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Improving reliability of radiopharmaceuticals synthesis system used in nuclear medicine

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The use of radioactive isotopes in nuclear medicine is crucial for diagnosis and treatment of many diseases, and the multi-purpose synthesis system plays a vital role in producing radiopharmaceuticals. However, due to the harsh radioactive operational conditions, the system must have high reliability to avoid failures that could have serious consequences. The purpose of the work presented in this paper is to develop a probabilistic assessment of system reliability using a mathematical modelling based on graph issued from Hasse diagrams and a reliability block diagram to compare the results. By dividing the synthesis system into small subsystems, the reliability of each subsystem and its possible architectures has been quantified. This approach allows identifying the components that have crucial impact on system reliability and clarifying their failure rates, taking into account operational conditions. The results show that it is possible to assess the reliability of a multi-purpose synthesis system used to produce radiopharmaceuticals for nuclear medicine using the proposed modelling and probabilistic assessment approach.

Keywords: System reliability assessment, nuclear medicine, Hasse diagram, reliability block diagram, redundancy, synthesis system, radiation and reliability.

1. Introduction

The nuclear medicine is an important branch of medicine that allow to diagnose and treat many serious diseases. The diagnostic and treatment of such diseases are based on radiopharmaceutical products which are synthesized using complex systems. Such systems implement nuclear radiation phenomena in the chemical synthesis process. If these nuclear phenomena are needed in the synthesis process of radiopharmaceutical products, they can have also a negative impact on the behaviour of the uses system and its components and more specifically in their reliability. The presented work on a first approach to probabilistic assessment of system reliability for a multi-purpose synthesis system used in nuclear medicine builds upon previous research in the field of reliability engineering.

Barni *et al.* (2003) proposed two approaches for reliability analysis of an Accelerator Driven System (ADS): a "top-down" and "bottom-up" approaches. The top-down approach involved techniques such as Fault Tree Analysis (FTA) and Reliability Block Diagram (RBD). These techniques help in identifying potential failure modes and analysing the system's reliability at a higher level of abstraction. The bottom-up approach, on the other hand, focused on Failure Mode and Effect Analysis (FMEA), particularly for large complex systems.

Burgazzi and Pierini (2007) conducted a study specifically on the availability and reliability analysis of ADS used in nuclear waste transmutation. They employed a Reliability Block Diagram (RBD) to quantitatively assess the reliability of different subsystems within the accelerator.

Blumenschein *et al.* (2019) proposed a systematic approach called Reliability Requirements and Initial Risk Evaluation (RIRE) for complex systems at CERN. Their study involved the use of various techniques such as a risk matrix, Failure Mode and Effect Analysis (FMEA), and Fault Tree Analysis (FTA). These techniques helped in determining reliability requirements and evaluating the initial risks associated with CERN's systems.

Building upon the knowledge and methodologies established by these previous studies, the present work focuses on the reliability assessment of multi-purpose synthesis systems in radiopharmaceutical production. The approach utilized in this work is based on Hasse diagrams and Reliability Block Diagrams (RBD).

The next section presents the description of the synthesis system used for the production of radiopharmaceuticals and it structure and components. The section 3 develops the reliability model in the form of Hasse diagram and, based on it, computes the minimal path-sets and the analytical expression of system reliability. To validate this result, a second approach of modelling and probabilistic assessment of system reliability by means of a reliability block diagram using a commercial software is also proposed. In order to improve the studied system, two more architectures are proposed in section 4 and their reliability are also calculated. Finally, the last section concludes this work and give some perspectives for the future.

2. System description

The research object being described is a synthesis system used for the production of radiopharmaceuticals, specifically for the synthesis of fluorodeoxyglucose (FDG) used in positron emission tomography (PET) for the diagnosis and treatment of oncological diseases. The system is made from commercial components and is designed to be highly reliable to ensure that it functions without failure. The synthesis system is composed of three parts (Fig. 1): a laptop with software for operator control, a control unit with several buttons and batteries for data transmission, and a synthesis module that performs all operations of the synthesis process, located inside a hot cell.

