EFFICIENT NUMERICAL APPROACHES TO CHALLENGING PROBLEMS IN THE FRONTIER OF MECHANICS AND BIOLOGY

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Summary Many challenging problems somewhere among Mechanics and Biology share an important characteristic, despite their very different nature. This class of problems is well known for being defined in state spaces of a high number of dimensions, leading to the well-known *curse of dimensionality*. This is related to the exponential increase in degrees of freedom with the number of state space dimensions, thus preventing the use of mesh-based numerical approaches such as finite element, volume or difference approaches. A very notable group of problems include those arising from Kinetic Theory (Fokker-Planck) modeling of phenomena such as polymer flows, cancer onset, traffic crowds, among others. In a very related framework, gene regulatory networks modeled by the chemical master equation share this same challenging characteristic. In this paper we overview a numerical technique coined as Proper Generalized Decomposition (PGD) that is based on the use of separated representations. We show how it efficiently beats the curse of dimensionality and how it allows for an efficient use of the concept of dimensionality in a problem, opening new insights in the way we tackle standard problems.

INTRODUCTION

High-dimensional models are frequent in science and engineering. To cite a few, we can consider quantum chemistry (in particular, descriptions arising from the Schroedinger equation [1]), kinetic theory descriptions of macromolecular fluids [2], the Chemical Master Equation governing biological processes such as cell signalling [3], or option pricing in financial mathematics [4], among other phenomena. Traditional, mesh-based, techniques such as finite differences or finite elements can not be applied for solving these models because of the exponential increase in the number of degrees of freedom associated with their discretizations.

In the context of evolution problems involving space and time coordinates, for instance, Proper Orthogonal Decompositions (POD) [5] [6], Singular Value Decomposition (SVD) [7], or Principal Component Analysis (PCA) [8] techniques, look for an optimal rank-m, a posteriori, separated representation of the solution $u(\mathbf{x},t)$ in the form

$$u(\mathbf{x},t) \approx \sum_{i=1}^{m} w_i(\mathbf{x}) \cdot \lambda_i(t) \tag{1}$$

as the one which minimizes the distance to the solution with respect to a particular norm. Functions $w_i(\mathbf{x})$ represent, therefore, the spatial functions that best (in a given norm) represent the solution throughout the considered time interval.

The so-called *radial approximation* [9] extended this approach in the sense that time and space functions were not computed *a posteriori*, as a statistical treatment of existing results, but *a priori*, by inserting the assumed approximation (1) into the variational or weak form of the evolution problem. The price to pay in using this method, however, is that we are faced to a non-linear problem even if the original differential equation was actually linear.

Proper Generalized Decompositions generalize this approach in the sense that propose a rank-m approximation of the type

$$u(\mathbf{x}_1,\ldots,\mathbf{x}_D) \approx \sum_{i=1}^{m} F_i^1(\mathbf{x}_1) \times \cdots \times F_i^D(\mathbf{x}_D) \tag{2}$$

and that these functions F_i^j are computed *a priori*, i.e., without any prior knowledge on the structure of the solution [10]. In order to compute these functions, a priori unknown, the method proceeds by constructing the variational, or weak, form of the problem and by projecting the sought functions into a finite element basis to obtain a discrete, algebraic, system of equations. If we restrict ourselves, for the sake of simplicity, and without loss of generality, to a two-dimensional framework with generic coordinates c_1 and c_2, the approximation of the solution will look like

$$u(c_1,c_2) \approx \sum_{i=1}^{m} F_i(c_1) \cdot G_i(c_2). \tag{3}$$

The method proceeds iteratively. Therefore, assuming that a set of functional couples $\{(F_i,G_i)\}_{i=1,\ldots,n}$ with $0 \leq n < m$ have been already computed, the method proceeds by seeking the $n+1$-th term, $R(c_1) \cdot S(c_2)$,

$$u(c_1,c_2) \approx \sum_{i=1}^{n} F_i(c_1) \cdot G_i(c_2) + R(c_1) \cdot S(c_2). \tag{4}$$

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Admissible variations of this approximation will therefore be given by

$$u^\star = S \cdot R^\star + R \cdot S^\star \tag{5}$$

By introducing (4) and (5) into the problem weak form and solving the resulting non-linear problem we obtain $R(c_1)$ and $S(c_2)$ that correspond to $F_{n+1}(c_1)$ and $G_{n+1}(c_2)$.

