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ISBN

978-1-4612-7690-6

Authors

Cain, William S. Cometto-Muniz, J. Enrique de Wijk, Rene A.

Publication Date

1992

Data Availability

The data associated with this publication are within the manuscript.

Peer reviewed

In: <u>The Science of Olfaction</u>. Michael Serby and Karen Chobor (Eds.). Springer-Verlag, New York, 1992, pp. 279-308.

Techniques in the Quantitative Study of Human Olfaction

William S. Cain, J. Enrique Cometto-Muñiz^{1,2}, and René A. de Wijk

John B. Pierce Laboratory and Yale University New Haven, CT 06519

¹Member of the Carrera del Investigador Científico, Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), República Argentina.

²Present affiliation: University of California, San Diego (UCSD). Correspondence to Dr. J. Enrique Cometto-Muñiz at: ecometto@ucsd.edu.

Introduction

This chapter will illustrate some techniques and procedures relevant to the study of the functional properties of human olfaction. Rather than deal with methodology in detail, we will deal largely with the outcome of psychophysical work on the premise that outcome illustrates methodology best. Although olfaction may be the least well understood of the five classical senses, there do exist solid data on various of its functions. We will cover only a few here and will occasionally highlight techniques that may prove of interest to a person who wishes to evaluate the modality clinically. First, however, we will look briefly at matters of stimulus control.

Stimulus Control and Measurement

The difficulty of controlling and delivering the olfactory stimulus is in some measure responsible for the slow pace of understanding of olfaction. The complications of stimulus control and measurement undoubtedly inhibit non-experts from entering the field and bringing new perspectives. It can appear to the non-expert that stimulus choice and control must conform to arcane rules known only to a few. To add to the burden, there exist almost no commercially available devices for stimulus control. One must not only choose a stimulus, but one must find a way to control it that often entails construction of a one-of-a-kind device. Some of the more elaborate olfactometers have required years to build, only to serve for one investigation and then to languish and fill lab space for years thereafter.

<u>Static Olfactometry</u>. Methods to generate odorants and deliver them to the nose divide themselves relatively well into the <u>static</u>, where odoriferous vapor exists in an enclosed or semi-enclosed volume, or the <u>dynamic</u>, where vapor flows continuously, carried by a dilution gas – generally odorless air – toward the nose of a subject. Glass bottles containing various dilutions of odorant in liquid provide the prototype for the static method, whereas olfactometers of many varieties provide examples of the dynamic method.

Elsberg and Levy (1935) developed a sort of hybrid technique, called the blast injection method, for clinical for clinical use by neurologists (Figure 1). It took the static headspace above undiluted odorant and expelled it through a nosepiece. With the nosepiece closed, the operator would push a syringe connected to one side of the odor vessel to a desired setting (thereby taking advantage of the compressability of air) and lock it in place. The pressure generated in the bottle would determine the flowrate and volume of air that exited when the operator opened the stopcock to the nosepiece placed just inside a patient's nostrils. Participants did not have to inhale to receive the odorant, which made the stimulation independent of inhalation pattern. The operator varied intensity of stimulation through the amount of pressure applied to the bottle, i.e., by the degree of compression, read as number of cubic centimeters on the syringe.

Figure 1 about here

Elsberg's technique had the flaws that it caused progressive drying of the nasal mucosa – eliciting pungent or irritant sensations with repetitive stimulation – and that it might also mistakenly measure air pressure thresholds rather than olfactory thresholds (Wenzel, 1948). Largely because of those concerns, it dropped out of the repertoire of clinical techniques. Nevertheless, it served as a forerunner of a technique used by Kobal (1981) who employs humidified air and adds odorant to a flowing airstream in such a manner as to preclude pressure artifacts. This recent development has proven useful for the measurement of the electro–olfactogram, a mass potential from the olfactory mucosa, and olfactory evoked potentials in humans (Fig. 2). In due course, such potentials may provide truly objective means to assess the olfactory functioning.

Figure 2 about here

Static olfactometry, generally the easiest form of stimulus control, customarily entails use of a number of glass or odorless plastic vessels each with a dilution of odorant in an odorless solvent. Choice of the solvent poses some challenge. Distilled and deionized water comprise one choice, but some odorants are not stable in it, e.g., esters slowly hydrolize to acids and alcohols, and many odorants have little or no water solubility. In those cases, mineral oil, propylene glycol U.S.P., or some low-vapor-pressure esters might be used. The actual stimulus in static olfactometry is the concentration of the odorant in the <u>headspace above a solution</u>. In principle headspace concentration varies proportionally with the concentration of the odorant <u>in the solution</u> by a factor known as the "activity coefficient." This factor differs among odorants diluted with the same solvent, among solvents, and sometimes among concentrations of the same odorant-solvent pair. A means to check vapor-phase concentration becomes the only safeguard against incorrect reliance on questionable assumptions about the relation between liquid-phase and vapor-phase concentrations. The majority of investigations of olfaction have unfortunately included no measurement of the concentration delivered to a subject's nose. Gas chromatography makes such calibration relatively simple.

