**Titre du projet: Machine learning for Healthcare Pathways analysis**

**Fiche «Membre 1»**

*Reviewing guidelines: Projects are reviewed with the best international standards in mind, considering 5 main criteria.*

## Project
*The evaluation must consider:*
- *The extent to which the project addresses the objectives of this "call for projects"*
- *The clarity and originality of the objectives beyond the current state-of-the-art*
- *The novelty of the approaches and their cancer relevance.*

This proposal addresses two fundamental aspects of healthcare pathways in the context of cancer. The 'collective approach' aims to model the overall healthcare pathway that will focus on population level studies and most likely impact health-economics. Here Dynamic Bayesian Networks will be explores as a primary modelling tool. The 'individual approach' aims to study the trajectory of an individual patient. Here, reinforcement learning will be utilised to analyse the data and make recommendations.

The team has already studied the application of relevant techniques in the context of Thyroid Cancer and leukaemia. The application of machine learning, in particular reinforcement learning, to modelling patient pathways is relatively new. While some of the general benefits, as for example the optimisation of therapeutic management or the measurement of impact of specific interventions, is clear the impact of this work is going to be less immediate.

## Innovation and development
*The evaluation must consider to what extent:*
- *is the proposal innovative in the technical and scientific fields?*
- *does the proposal contribute to unlock scientific bottlenecks?*
- *does the proposal open new scientific and technical perspectives?*
- *will the proposal have an effect towards the scientific community and policy makers ?*

While it will be possible to translate specific component solution into the clinic, the improved modelling of patient pathways will play a critical role in making broader changes in healthcare. Only if we test certain solution in the context of the patient pathway will it be possible to re-design specific pathways. This is of course a very complex problem and the risk of failure is high.

The work will advance the underlying methodology and highlight the utility of this technology in specific settings.

## Methodology and feasibility
*The evaluation must consider to what extent:*
- *the proposed methodology will be able to fulfill the objectives of the project in a competitive manner*
- *the proposed work is feasible within the project duration*

- *the appropriateness of the allocation and the integration of the work proposed to each participant*
- *the matching of the timetable and the methodology with the objectives of the project.*

The output and objectives of this research project are described at a higher level. A set of software libraries and software applications will be developed but it is not clear how these will be tested or validated.

Unfortunately, the problem of 'transparency in AI' is not being discussed in any meaningful way. While it is highlighted as one of the important fields for future work in the cited survey article (Yu et al) the proposal does not address the question on how clinicians or patients can trust this new technology.

I am confident that this well-qualified team will make significant progress. However, it is less clear what the precise output of the project will be. From the proposal it is not clear to me if the existing database is sufficient to support the proposed research.

## Consortium

*The evaluation must consider:*
- *the scientific excellence of the coordinator attested by the publications, the patents, and his/her aptitude to be a group leader able to manage the project*
- *the extent to which the participants collectively constitute a consortium of high quality and consider whether their complementarities and competences allow them to carry their tasks.*

The consortium is well qualified and reasonably well established. The team will also collaborate with M. Kosorok (Chapel Hill) and Erica Moodie (McGill). With the help of visits and extended research stays they will broaden the existing collaboration.

## Budget

*The evaluation must also consider whether the Budget requested is in adequation with the project for each of the following items, when necessary:*
- *Consumables*
- *Equipment*
- *Outsourcing of services*
- *Personnel*
- *Travel and other expenses*

Overall the budget makes sense but it is not clear how the computational costs will be covered.

## Overall comments

This proposal is both interesting and exciting. It is certainly a high-risk project and the anticipated output of the work is somewhat vague. Here I would argue that it is important to support this or similar efforts to take on the challenge of modelling very complex systems.

SAVY Nicolas

## Fiche «Membre 2»

*Reviewing guidelines: Projects are reviewed with the best international standards in mind, considering 5 main criteria.*

### Project
*The evaluation must consider:*
- *The extent to which the project addresses the objectives of this "call for projects"*
- *The clarity and originality of the objectives beyond the current state-of-the-art*
- *The novelty of the approaches and their cancer relevance.*

The project develops a machine learning framework for exploring healthcare pathways for individuals affected by chronic diseases such as cancer. While I see the importance of such study within the context life quality for cancer patients under treatment, the proposed project seems to point more in the direction of long term patient management (that pertain more to the "medico-economic" aspects) rather than addressing a fundamental scientific question that would advance our understanding about cancer or other chronic disease. So, I personally fail to distinguish the hard scientific question that the project would focus on.

