of an estimator $\hat{\theta}$. In practice, $\hat{\theta}$ and $\hat{\sigma}$ are usually used together to form the approximate confidence interval $\theta \in \hat{\theta} \pm \hat{\sigma} z^{(\alpha)}$, (1.7), where $z^{(\alpha)}$ is the $100 \cdot \alpha$ percentile point of a standard normal distribution. The interval (1.7) is claimed to have approximate coverage probability $1 - 2\alpha$. For the law school example of Section 2, the values $\hat{\theta} = .776$, $\hat{\sigma} = .115$, $z^{(.05)} = -1.645$, give $\theta \in [.587, .965]$ as an approximate 90% central interval for the true correlation coefficient.

We will call (1.7) the *standard interval for θ*. When working within parametric families like the bivariate normal, $\hat{\sigma}$ in (1.7) is usually obtained by differentiating the log likelihood function, see Section 5a of Rao (1973), although in the context of this paper we might prefer to use the parametric bootstrap estimate of σ, e.g., $\hat{\sigma}_{\text{NORM}}$ in Section 2.

The standard intervals are an immensely useful statistical tool. They have the great virtue of being automatic: a computer program can be written which produces (1.7) directly from the data **y** and the form of the density function for **y**, with no further input required from the statistician. Nevertheless the standard intervals can be quite inaccurate as Table 5 shows. The standard interval (1.7), using $\hat{\sigma}_{\text{NORM}}$, (2.5), is strikingly different from the exact normal theory interval based on the assumption of a bivariate normal sampling distribution F.

TABLE 5

Exact and approximate central 90% confidence intervals for θ, the true correlation coefficient, from the law school data of Fig. 1

1. Exact (normal theory)	[.496, .898]	R/L = .44
2. Standard (1.7)	[.587, .965]	R/L = 1.00
3. Transformed standard	[.508, .907]	R/L = .49
4. Parametric bootstrap (BC)	[.488, .900]	R/L = .43
5. Nonparametric bootstrap (BC_a)	[.43, .92]	R/L = .42

Note: R/L = ratio of right side of interval, measured from $\hat{\theta} = .776$, to left side. The exact interval is strikingly asymmetric about $\hat{\theta}$. Section 8 discusses the nonparametric method of line 5.

In this case, it is well known that it is better to make the transformation $\hat{\phi} = \tanh^{-1}(\hat{\theta})$, $\phi = \tanh^{-1}(\theta)$, apply (1.7) on the ϕ scale, and then transform back to the θ scale. The resulting interval, line 3 of Table 5, is moved closer to the exact interval. However, there is nothing automatic about the $\tanh^{-1}$ transformation. For a different statistic from the correlation coefficient or a different distributional family from the bivariate normal, we might very well need other tricks to make (1.7) perform satisfactorily.

The bootstrap can be used to produce approximate confidence intervals in an automatic way. The following discussion is abridged from Efron (1984 and 1985) and Efron (1982a, Chapter 10). Line 4 of Table 5 shows that the parametric bootstrap interval for the correlation coefficient θ is nearly identical with the exact interval. "Parametric" in this case means that the bootstrap algorithm begins from the bivariate normal MLE $\hat{F}_{\text{NORM}}$, as for the normal theory curve of Fig. 2. This good performance is no accident. The bootstrap method used in line 4 in effect transforms $\hat{\theta}$ to the best (most normal) scale, finds the appropriate interval, and transforms this interval back to the θ scale. All of this is done automatically by the bootstrap algorithm, without requiring special intervention from the statistician. The price paid is a large amount of computing, perhaps $B = 1000$ bootstrap replications, as discussed in Section 10.

Define $\hat{G}(s)$ to be the parametric bootstrap cdf of $\hat{\theta}^*$,

$$\hat{G}(s) = \text{Prob}_*\{\hat{\theta}^* < s\}, \tag{7.1}$$

where Prob_* indicates probability computed according to the bootstrap distribution of $\hat{\theta}^*$. In Fig. 2 $\hat{G}(s)$ is obtained by integrating the normal theory curve. We will present three different kinds of bootstrap confidence intervals in order of increasing generality. All three methods use percentiles of $\hat{G}$ to define the confidence interval. They differ in which percentiles are used.

The simplest method is to take $\theta \in [\hat{G}^{-1}(\alpha), \hat{G}^{-1}(1-\alpha)]$ as an approximate $1-2\alpha$ central interval for θ. This is called the *percentile method* in Section 10.4 of Efron (1982a). The percentile method interval is just the interval between the $100 \cdot \alpha$ and $100 \cdot (1-\alpha)$ percentiles of the bootstrap distribution of $\hat{\theta}^*$.

We will use the notation $\theta[\alpha]$ for the α level endpoint of an approximate confidence interval for θ, so $\theta \in [\theta[\alpha], \theta[1-\alpha]]$ is the central $1-2\alpha$ interval. Subscripts will be used to indicate the various different methods. The percentile interval has endpoints

$$\theta_P[\alpha] \equiv \hat{G}^{-1}(\alpha). \tag{7.2}$$

This compares with the standard interval,

$$\theta_S[\alpha] = \hat{\theta} + \hat{\sigma}z^{(\alpha)}. \tag{7.3}$$

Lines 1 and 2 of Table 6 summarize these definitions.

Suppose the bootstrap cdf $\hat{G}$ is perfectly normal, say

$$\hat{G}(s) = \Phi((s-\hat{\theta})/\hat{\sigma}), \tag{7.4}$$

where $\Phi(s) = \int_{-\infty}^{s} (2\pi)^{-1/2} e^{-t^2/2}\,dt$, the standard normal cdf. In other words, suppose that $\hat{\theta}^*$ has bootstrap distribution $N(\hat{\theta}, \hat{\sigma}^2)$. In this case the standard method and the percentile method agree, $\theta_S[\alpha] = \theta_P[\alpha]$. In situations like that of Fig. 2, where $\hat{G}$ is markedly nonnormal, the standard interval is quite different from (7.2). Which is better?

To answer this question, consider the simplest possible situation, where for all θ

$$\hat{\theta} \sim N(\theta, \sigma^2). \tag{7.5}$$

That is, we have a single unknown parameter θ with no nuisance parameters, and a single summary statistic $\hat{\theta}$ normally distributed about θ with constant standard error σ. In this case the parametric bootstrap cdf is given by (7.4), so $\theta_S[\alpha] = \theta_P[\alpha]$. (The bootstrap estimate $\hat{\sigma}$ equals σ.)

Suppose though that instead of (7.5) we have, for all θ,

$$\hat{\phi} \sim N(\phi, \tau^2), \tag{7.6}$$

for some monotone transformation $\hat{\phi} = g(\hat{\theta})$, $\phi = g(\theta)$, where τ is a constant. In the correlation coefficient example the function g was $\tanh^{-1}$. The standard limits (7.2) can now be grossly inaccurate. However it is easy to verify that the percentile limits (7.2) are still correct. "Correct" here means that (7.2) is the mapping of the obvious interval for ϕ, $\hat{\phi} \pm \tau z^{(\alpha)}$, back to the θ scale, $\theta_P[\alpha] = g^{-1}(\hat{\phi} + \tau z^{(\alpha)})$. It is also correct in the sense of having exactly the claimed converge probability $1-2\alpha$.

Another way to state things is that the percentile intervals are transformation invariant,

$$\phi_P[\alpha] = g(\theta_P[\alpha]) \tag{7.7}$$

for any monotone transformation g. This implies that if the percentile intervals are correct on some transformed scale $\phi = g(\theta)$, then they must also be correct on the original scale θ. The statistician does not need to know the normalizing transformation g, only that it exists. Definition (7.2) automatically takes care of the bookkeeping involved in the use of normalizing transformations for confidence intervals.

Fisher's theory of maximum likelihood estimation says that we are always in situation (7.5) to a first order of asymptotic approximation. However, we are also in situation (7.6), for any choice of g, to the same order of approximation. Efron (1984 and 1985) uses higher order asymptotic theory to differentiate between the standard and bootstrap intervals. It is the higher order asymptotic terms which often make exact intervals strongly asymmetric about the MLE $\hat{\theta}$ as in Table 5. The bootstrap intervals are effective at capturing this asymmetry.

