Contribution to Nosocomial Infections Detection via Biosensors Particles Spatial Simulation in Mixed Reality Environment

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Abstract. Nowadays, various studies show that many millions of patients globally are affected by healthcare-associated infections (HAIs) or nosocomial infections each year, causing hundreds of thousands direct deaths, presenting a crucial public health problem with serious social and economic implications with a predicted increasing tendency. Biosensor systems propose today a realizable way face to standard methods for detecting bacterial infections in clinical environments, as these standard methods are time-consuming and costly, presenting many limitations. This study involves interdisciplinary scientific areas to describe a theoretical frame of a real-time digital multi-system simulation of nosocomial infections in Mixed Reality environment. The theoretical description of the technical conditions and requirements of such a system will contribute to a future implementation of a real-time 3D spatial detection, quantification and simulation with future data monitoring of nosocomial bacteria rates. The proposed simulation system is based on combined simulation methods and mainly on voxels/point clouds technology with a potential comparison and evaluation with ideal rates in a comprehensible way. This will allow healthcare specialists and political decision makers to evaluate a hospital environment sanitary by taking suitable measures.

Keywords: Nosocomial infections simulation · AR 3D spatial simulation of nosocomial bacteria · Mixed Reality · Nosocomial bacteria detection with biosensors · 3D voxel simulation

1 Introduction

Nowadays, infectious diseases is a very serious healthcare problem as they are responsible for about 15% of all deaths worldwide [1]. In the last years, various studies show that almost 4 million patients in Europe are affected by healthcare-associated infections (HAIs) or nosocomial infections each year, causing approximately 37,000 direct deaths. By 2050, these deaths are expected to reach 10 million worldwide, presenting a crucial public health problem with serious social and economic implications [2].

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Some of the most serious public health problems causing hospital stays, higher medical expenses, and greater rates of death are indeed nosocomial infections and bacterial resistance [3]. Recent studies have also indicated that surgical and nosocomial infections may increase about 8 extra hospital days for patients with approximately $15 billion in additional expenses annually only in USA and $4.5 billion in the UK for 4 extra hospital days [4, 5]. Nosocomial infections affect between 5% and 20% of hospital patients worldwide while only in Europe the corresponding costs are estimated at almost € 7 billion per year [6].

According to the World Health Organization (WHO), Anti-Microbial Resistance (AMR) of bacteria, viruses and many parasites no longer respond effectively to medicines with traditional methods. So, AMR could lead almost 30 million people globally into extreme poverty [7].

Today, the traditional diagnostic methods of nosocomial infections have limitations because they rely on time-consuming laboratory procedures of 1–5 days [8] with significant delays in diagnosis and treatment process [1]. While new advanced microbiological techniques with molecular and nonmolecular methods reduce the time of bacteria detection [9], these traditional methods of detection and identify nosocomial bacteria still present limitations on their reliability, sensitivity, efficiency and range of applications [10]. They use PCR-based techniques, or mass spectrometry techniques, as Matrix-assisted laser desorption-ionization time of flight mass spectrometry (MALDI-TOF) [11], intricate and time-consuming techniques with no sufficient acid amplification and sample preparation at once, which is still remains a challenge [7].

On the other hand, at the new age of technology, biosensor systems that record biological parameters propose today a realizable way to traditional methods for detecting bacterial infections in clinical environments. Biosensors based on different materials develop new reliable methods to detect pathogens in many areas and they seem to offer greater stability and sensitivity [12]. They identify different infections quickly with accuracy, in real time and on-site [1]. In the past 10 years ASSURED criteria gave guidelines and the framework in order to develop numerous Point-of-Care (PoC) biosensors devices [13].

Studies in disease infections detection simulation have been undertaken by dynamic, complex and hybrid simulation models. These simulation models and surveillance systems focus, among others, to 2D diagrams for synthetic data generation, statistic comparison in 2D line charts, using developed data structures and data location, programming algorithms with 2D spatial distributions results, indoor location-based services for more efficient representation and management of indoor spatial data, etc. [14].

Thus, an effective and comprehensive bacterial infections simulation is significant factor to the contribution of the HAIs problem solution. This study is in the first phase of theoretical development and focuses on a technical preparation of future spatial simulation of nosocomial infections. The proposed methodology takes into account state-of-the-art spatial simulation techniques in 3D Mixed Reality (MR) environment (and no linear diagrams) by quoting related studies, technology of biosensors and their adaptation to the proposed simulation system by contributing to a hospital environment sanitarian evaluation by healthcare specialists and political decision makers.