When subjects open bottles containing odorant, bring the open end to their nose, and sniff from the headspace above the liquid solution, they also inhale a certain amount of surrounding room air, and thereby dilute the stimulus. Squeezable sniff bottles with pop-out spouts that fit into one or the other nostril for monorhinic testing can circumvent the problem of dilution (see Figure 3) (Amoore & Ollman, 1983; Cain, 1989; Cain, Gent, Catalanotto, & Goodspeed, 1983; Cain, Gent, Goodspeed, & Leonard, 1988). Subjects place the spout into the specified nostril, then squeeze and sniff simultaneously. In this way, the odorant vapor enters the nasal cavity efficiently and each nostril can be tested separately. The simplicity of the method, the ease of use and handling of the bottles, and the possibility for monorhinic testing make this procedure convenient in both clinical work (Cain, 1989) and in basic research (Cometto–Muñiz & Cain, 1990; J.C. Stevens & Cain, 1987).

Figure 3 about here

The headspace above an odorant solution requires time to regain its original – pre-squeeze – vapor concentration. If a bottle is left still, the duration would be in the order of minutes (around 30 min). Much faster re-equilibration – in the order of fraction of a minute – occurs if the liquid is shaken in a circular pattern (Dravnieks, 1975). If this precaution is supplemented with the availability of two bottles for each concentration step and alternative use of each, the problem of re-equilibration is essentially solved.

<u>Dynamic Olfactometry</u>. As noted above, dynamic olfactometry involves a stream of odorized air – generally at vapor saturation for that temperature – which can be mixed in various proportions with odorless air or nitrogen acting as solvent or carrier. An array of tubing, valves, flowmeters – either rotameters or capillaries with manometers – saturating and mixing vessels, deodorizing and air conditioning – temperature, humidity – devices, provide the necessary equipment for the generation and control of odorants.

Loading the carrier gas with vapors from liquid odorants can be achieved by direct vaporization into the carrier stream, by bubbling the odorless gas through the liquid, or by passing the gas over an extended surface of the odorant (Figure 4). The bubbling method has the disadvantage of forming aerosols – small droplets of the liquid suspended in the gas phase. These can be reduced by aerosol filters - typically glass wool - but may not always be completely eliminated.

Figure 4 about here

Dravnieks (1975) described the details of various dynamic olfactometers used for animal and human research, including Köster's (1967, 1971), Sanders's (1970), and Moulton's (1972). (Dravnieks also included an annotated bibliography with the complete reference and a brief summary of olfactometers described as early as 1930.) Particularly interesting was his own flexible, simple, valveless device, the Dravnieks Binary Dilution Olfactometer (Dravnieks, 1975), which combined stability of concentration and portability with ease of use and maintenance (see Figure 5).

In the Binary Dilution Olfactometer the odorous stimulus is generated by pumping air – at a pressure controlled by a water column manostat – across the surface of the odorant. The odorant–saturated air is mixed in desired proportions with odorless air. This is achieved via a stimulus splitter to which stainless steel capillaries of varying lengths and internal diameters are attached, providing an orderly series of various flows of odorous air (each related to the next by a fixed factor). The stimulus splitter is complemented with a makeup (odorless) air splitter that brings up the total flow from each sniffing port to a common value. An operator needs merely to place odorant into a small saturator and check a couple of flowrates. All the rest occurs automatically. The olfactometer is made of glass, stainless steel, very short pieces of neoprene tubing (to interconnect the capillaries), Tygon tubing for the initial pumping of the air, and teflon tubing to feed the sniffing ports.

The Dravnieks Binary Dilution Olfactometer, when allowed to run in a steady-state mode, essentially avoids the need for calibration through external analytical instruments, such as a gas chromatograph. Since the strongest stimulus is odorant-saturated air – the concentration of which may be calculated or looked up from tables – and the other stimuli are fixed dilutions (on a volume basis) of that vapor saturated stream, actual concentrations are simple to compute.

Figure 5 about here

Dravnieks also developed what is called a Dynamic Forced-Choice Triangle Olfactometer for measurement of thresholds (Dravnieks & Prokop, 1975; Dravnieks, Prokop, & Boehme, 1978). This instrument consists in six sniffing stations, each with three identical sniffing nozzles. One nozzle in each station delivers a certain dilution of the stimulus whereas the other two deliver odorless air. The stimulus varies in concentration by a factor of three from station to station. During threshold testing a subject starts with the first station (weakest stimulus) under instruction to choose the nozzle that smells different from (stronger than) the other two, and then goes to the next station (threefold more concentrated), where he seeks to do the same, and so on. The total flow rate emerging from each nozzle (blank or stimulus) is fixed at either 3 l/min or 0.5 l/min. The highest dilution achieved can also vary from 81-fold to 1700-fold. This device, like the Binary Dilution Olfactometer is available commercially from IIT Research Institute, Chicago, IL

