

Study of Oxygen Isotope Distillation for Applications in Medical Diagnostics

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The production of rare isotopes is difficult and carried out only in few sites in the World, though being of interest. For instance, the production of ¹⁸O and ¹⁷O is relevant for medical diagnostics, in particular to promote largescale application of breakthrough methods for early diagnostics for cancer, neurodegenerative diseases and lung diseases. ¹⁸O and ¹⁷O can be produced by cryogenic distillation, operating with a very high number of theoretical stages.

On this topic a PRIN 2022 project has been funded by the Ministero dell'Università e della Ricerca, with the aim of designing a distillation plant for increasing the amount of the isotopes of interest in the final product from the natural abundance up to 10%. The project is based on Aria, a major cryogenic distillation infrastructure in Nuraxi-Figus (South Sardinia), where a 350-meter-tall cryogenic distillation column is being installed to purify argon isotopes for dark matter searches. Extending 350 meters underground into a mineshaft of a former coal mine, Aria is today the only facility capable of producing stable light isotopes via cryogenic distillation in the European Union and has the potentiality to become the most powerful production plant of its kind in the world. This work focuses on the study of the cryogenic distillation column for treating a binary mixture of ¹⁶O₂ and ¹⁶O¹⁸O with the aim of producing a stream richer in ¹⁶O¹⁸O. The simulation of the process has been performed and sensitivity analyses on the main operating parameters have been carried out to define the best operating conditions of the column.

1. Introduction

Over the past 20 years, significant progress has been made in the research, production and application of stable isotopes. Their importance has increased in nuclear energy, medical diagnostics, and ecological studies. For example, medical applications have advanced with isotopes like ²H, ¹³C, ¹⁵N, ¹⁷O, and ¹⁸O playing a relevant role in the Nuclear Magnetic Resonance (NMR) for the disease detection and monitoring (Shulman et al., 1984), and in the Positron Emission Tomography (PET) for the effective cancer, cardiac and neurological diagnostics through non-invasive imaging using radioactive tracers (Ter-Pogossian et al., 1980). In the nuclear sector, the use of enriched isotopes such as ²³⁵U and ²³⁹Pu is needed for nuclear reactor fuels. Recently, ¹⁵N has gained attention for its potential use in uranium nitrides as fuel for the fourth-generation nuclear reactors, due to its exceptional thermal and mechanical properties.

The isotope separation has been carried out by employing several techniques to exploit the differences in the physical and chemical properties of isotopes, such as mass or boiling points. Among the many considered methods, cryogenic distillation is one of the best for the industrial-scale isotope production due to its efficiency and scalability (Andreev, 2007). It performs the separation of isotopes on the basis of their boiling point differences at extremely low temperatures, though the boiling point differences among different isotopes are

very low. The scalability and the cost-effectiveness of cryogenic distillation have made it an essential technology in the production of stable isotopes, a market that is projected to grow significantly in the coming decade.

One of the key projects on cryogenic distillation is Aria (INFN, 2020), that is part of the DarkSide-20k Collaboration. Aria is based on distillation columns initially designed for the purification of Underground Argon (UAr) from sources as the Kinder Morgan's Doe Canyon wells in Colorado in order to obtain a stream rich in ^{40}Ar (Aaron et al., 2023). The UAr is chosen for its significantly lower ^{39}Ar content compared to the one of atmospheric argon and therefore its higher easiness in increasing the ^{40}Ar content, reducing the radioactive interference in experiments aimed at detecting dark matter (Agnes et al., 2021). DarkSide-20k is an advanced experiment located at the Gran Sasso National Laboratory in Italy (Aalseth et al., 2018), employing Liquid Argon Time Projection Chambers (LAr TPCs) to detect weakly interacting massive particles (WIMPs) through nuclear recoil. The usage of purified and enriched argon in the chambers is to minimize radioactive interference from ^{39}Ar , which would otherwise contaminate the data and reduce the sensitivity of dark matter detection.

Aria is today the only facility capable of producing stable light isotopes via cryogenic distillation in the European Union and has the potentiality to become the most powerful production plant of its kind in the world. The facility for the isotope separation is located at the Seruci mine campus in Nuraxi-Figus at Gonnese, Carbonia in Sardinia (Italy) and is expected to be composed of two distillation columns (Seruci-I and Seruci-II) designed to enhance the mass transfer between the vapor phase and the liquid phase and the separation through an efficient packing. A closed-loop refrigeration system using liquid nitrogen to minimize the thermal losses and to optimize the energy efficiency is employed for cooling. The modules are tested at the Conseil Européen pour la Recherche Nucléaire (CERN) in Geneva (Switzerland) and then installed in the mine well. The height and the diameter of the wells, their configuration with multiple accesses and integrated security systems and the availability of a truckable motorway from the surface to a depth of 500 m are ideal conditions for the safe installation of a plant with unique features in the world (INFN, 2020).

