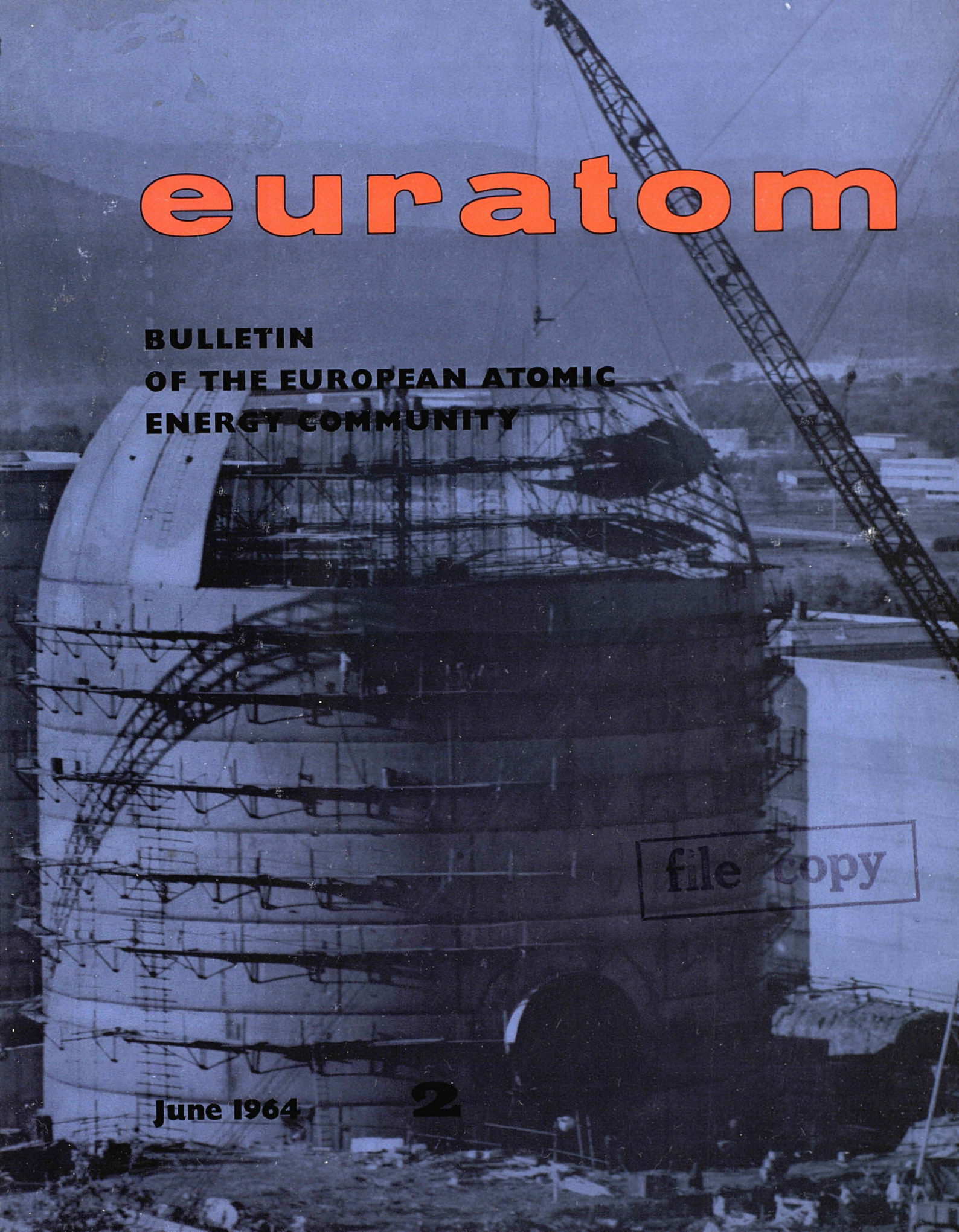

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June 1964 2

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1964-2

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◄ *Vacuum apparatus for the production of marked molecules*

Cover: The RAPSODIE reactor at Cadarache (France)

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Quarterly Information Bulletin of the European Atomic Energy Community (Euratom)

1964 - 2

The Community's mission is to create the conditions necessary for the speedy establishment and growth of nuclear industries in the member States and thereby contribute to the raising of living standards and the development of exchanges with other countries (Article 1 of the Treaty instituting the European Atomic Energy Community).

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Fast breeder reactors and "marked" molecules share the pages of this issue. Apart from the fact that they both come under the heading of nuclear energy, there is little in common between them.

In the case of the development of fast reactors, we have to do with an adventure, typical of the times in which we are living, which involves hundreds of highly qualified specialists, most of them concentrated in large research centres, working towards the solution of one big problem. The size of this adventure is indeed such that the countries of the European Community have decided to embark upon it together and not as separate entities.

"Marked" molecules belong to a totally different world, characterised by the modest scale of the apparatus required for their production and the relatively unspectacular nature of the experiments which make use of them.

Whereas the efforts needed to develop fast reactors are expressed in amounts which the imagination can hardly grasp, the money required to pay for the more easily produced marked molecules could be fetched out of one person's pocket.

And yet, if we were to add up all the contributions to knowledge which the various applications of marked molecules have yielded and will yield in the future, particularly in the field of biology, the sum total would undoubtedly be impressive.

The impressiveness of this total in Europe will depend to a large extent, as Mr. Sirchis shows in his article, on free exchanges across national boundaries, giving the specialists in the field a wide scope for their endeavours.

Fast reactors and marked molecules have thus found common ground, although they have reached it in different ways: they both have a role to play in the building of a united Europe.

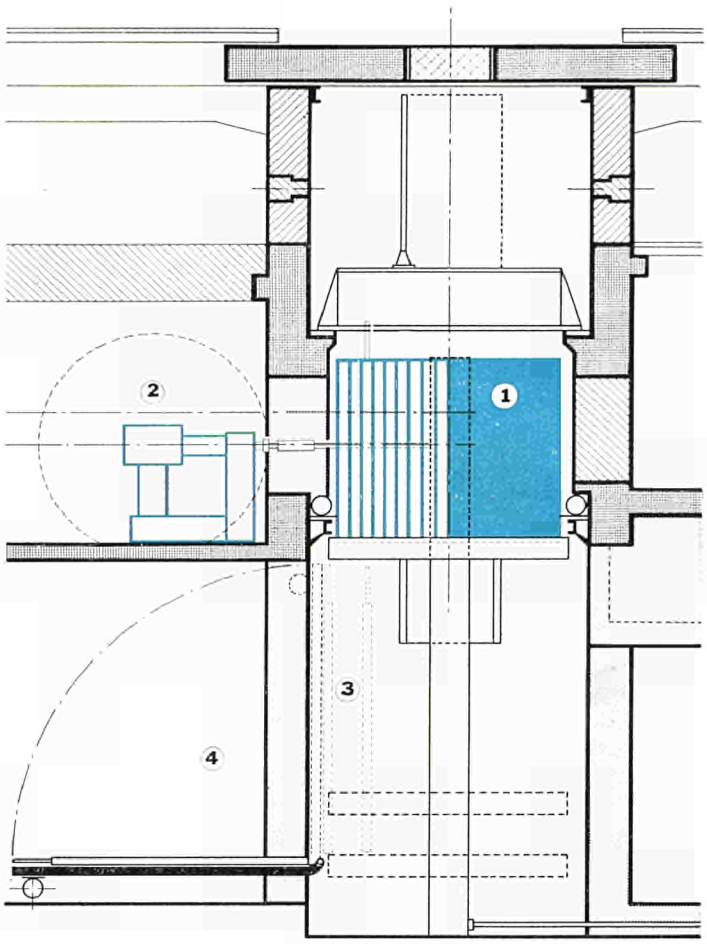


Figure 1—Schematic vertical section of the MASURCA fast critical assembly.
1 Reactor
2 Accelerator
3 Fuel
4 Tilting device for fuel loading

MASURCA, in Cadarache, is one of the two zero energy fast critical assemblies under construction in the European Community (the other is SNEAK in Karlsruhe).
The purpose of these critical assemblies is to provide accurate information on the behaviour of neutrons in fast reactors. Their flexibility will make it possible to vary conditions so as to obtain the data corresponding to the different types of fast reactor which are being envisaged.
Sound experimental data of this kind are obviously indispensable when it comes to putting the design of an actual reactor on the drawing board.
The accelerator shown on the left of the picture is used to give short bursts of neutrons to obtain "pulsed" conditions.

— a 1 MW loop) mocking-up the re-
— a 10 MW loop \ actor circuits
— a full-scale *RAPSODIE* reactor vessel.

The loops have been operating since 1962 and have been extremely useful in indicating several areas which had to be modified in the final reactor design; the experience so obtained has been recently reported by Mr. Vautrey at the Rome Symposium on Fast Reactors. The loops are now operating very smoothly and we think they are now well in hand. They will probably be converted in 1964 or 1965 so as to test different components for future reactors.

The vessel mock-up has been over a year late and the very experience of its construction has indicated areas on which more effort should be put into the real *RAPSODIE* vessel. It is going to be used for flow distribution measurement, loading and unloading experience using the actual *RAPSODIE* handling equipment, and, later on, for thermal shock experiments where the stresses in cases simulating reactor scrams will be measured. This vessel has already been filled with sodium and is now in operation.

The fuel for *RAPSODIE* has been developed by the CEA Plutonium Department at Fontenay-aux-Roses. It has been and is still being extensively tested under irradiation in the *EL-3* reactor before fabrication is started in 1964. Before it is used in *RAPSODIE*, we hope to be able to irradiate *RAPSODIE* pins in the *FERMI* reactor (Detroit, USA) to burn-ups of the order of 20,000 to 50,000 MWd/t in conditions closely similar to those which will exist in *RAPSODIE*.

A critical experiment on the *RAPSODIE* core is now under way in the *ZPR III* reactor (Arco, Idaho, USA) and is the first plutonium critical experiment at this facility; we are grateful for the possibility offered by the USAEC to carry out this essential experiment in their facility.

RAPSODIE should go critical in 1966 and we hope to use it as a reactor experiment and fuel irradiation facility from 1967 on.

Research and development aiming at future power reactors

The research and development programmes aiming at future power reactors are being initiated or pursued in all three associations: Cadarache will concentrate on solid-fueled sodium-cooled reactors, Karlsruhe has been and will continue looking into other cooling systems besides sodium, such as gas at high pressure and dry steam. The Casaccia Centre in Italy is considering advanced fuel systems of the "paste" type[2].

The Cadarache effort will soon start with the design of large industrial reactors (500-1000 MWe) which will be used for selecting the main lines of the prototype to be built as an intermediate step, and to guide the general research and development programme. It is planned that indus-

2. High-content suspensions of solid fuel particles in a liquid metal.

trial companies will share in this stage of the work and some of them are now presenting proposals.
The Cadarache programme will make full use of existing facilities at the site, which are to be converted into more general testing facilities after having accomplished their specific purpose for the *RAPSODIE* programme. In addition, steam generation is being studied on a 5 MW sodium loop now being completed at Grand-Quevilly (near Rouen, France).
In addition, *MASURCA*, the Cadarache critical facility (of which more later) will be fully used for this programme.

The Karlsruhe work started with a preliminary gas-cooled conceptual design which has been presented by Mr. Smidt at the recent Argonne meeting.
The work is now concentrated on the design of a sodium-cooled version, and a design study of a dry-steam-cooled reactor is being made in parallel.
These design studies will be carried out till the end of 1965, when it is hoped a decision will be made to concentrate on one of them and take it to the prototype stage.
The Karlsruhe programme includes the construction of experimental loops for helium and steam testing. Sodium testing is mainly concentrated on heat transfer work since Karlsruhe has full access to the Cadarache component testing experience as well as to the experiment developed in the framework of a programme supported by the German Government on sodium cooling of thermal reactors. The *SNEAK* critical facility will be extensively used for this programme.

Both programmes involve extensive fuel development. Cadarache will work on oxides, carbides, carbo-nitrides and metallic alloy. This will be mostly studied by the CEA Plutonium Department at Fontenay and Cadarache. The Karlsruhe programme will mostly concentrate on the mixed oxide solution and the work will mostly be carried out within the laboratories of the Euratom *Transuranium Institute* in Karlsruhe.

Casaccia has started only recently and is still in the preliminary evaluation stage.

Physics experiment facilities

The physics experiment facilities have been planned in proportion with the enormous problems which remain to be solved (and which have been emphasised once more by the recent Argonne meeting). These facilities should supplement, rather than duplicate, those already existing elsewhere, and so allow the Community to play a significant role in the overall effort in the field.
These experiments include:

SNEAK (Schnelle Null-Energie-Anordnung Karlsruhe—Fast zero energy assembly Karlsruhe)

SNEAK is a 2,000 liter core critical facility, the construction of which has just started in Karlsruhe with *Siemens* as architect-engineers. This facility will be ready by mid-1965. The plutonium-bearing elements will be in the form of sintered PuO_2-UO_2 pellets at 25% PuO_2, contained in stainless steel containers.
Internal cooling of the facility is provided to allow for use of "dirty"[3] plutonium.

MASURCA (MAquette SURgénératrice de CAdarache—Cadarache breeder assembly)

MASURCA is a 5,000 liter core critical facility the construction of which has also just started at Cadarache with *Belgo-Nucléaire* as architect-engineer. It will also be ready by mid-1965. The plutonium-bearing elements are to be used in the shape of cylindrical rods of 12,5 mm diameter of an alloy (uranium-plutonium-iron) developed at Cadarache.
Internal cooling of the assembly is also provided to allow for use of "dirty" plutonium.
In both *MASURCA* and *SNEAK* a central heated loop can be inserted for Doppler and sodium coefficient measurements.[4]
Both facilities are using the same modular dimension for the tubes of the assembly (which are also compatible with the *ZPR*'s, *ECEL* and *ZEBRA*). It is therefore possible to exchange fuel between the machines, and our two will actually share a common stock of approximately 400 kg of plutonium (for which negotiations are under way with UKAEA and the USAEC) according to the needs of a concerted programme.

Experimental fast oxide reactor for Doppler measurement

Because of the importance of the Doppler coefficient and of the difficulty of its evaluation at high temperatures, there was quite early the intention of having at Karlsruhe another experiment, the "Powder Godiva". The aim was to have an excursion reactor and to measure the Doppler effect "in action" when it terminates the excursion. But the amounts of additional plutonium required for such an experiment, as well as safety considerations, made that project a difficult one. Instead, steps have been taken to assure participation (financial, scientific and staff contributions), in the *SEFOR* (South West Experimental Fast Oxide Reactor) project of the *South West Atomic Energy Associates* which might be built by *General Electric* and used with the USAEC's support for research and development and operational tests. The aim is to measure the Doppler coefficient at high temperature in conditions representative of large fast reactors.

HARMONIE—fast source reactor

A 2 kW fast source reactor (*HARMONIE*) is being built at Cadarache for instrument calibration purposes, as well as for driving fast subcritical assemblies. Construction will be terminated in mid-1965. Experimental work on pulsed and modulated subcritical assemblies will also be initiated in the very near future at Cadarache.

SUAK (Schnelle Unterkritische Anordnung Karlsruhe—Fast subcritical assembly Karlsruhe)

A pulsed fast neutron subcritical assembly (*SUAK*) is being built at Karlsruhe. It is a

3. The conversion of U^{238} in a reactor does not lead to the production of Pu^{239} only, but also of several other isotopes of plutonium (Pu^{240}, Pu^{241}, etc.). Isotopes such as Pu^{239} and Pu^{241} are useful because they are fissile; Pu^{240} absorbs neutrons giving Pu^{241}. The term "dirty plutonium" refers to the fact that the element produced in a reactor is far from containing a single isotope.
It is of obvious interest to study the neutronic consequences of the presence of "dirty" plutonium and the design of *SNEAK* (and of *MASURCA*) provides for this. As the α-radiation emitted by "dirty" plutonium generates heat, cooling has to be provided in order to maintain the temperature in the reactor at a uniform low level.
4. A knowledge of the Doppler and sodium coefficients is essential to the assessment of the *safety* of fast reactors. The main consideration in this context is the effect of these coefficients on the behaviour of the reactor during a departure from stable conditions. An increase in the reactivity is accompanied by a rise in temperature. This in turn causes an expansion of the sodium which can result in a further *increase of the reactivity*. On the other hand, the heating of the fuel would lead to a *reduction of the reactivity* though the Doppler effect, because the resultant change in the relative motion of fuel atoms and the neutrons leads to a different pattern of nuclear reactions.
It is obviously of interest to study these two effects both separately and in combination with each other.

