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Meta-heuristic Optimization Techniques for the Production of Medical Isotopes Through Special Target Design

A Thesis Presented for the

Master of Science

Degree

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Dedication

This thesis is wholeheartedly dedicated to my father and mother, who always believed, and compelled me to believe, that honest hard work and determination will outlast any challenge that arises. I can not emphasize enough how none of what I have accomplished would be possible without the genuine love, continuous support, and seemingly never-ending sacrifices that my parents poured into my life.

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It would be impossible to name every individual and circumstance that contributed to this journey. From the character building lows to the celebrated highs, I have been blessed with an unmatched support system which shaped my perspective on life, work, and the importance of relationships.

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"The task is ... not so much to see what no one has yet seen; but to think what nobody has yet thought, about that which everybody sees."

— *Erwin Schrodinger*

Abstract

Medical isotopes are used for a variety of different diagnostic and therapeutic purposes Ruth (2008). Due to recent newly discovered applications, their production has become rapidly more scarce than ever before Charlton (2019). Therefore, more efficient and less time consuming methods are of interest for not only the industry's demand, but for the individuals who require radio-isotope procedures. Currently, the primary source of most medical isotopes used today are provided by reactor and cyclotron irradiation techniques, followed by supplemental radio-chemical separations Ruth (2008). Up until this point, target designs have been optimized by experience, back of the envelope calculations, and parametric studies Bevins (2017). Isotope production is, for many reasons, difficult and expensive, thus, more accurate isotope-specific data is required to build computational models to guide improvements on these processes. However, acquiring this data at large-scale production facilities is time-consuming and impractical Bogetic et al. (2018). The implementation of various optimization algorithms in the field of nuclear engineering and medical physics can be related to the increase in quality and safety of reactor cores, shielding, radiology, radiotherapy, and etc. Ghaheri et al. (2015); Charlton (2019). Thus, continuing these efforts to advanced medical isotope production techniques is inevitable. The work that follows proposes how the use of a meta-heuristic based optimization framework, with target design parameter variables, constraints, and objectives could lead to a more efficient production method. To accomplish this, we introduce Gnowee Bevins (2017), a meta-heuristic software package that

has been developed at the University of California, Berkeley Bogetic (2020). This multi variable/multi constraint optimization algorithm will provide a coherent and coordinated approach to tackling the difficult task of designing an optimal target for isotope production, enabling the capabilities to optimize the target using high fidelity neutronic simulations, with imposed constraints related to radio-chemical separations Hogle (2012). Therefore, this goal could potentially be accomplished by supplying Gnowee with the necessary variable options to choose materials and their respective thicknesses that (1) accurately degrade parts of the spectrum that are undesirable, (2) cause the least amount of reactions that require intensive separation techniques, and (3) maximize the production of the desired medical isotope.

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Chapter 1

Introduction

Radio-isotopes are useful in a wide array of medical applications including, but not limited to: diagnostic imaging techniques, therapeutic radiotherapy sources, and theranostic agents for human malignancies Charlton (2019). Due to the increased amount of applications, more efficient production techniques of these isotopes is more necessary Rad (2021). Therefore, this work aims to provide a target-design optimization methodology to better support the field by increasing the efficiency of commonly employed production methods through the use of target design.

The current route for producing medical isotopes can no longer meet this growing demand because of the copious amount of various types of isotopes that are useful in treatments, the increasing number of individuals who rely on these procedures, and the constrained optimization methods prior to irradiation due to the dependency of advanced nuclear facilities Ruth (2008). Up until this point, target designs have been optimized by experience, back of the envelope calculations, and parametric studies Rad (2021). These out-dated techniques, without the ability to limit other competing isotopes from being produced, cause the separation techniques following production to be complex and inefficient Hogle (2012). Current approaches in isotope separation require significant computational and manpower resources which often do not account for uncertainties present in isotope production cross sections during the

design process, as well as thermal mechanic limitations Charlton (2019). A new state-of-the-art optimization could increase the design space and help construct efficient targets within the experimental volume activation limitations. Alongside this, new experiments would need to be identified and designed to satisfy these optimization methods in order to obtain more certain data implementation.

In general, the implementation of various algorithms in the field of nuclear engineering and medical physics has been directly correlated to the increase in quality and safety of reactor cores, shielding, oncology, radiology, radiotherapy, etc. Ghaheri et al. (2015). Meta-heuristic algorithms particularly have been identified to significantly improve and efficiently automate what used to be laborious, conservative, time consuming, and expensive processes Bevins (2017). Furthermore, results from this work will provide the feasibility and advantages of using meta-heuristic algorithms like a genetic algorithm, to design optimal targets for isotope production. when coupled with particle transport simulations. The meta-heuristic algorithm used in this work is Gnowee. Bevins (2017). This project aims to expand the applicability of Gnowee for the specific purpose of neutron induced isotope production. Results from this work could impact many areas of target design as it provides a methodology that enables higher fidelity target designs. The goal of the presented project is to provide a new methodology to efficiently improve target designs for isotope production, rather than.

1.1 Motivation

Currently, there are over forty million nuclear-medicine procedures performed annually, and are projected to rise by a factor of five percent per year for the next foreseeable future Charlton (2019). The employed production methods do not possess long-term feasibility on their own due to expensive irradiation-time for intense flux environments, leading to a limited amount of experiments prior to irradiation events, and complex separation processes required for isotopically pure samples Rad (2021). Specifically, neutron induced isotope production techniques that exist today

have heavily relied on the use of nuclear reactor facilities Charlton (2019). This introduces another production challenge related of the limited access to state-of-the-art reactors, insufficient back-of-envelope neutron transportation calculations, the inability to efficiently perturb a reactor spectrum, and the complexity of separation techniques that fission products introduce Bogetic (2020).

Research has shown that the most constructive method to perturb a neutrons energy is by introducing various materials to degrade, or filter, an initial spectrum Hogle (2012). Energy Tuning Assemblies (ETA) take advantage of these properties by introducing various materials to filter unwanted neutron energies Bogetic (2020). Furthermore, optimizations of stacked material designs have verified the ability to effectively perturb an initial neutron spectrum Bevins et al. (2019). However, due to the wide array of reactions that take place at various neutron energies, competing objectives are introduced Ruth (2008). These include maximizing the intensity of the neutron flux for a particular energy where the reaction is most probable to occur, and minimizing reactions that would later require more time-consuming and complex separation techniques Bevins (2017).

In recent years, some automation involving systematic optimization of target design has been explored, including Dr. Hogle's work on the optimization of isotope production through the use of neutron filters Hogle (2012). The mechanism for producing many important isotopes relies on long production chains of neutron capture and subsequent decay **?**. The probability of neutron capture to occur depends strongly on the incident neutron energy, and this energy dependency is unique for each neutron capture reaction Bevins (2017). Parasitic reactions are undesirable captures in the product isotope and negatively impact the performance of a target design Hogle (2012). Leveraging the difference in the energy dependence of production capture reactions and parasitic reactions, neutron filters can be designed to improve target performance **?**. One of the difficulties she encountered is the large computational time for the predictive simulation for each of the proposed target designs Hogle (2012). Thus, a computationally efficient optimization algorithm to evaluate arbitrary

geometries could be a powerful tool to support this and similar efforts related to production of medical isotopes. The motivation for this work is to build on this research and maximize production yield, while reducing the parasitic reactions to improve the reliability of the production process. This project's objective is not to produce isotope, but rather to build and validate modern, advanced optimization methods into isotope production and apply them to the design of targets in the future production chain.

1.2 Objective

This work aims to provide a new methodology that could allow for small-scale proof of concept validations for more efficient use of reactor facilities. Specifically, through the use of The Fast Neutron Source (FNS) Pevey et al. (2021), which is a source-driven, sub-critical facility with an inter-changeable cassette configuration designed through similar optimization techniques as those explored in this work to mimic the shape of well-known industrial reactor spectra Pevey et al. (2021). Through the use of the FNS, an initiative has been undertaken at the University of Tennessee to inform industrial reactor facilities of more precise nuclear data, without the use of highly enriched Uranium. Because of the FNS's keen ability to match a spectrum of a state-of-the-art reactor, it becomes a vital resource in the future validation of this project as it will use lower intensity neutron generators to better inform reactor production facilities of more efficient flux-filtering target designs (refer to subsection 2.4.1) Pevey et al. (2021). Accomplishing this objective has the potential to allow for the highest isotopic return per unit time under irradiation, for a site specific reactor spectrum. This is planned to be accomplished by first building an optimization framework that, once initialized, will automatically simulate thousands of neutron transportation events to arrive at nearly optimal solution sets. By defining key variables related to a specific isotope of interest, utilizing Gnowee (a python-based, general-purposed, open-sourced optimization algorithm) Bevins and Slaybaugh (2018), implementing a

widely accepted neutron transportation code for stacked simulations, and establishing important objectives and constraints related to the problem, an optimization framework can be built to return solution sets of candidates that could be validated with the FNS, once fully assembled. Developing and documenting experimental capabilities of existing small-scale nuclear facilities, like the FNS, would allow for improved gathering of important data for the isotopes of interest (i.e. missing or improved cross-sectional data, cross-section uncertainties, and thermo-mechanical properties), in turn, accelerating the advancement of target production.

There are many factors limiting the successful optimization of isotope production targets **?**. One of them is the incomplete knowledge of the production and destruction cross sections, and the second one is the high cost of computational simulations of candidate production target designs Hogle (2012). High fidelity depletion simulations, with neutronic calculations at every time step, are required to predict the performance of a production target design, and these calculations take long times to converge Bogetic (2020). Thus, the research proposed is aiming to expand the physics modeling to include thermal limit calculations and dramatically increase the optimization search space to consider arbitrary geometric configurations of the production target. In this research, new developments are introduced which will enable efficient computational evaluation of candidate production target designs and intelligent optimization of the design, based on the predictive modeling. With this in mind, the primary objectives that will enable this more efficient approach to neutron induced medical isotope production are defined below.

List of primary objectives:

1. Develop and verify a general framework to couple Gnowee with Monte-Carlo transport code (MCNP) for target production to return candidate design sets.

2. Identify the neutron reactions that are required to filter specific energy ranges.

3. Choose and implement a relevant figure of merit, used as optimization function, which will require maximizing the reaction that leads to the isotope of interest, while minimizing the rest.

4. Analyze the potential to use multiple target materials to return the same isotope of interest at various energies of the neutron spectrum.

In conclusion, these primary objectives will be met by including the following tasks: (a) Generalization of the optimization methodology to include different neutron sources, design spaces, objective functions and sets of constrains for target design; (b) Generalization of neutron transport methodology to allow for coupling with MCNP version currently used; and (c) Development of validation experiments for specific neutron facilities, such as the FNS.

Chapter 2

Background

The objective of this project aims to involve the utilization of an optimization algorithm to design and evaluate special targets through the use of filter materials, in order to optimally produce a desired isotope of interest. As mentioned in chapter 1, this can be accomplished by building a software to automatically and iteratively create, simulate, and score neutron transport events based on a user defined figure of merit. To achieve the goal of building a robust optimization program one must first consider why the current techniques are rather slow, inefficient, wasteful.

