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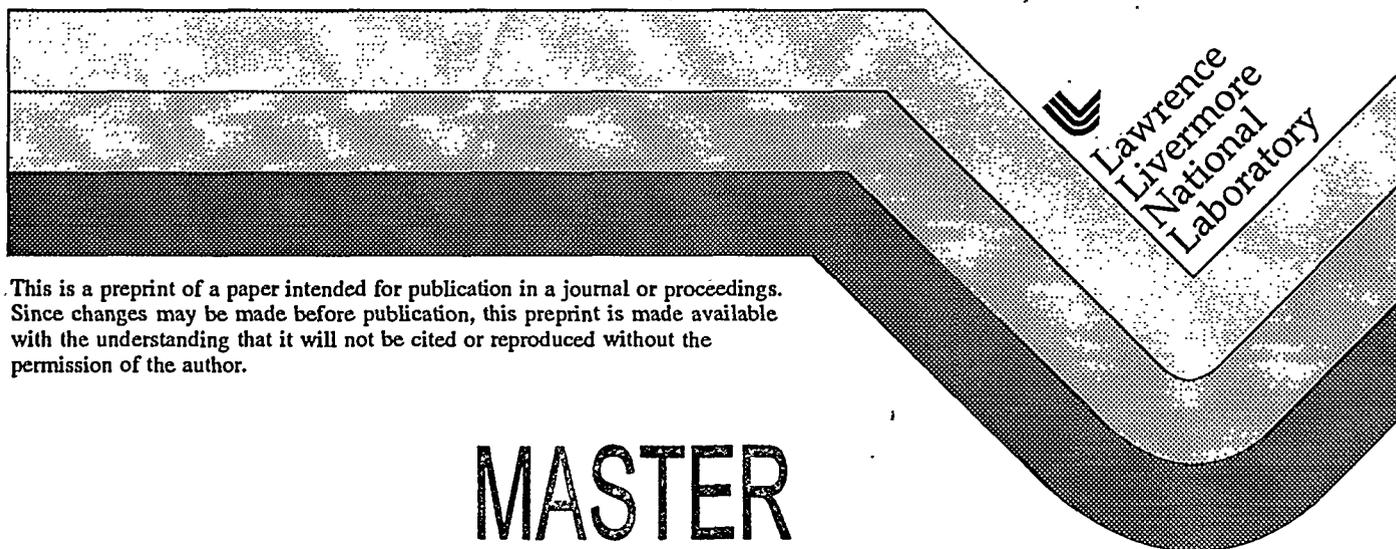
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Elements in Biological AMS

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Abstract

AMS provides high detection sensitivity for isotopes whose half-lives are between 10 years and 100 million years. ^{14}C is the most developed of such isotopes and is used in tracing natural and anthropogenic organic compounds in the Earth's biosphere. Thirty-three elements in the main Periodic Table and 17 lanthanides or actinides have long lived isotopes, providing potential tracers for research in elemental biochemistry. The overlap of biologically interesting heavy elements and possible AMS tracers is discussed.

Introduction

Life developed on Earth from common elements available in the prevailing aqueous solvent. The major nutritive elements are therefore light elements with high abundance at the earth's surface: hydrogen, carbon, nitrogen, oxygen, a few light metals such as calcium and magnesium, along with light non-metals like fluorine and chlorine. Primary biological chemistry of these elements takes place in aquatic solution within hydrophobic layers of ordered membranes to separate the balanced reactions and products of life from the less ordered surroundings. Trace amounts of elements and chemicals in nature are toxic to these reactions but are prevented from crossing membranes protecting the internal chemistry. Detoxification pathways also evolved to remove natural toxins that arose in or entered into life-forms. In comparison, anthropogenic chemicals are introduced in the biosphere too quickly for higher life forms to adopt protective membranes or detoxifying metabolism. Humans depend on bulk nutrition from light elements, but the technologies of civilization, from ore smelting to micro-chip production, make disproportionate use of heavy elements, primarily metals and metalloids along with "unnatural" organic compounds and solvents. Risk analyses and science-based decision processes in fields from pharmaceutical development to environmental management require better understanding of these chemicals.

Analytical methods for determining elemental biochemistry possess fundamental limitations due, among other things, to instrumental specificity: an inability to distinguish the traced label or element from a natural background. Accelerator MS (AMS) achieves sensitivities up to parts in 10^{15} (ppq) by using long lived isotopes. The isotope lifetimes are short in geochemical terms (10 years to 100 million years), leaving the isotope very rare in natural samples and lowering restrictions on instrumental specificity needed for high sensitivity. The isotope lifetimes are too

long for efficient decay counting, however, and the potential of their natural rarity was not exploitable without new detection methods. AMS is one analytical tool for studying biological and environmental chemistry of elements, including their distribution pathways and molecular interactions leading to sequestration or toxicity.

