X-RAY FLUORESCENCE—AN IMPROVED ANALYTICAL TOOL FOR TRACE ELEMENT STUDIES

FREDERICK S. GOULDING
LAWRENCE BERKELEY LABORATORY

1. Introduction

This conference is dominated by discussion of the hazards associated with radiation; the present author feels that this exaggerates the importance of radiation levels as a hazard to health, when compared to other environmental insults to which we are subjected. One such insult is that produced by toxic metals introduced into living systems via many routes from industrial and natural sources. The purpose of this paper is to describe the use of X-ray fluorescence analysis with semiconductor detector spectrometers as a tool to permit fast analysis of specimens for a broad range of chemical elements present in trace quantities (that is, < 1 ppm by weight).

Before discussing trace element analysis, it may be useful to examine some possible reasons for the emphasis on radiation seen at this meeting, and to relate these to the situation seen in regard to trace elements.

1.1 Sources of radiation exposure to living things are well defined both in location and time. Nuclear explosions, reactors, X-ray sources and other radiation sources are constantly scrutinized by local, national and international agencies. Contrasting with this situation, the release of toxic elements by natural and industrial sources is subject to virtually no control or monitoring.

1.2 Public and governmental sensitivity to the hazardous nature of radiation has resulted in large programs to improve radiation measurements, and to evaluate radiation effects. Minor parallel steps are only now being taken to establish similar parameters for trace elements.

1.3 Indices of radiation effects are fairly well established. While authorities may differ in their interpretation of such studies, incidence of cancer and leukemia, longevity, and infant mortality rates have all been used as indicators of radiation effects. Although relationships between trace elements and certain diseases are known to exist, and others are suspected, few large scale statistical studies have been made to define the range of possible connections. We should also note that the wide variety of trace elements, and of their effects, make

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studies equivalent to those of radiation effects much more complex and difficult in this area.

1.4 Many trace elements are known to be essential to life, but at higher concentrations they become toxic. Despite occasional murmurs to the contrary, it seems that any increase in radiation above natural background must be considered harmful. It is, therefore, much easier to define the objectives of radiation measurement and control programs than the equivalent objectives for trace element studies.

1.5 Synergistic effects are known to be extremely important in determining the behavior of trace elements in living systems, and any study of the effects of a trace element must take account of the presence of other elements. While synergistic effects are also observed in radiation studies it appears that they are much less important than in trace element studies.

In summary, we might conclude that the complexity of trace element work, the lack of funding, and the resulting shortage of suitable measurement techniques, weighed against the relatively better situation in radiation studies, makes the latter a more attractive field of research. *However, it does not necessarily follow that such research is more valuable or more important than research on other forms of insult to life.*

I am in the fortunate position, in this talk, of being able to point to a possible important contribution of one nuclear research program to the problems of trace element studies. The value of the technique lies in its potential to permit large scale statistical studies of trace element distributions in our environment, and in living things, and thereby to provide the basic data needed to understand their effect. Furthermore, the technique promises to provide the fast monitoring method required for control of certain environmental contaminants. Before illustrating some applications, we will discuss the method and recent improvements in it that have greatly enhanced its usefulness.

2. Physics of the X-ray fluorescence method

Every scientist is familiar with the brilliant yellow sodium light produced when salt falls into a flame, and with the fact that our knowledge of the constitution of stars derives from studies of the light they emit. Optical spectroscopy, thanks to our fine natural light detectors, and also to Newton's use of prisms to disperse light according to its color, is now a commonplace tool in chemical analysis. However, a casual observer is overwhelmed by the complexity of optical spectra, caused mostly by the abundance of levels in the outer shells of atoms involved in light production. By observing X-rays, we can do elemental analysis much more easily, for the inner atomic shell structure producing X-rays is quite simple, and only a few X-ray wavelengths are emitted. X-ray spectroscopy requires both detection of X-rays and measurement of their energy; both functions are performed conveniently and well by semiconductor detectors—hence, the power of these devices as analytical tools.

The simple design of a semiconductor X-ray fluorescence spectrometer is shown in Figure 1; the physical mechanisms involved in the fluorescence process are also illustrated. Spectroscopy of photoelectrons and Auger electrons can also be used for analysis purposes, and the outstanding energy resolution of electron spectrometers permits measurement of changes in energy levels due to chemical bonding effects. However, the short range of electrons in materials limits the use of electron (compared with X-ray) spectroscopy. A wide range of methods of exciting characteristic X-rays is available. We discuss here only X-ray excitation of the sample, as our objective is to illustrate a relatively simple instrument; other, more complex, methods of excitation may be employed and are favored for some purposes.

The atomic shell transitions generating the X-rays of interest in this paper

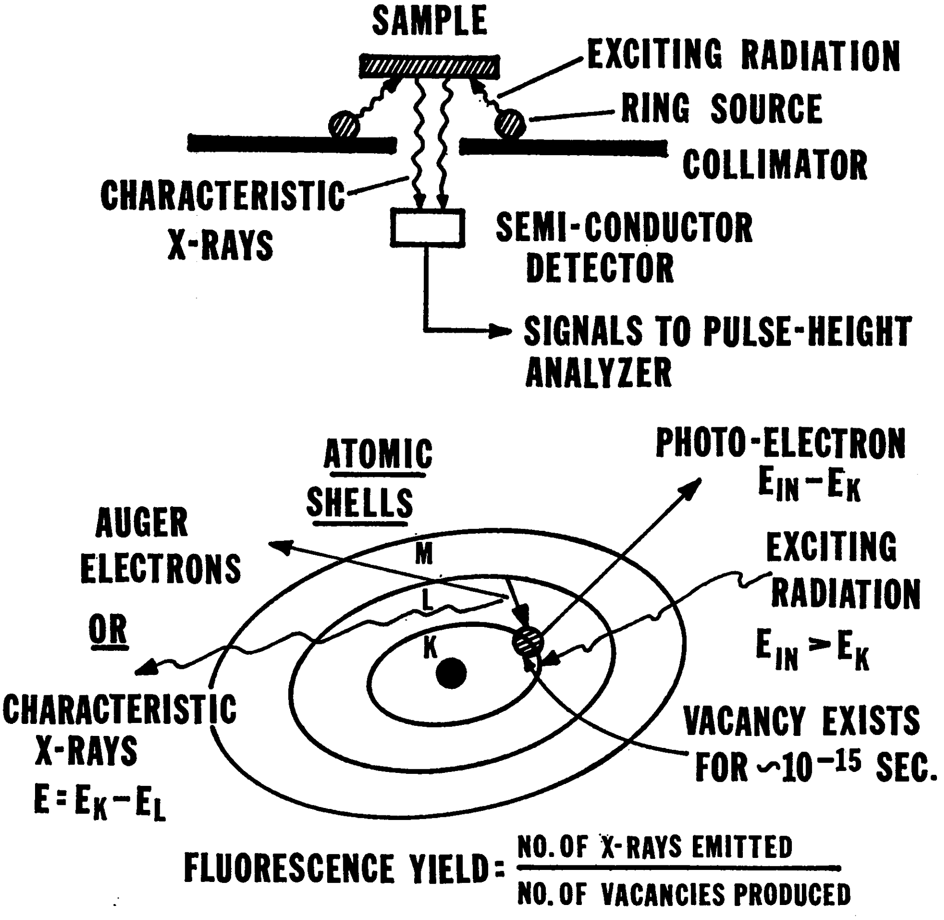

FIGURE 1

Basic X-ray fluorescence spectrometer and the atomic process.

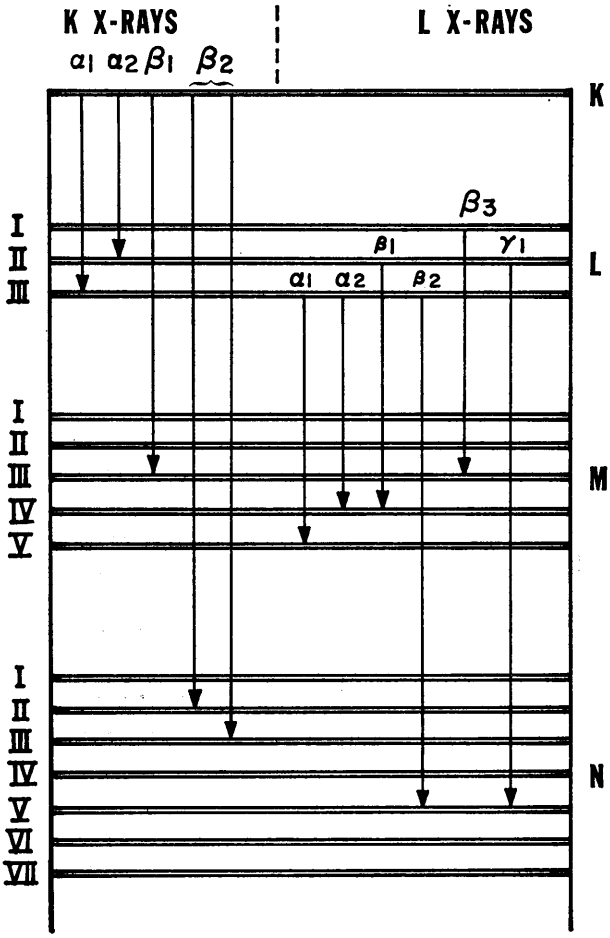

FIGURE 2

Atomic energy levels involved in the emission of X-rays of interest in this paper.

are shown in Figure 2. In the energy range of interest here, the energy resolution of semiconductor-detector spectrometers is such that the $K\alpha_1$ and $K\alpha_2$ lines are observed as a single line, as are the ($K\beta_1$, $K\beta_2$) and the ($L\beta_1$, $L\beta_2$, $L\beta_3$) lines. The intensity of the $K\beta$ peak is always much smaller than that of the $K\alpha$ line, while the $L\alpha$ and $L\beta$ lines are of similar intensity to each other, and are large compared with the other L X-rays.