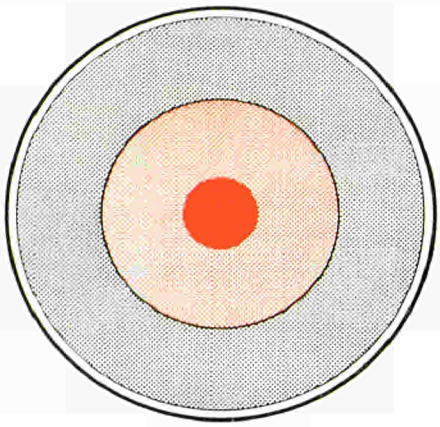


Figure 2—Schematic cross-section of the RAPSODIE reactor.
The central part (shown in full colour) is the core, where most of the fission reactions take place. The outer region (shown in lighter colour) is the blanket region, where most of the neutron captures by fertile material (U^{238}) occur, to produce fissile plutonium (Pu^{239}).
A full-scale prototype power reactor (the next logical step after the experience won from operating RAPSODIE) would typically be fueled with plutonium and natural uranium in the form of mixed oxide UO_2-PuO_2, the plutonium oxide accounting for about 25% of the total. The RAPSODIE fuel will have the same characteristics. However, as it is smaller, a critical mass can only be obtained by enriching the uranium in the isotope U^{235}.

rather ambitious flexible assembly housed in a special building to be completed next year. Specialised pulsed techniques successfully developed at the Centre for thermal reactors will be extensively applied to fast neutron problems.

STARK (Schnell-Thermischer Argonaut Reaktor Karlsruhe—Fast-thermal coupled Argonaut reactor Karlsruhe)

The *STARK* fast-thermal coupled reactor is being obtained by replacing the central graphite column of the Karlsruhe *Argonaut* with a fast neutron zone. This alteration will be completed by the end of this year, and the experiment will be used for fast-thermal coupled reactor study, and later on as a fast neutron source for instrument calibration.
In addition, the experimental physics programmes will make use of facilities provided by the Italian CNEN's RB 3 (thermal fast coupled assembly obtained by transforming the existing RB 1 of Bologna) and possibly a steady state or pulsed source reactor now in the preliminary design stage.

Van de Graaff accelerator installations existing at Karlsruhe, Bologna and Cadarache will also be extensively used in full support of the programmes.

Research and development support

The programmes carried out in the three associations are receiving full support from other sources. Among the most important contributions we might in particular mention:
— the CEA liquid metals section of Fontenay and Cadarache, where technological development as well as basic studies are carried out;
— the Euratom heat transfer department at Ispra, which is concentrating on basic heat transfer work;
— the CEA plutonium department, which is carrying out the laboratory scale work at Fontenay and the fabrication development work at Cadarache in the new plutonium hall;
— the Euratom *Transuranium Institute* at Karlsruhe which, now under construction, should be completed in 1965 but will shortly start active work in a small prototype laboratory;
— the Euratom-CEN Association for the high-flux BR 2 reactor in Mol, which is requested to carry out a large programme of structural material irradiation tests. Fuel irradiation is also planned in the central hole of BR 2, in a cadmium shielded loop, so that the irradiation would be carried out in an epithermal and fast neutron environment;
— the CEN neutron spectroscopy group, which will be fully employed in support of the Cadarache programme through a unique arrangement by which the complete team has been temporarily transferred to Cadarache;
— the Euratom *Central Bureau of Nuclear Measurements* at Geel, which is devoting a major part of its effort to the determination of the neutronic properties of elements according to priorities recommended by the European/American Nuclear Data Committee (where the representatives of our associations meet with their colleagues in other fields).
In addition to this list, we should also mention that we hope to be able to use the services of the reactor physics and technology departments at Ispra and maybe of the *SORA* pulsed fast source reactor should it be built there, and the irradiation services of the high-flux reactor of our Petten centre.

Looking to the future

The survey just made has to be completed by a survey of what we feel is missing to achieve our objective of establishing the industrial fast power reactor by 1975/1980. As others engaged in this field, we plan to have at least one prototype reactor operating in the early 1970's, which should be

the corner-stone of our effort in the third Euratom five-year programme.

The first pinch we feel in trying to fulfill this objective concerns the special nuclear materials which are needed in considerable quantities in the very near future, in particular to fuel our critical facilities. In order to start with the active plutonium work before the end of 1965, when our critical assemblies should have been completed, we need a minimum of about 350 kg of plutonium and ton amounts of uranium-235, at a time where there still does not exist a free market for these materials. We are, as already mentioned, negotiating for the supply of these materials and for possible more general collaboration with the USAEC as well as the UKAEA, since no Community facility will be in a position to supply the quantities we need in due time.

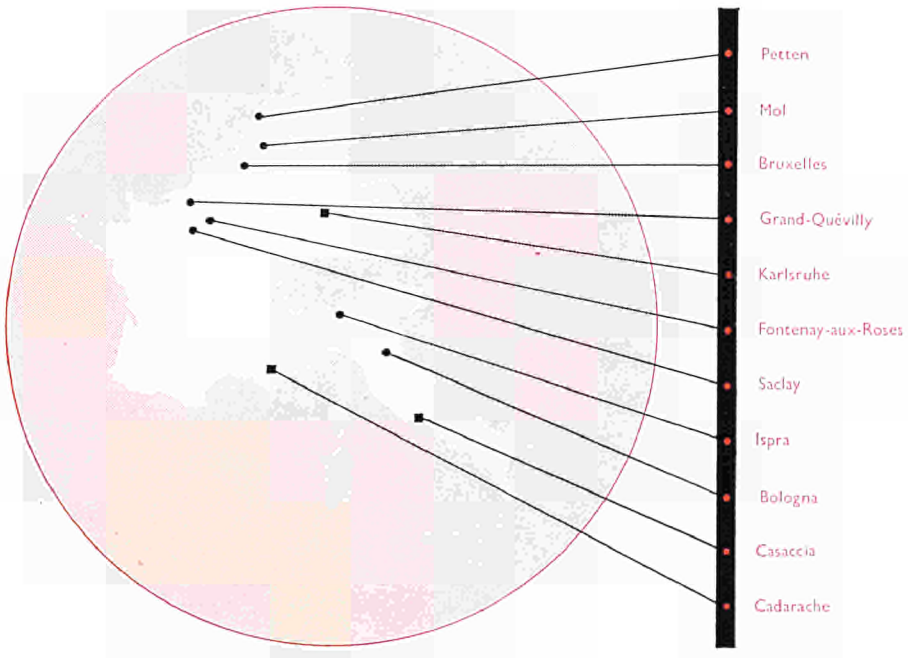
We also shall lack fast neutron irradiation facilities until *RAPSODIE* comes in to fill this gap in 1966 or 1967. As we have mentioned, the only fast neutron irradiation facility now available in the Community is the central hole of the BR 2 reactor, where a flux of about 5×10^{14} epithermal and fast neutrons can be obtained in a rather confined geometry which allows for the testing of only one pin at a time.

We are eager to find available space at reasonable conditions, in existing fast reactors outside of the Community, in particular in the *FERMI* reactor, which we feel is extremely well adapted for this type of testing. We are happy to have received the offer of making it accessible for Community users. I should also mention that negotiations are under way with the UKAEA for use of Dounreay. They are carried out by the CEA, acting on behalf of our Association.

The availability of *DFR* (Dounreay), *FERMI*, *EBR II* (Idaho) and *RAPSODIE* at a later date will not in our opinion solve the problem of finding the ultimate capability of the types of fast reactor fuel we are now considering or of future advanced types. We think that it may soon be necessary to plan for a specialised fast fuel test facility which will permit fully instrumented irradiation tests to be carried out exhaustively. We are, as everybody else, quite afraid of the large sums of money which would be involved in the construction and operation of this type of facility. We would therefore be extremely interested to examine any possible joint ventures which could be considered in this field.

We are also convinced that the ultimate safety evaluation of fast reactors is far from having been thoroughly investigated. This was apparent at the recent Argonne meeting and we are therefore encouraged to go on looking into this wide field; we have received the outline of a proposal from *BelgoNucléaire* concerning an improved *TREAT*[5] reactor and our department of reactor physics at Ispra had been in the meantime evolving an independent and parallel concept. Even though this type of facility can certainly accomplish a useful purpose in assessing the consequences of a fast reactor meltdown accident, we think it necessary to have a broader and deeper look in the safety field.

From the very beginning, we have been convinced that the study of fast reactors is ideally suited for international co-operation of the type we are at present consolidating within the Community and which we wish to extend beyond the Community. We are close, I hope, to the conclusion of an agreement of co-operation between the USAEC and Euratom and its associates; this agreement would provide for full flow of information and exchange of personnel between the different centres of activity.[6] We would certainly welcome such an exchange programme with the UKAEA, and possibly to be engaged into future joint ventures such as a common fast fuel test reactor and/or a safety test reactor. However dreamy these ideas might look today, we are confident that they should materialise in the future and shall always be ready to give them the most earnest consideration.



5. Thermal pulsed reactor for investigations in reactor safety.
6. This agreement was signed on 27 May 1964.

The European Transuranium Institute

LÉON STOULS, *Karlsruhe Establishment of Euratom's Joint Research Centre*

Uranium long occupied the last place in the periodical table of the elements, ranking with its atomic number 92, as the heaviest among them. However, during the winter 1940/41 four scientists, G. T. Seaborg, E. M. MacMillan, J. W. Kennedy and A. C. Wahl, succeeded in producing artificial elements which were even heavier: neptunium with atomic number 93 and plutonium with atomic number 94. These two first members of the family of "transuranium elements" as they soon came to be called, were joined as the years went on by americium, curium, berkelium, californium, einsteinium, fermium, mendelevium, nobelium and lawrencium.

Among all these transuranium elements plutonium has received the greatest attention. In fact plutonium is not only fissile, in the same way as uranium-235, but it is produced from uranium-238 in appreciable quantities by reactors in the course of their operation.

If we add the fact that natural uranium contains more than 99% of uranium-238, it is easy to see that effective conversion of this isotope into plutonium is of primary importance in meeting the world's long-term energy requirements.

In the fairly near future relatively large quantities of plutonium will already be available. It will naturally be important to know exactly how to put them to the best use in future reactors. This explains the creation in Karlsruhe of an Establishment of Euratom's Joint Research Centre, the *European Transuranium Institute*, with the task not only of carrying out basic research but more particularly of perfecting plutonium fuel elements.

This naturally implies the preparation of the appropriate fuels, alloys, oxides, carbides, etc.), the construction of prototype fuel elements, the verification of their behaviour when irradiated in a pile and, finally, the study of methods, machines and cost prices.

General description

The Institute is being built on a site ceded to Euratom in the north-east corner of the German Atomic Centre about 8 miles north of Karlsruhe. The fact that they are so close together is obviously very advantageous for relations between the European Institute and the various German institutes and at the same time enables the Institute to benefit from the Centre's general installations.

The various buildings of the Institute from North to South are as follows:

A Wing : Basic studies and analyses;

B Wing : Studies in shielded cells of samples and fuel elements after in-pile irradiation;

C Wing : Administration and personnel entrance;

D Wing : Dressing rooms, showers and connecting corridors between the wings;

E Wing : General workshops, services and cold laboratories;

F Wing : Preparation of fuels (metallurgy and ceramics), recovery of non-irradiated plutonium;

G Wing : Fabrication of prototype fuel elements.

The laboratories have, of course, been grouped as far as possible following a functional plan. For example F Wing, where the fuels will be prepared, and G Wing, where the rods will be built, adjoin each other. However, it is primarily the security aspect which has determined the grouping of the laboratories. Thus all those in which relatively large quantities of plutonium are handled have been placed near each other in F Wing, which thus includes metallurgy, ceramics and chemistry.

"Hot" and "cold" zones

It is well known that plutonium can be very dangerous if handled without proper precautions. Quantitative limitations must be observed, otherwise chain reactions can be set off. Once irradiated, moreover, plutonium emits radiations which necessitate using heavy biological protection (lead casks, shielded cells).

Above all, however, it is highly toxic. If it is absorbed by the organism it gathers most often in the bones, where its radiation can give rise to forms of anaemia and leukaemia.

This makes numerous precautions necessary. The atmosphere is protected by isolating the plutonium in glove-boxes or air-tight containers, and all premises in which plutonium may be present are surrounded by areas of controlled atmosphere, where the air is subjected to continuous analysis and is filtered before being expelled.

Access to these "hot areas" is through specially arranged air-locks fitted with emergency showers and control apparatus and only from an area with controlled but "cold" atmosphere. It was considered that this last area could facilitate movements within the Institute while also providing a rational link between the different hot areas and the exterior.

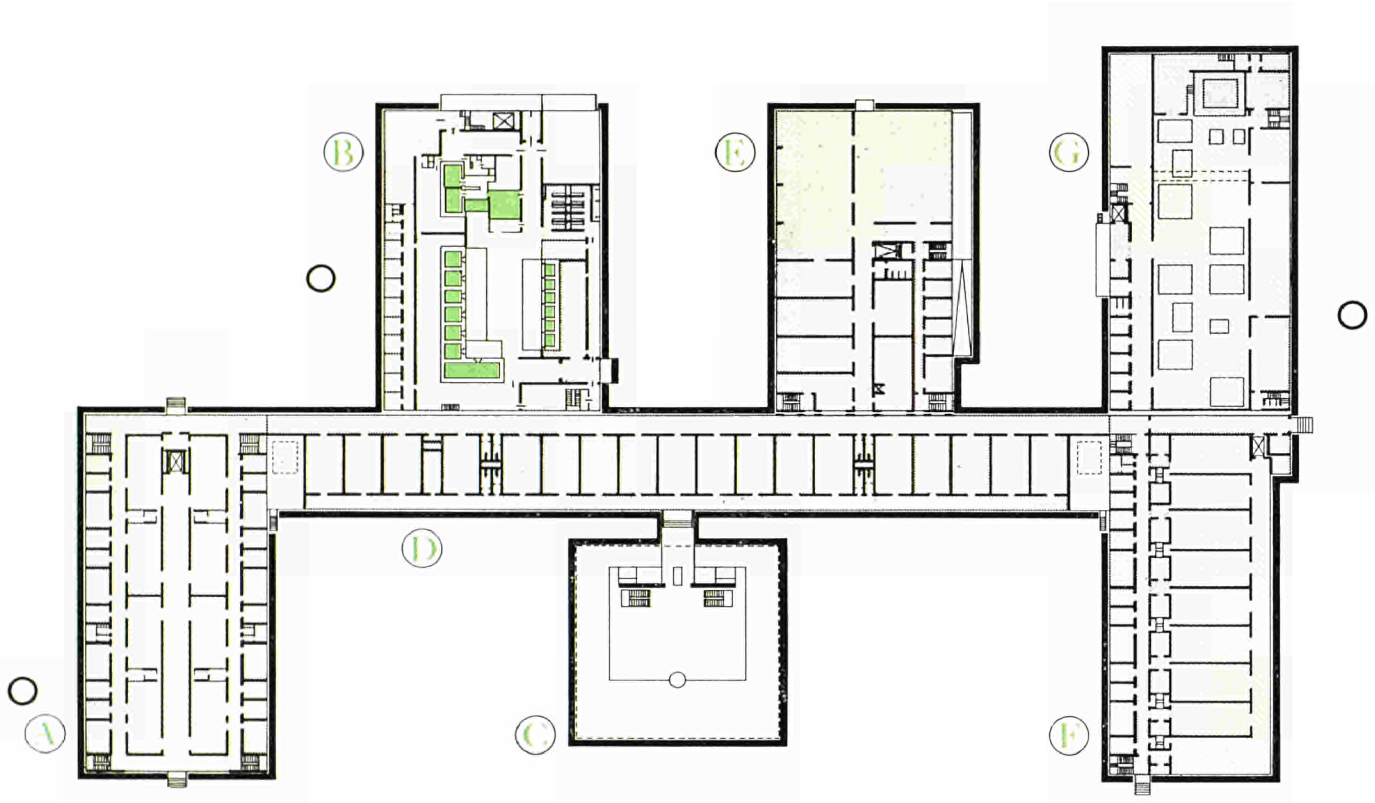
This controlled "cold" area branches out through all the wings. It includes all the corridors and cold premises used by personnel (offices, laboratories, workshops, etc.). Liaison with outside is only possible by passing through the dressing rooms and showers of D building. There is one single entrance for all personnel of the Institute, on the ground floor of the administrative wing.

