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ORIGINAL ARTICLE / ARTÍCULO ORIGINAL

EVENT RECONSTRUCTION ALGORITHM FOR CORONAVIRUS (COVID-19) 3D RECONSTRUCTION, ACCORDING TO STUDY ITS REACTION THROUGH ANTIVIRAL ANALYSIS TREATMENT

ALGORITMO DE RECONSTRUCCIÓN DE EVENTOS PARA LA RECONSTRUCCIÓN 3D DE CORONAVIRUS (COVID-19), SEGÚN EL ESTUDIO DE SU REACCIÓN A TRAVÉS DEL TRATAMIENTO DE ANÁLISIS ANTIVIRAL

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ABSTRACT

This research explains the applications of 3 dimensional (3D) reconstruction for COVID-19 families images, to look for the correlation between the mathematical model “event by event” with antiviral effect on the virus, furthermore, the mathematical model obtained from 3D reconstruction is correlated with “A general mathematical modelling for immune responses”. Therefore, the designed algorithm, provides support for medical doctors through a graphic analysis and predictions regarding “What happens with the virus before applying anti-malaria drugs?”. Many Countries are trying to find the vaccine against COVID 19; however, many Countries only have statistical strategies achieved by population displacement restrictions, which is not enough to avoid faster virus transmission. Hence, in this research is proposed a mathematical analysis to deal with the virus by a predictive model based on 3D COVID 19 images reconstruction, correlated with antiviral analysis applications. As a consequence of the model designed, the medical doctor can predict responses of cells damaged by the virus after application of antivirals or plasma. The algorithm is elaborated to be a support for COVID 19 treatment.

Keywords: COVID-19 – 3D reconstruction – mathematical modelling

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RESUMEN

Esta investigación explica las aplicaciones de reconstrucción tridimensional (3D) para las imágenes de las familias COVID-19, según la búsqueda de la correlación entre el modelo matemático "evento por evento" con efecto antiviral sobre el virus, además, el modelo matemático obtenido de la reconstrucción 3D está correlacionado con "Un modelado matemático general para las respuestas inmunitarias". Por lo tanto, el algoritmo diseñado, proporciona apoyo a los médicos a través de un análisis gráfico y predicciones con respecto a "¿Qué sucede con el virus antes de aplicar una acción como los medicamentos contra la malaria?". Muchos países están tratando de encontrar la vacuna contra COVID 19; sin embargo, muchos países sólo tienen estrategias estadísticas dadas por las restricciones de desplazamiento de la población, lo cual no es suficiente para evitar la rápida transmisión del virus. Por lo tanto, en esta investigación se propone un análisis matemático para tratar el virus mediante un modelo predictivo basado en la reconstrucción de imágenes 3D del COVID 19, correlacionada con aplicaciones de análisis antiviral. Como consecuencia del modelo diseñado, el médico puede predecir las respuestas de las células dañadas por el virus después de aplicar antivirales o plasma sobre ellas. El algoritmo proporcionado se elabora para ser un soporte para el tratamiento del COVID 19.

Palabras clave: COVID-19 – reconstrucción 3D – modelado matemático

INTRODUCTION 3D reconstruction.

According to achieve the mathematical model of an "event process" through 3D image reconstruction to be a support for medical doctor understanding of the virus damage over lungs, it was studied some figures of the virus effect in mice lungs. The permission of the figures was given by Lin *et al.* (2004).

Notwithstanding, "the main task of this research is to achieve the mathematical model of the interaction/effect among COVID 19 with antiviral treatment".

Hence, it is necessary to process at least 2 figures during different stage of the treatment due to get the

Figure 1 depicts the scheme of the algorithm. For which, "Tfi" represents the mathematical model of the "interaction/effect virus and cells". "Ui" is the input variables matrix, that represents "viral application, plasma application, chemical component" all of them as the input excitation signal. "Yi" is the output variables matrix, that represents every answer of the cells under the interaction/effect of the virus because of "Ui". "Yi" can give information (for a medical doctor) regarding the geometrical dimension of cells (as a consequence of some input variable applied as a viral over cells in interaction with the virus), also, it can give information of any kind of changes over system composed by "cells and virus interaction".