Environmental Chambers. Air-dilution olfactometers and static dilution devices may have limitations in the amount of air they deliver to the nose per unit time. Whether the limitations have any practical consequences remains largely unexplored. Work by Laing (1982, 1983) offers design endpoints of interest: An average human sniff lasts 0.4 sec, has a volume of 200 cm^3 , and reaches an instantaneous flowrate of 30 I/min. (Big sniffs do not necessarily increase odor magnitude over small sniffs.) Although suitably designed devices can accommodate these characteristics, an odor chamber offers the greatest freedom of human odor sampling. Such chambers provide a way to perform odor and pungency research with environmental realism. The results obtained permit an almost-in-the-field understanding of problems related to indoor air quality (Cain & Leaderer, 1982; Cain, Leaderer, Isseroff, Berglund, Huey, Lipsitt, & Perlman, 1983; Cain, See, & Tosun, 1986; Cain, Tosun, See, & Leaderer, 1987; Clausen, Fanger, Cain, & Leaderer, 1986), the perception of environmental fragrances (Schiet & Cain, 1990), and masking agents, and gas warning agents.

The air in the typical environmental chamber can be precisely controlled and monitored for temperature, humidity, and flowrate of both recirculation and outside – fresh – air. The air flow through the chamber should provide good mixing of any stimulus delivered and a fairly quick renewal of room air with fresh air, without creating disturbing air currents. A useful added feature is an anteroom to minimize perturbances created by entering and exiting the chamber.

Heating and cooling systems, as well as desiccant and humidifying devices, condition the air entering the chamber according to the requirements of each experiment. Measurement of decays of tracer gases – e.g., carbon dioxide – that are easy to deliver and monitor establish actual ventilation rates.

Thresholds

Odor thresholds have been measured since the middle of the nineteenth century (Cain, 1978). The corpus of published threshold data currently encompasses hundreds of materials (of hundreds of thousands of odorants), some of interest because of their flavors or their fragrancing effects, some because of their possible presence in polluted atmospheres, and some because olfactory researchers have arbitrarily The corpus of data has unfortunately little chosen to study them. A search through one or another published thematic uniformity. compilation may uncover thresholds for some members of a chemical series, but not for others, or for some isomers, but not others (Fazzalari, 1978; van Gemert & Nettenbreijer, 1977). The literature on smell contains disappointingly few prospective efforts to attack the molecular basis for odor potency via collection of thresholds for many related chemicals.

<u>Chemical Series and the Physicochemical Basis for Potency</u>. Occasionally investigators have explored some members of one or another chemical series in a search for insight into the physicochemical basis for odor potency. Figure 6 shows thresholds obtained in such efforts for various aliphatic series. The outcomes implied that within a series odor potency grows with molecular size and with lipid solubility. Once such factors are taken into account, the enormous odorant-toodorant range of thresholds of the sort seen in Table 1 foreshortens somewhat.

Figure 6 and Table 1 about here

Research of Cometto–Muñiz and Cain (1990) illustrates the point, both for olfaction and for pungency, e.g. irritation. Figure 7 displays thresholds for aliphatic alcohols in normal – normosmic – subjects (odor thresholds) and in persons – anosmics – without a functional sense of smell (pungency or trigeminal thresholds). As expected from general characteristics of olfaction and the common chemical sense, pungency thresholds lie well above odor thresholds, but both types of thresholds decline with chain length. When plotted in terms of what we might call incident vapor–phase concentration, measured via gas chromatography, the odor threshold changes by a factor of 2.1×10^5 from methyl to octyl alcohol and the pungency threshold changes by a factor of 50. When plotted in terms of percent saturated vapor, an index of thermodynamic activity, the odor threshold varies by a factor of 210 (and remains rather constant between ethyl and heptyl alcohol) and pungency threshold by a factor of 5 (Fig. 7).

Figure 7 about here

The reduction in range with the threshold data plotted in terms of percent saturated vapor implies that much of the change in threshold over the series results from variation in the amount of material that entered the biophase (watery mucus and lipid cell membrane). This was particularly true for pungency. With nonreactive materials such as the aliphatic alcohols, their ability to elicit pungency apparently comes from a non-specific effect derived from reaching a critical concentration in mucosal tissue. At equal concentrations in tissue, different alcohols cause the same degree of pungency.

As always, conclusions in olfaction rest upon only fragmentary data. Laffort and colleagues (Laffort, Patte, & Etcheto, 1974), however, used existing threshold data to build a reasonable model of odor potency from various molecular parameters.

