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ORIGINAL ARTICLE / ARTÍCULO ORIGINAL

PROPOSAL FOR AN EVENT RECONSTRUCTION ALGORITHM TO STUDY THE EVOLUTION OF CANCEROUS CELLS

PROPUESTA DE ALGORITMO DE RECONSTRUCCIÓN DE EVENTOS PARA ESTUDIAR LA EVOLUCIÓN DE LAS CÉLULAS CANCERÍGENAS

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ABSTRACT

In this work, a general algorithm is proposed to design the reconstruction of chemical/physical/biological process events as one of the most complicated today: the evolution of cancer cells. Studying the evolution of the boundary curves it is possible to make a three-dimensional (3D) integration, in addition the 3D figure obtained can be explained through a mathematical model to estimate its geometric evolution after physical/chemical reactions. In this work, there are analyzed images of each stage of the process based on the evolution of cancer cells. Each image was processed in order to obtain a mathematical equation as a reference to understand the geometry of the 3D structure based on its 2D image for each stage. On the other side, with this information and the processing of each stage image, a mathematical equation was achieved to describe the geometry of the structure between stages by "Optimal Prediction Analysis" which is so important to gain understanding of the geometry of the structure with the internal process.

Keywords: cancerous cells evolution – event reconstruction algorithm – 3D image reconstruction

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RESUMEN

En este trabajo se propone un algoritmo general para diseñar la reconstrucción de eventos de proceso químico/físico/biológico como uno de los más complicados hoy en día: la "evolución de las células cancerígenas". Estudiando la evolución de las curvas de frontera es posible hacer una integración en tres dimensiones (3D), además la cifra 3D obtenida se puede explicar a través de un modelo matemático para estimar su evolución geométrica después de reacciones físicas/químicas. En este trabajo, hay imágenes analizadas de cada etapa del proceso basadas en la evolución de las células cancerosas. Cada imagen fue procesada con el fin de obtener una ecuación matemática como referencia para entender la geometría de la estructura 3D basada en su imagen 2D para cada etapa. En el otro lado, con esta información y el procesamiento de cada imagen de etapa, se logró una ecuación matemática para describir la geometría de la estructura entre etapas mediante "Análisis de Predicción Óptima" que es tan importante para obtener la comprensión de la geometría de la estructura con el proceso interno.

Palabras clave: algoritmo de reconstrucción de eventos – evolución de células cancerígenas –reconstrucción de imágenes 3D

INTRODUCTION

Cancerous cells evolution is plenty studied nowadays (Tume-Farfán *et al.*, 2013, 2014; Villareño-Do-Dominguez *et al.*, 2020), because of its quite impact in human health since last century. In order to study cancer cell evolution, it was proposed many techniques that needed advanced mathematic analysis. These techniques were correlated with human genome and by medical doctor supervision they can be a good support to achieve successful diagnostics (Ribeiro & Shah, 2006). Nevertheless, the mathematic models use methodologies to propose every cause of the cancerous cell evolution, which can get an error during the estimation of the diagnostic. For this reason, in this work, it is proposed the algorithm that was based in the achieved experience (3 Dimensions) of nanostructures geometric analysis (Al-Haddad *et al*., 2015; Calderón *et al.*, 2021). By the designed algorithm, which depends of a mathematical model that was based in multiple input/output variables with support of image processing, it is achieved estimations of growing up of different structures and as a consequence to get diagnostic in possible situations during the evolution of the researched structure.

It means, the designed algorithm that was based in the 3D reconstruction by an optimal prediction of every input variable (not only images) can improve its own result as geometrical or physical parameter, that it is looked for a support for medical doctor interpretations to study cancerous cells evolution. In this work is proposed a general algorithm to design event reconstruction of chemical/physical/biological process, such as one of the most complicated nowadays "cancerous cells evolution".

The main objective in this article is to propose an algorithm that works with different events of cancerous cells evolution stage. The sequence of steps is described to be implemented in different software platforms, as for example Matlab, which was used in this work due to the versatility to operate with mathematical analysis calculations, process image and sequence of logic in order to simulate events connections. Furthermore, to achieve optimal predictions (not only 3D reconstructions) means to get optimal prediction support about events to study cancerous cells evolution. This is the reason, why it is proposed to monitory every suggestion of medical doctor, regarding the processed figure, as an input variable, from which can be possible to interpret changes of the mathematical model of the dynamical analysis consequence of the processed figures. (Ljung, 1994; Pearson, 1995; Wang, 2009; Li *et al*., 2010; Calderón *et al.*, 2019).