2 Objectives and Innovation

2.1 Objectives of the Research Proposal

This research addresses the technical requirements of spatial simulation proposal of nosocomial infections particles of hospital rooms via biosensors technology in order to contribute to a hospital environment sanitarian assessment. The proposed simulation system/methodology objectives are quite similar with a previous study of the same authors on Air Quality emissions from biosensors inside buildings [15] regarding, among others, the:

(1) detection and management of nosocomial infections particles inside a hospital environment via an adapted semi automatic biosensors network, with the use of trained personnel,
(2) representation of nosocomial infections particles in 3D VR spatial simulation environment based either on real or render images virtual tours with superimposed gradient spatial simulation [15],
(3) simulation of nosocomial infections particles in 3D volumetric point cloud/voxel simulation with spatial reference in AR environment [15],
(4) contribution to a wireless biosensors grid system creation adapted for infections particles measurement,
(5) theoretical description of an adapted methodology of 2D/3D effective spatial modelling for various simulation environments with the use of infections particles representation system [15],

2.2 Innovation of the Research Proposal

As this research is the extension of a previous study on Air Quality emissions from biosensors inside buildings [15], the innovation of this research proposal focuses on interdisciplinarity various simulation & modelling approaches and techniques to represent nosocomial infections particles from biosensors in a hospital environment. In particular, the innovation concerns, among others:

(1) a simultaneous 3D spatial structure modelling with nosocomial infections particles rates nebula representation in 3D point clouds/voxels either in immersive VR/AR environment as almost all studies simulate these rates only in 2D/3D linear diagrams or 2D spatial format [15],
(2) a method to obtain accurate measurements by improving a connection biosensors system to a network and the corresponding transferring data,
(3) a volumetric building modelling methodology for AR simulation,
(4) provide to any user the ability to real-time immersive experience, via VR/AR environment,
(5) a significant contribution to health experts or political decision-makers for (a) better understanding nosocomial infections behavior and (b) deliberating over the same understandable spatial simulation in order to take appropriate actions,
(6) ensure an immersive pedagogical experience of an academic student on nosocomial infections behavior via an interactive volumetric simulation.

3 BioSensors for Infections Detection

3.1 Types of Biosensors

The biosensors addressed to infections are classified in terms of pathogens detection and in terms of technical detection. In terms of pathogens detection, the biosensors are classified in three main categories [1]:

(a) immunosensors, which pose the potential to improve the pathogen and toxin diagnostic-processes, regarding pathogens, such as Leishmania, SARS-CoV-2, H1N1, Gram-positive bacteria, etc.,
(b) aptasensors, which detect target (bio) markers as biorecognition elements [16], regarding pathogens, such as S. aureus, E. coli, etc., and
(c) genosensors, which detect the hybridization reactions of target nucleic acids, either DNA or RNA [17], regarding pathogens, such as Human serum samples, DNA sample, Saliva sample, etc.

In terms of technical detection there are many biosensors based on several detection techniques, such as [18]:

(a) interferometric biosensor, which is a label-free sensitive biosensor with interference of two light waves [7],
(b) photonic biosensor, based on evanescent wave detection for point-of-care analysis which is the practice of diagnosing patients at the point of need [18],
(c) electrochemical biosensor, which is the most employed transducer including amperometric, potentiometric, conductometric & impedimetric techniques [19–21],
(d) piezoelectric biosensor, which is quartz crystal microbalance biosensor detecting resonance frequency changes of bacteria on the sensor surface) [18],
(e) optical biosensor, which is electromagnetic radiation that interacts with the analyte, [18], (see Fig. 1).