2.1 Medical Isotope Production and Applications

Up until this point, medical isotope production is accomplished by one of three ways including: Photo-nuclear enrichment, Cyclotron enrichment, and Reactor/Neutron enrichment. As it stands today the most optimal techniques exclude Photo-nuclear enrichment due to the difficulties of achieving the high energies and intensities of finely tuned gamma rays necessary to produce sufficient quantities of a given isotope. Cyclotron production methods are prominent for certain types of isotopes and are known to return a high specific activity, which is a measure of the number of radioactive atoms or molecules relative to the total number of atoms present in an initial sample. Furthermore, they also require fewer separation techniques due to the

minimal material waste compared to other sought out methods. This is due to the fact that charged particle beams can more easily tuned to the specific energy necessary to cause the reaction of interest, therefore other competing reactions are minimized, producing very little of waste. However, the major drawback that comes with cyclotrons often relies on the need for an enriched target due to low current or intensity constraints and in general there is a high capital cost associated with cyclotrons Ruth (2008). Finally, The use of nuclear reactors in isotope production relies on fission products which subsequently leads to larger quantities of waste, and a wide range of incident neutron energies. In the event that a fission product is not of interest, the neutrons produced from this reaction are often either used to induce threshold reactions, (n, p) and (n, α), at high energies, or thermally slowed down to take advantage of the neutron capture reactions (n, γ) Ruth (2008). Moreover, this often calls for the placement of a thin target in an experimental volume to be irradiated by the reactor specific spectrum. The wide array of interaction this unfiltered spectrum causes when incident on the target lends itself to multiple parasitic reactions taking place since there is typically only one route to the desired isotope.

Following an irradiation cycle, complex separation techniques are then required before it can be used for medical purposes, especially in the event of reactor production because of the large quantity of parasitic reactions. Once a sufficient amount of an isotope is chemically separated it can be implemented in imaging and therapeutic settings. Some of the more common isotopes used in medical procedures include: Yttrium-90, used for treatment of non-Hodgkin's lymphoma and liver cancer, and is for arthritis treatment; Fluorine-18, for diagnosis in Positron Emission Tomography (PET); and strontium-89, used for the relief of cancer-induced bone pain Rad (2021). For a given radioisotope, the practical application is based on the mode in which it decays in the body and must also have a half-life short enough to decay away after imaging is complete to limit the overall dose imparted by the decaying isotope (typically less than a few days). The modes of decay that make a radio-isotope advantageous for diagnostic medical purposes are the beta-plus and beta-minus

routes. The first is used for PET imaging techniques which relies on positron (positively charged beta/electron) emitting radioisotopes. Typically these decay types involve accelerator driven production due to the need for proton heavy nuclei which lends itself to the positively charged electron that is emitted once a proton trans-mutates to a neutron within the nucleus. The second decay type (Beta-minus) relies on the emitted gammas rays having enough energy to escape the body and be detected. This becomes relevant when choosing an isotope of interest to produce, as it is often based on the production routes available to the user.

On the other hand, a desirable therapeutic isotope varies with the procedure type: Internal radio-nuclide therapy which involves a finely peaked gamma and/or beta emitter implanted in the target area to impart dose to the surrounding area; and external irradiation (teletherapy) which utilizes an intense gamma peak from radioactive Cobalt-60 source to deliver the dose without the need for invasive procedures. With all of these applications in mind, it becomes imperative to simplify the number of various isotopes needed by taking advantage of certain isotopes that serve more than one single useful purpose.

Theranostic, the combination of therapeutic and diagnostic, medical isotopes include those that trans-mutates via positron, beta minus, and/or electron capture Yordanova et al. (2017). This allows these dual-purpose isotopes to be diagnostically useful for the various types of imaging, as described above, and therapeutically beneficial due to the beta particles and auger electrons often used for certain types of cancer therapies. This medical isotope is directed toward a specific location in the body by connecting it to a linking molecule, which attached a binding molecule Yordanova et al. (2017). A simplified model is shown below in Figure 2.1.

This theranostic isotope can be implemented for individual purposes, and/or lend key information to the dose distribution via imaging during cancer treatments. The increasing demand for these isotopes outweigh the current capabilities to produce, so utilizing advanced computational optimization methods are crucial for this development. Moreover, enhancing current traditional forms of isotope production

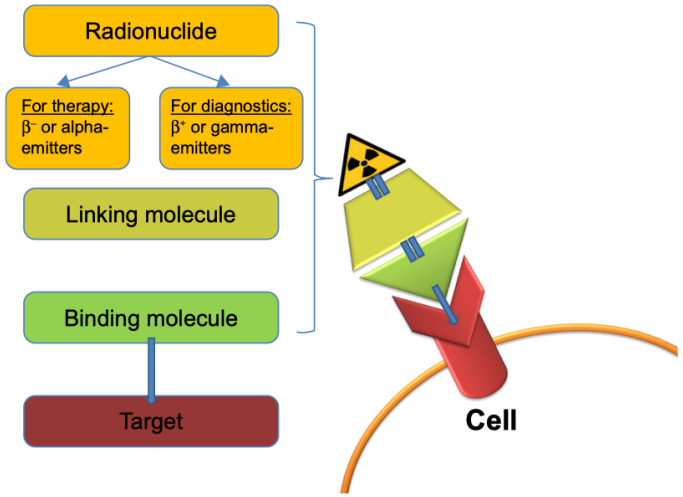


Figure 2.1: A simple model of a radio-pharmaceutical Yordanova et al. (2017)

through the use of theranostic isotopes will return advantageous benefits with a favorable safety profile. Lastly, taking advantage of dual-purpose radio-isotopes, point to the potential to increase necessary supply by simplifying the amount of various isotopes used in medicine Yordanova et al. (2017).

2.2 Neutron Induced Isotope Production

A well-known, diagnostically-significant isotope which is used in approximately 80% of all nuclear medicine procedures is Technetium-99m (Tc-99m). In order to obtain substantial quantities of this isotope most frequently has relied on the decay of a fission product, Molybdenum-99 (Mo-99), of enriched reactor fuel (Uranium-235). Because of Tc-99m's short half-life (6 hours), continuous and easily obtainable production of this isotope is imperative as it needs to be implemented in the patient before decaying away. Moreover, the Nuclear Energy Agency (NAE) released a report on the projected 2019-2024 medical isotope forecast exclaiming how disruptions in the supply-chain can lead to cancellations or delays in important medical procedures, with consequent effects on patients, their treatments, and their health. Furthermore, over the last 6 years unexpected delays and shutdowns of many Mo-99 production facilities lead to more recent chronic shortages. These include: The OSIRIS reactor in France (permanently ended operations in late 2015), the National Research Universal (NRU) reactor in Canada (ceased routine production of Mo-99 in late 2016, and permanently shut down all operations in March of 2018), and unplanned outages and limited capacity of the NTP Radioisotopes SOC Ltd facility in South Africa (since 2017) Charlton (2019).

Since the production of this widely used isotope depends on a Uranium fission product, the implementation of Tc-99m has primarily relied on the time-consuming, expensive, and complex Mo-99 fission product separation processes. However, The NorthStar RadioGenix System was granted FDA approval in 2018 for a non-conventional reactor-based production method that uses natural neutron-activated molybdenum targets

produced by an incident reactor spectrum to be supplied into the US market. This proved to serve as a substantial step in simplifying the necessary Mo-99 separation processes Charlton (2019). These advancements were crucial in moving supply to a more efficient state, but still obtain their own unique challenges. Reactor-based neutron induced reactions alike are advantageous because they provide an intense neutron flux; however, this presents expensive validation techniques due to the limited time allotted during controlled operation cycles to avoid flux disruption and difficulties associated with separating undesirable isotopes created from a general reactor spectrum. So, in order to most efficiently take advantage of these intense flux environments, and the limited time allotted for production, it becomes advantageous to build more robust verification and validation techniques prior to irradiation events. The factors that limit the use of a large-scale isotope production facility for generating new data are: modeling capabilities involve a time-consuming process of iteration between simulations and experiment, and running those machines is very expensive and beam times are limited.

Since reactor-based neutron production is reliant on the limited resources outlined above, maximizing the return of each irradiation becomes imperative. This can be done by implementing a given reactor's spectrum in MCNP simulations and optimizing various target designs prior to exposure in order to limit the creation of undesirable isotopes that are complicated to separate, while maintaining adequate production of the target isotope. To do this, a good understanding of the fundamental principles that govern how neutrons interact in a material is required for the validation of the enhanced production methods proposed by this work.

Neutrons undergo a multitude of various interactions while traversing a given material, based on the respective probabilities of interactions. These nuclear processes heavily rely on a material's cross-sections, incident neutron energies, and time during and post irradiation. Moreover, once reactions take place, the trans-mutated products will subsequently decay at constant rates. So, under a constant flux it will take various amounts of time for particular reactions to reach saturation equilibrium, where

the production and decay constants are equivalent. This is the point in which the maximum possible amount of a particular radio-isotope is reached. It is good to note that more efficient production is often found via reactors because they obtain a much higher flux intensity compared to well-known neutron generators.

2.2.1 The Bateman Equation

The Bateman equation Cetnar (2006), initially proposed in 1910, is an advanced analytical solution for the case of radioactive decay in non-linear nuclear transmutation systems to estimate the quantity of an isotope under a neutron flux. This equation is broken into sets of linear chains and can account for neutron build-up, self-absorption, and decay during and after an irradiation period. This is shown in Eq. 2.1 Cetnar (2006) below solving for $\lambda_{i,j}$, which is the transmutation constant, or the probability of the i-th nuclide production per unit time from the j-th nuclide destruction. This simple expression can be expanded for higher-order, multi-step interactions which adds complexity as it accounts each energy group in a neutron spectrum, multiple probabilistic reactions, and interactions with the desired product after it is created.

$$\lambda_{i,j} = b^d_{i,j} * \lambda^d_j + \sum_n \int \phi(E)\sigma^x_{i,j}(E)dE \quad Eq.\ (2.1)$$

Where $b^d_{i,j}$ is the branching ratio of j-th nuclides decay into the i-th nuclide; λ^d_j is the decay constant of the j-th nuclide; $\phi(E)$ is the particle (neutron) flux; $\sigma^x_{i,j}$ is the cross-section for the production of the i-th nuclide from neutron interactions with j-th nuclides. The resulting transmutation constant appears as the coefficient describing general, non-linear transmutation chains for neutron interactions. This is visualized in Eq. 2.2 Cetnar (2006) below.

$$\frac{dN_i}{dt} = \sum_{j=1} \lambda_{i,j} * N_j \quad Eq.\ (2.2)$$

Where N_i and N_j denote the concentration of i-th and j-th nuclides respectively. This points to the change in initial composition related to the probability that a specific reaction will occur. With this fundamental understanding of nuclear transmutation and decay for a neutron flux incident on a target, one can get an idea of the relative magnitude to expect from an experiment. Up until this point, many preliminary production calculations are performed by way of similar outdated analytical solutions. However, useful widely implemented nuclear transportation codes, such as ORIGEN developed by Oak Ridge National Laboratory, make these calculations much less time consuming BE- (2012).

As nuclear experiments continue to grow in complexity, there is much potential to increase the accuracy of these experiments through simulations, rather than back of envelope calculations which have been used to get a simple, and rather uncertain, approximations. This is due to the large array of potential reactions given a spectra of incident neutrons. Typically for thermal neutrons, one can expect a higher capture reaction (n,g) cross-section; whereas, fast neutrons primarily induce threshold reactions with a multitude of various products (n, 2n, p, d, He, etc.), inelastic and elastic scattering, and fission. Some instances of isotope production employ irradiating and separating for a known isotope that subsequently decays to the actual nuclide of interest. This points to the highly complex and stochastic nature of the problem that this work is aiming to address. There are minimal competing reactions for thermal neutron energies and many neutron induced methods of producing medical isotopes take advantage of the thermal-capture reactions. However, given the proper separation techniques, fast threshold reactions have potential to be equally as advantageous.