Tracing natural chemical cycles in the biosphere with cosmogenic isotopes preceded efforts to apply AMS to biological tracing by more than a decade. Kielson and Waterhouse [1] suggested chemical tracing with ^{14}C labels and AMS in 1978, but only in 1990 did our facility reduce it to routine practice for application in toxicology [2-4]. Elmore suggested AMS tracing of heavier elements in 1987 [5], but efforts at understanding aluminum kinetics using ^{26}Al [6,7] and quantifying bone chemistry using ^{41}Ca [8] did not begin until a few years later.

AMS Elements

The applicability and limitation of AMS to elemental tracing is demonstrated by the periodic table shown in Figure 1. Only "AMS elements" are shown. These have isotopes with half-lives between 10 years and 100 million years. AMS increases sensitivity for isotopes with half-lives as short as a few hundred days, but the added sensitivity is not worth the expense. Isotopes with half-lives that approach billions of years have abundances in natural matrices that significantly reduce the advantage of controlled radioisotope release. The eight elements in bold face in Figure 1 are already measured at the UC Center for AMS using routine chemical preparation and spectrometric quantification. The major, minor, suspected nutrient, and acutely toxic elements are also indicated in Figure 1 by various shadings [9].

Only four of the major nutrient elements are traceable by AMS. The wide variety of organic compounds studied at low concentrations using ^3H and ^{14}C is not discussed here. ^{36}Cl is used in botanical tracing using inefficient decay counting, a reasonable approach until a compelling application requires the more expensive AMS sensitivity. A study of the numerous toxic chlorinated hydrocarbons *in vivo* at low doses could use ^3H , ^{14}C , and ^{36}Cl in valuable synergy. The important application of AMS to bone study in humans using ^{41}Ca is covered by Freeman [10] in these proceedings. The "purely" toxic elements are represented only by beryllium, mercury, and plutonium. Seventeen of the AMS elements are rare-earths with few uses in biology. In between these extremes are the trace nutrient elements that have a significant overlap with toxic elements. For these, "the dose makes the poison", and their study at concentrations much greater than natural nutrient levels produces obviously incorrect results. The remaining AMS elements either substitute for other elements in their same chemical class without significant biological effects or are not important to living systems due to their rarity, insolubility, or inertness in the biosphere. The most important of these is aluminum, which was excluded from natural evolutionary importance by its

ubiquitous presence as inert aluminum oxide. Elemental aluminum was first refined in the last century and is now a common metal, as well as an important component in food products, cosmetics, and industrial chemicals. These proceedings contain several papers exploring metabolism of this "unnatural" element. Flack and Elmore [11] recently reviewed the subject.

The trace or suspected nutrients, and the toxic elements are of most interest to our planned development at CAMS. We report in these proceedings [12] about the development of routine chemical separation and measurement of nickel isotopes. We have completed preliminary tests on detection of ^{79}Se and believe that the PX-AMS method will be easily extended to ^{32}Si , ^{53}Mn , and ^{60}Fe . The latter two are especially interesting for biological study because manganese is entering the U.S. environment as a gasoline (petrol) additive [13], and iron has well known biological importance. These two isotopes are very difficult to produce, however, and their availability is uncertain. The elements marked with a small black triangle have long-lived fission-product isotopes that are "easily" obtained from spent reactor fuel for tracing purposes. They are also monitor isotopes of nuclear fuel reprocessing.

Human Elemental Abundances

Experimentation with human subjects raises ethical and legal considerations, but human biochemistry, nutrition, and toxicity are best studied directly. The possibility of using radioactive isotopes of toxic elements in such research seems remote at first. Both the chemical and radioactive dose to the subjects must be reduced to levels of harm considered negligible by even the most sceptical honest observer.

Figure 2 shows the known abundances of "AMS elements" as solid circles in a 70 kg human [14]. The light, nutrient elements are obvious with their gram to 15 kg abundances. The "trace" elements exist at the 10-100 milligram level in the whole human. The elemental abundance in 100 μl of easily drawn blood is shown as open boxes in Figure 2. Except for bulk nutrients, we obtain 0.5 to 50 nanograms of most elements in this low impact biopsy. For example, the necessary nutrient, molybdenum, is present at 1.5 ng, while the recognized toxin, mercury, is present at half that level; emphasizing the fine distinction between some nutrients and toxins. Note that more elements are represented in the blood data set, since whole body ashing with quantitative elemental capture is difficult. This data is derived from a 1975 compendium, and better determinations of specific elemental abundances may be available. However, a complete survey does not exist in the recent literature.

