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Programs for modeling and simulation of the SARS-COV virus

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Abstract

Simulation emerges as a valid alternative to studies and analysis of clinical practices in detriment of traditional public health solutions, including for actions to combat the new coronavirus. In this paper, the authors address the programs used in modeling and simulating the behavior and combat of Sars-Cov. The purpose of this approach is to verify the simulation programs, both in theoretical and practical studies, that were used in the current pandemic against this virus through a bibliographic study. For the analysis of the bibliographical reference, articles based on research about simulations of the Sars-Cov virus were selected as a priority, not being limited to the variables of the virus or to the area of action, thus the research focused on biological, mechanical and chemical simulations. The reflection about the results of the research points out that the most used programs in biological and chemical simulations, such as GROMAC and CHARMM are complex and difficult to access; the mechanical programs, on the other hand, are easier to acquire and study (such as ABAQUS), but this one, however, does not focus on the macro analysis of the viral structure, such as nucleus capsids, spikes, among others, but only on the creation of structures and/or equipment to fight the new pandemic. The research showed that the most used programs are paid or exclusive to a specific public, such as the CHARMM tool, which in turn is released only to researchers at Harvard College, limiting the range of researchers who use it.

Keywords: Biological simulation; Chemical simulation; SARS-COV virus; Sars-Cov virus modeling

1 Introduction

The outbreak of COVID-19 has been identified as a pandemic by the World Health Organization, and its containment relies on traditional public health measures. However, the explosive increase in the number of infections in a short period of time overloaded the health and research systems, which led to the movement of scientists from all over the world generating a huge effort in the area of simulations, which aims to help solve and/or resolve doubts and existing gaps of the new virus, which was leading patients to complete respiratory failure, and consequent death [1].

Simulation as a valid alternative to clinical practice studies and analysis is particularly pertinent. Several important factors lead to the consideration of this new approach, such as the accelerated risk of contagion in hospital environments due to the increased number of people attending these facilities imposing overload to professionals and, consequently, less availability to participate in the teaching process [2]. Currently, several simulation programs are available in the market, with applications in the most diverse sectors. This article will analyze biological and chemical programs, as is

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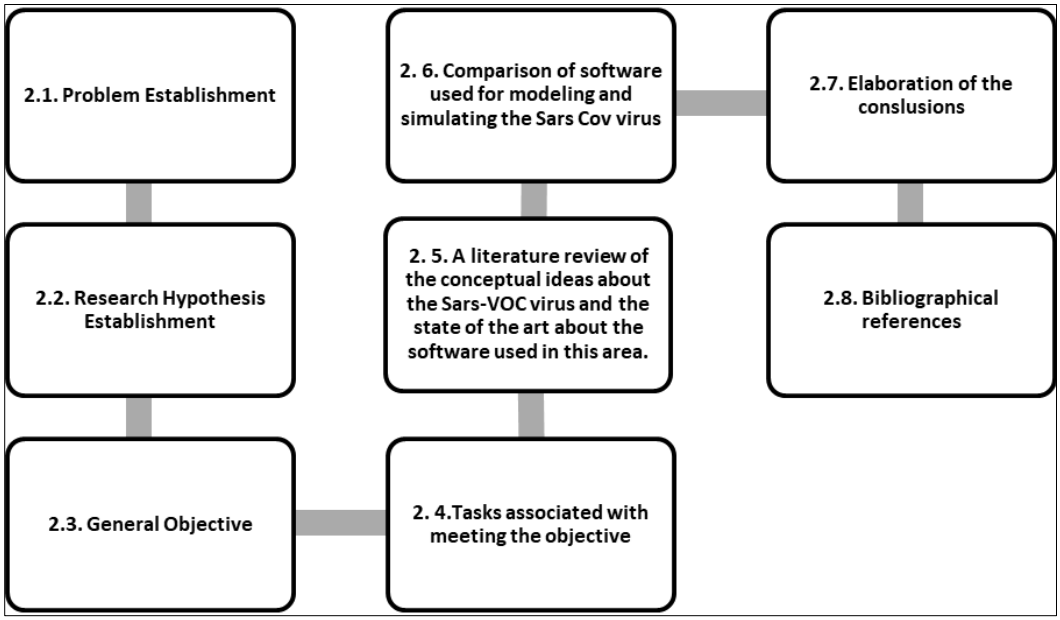
the case of CHARMM (Chemistry at Harvard Macromolecular Mechanics), which is a highly versatile and widely used molecular simulation program [3] and GROMACS (Groningen Machine for Chemical Simulations), which is a molecular dynamics package designed mainly for the simulation of proteins, lipids and nucleic acids [4], as well as expose the possibility of using electrical and mechanical programs, such as ABAQUS and the programs of the Ansys family.

