

# **ISOTOPIA-1.0**

**Simulation of medical isotope production with accelerators**

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## 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, and 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. For ISOTOPIA, we use the IAEA medical isotope data library for about 150 reaction channels, complemented by TENDL-2017 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  $^{99}\text{Mo}/^{99m}\text{Tc}$  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 a nuclear (research) reactor and via the photonuclear route.

At certain moments in time, a well-defined version of ISOTOPIA is frozen. You are now reading the manual of version 1.0. 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, [www.xxx.xxx](http://www.xxx.xxx), which allows to analyze production routes in an efficient way via a GUI.

ISOTOPIA-1.0 falls in the category of GNU General Public License software. Please read the

release conditions on the next page. Although I have invested some effort in the validation of this package, I will not make the mistake to guarantee perfection. Therefore, in exchange for the free use of ISOTOPIA: If you find any errors, or in general have any comments, corrections, extensions, questions or advice, I would like to hear about it. You can reach me at **A.koning@iaea.org**.

## Acknowledgements

I wish to thank a few persons who have contributed to the present state of ISOTOPIA:

- 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  $^{68}\text{Ga}$ ,
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- Roberto Capote Noy and the entire consortium responsible for the IAEA medical isotope data library, for helpful discussions and for providing the data library,
- Natalie Gaughan, for testing many of the isotope yield calculations with the TALYS code,
- Marco Verpelli, for integrating ISOTOPIA in the Medical Isotope Browser and for suggesting the associated improvements to the code.

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# Contents

<b>1</b>	<b>Introduction .....</b>	<b>7</b>
1.1	How to use this manual	8
<b>2</b>	<b>Installation and getting started .....</b>	<b>11</b>
2.1	The ISOTOPIA package	11
2.2	Installation	11
2.3	Verification	12
2.4	Getting started	12
<b>3</b>	<b>Medical isotope production .....</b>	<b>13</b>
3.1	Production and depletion of isotopes	13
3.2	Initial condition and stopping power	16
3.3	Nuclear reaction and decay rates	17
3.4	Activities	18
<b>4</b>	<b>Nuclear data libraries .....</b>	<b>19</b>
<b>5</b>	<b>Input description .....</b>	<b>21</b>
5.1	Basic input rules	22
5.2	ISOTOPIA keywords	22
<b>6</b>	<b>Sample cases .....</b>	<b>45</b>
6.1	Sample p-Mo100-Tc099m: Accelerator production of $^{99m}\text{Tc}$	45

<b>7</b>	<b>Outlook and conclusions .....</b>	<b>49</b>
	<b>Bibliography .....</b>	<b>51</b>
<b>A</b>	<b>Derivation of the isotope production equations .....</b>	<b>53</b>
<b>B</b>	<b>TERMS AND CONDITIONS FOR COPYING, DISTRIBUTION AND MODIFI- CATION .....</b>	<b>55</b>
	<b>Index .....</b>	<b>59</b>



# 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  $^{99}\text{Mo}/^{99m}\text{Tc}$  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 impurities after irradiation and after a cooling period?
- How much do the answers to the above questions depend on the use of an isotopically

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 based answers 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 list of bullets above.

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 impurities.
- 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 manual.
- 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-2017 nuclear data library [6], produced by the nuclear reaction model code TALYS [5],
- the IAEA medical isotope database, high-quality in-depth evaluations of important reaction channels, on the basis of available experimental data.

The current manual 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, [www.xxx.xxx](http://www.xxx.xxx), 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 manual

Although we would be honored if you would read this manual from the beginning to the end, we can imagine that not all parts are necessary, relevant or suitable to you. For example if you are just an interested physicist who does not own a computer, you may skip

Chapter 2: Installation guide for ISOTOPIA.

The general formalism employed for the production yield calculation of radioactive isotopes, which are formed in a nuclear reaction, can be found in

Chapter 3: General formalism for isotope production.

The nuclear reaction and structure information needed for the calculations are outlined in



Chapter 4: Cross section and decay data.

For your own calculations, you will need

Chapter 5: Input description.

