RADIOACTIVE ISOTOPES FOR THE STUDY OF TRACE ELEMENTS IN LIVING ORGANISMS[1]

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Radioactive trace elements are grouped according to certain selected characteristics and listed in tables. Indirect tracers are discussed in addition to the trace element itself. Two illustrative trace element experiments are detailed for the purpose of more clearly describing the Geiger–Müller counter technique of measurements of artificial radioactivity.

I. INTRODUCTION

The authors are pleased to have had the opportunity to contribute to the Symposium on Trace Elements, not only for the honor involved but also because it was a very helpful stimulus to their revision of the relative value of the radioactive isotopes as tracers on the basis of recent work in nuclear physics.

It is gratifying to present a critical analysis of artificial radioactivity in its primary significance, that is, in the service of mankind. We all remember the exciting time at the end of 1936 when Lawrence (19) disclosed that he had produced radioactive sodium in the cyclotron in an amount equivalent to 200 mg. of radium in its gamma radiation. This introduced a new era, signified by the fact that not only could thousands of dollars worth of radioactive matter of intensity comparable to that of radium be produced artificially and in a short time, but also by the fact that all chemical elements could be made radioactive and, as a result, all elements in living organisms could be traced by their corresponding radioactive isotopes.

However, the expectation of a simple solution of many important problems by means of artificial radioactivity soon was doomed to disappointment in many cases.

It was found early that radioactive isotopes could not be used as tracers for many of the most important elements in living organisms because they disintegrated so rapidly that it was impossible to trace the labeled elements or they disintegrated too slowly, emitting radiation of insufficient intensity for detection or, even if the half-life were favorable, weak radiation excluded easy experimental procedure.

After five years of the most extensive research in nuclear physics, the general picture can be presented as follows: (*1*) Many new isotopes of the most important elements, with sufficiently long life and high intensity of radiation, have been found. (*2*) The technique of measurement of radiation, developed to a

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very high degree, permits the application of tracers even with weak radiation. (*3*) The study of a number of elements still can not be benefited by the application of radioactive tracers, because of the lack of suitable isotopes.

A present trend in biology and related fields is to evaluate the significance and the effect in the living organism of elements present in traces. Some of these trace elements are necessary and therefore always present in living organisms, while others occur occasionally and may even be toxic. In this paper radioactive isotopes corresponding to both groups are presented, but their classification is based on their relative merits as tracers and not on the biological effects of the element traced.

The best yields of different radioactive isotopes are secured today by bombarding various elements in a cyclotron with high-velocity particles such as heavy hydrogen, ordinary hydrogen, helium, and neutrons, or, as more correctly expressed, they are obtained by means of different nuclear reactions[2].

An important criterion in the classification of nuclear reactions, for the production of radioactive isotopes to be used as tracers, is the atomic number of the active isotope formed. Is it the same as that of the element taken for activation, or is it different?

Since the quantity of stable element taken for activation ranges from 0.1 to 10 g., those radioactive elements formed which are isotopes of the same element as that used are mixed with the stable element. Those radioactive isotopes formed which have a different atomic number from that of the stable element bombarded are present in minute concentrations and as such can be chemically separated with or without addition of carrier, and the quantity of the latter may be controlled entirely by the requirements of the experiment. On this basis radioactive isotopes of different atomic number from that of the activated element are classified here as Group 1 tracers:

$$ {}_{z}A^{m} \longrightarrow {}_{z\pm1,2}A^{m\pm0,1,2} $$

that is, element A of charge number z produces upon activation radioactive isotopes of charge number $z \pm 1,2$; these first-group tracers, for the above reason, may be called "perfect tracers."

Radioactive isotopes of the same charge number as the activated element and, therefore, already diluted by the common element are classified here as Group 2 tracers:

$$ {}_{z}A^{m} \longrightarrow {}_{z}A^{m\pm1} $$

[2] The terms used in this paper are those generally accepted in the literature of nuclear physics. They are as follows: n for neutron; p for proton or hydrogen ion; d for deuteron or heavy hydrogen ion; α for alpha particle or helium ion. Nuclear reactions are expressed as follows:

$$ {}_{29}Cu^{63} \quad (d,p) \quad {}_{29}Cu^{64} $$

meaning that when the isotope of copper of atomic number 29 and mass number 63 is bombarded with deuterons, a proton is ejected and the result is the formation of an isotope of copper having a mass number of 64.

That is, element A of atomic number z produces upon activation radioactive isotopes of the same atomic number z but of different mass, $m \pm 1$, from that of the stable isotopes bombarded.[3]

II. RELATIVE SIGNIFICANCE OF DIFFERENT RADIOACTIVE ISOTOPES AS TRACERS

The importance of obtaining radioactive isotopes, uncontaminated by considerable quantities of inactive elements, for the study of living organisms can be demonstrated with arsenic.

In figure 1 are shown the radioactive isotopes of arsenic which are important as tracers. The stable isotopes are shown by rectangles, and the radioactive isotopes are shown by ovals. Stable arsenic is a single isotope ($_{33}As^{75}$). Germanium consists of five stable isotopes. Within the rectangle for each stable isotope its abundance is given in per cent. The arrows indicate the nuclear reactions forming different radioactive isotopes. From this drawing it can be seen that, if germanium is activated with protons (p,n reaction), the radioactive isotope of arsenic ($_{33}As^{74}$) is formed from the stable isotope of germanium ($_{32}Ge^{74}$). The quantity of arsenic formed after several hours' bombardment in the cyclotron is very small (less than 10^{-8} g.), but all the atoms of arsenic present are radioactive and the intensity of radiation emitted during their disintegration is sufficient to make this isotope applicable as a tracer.[4]

The minute quantities of radioactive arsenic can be separated from germanium after addition of a small quantity of common arsenic as carrier. The added arsenic may be 1 mg. or even considerably less, depending entirely on the nature of the experiments to follow.

Arsenic itself can be activated by fast neutrons, the reaction being $_{33}As^{75}$ $(n,2n)$ $_{33}As^{74}$. In this case the same radioactive isotope of arsenic will be formed as from germanium, but it will be mixed with 1 g. or even more of the common arsenic. This quantity of arsenic may be prohibitive for some studies of living organisms.