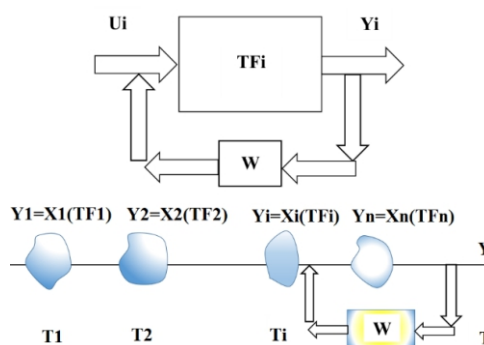


Figure 1. Event reconstruction algorithm scheme.

Therefore, to improve real information that the only doctor can verify or validate whether “U_i” has real information (according to analyze predictions or estimations), in that context, it is necessary feedback by adaptation of a weights matrix “W”. That is the reason, why, in the axis “Y” of figure 1, it is depicted for every instance “i”, in which was achieved an event “the response of the system after every internal feedback adaptation”, all of them executed during total time “T”. This research explains the applications of 3 dimensional (3D) reconstruction for COVID-19 families images, according to look for the correlation between the mathematical model “event by event” with antiviral effect on the virus.

MATERIALS AND METHODS

After to get the analysis of the 3D reconstruction model, separated from every stage of the treatment “virus and antiviral”, it is analyzed their curves through “Set Evolution Functions”. Therefore, the following equation takes the information of a curve from the figure processed, which is stored (by derivatives and divergences) its behaviour (their parameters α). That is the reason, why the dependence in position and time for level set functions “g” and “ φ ” can be solved by many models such as polynomial equations.

$$\frac{\partial \varphi}{\partial t} = g|\nabla \varphi| \operatorname{div} \left(\frac{\nabla \varphi}{|\nabla \varphi|} \right) + \nabla g \cdot \nabla \varphi + \alpha g|\nabla \varphi| \quad (1)$$

As it was described above, the treatment solutions worked in this research are based on polynomial models, like in equation (2). In that, the derivatives “P” with maximal order “n” is applied for the changes on time of the response function “y”, internal functions “x” and excitation signal (that causes changes in the system) “u”. Furthermore, its error “e”, the treatment solution to follow is given by “Modulating function analysis”.

$$P^n y(t) + \sum_{j=1}^n a_j p^{n-j} y(t) = \sum_{j=1}^n b_j p^{n-j} u(t) + e(t) \quad (2)$$

Where solution error analysis “e(t)” is the discrete error, and “V” keeps the Fourier series coefficients showed in equation (3).

$$e_n(m) = \sum_{k=m}^{n+m} \alpha(k, m, \theta_a) V(k) \quad (3)$$

Moreover, is the frequency parameter function in the equation (4), and C_{k-m} is the numerical combination of the physical parameters “a”.

$$\beta(k, m, \theta_a) = C_{k-m} \sum_{j=0}^n a_j (jk\omega_0)^{n-j} \quad (4)$$

For which, the nonlinear model for error analysis is given by equation (5). In that equation, “g” is the function for the parameters “ θ ”, “E and F” are the specified functions for the input variables “u” and responses “y”. Finally, “P” are the fixed polynomials as dependence on derivatives $p = \frac{d}{dt}$.

$$\sum_{j=0}^{n1} \sum_{k=1}^{n2} g_j(\theta) F_{jk}(u, y) P_{jk}(p) E_k(u, y) = 0 \quad (5)$$

