ISSN: 2633-4828 Vol. 5, No.2, June 2023

International Journal of Applied Engineering and Technology

Computational Modeling of HIV-TB Coinfection by Cellular Automata (Cell-DEVS)

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Date of Submission: 13th March 2023 Revised: 10th May 2023 Accepted: 20th May 2023

How to Cite: **Pino-Romero, N. et al. (2023). Computational modeling of HIV-TB coinfection by Cellular Automata (Cell-DEVS). International Journal of Applied Engineering and Technology, 5(2), pp 13-21.**

***Abstract*--** **In the present study, the computational modeling that describes the evolution and propagation of people susceptible to HIV-AIDS infection as well as Tuberculosis will be carried out. This additionally generates a coinfection in those infected that further complicates the epidemiological situation. Therefore, the presence of sanitary-epidemiological support personnel is important to consolidate prevention and control strategies. This epidemiological phenomenon could be modeled by differential equations, but we will focus on modeling by cellular automata to obtain computational simulations in time-space, and obtain possible scenarios and opt for the appropriate scenario to implement the most effective epidemiological strategies to obtain the results. better results and preserve the quality of life of society.**

***Keywords*- - computational modeling, HIV-AIDS, Tuberculosis, cellular automata, epidemiological coinfection, mathematical epidemiology**

INTRODUCTION

One of the most delicate problems that require particular attention is the coinfection between the infectious diseases HIV/AIDS and Tuberculosis. It is a reality that society faces that this complementarity of these diseases occurs in infected patients because they greatly affect society due to the reduction in the presence of infected [1]. HIV/AIDS is a disease that facilitates the spread of Tuberculosis (TB) due to the symptoms caused by HIV/AIDS.

The Ministry of Health of Peru through its National Center for Epidemiology, Prevention and Control of Diseases carries out prevention and control strategies according to the contextualized situation that is faced in the registered localities [2].The reality that occurs in each locality in terms of the dynamics of these two diseases must be analyzed and studied quickly enough to keep the rates low [3]. But also, the consideration of the use of economic and human resources to optimize the results [2].

The quality of life of patients is one of the priorities of the Peruvian government, but above all to reduce the prevalence of contagion of the two diseases that cause a coinfection that in many cases is not detected for a relatively long time, and this causes infections likely to cover an entire community unit [1]. And when this situation occurs, the health system can collapse and not cover all the patients to keep the disease controlled in each one of the patients, and, therefore, in the community as well. This perspective has been taking place in different Latin American countries because it is a worrying situation for public health [4].

On the other hand, mathematical and computational modeling continues to be one of the best ways to analyze the problem toconfront a dynamic system that represents the epidemiological problem for the choice of possible solutions and the impact they can generate [5]. Even more so when you have limited resources and you expect to get the best results from the epidemiological strategy to carry out.

Therefore, mathematical modeling allows us to analyze the evolution of the spread over time, and how we can intervene to disrupt this spread to generate a reduction in infections and introduce strategies to keep them that way [6]. Given this, being able to make a computational model that can observe the evolution in time and space would help us much more to specify the introduction of health personnel to cause a decrease in both evident and latent infections [7].

METHODOLOGY

I. Mathematical Model applied to Epidemiology

Since 1927, modeling by differential equations began with the proposal of W. O. Kermack and A. G. McKendrick that tried to describe the behavior of infectious diseases, then many more publications of different mathematical models have been generated by differential equations[8]. It is possible to perturb the different mathematical models developed by different authors, and obtain similar results where additional hypotheses have been included [9]. Mathematical models rely heavily on mathematical analysis focused on model stability theory, as well as the construction of computational simulations based on both discrete-time and discrete-event numerical methods [10].

Computer simulations help to visualize the evolution in time as well as in space for a suitable choice of solutions that follow some epidemiological strategy for the good of society. Therefore, the evolution of the spread of the disease must be considered in time and space, with which the study is focused according to the transition that is known between the epidemiological populations [11].

II. Cellular Automata Modeling

One of the ways to carry out computational modeling by cellular automata is by making simple rules that will allow describing complex systems.Therefore, a Cellular Automaton is a Mathematical Model of a Dynamic System that is structured by a set of cells that acquire different states or values during the simulation time [12]. The states of each cell evolve into another state depending on the rule that has been defined within the considered discrete time. It must be considered that modeling by cellular automata helps to describe complex systems using simple rules, there are also complications when carrying out the structure of the phenomenon that is being modeled, such as the case of "computational bugs" and the review of each cell with its respective neighborhood so that the model is well defined and structured [13].