2 Material and methods

The research work was developed following the methodological sequence below:



Source: Autor, 2023

Figure 1 Methodological sequence. Conclusions: drawing conclusions about the results obtained from the software analysis

Bibliographical references: In this task all the references reviewed were numbered, following the order and form established in the relevant standard.

3 Results and discussion

3.1 Problem Establishment

This is a topic of vital importance to the world society, specifically the use of technological software's that make it possible to model, simulate, and analyze (in the shortest time possible) the behavior of this virus under different scenarios such as pressure, temperature, vibrations, etc.

3.2 Research Hypothesis Establishment

It is possible to use technical and technological software to combat the Sars Covid Virus.

3.3 General Objective

To establish the theoretical basis necessary to select technical software in the process of modeling and simulating the Sars cov aiming to find efficient tools that allow its use in society applications.

3.4 Task associate with meeting the objective

The different tasks necessary to bring the research project to a successful conclusion will be surveyed.

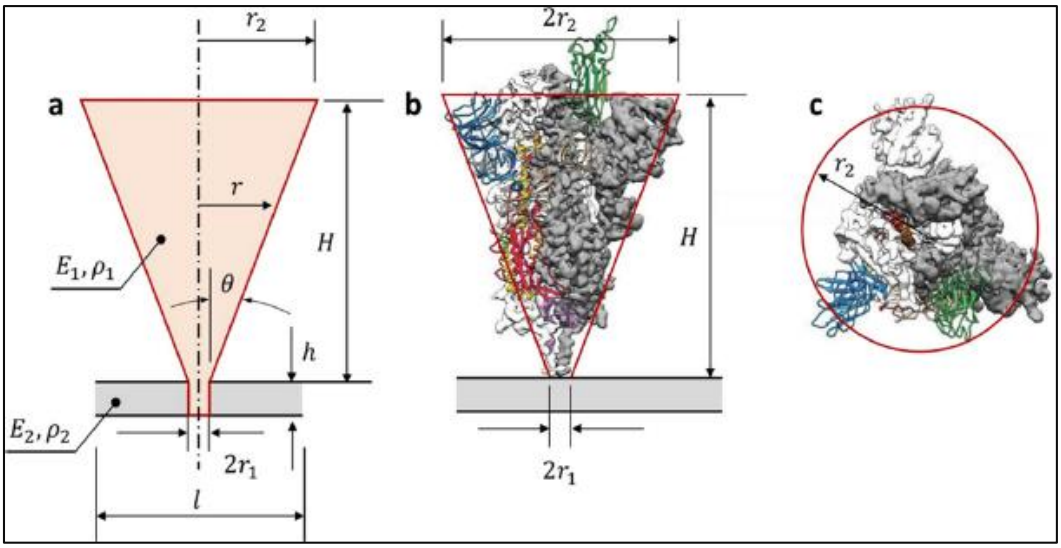
A literature review of the conceptual ideas about the Sars-VOC virus and the state of the art about the software used in this area: development of the software analysis applying the synthesis analysis and induction deduction method to

establish both the conceptual elements concerning the virus and the criteria concerning the applications used to combat Virus Sarc VOC.