<u>Threshold Methodology</u>. The odor threshold measured most often is the detection threshold, whereby subjects seek to distinguish the presence of odor from odorless air, and do not seek to specify or recognize odor quality. Compilations often include the so-called recognition threshold also, where subjects are required to specify quality. Such a threshold typically occurs at a concentration about threefold above the point of detection. It will come as no surprise that olfactory thresholds depend largely on the methodology used to gather them and that compilations suffer very much from methodological inconsistencies. Multiple entries for the same odorant may differ by as much as four orders of magnitude. Such differences can derive from such physical or chemical matters as the solvent used to dilute a material. Except for olfactometers arranged like the Dravnieks device, essentially every estimate of threshold is questionable without an assessment of vaporphase concentration. Nevertheless, psychophysical methodology per se also plays its role.

To take the simplest case, odor thresholds will vary according to whether the experimenter presents concentrations in ascending, descending, or random orders. An ascending series generally leads to a low threshold, a descending series to a high threshold, and a random series to an intermediate threshold (see Fig. 8). Higher thresholds found for descending stimuli probably occur because of adaptation (Köster, 1975). Adaptation may also play a role with stimuli presented in random order, particularly with short interstimulus intervals. Intervals of 60 sec generally lead to satisfactory results.

Figure 8 about here

Time figures pervasively in determinations of odor thresholds. Slow recovery from the effects of stimulation force the experiments to proceed at an often agonizing pace. In the experiments described in Fig. 8, subjects received no blanks. Unfortunately, then, the threshold could depend as much upon response criterion as upon olfactory sensitivity. Forced-choice methods, where subjects must choose between a stimulus and at least one blank, circumvent the problem, but only at the expense of time. Various experimenters have used an ascending method of limits in a forced-choice mode (two-alternatives).

In a forced-choice variation used in clinical evaluation, a correct answer at any given concentration leads to re-presentation of that same concentration until a criterion, e.g., five correct in a row, is reached, or until the subject makes an error, whereupon concentration increases by one step (Cain, 1989). In this variation, threshold is defined as the point of 100% detection rather than at the more conventional point halfway between chance and perfect performance. The procedure has limitations imposed by the inevitable occurrence of strings of correct answers by chance. Such limitations can be circumvented by increases in the number of correct answers required to quit testing, by repeat testing, and so on. Alternatively, another threshold procedure, such as the staircase method, could be employed (Doty, Gregor, & Settle, 1986). All such maneuvers take time, which may be plentiful in the laboratory, but not perforce in the clinic.

A somewhat less orthodox method for threshold measurement involves the extrapolation of threshold concentrations from psychophysical functions erected from ratings of perceived intensity. The procedure implies some knowledge of the form of the psychophysical function in the vicinity of threshold, a matter that remains unsettled (Marks & J.C. Stevens, 1968). The approach has yielded satisfactory results in some cases (Berglund, Hogman, & Johansson, 1988; Overbosch, de Wijk, de Jonge, & Köster, 1989), but seems a risky substitute for measuring thresholds directly. Random vs. Systematic Variability. Olfactory thresholds exhibit notorious person-to-person variability, sometimes as much as five log units, or 100,000 to 1, but more commonly three log units (Brown, Maclean, & Robinette, 1968). Although various methods of threshold measurement and various definitions of threshold (50% detection vs 100% detection; detection vs recognition) can account for some variability from study to study, they fail to account for variation within a study. This presumably arises from poor stimulus control, unreliability of methods, differences in the experience of subjects, and undoubtedly some true individual differences. Cain and Gent (1990) found that reliability increased from one threshold test to another over the course of four days. During this time, thresholds declined progressively. Hence, subjects become more uniform and seemingly more sensitive with practice.

In another experiment of how thresholds changed with repeated testing, Rabin and Cain (1986) found that practice generalized from one odorant to another and from one nostril to another, and presumably depended upon something other than peripheral sensory factors. Thresholds were still declining after three sessions of three hours (Fig. 9). De Wijk (1989) found stable individual threshold concentrations after subjects received approximately 30 hours of practice.

Figure 9 about here

Aging has an influence on olfactory thresholds more-or-less irrespective of the stimulus employed. In single threshold measurements, groups of elderly adults typically yield thresholds two- to tenfold above those of young adults (Cain & J.C. Stevens, 1989; J.C. Stevens, Cain, & Weinstein, 1987) (see Fig.10). Cain and Gent (1990) found that the apparent effect of age increased with the reliability of threshold measurements. Whereas age accounted for 15% of the variance of measurements made on a single day, it accounted for 50% of the variance of measurements averaged over four days (Fig. 11). Over a four-decade age-range from the 20's to the 50's, threshold averaged over four days of testing increased more than 60-fold with age. Residual individual differences, after accounting for age-related influences, equalled about 30 to 1, which lies well below the traditional 1,000 to 1 seen when age or other organismic variables are not taken into account.