Currently, various models use different formalisms to describe the behavior of dynamic systems that are represented by cell spaces[14]. In our study, modeling with the Cell-DEVS approach will be carried out, which is the complementary structuring of modeling by cellular automata and the DEVS formalism. Where each cell is defined as an atomic model, and the procedure is built to couple the cells in time with a spatial evolution. [13].

HIV/AIDS-TB COMPUTATIONAL MODEL

The computational model for cellular automata that is structured by strict rules allows to consolidate the good definition and configuration for the DEVS formalism. The computational simulation considers that the central cell represents the agent (individual) of the epidemiological population [13]. For the computational simulation, the interpretation of cells with the individuals of the epidemiological populations is considered. Where a cell when it is in contact with another cell depending on its nature can evolve to another state according to the defined rules, where a contact neighborhood has also been defined [12].

The area of the mesh that represents a geographic community also raises a study of position according to the neighborhood that has been defined for the propagation time and space of the disease, even more so, when there is a coinfection of two diseases [7].Now, cells will always be in contact with other cells, and in this interaction, there will be contact and contagion due to the presence of diseases, HIV/AIDS and TB, and how their presence evolves over time [13].

The realization of the evolution generates an expansion of infected becomes detrimental to the quality of life and coexistence for the community; this is one of the objectives that health institutions must keep under control through various strategies [2]. Now, it will be defined in a more formal way, in its mathematical sense, and together with the formalization of the respective local function that will systematically define the interaction between cells [13].

According to Wainer (2009), a definition can be formalized for the two-dimensional meshing of cellular automata over$\mathbb{Z}^2$. We will consider $\theta_n = \{0; 1; 2; \cdots; n-1\}$ being the set of potential states of the automaton. For this case, consider $H = [-a_1, b_1,] \times [-a_2, b_2,]$ where a rectangular region will be defined, and where the local function of the region will be defined. as follows: $\Psi(\theta_n)^H \rightarrow \theta_n$.

Most of the computational models are carried out using a rectangular mesh, this technique is carried out in various areas of modeling, for example, in Partial Differential Equations (PDE) where time and space are considered as independent variables[7]. In our model, the Neumann-type neighborhood will be considered where a rectangular mesh will be presented where the cells will be (in their different states) to be able to interact with each other [13], [14].

The rules that will describe the epidemiological model through cellular automata (Cell-DEVS) can be formalized in such a way that when representing them in the respective algorithm it is interpreted in the CD++ software [13]. Therefore, we will define the rules for our computational model [12], [13].

I. Rules for the computational model (Cellular Automata)

The following rules will define the structure of the computational model according to the phenomenology of the two epidemic diseases [15]. The presence of support staff represents the strategies carried out by health institutions. As well as each epidemiological individual can provide positive or negative support to others. These details allow us to approach the problem of the spread of the disease in a more heuristic way [13], [16].

Therefore, the rules of our computational model are as follows:

- Susceptible, HIV-infected, TB-infected, HIV-TB-infected, AIDS-infected, AIDS-TB-infected and recovered cells influence positively or negatively each unit of time.
- The cells of Support, Susceptible Temporary Support, Susceptible Permanent Support always positively influence each unit of time.
- The susceptible cell upon contact with HIV infected cells can contract the disease according to a probability of contact and contagion.
- The susceptible cell when coming into contact with TB infected cells can contract the disease according to a probability of contact and contagion.
- The susceptible cell when coming into contact with the Support cells can be considered as a support susceptible cell according to a probability of contact and contagion.
- The HIV infected cell after an incubation period becomes an AIDS cell.
- The HIV infected cell upon contact with TB cells can contract the disease according to a probability of contact and contagion, and would be in a state of coinfection.
- The TB infected cell upon contact with HIV cells can contract the disease according to a probability of contact and contagion, and would be in a state of coinfection.
- The HIV-TB infected cell after an incubation period becomes an AIDS-TB cell.
- When the HIV-TB infected cell comes into contact with the Support cells, they become HIV-infected cells according to a probability of contact and contagion.
- When the AIDS-TB infected cell comes into contact with the Support cells, they become AIDS-infected cells according to a probability of contact and contagion.
- The support susceptible cell when coming into contact with HIV infected cells can contract the disease according to a probability of contact and contagion.
- The cell susceptible to temporary support when coming into contact with TB infected cells can contract the disease according to a probability of contact and contagion.
- The cell susceptible to temporary support when coming into contact with the cells susceptible to Permanent Support can be considered as a support cell according to a probability of contact and contagion.
- The cell capable of permanent support does not catch any disease (immunity)
- The Support cell provides a strategy for TB cells to recover from disease.
- The Support cell does not catch any disease (immunity).
- All cells have a period of life according to their epidemiological status, when the time is up they leave the cell empty.
- When there is an empty cell, an epidemiological cell is randomly inserted.

