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Model order reduction of tumor growth model

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Abstract

In this paper, reduced order models (ROMs) for the tumor growth model, which is a nonlinear cross-diffusion system are presented. Linear-quadratic ordinary differential equations are obtained by applying the finite difference method to the tumor growth model for spatial discretization. The structure of the ROMs is the same as the structure of the full order model. Proper orthogonal decomposition method with tensorial form is sufficient to compute the reduced solutions efficiently and fast. The results of ROM are presented for one- and two-dimensional cases. Finally, the entropy structure for the reduced solutions, which are in decay form are presented.

Keywords: Tumor growth model, finite differences, entropy, proper orthogonal decomposition, tensor algebra.

2020 MSC: 37N25, 35K57, 35K61, 65M06, 65L05, 34C20.

1. Introduction

The model of tumor growth has been studied for a very long time. The reaction-diffusion model with cross-diffusion was used for mathematical modeling of tumor growth. In this model, two main biological behaviors are considered: diffusion (migration) and proliferation. Diffusion represents that tumor cells invade brain tissue. Proliferation illustrates the reactive behavioral function that explains tumor cell growth and death [1, 2, 7, 12, 13, 23].

The tumor growth model can be solved by some numerical methods such as finite element and finite difference methods. The tumor growth model has linear and quadratic parts, both in the cross-diffusion and reaction parts. The semi-discretization of the tumor growth model obtained by the second-order finite difference method in space has the structure of a linear-quadratic ordinary differential equation system (ODE). For time discretization of the semi-discrete tumor growth model, Kahan's method is used to obtain full solutions. The Kahan's method is a second-order linearly implicit method and requires only one step Newton iteration at each time step [9, 16, 17].

Recently, reduced-order models (ROMs) have been developed to minimize the computational cost of simulations of complex, large-scale dynamical systems such as tumor growth models. ROMs are efficient systems with small dimensions that can accurately replace full-order models (FOMs) and are able to make predictions in long-term integration. Proper orthogonal decomposition (POD) with Galerkin

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projection is the most popular ROM technique [6, 25]. POD satisfies the condition that the energy of a system can be characterized by a few modes. By applying the POD method to the tumor growth model, the dominant modes are extracted from the snapshots of the FOMs. The nonlinearities of the reduced systems have the same dimension of the full-solution, i.e., the online and offline phases are not separated. In the offline stage, the full-order solutions, reduced matrices, POD basis functions, and matricized tensors are computed. In the online stage, the reduced system is solved. To separate these two stages, matricization of tensors is used in the POD procedure [3, 5, 18, 20]. This is sufficient to construct ROMs in a computationally efficient way. Moreover, the sparse matrix technique MULTIPROD [22] is considered to speed up the computations of matricized tensors.

The paper is organized as follows. In Section 2, the tumor growth model is presented. In Section 3, the full order models of the tumor growth system for spatial and temporal discretization are presented. The reduced order model is obtained in Section 4 using the POD method. In Section 5, the computational efficiency and accuracy of ROMs for one- and two-dimensional tumor growth models are presented.

2. Tumor growth equation

When brain tissue is enclosed with diffuse and infiltrative growth, a brain tumor develops. The proliferation rate and migration speed of cells determine the progress of brain tumor growth. The system of equations of glioma cell concentration $u(x,t)$ is defined as Kolmogorov-Fisher equation and was introduced to describe the spread of a beneficial gene in a spatially extended population [11, 19],

$$\frac{\partial u}{\partial t} = D\Delta u + ru(1-u).$$

The diffusion coefficient D represents migration, while the growth rate r is described as a logistic growth function of tumor cell proliferation. It is one of the standard examples of a reaction-diffusion equation exhibiting traveling wave solutions. In [7, 12, 13], the cross-diffusion model has two different tumor cell: migration or proliferation. During the cell division process, there are two clearly separated states of cells: proliferating cells (denoted by u) and migrating cells (denoted by v) with a certain transition between these states. The transition between migration and proliferation, cell death, and birth is defined by the reaction terms. A proliferating cell produces offspring when the neighboring cell is empty. On the other hand, migrating cells can move their neighbouring cells when they are empty. Both cells can change their state under certain rates and also die with a certain rate.

In addition, cells may be randomly exchanged at certain rates during migration and proliferation and may also die at a certain rate. This results in the following cross-diffusion system, which is a tumor growth model:

$$\begin{aligned} \frac{\partial u}{\partial t} &= D_\alpha(1-u-v)\Delta u + \alpha u(1-u-v) - (\mu+q_2)u + q_1 v, \\ \frac{\partial v}{\partial t} &= D_v[(1-u)\Delta v + v\Delta u] - (\mu+q_1)v + q_2 u, \end{aligned} \tag{2.1}$$

in the spatial domain $\mathbf{x} \in \Omega \in \mathbb{R}$, $d = 1, 2$ with zero-flux Neumann boundary conditions, where q_1, q_2 are transition rates between migrating and proliferating cells. The constant $\mu > 0$ represents the cell death rate, while α is the cell division rate for component u. $D_\alpha = \alpha/2$ is the diffusion constant of proliferating cells.