Energies of primary interest lie below 30 keV, where the K X-rays of elements with $Z < 55$ are observed, and the L X-rays of the heavy elements also appear. Figure 3 shows the energies of these X-rays. The L X-ray energy of a heavy element may be the same as the K X-ray energy of a light element causing confusion in analysis; but most heavy elements are relatively rare in biological

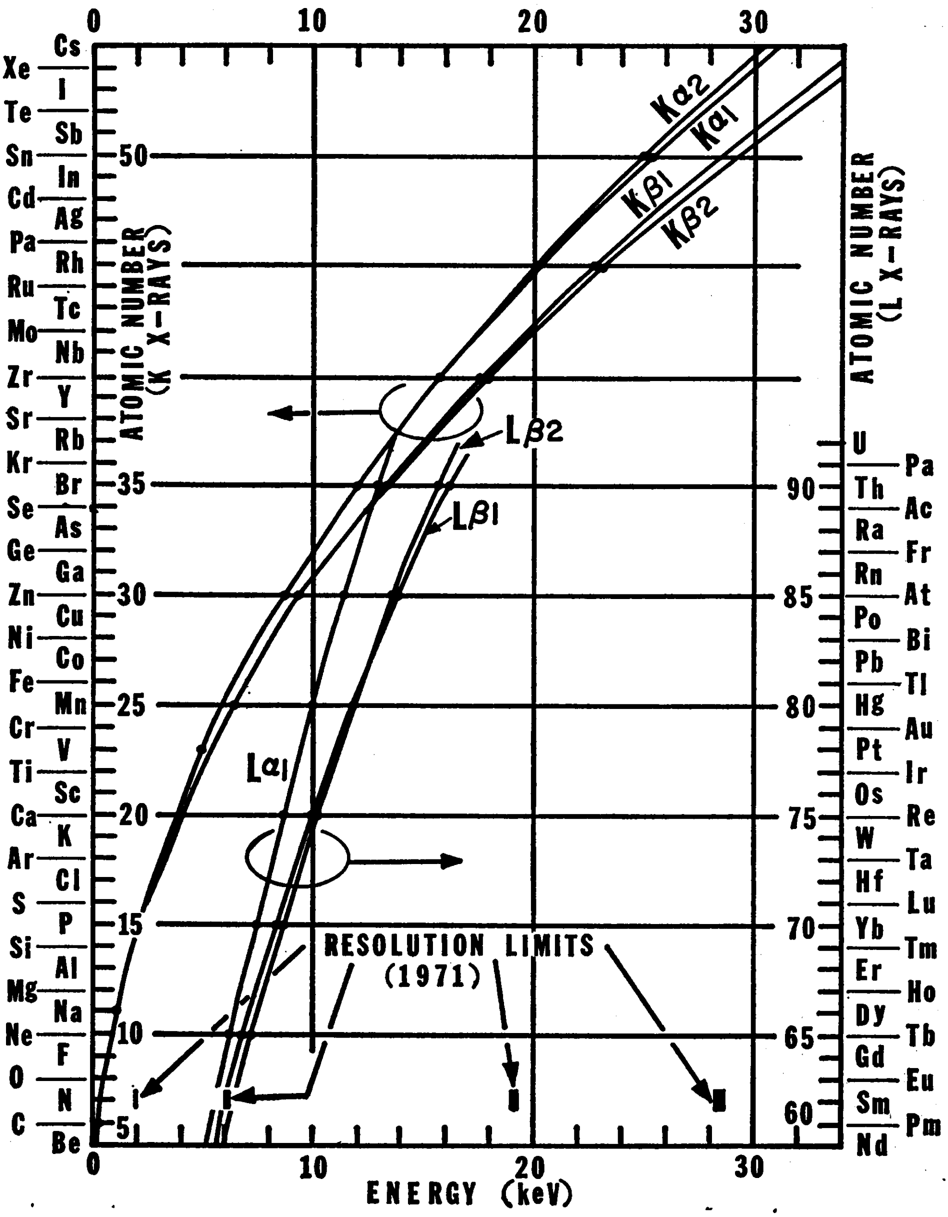

FIGURE 3

Energies of K and L X-rays up to 30 keV.

material, so the resulting problem is of less importance in practice than perhaps might be expected. Often, the presence of two strong L lines is useful—for example, Pb Lα coincides with the common As Kβ, but Pb Lβ only clashes with Kr, an uncommon contaminant. This fact permits determination of lead even when arsenic is present.

As shown in Figure 1, Auger electron emission provides an alternative method of filling vacancies in the atomic shells, thereby reducing the yield of fluorescent X-rays. Unfortunately, the emission of Auger electrons becomes highly probable for low energy transitions, so the fluorescent yield becomes very small for light elements, as shown in Figure 4. A similar behavior is seen for L X-rays emitted by heavy elements. The low fluorescent yield makes X-ray fluorescence spectrometers less sensitive for light elements; the problem is further exaggerated by the self-absorption of the fluorescent X-rays in the sample itself. This factor restricts analysis to a vanishingly small surface layer of the sample for low Z elements. Figure 5 shows the thickness of typical organic material required to attenuate different X-rays by a factor of $1/e$—this curve shows that samples less than 1 mm thick must be used to avoid severe attenuation even of elements as high as iron in the periodic table.

Two further efficiency factors are important in the design of an X-ray spectrometer. The efficiency of any detector falls at high energies causing a loss of counts. Lithium-drifted silicon detectors 5 mm thick were used in these studies; their efficiency is essentially unity in the energy range of interest here. Choosing the energy of the exciting radiation is a major step in the design of an X-ray fluorescence experiment; the probability of creating a vacancy is a maximum when the energy of the exciting radiation just exceeds the binding energy of the atomic shell involved. Figure 6 shows how the probability of vacancy creation in the K and L shells of various atoms depends on the energy of the exciting radiation. As an example of the use of these data, consider the case of a sample containing equal parts by weight of lead and bromine excited by Mo Kα radiation (17.4 keV). The lead L-shell vacancies will be excited 3.5 times as efficiently as the bromine K-shell vacancies; but since lead atoms are three times as heavy as bromine, only one-third as many lead atoms are present. Moreover, the fluorescent yield for Pb L X-rays is about 25 per cent less than that for Br K X-rays (Figure 4). The total number of lead X-rays from the sample will, therefore, be slightly smaller than that of bromine K X-rays.

We have so far considered only the fluorescent X-rays produced in the sample, their excitation and transmission to the detector, and their absorption in the detector. The main mechanism for absorption in the detector in this energy range is the photoelectric process; even where Compton scattering occurs in the detector, the scattered photon will nearly always be absorbed photoelectrically to produce a total charge in the detector proportional to the total energy of the original incoming X-ray. This situation is a pleasant contrast to the dominance of the Compton effect in spectra observed when detecting higher energy γ-rays. However, scattering processes are still a major factor in X-ray fluorescence

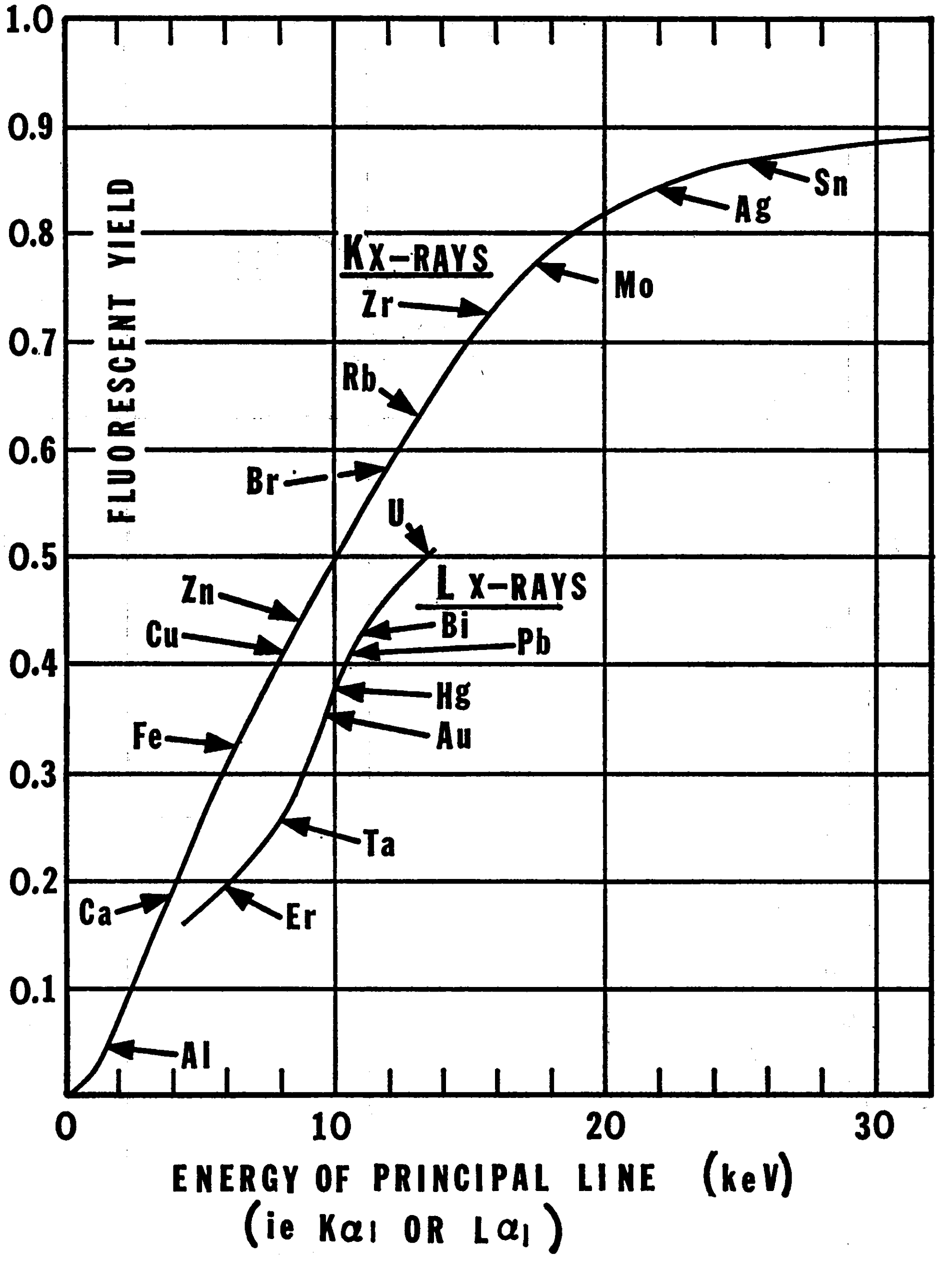

FIGURE 4

Variation of fluorescent yield with energy for K and L X-rays.

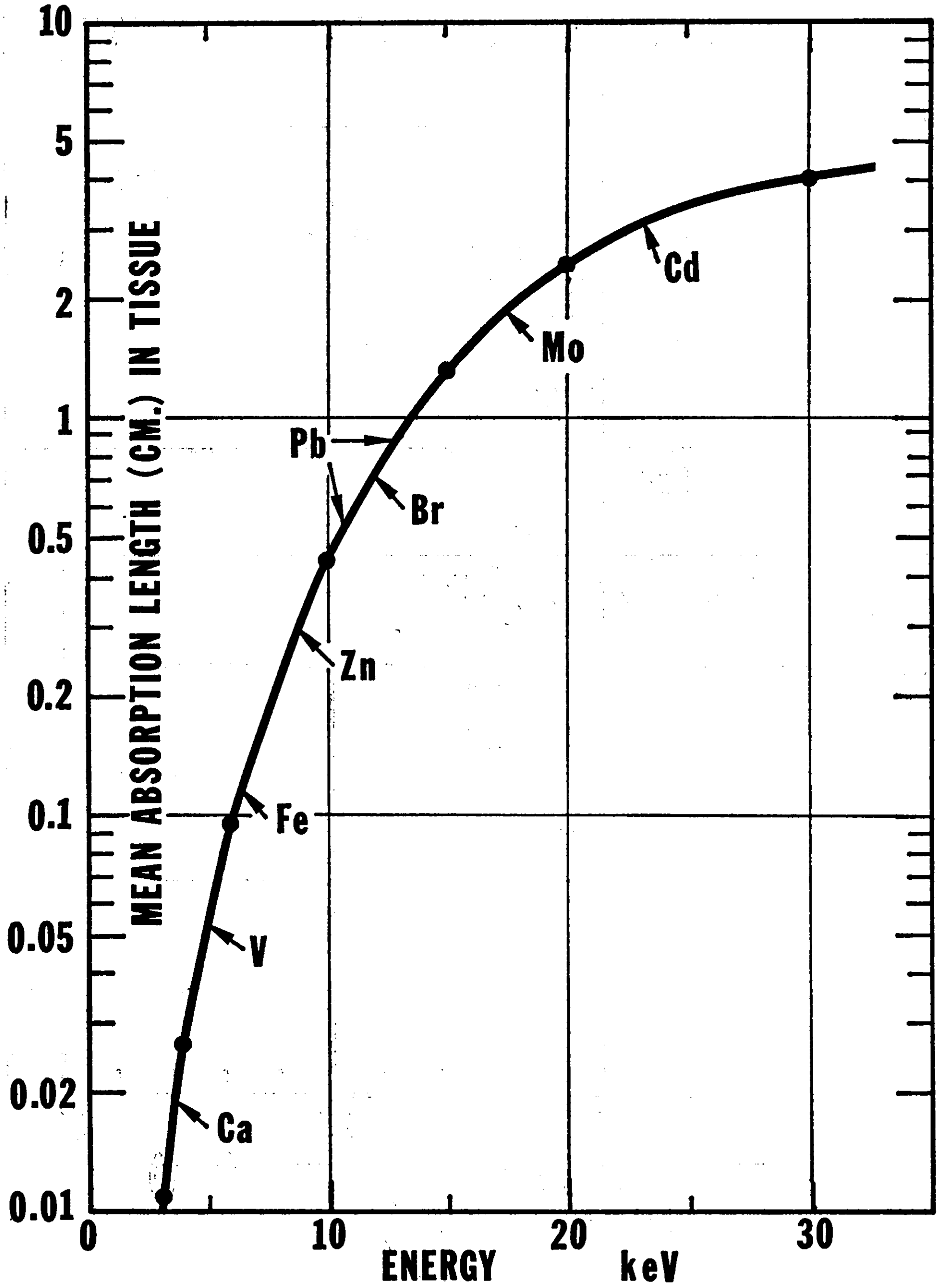

FIGURE 5

Absorption length of X-rays in typical organic material as a function of energy.