From here, the states of each cell (epidemiological individual) and the respective color will be defined for the computational simulation.

$$\textbf{Cells} = \begin{cases} 0 : Susceptible\ (green) \\ 1 : VIH\ Infected\ (red) \\ 2 : TB\ Infected\ (yellow) \\ 3 : VIH - TB\ Infected\ (magenta) \\ 4 : AIDS\ Infected\ (brown) \\ 5 : AIDS - TB\ Infected\ (silver) \\ 6 : Person\ Recovered\ (orange) \\ 7 : Support\ Person\ (blue) \\ 8 : temporary\ support\ susceptible\ (light\ green) \\ 9 : Permanent\ support\ susceptible\ (light\ blue) \\ 10 : Empty\ cell\ (white) \end{cases}$$

II. DEVS formalism applied to the Computational Model

To guarantee the good definition of the local functions (rules), the DEVS formalism must be carried out. This allows the proper functioning of the interacting cells [13].

Therefore, the algebraic structures for the construction of the computational model are presented according to the DEVS formalism [12], [13].

$$\boldsymbol{HIV - TB\_Model} =< X, Y, D, \{\boldsymbol{M_i}\}, \{\boldsymbol{I_i}\}, \{\boldsymbol{Z_i}\}, \boldsymbol{select} >$$

- $X = \emptyset$
- $Y = \emptyset$
- $D = \{cell\}$
- $M_{cell} = Cell\_Epidemics$
- $I_{cell} = \emptyset$
- $Z_i = \emptyset$
- $select = (Cell\_Epidemics)$

$$\boldsymbol{Cell\_Epidemics} =< \boldsymbol{X_{list}}, \boldsymbol{Y_{list}}, \boldsymbol{I}, \boldsymbol{X}, \boldsymbol{Y}, \boldsymbol{n}, \{\boldsymbol{t_1}, \boldsymbol{t_2}, \cdots, \boldsymbol{t_n}\}, \boldsymbol{\eta}, \boldsymbol{N}, \boldsymbol{C}, \boldsymbol{B}, \boldsymbol{Z}, \boldsymbol{select} >$$

- $X_{list} = \emptyset$
- $Y_{list} = \emptyset$
- $I =< p^x, p^y > \quad where:\ p^x = p^y = \emptyset$
- $X = \{0,1,2\}$
- $n = 2$
- $\eta = 2$
- $N = \{(-1,-1), (-1,0), (-1,1), (0,-1), (0,0), (0,1), (1,-1), (1,0), (1,1)\}$
- $B = \emptyset$
- $Z = \{P_{i,j}Y_1 \to P_{i,j-1}X_1, P_{i,j}Y_2 \to P_{i+1,j}X_2, P_{i,j}Y_3 \to P_{i,j+1}X_3, P_{i,j}Y_4 \to P_{i-1,j}X_4, P_{i,j}Y_5 \to P_{i,j}X_5, P_{i,j+1}Y_1 \to P_{i,j}X_1, P_{i-1,j}Y_2 \to P_{i,j}X_2, P_{i,j-1}Y_3 \to P_{i,j-1}X_3, P_{i+1,j}Y_4 \to P_{i,j}X_4, P_{i,j}Y_5 \to P_{i,j}X_5\}$

$$\boldsymbol{C_{i,j}} =<, I, X, Y, N, \boldsymbol{\delta_{int}}, \boldsymbol{\delta_{ext}}, \boldsymbol{d}, \boldsymbol{\tau}, \boldsymbol{\lambda} >$$