The next chapter we consider to be quite important, since it contains ready to use starting points (sample cases) for your own work,

Chapter 6: Sample cases and verification.

Finally, this manual ends with

Chapter 7: 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:

- *README* outlines the contents of the package.
- *isotopia.setup* is a script that takes care of the installation.
- *source/* contains the source code of ISOTOPIA: 26 Fortran subroutines, and the file *isotopia.cmb*, which contains all variable declarations and common blocks.
- *files/* contains the natural abundances and the decay data library.
- *doc/* contains the documentation: this manual 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.f* 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 dependences 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.f*.

ISOTOPIA has been successfully tested for the gfortran compiler.

### 2.2 Installation

The installation of ISOTOPIA is straightforward. The first steps are

- Copy the *isotopia.libs.tar* file to your hard disk.
- **tar xzf isotopia.libs.tar**, which installs the cross section database



- Copy *isotopia.tar* file to your hard disk.
- **tar xzf isotopia.tar**

The installation is expected to be handled by the *isotopia.setup* script, as follows

- edit *isotopia.setup* and set the first two variables: the name of your FORTRAN compiler and the place where you want to store the ISOTOPIA executable.
- **isotopia.setup**

If this does not work for some reason, we here provide the necessary steps to do the installation manually.

- Ensure that ISOTOPIA can read the data directory with cross sections and decay data. This is done in subroutine *machine.f*. If *isotopia.setup* has not already replaced the path name in *machine.f*, do it yourself. We think this is the only machine dependence of ISOTOPIA.
- **gfortran -c \*.f**
- **gfortran \*.o -o isotopia**
- **mv isotopia ~/bin** (assuming you have a *~/bin* directory which contains all executables that can be called from any working directory)

The above commands represent the standard compilation options. Consult the manual 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 5. Chapter 6 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 name *isotopia.inp* is not obligatory: you can use any name for this file. Besides the general output file *isotopia.out* various other output files are produced.

## 3. Medical isotope 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. This may be generalized in future versions.

### 3.1 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 (theoretically  $K$  may stand for the entire nuclide chart) 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:

$$\begin{aligned}\frac{dN_1(t)}{dt} &= \sum_{k=1, k \neq 1}^K \Lambda_{k \rightarrow 1} N_k(t) - \Lambda_1 N_1(t) \\ &\dots \\ \frac{dN_i(t)}{dt} &= \sum_{k=1, k \neq i}^K \Lambda_{k \rightarrow i} N_k(t) - \Lambda_i N_i(t) \\ &\dots \\ \frac{dN_K(t)}{dt} &= \sum_{k=1, k \neq K}^K \Lambda_{k \rightarrow K} N_k(t) - \Lambda_K N_K(t)\end{aligned}\tag{3.1}$$

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

$$\Lambda_{k \rightarrow i} = \lambda_{k \rightarrow i} + R_{k \rightarrow i} \quad (3.2)$$

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. (3.1) 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

$$\Lambda_i = \lambda_i + R_i \quad (3.3)$$

where the total decay rate for isotope  $i$  is

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

and the total nuclear reaction rate for isotope  $i$  is

$$R_i = \sum_{k=1, k \neq i}^K R_{i \rightarrow k} \quad (3.4)$$

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 (3.1) is often solved by methods developed by Bateman [1] for radioactive decay and later generalized for source terms by Rubinson [8].

Fortunately, the situation is often not as complex as sketched above, since very reasonable approximations can be introduced into Eq. (3.1), 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. (3.1) one by one for each target isotope and add these contributions at the end to get the answer for the target material. Then, for such a mono-isotopic target  $T$  we have at the start of the irradiation

$$\begin{aligned} t = 0 : N_T &= N_T(0) \\ N_i &= 0 \\ &\dots \\ N_K &= 0 \end{aligned} \quad (3.5)$$

Since in practice our target isotope is not radioactive, the loss terms reduce to  $\Lambda_T = R_T$  in Eq. (3.1) 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 irradiation times of the order of months or longer. 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

$$\frac{dN_T(t)}{dt} = -R_T N_T(t) \quad (3.6)$$

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

$$\frac{dN_i(t)}{dt} = \sum_{k=1, k \neq i}^K \lambda_{k \rightarrow i} N_k(t) + R_{T \rightarrow i} N_T(t) - \lambda_i N_i(t) \quad (3.7)$$

