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BIOLOGICAL AND MEDICAL

APPLICATIONS OF RADIOACTIVATION ANALYSIS

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PART I

In the life sciences activation analysis is employed in two different ways: 1) .. in the usual fashion as a quantitative elemental analytical method, 2) .. as a qualitative detection method for locating certain elements within biological structures or materials or for locating them following biochemical fractionation by electrophoresis, chromatography or other techniques. Both these approaches have been applied to the detection of the elements that are native to biological materials and also to the measurement of stable radioisotopes added in nonradioactive tracer studies.

In quantitative analysis the radioactivation approach often possesses three marked advantages in comparison with other methods: 1) For selected nuclides it possesses extraordinary sensitivity, 2) The element being measured is specifically identified by spectroscopic or half-life characteristics, and 3) It is usually free from exogenous contamination. In biological work either the first or third of these attributes may be particularly useful, as I shall discuss.

In material from living things the large number of macroconstituents characteristically present complicates quantitative elemental analysis by activation techniques. For this reason high-energy or charged particle activations are severely restricted in application. This is because of the strong likelihood of adventitious production of the radionuclides being assayed by means of competitive reactions on some of the many other elements present in typical biological samples. In the complex and variable mixture of elements present in living substances multiple nuclear reactions do occur. There is also apt to be troublesome heat release from the slowing down of poorly penetrating charged particles in thick biological samples. This also results in a change in parti-

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cle energy with depth, and since cross sections for charged particle interactions vary strongly with energy, there is the further complication of heterogeneous activation within the sample (1). Thus possible competitive transmutations in a polyelemental sample usually are so complicated (1) that they cannot be determined quantitatively; and it is often difficult just to catalogue them completely. Hence, for analysis of tissue constituents thermal neutron activations have been favored. With slow neutrons, adventitious reactions are few and are generally well known.

Nonetheless, in special cases, or with separated and fairly well purified biochemical substances, charged particle activations occasionally prove to be useful, as I shall point out later.

The general situation obtained after neutron activation of a biological sample is this: Daughter radioisotopes produced from those few elements present in all protoplasm that are particularly sensitive to neutron activation tend to over-shadow all radioactivities produced from trace constituents or from less readily activated elements. Thus, shortly after neutron bombardment of tissues the resulting gamma-ray activities are dominated by ^{24}Na and ^{38}Cl , and occasionally by ^{42}K ; while beta-ray emissions derive mainly from these same nuclides plus ^{32}P and rarely ^{35}S . This very dominance of the induced radioactivities by a few elements points out one of the limitations of neutron activation analysis in biology and medicine, yet it also provides a unique advantage that leads directly to one of the useful applications of the method in the life sciences.

The limitation of the technique to which I refer concerns the insensitivity toward radioactivation of the light elements that constitute the bulk of organic material, the so-called "matrix". Hydrogen and oxygen are not susceptible to low-energy neutron activation at all, and carbon and nitrogen are not activated to any

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useful extent. It is true that phosphorus and certain minor isotopes of hydrogen and oxygen can be measured by some of the special techniques that I shall discuss later, but this is useful primarily only in tracer studies. Yet it is this very inertness of the bulk light elements of tissue to neutron activation that permits the method to be applied profitably to the detection of trace constituents, metal ions, and some of the heavier elements in biological material.

As I indicated, sodium, chlorine, potassium and phosphorus are the prominent relatively heavy elements in tissue that are well activated by neutrons. Hence, one of the powerful applications of activation analysis to biology has been the measurement of these particular elements in very tiny amounts of tissue. For example, sodium, potassium and phosphorus have been quantitated in muscle biopsies from well people and from patients with muscle disease (2, 3); sodium and potassium have been analyzed in blood serum samples as small as one microliter (4); sodium and potassium have been assayed even in single, large nerve fibers (5); and sodium has been determined in bone (6), where the mineral matrix and great excess of calcium otherwise present great difficulty in sodium analysis.

In these applications of activation analysis to the detection of relative macroconstituents in microsamples, the great innate sensitivity of activation analysis for these particular elements has permitted microdeterminations that were simply beyond the pale of other quantitative methods. However, in the next general class of applications of activation analysis in biology and medicine it is not so much the extreme sensitivity of the method that has given it a marked advantage over other techniques, but rather its intrinsic relative freedom from exogenous contamination.