In table 1 are given different radioactive isotopes which fall into the Group 1 classification, the half-lives of which are long enough for experiments requiring considerable time. The half-life of each isotope, that is, the period in which the intensity of radiation and the number of radioactive atoms decreases by

[3] A few attempts to separate newly formed radioactive isotopes of a given element from the stable isotopes of the same element have been made. The procedure known as the Szilard–Chalmers method, however, has not yet found practical application in trace element technique (32).

[4] During the activation of germanium with protons, other isotopes of arsenic ($_{33}As^{73,76}$) are also formed from other stable isotopes of germanium but these have shorter half-lives than As^{74}. The same active isotopes of arsenic can be obtained from germanium by d,n and $d,2n$ reactions.

There is no need of discussing in this paper all the possible nuclear reactions for forming active isotopes from germanium. The aim is to point out one particular nuclear reaction for the production of the best yield of a desired radioactive isotope, in order to facilitate the selection of a radioactive isotope which fits the duration of the subsequent biological experiment.

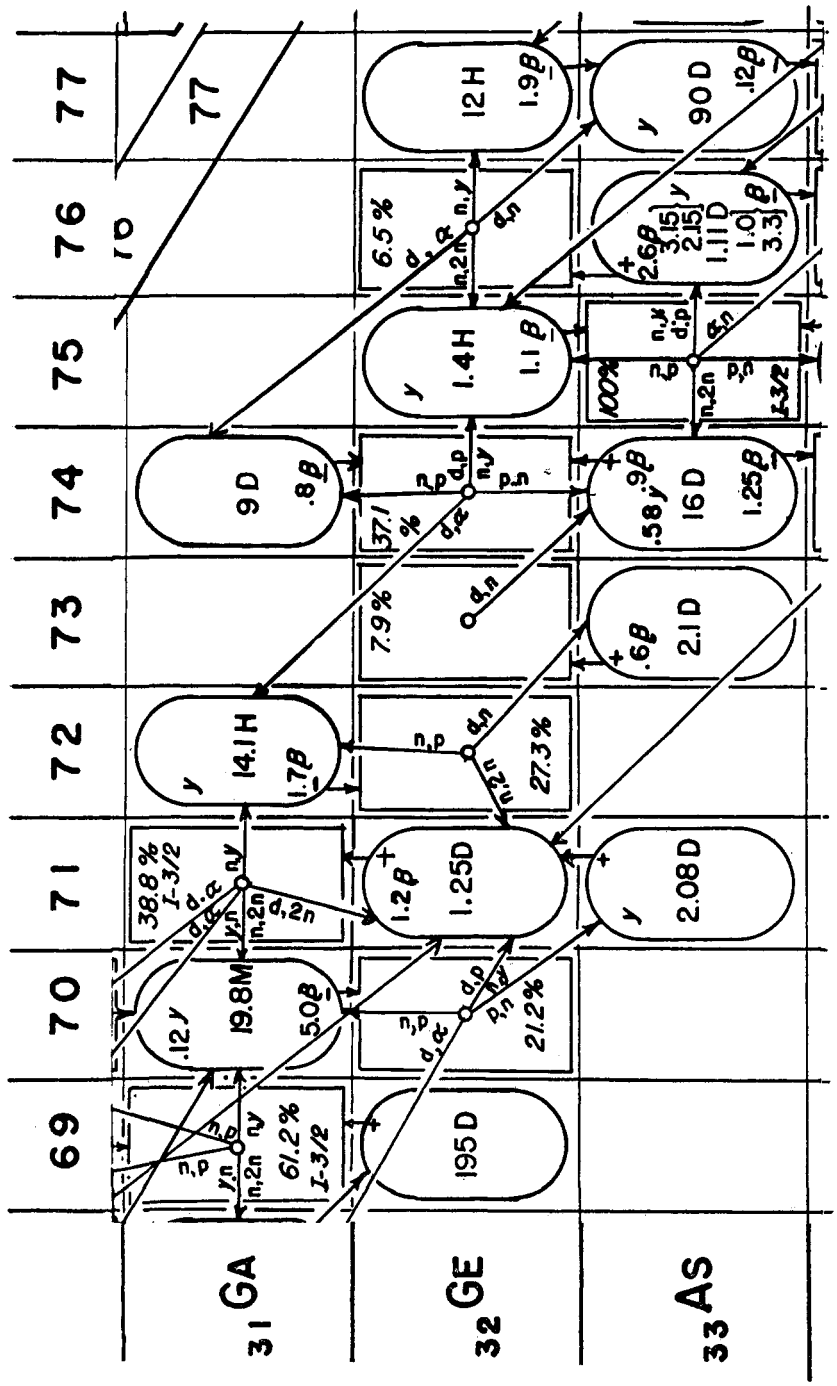

FIG. 1. Isotopic region of gallium, germanium, and arsenic

TABLE 1

Long-life tracers

Group 1: ${}_zA^m \rightarrow {}_{z\pm1}A^{m\pm0,1,2}$

RADIOACTIVE ISOTOPE	HALF-LIFE	BOMBARDED STABLE ISOTOPE AND NUCLEAR REACTION	ENERGY OF β-RAYS	ENERGY OF γ-RAYS	RELATIVE YIELD	REFERENCES
	days		*Mev.*	*Mev.*		
${}_{25}Mn^{52}$	7.4 D	Cr^{52} (p,n)	0.77 (+) K	0.90		(14)
${}_{25}Mn^{54}$	310 D	Fe^{56} (d,α)	K	0.85 0.12	1*	(7)
${}_{27}Co^{56,58}$	72 D	Fe^{56} $(d,2n)$ Fe^{57} (d,n) $Fe^{56,58}$ (p,n)	1.36 (+) 0.4 (+)	1.05 0.5 0.13 0.117		(23, 15)
${}_{30}Zn^{65}$	250 D†	Cu^{65} $(d,2n)$	0.7 (+)	1.14	0.5	(22, 8)
${}_{23}V^{48}$	16 D	Ti^{47} (d,n)	1.05 (+)	1.05		(35, 36)
${}_{33}As^{74}$	16 D	Ge^{74} $(d,2n)$ Ge^{73} (d,n)	0.9 (+) 1.25 (−)	0.58	2	(7)
${}_{33}As^{77}$	90 D	Ge^{76} (d,n)	0.12 (−)			(9)
${}_{34}Se^{76}$	160 D	As^{75} (d,n)	K	0.3		(17, 37)
${}_{39}Y^{88}$	105 D	Sr^{88} $(d,2n)$	K	1.92 0.95		(27, 18) (10, 13)
${}_{47}Ag^{106}$	8.2 D	Pd^{105} (d,n)	K	1.63 1.06 0.50		(8)
${}_{52}Te^{121}$	125 D	${}_{51}Sb^{121}$ $(d,2n)$	K	0.5		(30)
${}_{53}I^{131}$	7.8 D	Te^{130} (d,n)	0.59 (−)	0.37 0.08	20	(7, 33)