3.5 Use of mechanical and electrical simulation tools for biological simulation

At the heart of computational microscopy are simulation algorithms, for which molecular dynamics is most widely used. Molecular Dynamics (MD) is a computational simulation method that studies the physical motion of atoms and molecules, for which the potential interactions between these particles and the equations governing their motions are known [11]. The resulting time series, called a trajectory, can later be visualized and analyzed in detail. Molecular Dynamics (MD), Brownian Dynamics, Langevin Dynamics and Dissipative Particle Dynamics (DPD) have been implemented in several of the simulation program packages, the most widely used in the field of membrane modeling are AMBER, CHARMM, NAMD, OpenMM, LAMMPS and GROMACS, as well as ANTON with the DESMOND program [12].

The main limitation of simulations is the limited amount of sampling that can be performed, even when using the largest computers available today. As such, the mechanical and electrical simulation programs help in performing simulations outside the main scope of molecular dynamics, they are more commonly used in the area of the physical study of molecules in a macro scope, the main paper used as a basis for this topic clearly demonstrates the use of mechanical simulation for the analysis and study of Sars-Cov exposed to a varying mechanical field, and uses the laws of modern physics to calculate the physical efforts in its structure, mainly in its Spikes. For the accomplishment of the article in question, the authors counted on a junction of the molecular dynamics analysis to define the geometric shape of the Spike (Figure 1) and thus to apply the variable forces on it, being able to analyze the possible ruptures in the structure of protein S[13].



Source: Tomasz Wierzbicki et al, 2021.

Figure 2 Joining a mechanical program with a molecular dynamics program to define the geometry of the Spike

This use of programs with non-biological principles has been growing mainly in the COVID-19 pandemic, where scientists from all over the world came together with a single purpose, to acquire as much information as possible about the new unknown virus. According to the Web Of Science site (https://www.webofscience.com) there are currently 81,041 publications on the topic of Sars-Cov, of which 256 are from electrical/electronic engineering (0.316%) and 65 are from mechanical engineering (0.080%).

Comparison of software used for modeling and simulating the Sars Cov virus. This activity will be done through a characterization and evaluation of the most used software in this area.

4 Analysis of the most commonly used computer programs for biological simulation

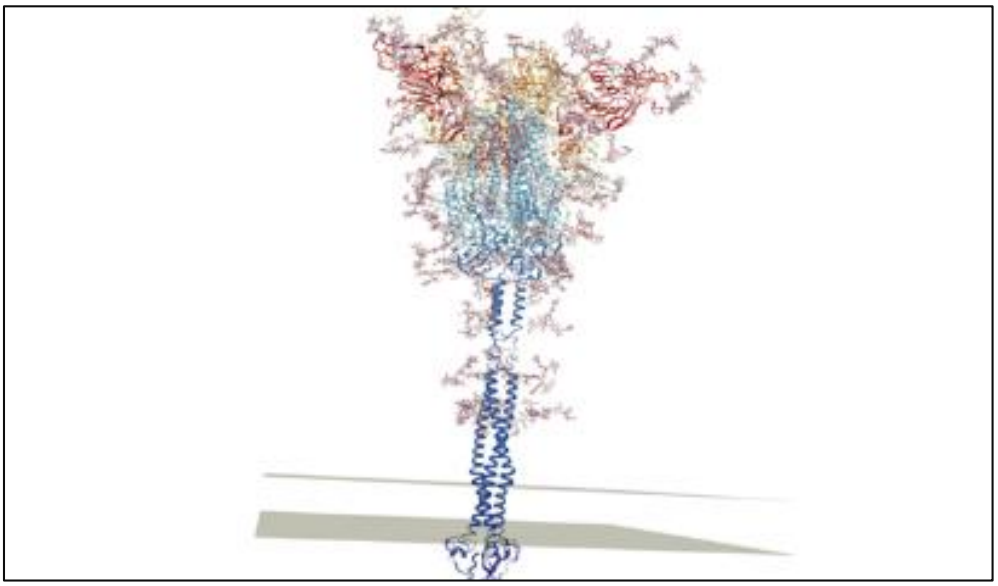
4.1 Program CHARMM and CHARMM-GUI: Biomolecular Modeling of Sars-Cov

CHARMM (Chemistry at Harvard Molecular Mechanics) is a very versatile and widely used molecular simulation program developed in the 1980s, focusing mainly on molecules of biological interest, including proteins, nucleic acids,

carbohydrates, lipids, their assemblies, and the small molecules that interact with these targets [5]. To study these systems, the program provides a wide range of computational tools, including different path and structure sampling methods, free energy estimators, molecular reduction techniques, dynamics and analysis, and modeling capabilities, in addition the program can run on a variety of UNIX-compatible platforms, with optional graphical output.