Finally, Figure 2 shows the sensitivity for reported AMS elements as diamonds. While light elements are quantified to attograms, heavier isotopes of metals and metalloids are detectable in 1-100 femtogram amounts. This sensitivity is a part in $10^4 - 10^6$ of what is available in the 100 μl blood biopsy. We can trace these elements in humans by introducing a bioavailable dose of the long-lived isotope equivalent to less than one part in 10^{4-5} of the natural elemental abundance. The chemical

form and method of introduction must be controlled to avoid local toxicity, especially if the element is injected as a single bolus. However, the a 0.001 to 0.01% change in a natural elemental abundance cannot be harmful overall.

The radiation dose can also be harmlessly small and depends on the biological half-life (assuming a simple linear model), the isotope half-life, and the energy of decay. ^{133}Ba is a worst case example with a radioactive half-life 10.5 yr. As a calcium analog, it could have a long biological half-life in bone, perhaps 20 years. The decay energy deposited is small, since the decay is through electron capture, and a significant energy is carried away by the emitted neutrino. The rest appears as x-rays totalling 356 keV. A dose equivalent to 10^{-5} of the whole body content in a 30 year old subject amounts to a lifetime dose (to 80 years old) of only 140mSv, on the order of one or two chest x-rays spread over the 50 years. Longer lived isotopes or shorter biological lifetimes produce even lower radiological doses. Many long lived isotopes decay through electron capture with similar low energy deposition. Thus, chemical and radiation issues in AMS tracing experiments are surmountable for long lived isotopes of biological interest.

Conclusion

We do not address the ease or difficulty of detecting these isotopes by AMS, the likelihood of practical chemical preparation of samples, or the availability of the required isotopes. We have considered only the overlap of biologically interesting elements with the realm of isotopes that have half-lives within the range that allows high sensitivity tracing using AMS. The figures in this paper are a guide to candidate elements as solutions to biomedical or environmental research interests. Science-based risk analysis in applications of metal and metalloid chemistry are possible justification for the development of AMS measurement capabilities for some of these isotopes.

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References

- [1] J. Kielson and C. Waterhouse, in H. Gove, ed., Proceedings of the First Conference on Radiocarbon Dating with Accelerators 1, no. 1 (1978) 391.
- [2] K.W. Turteltaub, J.S. Felton, B.L. Gledhill, J.S. Vogel, J.R. Southon, M.W. Caffee, R.C. Finkel, D.E. Nelson, I.D. Proctor and J.C. Davis, Proceedings Of the National Academy Of Sciences Of the United States Of America 87, no. 14 (1990) 5288.
- [3] K.W. Turteltaub, J.S. Vogel, C.E. Frantz and N. Shen, Cancer Research 52, no. 17 (1992) 4682.
- [4] C.E. Frantz, C. Bangerter, E. Fultz, K.M. Mayer, J.S. Vogel and K.W. Turteltaub, Carcinogenesis 16, no. 2 (1995) 367.
- [5] D. Elmore, Biological Trace Element Research 12 (1987) 231.