* Data on relative yields are taken from a paper presented by Dr. J. G. Hamilton before the Conference on Applied Nuclear Physics, Massachusetts Institute of Technology, October 28, 1940. These data are tentative and subject to large fluctuations.

† This isotope can be produced by deuteron bombardment of the same element with better yield, but the radioactive atoms will be contaminated by the bulk of stable element taken for bombardment.

‡ Emitted electrons are shown as (−); emitted positrons as (+).

half, is given in the second column in days (D). The third column shows the nuclear reaction by which the radioactive isotope is produced. In the fourth and fifth columns are given the energies of radiation in millions of electron volts

(1 electron volt is equal to 1.59×10^{-12} ergs).[5] Most artificial radioactive nuclei emit electrons, positrons, or gamma rays. Some, however, disintegrate by capturing one of their electrons in the K shell. This less familiar disintegration process is designated as K. The electrons and positrons emitted by nuclei during their transmutation are known as beta rays. While the individual electrons composing beta rays possess different kinetic energies, the maximum energy is significant, because this upper limit energy characterizes individual radioactive isotopes. For this reason only the upper limit energy is given in the tables of beta disintegration.

The intensity of radiation is a very important factor in an estimation of the relative value of radioactive isotopes as tracers. Thus, if disintegration occurs with emission of electrons (−) or positrons (+) with energy of more than a million electron volts the detection of radiation is very simple and such radiation may be classified conditionally as strong. Electrons emitted with an energy of between two hundred thousand and a million electron volts may be called medium energy electrons, and elements emitting electrons with an energy of one hundred thousand or less electron volts may be said to have weak radiation. Gamma rays, like x-rays, are electromagnetic and therefore can not be measured directly as the corpuscular types of radiation (for example, beta radiation which ionizes gases). However, gamma rays will eject electrons from molecules of gases, and these in turn produce ionization which is measurable.

Most of the isotopes shown in table 1 have already been used as tracers in various biological problems. Outstanding among these is the work with radioactive iodine on thyroid physiology and the distribution of iodine in normal and diseased thyroids.

The desirable duration of an experiment can be estimated on the basis of the half-life and relative yields of activities: for instance, for Mn^{54}, two half-lives, that is, a period of the order of 600 days; for Zn^{65}, one half-life or about one year; and for arsenic, three half-lives or about 48 days.

The considerable interest at present in the significance of traces of zinc in living organisms justifies more detailed description of the possibility of studying these phenomena with radioactive isotopes of zinc.

From figure 2 it can be seen that a long-life isotope of zinc can be produced by bombardment of zinc with deuterons ($_{30}Zn^{64}$ (d,p) $_{30}Zn^{65}$) or by bombardment of copper with deuterons or protons ($d,2n$ or p,n reactions). The yield of active zinc is considerably better when zinc is bombarded. However, in this case it is mixed with a large bulk of inactive zinc, while if copper is bombarded, the zinc added as carrier for separation of the active zinc can be limited to a desired ratio.

In case the tracer studies can be completed in 2 days it is sensible to limit the experiments to that time in order to use the isotope of zinc of shorter half-life,

[5] The data presented were collected from the literature cited up to October 1, 1942. Undoubtedly many data will be revised with time; new isotopes will be discovered, as may be expected in the rapid development of any new field of science.