The other major area of application of radioactivation for quantitative analysis in the life sciences concerns the detection of trace elements. Many of the microconstituent elements of protoplasm are present in concentrations of less than 1 p.p.m. -- especially the metal elements of the first transition group.

For example: Mn normally may exist in blood serum at about 1 p.p.b. (10^{-9} w/w) (7). Despite their presence at trace levels, these constituents play critical (or "catalytic") roles in biological structure and chemistry; and hence their measurement is important. Since many of these microconstituents possess nuclear characteristics favorable for neutron radio-activation, activation analysis has proven very useful in this area.

Nevertheless, it is only in a few instances that the intrinsic sensitivity of activation analysis has permitted analyses that were actually beyond the limits of other methods; because many ultramicrochemical techniques are available. Instead, it is the relative freedom from contamination that has made activation analysis more accurate rather than intrinsically more sensitive in trace analyses in biology. This is the case because the very low concentrations of some of the elements involved may be less than their contamination in even the best chemical reagents (7, 8). Furthermore, the complex chemical nature of biological material that I have mentioned usually forces the analyst to carry out complicated digestion and extraction maneuvers in addition to the analytical procedures per se. Each step in the resulting complex method is susceptible to contamination, and this is often sufficiently erratic or variable at the low levels pertinent to ultramicroanalysis to vitiate accurate compensation by the usual "blank" determinations. However, radioactivation procedures are sensitive to microcontamination only prior to the time of irradiation -- and hence before the addition of reagents, even when radiochemical separations are employed. Hence it is clear that they provide a powerful advantage in biological trace element determination.

However, it is also clear from my previous emphasis on the complexity of the radioemanations induced in biological materials by neutrons, that separation procedures are required for trace element analysis. These may be either radiochemical or instrumental in nature or a combination of the two. Since radiochemical

isolation techniques are now published for all elements of biological interest, it is evident that analyses for only one or a very few trace substances in samples may proceed using these standard procedures. In fact, applications of straightforward radiochemical procedures have resulted in the separate determinations of Cr, Mn, Co, Cu, Zn, Cd, Sr, W, and rare earths in biological and medical samples (9-20).

Despite the success of these essentially "conventional" radiochemical approaches in analyzing for one or a few elements at a time, the determination of the many constituents in tissue that are susceptible to radioactivation analysis would be cumbersome at best and might require excessive amounts of sample material. In order for activation analysis to provide simultaneous assay of many elements in one sample — such as can be accomplished by optical emission spectrometry, for example — the usual radiochemical methods must be modified. If procedures are developed that retain all elements but which provide isolation of radio-nuclides in fractions, then further separation of radioactivities may be effected by simple instrumental methods. Some very promising developments along these lines have been worked out by Samsahl and his collaborators. (21, 22). By means of serial passage of dissolved neutron-activated biological materials through a stack of short-ion-exchange columns, several elements can be measured in single samples. Radioactivated samples are wet digested, carriers are mixed in as necessary, and oxidizing agents are added. The dissolved sample is then distilled or passed serially through beds of ion-exchange resins, and the radioisotopes and carriers are separated in groups. Within each group the radioactivities may be completely resolved by gamma spectrometry. In one schema nineteen groups were obtained (23). ~~radioisotopes are~~ In these groups ^{are} thirteen elements which exist as essential macro- or microconstituents in tissues of man and higher animals. Biomedical investigators may also be interested in correlating with environmental

or pathological factors the levels of some of the nonessential trace elements measurable with this radiochemical separation. With procedures like this, Samsahl has determined simultaneously thirty trace elements in human tissues exposed for 24 hours to 2×10^{13} n/cm²/sec (23). The chemical separations are complete in 1 1/2 days, allowing radioisotopes with half-lives as short as 13 hour ⁶⁴Cu to be detected. Recently Samsahl has improved his apparatus for fast ion exchange separations by using a piston drive to allow exact and simultaneous adjustment of influent solutions to a series of exchange columns, thus separating six groups of trace elements in about 45 minutes (24). For neutron activation, samples are irradiated for 24 hours and decayed for three days to activate longer-lived radioisotopes and then re-irradiated for ten to thirty minutes to reactivate shorter radioactivities. Processing starts within three hours thereafter (24).

Another semiautomated system for determining trace elements in biological materials has been developed by Girardi and his colleagues at Euratom's Ispra Laboratory. A postactivation radiochromatographic separation is followed by gamma spectrometry, which is automatically evaluated by a computer (25, 26). Up to one hundred samples a month can be analyzed for twelve to fifteen elements.