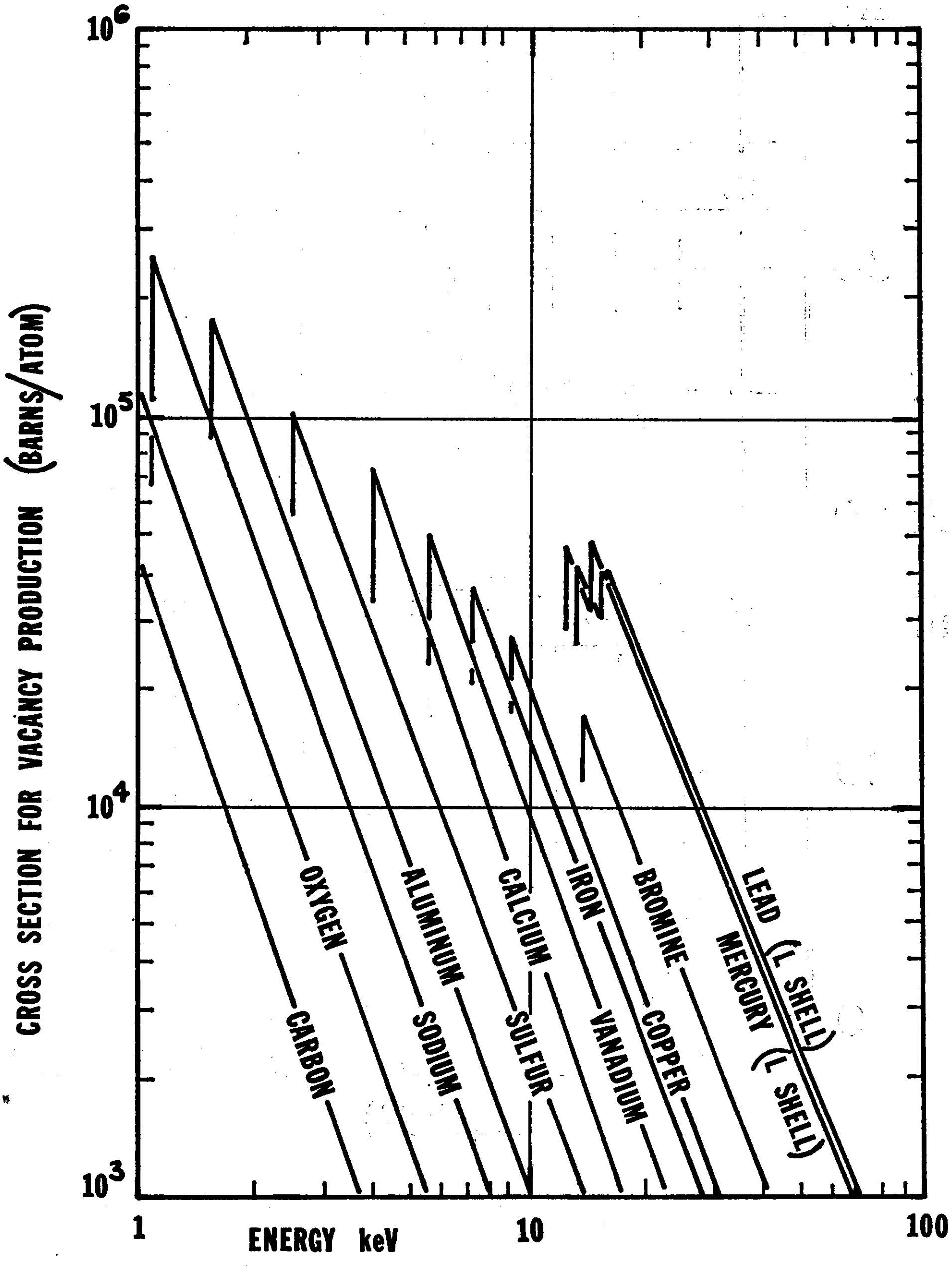

Figure 6

Cross section for K- (or L-) shell vacancy formation in several elements as a function of energy.

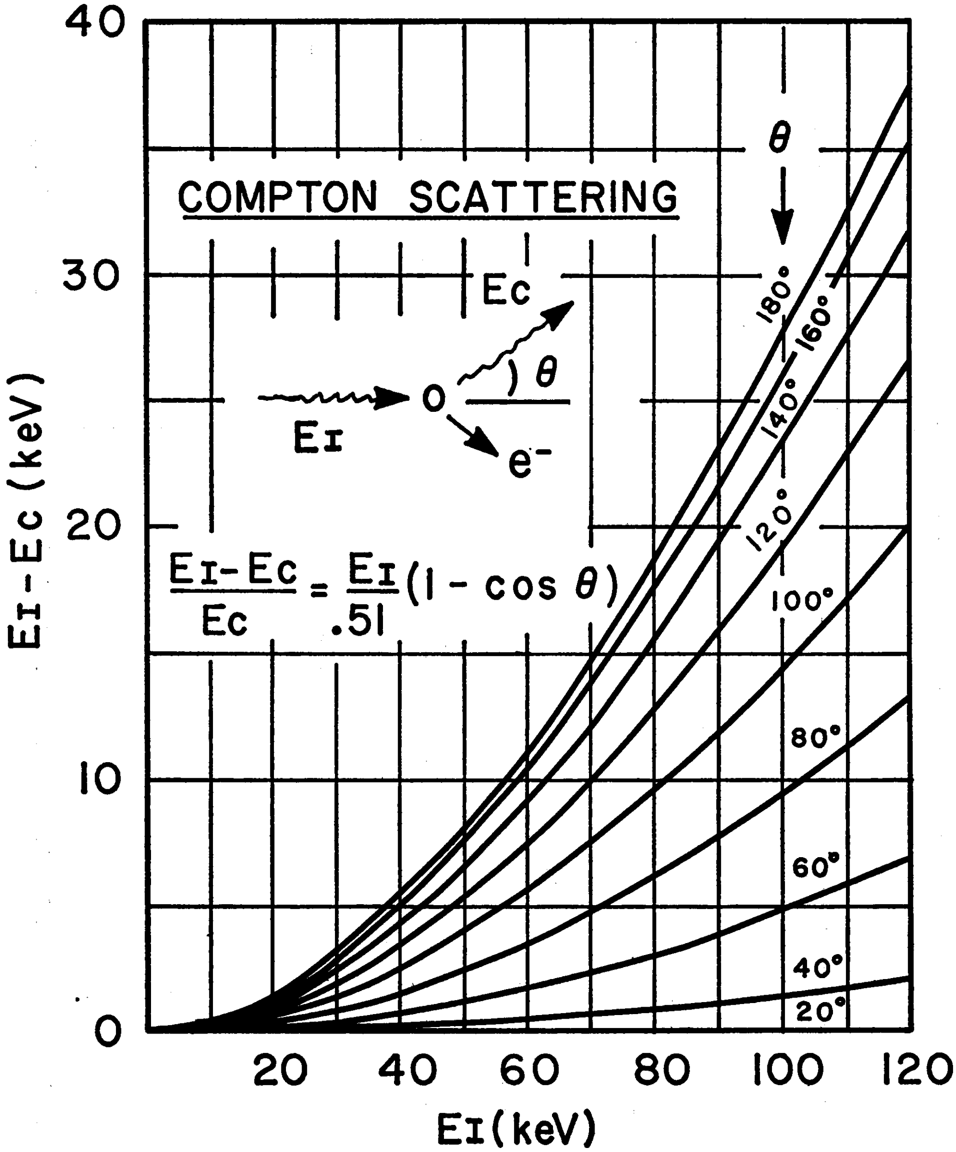

FIGURE 7

Energetics of the Compton-scattering process at energies below 120 keV.

spectroscopy—this time due to the effect of scattered radiation from the sample into the detector. Both coherent (elastic) and incoherent (Compton) scattering from the sample matrix, the organic base containing the trace elements, are present, the relative proportions depending on the ratio of light to heavy nuclei present. Figure 7 shows the energy exchanges involved in Compton scattering at these energies. Even 180° scattering of 20-keV photons involves a loss of energy of only about 1.5 keV to the photon involved in the scattering process.

We are now in a position to appreciate the general form of the spectrum (Figure 8) observed by a X-ray fluorescence spectrometer. The dominant feature of the spectrum is the large scatter peaks that may constitute 99 per cent of the total counts observed. At the very low energy end of the spectrum we see the effect of scattered photons from the sample which happen to Compton-scatter from electrons in the detector and escape, leaving only the knock-on electron energy in the detector. The central region of the spectrum contains the interesting information on fluorescent X-rays emitted by the sample—unfortunately, superimposed on a background that, in an ideal case, is due only to photoelectrons from the detector escaping from its surface. Since the photons producing these electrons are primarily those scattered from the sample, and only part of the photon energy is converted into ionization in the detector, a continuum of pulse heights below the scatter peaks is generated by this process. As we will see later, other processes in the detector degrade events that should appear in the scatter peaks, resulting in increased background in the region of interest, thereby limiting our ability to see minute traces of impurities. The results given in this paper are made possible only by the methods of background reduction described herein.

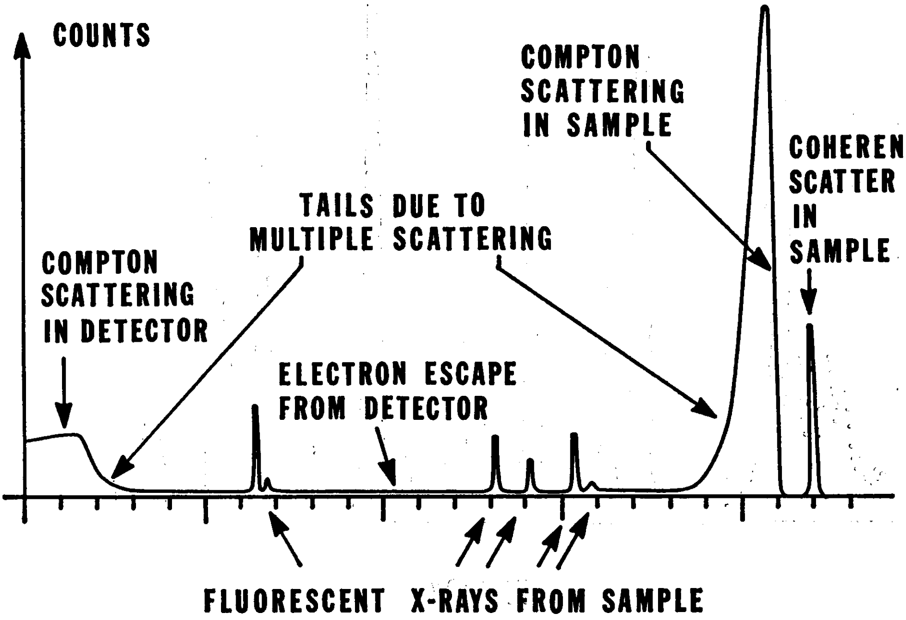

FIGURE 8

Idealized spectrum observed by an X-ray fluorescence spectrometer.