MATERIALS AND METHODS

As it was described in articles (Lei *et al.*, 2007; Sidow *et al.*, 2015), 3D image reconstruction from 2D image reconstruction was achieved by Level Set Functions (LSF) analysis that means by

equation 1 is summary of all the system of equations by equivalent of energy balance, in order to have a general equation to represent changes on time, furthermore, the changes on set of curves, where *"g"* means the indicator function border and *"α"* is the weight of curve area changes (Lei *et al.*, 2007).

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

For this reason, in order to propose a 3D reconstruction algorithm, it was necessary to get borders by correlating variables to get desired errors during geometrical reconstructions in every axis. It means that border changes analysis by LSF can be fixed by weights of optimal predictions that were applied to an identified mathematical model of the geometry dynamic that was achieved and described by equation 2.

$$Error = |corr(\phi_2, \phi_1) - h_0| \quad (2)$$

For all *"Error"* value belong to [$Error_o$, $Error_1$,..., $Error_m$] then it is possible to find the function "ϕ" to warrant 3D reconstruction. With sequence value of "ϕ" it is simple to create a movement sequence of figures *"Video"* that is composed by following equation 3, in which every instant *"t"* can be joined as a set of a period of time, which depends on the treatment time that is suggested by the medical doctor.

$$t = [t_0, t_1, \ldots, t_n] \quad (3)$$

it means *"Video"* is represented by equation 4

$$Video = [\phi_0, \phi_1, \ldots, \phi_n] \quad (4)$$

After to evaluate 3D initial sides view, "h_o" is a proposed value. Therefore, with the capability to make 3D reconstruction for every stage of real 2D image, it was obtained of the cancerous cells evolution process, so by "System Identification" it was possible to get physical and geometrical parameters of the 3D nanostructure image that was reconstructed during evolution of the process, carefully recognizing that real evolution of the process is elapsed many ranges of time, because of the quantity of internal process during real cell evolution, as it is depicted in Figure 1. Therefore, in this figure is showed the model as a system *"TF_i"*, in which an input variables matrix *"U"* causes responses *"Y"* that needs corrections/compensations that was achieved by an adaptive matrix of weights *"W"*, which is obtained for every sequence of package of figures *"Y_i"*.

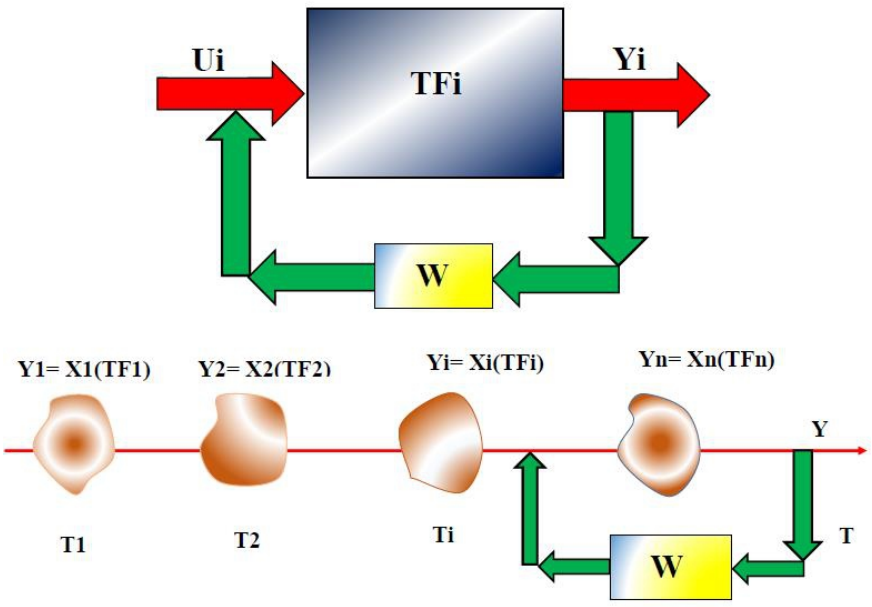

Figure 1. Proposed scheme to describe event reconstruction algorithm.