Figure 10 and 11 about here

Systematic influences of organismic and environmental factors on odor threshold often seem ephemeral. For example, one threshold study will uncover an effect of smoking and another will not (Hubert, Fabsitz, Feinleib, & Brown, 1980; Martin & Pangborn, 1970; Matzker, 1965; Venstrom & Amoore, 1968). One will find an advantage for females and another will not (Venstrom & Amoore, 1968; Koelega, 1970; Koelega & Köster, 1974; LeMagnen, 1952; Punter, 1983; Doty, Gregor, & Settle, 1986). Presumably, positive effects come closer to the truth than negative effects. The need seems clear: higher reliability will uncover the

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true effects more clearly and will give a more realistic picture of the true magnitude of an effect.

Temporal Integration and Adaptation. The threshold (or a comparable index of sensitivity) has often served as the workhorse of the psychophysical laboratory. If one wishes to study the effects of, say, time on the olfactory response, then a threshold study can usually reveal it. For instance, threshold studies have revealed that at the beginning of stimulation detectability increases with duration, i.e., temporal integration occurs, but that after a brief time detectability decreases, i.e., adaptation Stuiver (1958), who investigated the effects of temporal occurs. integration on olfactory thresholds, found that for very short stimulus durations (critical durations equal up to 160-200 msec), stimulus concentration and stimulus duration were completely interchangable (Fig. Detectibility increased with stimulus durations up to 1.6 sec. 12). Longer stimulus durations, however, led to a decrease in detectibility via adaptation (Fig. 13). Eventually, the threshold concentration may rise to equal the concentration of the adapting stimulus. As a result, the adapting stimulus may no longer be perceived. The Adaptation Time required for the Cessation of Smell or ATCS (de Wijk, 1989; Elsberg & Levy, 1935; Mullins, 1955; Stuiver, 1958; Woodrow & Karpman, 1917) increases with stimulus concentration, and varies with the test odorant (Fig. 14).

Figures 12 and 13 about here

Through the decades, researchers have sought one or another psychophysical maneuver to uncover what we might call the relatedness of odors. The phenomenon of cross-adaptation has often seemed the most likely route to such understanding, though various obstacles have stood in the way. In the cross-adaptation paradigm, an experimenter exposes a subject to one odorant and tests sensitivity with another. Although logic suggests that molecules that share receptor cells or receptor sites should cross-adapt more strongly than those that do not, the outcome of the experiments has yielded little in the way of discernible patterns (e.g. Köster, 1971). This may have occurred for several reasons. For example, receptor cells in the olfactory mucosa may have specific and nonspecific receptor sites and therefore every odorant may show some cross-adaptation with every other odorant. The amount of interaction, particularly that which arises from nonspecific interaction, may depend on how much material filters through to the relevant biophase. Alternatively, a given cell may possess unrelated specific receptor sites. Another possibility is that properties that have little to do with exactly which receptor sites a molecule stimulates, e.g., water solubility, may determine where the material deposits itself on the olfactory mucosa and accordingly related molecules may have little opportunity to show interaction. Without some fundamental insights into the biophysics of the olfactory mucosa, cross-adaptation may continue to frustrate as a means to solve the odor quality issue psychophysically (Cain & Polak, 1990; Köster, 1971).

Figure 14 about here

Common Chemical Sense. A final comment seems appropriate regarding thresholds for nasal pungency evoked by stimulation of the common chemical sense. Thresholds for such sensations as irritation, burning, prickling, tingling, freshness, stinging, piquancy, and the like, can prove difficult to measure because of simultaneous odor sensations elicited by the chemicals employed to provoke them, and because of mutual interactions between odor and pungency (Cain & Murphy, 1980). The use of anosmic subjects - i.e., persons lacking a functional sense of smell - provides one way to address common chemical functioning (see Cometto-Muñiz & Cain, 1990). A technique that measures the threshold for a momentary reflex interruption of inhalation evoked by nasal pungency provides another way and holds promise as an objective index of the functional status of the nasal common chemical sense (Cometto-Muñiz & Cain, 1982; Dunn, Cometto-Muñiz, & Cain, 1982; García-Medina, & Cain, 1982) (Figure 15). The reflex occurs well above the sensory threshold. Results from experiments on bilateral integration in the nose (García-Medina, & Cain, 1982), nasal pungency responses in smokers and nonsmokers (Cometto-Muñiz, & Cain, 1982), and temporal integration of nasal pungency (Cometto-Muñiz, & Cain, 1984) showed excellent agreement between the threshold for the reflex and psychophysical estimate of perceived pungency, suggesting that the threshold for the reflex occurs at a criterion level of pungency.

Figure 15 about here

Measurement of Perceived Odor Intensity

All of the phenomena of interest at threshold reflect themselves at suprathreshold levels, where the techniques of measurement differ from those used to study absolute sensitivity. In what follows, we will ignore the topic of differential sensitivity which has received relatively little attention (Cain, 1977), but will instead focus on magnitude of sensation.

