Herramienta para la simulacion del crecimiento de tumores en diversas regiones del cuerpo humano en 3 dimensiones.

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Resumo: Cancer is a disease characterized by the uncontrolled growth of abnormal cells in the body. It is a complex and multifaceted disease that has challenged researchers and doctors for decades. The ability to visualize and understand tumor growth can provide valuable insights into how cancer develops and spreads, leading to significant improvements in cancer diagnosis, treatment, and prevention. The three-dimensional tumor growth simulation tool that is being developed is an important step in this direction. It allows for detailed visualization of tumor growth in different parts of the human body, which can provide valuable insights into how cancer develops and spreads. Additionally, the ability of this tool to simulate tumor growth in different parts of the body means that it can be used to study a wide range of cancer types. This tool utilizes a cellular automaton and a small-world network to create connections between cells, allowing for a more accurate representation of organ and tumor structures. Furthermore, it allows for the loading of configurations and parameters from external files, providing great flexibility to the tool and allowing for customization of the simulation to the specific needs of each case. For 3D rendering, the Marching Cubes technique is used, which enables detailed and accurate three-dimensional representation of tumors.

Palavras-chave: Cellular Automaton, Marching Cubes, 3D, cancer, tumor

Introdução

The challenge of representing biological phenomena mathematically, physically, and computationally requires interdisciplinary synergy among experts in these fields. This collaboration enriches the traditional experimental method used in biological sciences by implementing mathematical models, which serve as tools to formulate and test hypotheses, guide experimental research, and refine the model based on the obtained results. [**?**]

Cancer is a disease that affects a large number of living organisms and is characterized by the presence of a group of abnormal cells that grow uncontrollably, disregarding the normal rules of cell division. It particularly affects humans, where its occurrence and development pose a threat to life. The malignancy of cancer varies and depends on factors such as the growth rate of cancer cells, their ability to spread to other tissues, and the possibility of recurrence after surgical removal.

The purpose of this type of research is to achieve a deeper understanding of biological processes through an iterative cycle of theory and experimentation. Additionally, mathematical models can be used to assist in the conception and design of therapeutic strategies, providing a more precise and personalized insight into the treatment of each patient.

In the case of this project, a cellular automaton and a small-world network are used to model the interactions between cells, providing a more accurate representation of tumor growth. The parameters and configurations can be loaded from external files, offering great flexibility in adapting the simulation to the specific needs of each case.

The technique of Marching Cubes [**?**] is used for 3D rendering, providing a detailed and precise visualization of tumors. This visualization can provide valuable insight into how cancer develops and spreads, which can be essential for the development of effective therapies and treatments. By visualizing tumor growth in three dimensions, doctors and scientists can gain a better understanding of tumor evolution and how it may affect surrounding tissues. This information can be crucial for the development of effective therapies and treatments for cancer.

Submissão

Cellular Automaton

In this section, the cellular automaton model presented in this work is conceived. It begins by formally defining a cellular automaton [5].

A cellular automaton is a tuple $(\mathscr{L};\mathscr{N};\mathscr{E};\mathscr{R})$ composed of the following representative elements:

$\mathscr{L}$: t is a potentially infinite set of cells.

$\mathscr{N}$: $\mathscr{L}\times\mathscr{L}\to\{0,1\}$ is a neighborhood function, which can be seen as a relation, usually reflexive and symmetric, between cells. This function shows which pairs of cells are neighbors, that is, the geometry of the cellular organization.

$\mathscr{E}$: It is a set of states. Each cell in the set $\mathscr{L}$ is assigned an associated state at each time step.

$\mathscr{R}$: $\mathscr{E}^{|\mathscr{N}(v)|}\to\mathscr{E}$ is a locally defined transition function. This function is the core of the dynamics of a cellular automaton and is commonly expressed through rules that define the state of the cell in the next time step based on the state of the neighboring cells. The set containing the state of the neighboring cells is obtained through the function $\mathscr{N}(v)$, wich is defined below **??**.

