world"; and I know from numerous kind comments I have received that other people did not read the letter that way.

Were I inclined to the ivory tower, surely I would not be a member in good standing of the American Civil Liberties Union, Americans for Democratic Action, the Congress of Racial Equality, the National Association for the Advancement of Colored People, and several similar organizations; I would not have helped to circulate the Pauling petition; nor would I have contributed much time, over the past 2 years, to the editing of the bulletin published by the Greater St. Louis Citizens' Committee for Nuclear Information. I think that Hedgpeth has developed a curious allergy that makes him break out into a rash of disagreement at the very sight of my name.

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Chemical Analysis by Mass Spectroscopy

In his very interesting article on the use of x-ray fluorescence analysis as a tool for chemical analysis in biology (*1*), Theodore Hall has included a table entitled "Capabilities of some methods for assay of chemical elements." Among these methods he lists mass spectroscopy. His Table 1 indicates that the minimum concentration detectable by this technique, "in the specimen fed to the device," is about 10^{-6} parts per million.

This statement, he says in his reference *31*, rests upon data given in a 1955 paper by M. G. Inghram (*2*). It is, however, a slight misinterpretation of Inghram's statement. It is the purpose of the present letter to make more clear the actual range of usefulness of mass spectroscopy. In brief, a sensitivity of one part in 10^{12} may well be attained in the near future, but it as yet has not even been approached by any commercial instrument. Nevertheless, present-day analytical mass spectrometers and spectrographs are indeed highly sensitive instruments; in fact, spark-source-equipped mass spectrographs are now pushing down into the one-part-per-billion (10^{-9}) region, in favorable cases. Some of the best electron-bombardment-source gas analysis instruments also approach this sensitivity. With a "tandem" instrument

(in which the ion beam passing through the image slit of the first spectrometer is again resolved into components of different mass-to-charge ratio in a second analyzer) the Knolls Atomic Power Laboratory research group has in fact demonstrated (*3*) an abundance sensitivity, in the low mass region, approaching 10^{11}. So it seems that the possibility of determining impurities present at the 10^{-12} level does in fact exist.

However, the sensitivity cited by Hall has been achieved only in certain isotope dilution experiments. And such experiments in general require some chemical processing of samples, usually with rather extensive preconcentration. In fact, the usable sensitivity of this technique is in general limited by contamination and instrumental background problems, the highest sensitivities being reported for nuclides that do not occur at all naturally, or that are of very small natural abundance, especially in laboratory and reagent environments.

Hall's Table 1 appears to state that mass spectroscopy *in toto* is appropriate to the analysis of only 68 elements. This statement likewise applies just to the isotope dilution technique, where the limiting factor is, of course, whether there exists an isotope of the element to be determined which is suitable for use as the internal standard (that is, which is in reasonably good supply and which is either stable or, if radioactive, of long enough half-life to permit one to perform the desired experiment). No such limitation applies when the spark, the crucible, or certain other ion sources are used. The N range of mass spectroscopy thus includes all the elements which have isotopes of long enough half-life to survive during the very short transit from ion source to detector. There is no Z limit for the instrument. And mass spectroscopy of course yields data on isotopic composition as well as on elemental abundance.

The minimum weight of element detectable by the technique may, in favorable cases, be well below the 10^{-12} grams listed by Hall; and, while the technique must in general be classed as destructive, amounts consumed in several ionization techniques are so small that it can, in these cases, be considered at least as nondestructive as, say, the electron-probe microanalyzer mentioned by Hall. Our organizations are in fact working jointly on the development of a mass spectroscopic analog of this device, which, we believe, will be able to exceed the sensitivity limit of the secondary x-ray microprobe by several orders of magnitude, while not being subject to its "blind spot" limitations.

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References

1. T. Hall, *Science* **134**, 449 (1961).
2. M. G. Inghram, in *Trace Analysis*, J. H. Yoe and H. J. Koch, Eds. (Wiley, New York, 1957).
3. F. A. White, F. M. Rourke, J. C. Sheffield, "A three-stage research mass spectrometer," *U.S. Atomic Energy Comm. Research and Development Rept. No. KAPL-1843* (1958).

The foregoing comment by Herzog and Marshall is a much fuller and better exposition of the capabilities of mass spectroscopy than appears in my article, partly because it is impossible to delineate a method's scope with one line in a table plus a brief footnote, and partly because I am not a mass spec-

troscopist. I must accept their main point: at present one cannot analyze directly down to a concentration of 10^{-12} for a wide range of elements in biological materials.

In extenuation, it should be noted not only that Table 1 in my article was characterized in the text as quite approximate but that the entry for mass spectroscopy posed a special problem. For most of the methods listed in Table 1 I drew on performance figures achieved during extensive biological research. For mass spectroscopy there is no comparable literature, and the technique has not had the benefit of comparable intensive biological trial. The inherent sensitivity of the method would be obscured by listing limits representing the present degree of mastery of contamination. I tried, rather, to tabulate the outstanding inherent sensitivity, leaving the implication that the method should play a larger role in biological trace work. This implication seems to be confirmed by the remarks of Herzog and Marshall.

May I add a few brief comments. I did not refer to commercial instruments, and I did not mean to imply that the isotope dilution method of mass spectroscopy (with its approximately 68 suitable isotopes) was the only method suitable for trace work.

I cannot quite agree with Herzog and Marshall's comment on nondestructive analysis. One hopes to analyze identified microentities; hence, much of the advantage of nondestructiveness is generally lost if the unconsumed and the analyzed regions are not identical. The degree of destructiveness of the electron microprobe is not yet established, but even if it destroys a circular area 1 micron in diameter, with the surroundings remaining recognizable, I believe conventional mass spectroscopy cannot hope to match it in nondestructiveness. Of course, mass spectroscopy with a microfocused ion beam could conceivably be similarly nondestructive.

With respect to "blind spots" I should mention that several laboratories are now seeking intensively to extend x-ray spectroscopy down to atomic number 6.

In summary, I think that the exposition by Herzog and Marshall should be stimulating to trace-element biologists, and I hope we may have even more detailed evaluations of the capabilities of the mass spectrometric method.

At this point I would like to make amends for an unrelated omission in my recent article: With respect to zinc concentrations in malignant prostatic tissue, although I did not seek to give a comprehensive bibliography, I should have listed a relatively early work, "The occurrence of zinc in the human prostate gland," by C. A. Mawson and M. I. Fischer [*Can. J. Med. Sci.* **30**, 336 (1952)].

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Sparing of Folinic Acid by Thymidine

In the recent report "Sparing of folinic acid by thymidine," by Grossowicz and Mandelbaum (*1*), it is quite clear that several important literature references are lacking.

The synergistic action of folinic acid and thymidine in stimulating the growth of *Pediococcus cerevisiae (Leuconostoc citrovorum)* ATCC 8081 was first noted by Bardos *et al.* (*2*). Furthermore, the finding that thymidine increased the