The percentile method automatically incorporates normalizing transformations, as in going from (7.5)–(7.6). It turns out that there are two other important ways that assumption (7.5) can be misleading, the first of which relates to possible bias in $\hat{\theta}$. For example consider $f_\theta(\hat{\theta})$, the family of densities for the observed correlation coefficient $\hat{\theta}$ when sampling $n = 15$ times from a bivariate normal distribution with true corre-

TABLE 6

Four methods of setting approximate confidence intervals for a real valued parameter θ

Method	Abbreviation	α level endpoint	Correct if	
1. Standard	$\theta_S[\alpha]$	$\hat{\theta} + \hat{\sigma}z^{(\alpha)}$	$\hat{\theta} \sim N(\theta, \sigma^2)$	σ constant
			There exists monotone transformation $\hat{\phi} = g(\hat{\theta})$, $\phi = g(\theta)$ such that:	
2. Percentile	$\theta_P[\alpha]$	$\hat{G}^{-1}(\alpha)$	$\hat{\phi} \sim N(\phi, \tau^2)$	τ constant
3. Bias-corrected	$\theta_{BC}[\alpha]$	$\hat{G}^{-1}(\Phi\{2z_0 + z^{(\alpha)}\})$	$\hat{\phi} \sim N(\phi - z_0\tau, \tau^2)$	z_0, τ constant
4. BC$_a$	$\theta_{BC_a}[\alpha]$	$\hat{G}^{-1}\left(\Phi\left\{z_0 + \frac{(z_0 + z^{(\alpha)})}{1 - a(z_0 + z^{(\alpha)})}\right\}\right)$	$\hat{\phi} \sim N(\phi - z_0\tau_\phi, \tau_\phi^2)$ where $\tau_\phi = 1 + a\phi$	z_0, a constant

Note: Each method is correct under more general assumptions than its predecessor. Methods 2, 3, and 4 are defined in terms of the percentiles of $\hat{G}$, the bootstrap distribution (7.1).

lation θ. In fact it is easy to see that no monotone mapping $\hat{\phi} = g(\hat{\theta})$, $\phi = g(\theta)$ transforms this family to $\hat{\phi} \sim N(\phi, \tau^2)$, as in (7.6). If there were such a g, then $\text{Prob}_\theta\{\hat{\theta} < \theta\} = \text{Prob}_\phi\{\hat{\phi} < \phi\} = .50$, but for $\theta = .776$ integrating the density function $f_{.776}(\hat{\theta})$ gives $\text{Prob}_{\theta=.776}\{\hat{\theta} < \theta\} = .431$.

The *bias-corrected percentile method* (BC method), line 3 of Table 6, makes an adjustment for this type of bias. Let

$$z_0 = \Phi^{-1}\{\hat{G}(\hat{\theta})\}, \tag{7.8}$$

where Φ^{-1} is the inverse function of the standard normal cdf. The BC method has α level endpoint

$$\theta_{\text{BC}}[\alpha] = \hat{G}^{-1}(\Phi\{2z_0 + z^{(\alpha)}\}). \tag{7.9}$$

Note: if $\hat{G}(\hat{\theta}) = .50$, that is if half of the bootstrap distribution of $\hat{\theta}^*$ is less than the observed value $\hat{\theta}$, then $z_0 = 0$ and $\theta_{\text{BC}}[\alpha] = \theta_P[\alpha]$. Otherwise definition (7.9) makes a bias correction.

Section 10.7 of Efron (1982a) shows that the BC interval for θ is exactly correct if

$$\hat{\phi} \sim N(\phi - z_0\tau, \tau^2) \tag{7.10}$$

for some monotone transformation $\hat{\phi} = g(\hat{\theta})$, $\phi = g(\theta)$ and some constant z_0. It does not look like (7.10) is much more general than (7.6), but in fact the bias correction is often important.

In the example of Table 5, the percentile method (7.2) gives central 90% interval [.536, .911] compared to the BC interval [.488, .900] and the exact interval [.496, .898]. By definition the endpoints of the exact interval satisfy

$$\begin{aligned} \text{Prob}_{\theta=.496}\{\hat{\theta} > .776\} &= .05 \\ &= \text{Prob}_{\theta=.898}\{\hat{\theta} < .776\}. \end{aligned} \tag{7.11}$$

The corresponding quantities for the BC endpoints are

$$\begin{aligned} \text{Prob}_{\theta=.488}\{\hat{\theta} > .776\} &= .0465, \\ \text{Prob}_{\theta=.900}\{\hat{\theta} < .776\} &= .0475, \end{aligned} \tag{7.12}$$

compared to

$$\begin{aligned} \text{Prob}_{\theta=.536}\{\hat{\theta} > .776\} &= .0725, \\ \text{Prob}_{\theta=.911}\{\hat{\theta} < .776\} &= .0293. \end{aligned} \tag{7.13}$$

for the percentile endpoints. The bias correction is quite important in equalizing the error probabilities at the two endpoints. If z_0 can be approximated accurately (as mentioned in Section 9), then it is preferable to use the BC intervals.

Table 7 shows a simple example where the BC method is less successful. The data consists of the single observation $\hat{\theta} \sim \theta(\chi^2_{19}/19)$, the notation indicating an unknown scale parameter θ times a random variable with distribution $\chi^2_{19}/19$. (This definition makes $\hat{\theta}$ unbiased for θ.) A confidence interval is desired for the scale parameter θ. In this case the BC interval based on $\hat{\theta}$ is a definite improvement over the standard interval (1.7), but goes only about half as far as it should toward achieving the asymmetry of the exact interval.

TABLE 7

Central 90% confidence intervals for θ having observed $\hat{\theta} \sim \theta(\chi^2_{19}/19)$

1. Exact	$[.631 \cdot \hat{\theta}, 1.88 \cdot \hat{\theta}]$	R/L = 2.38
2. Standard (1.7)	$[.466 \cdot \hat{\theta}, 1.53 \cdot \hat{\theta}]$	R/L = 1.00
3. BC (7.9)	$[.580 \cdot \hat{\theta}, 1.69 \cdot \hat{\theta}]$	R/L = 1.64
4. BC$_a$ (7.15)	$[.630 \cdot \hat{\theta}, 1.88 \cdot \hat{\theta}]$	R/L = 2.37
5. Nonparametric BC$_a$	$[.640 \cdot \hat{\theta}, 1.68 \cdot \hat{\theta}]$	R/L = 1.88

Note: The exact interval is sharply skewed to the right of $\hat{\theta}$. The BC method is only a partial improvement over the standard interval. The BC$_a$ interval, $a = .108$, agrees almost perfectly with the exact interval.

It turns out that the parametric family $\hat{\theta} \sim \theta(\chi^2_{19}/19)$ cannot be transformed into (7.10), not even approximately. The results of Efron (1982b) show that there does exist a monotone transformation g such that $\hat{\phi} = g(\hat{\theta})$, $\phi = g(\theta)$ satisfy to a high degree of approximation

$$\hat{\phi} \sim N(\phi - z_0\tau_\phi, \tau_\phi^2) \quad (\tau_\phi = 1 + a\phi). \tag{7.14}$$

The constants in (7.14) are $z_0 = .1082$, $a = .1077$.

The BC$_a$ method (Efron, 1984), line 4 of Table 6, is a method of assigning bootstrap confidence intervals which are exactly right for problems which can be mapped into form (7.14). This method has α level endpoint

$$\theta_{\text{BC}_a}[\alpha] = \hat{G}^{-1}\left(\Phi\left\{z_0 + \frac{z_0 + z^{(\alpha)}}{1 - a(z_0 + z^{(\alpha)})}\right\}\right). \tag{7.15}$$

If $a = 0$ then $\theta_{\text{BC}_a}[\alpha] = \theta_{\text{BC}}[\alpha]$, but otherwise the BC$_a$ intervals can be a substantial improvement over the BC method as shown in Table 7.

The constant z_0 in (7.15) is given by $z_0 = \Phi^{-1}\{\hat{G}(\hat{\theta})\}$, (7.8), and so can be computed directly from the bootstrap distribution. How do we know a? It turns out that in one-parameter families $f_\theta(\hat{\theta})$, a good approximation is

$$a \doteq \frac{\text{SKEW}_{\theta=\hat{\theta}}(\dot{l}_\theta(t))}{6}, \tag{7.16}$$

where $\text{SKEW}_{\theta=\hat{\theta}}(\dot{l}_\theta(t))$ is the skewness at parameter value $\theta = \hat{\theta}$ of the score statistic $\dot{l}_\theta(t) = (\partial/\partial\theta)\log f_\theta(t)$. For $\hat{\theta} \sim \theta(\chi^2_{19}/19)$ this gives $a \doteq .1081$, compared to the actual value $a = .1077$ derived in Efron (1984). For the normal theory correlation family of Table 5 $a \doteq 0$ which explains why the BC method, which takes $a = 0$, words so well there.

The advantage of formula (7.18) is that we need not know the transformation g leading to (7.14) in order to approximate a. In fact $\theta_{BC_a}[\alpha]$, like $\theta_{BC}[\alpha]$ and $\theta_P[\alpha]$, is transformation invariant, as in (7.7). Like the bootstrap methods, the BC_a intervals are computed directly from the form of the density function $f_\theta(\cdot)$, for θ near $\hat\theta$.