Furthermore, schematic proposal above is supported through a mathematical base, which are described in following equations. Therefore, it is required a model that could work with different changes through the operations (as derivatives), the model to represent a nonlinear system as dependence of many input/output variables. It means, it was proposed a polynomial model that is described in equation 5. *"P"* and *"n"* are the derivatives and order respectively, *"a"* and *"b"* are the parametric coefficients, which contain information of the system. For this scenery the "system" is defined as the package of figures as dependence of variables *"y"* and *"u"* in time domain *"t"* (Pearson, 1995; Calderon *et al*, 2019).

$$P^n y(t) + \sum_{j=1}^{n} a_j P^{n-j} y(t) = \sum_{j=1}^{n} b_j P^{n-j} u(t) + e(t) \quad (5)$$

Therefore, by the costing function equation *"J"* analysis, it was achieved an adaptive prediction over processed image, as it is showed by equation 6, for which *"Y_c"* is the expected output variables matrix, *"Γ_c"* is the output variables matrix, *"θ"* is the regression coefficients matrix and *"W"* is the adaptive weight coefficient matrix.

$$J = (\Upsilon_c - \Gamma_c\theta)'\Gamma'_c W^{-1}(\Upsilon_c - \Gamma_c\theta) \quad (6)$$

By solving equation 6, it is obtained the matrix of parameters *"θ"* that is depicted by equation 7

$$\theta = (\Gamma'_c\omega^{-1}\Gamma_c)^{-1}\Gamma'_c\omega^{-1}\Upsilon_c \quad (7)$$

In figure 2 is shown first part of the flowchart for the algorithm that was designed, in which is necessary to choose parameters as a dependence of sampling time, computing time, response time and estimated growing time as optimal value studied in this research. The methodology, which was analyzed in order to design this algorithm, was proposed by authors (Wang, 2009; Calderón *et al.,* 2019). The algorithm needs border curves as a potential reflection according to get 2D to 3D reconstruction. Through every 3D reconstruction it was obtained mathematical information by "System Identification".

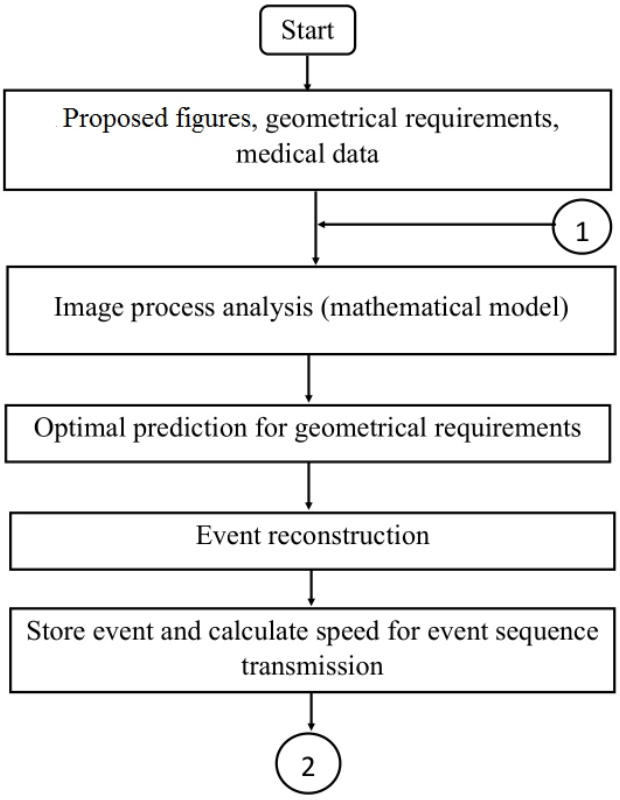

Figure 2. Proposed flowchart to explain the event reconstruction designed algorithm (Calderón *et al.*, 2019), part 1.

Therefore, with these mathematical equations, because of identification, it was possible to design subroutines in the main algorithm to achieve the optimal predictions of images for every stage of the cancerous cells evolution. Furthermore, by a simple subroutine, it was possible to organize "video sequence" and to get a video of all the process after filtering geometrical information, which were predicted as not a part of the final 3D image, in order to achieve the optimal reconstruction, as it is depicted in figure 3 as a second part of the proposed algorithm.

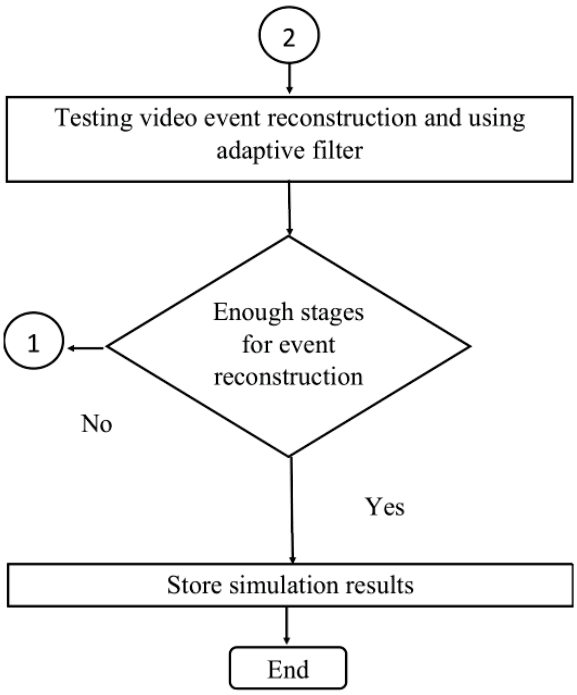

Figure 3. Proposed flowchart to explain the event reconstruction designed algorithm (Calderón *et al.*, 2019), part 2.