The aim has been to keep the movement of equipment separated from that of personnel as systematically as possible by reserving an area of its own to equipment. In each wing this includes a special corridor linked by a goods-lift with the central "equipment" corridor, which runs in the cellar of the Institute from end to end. At the back of the building three doors are reserved for α, $\alpha\gamma$ and "cold" materials, in the G, B and E wings respectively.

Ventilation

The ventilation installations are of capital importance since they are linked with safety problems. It is thanks to them that air pollution can be prevented by maintaining glove-boxes and premises susceptible to contamination below atmospheric pressure.

Each wing of the Institute has its own ventilation plant. It was considered preferable that each should form a technically independent unit so that the Institute could begin to function by stages and subsequent-



ordinary "cold" zone

controlled "cold" zone

"hot" zone (permanent $\alpha\gamma$ activity)

zone which can be exposed accidentally to $\alpha\gamma$ radiation

zone which can be exposed accidentally to α radiation

zone which can, in exceptional cases, be exposed to α radiation

Figure 1. General plan of the Karlsruhe Transuranium Institute

ly maintain greater flexibility of operation. In each wing a blower plant draws in the external air and filters, warms and humidifies it before dispatching it to the various premises. Before being expelled from the building by the extraction plant, the air passes successively through three incombustible high performance filters if it comes from a glove-box. If it comes from a laboratory the number of filters is reduced to two.

An overall regulation system maintains the depression in the premises at such values that it would be difficult for any room accidentally contaminated to infect a neighbouring "clean" room. Finally, in the event of an electricity supply breakdown, an emergency group starts up automatically to maintain ventilation. A general control room situated in the centre of the Institute at the entrance to E wing groups all security and supervision installations for the whole complex and, in particular, enables the proper operation of all the ventilation circuits to be checked.

Effluents and waste

Everything that emerges from the Institute must be checked to avoid any risk of radioactive pollution outside. This is particularly the case with effluents. Those known in advance to be radioactive—they will generally be of small quantity and originate from specific operations—will be stocked in special bottles and then transported and treated in the German Nuclear Centre along with similar residues of its own.

All other effluents from the Institute without exception will be considered as doubtful. They will all be led into a central depot in the cellars of D wing, where a number of reservoirs with a total capacity of 330 m^3 will make possible complete classification by origin and, after analysis, dispatch to the Centre for appropriate treatment.

Solid waste will be gathered in special containers in stocking points close to the exits before being evacuated by the German Nuclear Centre.

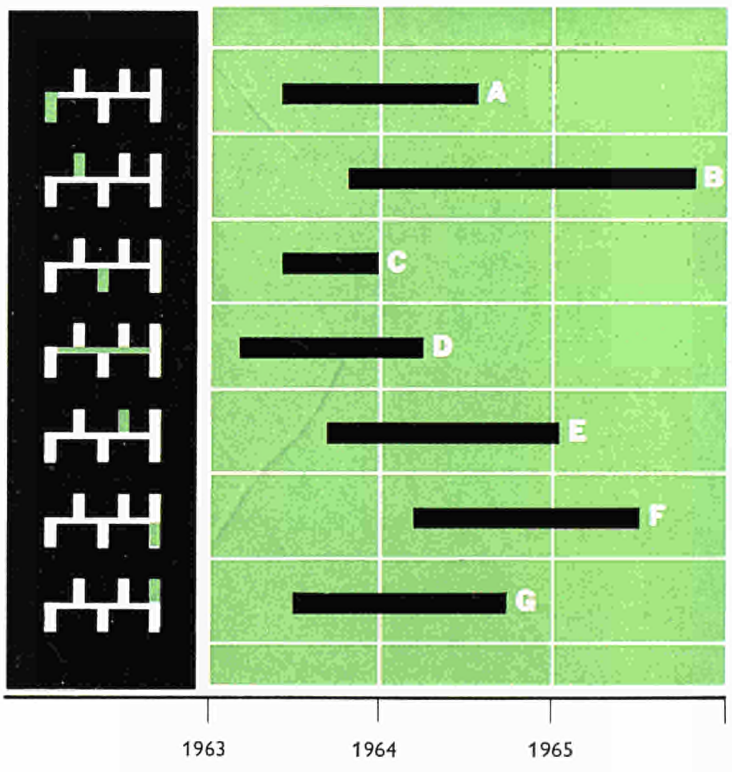
Time-table of the work

Although the Institute is still building some dates might be of interest.

The agreement laying down the basis of collaboration between Euratom and Germany in building the Institute goes back to 21 December 1960. But it was not until the framework programme of December 1961 that the Euratom/German Karlsruhe Centre Joint Planning Group could submit the real preliminary project on 7 January 1962. The size of the Institute[1] and the need to bring a part of it into operation as soon as possible have, of course, led to staggering of the work, which began as soon as the building permit was received. Diagram 2 shows the work schedule, which is subject to the usual reservations, although we would point out that it has so far been adhered to.

1. The volume of the Institute is 180,000 m^3 and it covers a ground area of 16 000 m^2.

Figure 2. Time-table of the work



"Marked" molecules: modern research tools

JEAN SIRCHIS,

Directorate-General for Research and Training, Euratom

More than 160 specialists from the countries of the European Community and 13 non-member countries met in Brussels from 13 to 16 November 1963 at the invitation of Euratom for a conference in a field of interest to many research workers, the field of labelled compounds, or "marked" molecules. This was the first international conference devoted exclusively to the problems of preparing and conserving these products.

"Marking" a molecule

To "mark" a product means introducing into the molecule a naturally rare nuclide, which may be stable or radioactive, so as to render it easily recognizable. Thus, glycine (Figure 1) can be marked by introducing into its structure radioactive carbon-14 in position 2, which is normally occupied by the most frequent isotope of this element, carbon-12. Similarly, the nitrogen (^{14}N) of the molecule can be replaced by the stable isotope ^{15}N.

To detect a molecule marked by a stable isotope requires the use of a mass spectrometer, a costly apparatus difficult to handle. As against this, radioactive marked molecules are betrayed by the radiation they give off and thus detected much more easily. For this reason, they are the most generally used.

Why produce "marked" molecules?

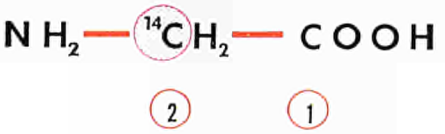
The preparation of marked molecules is not an end in itself. They are intended as a tool for experiments by researchers in most fields of basic or applied science. The generalisation of their use is explained by the possibility they offer of increasing the sensitivity and effectiveness of certain conventional techniques, but especially because they make it possible to attack and resolve problems which defy other methods. Some examples should therefore be mentioned to justify the efforts expended on their preparation.

Applications in chemistry

In order to study the mechanism of chemical reactions involving complex organic substances, the intermediate compounds which form must be identified, and atoms and radicals which are chemically identical but of differing origin must be distinguished. With the exception of a few simple reactions for which physico-chemical methods could provide the answer, the organic chemist was reduced to formulating hypotheses. Since marked molecules appeared on the scene it has become possible to differentiate the parts played in a reaction by the atoms of an element by following the trace of one of them.

Let us take the simple example of the hydrolysis of esters, a current reaction in organic chemistry with numerous applications in industry. In theory, this reaction

Figure 1. Marked glycine



glycine marked with carbon-14 (radioactive isotope) on carbon atom 2

glycine marked with nitrogen-15 (stable isotope)

can take place according to the two mechanisms outlined in Figure 2.

By utilising water marked with oxygen-18 ($H^{18}OH$), the behaviour of the three oxygen atoms can be differentiated. In fact, it has been possible to determine that oxygen-18 was found in the acid formed. Consequently, the reaction follows the second pattern.

Another example: the use of glucose marked with ^{14}C has made it possible to establish the complex mechanism of its degradation under the effect of brewer's yeast and to determine the part played by each of the 6 atoms of the molecule up to the final stage of formation of acetic acid and CO_2.

The use of marked reagents also makes it possible to specify the structure of high polymers and to study the mechanism by which they are obtained. Certain chemical substances, when present in trace quantities, have the property of acting on the speed of polymerisation by combining with the monomer or by initiating the formation of free radicals. By using these substances marked with an isotope the number of molecules concerned can be evaluated and, consequently, the effectiveness of the substances determined.

Study of the mechanism of reactions and of other problems of a chemical nature requires precise knowledge of the quantity of one or several substances in a mixture. Here again the help of marked molecules is appreciable, since they make it possible to dose the components of a complex mixture without any important losses. The method known as "isotopic dilution" consists of adding to the mixture a small quantity, marked with an isotope and of known specific activity, of the compound "A" to be dosed. Product "A" is then isolated in a sample taken from the mixture and its specific radioactivity, which is necessarily lower than that of the initial marked product, is measured. A simple formula relating this decrease in specific activity to the total quantity of the product makes it possible to calculate the latter rapidly.

The applications of marked molecules to chemistry extend, of course, to those sciences and techniques where chemical phenomena come into play.

Applications in biology and medicine

It is particularly in biology and medicine that the use of marked molecules has led to considerable progress.

When a marked molecule is introduced into a biological system—a living being or an isolated organism—it is possible to follow its trace as it passes from one cell or organ into other cells or organs and to study the processes by which it degenerates, becomes reconstituted or combines with other substances (see Figure 3).

It has thus been possible to identify the majority of the intermediaries formed in the course of photosynthesis from the carbon dioxide of the air up to the most complex compounds of very high molecular weights, such as the proteins. In the same way it has been possible to establish that blood pigments are formed on the basis of an amino-acid, the role played by each carbon atom being specified.

Medical diagnosis has largely profited from the utilisation of marked molecules. We may mention the detection of tumors with the help of albumin marked with radioactive iodine (see Figure 4). This substance has the property of being fixed by the tumors, whose membrane is more permeable than other tissues. Thus it is possible to localise a tumor rapidly and precisely by detecting where the radioactive iodine is concentrated, with the help of a counter or a photographic plate.

Studies now going on permit the hope that by using a similar method it will be possible not only to detect malignant tumors but also to treat them internally by fixing selectively on them a marked molecule of high radioactivity whose radiation will be able to destroy them[1].

Other uses of marked molecules could be mentioned. Several are finding a recognised place in industries using certain physico-chemical processes. An example is given in Figure 5.

However, the very diversity of the possible uses of marked molecules gives rise to obstacles to their full exploitation.

1. The applications of marked molecules in biology are innumerable. Professor Lettré gave some examples in an article published in Euratom Bulletin 1962, No. 4.

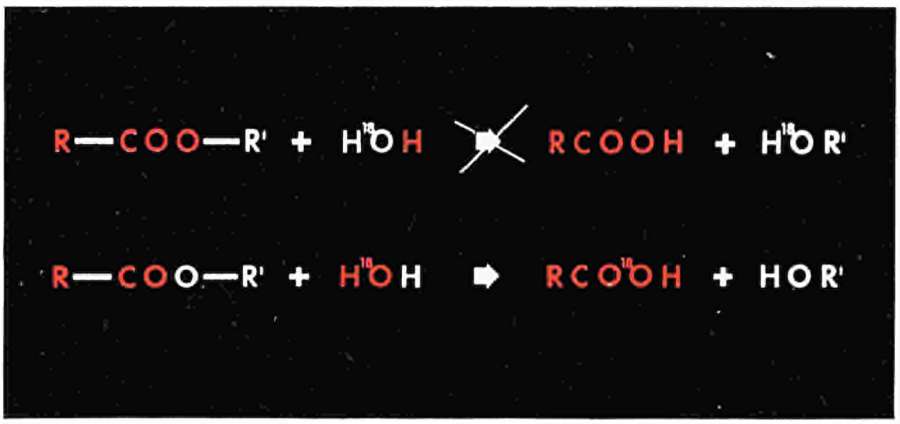
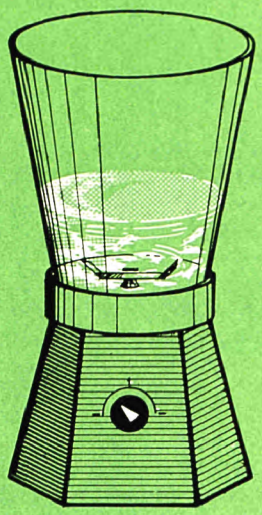


Figure 2. Determination of the hydrolysis mechanism of esters. Thanks to the use of water marked with oxygen-18 ($H^{18}OH$) we can determine that the drolysis reaction follows the second pattern.

1

2



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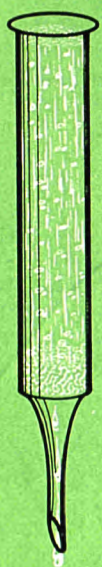

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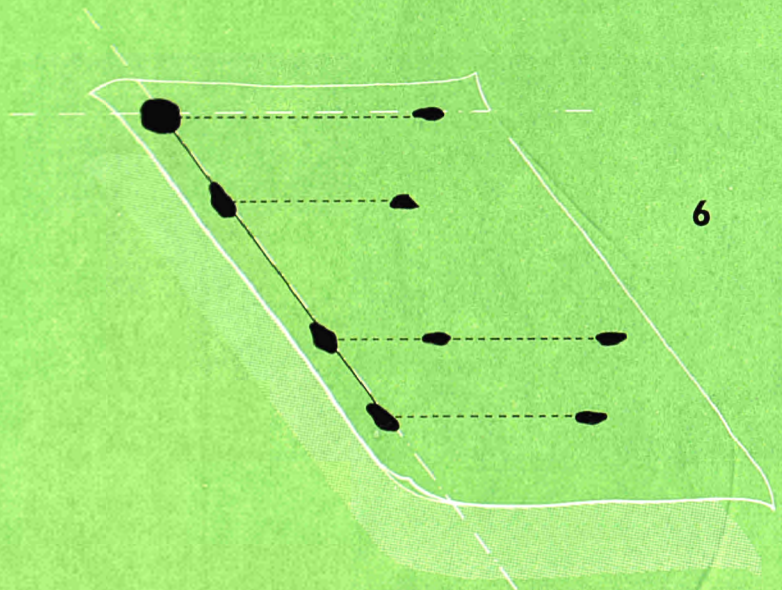

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Figure 3. An example of the biochemical study of the mode of action of a vegetable hormone.

Up to the present nothing has been known of the behaviour at molecular level of gibberellic acid, a vegetable hormone which possesses the interesting property of stimulating growth.

A certain quantity of marked gibberellic acid was recently synthesised. It is therefore hoped that it will be possible to determine with exactitude the transformation products of this hormone and thus discover the mechanisms of its action.

The figure gives the stages of a typical experiment in outline.

1. Application of gibberellic acid to the plant; accelerated growth results;

2. Taking a sample leaf;

3. Grinding of the leaf in an aqueous medium;

4. Filtering (to eliminate insoluble particles);

5. Separation by ion-exchange resins of three groups of substances: organic acids, amino-acids and sugars;

6. Determination by paper chromatography of the components of each of these groups. The radioactive components are localised by auto-radiography and their radioactivity measured with a Geiger-Müller counter.

The obstacles

Very often a given product interests only a small number of research workers. Quite irrespective of the extra problems inherent in the manipulation of radioactive sources, all these products, like most organic compounds, are particularly delicate and difficult to produce; it will therefore be understood that the restricted market for them results in very high prices and very long delivery dates.

To these two drawbacks must be added a third: when products of high specific activity have to be stocked, they destroy themselves. The effect of radiation involves a degradation of the molecule, so that it cannot be conserved beyond a certain time which, in some cases, is no more than a few days.

Finally, an even more serious problem arises: it very often happens that researchers need compounds which no laboratory, private or public, has ever produced.

It is true that specialised laboratories are making a considerable effort to remedy this difficult situation, but most of them are very naturally anxious to cover their production costs and can hardly be expected to launch into the synthesis of products which interest too few clients.