Formula (7.16) applies to the case where θ is the only parameter. Section 8 briefly discusses the more challenging problem of setting confidence intervals for a parameter θ in a multiparameter family, and also in nonparametric situations where the number of nuisance parameters is effectively infinite.

To summarize this section, the progression from the standard intervals to the BC_a method is based on a series of increasingly less restrictive assumptions, as shown in Table 6. Each successive method in Table 6 requires the statistician to do a greater amount of computation: first the bootstrap distribution $\hat G$, then the bias correction constant z_0, and finally the constant a. However, all of these computations are algorithmic in character, and can be carried out in an automatic fashion.

Chapter 10 of Efron (1982a) discusses several other ways of using the bootstrap to construct approximate confidence intervals, which will not be presented here. One of these methods, the "bootstrap t," was used in the blood serum example of Section 4.

8. NONPARAMETRIC AND MULTIPARAMETER CONFIDENCE INTERVALS

Section 7 focused on the simple case $\hat\theta \sim f_\theta$, where we have only a real valued parameter θ and a real valued summary statistic $\hat\theta$ from which we are trying to construct a confidence interval for θ. Various favorable properties of the bootstrap confidence intervals were demonstrated in the simple case, but of course the simple case is where we least need a general method like the bootstrap.

Now we will discuss the more common situation where there are nuisance parameters besides the parameter of interest θ; or even more generally the nonparametric case, where the number of nuisance parameters is effectively infinite. The discussion is limited to a few brief examples. Efron (1984 and 1985) develops the theoretical basis of bootstrap approximate confidence intervals for complicated situations, and gives many more examples. The word "approximate" is important here since exact nonparametric confidence intervals do not exist for most parameters (see Bahadur and Savage, 1956).

Example 1. Ratio Estimation

The data consists of $\mathbf{y} = (y_1, y_2)$, assumed to come from a bivariate normal distribution with unknown mean vector η and covariance matrix the identity,

$$\mathbf{y} \sim N_2(\eta, I). \tag{8.1}$$

TABLE 8

Central 90% confidence intervals for $\theta = \eta_2/\eta_1$ and for $\phi = 1/\theta$ having observed $(y_1, y_2) = (8, 4)$ from a bivariate normal distribution $\mathbf{y} \sim N_2(\eta, I)$

	For θ	For ϕ
1. Exact (Fieller)	[.29, .76]	[1.32, 3.50]
2. Parametric boot (BC)	[.29, .76]	[1.32, 3.50]
3. Standard (1.7)	[.27, .73]	[1.08, 2.92]
MLE	$\hat\theta = .5$	$\hat\phi = 2$

Note: The BC intervals, line 2, are based on the parametric bootstrap distribution of $\hat\theta = y_2/y_1$.

The parameter of interest, for which we desire a confidence interval, is the ratio

$$\theta = \eta_2/\eta_1. \tag{8.2}$$

Fieller (1954) provided well known exact intervals for θ in this case. The Fieller intervals are based on a clever trick, which seems very special to situation (8.1), (8.2).

Table 8 shows Fieller's central 90% interval for θ having observed $\mathbf{y} = (8, 4)$. Also shown is the Fieller interval for $\phi = 1/\theta = \eta_1/\eta_2$, which equals $[.76^{-1}, .29^{-1}]$, the obvious transformation of the interval for θ. The standard interval (1.7) is satisfactory for θ, but not for ϕ. Notice that the standard interval does not transform correctly from θ to ϕ.

Line 2 shows the BC intervals based on applying definitions (7.8) and (7.9) to the parametric bootstrap distribution of $\hat\theta = y_2/y_1$ (or $\hat\phi = y_1/y_2$). This is the distribution of $\hat\theta^* = y_2^*/y_1^*$ when sampling $\mathbf{y}^* = (y_1^*, y_2^*)$ from $\hat F_{\text{NORM}} \sim N_2((y_1, y_2), I)$. The bootstrap intervals transform correctly, and in this case they agree with the exact interval to three decimal places.

Example 2. Product of Normal Means

For most multiparameter situations, there do not exist exact confidence intervals for a single parameter of interest. Suppose for instance that (8.2) is changed to

$$\theta = \eta_1\eta_2, \tag{8.3}$$

still assuming (8.1). Table 9 shows approximate intervals for θ, and also for $\phi = \theta^2$, having observed $\mathbf{y} = (2, 4)$. The "almost exact" intervals are based on an analog of Fieller's argument (Efron, 1985), which with suitable care can be carried through to a high degree of accuracy. Once again, the parametric BC intervals are a close match to line 1. The fact that the standard intervals do not transform correctly is particularly obvious here.

TABLE 9

Central 90% confidence intervals for $\theta = \eta_1\eta_2$ and $\phi = \theta^2$ having observed $\mathbf{y} = (2, 4)$, where $\mathbf{y} \sim N_2(\eta, I)$

	For θ	For ϕ
1. Almost exact	[1.77, 17.03]	[3.1, 290.0]
2. Parametric boot (BC)	[1.77, 17.12]	[3.1, 239.1]
3. Standard (1.7)	[0.64, 15.36]	[−53.7, 181.7]
MLE	$\hat{\theta} = 8$	$\hat{\phi} = 64$

Note: The almost exact intervals are based on the high order approximation theory of Efron (1985). The BC intervals of line 2 are based on the parametric bootstrap distribution of $\hat{\theta} = y_1 y_2$.

The good performance of the parametric BC intervals is not accidental. The theory developed in Efron (1985) shows that the BC intervals, based on bootstrapping the MLE $\hat{\theta}$, agree to high order with the almost exact intervals in the following class of problems: the data $\mathbf{y}$ comes from a multiparameter family of densities $f_\eta(\mathbf{y})$, both $\mathbf{y}$ and η k-dimensional vectors; the real valued parameter of interest θ is a smooth function of η, $\theta = t(\eta)$; and the family $f_\eta(\mathbf{y})$ can be transformed to multivariate normality, say

$$(8.4) \qquad g(\mathbf{y}) \sim N_k(h(\eta), I),$$

by some one-to-one transformations g and h.

Just as in Section 7, it is not necessary for the statistician to know the normalizing transformations g and h, only that they exist. The BC intervals are obtained directly from the original densities f_η: we find $\hat{\eta} = \hat{\eta}(\mathbf{y})$, the MLE of η; sample $\mathbf{y}^* \sim f_{\hat{\eta}}$; compute $\hat{\theta}^*$, the bootstrap MLE of θ; calculate $\hat{G}$, the bootstrap cdf of $\hat{\theta}^*$, usually by Monte Carlo sampling, and finally apply definitions (7.8) and (7.9). This process gives the same interval for θ whether or not the transformation to form (8.4) has been made.

Not all problems can be transformed as in (8.4) to a normal distribution with constant covariance. The case considered in Table 7 is a one-dimensional counter example. As a result the BC intervals do not always work as well as in Tables 8 and 9, although they usually improve on the standard method. However, in order to take advantage of the BC_a method, which is based on more general assumptions, we need to be able to calculate the constant a.

Efron (1984) gives expressions for "a" generalizing (7.16) to multiparameter families, and also to nonparametric situations. If (8.4) holds, then "a" will have value zero, and the BC_a method reduces to the BC case. Otherwise the two intervals differ.

Here we will discuss only the nonparametric situation: the observed data $\mathbf{y} = (x_1, x_2, \cdots, x_n)$ consists of iid observations $X_1, X_2, \cdots, X_n \sim F$, where F can be *any* distribution on the sample space $\mathscr{X}$; we want a confidence interval for $\theta = t(F)$, some real valued functional of F; and the bootstrap interval are based on bootstrapping $\hat{\theta} = t(\hat{F})$, which is the nonparametric MLE of θ. In this case a good approximation to the constant c is given in terms of the empirical influence function U_i^0, defined in Section 10 at (10.11).

$$(8.5) \qquad a \doteq \frac{1}{6} \frac{\sum_{i=1}^n (U_i^0)^3}{\{\sum_{i=1}^n (U_i^0)^2\}^{3/2}}.$$

This is a convenient formula, since it is easy to numerically evaluate the U_i^0 by simply substituting a small value of θ into (10.11).

Example 3. The Law School Data

For $\hat{\theta}$ the correlation coefficient, the values of U_i^0 corresponding to the 15 data points shown in Fig. 1 are −1.507, .168, .273, .004, .525, −.049, −.100, .477, .310, .004, −.526, −.091, .434, .125, −.048. (Notice how influential law school 1 is.) Formula (8.5) gives $a \doteq -.0817$. $B = 100{,}000$ bootstrap replications, about 100 times more than was actually necessary (see Section 10), gave $z_0 = -.0927$, and the central 90% interval $\theta \in [.43, .92]$ shown in Table 5. The nonparametric BC_a interval is quite reasonable in this example, particularly considering that there is no guarantee that the true law school distribution F is anywhere near bivariate normal.