- $X_{list} = \emptyset$
- $Y_{list} = \emptyset$

- $p^x = \{X_k \in \{0,1,2,3,4,5,6,7,8,9,10\} \ donde \ k = \overline{1,10}\}$
- $p^y = \{X_k \in \{0,1,2,3,4,5,6,7,8,9,10\} \ donde \ k = \overline{1,10}\}$
- $X = \{0,1,2\}$
- $Y = \{0.1.2\}$
- $N = \{(-1,-1),(-1,0),(-1,1),(0,-1),(0,0),(0,1),(1,-1),(1,0),(1,1)\}$
- $d = Time$
- $SX : Descriptive\ Variables$

$$SX = \begin{cases} Cell\ 0 : Susceptible \\ Cell\ 1 : VIH\ Infected \\ Cell\ 2 : TB\ Infected \\ Cell\ 3 : VIH - TB\ Infected \\ Cell\ 4 : AIDS\ Infected \\ Cell\ 5 : AIDS - TB\ Infected \\ Cell\ 6 : Person\ Recovered \\ Cell\ 7 : Support\ Person \\ Cell\ 8 : Temporary\ support\ susceptible \\ Cell\ 9 : Permanent\ support\ susceptible \end{cases}$$

Now, we have the rules for the computational model as well as its good structure as well as with the mathematical models where the good definition is made to guarantee its existence and uniqueness of solutions [17], [18].We will continue with the contextualization of the mesh and the initial populations that will be considered to start the computational simulation, and be able to analyze how it evolves in time and space [13]. From there, locate the support cells appropriately according to the control and prevention strategies, as well as the location of the infected cells to be able to address them in the best way according to Public Health [2], [15].

III. Initial State of the Computational Model

For the computational simulation, the initial state will be considered to begin the evolution of the model (cellular automata). A 50×50cell-mesh will be considered where it contains the various initial populations [16].

The computational algorithm carried out in CD++ to obtain the data collection, and thus, have the population evolution graph available. The algorithm performs the computational operations according to the absolute error(10^{-6})in order to guarantee the convergence of the computational model which is a crucial point of computer modeling [13], [19].

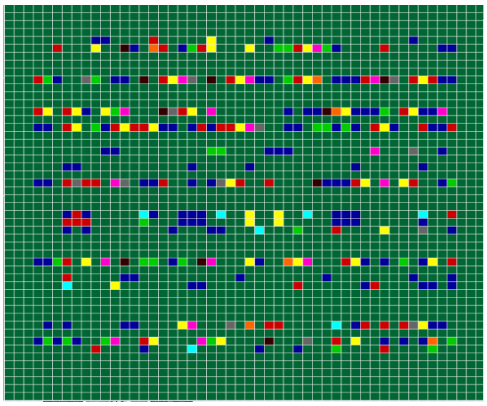

Fig. 1 Initial State of the Model

From figure 1, the evolution of the model (cellular automaton) will be taken according to the computational time that is imposed, where care is taken with the limitations of computational operation (finite resources) at the time of obtaining the data [13], [20].

Now, the epidemiological populations will start with a number and various positions in the region that comprises the model. This will help strategic placements on the part of the country's health institutions [2].

TABLE I
INITIAL EPIDEMIOLOGICAL POPULATIONS

Populations	Cell	Initial
Susceptible Person	0	2238
VIH Infected	1	52
TB Infected	2	38
VIH-TB Infected	3	18
AIDS Infected	4	12
AIDS-TB Infected	5	10
Recovered Person	6	7
Support Person	7	90
T-Support Susceptible	8	30
P-Support Susceptible	9	5

Algorithm optimization will always work with the compilation and simulation time to obtain more reliable results, thus also improve the rules of the computational model. [20], [21]. Therefore, the improvement of the algorithm as well as the good use of computer resources contributes enormously both in structured and parallel programming [13], [22].

In the next section, we will address the results obtained from computer simulations to analyse the evolution of epidemiological populations [2], [3].

RESULTS AND DISCUSSIONS

The results of the computational simulations carried out with the algorithm (Cell-DEVS) will be shown, where the evolution compiled in the simulation time has been 5000 ms (500 frames), in addition to an application of a total of 100 simulations. with the same initial state for the different simulation meshes and their analysis at compile time. This helps us to address the problem of the spread of the disease, even more so, the coinfection of HIV/AIDS and TB [13].

The evolution of the spread is a sensitive and delicate issue to address because resources are limited and the priority of each epidemiological strategy is the life of each individual who remains in good health [25], [26].