According to [3], the CHARMM program is applicable to problems involving a much broader class of multi-particle systems. Calculations with CHARMM can be performed using a variety of models and energy functions, from mixed molecular quantum mechanical force fields to classical potential energy functions of all atoms with a clear solvent and different boundary conditions, in solvent and subterranean membrane models.

The program in question was used extensively in the simulations of the new virus, with a major focus on atomic simulations of the Spike structures, structures that promote entry into cells and are the main target of antibodies [6]. The use of CHARMM was important for the initial creation of the basic molecular structures of the Spike protein, as shown in Figure 3 (experimental visualization of the simulation), generated by the authors.



Source: Authors, 2022.

Figure 3 Spike protein generated in the Charmm-Gui graphics tool

The tool also has an extension called CHARMM-GUI (http://www.charmm-gui.org), which manages all the graphics and has a free online repository (http://www.charmm-gui.org/docs/archive/covid19) containing all the simulations of the COVID-19 related proteins. CHARMM-GUI was developed to provide a web-based graphical user interface to generate various input files, molecular systems to facilitate and standardize the use of common and advanced simulation techniques in CHARMM. The web environment provides an ideal platform to build and validate a molecular model system interactively, so that if a problem is found through visual inspection, one can revert to the previous configuration and regenerate the entire system again [7].

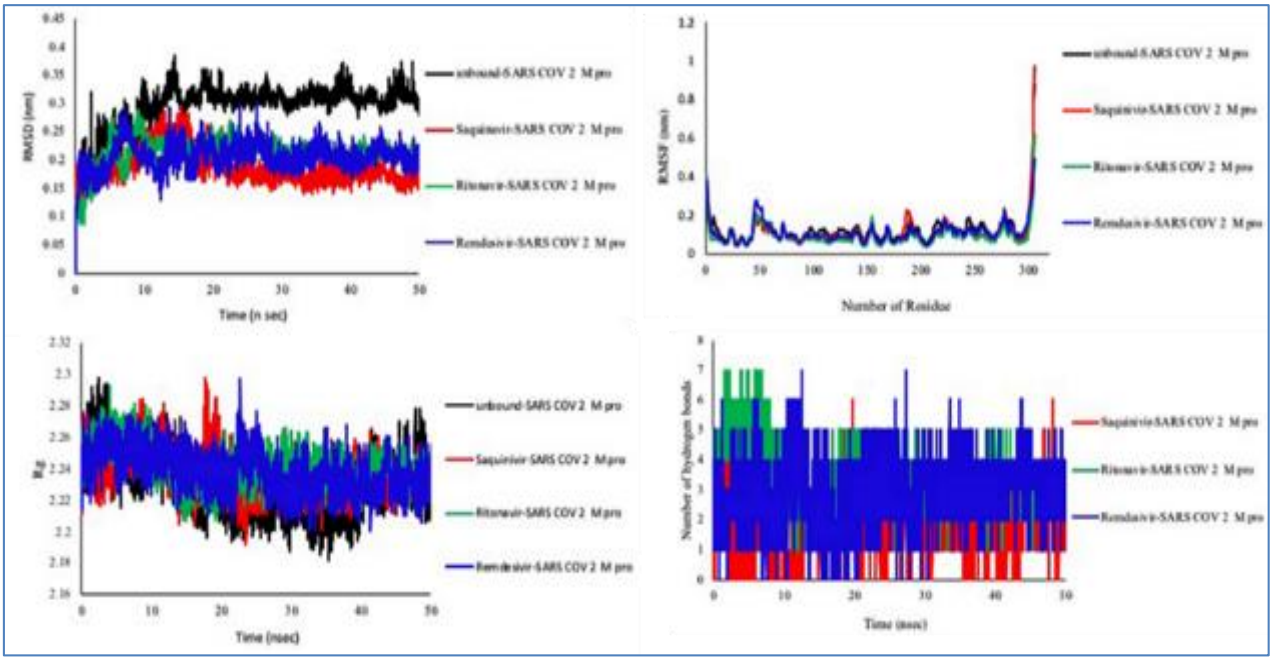
The base publication used to create this topic also shows the utility of the CHARMM-GUI tool for generating clear and easily shareable biological models in academia to be used for simulation, modeling, and/or used for vaccine and antiviral drug development [8]. The CHARMM tool, despite being very useful, has a difficult access, being shared only with Harvard faculty researchers and having as "open to the public" only the CHARMM-GUI graphical generator.