Example 4. Mouse Leukemia Data (the First Example in Section 3)

The standard central 90% interval for β in formula (3.1) is [.835, 2.18]. The bias correction constant $z_0 \doteq .0275$, giving BC interval [1.00, 2.39]. This is shifted far right of the standard interval, reflecting the long right tail of the bootstrap histogram seen in Fig. 3. We can calculate "a" from (8.5), considering each of the $n = 42$ data points to be a triple (y_i, x_i, δ_i): $a \doteq -.152$. Because a is negative, the BC_a interval is shifted back to the left, equaling [.788, 2.10]. This contrasts with the law school example, where a, z_0, and the skewness of the bootstrap distribution added to each other rather than cancelling out, resulting in a BC_a interval much different from the standard interval.

Efron (1984) provides some theoretical support for the nonparametric BC_a method. However the problem of setting approximate nonparametric confidence intervals is still far from well understood, and all methods should be interpreted with some caution. We end this section with a cautionary example.

Example 5. The Variance

Suppose $\mathscr{X}$ is the real line, and $\theta = \mathrm{Var}_F X$, the variance. Line 5 of Table 2 shows the result of applying the nonparametric BC_a method to data sets $x_1, x_2, \cdots, x_{20}$ which were actually iid samples from a $N(0, 1)$ distribution. The number .640 for example is the average of $\hat{\theta}_{BC}[.05]/\hat{\theta}$ over 40 such data sets. $B = 4000$ bootstrap replications per data set. The upper limit $1.68 \cdot \hat{\theta}$ is noticeably small, as pointed out by Schenker (1985). The reason is simple: the nonparametric bootstrap distribution of $\hat{\theta}^*$ has a short upper tail, compared to the parametric bootstrap distribution which is a scaled χ^2_{19} random variable. The results of Beran (1984), Bickel and Freedman (1981), and Singh (1981) show that the nonparametric bootstrap distribution is highly accurate asymptotically, but of course that is not a guarantee of good small sample behavior. Bootstrapping from a smoothed version of $\hat{F}$, as in lines 3, 4, and 5 of Table 2 alleviates the problem in this particular example.

9. BOOTSTRAP SAMPLE SIZES

How many bootstrap replications must we take? Consider the standard error estimate $\hat{\sigma}_B$ based on B bootstrap replications, (2.4). As $B \to \infty$, $\hat{\sigma}_B$ approaches $\hat{\sigma}$, the bootstrap estimate of standard error as originally defined in (2.3). Because $\hat{F}$ does not estimate F perfectly, $\hat{\sigma} = \sigma(\hat{F})$ will have a non-zero coefficient of variation for estimating the true standard error $\sigma = \sigma(F)$; $\hat{\sigma}_B$ will have a larger CV because of the randomness added by the Monte Carlo bootstrap sampling.

It is easy to derive the following approximation,

$$\text{(9.1)} \qquad \mathrm{CV}(\hat{\sigma}_B) \doteq \left\{ \mathrm{CV}(\hat{\sigma})^2 + \frac{E\{\hat{\delta}\} + 2}{4B} \right\}^{1/2},$$

where $\hat{\delta}$ is the kurtosis of the bootstrap distribution of $\hat{\theta}^*$, given the data $\mathbf{y}$, and $E\{\hat{\delta}\}$ its expected value averaged over $\mathbf{y}$. For typical situations, $\mathrm{CV}(\hat{\sigma})$ lies between .10 and .30. For example, if $\hat{\theta} = \bar{x}$, $n = 20$, $x_i \sim_{\text{iid}} N(0, 1)$, then $\mathrm{CV}(\hat{\sigma}) \doteq .16$.

Table 10 shows $\mathrm{CV}(\hat{\sigma}_B)$ for various values of B and $\mathrm{CV}(\hat{\sigma})$, assuming $E\{\hat{\delta}\} = 0$ in (9.1). For values of $\mathrm{CV}(\hat{\sigma}) > .10$, *there is little improvement past* $B = 100$. In fact B as small as 25 gives reasonable results. Even smaller values of B can be quite informative, as we saw in the Stanford Heart Transplant Data (Fig. 7 of Section 3).

TABLE 10

Coefficient of variation of $\hat{\sigma}_B$, the bootstrap estimate of standard error based on B Monte Carlo replications, as a function of B and $\mathrm{CV}(\hat{\sigma})$, the limiting CV as $B \to \infty$

		$B \to$				
		25	50	100	200	∞
$\mathrm{CV}(\hat{\sigma})$	.25	.29	.27	.26	.25	.25
↓	.20	.24	.22	.21	.21	.20
	.15	.21	.18	.17	.16	.15
	.10	.17	.14	.12	.11	.10
	.05	.15	.11	.09	.07	.05
	0	.14	.10	.07	.05	0

Note: Based on (9.1), assuming $E\{\hat{\delta}\} = 0$.

The situation is quite different for setting bootstrap confidence intervals. The calculations of Efron (1984), Section 8, show that $B = 1000$ is a rough minimum for the number of Monte Carlo bootstraps necessary to compute the BC or BC_a intervals. Somewhat smaller values, say $B = 250$, can give a useful percentile interval, the difference being that then the constant z_0 need not be computed. Confidence intervals are a fundamentally more ambitious measure of statistical accuracy than standard errors, so it is not surprising that they require more computational effort.

10. THE JACKKNIFE AND THE DELTA METHOD

This section returns to the simple case of assigning a standard error to $\hat{\theta}(\mathbf{y})$, where $\mathbf{y} = (x_1, \cdots, x_n)$ is obtained by random sampling from a single unknown distribution, $X_1, \cdots, X_n \sim_{\text{iid}} F$. We will give another description of the bootstrap estimate $\hat{\sigma}$, which illustrates the bootstrap's relationship to older techniques of assigning standard errors, like the jackknife and the delta method.

For a given bootstrap sample $\mathbf{y}^* = (x_1^*, \cdots, x_n^*)$, as described in step (i) of the algorithm in Section 2, let p_i^* indicate the proportion of the bootstrap sample equal to x_i,

$$\text{(10.1)} \qquad p_i^* = \frac{\#\{x_j^* = x_i\}}{n} \qquad i = 1, 2, \cdots, n,$$

$\mathbf{p}^* = (p_1^*, p_2^*, \cdots, p_n^*)$. The vector $\mathbf{p}^*$ has a rescaled multinomial distribution

$$\text{(10.2)} \qquad \begin{aligned} &\mathbf{p}^* \sim \mathrm{Mult}_n(n, \mathbf{p}^0)/n \\ &\qquad (\mathbf{p}^0 = (1/n, 1/n, \cdots, 1/n)), \end{aligned}$$

where the notation indicates the proportions observed from n random draws on n categories, each with probability $1/n$.

For $n = 3$ there are 10 possible bootstrap vectors $\mathbf{p}^*$. These are indicated in Fig. 15 along with their multinomial probabilities from (10.2). For example, $\mathbf{p}^* = (1/3, 0, 2/3)$, corresponding to $\mathbf{x}^* = (x_1, x_3, x_3)$ or any permutation of these values has bootstrap probability 1/9.

To make our discussion easier suppose that the statistic of interest $\hat{\theta}$ is of functional form: $\hat{\theta} = \theta(\hat{F})$, where $\theta(F)$ is a functional assigning a real number to any distribution F on the sample space $\mathcal{X}$. The mean, the correlation coefficient, and the trimmed mean are all of functional form. Statistics of functional form have the same value as a function of $\hat{F}$, no matter what the sample size n may be, which is convenient for discussing the jackknife and delta method.

For any vector $\mathbf{p} = (p_1, p_2, \cdots, p_n)$ having nonnegative weights summing to 1, define the weighted

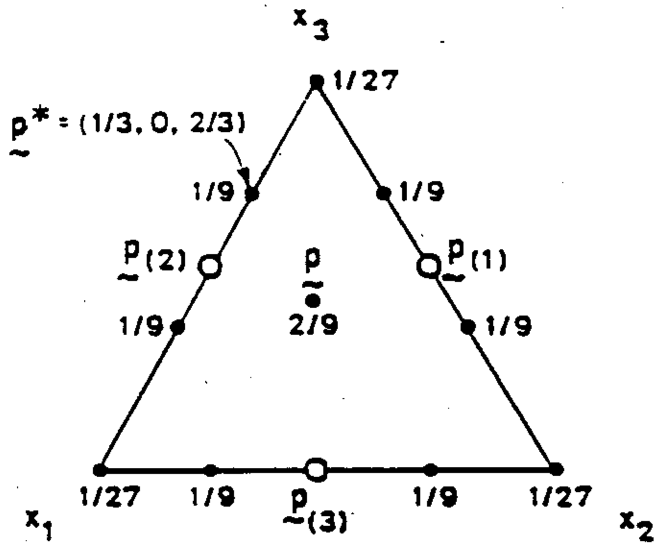

FIG. 15. *The bootstrap and jackknife sampling points in the case $n = 3$. The bootstrap points $(\cdot)$ are shown with their probabilities.*

empirical distribution

(10.3) $\hat{F}(\mathbf{p})$: probability p_i on x_i $\quad i = 1, \cdots, n$.