TABLE II
COMPILE TIME SUMMARY

Simulation Mesh	Total Cells	Real Compilation Time (minutes)	Verification Time (seconds)
50×50	2500	1.821 min	35.486 s
70×70	4900	3.215 min	41.794 s
75×75	5625	3.554 min	45.652 s
80×80	6400	3.869 min	51.314 s
90×90	8100	4.789 min	89.652 s
100×100	10000	5.429 min	138.652 s

On the other hand, the mortality of people infected by TB or HIV/AIDS will always be very careful because the mission of health institutions is to ensure their integrity [27]. Within the computational model, the mortality of the cells and a random insertion in their place are considered in order to generate an introduction that can be positive or negative within the community [28]. Many of the impacts generated by those infected must be foreseen in time so that they do not cause an explosive expansion of the disease, for which reason epidemiological support personnel are vital to be present but at the same time help those likely to be prevented. of contracting the disease or that the spread of contagion from them is reduced [29].

In figure II, it is possible to analyze the evolution in time and space of the two diseases (HIV and TB), and how it spreads in the susceptible population within the considered region [2]. This evolution, which takes considerable time, allows us to observe the influence that the support population has on other populations, but HIV infection is also predominant in regions where there is an absence of support populations. Always the inclusion of good support allows the prevalence to maintain susceptible in the midst of infected [4], [9].

This figure represents the average evolution of our model, in addition to the fact that only the 50×50 mesh is presented, although in the different higher order meshes, the behavior is similar in the medium and long term of evolution [21]. But the short-term spread tends to differ due to the initial position as well as the random influence that is considered [11].

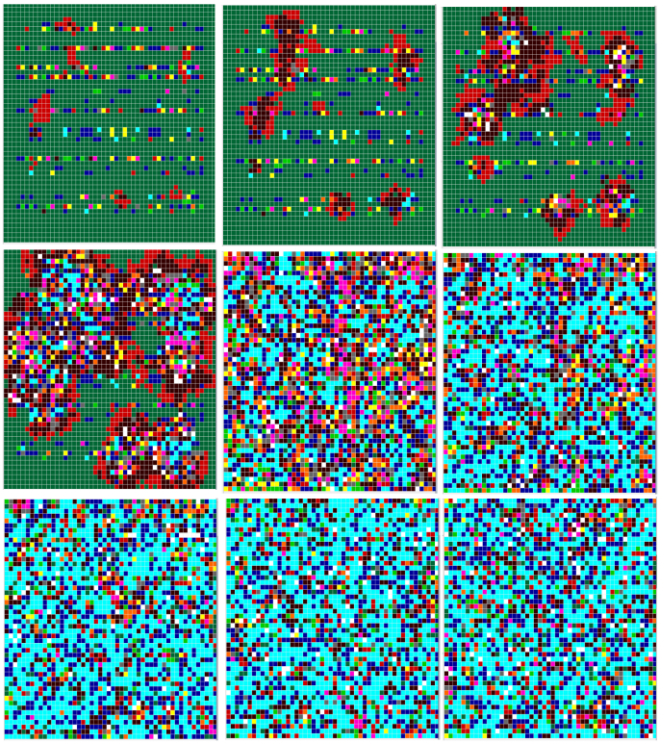

Figure II Evolution Of The Computational Model($\mathbf{50 \times 50}$)

Figure II shows an evolution of the diseases, but in the medium and long term the presence of those susceptible to permanent support is undeniable [1]. This presence is important because it reflects the influence and application of the control and prevention strategy for the disease [16]. But unfortunately, the presence of infected people (HIV or TB or both) remains, even in isolated foci by support personnel (epidemiological or susceptible), and thus contagion is kept to a minimum and a specialized location is maintained to prevent the spread of the disease, being the first objective of health institutions [2], [3].

In addition, the positions in the face of mortality generate a possible focus of infection or protection, the random insertion allows us to observe how its introduction causes a brake on the epidemic or an epidemic focus to be prevented [27]. Finally, the computational simulation where the evolution of the benefits of the epidemiological strategies can be appreciated helps us to maintain or change them to obtain better results [3].

As well as the location of potential installation points for epidemiological support personnel to obtain positive results in the face of coinfection that generates more evident or latent infected, and this is the problem that is faced in the prevention of HIV or TB infection that coexist in the region and it must be prevented from arising in the community [5], [26].