The validity of this general picture is illustrated in an X-ray fluorescence

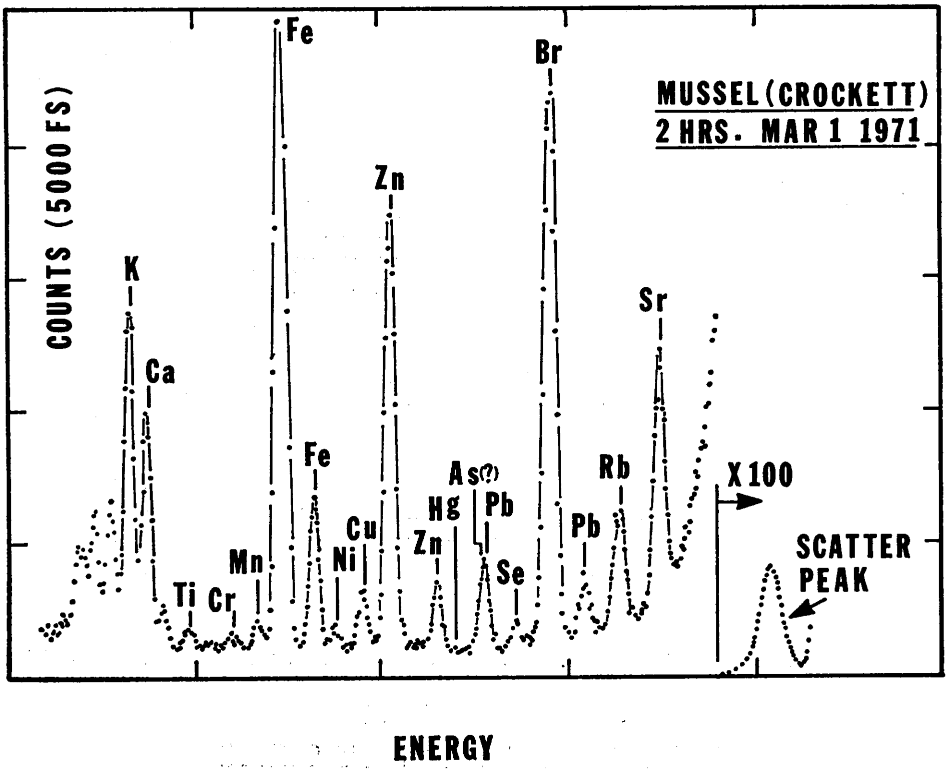

FIGURE 9

A practical spectrum obtained with Mo X-ray excitation of a freeze dried mussel sample.

spectrum obtained recently, shown in Figure 9. The large incoherent scatter peak is shown, while the coherent scatter peak is just beyond the right margin of the figure. The Compton edge due to the detector, which would normally appear at the left of this figure, has been removed by a discriminator in the electronic pulse pileup rejection system employed in this experiment. The background level seen in this figure, while low, is at least ten times as high as can be explained by photoelectrons escaping from the detector surface.

In the next section we will discuss the origins of background in X-ray spectrometers and the factors that determine the sensitivity of the spectrometers for analysis of trace elements.

3. Background and sensitivity factors

3.1 *Energy resolution and counting-rate performance.* The ability of an X-ray spectrometer to identify elements clearly depends on the width of the peaks produced in a spectrum like that shown in Figure 9—if lines due to adjacent elements are not separated, then separate identification of these elements is impossible. It is only in the last six years that electronic noise sources have been reduced sufficiently to make semiconductor detector X-ray fluorescence spectrometers a practical tool [1]. Recent work [2] has improved energy resolution to the point where even lines due to elements as light as carbon are well resolved [3].

A further benefit results from improvements in resolution—narrower peaks stand higher above the flat background observed in a spectrum like that in Figure 9. Therefore, better resolution results not only in the ability to resolve peaks due to adjacent elements, but also in lower detection limits for these elements.

The ultimate lower detection limit for an element is determined by comparing the statistical variations in background below a peak with the counts produced in a peak by a trace element contained in a sample. The number of counts in a peak is obviously proportional to the integrated dose of X-rays on the sample in the counting time. The background level is also proportional to the dose, though we will see later (Section 3.3) that the constant of proportionality is very dependent on the actual spectrometer design, and on the type of source of exciting radiation. Statistical fluctuations in the background are proportional to the square root of the dose. The detection limit for a peak is, therefore, proportional to $1/(\text{dose})^{1/2}$ (that is the sensitivity is proportional to $(\text{dose})^{1/2}$).

A consequence of these considerations is that fast determination of trace elements demands both intense X-ray excitation sources (see Section 3.2), and also electronics capable of handling high counting rates. Recent work [4] has resulted in electronics capable of handling adequate counting rates (2×10^4 to 10^5 c/sec) with virtually no degradation of resolution.

3.2 *Choice of excitation source.* In the work described in this paper we have chosen to use X-ray excitation of the fluorescent X-rays of elements in the sample. Possible alternative methods of excitation include charged particles [5] and electrons. The first alternative is eliminated partly because it requires a rather elaborate piece of equipment in the particle accelerator; also because comparisons between our own results and these achieved with charged-particle excitation have indicated that the sensitivity achieved in a short time is generally better with X-ray excitation of the right type. Direct-electron excitation of the sample is only useful for examination of very thin samples, and is, therefore, unsuitable for analysis of a broad range of samples. Furthermore, the Bremsstrahlung background produced by electron bombardment masks lines produced by trace elements, thereby seriously limiting sensitivity of the spectrometer.

Having chosen to use X-ray excitation, choice of the actual method of generation of X-rays must be considered. Radioactive sources such as I 125 (producing Te X-rays) are commonly employed, but such sources (of reasonable size) provide only relatively weak excitation. Consequently, long counting periods must be used to provide good trace element sensitivity. An attractive alternative is to use a small X-ray tube for excitation—intensities equivalent to tens of curies of radioisotopes are produced by X-ray tubes dissipating only a watt or two of electrical power. Furthermore, the emission of X-ray tubes can be cut to zero when not required—a contrast to radioactive sources which must be considered potentially hazardous to the general public when used on a large scale.

Unfortunately, the output of conventional X-ray tubes consists mostly of continuous Bremsstrahlung X-rays with the characteristic anode material X-rays superimposed on the continuum. When such a tube is used for excitation in a X-ray fluorescence spectrometer, the continuous X-ray spectrum is scattered from the sample to produce a large background in the spectral region where the characteristic fluorescent X-ray peaks should be observed. The flat background seen in Figure 8 is made very large in this case, and sensitivity to trace elements is very poor.

To overcome this limitation we have adopted two new designs of X-ray tube [6].

3.2.1 *Transmission anode tube.* In this tube a thin foil is used for the anode of a small X-ray tube, and the X-ray output is taken from the side of the anode opposite that bombarded by electrons. The filtering effect produced by passage of the X-rays through the thin anode foil cuts out most of the Bremsstrahlung spectrum, so that the output spectrum consists of almost monoenergetic X-rays characteristic of the anode material. A diagram of a tube of this type is shown in Figure 10.

3.2.2 *Secondary fluorescence anode tube.* In this tube a reflection X-ray output geometry is used for the anode, with the X-rays produced by the anode exciting fluorescent X-rays from a secondary target. Collimation of the output permits only the secondary-target X-rays to leave the tube. To obtain high output intensities from the tube it is necessary to have very close coupling between the primary anode X-rays and the secondary fluorescence target. Figure 11 shows an X-ray tube of this type. Its output is almost monochromatic, consisting of the X-rays characteristic of the secondary fluorescence target, with almost no background at lower energies.

These tubes have been demonstrated to be ideal excitation sources for fluorescence X-ray spectrometers, permitting fast analysis of samples for trace elements (for example, 0.1 ppm sensitivity in 15 minutes in some cases).

3.3 *Conventional detectors.* Figure 12 shows three silicon detector configurations used in X-ray spectrometers. The first type, originally used by Miller [7] is referred to as the "top hat" geometry, and is characterized by low leakage current and excellent high voltage behavior. Both characteristics are desirable in high resolution spectrometers, so this configuration is commonly used in these applications. The second type, the "grooved" detector, was used originally by E. Woo, and now employed in "Kevex" X-ray systems, possesses the same advantages as the "top hat" geometry. The third geometry, generally referred to as "planar" exhibits higher leakage current and capacity than the other two

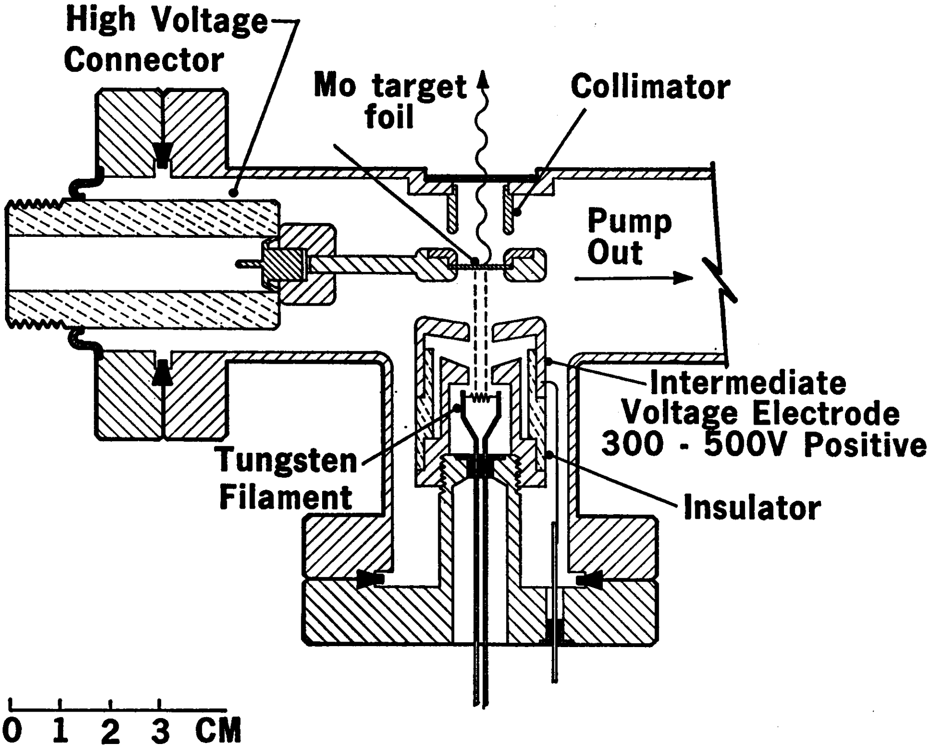

FIGURE 10

Schematic of transmission X-ray tube.

types, and is, therefore, rarely used in X-ray spectrometers. However, its background properties probably deserve investigation. Llacer [8] analyzed the behavior of these geometries with regard to their ability to sustain high voltage operation, and to produce low leakage current. His results, and those obtained in our laboratory, indicate that an *n*-type surface channel normally exists on the surface of silicon detectors. This channel acts as an extension of the *n*-type lithium-diffused region, and since it represents a poor junction to the bulk material, it contributes most of the leakage current, and sets the voltage limitation on detector operation. The fact that such channels can be "pinched off" by internal electric fields normal to the surface explains the difference in behavior between the structures (a) and (b) of Figure 12 and that of structure (c) of Figure 12.

