then increase in tone and consequently raise the blood pressure. The increase in the peripheral vascular tone must result from an increase in calcium load in vascular smooth muscle cells, because cytosolic calcium is the penultimate signal for vascular smooth muscle contraction. Hence, the effective use of calcium channel blockers as antihypertensive drugs. However, renal dysfunction in salt excretion might also be expressed by a rise in the calcium load in cells other than vascular smooth muscle cells. Because the cytosolic calcium is a second messenger for multiple cellular functions, it is possible that "salt sensitivity" is in fact a reflection of renal dysfunction in excreting a high salt load, expressed bv cellular abnormalities that exert deleterious effects on the cardiovascular system regardless of whether or not there is a rise in blood pressure.

The important question is not whether a high salt intake causes hypertension in some humans, but whether it increases (or for that matter diminishes) morbidity and mortality from any cause.

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Permit a physicist to make a few comments. Chemical potentials are typically proportional to the logarithm of concentrations. Most of the comparisons of sodium ingestions have been over a narrow range (between 6 and 9 grams daily, for example), which may be too small to show an effect, even if one is present. In order to demonstrate the existence of an effect, genuinely low sodium diets (less than 100 milligrams daily) should be used. But this was done, successfully, at least for severe hypertensives, by Kempner half a century ago. The open, and perhaps unanswerable, question is whether these results can be extrapolated to small reductions of sodium intake in the general population. This question resembles the similarly unanswered question of the validity of linear extrapolation of the effects of ionizing radiation to small doses. In the case of sodium ingestion, because of the chemical potential argument, a plausible hypothesis is that effects are proportional to the logarithm of the ingestion rather than to the ingestion itself.

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Quantum Computing

In April 1996, 5 milliliters of di-bromothyophene, a molecule containing two coupled hydrogen atoms, were placed inside a 500-megahertz magnet. The sample was then subjected to a sequence of radio frequencies (rf) and gradient pulses, after which the collective behavior of the molecules of the sample was that of a quantum system in a pure state. Another sequence of rf pulses implemented the first quantum logic gate produced by nuclear magnetic resonance (NMR). The nuclei of the hydrogen atoms acted as two quantum bits, and thus the first implementation of a two-qubit NMR quantum computer came to be. This experiment was performed at the Francis Bitter Magnet Laboratory at Massachusetts Institute of Technology by David Cory, Tim Havel, and me. We wrote up our exciting results and submitted them to Tom Toffoli of Boston University, chair of Physcomp '96, where the paper appeared on the conference Web site in July and in the proceedings in November 1996 (*1*).

In a Research Commentary, "Fast searches with nuclear magnetic resonance computers" (*Science*'s Compass, 10 Apr., p. 229), Jonathan A. Jones states that "two different two-qubit NMR computers have been built: one by Chuang and co-workers [he cites a paper then in press (*2*)] . . . and one by my research group in Oxford . . . [he cites work then in preparation (*3*)]." Although the *Physcomp '96* paper was mentioned (but not cited) by Gary Taubes in a Research News article ("Putting a quantum computer to work in a cup of coffee," 17 Jan. 1997, p. 307), this first implementation was not cited in a *Science* report ("Bulk spin-resonance quantum computation" by N. A. Gershenfeld and I. L. Chuang, 17 Jan. 1997, p. 350) or technical comments ("The usefulness of NMR quantum computing" by W. S. Warren, 12 Sept. 1997, p. 1688; response by N. Gershenfeld and I. Chuang, p. 1689) concerning quantum computation by NMR.

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Response

Fahmy is quite right to draw attention to his seminal work in NMR quantum computing. His pioneering studies of 2,3-dibromothiophene, conducted with Cory and Havel, included the first experimental demonstrations of effective pure states and quantum logic gates in NMR. This work was originally described in the proceedings of *Physcomp '96* (*1*) and was swiftly followed by a detailed theoretical paper

(*2*). In my Research Commentary, I did refer to this later paper, but as it does not contain experimental results, I agree that I should have also referred to the original paper (*1*).

Whether the system of Fahmy *et al.* constitutes a true quantum computer is open to debate, as they implemented quantum gates, but apparently did not attempt to implement quantum algorithms. They did, however, demonstrate all the basic elements required to build such a computer and therefore could be called the "fathers" of the NMR quantum computer. I am delighted to have this opportunity to clarify the matter.

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Crystallography of a Photocycle Intermediate

In their report "Energy transduction on the nanosecond time scale: Early structural events in a xanthopsin photocycle" (20 Mar., p. 1946), Benjamin Perman *et al.* discuss how proteins change when light energy is converted into a chemical signal in a halophilic phototrophic bacterium (*1*). It seems to us, however, that the crystallography in the report is in error. The most serious problem is that the proposed structure of the intermediate does not agree with the difference electron density map. The largest negative electron density feature (M) is appropriately ascribed to movement of the carbonyl oxygen, but the large positive density (L), which would logically be associated with the carbonyl, is incorrectly ascribed to movement of the carbon-carbon double bond.

The results reported by Perman *et al.* should be compared with those of Genick *et al.* (*2*), which was also about a photoactive yellow protein photocycle early intermediate (*3*). The differences that are present may be ascribed to a lower resolution of the data in the report by Perman *et al.*, which in our view has led to an incorrect interpretation. The higher resolution results obtained by Genick *et al.* (*2*), during isomerization of the carbon-carbon double bond, show that it is the carbonyl group that rotates.

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3. We also prefer the nomenclature used by Genick *et al.* (*2*) and established earlier by our group (*1*) to that used in the report by Perman et al.; that is, photoactive yellow protein, not xanthopsin, and intermediates I^1 and I^2, instead of pR and pB.

Response

Meyer *et al.* raise an interesting point concerning the structural interpretation presented in our report, which was derived from real-time, ambient temperature measurements, in contrast with that derived from data obtained at cryogenic temperature by Genick *et al.* (*1*). These interpretations unquestionably differ. The interpretation of our results now advanced by the Arizona group was in fact the one we considered first immediately on inspecting our results. In our initial attempts, the intermediate did not behave as well under crystallographic refinement as the one we presented in our report. When we became aware of the Genick *et al.* results [one of us (K.M.) and Elizabeth Getzoff presented their results back-to-back at a meeting in Grenoble, France, in January 1998], we reexamined our structural interpretation and concluded that our crystallographic data was not compatible with the model proposed by Genick *et al.*

It is possible for the interpretations in both our report and in the paper by Genick *et al.* (*1*) to be correct because the conditions under which the data were obtained are so different. Structural relaxation is greatly hindered at cryogenic temperatures and may be qualitatively (not just quantitatively) altered from that at ambient temperature. Freeze-trapping of authentic reaction intermediates is therefore not necessarily a straightforward process (*2*). Related studies, from our laboratory, of time-resolved crystallography on myoglobin at both ambient and cryogenic temperatures (*3*) also encounter this question. We maintain that our data and interpretation are correct (*4*).

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4. "Xanthopsins" refers to the family of photoactive yellow proteins [R. Kort *et al.*, *EMBO J.* **15**, 3209 (1996)].