Therefore, the estimation matrix is given by the following equation:

$$\hat{\beta}_w = (X^T W^{-1} X)^{-1} X^T W^{-1} Y \quad (6)$$

For which, the weighting matrix “W” was solved by “Feasible Generalized Least Square (FGLS), Cochrane Orcutt Procedure (COCR)”. It must be known ρ take values between -1 and 1:

$$W^{-1} = \begin{pmatrix} 1 & -\rho & 0 & \dots & 0 \\ -\rho & 1 + \rho^2 & -\rho & \dots & 0 \\ 0 & -\rho & 1 + \rho^2 & -\rho & 0 \\ \vdots & \vdots & -\rho & 1 + \rho^2 & -\rho \\ 0 & 0 & 0 & -\rho & 1 \end{pmatrix} \quad (7)$$

That is the reason why the general solution is given by the following equation:

$$\hat{y}_w = X \hat{\beta}_w \quad (8)$$

In figure 2, it is showing a Representative lung histopathology” kindly provided by Yan *et al.* (2013), in which is described the interaction between virus H5N1 with the antiviral, that sequence of figures is quite necessary to achieve the 3D image reconstruction of the “interaction stages between the virus and antiviral”, even

though “it is more necessary to apply this research for COVID 19”. In the image provided is not known the scale (only magnifications: 200x and 400x), hence, the equivalent scale in every 3D reconstruction image (from figure 3 to figure 10) is depicted by colours while growing up the size in “Z” axis: blue, light blue, yellow, orange and red.