These arguments fail to take into account the collection of charge produced by radiation in the bulk of the detector. The presence of *n*-type surface layers distorts the internal electric field pattern in the detector in such a way that collection of charge produced by X-rays interacting in some parts (shown by horizontal line shading in Figure 12) is via the surface layers. This causes a loss

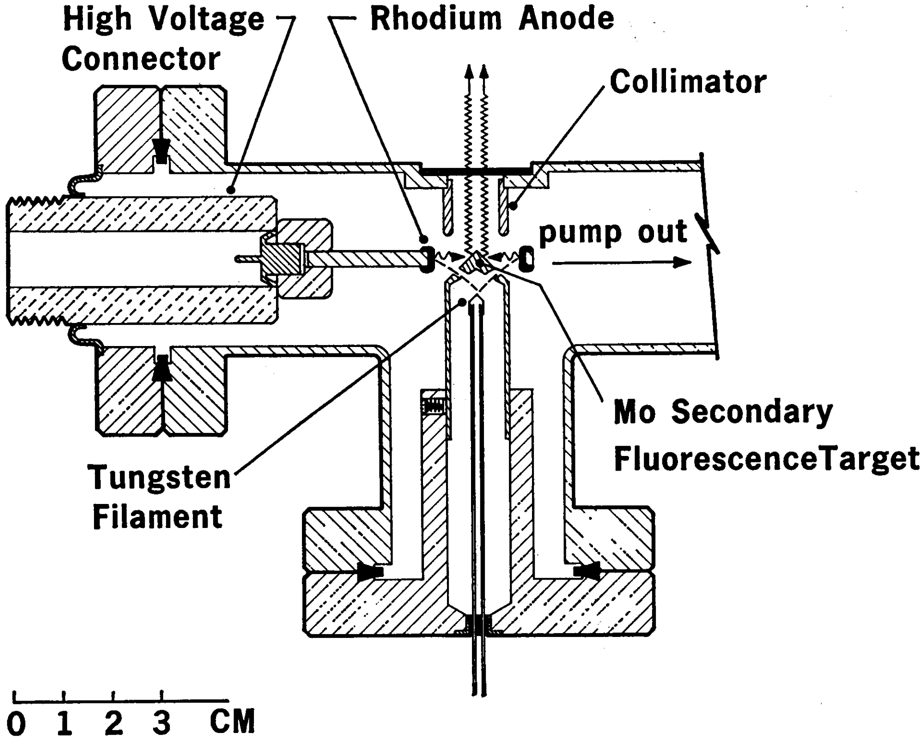

FIGURE 11

Schematic of secondary fluorescence tube with a rhodium anode and molybdenum secondary target.

of charge, so that signals that should appear in the backscatter peaks appear in the general background in spectra. The tests presented in this paper show that this is the predominant source of background in existing spectrometers.

At first sight, it may appear that collimation of X-rays to prevent their interaction in the poor field regions might reduce background, and, indeed, tests show that some improvement can be achieved by this method. It is also obvious that improvement results from increasing the detector area while collimating to a small central region, but the large consequent increase in detector capacity seriously degrades the system resolution—an intolerable price to pay. The degree of collimation that can be used is determined by the requirement for good sample detector geometry; as shown in the typical geometry shown in Figure 13, this implies a wide divergence of X-rays hitting the detector. Despite the possible auxiliary collimator shown in this figure, mounted on the detector face—an expedient rarely adopted as it is difficult to change this collimator to suit the energy range of interest—X-rays like that travelling from A to B still interact in regions of poor charge collection. On the other hand, the X-ray from

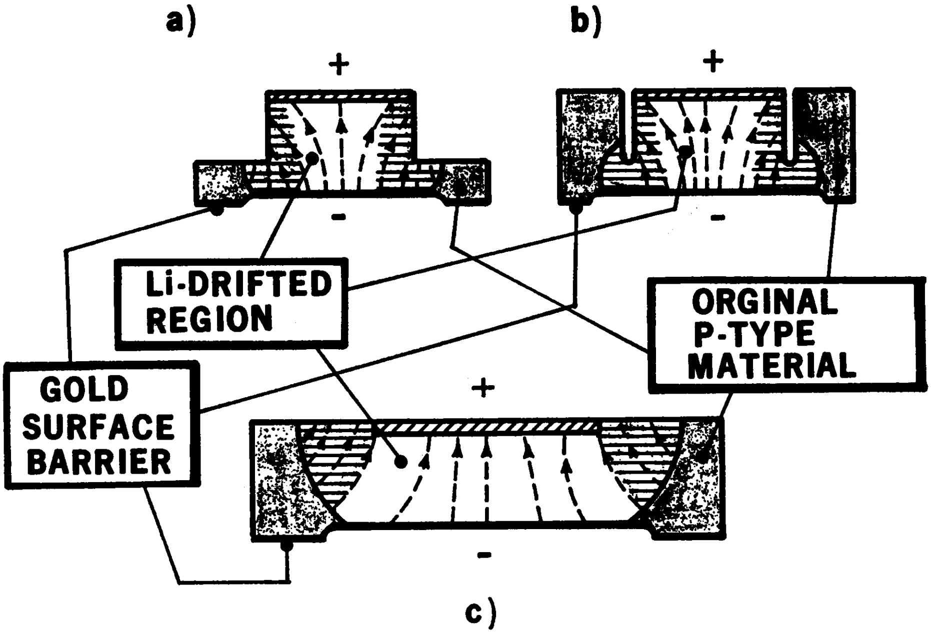

FIGURE 12

Types of detector configuration used in X-ray spectrometers. (a) Top hat detector, (b) grooved detector, (c) planar detector.

C to D interacts in a region of good charge collection, and produces the correct signal.

As shown in Figure 14, the background due to degraded pulses increases as the energy of the X-rays impinging on the detector increases. For cadmium X-rays, the total integrated background count approaches the total number of counts in the main X-ray peak. The proportion of counts in the background decreases considerably in the case of zirconium, and still further for lower energy X-rays.

3.4 *Guard ring detectors.* Guard rings have been employed for many years to overcome fringing field effects in standard capacitors, and have also found application in semiconductor detectors as a device to reduce edge leakage [9]. It, therefore, seems an obvious step to use a guard ring to define the boundary of the sensitive volume of a detector by internal electric field lines rather than by a physical surface with its unknown charge-trapping characteristics. This can also be considered as an electronic collimation technique. Figure 15(a) shows the simple implementation of the idea; note that the output signal is derived only from the central region, while the guard ring and the central region are maintained at the same dc potential (ground).

Even this configuration suffers from a signal degradation problem at the edge

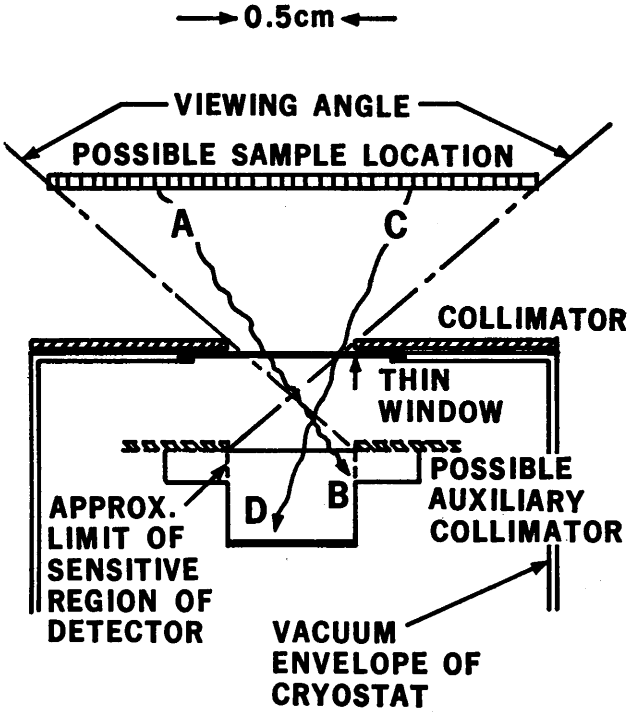

FIGURE 13

Preferred collimation geometry for an X-ray spectrometer.

of the central region. The initial X-ray interaction in this peripheral region produces a dense cloud of charge ~5 microns in diameter; in the electric field, holes and electrons are separated, drifting toward their appropriate electrode. The internal repulsive fields existing within the hole and electron clouds are very large compared with the drift field in the detector—therefore, the cloud dimensions rapidly increase until the internal repulsive field approaches the same value as the drift field. This means that the cloud dimensions reach about 100 microns during the charge collection process. Consequently, a peripheral region of 100 microns thickness exists around the sensitive region from which only part of the charge due to an event is collected in the central region—this means that many of the backscattered events appear in general background. Our measurements show that the background present with a simple guard ring detector is from 2 to 10 times smaller than that with a top hat detector, the exact factor depending on the energy of the backscatter peak.

A further reduction in background is achieved by sensing coincident signals between the guard ring and central regions, and rejecting the central region signal when such a coincidence is registered. This "guard ring reject" system

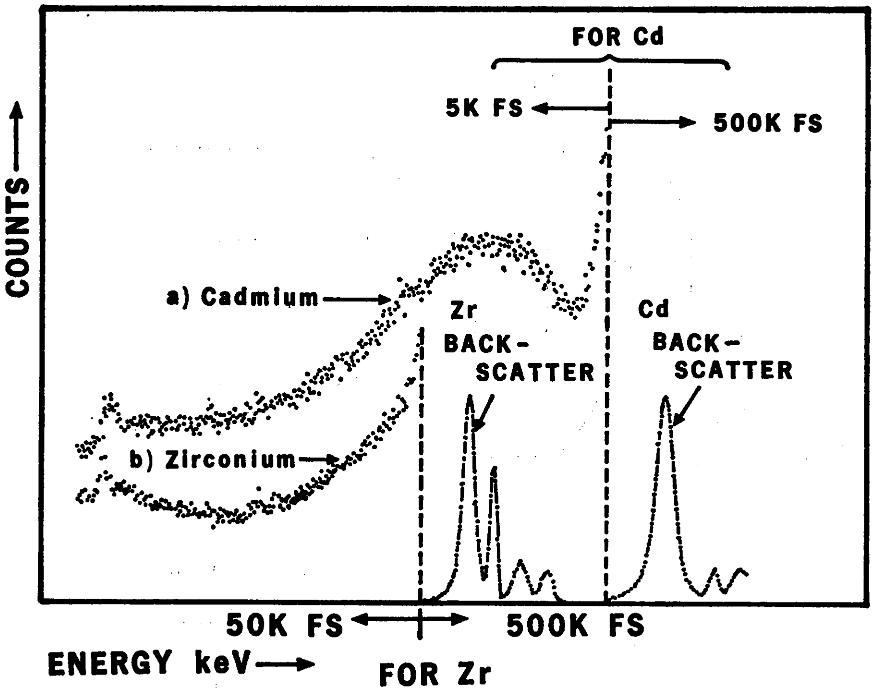

FIGURE 14

The variation in background of a top hat detector as a function of the energy of radiation striking the detector. (a) Cd X-rays scattered by lucite, (b) Zr X-rays scattered by lucite.

effectively eliminates the partial collection from the peripheral region of the sensitive volume of the detector. With such an arrangement, we approach the background level expected due to electron escape from the detector surface. In our actual detector, shown in Figure 15(b), a double guard ring is used, the outer ring serving to reduce edge leakage in the inner ring, and thereby improving its noise properties so that the inner guard ring signal discriminator can be set low to detect very small signals.