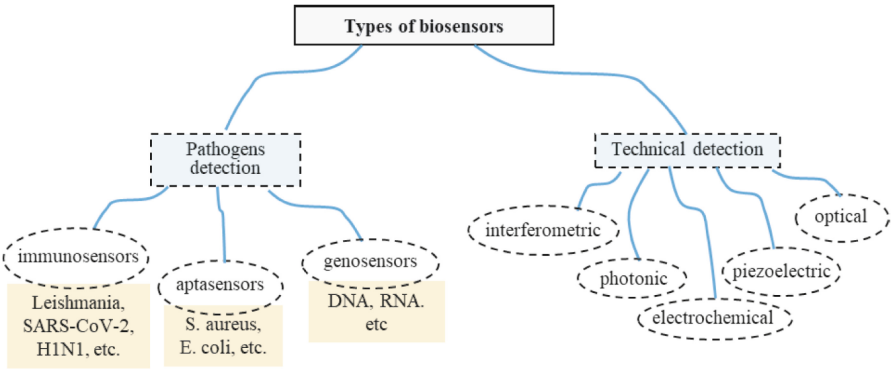

Fig. 1. Types of biosensors in terms of pathogens & technical detection

Certain low-cost biosensors produced by inject-printed techniques and exhibited better sensitivity in biosensor performance [22–24].

3.2 Advantages and Limits of Biosensors

Traditional diagnostic methods have disadvantages, such as:

(a) increased costs, longer diagnostic times,
(b) specialized equipment and trained personnel,
(c) greater sample volumes and sample handling protocols,
(d) increasing the possibility of contamination and human error [25].

On the other hand, biosensors present many advantages, such as

(a) quick analysis times and high loading capacity [26],
(b) great sensitivity [27],
(c) selectivity, which is the capacity to interact with a particular target analyte (molecule) [28],
(d) reproducibility by performing under difficult conditions [29],
(e) response time, which is the duration to read and generate a signal [25],
(f) distinguish between different strains of pathogens within a single sample and
(g) conditions requiring continuous monitoring.

However, the bigger limit of biosensors is the high cost [30] while scalability presents financial and logistical difficulties, although using cost-effective materials and promoting open-source designs can reduce overall costs [31]. In addition, no biosensor currently in use can perform real-time quantitative testing for huge arrays.

4 Infections Detection and Simulation Studies–Discussions

Researches in disease infection detection and simulation are based on 2D statistic charts using mainly structure and location data with algorithms of 2D spatial distribution results.

Agent-Based Model (ABM) is a bottom-up simulation method for dynamic modelling with autonomous entities called agents. This method is often use in disease infection simulation in order to discover spatial and temporal patterns analysis via 2D diagrams for synthetic data generation, while other microscale simulation with surveillance system on hospital-acquired infection prevention and control use comparison in 2D line charts simulation [32].

Agent based modelling is an effective simulation method to simulate the spread of infection via interactions of agents which are individual and/or collective entities. In GAMA platform which is an open-source development environment for an agent-based modelling language (GAML) a simulator was created in order to simulate infection spread, infected people and the level of infectivity in QGIS, an open-source GIS environment [33].

System Dynamics (SD) is a top-down continuous simulation modelling method capable to simulate non-linear relationships using differential equations [34].

Discrete Event Simulation (DES) models the sequence of activities and events in time of a detection system operation [32]. DES captures the variability and the randomness of multiple elements (e.g. individual objects behavior, age, health status, etc.) within a detection system [35].

Hybrid Simulation Models (HSM is a simulation modelling method combining at least 2 different simulation modelling methods [36].

Another method called LAMP has been integrated into a specific biosensor surface (Surface Plasmon Resonance – SPR) in order to detect S. aureus and methicillin-resistant genes [37]. Similar studies use LAMP method with a nucleic acid biosensor (LFNAB) in order to identify the amplification products via immunoreactions and visual detection [38] while other study use LAMP with integrating DNA extraction and colorimetric detection in order to identify E. faecium gene by even naked eye in 1 h [39].

Another simulation model called Montel Carlo simulates antibiotic-resistant bacteria in hospital units. It represents patients and staff members and their interactions, such as handwashing compliance, via colonization curves by allowing to study the impact of infection control measures and being a precious educational tool for staff [40].

An infectious disease simulator is based on contact network generator using techniques from location-aware search into the hospital environment by processing millions of locations and structures data in order to simulate spatial distributions [41].

Several infectious disease simulators, represent only parameter variation with calibration results [42], parameters values by estimating the transmission dynamics [43] or surveillance systems for infection prevention and control by 2D statistics data comparison [44].

5 Research Methodology

5.1 Introduction

The research methodology of the present study is based on a previous study of the same authors on Air Quality emissions from biosensors inside buildings [15]. It takes into account modelling and simulation techniques, communication and connection specifications affection the research organization. The methodological steps consist in (1) BioSensors implementation and measurements of nosocomial infections parameters (2) Geometry modelling (3) Simulation techniques (4) Spatial 3D representation in VR/AR environment (see Fig. 2).

