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Supplementary Material for

Humans Can Discriminate More Than 1 Trillion Olfactory Stimuli

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Materials and Methods

Fig. S1

Other Supplementary Material for this manuscript includes the following:
(available at www.sciencemag.org/content/343/6177/1369/suppl/DC1)

Tables S1 and S2

Materials and Methods

Study Subjects

Each subject in the study completed the same 264 discrimination tests over three visits to the Rockefeller University Hospital Outpatient Unit. Each subject completed the three visits over a period of three to nine days. The median duration of the visits was 1 h and 6 min (range: 38 min to 2 h 54 min). Only English-speaking subjects aged 18 to 50 with no allergies to fragrances or smells were enrolled in this study. Further exclusion criteria were active head cold, upper respiratory infection, or seasonal nasal allergies as well as a history of nasal health problems, and any other pre-existing medical conditions that may cause reduced olfactory acuity, such as: head injury, cancer therapy, radiation to head and neck, and alcoholism. All subjects gave their informed consent to participate and all procedures were approved by the Rockefeller University Institutional Review Board. Subjects were compensated for their participation in the study.

Psychophysics

Subjects performed olfactory three-alternative forced-choice discrimination tests that are also known as triangle tests. For these tests, subjects were presented with three odor vials, two of which contained the same mixture, whereas the third contained a different mixture. The testing procedure was computerized using a custom-written Microsoft Access application in which subjects were instructed to identify the odd odor vial based on odor quality and scan the bar code affixed to the side of that vial. The application was written so that the order of the visits as well as the order of the tests during a visit was randomized. A tray containing all the vials was presented to the subjects. Subjects were instructed to open the vials, sniff the contents, and follow instructions on the computer screen. Subjects are numbered in Table S2 according to their overall performance in discriminating the 260 mixture pairs, such that Subject 1 had the worst performance and Subject 26 the best. Although Subject 1 successfully discriminated 3 of 4 control discrimination tests, this individual performed close to chance for the 260 mixture pairs (34.6% correct). In showing extremes of inter-individual discrimination ability in Fig. S1, we therefore show data from Subject 2 and not Subject 1.

Calculation of the Number of Mixtures and Mixture Pairs

There are C = 128 odorous molecules in the collection from which the components of the mixtures were picked. The 13 types of mixture pairs differ in the number of components (N = 10, 20, or 30) in the mixtures and in the number of components in which the two mixtures overlap (O, where $0 \leq O < N$). The formula to calculate the number of possible mixtures is:

$$\binom{C}{N} = \left(\frac{C!}{(C-N)!\,(N!)}\right)$$

The procedure to calculate the number of possible pairs of mixtures of N components that overlap by O components is to choose one of the two members of the pair, which is chosen arbitrarily as N out of C. Then we have to choose O elements. The formula to calculate the number of possible pairs is:

$$\binom{C}{N}\binom{N}{O}\binom{C-N}{N-O}/2$$

Numbers are rounded for display but were computed with arbitrary precision using Mathematica.

Calculation of the Number of Discriminable Mixtures From the Empirically Determined Resolution

When calculating the number of discriminable stimuli that differ along a single dimension, such as the wavelength of monochromatic light, we parcel the range of stimuli into segments whose size equals the difference limen (or resolution). For a hypothetical example, if we could perceive light with wavelengths in the range between 400 and 700 nm and discriminate two lights when they differ by more than 10 nm, there would be 30 segments of size 10 nm:

400 nm ↔ 410 nm, 410 nm ↔ 420 nm, ..., 690 nm ↔ 700 nm.

An equivalent representation of these segments can be given by labeling them by their center:

405 nm +/- 5 nm, 415 nm +/- 5 nm, ..., 695 nm +/- 5 nm.

In this second representation we have chosen one particular stimulus from each segment, the center of the interval, as an explicit representative. There are 30 stimuli (405 nm, 415 nm, ..., 695 nm) each of which is separated from the others by at least one difference limen. The 30 stimuli form a set of stimuli that are mutually discriminable, so in this hypothetical example we can discriminate 30 different colors. Notice that in moving from the first to the second representation of these segments, we switched from describing segments as having a width (or diameter) equal to the limen (10 nm) to having a center and a radius around that center of half the limen (5 nm).

When the stimulus space is two-dimensional, instead of calculating the number of segments of a certain width, one would calculate how many circles of a certain diameter can be packed into the stimulus space. For a three-dimensional stimulus space, one would count spheres that can be packed into the three-dimensional space. This mathematical procedure can be generalized to stimulus spaces with more than three dimensions. Thus, the number of stimuli that can be discriminated in a multidimensional stimulus space can be determined through *sphere packing* (*14*). Regardless of the number of dimensions of the stimulus space, one can calculate how many spheres of a diameter equal to the difference limen can be packed into the stimulus space. The number of these spheres that can be packed into the stimulus space is the number of discriminable stimuli, just as in a one-dimensional stimulus space the number of segments with width equal to the difference limen that can be packed into the space is the number of discriminable stimuli.

