calculations, the notion of an  $H_2$  moiety attached to a CH<sub>3</sub> tripod is only lost before dissociation if the temperature is very high (Fig. 2B) (13).

If the theoreticians are right in thinking that  $CH_5^+$  is a highly fluxional molecule, it should come as no surprise that CH<sub>5</sub><sup>+</sup> is quite resistant to direct experimental characterization. Kenzo Hiraoka and co-workers found their mass spectrometric data to be compatible with a 3c-2e bonded structure of  $C_s$  symmetry (14). However, this conclusion was arrived at by attaching methane molecules as thermochemical sensors to a CH5<sup>+</sup> core. Using less perturbing H<sub>2</sub> molecules instead of CH<sub>4</sub> yielded somewhat less clear evidence in favor of 3c-2e bonding (14). Mass spectrometric evidence for the  $C_s$  structure was also found by contrasting the reactivity of  $CH_4D^+$  and  $CD_4H^+(15)$ . Stabilizing  $CH_5^+$ by attaching H<sub>2</sub> molecules led to the first infrared spectra of the C-H stretching bands of  $CH_5^+$  cores in trapped  $CH_5^+$  $(H_2)_n$  complexes (n > 1) (16). As expected, solvation clearly affected hydrogen scrambling in the CH<sub>5</sub><sup>+</sup> core, which became frozen when at least three H<sub>2</sub> molecules were attached. However, none of these studies can claim to have resolved the puzzle of unperturbed CH<sub>5</sub><sup>+</sup>. Takeshi Oka started his quest for free  $CH_5^+$  in the spring of 1983 (17), the fruits of which he presents now (3). The resulting determination of the high-resolution infrared spectrum of the C–H stretching band of  $CH_5^+$  is a major achievement. However, we will not know the real structure of  $CH_5^+$  until the jungle of 1000 lines resolved by Oka's group in a very narrow spectral range is assigned.

To arrive at a comprehensive understanding of CH<sub>5</sub><sup>+</sup>, cutting-edge experimental and theoretical studies will be needed. Embedding molecules in nanofridges, that is, small superfluid helium droplets, may allow high-resolution rotational-vibrational spectra to be obtained at a temperature of only 0.4 K, with minimal interaction between the molecule and the cooling agent (18). At this extremely low and controlled temperature, the CH<sub>5</sub><sup>+</sup> spectrum will hopefully become somewhat simpler. Another exciting perspective is the use of Coulomb explosion imaging (19), which allows direct measurement of the many-body nuclear probability density, reconstructed from many independent "snapshots" of the vibrating nuclear skeleton. In this way, a representation like that depicted in the figures could be inferred directly from experiment. Theoretical studies must seek a solution to the time-dependent quantum motion of  $CH_5^+$  on a potential energy surface of the quality provided in (9, 10), while simultaneously taking into account all degrees of freedom—a highly complex endeavor. CH<sub>5</sub><sup>+</sup> will certainly continue to challenge many groups in various fields of expertise for some time to come.

