ISOTOPIA-2.2

Simulation of medical isotope production with accelerators

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nds.iaea.org/talys

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About the author

Arjan Koning is a nuclear physicist with a Masters Degree in Theoretical physics at the Univ. of Amsterdam, a PhD in the Natural Sciences on Multi-step direct reactions at the Univ. of Groningen, and a Professorship at the Univ. of Uppsala on theoretical nuclear reactions.

Arjan is currently Head of the Nuclear Data Section at the IAEA in Vienna. Before that, he has worked at ECN/NRG Petten, the Netherlands, on nuclear reaction data for science and technology, and as guest scientist at CEA/Bruyères-le-Châtel and Los Alamos National Laboratory on the development and computational implementation of nuclear reaction models. He has led several students to PhD degrees, has coordinated and chaired various international nuclear data projects such as the OECD/NEA JEFF and WPEC projects, and has advised governments and international organisations on nuclear research and development. Among his scientific accomplishments are innovations in nuclear reaction physics, especially for the optical model and pre-equilibrium reactions, and initiating the ’3 T’s’: the TALYS nuclear model code, Total Monte Carlo uncertainty propagation and the TENDL nuclear data library. He has been awarded the Oppenheimer Coin from Los Alamos National Laboratory, and the title of Doctor Honoris Causa by Uppsala University. As of 2025, his h-index is 62 with more than 26 000 citations.

Although Arjan is currently in a managerial role, he aims to keep his scientific creativity alive by maintaining and extending TALYS plus all software that emerges from that. Pleas from his friends to also spend time on other things are sometimes honoured.

Preface

ISOTOPIA is a software package for the prediction of medical isotope production with charged-particle accelerators. In principle, the isotope yields for any production route with incident protons, deuterons, tritons, helions or alpha particles, for natural or enriched targets, can be calculated. While most computational ingredients for the simulation of isotope-producing accelerators are rather straightforward, the *crucial* ingredients for reliable simulation of the isotope yield are nuclear reaction cross sections radioactive decay data. For ISOTOPIA, we use the IAEA medical isotope data library for about 150 reaction channels, complemented by TENDL-2023 for all other reactions.

The idea to construct ISOTOPIA is rooted in the belief that radioisotopes produced with *both* reactors and accelerators are needed in the foreseeable future, to ensure that medical diagnosis and therapy remain successful *and* economically affordable. Since several years, this issue has entered the discussion with the need for the replacement of old reactors that produce isotopes. Accelerators, which are mostly used to produce neutron-poor PET isotopes, and also several therapeutic isotopes, are now also suggested as a possible alternative production device for “reactor nuclides” with the ^{99}Mo/^{99m}Tc generator as the most important case. While this issue has economical, logistic and political aspects, the current code will at least help to answer its scientific aspects. ISOTOPIA predicts the production yield of any diagnostic, therapeutic or theranostic isotope with an accelerator. Obviously, the *reliability* of that prediction depends strongly on the quality of the nuclear reaction cross sections.

To complete ISOTOPIA, we are working on an extension for isotope production by nuclear (research) reactors and via the photonuclear route. The cross section libraries are already available for that, but we still need to implement the correct neutron and photon particle sources in the equations.

At certain moments in time, a well-defined version of ISOTOPIA is frozen. You are now reading the tutorial of version 2.2. Future versions should become more and more reliable through improvements in both the ISOTOPIA code and the underlying cross section and radioactive decay data libraries.

ISOTOPIA is the engine behind the Medical Isotope Browser, nds.iaea.org/mib, which allows to analyze production routes in an efficient way via a GUI.

License, contact and reference

As mentioned on the first page and in the source code, ISOTOPIA falls in the category of MIT License software.

In addition to the MIT *terms* I have a *request*:

- When ISOTOPIA is used for your reports, publications, etc., please make a proper reference to the code. At the moment this is:
  A.J. Koning, ISOTOPIA: Simulation of medical isotope production with accelerators, unpublished tutorial (2025).

The webpage for ISOTOPIA is **nds.iaea.org/talys**.

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- Marieke Duijvestijn, who set up the first calculation routes with the TALYS code for isotopic yields, which we needed for a project on the production of ^{68}Ga, when we were still working at NRG Petten,
- Marco Verpelli, for integrating ISOTOPIA in the Medical Isotope Browser and for suggesting the associated improvements to the code.
- Steven van der Marck for his initial help to construct a software tool like this and useful discussions,
- Will Webster and Bernard Erasmus for important feedback on the implementation of ISOTOPIA in the TALYS code,
- Roberto Capote Noy and the entire consortium responsible for the IAEA medical isotope data library, for helpful discussions and for providing the specific data library for about 150 isotopes,
- Natalie Gaughan, for testing many of the isotope yield calculations with the TALYS code,
- Ulli Koester, for taking a critical look at our Medical Isotope Browser and suggesting improvements.

Arjan Koning

Contents

1. Introduction

There is an increasing demand for radioisotopes for medical diagnosis or therapy. For diagnosis, almost all radioisotopes fall into the categories of single photon emission computed tomography (SPECT) or positron emission tomography (PET). Although PET scans are qualitatively superior and therefore its market is enlarging, the ease of use and cost effectiveness of SPECT, with the ^{99}Mo/^{99m}Tc generator as the workhorse, entails that its dominance will probably not disappear in the coming decade. As a rule of thumb (exceptions exist!) neutron-rich nuclides, often retrieved as fission products or by neutron capture in a nuclear reactor, are used for SPECT scans while neutron-poor nuclides, produced with accelerators, are used for PET scans. For therapy, also both reactor-produced and accelerator-produced isotopes are on the market.

The current version of ISOTOPIA is completely devoted to the production of isotopes with a charged-particle accelerator. (The underlying physics for isotopes produced with a reactor or by photonuclear reactions is somewhat different and will be added in a future version).

Often, on the basis of its biological, chemical and nuclear decay properties a radioisotope is identified as a promising candidate for medical diagnosis or therapy. The subsequent question "Can we produce that medical isotope with an accelerator?" can usually not be answered by a firm "yes" or "no" but fragments into several other questions, such as:

- What is the optimal production route for the isotope, i.e., what is the best target + projectile combination?
- What is the optimal incident beam energy?
- What is the optimal target thickness, or equivalently, what is the projectile energy range inside the target?
- What is the optimal irradiation time and cooling period?
- What is the isotopic yield during and directly after irradiation and after a cooling period?
- What is the yield of elemental and isotopic contaminations after irradiation and after a cooling period?
- How much do the answers to the above questions depend on the use of an enriched or a

natural target?

To answer such questions, we have implemented an analytical model which allows to parameterize the various characteristics of an accelerator + target combination and which calculates the isotopic yields of various production routes as a function of irradiation time on the basis of modern cross section and decay data libraries.

Of course, the nuclear physics aspects to the above questions are not the end of the story. Several questions on economics and logistics (often correlated) need to be answered as well, e.g.

- How many accelerators are needed to meet the current demand?
- What are the logistical implications of the radioactive decay time of the desired product and its purity, which may depend on the production route?
- What are the costs to make a sufficiently enriched target?

Finally, a political decision to build a production facility is made which may discard the scientific and economical answers, but we have decided not to touch economical, logistical or political aspects here and concentrate ourselves on the purely scientific aspects.

As specific features of ISOTOPIA we mention

- Estimation of isotopic yield on the basis of a user-specified accelerator beam current and energy range, target thickness, irradiation time and cooling period. Covered are incident protons, deuterons, tritons, helions and alpha particles, on any type of target material.
- The activities of all residual products are presented as yields as a function of irradiation time. When appropriate, results are averaged over time to obtain the average yield in [MBq/mAh].
- Estimate of simultaneous production of contaminations.
- Robustness: thanks to the complete TENDL data library augmented by well-evaluated reaction channels of the IAEA medical isotope library, ISOTOPIA can be used for the prediction of any isotope that one is interested in: it is generally applicable and has been thoroughly tested on a basic quality level.
- A transparent source program.
- Input/output communication that is easy to use and understand.
- A user tutorial.
- A few sample cases.

The starting point of all calculations are cross sections for all reaction channels. They are obtained from two sources,

- the TENDL-2023 nuclear data library [1], produced by the nuclear reaction model code TALYS [2],
- the IAEA medical isotope database, high-quality in-depth evaluations of important reaction channels, on the basis of available experimental data [3, 4, 5, 6].

The current tutorial only describes the ISOTOPIA code and its input and output. We stress however that a powerful Graphical User Interface has been built around it at IAEA, the Medical Isotope Browser, nds.iaea.org/mib, which drives the ISOTOPIA code and which is a very efficient way to study medical isotope production as a function of the accelerator characteristics.