Fechner's Law. Researchers in psychophysics have long grappled with how to measure the basic input-output function of a sensory Gustav Fechner, the father of psychophysics, sought the modality. answer by construction of a scale of cumulative just noticeable differences (ind's) in sensation (Fechner, 1860). The ind thereby came to be treated as a unit of perceived magnitude. To construct such a scale empirically, i.e., by the actual measurement and cumulation of jnd's along the dynamic range of a modality, would prove a formidable obstacle to progress. Fechner, however, found a way around the obstacle. He accepted that the magnitude of stimulation that would prove just resolvable, i.e., would give a jnd, equalled a constant fraction of the reference stimulus. Hence, if it took a one-unit change in a stimulus of a magnitude of 10 units to resolve a difference, then it would take a 10unit change in a stimulus of 100 units, a 100-unit change in a stimulus of 1,000 units, and so on.

The rule of proportionality of resolving power is known as Weber's Law. Fechner showed that joint acceptance of Weber's Law and of the assumption that all jnd's had equal subjective size, i.e., formed a true unit of subjective magnitude, led to a simple <u>logarithmic rule</u> relating sensation

to stimulus magnitude. For almost a century, Fechner's logarithmic law prevailed for characterization of input-output.

The logarithmic law stayed alive in part because a simple method of judgment, known as category rating, often tended to yield logarithmic functions (Marks, 1968). Such a simple method of judgment, e.g., use of a 5-point scale, saw relatively little use in work designed to understand sensory processes, but often served in practical work. Figure 16 offers one example of many sets of odor/irritation functions derived from screening gas warning agents by the U. S. Bureau of Mines (Katz & Talbert, 1930). The data illustrate that the same vapor that stimulates olfaction at low concentrations may stimulate both olfaction and the irritation sense, often called the common chemical sense (Cain, 1990), at higher concentrations. These results also reveal that both odor intensity and irritation intensity functions, but that irritation functions are much steeper than odor functions.

Figure 16 about here

Ratio Scaling and the Power Law. About 40 years ago, category scaling came under attack, as did Fechner's Law again, with the introduction of what are commonly called ratio scaling techniques. In the terminology of measurement theory, scales formed from category ratings fall into a class called interval scales. Such scales, exemplified in physical science by the Celsius and Fahrenheit scales of temperature, possess no true zero and do not allow statements regarding the ratios of scale values. On a seven-point category scale, a judgment of six does not equal twice as much as a judgment of three. Its interval properties do, however, allow such statements as that a scale value of six falls the same distance from a scale value of four as does a scale value of two.

The introduction of ratio scaling techniques by S. S. Stevens (e.g., 1957) and his colleagues at the Harvard Laboratory of Psychoacoustics injected the discipline of psychophysics with considerable life and with unparalleled activity. The most commonly used ratio judgment technique, called magnitude estimation, requires subjects to emit numbers to match sensations and to preserve in those numbers the ratio relations among the impressions (S.S. Stevens, 1956). If one sensation seems twice as strong as another, it deserves a number twice as large. If it seems half as strong, it deserves a number half as large. And so on. Data obtained via magnitude estimation, and companion techniques called magnitude production, ratio estimation, and ratio production, gave birth to a new formulation of the psychophysical law, based upon a power function: $Y = kg^{\beta}$, where ø refers to physical magnitude, Y to perceived magnitude, k to a constant of proportionality, and ß to the shape and rate of growth of the function.

Whereas the logarithmic law implied that a geometric progression of stimulus magnitudes would lead to an arithmetic progression of sensation magnitudes, e.g. progressive doubling, Stevens's psychophysical power law implied that a geometric progression of stimulus magnitudes would lead to a geometric progression of sensation magnitudes. For example, if stimulus magnitude progressed according to the series 1, 2, 4, 8, and 16, a logarithmic law would predict that sensation might progress in the following manner: 0.5, 1.0, 1.5, 2.0, and 2.5, i.e., each multiple of stimulus magnitude might yield a constant half-unit increment in sensation. The power law would predict, however, that sensation would progress according to equal percentage increments in magnitude. In the case of a square-root relation, for example, sensation would grow by 41% for each doubling of stimulus magnitude. Hence, for the series above, sensation would progress: 0.5, 0.7, 1.0, 1.41, and 2.0.

A square-root relation may hold in some cases, but in actuality the exponent can have any value and does vary substantially from one sensory continuum to another. For loudness re sound pressure level, for instance, it equals two-thirds and, for brightness, it equals one-third. To some degree, an exponent will vary with the frequency of a sound and the wavelength of a light. In olfaction, variation of the exponent of the power function commonly varies from one stimulus to another (Fig. 17) (Cain, 1969). It may vary from under 0.10 to over 0.70. It virtually always falls below 1.0, which implies a compression of sensation magnitude over stimulus magnitude (Cain & Moskowitz, 1974). Often, the compression is very marked, i.e., the exponents are very low. As examples, let us consider exponents of 0.7 and 0.1. In the former case, a tenfold increase in concentration would lead to a fivefold increase in perceived odor intensity. In the latter case, the tenfold increase in concentration would lead to just a 25% increase in perceived odor Patte and colleagues (1975) have related variation of the intensity. exponent to various physicochemical properties.