We applied this strategy of sphere packing in a multi-dimensional stimulus space to calculate the number of discriminable mixtures from the difference limens that we empirically determined in the psychophysical experiments presented here. The question that we addressed by this calculation was how many mixtures of N components out of a collection of C components exist that all differ from one another by more than D components. If two mixtures of N that differ by more than D components can be discriminated, this is also the number of discriminable mixtures. D is the difference limen. For pairs of mixtures, D is the number of components in the mixtures (N) minus the number of components that are present in both (the overlap O) for pairs which still can be discriminated (D = N-O). In the geometric analogy, the question how many discriminable mixtures there are, is the problem of how many balls of diameter D (or radius R; D = 2*R) can be packed into a C-dimensional space.

Calculating the number of balls that can be packed into a multidimensional space is a two-step process. First, we had to calculate how many mixtures are contained in each ball of a diameter equal to the difference limen [formula (2) below]. These are mixtures that cannot be discriminated from one another. Then, the total number of all mixtures in the stimulus space has to be divided by the number of mixtures contained in each of these balls to arrive at the number of balls that can be packed into the stimulus space [formula (3) below]. This is the number of discriminable mixtures.

To calculate how many mixtures are contained in a ball of a certain diameter, we first calculated how many mixtures are contained in a *sphere* of a certain diameter [formula (1) below] and then, using the results of this calculation, the number of mixtures in a *ball* of that diameter [formula (2) below]. A *sphere* is a spherical surface or shell, so a sphere of radius R around its center X is the set of all points which is *precisely* at distance R from X. A *ball* is the spherical surface and everything within it, so a ball of radius R around its center X is the set of all points at distances *smaller than or equal to* R. Spheres are hollow while balls are solid. In our case, the points in stimulus space represent mixtures. The mixtures on the sphere around any give mixture X all differ by exactly R components from mixture X. The mixtures in the ball all differ by R or less components from X. More importantly, all mixtures in one ball differ from each other by less than the difference limen D (=N-O). Therefore, all the mixtures in a ball are indiscriminable, just as for all the light stimuli between 400 and 410 nm in the above example.

How many different mixtures of N components are contained in a sphere of radius R around a mixture X in a C-dimensional space? The sphere of radius 1 around mixture X consists of all the mixtures in which precisely one component has been changed. They all overlap with mixture X by N-1 components. There are N choices of the single component to be changed, and each one can be changed to any component not already in X, of which there are C-N. Thus the sphere of radius 1 contains N*(C-N) odor mixtures. Similarly, for the sphere of radius 2 we have to choose 2 components from X. There are N(N-1)/2=$\binom{N}{2}$ such choices, and these two components can be changed to any of the C-N components not in X, giving us $\binom{C-N}{2}$ such choices. Since these choices are independent, the formula to calculate how many different mixtures of N components are contained in the sphere of radius R in a C-dimensional space is:

$$sphe(R) = \binom{N}{R}\binom{C-N}{R}$$ Formula (1)

Formula (1) allows us to calculate the number of mixtures that differ by *exactly R* components from a mixture X. To calculate how many mixtures differ by *R or less* components, it has to be calculated how many mixtures are contained in a ball (not a sphere) with a diameter equal to the difference limen. The number of stimuli contained in a ball is calculated by summing the numbers of stimuli contained in the spheres that make up the ball. Because we cannot change components fractionally, the number of stimuli contained in a ball with radius R it the sum of the numbers of mixtures in the spheres of radius R, R-1, R-2, ..., , and 0 (The sphere of radius 0 contains only mixture X itself). Thus, the formula to calculate how many different mixtures of N components are contained in the ball of radius R in a C-dimensional space is:

$$ball(R) = \sum_{r=0}^{R} sphe(r)$$ Formula (2)

Formula (2) allows us to calculate the number of mixtures that differ by *R or fewer* components from a mixture X. If two mixtures can only be discriminated if they differ by more than D (=2*R) components, then *ball(R)* is the number of mixtures that cannot be discriminated from one another. In the geometric analogy, it is the size of the ball around a point X that contains all the mixtures that cannot be discriminated from the mixture at its center and from each other.