Although the concept and practice of radiochemical separations is undoubtedly sound, it does suffer several disadvantages: 1) It is time-consuming and involves many separate chemical treatments of each sample; and 2) A separation designed to isolate one element may cause losses of other important components of a sample--although the Samsahl approach seeks to get around this shortcoming. In other words; radiochemical analysis is a destructive method. 3) As a result of this, samples can be analyzed only once; and 4) The short lifetimes of the daughter radionuclides from several biologically significant elements are poorly compatible with the time lost in radiochemical manipulations.

As has been pointed out for several years (27-29), purely instrumental (or radiometric) measurements seek to avoid these shortcomings. Without chemical

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To indicate further the versatility of activation analysis in its application to biology and medicine, I shall catalogue briefly two more examples: Sulfur has been measured at the microgram level by activation analysis using deuterons by means of detecting positrons from the 3-minute ^{30}P produced by the (d,α) reaction on ^{32}S (46). And last, in an application that is not strictly activation analysis, induced radio-activities have been employed to determine neutron exposures of animals (47) and following reactor accidents involving humans (48).

In conclusion, it can be stated that these selected examples of activation analysis show clearly that the method has many useful applications to biology and medicine at the level of research studies, even though routine or clinical uses have not developed as yet. Activation analysis has permitted some experimental determinations that were impossible without it; it has made other analyses more accurate; and in other cases its major contribution has been to provide feasibility or simplicity to procedures that were at least attainable by other methods. The play of imaginative minds clearly can expand further the application of radio-activation to the life sciences.

PART II:

As an appendix to this broad — although incomplete — review of biomedical applications of radioactivation analysis, I want to present some aspects of work that has been proceeding for some years in our department at Brookhaven National Laboratory. As I indicated earlier, this work has to do with a purely instrumental and physical approach to activation analysis, eschewing all radiochemical separations — even for radiosodium. The basic concept has been to apply special types of coincidence spectrometry along with selective neutron activation. In order to give some coherence to the presentation, I shall review the major aspects much

as they occurred chronologically, ending with our plans for applying newly developed techniques and equipment so as to give maximum power to this approach. For clarity I will use only one or a few sample problems, but the method can be generalized (30). In fact, one of the great strengths of the method — aside from minimum sample preparation — is its great flexibility in resolving many mixtures of radionuclides, whether from radioactivated samples or from a multiple radiotracer study.

As a graphic example of interference from ^{24}Na Compton distribution which limits instrumental detection based on gamma ray scintillation spectroscopy, there is the example of neutron irradiated blood and serum. The gamma spectrum of untreated blood is seen to be essentially that of ^{24}Na alone. Following radiochemical "purification" of ^{56}Mn from the same samples, excellent total absorption peaks corresponding to the dominant 850 Kev gamma emission of ^{56}Mn are recorded (8). Of course the same ^{56}Mn radioactivity was originally present in the unpurified samples, but it was statistically undetectable in the face of the much more abundant ^{24}Na decays, as was discussed previously.

The radioanalytical approach to such minor constituent analysis is based upon selective suppression of the detection of matrix radioactivity — in this case, ^{24}Na . Coincidence spectroscopy seeks to identify radioactive decay processes by "simultaneously" detecting two or more emissions from a particular decay branch. Gamma-gamma coincidence detection is often useful, but in the comparison of ^{56}Mn and ^{24}Na decay schemes (30), it can be seen that an "ideal" radiation detector that could discriminate perfectly between beta rays and gamma rays could totally suppress all detection of ^{24}Na radioactivity, provided it was gated to reject all beta rays with an energy below 1.4 Mev. The decay scheme of ^{24}Na provides essentially no beta to exceed this threshold, so an "ideal" beta-gamma coincidence spectrometer with a beta detection threshold of 1.4 Mev would not record ^{24}Na events at all. On the other hand, about two thirds of the ^{56}Mn

radioactive decays proceed by a branch with a beta emission of 2.85 Mev maximum energy, followed by the 850 Kev gamma. Since some of the radiomanganese betas exceed the detector threshold, gamma emission detected in coincidence with such events could be analyzed; and the beta-gamma spectrometer would record a significant fraction of the ^{56}Mn disintegrations. Of course the detection efficiency of the beta-gamma coincidence spectrometer for purified ^{56}Mn would be significantly less than the efficiency of a gamma singles spectrometer; but since the radiosodium background would be completely suppressed in the idealized case, the ^{56}Mn spectrum that was recorded would be completely resolved from the ^{24}Na matrix, and the overall sensitivity of the system for radiomanganese measurement in neutron activated tissues would be vastly increased due to the tremendously enhanced ^{56}Mn ; ^{24}Na detection ratio (30).