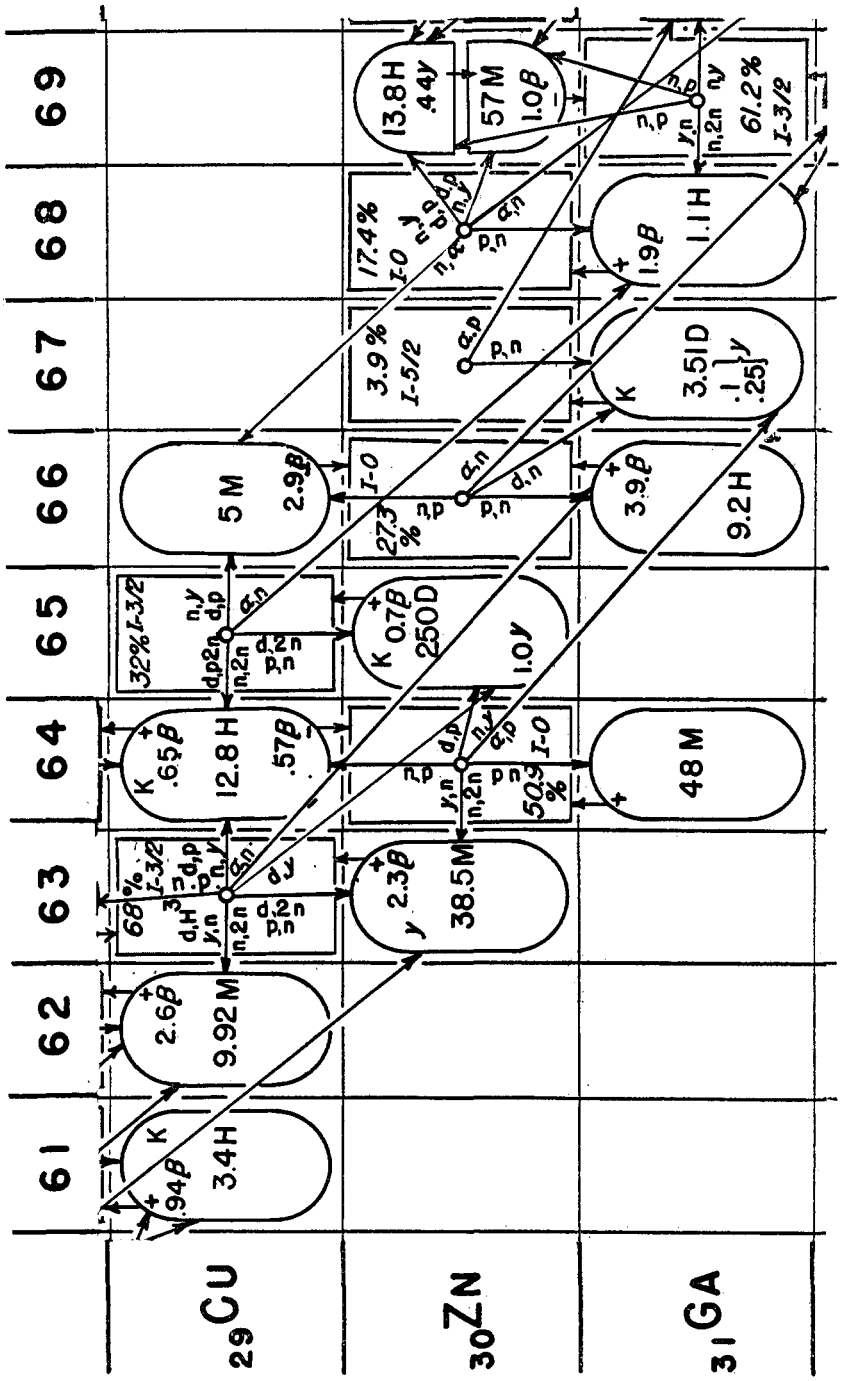

FIG. 2. Isotopic region of copper, zinc, and gallium

because of its greater intensity of radiation. In this connection it may be said that, in general, the activity of a long-life isotope is weaker than that of a short-life isotope when they have similar types of radiation.

An additional consideration in planning tracer studies is the extent of distribution of the element, say zinc, through the whole body of the living organism, as compared to the amount in that part of the organism actually undergoing measurement. This is more of a limiting factor in the application of a long-life

TABLE 2

Intermediate-life tracers

RADIOACTIVE ISOTOPE	HALF-LIFE	BOMBARDED STABLE ISOTOPE AND REACTION	ENERGY OF β-RAYS	ENERGY OF γ-RAYS	TRACER GROUP	REFERENCES
	hours		*Mev.*	*Mev.*		
$_{27}Co^{55}$	18.2 H	Fe^{54} (d,n)	1.5 (+)	1.2 0.8	1	(20, 22)
$_{29}Cu^{64}$	12.8 H	Cu^{63} (d,p)	0.58 (−) 0.66 (+) K		2*	(31, 34)
$_{30}Zn^{69}$	13.8 H† 57 M†	Zn^{68} (d,p)	 1.00 (−)	0.44	2	(16, 22)
$_{33}As^{76}$	26.7 H	As^{75} (d,p)	3.24 (−)	2.05	2	(24)
$_{35}Br^{82}$	36 H	Br^{81} (d,p)	0.46 (−)	1.35 0.79 0.55	2*	(28)
$_{53}I^{130}$	12.6 H	Te^{130} $(d,2n)$	1.07 (−) 0.55 (−)	0.74 0.67 0.53 0.42	1	(7, 9)

* These isotopes can be obtained as tracers of Group 1 from the element of previous charge number but in lower yield.

† Isomers: M indicates half-life in minutes.

isotope of weak radiation than it is for a short-life isotope with strong radiation, for the latter can be detected locally even after wide distribution in the body.

The last isotope of zinc shown on the chart, with a half-life of 13.8 hr., can be obtained by activation of zinc with deuterons and, of course, is contaminated with inactive zinc. This active isotope, Zn^{69}, does not disintegrate directly to gallium but first produces another radioactive isotope of the same mass (nuclear isomer) but with a half-life of only 57 min. The latter disintegrates into gallium with emission of electrons having an energy of one million electron volts. As long as the 13.8-hr. isotope exists, the 57-min. isotope is present too. Thus two

radiations, gamma and beta,—the first emitted by the 13.8-hr. period and the second by the 57-min. period,—will be observed together.

In table 2 are given the radioactive isotopes of different elements having half-lives similar to that of Zn^{69}. In all cases in which experiments can be completed in not more than 3 days and do not require minute quantities, that is, 10^{-8} g. or less, these isotopes should be selected, even though some of the elements have active isotopes of longer half-life. The reason for this is that the yields in terms of activity units are many times greater than those of the elements in table 2. The radioactive isotopes of copper and bromine shown in the table have the longest half-lives known for these elements today.

The next series of radioactive isotopes (see table 3) consists of tracers with half-lives which require completion of an experiment within 24 hr. These

TABLE 3

Short-life tracers

Group 2: ${}_zA^m \rightarrow {}_zA^{m+1}$

RADIOACTIVE ISOTOPE	HALF-LIFE	BOMBARDED STABLE ISOTOPE AND REACTION	ENERGY OF β-RAYS	ENERGY OF γ-RAYS	REFERENCES
	hours		*Mev.*	*Mev.*	
${}_{25}Mn^{56}$	2.59 H	Mn^{55} (d,p)	2.8 (−) 1.15 (−)	2.2 0.83	(1, 7, 11)
${}_{28}Ni^{63}$	2.60 H	Ni^{62} (d,p)	1.65 (−)	0.93 0.65 0.28	(11)
${}_{56}Ba^{139}$	1.42 H	Ba^{138} (d,p)	1.0 (−)	0.6	(26)
${}_{14}Si^{31}$	2.60 H	Si^{30} (d,p)	1.37 (−)		(8, 25, 38)

isotopes, which have a very strong intensity of radiation, are produced by short bombardment. They belong to the second group of tracers, with the exception of Mn^{56}, which can be produced by activation of chromium. For experiments of a type which can be performed in small volumes, that is, of the order of 100 cc., there are radioactive isotopes of chromium, nickel, and barium of longer half-life. These can be obtained as tracers of the first group but of rather weak radiation.