CHALLENGING PROBLEMS BETWEEN MECHANICS AND BIOLOGY

As stated before, many models in science and engineering are defined in a high-dimensional framework. We refer to the Chemical Master Equation (CME) governing gene regulatory networks as one of these examples. In chemical systems involving several species each one composed by a few number of individuals, the state of the system is given by a probability (the deterministic approach fails when the number of individuals is too reduced for introducing the concept of chemical concentration): $P(\mathbf{z}, t|\mathbf{z}_0, t_0)$ where $\mathbf{z} = (z_1, \cdots z_D)$ and z_i refers to the number of individuals of each species s_i. Obviously z_i is changing in time because the different chemical reactions that are producing or destroying individuals in the population s_i. The CME thus reads:

$$\partial_t P(\mathbf{z}, t|\mathbf{z}_0, t_0) = \sum_j \left(a_j(\mathbf{z} - \mathbf{v}_j)P(\mathbf{z} - \mathbf{v}_j, t|\mathbf{z}_0, t_0) - a_j(\mathbf{z})P(\mathbf{z}, t|\mathbf{z}_0, t_0)\right) \tag{6}$$

where a_j are the propensities (the chemical reaction j operates growing the population $\mathbf{z}$ from $\mathbf{z} - \mathbf{v}_j$: $\mathbf{z} - \mathbf{v}_j \rightarrow \mathbf{z}$, and simultaneously population $\mathbf{z}$ decreases originating individuals of other populations).

When modeling the onset and progression of cancer cells, see [13], the framework is similar from the mathematical point of view. We can consider the stochastic modification of the microscopic state of genes or cells due to interaction with other cells, the genetic alteration of cells which may increase the the progression of tumor cells or generate news cancer cells, the proliferation or destruction of cells due to the interaction with other populations or, finally, external actions, such as therapies. All these effects govern the time evolution of the probability distribution function of each cell population, $f_i(t, u) : [0, T] \times D_u \rightarrow \mathbb{R}_+$ in the following way:

$$\partial_t f_i(t, u) + F_i(t)\partial_u f_i(t, u) = J_i[f](t, u) \tag{7}$$

where $u \in D_u$ represents the microscopic state of the active particles (cells) such that $dn_i = f_i(t, u)du$ denotes the number density of active particles which, at time t, are in the element $[u, u+du]$ of the space of the microscopic state. Here, $F_i(t)$ models the external action over the i-th cell population and $J_i[f](t, u) = C_i[f](t, u) + D_i[f](t, u) + P_i[f](t, u)$. $C_i[f](t, u)$ represents the flow, at time t, into the elementary volume of the state space of the i-th population due to conservative interactions, $D_i[f](t, u)$ models the flow due to proliferative and destructive interactions without transition of population and, finally, $P_i[f](t, u)$ models the flow due to proliferation. In the existing works (see [13]) the number of populations, and hence the dimensionality of the model, is always limited. With PGD methods we can efficiently afford high dimensional models in which a spatial dependence and vectorial u exist.

As can be noticed, the above problems (6) and (7) share a similar structure (discrete in the first case, continuous in the second one) of the Fokker-Planck approach to modeling the miscrostructural behavior of polymer flows, see [10].

CONCLUSIONS

In this work we will show the capabilities of the PGD method to treat efficiently some challenging problems defined in high dimensional state spaces. The PGD method even allows to incorporate parameters as additional space dimensions, thus allowing to obtain a sort of meta-modeling technique in which no prior computer experiment is necessary. This is specially important in biological setting, where equation parameters are often very difficult to obtain experimentally. PGD approximations could greatly help in the design of experiments, for instance, as will be shown in the examples.

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