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. (3.7) reduces to

$$\frac{dN_i(t)}{dt} = \lambda_{p \rightarrow i} N_p(t) + R_{T \rightarrow i} N_T(t) - \lambda_i N_i(t) \quad (3.8)$$

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,

$$\frac{dN_p(t)}{dt} = R_{T \rightarrow p} N_T(t) - \lambda_p N_p(t) \quad (3.9)$$

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.  $^{120}\text{Te}(p, 2p)^{119}\text{Sb}$  and the contribution from its feeding channel  $^{120}\text{Te}(p, 2n)^{119}\text{I} + 2\beta^+$ . 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. (3.1) 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.

If we now use the boundary conditions  $N_T(t=0) = N_T(0)$  and  $N_p(t=0) = N_i(t=0) = 0$ , the solutions to these equations are given by:

$$\begin{aligned} N_T(t) &= N_T(0) e^{-R_T t}, \\ N_p(t) &= N_T(0) \frac{R_{T \rightarrow p}}{\lambda_p - R_T} [e^{-R_T t} - e^{-\lambda_p t}], \\ N_i(t) &= N_T(0) \frac{R_{T \rightarrow i}}{\lambda_i - R_T} [e^{-R_T t} - e^{-\lambda_i t}] + N_T(0) \frac{R_{T \rightarrow p} \lambda_{p \rightarrow i}}{\lambda_p - R_T} \left[ \frac{e^{-R_T t} - e^{-\lambda_i t}}{\lambda_i - R_T} - \frac{e^{-\lambda_p t} - e^{-\lambda_i t}}{\lambda_i - \lambda_p} \right] \end{aligned} \quad (3.10)$$

This is derived in the Appendix. Note that the 3 equations in Eq. (3.10) are more general than what is used in most studies. Often the only term that is used is that of a radioactive isotope which is directly produced from the target and which radioactively decays itself. Eq. (3.10) considers, with the first line, the burn-up of the target, and also, with the second line, the possible production of the isotope of interest via an indirect route. The rate  $R_T$  is in general very small compared to the irradiation time, of the order of  $10^{-10} \text{ s}^{-1}$ , i.e.  $N_T(t) \sim N_T(0)$  and one could discard the first line of Eq. (3.10). 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. (3.10) will then 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. (3.10).

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

$$t_{max} = \frac{\ln(\lambda_i/R_T)}{\lambda_i - R_T} \quad (3.11)$$

The production of  $i$  is restrained by its  $\beta$ -decay on the one hand and by the decreasing number of available target atoms on the other hand. Hence, this observable  $t_{max}$  depends on the decay constant  $\lambda_i$  and the total production rate  $R_T$ .

Now that the analytical formulae for production are set with Eq. (3.10), the remaining ingredients needed to evaluate Eqs.(3.10) and (3.11) are:  $N_T(0)$ ,  $R$ , and  $\lambda$ , and this will be done in the next two sections.

### 3.2 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:

$$N_T^m(0) = \frac{N_A}{A} B_m \rho V_{tar}, \quad (3.12)$$

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

$$V_{tar} = S_{beam} \int_{E_{back}}^{E_{beam}} \left( \frac{dE}{dx} \right)^{-1} dE, \quad (3.13)$$

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  $[\text{MeV}/\text{cm}]$ . We use the Bethe-Bloch formula [7]:

$$\frac{dE}{dx} = 0.1535 \rho \frac{Z}{A} \frac{z_p^2}{\beta^2} \left[ \ln \left( \frac{2m_e \gamma^2 v^2 W_{max}}{I^2} \right) - 2\beta^2 \right], \text{ MeV}/\text{cm} \quad (3.14)$$

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

$$\beta = \frac{v}{c} = \sqrt{\frac{E_{beam}(E_{beam} + 2m_0c^2)}{(E_{beam} + m_0c^2)^2}}, \quad (3.15)$$