2.3 Radio-Chemical Separation Techniques

In order to obtain a purified isotope of interest following irradiation, radio-chemical separation techniques are introduced. Since pure isotopic concentrations are required

for medical applications, the necessary separation processes must be taken into account prior to inducing a neutron flux on a given material. The techniques required depend on the initial target composition and the residual nuclides formed during irradiation.

The measure of the number of radioactive atoms relative to the total number of atoms in the sample following irradiation is simply quantified by an isotope's specific activity. So, utilizing the equations above one is returned with the expected activities of reaction products. From here, one can subsequently solve for the specific activity of any product in the final target, guiding the choice of needed separation techniques for the isotope of interest. Eq. 2.3 Ruth (2008) shows how the disintegration (decay) rate ($\frac{dN}{dt}$) is represented by its relationship with the number of radio-active atoms, N, in a sample, and its decay constant ($\lambda = \frac{ln(2)}{t_{1/2}}$), which is dependant on its respective half-life ($t_{1/2}$) Ruth (2008).

$$\frac{dN}{dt} = -\lambda N \quad Eq.\ (2.3)$$

Therefore, with an expected activity of a sample one can solve for the number of specific radioactive elements. This allows one to assess which separation techniques are required to obtain the maximum amount of the isotope of interest Ruth (2008). Once an accurate assessment of the differences between the atomic structures of the atoms present is well-understood, one can correctly choose one, or multiple, separation techniques to employ. Below are listed some examples of commonly used, and new-found, methods to separate for high-purity medical radio-nuclides.

(1) Ion Exchange Resin (IER) Kim et al. (2009) is used for separation and purification of an isotope which is accompanied by those of a different charge. The IER anion is positively charged, therefore negatively charged particles are left behind. This is done by dissolving the irradiated foil in hydro-chloric acid, followed by being eluted through a column cartridge to separate isotopes based on charge, then finishing with a distilled water bath Kim et al. (2009).

(2) Vacuum Metallurgy Separation (VMS) Zhan et al. (2009) techniques utilize different vapor pressures of various metals to separate, and then recycles a multitude of pure metals types through condensation under different conditions. Therefore, metals with a high vapor pressure and a low boiling point can be separated from the mixture by means of sublimation or distillation as non-volatile impurities are left behind Zhan et al. (2009).

(3) Plasma Centrifuge Isotope Separation (PCIS) James and Simpson (1976) works to separate isotopes with varying mass through the use of plasma accelerated to a high rotational velocity. This rotation is produced by introducing an electric current flowing through the plasma with a transverse magnetic field. By doing this, isotopes are separated in a gradient along the radius of a rotating container. Samples are then extracted from the plasma utilizing a fast-acting gas valve James and Simpson (1976).

These notable separation methods involve multiple steps before a final solution is returned and are incredibly intricate by nature. However, published work include separation efficiencies of 95 to 99.9 wt%, meaning that nearly pure concentrations of the isotope of interest can be obtain Zhan et al. (2009). Although the techniques addressed above will not necessarily be required to validate the work that follows, taking these complications and results into account when building a multi-purpose optimizer is of interest in order to minimize required separation techniques when industrially implemented. This is to ensure proper counting statistics can be made for an accurate assessment of the returned specific activity.

2.4 Neutron Flux Spectrum Filtering

Unlike charged particles, predicting the means of which a neutron is transported through a material is difficult. This is because of the inherently possessed stochastic processes of neutrally charged particles while traveling through a material. Research has shown that implementation of various filter materials is the only truly effective

route in tailoring a neutron to a specific energy. However, because of the limited access to state-of-the-art reactors and a seemingly infinite amount of materials to choose from, assessing performance of a material's ability to shape a given neutron spectrum becomes time-consuming and computationally expensive. By building a more efficient computational method to test filtering materials to degrade parts of the neutron spectrum leading up to a primary target one can combat these current production challenges, which is the primary objective of this work. In general, by using a stack-up of materials one has the ability to shape an initial source spectrum to produce a sufficient quantities of a desired isotope and/or incident target spectrum Bogetic et al. (2018).

Competing with the objective to filter a flux spectrum and limit parasitic reactions, is the goal of maximizing the overall intensity of that neutron energy in the target. This creates competing objectives of maximizing the flux in the target, and providing the correct neutron energy for the simplest separation techniques. A simple example of this would be utilizing a characteristic neutron thermalizer, with a thickness that allows for sufficient neutron transparency, to minimize subsequent reactions in the target that are typically more difficult to separate. Whether one desires to tailor a spectra for a fast or slow reaction, this competing objective will always present itself. In summary, it is near impossible to obtain a narrowly peaked neutron spectra because of the inherently stochastic characteristics of neutrally charged particles (especially once implementing multiple filters leading to the target) Bogetic (2020). Therefore, optimizing to a nearly thermal target spectra allows for fewer competing reactions. Whereas, in the scenario of targeting a faster neutron flux, even with the most advance material combinations, a distribution of reactions will occur due to overlapping cross-sections at higher neutron energies, complicating future separation requirements. These factors directly contribute to the need for small-scale validation techniques prior to reactor environments to most efficiently take advantage of the respective more intense neutron flux. The University of Tennessee's Department of Nuclear

Engineering is working to develop these methods, and other validations alike, through the use of a Fast Neutron Source.

2.4.1 The Fast Neutron Source (FNS)

Although this project will not address the feasibility of industrial implementation of this work, it will lay the foundation for small-scale validation to be completed through the use of a neutron generator, which has a less-intense flux compared to an industrial reactor. Unlike reactor facilities their fusion-based spectra are mono-energetic with mean energies of 2.5 MeV for Deuterium-Deuterium (D-D) and 14 MeV for Deuterium-Tritium (D-T) generators Lou (2003). The FNS Pevey et al. (2021) will utilize a D-D or D-T neutron generator, which provide spectrum distribution with a mean energy of 2.5 and 14 MeV respectively, and an interchangeable cassette configuration of various materials to produce a neutron flux in a target volume that is comparable in spectral shape to that of a state-of-the-art reactor. The preliminary designs have been verified with genetic algorithms and neural training networks to create and score various cassette configurations based on a desired flux spectrum. Following neutron transportation simulations, each of the simulated FNS design candidates were scored relative to how well the resulting spectrum was representative of the one desired. Specifically, a well-representative Sodium Fast Reactor (SFR) Pevey et al. (2021) configuration was achieved without the use of highly enriched uranium, which makes this facility specifically advantageous as natural Uranium is less expensive to use and requires much less regulations. This points to the competing objectives which include: maximizing the total flux and maximizing how well the shape of an ideal spectrum is represented. The initial schematics heed 10^5 n/cm^2s for a highly representative SFR spectrum Pevey et al. (2021). Although this intensity may not be sufficient for large-scale isotope production, it has much potential to validate previously known expensive and time consuming experiments to better inform, and more efficiently use, industrial facilities.

The ability to reconfigure the FNS for nearly any desired spectrum returns the flexibility to experiment and validate stack-up target designs for efficient production of neutron induced medical isotopes. Because of the early stages of the FNS, this work will reflect only three of the possible spectra able to be produced. These include: an FNS represented SFR spectrum, and D-D/D-T neutron generator sources. Furthermore, the section that follows will explain how the optimization methods required for variable generator spectra can help inform and accelerate the production of medical isotopes through the creation and simulation of numerous simply designed stack-up candidates. Specifically addressing how the desired target flux energy distribution and intensity dictates an optimally chosen source spectrum. Lastly, the incredible opportunity that the FNS facility brings for proof of concept allows for the integration of small University facilities to support the isotope production industry by using them to validate target design methodology, so that it may be applied to large, expensive machines.

2.4.2 Design Methodology for Isotope Production Target

Research presented by the Dr. Hoggle and the Office of Nuclear Physics at the Oak Ridge Nuclear Laboratory verified the ability to optimize the production of transcurium isotopes in the High Flux Isotope Reactor (HFIR) in order to prolong the use of high-quality heavy curium feed-stock Hogle (2012). This was accomplished by analyzing the transcurium isotope production process and identifying means of optimizing the production of the heavy actinides relative to the consumption of the curium feed-stock. Furthermore, they showed that by filtering the HFIR flux spectrum, it was possible to increase the fraction of capture reactions per neutron absorption. So, by using neural networks and genetic algorithms, a framework was created to better evaluate performance of filter materials prior to irradiation exposure. Lastly, these processes were also validated by irradiating experimental capsules and examining the resulting fission and activation products Hogle (2012). This work

provided a crucial preliminary understanding of verified techniques to validate a flux-filtering optimization method for production of neutron induced isotopes of interest.

2.5 Cu-64 A Theranostic Isotope

In general, medical isotopes are more widely implemented in common practice today than every before Charlton (2019). Because of this demand, creating isotopes for multi-purpose (theranostic) applications with an emphasis on the efficiency of production is of great interest. Doing this would allow industry to focus on fewer isotopes to meet the growing demand, greatly simplifying the problem at hand. This section will address a potential medical applications of Copper (Cu), which has a naturally occurring isotopic composition of Cu-63 (69.15%) and Cu-65 (30.85%). Furthermore, what follows will focus on the primary modes of production and separation for this theranostic isotope Kim et al. (2009).

2.5.1 Medical Applications

Cu-64 is known to obtain properties which are complimentary to both diagnostic and therapeutic processes. This radio-isotope trans-mutates via three different routes: positron decay, beta decay, and electron capture. So, diagnostically, it can be used for positron emission tomography (PET) imaging; and therapeutically beneficial due to its beta particles and Auger electron which are often used in cancer therapy Kim et al. (2009). Moreover, when in its most simple form (with other bio-active molecules) it can be used as theranostic agent in human malignancies like prostate, glioblastoma, melanoma, and breast cancers and has been shown to also be beneficial in the diagnosis of human copper-associated diseases. However, at this time there has been no significant clinical development in industry, but a research group out of Korea is one recent study which confirmed Cu-64 showing similar results to that of Fluorine-18 in microPET scanner Kim et al. (2009).

2.5.2 Production Methods

Up until this point, industry has produced Cu-64 by means of cyclotron irradiation of an enriched Nickle-64 target, focusing on the Ni-64(p,n)Cu-64 reaction due to the high specific activity returned Kim et al. (2009). Due to the way in which charged particles interact in a material, the separation process becomes relatively simple compared to neutron enrichment production techniques. This method primarily returns Ni-64 and Cu-64 and research has shown the ability to use ion exchange resin in plastic column cartridge for separation and purification because of the varying charged states Kim et al. (2009). The amount of the specific activity present has be found by obtaining the gamma intensities and energies of the decaying isolated material. So with this known, one can use a High Purity Germanium (HPGe) detector, known for its high resolution, to detect Cu-64 gamma decay peaks at 511, 1022, and 1346 KeV which allows an understanding of the amount of isotopes present from given experimental conditions. The radioactive species produced and separated through these methods often return over 99% pure Cu-64, following the initial 95% enriched Ni-64 Kim et al. (2009).

Although, the current methods of producing Cu-64 is known to have high specific activity and purity, the use of cyclotron beam time is typically costly and/or hard to come by, as mentioned before. This calls for more efficient production methods that could supplement and/or replace novel production techniques, increasing the supply while decreasing the price for the ever-rising demand. Furthermore, as new separation techniques continue to be developed there is a rise in interest to explore other production types. One well-known method that could take advantage of these new separation techniques is through the neutron induced production pathways: Cu-63(n,g)Cu-64 and Zn-64(n,p)Cu-64.