From figure 3 it can be seen that the radioactive isotope of nickel, Ni^{57}, is obtained by activation of iron with alpha particles. This isotope is produced in minute concentrations of half-life 1.5 days. The relative yield and intensity of radiation are rather moderate. By activation of titanium with alpha particles, the 26.5-day radioactive isotope of chromium can be secured in minute concentrations. Bombardment of cesium with deuterons yields the active isotope of barium of half-life 39.5 hr. (4).

The last series of radioactive isotopes, given in table 4, are of rather short life, but their use as tracers is of considerable value in the solution of problems the

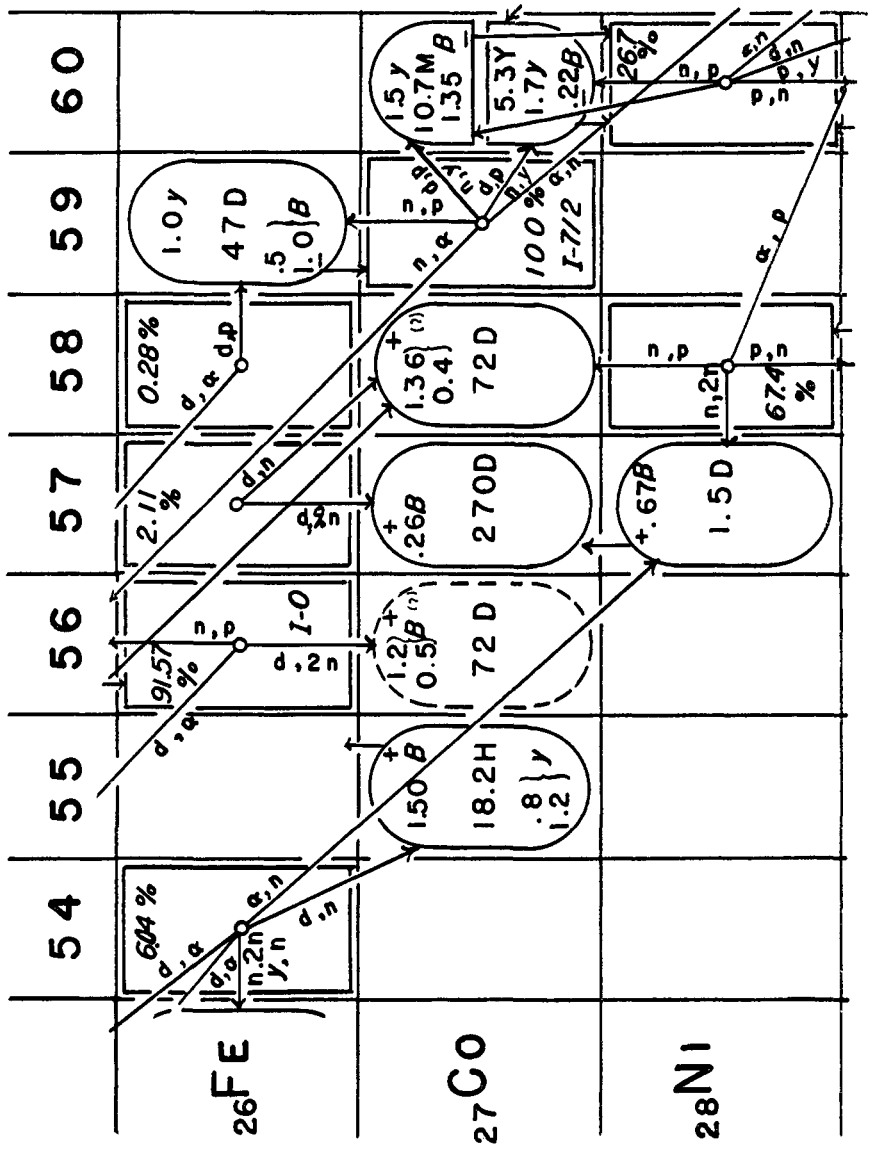

FIG. 3. Isotopic region of iron, cobalt, and nickel

duration of which is not more than several hours. All these isotopes are first-group tracers and can be secured with strong intensity of radiation. In addition, the radioactive isotope F^{18}, with half-life 1.9 hr., is the longest known isotope of the element fluorine.

TABLE 4

Short-life tracers

Group 1: ${}_zA^m \rightarrow {}_{z+1}A^{m+0,1}$

RADIOACTIVE ISOTOPE	HALF-LIFE*	BOMBARDED STABLE ISOTOPE AND REACTION	ENERGY OF β-RAYS	ENERGY OF γ-RAYS	REFERENCES
			Mev.	*Mev.*	
${}_9F^{18}$	1.9 H	O^{18} (p,n)	0.74 (−)		(6)
${}_{25}Mn^{51}$	46 M	Cr^{50} (d,n)	2.0 (−)		(21)
${}_{30}Zn^{63}$	38.5 M	Cu^{63} $(d,2n)$	2.3 (−)	γ	(31)
${}_{34}Se^{75}$	1.81 H	As^{75} (p,n)	β (+)		
${}_{53}I^{128}$	25.6 M	Te^{128} $(d,2n)$	2.44 (−)	0.4	(33)

* H = hours; M = minutes.

† Can be obtained as tracer of the second group by activation of iodine with deuterons.

III. INDIRECT TRACERS

From the above review of different groups of radioactive isotopes it is obvious that not all trace elements in living organisms have radioactive isotopes suitable to be used as tracers. Thus, aluminum, magnesium, lithium, and boron have no active isotopes of sufficiently long life to be used as tracers in biological experiments. The longest lived isotope of aluminum has a half-life of only 6.7 min., that of magnesium a half-life of 10.0 min., that of lithium a half-life of 0.89 sec., and that of boron a half-life of only 0.02 sec. In such cases as these it is justifiable to use indirect tracers, that is, radioactive isotopes of chemically similar elements.