For $\mathbf{p} = \mathbf{p}^0 = 1/n$, the weighted empirical distribution equals $\hat{F}$, (1.4).

Corresponding to $\mathbf{p}$ is a resampled value of $\hat{\theta}$,

$$\hat{\theta}(\mathbf{p}) = \theta(\hat{F}(\mathbf{p})). \tag{10.4}$$

The shortened notation $\hat{\theta}(\mathbf{p})$ assumes that the data $(x_1, x_2, \cdots, x_n)$ is considered fixed. Notice that $\hat{\theta}(\mathbf{p}^0) = \theta(\hat{F})$ is the observed value of the statistic of interest. The bootstrap estimate $\hat{\sigma}$, (2.3), can then be written

$$\hat{\sigma} = [\mathrm{var}_* \hat{\theta}(\mathbf{p}^*)]^{1/2}, \tag{10.5}$$

where var_* indicates variance with respect to distribution (10.2). In terms of Fig. 15, $\hat{\sigma}$ is the standard deviation of the ten possible bootstrap values $\hat{\theta}(\mathbf{p}^*)$ weighted as shown.

It looks like we could always calculate $\hat{\sigma}$ simply by doing a finite sum. Unfortunately, the number of bootstrap points is $\binom{2n-1}{n}$, 77,558,710 for $n = 15$ so straightforward calculation of $\hat{\sigma}$ is usually impractical. That is why we have emphasized Monte Carlo approximations to $\hat{\sigma}$. Therneau (1983) considers the question of methods more efficient than pure Monte Carlo, but at present there is no generally better method available.

However, there is another approach to approximating (10.5). We can replace the usually complicated function $\hat{\theta}(\mathbf{p})$ by an approximation linear in $\mathbf{p}$, and then use the well known formula for the multinomial variance of a linear function. The *jackknife approximation* $\hat{\theta}_J(\mathbf{p})$ is the linear function of $\mathbf{p}$ which matches $\hat{\theta}(\mathbf{p})$, (10.4), at the n points corresponding to the deletion of a single $\mathbf{x}_i$ from the observed data set $x_1, x_2, \cdots, x_n$,

$$\mathbf{p}_{(i)} = \frac{1}{n-1}(1, 1, \cdots, 1, 0, 1, \cdots, 1) \tag{10.6}$$

$i = 1, 2, \cdots, n$. Fig. 15 indicates the jackknife points for $n = 3$; because $\hat{\theta}$ is the functional form, (10.4), it does not matter that the jackknife points correspond to sample size $n - 1$ rather than n.

The linear function $\hat{\theta}_J(\mathbf{p})$ is calculated to be

$$\hat{\theta}_J(\mathbf{p}) = \hat{\theta}_{(\cdot)} + (\mathbf{p} - \mathbf{p}^0) \cdot \mathbf{U} \tag{10.7}$$

where, in terms of $\hat{\theta}_{(i)} = \hat{\theta}(\mathbf{p}_{(i)})$, $\hat{\theta}_{(\cdot)} = \sum_{i=1}^n \hat{\theta}_{(i)}/n$, and $\mathbf{U}$ is the vector with ith coordinate

$$U_i = (n-1)(\hat{\theta}_{(\cdot)} - \hat{\theta}_{(i)}). \tag{10.8}$$

The jackknife estimate of standard error (Tukey, 1958; Miller, 1974) is

$$\hat{\sigma}_J = \left[\frac{n-1}{n}\sum_{i=1}^n \{\hat{\theta}_{(i)} - \hat{\theta}_{(\cdot)}\}^2\right]^{1/2} = \left[\frac{\sum_1^n U_i^2}{n(n-1)}\right]^{1/2}. \tag{10.9}$$

A standard multinomial calculation gives the following theorem (Efron, 1982a),

THEOREM. *The jackknife estimate of standard error equals $[n/(n-1)]^{1/2}$ times the bootstrap estimate of standard error for $\hat{\theta}_J$,*

$$\hat{\sigma}_J = \left[\frac{n}{n-1}\mathrm{var}_* \hat{\theta}_J(\mathbf{p}^*)\right]^{1/2}. \tag{10.10}$$

In other words, the jackknife estimate is itself almost a bootstrap estimate applied to a linear approximation of $\hat{\theta}$. The factor $[n/(n-1)]^{1/2}$ in (10.10) makes $\hat{\sigma}_J^2$ unbiased for σ^2 in the case where $\hat{\theta} = \bar{x}$, the sample mean. We could multiply the bootstrap estimate $\hat{\sigma}$ by this same factor, and achieve the same unbiasedness, but there does not seem to be any consistent advantage to doing so. The jackknife requires n, rather than $B =$ 50 to 200 resamples, at the expense of adding a linear approximation to the standard error estimate. Tables 1 and 2 indicate that there is some estimating efficiency lost in making this approximation. For statistics like the sample median which are difficult to approximate linearly, the jackknife is useless (see Section 3.4 of Efron, 1982a).

There is a more obvious linear approximation to $\hat{\theta}(\mathbf{p})$ than $\hat{\theta}_J(\mathbf{p})$. Why not use the first-order Taylor series expansion for $\hat{\theta}(\mathbf{p})$ about the point $\mathbf{p} = \mathbf{p}^0$? This is the idea of Jaeckel's *infinitesimal jackknife* (1972). The Taylor series approximation turns out to be

$$\hat{\theta}_T(\mathbf{p}) = \hat{\theta}(\mathbf{p}^0) + (\mathbf{p} - \mathbf{p}^0)'\mathbf{U}^0$$

where

$$U_i^0 = \lim_{\epsilon \to 0} \frac{\hat{\theta}((1-\epsilon)\mathbf{p}^0 + \epsilon\delta_i) - \hat{\theta}(\mathbf{p}^0)}{\epsilon}, \tag{10.11}$$

δ_i being the ith coordinate vector. This suggests the infinitesimal jackknife estimate of standard error

$$\hat{\sigma}_{IJ} \equiv [\text{var}_* \hat{\theta}_T(\mathbf{p}^*)]^{1/2} = [\Sigma U_i^{0 2}/n^2]^{1/2} \tag{10.12}$$

with var_* still indicating variance under (10.2). The ordinary jackknife can be thought of as taking $\varepsilon = -1/(n-1)$ in the definition of U_i^0, while the infinitesimal jackknife lets $\varepsilon \longrightarrow 0$, thereby earning the name.

The U_i^0 are values of what Mallows (1974) calls the empirical influence function. Their definition is a nonparametric estimate of the true influence function

$$IF(x) = \lim_{\varepsilon \to 0} \frac{\theta((1-\varepsilon)F + \varepsilon\delta_x) - \theta(F)}{\varepsilon},$$

δ_x being the degenerate distribution putting mass 1 on x. The right side of (10.12) is then the obvious estimate of the influence function approximation to the standard error of $\hat{\theta}$ (Hampel, 1974), $\sigma(F) \doteq [\int IF^2(x)\, dF(x)/n]^{1/2}$. The empirical influence function method and the infinitesimal jackknife give identical estimates of standard error.

How have statisticians gotten along for so many years without methods like the jackknife and the bootstrap? The answer is the delta method, which is still the most commonly used device for approximating standard errors. The method applies to statistics of the form $t(\bar{Q}_1, \bar{Q}_2, \cdots, \bar{Q}_A)$, where $t(\cdot, \cdot, \cdots, \cdot)$ is a known function and each $\bar{Q}_a$ is an observed average, $\bar{Q}_a = \sum_{i=1}^n Q_a(X_i)/n$. For example, the correlation $\hat{\theta}$ is a function of $A = 5$ such averages; the average of the first coordinate values, the second coordinates, the first coordinates squared, the second coordinates squared, and the cross-products.

In its nonparametric formulation, the delta method works by (a) expanding t in a linear Taylor series about the expectations of the $\bar{Q}_a$; (b) evaluating the standard error of the Taylor series using the usual expressions for variances and covariances of averages; and (c) substituting $\gamma(\hat{F})$ for any unknown quantity $\gamma(F)$ occurring in (b). For example, the nonparametric delta method estimates the standard error of the correlation $\hat{\theta}$ by

$$\left\{\frac{\hat{\theta}^2}{4n}\left[\frac{\hat{\mu}_{40}}{\hat{\mu}_{20}^2} + \frac{\hat{\mu}_{04}}{\hat{\mu}_{02}^2} + \frac{2\hat{\mu}_{22}}{\hat{\mu}_{20}\hat{\mu}_{02}} + \frac{4\hat{\mu}_{22}}{\hat{\mu}_{11}^2} - \frac{4\hat{\mu}_{31}}{\hat{\mu}_{11}\hat{\mu}_{02}} + \frac{4\hat{\mu}_{13}}{\hat{\mu}_{11}\hat{\mu}_{02}}\right]\right\}^{1/2}$$

where, in terms of $x_i = (y_i, z_i)$,

$$\hat{\mu}_{gh} \equiv \Sigma(y_i - \bar{y})^g(z_i - \bar{z})^h/n$$

(Cramér (1946), p. 359).