1.1 How to use this tutorial

Although we would be honored if you would read this tutorial from the beginning to the end, we can imagine that not all parts are necessary, relevant or suitable to you. the contents are as follows:

Chapter 2: Installation guide for ISOTOPIA.
Chapter 3: The main input rules
Chapter 4: General formalism for isotope production.
Chapter 5: The nuclear reaction and structure information needed in the form of cross section and decay data.
Chapter 6: The reference guide with all the keywords

Chapter 7: Sample cases and verification.
Chapter 8: Outlook and conclusions.

2. Installation and getting started

2.1 The ISOTOPIA package

In what follows we assume ISOTOPIA will be installed on a Linux or MacOS operating system. The total ISOTOPIA package is in the *isotopia/* directory and contains the following directories and files:

- *LICENSE* is the license file,
- *README.md* outlines the contents of the package.
- *install_isotopia.bash*, *code_build.bash* and *path_change.bash* are scripts that take care of the installation,
- *source/* contains the Fortran source code of ISOTOPIA
- *files/* contains the natural abundances and the decay data library.
- *doc/* contains the documentation: this tutorial in pdf format.
- *samples/* contains the input and output files of the sample cases.

Outside *isotopia/*, you need to have the directory *isotopia.libs/* which contains all cross section data. In fact the place of this directory can be set in the *machine.f90* subroutine.

In total, you will need about 20 Gb of free disk space to install ISOTOPIA, which is almost entirely due to the cross section database in the *isotopia.libs/* directory. The code has so far *only* been tested on various Linux and MacOS systems, so we can not guarantee that it works on all operating systems. The only OS dependencies we can think of are the directory separators '/' we use in pathnames that are hardwired in the code. If there is any dependence on the operating system, the associated statements can be altered in the subroutine *machine.f90*.

ISOTOPIA has been successfully tested for the gfortran compiler.

2.2 Installation

The installation of ISOTOPIA is straightforward. You can download ISOTOPIA via either git

- **git clone https://github.com/arjankoning1/isotopia.git** or by getting the tar file

- from **https://nds.iaea.org/talys/isotopia.tar**
- **tar zxf isotopia.tar**

We here provide the necessary steps to do the installation, For a Unix/Linux system, the installation is expected to be done by the simple command

- *install_isotopia.bash*

which calls the scripts

- *code_build.bash* where you may set, if needed, the name of your compiler and the place where you want to store the ISOTOPIA executable.
- **path_change.bash** to set the pathname in the source code.

An alternative installation option is

- **cd isotopia/source**
- **make**

If this does not work for some reason, we here provide the necessary steps to do the installation manually. For a Unix/Linux system, the following steps should be taken:

- **cd isotopia/source** If *code_build.bash* has not already replaced the path name in *machine.f90*, do it yourself. We think this is the only Unix/Linux machine dependence of ISOTOPIA. We expect no complaints from the compiler.
- **gfortran -c *.f90**
- **gfortran *.o -o isotopia**
- **mv isotopia ../bin**

The above commands represent the standard compilation options. Consult the tutorial of your compiler to get an enhanced performance with optimization flags enabled. We note that an ISOTOPIA run generally takes only less than a second so extreme optimization is not necessary.

2.3 Verification

If ISOTOPIA is installed, testing the sample cases is the logical next step. The *samples/* directory contains the script *verify* that runs all the test cases. Each sample case has its own subdirectory, which contains a subdirectory *org/*, where we stored the input files and *our* calculated results. It also contains a subdirectory *new*, where we have stored the input files only and where the *verify* script will produce *your* output files. A full description of the keywords used in the input files is given in Chapter 3. Chapter 7 describes all sample cases in full detail. Note that in each subdirectory a file with differences with our original output is created.

2.4 Getting started

If you have created your own working directory with an input file named e.g. *isotopia.inp*, then a ISOTOPIA calculation can easily be started with:

isotopia < **isotopia.inp** > **isotopia.out**

where the names *isotopia.inp(out)* are not obligatory: you can use any name for these files. Besides the general output file *isotopia.out* various other output files, with activities per isotope,are produced.

3. Input description

For the communication between ISOTOPIA and its users, we have constructed an input/output method which shields beginners from all the possible options for parameters that can be specified in ISOTOPIA, while enabling at the same time maximal flexibility for experienced users.

An input file of ISOTOPIA consists of keywords and their associated values. Before we list all the input possibilities, let us illustrate the use of the input by the following example. It represents a minimum input file for ISOTOPIA:

```
projectile p
element    Mo
mass       100
ebeam     16.
```

This input file represents the simplest question that can be asked to ISOTOPIA: if a 100 % enriched ^{100}Mo target is bombarded by 16 MeV protons, what isotopes are produced as a function of time, and what is the radioactive yield? Behind this simple input file, however, there are several default values for the various assumptions, parameters, output flags, etc., that you may or may not be interested in. When you use a minimal input file like the one above, you leave it to the author of ISOTOPIA to choose all the parameters for you, including accelerator and target specification, as well as the level of detail of the output file. If you want to use specific parameters other than the default, or want to have more specific information in the output file(s), more keywords are required. Obviously, more keywords means more flexibility and, in the case of adequate use, better results. For example, one probably would like to enter the accelerator beam current, target size and material density in the input. In this Chapter, we will first give the basic rules that must be obeyed when constructing an input file for ISOTOPIA.

3.1 Basic input rules

Theoretically, it would be possible to make the use of ISOTOPIA completely idiot-proof, i.e. to prevent the user from any input mistakes that possibly can be made and to continue a calculation with "assumed" values. Although we have invested a relatively large effort in the user-friendliness of ISOTOPIA, we have not taken such safety measures to the extreme limit and ask at least some minimal responsibility from the user. Once you have accepted that, only very little effort is required to work with the code. Successful execution of ISOTOPIA can be expected if you stick to the following simple rules and possibilities of the input file:

1. One input line contains one keyword. Usually it is accompanied by only one value, but some keywords (e.g. **Tcool**) need to be accompanied by more than one value on the same line.
2. A keyword and its value(s) *must* be separated by at least 1 blank character.
3. The keywords can be given in arbitrary order. If you use the same keyword more than once, the value of the last one will be adopted.
4. All characters can be given in either lowercase or uppercase.
5. A keyword *must* be accompanied by a value. To use default values, the keywords should simply be left out of the input file.
6. An input line starting with a # in column 1 is neglected. This is helpful for including comments in the input file or to temporarily deactivate keywords.
7. A minimal input file always consists of 4 lines and contains the keywords **projectile**, **element**, **mass** and **ebeam**. These 4 keywords *must* be given in any input file.
8. An input line may not exceed 80 characters.

As an example of rules 3, 4, and 6, it can be seen that the following input file is completely equivalent to the one given in the beginning of this chapter:

```
Ebeam     16.
Element    Mo
MASS       100
projectile p
#rho 5.
```

In the following erroneous input file, only the second and third lines are correct, while rules 2, and 5 are violated in the other lines.

```
Ebeam22.
projectile p
MASS 103
Element
```

In cases like this, ISOTOPIA will give a specific error message for the first encountered problem and the execution will be stopped. We like to believe that we have covered all such cases and that it is impossible to let ISOTOPIA crash (at least with our compilers) without giving an appropriate error message, but you are of course invited to prove and let us know about the contrary (Sorry, no cash rewards). Typing errors in the input file should be spotted by ISOTOPIA, e.g. if you write **projjectile d**, it will tell you the keyword is not in our list, and the code will gracefully stop.

4. Radioisotope production

This section describes the formalism to calculate the production yield of a radioactive nucleus by a nuclear reaction. Starting from the general formalism we will introduce realistic approximations and derive simpler equations that hold in basically all cases of interest. In ISOTOPIA we have implemented only analytical solutions to the production and depletion equations, which are expected to be sufficient for isotopes formed by activation. The production via fission to fission products is not yet included. This may be generalized in future versions.