For the case of neutron irradiation incident on a thin Cu-63 target, obtaining a finely tuned beam is much more difficult compared to charged particle induced methods. Furthermore, because of this inevitable spread-out energy distribution other reactions

are more likely to be created. However, given that the separation techniques defined above are available (VMS, IER, and PCIS), and assuming proper intensities of total flux can be reached to induce sufficient quantities in the target, one could use degrading filtering materials to suppress the flux in the energy range that causes other products to be created. Figure 2.2 on the next page shows the reaction cross-sections for the Cu-63 material, proving that the mode of neutron induced Cu-64 production would require a thermally dominant spectrum (blue), in order to limit multiple competing threshold reactions.

A similar case could be made for the Zn-64(n,p)Cu-64 reaction as it has been found to have a large cross-section at 5 MeV. Because this is a threshold reaction, there are of course more competing reactions around this peak probabilistic region. However, recalling the same assumptions as above, if one could use nearly pure Zinc-64 as a filter material this could return a better method that could increase the efficiency of this production even further. For the purposes of this study and the potential validation with the FNS, pure Cu-63 is the primary desired target with Zinc-64 as a potential secondary (or supplemental) target/filter. As the magnitude of production grows trade-offs will arise between material purity and cost, which is dependant on accessible radio-chemical separation techniques and concentration requirements.

Cu-64 is a highly sought after dual-purpose radioactive isotope that has potential to be implemented in PET imaging, cancer diagnostics and treatments, and more. The current constraint on industry utilizing this is the means by which sufficient production and separation can be made in a way that is valuable to both the user and producer. By using Meta-heuristic algorithms, one can quickly and more accurately understand a wide range of geometrical designs that cause the maximum production of Cu-64 from an incident neutron flux before an experiment begins. Furthermore, implementing these optimization techniques for the production of Cu-64 will lead to other capabilities for understanding the most efficient route of production given any target and/or source spectrum of interest.

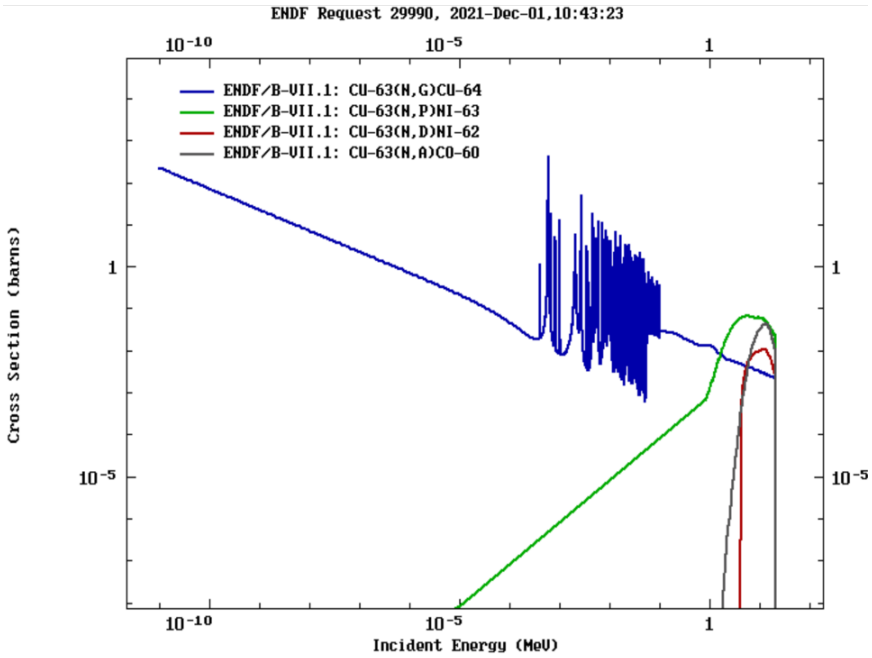


Figure 2.2: ENDF/B-VIII Cross-Section Data for Cu-63

Therefore, this verification will serve as a step to a more robust and efficient isotope production community, enhancing the way in which treatments and diagnosis are administered today. All of this being primarily dependant on the ability to shape, or filter, an initial neutron spectrum, prior to interaction with the target. This points to the need to accurately assess how each of the parameters described effect the overall production result. So, through the use of the optimization algorithm described next coupled with MCNP, these competing objectives and constraints can be appropriately evaluated, returning a set of the top performing designs that are scored based on a user-defined objective function.

2.6 Advantages of Optimizing Special Target Designs

Much of the knowledge applied leading up to neutron induced isotope production has come from simple calculations/approximations and sensitivity studies, producing unrefined and lacking results. However, research shows that given the proper initializing variables, there is great potential to further explore this production design space by automatically simulating stacked material geometries in various irradiation environments Robinson et al. (2020). The iteration and optimization of this is shown to lead to the ability to autonomously create and score thousands of candidate designs in a rapid and extremely efficient manner compared to commonly employed methods today Bogetic et al. (2018).

Furthermore, it is likely that the optimizer will arrive at a solution that would not have been previously discovered using the outdated verification methods described earlier because of the complex search parameters employed to sample large and complex design spaces Bevins and Slaybaugh (2018). With the advantages of using an optimization algorithm to create a proof of concept methodology known, the work

that follows aims to build a meta-heuristic framework and is more deeply explained in chapter 3.

Chapter 3

Methodology

3.1 Problem Definition

Medical isotope production is a large and rapidly growing industry, and it appears that the target designs have typically been optimized by experience, back of the envelope calculations, and parametric studies. Where the fundamental principle is the desire to generate as much of a certain isotope as possible while avoiding other isotopes that are difficult to separate from the irradiated sample. Based on the relative cross-section of the two or more reactions, there will be an optimal target flux spectrum obtained by tuning an initial neutron source through the use of filtering materials. Because these environments are expensive and limited, a more optimal filter selection method was necessary prior to irradiation events. This leads to stack-up MCNP simulations to assess what set of materials give the highest probability for the reaction of interest to occur. Furthermore, by optimizing this selection based on well-scored parents, the ability to automatically simulate thousands of cases and arrive at a set of potential target designs has been effectively demonstrated. Moreover, there is potential to use filtering materials as secondary targets, and optimize accordingly, pending appropriate separation techniques are available.

3.1.1 Origins of Gnowee

In 2018, a meta-heuristic optimization algorithm (Gnowee Bevins and Slaybaugh (2018)) was designed specifically for engineering applications that fell into the sub-category of single-objective, nonlinear, combinatorial and mixed-integer optimization problems. The intricacies of Gnowee will be more deeply defined in the next chapter, but for now it is sufficient say that it is a general-purpose tool that can be applied to a wide-array of problems Bevins (2017), however, the implementation of it requires an enhanced framework that properly simulates (i.e. radiation transport calculations) and evaluates (via user-defined objective function) to achieve an optimized solution Bogetic et al. (2018).

An initial application of designing an Energy Tuning Assembly (ETA) for modification of the National Ignition Facility (NIF) neutron spectrum relied on Coeus, which was the interface between Gnowee and a radiation transport code to evaluate the ETA objective function and constraints. The objective function formulated was a flux-weighted relative least squares minimization to compare an objective spectrum to that of a candidate design Bogetic (2020). Each design outcome corresponded to a chosen vector which contained discrete (materials, densities, numbering of cells), continuous (cell dimensions), and combinatorial (ordering of cells in geometry) variables. This allowed for an extremely complex design problem to be simplified to a single figure of merit, minimizing the difference in comparison of two neutron spectra. The results verified Gnowee's ability to create designs that returned a nearly optimally shaped flux in the sample cavity Bogetic et al. (2018). One of these top performing candidates can be visualized in Figure 3.1 below, which also shows the objective spectrum comparison to that produced by the ETA design.

This research validates Gnowee's ability to be able to optimize a target spectrum via complex design Bogetic (2020). Moreover, it lays the foundation for the work that follows as it aims to build an enhanced optimization framework that converges on more efficient medical isotope production target designs than those employed today.

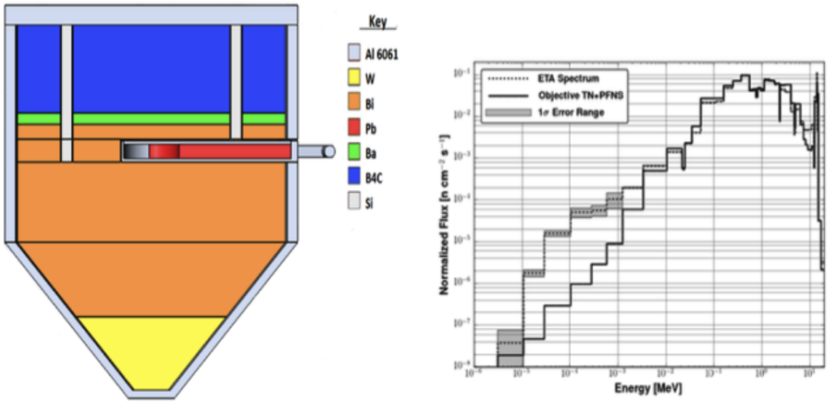


Figure 3.1: Design of the nearly optimum ETA production of synthetic fission and activation products, with the shaped flux in the sample cavity Bogetic et al. (2018); Bevins (2017)

3.2 Optimization Method

The tools needed to verify the use of special target design in medical isotope production included a particle transport code, an optimization algorithm, and the supplemental python functionality for pre- and post-processing. For this work, MCNP is the chosen simulator which informs Gnowee of a given design candidate's performance.

3.2.1 Gnowee - A General Purpose Hybrid Meta-heuristic Optimization Algorithm

As briefly defined in the previous chapter, Gnowee Bevins (2017) is a modular, open-source, general-purpose optimization algorithm that uses meta-heuristic search patterns to efficiently sample a design space for nearly any optimization problem Lones (2014). Its meta-heuristics can be better explained as a problem-independent search technique that provides guidelines to develop optimized solutions Bevins (2017).

Gnowee relies on a user-defined, black-box objective function, to score mixed-integer, combinatorial design vectors of continuous and discrete variable types Bogetic et al. (2018). Meaning that Gnowee requires a figure of merit to assess the performance of the variables chosen. It rapidly samples potential combinations of variables and relies on the user defined objective to assess the various candidates' performance. The best candidates become the algorithms parent population and Gnowee continuously optimizes appropriately balancing diversification and intensification strategies. This is an advantage of it's meta-heuristics, which allow high-level search parameters to assess the parent population. Once each parent has been replaced by a better performing candidate, a new generation begins. This approach allows for rapid convergence for nearly any user-defined complex design challenge Bevins and Slaybaugh (2018). Figure 3.2 below shows the Gnowee's Flowgorithm simply illustrating its functionality.