### Innovation and development
*The evaluation must consider to what extent:*
- *is the proposal innovative in the technical and scientific fields?*
- *does the proposal contribute to unlock scientific bottlenecks?*
- *does the proposal open new scientific and technical perspectives?*
- *will the proposal have an effect towards the scientific community and policy makers ?*

The project is certainly useful for policy makers, and from that perspective, indeed, the project is innovative. However, the project does not identify a clear scientific contribution nor a novel technical advancement.

### Methodology and feasibility
*The evaluation must consider to what extent:*
- *the proposed methodology will be able to fulfill the objectives of the project in a competitive manner*
- *the proposed work is feasible within the project duration*
- *the appropriateness of the allocation and the integration of the work proposed to each participant*
- *the matching of the timetable and the methodology with the objectives of the project.*

The approach has in itself is useful for policy makers, and for that purpose the methodology seems appropriate. However, the project does not have a clear and focussed plan to addressing a specific aspect (say in cancer or other chronic disease) that would lead to an advancement of science.

### Consortium
*The evaluation must consider:*
- *the scientific excellence of the coordinator attested by the publications, the patents, and his/her aptitude to be a group leader able to manage the project*
- *the extent to which the participants collectively constitute a consortium of high quality and consider whether their complementarities and competences allow them to carry their tasks.*

There is no doubt that the consortium is of very high quality, involving highly experienced PIs that bring together complementary expertise in machine learning, statistics, and data analysis. Certainly, with this wealth of expertise, the consortium will have no problem in achieving and exceeding the goals assumed in this proposal.

## Budget
*The evaluation must also consider whether the Budget requested is in adequation with the project for each of the following items, when necessary:*
- *Consumables*
- *Equipment*
- *Outsourcing of services*
- *Personnel*
- *Travel and other expenses*

The budget planning is appropriate

## Overall comments

The project proposes a machine learning framework based on a wealth of artificial intelligence methods to explore and assess the long term trajectories of individual affected by chronic diseases (as it is the case for instance in several forms of cancer). While this is important for instance for long-term medical management purposes, I personally failed to distinguish a hard scientific question that the proposal would focus on.

*Reviewing guidelines: Projects are reviewed with the best international standards in mind, considering 5 main criteria.*

## Project

*The evaluation must consider:*
- *The extent to which the project addresses the objectives of this "call for projects"*
- *The clarity and originality of the objectives beyond the current state-of-the-art*
- *The novelty of the approaches and their cancer relevance.*

The project titled "Machine learning for Healthcare Pathways analysis" addresses the objectives of developing technologies to optimize the so-called "healthcare pathways" that is the sequence of health-treatment events in the life of an individual affected by some form of chronic diseases such as cancer. At the individual level, the project aims to optimize a cancer-specific (myeloid leukemia is the use case) treatment management increasing the treatment success rate while at the societal level the goal is to optimize health management costs. In this regards the project fits the objectives of the present "call for projects"; specifically it aims to develop computational methods to optimize "Diagnostic aids, prognosis, therapeutic follow-up" The originality of the envisaged approach is beyond the current state-of-the-art. Indeed the suggested work includes recent improvements in machine learning and AI techniques.These approaches are however completely independent from the cancer field as they relate to the field of computer science. In this respect, cancer appears as a viable proof of concept where to apply the mentioned techniques.

## Innovation and development

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- *will the proposal have an effect towards the scientific community and policy makers ?*

The project is certainly innovative. It aims at applying state-of-art machine learning and artificial intelligence methods/concepts/technologies to the field of chronic patient treatments pathways. It could potentially deliver interesting solutions and/or open new scientific technical perspectives thus having an effect toward the scientific community and policy makers.