5.2 Biosensors Implementation & Nosocomial Infections Measurements

A biosensor is an analytical device composed of a biological sensing element (antibody, enzyme, DNA) in close contact with a physical transducer (converts bio-recognition event into a measurable signal) which together relate the concentration of an analyte (substance of interest that needs detection) to a measurable electrical signal with the aid of an amplifier (signal amplification), a biocomponent (target analyte) and a bioreceptor (molecule that specifically recognizes the analyte) [25]; the schematic representation of the biosensor (see Fig. 3).

The biosensor implementation is a process with many problems that principally have to do with the biosensor transitioning from the lab to the clinic 45]. In real, only a few biosensors, such as glycose sensor have been successfully translated from research labs to clinical settings [45].

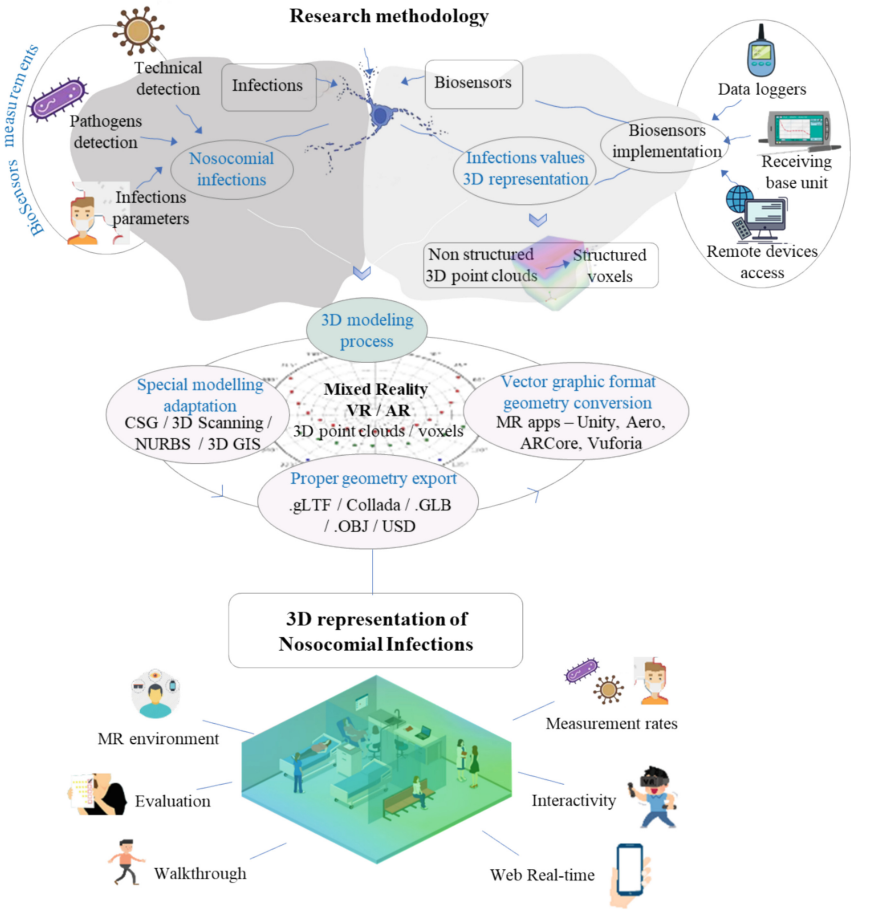

Fig. 2. Research schematic methodology

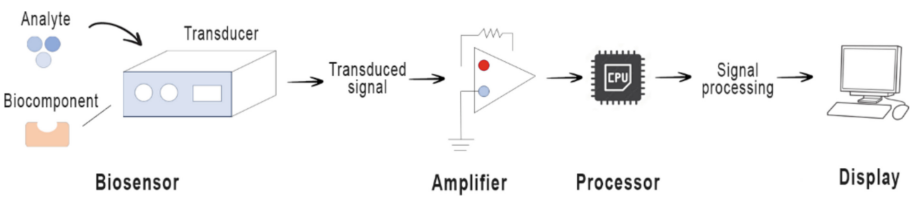

Fig. 3. Schematic representation of a typical biosensor [25]

Today, many implementation methods are being actively researched aiming to novel fabrication procedures, lower costs, accessibility increase, incompatibilities resolution, standardization data formats, data management platforms and biosensors connection, etc. [25]. Another research area is the buildup of organic material on the biosensor surface ("biofouling") in order to increase performance [46].