Another insight that the computational model gives us is the temporal evolution of epidemiological populations [10]. The graph of population growth according to their interaction allows analyzing the epidemiological curve in the face of disease prevalence, as well as its decrease to consolidate strategies or change intervention methodologies [2], [5]. Undoubtedly, the temporal graph will help us to visualize the presence of HIV and TB coinfection in the medium and long term [26]; but also, the interaction of both HIV (non-curable disease) and TB (curable disease), which causes a faster mortality to infected people, and it is here where health institutions must anticipate and maintain low levels of prevalence [18], [29].

The following figures contain the information of $150ms$ only because the following the variation of the populations are not very significant and a stable model could be considered [13]. In this sense, temporal evolution allows us to analyze in the short and medium term to evaluate epidemiological strategies that are the most effective [3], [26].

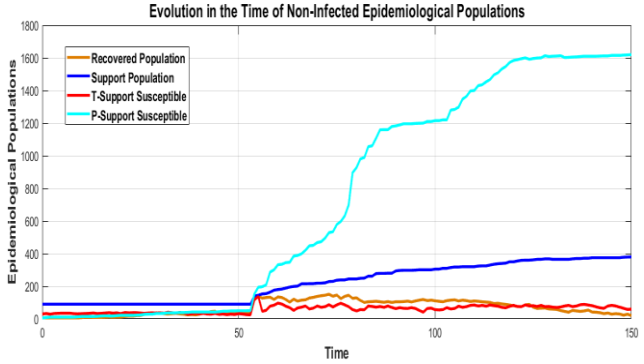

Figure III Temporal evolution of the epidemiological populations: Not infected

In figure III, the evolution in the time of these populations allows visualizing how at the beginning of the simulation they remain almost at the same level, because there is a certain growth of infected populations [2]. But there comes a time in which they begin to increase, especially the permanent susceptible support population (people with social conscience and seeks to promote prevention of infection of diseases) by while the epidemiological support population is slowly stabilized [3]. This evolution provides an epidemiological visualization to promote or change strategies to obtain good results where the community is maintained in a healthy coexistence [26]. The low presence of recovered and susceptible temporary support supports the growth of the permanent susceptible population to maintain a community aware of the disease and how it can be lived with a good quality of life. [5].

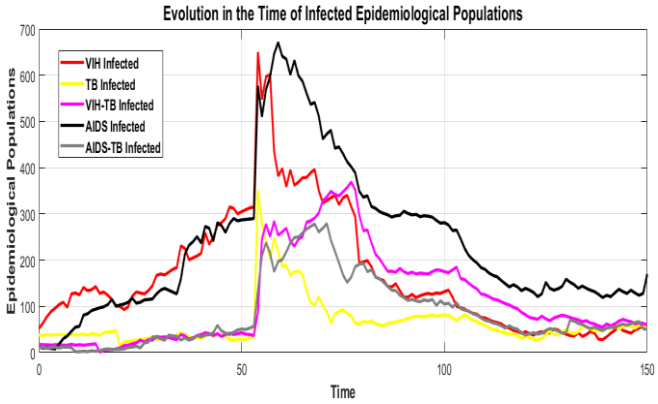

Figure IV Temporal Evolution of The Epidemiological Populations: Infected

In Figure IV, the growth of infected populations is displayed cause the spread of diseases (HIV, TB and coinfection) to a threshold point where it begins to descend [2]. Coinfection Although it has a lower propagation, this does not indicate that it does not affect society because the introduction to the infected population will always be HIV or TB [26]. The AIDS population marks a greater presence because it is the final evolution of HIV, and its infection is stronger and more present in society that should always be addressed, not because they are going to heal the disease but because they deserve special care and Attention of health institutions [3].

The growth of infected populations at first will always be of explosive tendency until the adequacy of epidemiological strategies by health institutions or also of the same population that seeks the common good and healthy coexistence [9]. The infection of a disease is always due to the probability of contact and contagion with infected people, this peculiarity of every epidemic can be better visualized with time-space models because the geographical space will always be limited according to the rooms that exist within the region [21].

Moreover, the presence of infected does not guarantee that one is infected because each person has their own immune system as well as their closeness or remoteness [29].Without a doubt, considering the positive or negative influence rule of all people allow to model this epidemiological behavior in a simple but important way to fence the reality of the propagation of coinfection [5], [28].

The decrease in infected populations will always be sought to avoid the spread of the disease, but also the consideration of the non-curable disease, it is not to include mortality as a means of reduction but rather the care of this population as a maximum end of the part of the part of the health institutions of the Peruvian State [2], [24]. In addition, the location of epidemiological populations will always be part of epidemiological strategies to implement them with a minimum margin of error to optimize the resources available within the normative frameworks provided by the Ministry of Health [1], [3].