The tumor growth model can also be expressed in the following form [15]:

$$\begin{pmatrix} \frac{\partial u}{\partial t} \\ \frac{\partial v}{\partial t} \end{pmatrix} = \operatorname{div}\left(\sum_{i=1}^{2} \mathcal{A}_{ij}(u,v)\nabla u \right) + \begin{pmatrix} f(u,v) \\ g(u,v) \end{pmatrix} \tag{2.2}$$

with the diffusion matrix $\mathcal{A}_{ij}(u,v)$,

$$\mathcal{A}(u,v) = \frac{1}{2+4u+v} \begin{pmatrix} 1+2u & u \\ 2v & 2+v \end{pmatrix}.$$

The tumor growth model involves coupled nonlinear parabolic PDEs, and the matrix $\mathcal{A}$ is not symmetric, so the maximum principle does not apply. Moreover, the diffusion matrix $\mathcal{A}$ is also not positive definite. The entropy variable is sufficient to transform the diffusion matrix A into a symmetric and positive definite matrix. The entropy function allows us to examine long-term behavior and leads to a nonnegative and bounded solution. Equation (2.2) can be written in terms of the entropy function gradient form [10, 15],

$$\partial_t u - \operatorname{div}(\mathcal{B}\nabla \operatorname{grad} \mathcal{E}[u]) = f(u), \quad \text{in} \quad \mathcal{R}^d, \quad t > 0,$$

where $\mathcal{B}$ is a semidefinite positive matrix and grad $\mathcal{E}$ is the Fréchet derivative of the entropy functional $\mathcal{E}[u,v] = \int_{\mathcal{R}^d} \epsilon(u,v)d\Omega$, and $\epsilon(u,v)$ is the entropy density. With time, the entropy decreases with $\frac{d\mathcal{E}}{dt} \leqslant 0$. Tumor growth models have a partial entropy functional that excludes the reaction terms in (2.1). The entropy satisfies a priori estimates and also defines a change in variables that makes the diffusion matrix positive-definite [15].

3. Full order model

We can discretize the tumor growth model (2.1) by using the finite difference method for spatial discretization, yielding a system ODE as

$$\begin{aligned} \frac{d\mathbf{u}(t)}{dt} &= d_1 A\mathbf{u} - d_1\mathbf{u}\circ(A\mathbf{u}) - d_1\mathbf{v}\circ(A\mathbf{u}) + \alpha\mathbf{u} - \alpha\mathbf{u}^2 - \alpha\mathbf{u}\circ\mathbf{v} - (q_2+\mu)\mathbf{u} + q_1\mathbf{v}, \\ \frac{d\mathbf{v}(t)}{dt} &= d_2 A\mathbf{v} - d_2\mathbf{u}\circ(A\mathbf{v}) + d_2\mathbf{v}\circ(A\mathbf{u}) - (q_1+\mu)\mathbf{v} + q_2\mathbf{u}, \end{aligned} \tag{3.1}$$

where powers are controlled component-wise together with the product operator $\circ$. $\mathbf{u}(t)$ and $\mathbf{v}(t)$ are approximations to the exact solutions u and v in one- and two- dimensional regions, which are given as continuous time semi-discrete solution vectors (2.1) in space,

$$\mathbf{u}(t) = (u_1, \ldots, u_{n_x}), \quad \mathbf{u}(t) = (u_{1,1}, \ldots, u_{1,n_x}, u_{2,1}, \ldots, u_{n_x,n_y})^T,$$

where $\mathbf{v}(t)$ is defined in a similar way. For one-dimensional problems, the degree of freedom (DOF) is $N = n_x$, and for the two dimensional case, $N = n_x n_y$, where $n_x = L_x/\Delta x$ and $n_y = L_y/\Delta y$ are the number of partitions in the x and y directions, respectively. In the rest of the paper, we denote the state vectors as $\mathbf{u}(t), \mathbf{v}(t)$ and omit the dependence on time t.