A main biosensor implementation problem, is also to guarantee the reproducibility of experiments and diagnostic procedures and not only to ensure the accuracy of results via adequate adjustments [25].

Another research about immunological biosensor implementation focuses on the improvement antibody immobilization methods in order to increase sensitivity [47] while research about DNA-based biosensors explore methods of amplification techniques [48].

Another challenge is the incorporation of biosensor-generated data into existing Information Management System of a Laboratory (LIMS) with the implementation of open-source biosensor platforms in order to enhance data accessibility and facilitate the real-time diagnostic process [49].

The proposed implementation process is based on a data recording system which is generally made of 3 components [50]:

(a) a network of biosensors at the measuring points converting nosocomial diseases values into electrical analog or digital signals
(b) an acquisition system (digital or analog) reading and logging electrical signals from biosensors
(c) a computer allowing the storage, the processing and the analysis of the acquired values.

The connection of the 3 components can be implemented via (a) wired connection and (b) wireless connection by radio frequency transmission. Each type of connection present advantages/disadvantages depending on the components distance, the ease and the cost of installation and finally the potentiality to modify the system with electromagnetic interferences. In case of radio wireless connection, the acquisition system positions the transmitting part close to the biosensor facilitating the transmission of the measured values to the receiving part. At the same time, modern sophisticated systems integrate the transmitting part and the biosensor in the measuring instrument by placing the receiving part near to the computer in order to facilitate the values transmission [1].

The proposed system, running in web environment, requires the creation of recording stations (Stations) of the biosensor results in special data loggers which are located appropriately in the hospital area. The data is then sent to the central base unit and then stored, processed and visualized, according to what was mentioned in the technical part of the data transfer. The entries will be made by trained hospital personnel (see Fig. 4).

5.3 Simulation System and Techniques

Simulations of spatial elements and descriptive forms with interdisciplinary approaches [51] is almost an inevitable way with an added value for particles spatial simulation.

This study is based on a state-of-the-art 3D spatial simulation system in either a modern 3D point cloud/voxels nebula surround environment or an immersive VR/AR evolving environment [15]. The proposed system can be transformed in a power educational tool contributing either to medicine students or to a common language creation between medicine experts and political decision makers for a social policy.

Today, several interdisciplinary simulation techniques are used in complex spatial simulation issues providing access to complex databases [52], 3D modelling based

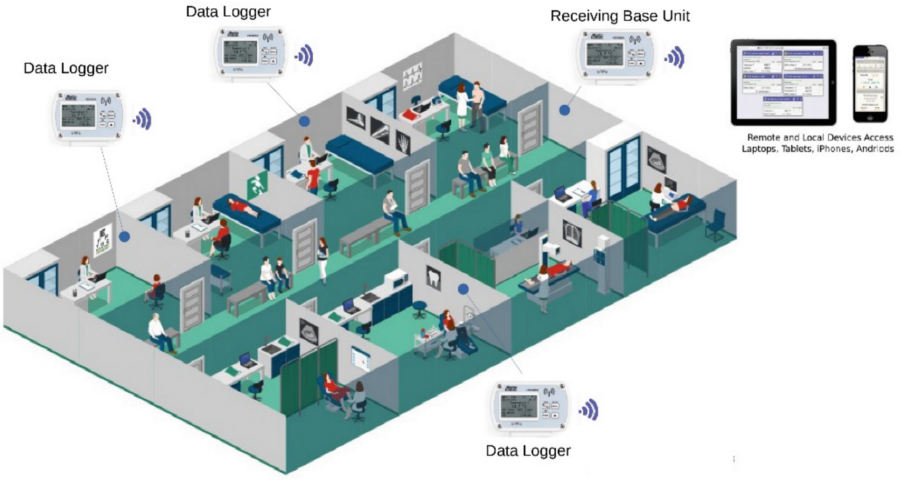

Fig. 4. Schematic 3D diagram of sensor installation and data transmission [50, 74]

either on VRML programming or even on modern CAD systems integrating Building Information Modelling (BIM) procedures, displays interpolation technology, etc.