An impasse

All in all, we are threatened with a vicious circle: producers observing the elementary rules of prudence hesitate to bring into the market products which they are not practically certain to sell. On the other hand, research workers, however alive they may be to the advantages of marked molecules, will tend to make do without them if they have to face constant problems of availability and delivery dates. It is evident that the unfavourable influence of this reflex on demand directly affects the attitude of producers. The vicious circle is thus complete.

How to get out of the impasse

To extricate ourselves from this impasse we must first of all widen the "market" for marked molecules, which is tantamount to saying that we must encourage its "internationalisation". It is therefore no surprise that Euratom has been given an important role in this field.

In the course of an address at the conference already mentioned, Professor Medi, Vice-President of the Euratom Commission, spoke as follows: " . . . when referring to the effort put forth by Euratom to harmonise research and industrial production in the field of atomic energy, the expression 'atomic energy' is not to be taken literally. Our role is to promote the study and utilisation of the properties of the atomic nucleus . . .

Consequently, marked molecules, radioisotopes, and biology enter directly into our field of action; we are not here simply to produce units of electricity of nuclear origin . . .".

Euratom's activity consists chiefly of a permanent inquiry among more than 5.000 specialists who are interested in the preparation and utilisation of marked molecules. The first stage in this activity was a census of requirements in the six Community countries and an inquiry with research laboratories which had already synthesised, for their own studies, marked molecules which they could not find in the trade.

A marked molecules "bank"

Products prepared by research workers for their own requirements and of interest to others have been the subject of agreements under which the producing laboratory prepares a surplus whose existence is widely publicised. In this way, a veritable marked molecules "bank" has sprung up. Actually it has already done good service in procuring marked products for laboratories in the European Community and in non-member countries.

New syntheses

Furthermore, research contracts ensure the synthesis of certain products which have never been prepared before. Once the synthesis is achieved, these products are included in the bank.

M. P. De Groote, member of the Euratom Commission, speaking of these research

contracts at the conference, specified that "in order to avoid dispersion of effort, the stress is laid as far as possible on *general methods* applicable to the synthesis of *groups* of products rather than the preparation of particular compounds".
These measures, which are justified in themselves, since they enable several users of marked molecules to find the product indispensable for their research work, often result in an extension of the usefulness of the product. In fact, researchers working in the same field become interested in a new product as soon as it exists, and demand increases. This in turn can justify the preparation of the product on a commercial scale. It can therefore be noted that in effect Euratom, far from competing with private bodies, tends on the contrary to favour their activities by saving them over-costly research. Thus, certain commercial producers, after noting the interest shown for molecules promoted in this way have decided to prepare them on an industrial footing.

Methods of preparing marked molecules

The present methods of preparing marked molecules may be grouped under three main heads: chemical synthesis, biosynthesis and "radiochemical" methods.

Chemical synthesis

The synthetic methods of preparation follow the traditional techniques of organic chemistry, suitably adapted to the small quantity of substances on which the work is done. In the case of ^{14}C it is generally a matter of total syntheses—carried out, that is to say, by progressively building up the molecular structure from very simple inorganic substances—while with ^{3}H less complicated exchange and addition reactions are often possible.
Chemical synthesis is at present the method which furnishes the greatest number of labelled compounds. It has attained a very high degree of sophistication and efficiency, and the labelled compounds prepared are generally very pure. Furthermore, the position of the radioactive element in the molecule is well known.
But chemical synthesis has its limits, which are the impossibility of producing very complex marked molecules, which are precisely those most useful in biological research (proteins, enzymes, many alkaloids, etc.) and the laborious nature of the processes needed to obtain many marked molecules.

Biosynthetic methods of marking

On the other hand, even very complex compounds can be obtained by biosynthesis. By this technique a living organism is supplied with a very simple labelled compound which it utilises to synthesise other substances, in particular the product sought.
There are no limits to the molecular complexity of the compounds which can be

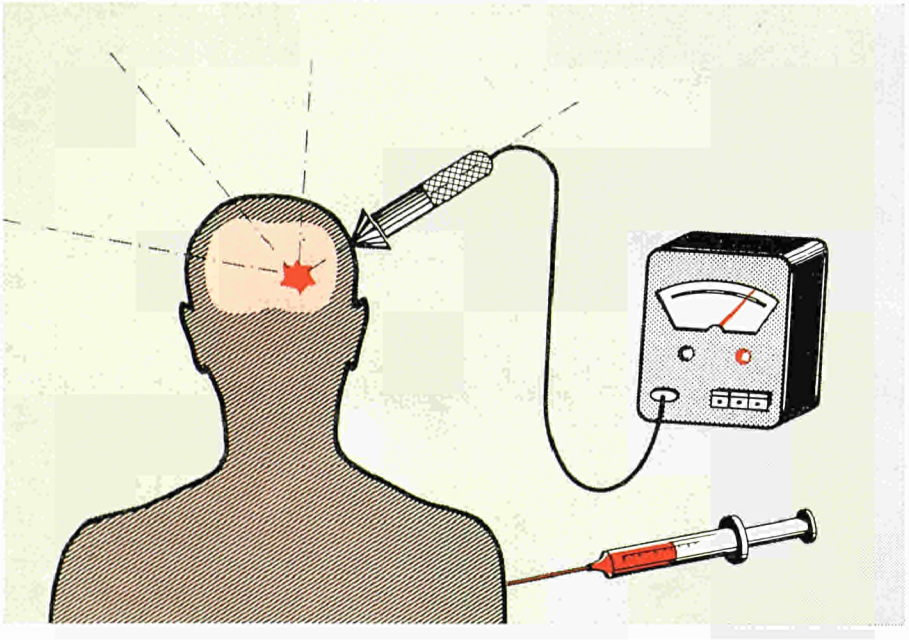


Figure 4. Detection of a tumor with the help of marked albumin.
— An iodised protein (most usually a human albumin marked with iodine-131) is injected.
— The albumin molecules are distributed in the body by blood circulation but, normally, do not penetrate into the tissues and organs because they are too big to pass through the membranes covering them.
— In a normal subject the product will therefore be eliminated, but in the case of a tumor the membrane becomes permeable and the result is localisation which can easily be traced from outside thanks to the γ radiation of the iodine.

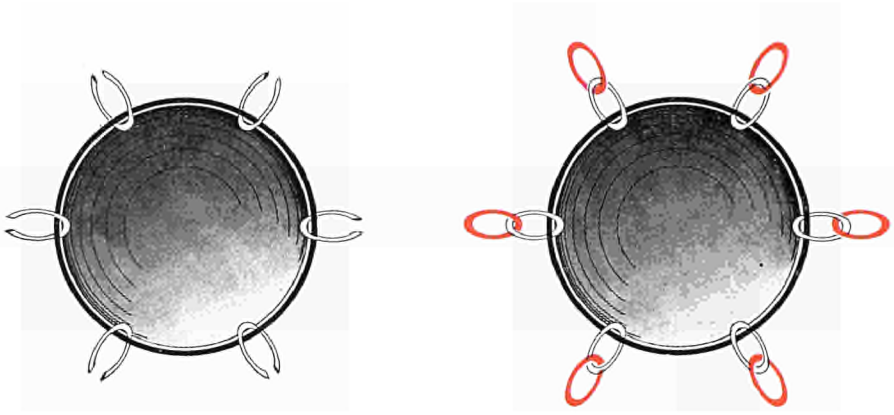


Figure 5. Determination of the chemically active sites on the surface of a particle of carbon black with the help of marked molecules.
It is often desirable, for instance in order to perfect an industrial process, to know exactly the chemical reactivity of a substance. In the case of substances like carbon black, which occur in the form of very finely divided solids, the traditional chemical methods have proved insufficiently sensitive. The idea of using marked molecules therefore emerged.
The diagram on the left represents a particle of carbon black and the chemically active sites on its surface.
After making the particle react with a marked product, bonds are obtained which are represented in the diagram on the right: molecules of this product have fixed themselves on these sites.
The method therefore consists in bringing about the reaction of a known quantity of particles with a product marked with carbon-14 of known specific radioactivity. After burning the sample, it is sufficient to measure the radioactivity of the CO_2 produced in order to calculate the initial number of active sites per gramme of matter.

labelled by biosynthesis. Enzymes, nucleic acids, proteins, steroids, alkaloids, etc. . . can be obtained.
However, the very nature of the biosynthetic methods imposes very severe limits on their employment. In the first place, the organism chosen to receive the labelled compound utilises it to synthesise a great number of molecules, with the consequence that a very low fraction of the initial activity is found in the desired compound. Moreover, as the latter is accompanied by numerous other substances which are also labelled, careful purification has to be undertaken. Finally, the position of the radioactive atom in molecules marked by biosynthesis is generally not known.
Allowing for all these limitations biosynthetic methods are nevertheless the only ones available for labelling certain types of organic substances.

Radiochemical methods

Finally, there exists a third group of techniques for the introduction of radioactive atoms into an organic compound. These are the "radiochemical" marking methods.
Their essential feature is the direct introduction of a radioactive atom into a molecule without recourse to synthesis. This substitution is sparked off with the help of energy supplied either by external radiation or by the kinetic energy or the radiation of the radioisotope itself.
The advantages of this group of methods are evident when it is a matter of preparing compounds whose complexity precludes any appeal to chemical procedures and in cases where biosynthesis cannot provide an adequate specific radioactivity.

In the following pages, eminent specialists from the European Community, whose contributions to the conference attracted much attention, describe the three groups of methods of preparing radioactive marked molecules and give an idea of the difficulties resulting from the self-destruction of these molecules. Thus we now leave the plane of generalisation and enter the laboratories.

Chemical syntheses of marked molecules

LOUIS PICHAT, *Head of the Marked Molecules Section, CEN, Saclay, France*

Although they use methods which are already well known, chemical syntheses of marked molecules present interesting and notable differences when compared with syntheses in "classical" organic chemistry.

High cost of the isotopes

Radioisotopes like tritium (^3H) and sulphur-35 are relatively cheap. On the other hand, carbon-14, which is the most generally used radioisotope, is still a costly raw material. It is therefore essential to obtain an optimum yield at every stage of a synthesis. Products of biological interest marked with ^{14}C can easily be worth as much as 300 to 500 dollars per millicurie. It is therefore no rare thing in the course of syntheses on high activities at production centres like Saclay for several thousand dollars' worth of products to be manipulated in microchemical apparatus during each operation.

An unusual raw material

Carbon-14 is supplied to the organic chemist in the form of barium carbonate ($^{14}CO_3Ba$). By decomposing this product with the help of an acid, ^{14}C is obtained in the form of $^{14}CO_2$. It is therefore on the basis of $^{14}CO_2$ that the chemist must fashion molecules and introduce the ^{14}C in very specific positions. In this way certain so-called basic molecules such as calcium carbide, potassium cyanide, sodium formate and methanol can be obtained to serve for the syntheses of more complex molecules.

The carbonation of an organo-magnesium compound is a reaction widely exploited for the synthesis of marked molecules, since the radical R can be extremely varied (see Figure 1).

Health considerations

As soon as millicurie level is reached, protection by lead or concrete screens must be provided when preparing molecules marked with iodine-131 or bromine-82. Luckily, since the isotopes most commonly used to mark organic products (^{14}C, ^{35}S, ^3H) emit soft β-rays which are absorbed by the glass walls of the apparatus, only precautions against internal contamination need to be taken. For this purpose the operations are carried out in well-ventilated hoods or glove-boxes.

Need to work on microquantities

For biological experimentation it is generally necessary to obtain a product containing maximum radioactivity (in millicuries) for minimum of weight. If, therefore, it is not possible to bring a large number of millicuries into play, work has to be done on very small ponderal quantities (from 50 mg to 1 g), and this seriously complicates the task.

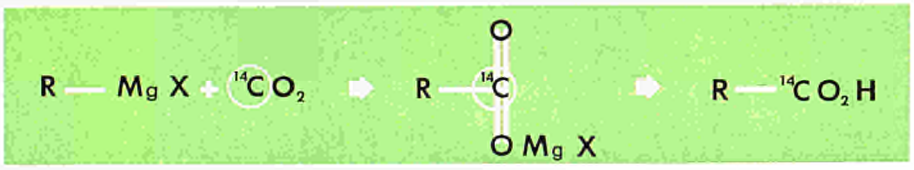


Figure 1. Preparation of ^{14}C labelled organo-magnesium compound

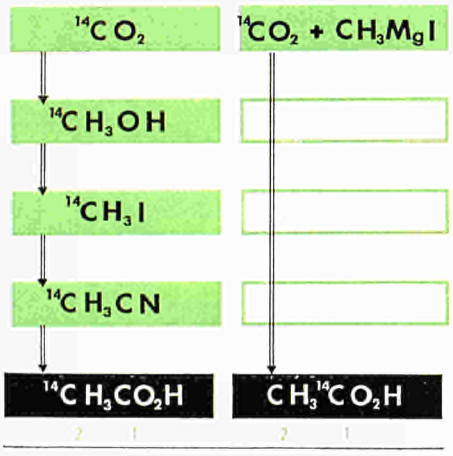


Figure 2. Preparation of marked acetic acid: acetic acid ^{14}C-1 (marked on carbon atom 1); acetic acid ^{14}C-2 (marked on carbon atom 2).

Position of the marked atom and difficulty of synthesis

Even for very ordinary products like acetic acid the difficulties of preparation vary enormously with the atom which it is proposed to mark. Acetic acid ^{14}C-1 is prepared by a single reaction, whereas to obtain acetic acid ^{14}C-2 four stages must be gone through (see Figure 2).
These differences in difficulty are reflected in differences in price (acetic acid ^{14}C-2 costs two-and-a-half times as much as acetic acid ^{14}C-1).

Preparation of tritiated molecules by exchange reactions

With a few exceptions molecules marked with ^{14}C must be prepared by chemical or biological synthesis. In the case of tritiated molecules it may be possible to dispense with synthesis and carry out a direct exchange of an atom of ordinary hydrogen with an atom of tritium. This can be done by simple incubation with pure gaseous tritium (Wilzbach mehod)[1] or by simple heating with tritiated water in the presence of a suitable catalyst such as platinum.

Techniques for preparing marked molecules

In many cases preparation is done in a vacuum apparatus in which the products move and react without escaping from the enclosure. This precludes any loss or any danger to the operator.
Figure 5 gives the outline diagram of such an apparatus.

Chromatographic methods of purification and isolation

The need to work on small quantities calls for methods of isolation and purification which reduce losses to a minimum, and chromatographic methods occupy a leading place. Use is made, according to the case, of chromatography on alumina,

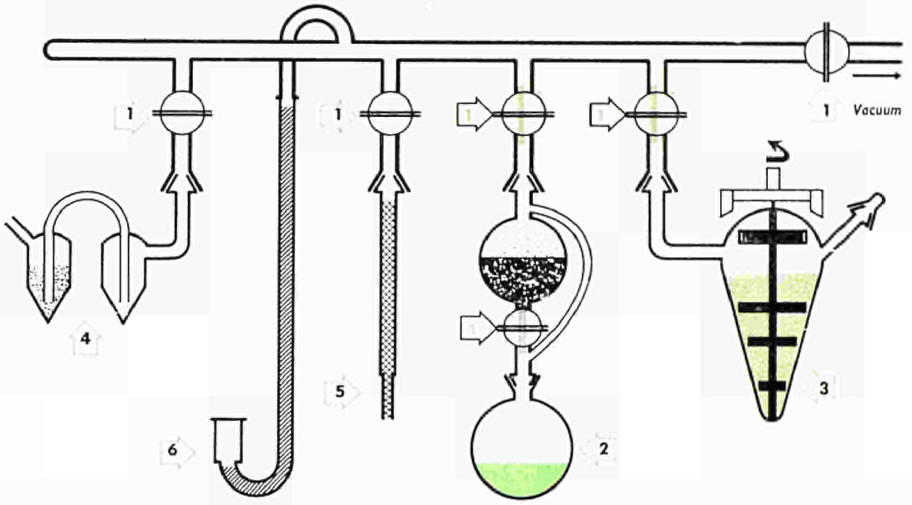
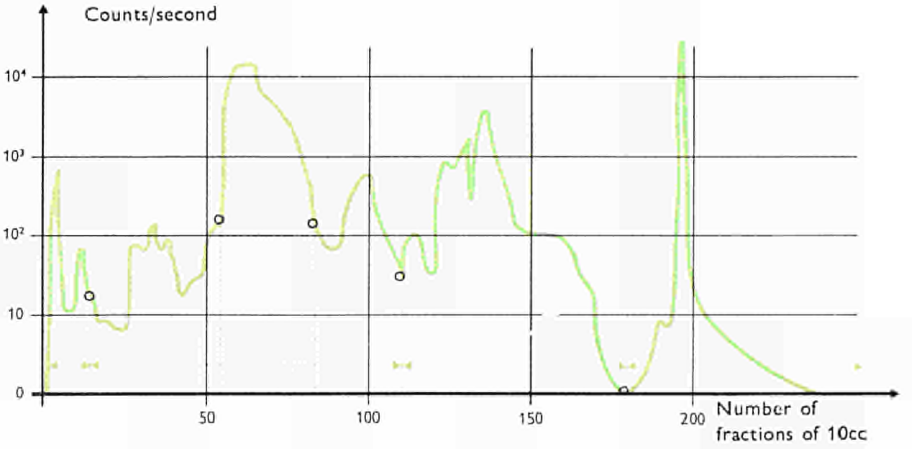


Figure 3. Working principle of the vacuum apparatus used for synthesising ^{14}C carboxylic acids.
1. Taps
2. CO_2 generator
3. Flask containing the organo-magnesium compound (intermediary of the synthesis)
4. CO_2 trap
5. Nitrogen used to scour the apparatus after an operation is completed
6. Vacuum-gauge
$^{14}CO_2$ is obtained from barium carbonate by sulfuric acid attack (2); it is then transferred to the flask containing the organo-magnesium compound (3). Once the synthesis is completed the excess $^{14}CO_2$ is trapped in sodium hydroxyde (4) and the vacuum line is scoured with nitrogen (5).