4.1 Equations for production and depletion of isotopes

In virtually all cases of interest for radioisotope production by means of activation, the temporal development of a system of isotopes during irradiation can be expressed as follows

$$
\begin{aligned}
N_T(t) &= N_0\, e^{-R_T t}, \\
N_p(t) &= N_0\, \frac{R_{T\to p}}{\lambda_p - R_T}\, [e^{-R_T t} - e^{-\lambda_p t}], \\
N_i(t) &= N_0\, \frac{R_{T\to i}}{\lambda_i - R_T}\, [e^{-R_T t} - e^{-\lambda_i t}] + N_0 \frac{R_{T\to p}\lambda_{p\to i}}{\lambda_p - R_T} \left[\frac{e^{-R_T t} - e^{-\lambda_i t}}{\lambda_i - R_T} - \frac{e^{-\lambda_p t} - e^{-\lambda_i t}}{\lambda_i - \lambda_p} \right],
\end{aligned}
\tag{4.1}
$$

where,

- N_T: the number of target isotopes at any time t,
- N_i: the number of produced isotopes of interest at any time t,
- N_p: the number of parent isotopes, possibly feeding into N_i at any time t,
- N_0: $= N_T(t = 0)$, the initial number of target isotopes,
- λ_i: total radioactive decay rate for isotope i, respectively, where $\lambda_i = \ln 2/T_{i,1/2}$, with $T_{i,1/2}$ the half life. Similar for isotope p,

- $\lambda_{p\to i}$: radioactive decay rate for isotope p decaying to isotope i,
- R_i: total nuclear reaction rate for isotope i. Similar for isotope p,
- $R_{p\to i}$: partial nuclear reaction rate for parent isotope p to isotope i,

These equations are derived in the Appendix. Note that Eq. (4.1) is more general than what is used in most analyses. Often the only term that is used is that of a radioactive isotope which is directly produced from the target and which decays itself, i.e. the first term of the third line (or equivalently, the second line with p replaced by i). Eq. (4.1) considers, with the first line, the burn-up of the target, and also, with the second and third lines, the possible production of the isotope of interest via an indirect route. The rate R_T is often very small compared to the irradiation time, of the order of 10^{-10} s^{-1}, i.e. $N_T(t) \sim N_0$ and therefore one often discards the first line of Eq. (4.1). For very high burn-up it is better to include this though. If there is no indirect feeding via a parent to the final isotope i, we can also discard the second line and the second term of the last line. With a negligible R_T, Eq. (4.1) will then be be reduced to one term proportional to $1-\exp(-\lambda_i t)$, which is the one used in most analyses. We have however implemented the full set of Eq. (4.1).

By setting the derivative of $N_i(t)$ to zero, the irradiation time for which a maximal yield is obtained can be derived:

$$t_{max} = \frac{ln(\lambda_i/R_T)}{\lambda_i - R_T} \tag{4.2}$$

Hence, this observable t_{max} depends on the decay constant λ_i and the total production rate R_T.

4.2 Activities

With $N_i(t)$ known, the expression for the activity A_i of the produced isotope i as a function of the irradiation time can now be given by

$$A_i(t) = \lambda_i\, N_i(t). \tag{4.3}$$

Usually the activity is given in GBq or MBq. For small irradiation times the expression for $N_i(t)$, Eq. (4.1), behaves as:

$$N_i(t) = N_0\, R_{T\to i}\, t, \tag{4.4}$$

and hence the activity of i as

$$A_i(t) = \lambda_i\, N_0\, R_{T\to i}\, t, \tag{4.5}$$

Under these circumstances, the yield scales linearly with the irradiation time t and the production rate $R_{T\to i}$. Only then, the production yield expressed in [MBq/mAh] is a meaningful quantity.

The formalism given above is still general with respect to the irradiation source. The activation equations apply to neutron, charged-particle or photon irradiation. It is the production rate R which differs for the three types of irradiation. It depends on two important ingredients: the particular geometry-dependent aspects of the reaction rate, and the cross sections. We will now first outline the expressions for the reaction rate. The cross sections will be discussed in a separate Section.

4.3 Charged-particle irradiation

Now that the analytical formulae for production are set with Eq. (4.1), the remaining ingredients needed to evaluate Eqs.(4.1) and (4.2) are: $N_T(0)$, R, and λ, and this will be done in the next two sections.

4.4 Initial condition and stopping power

The number of target atoms at t=0, $N_T^m(0)$, for $1 \leq m \leq M$ (with M the number of natural isotopes constituting the element) equals:

$$N_T^m(0) = \frac{N_A}{A} B_m \, \rho \, V_{tar}, \tag{4.6}$$

where $N_A = 6.022 \; 10^{23}$ is Avogadro's number, A is the mass number, B_m is the abundance of isotope m with $\sum_m^M B_m = 1$, ρ the mass density in [g/cm^3], and V_{tar} the active target volume in [cm^3]. V_{tar} is given by the product of the beam surface S_{beam} in [cm^2] and the effective target thickness in [cm], which can be expressed in terms of the stopping power $\frac{dE}{dx}$,

$$V_{tar} = S_{beam} \int_{E_{\mathrm{back}}}^{E_{\mathrm{beam}}} \left(\frac{dE}{dx} \right)^{-1} dE, \tag{4.7}$$

where E_{beam} denotes the incident beam energy and E_{back} is the average projectile energy available at the backside of the target. If the projectiles travels through the target, the average projectile beam energy will decrease. The amount of energy loss inside the target is determined by the target thickness and the stopping power. The integration limits E_{beam} and E_{back} are fixed by the requested projectile energy range inside the target, which is determined by the cross section as function of projectile energy (excitation function). This formula neglects the spreading of the beam inside the target.

The stopping power describes the average energy loss of projectiles in the target by atomic collisions as a function of their energy in [MeV/cm]. We use the Bethe-Bloch formula [7]:

$$\frac{dE}{dx} = 0.1535 \, \rho \, \frac{Z}{A} \frac{z_p^2}{\beta^2} \, [ln \left(\frac{2m_e \gamma^2 v^2 W_{max}}{I^2} \right) - 2\beta^2], \;\; \mathrm{MeV/cm} \tag{4.8}$$

with Z the target charge number, and z_p the projectile charge number, while β represents a beam particle traveling at a relative velocity

$$\beta = \frac{v}{c} = \sqrt{\frac{E_{beam}(E_{beam} + 2m_0 c^2)}{(E_{beam} + m_0 c^2)^2}}, \tag{4.9}$$

with rest mass m_0. Further, m_e is the electron mass, and $\gamma = \frac{1}{\sqrt{1-\beta^2}}$. The maximum energy transfer in a single collision, W_{max} is given by

$$W_{max} = 2m_e c^2 (\beta\gamma)^2, \tag{4.10}$$

if the incident particle is much heavier than the electron mass. For the mean excitation potential I a semi-empirical formula is adopted:

$$\frac{I}{Z} = 9.76 + 58.8 Z^{-1.19} \;\; \mathrm{eV}. \tag{4.11}$$

This expression is claimed to be tested only if $Z \geq 13$, but we use it for all values.

Note that after insertion of the stopping power the mass density ρ cancels out in the final expression of Eq. (4.6).

4.5 Nuclear reaction and decay rates

When the full beam hits the target (i.e., assuming that the beam diameter is smaller than the target dimensions), the production rate in [atoms/s] of isotope i through the nuclear reaction on the target isotope T is given by the following expression

$$R_{T\to i} = \frac{I_{beam}}{z_p\, q_e} \frac{1}{V_{tar}} \int_{E_{\text{back}}}^{E_{\text{beam}}} \left(\frac{dE}{dx}\right)^{-1} \sigma_i^{rp}(E)\, dE \tag{4.12}$$

where I_{beam} is the beam current in [A] and q_e is the electron charge. The factor $I_{beam}/(z_p q_e)$ corresponds to the number of projectiles impinging on the target per [s]. The residual production cross section of i in [mb] is denoted by $\sigma_i^{rp}(E)$.

Analogously, the production rate in [s^{-1}] of all reaction channels, from the target, is given by:

$$R_T = \frac{I_{beam}}{z_p\, q_e} \frac{1}{V_{tar}} \int_{E_{\text{back}}}^{E_{\text{beam}}} \left(\frac{dE}{dx}\right)^{-1} (\sigma_{non}(E) - \sigma_{in}(E))\, dE \tag{4.13}$$

where σ_{non} is the non-elastic cross section and σ_{in} is the inelastic cross section of i in [mb]. The difference $\sigma_{non} - \sigma_{in}$ provides the probability to create an isotope different from the original target atom in the nuclear reaction.

The decay rate of i is given by the simple relation

$$\lambda_i = \frac{\ln 2}{T_i^{1/2}}, \tag{4.14}$$

where $T_i^{1/2}$ is the half-life of isotope i in [s]. The λ_i in the loss term usually feeds only one or two different channels, namely by beta decay to the ground state or isomer of the daughter isotope d,

$$\lambda_i = \lambda_{i\to d} = \lambda_{i\to d}^{g.s.} + \lambda_{i\to d}^{iso}. \tag{4.15}$$

With this, all ingredients of Eq. (4.1) are defined and we may calculate the nuclide inventory $N_i(t)$ at any time during or after the irradiation process.

All quantities needed to calculate the activity are easy to obtain with one exception: the production cross sections.