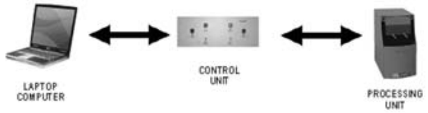

Fig. 1. Synthesis system components

The synthesis module is made up of actuators, including solenoid valves, reed switches, pneumatic cylinders, pneumatic 90-degree rotary actuator, heating element, vacuum pump, pressure regulator, RFID sensor, radiation sensor, thermocouple sensor, and pressure sensor. The control part of the synthesis module includes two printed circuit boards - relay and control. The relay board includes relays, diodes, resistors, fuse, and capacitors. The control board consists of an 8-bit PIC microcontroller, operational amplifiers, linear drivers and receivers, voltage reference, voltage regulators, potentiometers, diodes, resistors, and capacitors.

3. Reliability assessment

During its lifetime, the synthesis system for producing FDG operates in radioactive environment, so it must have high reliability in order to fulfil its mission. To assess the reliability of the system, the following methodology was proposed:

(i) a functional diagram of the system is built by highlighting functional parts (subsystems);
(ii) based on the obtained functional diagram, a reliability block diagram is built;
(iii) the reliability of individual elements of the subsystem is assessed;
(iv) the reliability of the entire system is calculated.

Using this technique, the reliability of the cartridge fixation subsystem was calculated. A functional diagram of the subsystem was built (Fig. 2), where MCU is a PIC microcontroller, R is a relay, RS is a reed switch, EV is a solenoid valve, and PC is a pneumatic cylinder.

A reliability block diagram (RBD) of the cartridge fixation subsystem was made from functional block diagram (Fig. 3). For this block diagram, the following structure function of the system is obtained:

$$y = x_{MCU} \wedge \left(x_{R12} \wedge x_{RS2} \wedge x_{EV11} \wedge x_{PC3} \wedge x_{PC4} \vee x_{R13} \wedge x_{RS1} \wedge x_{EV12} \wedge \left(x_{PC1} \wedge x_{PC2} \vee x_{PC5} \wedge x_{PC6}\right)\right) \qquad (1)$$

As an alternative approach, a Hasse diagram of the subsystem was constructed (Fig. 4). Each node of this Hasse diagram represents a state vector of the system. The state vector considered in the diagram of Fig. 4 is the following: For a more compact representation of the Hasse diagram, the following simplifications were made the subsystem binary word has been simplified to the following form:

$$< x_{MCU},\ x_{L1},\ x_{L2\_el},\ x_{L2\_PC1\&2},\ x_{L2\_PC5\&6} > \qquad (2)$$

where:

(i) L1 represents the first line of the reliability block diagram R12-RS2-EV11-PC3-PC4 and the state value of this line is given by only one Boolean variable x_{L1}
(ii) L2_el represents the electrical part of the second line of the reliability block diagram R13-RS1-EV12 and its state value is given by the Boolean variable x_{L2_el}
(iii) L2_PC1&2 and L2_PC5&6 represent the pneumatic actuators parts PC1 in series with PC2 and, respectively PC5 in series with PC6 and their state values are given by the Boolean variables $x_{L2\_PC1\&2}$ and $x_{L2\_PC5\&6}$.

The Hasse diagram obtained in figure 4 allow us to obtain firstly the minimal cuts-sets and path-sets of this system (Duroeulx *et al.* 2017) by using satisfiability approach (Biere *et al.* 2009). This system has three minimal pats-sets represented by the state vectors <10110>, <10101> and <11000>. For example, the first state vector <10110> means that it is sufficient that the three components MCU, L2_el and L2_PC1&2 work (and to other two components L1 L2_PC5&6 are failed) to assure that the system is operational and realize its function. The system has also three minimal cut-sets represented by the following state vectors: <01111>, <10011> and <10100>. For example, the first state vector <01111> representing a minimal cut-set means that if the only one component MCU is failed, then the whole system is completely failed.

