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Robust System of Algorithms for the Functioning of Biocompatible Artificial Liver Devices †

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Abstract: This article concerns liver transplantation and its associated difficulties and risks, and also describes a more progressive method of saving people in need of a liver transplant—an artificial liver. An analysis of the BioUML software platform for modeling bioartificial liver systems is also presented.

Keywords: re-engineering; energy sector; energy security; cognitive modeling; mathematical modeling

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1. Main Text

The liver is one of the most complex and metabolically active organs in the body, and it performs many functions such as detoxification and protein synthesis, which are necessary for life. Extracorporeal bioartificial liver systems (BAL), consisting of functioning viable hepatocytes, can provide temporary support to patients with acute liver failure and save the lives of patients awaiting orthotopic liver transplantation (OLT).

To date, one of the most dangerous diseases in the world that leads to a fatal outcome is Fulminant hepatic failure (FHF). Few experiments and studies have been conducted in this area, which have brought significant results in therapy, but have had no effect on mortality; rates are close to 80%. Some patients can be saved when provided with short-term liver support, which, in turn, helps theirs regenerate. However, this procedure can only help those with reversible liver failure. It is also worth noting the fact that patients who have gone through the procedure described above, after it was carried out, had liver function completely restored and returned to their usual life. But this was not always the case; for many years, there was only one method of treating FHF—liver transplantation. There are many disadvantages to this method; for example, there are patients with liver failure who absolutely cannot have this operation for medical reasons such as: concomitant infection, cancer with metastases, chronic alcoholism, etc. Another disadvantage of liver transplantation surgery is the lack of donors; as a consequence, the liver, that is, the patient, may die whilst waiting for their turn for transplantation, simply because there was no donor. In this regard, a new method has been invented that will help both patients who cannot undergo liver transplantation for medical reasons and those who are on the waiting list for this operation. For example, patients with acute hepatitis, potentially reversible, may benefit from temporary artificial liver support. For this purpose, special bio-artificial devices have been developed that can replace a number of liver functions: synthetic, metabolic, and detoxification processes. Some of these devices have been evaluated in clinical trials [1–3].

To study both BAL and OLT systems, several articles were analyzed. The primary sources of these articles were also found.

Both adults and children are susceptible to liver diseases. Doctors have noted in recent years that the number of patients suffering from liver diseases has increased sixfold. In addition, mortality in liver diseases remains high. It is also known that it is very difficult to recognize these diseases [4].

Today, transplantation operations are the only method of radical treatment for patients in the late stages of liver disease. More than 25 thousand orthotopic liver transplants are performed annually in the world. Despite this, the need for this operation, according to UNOS, is four times greater and ranges from 20 to 30 per 1 million people. In order to reduce orthotopic liver transplantation, in our work, we will consider replacing an ordinary liver with an artificial one using a robust method. To achieve this, an analysis of BAL systems was carried out. Over the past few years, several clinical studies have been conducted in which the effectiveness of BAL devices has been tested. These preliminary studies have yielded some promising results, although the current generation of liver aid devices has not yet demonstrated sufficient effectiveness for normal use. Some of the problems that the BAL development area continues to struggle with are the following:

1. How to maintain a large cell mass without restrictions on the substrate so that the cells function with maximum efficiency;
2. How to maintain high levels of stable, long-term, liver-specific function in an artificial (and potentially inhospitable) environment;
3. How to minimize the amount of filling (or dead space) that needs to be filled with the patient's blood or plasma.

It is becoming clearer every day that a more fundamental understanding of the influence of environmental parameters on the function of hepatocellular diseases, as well as the interaction of the host and BAL, is needed before the concept of BAL becomes a reality available at a reasonable price [5–7].

Also, a software platform is needed to model bioartificial liver systems. BioUML was taken used as a basis. Figure 1 shows an example of working in the BioUML software environment.

BioUML is an open source software platform for the data analysis of omics scientific research and other advanced computer biology analyses developed by scientists from the Institute of Systems Biology in Novosibirsk, Russia [8].