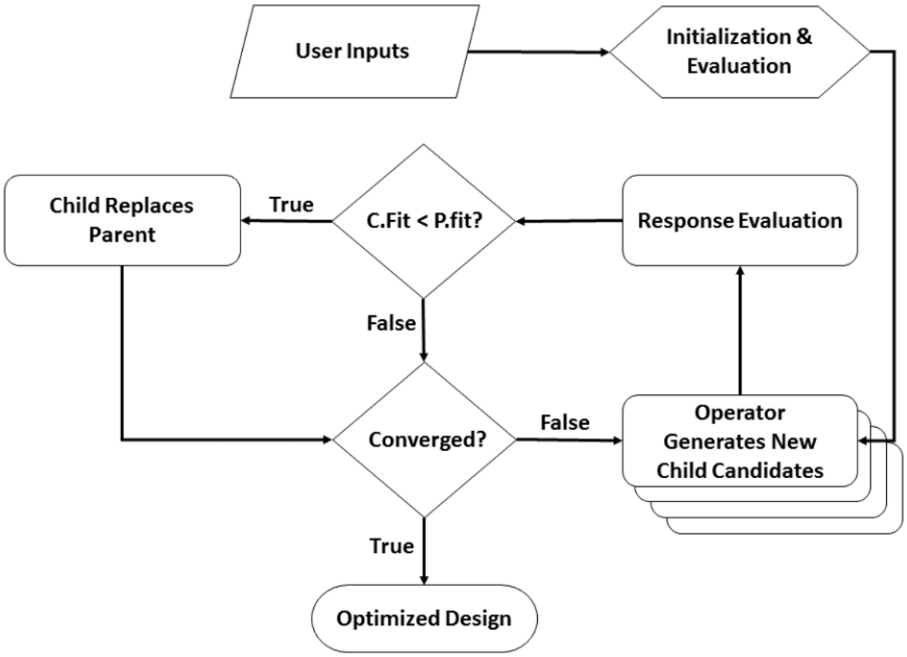


Figure 3.2: Gnowee's Optimization Flowgorithm Bevins (2017)

The routines presented above shows that by outlining the user-specified bounds and variables, Gnowee will create multi-combinatorial design vectors to be scored by a user-defined objective function following simulations. Therefore, by simply outlining the objectives and constraint this work aims to definitively use Gnowee, and supplemental functionality, to design a stack-up target that returns nearly optimal targets for the production of the isotope of interest. Moreover, Gnowee has been proven to converge quickly, but is often limited by the employed transportation code run-time when applied to similar applications Bogetic et al. (2018). The last parameters to define include the identification of continuous and discrete variables, and the bounds and list of options needed for Gnowee to choose respectively.

3.2.2 MCNP - Monte Carlo N-Particle Transport Code System

MCNP Werner (editor) is a general-purpose, time-dependant Monte Carlo transport code which uses continuous-energy and generalized geometry. It has been implemented in the nuclear field for the verification of a wide variety of radiation transport problems, especially those related to neutron simulations. The default cross-section data used by MCNP consists of the ENDF/B-VII libraries Werner (editor). Because of its inherent simplicity and high regards, it was the most viable option for an optimization framework that required python code to automatically manipulate respective variables.

Although there were advantages to using MCNP, one challenge that came with it was the need for large amounts of computational time in order to be returned with certain results. Moreover, since a multitude of simulations were required for proper assessment of the design space, it was not advantageous to maximize this run-time for every simulation. Thus, a variance reduction technique was implemented to increase precision of statistics, while minimally effecting a candidate's simulation rate. One of MCNP's inherent techniques that was chosen based on its simplicity and direct

effect on the simulation's uncertainty, was the cell-based weight windowing. This method utilized a cell's importance value to assess the portion of geometry where the most precise statistics are desirable Werner (editor). With that being said, python functionality allows for automatic increases to be applied to each cell's importance while the optimization nears trends toward convergence. This allows the optimizer to best take advantage of more precise statistics for the cases that are more likely to be better performers, which are most likely to occur following a good parent population. Furthermore, if a best case is found early in the sampling process, it is still advantageous to rerun this candidate/a similar one for better statistics (once the weighted cell windowing is increased).

3.2.3 Development of Coupling Framework for Reaction Rate Optimization

Gnowee is introduced following the creation of the MCNP mock input file. This input deck contained the overall geometric design and supplemental information that remained constant through each run. Also, specifically defined variables are required to inform Gnowee of the potential options which are used to update the mock file via necessary python functionality. The python code searches the mock input for identifying place holders to change with the chosen variables. This functionality leads to the ability to automatically read and create new MCNP input decks based on discrete and continuous variables that was iteratively chosen by Gnowee.

The routines and processes that our created framework obtains can be better visualized in Figure 3.3 below. This figure accurately represents the iterative cycle that our framework follows to submit design candidates. These design variables are chosen by Gnowee based on the list of options and bounds related to discrete and continuous variable types respectively. Following this, supplemental python functionality replaces variable names inside the mock transport code input file and automatically submits it to run the neutron particle simulations.

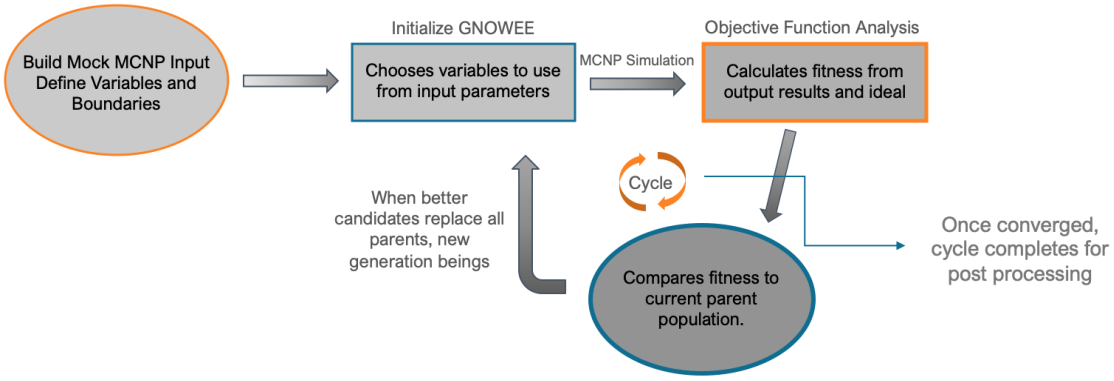


Figure 3.3: Block Schematic of Optimization Routines

Gnowee's meta-heuristic search parameters allowed for the creation of a special flux filtering target by means of variable selection. This was done through informing the optimizer of nine discrete variables (eight materials and one source), and eight continuous variables (material size). With these came a list of options to choose from along with lower and upper bounds respectively for each variable type.

Before the algorithm is able to optimize a set of well-performing parents, a wide variety of combinations needed to first be sampled to properly assess the design space and later arrive at a final diverse solution set. This began by introducing the Latin hypercube (LHC) sampling technique to find thirty well-performing evaluations to store as parents Bevins (2017). This sampling method is known to adequately increase the diversity of initial solution sets, compared to other sampling techniques its capable of, to better explore a large design space Bevins and Slaybaugh (2018). Gnowee simulates hundreds of evaluations until a top-performing parent population was found.

From this the optimizer crossed and mutated the population until new evaluations out-performed the previous set. This new solution set is similarly cycled through consecutive generations until the previously defined max evaluations or generations is reached, or an optimal is found.

3.2.4 Neutron Flux Spectra Considered

The spectra selected as variables were chosen based on their availability to the University of Tennessee and their practical implementation in the field. Again, these MCNP source definitions include: a D-D (2.5 MeV) and a D-T (14 MeV) Maxwellian distributed neutron source, and the FNS spectrum which is representative of a Sodium Fast Reactor Pevey et al. (2021). These spectra are shown in Figure 3.4 below.

By allowing the optimizer to choose from these spectra a more robust algorithm was created enabling the implementation of any user defined neutron source. Furthermore, these capabilities will serve to be more advantageous when optimizing to a fast

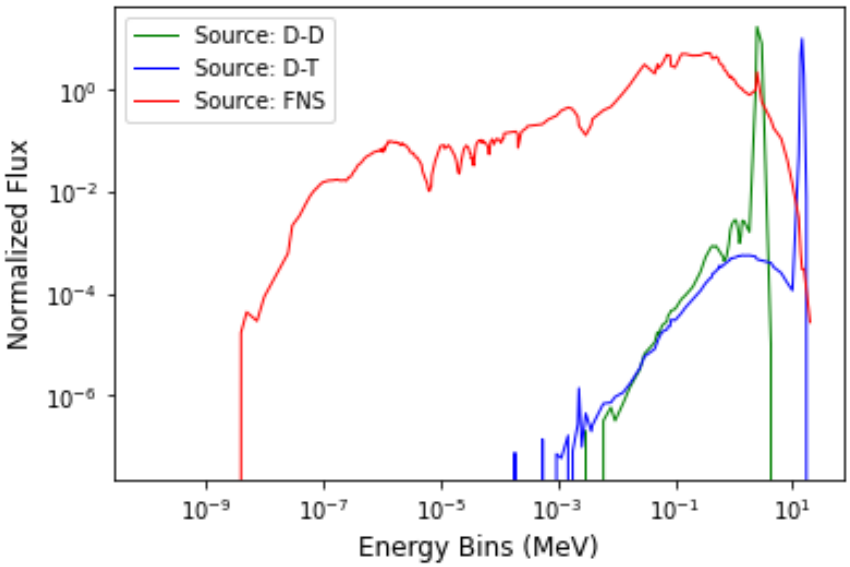


Figure 3.4: Source Variables for Optimizer

threshold reaction and/or utilizing production of a target isotope from a secondary target in the design.

As mentioned before, the preliminary designs of the FNS do not include well represented spectra outside that of a SFR. Moreover, since future plans of the FNS include utilizing a D-T neutron generator (currently designed with D-D), these were chosen as potential validating sources as well. On the other hand, as various FNS designs are validated, more spectrum variables can be implemented to better inform the respective reactor facility of more efficient target designs. Overall, the capability to optimize and select a best performing spectra (based on a set of inputs) will continue to return a deeper understanding of methods and resources necessary to validate a most efficient production route. Furthermore, this selection process lead to a deeper assessment of neutron events while traversing a respective material's (or stacked set of materials') effect on an initial flux.

3.2.5 Degrading Materials

The process of choosing a material to filter a portion of the neutron spectrum introduces competing objectives as we desired to maximize the intensity of neutrons that are transmitted in the desirable energy range; and minimize those which are not. This again is necessary because of the objectives to obtain the highest specific activity of the desirable isotope. The wide variety of materials that were given as options for the optimizer to choose from allow for proper assessment of the large design space, which lead to a better understanding of intrinsic characteristics that attribute to a good filter material. Furthermore, by using the Pacific Northwest National Laboratory's (PPNL) compendium of material composition data for radiation transport modeling, we were most accurately able asses neutron behaviors within materials Customs et al. (2011).

Of the large array of filter options there were a handful of well-known materials that were of interest to us due to their keen abilities to thermalize cold neutrons.

This is important to note, as the overall goal was to slow neutrons to acceptable capture energy range in the Cu-63 target (recalling Figure 2.3 of Cu-63 cross-section data), to produce Cu-64. Moreover, a well-performing filter is known to have a large scatter, and relatively low absorption, cross-section(s). This is verified as the maximum amount of neutrons slow down, and transmit, through the filter. A couple examples of a known well-performing fast neutron filters that this work will confirm include various forms of polyethylene, Iridium (Ir-191 specifically), stainless steel, and Indium Hogle (2012).

Polyethylene is one example that has a high scatter cross-section for energetic neutrons because of its relatively similar mass, compared to a neutron. Furthermore, the conservation of energy requires there to be a high probability that much of the neutron's energy is lost in a single collision somewhere along its path length. Since neutrons are typically to be slowed immediately, not many traversed the entire thickness of the species and made it to the target. Moreover, doped species of polyethylene allowed for more scattering, and in turn a higher intensity of thermal neutrons in the Cu-63 target. For the purposes of this work, lithiated, dueterated, and non-borated polyethylene were some of the options that Gnowee could choose for materials leading up to the target, the material following the target, and that which made up the encapsulating cylinder. With all of this in mind, prior to running simulations we expected the latter polyethylene choices to be good candidates specifically for the surrounding cylinder. However, other materials, like stainless-steel, showed more promising capabilities to reflect neutrons back to the target, without the loss of absorption. This increased a neutrons chance to scatter at a higher energy and subsequently reach the target, compared to a poly-type species.