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

$$W_{max} = 2m_e c^2 (\beta\gamma)^2, \quad (3.16)$$

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

$$\frac{I}{Z} = 9.76 + 58.8Z^{-1.19} \text{ eV}. \quad (3.17)$$

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

### 3.3 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

$$R_{T \rightarrow i} = \frac{I_{beam}}{z_p q_e} \frac{1}{V_{tar}} \int_{E_{back}}^{E_{beam}} \left( \frac{dE}{dx} \right)^{-1} \sigma_i^{rp}(E) dE \quad (3.18)$$

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:

$$R_T = \frac{I_{beam}}{z_p q_e} \frac{1}{V_{tar}} \int_{E_{back}}^{E_{beam}} \left( \frac{dE}{dx} \right)^{-1} (\sigma_{non}(E) - \sigma_{in}(E)) dE \quad (3.19)$$

where  $\sigma_{non}$  is the non-elastic cross section and  $\sigma_{in}$  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

$$\lambda_i = \frac{\ln 2}{T_i^{1/2}}, \quad (3.20)$$

where  $T_i^{1/2}$  is the half-life of isotope  $i$  in [s]. The  $\lambda_i$  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  $d$ ,

$$\lambda_i = \lambda_{i \rightarrow d} = \lambda_{i \rightarrow d}^{g.s.} + \lambda_{i \rightarrow d}^{iso}. \quad (3.21)$$

With this, all ingredients of Eq. (3.10) are defined and we may calculate the nuclide inventory  $N_i(t)$  at any time during or after the irradiation process.



### 3.4 Activities

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

$$A_i(t) = \lambda_i N_i(t). \quad (3.22)$$

For small irradiation times the expression for  $N_i(t)$ , Eq. (3.10), behaves as:

$$N_i(t) = N_T(0) R_{T \rightarrow i} t, \quad (3.23)$$

and hence the activity of  $i$  as

$$A_i(t) = \lambda_i N_T(0) R_{T \rightarrow i} t, \quad (3.24)$$

Under these circumstances, the yield scales linearly with the irradiation time  $t$  and the production rate  $R_{T \rightarrow i}$ . Only then, the production yield expressed in [MBq/mAh] is a meaningful quantity, which can be used to determine the yield, given a certain irradiation time and beam current.

All quantities needed to calculate the activity are easy to obtain with one exception: the production cross sections. These are accompanied by larger uncertainties than the other quantities mentioned above and therefore deserve their own chapter.

## 4. Nuclear data libraries

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

- the solution of the production and decay equations, Eq. (3.10),
- a model for the stopping power, in our case Eq. (3.14),
- 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 it 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,

- The IAEA Medical Isotope database [2, 3, 4, 9], 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, energy ranges,
- TENDL-2017 [6], is a complete nuclear data library for all projectile, target, product, energy combinations. For projectiles on any target, cross sections for all residual products cross sections which can be produced for incident energies up to 200 MeV are included. For incident charged-particles, TENDL has been automatically produced, because the time-consuming nuclide-by-nuclide adjustment to experimental data has only been performed for incident neutrons so far. That means that compared to experimental data the TENDL curves can be excellent, good, reasonable or bad. Statistical analyses of the overall quality, also in comparison with other high-energy libraries, exist.

The medical isotope data library for ISOTOPIA is the result of a smooth merger between the

above two data libraries. Obviously, TENDL is used for projectiles, targets, products and reaction channels which do not exist in the IAEA database. Moreover, we have complemented the IAEA database by TENDL at the energy limits of 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 impurities to consider.

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

## 5. 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  $^{100}\text{Mo}$  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. Next, we give an outline of all the keywords, which have been categorised in several groups. Finally, we summarize all keywords in one table.