The sets $A^n(G)$ and $A^d(G)$ group the edges of the graph that correspond to immediate and distant connections, respectively. These sets have the following properties:

$$A^n(G)\cup A^d(G)=A(G), \tag{1a}$$

$$A^n(G)\cap A^d(G)=\emptyset. \tag{1b}$$

These properties indicate that the subsets of edges $A^n(G)$ and $A^d(G)$ form a partition of the set of edges $A(G)$

Based on the sets of vertices $V(G)$ and edges $A(G)$, the representative elements $\mathscr{L}$ and $\mathscr{N}$ of the cellular automaton model are defined as follows:

The set of cells $\mathscr{L}$ is defined based on the set of vertices of the graph $V(G)$ as shown below:

$$\boxed{\mathscr{L}=V(G)}\,. \tag{2}$$

The neighborhood function $\mathscr{N}$ s defined based on the set of edges of the graph $A(G)$ as shown below:

$$\boxed{\mathscr{N}:V(G)\times V(G)\to\{0,1\}}\,, \tag{3a}$$

$$\boxed{\mathscr{N}(v,w)=\begin{cases}0 & si\ \{v,w\}\notin A(G)\\ 1 & si\ \{v,w\}\in A(G)\end{cases}}\,, \tag{3b}$$

In other words, the vertices $v \in V(G)$ and $w \in V(G)$ are neighbors in the cellular automaton if there exists an edge in G that connects them.

The neighborhood of the vertex $v \in V(G)$ is defined based on the neighborhood function $\mathcal{N}(v,w)$ as the set of vertices $\mathcal{N}(v)$ that have edges with the vertex v:

$$\mathcal{N}(v) = \{w \mid \mathcal{N}(v,w) = 1\}. \tag{4}$$

Set of cells: Watts-Strogatz model

In the presented study, a soft tissue is defined as a set of cells that exhibit two types of connections: between nearby neighboring cells and between distant cells. To represent these types of connections, a cellular automaton model based on a graph network is used. In their work[31], Duncan J. Watts and Steven H. Strogatz showed that there are many biological, technological, and social networks that lie between regular and random networks, which have traditionally been used to model different types of dynamic systems.

Let v be a vertex of the graph that has k_v edges connecting it to k_v vertices. The value between the actual number of edges K_v that exist between these k_v vertices and the maximum number of possible edges[1] $k_v(k_v-1)/2$ e is the clustering coefficient of vertex v and is determined as [**?**]:

$$C_v = \frac{2K_v}{k_v(k_v-1)}. \tag{5}$$

The global clustering coefficient of the graph C_G is the average of all individual clustering coefficients C_v, that is [**?**]:

$$C_G = \frac{1}{|V(G)|}\sum_{v=1}^{|V(G)|} C_v. \tag{6}$$

The average path length is the mean of the distances between every pair of vertices belonging to the graph and is denoted as ℓ_G. Due to the existence of numerous distant connections through the circulatory system, the average path length in the network of cells is relatively small.

Therefore, it is hypothesized that a living tissue possesses a high clustering coefficient and a small average path length. These characteristics are characteristic of small-world networks, and they are used to represent living tissue. To generate small-world networks with these characteristics, the Watts and Strogatz model is used [9]. This model starts with a graph with q vertices, each connected to k immediate neighbors, and then randomly rewires each edge of the graph with a probability p, introducing edges that connect distant vertices.

Marching Cubes

The Marching Cubes technique is a computer graphics algorithm used to extract a polygonal mesh of an isosurface from a three-dimensional discrete scalar field, such computed tomography (CT) scans and magnetic resonance imaging (MRI) data [7]. In the context of this project, it is used for the three-dimensional representation of tumors, providing detailed and accurate visualization.

This algorithm works by processing the cells of volume data (also known as voxels), checking the intersection between their respective edges and the isosurface. The values of each vertex of the cells are compared with a given isosurface value, and these vertices are classified as ”inside”or ”outside”the isosurface. Once the type of intersection is determined, an approximation of the isosurface contained in the cell is constructed by building triangles [6].

[1]The maximum number of possible edges is reached when the neighbors, denoted as k_v of vertex v belong to a clique. In an undirected graph, a clique is a set of vertices such that every pair of vertices is connected by an edge. https://www.baeldung.com/cs/graphs-max-number-of-edges

The resulting visualization can provide valuable insights into how cancer develops and spreads. By visualizing tumor growth in three dimensions, doctors and scientists can gain a better understanding of tumor evolution and how it may impact surrounding tissues. This information can be essential for the development of effective cancer therapies and treatments.