The knowledge of minimal path-sets helps us to directly obtain the expression of the system reliability from the Hasse diagram. The idea of this approach (Brinzei and Aubry, 2018) is to associate a weight equal to “1” to each minimal path-set and to propagate it to all of each their upper nodes of the diagram. At this step of the algorithm the weight of each upper node lets us to know how many times they have been counted if we consider only the minimal path-sets. In terms of probability, this means if we consider the probability of the monomials corresponding to the path-sets (in the expression of system reliability), then the probabilities of the upper nodes will be counted many times, and this give a overvaluation of the system reliability. In order to obtain the exact expression of system reliability it is necessary to reduce the weight of each upper node to “1” and when it is realized to delete the node from the Hasse diagram. The algorithm proposed in (Brinzei and Aubry, 2018) performs this in a iterative way and it allow to obtain the following analytical expression of system reliability:

$$R_{Sys}(t) = R_{MCU}(t) \cdot R_{L1}(t) + R_{MCU}(t) \cdot R_{L2el}(t) \cdot R_{L2\_PC1\&2}(t) + R_{MCU}(t) \cdot R_{L2el}(t) \cdot R_{L2\_PC5\&6}(t) + R_{MCU}(t) \cdot R_{L1}(t) \cdot R_{L2el}(t) \cdot R_{L2\_PC1\&2}(t) \cdot R_{L2\_PC5\&6}(t) - R_{MCU}(t) \cdot R_{L1}(t) \cdot R_{L2el}(t) \cdot R_{L2\_PC1\&2}(t) - R_{MCU}(t) \cdot R_{L1}(t) \cdot R_{L2el}(t) \cdot R_{L2\_PC5\&6}(t) - R_{MCU}(t) \cdot R_{L2el}(t) \cdot R_{L2\_PC1\&2}(t) \cdot R_{L2\_PC5\&6}(t) \qquad (3)$$

To calculate the reliability of the subsystem, the values of the failure rate of individual elements were found:

Table 1. Failure rates of the subsystem elements.

PIC MCU:	$\lambda_{MCU} = 3.27 \cdot 10^{-9}\, h^{-1}$
Relay:	$\lambda_R = 3.54 \cdot 10^{-8}\, h^{-1}$
Reed switch:	$\lambda_{RS} = 5 \cdot 10^{-9}\, h^{-1}$
Electric valve:	$\lambda_{EV} = 3.12 \cdot 10^{-6}\, h^{-1}$
Pneumatic cylinder:	$\lambda_{PC} = 1.37 \cdot 10^{-6}\, h^{-1}$

Failure rate values were taken from various sources (such as MIL217, manufacturer reliability databases, and analogue equipment reliability databases). According to the failure rates og table 1, the reliability of each component can be computed by $R_i(t) = e^{-\lambda_i t}$. For the macro-components L1, L2_el, L2_PC1&2, L2_PC5&6, we compute firstly their equivalent failure rate as a sum of the failure rates of their elementary components due to series configurations.

In order to validate our approach by Hasse diagram, we use also the GRIF® software (GRIF 2023) that allow us to compute directly from the reliability block diagram of figure 3 the numerical values of system reliability. The GRIF software uses a BDD (Binary Decision Diagram) approach to compute the system reliability, but it does not provide the analytical expression of the system reliability, just the numerical values of this reliability. The results of reliability calculations by two approaches are shown in the form of curves in Fig. 5, they allow to validate the approach by Hasse diagram.