The facility has then been thought to be used for the purification of other isotopes in addition to Ar, to set up a production with the aim of satisfying the increasing demand of these species, for instance in medical diagnostics. This work has been carried out within the research project "Production of rare oxygen isotopes with the Aria cryogenic distillation plant for innovative applications in medical diagnostics" and aims at studying the cryogenic distillation column for treating a binary mixture of $^{16}\text{O}_2$ and $^{16}\text{O}^{18}\text{O}$ for the production of a stream richer in $^{16}\text{O}^{18}\text{O}$, with a target of 10 % ^{18}O in the product.

2. Isotopes of the molecular O_2

^{16}O , ^{17}O and ^{18}O are the three oxygen isotopes present in nature. Their abundances (LibreText Chemistry, 2024) are reported in Table 1.

Table 1: Natural abundances [%] of oxygen isotopes

Isotope	Isotope abundance [%]
^{16}O	99.757
^{17}O	0.038
^{18}O	0.205

The combinations of these isotopes for constituting the molecular oxygen are obtained by considering the probability of formation of these molecules, as the product between the concentrations of the two isotopes constituting the molecule and the normalization of all the molar fractions. The results are reported in Table 2.

Table 2: Mole fractions of molecular oxygen isotopes, determined on the basis of the natural abundances of each isotope

Molecule	Mole fraction
$^{16}\text{O}_2$	0.99757
$^{16}\text{O}^{18}\text{O}$	0.00205
$^{16}\text{O}^{17}\text{O}$	0.00038
$^{18}\text{O}_2$	4.21E-06
$^{17}\text{O}^{18}\text{O}$	7.81E-07
$^{17}\text{O}_2$	1.45E-07

$^{18}\text{O}_2$, $^{17}\text{O}^{18}\text{O}$ and $^{17}\text{O}_2$ are present in traces. The production of the isotope ^{18}O could be obtained by $^{16}\text{O}^{18}\text{O}$. In this work, the mixture of isotopes has been assumed to be composed of only the two isotopes $^{16}\text{O}_2$, that is the

main one, and $^{16}\text{O}^{18}\text{O}$, that, though being characterized by a much lower amount, is the one with the highest composition excluding $^{16}\text{O}_2$. Considering that the target is 10 % of ^{18}O and that ^{18}O is present in the molecule $^{16}\text{O}^{18}\text{O}$, the distillation column should produce a bottom stream with 20 % of $^{16}\text{O}^{18}\text{O}$ on a molar basis.

3. Methodology

3.1 Properties of the binary system

The composition of the binary mixture with $^{16}\text{O}_2$ and $^{16}\text{O}^{18}\text{O}$ has been normalized by neglecting the molecules present in very low amount and by adding the amount of $^{16}\text{O}^{17}\text{O}$ (with a molar fraction equal to 0.00038) to the amount of $^{16}\text{O}_2$. The considered mixture is characterized by a molar fraction of $^{16}\text{O}_2$ and of $^{16}\text{O}^{18}\text{O}$ as reported in Table 3.

Table 3: Composition of the binary mixture with $^{16}\text{O}_2$ and $^{16}\text{O}^{18}\text{O}$ considered in this work

Molecule	Mole fraction
$^{16}\text{O}_2$	0.99795
$^{16}\text{O}^{18}\text{O}$	0.00205

Given the very low concentration of the heavy isotope of interest (only 0.2 %) in the feed of the distillation column, the enrichment up to 20 % is very difficult to achieve and is a general characteristic of separation of isotopes. Therefore, a tall distillation column is needed, with a high reflux ratio and a low bottom product flowrate, as the one designed for Seruci-I.