4.2 GROMACS program: Simulation of proteins, lipids and nucleic acids from the epidemic-causing virus COVID-19

Molecular dynamics is a computational tool used in the field of pharmaceutical chemistry for the creation of drugs and extends beyond the field of molecular mechanics. Computational chemistry is a subdivision of the field of chemistry that covers its content and technology. Its goal is to develop biological and chemical solutions by means of specialized programs. One of the well-known programs for this type of application is GROMACS.

According to [9], GROMACS is a program for performing molecular dynamics simulations and energy minimization. These are two of the many techniques that belong to the domain of computational chemistry and molecular modeling. The goal of the GROMACS program is to provide a versatile and efficient program, especially targeted at the simulation of macromolecules in aqueous and membrane media, capable of running on single processors as well as on parallel operating systems [10].

For this topic, an article that addresses integrated computational methods to identify a safe treatment for Sars-Cov was used as a basis. The molecular dynamics simulations in the researched article performed an inspection to verify the stability of protein-drug complexes (figure 4).



Source: Khattab, Al-Khafaji, Dunya AL-Duhaidahawi & Tugba Taskin Tok et all, 2020

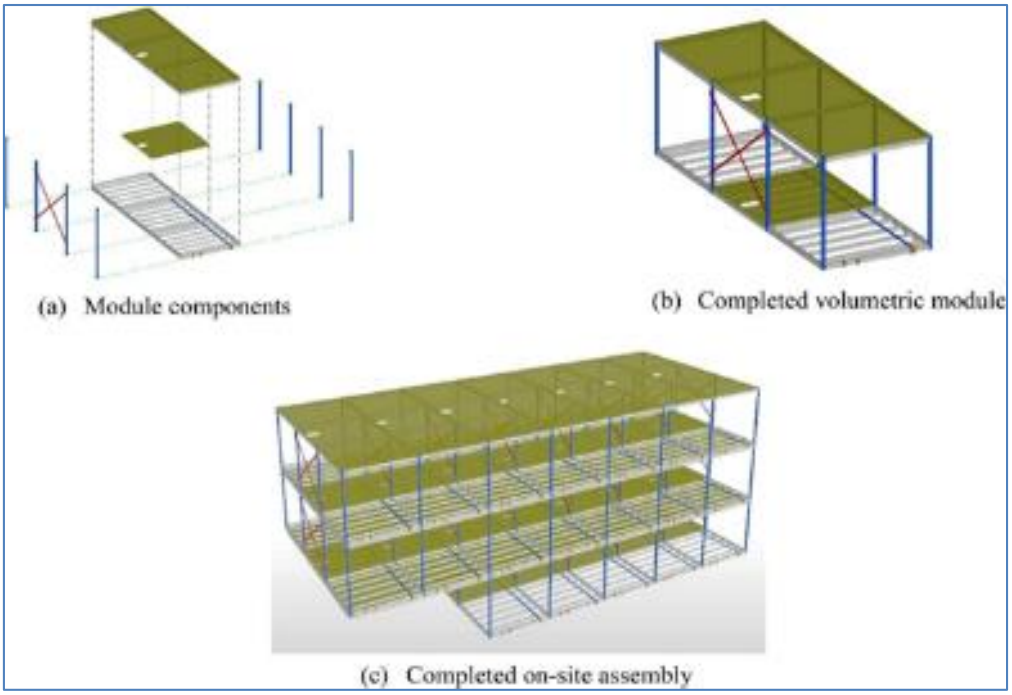
Figure 4 Molecular dynamics simulation for three drug-protein systems.