5. Nuclear data libraries

In the previous chapter it was outlined that the entire simulation of isotope production basically depends on 4 ingredients,

- the solution of the production and decay equations, Eq. (4.1),
- a model for the stopping power, in our case Eq. (4.8),
- a radioactive decay data library,
- a cross section data library,

For the radioactive decay data library, we have taken the JEFF-3.3-RD. For the current version of ISOTOPIA, all we use is a basic decay mode, i.e. whether the nuclide decays via electron or positron emission along the decay chain, and of course the half life.

The cross section database of ISOTOPIA is a merger of two sources,

- TENDL-2023 [1], is a complete nuclear data library for all projectile, target, product, energy combinations. For projectiles on any target, cross sections are included for all residual products which can be produced for incident energies up to 200 MeV. For incident charged-particles, TENDL has been automatically produced, using adjusted nuclear model parameters for those reactions where experimental data are available. That means that compared to experimental data the TENDL curves are usually good. Statistical analyses of the overall quality, also in comparison with other high-energy libraries, exist.
- The IAEA Medical Isotope database [3, 4, 5, 6], has been produced by a series of IAEA collaborations and has resulted in a recommended database for about 150 cross section sets for important medical isotopes produced by charged-particle induced reactions. For these reactions, the experimental data were considered to be so abundant and/or of so high quality that empirical Pade fits were made to produce the final evaluation, and no nuclear model code was required. This has led to excitation functions for restricted, though often the most important, nuclides and energy ranges,

The medical isotope data library for ISOTOPIA is the result of a smooth merger between these two data libraries. Obviously, TENDL is used for projectiles, targets, products and reaction channels which do not exist in the IAEA database. For the 150 reaction channels of the IAEA database, we have complemented the IAEA database by simply normalizing TENDL to the first and last energy point of the IAEA excitation functions. Often, but not always(!), the most relevant energy range is considered by the IAEA tables. Of course, for totally new production routes only the TENDL cross sections are available. Also, though for the about 150 well-known reaction channels a nuclear model estimate may be redundant, the better a nuclear model code can reproduce the experimental data or its Pade fit, the more confidence we may have for the *other* produced channels for the same reaction, which could represent important contaminations to consider.

The combination of IAEA database and TENDL currently may bring the most complete and best quality library for medical isotope production, but may be improved by adjusting TALYS nuclear model parameters to (even) better fit experimental data for many nuclides.

5.1 Creation of medical isotope data library

The nuclear data library that is used by ISOTOPIA is called *isotopia.libs*. For future reference, we describe here how it is created.

- First, the "raw" data file from the IAEA medical isotope database are renamed to filenames consistent with the entire system around TALYS. For example, the ^{100}Mo(p,2n)^{99m}Tc cross section is stored in p-Mo100-rp043099m.iaea.med. This is a manual or semi-automated step.
- Next, we rename the headers of the files to bring them in sync with the rest of the *libraries/* database. For this we use the script /isotopia/misc/medrename.bash
- To unify with the rest of the database even more, we extend every IAEA file up to 200 MeV, for which we use /isotopia/misc/medmerge.bash.
- Note that there are various collections of historic IAEA files, for therapeutic, diagnostic, monitor reactions etc. They all get the treatment mentioned above, and older files are overwritten with newer files.
- In directory *isotopia.libs* there is a script *create.isotopia.libs*. This script basically merges the latest version of TENDL with the collection of specific IAEA medical isotope files. In practice this goes as follows: every single reaction file from TENDL is copied, and only those files which exist in the IAEA database are overwritten by the latter. For completeness, also all data from the EXFOR database are included.

This process leads to a data library *isotopia.libs* which has at the highest level the incident particles,

```
p/
d/
t/
h/
a/
```

The next level contains the nuclides

```
....
p/Mo097/
p/Mo098/
p/Mo100/
etc.
```

The next level contains the nuclear data library and EXFOR,

```
p/Mo100/exfor/
p/Mo100/iaea.2024/
```

All relevant EXFOR data that is available in computational XC4 format is stored in the exfor/ directory. For the particular case of medical isotope production we need only 2 subdirectories

```
p/Mo100/exfor/xs      : the channel cross sections, in particular the non-elastic
p/Mo100/exfor/residual: all residual production cross sections
```

Next, the *iaea* directory contains the evaluated nuclear data tabulated per reaction channel in simple tables. For consistency with the *libraries/* database used for other projects we have kept the same directory structure. For *isotopia.libs*, we have

```
p/Mo100/iaea.2024/tables/xs      : the non-elastic cross section p-Mo100-MT005.iaea.2024
p/Mo100/iaea.2024/tables/residual: all residual prod. c.s. e.g. p-Mo100-rp043099m.iaea.2024
```

Finally, as an example of a file with residual production cross sections, *p-Mo100-rp043099m.iaea.2024* looks as follows

```
# header:
#   title: Mo100(p,x)Tc99m cross section
#   source: IAEA medical isotope consortium
#   user: Arjan Koning
#   date: 2024-10-06
#   format: YANDF-0.2
# endf:
#   library: iaea.2024 + TENDL-2023
#   author: IAEA medical isotope consortium
#   year: 2024
# target:
#   Z: 42
#   A: 100
#   nuclide: Mo100
# reaction:
#   type: (p,x)
#   ENDF_MF: 6
#   ENDF_MT: 5
# residual:
#   Z: 43
#   A: 99
#   nuclide: Tc99m
#   level:
#     isomer: 1
# datablock:
#   quantity: cross section
#   columns: 3
#   entries:     457
```

```
##       E              xs            dxs
##     [MeV]           [mb]           [mb]
   6.000000E+00   1.100000E+00   1.100000E+00
   6.100000E+00   9.000000E-01   9.000000E-01
   6.200000E+00   8.000000E-01   8.000000E-01
   6.300000E+00   8.000000E-01   8.000000E-01
..................
```

where this particular example contains data from the IAEA evaluation, extended with TENDL. By far, the majority of files come straight from TENDL, as e.g. *p-Mo100-rp043098.iaea.2024*

```
# header:
#   title: Mo100(p,x)Tc98 cross section
#   source: ENDF
#   user: Arjan Koning
#   date: 2024-10-07
#   format: YANDF-0.2
# endf:
#   library: tendl.2023
#   author: A.J. Koning
#   year: 2023
# target:
#   Z: 42
#   A: 100
#   nuclide: Mo100
# reaction:
#   type: (p,x)
#   ENDF_MF: 6
#   ENDF_MT: 5
# residual:
#   Z: 43
#   A: 98
#   nuclide: Tc98
# datablock:
#   quantity: cross section
#   columns: 2
#   entries: 31
##       E              xs
##     [MeV]           [mb]
   1.685404E+01   0.000000E+00
   1.700000E+01   6.829083E-02
   1.800000E+01   3.388542E+01
   1.900000E+01   1.525024E+02
..................
```

In sum, TENDL is used for the energy ranges outside the IAEA evaluations and for all other isotopes.

6. Reference Guide

In this part, all ISOTOPIA keywords will be described, one per page. The description of each keyword is as follows:

- Name of the keyword
- Explanation
- Examples
- Range of allowed values
- Default value
- Comments (optional), when we feel that some extra warnings or explanation for proper use is appropriate.

In principle, all keywords may be referred to in the other parts of this tutorial.

6.1 ISOTOPIA keywords

As explained above, the minimum input file has 4 keywords, and leaves all choices for the other parameters to the author. In general, you probably want to be more specific. Below, we will explain all the possible keywords. For each keyword, we give an explanation, a few examples, the default value, and the theoretically allowed numerical range. Remember that you can always find all adopted default values for all parameters at the top of the standard *output* file of ISOTOPIA.

abundance

File with tabulated abundances. The **abundance** keyword is only active for the case of a natural target, i.e. if **mass 0**. By default, the isotopic abundances are read from the *isotopia/files/abundance/* database. It can however be imagined that one wants to analyze production from targets of a certain isotopic enrichment. On the input line, we read **abundance** and the filename. From each line of the file, TALYS reads *Z*, *A* and the isotopic abundance with the format (2i4,f11.6). An example of an abundance file, e.g. *abnew*, different from that of the database, is

```
82 206  24.100000
82 207  22.100000
82 208  52.400000
```

where we have left out the "unimportant" ^{204}Pb (1.4%). ISOTOPIA automatically normalizes the abundances to a sum of 1, leading in the above case to 24.44 % of ^{206}Pb, 22.41 % of ^{207}Pb and 53.14 % of ^{208}Pb in the actual calculation.

Examples

abundance abnew

Range

abundance can be equal to any filename, provided it is present in the working directory.

Default

If **abundance** is not given in the input file, abundances are taken from *files/abundance* and calculations for all isotopes are performed.

Adepth

The depth, relative to the target mass number, to which isotopes are scanned for cross sections that contribute to the production path. For example if **Adepth 5** for the p + ^{100}Mo reaction, only yields for elements defined by **Zdepth** and isotopes with mass numbers between 95 and 101 will be calculated.