3.2 Simulation of the unit

The commercial process simulator ASPEN Plus[®] V14 has been used for the simulation of the distillation column. It is provided by default in the database with only one molecule of O_2 , that has been assumed to be representative of the isotope $^{16}\text{O}_2$, the main common one. Another component, representing the $^{16}\text{O}^{18}\text{O}$ isotope, has been added to the database, with a different molecular weight because of the different atomic composition and a different vapor pressure. The vapor pressure has been determined on the basis of the value provided by Ancona et al. (1962). The $^{16}\text{O}^{18}\text{O}$ isotope is characterized by the same specific heat capacity of the vapor phase and of the liquid phase, the same heat of vaporization and the same liquid molar volume of the the $^{16}\text{O}_2$ isotope (Baraldi, 2024).

The Seruci-I column is provided with 28 central modules, each one of height equal to 10.28 m and diameter of 0.71 m, with an internal packing characterized by a Height Equivalent to a Theoretical Plate (HETP) of 10 cm, in addition to be provided with a top module and a bottom module and liquid distributors. The total column height is equal to 349 m and the total number of theoretical stages is 2871.

The DSTWU column has been employed for the simulation in this work. It performs a Winn-Underwood-Gilliland shortcut design calculation for a distillation column, with a partial or a total condenser and with a single feed and two products. For the specified recovery of the light and the heavy key components, the minimum number of theoretical stages with the Winn correlation, the minimum reflux ratio with the Underwood correlations, the required reflux ratio for a specified number of theoretical stages or the required number of stages for a specified reflux ratio with the Gilliland method are estimated.

In this work, the number of stages has been set equal to the one of the Seruci-I distillation column and the reflux ratio has been determined for different recovery ratios (from 60 % to 99 %) in the bottom product of the heavy isotope of interest. Then, the maximum feed that can be provided on the basis of fluid dynamic performances has been determined and the productivity of the unit has been analyzed.

4. Results and Discussion

Firstly, the minimum number of stages (reported in Figure 1a)) required for the separation has been checked. The required binary distillation is possible for every recovery ratio of the heavy isotope $^{16}\text{O}^{18}\text{O}$, because the minimum number of stages is always lower than the number of available ones from Seruci-I.

The molar fraction of $^{16}\text{O}_2$ in the distillate product slightly increases as the recovery ratio of $^{16}\text{O}^{18}\text{O}$ increases because more $^{16}\text{O}^{18}\text{O}$ is recovered in the bottom product (Figure 2). The distillate stream, also for a recovery ratio equal to 60%, is characterized by a molar fraction of the light isotope $^{16}\text{O}_2$ equal to more than 0.999. The molar compositions of the bottom product do not change because of the specification of molar fraction of $^{16}\text{O}^{18}\text{O}$ equal to 0.20.

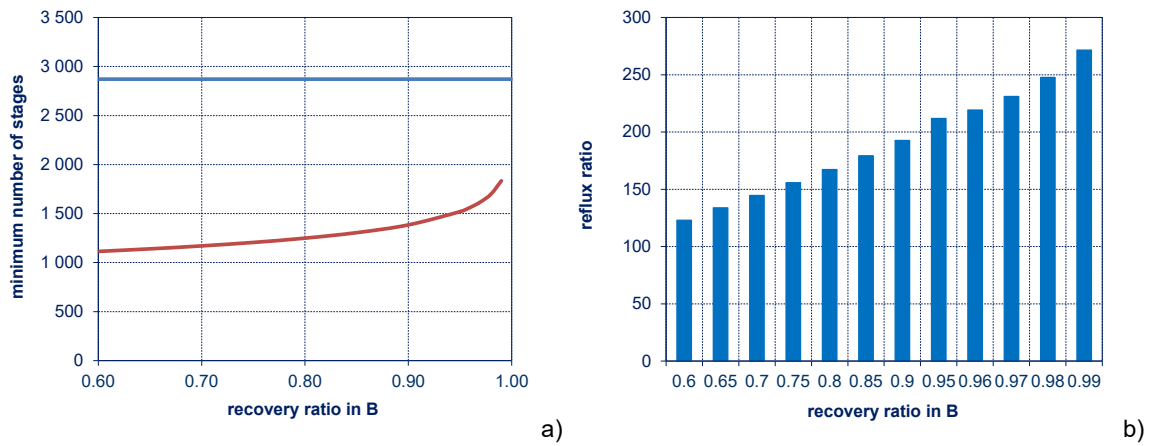


Figure 1: Variation a) of the minimum number of stages and b) of the reflux ratio as the recovery ratio of $^{16}\text{O}^{18}\text{O}$ in the bottom stream varies, obtained with a molar fraction of 20% of $^{16}\text{O}^{18}\text{O}$ in the bottom product