Gallium is similar to aluminum and has two radioactive isotopes; Ga^{66}, 9.2 hr. half-life and strong positron radiation; Ga^{67}, 84.4 hr. of 0.25 Mev. gamma radiation. Both are isotopes of Group 1 and are easily produced simultaneously by activation of zinc with protons (see figure 2) (2, 3).

The isotope of silicon has a rather short half-life of 2.6 hr., but the chemically similar element germanium has several isotopes with long half-lives. For example, Ge^{71}, produced by deuteron bombardment of gallium, belongs to the Group 1 tracers and is a strong emitter of positrons (see figure 1) (23).

In table 5 are given radioactive isotopes of Group 2 which are of long life and have strong radiation. These have already been applied as indirect tracers. It might be mentioned that Sr^{89} has been used as a tracer for calcium in the solution of biological problems, since the long-life radioactive isotope of calcium, Ca^{46}, has weak intensity of radiation. Similarly, rubidium can be used to trace potassium when the 12.4-hr. period of K^{42} is not sufficiently long (10, 12, 13, 18).

For a comparative study of the effects of light and heavy elements of the same periodic group, radioactive isotopes of sulfur, selenium, and tellurium may be

used as examples. The isotopic region of tellurium is shown in figure 4, from which it is evident that a variety of isotopes are available.

Sulfur has a long-life isotope with a half-life of 88 days. However, it has a rather weak electron radiation—0.107 Mev.—which requires a somewhat different condition of measurement.

For a comparative study of the elements iron, nickel, and cobalt, suitable radioactive isotopes of cobalt (shown in figure 3) can be selected for experiments of various lengths (5, 15, 23).

TABLE 5

Long-life tracers

Group 2: ${}_{z}A^{m} \rightarrow {}_{z}A^{m+1}$

RADIOACTIVE ISOTOPE	HALF-LIFE	BOMBARDED STABLE ISOTOPE AND REACTION	ENERGY OF β-RAYS	ENERGY OF γ-RAYS	RELATIVE YIELD*	REFERENCES
	days		*Mev.*	*Mev.*		
${}_{32}Ti^{51}$	72 D	Ti^{50} (d,p)	0.36 (−)	1.00		(31)
${}_{37}Rb^{86}$	19.5 D	Rb^{85} (d,p)	1.56 (−)		10	(13)
${}_{38}Sr^{89}$	55 D	Sr^{88} (d,p)	1.50 (−)		7	(10)

* Relative yield is given in the same units as in table 1.

IV. DETERMINATION OF TRACE ELEMENTS BY MEANS OF RADIOACTIVE TRACERS AND TECHNIQUE OF MEASUREMENTS

A quantitative determination of any element in any of its chemical compounds by means of radioactive tracers is based on acceptance of the fact that radioactive isotopes mixed homogeneously with inactive isotopes of the same chemical element will accompany the stable element, always being in the same ratio as in the initial mixture, so long as no conditions for separation of isotopes are involved.

From this statement it follows at once that there is no necessity (except in some specific cases) for knowing the actual weight of the radioactive isotope added. It is, however, necessary to know the total weight of the stable element and the radiation of the added active isotope.

At the present time the intensity and nature of radiation, that is, whether the radiation is corpuscular or electromagnetic, can be determined with equal simplicity by means of two main types of instruments: (*1*) the electrometer and (*2*) counters.

An electrometer measures with great exactness the ionization produced by the radiation as a whole or a summarized effect from all particles penetrating into the ionization chamber from the active source. Consequently, the geometrical arrangement of a solid active substance with regard to the ionization chamber is of primary significance when the reproducibility of experiments with the same intensity of radiation is required, as in many biological problems.

In figure 5 is shown a typical arrangement of a unifilar electrometer with ionization chamber on top, for measurement of solid radioactive substances.

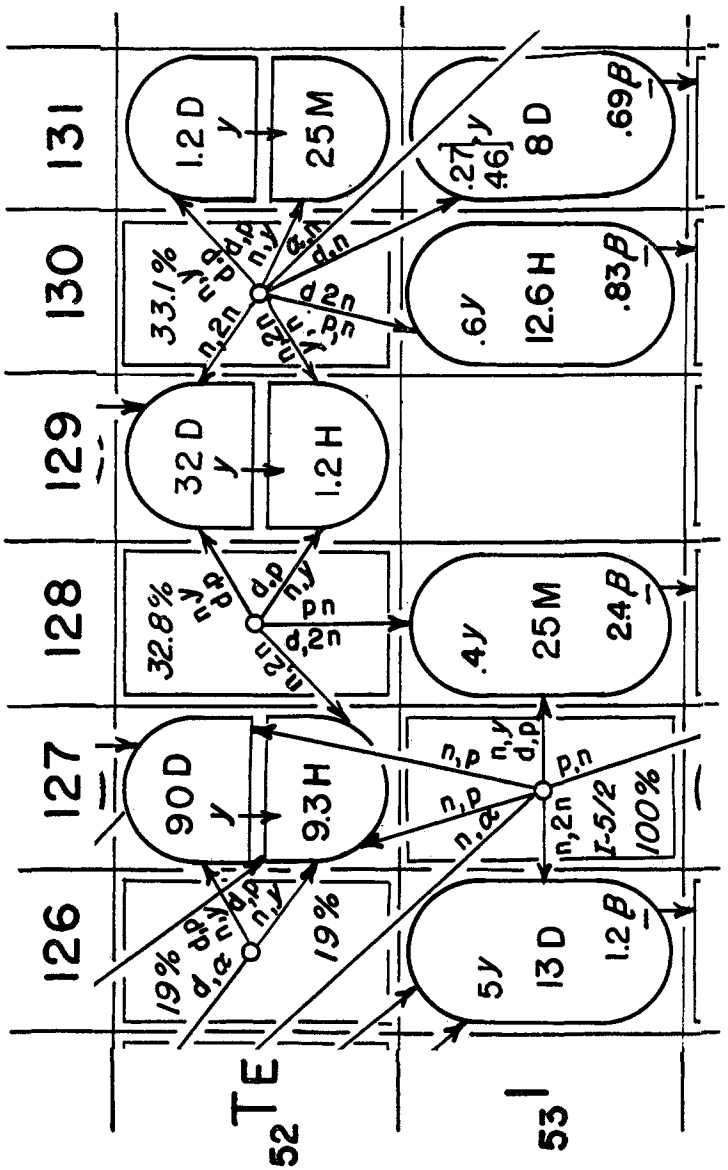

FIG. 4. Isotopic region of tellurium and iodine

From the diagram one can see that the batteries, through resistances, are connected to the plate P of the electrometer and to the inner cylinder A of the ionization chamber I. When rod r of the ionization chamber is disconnected from the ground and the gas in the chamber is ionized, the rod will become charged. The fiber of the electrometer which is connected to the rod will then move toward the appropriately charged plate P, to the left in this diagram. With proper strength potential applied to the cylinder of the ionization chamber, the