However, "ideal" coincidence spectrometers or beta and gamma detectors do not exist; coincidence timing is never truly instantaneous, so non-coincident emissions from separate disintegrations in the sample may be recorded as so-called "accidental" coincident events; and the background due to these accidentals will increase as the square of the radioactive intensity of the source (30). Furthermore, the counting efficiency of a coincidence spectrometer is the product of the singles efficiencies of the separate detector components for the different emissions of the decay branch that is to be detected (30, 49). Therefore, for reasonable counting efficiencies of minor radioactivities in neutron-activated biological materials, the separate beta and gamma detection components must be made as efficient as is feasible.

Gamma detection is accomplished spectroscopically, so to optimize the efficiency of gamma counting one seeks to maximize the likelihood of recording a total absorption gamma spectral peak while maintaining the best possible resolution of line width, because the detection sensitivity expressed in terms of a signal-to-noise ratio is an inverse function of line width. The extraordinary

resolution of Ge(Li) solid-state detectors will be discussed later, but for the initial coincidence work only NaI(Tl) scintillation detectors were used. It is clear that for these the efficiency of counting in the total absorption peak increases with larger crystal size. However, spectral resolution declines somewhat with very large crystals, so for the initial work reported here 13 x 10 or 13 x 13 cm NaI(Tl) crystals specially selected for good resolution were employed for gamma detection (30).

Beta detection using magnetic spectrometers was attempted, because the gamma response of focusing spectrometers can be made very low. For reasons that will not be reviewed here these trials were unsatisfactory (30), but recent changes in the outlook for magnetic detectors will be noted later. Alternatively, beta scintillation detectors were employed because of their high efficiency, good geometry, and fast response. However, even when scintillators composed of low atomic number elements were used to minimize Compton interactions with gamma rays from samples, an appreciable gamma sensitivity remained in all crystals sufficiently deep to discriminate beta ray energies in the 1.5 Mev region. It can be seen that the theoretical Compton electron spectrum from the 2.76 Mev photon from ^{24}Na seriously overlaps that fraction of the ^{56}Mn beta spectrum above 1.4 Mev which is to be used for coincidence detection of the radiomanganese. As a result, Compton events in the beta scintillator due to the 2.76 Mev gamma line from ^{24}Na may "masquerade" as ^{56}Mn betas with energy above 1.4 Mev and thus open ~~and~~ the coincident circuits. This allows the spectrometer to record coincident 1.37 Mev gamma interactions from ^{24}Na in its NaI(Tl) crystal, thereby causing the coincidence spectrometer to escape from the desired nearly total suppression of gamma response to radiosodium (30).

The Compton response of the beta detector was reduced by converting it into a double-crystal "counter telescope" and then demanding a triple coincidence between these two counters and the gamma crystal before the coincidence control

circuitry opened the spectrometer's recording analyzer to accept pulses from the gamma counter. A crystal barely thick enough to elicit a light pulse from penetrating beta rays was placed between the radioactive source and the thicker beta energy discriminator. All true beta rays passing from the sample to the beta counter would also trigger the thin intervening crystal, but the likelihood of a Compton interaction from an energetic gamma emanating from the source would be negligible, so the triple coincidence requirement could be expected to lower the gamma response of the beta detector—ideally by a factor equal of the ratio of their thickness. In actuality this degree of suppression ^{of} ^{24}Na events did not occur, because sodium betas and scattered electrons were also present near the sample, and these could trigger the thin crystal (30). Nonetheless, impressive gains in the ratio of ^{56}Mn to ^{24}Na detection were registered by the triple coincidence beta-gamma spectrometer. In one geometry the ratio of manganese-to-sodium detection by coincidence counting increased approximately one hundred-fold over that achieved with singles spectroscopy with the same gamma detector (30). Of course the absolute counting rates decreased in the coincidence mode, but the enhancement of the manganese gamma peak from the ^{24}Na background was dramatic.