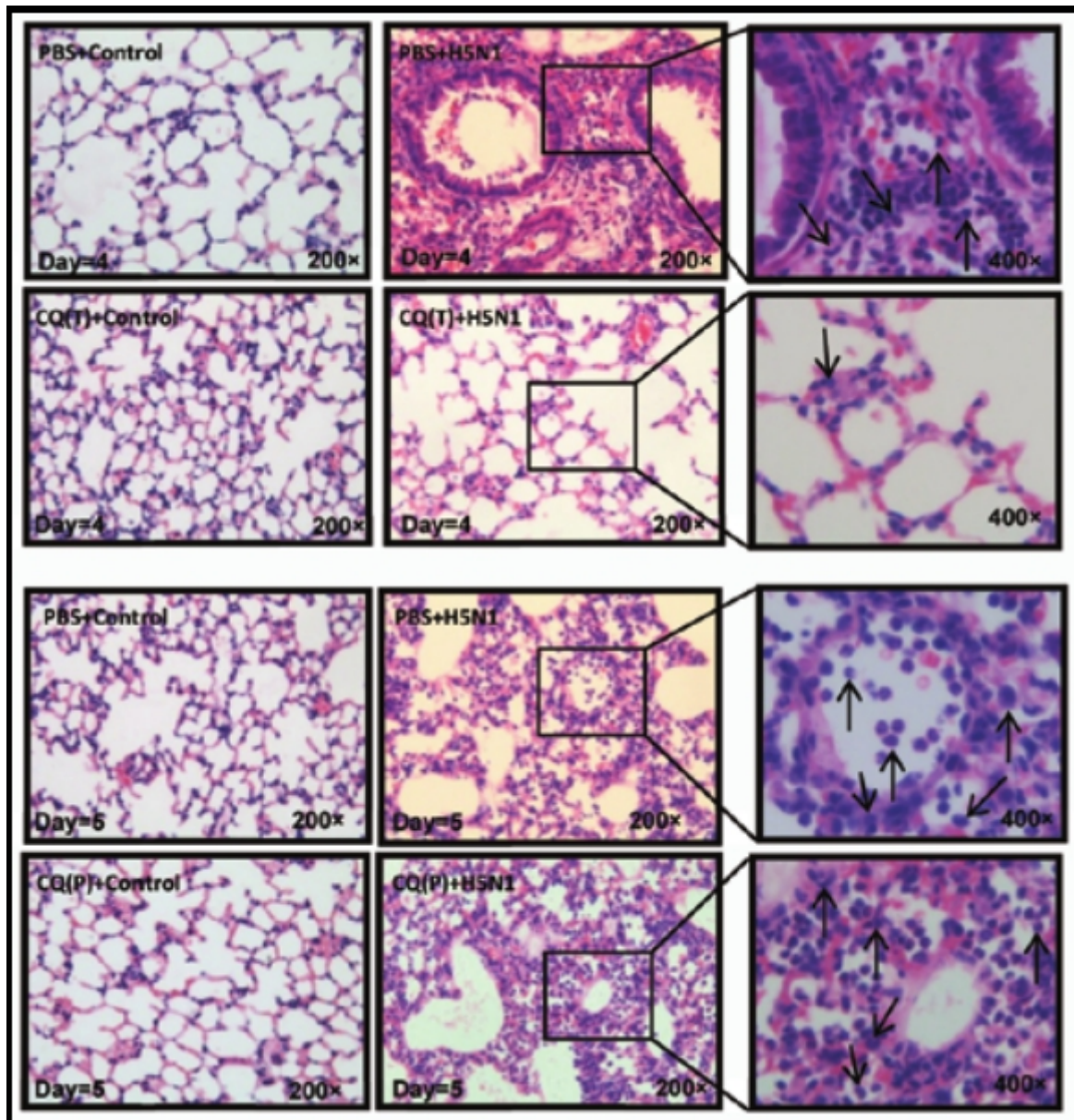


Figure 2. Representative lung histopathology provided by Yan *et al.* (2013).

Therefore, it was executed the algorithm designed and described above owing to achieve 3D reconstruction. The following figure shows the 3D reconstruction of mice lung cells under PBS (Phosphate Buffered Saline) control around 200x magnification due to the original figure (cells

inside “C” curve [1] during the test day 4) was under that magnification value. It means that “C1, C2 and C3” achieved similar scale reconstruction, these reconstructions give geometrical details of the internal sizes (estimated) for the “PBS control” applied.

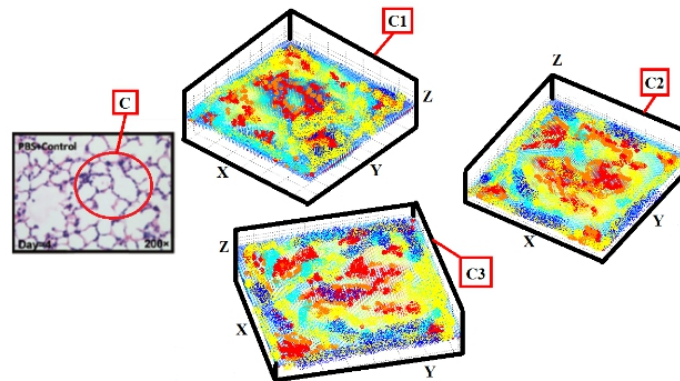


Figure 3. Mice lung cells under PBS control (Yan *et al.*, 2013), original magnification was 200x by the SEM and the 3D reconstruction under that magnification (during the test day 4). C = circumference. C1, C2 and C3 = 3D reconstruction in SEM.

Moreover, the following figure shows the same mice lung cells under PBS but infected by H5N1 (during day 4 after virus infection) in magnification SEM of 400x (Yan *et al.*, 2013) inside the circumference “C”, also, “C1, C2 and

C3” show the 3D reconstruction at 400x in magnification SEM (Figure 4). It is possible to identify better view from “monocytes and neutrophils of the infiltrating cells”.

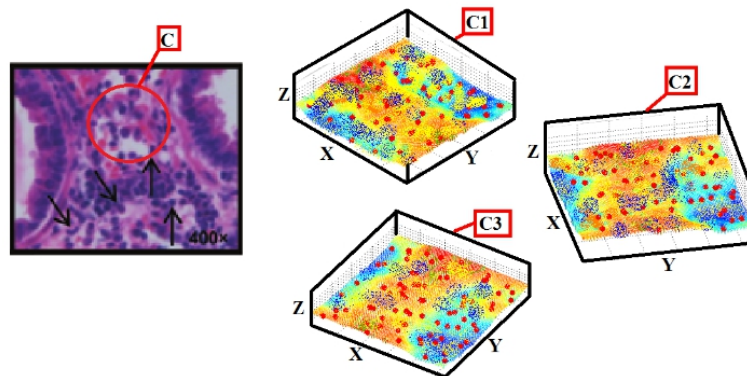


Figure 4. 3D reconstruction at 400x magnification SEM of mice lung cells infected by H5N1 (during the test day 4). C = circumference. C1, C2 and C3 = 3D reconstruction in SEM.