Iridium is a well-known flux filter that has been implemented in sensitivity studies to slow down initially cold neutrons Hogle (2012). Figure 3.5 below shows the ENDF evaluated cross-sections for Iridium-191; and subsequently the reason for its ability to thermalize high energy neutrons before interaction with the primary target.

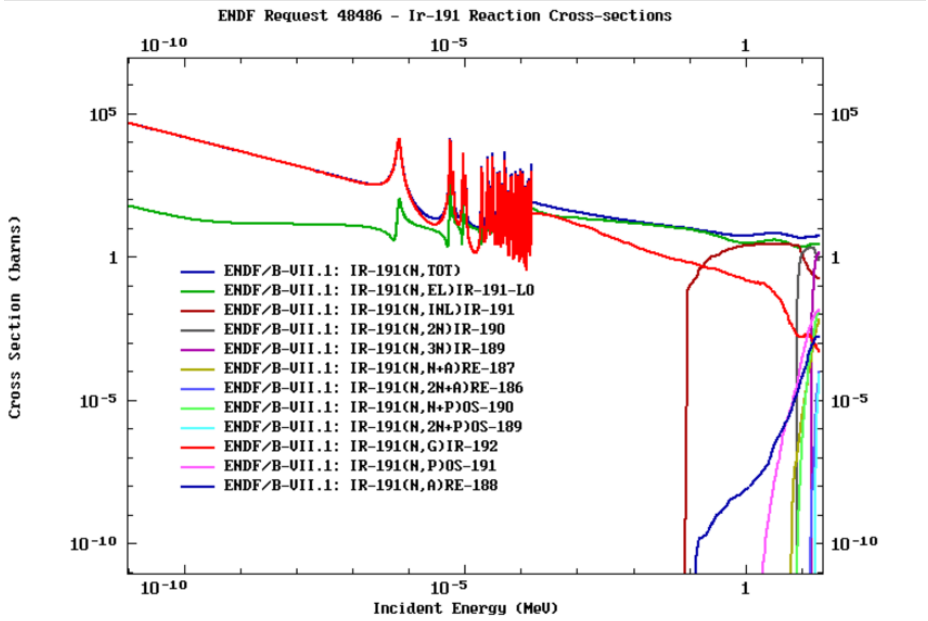


Figure 3.5: ENDF/B-VIII Cross-Section Data for Iridium-191

Iridium-191 has shown to have favorable scatter cross-sections and is the most probable mode of interaction as it contributes the most to the total cross-section at nearly all neutron energies above the resonance region (10^{-3} MeV). However, in the thermal energy range (below resonance region), it is seen that Iridium is more likely to trans-mutate via the capture reaction (n, λ). Furthermore, only few other cross-sections reach values higher than 10^{-2} *barns* (especially for the energy ranges of the sources that were simulated). These attributes point to the reason Iridium is better used as one of the initial cassettes, instead of the latter. As the intensity of thermal neutrons are higher near the primary target (after being slowed down from the source), implementation of Ir-191 at this location is likely to cause more captures than when it is placed closer to the source. Moreover, since the targeted reaction is the Cu-63 (n, γ) Cu-64 capture reaction, placement of Ir-191 near the primary target is not optimal as it attributes to less overall production of the isotope of interest. Other notable filters with similar intrinsic properties included: Gold, Titanium, Nickel, Indium, and various forms of Aluminum.

Recalling that this project required a thermally induced reaction, the optimizer simply chose the best set of materials, and their respective sizes, for the most efficient design that yields the least difference in comparison to the objective reaction rate. Therefore, it is expected that the optimizer will work to place materials with probable high energy scatter reactions before the placement of a material with favorable lower energy scatters. This design approach allows for the most neutron transmission for interaction with the target down stream. With a good understanding of filtering materials and their supplemental effects on an initial source spectra, simulations and optimizations of this special target design are carried out.

3.2.6 Geometric Design and User Specified Variables

The geometry setup in the mock input is a variably sized cylindrical setup with a diameter of 1.27 cm. This cylinder was separated by planes at variable depths (six

materials before target, one following). Pre-processing with python allows Gnowee to choose from a list of materials and thicknesses in the range of zero to twenty centimeters, keeping the thickness of the target constant at 0.0127 cm (similar to that of common activation foils). Encapsulating this was another cylinder with a variable material and thickness (bounded from zero to thirty centimeters).

With lower and upper bounds for continuous (size) variables defined, the material choices Gnowee chose to fill these cells were selected from a list of discrete variables with compositions based on the PNNL material's library Customs et al. (2011). The optimizer is given this list of these material identifiers which require more pre-processing to relate the identifier to the material definition information MCNP needed for simulation. It is good to note, air and void options are available, as well as widely known energy specific filtering materials. Lastly, utilizing the neutron flux spectra presented in the previous sections, the source spectrum is defined as another discrete variable for Gnowee to choose from. This allows for a more complex design space and potentially a wider variety of returned candidate designs. Furthermore, by implementing variable preliminary sources to choose from (FNS spectrum, D-D, and D-T distributions), this work also shows a potential method for discerning which isotope production routes work best for reactor facilities used today. Now that all variables in the target design have been defined, the constraints and objectives are defined next to assess the figure of merit for each evaluation submitted by optimizer.

3.2.7 Constraints

The governing constraint on problems similar to the one discussed here, typically are not outside of the physical principles involved with neutron transportation. Meaning that space and mass are primarily the only limiting factor of the facilities often used to validate their research (materials, source spectra, separation techniques). However, because of the intricate design of the FNS, the validation of this work is not a limited by that of most reactor facilities. Recalling that the FNS cannot produce similar

magnitudes of flux intensity as that of reactor facilities, a smaller quantity of materials can be more feasibly obtained and a wide variety of spectra potentially experimented with. In general, the only constraints implemented in this work were related to the number of reactions occurring in the target volume.

Because of the time taken for each simulation to complete, a trade-off presented itself involving the statistics of the returned values. Because of long run times introduced with more precise simulations, it was advantageous to set a minimum constraint on the reaction rate value that is desired to be maximized in order to efficiently make use of computational time. Furthermore, given the reaction rate to maximize is greater than the imposed constraint, case's that returned no reactions for the transmutation to minimize was set equal to that of the objective ratio's denominator. This allows all case's to be scored based on the difference between reactions while avoiding infinite fitness values (by dividing by zero) for cases that were actual well-performers.

3.2.8 Objectives Function

As it relates to this project, the objective function assesses the difference in the reaction rate to maximize relative to a competing reaction, returning a ratio to be compared to a nearly theoretical reaction rate ratio. This allows the optimizer to maximize the difference between the desired and competing reactions and assess the vector of variables chosen with a single fitness value. Gnowee is known to best optimize when the fitness values are between zero and one Bevins and Slaybaugh (2018), this is the reason a candidate's reaction rate ratio is subsequently compared to a theoretically optimal calibration ratio and returns the difference of this comparison. This figure of merit allows Gnowee to evaluate and optimize this ratio by choosing various materials (and sizes) for a stack-up design by comparison of reaction rates in the primary target material (Cu-64). A fitness value of zero informs the optimizer that there is no difference between the objective and test ratios. As the optimal value will never actually reach zero, it will only approach it as the optimizer converges on

a set of solutions. It is also good to note that the reaction chosen to be minimized in the Cu-63 target is the Cu-63(n,p)Ni-64 reaction, which requires the lowest incident energy of Cu-63's threshold reactions.

For visualization purposes, the formulas below accurately asses the objective function decided on for this work (including constraints introduced above), where RR(I) is the reaction rate of interest (maximized), and RR(N) is the competing reaction rate (minimized).

$$TestRatio = log(RR(I)/RR(N)) \quad Eq.\ (3.1)$$

$$Fitness = |ObjectiveRatio - TestRatio|/ObjectiveRatio \quad Eq.\ (3.2)$$

The optimization continues to converge until the difference between these ratios is less than or equal to an initialized optimum of 0.001. With this figure of merit, the optimization algorithm can be used to design targets for more efficient medical isotope production, returning much insight on a material's ability to accurately filter neutron energy ranges that contribute to reactions that are not of interest.

Lastly, for the sake of this project, it is desirable to explore the use of a filter material as secondary target. Specifically, by implementing Zinc as a potential degrading material for the fast neutron energy range to be chosen by Gnowee because one of it's isotopes (Zn-64) has a large neutron-proton reaction cross-section that could lead to the production of Cu-64 as well. Since competing reactions make-up our figure of merit, a single optimal solution will not be returned, but a solution set of optimums.

3.2.9 Preparation and Initialization

The optimization begins by implementing the outlined bounds and variables for Gnowee to change within the general cylindrical design parameters. Outside of this, a maximum number of generations to optimize, if convergence is not met, is initially set to 500. Furthermore, 30 parents are initially found following hundreds of

evaluations through the use of the LHC sampling method. This set of parents then serve as the first generation's population for the nature based optimization algorithm to further explore. It is also good to note, that since our objective reaction rate ratio will not necessarily be arrived at, Gnowee terminated its optimization once two consecutive parents populations are the same Bevins (2017). Nonetheless, this optimization framework returns a wide variety of candidates that have similar fitness values with varying reaction rate values and design vectors.

3.3 Challenges

As mentioned before, given the long run time required by MCNP, returned uncertainties are initially poor, but increase as the optimization continues. Therefore, once a solution set of candidates are found, Gnowee is informed to rerun top performers for more precise assessments of future experiments. Furthermore, the implementation of variance reduction techniques, through MCNP's weighted cell windowing, return more precise statistics while requiring less overall optimization time. Specifically the importance of target volume, where the most accuracy is desired, is given a higher value than surrounding cells. This allows for the most efficient use of computational power as the optimizer can better asses poor performing candidates to throw out.
Lastly, the inability to have multiple user specified objective functions made from a combination of a various tallies did pose a challenge. This is the main reason a reaction rate ratio objective function is implemented, as it informs the optimizer of the case's fitness based on results from a combination of tallies. Furthermore, for future optimization it may be advantageous to also optimize to an ideal spectrum in the target, based on the energy range of the cross-section of interest and others competing with it. Our created framework has this ability if desired by the user. However, a fallback of this approach is the increase in optimization time as the spectra figure of merit posed less sensitivity to poor performers, and in turn inefficiently informs Gnowee of negative moves.

3.4 Solution Set Evaluation Methods

Due to the nature of the employed objective function (comparison of multiple competing reaction rates) and the stochastic characteristics neutral particles possess, it is unlikely a single-optimal candidate design will be found. Moreover, a set of top performing candidates are returned which shows trade-offs between the reaction that is desirable to maximize and the competing reaction to minimize. As the optimization continues, the initial parent population is updated respectively. Once convergence, or a set maximum number of evaluations/generations, is reached, post-processing begins by resubmitting the top candidate(s) represented by a pareto front for higher quality statistics, and assessing the performance of the optimization process as a whole. The results of this work will show how the pareto front functionality presents the respective reaction rates for top performers with the ability to visualize a set of well-performing solutions that include a variety of different variable choices.

Chapter 4

Target Design Optimization

4.1 Optimization Results

The target design optimization worked within the bounds/limitations of the initializing parameters to arrive at a set of solutions. Although many of the top performers have similar variable choices, each of the candidates that these results present are based on the general mock design described in the previous chapter and better visualized in Figure 4.1 on the following page. With this mock design, the location and thickness of the thin target is the only parameter held constant. Therefore, Gnowee chooses discrete materials, continuous sizes, and a source variable which represents the incident spectra on the target design.