The two most prevailing particle methods of "Smooth Particle Hydrodynamics - (SPH)" and "Moving Particle Semi-implicit (MPS)" allowing integral representation of quantities and spatial derivatives and incompressible fluid flow are used today for fluid mechanics [53]. Thus, particles spatial simulation techniques, such as infection and comfort conditions can be supported by VR/AR techniques for volumetric representation [15] dealing with OpenGL techniques, other approaches that convert particles to volumetric data representing point density and texture-mapping [54], image overlay, telecommunications and wireless, etc. However, points cloud/Voxel simulation method is a sophisticated and optimal way to represent this kind of particles as this method segments the space into cubes of precise dimensions and structure with a 3D cube table [55]. This method exploits the screen technology and energy visualization, such as Cave Automatic Virtual Environment [15], as well as special devices capable to see superimposed rendering images over the real word, such as Head Mounted Displays (HMD) and See-through Displays by using Tracking and Client-Server Network Architecture technology [56], etc.

5.4 3D Spatial Geometry Modelling Process

A lot of 3D complex spatial modelling methods and techniques are implementing in volumetric visualization such as Grid Mapping and voxels [57], point clouds [58], Constructive Solid Geometry – CSG, NURBS surfaces [59], 3D scanning and object's recognition [60] 3D GIS topology elements [61], Boundary Representations, Spatial subdivision representations, etc. The 3D spatial modelling and representation of nosocomial infections is a technically painful procedure due to the Mixed Reality communication protocols and the complex connection of special devices [15].

These 3D model's creation methods [62] representing the spatial surrounds in AR environment need to be converted into appropriate formats such as OBJect format, Collada, etc. [63] by specific AR software allowing create interactive experiences by blending virtual elements with the real world, such as, Unity platform, Adobe Aero, ARCore, Vuforia, etc.

In addition to standard CAD software, many software using photogrammetric methods with multiple angles, extract 3D geometry and texture data that need to be converted in proper format such as GL Transmission Format (gLTF), gLB format, USDZ format or Universal Scene Description (USD) format, etc. [64]. The necessary technical synchronization and adaptation between the plethora of formats/protocols and the biosensors implementation requirements in practice from the lab to the clinic is a very difficult interdisciplinary challenge that many researchers are working on [15, 31].

5.5 Nosocomial Infections Values 3D Representation

VR Simulation. Architectural and urban spatial digital simulations [65], as well as many CAD and rendering environments create 3D models with solids, surfaces, meshes, NURBS and Bezier polygons tools [51]. These 3D models have to be converted into appropriate VR 360° scene format based on

(a) directly 3D vector models,
(b) 360° bitmaps from 3D models or
(c) 360° real photos superposition (see Fig. 5).

User-friendly digital tools and visualization methods [66] are adapted to the final VR 360° scene into multimedia elements, such as interactive superimposed areas, 360° panoramas et video, block of images, popup information, interactive HTML5 or JAVAScript programming elements, etc. [67].

Other different interpolation techniques and algorithms in 2D within GIS systems, such as Inverse Distance Weighting (IDW) and radial basis function (RBF) contribute to infection modelling and simulation by grouping points with similar characteristics. The GIS "nebula" simulation results can be also used as a superimposed multimedia element in the final VR 360° environment [15].

AR 3D Cloud/Voxel Simulation

The modelling/simulation of the space (e.g. hospital room, etc.) will be implemented either in VR and/or AR environment [15]. This simulation will be supported by specifics techniques, such as point cloud data, CSG, Boundary and Spatial sub-division simulation [62] generated from CAD/GIS software, taking into account specific requirements of biosensors integration, geometry modelling, 3D clouds points, etc.

The Lidar technique will convert spatial 3D model of points cloud into an appropriate file (CSV) with geometry definition (OBJ) [68] and finally into a voxel model based on voxel-algorithm from points cloud [15, 69]. It is crucial to say that point cloud representation nowadays is cheaper and easiest to generate, due to low cost lidar systems with SLAM technology [70].

More specifically voxelization is a process of transferring vector data into a structure that represents discretely geometry and semantics. Three are the main components of



Fig. 5. VR 360° "nebula" simulation results with superimposed multimedia elements

the procedure starting a) with the input geometry, b) the voxelization and c) the data storage, visualization and export [71]. Although, is extremely important the choice of certain criteria in the voxelization procedure such as voxelization algorithms that will be implemented, the availability of common software that will be used, different libraries (Open3D, Unity Point Cloud Viewer etc.), the compression and decompression method that will be selected, the testing platform and other [71].