The matrix A is the finite difference matrix that approximates the Laplace operator Δ by second order centered finite differences under homogeneous Neumann boundary conditions. For the one-dimensional tumor growth equation (2.1), the matrix $A \in \mathbb{R}^{n_x^2}$ has the form

$$A = \frac{1}{\Delta x^2}\begin{pmatrix} 1 & -1 & & & \\ -1 & 2 & -1 & & \\ & \ddots & \ddots & \ddots & \\ & & -1 & 2 & -1 \\ & & & -1 & 1 \end{pmatrix}.$$

For the two-dimensional tumor growth equation (2.1), the matrix $A \in \mathbb{R}^{n_x^2 \times n_y^2}$ is given as

$$A = \frac{1}{\Delta x \Delta y}\begin{pmatrix} B & -2I & & & \\ -I & B & -I & & \\ & \ddots & \ddots & \ddots & \\ & & -I & B & -I \\ & & & -2I & B \end{pmatrix}, \quad B = \begin{pmatrix} 4 & -2 & & & \\ -1 & 4 & -1 & & \\ & \ddots & \ddots & \ddots & \\ & & -1 & 4 & -1 \\ & & & -2 & 4 \end{pmatrix},$$

where I_n denotes the n-dimensional identity matrix. Here, linear and quadratic parts are first collected, then (3.1) is obtained as a linear-quadratic ODE system,

$$\frac{du}{dt} = \underbrace{L_{11}\mathbf{u} + L_{12}\mathbf{v}}_{\text{linear}} - \underbrace{d_1\mathbf{u}\circ(A\mathbf{u}) - d_1\mathbf{v}\circ(A\mathbf{u}) - \alpha\mathbf{u}^2 - \alpha\mathbf{u}\circ\mathbf{v}}_{\text{quadratic}},$$
$$\frac{d\mathbf{v}}{dt} = \underbrace{L_{21}\mathbf{u} + L_{22}\mathbf{v}}_{\text{linear}} - \underbrace{d_2\mathbf{u}\circ(A\mathbf{v}) + d_2\mathbf{v}\circ(A\mathbf{u})}_{\text{quadratic}},$$

where $L_{ij},\ i,j = 1,2,$

$$L_{11} = d_1A + (\alpha - \mu - q_2)I, \quad L_{12} = q_1I, \quad L_{22} = d_2A - (\mu + q_1)I, \quad L_{21} = q_2I.$$

The compact form of linear-quadratic systems is given as

$$\frac{d\mathbf{w}}{dt} = \mathbf{F}(\mathbf{w}) = L\mathbf{w} + Q(\mathbf{w}), \tag{3.2}$$

where $\mathbf{w} = (\mathbf{u},\mathbf{v}) \in \mathbb{R}^{2N}$ is the vector of the two components u and v. The linear terms $\mathbf{L} \in \mathbb{R}^{2N\times 2N}$ are represented as follows

$$L = \begin{pmatrix} L_{11} & L_{12} \\ L_{21} & L_{22} \end{pmatrix},$$

and the quadratic terms $Q = (Q_1, Q_2) \in \mathbb{Q}^{2N}$ are represented as

$$Q(\mathbf{w}) = \begin{pmatrix} -d_1H(A\mathbf{u}\otimes\mathbf{u}) - d_1H(A\mathbf{u}\otimes\mathbf{v}) - \alpha H(\mathbf{u}\otimes\mathbf{u}) - \alpha H(\mathbf{u}\otimes\mathbf{v}) \\ -d_2H(A\mathbf{v}\otimes\mathbf{u}) + d_2H(A\mathbf{u}\otimes\mathbf{v}) \end{pmatrix},$$

where

$$Q_1 = \begin{pmatrix} Q_{11} & 0 \\ 0 & Q_{22} \end{pmatrix}\begin{pmatrix} H(\mathbf{u}\otimes\mathbf{u}) \\ H(\mathbf{v}\otimes\mathbf{v}) \end{pmatrix}, \qquad Q_2 = \begin{pmatrix} 0 & Q_{12} \\ Q_{21} & 0 \end{pmatrix}\begin{pmatrix} H(\mathbf{u}\otimes\mathbf{v}) \\ H(\mathbf{u}\otimes\mathbf{v}) \end{pmatrix},$$

where $\otimes$ is the Kronecker product, and $H \in \mathbb{R}^{N\times N^2}$ is the matricized tensor and the identity is defined as $H(\mathbf{w}\otimes\mathbf{v}) = \mathbf{w}\circ\mathbf{v}$ for any vector $\mathbf{w},\mathbf{v} \in \mathbb{R}^N$.

Various explicit and implicit methods can be used to solve the compact system of equations (3.2) in time. While explicit methods solve the problem with small time steps, unstable solutions arise. The implicit integrators solve the nonlinear equations iteratively at each time point. The semi-discrete linear-quadratic tumor growth model (3.2) is solved in time using the linear implicit Kahan's method [16, 17].