## 5.1 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.

## 5.2 ISOTOPIA keywords

As explained above, the minimum input file is a blank file, i.e. to leave all choices for the parameters to the author. In general, you probably want to be more specific. Below, we will explain all the

---

possible keywords. We have classified them according to their meaning and importance. 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”  $^{204}\text{Pb}$  (1.4%). ISOTOPIA automatically normalizes the abundances to a sum of 1, leading in the above case to 24.44 % of  $^{206}\text{Pb}$ , 22.41 % of  $^{207}\text{Pb}$  and 53.14 % of  $^{208}\text{Pb}$  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  $p + {}^{100}\text{Mo}$  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

$0 \leq \text{Adepth} \leq \text{Atarget}$  where Atarget is the mass number of the target.

### Default

**Adepth 20.**



**Area**

Area of the target in cm<sup>2</sup>.

**Examples**

Area 1.

**Range**

$0 \leq \text{Area} \leq 10000$ .

**Default**

Area 10. cm<sup>2</sup>.

**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**

$0. \leq \text{Eback} < \text{Ebeam}$

**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**

$3 \leq \text{element} \leq 124$  or  $\text{Li} \leq \text{element} \leq \text{C4}$ .

**Default**

None.

**Comments**

- To accomodate 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.

**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. 24), after which the results will be properly weighted and summed.

**Examples**

**mass 112**

**mass 0**

**Range**

**mass 0** or  $5 < \text{mass} \leq 339$ . 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,  $^3\text{He}$ , 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.

*The following units are possible:*

**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<sup>3</sup>.

**Examples**

**rho 10.**

**Range**

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

**Default**

**rho** is read from a hardwired material density table.

**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**

<b>Tirrad</b>	<b>2 d 5 h</b>
<b>Tirrad</b>	<b>32 h 30 m</b>
<b>Tirrad</b>	<b>1 d 6 h 24 m 12 s</b>

**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**

$0 \leq \text{Tcool} \leq 1\text{e}6$  for every time unit.

**Default**

**Tcool 1 d.**



**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.

*The following units are possible:*

**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**

$0 \leq \text{Zdepth} \leq \text{Ztarget}$  where  $\text{Ztarget}$  is the mass number of the target.

**Default**

**Zdepth 10.**

Table 5.1: The keywords of ISOTOPIA.

Keyword	Range	Default	Page
abundance	filename	no default	24
Adepth	0-Atarget	20	25
Area	0. - 10000.	10.	26
crosspath	directory name	~/libraries/	27
decay	y,n	y	28
Eback	1.e-11 - 200.	Ebeam - 5	29
Ebeam	1.e-11 - 200.	None	30
element	3 - 124 or Li - C4	None	31
Ibeam	0. - 10000.	10.	32
mass	0, 5 - 339	None	33
outcross	y,n	n	34
projectile	p,d,t,h,a,	None	35
radiounit	(k,M,G)Bq, (m,k)Ci	Gbq	36
rho	0. - 100.	1.	37
Tirrad	0 - 1.e6	1 d	38
Tcool	0 - 1.e6	1 d	39
xsfile	file name	none	40
yieldunit	num, mug, mg, g or kg	num	41
ZAoutput	y,n	n	42
Zdepth	0-Ztarget	10	43

## 6. 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 many different 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 TALYS 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 on your computer, and (b) validation of ISOTOPIA: the results should be comparable to those obtained in other publications. The computation time of ISOTOPIA is very short, i.e. you can wait on the results of the sample cases. In general, we will explain the keywords again as they appear in the input files below. If not, consult Table 5.1, which will tell you where to find the explanation of a keyword.

### 6.1 Sample p-Mo100-Tc099m: Accelerator production of $^{99m}\text{Tc}$

```
projectile p
element Mo
mass 100
Ebeam 16.
Eback 12.
Ibeam 0.025
```

## Prediction of medical isotope production with accelerators

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

USER INPUT FILE

```

projectile p
element mo
mass 100
ebeam 16.
eback 12.
ibeam 0.025

```

USER INPUT FILE + DEFAULTS

Keyword	Value	Variable	Explanation
#			
# 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	0.025	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 <sup>2</sup>
Tcool	1	Tcool	d of cooling time
rho	-1.000	rhotarget	target density [g/cm <sup>3</sup> ]
#			
# 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

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
Energy range             : 16.000 --> 12.000 MeV

```