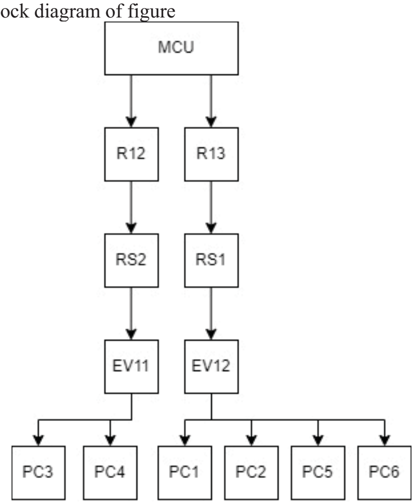

Fig. 2. Functional diagram of the cartridge holder subsystem

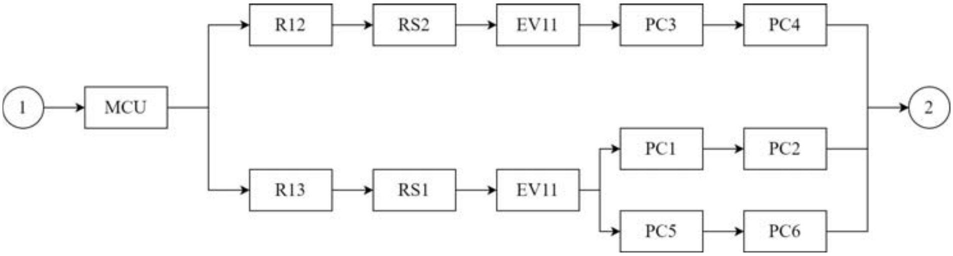

Fig. 3. RBD of the cartridge holder subsystem

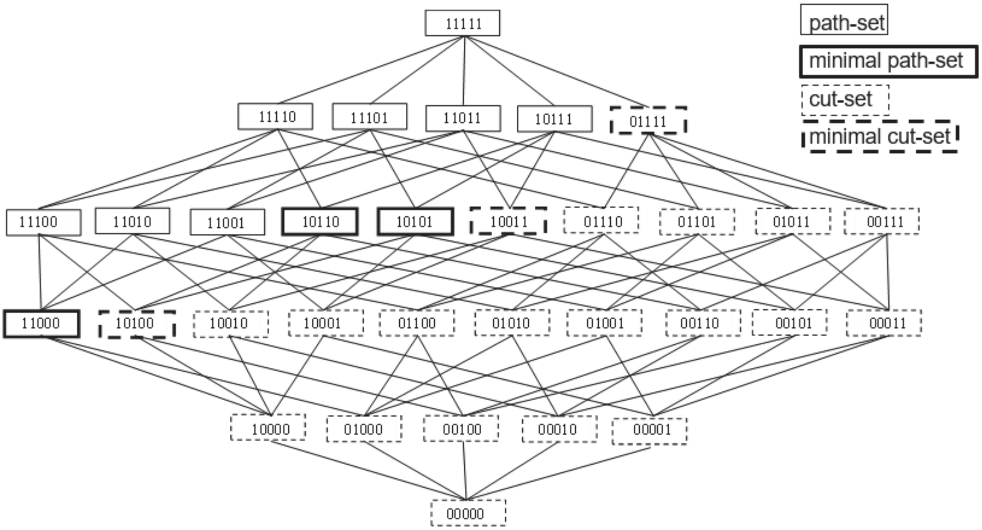

Fig. 4. Hasse diagram of the cartridge holder subsystem

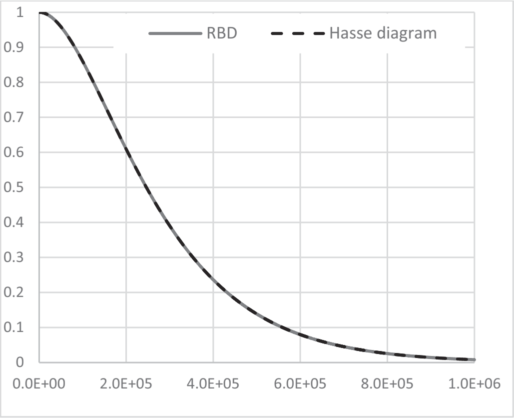

Fig. 5. Subsystem reliability calculation results

4. Improvement of the cartridge holder subsystem reliability

Firstly, to improve the cartridge holder subsystem new architecture was proposed (Fig. 6). There were added new dependencies between PC's. For this block diagram, the following Boolean structure function is obtained:

$$y = x_{MCU} \wedge (x_{R12} \wedge x_{RS2} \wedge x_{EV11} \wedge x_{PC3} \wedge x_{PC4} \vee x_{R13} \wedge x_{RS1} \wedge x_{EV12} \wedge (x_{PC1} \wedge x_{PC2} \vee x_{PC5} \wedge x_{PC6}) \vee x_{R12} \wedge x_{R13} \wedge x_{RS1} \wedge x_{RS2} \wedge x_{EV11} \wedge x_{EV12} \wedge (x_{PC2} \wedge x_{PC3} \vee x_{PC4} \wedge x_{PC5} \vee x_{PC1} \wedge x_{PC4} \vee x_{PC3} \wedge x_{PC6})) \quad (4)$$

Secondly, from the previously proposed architecture another system architecture was made (Fig. 7), it contains one redundant element – electric valve (EVr1). The binary Boolean structure function of this architecture is the following:

$$y = x_{MCU} \wedge (x_{R12} \wedge x_{RS2} \wedge x_{EV11} \wedge x_{PC3} \wedge x_{PC4} \vee x_{R13} \wedge x_{RS1} \wedge (x_{EV11} \wedge x_{PC1} \wedge x_{PC2} \vee x_{EVr1} \wedge x_{PC5} \wedge x_{PC6}) \vee x_{R12} \wedge x_{R13} \wedge x_{RS1} \wedge x_{RS2} \wedge (x_{EV11} \wedge x_{EV12} \wedge (x_{PC2} \wedge x_{PC3} \vee x_{PC4} \wedge x_{PC5}) \vee x_{EV11} \wedge x_{EVr1} \wedge (x_{PC1} \wedge x_{PC4} \vee x_{PC3} \wedge x_{PC6}) \quad (5)$$

Using previously given failures rates the reliability the two proposed architectures were made. The results of them with comparison with original architecture depicted on Fig. 8. Architecture #1 is more reliable than the original one, while architecture #2 is even better than the second one. The results show that the addition of redundant elements such as electric valve EVr1 in architecture #2 has contributed significantly to the subsystem's reliability.

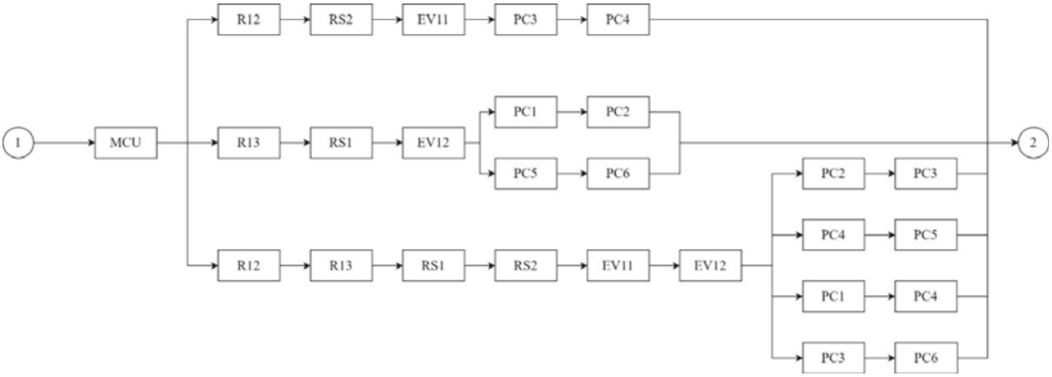

Fig. 6. Architecture of the cartridge holder subsystem #1.

