CSP and "omics" Technology Applied on Versatile and Intelligent Portable Platform for Modeling Complex Bio-medical Data

Luige Vladareanu, Mihaiela Iliescu*
Robotics and Mechatronics Department
Institute of Solid Mechanics of the Romanian Academy
010141, C-tin Mille 15, Romania, Bucharest
luigiv2007@yahoo.com.sg; iliescumihaiela7@gmail.com

Hongbo Wang, Feng Yongfei
Parallel Robot and Mechatronic System
Laboratory of Hebei Province, Yanshan University,
Qinhuangdao, China
hongbo_w@ysu.edu.cn;

Victor Vladareanu*
Faculty of Electronics II,
University Politehnica of Bucharest,
313 Splaiul Independentei, *060042,* Buchatrest, Romania
vladareanuv@gmail.com

Hongnian Yu
School of Design, Engineering and Computing
Bournemouth University, Poole,
Dorset BH12 5BB, UK,
yuh@bournemouth.ac.uk

Florentin Smarandache
Department of Mathematics,
University of New Mexico,
705 Gurley Avenue, Gallup, NM 87301, USA
fsmarandache@gmail.com

***Abstract* - This paper presents relevant aspects of the idea of using the digital medicine in cancer, so that to shape a viable strategy for creating and implementing an interactive digital platform, NEO-VIP, that should be the basic support to design the strategy for integration of basic, clinical and environmental research on neoplasia progression to cancer. The two main components of the VIPRO Platform are represented by the workstation "Engineering Station" for CPS (Cyber Physical System) and "omics" technology and by the "Graphical Station" for the development of a virtual mechatronic system environment and virtual reality for system components' motion. The NEO-VIP Platform will consolidate the collaboration of specialized institutions in IT, medicine, health, life standards so that to enhance their capabilities to work as a consortium. The results lead to the possibility developing NEO-VIP Platform in the IT modelling field, applied on bio-medical data, as a new player alongside with the existing ones. So, new improved methodologies for investigating social implications of machines working with and for people will be applied.**

Keywords—intelligent control systems; cyber physical system, "omics" technology; modelling system; virtual reality; digital medicine in cancer

I. INTRODUCTION

In recent years the identification of missing information/links/principles on different biological, medical, and organizational levels regarding carcinogenesis and possible solutions for designing an integrative platform able to use the data and merge, complement and develop in a transformative approach the high impacting tools have gained attention among the research community [1-3], but also in manufacturing industry, resulting in an outstanding development in terms of hardware and software [4-6].

According to the World Health Organization (WHO) report "Health in 2015: from MDGs to SDGs", cancer is a leading cause of death worldwide and accounted for 8.2 million deaths (22% of all non-communicable disease deaths) in 2012. The emergence of this disease is caused by molecular, genetic,

*** Corresponding Authors***

epigenetic alterations and environmental factors that favor neoplasia. Cancer incidence and mortality increase with age, and both the absolute number and the percentage of the population that is older are increasing in all regions of the globe. Dealing with a context characterized by ageing populations, rapid urbanization and globalization of markets that promote inactivity and unhealthy diets is a priority for WHO that will focus on the development and implementation of strong national plans that emphasize prevention and treatment access for all [7, 8].

The paper main objective is that of supporting the use of digital medicine in cancer, so that to shape a viable strategy for creating and implementing an interactive digital platform that should be the basic support, to design the strategy for integration of basic, clinical and environmental research on neoplasia progression to cancer.

The paper main objective supporting the use of digital medicine in cancer, is to shape a viable strategy for creating and implementing an interactive digital platform, and to design the strategy to integrate basic, clinical and environmental research on neoplasia progression to cancer and use the support of the NEO-VIP platform, by developing of the VIPRO Platform [9-11], to progress beyond the state of art.

A lot of initiatives were launched in the last decade in the purpose of coordinating research projects that have the common aim to elucidate comprehensively mainly the genomic changes present in many forms of cancers. One of these initiatives, the International Cancer Genome Consortium (ICGC) was launched in 2010 [12] with the scope to generate comprehensive database of genomic abnormalities (somatic mutations, abnormal expression of genes, epigenetic modifications) in tumors from 50 different cancer types and/or subtypes which are of clinical and societal importance and make the data available to the entire research community.

In United States exists a wide interest in developing databases on different types of cancers that would be fit to be connected and explored by a the new integrative NEO-VIP Platform presented in paper. The NAR Database (https://www.oxfordjournals.org/our_journals/nar/database/subcat/8/33) provides a summary of the most known and used databases grouped on categories addressing to genomic, trascriptomic, and proteomic-field, and also library databases on several others domains.