The expected result of the algorithm execution is shown in figure 4, in which is represented how geometrical parameters change, while time elapses (Calderón *et al.*, 2019). Thus, by analysis of every input variable as the part of the adaptive costing error analysis in the main algorithm, it was looked for a 3D reconstruction that was depicted in figure 4.

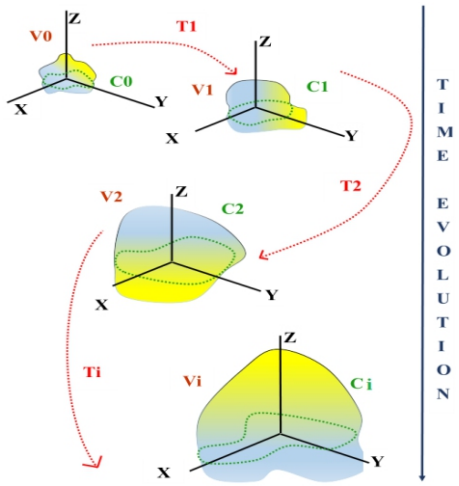

Figure 4. Geometrical representation of the "cancerous cells evolution" (Calderón *et al.*, 2019).

Ethical aspects: This research has not ethical conflicts in the proposed article, it was cited every bibliographic reference for every analysis described, moreover the image from which was made the three-dimension reconstruction, as a consequence of the algorithm designed for this research, this image was proportionated by the Medical Julio Guevara. Hence, it is warranted that the ethical aspects are applied for this research.

RESULTS AND DISCUSSION

In order to prove the designed algorithm, it was made different experiments over aluminum elaborating electropolishing and anodization (Wang, 2009; Inan & Marshall, 2011; Calderón *et al.*, 2019). These processes are based in chemical procedures, which produce chemical changes over aluminum foil as it was given by "Anodic Aluminum Oxide" (AAO) (Poinern *et al.*, 2011), furthermore, some physical changes in their geometry. It is necessary to use microscope to evaluate reactions over the aluminum foil. Nevertheless, for this research, it was used a "Leitz" microscope at resolution in micrometers, owing to watch geometrical deformations in millimeters scale. After to verify the results that were achieved by the algorithm, it was proved the capacity to achieve 3D reconstruction in a real figure of lung cancer cells (Kraeft *et al.*, 2000).

In this context, figure 5 shows a piece of aluminum foil (figure 5A) and its 3D reconstruction in figure 5B, for which colors red, yellow and light blue represent interval scales between 0.9mm, 0.6mm and 0.3mm respectively.

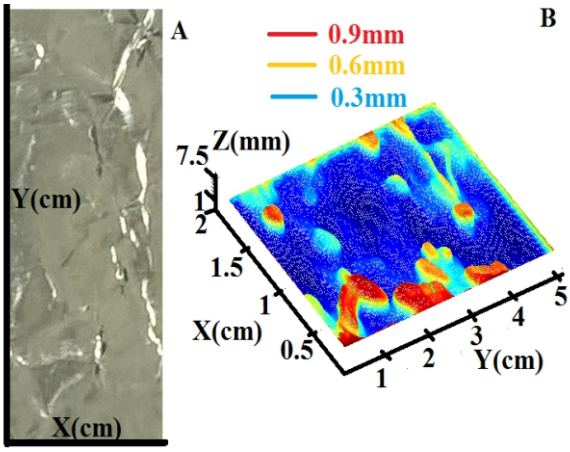

Figure 5. 3D reconstruction of Aluminum foil.

After electropolishing and anodization processes (Calderón *et al.*, 2019), according to study the behaviour of physical/chemical changes over a structure (aluminum foil for this experiment), it was achieved AAO that is showed in figure 6A and its respective 3D reconstruction that is depicted in figure 6B, for which colors red, yellow and light blue represent interval scales between 0.9mm, 0.6mm and 0.3mm respectively.