The improvement in background resulting from use of the guard ring reject method is shown in Figure 16. Using exactly the same geometry, cadmium X-rays scattered from lucite were used to irradiate a standard top hat detector (a), and the guard ring reject detector system (b). For the same number in the cadmium peak, total counts recorded in the background is 40 times smaller for the guard ring reject system than for the top hat detector. Larger factors are obtained when the detectors are irradiated by radiation of higher energy than cadmium X-rays.

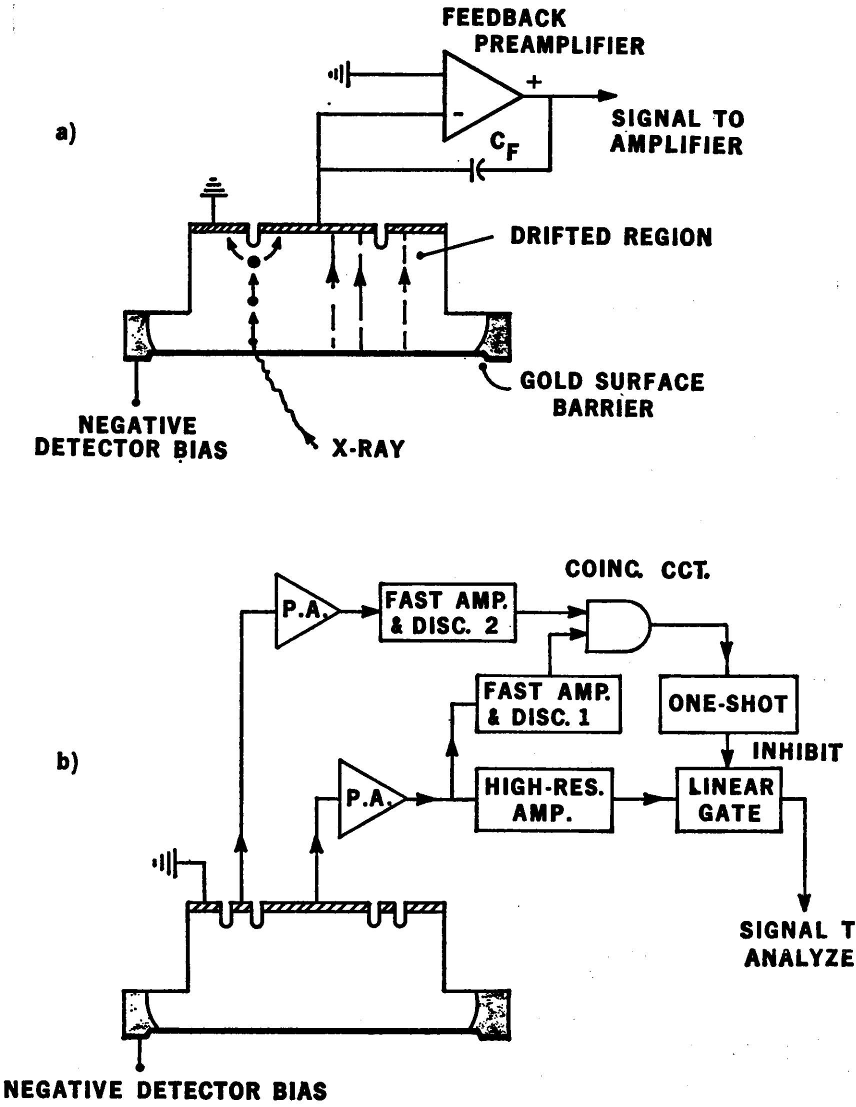

FIGURE 15

Guard ring detectors. (a) Simple guard ring approach showing the mechanism for degraded pulses, (b) double guard ring detector with pulse-reject circuitry to remove degraded pulses.

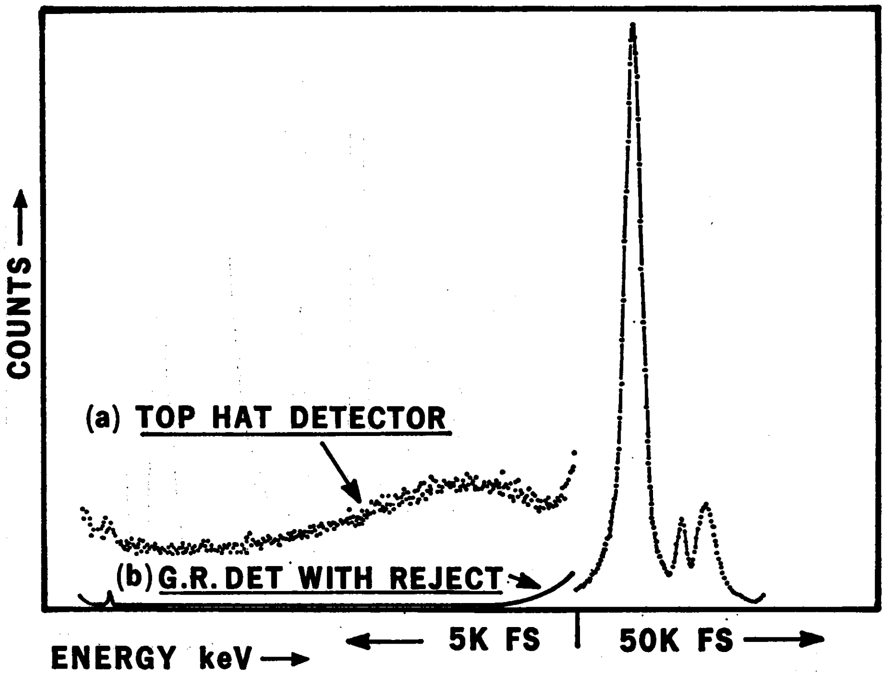

FIGURE 16

Background produced in detector systems by de X-rays. (a) Top hat detector, (b) guard ring detector with reject circuitry.

Figure 17 illustrates the improvement achieved by using this technique on a typical sample. A blood serum sample was examined by a system using a top hat detector, then by one using a guard ring detector, and the same total number of counts were accumulated in the molybdenum X-ray backscatter peak. The reduction in background seen in the second spectrum, averaged over the full energy range, is about a factor of 15. Much larger factors, ranging up to about 60, have been observed for higher energy excitation. Comparison of the two results in Figure 17 shows the improvement in ability to see small traces of elements, such as nickel, present in the specimen at a level near 0.1 ppm. Better statistics realized by a longer count, or with more intense excitation, would further reduce the detection limit.

4. Some experimental results and applications

Semiconductor X-ray spectrometers are distinguished by their ability to simultaneously survey a whole spectrum of trace elements present in samples at levels less than 1 ppm. More sensitive methods can be devised for particular elements; for example, atomic absorption can be used for such elements as

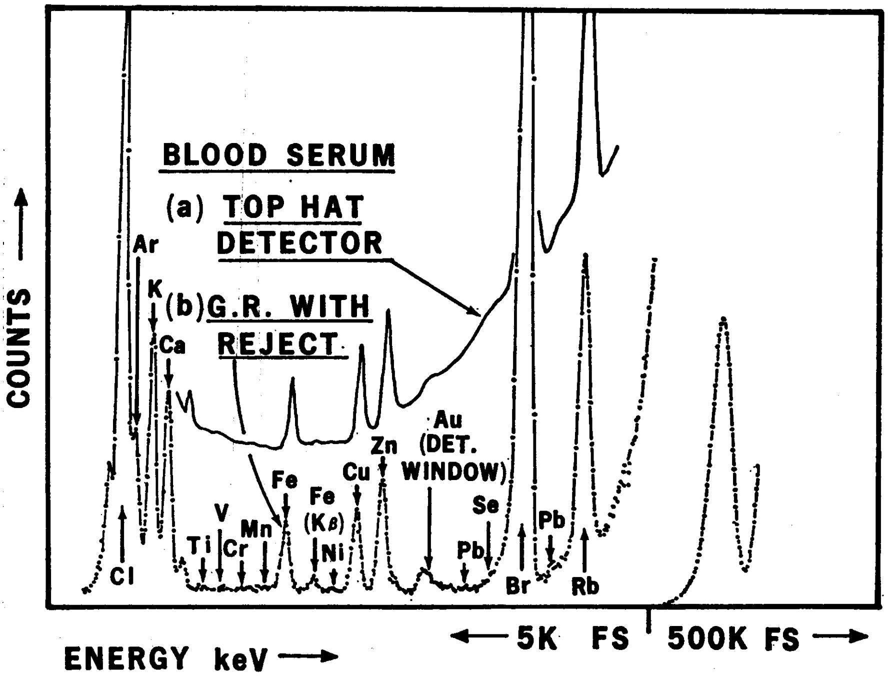

FIGURE 17

Fluorescence X-ray spectrum obtained on a blood serum specimen using a spectrometer equipped with guard ring detector and reject circuitry (b). For comparison, the spectrum obtained on the same sample with the same geometry, and the same total counts in the scatter peak, but with a simple top hat detector, is also shown (a).

mercury. Neutron activation can exhibit greater sensitivity than X-ray fluorescence for some elements, but its sensitivity is poor for many elements, and the activation process is slow and costly. The activation of sodium in biological samples necessitates a long "cooling off" period (often a month) before a sample can be analyzed. Other methods, including atomic absorption, require extensive sample preparation, while X-ray fluorescence requires very little, though removal of water by freeze drying is useful in many cases. For these reasons, it seems that X-ray fluorescence analysis may find a wide range of applications. A few of these are discussed in this section, and some early results are presented.

4.1 *Analysis of foods.* Public attention has recently been focused on the adverse effects of certain trace elements in foods. Mercury and cadmium, in particular, have received attention. The toxicity of these elements results from their accumulating in the body and inhibiting important organic functions. This is to be distinguished from the toxicity of chemicals that cause immediate effects on body functions. Furthermore, the toxicity of an element depends a great deal on its chemical form. In the well-known case of mercury, organic mercury compounds are more toxic than are most of its inorganic salts. X-ray fluorescence gives no information on the chemical form of elements, so it can only be used to flag possible hazards.

Since some trace elements are toxic while others are essential to life, detailed maps of trace elements in a wide range of foods should be of value in nutritional studies.

With these points in mind, we will examine a few measurements on foods made with Mo X-ray excitation. In practice, Mo X-ray excitation restricts the range of elements measured with good sensitivity to the heavy elements (L X-rays), and to the light elements from iron through rubidium. Higher energy excitation must be used for elements heavier than rubidium. Measurements of elements below iron demand lower energy excitation, and also the use of thin samples. In both cases, a slight loss of sensitivity will result.

A test on a freeze dried tuna sample, depicted in Figure 18, shows the presence of mercury (~0.5 ppm). However, the sample was concentrated by freeze drying; the original tuna would have assayed at 0.1 ppm of Hg—far below the FDA tolerance (0.5 ppm).