Most of existing databases are “niche specific” and an represent integration approach of different "omics" with suggestions for treatment or adequate nutrition to minimize the risks of cancer development , so this is why they might be very useful for clinical practice and ultimately to the patients. To the best of our knowledge, none of the existing databases focus on the early detection of neoplastic transformation and none of them relates to the prevention.

The innovative NEO-VIP platform, developed as open architecture system and adaptive networks integrates Future Internet Systems vision enabling: cyber-physical systems by adaptive networks, intelligent network control systems, human in the loop principles, data mining, big data, intelligent control interfaces, network quality of service, shared resources and distributed server network - remote control and e-learning users by interconnected global clouds. Based on all the above, the challenges and, therefore, expected progress of NEO-VIP are its ability to be interactive, integrated and competitive with scientific research DMC (Digital Medicine for Cancer) platforms such as ICGC Data Portal, TCGA Data Portal, NCI Genomic Data Commons (GDC) thus supporting the ITfoM (IT Future of Medicine) concepts.

II. CSP AND OMICS TECHNOLOGY APLLIED ON NEO-VIP PLATFORM

NEO-VIP is extendable for integration, testing and experimenting clinical research on neoplasia progression through building an open architecture system and adaptive networks, combining the expertise of a team of specialists in biomedical engineering, electronics, mathematics, computer sciences with the expertise of a diverse group of researchers in different oncologic specialties (hematologic, head and neck, breast, hepatic, gastric, pancreatic, lung, cervical), immunology, pharmacogenomics. NEO-VIP will facilitate new ways to corroborate data to produce predictive models of neoplastic transformation and prevention and nucleate scientific groups that will be able to answer the extremely complex problems posed by oncogenesis. The computational platform NEO-VIP developed in this project is based on the virtual projection method [9, 13- 15].

Human remotely controlled intelligent networks, are estimated to have an increasingly significant role in events that could put at risk human lives. This is why, the development of an Interactive and Versatile Intelligent Portable Platform, NEO-VIPP is of high benefit. This platform should be able to integrate clinical research on neoplasia progression to cancer and fit these data in predictive patterns of oncogenesis. Nowadays neoplasia research encounters some barriers that prevent researchers from completely exploring all the genomic data available, thus impeding progress. Some of these weaknesses are mentioned next

- Neoplasia data that would be available from various projects, clinical trials, and neoplasia tests are stored on various media with secured management systems, for accessing these data.

- Neoplasia data are many times generated by different methods, so that even if two different datasets are explored, the researcher cannot use both in the same time
- Large size of datasets files, difficult access to efficient storage media and specific software represent a barriers for researchers to get efficient knowledge and information.

The Versatile, Intelligent, Portable NEO-VIPP platform breaks down these barriers by bringing neoplasia progression datasets and associated clinical data into one location that any researcher may access, and "harmonizing" the data so that datasets that were generated with different protocols can be studied side by side. These data are available by modern computing and network technology, so that NEO-VIPP enables any researcher to study, search and ask new and fundamental questions about cancer.

As foster of large scale cooperation at the European level is the development of an e-learning and remote-control platform that should enable community interested in the topic and long-term plans to further develop research and innovation. This, in fact, is the tool of ensuring the ability of continuously learning, adapting and improving in "real world" complex environments, modeling in real time the information gathered by "**omics**" technologies, clinical, imaging so as to provide support in "big data" management and development of international clusters able to process the information in an unifying vision. This way, networking activities will be in good balance with scientific and technical activities contributing equally to advance the scientific research and to improve people life by prevention of neoplasia progression to cancer.

The VIPRO architecture for humanoid and cooperative robots [9, 11], is extendable for integration, testing and experimenting clinical research on neoplasia progression through building an open architecture system and adaptive networks over the classic control system, as shown in Figure 1. The virtual platform developed and extended, NEO-VIPP, is the tool for transforming data in knowledge on oncogenesis and use it in personalized/precision medicine. The need to manage all behaviours and interactions is solved by developing a new interface for intelligent control based on advanced control strategies, such as extended control (Extenics), neutrosophic control, human adaptive mechatronics, implemented by high speed processing IT&C techniques in real time communication for a high amount of data processing, including a remote control & e-learning component and an adaptive networked control. This will allow the development of new methodologies, evaluation metrics, test platforms, reproducibility of experiments, novel approaches to academia-industry co-operation for enabling disruptive product and process innovation and last but not least an inter-academic network for research and modeling complex bio-medical data for neoplasia early diagnosis of progression and management towards personalized medicine.