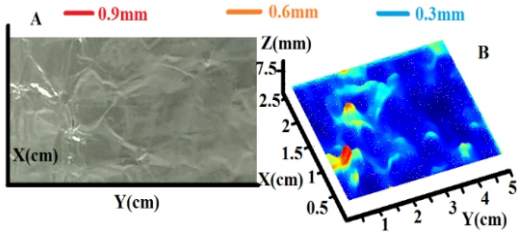

Figure 6. 3D reconstruction of AAO.

It was necessary to achieve deep chemical changes in copper sulphate, as it is depicted in figure 7A and its 3D reconstruction showed in figure 7B, for which colors red, yellow and light blue represent interval scales between 0.9mm, 0.6mm and 0.3mm respectively.

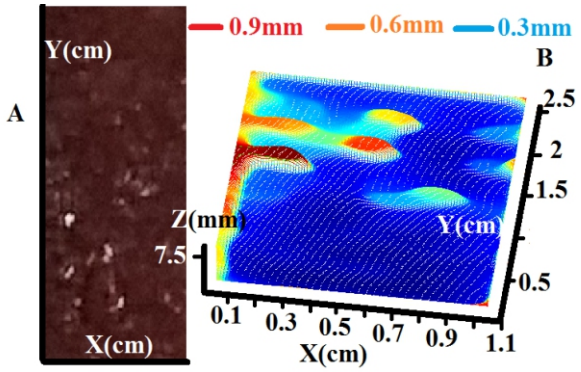

Figure 7. Copper sulphate over AAO foils and its 3D reconstruction.

In spite of the geometrical changes, it was verified the 3D reconstruction from figures above and it was increased time from last reaction at 20%. Therefore, it was damaged the foil (figure 8A) that was necessary to evaluate geometrical reconstructions in more complicated situation as it was achieved in figure 8B, for which colors red, yellow and light blue represent interval scales between 0.9mm, 0.6mm and 0.3mm respectively.

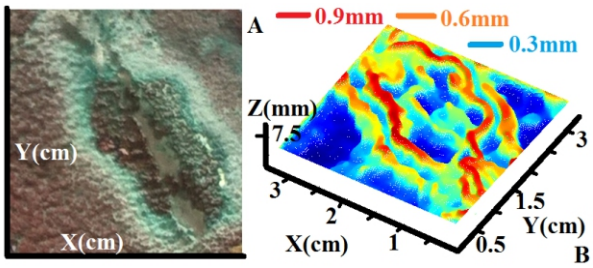

Figure 8. Damaged foil after to increase time reaction at 20%.

Finally, according to evaluate the performance of the algorithm, it was analyzed a lung cancer cell in figure 9, from which there are tumor cells surrounding lung cancer cells as depicted by figure 9A1, 9A2, 9A3, and 9A4. Therefore, the algorithm was evaluated and it was achieved their respective 3D reconstruction, as it is showed by figures 9B, 9C, 9D and 9E, from which was obtained the possibility to see an estimation of geometrical parameters as the size that was not possible to see in 2D. Furthermore, the mathematical model as dependence not only on figures that were introduced in the algorithm, it means that every diagnostic of the medical doctor can be translated as an input variable to explain the final result of the model in order to achieve estimation.

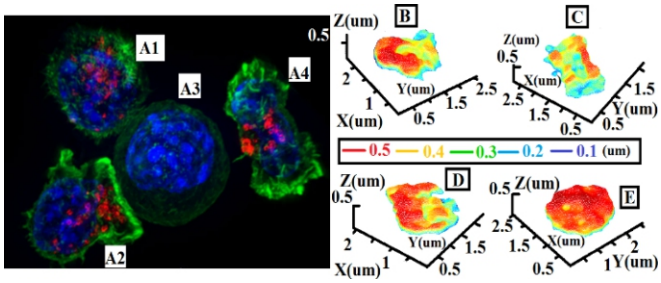

Figure 9. Lung cancer cells and its 3D reconstruction.

It was evaluated the algorithm in order to get geometrical image details that cannot be simple to see through the microscope. Therefore, a 3D image reconstruction can be a support for oncology analysis. Nevertheless, this is only an algorithm support.

It was achieved numerical data from the estimated physical variables (medical interpretation of tested images), for which it can be expected geometrical parameters of the expected evolution of cancerous cells and to model mathematical equations as the diagnostic that needs to be evaluated by medical doctor.

It is suggested to verify this algorithm with more different cases of cancer cells photos, in order to find applications of predictive behavior of the researched mathematical model, which supports the designed algorithm. These applications could be a support for predictive diagnostic of medical doctors.

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