$$\frac{\mathbf{w}^{n+1} - \mathbf{w}^n}{\Delta t} = \frac{1}{2}L(\mathbf{w}^n + \mathbf{w}^{n+1}) + \tilde{Q}(\mathbf{w}^n, \mathbf{w}^{n+1}),$$

where $\tilde{Q}(\mathbf{w}^n, \mathbf{w}^{n+1})$ is the symmetric bilinear form and is obtained by polarization of quadratic vector field Q [8]:

$$\tilde{Q}(\mathbf{w}^n, \mathbf{w}^{n+1}) = \frac{1}{2}Q(\mathbf{w}^n + \mathbf{w}^{n+1}) - Q(\mathbf{w}^n) - Q(\mathbf{w}^{n+1})$$

and Δt is the time step, $\mathbf{w}^{n+1}$ and $\mathbf{w}^n$ are the approximations of $\mathbf{w}$ at time t_{n+1} and t_n. It is time-reversal and symmetric, linearly implicit, i.e., computing a single linear system yields $\mathbf{w}^{n+1}$,

$$\left(I - \frac{\Delta t}{2}\mathbf{F}_J(\mathbf{w}^n)\right)\tilde{\mathbf{w}} = \Delta t\mathbf{F}(\mathbf{w}^n), \qquad \mathbf{w}^{n+1} = \mathbf{w}^n + \tilde{\mathbf{w}},$$

where $\mathbf{F}_J(\mathbf{w}^n)$ is the Jacobian evaluated at time t_n.

Kahan's method also takes form of a second-order convergent Runge-Kutta method [9]:

$$\frac{\mathbf{w}^{k+1}-\mathbf{w}^{k}}{\Delta t}=-\frac{1}{2}f(\mathbf{w}^{k})+2f\left(\frac{\mathbf{w}^{k+1}+\mathbf{w}^{k}}{2}\right)-\frac{1}{2}f(\mathbf{w}^{k+1}).$$

If fully implicit methods are chosen for the time discretization, the nonlinear equations must be solved iteratively at each time step using Newton's method. The Kahan's methods solve the nonlinear problem faster than the fully implicit methods such as the implicit Euler and mid-point rules.

4. Reduced order model

In this section, we present the construction of reduced order model solutions for the tumor growth model (2.1). Proper orthogonal decomposition method is used to reduce the dimension of the full discrete solutions [21]. The POD basis functions are computed by applying singular value decomposition (SVD) to the snapshots matrix,

$$S_u=[\mathbf{u}_1,\cdots,\mathbf{u}_{N_t}]\in\mathbb{R}^{N\times N_t},\quad S_v=[\mathbf{v}_1,\cdots,\mathbf{v}_{N_t}]\in\mathbb{R}^{N\times N_t}.$$

Each column of the snapshots matrix is formed from the full solutions $\mathbf{u}$ and $\mathbf{v}$ at time t_n, $n=1,\cdots,N_t$. The SVD of the snapshot matrices is calculated as

$$S_{\mathbf{u}}=W_{\mathbf{u}}\Sigma_{\mathbf{u}}Z_{\mathbf{u}}^{T},\quad S_{\mathbf{v}}=W_{\mathbf{v}}\Sigma_{\mathbf{v}}Z_{\mathbf{v}}^{T},$$

where the columns of $W_{\mathbf{u}},W_{\mathbf{v}}\in\mathbb{R}^{N\times N_t}$ and $Z_{\mathbf{u}},Z_{\mathbf{v}}\in\mathbb{R}^{N_t\times N_t}$ represent the left singular vectors of S_u and the right singular vectors of S_v, and $\Sigma_{\mathbf{u}},\Sigma_{\mathbf{v}}\in\mathbb{R}^{N_t\times N_t}$ are the diagonal matrices representing the singular values in descending order $\sigma_1\geqslant\sigma_2\geqslant\cdots\geqslant\sigma_{N_t}\geqslant 0$. The k-POD basis matrix $\Psi_{\mathbf{u},k}\in\mathbb{R}^{N\times k}$, similarly $\Psi_{\mathbf{v},k}\in\mathbb{R}^{N\times k}$, is calculated by solving the minimization problem

$$\min_{\Psi_{\mathbf{u},k}\in\mathbb{R}^{N\times k}}\|S_u-\Psi_{\mathbf{u},k}\Psi_{\mathbf{u},k}^{T}S_u\|_F^2=\min_{\Psi_{\mathbf{u},k}\in\mathbb{R}^{N\times k}}\sum_{n=1}^{N_t}\|\mathbf{u}^n-\Psi_{\mathbf{u},k}\Psi_{\mathbf{u},k}^{T}\mathbf{u}^n\|_2^2=\sum_{n=k+1}^{N_t}\sigma_{\mathbf{u},n}^2,$$

where $\|\cdot\|_F$ indicates the Frobenius norm. The k-largest singular values are selected from the left singular values of the snapshot matrices S_u using the relative information content (RIC) defined as

$$\frac{\sum_{n=1}^{k}\sigma_n^2}{\sum_{n=1}^{N_t}\sigma_n^2}<\text{tol}_{\text{RIC}},$$