## Methodology and feasibility

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- *the proposed methodology will be able to fulfill the objectives of the project in a competitive manner*
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- *the matching of the timetable and the methodology with the objectives of the project.*

The proposal has many merits. The topic is interesting and addresses one of the scopes of the call.However, its feasibility appears its main weakness.The project is quite ambitious given the paucity of data. Indeed this aspect reveals the main pitfall of the proposal.The question of data availability is poorly addressed. It is not clearly described where are they going to find all the data needed. I would have seen a table summarising all the data sources with numbers, cases, etc. Also, there is no

estimation of these numbers.The proposal has a major flaw: it concentrates very much on the general theoretical questions without a dip into a concrete description of the real problem. The optimization of healthcare pathways is identified as a very complex problem where the most relevant source of problems comes from the enormous diversity of cases which is not paralleled by as much available data. The techniques mentioned in the proposal require a very large data set to be set up and tested and it is not clear (since it is very vaguely stated in the proposal) what is the amount of data available to support such statistical inference methods.Also, while many techniques are mentioned with a clear idea of how to combine them, they are not sufficiently described to convey the message that the details of the implementation are clear and not yet a blue sky research topic. The timetable seems appropriate. What is missing is a clear deliverable/milestone plan to demonstrate project progresses.

## Consortium

*The evaluation must consider:*

- *the scientific excellence of the coordinator attested by the publications, the patents, and his/her aptitude to be a group leader able to manage the project*
- *the extent to which the participants collectively constitute a consortium of high quality and consider whether their complementarities and competences allow them to carry their tasks.*

The consortium is well sorted with skills in the different areas of the required research areas such as machine learning, statistics, data analysis, epidemiology but also cancer clinics.Each team is hosted in renowned scientific institutions and connected with groups with consolidated backgrounds in the specific knowledge required by the proposed research. The integration of these skills is the strength of the consortium.Certainly, the investigators are experts in the field and know what to do. They have experience in similar applications of artificial intelligence methods and want to use it in another contest (chronic leukemia).

## Budget

*The evaluation must also consider whether the Budget requested is in adequation with the project for each of the following items, when necessary:*

- *Consumables*
- *Equipment*
- *Outsourcing of services*
- *Personnel*
- *Travel and other expenses*

The requested budget appears adequate. It includes personnel costs and some money for disemination activities. It also includes money for travel, for computer equipment and to conduct extensive numerical experiments.

## Overall comments

The proposal describes a plethora of AI methods that, while orchestrated with the ability of the experienced project proponents, carry an enormous risk: if only one of the envisaged step fails, the overall project will not be able to deliver a working solution. Each of the techniques mentioned (Q-learning, PAC, ABM, DNN) requires great care, large data sets, heuristics, computational resources to train/simulate, time to set up and test.The proposed work seems more concentrated on solving theoretical/methodological problems rather than applying state-of-art to the clinical problem itself.The use of deep Q-learning implies the use of deep learning (deep NN) which has a huge number of parameters: the problem of available data to train the agent (needed to approximate the Q-value function to be used in the reinforcement learning algorithm) seems mined on its ground.In another paragraph, the proposal mentions the potential use of the PAC method to solve the problem of "policy evaluation" while interesting from the theoretical viewpoint, carries the risk of failing.It is not clear

how a GAN approach can escalate meaningful information (virtual patients) if the available data for them to be trained is low. It looks like a chicken-egg problem.Also, if the potential phase space is poorly represented by the limited data, there are no guarantees that a GAN approach will be able to cover holes in the manifestations.The question of "interpretability of the results" when using putative sophisticated learning techniques is a problem left unsolved. It is not clear whether this might translate into a successful outcome.This shows that the project while good in the intention, is likely not to deliver what promised. It will certainly lead to interesting scientific signs of progress in the field of artificial intelligence but not in cancer management or cancer research which is the real aim of this call for projects.

**Interdisciplinary approaches in oncogenic processes and therapeutic perspectives:**
**Contributions of mathematics and informatics to oncology**
**Edition 2021**


**SAVY Nicolas**

Committee Feedback



## Strength:

- The output of this proposal is advancement in methodology

## Weakness:

- The proposal lacks novelty
- The proposal does not tackle a specific question that is translatable and does not have one specific scientific question to focus

## Global opinion and Recommendation:

- The main concerns of the panel members is the scientific question
- From the proposal it is not clear if the existing database is sufficient to support the proposed research.