Figure 4. Purification of methionine ^{35}S by radiochromatography on Dowex 50 ion-exchange resin. Methionine ^{35}S with its impurities is adsorbed on a column of resin and the different components of the mixture are separated one by one by using different reagents. The surface of each "peak" in the diagram represents one component. The one which corresponds to methionine ^{35}S is shaded. The product may not be considered "radio-chromatographically" pure until the "peak" of methionine ^{35}S appears alone on the diagram.



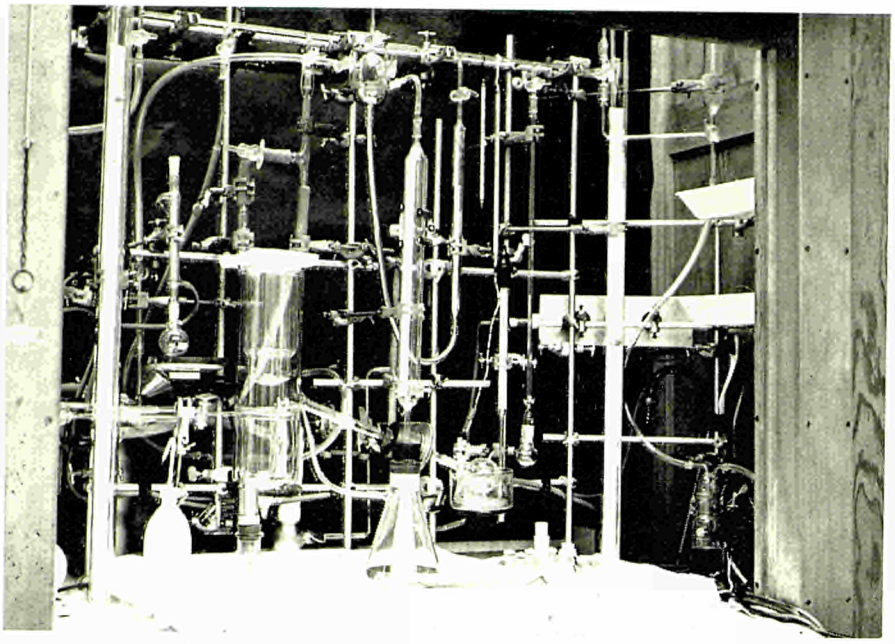
1. See page 28.

on ion-exchange resins, or vapour phase chromatographs. With each of these techniques the automatic continuous registration of the radioactivity is ensured by appropriate apparatus.

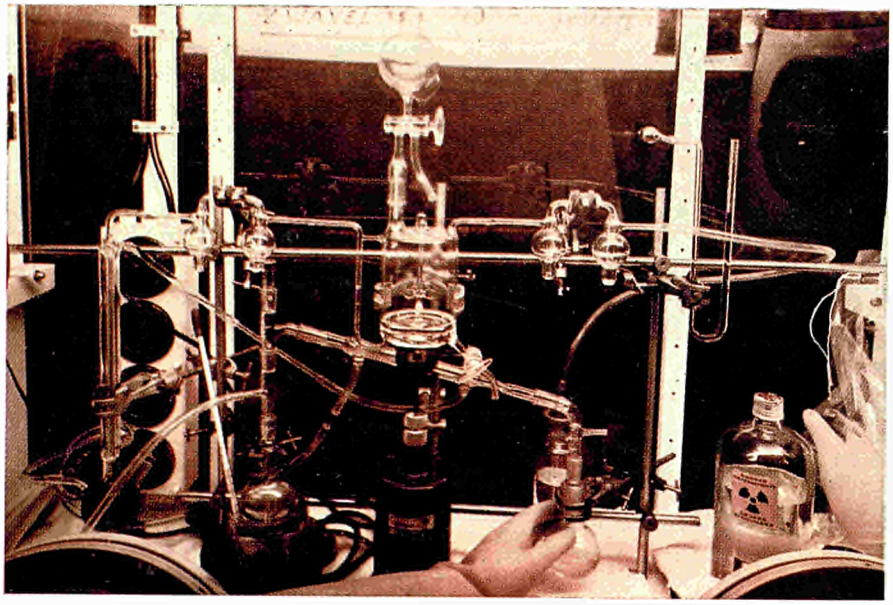
Importance of checking the radiochemical purity of marked molecules

Thanks to the extreme sensitivity of radioactivity measurements, it is possible to detect traces of impurities which cannot be discovered on inactive products. It is therefore essential to verify the strict purity of the labelled products, otherwise the biologist making use of them runs the risk of erroneous interpretations. The usual purity criteria for organic compounds apply to marked molecules, but they are insufficient. For this reason it is usual to associate "paper chromatography" with a measurement of radioactivity (see Figure 4).
The components of the mixture are first separated by paper chromatography. Then the radioactivity of the chromatograph is measured with a scanner and a radiochromatograph of the product tested is thus obtained. The scanner is an apparatus which unrolls the chromatograph in front of the window of a suitable Geiger-Müller counter and simultaneously registers the radioactivity. If the radio-chromatograph contains only one "radioactive peak", the product may be considered as radiochromatographically pure.

The chemical preparation of marked molecules is effected by the general methods of synthesis in organic chemistry with suitable adaptation. The need to work on small quantities of costly radioactive products results in the use of vacuum techniques familiar to the physical chemist and of all forms of chromatography.
This fine organic chemistry means that it is sometimes a very long business to perfect the synthesis of a new marked molecule. Because of the increasing demand fur such molecules and the growing complexity of the marked products required by biologists, the needs of research workers are outrunning the possibilities of preparing the products in the various European centres. It would therefore seem necessary to expand the preparation of marked molecules, which are an indispensable tool of biological research.



Vacuum apparatus in a protected enclosure.



Distillation of a radioactive compound in a protected enclosure. The gloved hand of the operator can be seen.

Preparation of marked molecules by biosynthesis

BY PROF. WALTER G. VERLY, *Isotope Laboratory, Department of Biochemistry, University of Liège*

Since this chapter deals with the biosynthesis of marked molecules[1] the carbonaceous substances, also called organic, will attract our attention exclusively.

A great number of these exist in the tissues of living beings, where they undergo the chemical transformations known as metabolism.

Marked organic molecules are in demand among biologists mainly for physiological studies and among doctors for use in diagnoses based on pathological deviations in the utilisation of these products by the human organism. This clientele therefore mainly desires marked molecules which correspond to natural products elaborated in living matter.

Marked molecules can be prepared by *chemical synthesis* using all the resources available to the expert chemist. But it is also possible to give a living organism in suitable chemical form the marker nuclide, which will be incorporated into the required product normally elaborated by this organism. It is this technique which is called "*marking by biosynthesis*". The procedure seems very easy, since the living organism spontaneously achieves a synthesis which would have demanded long work from the organic chemist. However, biosynthesis is rarely directed to a single end and its result is usually an extremely complex mixture of labelled substances: the action of the chemist therefore remains necessary to separate these. Both biosynthesis and chemical synthesis therefore have their advantages and drawbacks, and these have to be weighed in each particular case so that the easiest method, which is necessarily the least costly, is always chosen.

The rare isotopes, radioactive or heavy, of all the elements which make up living protoplasm can serve for marking by biosynthesis. The most important are probably: ^{14}C, ^{3}H, ^{2}H, ^{32}P, ^{35}S, ^{131}I, ^{15}N, ^{18}O, etc.

These marker nuclides must be presented in a suitable chemical form. The marked precursor, which is introduced into the biological medium, can be a very simple molecule, if necessary inorganic such as carbon dioxide, water or the sulfate ion. It may also be much more complex; we will see below that use has been made of tritiated progesterone (i.e. marked with ^{3}H), that is to say a hormone whose molecule contains 53 atoms ($C_{21}H_{30}O_2$)!

The biological system which achieves the biosynthesis can be a whole organism, multicellular like a tobacco plant, or monocellular like the chlorella alga. It can be an isolated organ, such as a liver, kept alive by artificial circulation, into which the marked precursor is introduced. Sections of an organ of a few tenths of a millimetre thickness (for instance sections of adrenal gland) may be suspended in a nourishing medium. It is also possible to use a homogenous solution of more or less carefully purified enzymes.

Very many variables influence marking by biosynthesis and determine its practical value: the nature of the marker nuclide used and its price, the chemical nature of the marked precursor, the quality demanded of the marked molecule which it is desired to prepare, the composition of the biological system used. Lastly, the toxic effect of ionising radiations cannot be left out of account and sets limits to the method when radionuclides are employed.

These variables may combine in multiple ways but they are not independent, and this makes a systematic survey of the problem difficult. Account must also be taken of the isotopic yield, that is to say of the relation between the quantity of the marker isotope (or the radioactivity—which is proportional to it—in the case of a radioisotope) which is found in the final product, and the quantity used under the form of the marked precursor. Generally, the isotopic yield will be the higher the more complex and specific the precursor and the simpler the biological system, so as to avoid a deviation of the marker nuclide

1. The term "marked molecule" is not strictly correct. For instance, a molecule which contains a radionuclide cannot be traced: it only manifests its existence at the precise moment when the radioactive atom disintegrates. Before this disintegration it is as silent as a molecule containing only stable atoms and after disintegration it ceases to be of any interest: its marker nuclide has disappeared and its chemical nature has been completely changed by the transmutation. The problem should therefore not be considered at the scale of a molecule, but rather statistically, and it is more correct to speak of a labelled *product*. A quantity — even a small one—of this product contains billions of molecules, and the suicide of some of these does not alter the properties of the whole; these suicides form an almost continuous fireworks display which makes it possible to localise the product easily. Despite this introductory remark we will use the terms "marked molecules", "labelled product" or "substance" without distinction and in the same sense.

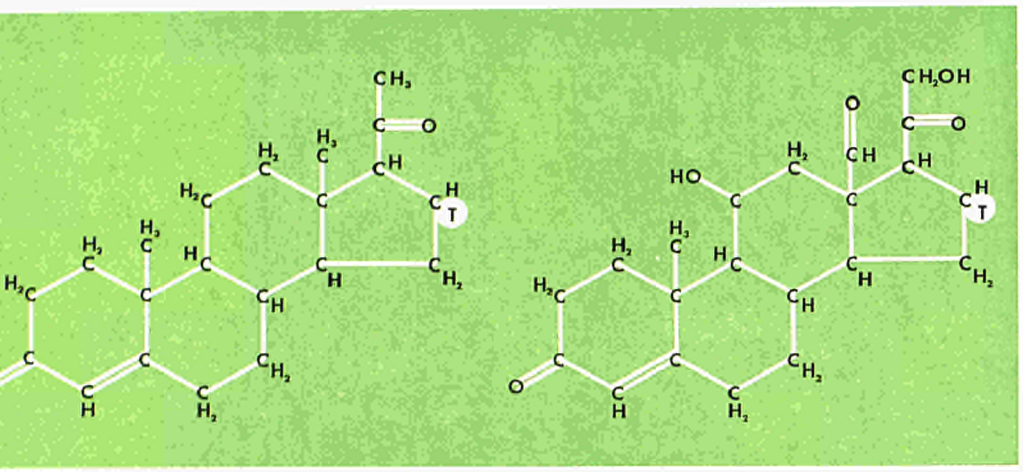


Figure 1.
16-^{3}H-progesterone→16-^{3}H-aldosterone
In the formulae the symbol T replaces H^{3}

towards the products of secondary parasitical reactions. But the best yardstick of the practical value of a technique is the product: isotopic yield × the cost of the quantity of the marked precursor containing a unit of the marker nuclide.

We will now see some examples of the preparation of marked molecules by biosynthesis and briefly discuss the problems posed by the interaction of the variables we have just mentioned.

It is possible to use a non-specific precursor marked with a costly radioisotope in a complex biological system if the intention is to label substances which are naturally abundant in the organism chosen. $^{14}CO_2$ is given to illuminated chlorellae to prepare amino-acids marked with ^{14}C; the isotopic yield is good. The $^{14}CO_2$ is utilised completely by the alga, which is rich in proteins (macromolecules which can be cut up into amino-acids by hydrolysis). The endeavour may even be made to improve the global isotopic yield by extracting from the same cells other products such as lipids, sugars, nucleic acids, etc. In fact, alga has become a veritable mine of the most divers labelled substances. It must be realised, however, that the most effective methods of extraction for one product are not necessarily those which are best suited to another, so that the global yield is not the sum of the possible individual yields. It should be added that, as this monocellular alga multiplies very rapidly, it may be given very active $^{14}CO_2$ without fear of any lethal effect of the radiations on the organism: the isolated products haven therefore, a very high specific radioactivity.[2]

The problem is different when it is a matter of preparing a rare substance such as digitoxin (cardiotonic glucoside) elaborated by a slow-growing plant. It is possible to grow a digitalis (digitalis purpurea) in an atmosphere of $^{14}CO_2$, but the yield is necessarily very poor, since glucoside is present in the plant only in small quantities. Preparations of this kind have come to be called "isotopic culture" or "isotope farming". The slow growth of the plant allows only small quantities of ^{14}C to be employed in order to avoid killing it by irradiation; the products finally obtained have only very low radioactivity.

The idea of giving animals chlorellae cultivated in the presence of $^{14}CO_2$ to mark rare substances such as certain hormones which are elaborated only in their tissues has had to be abandoned: the process yields only products of very low activity which are extremely costly.

The problem would be of a different kind in the case of a nuclide belonging to another element. Let us take the case of ^{3}H which, contrary to ^{14}C, costs practically nothing and whose radioactivity per atom-gramme is about a thousand times higher. One of the outstanding advantages of ^{3}H is that it permits the preparation of highly radioactive molecules which are ultrasensitive indicators for metabolic studies: problems can be tackled with ^{3}H which are beyond the possibilities of ^{14}C. We could imagine that tritiated water would make it possible to prepare simply, by biosynthesis, a whole range of marked molecules beginning with those which are most plentiful in protoplasm, but this is not the case: the percentage of the hydrogen passing through the cell in the form of water involved in the biosynthesis of organic molecules is very low. The poverty of this isotopic yield is not serious from the economic point of view, since ^{3}H costs practically nothing and the tritiated water can be recovered. But water forms the major part of living tissue and a low percentage of tritium is sufficient to bring about the rapid death of the cells through irradiation. The method, therefore, is suited only to the preparation of molecules of low radioactivity which are without interest for many studies.

To prepare a complicated product which is not plentiful in living organisms, such as an alkaloid or a hormone, the best technique is often to begin with a more specific precursor, which can then have a

2. activity per unit of weight.