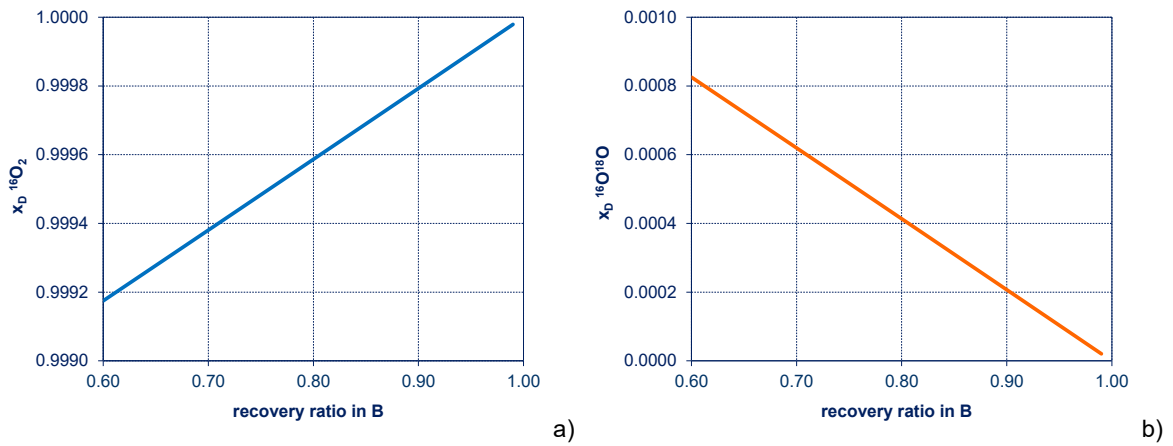


Figure 2: Variation of the mole fraction of a) $^{16}\text{O}_2$ and b) of $^{16}\text{O}^{18}\text{O}$ in the distillate product as the recovery ratio of $^{16}\text{O}^{18}\text{O}$ in the bottom stream varies, obtained with a molar fraction of 20% of $^{16}\text{O}^{18}\text{O}$ in the bottom product

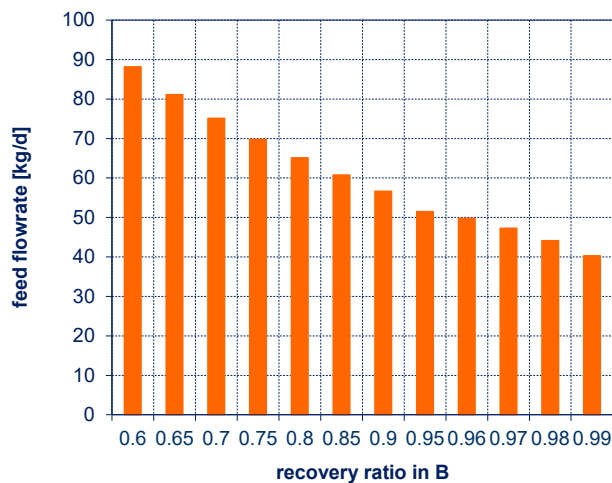


Figure 3: Variation of the feed flowrate as the recovery ratio of $^{16}\text{O}^{18}\text{O}$ in the bottom stream varies, obtained with a molar fraction of 20% of $^{16}\text{O}^{18}\text{O}$ in the bottom product