Temporal integration and Adaptation. Phenomena measured quantitatively at the threshold level often occur over a different timescale above threshold. Whereas temporal integration occurred over intervals up to about 2 sec at threshold, it occurs over intervals as long as 6 sec above threshold (Fig. 18). Critical durations of such length occur infrequently in the sensory domain (de Wijk, 1989; von Békésy, 1964). For the common chemical sense, suprathreshold temporal integration can even occur over durations as long as an hour (Cain, See, & Tosun, 1986; Cain, Tosun, See, & Leaderer, 1987; Cometto–Muñiz, & Cain, 1984).

Figure 18 about here

Phenomena such as adaptation also hold as much or even more interest interest at suprathreshold levels as at the threshold. Ratio scaling techniques and the coincident formulation of the psychophysical power law also led to a coherent way to describe phenomena such as adaptation. Various investigators have asked how adaptation to a particular concentration of an odorant transforms the the psychophysical function for odor intensity.

Figure 19 gives an example of families of adaptation functions for two odorants with very similar earthy-chocolate odor qualities (Cain & Polak, 1990). The uppermost functions in each set describe perceived magnitude when subjects were adapted to room air before they judged the various test stimuli. The functions fitted to the data conform to a generalized version of the psychophysical power law, $Y = k(\phi - \phi_0)^{\beta}$, where ϕ_0 is an estimated constant. With subjects adapted to a concentration of the test odorant (self-adaptation) before smelling the test stimuli, perceived magnitude fell, more in the case of adaptation to a stronger than a weaker concentration. With subjects adapted to a concentration of the other odorant (cross-adaptation), perceived magnitude also fell, though not quite so severely as with self-adaptation. Severity of adaptation, generally more evident at low than at high test concentrations, revealed itself largely by increases in the exponents of the psychophysical functions. As Fig. 20 shows, comparable conditions of self-adaptation and cross-adaptation led to almost identical changes in perceived magnitude from the one odorant to the other. In this case, the data suggested that the adapting stimuli matched in perceived intensity will produce equal degrees of self-adaptation and, at least in very similar smelling substances, equal degrees of mutual crossadaptation.

Figures 19 and 20 about here

<u>Gender, Aging and Smoking</u>. A technique called magnitude matching, devised to compare absolute values of perceived magnitude across groups of subjects, has rather recently entered the psychophysical repertoire (J.C. Stevens & Marks, 1980). It has seen use in the study of olfaction and nasal pungency in relation to aging (J.C. Stevens & Cain, 1986; 1987), gender (Cometto-Muñiz & Noriega, 1985), and smoking (Cometto-Muñiz & Cain, 1982).

The magnitude matching procedure requires subjects to assign numbers to perceived intensity in more than one sensory modality in a given session. Subjects are instructed to use a common scale across modalities. One modality serves as a reference. In the study of the influence of aging on the sense of smell, the taste modality has served often as reference because aging has little or no influence on perceived Subjects have judged both saltiness and the odor taste intensity. intensity of interest. Figure 21 shows functions for the odor intensity of isoamyl butyrate (Cain &, J.C. Stevens, 1989). The vertical positions of the functions reflect odor intensity after normalization to taste intensity. The technique has consistently found that the threshold difference between young and elderly subjects translates itself rather uniformly up the concentration scale, so that elderly subjects find both strong and weak odors comparably weakened. A similar parallel shift in the functions also characterizes nasal pungency perceived by young and elderly (J.C. Stevens, Plantinga, & Cain, 1982; J.C. Stevens, & Cain, 1986); by nonsmokers and smokers, with smokers finding nasal pungency weaker than nonsmokers (Cometto-Muñiz & Cain, 1982), and by females and males, with males finding nasal pungency weaker than females (Cometto-Muñiz, & Noriega, 1985).

Figure 21 about here

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Preparation supported by NIH Grant DC00268

Figure Captions

<u>Figure 1</u>. The arrangement for the blast injection technique. A: "Loading" the bottle for testing. B: Upon signal from the subject – who raises his finger while holding his breath – the experimenter presses the valve to release the blast of odorized air. From Elsberg and Levy, 1935.

<u>Figure 2.</u> Human electro-olfactogram, a potential that reflects the activity of many receptors, elicited by hydrogen sulfide at two stimulus durations (adapted from Kobal, 1981)

<u>Figure 3</u>. Squeezable bottles with pop-out spouts used for clinical testing (from Cain, 1989).

<u>Figure 4</u>. Various techniques for introducing odorant into a stream of non-odorous air (from Dravnieks, 1975).

<u>Figure 5</u>. Top: Schematic representation of the Dravnieks Binary Dilution Olfactometer (from Dravnieks, 1975). Bottom: A perspective drawing of the olfactometer (from Dravnieks, 1977).

<u>Figure 6.</u> Odor thresholds for human subjects of four aliphatic series (from Cain, 1988, data from Laffort, 1969).