The Biological Unified modeling language is an integrated extensible environment for the visual modeling of biological systems. The vision of BioUML is to provide a computing platform for creating a virtual cell, virtual human physiology, and a virtual patient. BioUML allows the user to conduct the visual modeling of complex systems, adjust model parameters based on several experiments, analyze data, and conduct joint research, and it also contains tools such as: visual modeling, simulation, parameter selection and analysis, genome browser, scripts (R, JavaScript), and a workflow mechanism. Thanks to its integration with the Galaxy and R/Bioconductor platforms, BioUML provides extensive opportunities for omic data analysis. The plug-in architecture allows the user to add new functions using plug-ins. To help the user focus on a specific task or database, several predefined perspectives have been developed that display only those elements of the web interface that are necessary for a specific task [9–11].

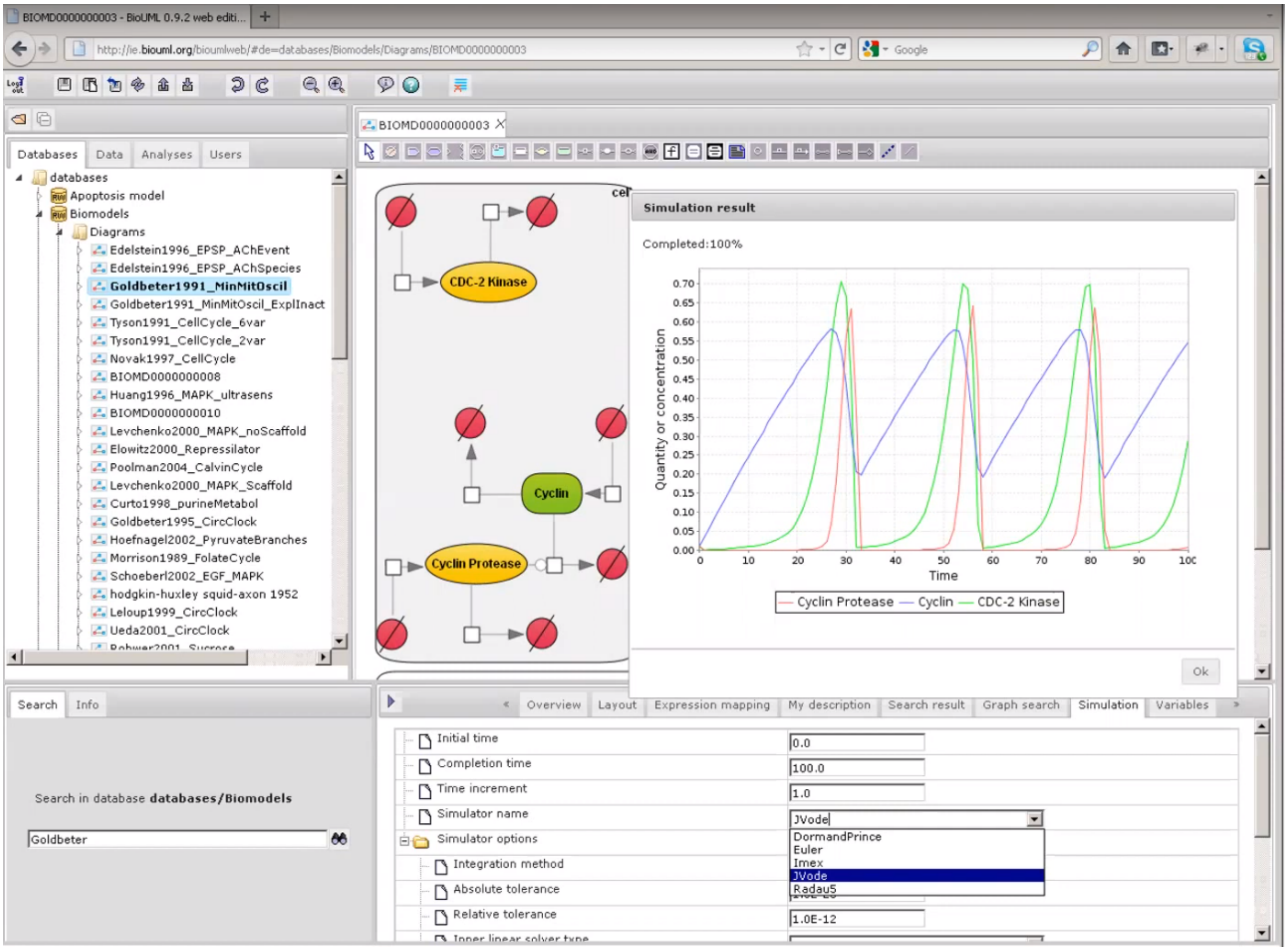

Figure 1. Example of visual modeling.