THEOREM. *For statistics of the form $\hat{\theta} = t(\bar{Q}_1, \cdots, \bar{Q}_A)$, the nonparametric delta method and the infinitesimal jackknife give the same estimate of standard error* (Efron, 1982c).

The infinitesimal jackknife, the delta method, and the empirical influence function approach are three names for the same method. Notice that the results reported in line 7 of Table 2 show a severe downward bias. Efron and Stein (1981) show that the ordinary jackknife is always biased upward, in a sense made precise in that paper. In the authors' opinion the ordinary jackknife is the method of choice if one does not want to do the bootstrap computations.

ACKNOWLEDGMENT

This paper is based on a previous review article appearing in *Behaviormetrika*. The authors and Editor are grateful to that journal for graciously allowing this revision to appear here.

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Comment

J. A. Hartigan

Efron and Tibshirani are to be congratulated on a wide-ranging persuasive survey of the many uses of the boostrap technology. They are a bit cagey on what is or is not a bootstrap, but the description at the end of Section 4 seems to cover all the cases; some data y comes from an unknown probability distribution F; it is desired to estimate the distribution of some function $R(y, F)$ given F; and this is done by estimating the distribution of $R(y^*, \hat{F})$ given $\hat{F}$ where $\hat{F}$ is an estimate of F based on y, and y^* is sampled from the known $\hat{F}$.

There will be three problems in any application of the bootstrap: (1) how to choose the estimate $\hat{F}$? (2) how much sampling of y^* from $\hat{F}$? and (3) how close is the distribution of $R(y^*, \hat{F})$ given $\hat{F}$ to $R(y, F)$ given F?

Efron and Tibshirani suggest a variety of estimates $\hat{F}$ for simple random sampling, regression, and autoregression; their remarks about (3) are confined mainly to empirical demonstrations of the bootstrap in specific situations.

I have some general reservations about the bootstrap based on my experiences with subsampling techniques (Hartigan, 1969, 1975). Let $X_1, \ldots, X_n$ be a random sample from a distribution F, let F_n be the empirical distribution, and suppose that $t(F_n)$ is an estimate of some population parameter $t(F)$. The statistic $t(\hat{F}_n)$ is computed for several random subsamples (each observation appearing in the subsample with probability ½), and the set of $t(\hat{F}_n)$ values obtained is regarded as a sample from the posterior distribution of $t(F)$. For example, the standard deviation of the $t(\hat{F}_n)$ is an estimate of the standard error of $t(F_n)$ from $t(F)$; however, the procedure is not restricted to real valued t.

The procedure seems to work not too badly in getting at the first- and second-order behaviors of $t(F_n)$ when $t(F_n)$ is near normal, but it not effective in handling third-order behavior, bias, and skewness. Thus there is not much point in taking huge samples $t(\hat{F}_n)$ since the third-order behavior is not relevant; and if the procedure works only for $t(F_n)$ near normal, there are less fancy procedures for estimating standard error such as dividing the sample up into 10 subsamples of equal size and computing their standard deviation. (True, this introduces more bias than having random subsamples each containing about half the observations.) Indeed, even if $t(F_n)$ is not normal, we can obtain exact confidence intervals for the median of $t(F_{n/10})$ using the 10 subsamples. Even five subsamples will give a respectable idea of the standard error.

Transferring back to the bootstrap: (A) is the boot-

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strap effective for non-normal situations? (B) in the normal case, does the bootstrap give accurate assessment of third-order terms? If not, it is scarcely justified to do many bootstrap simulations, since you will only use them to estimate a variance. The asymptotic justifications of the bootstrap such as in Bickel and Freeman (1981) or Singh (1981) do consider behavior near the normal.

To be specific, consider the case where a statistic $t(F_n)$ estimates a parameter $t(F)$. The first kind of bootstrapping might be on the quantity $t(F_n) - t(F)$; to estimate its variance $\sigma^2(F)/n$ we compute repeatedly $t(\hat{F}_n) - t(F_n)$ where $\hat{F}_n$ is the empirical distribution of a sample of size n from F_n. Thus $\sigma^2(F_n)$ will be used to estimate $\sigma^2(F)$. We might hope that

$$t(F_n) = t(F) + \xi \frac{\sigma(F)}{\sqrt{n}} + O\left(\frac{1}{n}\right)$$

where $\xi \sim N(0, 1)$. This is the case referred to above where $t(F_n)$ is normal and numerous resampling estimates are available to estimate $\sigma^2(F)$. To do better, consider the higher order terms:

$$t(F_n) = t(F) + \xi \frac{\sigma(F)}{\sqrt{n}} + \frac{s_3(F)}{n} (\xi^2 - 1) + \frac{b(F)}{n} + O(n^{-3/2}).$$

Then

$$t(\hat{F}_n) = t(F_n) + \xi \frac{\sigma(F_n)}{\sqrt{n}} + \frac{s_3(F_n)}{n} (\xi^2 - 1) + \frac{b(F_n)}{n} + O(n^{-3/2}).$$

We might expect that the sample quantities $\sigma(F_n)$, $s_3(F_n)$; $b(F_n)$ are within $O(n^{-1/2})$ of the population quantities; but since $\sigma(F_n) - \sigma(F) = O(n^{-1/2})$, the error in approximating the distribution of $t(F_n) - t(F)$ by that of $t(\hat{F}_n) - t(F_n)$ is $O(n^{-1/2})$, so that the additional skewness and bias terms are of no interest:

$$P\left[(t(F_n) - t(F) \le \frac{a}{\sqrt{n}}\right] - P\left[t(\hat{F}_n) - t(F_n) \le \frac{a}{\sqrt{n}}\right] = O(n^{-1/2}).$$

The bootstrap distribution is no better than any normal approximation using an estimate of variance accurate to $O(n^{-1/2})$!

On the other hand, if

$$R(y, F) = [t(F_n) - t(F)]/\sigma(F),$$

$$[t(F_n) - t(F)]/\sigma(F) = \frac{\xi}{\sqrt{n}} + \frac{s_3'(F)}{n} (\xi^2 - 1) + \frac{b'(F)}{n} + O(n^{-3/2})$$

$$[t(\hat{F}_n) - t(F_n)]/\sigma(F_n) = \frac{\xi}{\sqrt{n}} + \frac{s_3'(F_n)}{n} (\xi^2 - 1) + \frac{b'(F_n)}{n} + O(n^{-3/2}).$$

Now $s_3'(F_n)$ estimates $s_3'(F)$ and $b'(F_n)$ estimates $b'(F)$ to within $O(n^{-1/2})$, and the Cornish-Fisher expansion is accurate to skewness and bias terms:

$$P\left(\frac{t(F_n) - t(F)}{\sigma(F)} \le \frac{a}{\sqrt{n}}\right) - P\left(\frac{t(\hat{F}_n) - t(F_n)}{\sigma(F_n)} \le \frac{a}{\sqrt{n}}\right) = O(n^{-1}).$$

These results are given for $t(F_n) = \bar{X}$ in Singh (1981).

The conclusion is that for $t(F_n)$ near normal there is no advantage for the bootstrap over other resampling methods, unless the pivotal $[t(F_n) - t(F)]/\sigma(F)$ is used. Usually $\sigma(F)$ is not known: that's why we are resampling in the first place. We would need to estimate it by bootstrapping and use the pivotal $(t(F_n) - t(F))/\sigma(F_n)$. And the distribution of this pivotal would be determined by bootstrapping to obtain $[t(\hat{F}_n) - t(F_n)]/\sigma(\hat{F}_n)$. Note that $\sigma(\hat{F}_n)$ requires two levels of bootstrapping; this might get close to Professor Efron's objective of soaking up all the spare cycles on the West Coast!