$\Psi_{\mathbf{u},k}$ and $\Psi_{\mathbf{v},k}$ basis matrix are given by k left singular vectors. Then the POD approximations are given $u\approx\Psi_{\mathbf{u}}\widehat{\mathbf{u}}$ and $v\approx\Psi_{\mathbf{v}}\widehat{\mathbf{v}}$, where $\widehat{\mathbf{u}},\widehat{\mathbf{v}}\in\mathbb{R}^k$. The reduced solutions approximate the full order solution $\mathbf{w}\approx\Psi\widehat{\mathbf{w}}$. Then, the ROM solutions of the tumor growth model are obtained as follows:

$$\frac{d}{dt}\widehat{\mathbf{w}}=\widehat{L}\widehat{\mathbf{w}}+\widehat{Q}(\widehat{\mathbf{w}}),\tag{4.1}$$

where $\widehat{\mathbf{w}}=(\widehat{\mathbf{u}},\widehat{\mathbf{v}})$, $\widehat{L}=\Psi^{T}L\Psi$, $\widehat{Q}(\widehat{\mathbf{w}})=\Psi^{T}Q(\Psi\widehat{\mathbf{w}})$, and

$$\Psi=\begin{pmatrix}\Psi_{\mathbf{u}} & 0\\ 0 & \Psi_{\mathbf{v}}\end{pmatrix}\in\mathbb{R}^{2N\times(2k)}.$$

4.1. Fast solution of the reduced-order equations with tensor techniques

The nonlinearities in ROM solutions have the same dimension as the FOM solutions. To deal with this, tensor matricization with the Kronecker product property and the separation of offline and online stages are used. Using matricized tensor satisfies to construct the ROM with low computational costs

instead of using nonlinearity reduction methods such as the discrete empirical interpolation method. The MULTIPROD technique for sparse matrix is used to speed-up the computation of the matricized tensor.

The reduced quadratic terms in the tumor growth model (4.1) have the following structure:

$$\widehat{Q}_1(\widehat{\mathbf{w}}) = \Psi^\top Q_1(\Psi\widehat{\mathbf{w}}) = \begin{pmatrix} \Psi_{\mathbf{u}}^\top Q_{11} H((\Psi_{\mathbf{u}}\widehat{\mathbf{u}}) \otimes (\Psi_{\mathbf{u}}\widehat{\mathbf{u}})) \\ \Psi_{\mathbf{v}}^\top Q_{22} H((\Psi_{\mathbf{v}}\widehat{\mathbf{v}}) \otimes (\Psi_{\mathbf{v}}\widehat{\mathbf{v}})) \end{pmatrix}, \quad \widehat{Q}_2(\widehat{\mathbf{w}}) = \Psi^\top Q_2(V\widehat{\mathbf{w}}) = \begin{pmatrix} \Psi_{\mathbf{u}}^\top Q_{12} H((\Psi_{\mathbf{u}}\widehat{\mathbf{u}}) \otimes (\Psi_{\mathbf{v}}\widehat{\mathbf{v}})) \\ \Psi_{\mathbf{v}}^\top Q_{21} H((\Psi_{\mathbf{v}}\widehat{\mathbf{v}}) \otimes (\Psi_{\mathbf{u}}\widehat{\mathbf{u}})) \end{pmatrix},$$

or in compact general form

$$\Psi_i^\top Q_{ij} H((\Psi_i\widehat{\mathbf{u}}) \otimes (\Psi_j\widehat{\mathbf{v}})),$$

where $\Psi_i = \Psi_{\mathbf{u}}$ and $\Psi_j = \Psi_{\mathbf{v}}, i, j = 1, 2$. The calculation of H is obtained by using the properties of the Kronecker product and the reduced tensor $\widehat{H} = H(\Psi_i \otimes \Psi_j) \in \mathbb{R}^{N \times k_i k_j}$, so that it is obtained

$$\Psi_i^\top Q_{ij} H((\Psi_i\widehat{\mathbf{u}}) \otimes (\Psi_j\widehat{\mathbf{v}})) = \Psi_i^\top Q_{ij} \widehat{H}(\widehat{\mathbf{u}} \otimes \widehat{\mathbf{v}}), \tag{4.2}$$

where the small matrix $\Psi_i^\top Q_{ij} \widehat{H} \in \mathbb{R}^{k_i \times k_i k_j}$, which is precomputable, is computed in the offline stage. By separating the high dimensional variables in (4.2), the computational cost of the reduced quadratic nonlinear terms in the online stage is reduced and their dimension is equal to the dimension of the ROMs, i.e., $\mathcal{O}(k_i^3)$. Without using the tensor techniques, the online computational cost scales with the dimension N of the FOM, i.e., $\mathcal{O}(Nk_i)$ since the dimension of the reduced quadratic terms depends on the high-dimensional FOM, e.g., $(\Psi_i\widehat{\mathbf{u}}) \odot (\Psi_j\widehat{\mathbf{v}})$ [26].