Examples

Adepth 2
Adepth 10

Range

0 $\leq$ **Adepth** $\leq$ **Atarget** where Atarget is the mass number of the target.

Default

Adepth 20.

Area

Area of the target in cm^2.

Examples

Area 1.

Range

0 <= **Area** <= **10000**.

Default

Area 10. cm^2.

crosspath

Path for the cross section database. You should have this path hardwired in subroutine *machine.f*, but it may be helpful to easily change between different versions of the cross section database.

Examples

crosspath /home/koning/isotopia.libs
crosspath /home/qaim/tendl.2019

Range

crosspath should exist.

Default

Default: **crosspath ∼/libraries/**

decay

Flag to include decay from parent nuclide. Used mostly for code diagnostics.

Examples

```
decay y
decay n
```

Range

y or **n**

Default

decay y

Eback

The lower end of the energy range at the back end of the target in MeV. This energy degradation is directly related to the effective thickness of the target.

Examples

Eback 130.
Eback 12.

Range

0. $\leq$ **Eback** $<$ **Ebeam**

Default

Eback = Ebeam - 5 MeV.

Ebeam

The incident energy of the particle beam in MeV.

Examples

Ebeam 140.
Ebeam 16.

Range

Ebeam $<$ 250. MeV.

Default

None.

element

Either the nuclear symbol or the charge number Z of the target nucleus can be given. Possible values for **element** range from Li (3) to C4 (124).

Examples

element pu
element 41
element V
element B9

Range

3 $\leq$ **element** $\leq$ **124** or **Li** $\leq$ **element** $\leq$ **C4**.

Default

None.

Comments

- To accommodate target nuclides with $Z > 110$ the element names are defined as follows: Rg(111), Cn(112), Nh(113), Fl(114), Mc(115), Lv(116), Ts(117), Og(118), B9(119), C0-4(120-124), which takes as a basis for $Z = 100$ the symbol $A0$, etc. unless an official name has been assigned to it, which is currently the case for $Z \leq 118$. Clearly, if we ever need or wish to go beyond $Z = 124$, there are enough symbols left. Obviously the symbols for Z above 118 will be changed as soon as official names are assigned to them.

format

The format of the metadata in the output files. It may be helpful to specify the version. You may edit the ’format’ variable variable in input.f90 and put your own version there. However, you can also use the input keyword.

Examples

format YANDF-0.3beta2

Range

Any string

Default

YANDF-0.2

Ibeam

Particle beam current in mA.

Examples

Ibeam 0.1
Ibeam 5.

Range

0 <= **Ibeam** <= **10000**.

Default

Ibeam 1. mA.

mass

The target mass number *A*. The case of a natural element can be specified by **mass 0**. Then, an ISOTOPIA calculation for each naturally occurring isotope will be performed (see also the **abundance** keyword, p. 26), after which the results will be properly weighted and summed.

Examples

mass 112
mass 0

Range

mass 0 or **5** $<$ **mass** $\leq$ **339**. The extra condition is that the target nucleus, i.e. the combination of **mass** and **element** must be present in the cross section database, which corresponds to all nuclei with a half life longer than 1 day.

Default

None.

outcross

Flag to output cross sections to separate files.

Examples

outcross y
outcross n

Range

y or **n**

Default

outcross n

projectile

Five different symbols can be given as **projectile**, namely **p, d, t, h, a** representing proton, deuteron, triton, ^{3}He, and alpha, respectively.

Examples

projectile p
projectile d

Range

projectile must be equal to **p, d, t, h, a**.

Default

None.

radiounit

Unit for radioactivity, to be used in the output files for isotope production.

Examples

radiounit Bq: Becquerel
radiounit kBq: kiloBecquerel
radiounit MBq: MegaBecquerel
radiounit GBq: GigaBecquerel
radiounit Ci: Curie
radiounit mCi: milliCurie
radiounit kCi: kiloCurie

Range

radiounit should be equal to one of the units above.

Default

radiounit Mbq.

rho

Material density of the target in g/cm^3.

Examples

rho 10.

Range

0 <= **rho** <= **100**.

Default

rho is read from a hardwired material density table.

source

The source of the calculations. obviously this is ISOTOPIA, but it may be helpful to specify the version such that it appears in the metadata of the many output files. You may edit the 'source' variable variable in input.f90 and put your own version there. However, you can also use the input keyword.

Examples

source TALYS-2.01beta3v20240223

Range

Any string

Default

ISOTOPIA

Tirrad

Irradiation time. A general input for the irradiation time has been enabled. On the input line we read integer values and time units, which can be y (years), d (days), h (hours), m (minutes) or s (seconds). These all need to be separated by blanks.

Examples

Tirrad	**2 d 5 h**
Tirrad	**32 h 30 m**
Tirrad	**1 d 6 h 24 m 12 s**

Range

0 <= **Tirrad** <= **1e6** for every time unit.

Default

Tirrad 1 d.

Tcool

Target cooling time. A general input for the cooling time has been enabled. On the input line we read integer values and time units, which can be y (years), d (days), h (hours), m (minutes) or s (seconds). These all need to be separated by blanks.

Examples

Tcool	**2 d 5 h**
Tcool	**32 h 30 m**
Tcool	**1 d 6 m 24 m 12 s**

Range

0 <= **Tcool** <= **1e6** for every time unit.

Default

Tcool 1 d.

user

The current user who produces the result. You may edit the ’user’ variable in input.f90 and put your own name there. It will appear in the metadata of the various output files. However, you can also use the input keyword.

Examples

user Vlad Avrigeanu

Range

Any string

Default

Arjan Koning

xsfile

Local file with cross sections. With this keyword, residual production cross sections from TENDL can be overruled with values given in your working directory. On the input line, we read **xsfile**, Z and A of the residual product, the filename, and optionally the number of the produced isomer. This file should consist of Energy [MeV] - cross section [mb] values in x-y form, with a similar structure as those of the cross section database.

Examples

xsfile 25 56 Mn56.exp
xsfile 42 100 Mo100.loc 1

Range

xsfile should exist.

Default

None.

yieldunit

Unit for isotope yield, in weight or number of isotopes.

Examples

yieldunit mug: microgram
yieldunit mg: milligram
yieldunit g: gram
yieldunit kg: kilogram
yieldunit num: number of isotopes

Range

yieldunit should be equal to one of the units above.

Default

yieldunit num.

ZAoutput

Flag to use numerical Z and A values in the filenames instead of nuclide names.

Examples

ZAoutput y
ZAoutput n

Range

y or **n**

Default

ZAoutput n

Zdepth

The depth, relative to the target charge number, to which isotopes are scanned for cross sections that contribute to the production path. For example if **Zdepth 2** for the p + Mo reaction, only yields for Tc, Mo, Nb and Zr isotopes will be calculated.

Examples

Zdepth 2
Zdepth 10

Range

0 $\leq$ **Zdepth** $\leq$ **Ztarget** where Ztarget is the mass number of the target.

Default

Zdepth 10.

Table 6.1: The keywords of ISOTOPIA.

Keyword	Range	Default	Page
abundance	filename	no default	26
Adepth	0-Atarget	20	27
Area	0. - 10000.	10.	28
crosspath	directory name	˜/libraries/	29
decay	y,n	y	30
Eback	1.e-11 - 200.	Ebeam - 5	31
Ebeam	1.e-11 - 200.	None	32
element	3 - 124 or Li - C4	None	33
format	format name	YANDF	34
Ibeam	0. - 10000.	10.	35
mass	0, 5 - 339	None	36
outcross	y,n	n	37
projectile	p,d,t,h,a,	None	38
radiounit	(k,M,G)Bq, (m,k)Ci	Gbq	39
rho	0. - 100.	1.	40
source	name of source	ISOTOPIA	41
Tirrad	0 - 1.e6	1 d	42
Tcool	0 - 1.e6	1 d	43
user	your name	no default	44
xsfile	file name	none	45
yieldunit	num, mug, mg, g or kg	num	46
ZAoutput	y,n	n	47
Zdepth	0-Ztarget	10	48

7. Sample cases

The purpose of ISOTOPIA is that every imaginable production route for a medical isotope can be simulated. To strengthen this statement, we will discuss a few sample cases. In each case, the ISOTOPIA input file, the relevant output and if appropriate, a figure will be presented. The description of the first sample case is the longest, since the output of ISOTOPIA will be discussed in complete detail. Obviously, that output description is also applicable to the other sample cases. The entire collection of sample cases serves as (a) verification of ISOTOPIA: the sample output files should coincide, apart from numerical differences of insignificant order, with the output files obtained by you, and (b) validation of ISOTOPIA: the results should be comparable to those obtained in other publications. The computation time of ISOTOPIA is very small. In general, we will explain the keywords again as they appear in the input files below. If not, consult Table 6.1, which will tell you where to find the explanation of a keyword.