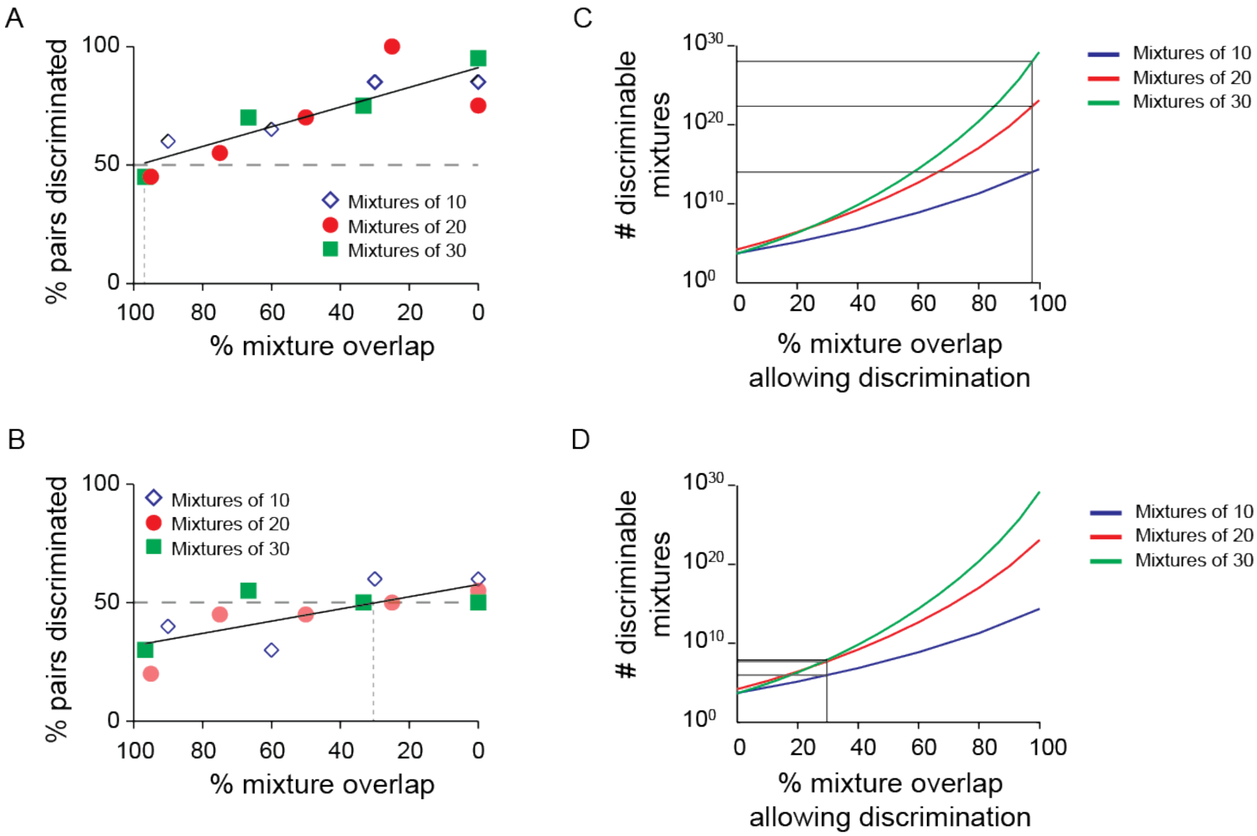
In a final step, to approximate the number of discriminable mixtures, it has to be calculated how many balls of size *ball(R)* can be packed into the stimulus space. This is done by dividing the total number of mixtures in the stimulus space by the number of mixtures contained in a ball of diameter D. The formula to calculate this is:

$$disc(D) = \frac{\binom{C}{N}}{\sum_{r=0}^{D/2}\binom{N}{R}\binom{C-N}{R}}$$ Formula (3)

disc(D) is the number of discriminable mixtures of N out of a collection of C if only mixtures that differ by more than D components can be discriminated (D=2*R=N-O). This is an upper bound as it fails to count the “dead space” in the corners between spheres.

Formula (3) was used to generate the graphs in Fig. 3 C/D and Fig. S1 C/D. C is 128 in these cases and the value of O changes along the x-axis. The three lines are the results of formula (3) for three different values of N (10, 20, and 30). The numbers of discriminable mixtures reported in this paper were then extrapolated from the graphs using Mathematica by determining the number of discriminable mixtures that correspond to the values of O (in percentage) that were shown in the psychophysical testing to correspond to the difference limen.

Fig. S1.



Inter-individual variability in the discrimination capacity of subjects. (A) Discrimination capacity of subject 26 (Table S2) according to % mixture overlap. (B) Discrimination capacity of subject 2 (Table S2) according to % mixture overlap (C, D) Extrapolation of the number of discriminable mixtures derived from A and B, respectively.

Additional table S1 (separate file)
The 128 odorous molecules used in this study.

Additional table S2 (separate file)
The odor mixtures used in this study and the results of the discrimination tasks.