```

Beam current           :      0.025 mA
Target material density :      10.220 g/cm^3
Target area            :      1.000 cm^2
Effective target thickness :      0.021 cm
Effective target volume :      0.021 cm^3
Effective target mass   :      0.214 g
Number of target atoms  :      1.29158E+21
Number of incident particles: 1.56038E+14 [s^-1]
Produced heat in target :      0.100 kW

```

(Maximum) production and decay rates per isotope

Production rate for all isotopes: 1.66066E-10 [s^-1]

# Nuc #	Prod.rate [s^-1]	Decay rate [s^-1]	Activity EOI [GBq]	#isotopes EOI [ ]	Yield BOI [GBq/mAh]	Isotopic fraction EOI			Hal
Tc 101	1.54784E-13	8.13553E-04	1.99915E-01	2.45730E+11	1.22953E+01	0.00003		0 y	0 d
Tc 100	9.24118E-12	4.38701E-02	1.19357E+01	2.72069E+11	9.54856E+02	0.00041		0 y	0 d
Tc 99	1.39410E-10	1.02640E-13	1.60186E-06	1.56066E+16	2.66149E-06	0.53072	213995 y	133 d	
Tc 99 g	1.11455E-10	1.02640E-13	1.27658E-06	1.24374E+16	2.12764E-06	0.42295	213995 y	133 d	
Tc 99 m	3.60405E-11	3.20368E-05	4.36259E+01	1.36175E+15	2.08670E+02	0.04631		0 y	0 d
Mo 100	1.56171E-11	0.00000E+00	0.00000E+00	1.29158E+21	0.00000E+00	1.00000	stable		
Mo 99	3.83200E-12	2.91994E-06	1.10357E+00	3.77942E+14	2.07559E+00	0.00000		0 y	2 d

End of ISOTOPIA calculation for p + Mo100



## 7. Outlook and conclusions

This manual describes ISOTOPIA-1.0, a software package for the prediction of medical isotope production using an accelerator.

The formalism employed in version 1.0 to calculate all isotopic activity yields, is based on the direct production and  $\beta$ -decay of the isotopes. Feeding of the isotope through  $\beta$ -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  $\beta$ -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-2017. 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.

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

Here we derive the solutions (3.10) of the differential equations (3.6)-(3.9). Eq. (3.10) has been implemented in ISOTOPIA.

For the target nuclide we have

$$\frac{dN_T(t)}{dt} = -R_T N_T(t). \quad (\text{A.1})$$

This is easily integrated to give

$$N_T(t) = N_T(0) e^{-R_T t}. \quad (\text{A.2})$$

For every parent nuclide we have

$$\frac{dN_p(t)}{dt} = R_{T \rightarrow p} N_T(t) - \lambda_p N_p(t). \quad (\text{A.3})$$

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

$$e^{\lambda_p t} \frac{dN_p(t)}{dt} = e^{\lambda_p t} [R_{T \rightarrow p} N_T(t) - \lambda_p N_p(t)], \quad (\text{A.4})$$

or,

$$e^{\lambda_p t} \frac{dN_p(t)}{dt} + e^{\lambda_p t} \lambda_p N_p(t) = e^{\lambda_p t} R_{T \rightarrow p} N_T(t), \quad (\text{A.5})$$

or,

$$\frac{d[e^{\lambda_p t} N_p(t)]}{dt} = e^{\lambda_p t} R_{T \rightarrow p} N_T(t). \quad (\text{A.6})$$

Integrating this, after insertion of Eq. (A.2), gives

$$\begin{aligned} e^{\lambda_p t} N_p(t) &= N_T(0) R_{T \rightarrow p} \int dt e^{(\lambda_p - R_T)t} \\ &= \frac{N_T(0) R_{T \rightarrow p}}{\lambda_p - R_T} e^{(\lambda_p - R_T)t} + C, \end{aligned} \quad (\text{A.7})$$