## References

- 1. R. J. Saykally, Science 239, 157 (1988).
- V. L. Tal'roze and A. K. Lyubimova, Dokl. Akad. Nauk SSSR 86, 909 (1952).
- 3. E. T. White, J. Tang, T. Oka, Science 284, 135 (1999).
- G. A. Olah, Angew. Chem. Int. Ed. Engl. 34, 1393 (1995); see also F. Flam, Science 266, 369 (1994).
- E. Herbst, S. Green, P. Thaddeus, W. Klemperer, Astophys. J. 215, 503 (1977); D. Talbi and R. P. Saxon, Astron. Astrophys. 261, 671 (1992).
- A. Gamba, G. Morosi, M. Simonetta, *Chem. Phys. Lett.* 3, 20 (1969); G. A. Olah, G. Klopman, R. H. Schlosberg, *J. Am. Chem. Soc.* 81, 3261 (1969); W. T. A. M. van der Lugt and P. Ros, *Chem. Phys. Lett.* 4, 389 (1969).
- V. Dyczmons and W. Kutzelnigg, Theoret. Chim. Acta 33, 239 (1974); see V. Dyczmons, V. Staemmler, and W. Kutzelnigg [Chem. Phys. Lett. 5, 361 (1970)], for the corresponding Hartree-Fock reference calculations.
- D. Marx and A. Savin, Angew. Chem. Int. Ed. Engl. 36, 2077 (1997).
- H. Müller, W. Kutzelnigg, J. Noga, W. Klopper, J. Chem. Phys. 106, 1863 (1997).
- P. R. Schreiner, S.-J. Kim, H. F. Schaefer III, P. von Ragué Schleyer, J. Chem. Phys. 99, 3716 (1993).
- 11. D. Marx and M. Parrinello, *Nature* **375**, 216 (1995). 12. \_\_\_\_, *Z. Phys. B* **95**, 143 (1994).
- 13. . . Z. Phys. D 41, 253 (1997).
- K. Hiraoka and P. Kebarle, J. Am. Chem. Soc. 97, 4179 (1975); K. Hiraoka and T. Mori, Chem. Phys. Lett. 161, 111 (1989); K. Hiraoka, I. Kudaka, S. Yamabe, *ibid.* 184, 271 (1991).
- A. J. R. Heck, L. J. de Koning, N. M. M. Nibbering, J. Am. Soc. Mass Spectrom. 2, 453 (1991).
- D. W. Boo and Y. T. Lee, *Chem. Phys. Lett.* **211**, 358 (1993); D. W. Boo, Z. F. Liu, A. G. Suits, J. S. Tse, Y. T. Lee, *Science* **269**, 57 (1995).
- 17. T. Oka, Philos. Trans. R. Soc. London Ser. A **324**, 81 (1988).
- S. Grebenev, J. P. Toennies, A. F. Vilesov, *Science* 279, 2083 (1998); see also K. K. Lehmann and G. Scoles, *ibid.*, p. 2065.
- 19. Z. Vager, R. Naaman, E. P. Kanter, *ibid*. **244**, 426 (1989).

## NOTA BENE: MEDICINE

## Fear of Flying!

The meager peanut snacks offered on airplanes may be a source of irritation for most passengers, but for those unfortunate enough to be allergic to peanuts they pose a serious health hazard. In the United States, about 100 individuals allergic to different foods (primarily peanuts) die each year from anaphylactic shock after accidental exposure to the culinary culprit. Peanut allergy appears to be on the increase particularly among young children, so much so, that U.S. lawmakers may mandate peanut-free zones in schools and on airplanes.

Anaphylaxis is an immune reaction initiated by an allergen such as peanut protein that crosses the mucosa and binds to immunoglobulin E (IgE) on the surface of mast cells. Cross-linking of IgE triggers mast cells to release histamine and other mediators that cause a systemic anaphylactic reaction, which includes the contraction of smooth muscle in the tissues lining the airways. Unless epinephrine is administered quickly, anaphylaxis can be fatal.

The approach outlined in a paper in this month's *Nature Medicine* (1) may provide a solution for individuals suffering from food allergies or other types of IgE-mediated (atopic) diseases, such as hay fever and asthma. Roy and his colleagues at the Johns Hopkins University in Baltimore used an oral DNA vaccine to induce tolerance to peanut allergen in mice. Animals were fed nanoparticles composed of DNA encoding Arah2 (the principal allergen in peanuts) and chitosan, a biodegradable component of crustacean shells that protects the DNA and delivers it to the epithelial cells lining the intestine. In nanoparticle-fed mice, mucosal IgA levels increased as did the T helper cell type I immune response, with a concomitant decrease in peanut allergen–specific IgE antibody. When orally immunized animals were sensitized to peanuts and then challenged with Arah2, they

showed a delayed and much milder anaphylactic reaction than nonimmunized mice or mice that received control DNA instead of peanut allergen DNA.

The authors note that this is a preventive vaccine model in which mice are orally immunized before sensitization to peanut protein. Closer to the human situation, but less likely to succeed, is a therapeutic vaccine model in which the peanut allergen DNA is administered to animals

that are already sensitized, with the goal of rerouting an immune response that is already under way. If Roy *et al.* can reproduce their findings in sensitized mice, then an oral vaccine to induce tolerance in humans with peanut allergy may be on the horizon. And passengers allergic to peanuts need fear flying no more.

References

1. K. Roy et al. Nature Med. 5, 387 (1999).

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