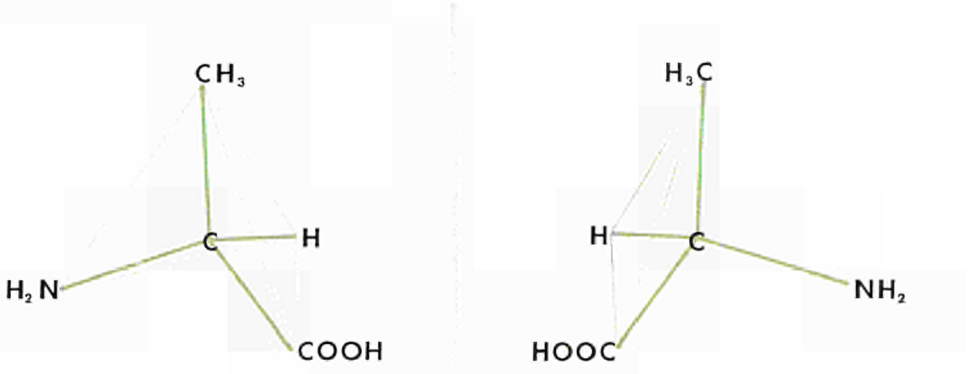
very great specific radioactivity. The danger of excess irradiation no longer exists, since the concentration of this precursor in the biological medium is never very high. At the same time, there will often be advantage in simplifying the biological system to avoid any waste through parasitical transformation. In this way, sections of adrenal gland have been used to prepare ^{3}H-aldosterone from ^{3}H-progesterone (Figure 1). Ideally, a solution of the enzymes needed for the biochemical reactions which it is desired to utilise would be sufficient: ^{14}C-thymidine has been prepared from ^{14}C-thymine and deoxyribose-phosphate in presence of the specific transferase (enzyme) extracted from the liver of rats (Figure 2).

Biosynthesis can have a decisive advantage in the preparation of marked natural products "optically active". The chemical synthesis of a substance which possesses an atom of carbon around which the rest of the molecule may be disposed in two different ways (optical isomers—see Figure 3) usually gives the mixture of the two forms (racemic); whereas the natural products possess one of the structures to the exclusion of the other. Biosynthesis obviously leads to the *natural* marked isomer which is much more useful than the racemic in biological work. In this way, the amino-acids elaborated by Chlorella are all of the L variety.

At other times it is biosynthesis which is in an unfavourable position compared with chemical synthesis. When a non-specific marked precursor such as $^{14}CO_2$ is used, the final molecule is often marked simultaneously in several of its atoms. For instance, amino-acids synthesised by Chlorella in the presence of $^{14}CO_2$ are marked in all the carbons. These radioactive products are suitable in studying the biosynthesis of the proteins, where they are entirely incorporated, but they cannot be used for research into intermediary metabolism or catabolism in which it is desired to follow the fate of each of the carbon atoms. A molecule marked only at the carbon atom whose fate is of interest is therefore necessary, and this more often than not, can be prepared only by an organic chemist.

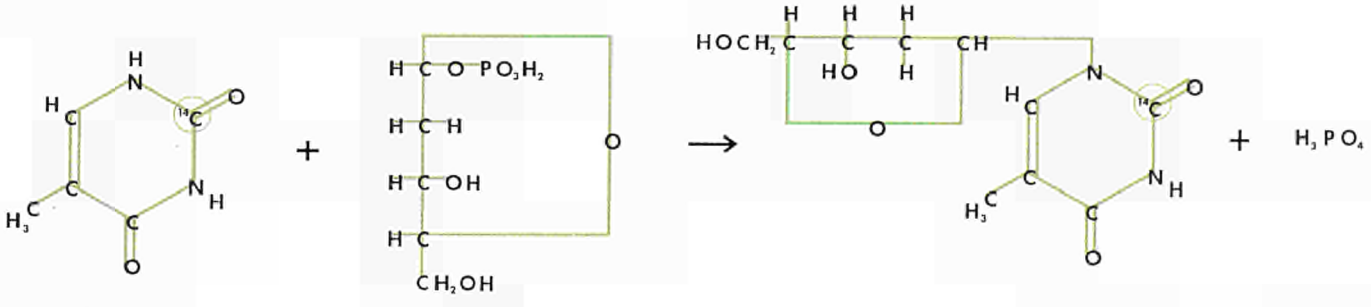
The restriction we have just indicated in the use of biosynthesis, which holds in the case of $^{14}CO_2$ supplied to a plant, is not of general application. The problem is different for other elements. If Chlorella is given ^{35}S in sulphate form, it is evident that all the substances elaborated which contain only one atom of sulphur per molecule will not be different from those which it would have been possible to prepare by cheimcal synthesis. This is particularly the case for the sulphurated amino-

Figure 3. Alanine "optical" isomers

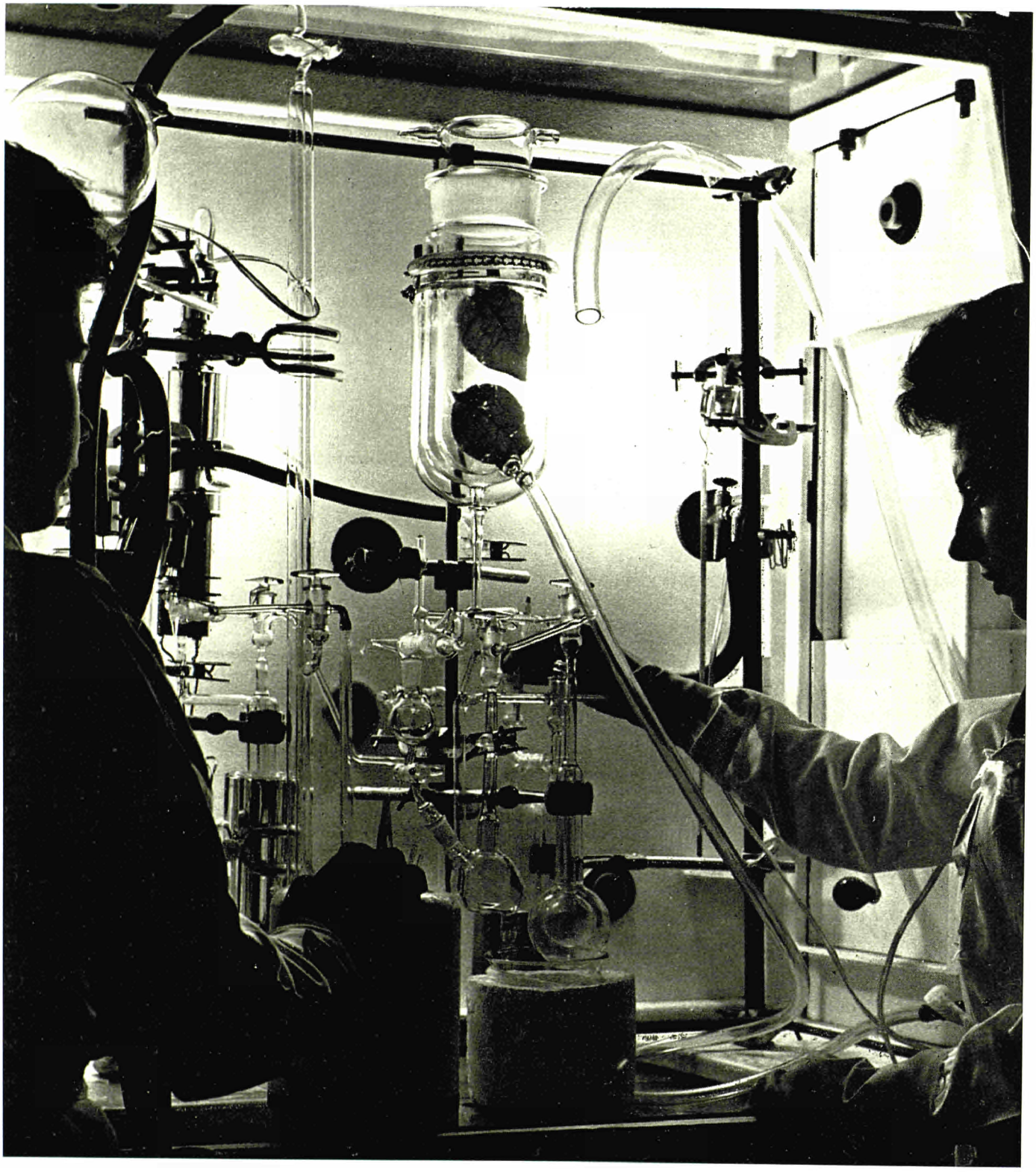


L-alanine *D-alanine*

Figure 2. Biosynthesis of ^{14}C-thymidine



2-^{14}C-thymine *deoxyribose-1-phosphate* *2-^{14}C-thymidine* *phosphate*



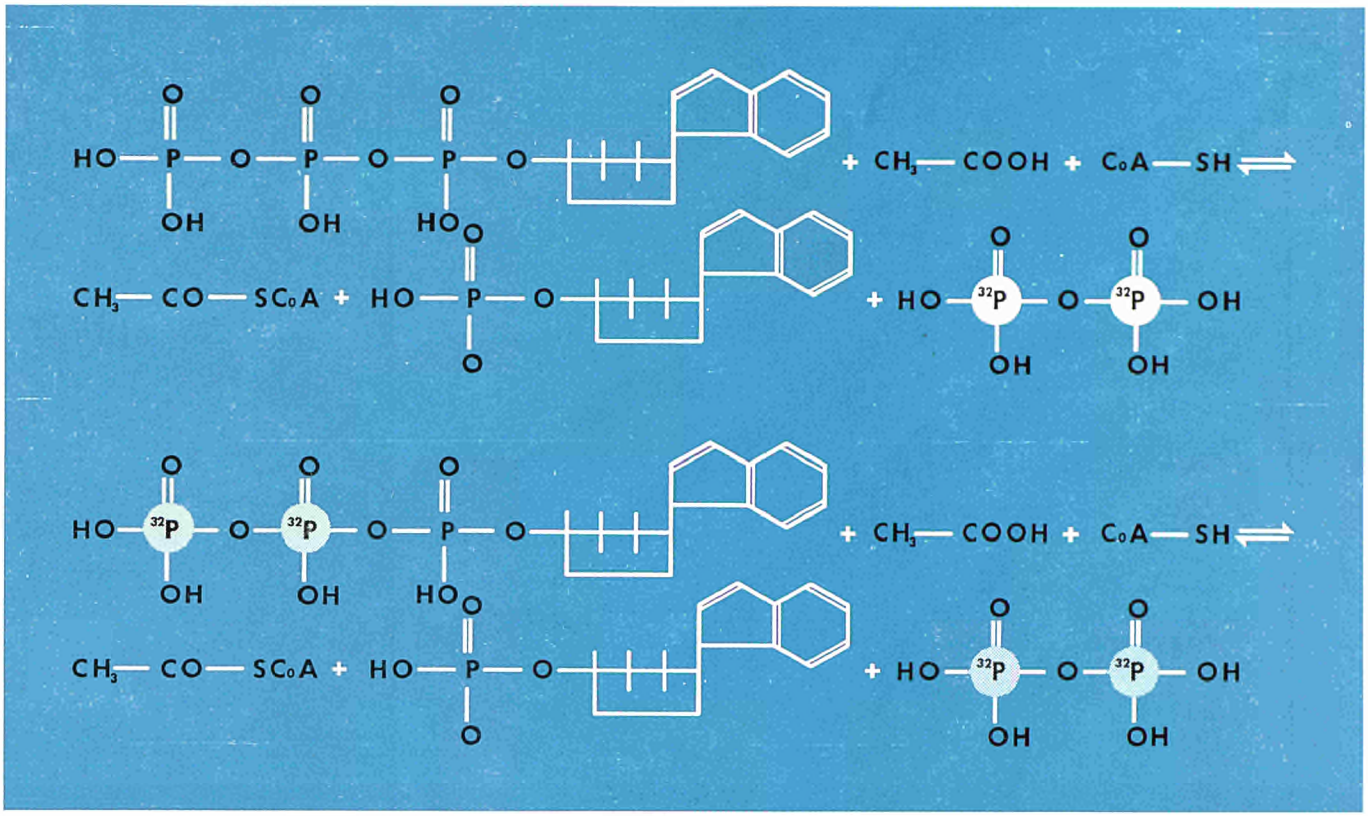


Figure 4. adenosine triphosphate + acetate + coenzyme A ⇌ acetyl-coenzyme A + adenosine monophosphate + pyrophosphate. The formula of coenzyme A, which is extremely complicated is not elaborated because only the SH Group participates in the bio-reaction.

Above: The reversible reaction is under way. ^{32}P is supplied in the form of pyrophosphate.

Below: After a time, some of the ^{32}P finds its way into the adenosine triphosphate.

Cell for photosynthesis of ^{14}C labelled sugars. Radioactive carbon dioxide ($^{14}CO_2$) is introduced into the cell, which contains freshly cut tobacco leaves. Under the effect of powerful lamps (2000 watts) the gas participates in the phenomenon of photosynthesis and gives birth to a whole series of radioactive compounds, including sugars marked with ^{14}C.

acids, known as cysteine and methionine, and biosynthesis will here have the advantage already mentioned of supplying the natural stereoisomer without it being necessary to carry out a laborious separation of the racemic.

Biosynthesis is an elegant way of marking very complex molecules such as proteins, polymers formed by the union of several hundreds of amino-acids. The immunity reactions of an organism enable it to neutralise the action of the foreign bodies called antigens by the production of antibiotics; these are proteins of the globulin class which are found in blood plasma. It is possible to prepare marked antibiotics by administering radioactive amino-acids to an animal which is subjected to the action of an antigen. Processes other than biosynthesis exist for marking protein, but none gives the same guarantees. A protein can be tritiated by exposing it to molecular ^3H-hydrogen (Wilzbach process); the greater part of the ^3H fixed is found in decomposition products of the macromolecule the purification of which becomes very difficult: one can never be certain of attaining radiochemical purity, that is to say of having the ^3H exclusively in molecules with the same constitution and structure as the native protein. It is also possible to fix an atom of ^{131}I on the protein. Here the radioactive molecule is obviously different from the protein to which it is desired to give an indicator, whereas protein marked by biosynthesis is chemically identical with the natural macromolecule.

We will end by pointing out that certain labelling processes obtained in biological systems are not biosyntheses but mere exchanges. This is particularly true of the preparation of numerous phosphorus compounds and is explained by the fact that phosphorus is found in organisms exclusively in the form of phosphoric acid and its derivatives. Two enzymes catalyse a reversible reaction which makes it possible to introduce into adenosine triphosphate (ATP) the ^{32}P given in the form of pyrophosphate without the balance-sheet showing a synthesis of ATP (Figure 4).

Labelling by radiochemical methods

PROF. FULVIO CACACE *Lecturer in Radiochemistry at the University of Rome*

There exists a group of techniques for the introduction of radioactive atoms into an organic compound generally referred to as "radiochemical" labelling methods.