4.1.1 Pareto Solution Set

Due to the nature of our ratio objective, when the reaction rate to minimize equals zero, cases were said to have the most optimal parasitic reaction rate (as a denominator of zero does not accurately represent a candidates performance with respect to the the employed objective function). For this reason, many top performing cases, including the two with the best score, are shown to have 1E-14 reactions per source neutron as doing this allowed the objective function to return a similar fitness

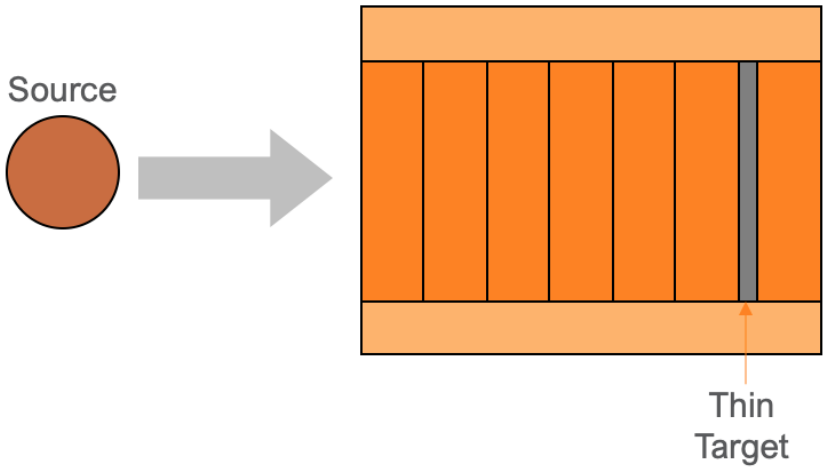


Figure 4.1: General cylindrical design for optimization

to that of the cases with slightly larger values for the competing threshold reaction. Since the uncertainty associated with some filtering material's reaction cross-section data is large, the initial, noisy results do not accurately represent the true performance of a design. This leads to a deviation from a candidate's initial fitness following re-simulation with more neutrons for more precise results. Therefore, the cases that are reran and deviate the least from their initial fitness, are chosen to be further analyzed. Furthermore, the results related to a top performer, when the parasitic reaction was not equal to zero (denoted in red), proves to be comparable following re-simulation, which is directly related to various material's uncertain data particularly at thermal neutron energies.

Since competing values make up the figure of merit implemented in this work, Figure 4.2 represents the spread of the top 731 cases in the form of a Pareto Front. This shows the distribution of candidates' scores with the reaction rate to be maximized on the vertical axis, and the reaction rate to be minimized on the horizontal axis. This figure further points to the top performing candidates residing in the upper-leftmost portion, deemed the pareto front.

Of the top performers there are notable trends that need be mentioned. The FNS spectra is chosen for nearly all cases in this solution set because of it's larger thermal tail (necessary for maximal Cu-63 captures), compared to the general neutron generator spectra (D-D and D-T) presented in chapter 3. Outside of this, some common materials were also used. These include many of those outlined in previous chapters (various forms of Polyethylene, Iridium, Aluminum, ect.), and some seemingly non-characteristic materials like borated poly, Titanium, and heavy water equivalent plastic. Although complex combinations of these materials were verified to produce similar results, the desire to minimize cross-section data uncertainties with the FNS (for future validation) became the primary motive in choosing final cases to analyze. Furthermore, the trade off of having a lower magnitude reaction rate to maximize in order to further limit competing reactions is imposed because of the flux intensity constraint of the FNS facility. However, when implementing

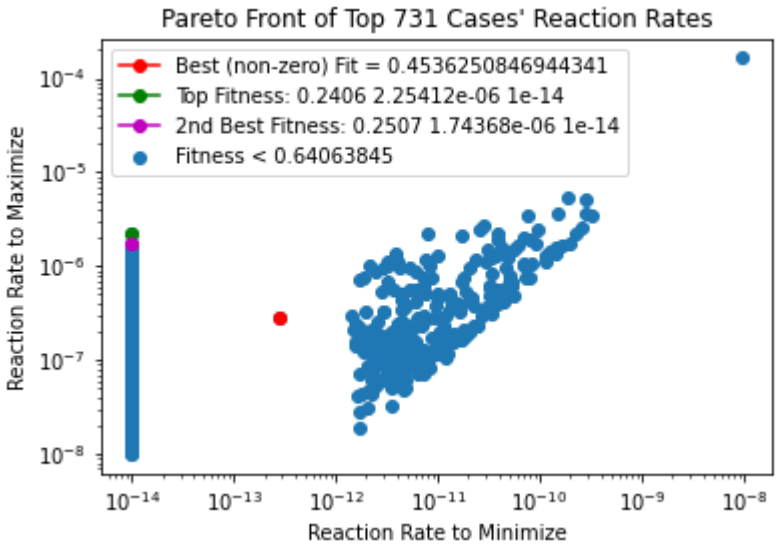


Figure 4.2: Pareto front of the set of solutions for the optimization of Cu-64 production

on a larger scale, more careful considerations would need to be taken into account regarding the production of undesirable isotope(s) and separation processes available to the production facility.

4.2 Top Performing Candidates

Of the top cases that were reran following completion of the optimization, those that deviate the least from their initial fitness are chosen to be presented here. These include: a top case with (a) the competing reaction equal to zero, (b) competing reaction not equal to zero, and (c) one which included Zinc-64 as a filter material (to further analyze potential of using it as a secondary optimization target).

4.2.1 Best Candidate with Zero Parasitic Reaction Rate

The top case that deviated the least from its initial fitness (that initially returned a parasitic reaction rate value of zero) is shown below in Figure 4.3. This includes the materials leading up to the target, the material that follows the target, and the encapsulating cylinder. All of these obtaining crucial reflective properties that lead to maximal scatter for captures to occur in the target.

The scattering affect of this stack-up of materials ability to thermalize/shape the initial FNS spectrum can be better visualized in Figure 4.4 on the following page. From this one could further conclude that various forms of highly hydrogenated materials and special metals most efficiently contribute to maximal captures, and minimal adsorptions in the Cu-63 target. Furthermore, this figure points to uncertain nuclear data as a large deviation was noted from its initial fitness. Lastly, the effect of the neutron spectrum following incidence on a given material (and its thickness in centimeters) is shown, in general, to maximize the thermal region of the spectrum and filter unwanted fast neutrons.

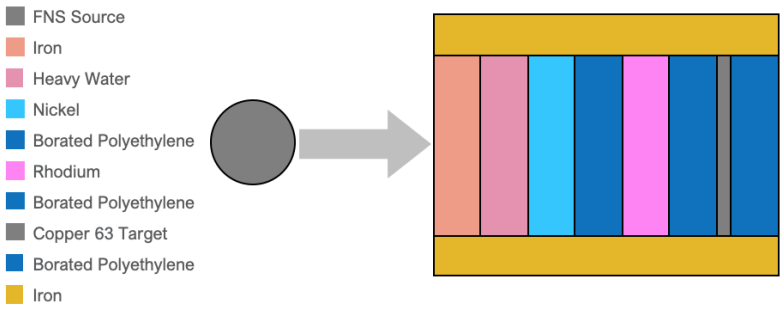


Figure 4.3: 2-D cross-sectional view of simulation target design

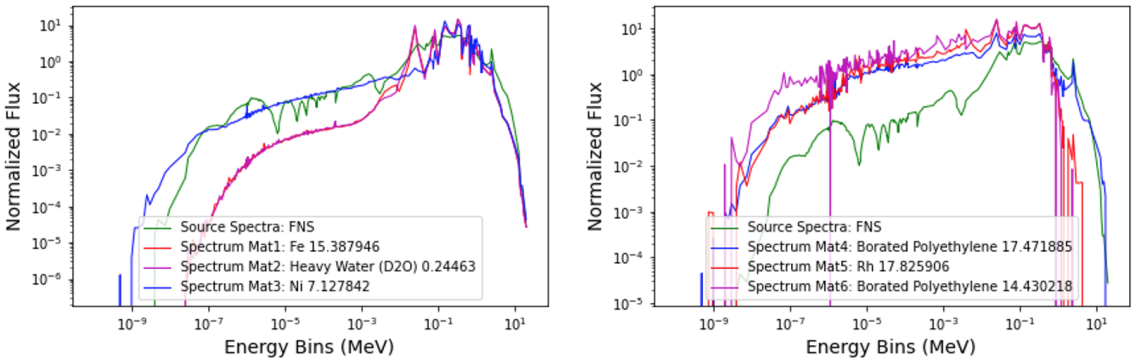


Figure 4.4: Normalized flux through materials prior to target

These chosen materials lead to a primarily thermal spectrum in the target. A comparison to a theoretical objective (or ideal) spectrum which is based on the desired capture cross-section spoken about in previous chapters. These spectra are shown in Figure 4.5 on following page, along with the FNS spectrum chosen by the optimizer. This case showed a final reaction rate fitness value of 0.533 after an initial fitness of 0.267. Furthermore, if this were to be validated under a flux intensity of around 1E9 neutrons per second (general neutron generator magnitude), this incident spectrum could potentially impose hundreds of capture reactions per second in the Cu-63 target and nearly 1E-3 (n,p) absorptions per second.

Due to the aforementioned deviations in the fitness values, when the reaction rate to minimize equalled zero (which is related to uncertain nuclear data at thermal energies), it is advantageous to compare it to one of the highly scored cases that did not initially return a parasitic reaction rate value of zero.

4.2.2 Best Candidate with Non-Zero Parasitic Reaction Rate

In general, the change in fitness was much smaller after re-running for better statistics compared to the previous candidate. Furthermore, the final fitness came out to 0.528, which is actually better than that of the first case described. Again, this case is specified in Figure 4.2 in section 4.1.1 (denoted in red), and showed final reaction values of similar magnitude as the one previously mentioned. Figure 4.6 below shows the design of this candidate, which utilized much less borated polyethylene, leading to more precise results.

The neutron flux produced from the FNS spectrum, filtered by the optimization design is compared to the same theoretical thermal objective described above and is shown in Figure 4.7.