or,

$$N_p(t) = \frac{N_T(0)R_{T \rightarrow p}}{\lambda_p - R_T} e^{-R_T t} + C e^{-\lambda_p t}. \quad (\text{A.8})$$

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

$$0 = \frac{N_T(0)R_{T \rightarrow p}}{\lambda_p - R_T} + C, \quad (\text{A.9})$$

giving the solution for the parent nuclide,

$$N_p(t) = \frac{N_T(0)R_{T \rightarrow p}}{\lambda_p - R_T} [e^{-R_T t} - e^{-\lambda_p t}]. \quad (\text{A.10})$$

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

$$\frac{dN_i(t)}{dt} = \lambda_{p \rightarrow i} N_p(t) + R_{T \rightarrow i} N_T(t) - \lambda_i N_i(t). \quad (\text{A.11})$$

Multiplying both sides with  $e^{\lambda_i t}$  gives analogous to Eqs. (A.4)-(A.6),

$$\frac{d[e^{\lambda_i t} N_i(t)]}{dt} = e^{\lambda_i t} [\lambda_{p \rightarrow i} N_p(t) + R_{T \rightarrow i} N_T(t)], \quad (\text{A.12})$$

or, after insertion of the solutions for  $N_T$ , Eq. (A.2), and  $N_p$ , Eq. (A.10),

$$\frac{d[e^{\lambda_i t} N_i(t)]}{dt} = e^{\lambda_i t} \left[ \lambda_{p \rightarrow i} \frac{N_T(0)R_{T \rightarrow p}}{\lambda_p - R_T} (e^{-R_T t} - e^{-\lambda_p t}) + N_T(0)R_{T \rightarrow i} e^{-R_T t} \right]. \quad (\text{A.13})$$

Integrating this gives

$$\begin{aligned} e^{\lambda_i t} N_i(t) &= \frac{N_T(0)\lambda_{p \rightarrow i}R_{T \rightarrow p}}{\lambda_p - R_T} \left[ \int dt e^{(\lambda_i - R_T)t} + \int dt e^{(\lambda_i - \lambda_p)t} \right] \\ &+ N_T(0)R_{T \rightarrow i} \int dt e^{(\lambda_i - R_T)t} + C, \end{aligned} \quad (\text{A.14})$$

or,

$$\begin{aligned} N_i(t) &= \frac{N_T(0)\lambda_{p \rightarrow i}R_{T \rightarrow p}}{\lambda_p - R_T} \left[ \frac{e^{-R_T t}}{\lambda_i - R_T} + \frac{e^{-\lambda_p t}}{\lambda_i - \lambda_p} \right] \\ &+ \frac{N_T(0)R_{T \rightarrow i}}{\lambda_i - R_T} e^{-R_T t} + C e^{-\lambda_i t}. \end{aligned} \quad (\text{A.15})$$

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

$$0 = \frac{N_T(0)\lambda_{p \rightarrow i}R_{T \rightarrow p}}{\lambda_p - R_T} \left[ \frac{1}{\lambda_p - R_T} + \frac{1}{\lambda_i - \lambda_p} \right] + \frac{N_T(0)R_{T \rightarrow i}}{\lambda_i - R_T} + C, \quad (\text{A.16})$$

so we finally obtain

$$N_i(t) = N_T(0) \frac{R_{T \rightarrow i}}{\lambda_i - R_T} [e^{-R_T t} - e^{-\lambda_i t}] + N_T(0) \frac{\lambda_{p \rightarrow i}R_{T \rightarrow p}}{\lambda_p - R_T} \left[ \frac{e^{-R_T t} - e^{-\lambda_i t}}{\lambda_i - R_T} - \frac{e^{-\lambda_p t} - e^{-\lambda_i t}}{\lambda_i - \lambda_p} \right]. \quad (\text{A.17})$$

The three solutions of interest are thus given by Eqs. (A.2), (A.10), and (A.17).

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## Index

### A

abundance..... 16  
activity..... 18

### B

beam surface..... 16

### D

decay rate..... 14, 17

### I

input..... 21  
installation..... 11  
irradiation time..... 16

### M

mass density..... 16

### N

nuclear reaction rate..... 14

### P

production rate..... 17

### S

samples..... 45  
stopping power..... 16

### T

target volume..... 16