Even if the computation of $\widehat{H}$ is completed in the offline phase, the dimension of $\Psi_i \otimes \Psi_j$ is still the full dimension N. This leads to inefficiency. By using μ-mode matricization of tensors [3, 4], $\Psi_i \otimes \Psi_j$ is computed in an efficient way, and the computational cost is reduced. The particular structure of Kronecker product is exploited to develop tensorial algorithms [4, 5]. The reduced matrix $\widehat{H}$ can be defined as follows:

$$\widehat{H} = \begin{pmatrix} \Psi_i(1,:) \otimes \Psi_j(1,:) \\ \vdots \\ \Psi_i(N,:) \otimes \Psi_j(N,:) \end{pmatrix}, \tag{4.3}$$

it exploits the structure of $H(\Psi_i \otimes \Psi_j)$ without constructing H explicitly. "MULTIPROD" [22] is used to increase computational efficiency. It is a fast and memory efficient MATLAB operator. For any two vectors $\mathbf{a}$ and $\mathbf{b}$, the Kronecker product property is given as

$$(\mathrm{vec}(\mathbf{b}\mathbf{a}^\top))^\top = (\mathbf{a} \otimes \mathbf{b})^\top = \mathbf{a}^\top \otimes \mathbf{b}^\top, \tag{4.4}$$

where $\mathrm{vec}(\cdot)$ denotes the vectorization of a matrix. The matrix $\widehat{H} = H(\Psi_i \otimes \Psi_j)$ can be written with the identity in (4.4) as

$$\widehat{H}(m,:) = (\mathrm{vec}(\Psi_i(m,:)^\top \Psi_j(m,:))^\top, \quad m \in \{1, 2, \ldots, N\}.$$

Reshaping the matrix $\Psi_i \in \mathbb{R}^{N \times k_i}$ as $\widetilde{\Psi}_i \in \mathbb{R}^{N \times 1 \times k_i}$ and calculating MULTIPROD of Ψ_j and $\widetilde{\Psi}_i$ in the second and third dimensions, it is obtained

$$\widehat{\mathcal{H}} = \mathrm{MULTIPROD}(\Psi_j, \widetilde{\Psi}_i) \in \mathbb{R}^{N \times k_j \times k_i},$$

where the reduced matricized tensor $\widehat{H} \in \mathbb{R}^{N \times k_i k_j}$ is taken by reshaping the matrix $\widehat{\mathcal{H}}$ into a matrix of dimension $N \times k_i k_j$. The computation of $\widehat{\mathcal{H}}$ in (4.3) requires N for loops, where in each iteration the matrix product of two matrices of sizes $k_j \times 1$ and $1 \times k_i$ is formed. However with MULTIPROD, the matrix products are computed simultaneously in a single loop, which reduces the computational cost of the reduced matricized tensor in the offline stage [18]. Matricized tensor $\widehat{H} \in \mathbb{R}^{N \times k_i k_j}$ can also be computed using the Hadamard product which is defined as $H(\mathbf{w} \otimes \mathbf{v}) = \mathbf{w} \odot \mathbf{v}$. The matricized tensor is evaluated over the reduced dimensions k_i and k_j, which are smaller than the dimension N of the FOMs.

5. Numerical results

In this section, the numerical results for the one- and two- dimensional tumor growth systems are presented. The solutions of FOM and POD are compared and the entropy structures are shown. The time averaged relative L^2-error is used to show the efficiency of the solutions of ROM

$$\|\mathbf{w} - \Psi\widehat{\mathbf{w}}\|_{\text{rel}} = \frac{1}{N_t}\sum_{n=1}^{N_t}\frac{\|\mathbf{w}^n - \Psi\widehat{\mathbf{w}}^n\|_{L^2}}{\|\mathbf{w}^n\|_{L^2}}. \tag{5.1}$$

5.1. Tumor growth model in one dimension

The first example is a one-dimensional tumor growth model (2.1) in the space-time domain $[0,100]\times(0,50]$ with 600 number of mesh points and time step $\Delta t = 0.05$. The parameters and initial conditions are set as in [12] as

$$\alpha = 1,\ d_1 = \alpha/2,\ d_2 = 5/2,\ \mu = 0,\ q_1 = 10,\ q_2 = 20,\ (u_0, v_0) = (\exp(-10x), 0).$$

In Figure 1, the normalized singular values decay slowly (linearly) which is characteristic of traveling wave solution problem such as the tumor growth model. The decay of the Kolmogorov-n-widths of, e.g., $n^{-1/2}$ [14, 24] describes the best-possible error for a linear-subspace ROM of size r. Due to the slow decay of the normalized singular values, the FOM is captured by the ROM with a relatively large number of the POD modes in Figure 2 and Table 1 with the RIC tolerance $\text{tol}_{\text{RIC}} = 10^{-4}$.

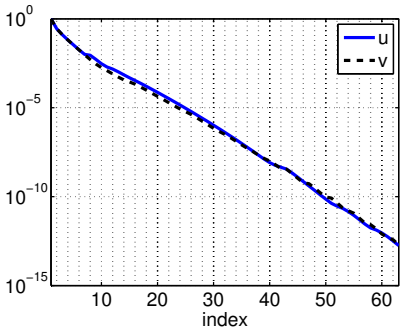

Figure 1: Decay of the singular values for one dimensional problem.