This simulation is used to explain the dynamic behavior of biological systems at the atomic level. GROMACS was used to simplify the effect of drugs on the movement of the analyzed protein and extracting this dynamic movement in simulations. Based on the presented article, one can see the importance of using simulation programs to study not only Sar-Cov, but also other subjects related to chemistry, complementing the academic environment.

4.3 The ABAQUS program and its assistance in research regarding Sars-Cov

With the advent of mathematical models for simulation, a methodology called Finite Element Method or FEM emerged that helps to satisfactorily obtain theoretical models and analyze their structural behavior. One of the most established programs that uses this method is the commercial program package ABAQUS marketed under SIMULIA.

The ABAQUS program proved to be one of the benefactors during the battle at the peak period of the COVID-19 outbreak in Wuhan, China, where quick and accurate work was needed to combat the disease. In the work of [14], the design of new modular steel frame units accessible for efficient construction was developed, which are ideally suited for emergency response situations such as health, structural and fire as per figure 5. The work turned out to be of utmost importance in dealing with the demand for faster construction of the emergency Huoshenshan Hospital during the outbreak, with the design depicted in figure 5, and left its legacy for similar emergency response in the future.



Source: Perampalam Gatheeshgar et al, 2021

Figure 5 Modular construction - Module assembly for modular construction completed

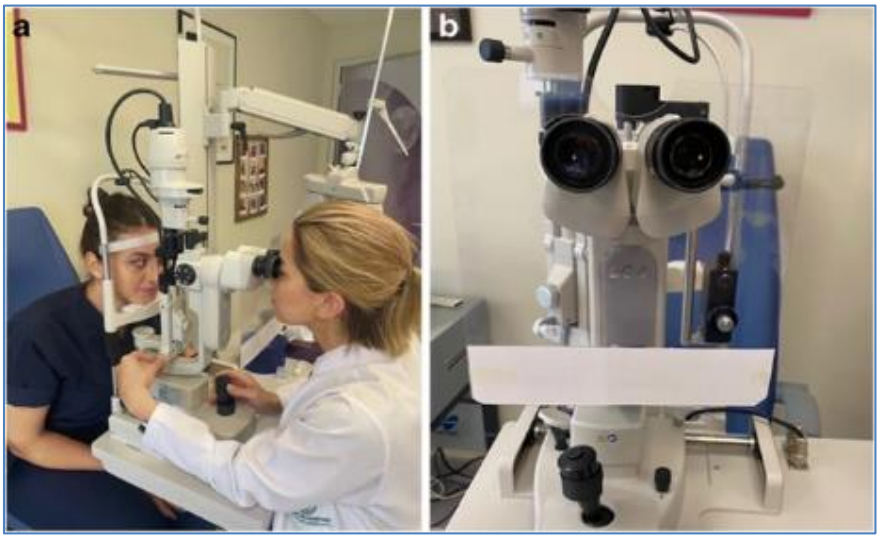
Source: Perampalam Gatheeshgar et al, 2021

Figure 6 Hospital built using modular techniques around the world

Another research that works with the COVID theme and using the ABAQUS finite element simulation tools is the work of [15], which brings an interesting approach on the dissemination of the virus in ophthalmologic examinations leading to the contamination cycle between doctor and patient.