The following figure shows the 3D reconstruction of mice lung cells under CQ (chloroquine) control around 200x magnification due to the original figure (cells inside C curve (Yan *et al.*, 2013)) was achieved under that magnification value, in both contexts (SBS and CQ control) were analyzed for the day 4 of infection. It means that “C1, C2 and

C3” achieved similar scale reconstruction, these reconstructions give geometrical details of the internal sizes (estimated) for the “CQ control” applied (Figure 5). It is necessary to remind “CQ is a highly effective therapeutic but not prophylactic agent against avian influenza AH5N1 (Yan *et al.*, 2013)”.

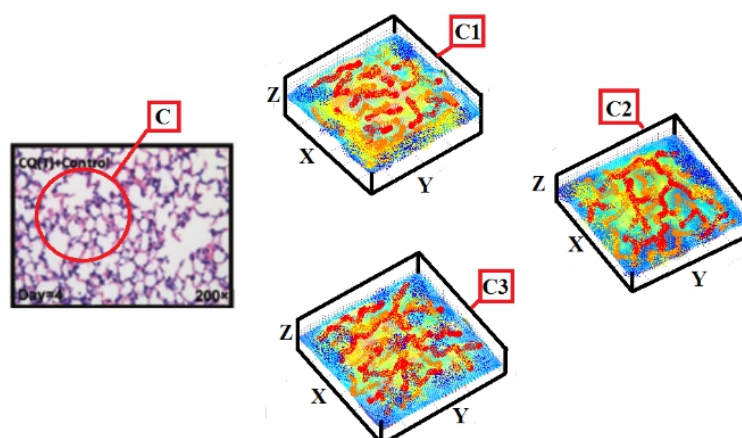


Figure 5. Mice lung cells under CQ control (Yan *et al.*, 2013), original magnification was 200x by the SEM and the 3D reconstruction under that magnification (during the test day 4). C = circumference. C1, C2 and C3 = 3D reconstruction in SEM.

Furthermore, the following figure shows the same mice lung cells under CQ but infected by H5N1 (during day 4 after virus infection) in magnification SEM of 400x (Yan *et al.*, 2013) inside the circumference “C”, also, “C1, C2 and C3” show the 3D reconstruction at 400x in

magnification SEM (Figure 6). It is possible to identify a better view from “monocytes and neutrophils of the infiltrating cells”. This reconstruction can be used by a medical doctor to evaluate the effects of CQ in mice lungs.

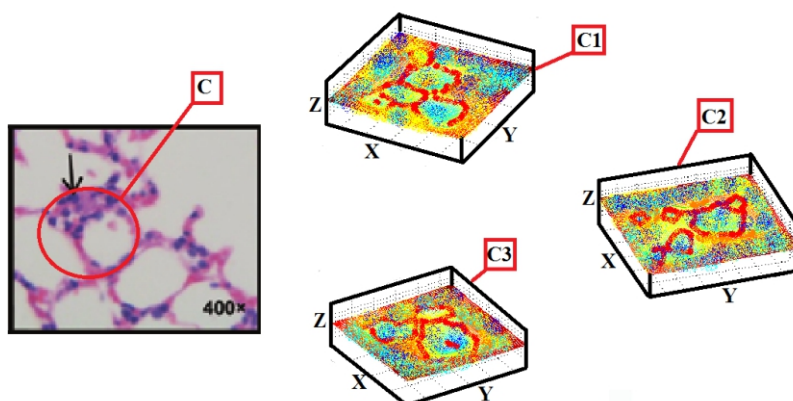


Figure 6. 3D reconstruction at 400x magnification SEM of mice lung cells infected by H5N1 (during the test day 4). C = circumference. C1, C2 and C3 = 3D reconstruction in SEM.