Despite the gain in manganese-to-sodium detection ratios achieved by coincidence counting, the dilute concentration of manganese in some tissues—especially body fluids—eluded measurement following neutron activation. It was therefore decided to increase the initial radioactivation of manganese relative to the radioactivity induced in the sodium content of the same sample. This was achieved by taking advantage of low-energy resonances (in the several hundred electron volt region) of the neutron cross sections of manganese, cobalt, bromine, and several other biologically important trace elements (50); because ^{23}Na has no resonance below about 2.85 Kev. Although the total cross section curves contain a large neutron scatter component in their resonances, there is appreciable resonance for the (n,γ) reaction also (30). If samples could be irradiated with

neutrons in an energy region corresponding to a ^{55}Mn resonance but free of a ^{23}Na resonance, for example, the initial radioactivation ratio of ^{56}Mn -to- ^{24}Na could be markedly increased over that produced by slow neutrons in the energy region where the thermal (n, γ) cross sections largely determine the activation ratio. Unfortunately, monoenergetic neutron sources in this energy region are too weak for sensitive activation analysis, but the moderated neutron flux of a reactor consists of a sharp thermal-energy spike and a "1/energy" spectrum in the resonance region. If the samples are separated from the reactor flux by appropriate amounts of filtering material—such as ^{10}B or cadmium, they may be effectively sealed off from the thermal-epithermal region of the neutron spectrum. Although the total irradiation flux will then be decreased at the sample, the fraction of the activating neutron flux ^{that is} in the resonance region will be significantly elevated; and elements possessing neutron resonances in this energy range will be "selectively activated" with respect to elements that ~~lack~~ ^{lack} them, such as sodium and chlorine in most tissue matrices (30).

The gain in the ratio of ^{56}Mn radioactivity to ^{24}Na radioactivity in comparing such "selective" or resonance activation with conventional "pile" irradiation in a largely thermalized reactor neutron flux is a factor of about seven. The enhancement of ^{56}Mn induction relative to ^{38}Cl formation is even greater (about fourteen times) when using "selective" neutron irradiation (30). Of course the gain in manganese detection sensitivity realized by resonance neutron activation can be combined with the gains secured by using coincidence spectrometry in order to offer a maximum overall sensitivity for tissue manganese measurement, by instrumental neutron activation procedures.

Two examples will serve to illustrate some of the potential of these combined methods. In the first case the gamma singles spectrum from conventional "pile" neutron irradiation of a sample of brain tissue reveals a dominant ^{24}Na with only an equivocal ^{56}Mn peak superimposed. Selective neutron activation with

cadmium and boron shielding of the sample increases the ratio of the ^{56}Mn and ^{24}Na gamma peaks by approximately six or seven times. Coincidence spectrometry of the pile-activated sample using only double coincidence (and no thin third crystal) produces a comparable enhancement. Then, as one would expect, the combination of resonance activation and coincidence spectrometry yields a ^{56}Mn detection gain that is roughly the product of these two increments, such that the initially borderline ^{56}Mn gamma spectral peak becomes as large as the 1.37 Mev ^{24}Na peak, if not larger (29). In the case of blood and serum, where the ratio of manganese to sodium is even lower than in brain, the gamma singles spectrum of even the selectively activated sample appears to reveal nothing but ^{24}Na . However, triple coincidence spectroscopy (in a favorable sample geometry that favors detection of ^{56}Mn over ^{24}Na at the further loss overall counting efficiency) barely brings out the ^{56}Mn peaks over the statistical background (30).

Although the results just discussed represent particular examples, the applications of coincidence spectrometry and selective radioactivation have a general utility (30). Nonetheless, for some cases readily handled by destructive radiochemical procedures — such as serum manganese levels (7) — the instrumental approach outlined above provided only marginal results on a demonstration level and was not feasible for accurate, routine analysis. However, in the interval since it was first developed (30), notable instrumental and technical advances have occurred; and the application of the full power of contemporary techniques should greatly magnify the scope and resolving power of these methods. Presently just such a modification program is under way at Brookhaven, and significant improvement can be anticipated in the combined use of selective activation and coincidence spectrometry for instrumental radioactivation analysis in at least six areas:

1) Improved coincidence circuitry: The previous work used a coincidence control with timing based on the leading edges of the amplifier output pulses and had a resolving time of about 10^{-7} sec. With sample radioactivities usually about as intense as the gamma counter could accept without saturation (in order to maximize the counting statistics of the very inefficient triple coincidence spectrometer), an important spectral background existed due to the recording of accidental coincidences. Present coincidence controls with time resolution of about 10^{-8} sec., based on the cross-over point of double delay line shaped pulses, should decrease markedly the background component from accidental coincidences.

