LETTER TO THE EDITOR

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This journal recently published a review of the paperback edition of my book *The Secret of Scent*. The reviewer is free to disagree with the ideas, of course, but inaccurate criticism expressed as ad hominem arguments should not be acceptable in any responsible journal. He dismisses one class of mechanisms proposed (in the same journal, incidentally) for primary olfactory reception as a "myth", "alchemy", and "contrary to facts and basic scientific principles". These claims are based on a number of straightforward errors on his part. I write to correct the record.

The reviewer claims I invented the longestablished technique of inelastic electron tunneling

He states that inelastic electron tunneling spectroscopy (IETS) is "an outrageous mechanism" that I "invent" for the detection of molecular vibrations. I would of course be immensely proud to have invented IETS, but alas Jaklevic and Lambe beat me to it in 1966 (Jaklevic and Lambe 1966). Furthermore, Troisi et al. (2007) showed that it works at the single-molecule level.

The reviewer does not accept that different spectroscopies have different selection rules

The reviewer does not appear to be aware that IETS is a working spectroscopic method. This serious gap in his knowledge is why he refers solely to infrared (IR) absorption bands. He also seems unaware of selection rules that determine the amplitude and sometimes the very existence of a spectroscopic "line"; such selection rules underpin many spectroscopies. His conviction that my theory relies on IR absorption is particularly vexing in a review of a book that devotes considerable pages to discussing the various spectroscopic methods.

The reviewer makes condescending comments on a paper by Brookes et al. (2007) published in *Physical Review Letters*, the premier journal in its field, whose editors singled out the findings as of special interest. Yet, according to the reviewer: "Bands in this region were calculated by Brookes et al. (2007) to be weak. However, these presumptions are not borne out by the facts that show prominent IR absorption bands [...] for all 3 carborane isomers." The amplitude of a spectroscopic band on a published IR spectrum is not quantitative because the person operating the spectroscope routinely alters cell thickness to achieve full scale on the biggest peak. In the case of carboranes, the bonds are all very nonpolar (as DFT 6-31G** B3LYP calculations of Brookes et al. 2007 confirm), all the peaks are small, and the boron-hydrogen (BH) bond stretch intensity, though much smaller than in boranes, is thus magnified severalfold.

The reviewer is unwilling to accept that boranes smell sulfuraceous, despite never having smelled them

The article takes me to task for insisting on the importance of the fact that nothing in nature smells like an -SH group save a -BH group and that the only thing these 2 have in common is a vibrational frequency around 2500 wave numbers. It is also pointed out that I describe the smell of decaborane variously as reminiscent of sulfur, rotten eggs, thiols, leeks, or boiled onions—an "imprecision" the reviewer finds disturbing. Readers with some knowledge of aromachemicals will understand that all these descriptors refer to the unmistakable odor of -SH and that this, rather than the difference between leeks and onions, is the important point. In support of this characterization, my book mentions Alfred Stock, recipient of the Nobel Prize for his work on boranes, who described their odor as "reminiscent of hydrogen sulphide."

The reviewer, although unfamiliar with the significant number of isotope experiments, is nonetheless adamant that no isotope effects exist

His discussion of the vital question of whether isotopes can be distinguished by smell is confused. He makes a general, unsupported claim that "normal and deuterated compounds have essentially the same odor" and insists that they should smell vastly different, not slightly different, and that more people should be able to smell the difference. Given that normal and deuterated compounds are practically identical in shape and chemical behavior, mainstream theories of olfaction are hard put to explain even a slight difference in smell, let alone one that 47% of subjects (as found in one study, Haffenden et al. 2001) can perceive reliably. I believe that there is still important experimental work to be done in this area.

The reviewer fails to accept that electrochemical reactions involve both electrons and chemistry

He asserts that the specific proposed mechanism of electron tunneling spectroscopy is incorrect because it uses "free" electrons from nicotinamide adenine dinucleotide (NADH) and nicotinamide adenine dinucleotide phosphate. However, he seems to be aware only of the purely chemical aspect of NADH, namely, hydrogen transfer, and totally unaware of the electrochemical aspect, in which 2 half reactions separated in space—one producing electrons and H+ ions and one consuming electrons—occur in a coupled fashion. Two things make such reactions possible: the buffering of H+ ions in aqueous media and the conduction of electrons, sometimes over large distances, within proteins. For example, membrane oxidoreductases use intracellular NADH to reduce extracellular oxygen and transport electrons over 5-nm distances Baker et al. (2003). The literature on this is vast, and the transfer of electrons within proteins has been amply demonstrated by elegant spectroscopic experiments Gray and Winkler (2005). Given the importance of such electron transport in mitochondria, we would not be alive if the reviewer's assertions were true.

The reviewer claims all is well in the understanding of smell so a spectroscopic theory is unnecessary

He asserts "there exists a close relationship between the types of odors and the steric and electronic chemical features of odor molecules." Surprisingly, he quotes Rossiter and Moncrieff in support of this assertion, though anyone who has read these reviews knows that they are catalogues of exceptions, not of rules. Rossiter's article was part of her PhD thesis, and her former supervisor at Quest, Charles Sell, has since written a candid review titled "On the unpredictability of odor" (Sell 2006) that sets the record straight: *odor cannot be predicted by molecular shape*.

Has this reviewer got anything right? To his credit, he offered 7 valid corrections of detail in figures and text. I am grateful to him for pointing these errors out and will be sure they are corrected in subsequent editions; I wish my publisher had hired him as a proofreader. Also correct is his first observation: the paperback edition is indeed essentially the same as the hardback.

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