Therefore, it was executed the algorithm designed and described above owing to achieve 3D reconstruction. The following figure shows the 3D reconstruction of mice lung cells under PBS control around 200x magnification due to the original figure (cells inside C curve (Yan *et al.*,

2013) during day 5 after virus infection) was achieved under that magnification value. It means that “C1, C2 and C3” achieved similar scale reconstruction, these reconstructions give geometrical details of the internal sizes (estimated) for the “PBS control” applied (Figure 7).

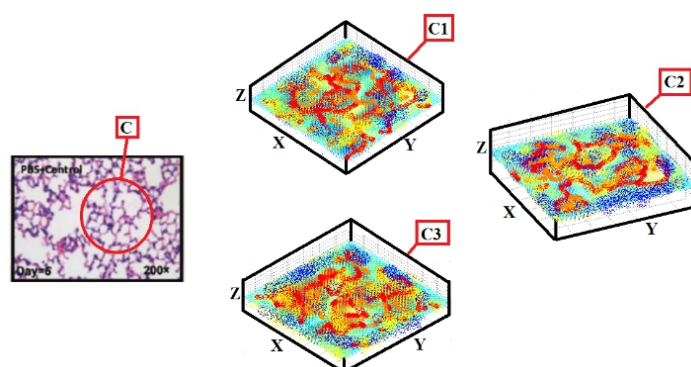


Figure 7. Mice lung cells under PBS control (Yan *et al.*, 2013), original magnification was 200x by the SEM and the 3D reconstruction under that magnification (during the test day 5). C = circumference. C1, C2 and C3 = 3D reconstruction in SEM.

Furthermore, the following figure shows the same mice lung cells under PBS but infected by H5N1 (during day 5 after virus infection) in magnification SEM of 400x (Yan *et al.*, 2013) inside the circumference “C”, also, “C1, C2 and

C3” show the 3D reconstruction at 400x in magnification SEM (Figure 8). It is possible to identify better view from “monocytes and neutrophils of the infiltrating cells”.

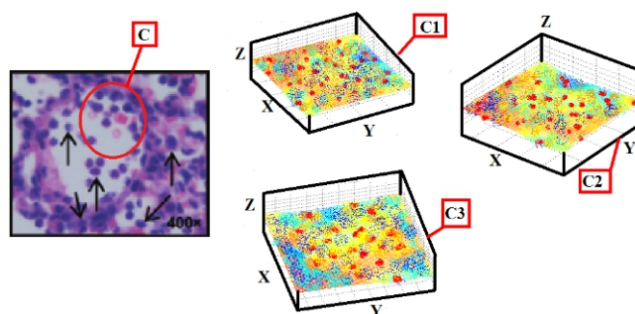


Figure 8. 3D reconstruction at 400x magnification SEM of mice lung cells infected by H5N1 (during the test day 5). C = circumference. C1, C2 and C3 = 3D reconstruction in SEM.

Therefore, it was executed the algorithm designed and described above owing to achieve 3D reconstruction. The following figure shows the 3D reconstruction of mice lung cells under CQ control around 200x magnification due to the original figure (cells inside C curve (Yan *et al.*, 2013)

during day 5 after virus infection) was achieved under that magnification value. It means that “C1, C2 and C3” achieved similar scale reconstruction, these reconstructions give geometrical details of the internal sizes (estimated) for the “CQ control” applied (Figure 9).

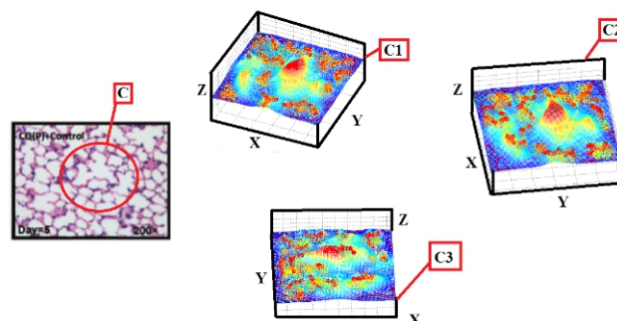


Figure 9. Mice lung cells under PBS control (Yan *et al.*, 2013), original magnification was 200x by the SEM and the 3D reconstruction under that magnification (during the test day 5). C = circumference. C1, C2 and C3 = 3D reconstruction in SEM.