7.1 Sample p-Mo100-Tc099m: Accelerator production of ^{99m}Tc

This sample case considers one of the most discussed alternatives for reactor-produced ^{99}Mo: the direct production of ^{99m}Tc from ^{100}Mo with a proton accelerator via the (p,2n) reaction. The input file for this case is as follows,

```
projectile p
element Mo
mass 100
Ebeam 16.
Eback 12.
Ibeam 0.15
```

Running this input file with

isotopia < isotopia.inp > isotopia.out

gives an output file with the general characteristics of the reaction. The output file starts with a display of the version of ISOTOPIA you are using, the name of the author, the Copyright statement and then an exact copy of the input file as given by the user is returned.

```
   ISOTOPIA-2.1    (Version: December 29, 2024)

          Prediction of medical isotope production with accelerators

Copyright (C) 2024  A.J. Koning

User: Arjan Koning
Date: 2024-12-22

########## USER INPUT ##########

USER INPUT FILE

projectile p
element mo
mass 100
ebeam 16.
eback 12.
ibeam 0.15

USER INPUT FILE + DEFAULTS

Keyword           Value   Variable     Explanation

user      Arjan Koning    user         user for this calculation
source    ISOTOPIA        source       source for this calculation
format    YANDF-0.2       oformat      format for output
#
# Nuclear reaction
#
projectile          p     ptype0       type of incident particle
element            Mo     Starget      symbol of target nucleus
mass              100     Atarget      mass number of target nucleus
#
# Accelerator
#
Ebeam              16.000 Ebeam        incident energy in MeV
Eback              12.000 Eback        lower end of energy range in MeV
Ibeam               0.150 Ibeam        beam current in mA
Tirrad              1     Tirrad       d of irradiation time
radiounit             gbq radiounit    unit for radioactivity
yieldunit             num yieldunit    unit for isotope yield
#
# Target
#
```

```
 Area                1.000 Area         target area in cm^2
 Tcool               1     Tcool        d of cooling time
 rho                -1.000 rhotarget    target density [g/cm^3]
 #
 # Cross section and decay data
 #
 Zdepth             10     Zdepth       depth to which Z numbers are scanned for cross sections
 Adepth             20     Adepth       depth to which A numbers are scanned for cross sections
```

Not only the keywords that you have specified in the input file are listed, but also all the defaults that are set automatically. The corresponding Fortran variables are also printed, together with a short explanation of their meaning. This table can be helpful as a guide to change further input parameters for a next run. You may also copy and paste the block directly into your next input file.

In the next output block we print the main parameters that characterize the production process. Note that some of these have been given in the input, while others are automatically calculated.

```
 Summary of isotope production for p + Mo100

 Maximal irradiation time:       0 years   1 days  0 hours  0 minutes  0 seconds
 Cooling time:       0 years   1 days  0 hours  0 minutes  0 seconds
 E-beam [MeV]:   1.600000E+01
 E-back [MeV]:   1.200000E+01
 Beam current [mA]:        0.150 mA
 Target material density [g/cm^3]:   1.022000E+01
 Target area [cm^2]:   1.000000E+00
 Effective target thickness [cm]:   2.097696E-02
 Effective target volume [cm^3]:   2.097696E-02
 Effective target mass [g]:   2.143845E-01
 Number of target atoms:    1.291053E+21
 Number of incident particles [s^-1]:   9.362260E+14
 Produced heat in target [kW]:   6.000000E-01
```

The block with final results is

```
 (Maximum) production and decay rates per isotope

 Total production rate [s^-1]:   9.624934E-10

#  Nuc     Production rate Decay rate     Activity       #isotopes      Yield          Isotopic fr
#             [s^-1]         [s^-1]         [GBq]          [   ]        [GBq/mAh]
 Tc 101     9.115965E-13   8.135531E-04   1.176901E+00   1.446618E+12   3.427384E-03   0.00004
 Tc 100     6.088757E-11   4.387007E-02   7.860895E+01   1.791858E+12   3.032753E-01   0.00051
 Tc  99     7.742050E-10   1.026401E-13   2.616365E+02   7.370476E+16   6.840031E-10   0.54037
 Tc  99 g   5.875616E-10   1.026401E-13   6.726828E-06   6.553800E+16   5.190665E-10   0.40869
 Tc  99 m   2.162431E-10   3.203675E-05   2.616365E+02   8.166760E+15   5.800662E-02   0.05093
 Mo 100     1.174375E-10   0.000000E+00   0.000000E+00   1.290946E+21   0.000000E+00   1.00000
..................
  End of ISOTOPIA calculation for p + Mo100
```

The time-dependent production of each isotope is found the files *ZZAAA.act* or *ZZAAAm.act* if is concerns isomeric production, with ZZ the charge number in (i2.2) format and AA the mass number in (i3.3) format.

For this case, obviously most important is the production of ^{99m}Tc, given in file *Tc099m.act*, which looks as follows,

```
# header:
#   title: Mo100(p,x)Tc99m Isotope production
#   source: ISOTOPIA
#   user: Arjan Koning
#   date: 2024-12-22
#   format: YANDF-0.2
# target:
#   Z: 42
#   A: 100
#   nuclide: Mo100
# reaction:
#   type: (p,x)
#   ENDF_MF: 6
#   ENDF_MT: 5
# residual:
#   Z: 43
#   A: 99
#   nuclide: Tc99m
# parameters:
#   Beam current [mA]:  1.500000E-01
#   E-Beam [MeV]:  1.600000E+01
#   E-Back [MeV]:  1.200000E+01
#   Initial production rate [s^-1]:  2.162431E-10
#   Decay rate [s^-1]:  3.203675E-05
#   Initial production yield [GBq/mAh]:  5.800662E-02
#   Total activity at EOI [GBq]:  2.616365E+02
#   Irradiation time:       0 years   1 days  0 hours  0 minutes  0 seconds
#   Cooling time:       0 years   1 days  0 hours  0 minutes  0 seconds
#   Half-life:       0 years   0 days  6 hours  0 minutes 36 seconds
#   Maximum production:       0 years   3 days 18 hours 17 minutes 18 seconds
# datablock:
#   quantity: Isotope production
#   columns: 6
#   entries: 100
##     Time         Activity       Isotopes         Yield      Isotopic_frac.      Time
##     [sec]          [GBq]           []          [GBq/mAh]          []              [h]
   1.728000E+03   1.503532E+01   4.693146E+14   5.800662E-02   1.336947E-01   4.800000E-01
   3.456000E+03   2.926088E+01   9.133534E+14   5.488257E-02   1.306088E-01   9.600000E-01
   5.184000E+03   4.272030E+01   1.333478E+15   5.192677E-02   1.275825E-01   1.440000E+00
   6.912000E+03   5.545484E+01   1.730975E+15   4.913017E-02   1.246355E-01   1.920000E+00
   8.640000E+03   6.750352E+01   2.107065E+15   4.648413E-02   1.217707E-01   2.400000E+00
.....................
```

In the file above, the general irradiation characteristics are repeated, as well as the total production rates. The activity as a function of time is presented in Fig. 7.1. Note that the production yield decreases as a function of time since ^{99m}Tc has a half life of 6 hours. Also the last column in this file can be related to the purity or specific activity of ^{99m}Tc relative to the other Tc isotopes and ^{99c}Tc.

Note that the directory also lists the following files

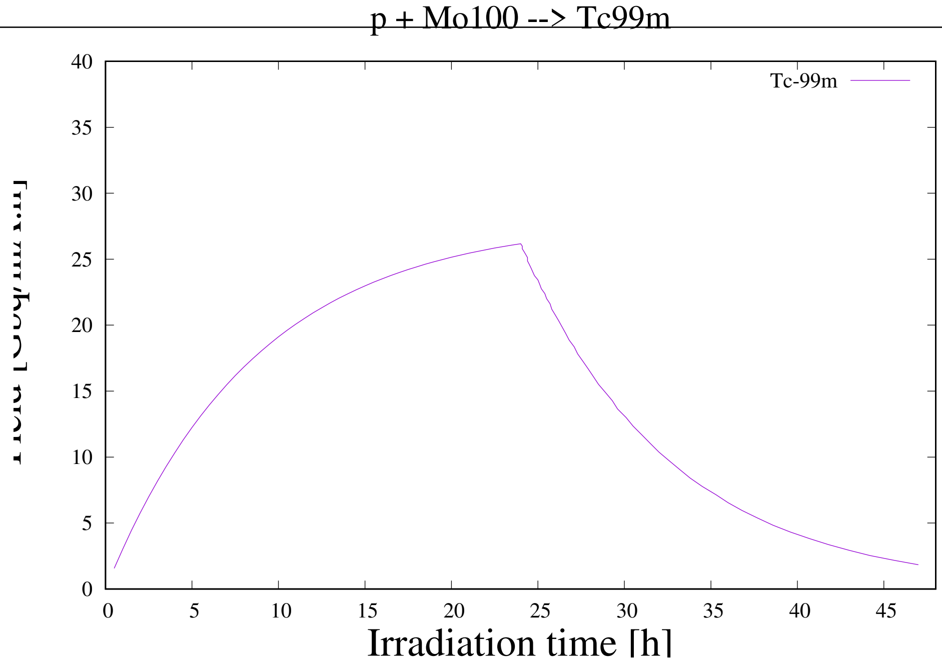

Figure 7.1: Production of Tc-99m

```
Mo099.act
Mo100.act
Tc099.act
Tc099g.act
Tc099m.act
Tc100.act
Tc101.act
```

which represent the isotopes, of which some can be regarded as 'impurities', which are produced simultaneously.