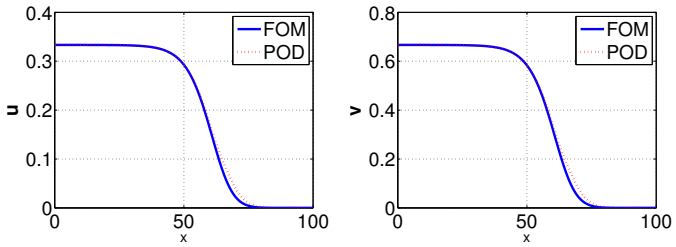

Figure 2: FOM and ROM solutions for one dimesional problem.

Table 1: FOM-ROM errors for tol=10^{-4} and speedups for one dimensional problem.

# POD-u	# POD-v	Error-u	Error-v	Wall clock time FOM	Wall clock time ROM	Speedup
25	25	5.89e-03	1.15e-02	4.0034	2.5383	1.6

5.2. Tumor growth model in two dimensions

As a second example, we consider the two-dimensional tumor growth model in [7] with parameters $\alpha = 2,\ D_\alpha = D_\nu = 0.025,\ q_2 = 20,\ q_1 = 10,\ \mu = 0$. The initial condition is given by

$$u_0(x,y) = \chi_C(x,y)\exp^{-0.25(x^2+y^2)}, \quad \nu_0(x,y) = 0,$$

where $\chi_C(x,y)$ denotes the characteristic function

$$C = (x,y) \in \mathbb{R}^2 : (x-0.55)^2/4.5 + (y-1.4)^2/0.5 - 2 > 0.$$

Number of mesh points is taken as 200 and the time step is $\Delta t = 0.1$. Figure 3 shows singular values that slowly decay as in the one-dimensional tumor growth model in Figure 1. The tolerance of RIC is assumed to be $tol_{RIC} = 10^{-5}$. The ROM solutions in Figure 5 are very close to the full solutions in Figure 4, with a small L_2 error, as shown in Table 2. In both numerical tests, the speed-ups are small due to the large number of POD modes required to capture full-order solutions.

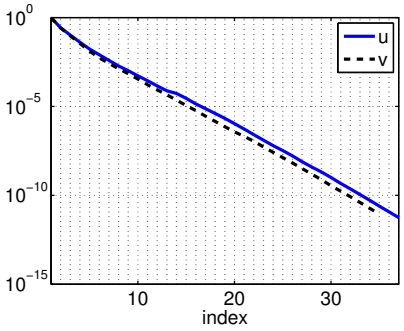

Figure 3: Decay of the normalized singular values for two dimensional problem.

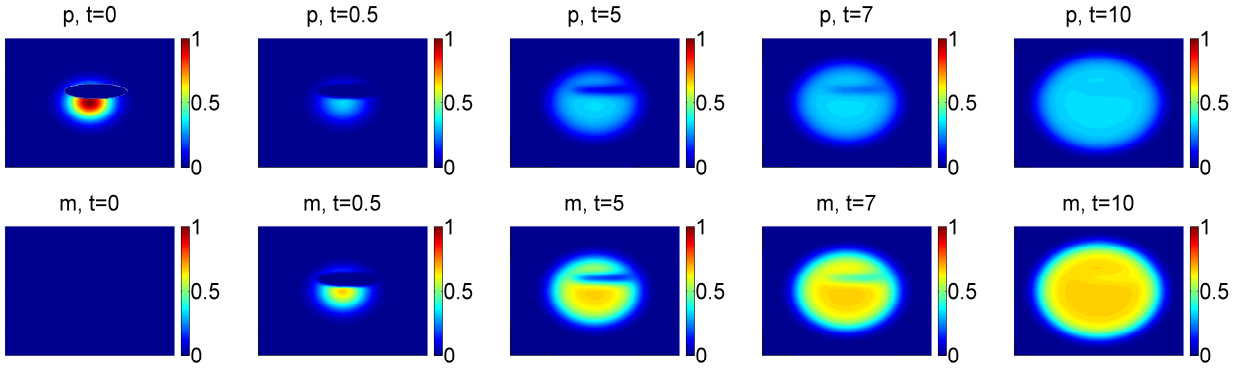

Figure 4: FOM solutions of u (top) and ν (bottom) components for two dimensional problem.

Table 2: FOM-ROM errors for tol= 10^{-5} and speedups for two dimensional problem.