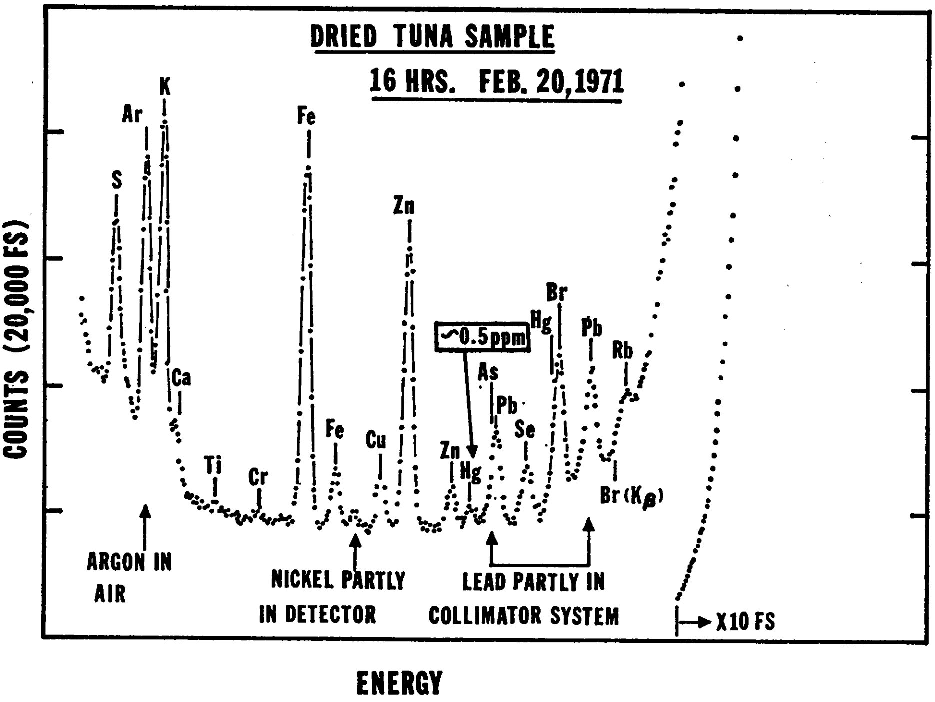

FIGURE 18

Dried tuna spectrum. Features due to the collimator system and other extraneous materials are indicated.

Several features in this spectrum are due to instrumental artifacts. The lead peaks are due mainly to lead contamination of the collimator, while the nickel peak is partly due to the nickel surface barrier used in this particular detector. These factors are not present in the remaining spectra in this paper. The argon peak is due to excitation of argon present at a level of 1 per cent in the air surrounding the system. We also note that krypton—present to only 1 ppm in air—is observed in some spectra. Helium can be used to displace air when necessary.

A word about calibration is in order at this point. A calibration procedure devised by J. Jaklevic and R. Giauque uses thin metal layers of known weight to determine geometry factors, excitation efficiency, and sample absorption [10]. This method permits rapid quantitative assessment of the concentrations of impurities observed in spectra.

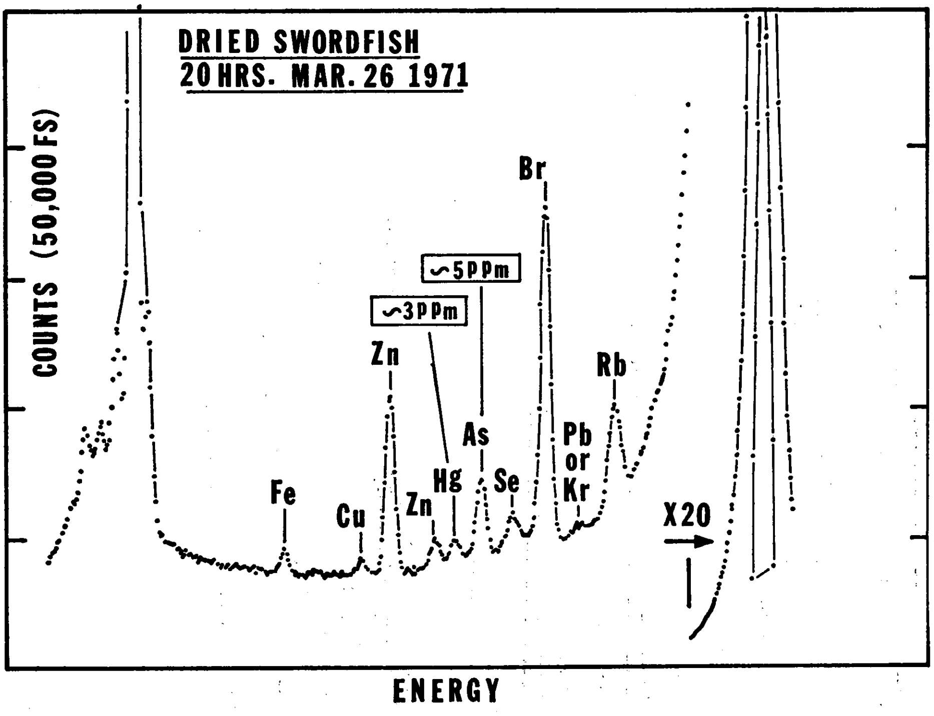

FIGURE 19

Dried swordfish spectrum.

A test on dried swordfish (see Figure 19) is to be compared with that on tuna shown in Figure 18. A very different distribution of elements is seen: iron is almost absent in swordfish, while much more mercury and arsenic are present. Arsenic is probably not a serious problem, but this sample of swordfish (recently purchased) certainly contains more mercury than the FDA limit.

The results of a test on liver sausage (freeze dried) are seen in Figure 20.

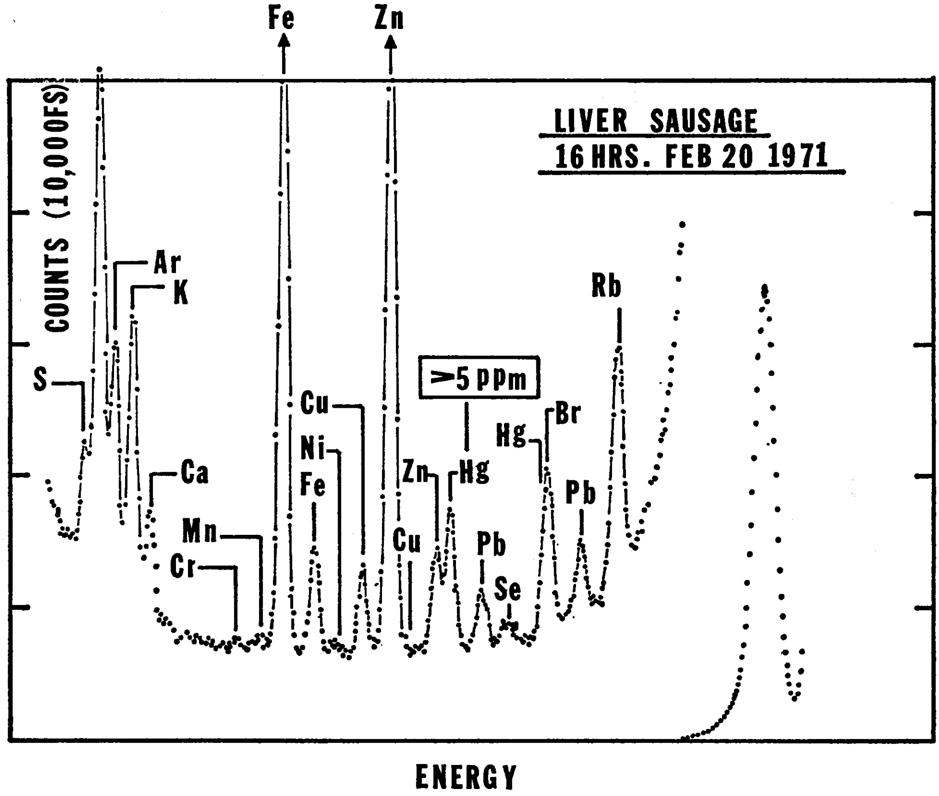

FIGURE 20

Liver sausage spectrum.

Both mercury and lead are present in higher concentrations than in Figure 18, but the mercury in this case might well be largely in the form of an inorganic salt. Although the FDA limit of 0.5 ppm contains no qualification as to chemical form, eating liver sausage might not be a hazardous pursuit!

4.2 *Plants.* Trace elements are known to be an important factor in the growth of plants, and examination of plant material and soils may provide useful information in agriculture. Perhaps the most surprising result of our analysis of plant material has been the high concentration of relatively uncommon elements.

Figure 21 shows the spectrum obtained with a camellia leaf. We show it as a contrast to the other spectra presented here. The large quantities of manganese and strontium were surprising. The ubiquitous lead peak is seen although this particular plant grows far from freeways or city traffic.

4.3 *Medical uses.* Medical applications of this technique could turn out to be the most important. Studies have shown that trace elements in blood may correlate with disease states, indicating a possible diagnostic technique [11].

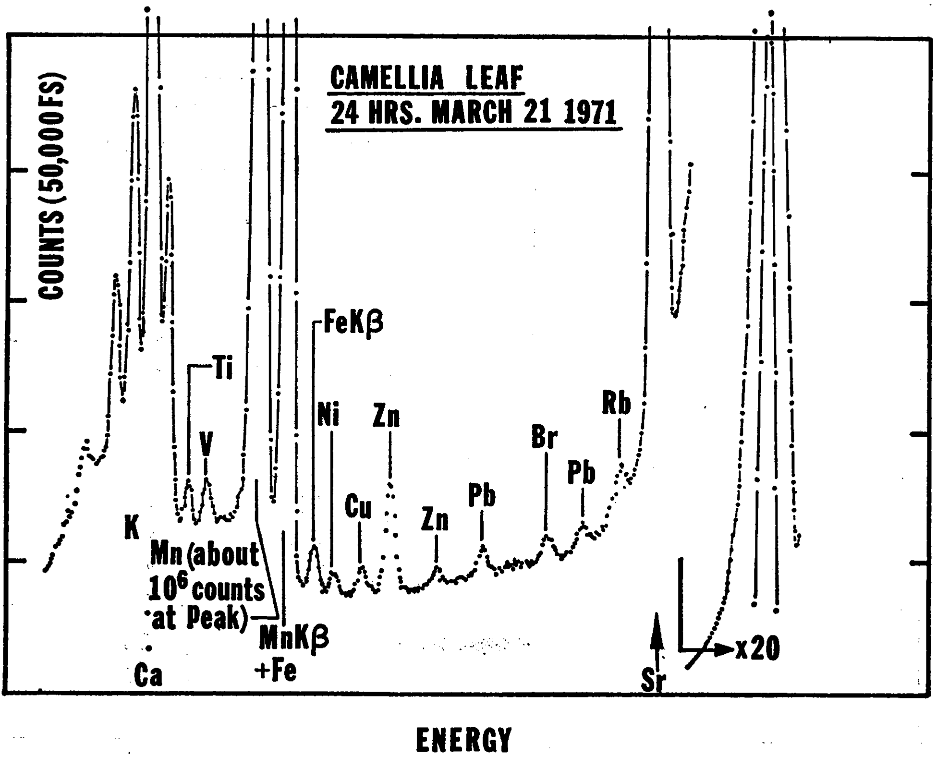

Figure 21

Camellia leaf spectrum.

Other readily available samples include urine, hair, fingernails, and so forth. The statistical correlations between trace elements in these various samples and disease have hardly been studied at all—mostly due to the lack of a suitable fast, convenient, and accurate method of measurement. Semiconductor detector X-ray fluorescence spectrometers may well stimulate new interest in this field of study.