7.2 Sample a-Bi209-At211: alpha-induced production of therapeutic nuclide ^{211}At

This production route is listed in Table 1 of Ref. [8]. The corresponding input file for this case is

```
projectile a
element Bi
mass 209
Ebeam 28.
Eback 10.
Ibeam 0.100
```

Ref. [8] lists an initial production yield of 17.5 Mbq/(μA.h), while ISOTOPIA produces a value of 22.5, see the output file. Note that there is still some uncertainty with regards to the production cross section.

7.3 Sample p-Ga069-Ge068: Production of the ^{68}Ge generator for ^{68}Ga

There are various production routes for this isotope. The input file for this case is

```
projectile p
element Ga
mass 69
Ebeam 25.
Eback 15.
Tirrad 7 d
radiounit Ci
outcross y
```

Note that in this input file we have include some other features of ISOTOPIA, which of course can also be used in all other input files. The irradiation time is 7 days, while we request the output to be in Ci instead of GBq. In this case, the output file of most interest is probably *Ge068.act*. Also, all residual production cross sections for this reaction are printed in separate files.

7.4 Sample p-Th232-Ac225: Production of ^{225}Ac from ^{232}Th

As an example of the high-energy end of the domain of ISOTOPIA, we include the following sample case,

```
projectile p
element Th
mass 232
Ebeam 192
Eback 170.
Ibeam 0.10
```

Note that activation files for many isotopes are produced. The higher the incident energy, the more side-products are made, and many of them could be unwanted.

8. Outlook and conclusions

This tutorial describes ISOTOPIA-2.2, a software package for the prediction of medical isotope production using an accelerator.

The formalism employed in version 2.2 to calculate all isotopic activity yields, is based on the direct production and β-decay of the isotopes. Feeding of the isotope through β-decay of other nuclei produced in the nuclear reactions is taken into account for one parent nuclide only, which for charged-particle induced reactions is generally sufficient. In general, one would like to include the processes of all β-decay feeding as well as nuclear reactions of already produced nuclei (which occurs at a high target burn-up) in an exact calculation. This can only be achieved by fully simulating the radiation transport and the burn-up of the target. For most cases of interest, this is however not necessary. Nevertheless, we may upgrade ISOTOPIA with a general differential equation solver in the future.

ISOTOPIA is complete in the sense that it produces results for all possible isotope production paths. The quality of the prediction is directly related to the current quality of the cross section database. The backbone of the cross section database is TENDL-2023. TENDL is gradually transforming from a calculated data library into an evaluated data library. This means that in addition to global theoretical improvements in the TALYS code, an increasing number of experimental cross section sets will be taken into account in future versions of TENDL. Until that time, and probably also after, the addition of the IAEA medical isotope database is indispensable.

In terms of functionality, we can think of at least one obvious extension, which is the ability to answer the "inverse question": *Given a desired isotope*, how do the various production routes relate to each other, in terms of projectile type, energy ranges, impurities, etc. and what is the optimal production route? In the current version of ISOTOPIA, we can only perform the "forward route": on the basis of an intuitively promising production route, we calculate all results of interest. A loop over the entire ISOTOPIA code needs to be built for this extension, after which a clever optimization (search) routine would provide the answer. Given the short calculation time of a typical ISOTOPIA run, this looks feasible.

Another addition is to allow calculations with multiple incident energies. At the moment only one incident energy is given. If an incident energy grid would be given, the production yield as a function of incident energy can be calculated in one run, rather than performing several ISOTOPIA runs for each incident energy.

Finally, at the moment ISOTOPIA can only be used for charged-particle accelerator beams. With the addition of photonuclear and neutron (e.g. from a reactor) induced reactions it would become a “complete” isotope production code. Two issues need to be solved for that:

- For photonuclear reactions: the equivalent of stopping power for charged-particles needs to be taken into account
- For neutron-induced reactions: a folding over the (reactor) spectrum needs to be included.

Both extensions seem to be feasible, at first sight.

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A. Derivation of the isotope production equations

A.1 Differential equations for production and depletion of isotopes

The most general situation is that of the irradiation of a piece of material, consisting of many different isotopes, which were either present at the start of the irradiation, have been formed, or will be formed during the irradiation, by either the primary flux of particles, by secondary particles, or by radioactive decay. If we have a total of K different isotopes and the number of each isotope k is N_k, then the temporal development of such a system, during irradiation and decay, is described by K differential equations:

$$\begin{aligned}
\frac{dN_1(t)}{dt} &= \sum_{k=1,k\neq 1}^{K} \Lambda_{k\rightarrow 1} N_k(t) - \Lambda_1 N_1(t) \\
&\dots \\
\frac{dN_i(t)}{dt} &= \sum_{k=1,k\neq i}^{K} \Lambda_{k\rightarrow i} N_k(t) - \Lambda_i N_i(t) \\
&\dots \\
\frac{dN_K(t)}{dt} &= \sum_{k=1,k\neq K}^{K} \Lambda_{k\rightarrow K} N_k(t) - \Lambda_K N_K(t) \qquad \text{(A.1)}
\end{aligned}$$

In each equation, the first term is a feeding term. In the most general case, various parent nuclides k may contribute to the formation of isotope i, hence the summation over k, with $\Lambda_{k\rightarrow i}$ the partial formation rate for any possible parent isotope k to isotope i. Each partial formation rate can be expressed as

$$\Lambda_{k\rightarrow i} = \lambda_{k\rightarrow i} + R_{k\rightarrow i} \qquad \text{(A.2)}$$

with $\lambda_{k\rightarrow i}$ the (partial) radioactive decay rate and $R_{k\rightarrow i}$ the (partial) nuclear reaction rate for any possible parent isotope k to isotope i. The second terms of Eq. (A.1) are loss terms due to radioactive decay and nuclear reactions from isotope i to any other isotope. Here the total depletion rate (we interchange "depletion" with "formation" whenever appropriate) for isotope i is

$$\Lambda_i = \lambda_i + R_i \tag{A.3}$$

where the total decay rate for isotope i is

$$\lambda_i = \sum_{k=1,k\neq i}^{K} \lambda_{i\to k}$$

and the total nuclear reaction rate for isotope i is

$$R_i = \sum_{k=1,k\neq i}^{K} R_{i\to k} \tag{A.4}$$

The entire loop over k may run over isotopes in their ground or isomeric states. Theoretically, the sum over reaction rates could include secondary particles (neutrons, photons, alpha particles etc.) formed after the first interaction of the incident beam with the material, over the entire outgoing energy spectrum. Since the number of isotopes i, $N_i(t)$ may appear simultaneously in many equations, due to its possible formation, or depletion, by many different nuclear reactions, it is clear that such a coupled system can only be solved by complicated mathematical and computational techniques. In fact, the most exact simulation would involve a Monte Carlo 3D transport calculation in which all primary and secondary particles are taken into account, including complete cross section libraries for all possible particles, coupled with an activation code that keeps track of the nuclide inventory. If we neglect such thick target transport issues, a system of equations like (A.1) is often solved by methods developed by Bateman [9] for radioactive decay and later generalized for source terms by Rubinson [10].