Furthermore, the following figure shows the same mice lung cells under CQ but infected by H5N1 (during day 5 after virus infection) in magnification SEM of 400x (Yan *et al.*, 2013) inside the circumference “C”, also, “C1, C2 and

C3” show the 3D reconstruction at 400x in magnification SEM. It is possible to identify better view from “monocytes and neutrophils of the infiltrating cells” (Figure 10).

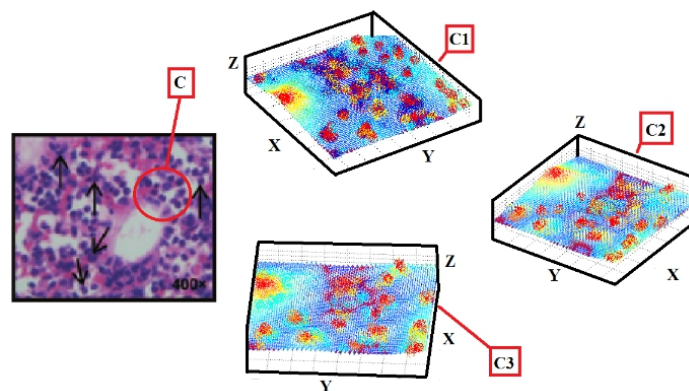


Figure 10. 3D reconstruction at 400x magnification SEM of mice lung cells infected by H5N1 (during the test day 5). C = circumference. C1, C2 and C3 = 3D reconstruction in SEM.

RESULTS AND DISCUSSION

It was designed an algorithm according to be a support for medical doctors, who are dealing with COVID 19 treatment in Peruvian hospitals (Haerberle *et al.*, 2016; Goldsmith & Miller, 2009; Bhalla *et al.*, 2020; Duan *et al.*, 2020; İnandıklioğlu & Akkoc, 2020; Kaniyala-Melanthota *et al.*, 2020). At the time that was finished this research, the world and Perú are losing many lives, even though some countries are crossing this epidemic. However, there are countries such as Perú in which the epidemic makes that medical doctors need to research new strategies as did colleagues from other countries (Prompetchara *et al.*, 2020; Shah *et al.*, 2020). Yan *et al.* (2013), who let to analyze their images, researched responses from viral against H5N1, and that results helped to this research owing to make 3D reconstructions of that figures, and getting a mathematical model in which medical doctors can evaluate the different response of different excitation signals (viral, plasma, medicines) that are translated as input excitation signals to the model, from which was elaborated the algorithm. Therefore, every answer and prediction of this research help to medical doctors to accelerate reaction over patients, it is looking for

a faster understanding of what can happen with the patient under different excitation signal.

Furthermore, it is possible to analyze the behaviour inside of the body, that means reaction from the lung and cells damaged by the virus, because of images help to validate information expected by medical doctors, which are formalized by the mathematical model, and that can warrant to find different solutions to estimate the best response that medical doctor can use according to enhance treatment to deal with this virus. The performance of this research is constantly corrected while there is more and more database to adapt its parameters, which depend on many conditions due to every patient has different characteristics, even similitude but the difference are modelled by the coefficient of the polynomial that represents the behaviour of the general immunity response, supported by the image processed and excitation signal response evaluated to find the more adapted model.

It is expected to complement this research for plasma analysis application. Hence, it waits that this research could be a support to correlate advanced predictive polynomial models to achieve adaptive predictions, in the image analysis of

figures achieved from cells damaged by COVID 19, and as consequence, the medical doctors could get faster emulations to study better answers to understand new treatments against this virus.

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