While VR representation needs either specific VR head glasses, the AR representation needs a specific tablet/smartphone with integrated sensors that track movements and objects position. Theoretically the nosocomial infections rates in form of interpolated 3D voxels will be transparent allowing visual and spatial perception of the user (see Fig. 6).

The above system which consists of many individual functions that have to be performed, the integration of different data (biosensors, etc.), the implementation of communications between the various sub-systems, the visualization products for end users and much more, requires the adoption of modern frameworks or architectures such as a Service-Oriented System [72].

5.6 Advantages/Limitations of Simulation and Modelling Processes

The processes of modelling and representation have many advantages but also present a lot of limitations.

The main advantage of the simulation process is the use of voxels which allows accurate particles volumetric simulation of complex objects, almost impossible to be simulated with other methods.

The main advantage of the modelling process is the implementation and the complementarity of interdisciplinary spatial modelling methods such as grid mapping & voxels, point clouds, 3D scanning, CSG, etc.

On the other hand, the main limitation of the simulation process is the complexity of the biosensor's implementation in relation to the values extraction and representation with a multitude of devices and software.

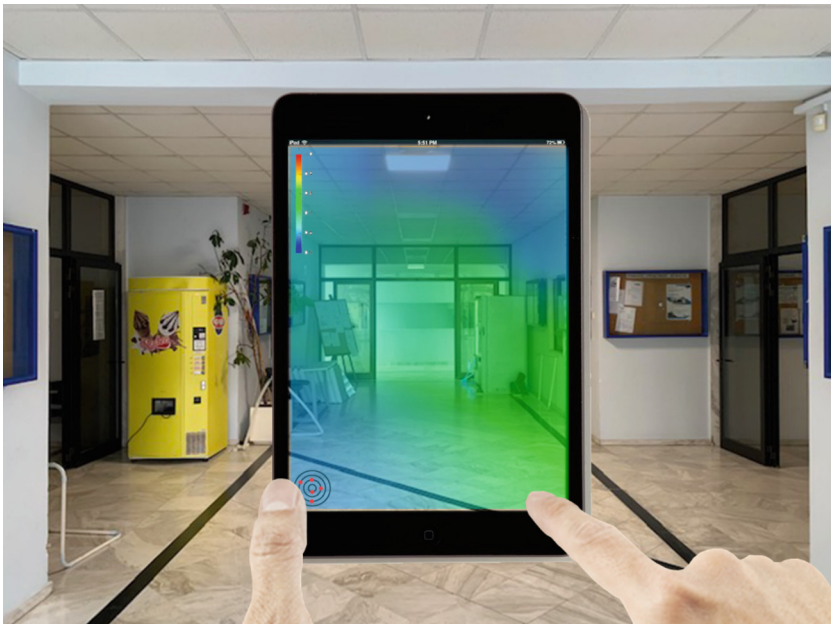

Fig. 6. Theoretical representative simulation results of the proposed pilot representation system in AR environment after future implementation

The main limitation of the modelling process is the exhaustive technical requirements due mainly to the format incompatibilities resolution and standardization data of the different modelling software and the specific MR devices communication protocols.

6 Conclusions

The infectious diseases are considered as a major global health challenge. Current diagnostic methods present a lot of limitations related to time-consuming laboratory procedures, while biosensors facilitate with accuracy the on-site detection of various pathogens.

The theoretical development of the proposed nosocomial infections particles rates spatial simulation allows an understandable and accurate 3D representation via modern point clouds/voxel techniques. This simulation allows a real-time VR/AR immersive walkthrough with significant scientific and social impact [73], while current systems offer 2D/3D charts statistics [15].

The use of 3D point clouds/voxels technique allows an accurate particles volumetric simulation in relation with interdisciplinary spatial modelling methods. However, these simulation and modelling techniques present implementation and incompatibilities limitations.

The proposed spatial simulation could facilitate the communication between a medicine experts and non-expert users, such as clients, hospital staff, even public authorities in social health plans discussion.

The biosensor chip technology progress and the biosensing systems with artificial intelligence (AI) and machine learning (ML) for huge amounts and high-quality representative datasets management is an imminent perspective [7]. The involvement of modern technologies, such as Internet of Things and 5G network's fast transmission rate will increase the effectiveness of detection and simulation methods of infectious diseases or even chronic ailments [25].

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