More specific types of problem also arise in medicine. The examination of organs for trace elements may be an important tool in studying the accumulation of elements in organs and its relationship to diseases, including cancer. One example is the analysis of blood samples for lead, as an indicator of lead poisoning in infants. The X-ray fluorescence method is sensitive enough for this purpose as illustrated in Figure 22, where lead is clearly determined in a freeze dried sample (about 3 ml) of blood obtained from an infant with symptoms of lead poisoning. The sensitivity is adequate to permit use of very small samples (~0.25 milliliters).

Two other features should be noted in Figure 22. The large iron peak results in an increase in background at energies below that of the peak. This is due to

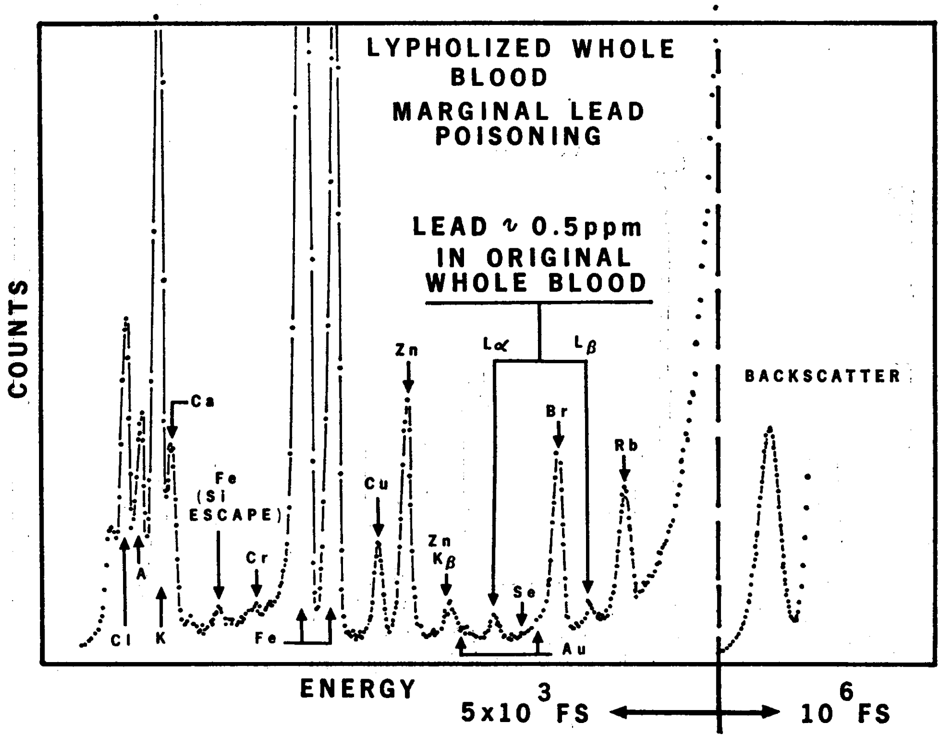

Figure 22

Freeze dried whole blood—original blood volume = 3 ml.

a small dead layer in this particular detector. We also note a small peak resulting from escape of silicon K X-rays excited by the iron X-rays. This indicates the care required in interpretation of results, as the escape peak is quite close to the expected location of a vanadium peak (but resolvable by the system).

4.4 *Air pollution studies.* Elemental analysis of particulate deposits on air pollution filters presents a simple problem for this technique. With short sample collection times, the mass of the particulate deposit becomes a substantial fraction of the air filter material. Consequently, when the filter is subjected to analysis, background due to backscatter in the filter material is quite small. An example of air filter analysis is shown in Figure 23. The quantity of lead measured in this sample (from Detroit) corresponds to almost 2 $\mu g/\text{meter}^3$ of air, a typical number for air in an industrial area.

Figure 23 also illustrates the use of an X-ray tube to speed up analysis. The transmission-anode tube of Figure 10 was used to expose the sample for only ten minutes to produce this result—opening up the possibility of on-line analysis of pollution with the capability of seeing fluctuations in particulate pollutants on a time scale much shorter than an hour.

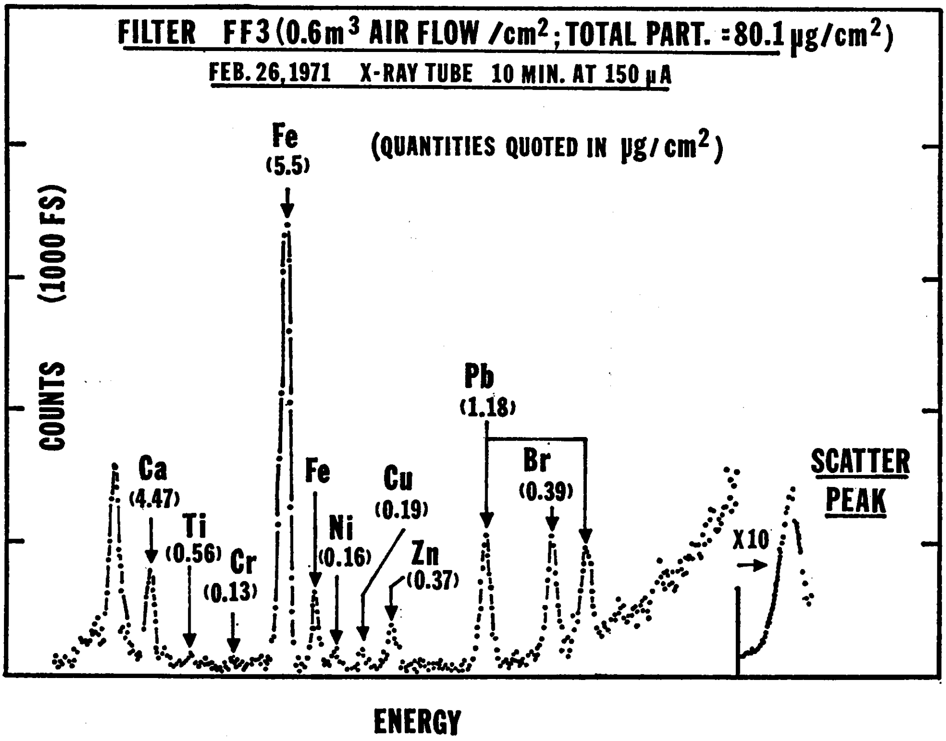

FIGURE 23

Air filter spectrum.

5. Conclusions—relationship to epidemiological study

The instrument described here provides the potential for study, on a large scale, of a broad range of elements present at the <1 ppm in many types of sample. Sample preparation can be very simple at this level of sensitivity, and the measurement time can be short. It is possible to envisage a broad range trace element analysis facility capable of analyzing 50 or more samples per day down to a level of about 0.1 ppm by weight at a cost in the region of $100,000. A limited range of elements could be examined at much lower cost. When this is combined with a computer analysis system, direct readout of trace element concentrations for this large number of samples would be possible.

The samples analyzed with the instrument may cover the whole range required for epidemiological studies. Foods, water, air, particulates, plants, and other environmental factors can be subjected to analysis, and studies of the deposition of trace elements in the human body may also be facilitated. The broad range capability of the method will permit studies of synergistic relationships between the elements.

A necessary factor in any epidemiological study would seem to be the data base available on the problem to be studied. We believe that the use of X-ray fluorescence analysis represents a significant new technique in acquiring such a data base for trace element studies.

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It is a pleasure to acknowledge the cooperation and advice of J. Jaklevic, B. Jarrett, R. Pehl, D. Landis and J. Walton throughout this program. The assistance of R. Giauque in some of the analytical chemistry aspects of the work is also recognized.

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Discussion

Question: E. Tompkins, Human Studies Branch, Environmental Protection Agency

Would you please relate the level of lead shown in the blood of the child to that which would be seen in a child with acute lead poisoning?

Reply: F. S. Goulding

Based on published data, the 0.5 ppm lead (in whole blood), seen in this case, produces minimum clinical symptoms. Acute cases involve levels many times higher than seen in this case.

Question: Emanuel Hoffer, California Department of Public Health

You said we didn't have any information or work on trace elements in human tissues. What about the work of Isabel Tipton in spectroscopy at Oak Ridge?

You also made a statement that we do not have any information on the distribution of these elements in human tissues. There is the work of a statistician at the University of Cincinnati who studied lead, chromium, mercury, and others, and found that these trace elements followed a log normal distribution.

And finally, you made the statement that the level of detection for your fluorescence method would detect the lowest levels of lead where you would get clinical symptoms. What about the delta-aminolevulinic acid test which can detect subclinical levels of symptomology?

Reply: F. S. Goulding

I plead guilty to the charge of minimizing work already done in trace elements. I think, however, that it is fair to say that there is a lack of sufficient data on trace element distributions in human organs, on the normal fluctuations in the levels, on the levels in the environment, foods and other species, and their effect on human beings. I try to relate the few good studies in this area to the vast amount of work on radiation effects, bearing in mind that trace elements represent a much more complex problem.

As seen in the spectrum of Figure 22 the level of lead in this specimen is easily seen, though it is characteristic of just detectable poisoning symptoms. The method is clearly capable of observing levels 5 to 10 times below the clinically observable amount. The ALA in urine test does not appear to be as sensitive since very little change in ALA in urine occurs until lead approaches the clinically detectable level. A nonlinear relationship exists in a plot of ALA in urine against the ALA activity in blood.

Question: Thomas F. Budinger, Donner Laboratory, University of California, Berkeley

We have some data on the distribution of trace elements in tissues of normal and diseased individuals. I would guess that between Professor Isabel Tipton, Dr. Schroeder, and others, even including Dr. John Gofman who worked in this field before he took up his chromosome and linear radiation work, there are over 2000 cadaver studies. These studies include measurements of quantities of about 40 elements above the 1 to 2 ppm lower sensitivity range. Furthermore, we have measures of the variance of concentration in organs and the change in content with age, for example, cadmium. I agree the possible threat from trace elements which accumulate irreversibly in body organs such as kidney and liver is perhaps far greater than anticipated radiation pollution. However, I plead that we avoid trace element fishing trips.

For example, we have collected about 2000 food measurements of Cd and well over 300 references, some of which would seduce us to conclude Cd causes hypertension and tumors. Perhaps it has an important role as perhaps chromium deficiency is involved in diabetes. However, without critical experiments aimed at elucidating mechanisms, I do not see how we are going to establish cause effect. One element is a lifetime work for one man. Or study of many trace elements in one plant or animal system is a lifetime work. Not both.

Reply: F. S. Goulding

Thank you for detailing the scope of existing studies. While I agree that the purely statistical approach to trace elements will be time consuming, and the problem might better be approached in terms of specific mechanisms, we should recognize that accumulation of statistical data often points to mechanisms that might not be predicted.

George B. Morgan, Monitoring Support Division, Environmental Protection Agency

The X-ray fluorescent instrument is excellent for biological tissue. It definitely lacks sufficient sensitivity for measuring concentrations in the environment. To determine transport of pollutants through the media of air, water and food, sensitivities 50 to 100 times the X-ray instrument are needed.

EPA is using the X-ray instrument described for source samples. For ambient samples the following instruments are necessary because some are particularly sensitive for certain elements: (1) emission spectrometer (computerized)—40 elements simultaneously; bad for zinc, arsenic, lithium, mercury, and so forth; (2) spark and plasma TET; good for Pb, Cr, U, Cu, Be, Co, Ti, Fe, Mn, Sr, and so forth; (3) activation analysis—very good for selenium, mercury, arsenic, (4) atomic absorption spectrometer—100 samples per hour for two elements.

There is no one instrument that can do the entire job for environmental measurements. To select the optimum instrument, the researcher must consider the pollutant and the type of sample. The cost for a comprehensive laboratory is about 700 to 800K which includes data acquisition.