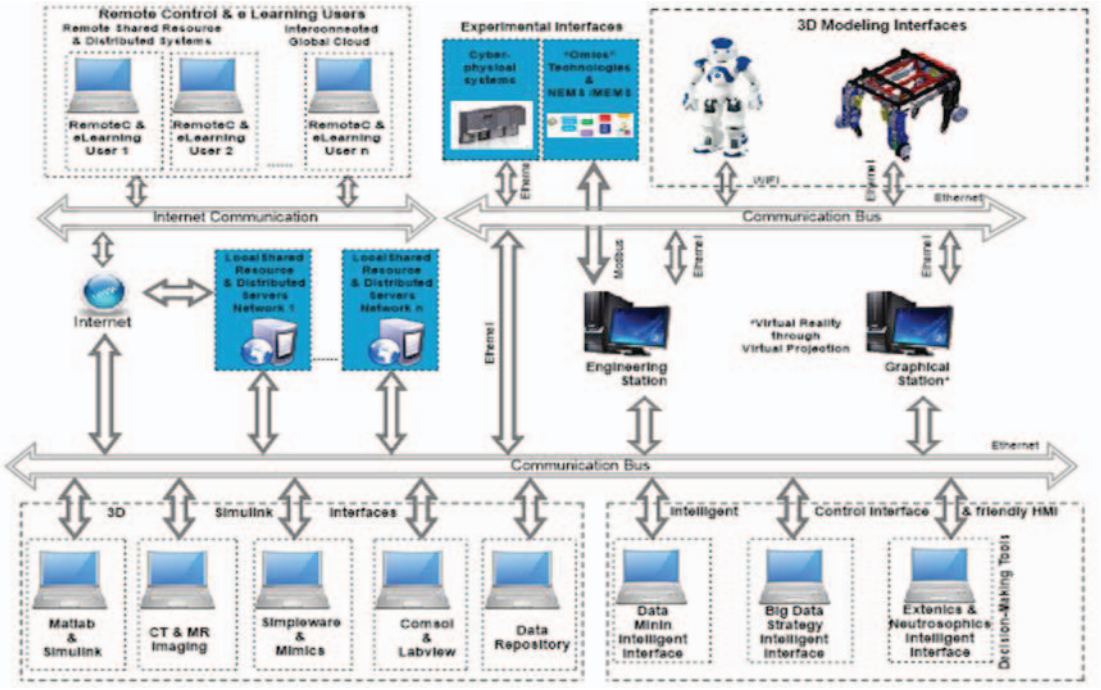

Fig. 1. Architecture of the NEO-VIP Platform

The NEO-VIPP innovative platform will be competitive with other similar DMC virtual application platforms, ICGC Data Portal, TCGA Data Portal, NCI Genomic Data Commons (GDC), or the powerful worldwide platforms for CAD applications (SolidWorks), medical imaging reconstruction (Simpleware, Mimics), multiphysics numerical modeling (Comsol), mathematical and biomedical modeling (Matlab+Simulink, Mathematica), virtual instrumentation and measurements (Labview), or virtual reality environment (Coreograph, Webot, USARSIM, V-RAP), but additionally to these platforms, it enables the design, test and experimentation by intelligent control methods in real time integrating classical control in modelling and simulation [16-18].

The VIPRO Platform architecture for modelling and simulation of mobile robots is based on the virtual projection method, through which robotics and mechatronics systems are developed in a virtual environment.

The technical solution, presented in an open architecture real time control structure, contains the main modules of the VIPRO Platform. The intelligent control interface module uses advanced control strategies adapted to the research environment such as research data mining, big data or decision control through extenics [19-20], neutrosophic logics control [21-23], etc., implemented through computational techniques for fast processing and real time communication. The following intelligent control interfaces have been designed and implemented on the NEO-VIP Platform: data mining intelligent interface, big data strategy intelligent interface, extenics & neutrosophic intelligent interface.

The two main components of the VIPRO Platform are represented by the workstation "Engineering Station" for CPS (Cyber Physical System) and "omics" Technology and by the "Graphical Station" for the development of a virtual robot environment and virtual reality for system motion.

The NEO-VIP Platform has allotted 5 user stations dedicated to simulation using data repository, Comsol & Labview, Simpleware & Mimics, CT&MR Imagingor Matlab &Simulink.

For remote control in establishing the e-learning component of the NEO-VIP Platform, a PC server was integrated to ensure large data traffic for internet communication, with two addition workstations for end-user applications.

The "Engineering Station" component is mainly aimed at integrating the AC500 development environment for programmable automate (PLC) applications, control of the CPS application through the virtual projection method and decision testing of the intelligent neutrosophic control, extenics control, and dynamic hybrid force position control DHFPC interfaces.

After testing, these are integrated in real-time control of a new CPS or "omics" technology with improved system performance through the Graphical Station, as follows: for multi-users through the components of the NEO-VIP Platform consisting of Remote_Control & eLearning_User1, Remote_Control&eLearning_User2 or individually through the NEO-VIP Platform components consisting of the dedicated intelligent interfaces on the Notebook workstations, namely simulation by data repository, Comsol_ & Labview, Simpleware_& Mimics, CT&MR Imaging or Matlab_& Simulink or intelligent interfaces: neutrosophic, extenics and DHFPC interfaces.