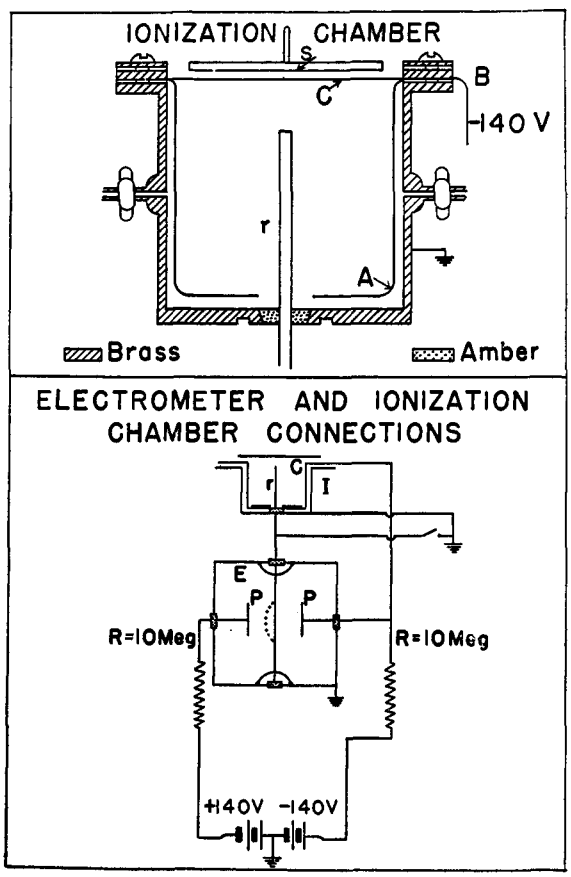

FIG. 5. Arrangement of unifilar electrometer

velocity of the fiber in the electrometer will be proportional to the ionization current obtained in the chamber and this current, at saturation, is proportional to the intensity of ionization produced by the radioactive sample.

The ionization chamber shown in the upper part of figure 5 has a thin aluminum window, C, supporting sample S of radioactive substance. The diameter of sample S, its thickness, and even the bulk of the material within it are of great significance in obtaining the same results with identical samples. The time required for preparing geometrically identical solid samples prohibits the use

of the electrometer in many cases and results in a real advantage in the use of Geiger-Müller counters.

The general recognition of Geiger-Müller counters as the instruments best fitted for measuring radiations in tracer studies is well founded upon its convenience and speed of operation. In figure 6 is shown a general diagram of a Geiger-Müller counter and in figure 7 a picture of part of a counter tube. The counter tube consists of a closed glass cylinder filled with a mixture of air and argon, or sometimes with other gases, at a pressure of several centimeters of mercury. The cylindrical part of the tube is made of very thin glass which permits electrons to penetrate if they have sufficient kinetic energy. The inside of the tube is covered with either a very fine deposit of some metal or its oxide or has just a metal screen. A tungsten wire is sealed into the glass at the bottom and the top of the tube. The wire usually is charged positively and the metal wall negatively.

The principle of operation of the counter consists in the following: Until the potential difference between the wire and the plated metal attains a definite

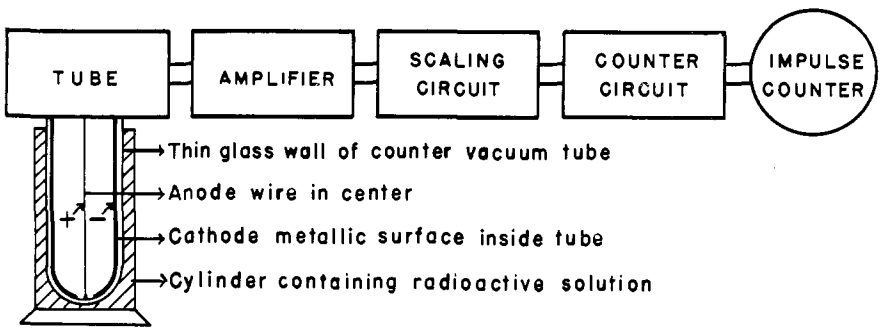

FIG. 6. Diagram of Geiger-Müller counter

value, depending upon the dimensions, the inner gas, and its pressure, etc., no discharge takes place even if some radioactive substance is placed near the counter tube. When the potential is raised to a definite value, known as the threshold voltage, a discharge takes place in the presence of a radioactive substance. One particle, such as an electron with sufficient kinetic energy, penetrating the tube is sufficient to produce a discharge. The discharge or count is transmitted through an amplifier and counter circuit to the impulse counter, which registers the discharge on a watch-type dial.

As soon as a discharge occurs, the potential through the tube drops to some low value at which (by means of radio tubes connected to the counter tube, shown in figure 7) the discharge is extinguished and the potential across the counter tube recovers its initial value. The quenching of discharge and recovery of potential of the tube can be obtained by partially filling the tube with alcohol or some other volatile organic compound, with an action similar to that of the radio tube quenching circuit. The resolving time of the tube, that is, the time which is required for discharge and recovery, in a properly constructed tube is very small, of the order of 10^{-5} sec.

From this figure it is evident that a counter tube is capable of producing many thousand discharges per minute. However, mechanical counters are able to register only several hundred pulses per minute. If the source of radiation is too strong, a special circuit, known as a scaling circuit, is included in the counting system. The scaling circuit facilitates the work of the impulse counter by delivering only a definite fraction of the total discharge per minute. Frequently the scaling circuit is so made that only each sixteenth discharge will be registered by the impulse counter.