Let us consider the modest objective of estimating the variance of $t(F_n)$. The various resampling techniques compute the variance of $t(W^1)$, $t(W^2)$, ..., $t(W^k)$ where $t(W^j)$ denotes the statistic computed on X_i repeated W_i^j times, $1 \le i \le n$. What is a good choice of $W^1, W^2, \ldots, W^k$? If in fact $X_1, \ldots, X_n$ are sampled from $N(\mu, \sigma^2)$ and $t = \bar{X}$, a minimum variance unbiased estimate of σ^2 is obtained by setting $W_i^j = 1 + \sqrt{n}\xi_i^j$ where $\xi^1, \sigma^2, \ldots, \xi^k$ are any k orthonormal vectors orthogonal to 1. The quantities $\sqrt{n}\xi_i^j$ can be obtained roughly by sampling each of them independently from $N(0, 1)$. Bootstrap resampling, for large n, has W_i^j approximately independently Poisson with expectation 1. Random subsampling, for large n has W_i^j approximately independent and approximately taking values 0 and 2 with probability ½. The Dirichlet distribution for F given F_n produces weights W_i^j that are approximately exponential with expectation 1. Any resampling scheme in which the weights are approximately independent with mean and variance 1 will give the right expected variance, but the efficiency of the estimate (at normal means) is optimal for $W_i^* = 1 + \sqrt{n}\xi_i^*$.

For $n = 8$, obtain an efficient estimate from subsamples (1234), (1256), (1278), (1357), (1368), (1458), (1467); use as many as you need, and if $n > 8$ divide the sample into 8 groups as evenly as possible. I think it must be rare that the various approximations needed to connect the resampled computation to the computation of interest will be satisfied well enough to justify more than a few resamples. Perhaps this method might be called the *shoestring*.

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Rejoinder

B. Efron and R. Tibshirani

Professor Hartigan, who is one of the pioneers of resampling theory, raises the question of higher order accuracy. This question has bothered resamplers since the early days of the jackknife. Sections 7 and 8 of our paper show that the bootstrap can indeed achieve higher levels of accuracy, going the next step beyond simple estimates of standard error. The bootstrap confidence intervals we discuss are *not* of the crude (although useful) first-order form $\hat{\theta} \pm \hat{\sigma} z^{(\alpha)}$. They explicitly incorporate the higher order corrections about which Hartigan is legitimately concerned.

In particular the "z_0" term (7.8) is a correction for bias, and the acceleration constant "a," (7.16), is a correction for skewness. These correspond to Hartigan's $b(F)$ and $s_3(F)$, respectively. The reader who follows through Tables 5 and 7 will see these corrections in action. The fact that they produce highly accurate confidence intervals is no accident. The theory in Efron (1984a, 1984b) demonstrates higher order accuracy of the BC_a intervals in a wide class of situations. This demonstration does not yet apply to fully general problems, but current research indicates that it soon will. (The impressive higher order asymptotic results of Beran, Singh, Bickel, and Freedman, referred to in the paper, underpin these conclusions.)

It is worth mentioning that the bias and skewness corrections of the bootstrap confidence intervals are not of the simple "plug into an approximate pivotal" form suggested in Hartigan's remarks. The theory is phrased in a way which automatically corrects for arbitrary nonlinear transformations, even of the violent sort encountered in the correlation example of Table 5. In this sense the bootstrap theory does handle "non-normal situations."

Since this paper was written, research by several workers, including T. Hesterberg, R. Tibshirani, and T. DiCiccio, has substantially improved the computational outlook for bootstrap confidence intervals. It now appears possible that bootstrap sample sizes closer to $B = 100$ than $B = 1000$ may be sufficient for the task. However, these improvements are still in the process of development.

Professor Hartigan's last remarks, on the comparative efficiency of different resampling methods, need careful interpretation. There are two concepts of efficiency involved: the efficiency of the numerical algorithm in producing an estimate of variance, and the statistical efficiency of the estimate produced. There is no question that other resampling techniques, for example, the jackknife, can produce variance estimates more economically than does the bootstrap. We have argued, both by example and theory, that the bootstrap variance is generally more efficient as a statistical estimator of the unknown true variance.

This is not surprising given that methods like the jackknife are Taylor series approximations to the bootstrap (see Section 10). The simple idea in (2.3), substituting $\hat{F}$ for F, lies at the heart of all nonparametric estimates of accuracy. The bootstrap is the crudest of these methods in that it computes $\sigma(\hat{F})$ directly by Monte Carlo. For this reason it is also the method that involves the least amount of analytic approximation. It is perhaps surprising, and certainly gratifying, that a method based on such a simple form of inference is capable of producing quite accurate confidence intervals.

To say that the bootstrap is good, as we have been blatantly doing, doesn't imply that other methods are bad. Professor Hartigan's own work shows that for some problems, for example, forming a confidence interval for the center of a symmetric distribution, other methods are better. We hope that resampling methods in general will continue to be a lively research topic.

APPENDIX E

GLOSSARY

GLOSSARY

Air-exchange rate: The speed with which a volume of air in an enclosed space is replaced by a volume of air from another source (i.e., outdoor air through infiltration or active ventilation). The air-exchange rate may be used to indicate whether or not an indoor environment has a sufficient outdoor air supply.

Ambient: outdoor air

Atmospheric lifetime: See tropospheric lifetime.

Centroid: See population centroid.

Dielectric fluid: A fluid used to inhibit the conduction of electrical current in transformers.

Dry deposition: Removal of gases or particles from the atmosphere to surfaces, including moist surfaces.

Electron capture detector: A detector used in association with gas chromatography for the analysis of compounds with electronegative groups, e.g., halogens. A decrease in current results from the change in electron flow as a compound enters the detector. The attenuated current is compared to a reference current.

Electron-inductive effect: A molecule becomes charged as a result of being near an electron.

Electrophilic attack: A molecule with an affinity for electrons (electron-seeking) reacts with the electrons associated with another molecule.

Gas chromatography: A sample of air mixed with "carrier" gas flows through a column containing a liquid or solid "stationary" phase. Each pollutant in the sample has a different chemical structure and therefore a different affinity for the stationary phase. The pollutants are retained (adsorbed or absorbed) on the column for different lengths of time and are detected separately. The retention time of the pollutants may be compared to those of a standard with known chemical constituents.

Half-life: The time required for the concentration of a reactant to be reduced to one-half of its initial value.

Industrial Source Complex Short Term (ISCST) model: A dispersion model which estimates ambient concentrations at locations (receptors) downwind of a source, or an array of sources, based on emission rates, release specifications, and meteorological factors such as wind speed, wind direction, atmospheric stability, mixing height, and ambient temperature.

Limit of detection (LOD): The concentration at which the amount of signal measured in response to analyte is significantly different from that of background. Please see Appendix B for the Air Resources Board (ARB) Monitoring and Laboratory Division's method for determining LOD.

Log-normal distribution: A random variable's distribution is log-normal if the distribution of the log of the variable is a normal distribution.

Microgram (ug): A unit of weight equal to one-millionth of a gram (one gram= 0.035 ounces).

Partition coefficient: In a static situation, the distribution of a substance between two solvents at equilibrium is constant at a given temperature.

Personal sampler: A small apparatus for sampling airborne particles or chemicals that can be carried by a person for a specified sampling period. Air is either drawn through the sampler actively by powered pumps or passively by natural air flow.

Photolysis: Chemical decomposition by the action of radiant energy (such as sunlight).

Photo-oxidation: The oxidation of a chemical initiated by radiation such as sunlight, although the actual reaction need not involve photolysis. Reactions initiated by hydroxyl radicals and ozone are examples of photo-oxidative processes.

Population centroids: The point where the population of a particular geographical area is assumed to be located based on the distribution of population as indicated by the census tracts.

Population-weighted concentration: The population-weighted exposure divided by the total population.

Population-weighted exposure: The sum of the annual average ambient concentration (C) estimated for each population cell (e.g., census tract) multiplied by the population (P) exposed in each cell, e.g., $(C_1 \times P_1) + (C_2 \times P_2) + (C_3 \times P_3)$.

Quantile: A set of values (arranged in order of value) is divided into intervals containing the same number of values. The dividing lines between these intervals or parts are called quantiles.

Rate constant: A quantitative measure of how fast chemical reactions proceed.

Reaction rate: The change in the concentration of a reactant or product with time.

Steric protection: A reaction between two chemicals is hindered when the reactive site of one of the chemicals (e.g., the carbon-carbon double bond) is shielded by bulky substituent groups.

Troposphere: The portion of the earth's atmosphere which extends outward seven to ten miles above the earth's surface.

Tropospheric lifetime: The time required for the concentration of a reactant to be reduced to 1/e of its initial value where "e" is the base of natural logarithms (2.718).

Vapor pressure: The pressure exerted by a vapor that is in equilibrium with its solid or liquid form is constant at a given temperature. Generally, the higher the vapor pressure at a specified temperature, the greater the tendency for a substance to exist as a vapor.

Wet deposition: Removal of gases or particles by absorption into rain, snow, cloud, or fog followed by precipitation to the earth's surface.