NEO-VIPP is an innovative platform which makes the difference from existing ones in that it is the only one which ensures real-time testing and experimentation on its own real time control system and adaptive networked control for remote users through e-learning & remote communication in addition to the design, modelling and simulation facilitated by scientific research platforms such as ICGC Data Portal, TCGA Data Portal, NCI Genomic Data Commons (GDC), being integrated into the DMC platforms ~~through~~ using the ITfoM (IT Future of Medicine) concepts.

The NEO-VIPP platform is more than just a data repository; it will continue to evolve by encouraging scientists to submit the data for early diagnosis of **neo**plasia progression from their own investigations. When researchers submit data to the NEO-VIPP, they will be able to access and, analyze all NEO-VIPP available datasets in neoplasia, while further expanding these resources to the cancer research community.

The NEO-VIPP will also house data from a new era of NCI programs that will sequence the DNA of patients enrolled in clinical trials. These datasets will lead to a much deeper understanding of which therapies are most effective for individual neoplasia patients. There is also to be developed an interface to e-Health Literacy that ensures that data and results from NEO_VIPP will be accessed, explored and applied by all interested people.

Each new datasets entry to NEO-VIPP will evolve into a smarter, more comprehensive knowledge base that will foster important achievements in neoplasia research. It will increase the success of neoplasia early diagnosis and management, basically from Virtual Patient" health models to personalized cancer treatment.

Personalized treatment may benefit of using reliable biomedical numerical models concerning patient-specific, morphologically realistic computational domains (built out of medical MRI, CT, PET, Doppler, etc. images) that present detailed and accurate virtualizations of organs, tissues or regions of interest (ROI) that may produce results, which can

be checked against experimental data. Along this path, medication delivery through existing or yet to be accepted techniques (*e.g.*, magnetic drug targeting, general or localized hyperthermia) may be explored.

III. Resultes and Conclusions

NEO-VIP Platform aims to demonstrate and validate the usability and benefit of DMC in healthcare as well as to enable stockholders to adopt and implement models, strategy and the platform.

The platform represent a tool and a warrant of sustainable learning, testing, adjusting and improving in "real world" various complex environments, mining data gathered from H2020 research programs such as FET (Future and Emerging Technologies) and HDCW (Health, Demographic Change and Wellbeing). It should also enable real time modeling of the information got from "omics" technologies, validation by multinational and multidisciplinary scientists work, appropriate link with various medical, imaging, environmental exposure data, in predictive patient treatment algorithms and strategies for patient management.

New enabling methodologies, and techniques, relying inclusively on medical physics, statistical and applied mathematics (methods, protocols and algorithms, implementation; procedures for data mining; procedures for exploring, handling and connecting big data, etc.), and biomedical engineering, developed by NEO-VIP Platform, may be needed to provide the patient-related approach in DMC.

To provide the patient-related approach in Digital Medicine for Cancer, the NEO_VIPP platform would represent a reliable tool for providing vital support to "big data" management so that data processing in an unified vision to be ensured.

The platform aims to bring high value and positive impact on accessing, exploring and management of impressive amount of data generated by research prevention, detection, treatment and management of neoplasia and its associated diseases. Establishing original links, by the NEO-VIP Platform, between novel genomic alterations in oncogenesis, is estimated to make possible the identification of new, relevant biomarkers and, consequently to indicate new ways of cancer therapy.

At the same time, NEO-VIP Platform allows in a dynamic way, our understanding of the causes and mechanisms underlying healthy ageing and disease, providing opportunity an approach for multiscale modeling in real time the information gathered by "omics" technologies, clinical, imaging, nutritional, and environmental exposure data, in predictive algorithms and personalized strategies for patient management, completing and increasing the impact of the existing initiatives in disease prevention, detection, treatment and management.

Multidisciplinary, large scale cooperation in the development and implementation of the NEO_VIP Platform, will establish a nucleus of competence that will integrate various specialists (biomedical engineers, mathematicians, biochemists, biologists, physicians, bio-physicists, etc.) and will deliver coherent recommendations for implementing this interactive platform. So, through the networking activities will increase the awareness of all stakeholders, including healthcare professionals and patients. The NEO-VIP Platform will consolidate the collaboration of the specialized institutions in IT, medicine, health, life standards so that to enhance their capabilities to work as a consortium.

This will lead VIP Platform to be integrated in the IT modelling field as a new player alongside with the existing ones. The NEO-VIP knowledge transfer facility aims to achieve a strategic, sustainable and long-term partnership (pole of excellence) that will improve the theoretical, technical and best practices of researchers in the EU and worldwide on neoplasia progression. So, new improved methodologies for investigating social implications of machines working with and for people will be applied.

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