Labelling by nuclear recoil

Let us briefly consider the nuclear reaction by which a radioactive isotope, for instance tritium (^3H or T), is produced.
To obtain tritium, a lithium salt is introduced into a nuclear reactor where it is continuously bombarded by neutrons. The nuclear reaction is as follows[1]:

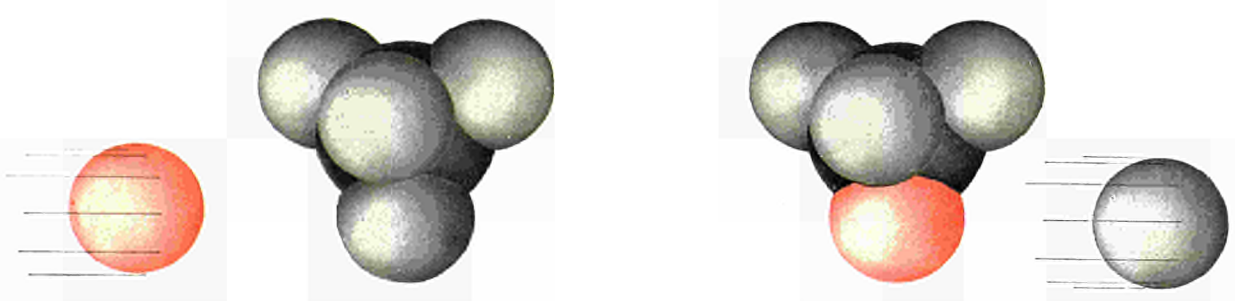
$$^{6}_{3}\mathrm{Li} + {}^{1}_{0}\mathrm{n} \rightarrow \left[{}^{7}_{3}\mathrm{Li}\right] \rightarrow {}^{3}_{1}\mathrm{H} + {}^{4}_{2}\mathrm{He}$$

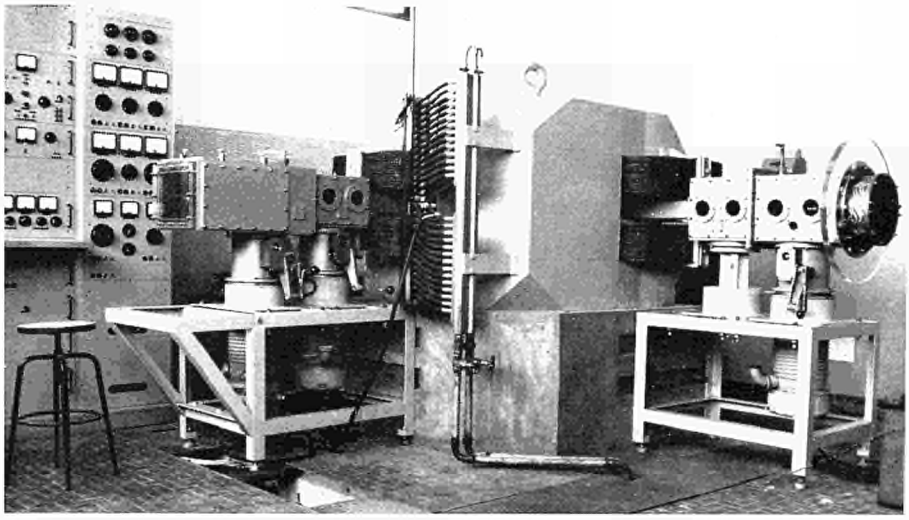
1. In a formula representing a *nuclear* reaction, the exponent preceding the symbol indicates the mass — protons plus neutrons—of the atom, and the index the number of charges.

It can be imagined that an unstable lithium nucleus is first formed and in a very short time breaks down, expelling a nucleus of tritium and a helium nucleus at high velocity.
Applying the law on the conservation of momentum, it will be noted that, whereas the helium nucleus is projected in one direction, the tritium nucleus will move in the opposite direction following the phenomenon which, by analogy with the known example of a gun, has been called nuclear "recoil". In all events, the atom of ^3H is not born in a state of rest but is endowed with considerable kinetic energy and consequently will move rapidly within the irradiated substance. Let us now suppose that the lithium salt was mixed before irradiation with the organic compound to be marked, for instance methane.
In its rapid movement the atom of ^3H produced by the recoil will strike the molecules present, progressively dissipating its kinetic energy in a series of shocks.
Initially, it will not be able to set up stable chemical combinations because of its excessive energy, but when it has been slowed down sufficiently it will be able to strike an atom of methane hydrogen, displace it and occupy its position in its stead (Figure 1).

It is clear that with this substitution reaction we obtain a molecule marked with ^3H similar to that which was irradiated.
Naturally, other reactions are produced which lead to the formation of other marked molecules. However, it is possible, with suitable separation and purification techniques, to isolate the compound sought. This method has made it possible to prepare numerous compounds labelled with ^3H.
Among these should be mentioned amino-acids, alkaloids, steroids and sugars.

Figure 1. An atom of high-energy tritium replaces a hydrogen atom in methane and produces tritiated methane.





General view of an isotope separator

One advantage of this technique is that even large quantities of substances can be labelled without any need for synthesis. But the products have to be purified carefully and the activity obtained is often low. This technique has not been adopted only for tritium. Actually, in 1934 Szilard and Chalmers discovered it by irradiating ethyl iodide with neutrons.

Another very interesting reaction is ^{14}N (n, p)^{14}C which has been much studied for the labelling of organic compounds. In the course of this reaction the nitrogen atom gives birth to a radioactive atom of ^{14}C by capturing a neutron and emitting a proton. By irradiating pyridine with neutrons we obtain, for instance, radioactive pyridine and benzene, as shown in Figure 2. In these experiments the sample to be labelled must always be irradiated in a nuclear reactor where it undergoes considerable decomposition as a result of the gamma rays, fast neutrons and high temperatures.

Since a radioactive atom with high kinetic energy is required for the marking reaction, the idea of producing these atoms by processes other than a nuclear reaction has suggested itself.

Figure 2. An atom of high-energy ^{14}C (coloured sphere) replaces the nitrogen atom (black sphere) of pyridine and gives marked benzene; or it replaces an atom of ^{12}C (white sphere) and produces marked pyridine.

Labelling by accelerated radioactive ions

As a general rule these ions are produced and accelerated by an electric discharge in a vessel containing the substance to be marked; they react with it and produce a whole series of marked substances.

However, organic substances marked with ^{14}C have been prepared by Giacomello and Croatto according to the following technique: $^{14}C^+$ ions (that is to say ^{14}C atoms with a positive charge) have been produced from $^{14}CO_2$, accelerated with a suitable electric field, separated from other non-radioactive ions by a magnetic field and projected against the compound to be labelled (Figure 3).

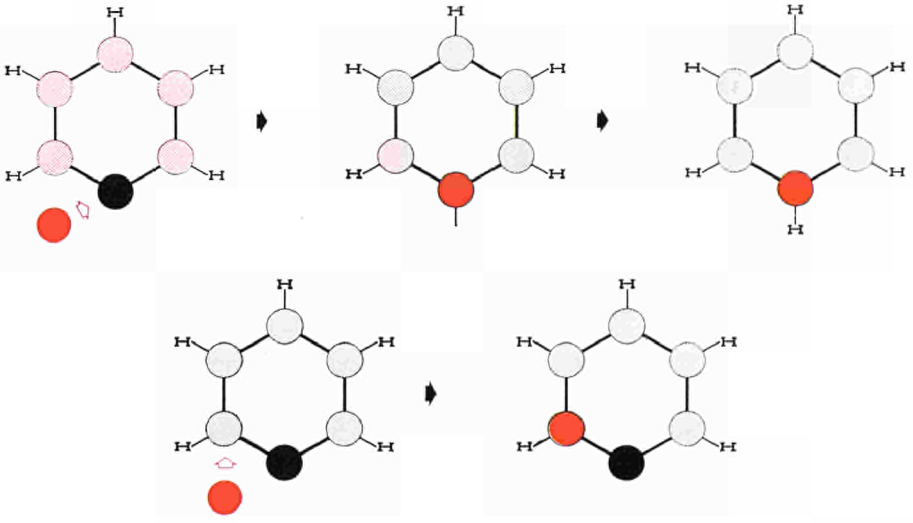
Techniques based on a similar principle have been adopted to label different organic compounds with ^3H and ^{14}C.

However, in a good number of these experiments it has been found unnecessary for the ions to have high kinetic energy in order to produce marking reactions.

Marking by ionising radiations

Another technique has therefore been worked out by which a mixture of marked and non-marked substances is ionised by radiation. Groups of ionised and radioactive atoms then form and combine with the substance to be marked, which is itself ionised by the radiation.

Substances marked with tritium have been obtained from a ^{60}CO source by irradiating organic substances with γ rays in the presence of ^3H. Similar labelling reactions have been used by irradiating systems containing a very simple compound including ^{14}C (for instance, $^{14}CO_2$, ^{14}CO, $^{14}CH_4$,) with an organic substance. As radiation source, use has been made of various



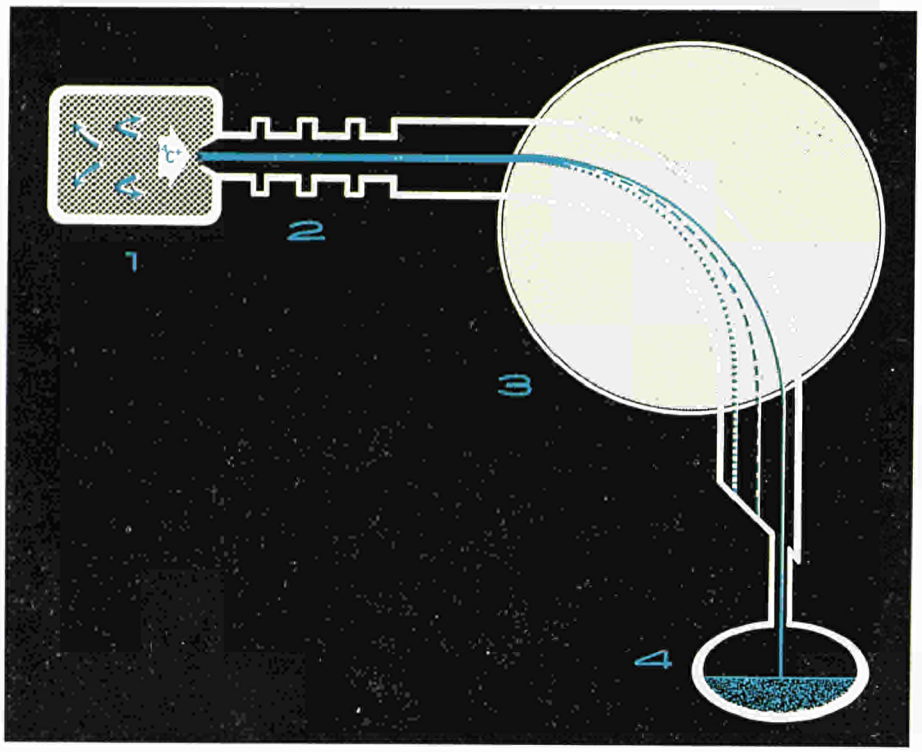


Figure 3. Marking of organic substances with accelerated radioactive ions: (1) ion source (2) acceleration chamber (3) magnetic field (which makes it possible to select the ions; the clusters of non utilised ions are shown by dotted lines) (4) substance to be marked.

radioelements such as ^{85}Kr, ^{204}Tl, γ rays from exhausted nuclear fuel elements, etc. On the basis of a system composed of heptane and $^{14}CH_4$ subjected to 10^8 rad of γ rays, labelled iso-octanes have been obtained by using the following synthesis reactions:

1 $^{14}CH_4 \rightarrow {}^{14}CH_3\cdot + H$

2 $C_7H_{16} \rightarrow \cdot C_7H_{15} + H$

3 $^{14}CH_3\cdot + \cdot C_7H_{15} \rightarrow {}^{14}CH_3\text{–}C_7H_{15}$

All these methods naturally produce a great number of labelled compounds and therefore demand effective systems to isolate and purify the reaction products. On the other hand, many types of research (for instance into hydrocarbons contained in fuels) demand, not one compound, but a whole mixture of marked substances. In this case, this method of labelling can prove very useful.

The Wilzbach method for marking with ^3H

Special mention must be made of the technique, introduced in 1957 by Wilzbach for labelling organic compounds with tritium, which is the most current "radiochemical" method. The compound to be labelled is simply introduced into a flask with a few curies[2] of gaseous tritium. A few days later the tritium is eliminated: some of the ^3H atoms have, however, replaced H atoms in the organic substance, which is therefore labelled. The exchange reaction produced by the disintegration of the tritium:

$$T_2 + R\text{-}H \rightarrow R\text{-}T + HT$$

has been applied to a large number of organic compounds from the simplest to the most complicated right up to antibiotics, proteins and enzymes. The tremendous advantage of the Wilzbach method is that to obtain the substance labelled with ^3H it is sufficient to have available the same non-labelled compound and to bring it into contact with the gaseous tritium.

This is an extremely simple process but its application is often hampered by very long and laborious purifications to eliminate the radioactive impurities produced in the course of the reaction. Furthermore, the specific radioactivity obtained is not always as high as could be wished.

Some of the compounds labelled by the Wilzbach technique and the ^3H activities introduced into them are shown below:

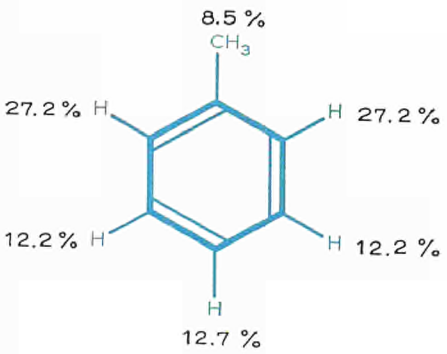
2. A curie, which is the unit of measurement of radioactivity, corresponds to 3.7×10^{10} disintegrations per second. Its sub-multiple is the millicurie equal to 3.7×10^7 d.p.s.

Compound	*Specific radioactivity (mC per gramme)*
Toluene	22.1
n-heptane	1.3
Benzoic acid	14.0
Saccharose	5.3
Cholesterol	64.3
Digitoxin	90

Numerous other substances have been marked in this way. Steinberg has prepared tritiated lysozyme and ribonuclease. They include complex molecules such as β-20-hydroxycholesterol, dehydroisoandrosterone, desoxycorticosterone, morphine, adenine, thymidine, gibberellic acid, different antibiotics and numerous other substances. In general, the distribution of the tritium in these substances is not selective nor completely uniform. This is shown in Figure 4, which gives the percentage of activity present in the various positions of toluene labelled by Wilzbach's method. It may be observed that there exists a certain preference for labelling in the benzene ring and within this for the two ortho positions. The Wilzbach method is, therefore, particularly useful when it is not necessary to know the exact position of the radioactive atom in the molecule marked.

Despite this limitation the Wilzbach technique is much in use today and many commercial organisations make available to laboratories utilising marked molecules a "tritium labelling service". This service receives from the client one or other organic substances, labels it by exposure to tritium and, in many cases, is also in a position to subject the tritiated product to suitable purification.

Figure 4. Distribution of tritium in toluene marked by the Wilzbach method.



The storage of marked molecules

DR. KLAUS HEMPEL, *Institute for Medical Isotope Research, University of Cologne*

For the synthesis of radioactive labelled organic compounds the radioisotopes of hydrogen (^{3}H), carbon (^{14}C), phosphorus (^{32}P) and sulphur (^{35}S) are mainly used. These radioisotopes disintegrate with differing half-lives by emitting a high-energy β-particle which is easy to trace by appropriate physical methods.

The problems

A serious disadvantage of radioactive labelled organic compounds is that they undergo far more rapid chemical changes than the rate of radioactive disintegration would lead to expect. The reason is that the radiation sets up radiochemical reactions which lead to the destruction of the labelled substance. In this way radioactive labelled disintegration products originate which, in certain circumstances, can give rise to erroneous interpretations of experimental findings.

Radioactive disintegration products are in principle the result of one of the three radiation effects briefly sketched below:

Primary internal radiation effect—When radioactive disintegration occurs, the radioisotope of one element is transformed into the stable isotope of another. Thus, for instance, a stable isotope of helium (^{3}He) arises from the radioactive isotope of hydrogen (^{3}H).

$$^{3}_{1}H \rightarrow {}^{3}_{2}He + e^{-}$$

If the radioactive hydrogen is bonded in an organic molecule, organically bonded helium is formed from it as an intermediary stage. This compound immediately disintegrates further into elementary helium and an inactive organic residue which generally continues to change chemically. Primary internal radiation effects always give rise to radioactive labelled disintegration products when the marked molecule originally contains more than one radioactive atom. This is often the case, particularly with macromolecules.

Primary external radiation effect—By this we mean the destruction of a molecule through the direct interaction of high-energy radiation, for instance high-energy β-particles, coming from outside. Under this effect radioactive labelled impurity elements arise from radioactive labelled compounds. One high-energy β-particle can transform many molecules.

Secondary radiation effect—In some circumstances compounds of considerable chemical reactivity can arise from the exposed substance itself through the high-energy radiation: from water, for instance, peroxide, ions and radicals can be produced, which have a secondary reaction with the marked molecules and induce chemical changes in them.