APPENDIX F

ABBREVIATIONS AND ACRONYMS

ABBREVIATIONS AND ACRONYMS

ARB: Air Resources Board

CDHS or DHS: California Department of Health Services

EPA: Environmental Protection Agency

LOD: Limit of detection (see Glossary, Appendix E)

ISCST: Industrial Source Complex Short Term (see Glossary, Appendix E)

PPBV: Parts per billion by volume

PPBW: Parts per billion by weight

PPB(W/W): The ratio of the weight of the chemical in ppb to the total weight of the water

TEAM: Toxic exposure assessment methodology

TPY: Tons per year

ug/m^3: Micrograms per cubic meter (see Glossary, Appendix E)

APPENDIX G

PUBLIC INFORMATION REQUEST LETTER

STATE OF CALIFORNIA GEORGE DEUKMEJIAN, Governor

AIR RESOURCES BOARD
1102 Q STREET
P.O. BOX 2815
SACRAMENTO, CA 95812

April 7, 1986

Dear Sir or Madam:

Request for Information Regarding Perchloroethylene (tetrachloroethylene)

I am writing to request information on the health effects of perchloroethylene (tetrachloroethylene) as part of our toxic air contaminant program. This program is based on Health and Safety Code Sections 39650, et seq. which require the Air Resources Board (ARB) to prepare a report which would serve as the basis for regulatory action and to determine by regulation, whether a substance is a toxic air contaminant. Once identified as a toxic air contaminant, the law further requires that the ARB prepare a report on the need and appropriate degree of regulation for the substance. After consultation with the staff of the Department of Health Services (DHS), we have selected perchloroethylene as a candidate toxic air contaminant to be evaluated in accordance with the provisions of Health and Safety Code Sections 39650, et seq. During our evaluation of perchloroethylene, we will consider all available health information regarding this substance. Additionally, we are soliciting information regarding possible biological transformations of perchloroethylene.

Before the ARB can formally identify a substance as a toxic air contaminant, several steps must be taken. First, the ARB must request the Department of Health Services to evaluate the health effects of the candidate substance. Second, the ARB staff must prepare a report which includes the health effects evaluation and then submit the report to a Scientific Review Panel for its review. The report submitted to the Panel will be made available to the public. Information submitted in response to this request will be considered in the report to the Panel. I urge you to submit all information at this time for our consideration in the development of the report for the Panel. The Panel reviews the sufficiency of the information, methods, and data used by the DHS in its evaluation. Last, after review by the Scientific Review Panel, the report with the written findings of the Panel will be considered by the Air Resources Board and will be the basis for any regulatory action to identify a substance as a toxic air contaminant.

I would appreciate receiving any relevant information you wish to submit by May 16, 1986. Your help in expediting our review will be greatly appreciated. Please send the information in duplicate to the attention of:

William V. Loscutoff, Chief
Toxic Pollutants Branch
Re: Perchloroethylene
California Air Resources Board
P. O. Box 2815
Sacramento, CA 95812

If you have any further questions regarding health effects information, please contact Mr. John Batchelder at (916) 323-1505. For any other questions, please contact Mr. Gary Murchison at (916) 322-8521.

If you are not the person to whom this request should be addressed, please forward it to the appropriate person in your organization. Also, please let us know whether you would like to continue to receive information inquiries for other candidate substances, and if not, if there is anyone in your organization to whom such requests should be sent.

Sincerely,

for Peter D. Venturini, Chief
Stationary Source Division

Attachment

cc: Alex Kelter, DHS
Lori Johnston, DFA
Wayne Morgan, President, CAPCOA
Jan Bush, Executive Secretary, CAPCOA
David Howekamp, EPA Region IX
Assemblywoman Sally Tanner, Chairwoman, Committee on Toxic Materials
Senator Ralph Dills, Chairman, Committee on Governmental Organization
Senator Art Torres, Chairman, Committee on Toxics and Public Safety Management
Emil Mrak, Chairman, and Scientific Review Panel Members
APCOs

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George J. Laumann, Jr.
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C. Halogenated Solvents Industry Alliance (HSIA)

Paul A. Cammer, Ph.D.
May 22, 1986

Note: These references are in the order in which they were listed in Dr. Cammer's letter.

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D. E. I. Du Pont De Nemours and Company

Pamela Meitner
May 14, 1986

- Comments of E. I. Du Pont De Nemours and Company on the Notice of Intent-to-list Perchloroethylene as a Hazardous Air Pollutant, Docket No. A-85-03, EPA, April 17, 1986.

E. New York State Department of Environmental Conservation

Carlos L. Montes
April 24, 1986

- Riano, M. M.. and S. T. Rao, no date given. "Quantitative Risk Assessment for Tetrachloroethylene (Perchloroethylene)," Preliminary Report, Toxic Assessment Section, Bureau of Air Toxics, Division of Air Resources, New York State Department of Environmental Conservation.

F. Phillips Manufacturing Company, Chicago, Illinois

April 11, 1986

- Material Safety Data Sheet: Perclene, Diamond Shamrock, Corp., CA-MSDS-0383.

APPENDIX H

HEALTH EFFECTS EVALUATION LETTER OF REQUEST TO THE DEPARTMENT OF HEALTH SERVICES

ate of California

lemorandum

. : Kenneth W. Kizer, M.D., Director
Department of Health Services
714 P Street
Sacramento, CA 95814

James D. Boyd
Executive Officer
om Air Resources Board

Date : July 22, 1986

Subject: Evaluation of
Perchloroethylene
(Tetrachloroethylene)

I am writing to formally request that the Department evaluate the health effects of perchloroethylene as a candidate toxic air contaminant in accordance with Assembly Bill 1807 (Tanner). According to Health and Safety Code Sections 39660-62, your Department has ninety days to submit a written evaluation and recommendations on the health effects of perchloroethylene to the Air Resources Board. If necessary, the Department may request a thirty-day extension. Attached for your staff's consideration in evaluating perchloroethylene are: Attachment I - ambient perchloroethylene concentrations which should be used to estimate the range of risk to California residents as required in Health and Safety Code Section 39660(c); Attachment II - a supplemental list of references provided by the public in response to the ARB inquiry letter; and Attachment III - a list of references on perchloroethylene health effects which were identified in an ARB letter of public inquiry.

My staff is available for consultation in conducting this health effects evaluation. We look forward to continuing to work closely with you and your staff in carrying out this legislative mandate. If you have any further questions regarding this matter, please contact me at 445-4383 or have your staff contact Peter D. Venturini, Chief of the Stationary Source Division, at 445-0650.

Attachments
cc: Jananne Sharpless, Secretary of Environmental Affairs
Clare Berryhill, Director, Dept. of Food and Agriculture
Emil Mrak, Chairman, Scientific Review Panel
Members of the Scientific Review Panel
Assemblywoman Sally Tanner
Senator Ralph Dills
Senator Art Torres
Alex Kelter, DHS, w/attachments
Raymond Neutra, DHS, w/ attachments
Peter D. Venturini, ARB

ATTACHMENT I

During 1985, the ARB conducted ambient monitoring for perchloroethylene at 21 sites in various areas of California. The maximum concentration measured was 5.2 ppb; the minimum concentration measured was below the detection limit of 0.01 ppb. Annual average concentrations ranged from 0.32 ppb in Citrus Heights to 1.6 ppb in El Monte.

The major uses of perchloroethylene are as a dry cleaning solvent, a general cold cleaning solvent for fabrics and upholstery, a paint remover, a heat transfer media ingredient, a chemical intermediate in the manufacture of other organic chemicals and a metal degreaser. Extensive public exposure to perchloroethylene occurs as a result of extensive use of perchloroethylene by the dry cleaning industry and in consumer products.

ATTACHMENT II

MATERIALS PROVIDED IN RESPONSE TO PUBLIC INFORMATION REQUEST ON PERCHLOROETHYLENE

National Institute for Occupational Safety and Health

Retrospective Cohort Mortality Study of Dry Cleaner Workers Using Perchloroethylene - Samuel D. Kaplan, SRI, December, 1985.

Listing of NIOSH Reports Containing Information on PERC

New York State Department of Environmental Conservation

Quantitative Risk Assessment for Tetrachloroethylene (Perchloroethylene) - Dr. Moises M. Riano, New York State Department of Environmental Conservation

Diamond Shamrock

Perchloroethylene Material Safety Data Sheet

E.I. DuPont DeNemours and Company

Comments of E. I. DuPont De Nemours and Company to the Environmental Protection Agency Notice of Intent to List Perchloroethylene as a Hazardous Air Pollutant

California Fabricare Institute

Comments of International Fabricare Institute and the Institute of Industrial Launderers on Proposed Listing of Perchloroethylene as Hazardous Air Pollutant - submitted to EPA, 4/21/86

Halogenated Solvents Industry Alliance

(see attached)

ADDITIONAL REFERENCES SUBMITTED TO THE CALIFORNIA AIR RESOURCES BOARD ON PERCHLOROETHYLENE

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10. Letter to Mr. Gerald A. Emison (EPA) from Dr. Ernest E. McConnell (NTP) (June 11, 1985).

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ATTACHMENT III

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