Fortunately, the situation is often not as complex as sketched above, since very reasonable approximations can be introduced into Eq. (A.1), which represent cases which are used in practice. First, let us start with the common case of the irradiation of a target which contains of only one natural element at the start of the irradiation. This set of equations can be then be separated into a linear combination of contributions by each target *isotope*. Hence, we solve Eq. (A.1) one by one for each target isotope and add these contributions at the end to get the activation for the target material. Then, for such a mono-isotopic target T we have at the start of the irradiation

$$\begin{aligned} t = 0 : N_T &= N_T(0) = N_0 \\ N_i &= 0 \\ &\dots \\ N_K &= 0 \end{aligned} \tag{A.5}$$

Since in practice our target isotope is not radioactive, the loss terms reduce to $\Lambda_T = R_T$ in Eq. (A.1) for N_T. Next, if a substantial part of the target is converted into other isotopes, beam particles may interact with atoms other than the original target atoms. However, this is only a concern for very long irradiation times. For most practical applications, like medical isotope production, we can often assume that the burn-up of the target is small and that the target composition does not change much during the irradiation (this will be confirmed by some of our sample cases). Hence, in addition we will assume there are no nuclear reaction or radioactive decay feeding terms for the *target* isotope T.

This means that the temporal evolution of the target isotope is described by the following simple equation

$$\frac{dN_T(t)}{dt} = -R_T N_T(t) \tag{A.6}$$

which basically states that the only thing that happens to the target material is burn-up through nuclear reactions.

For the isotopes that are produced during the irradiation, which are of course more interesting, we can make similar reasonable assumptions. We assume there is no loss of *produced* isotopes of interest through nuclear reactions with beam particles, i.e. we assume nuclides which are produced are not hit twice (again, this assumption becomes less accurate at very long irradiation times). This is equivalent to stating that the isotopes of interest are only produced from nuclear reactions on the target isotopes or from decay of other products formed during the irradiation. Also, consistent with the assumption for the target isotope that nuclides are not hit twice, we have $\Lambda_i = \lambda_i$ for the depletion term, and assume that no other nuclear reactions lead to the isotope of interest. Thus for the produced isotopes i we obtain

$$\frac{dN_i(t)}{dt} = \sum_{k=1,k\neq i}^{K} \lambda_{k\rightarrow i} N_k(t) + R_{T\rightarrow i} N_T(t) - \lambda_i N_i(t) \tag{A.7}$$

Nuclides often have only one or a few radioactive decay modes. Usually, only beta decay to the ground state or an isomer needs to be considered, although in some cases alpha decay may occur as well. If we neglect alpha decay, the summation in the first term above reduces to only one term. Thus, Eq. (A.7) reduces to

$$\frac{dN_i(t)}{dt} = \lambda_{p\rightarrow i} N_p(t) + R_{T\rightarrow i} N_T(t) - \lambda_i N_i(t) \tag{A.8}$$

where we now use the subscript p for the parent isotope which decays to isotope i. The parent isotope itself is produced from nuclear reactions on the target and is described by the equation,

$$\frac{dN_p(t)}{dt} = R_{T\rightarrow p} N_T(t) - \lambda_p N_p(t) \tag{A.9}$$

where for simplicity we have left out a possible feeding term $\lambda_{g\rightarrow p} N_g(t)$ from its own parent (i.e. the grandparent g of isotope i). It neglects radioactive decay to channels produced by multiple proton emission, e.g. ^{120}Te(p,2p)^{119}Sb and the contribution from its feeding channel ^{120}Te(p,2n)^{119}I + $2\beta^+$. Although the (p,2p) channel is generally smaller and therefore often not relevant for most practical medical isotope production routes, it would be safer that at higher energies feeding from radioactive decay is taken into account. For that a more general solution of Eq. (A.1) would have to be implemented, similar to solutions for neutron-induced problems where processes like e.g. multiple decay of fission fragments needs to be taken into account. For most charged-particle induced reactions of interest, the current approximation is justified.

A.2 Solution of the differential equations

Here we derive the solutions (4.1) of the differential equations (A.6)-(A.9). Eq. (4.1) has been implemented in ISOTOPIA.

For the target nuclide we have

$$\frac{dN_T(t)}{dt} = -R_T N_T(t). \tag{A.10}$$

This is easily integrated to give

$$N_T(t) = N_0\, e^{-R_T t}. \tag{A.11}$$

For every parent nuclide we have

$$\frac{dN_p(t)}{dt} = R_{T\to p} N_T(t) - \lambda_p N_p(t). \tag{A.12}$$

Multiplying both sides with $e^{\lambda_p t}$ gives

$$e^{\lambda_p t}\frac{dN_p(t)}{dt} = e^{\lambda_p t}\left[R_{T\to p} N_T(t) - \lambda_p N_p(t)\right], \tag{A.13}$$

or,

$$e^{\lambda_p t}\frac{dN_p(t)}{dt} + e^{\lambda_p t}\lambda_p N_p(t) = e^{\lambda_p t} R_{T\to p} N_T(t), \tag{A.14}$$

or,

$$\frac{d[e^{\lambda_p t} N_p(t)]}{dt} = e^{\lambda_p t} R_{T\to p} N_T(t). \tag{A.15}$$

Integrating this, after insertion of Eq. (A.11), gives

$$\begin{aligned} e^{\lambda_p t} N_p(t) &= N_0 R_{T\to p}\int dt e^{(\lambda_p - R_T)t} \\ &= \frac{N_0 R_{T\to p}}{\lambda_p - R_T} e^{(\lambda_p - R_T)t} + C, \end{aligned} \tag{A.16}$$

or,

$$N_p(t) = \frac{N_0 R_{T\to p}}{\lambda_p - R_T} e^{-R_T t} + C e^{-\lambda_p t}. \tag{A.17}$$

Inserting the initial condition $N_p(t=0) = 0$ gives

$$0 = \frac{N_0 R_{T\to p}}{\lambda_p - R_T} + C, \tag{A.18}$$

giving the solution for the parent nuclide,

$$N_p(t) = \frac{N_0 R_{T\to p}}{\lambda_p - R_T}\left[e^{-R_T t} - e^{-\lambda_p t}\right]. \tag{A.19}$$

For every isotope i, directly produced by a nuclear reaction on the target isotope or from decay of the parent nuclide, we have

$$\frac{dN_i(t)}{dt} = \lambda_{p\to i} N_p(t) + R_{T\to i} N_T(t) - \lambda_i N_i(t). \tag{A.20}$$

Multiplying both sides with $e^{\lambda_i t}$ gives analogous to Eqs. (A.13)-(A.15),

$$\frac{d[e^{\lambda_i t} N_i(t)]}{dt} = e^{\lambda_i t}\left[\lambda_{p\to i} N_p(t) + R_{T\to i} N_T(t)\right], \tag{A.21}$$

or, after insertion of the solutions for N_T, Eq. (A.11), and N_p, Eq. (A.19),

$$\frac{d[e^{\lambda_i t}N_i(t)]}{dt} = e^{\lambda_i t}\left[\lambda_{p\to i}\frac{N_0 R_{T\to p}}{\lambda_p - R_T}(e^{-R_T t} - e^{-\lambda_p t}) + N_0 R_{T\to i} e^{-R_T t}.\right] \tag{A.22}$$

Integrating this gives

$$\begin{aligned} e^{\lambda_i t}N_i(t) &= \frac{N_0\lambda_{p\to i}R_{T\to p}}{\lambda_p - R_T}\left[\int dt e^{(\lambda_i - R_T)t} + \int dt e^{(\lambda_i - \lambda_p)t}\right] \\ &+ N_0 R_{T\to i}\int dt e^{(\lambda_i - R_T)t} + C, \end{aligned} \tag{A.23}$$

or,

$$\begin{aligned} N_i(t) &= \frac{N_0\lambda_{p\to i}R_{T\to p}}{\lambda_p - R_T}\left[\frac{e^{-R_T t}}{\lambda_i - R_T} + \frac{e^{-\lambda_p)t}}{\lambda_i - \lambda_p}\right] \\ &+ \frac{N_0 R_{T\to i}}{\lambda_i - R_T}e^{-R_T t} + Ce^{-\lambda_i t}. \end{aligned} \tag{A.24}$$

Inserting the initial condition $N_i(t = 0) = 0$ gives

$$0 = \frac{N_0\lambda_{p\to i}R_{T\to p}}{\lambda_p - R_T}\left[\frac{1}{\lambda_p - R_T} + \frac{1}{\lambda_i - \lambda_p}\right] + \frac{N_0 R_{T\to i}}{\lambda_i - R_T} + C, \tag{A.25}$$

so we finally obtain

$$N_i(t) = N_0\,\frac{R_{T\to i}}{\lambda_i - R_T}\,[e^{-R_T t} - e^{-\lambda_i t}] + N_0\frac{\lambda_{p\to i}R_{T\to p}}{\lambda_p - R_T}\left[\frac{e^{-R_T t} - e^{-\lambda_i t}}{\lambda_i - R_T} - \frac{e^{-\lambda_p t} - e^{-\lambda_i t}}{\lambda_i - \lambda_p}\right]. \tag{A.26}$$

The three solutions of interest are thus given by Eqs. (A.11), (A.19), and (A.26).