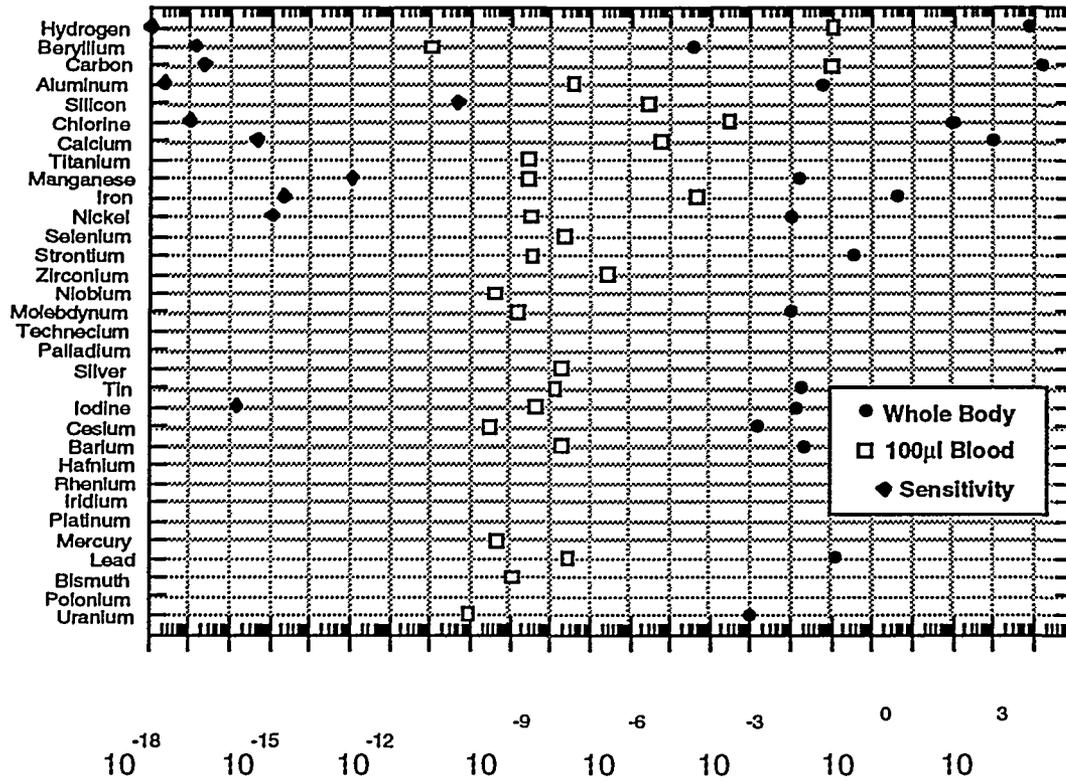
- [6] K. Kobayashi, S. Yumoto, H. Nagai, Y. Hosoyama, M. Imamura, S. Masuzawa, Y. Koizumi and H. Yamashita, Proceedings Of the Japan Academy Series B-Physical and Biological Sciences 66, no. 10 (1990) 189.
- [7] J. Barker, J.P. Day, T.W. Aitken, T.R. Charlesworth, R.C. Cunningham, P.V. Drumm, J.S. Lilley, G.W.A. Newton and M.J. Smithson, Nuclear Instruments & Methods In Physics Research Section B-Beam Interactions With Materials and Atoms 52, no. 3-4 (1990) 540.
- [8] R.R. Johnson, D. Berkovits, E. Boaretto, Z. Gelbart, S. Ghelberg, O. Meirav, M. Paul, J. Prior, V. Sossi and E. Venczel, Nuclear Instruments & Methods In Physics Research Section B-Beam Interactions With Materials and Atoms 92, no. 1-4 (1994) 483.
- [9] J.J.R. Frausto da Silva and R.J.P. Williams, The Biological Chemistry of the Elements (Clarendon, Oxford, 1991).
- [10] S.P.H.T. Freeman, J.C. King, N.E. Vieira, L.R. Woodhouse, and A.L. Yergey Nuclear Instruments & Methods In Physics Research Section B-Beam Interactions With Materials and Atoms: These Proceedings.
- [11] R. Flack and D. Elmore, in P. Zatta and A.C. Alfrey, eds. Aluminum in Infants Health and Nutrition (World Scientific, Singapore, In Press).
- [12] J.E. McAninch, L.J. Hainsworth, A.A. Marchetti, M.R. Leivers, P.R. Jones, A.E. Dunlop, R. Mauthe, J.S. Vogel, I.D. Proctor, and T. Straume Nuclear Instruments & Methods In Physics Research Section B-Beam Interactions With Materials and Atoms: These Proceedings.
- [13] V.S. Giand, K. Vohra, and F. Chai, Analyst 117 (1992) 161.
- [14] W.S. Snyder, M.J. Cook, E.S. Nasset, L.R. Karhauseen, G. Parry Howells, and I.H. Tipton, Report on the Task Group on Reference Man, ICRP No. 23 (Pergamon, Oxford, 1975).

Figures

- 1.) The periodic table has been shaded to indicate the primary, secondary and putative nutrients. Only elements for which there is a long-lived isotope suitable for AMS tracing are named. Routine measurement capabilities at CAMS/LLNL include the bold-faced subset of elements. Future development will emphasize important trace nutrients that are also toxic elements.
- 2.) The gram elemental abundances of a 70 kg reference person are shown for elements having "AMS" isotopes. A simple 100 μ l biopsy provides nanograms of these elements, while AMS sensitivity is on the order of 10 femtograms. Thus, long-lived isotopes can be used as tracers in the human body at levels corresponding to parts in 10^4 to 10^6 of the naturally occurring abundances of many heavy elements.

Sensitivity (g)

Abundance (g)



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