# POD-u	# POD-ν	Error-u	Error-ν	Wall clock time FOM	Wall clock time ROM	Speedup
15	15	8.20e-04	6.62e-04	57.5272	10.2238	5.6

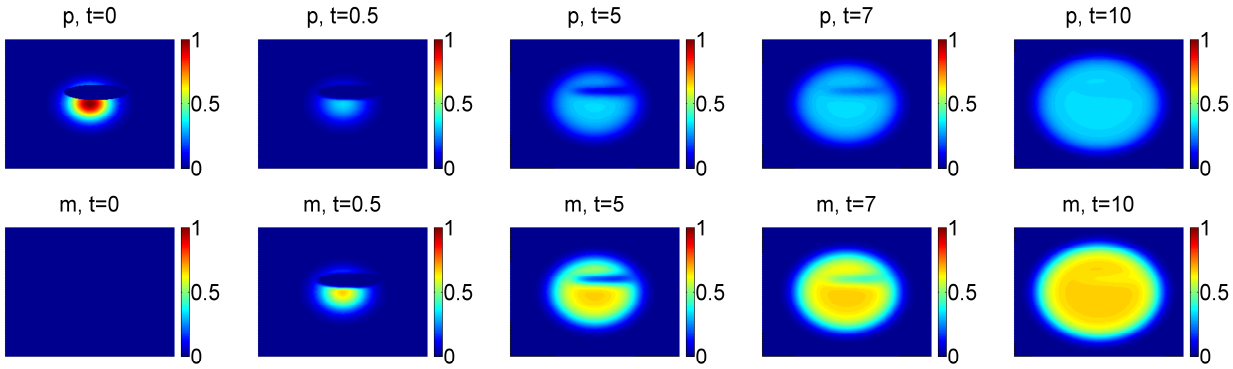

Figure 5: ROM solutions of u (top) and v (bottom) components for two dimensional problem.

5.3. *Entropy preservation*

The entropy $\mathcal{E}$ of the tumor growth model is defined as

$$\mathcal{E} = \int_\Omega \epsilon \, d\Omega = \int_\Omega (v \log(v) + (1-u-v)\log(1-u-v)) \, d\Omega.$$

Figures 6-7 show the decay of entropy of FOM and ROM entropy are illustrated for one- and two-dimensional cases [7]. The entropy is well preserved by the ROMs.

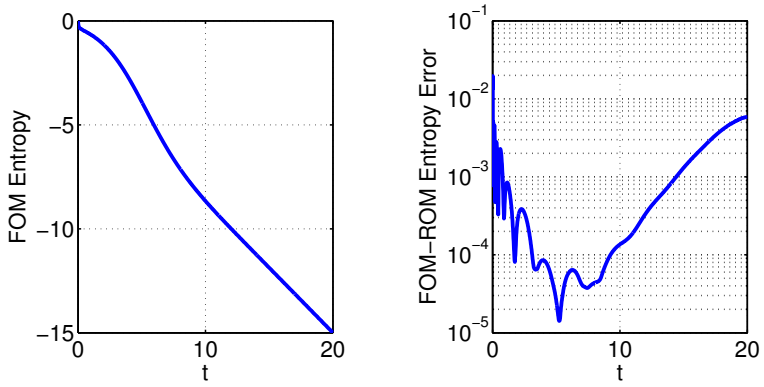

Figure 6: Entropy decay for one dimesional problem.

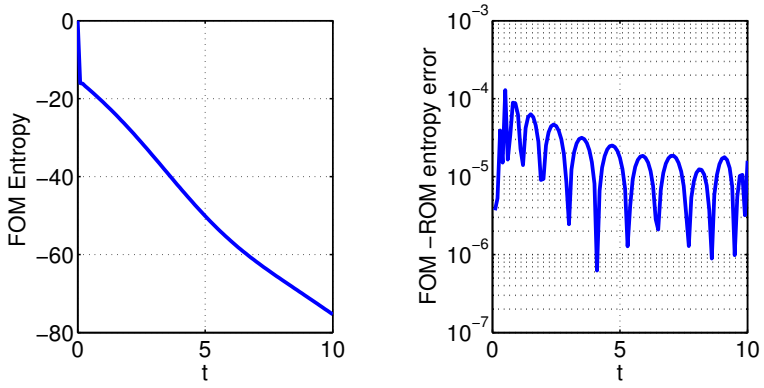

Figure 7: Entropy decay for two dimensional problem.

6. Conclusions

Semi-discretization with finite differences in space leads to linear-quadratic ODE systems for the tumor growth model, allowing separate offline and online computation. The full-order solutions are computed using the linearly implicit Kahan's method by solving one nonlinear system of equations for each time step. In this way, FOMs are computed accurately and quickly for fine spatial and temporal discretizations. By applying tensor techniques to the linear-quadratic systems of tumor growth model the online computation of the ROMs is further accelerated. This results in the solutions of the reduced-order system requiring much less computation time. The solutions of ROM depend affinely on the parameters in both the linear and quadratic parts. This allows the prediction of patterns of the tumor growth model for different parameter values without interpolation. The bifurcation of the tumor growth model can be studied by using the ROMs technique.

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