The solutions

The formation of radioactive disintegration products can be avoided by suitable storage of radioactive labelled organic compounds if the disintegration is caused by primary external or secondary radiation effects. Primary internal radiation effects, on the other hand, cannot be influenced by external measures. Chemical reactions through primary internal radiation effects run their course in the same spontaneous way as

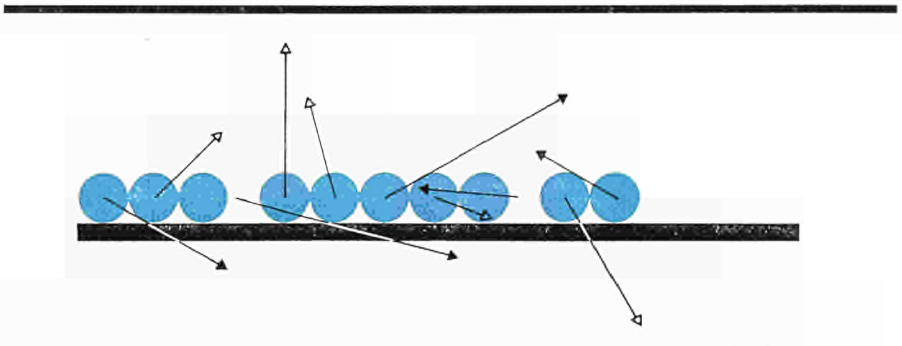


Figure 1. Storage of radioactive labelled organic compounds in a monomolecular layer

Table I. Dependence of the radiation dose on the concentration of the radioisotope

Concentration (mc^{+}/g)	*Radiation dose* (rad^{++} *per diem*)			
	^{3}H	^{14}C	^{32}P	^{35}S
1	2.9×10^{2}	2.3×10^{4}	3.5×10^{4}	2.6×10^{3}
10	2.9×10^{3}	2.3×10^{5}	3.5×10^{5}	2.6×10^{4}

\+ *1 millicurie (mc) = 3.77×10^{7} disintegrations per second*

\++ *1 rad = 100 erg per gramme = 2.4×10^{-6} calories per gramme*

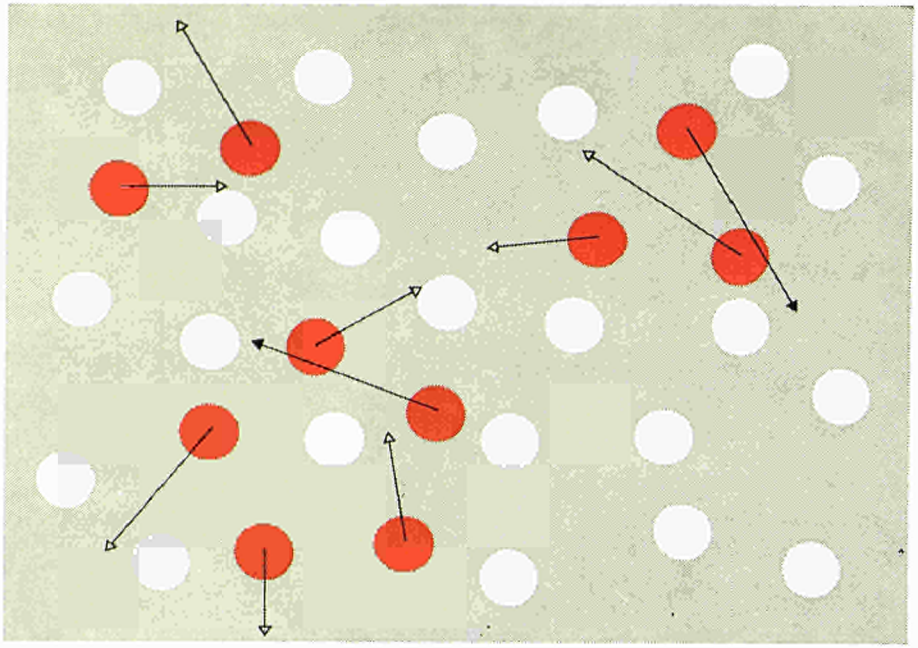


Figure 2. Storage of radioactive labelled compounds in a solution

Radioactive marked molecule

Molecule of the solvent

radioactive disintegration. This effect can only be avoided if care is already taken at the stage of synthesis of the labelled compounds that one radioactive atom at the most per molecule is included.

The extent of the primary external radiation effect and of the secondary radiation effect depends, apart from the nature of the exposed substance, primarily on the radiation dose which is absorbed by the radioactive sample. The radiation dose can be calculated from the number of radioactive disintegrations per gramme and the average energy per disintegration. Table 1 gives the radiation doses for the most important radioisotopes when one gramme of the substance contains one or ten millicuries of the radioisotope.

The chemical disintegration through radiation of the labelled compounds can be reduced if the proportion of the radiation energy absorbed by the labelled substance is kept low. This can be done in two different ways:

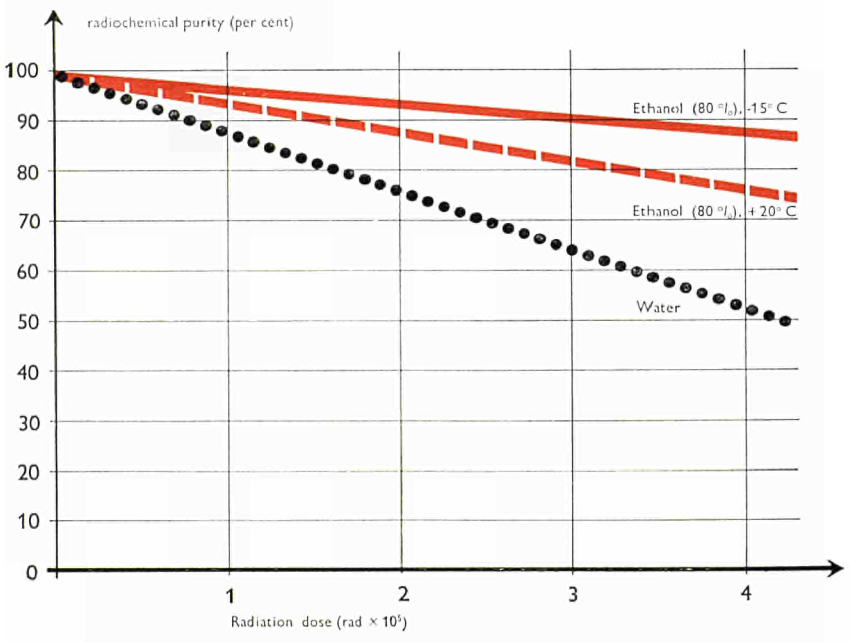
First, as shown in outline in Figure 1, the radioactive labelled organic compound can be placed upon a suitable carrier in a monomolecular layer. The thickness of the layer is then considerably smaller than the radius of action of the β-particles. The β-particles liberated by the radioactive disintegration then no longer strike the marked molecules exclusively but in particular the carrier. Paper is mostly used as a carrier.

Secondly, the marked molecules can be protected by thinning them out with inactive molecules. The molecules used for this may be chemically identical with the radioactive molecules or different from them. If the thinning out is done with a foreign molecule, for instance by dissolving the radioactive compound in a suitable solution, as indicated in Figure 2, the danger exists that the radiation will produce highly reactive compounds from the solution, and that these will disintegrate the labelled compounds which are to be protected.

Thus water is very unsuitable as a solution for the storage of radioactive labelled compounds, since the radiation gives rise *inter alia* to hydrogen peroxide which reacts with many organic compounds. Benzene, on the other hand, is very resistant to radiation and is highly suitable as a solution for radioactive compounds. However, many organic compounds are not soluble in benzene. In these cases, other less stable solutions, such as ethanol, must be used. Figure 3 gives as an example the differing stability of a radioactive amino-acid dissolved in water and in ethanol. For the dissolution in ethanol stability is moreover shown at two different temperatures, + 20 and —15 degrees. The labelled compound is noticeably more stable at the lower temperature, since secondary radiation effects generally decline with falling temperature.

A further possibility of keeping secondary radiation effects at a low level is to add radiation protective materials to the solution. These protective materials react most readily with the radicals and peroxides produced by the radiation and thus protect the labelled organic compound.

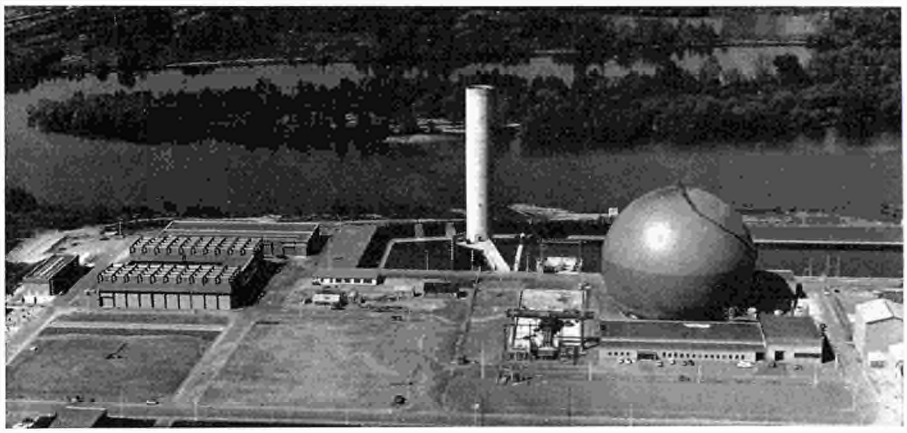
Figure 3. Influence of the solvent on the radiochemical stability of radioactive labelled compounds (based on experiments with ^{3}H-lysin)



EURATOM NEWS

Two full-scale nuclear power plants producing electric current in the Community

At the beginning of 1964, for the first time in the Community, full-scale nuclear power plants supplied electricity under normal commercial conditions over a substantial period. They are the Latina (Italy) and Chinon – EDF I (France) plants, both equipped with gas-graphite reactors.
For March 1964, the load factor of the more powerful of these plants, i.e. the one at Latina, averaged 91.4%, the rated capacity being 200 MWe.



EDF 1 power reactor of Electricité de France at Chinon

A further step towards a common European energy policy?

During its meeting on 21 April 1964, the Special Council of Ministers of the *European Coal and Steel Community* (ECSC) adopted a Protocol of Agreement on energy problems which confirms the Governments' desire to formulate a common energy policy in the context of the gradual fusion of the Communities.
As regards coal in particular, the Protocol empowers the High Authority of the ECSC to set up, by agreement with the Council, a unified system for the granting of state aid to the coal industry.
With regard to petroleum, the Protocol embodies a number of provisions which will help the Commission of the *European Economic Community* in its efforts to develop, pursuant to the Treaty of Rome, a common policy in this field too.

Finally, the Protocol contains the following text on nuclear energy:
"As regards nuclear energy, the Governments are disposed, within the framework and in accordance with the provisions of the Treaty establishing the *European Atomic Energy Community*:
to promote and step up research, experimental work and aid in the development of nuclear industries in the Community in order to enable this new source of energy to make, as soon as possible, the full contribution of which it is capable, under economic conditions, towards meeting the Community's energy requirements."

Seventh General Report on Euratom's Activities

On 23 April 1964, the Euratom Commission published its Seventh General Report, which provides ample evidence that nuclear energy in the Community has now entered the industrial stage in the true sense.
Europe is the world's largest importer of energy. In 1960 these imports represented 27% of its total supplies, and by 1970 this figure will have risen to 50%. The use of nuclear energy may gradually slow down this upward trend, and, since its cost is falling rapidly, may exercise a restraining influence on energy prices in general.
The industrial applications of nuclear energy must be backed up by research, and it is only by dovetailing the research activities of Euratom and all the Member States that Europe can maintain a leading role in the field of nuclear technology.
Furthermore, in order that industrialists can map out their own activities, it is imperative that the Community's industrial targets be clearly defined. These targets are based on the assumption of an installed power of 40,000 nuclear MWe by 1980, entailing investments of the order of 8-10,000 million dollars.

EURATOM NEWS

Higher burnup for gas-graphite-reactor fuel elements?

A theoretical study, carried out by the French Atomic Energy Commission (CEA) under a contract concluded with Euratom, has shown that from the neutronics standpoint, burnups averaging 5.000 – 6.000 megawatt-days per ton and more are a practical prospect for gas-graphite-reactor fuel elements, the economic optimum being in the region of 5,500 MWd per ton. These figures are distinctly higher than those previously envisaged, which were around 3,500 MWd per ton.

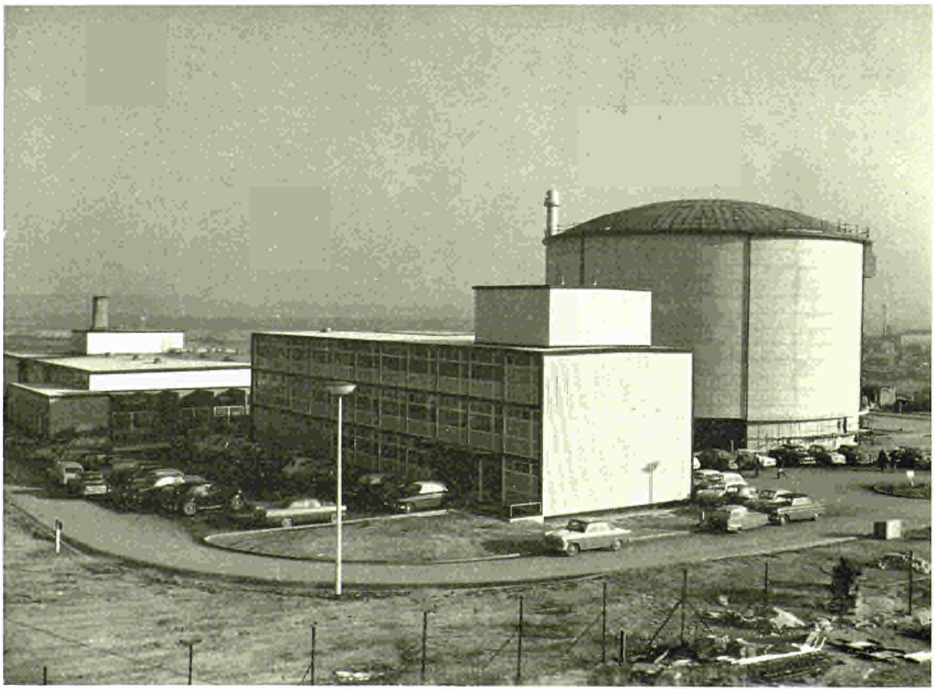
The study, which was based on EDF 2 fuel elements containing 1.1% molybdenum, took into account the most recent theoretical "thermalisation" patterns. These have already been verified to some extent by experiment, a fact which promises well for the validity of the calculations.

Euratom meeting with Community Trade Union leaders

Some forty leaders of the main trade union organisations of the Community met at Stresa, Italy, on 20-22 May, for a round-table discussion arranged by Euratom.
The meeting, which afforded the Euratom Commission an opportunity to acquaint the labour organisations with its activities, prompted a wide exchange of views, in particular on the social consequences of the development of nuclear industries.

DRAOGN to go critical soon

The *DRAGON* experimental reactor is almost complete and should go critical for the first time within the next few months. THE *DRAGON* high temperature gas-cooled reactor is being built as an international project under the auspices of the *European Nuclear Energy Agency* (ENEA) of the *Organisation for Economic Co-operation and Development* (OECD). The agreement launching the project involved 12 countries, including the six countries of the European Community, represented by the Euratom Commission. The European Community's share in the cost of the project is 46%.
The reactor will run on 37 fuel elements, the first few of which have already been manufactured. The fuel elements of the central zone will contain thorium as well as uranium, allowing conversion of thorium into fissile uranium-233 to take place.



General view of the DRAGON reactor

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ORGEL – a thermal breeder reactor?

The attractions of breeder reactors no longer need to be proved; it is evident that this type of reactor will permit the most rational possible utilisation of the available uranium and thorium reserves.

Up till now the most thoroughly explored reactor in this category is the fast-neutron breeder type, and it is in fact hoped to obtain high breeding factors with this, of the order of 1.4. Slow-neutron breeders will never be capable of such high performances, but they will, on the other hand, have the advantage of being able to operate on thorium, a fuel which is much more difficult to use in fast-neutron reactors. Studies in this connection have already been launched in the USA and elsewhere.

Are there good grounds for hoping that it will prove possible to "breed" fuel by means of an *ORGEL*-type reactor? Preliminary studies suggest that there may be a good chance, but they must be followed up further in order to make sure.

Construction of ESSOR at Ispra

The *ESSOR* reactor is now under construction at the Ispra establishment of the Euratom Joint Research Centre. It is a reactor for specific experiments connected with heavy-water-moderated pressure-tube reactors, and is equipped primarily for *ORGEL* string studies (see Euratom Bulletin 1963, No. 2).

The GAAA-Interatom-Montecatini group have been appointed as industrial architects. The first earthworks began in April 1963. The foundations were sufficiently advanced in December of the same year for work to begin on the construction of the leaktight containment shell; at the beginning of May 1964 the wall of the containment shell had reached a height of 20 metres.

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