As mentioned above, one of the advantages of this platform is visual modeling, which greatly simplifies working with complex systems.

2. Considering One of the Languages of Systems Biology

Systems Biology Graphics Notation (SBGN) is a standard graphical representation designed to facilitate the efficient storage, exchange, and reuse of information about signaling pathways, metabolic networks, and gene regulation networks among communities of biochemists, biologists, and theorists (Figure 2). The system was created several years ago by a community of biochemists, model developers, and computer scientists. It is believed that SBGN will contribute to the efficient and accurate representation, visualization, storage, exchange, and reuse of information about all types of biological knowledge, from gene regulation to metabolism and cell signaling.

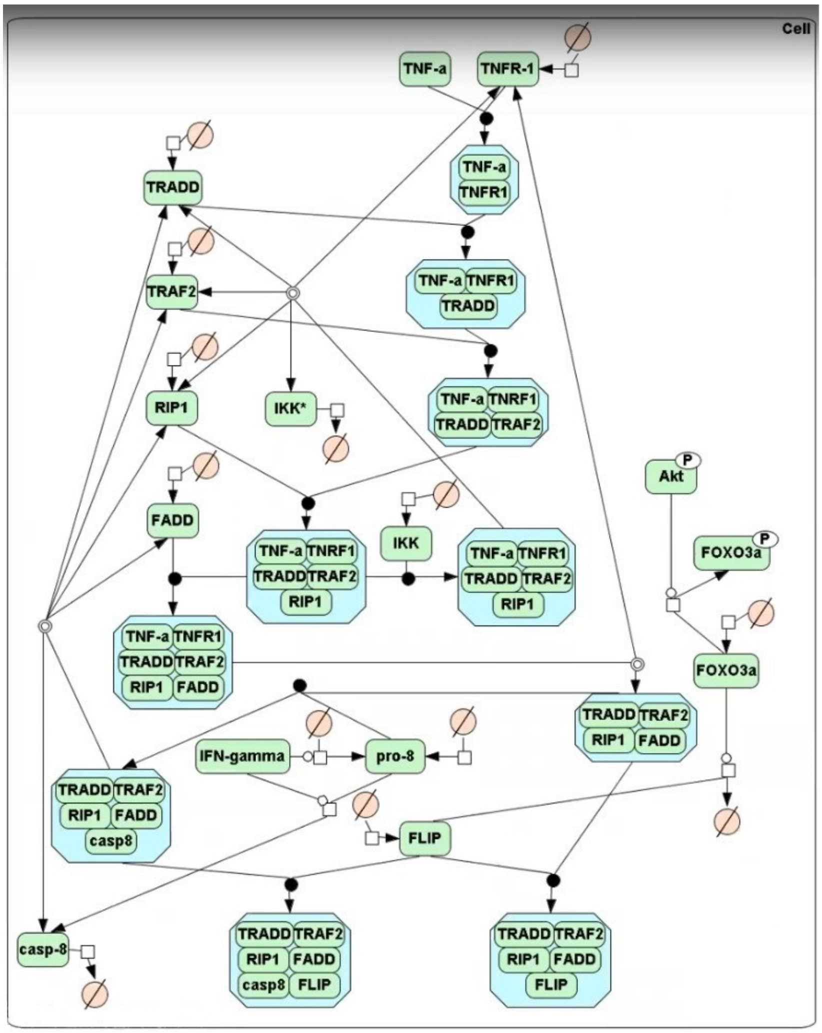

Figure 2. Example TNF-α module (SBGN).

This example demonstrates the convenience of this platform. All elements are reflected and, if necessary, the user can combine some objects together, which is also shown in the diagram [12].

Consider the architecture of a universal platform for analyzing a wide range of biomedical data (Figure 3). It consists of:

1. Computer programs whose main function is data analysis and visualization. For example, Docker is an open source project to automate the deployment of applications in the form of portable standalone containers running in the cloud or on premises. Common Workflow Language (CWL) is a specification for describing the analysis of workflows and tools in such a way as to make them portable and scalable in a variety of software and hardware environments, from workstations to clusters, the cloud, and high-performance computing environments (HPC).
2. The BioUML platform acts as the core [1], which acts as a link with integrated tools (Galaxy, Jupyterhub, R, Docker, noVNC, etc.).
3. IT infrastructure. This means the one on which the platform is installed.
4. External resources are connected via a special API. They are necessary for storing user data.