Due to the high computational cost of representing and applying the Marching Cubes algorithm to realistic models containing millions of cells, this work implements a model scaling technique that reduces the length of the dimensions of the original cellular automaton model. The reduction process is as follows:

- Cells are grouped into quadrants of dimensions provided by the user.
- The states of all cells belonging to the quadrant are examined.
- The quadrant adopts the state that is most repeated among the cells in it.
- fter performing this process for several quadrants, each quadrant reduces its size from $(nxmxl)$ to $(1x1x1)$, where $n \leq S_x, m \leq S_y, l \leq S_z$.

In summary, the Marching Cubes technique is a powerful tool for the three-dimensional visualization of medical data. In the context of cancer research, it can provide a detailed and accurate representation of tumor growth, which can significantly contribute to our understanding of this disease and the development of effective therapies and treatments.

Configuraciones y Parametros de la simulacion
me of the parameters and configurations that can be modified are:

- S_x - Dimension of the space declared on the x-axis.
- S_y - Dimension of the space declared on the y-axis.
- S_z - Dimension of the space declared on the z-axis. [**?**] The ranges of values for the spatial components of the graph vertices are as follows: $0 \leq x \leq S_x$, $0 \leq y \leq S_y$ y $0 \leq z \leq S_z$.
- p - Probability of reconnection in the Watts-Strogatz model
- P_0^a, P_0^v - Initial populations of the avascular and vascular stages respectively. [**?**]
- Parameters corresponding to the number of states that the automaton cells can have and their descriptions.
- Parameters for possible transitions between the states of the automaton.
- Parameters for the probabilities of the transitions between states. When including parameters for the calculation of certain probabilities, one can take into account the calculation of the probability of interaction between tumor cells and the immune system. [2].
- Parameters corresponding to the shape of the organs where the simulation will take place.
- Parameters to describe the schema of the organs where the simulation will be performed. This allows for the consideration of the characteristics of each organ separately and enables a more realistic simulation.

There are many other configurable parameters.

Seleção de trabalhos

Os trabalhos submetidos, dentro do prazo estabelecido, serão enviados aos revisores do Comitê Científico. Com base nos pareceres do comitê, o trabalho poderá ser (1) aceito plenamente, (2) aceito sob a condição de que correções menores sejam feitas em curto prazo ou (3) rejeitado.

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Devem seguir as normas da ABNT NBR 10520. Nas citações, as chamadas pelo sobrenome do autor devem ser em letras maiúsculas e minúsculas e, quando estiverem entre parênteses, devem ser em letras maiúsculas.

Exemplos:

A ironia seria assim uma forma implícita de heterogeneidade mostrada, conforme a classificação proposta por Authier-Reiriz (1982).

"Apesar das aparências, a desconstrução do logocentrismo não é uma psicanálise da filosofia [...]" (DERRIDA, 1967, p. 293).

a) As citações diretas, no texto, com mais de três linhas, devem ser destacadas com recuo de 4 cm da margem esquerda, espaço entre linhas simples e sem aspas, em fonte Times New Roman, tamanho 10.

> A teleconferência permite ao indivíduo participar de um encontro nacional ou regional sem a necessidade de deixar seu local de origem. Tipos comuns de teleconferência incluem o uso da televisão, telefone, e computador. Através de áudio-conferência, utilizando a companhia local de telefone, um sinal de áudio pode ser emitido em um salão de qualquer dimensão. (NICHOLS, 1993, p. 181).

b) As citações diretas, no texto, de até três linhas, devem ser escritas entre "aspas" duplas e incorporadas ao texto. Exemplos: Barbour (1971, p. 35) descreve: "O estudo da morfologia dos terrenos [...] ativos [...]"

"Não se mova, faça de conta que está morta." (CLARAC; BONNIN, 1985, p. 72).

Segundo Sá (1995, p. 27): "[...] por meio da mesma 'arte de conversação' que abrange tão extensa e significativa parte da nossa existência cotidiana [...]"

c) Nas citações diretas, especificar no texto o ano de publicação e a(s) página(s) da fonte consultada. Estes dados devem ser colocados entre parênteses e separados por vírgula. Nas citações indiretas, a indicação da(s) página(s) consultada(s) é opcional, mas o ano de publicação da obra é obrigatório e deve estar entre parênteses.