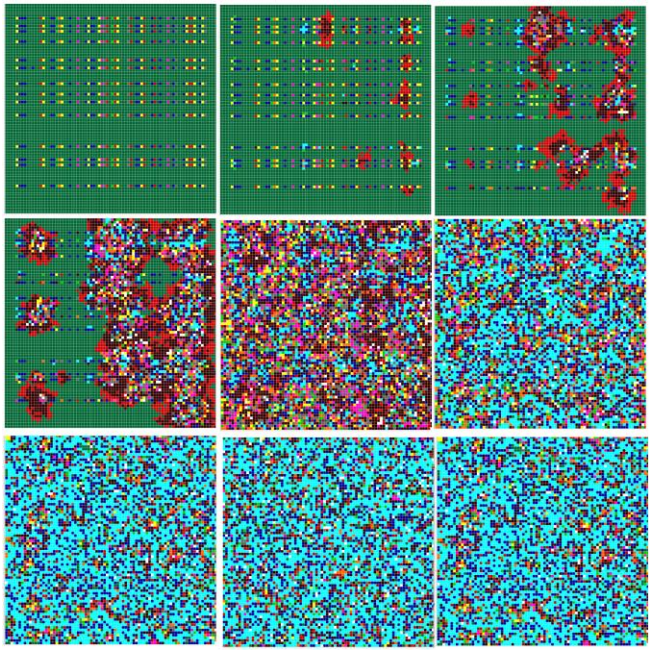

Figure V Evolution of the Computational Model(80×80)

In a similar way that a simulation was carried out with a 50×50 mesh, an 80×80 mesh was carried out to extend the region of consideration of the contagion dynamics [21]. In the same simulation time, similar results are obtained in terms of average, but the important thing about time-space simulations is that they allow analyzing the evolution of the location of the infected cells in order to introduce control and prevention strategies [3]. In this way, better results can be obtained according to the resources that are available from the health institutions [1], [26]. The vision of training and awareness of the importance of caring for infectious diseases (HIV and TB) allows maintaining very low rates in the community, since there is not a strong dependence on epidemiological support personnel, but rather on susceptible people [2]. They go through a period of training to become support staff for the other infected people.

This is evidenced in the simulations shown in figures II and V, where the presence of these permanent susceptible support personnel who support their community prevail in the medium term, and although there are infected cells, they do not go on to an epidemic outbreak of the diseases. even more so, the HIV-TB coinfection that causes a silent propagation [16], [29].

Computational modelling of the propagation of infectious diseases will always require an analysis of infection data, prevalence, statistics, projections to evaluate the best way to collect and apply them to implement them in a mathematical model [1], [16]. This help will always be of vital importance to obtain the best epidemiological results [3].

CONCLUSSIONS

Computational modeling to address the spread of infectious diseases will always have complications due to human behavior that can be unpredictable or collectively driven [30]. In this sense, the model by cellular automata provides us with a connection between contact and contagion according to a small neighborhood than a mathematical model by differential equations that addresses contact and contagion with the entire population [3], [28]. In addition, including the coexistence of a coinfection is always delicate because two diseases coexist with their symptoms, which the epidemiological support staff and the susceptible population cannot easily distinguish to avoid contagion [16].Therefore, the implementation of intervention strategies as a school of learning about diseases is essential to reduce risk [24].

- The computational modeling by cellular automata allows us to visualize the evolution of the pandemic in time and space to approach a more focused analysis of intervening with some epidemiological strategy [30].
- The consideration of the support population and the evolution of the temporary to permanent susceptible population evidence the effectiveness of prevention strategies as well as control towards infected populations to maintain low levels of prevalence [2], [16].
- The coinfection presents a concern for the susceptible population because it has a contagion of two related diseases and makes it more difficult to carry out an adequate treatment. Therefore, prevention and control strategies should be better focused according to the locations of the infected populations [16], [26].
- The evolution of the mathematical model stabilizes where it represents the coexistence of epidemiological populations over time. But the spatial location allows us to analyze the infected populations to carry out control strategies [7], [15].
- The computational model (Cell-DEVS) can be complemented with mathematical models to address the problem of HIV-TB coinfection where prevention and control is essential for public health, even more so, for the quality of life and coexistence of the population. Community [24], [27].

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