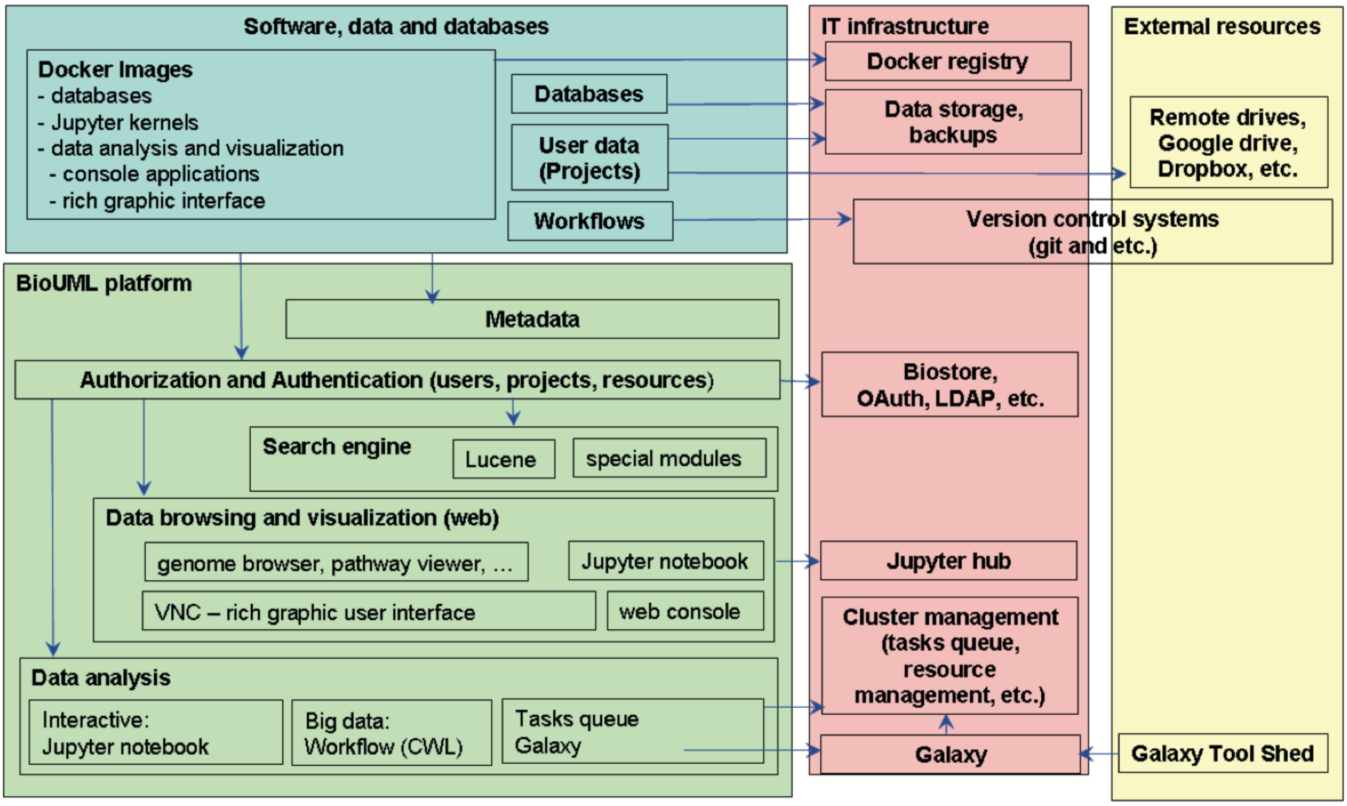

Figure 3. Architecture of a universal platform for the analysis of a wide range of biomedical data.

3. Conclusions

Thus, the shortage of donor organs, in particular, the liver, remains a problem today. This problem is global in nature, and one of the ways to solve it is using a bioartificial liver. In the article, we examined the BAL system, which supports the liver of a person suffering from acute liver failure. The analysis of this system was carried out for the further construction of an artificial liver model using a robust method. The BioUML platform is used to model such complex systems. In the future, this system will be able to save many lives.

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