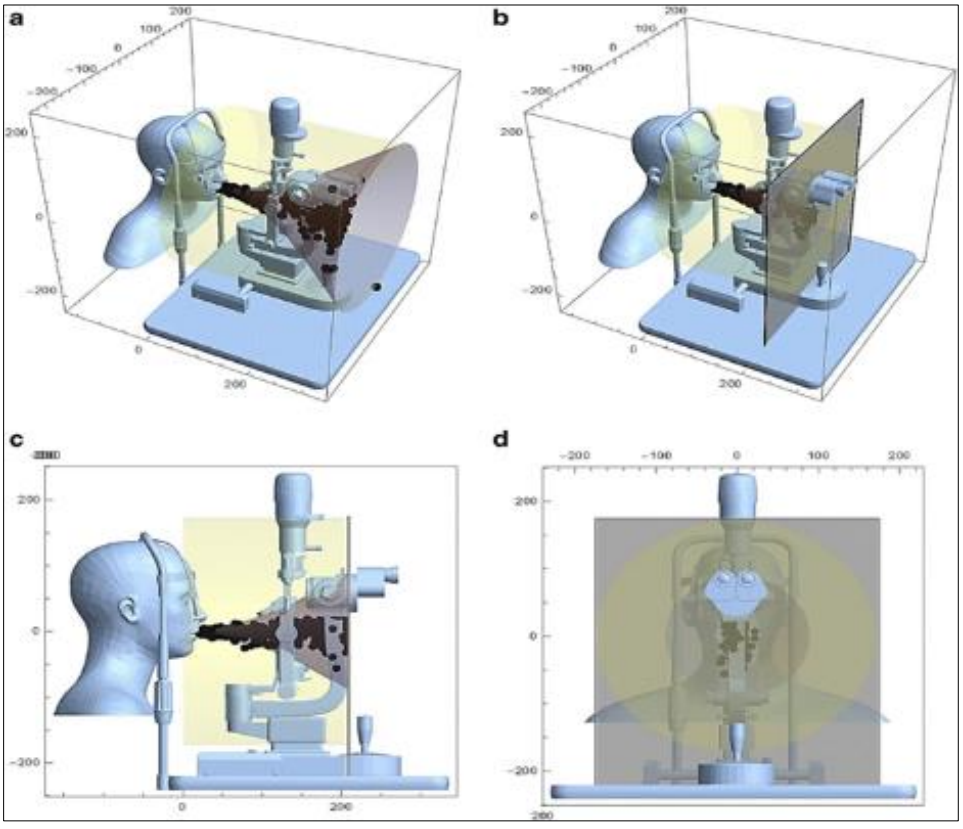
As ophthalmology professionals work in close proximity with their patients during eye examinations, figure 6, a physical barrier is of great importance in order to avoid contamination by coughing or sneezing since masks would not have guaranteed efficiency in this proximity. Thus, the research of [15] used ABAQUS to model the people and simulate the

distribution of the contaminant in the format of an air jet with liquid droplets, arriving at the result presented in figure 7, which shows the geometry needed for protection of the areas of risk and contamination.



Source: Basak Bostanci Ceran et al, 2020

Figure 7 (a) A standard eye examination with the biomicroscope. (b) Biomicroscope with respiratory protection



Source: Basak Bostanci Ceran et al, 2020.

Figure 8 Conceptual shield design based on simulation results: a) no shield, b) effect of the shield in case of coughing/sneezing (isometric view), c) front view of the shield, d) examiner's view

5 Conclusion

At the end of the analysis of this research, it is pointed out that the simulation programs that most help in the understanding of the structure of the virus and the ways to combat it were the biological and chemical ones, in this context, CHARMM and GROMAC stand out; ABAQUS, being a mechanical/physical program, is not used to perform biological representations due to its limitations in performing biological calculations and structures. The mechanical programs are little used to combat the new virus due to the difficulty in joining the results obtained through the DM (Molecular Dynamics) with the mechanical simulation tools, being located only one article where this was accomplished.

Finally, as a recommendation for future work, it is worth an analysis focusing on the simulation tools open to the market, considering that all the programs studied in this article are paid or released only to a specific audience, such as the CHARMM tool, which in turn is released only to researchers at Harvard College.

Compliance with ethical standards

Acknowledgments

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Disclosure of conflict of interest

There are no conflicts of interest for the authors of this article.

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