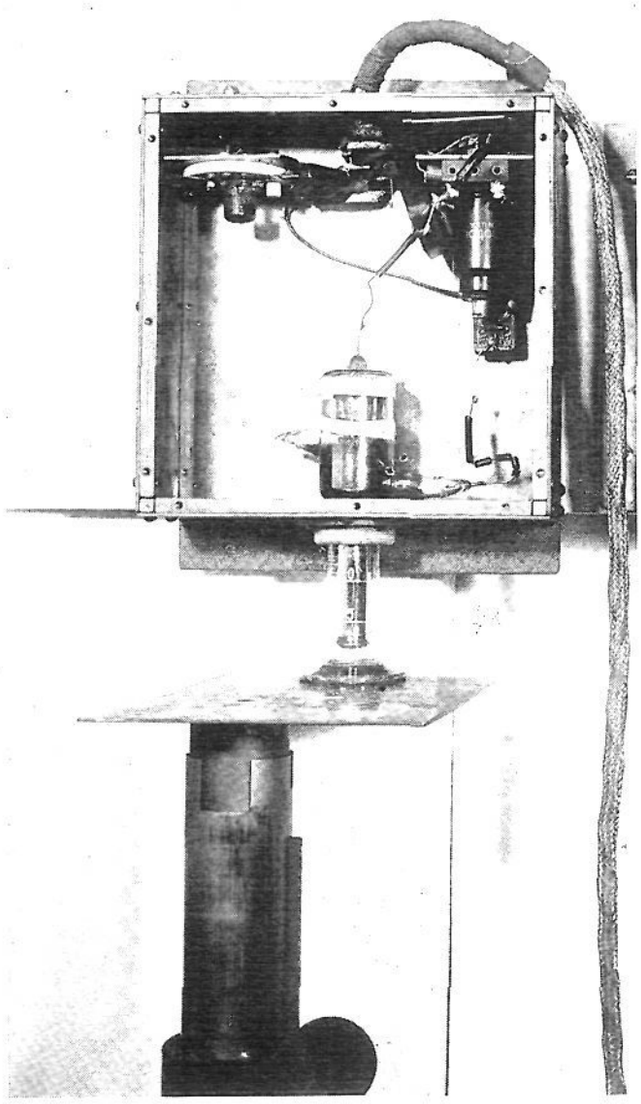

FIG. 7. Geiger–Müller immersion tube with cylinder containing radioactive solution

From this description it can be seen that, in contrast to the electrometer, which measures the total ionization effect of all particles penetrating the ionization chamber, a Geiger–Müller counter tube registers the number of individual atomic disintegration particles that enter the tube. However, the reproducibility of the geometrical position of a sample in regard to the Geiger–Müller tube is just as important as with the electrometer. The principal advantage of a Geiger–Müller counter is that it may be used with liquid samples. Liquid samples in many experiments are readily obtained, and in such cases a Geiger–Müller tube can be immersed directly in liquid.

As is shown in figures 6 and 7, the displacement of liquid by the counter tube is always the same and the geometrical conditions are easily reproducible, provided the volume of liquid is kept constant. Furthermore, the time required for preparation of solid samples is eliminated. As shown in figure 7, the proper displacement of liquid is obtained by a graduated lift table. The graduated cylinders used for the radioactive substances have always the same diameter.

The reliability of a Geiger–Müller counter depends upon several characteristics. The first of these is the stability and range of the plateau of the counter, that is, the range of voltage at which the counter delivers the same number of counts for a given activity of sample. For example, a satisfactory counter tube may start operating at 1200 volts, have a plateau from 1200 to 1500 volts, and only above 1500 volts show an anomalous increase in the number of counts. With a typical background count of about twenty counts per minute (number of counts delivered by Geiger–Müller counter in the absence of any radioactive substance), a liquid sample containing a radioactive substance and producing not less than two hundred counts per minute provides reproducible results.

In conclusion the proper procedure with tracers can be illustrated by two examples:

(*1*) Assume that the first problem is stated as follows: The effect of nickel (in the form of one of its salts) on some organisms is to be studied. The duration of the experiments is only several hours and the quantity of common nickel present must be strictly controlled and is not to exceed 1 mg. per experiment. The last condition prohibits the use of Ni^{63}, since a large quantity of a stable nickel will be mixed with the radioactive Ni^{63}. The nickel isotope Ni^{57}, 1.5 days, fits the requirements better because it is a Group 1 tracer and can be separated from the bombarded iron with proper quantities of stable nickel.

Thus, having obtained the solution of nickel salt with the desired concentration of nickel, a 10-ml. sample should be set aside for measurement of activity from time to time to follow the disintegration curve. From the disintegration curve the ratio of the number of counts to the quantity of stable nickel can be obtained for each time at which the biological experiments are measured. This example demonstrates favorable conditions for supplying radioactive tracers of the first group having weak intensity of radiation.

(*2*) The second problem can be presented as follows: A living organism having a total weight of 1 kg. is to be studied with regard to the distribution and concentration of manganese in different parts of the body. The duration of the experiment is to be 100 days and 50 g. of the body are to be removed for study.

For this work the radioactive isotope of manganese Mn^{54}, 310 days, can be considered suitable. It is obtained by activation of iron with deuterons. The manganese so formed is separated from iron by the usual analytical procedures and purified, using iron, cobalt, and other carriers in order to obtain the manganese in a pure radioactive state.

A part of the manganese salt so prepared should be measured on a Geiger–Müller counter and the activity followed for a few weeks to make sure that the period of disintegration corresponds to that of Mn^{54}. The established ratio (counts of activity)/(grams of stable manganese) at the beginning of the experi-

ment and in the analyzed material at the end should be sufficiently high to permit accurate radioactive measurements.

It may now be concluded that, in order successfully to apply radioactive isotopes as tracers, it is necessary (*1*) to determine the duration of the experiment, (*2*) to find out if a suitable radioactive isotope exists, and (*3*) to evaluate the experimental conditions in regard to the optimum ratio of intensity of radiation in counts to the quantity of inactive traced element in grams.

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