Although this candidate did not initially show promise of being a top performing case, once reran it outperformed nearly other cases, including many of those that initially returned an optimal reaction rate to minimize. The primary difference in these two

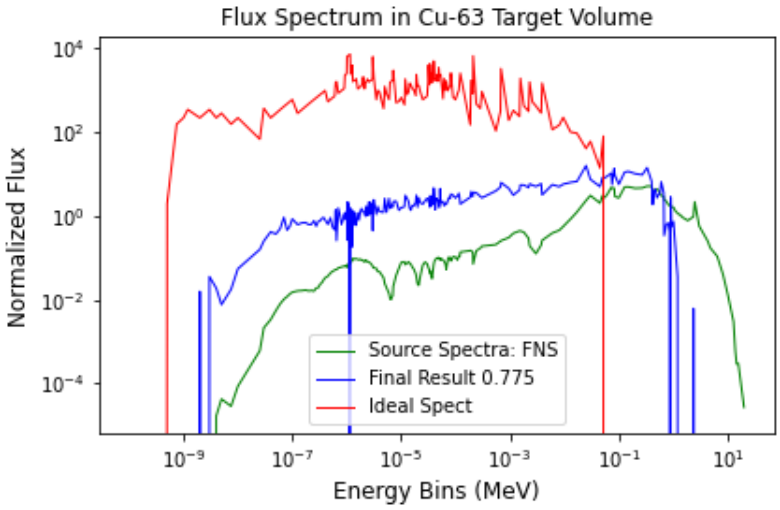


Figure 4.5: A top candidate's normalized flux in target volume

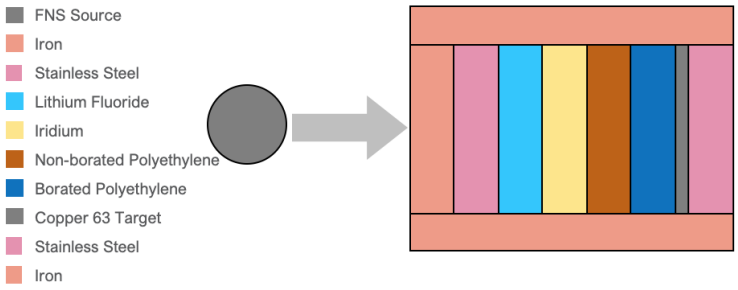


Figure 4.6: 2-D cross-sectional view of target design with non-zero RR(N)

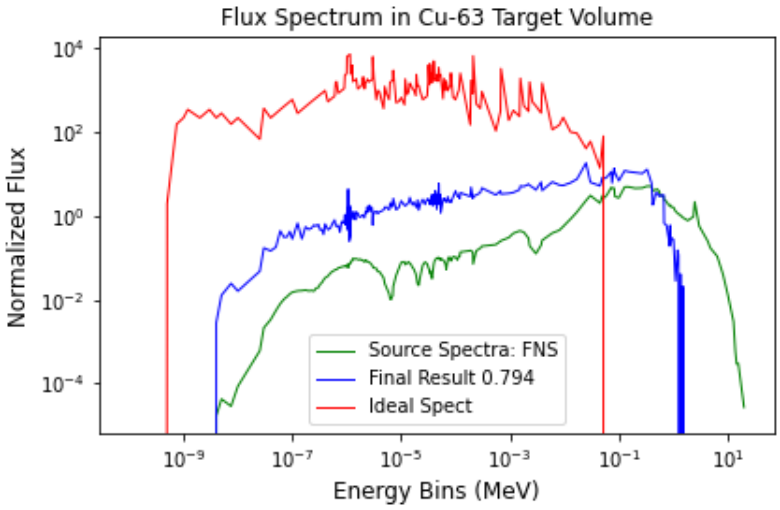


Figure 4.7: A top candidate's normalized flux in target with non-zero RR(N)

cases regards the uncertain cross-section data associated with borated polyethylene, as this case showed substantially less use of it compared to the previous candidate shown.

4.2.3 Best Candidate with Zinc Chosen as Filter Material

Finally, one special top performer chose Zn-64 as a filter material leading up to the target. This is interesting because it proves Zn-64's ability to filter fast neutrons, and is also known to obtain a high (n, p) reaction probability, which could be further implemented as a secondary target to produce Cu-64 by way of neutrons absorption. The cross-sectional view of the entire target design is shown below in Figure 4.8.

The resulting spectrum from this case is shown in Figure 4.9 and it's final reaction rate fitness came out to 0.597 (following an initial fitness of 0.27). It is similarly uncertain for the same reasons as the first presented case, regarding the simulation of materials with uncertain nuclear data. This is important as the associated uncertainties of certain materials need be taken into account when validating these methods.

By re-simulating this case and tracking the number of neutron-proton reactions that occur in the Zinc-64 sample, this reaction rate showed to be one order of magnitude lower than the primary target reaction in Cu-63 sample. This verifies the potential ability to use it as a secondary target material to also contribute to the overall amount of Cu-64 obtained from an irradiation cycle. Furthermore, it could be more so advantageous to implement this technique into the objective function and optimizing accordingly.

This updated optimization is currently in-progress and has already returned results with much better fitness values and a thinner target compared to the case returned from the original optimization (20 centimeters).

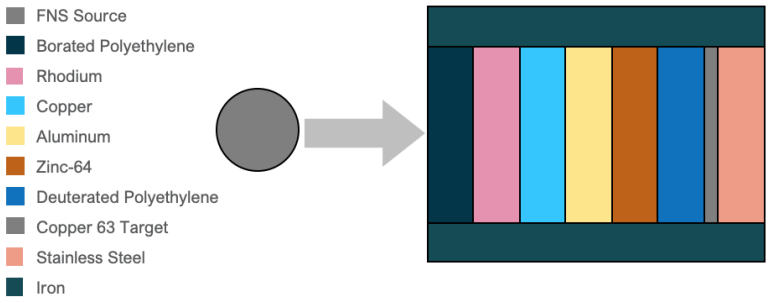


Figure 4.8: 2-D cross-sectional view of target design with Zinc-64 as filter

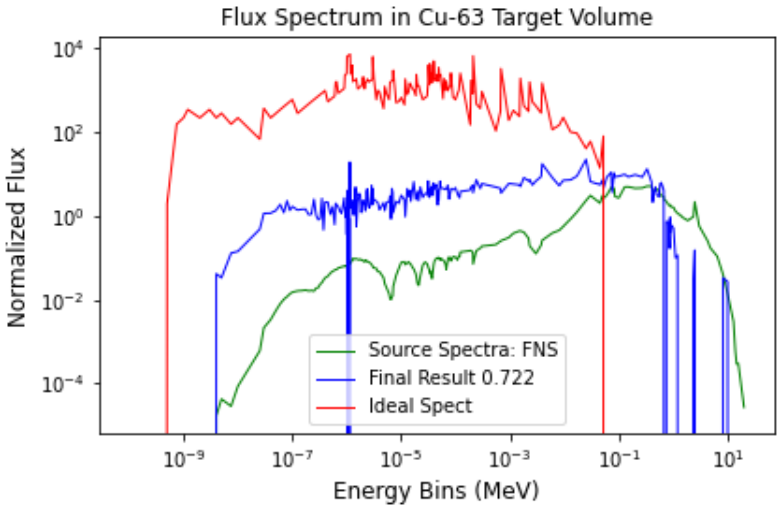


Figure 4.9: A top candidate's normalized flux in target with Zinc-64 as filter

4.3 Population Fitness Analysis

As mentioned before, after hundreds of evaluations, the first generation's population (30 complex individuals) was found. As variants of these parents were created and evaluated, the parent population was replaced by better performers. This resulting trend is shown below in Figure 4.10 as the best, worst, and average population fitness is represented as the optimizer continuously converged for 204 generations, until two consecutive populations concluded the run.

Overall, this optimization concluded after over 5500 individuals were evaluated over the short time frame of a week, with each simulation taking on average 4-7 minutes. Gnowee's efficient framework took seconds to analyze each evaluation and submit a new case which pointed to the neutron transport code taking the majority of the time. Nonetheless, these results verified the ability of our optimization framework to evaluate immensely more target designs for neutron induced production methods compared to current sensitivity calculations used up until this point. Furthermore, with the ability to optimize any highly intense reactor spectra this could potentially further inform the production community of the most efficient isotope for a specific site.

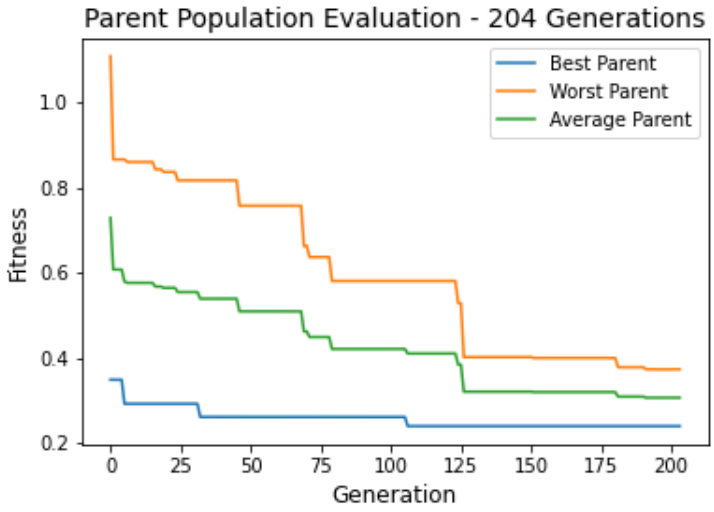


Figure 4.10: Parent population average, best, and worst fitness

Chapter 5

Conclusions

The goal of this research was to develop a meta-heuristic optimization framework that served neutron induced production facilities by way of enhanced spectra modification techniques. Specifically, the work aimed to enable more efficient production methods through flux filtering target design. The work presented accomplished this goal by coupling a general-purpose optimization algorithm with MCNP, identifying neutron reactions that were required to filter specific energy ranges, and building a personalized figure of merit that was used as the optimization function and required maximizing the reaction of interest while minimizing competing, parasitic production. Furthermore, this optimization evaluated over 5500 various designs in about a weeks time. Comparing this to hand calculations, it is easy to see the magnitude of importance these optimization methodologies bring. Lastly, the framework optimized these various designs and returned a solution that appropriately maximized the difference in the reaction of interest and the competing one desired to be minimized. Moreover, the solution set demonstrated that the reaction rate of interest was on the order of 10 of thousands times more likely to occur, than the parasitic one, desired to minimized.

Moreover, the objective of evaluating the ability to implement a secondary target material to return a single theranostic isotope in faster energy regions of the

neutron spectrum was also accomplished. This optimization framework proves to obtain keen characteristics that have potential to greatly advance commonly employed optimization techniques because of its ability to simulate and evaluate thousands of various target designs. Finally, by utilizing a python based meta-heuristic optimization algorithm, a robust and adaptable medical isotope production framework was created with the potential to strengthen the current state of production and help ensure patients receive the necessary treatments and diagnoses for the foreseeable future.

Chapter 6

Future Work

The methods and procedures used for this project helped to improved the value of meta-heuristic algorithms in the isotope production industry. Moreover, this research illuminated many areas of potential work and improvements that would be significant for further informing medical isotope production facilities and enhancing these created frameworks. These include updating the Gnowee/MCNP framework and utilizing the a small-scale generator-driven neutron facility to validate proposed target design optimization methods.

6.1 Optimization Framework Enhancements

Future work that relates to the optimization framework enhancements include the list defined below.

- Implementation of multi-objectivity Gnowee within medical isotope production framework
- Enhance Gnowee to simulate charged particle transport code
- Enable the ability to compare multiple particle type productions for a isotope of interest.

- Develop adaptation and analysis of using multiple targets to create a variety of commonly used medical isotopes.

6.2 Isotope Production Optimization Validation

Lastly, future work that will allow these optimization methods to one day be usefully applied in industry include a proof of concept validation of the proposed isotope production target optimization methodologies. This has much potential to be validated with the FNS, which will conveniently be located on the University of Tennessee's campus.

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Vita

Cameron Salyer is from Norton, Virginia and attended Central High School as a mutli-sport athlete. With the hopes of a one-day football scholarship he looked to walk-on at East Tennessee State University. After two years there work and school overtook his life and he dreamed for a more intellectual and stimulating field of study. Upon the acceptance of the University of Tennessee's College of Engineering, he moved to Knoxville with the pursuit of a Bachelors degree in Nuclear Engineering. Along the way, he further nurtured the hard-worker in him as a server, bartender, intern, research assistant, and indoor cycling instructor. Upon graduation, he quickly returned to pursue a Master's Degree in Medical Physics while working as a medical physics intern at the Provision Proton Therapy Center. All these experiences, and people met along the way, equipped him with the tools and resources needed to complete the assignment at hand. Following this, he hopes to continue his education and research in order to obtain a PhD in Nuclear Engineering. He further dreams of applying this new-found knowledge to enhance the way in which nuclear and radiation practices are implemented in the medical field.