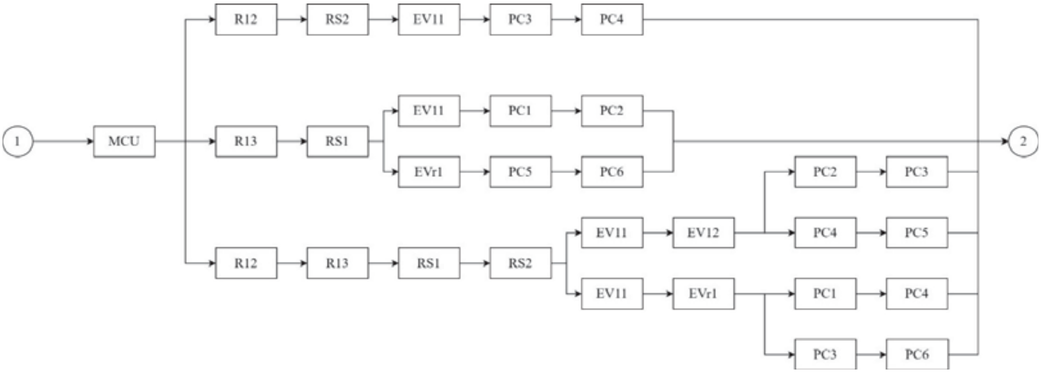

Fig. 7. Architecture of the cartridge holder subsystem #2, with redundancy.

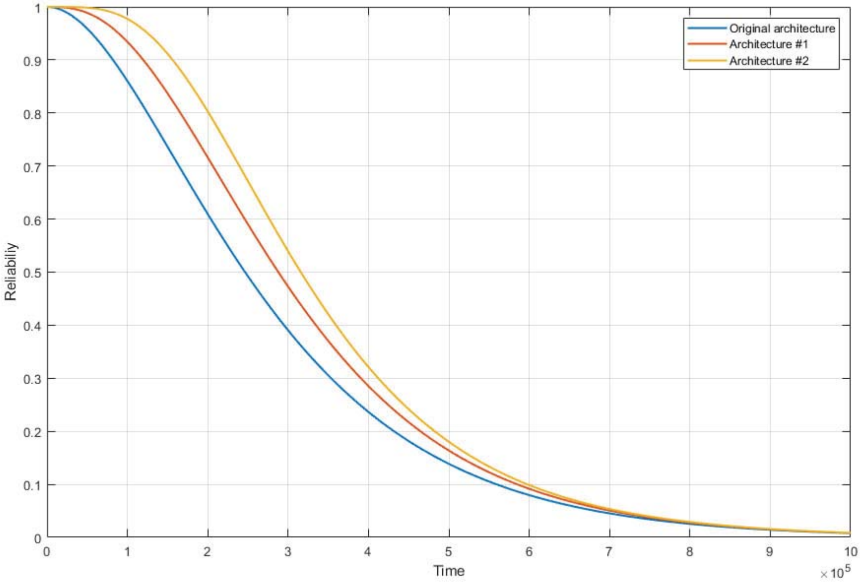

Fig. 7. The comparison between the three subsystem architectures.

5. Conclusions

The identification of functional block diagrams and the development of reliability models using Boolean structure function and Hasse diagram are important steps in assessing the reliability of complex systems such as the multi-purpose synthesis system used in nuclear medicine. Such systems are submitted to radiation effects which can have a significant impact on the reliability of the system and its components. The analytical expression obtained for probabilistic assessment can provide valuable information for optimizing the system and improving its reliability. Redundancy is a common approach to improve the reliability of a system, as it allows for backup elements to take over in case of a failure. Proposed architecture with a redundant element (electric valve EVr1) improves the overall reliability of the system. This redundancy provides an additional level of protection against system failures, which is reflected in the reliability curve of architecture #2 being higher than that of architecture #1.

However, it is important to note that the model and estimation of reliability are only as good as the assumptions and input data used in the analysis. Therefore, it is important to carefully consider the factors that can affect the reliability of the system and to obtain accurate and up-to-date information on the failure rates of its components. To achieve this, we propose in the future research work to determine the impact of radiation on the system components (Dodd and Massengill, 2003) in order to compute the values of failure rates including the radiation effects and, also, the impact on software errors (Asadi et al. 2007).

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