2) Better facilities for resonance activation: The cadmium-boron cladding of sample containers was awkward to handle. Because of its depressing effect on pile reactivity, it could be placed only in irradiation facilities where cadmium-ratios were about 30:1 — i.e. only about 3% of the total neutron flux of about $1-2 \times 10^{13}$ n/cm²/sec was in the energy region above epithermal. Today at Brookhaven the High Flux Beam Reactor is approaching experimental use and may provide resonance neutron fluxes exceeding 10^{14} n/cm²/sec without the need for special neutron filters.

3) Anticoincidence suppression of Compton background: The use of annular gamma detectors around the primary gamma counter allows escaping secondary photons from Compton events in the primary crystal to be recorded. If the annulus is connected in anticoincidence with the analyzing detector, many of the Compton events occurring in the latter will not be recorded, so that Compton background from which less energetic gamma peaks must be statistically resolved is much reduced. Ratios of total absorption peak: Compton shoulder or continuum are increased by two to ten times with present annular geometries.

4) Magnetic beta spectrometers with high transmission: Focusing magnetic beta spectrometers have intrinsic low contamination from source gamma rays. Older

intermediate image configurations had low beta transmission and interfered with simultaneous gamma spectrometry. Now magnetic spectrometers of the type first developed by Slatis are readily available. They have high electron transmission; and with both sample and detector at or near the exterior of the device, coincidence spectroscopy is facilitated (30). Another broad-range extremely high-transmission electron spectrometer with a solenoidal magnetic field (51) is being investigated as a "gamma-free" beta detector for the improved beta-gamma coincidence apparatus.

5) Multiparameter, multichannel analyzers: Previously coincidence spectroscopy was accomplished by recording gamma spectra on a multichannel analyzer gated in coincidence with a single-channel beta counter-telescope detector. In general, the recording of gamma peaks corresponding to only one decay branch of one of the radioisotopes in the sample could be optimized at one time. For greatest sensitivity in resolving decay schemes of other radio-nuclides present in neutron activated biological materials, sequential spectra were necessary; and with the long counting times resulting from the low efficiency of coincidence spectrometers, much data was ignored. Current multiparameter analyzers allow random access to each memory location, so all coincidence information available from a sample can be recorded concurrently. Interchange between beta-gamma and gamma-gamma coincidence modes is readily accomplished, and data processing by direct communication with a computer is anticipated.

6) Solid-state gamma detectors of high resolution: Lithium-drifted germanium crystals at 77°K have recently become increasingly accessible. Their resolution is approximately twenty times sharper for gamma absorption peaks than is the case with NaI(Tl) scintillation detectors. The resulting improvement in signal-to-noise dramatically enhances detection of weak lines, and the sharpness of the peaks frequently completely separates lines that seriously overlap and cannot be identified in gamma scintillation spectra. The small size of most Ge(Li)

detectors seriously reduces the absolute efficiency for detection of full absorption peaks, but the extraordinary resolution of these crystals may more than compensate for this, even with the 2-to-4 ml volume detectors now in use (33, 49). Gamma singles spectra of neutron activated tissues with 4 ml Ge(Li) detectors occasionally reveals minor peaks that are not resolved in spectra from 13 x 13 cm NaI(Tl) scintillators. Because of the already low counting efficiency of coincidence spectrometers, the low absolute detection efficiency of small Ge(Li) crystals does not appear to encourage their routine application to coincidence spectrometry in activation analysis, although some coincidence work has been done with Ge(Li) detectors in physics experiments (49). However, Ge(Li) efficiency improves with thickness, and the feasibility of coincidence counting also increases with larger detectors; so the present preparation of 20-to-30 ml Ge(Li) crystals (with lithium drifting from several surfaces) at Brookhaven and other laboratories may make high resolution Ge(Li) gamma detectors compatible with coincidence spectrometers for use with instrumental activation analysis. In any case, the peak-to-Compton ratios of gamma singles or coincidence spectra recorded with Ge(Li) crystals may be enhanced by using annular anticoincidence counters, just as was found to be the case previously with NaI(Tl) spectra. In fact, the anticoincidence suppression of Compton background has been even more noticeable with Ge(Li) detectors than with larger NaI(Tl) scintillating crystals (52).

The degree of improvement in instrumental activation analysis that may result from the application of these different improvements in combination or alone remains to be determined.

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