Conclusões

The growth of a tumor can be visualized in 3D using the Marching Cubes technique. It is widely used for medical visualizations, such as computed tomography (CT) and magnetic resonance imaging (MRI) images. Additionally, the Marching Cubes algorithm can reduce the computational time used for sampling in 3D reconstruction. However, one of the main issues with Marching Cubes is the presence of unused voxels that can be generated during the analysis of the coordinates and intensity values of 2D images. These unused voxels can affect the smoothness of the 3D surface. [8]

La creación de una herramienta para simular el crecimiento de un tumor con un autómata celular en cualquier órgano del cuerpo humano es un avance significativo en el campo de la modelación y simulación de sistemas biológicos. Esta herramienta proporciona un enfoque innovador y flexible para

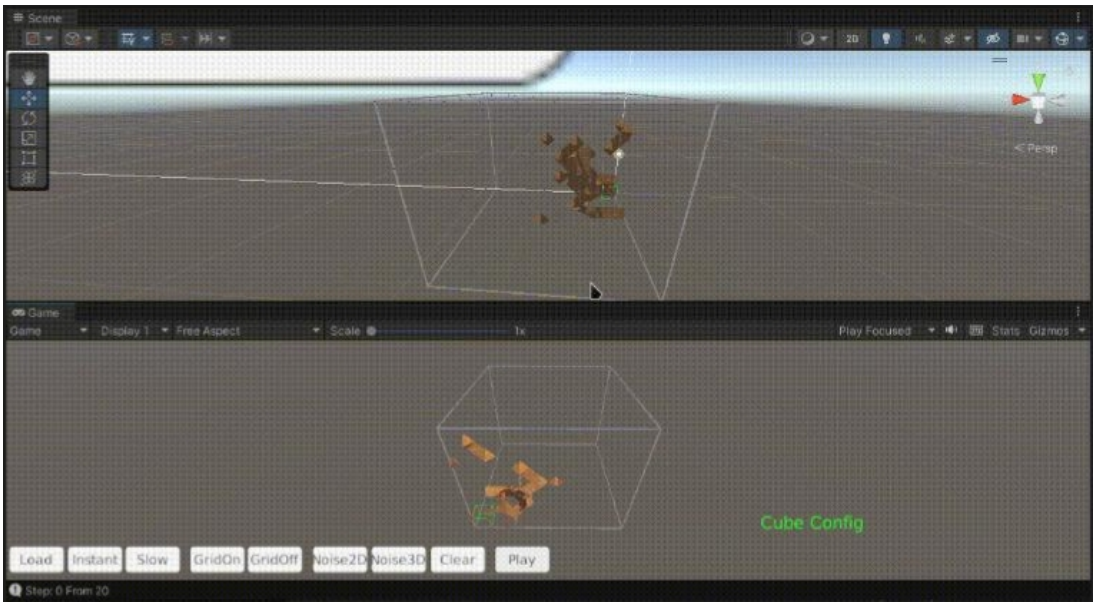

Figura 1: An example of simulating tumor growth in 3D at early stages.

estudiar el crecimiento de los tumores, lo cual tiene importantes implicaciones tanto en la investigación básica como en la clínica.

La capacidad de cargar configuraciones específicas y ajustar, agregar o eliminar parámetros que influyen en el realismo de la simulación permite adaptar el modelo a diferentes escenarios y condiciones. Esto hace que la herramienta sea altamente versátil y aplicable a una amplia gama de situaciones y tipos de tumores.

El uso de autómatas celulares para simular el crecimiento del tumor proporciona una representación detallada y dinámica del proceso. Los autómatas celulares son especialmente adecuados para este tipo de modelado, ya que permiten representar de forma precisa y realista la interacción entre las células y su entorno, así como los cambios que ocurren en el tiempo.

Finalmente, la visualización en 3D del crecimiento de un tumor utilizando la técnica de Marching Cubes puede proporcionar una herramienta valiosa para los profesionales de la salud para entender mejor la dinámica del crecimiento del tumor y desarrollar estrategias de tratamiento más efectivas.

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Referências

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