<u>Figure 7.</u> Top: Odor thresholds measured in normosmics (empty symbols) and pungency thresholds measured in anosmics (filled symbols) for the eight alphatic alcohols from methanol to 1-octanol. Bottom:

Thermodynamic activity at the odor threshold (from normosmics) (empty symbols) and at the pungency threshold (from anosmics) (filled symbols). The activity was calculated as the ratio between vapor concentration at threshold odor or pungency to saturated vapor concentration, multiplied by 100. From Cometto-Muñiz and Cain, 1990.

<u>Figure 8.</u> Psychometric functions for 2-heptanone obtained by three methods of stimulus presentation (from Pangborn, Berg, Roessler and Webb, 1964).

<u>Figure 9.</u> Odor thresholds measured over three days. Bars depict standard errors computed with and without normalization for a general factor of sensitivity across subjects. From Rabin and Cain, 1986.

<u>Figure 10.</u> Detection thresholds for the gas warning agent ethyl mercaptan in young and old subjects. The standard level refers to the concentration of ethyl mercaptan (14 ppb) that would be achieved when a leak of propane from a freshly filled cylinder achieves a concentration of 0.47 % (one fifth of the lower explosive limit). From J.C. Stevens, Cain and Weinstein, 1987.

<u>Figure 11.</u> Relationship between threshold and age for 1-butanol, pyridine, isoamyl butyrate (IAB) and phenylethylmethylethyl carbinol (PEMEC). Each point represents a participant. From Cain and Gent, 1990. <u>Figure 12.</u> Detection thresholds, expressed in terms of number of molecules per sec, as a function of stimulus injection time for sec- butyl mercaptan and m-xylene. Flow rate was 100 ml/sec. From Stuiver, 1958.

<u>Figure 13.</u> Increase of the threshold for 2-octanol during adaptation to various stimulus concentrations. Both adapting and threshold concentrations are expressed in multiples of the unadapted threshold concentration. From Stuiver, 1958.

<u>Figure 14.</u> Relation between the concentration of the adapting stimulus (expressed in multiples of the unadapted threshold concentration) and the adaptation time required for the cessation of the smell sensation (ATCS) for 2-octanol and m-xylene (from Stuiver, 1958).

<u>Figure 15</u>. Breathing patterns detected by changes in temperature of a nasal thermocouple before, during and after presentation of carbon dioxide at a concentration sufficient to disrupt breathing, eliciting a reflex, transitory apnea (from Cometto–Muñiz and Cain, 1982). Such measurements confirmed that smokers showed the threshold at a significantly higher carbon dioxide concentration (52.3 ± 2.2 %) than nonsmokers (41.8 ± 2.6 %).

<u>Figure 16.</u> Psychophysical functions, derived from category scaling, for eye irritation, nasal irritation, and odor of benzyl mercaptan (from Katz and Talbert, 1930).

<u>Figure 17.</u> Magnitude estimation as a function of concentration for five odorants. The functions have been displaced in the vertical direction for clarity. The arrows indicate points of equal intensity across odorants and provide the means to relate the functions to each other. From Cain, 1969.

<u>Figure 18.</u> Individual temporal integration functions for n-hexane. Each point represents the mean of 50 magnitude estimations. From de Wijk, 1989.

<u>Figure 19.</u> Families of psychophysical functions for the odor intensity of trimethyl pyrazine (TMP) and 2-propionyl-3-methyl furan (PMF) under two conditions of self-adaptation (low and high adapting concentrations) and two conditions of cross-adaptation (low and high) of one substance by the other (from Cain and Polak, 1990).

<u>Figure 20</u>. Same data as in Fig. 19, but plotted as perceived odor intensity of TMP and PMF after odor adaptation vs. perceived odor intensity after adaptation with air (from Cain and P{olak, 1990).

<u>Figure 21</u>. Magnitude matching functions for odor intensity of isoamyl butyrate in three age groups. The functions were normalized according to intensity of the salty taste of sodium chloride in the three groups (see text). From Cain and J.C. Stevens, 1989.

FIGURE 1



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FIGURE 5















FIGURE 12



FIGURE 13











FIGURE 18







FIGURE 21



<u>Table</u>

Table 1. Odor detection thresholds of selected compounds (adapted from Amoore, 1982).

Compound	Odor threshold concn. in air	
	(mg/m ³)	(ppm, v/v)
Ethane	1.5 × 10 ⁵	120.000
Methanol	6.6×10^{2}	500
Chloroform	3.2×10^{2}	65
Benzene	1.7×10^{1}	5.2
Camphor	1.1×10^{0}	0.17
Furfural	2.3×10^{-1}	0.059
Isoamyl acetate	3.8×10^{-2}	0.0071
5a-Androst-16-en-3-one	2.1×10^{-3}	0.00019
2-Methoxy-3-isobutylpyrazine	3.6×10^{-5}	0.00000054

Adapted from Amoore (1982).

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