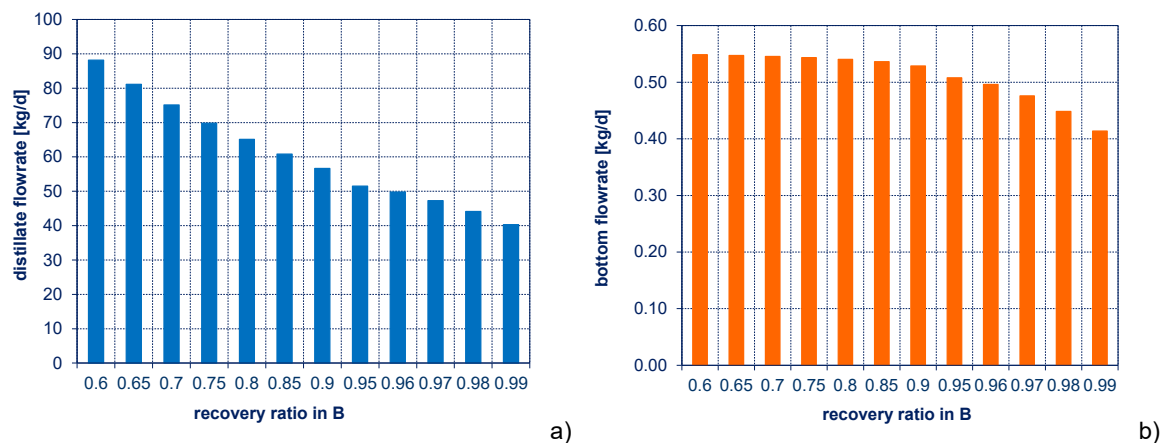


Figure 4: Variation a) of the distillate flowrate and b) of the bottom flowrate as the recovery ratio of $^{16}\text{O}^{18}\text{O}$ in the bottom stream varies, obtained with a molar fraction of 20% of $^{16}\text{O}^{18}\text{O}$ in the bottom product

The reflux ratio, that is much higher than the value usually considered for the separation of traditional systems, significantly increases as the recovery ratio of $^{16}\text{O}^{18}\text{O}$ increases, up to more than 300, because of the increased difficulty in the separation (Figure 1b)). Generally, the increase in the reflux ratio causes an increase in the operating costs of the distillation column, mainly related to the condenser duty and to the reboiler duty, because of the higher circulating flowrates.

The feed flowrate depends on the maximum circulating flowrates of vapor and liquid inside the column, that increase as the recovery ratio of the heavy isotope increases. As the circulating flowrates inside the column increase, the maximum feed flowrate decreases, as reported in Figure 3. For a recovery ratio of 99% the feed flowrate is lower than half of the one obtained for a recovery ratio of 60%. Therefore, also the productivity varies and the flowrates of the distillate and of the bottom products decrease as the recovery of the isotope $^{16}\text{O}^{18}\text{O}$ in the bottom stream increases (Figure 4), for the same molar fraction of $^{16}\text{O}^{18}\text{O}$ in the bottom product, equal to 20%.

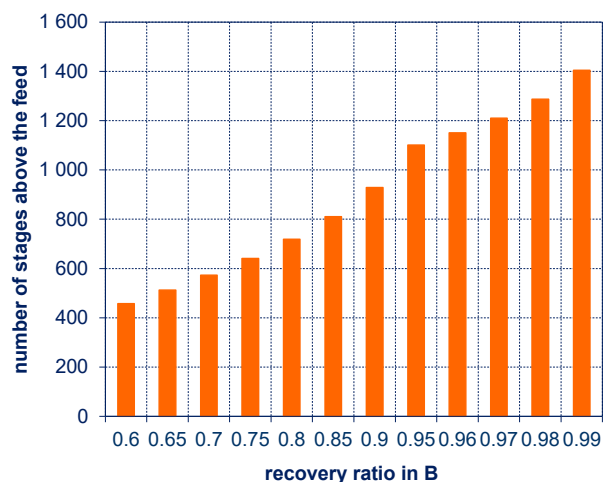


Figure 5: Variation of the number of stages above the feed stage as the recovery ratio of $^{16}\text{O}^{18}\text{O}$ in the bottom stream varies, obtained with a molar fraction of 20% of $^{16}\text{O}^{18}\text{O}$ in the bottom product

The number of theoretical stages above the feed inlet position increases as the recovery ratio of the heavy isotope in the bottom product increases and the feed stage tends to move closer to the bottom of the column (a higher number of theoretical stages above the feed is needed, as reported in Figure 5). A higher section of rectification and a lower section of stripping are needed, with a relevant variation if considering a recovery ratio of $^{16}\text{O}^{18}\text{O}$ in the bottom stream equal to 60 % or equal to 99 %.

An experimental activity on the Seruci-I distillation column is scheduled and it is of interest to compare the results obtained in this work with the experimental points.

5. Conclusions

This paper focused on the study of a cryogenic distillation column for producing isotopic mixtures rich in the isotope ^{18}O , with the analyses of the performances of a unit within the Aria Project. In particular, the database of the ASPEN Plus[®] software has been implemented with the ^{18}O isotope and several simulations of the distillation column have been performed, by analyzing the variation of the main parameters as the recovery ratio of the heavy isotope in the bottom stream varies, for the same purity of the bottom product. The Aria plant can provide an oxygen isotope production, with a potential for the facility to enter the global market. As the research project is being developed, the isotope production capacities could be expanded with Seruci-II, the second column with a larger diameter, that is planned to be built and to start its operation, contributing to the development of the industry focusing on stable isotopes production.

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