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A new discontinuous Galerkin method for the nonlinear Poisson–Boltzmann equation

Weishan Deng[a], Xiaohe Zhufu[a], Jin Xu[a], Shan Zhao[b,*]

[a] *Institute of Software, Chinese Academy of Sciences, Beijing, 100190, PR China*
[b] *Department of Mathematics, University of Alabama, Tuscaloosa, AL 35487, USA*

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ABSTRACT

A novel discontinuous Galerkin (DG) method is proposed in this letter to solve the three-dimensional (3D) nonlinear Poisson–Boltzmann (PB) equation for the electrostatic analysis of solvated biomolecules. A regularization formulation is employed in constructing the DG method, which decomposes the electrostatic potential into singular, harmonic, and regular components, so that the inaccurate approximation of singular charge sources can be bypassed. Based on a pseudo-transient continuation approach, the nonlinear term of the PB equation is analytically integrated in our DG method, which avoids the nonlinear instability. A nodal based DG variational formulation is introduced to effectively handle the nonsmooth potential owing to a piecewisely-defined dielectric profile. The stability, convergence, and accuracy of the proposed DG method are numerically verified via a benchmark study.

1. Introduction

The Poisson–Boltzmann (PB) equation is commonly used to characterize electrostatic interactions in charged systems with distributed mobile charges, which are vital for the study of a protein system immersed in an ionic solvent environment [1]. Solving the nonlinear PB equation numerically is very challenging due to various factors of the PB model, such as complex geometry of protein structures, singular source terms, strong nonlinearity of ionic effects [2]. Moreover, the coefficients of the PB model are discontinuous across the solute–solvent interface or molecular surface, so that continuous polynomial based numerical methods may perform poorly in treating the nonsmooth electrostatic potential of the PB equation [3,2].

Various numerical PB solvers have been successfully developed in the literature, based on finite element method [4], finite difference method [3], and others. We refer to a recent review [2] for more details of these studies. Recently, Bedin and Bosing have developed an interior penalty discontinuous Galerkin (IPDG)

* Corresponding author. Tel.: +1 205 3485303; fax: +1 205 3487067.
E-mail addresses: weishan2012@iscas.ac.cn (W. Deng), xiaohe@iscas.ac.cn (X. Zhufu), xu_jin@iscas.ac.cn (J. Xu), szhao@ua.edu (S. Zhao).

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method for solving a two-dimensional (2D) linear PB equation [5]. In this IPDG method, a regularization scheme [4] is first employed to transform the PB problem to one free of singular source terms. Then the nonsmoothness of the solution is addressed by replacing the discontinuous coefficients with a suitable Lipschitz approximation. More recently, an iterative DG method has been introduced by Yin et al. [6] for solving a source-free PB model with an exponential nonlinear term. This iteration scheme approximates the 2D nonlinear PB equation by a series of linear PB equations, which are numerically discretized by the direct DG method. We note that this iteration scheme can be regarded as a pseudo-transient continuation approach [7,8] for the PB equation with an implicit Euler time discretization of the linear terms and an explicit evaluation of the nonlinear term. Given the potential of the DG variational formulation in handling complex geometries and nonsmooth solutions, it is of great interests to further develop three-dimensional (3D) DG methods to solve the nonlinear PB equation with full features including discontinuous solute–solvent coefficients, singular source terms, and a hyperbolic sine nonlinear term.

The goal of this letter is to introduce a 3D DG method for solving the nonlinear PB equation, which takes advantage of various latest numerical schemes in the literature. In particular, a regularization formulation of the nonlinear PB equation [3,2] will be employed to decompose the electrostatic potential into singular, harmonic, and regular components. The singular solution is given analytically by Green's functions, while other two components are governed by source-free Poisson's and PB equations. In the proposed approach, the Poisson boundary value problem will be simply solved by a continuous finite element method, while the nonlinear PB equation will be recast into a time-dependent process using the pseudo-transient continuation method [7,8]. An operator splitting [7,8] will then be conducted so that the nonlinear term can be treated analytically, which greatly enhances the stability of our pseudo-time computation. The resulting time-dependent linearized PB equation will be discretized based on the forward Euler scheme in time and a nodal based DG method [9] in space. The details of the proposed DG method will be discussed in Section 2. Numerical validations through a benchmark example with analytical solution will be considered in Section 3. Finally, this letter ends with a conclusion.

2. Mathematical models and numerical algorithms

Consider the 3D nonlinear PB equation in the dimensionless form [2,7]

$$-\nabla\cdot(\epsilon\nabla u)+\kappa^2\sinh(u)=\rho:=C\sum_{j=1}^{N_m}q_j\delta(\vec{x}-\vec{x}_j),\quad \text{for } \vec{x}\in\Omega=\Omega^-\cup\Omega^+, \tag{1}$$

$$u=g(\vec{x}),\quad \text{for } \vec{x}\in\partial\Omega, \tag{2}$$

where u is the electrostatic potential and g is a boundary data. The domain Ω consists of two regions, i.e., a solute domain Ω^- occupied by a macromolecule, and a solvent domain Ω^+ for the surrounding aqueous environment. Here C is a constant, N_m is the total atom number of the solute macromolecule, and q_j is the partial charge on the jth atom located at position $\vec{x}_j=(x_j,y_j,z_j)$. Across the molecular surface Γ [2], separating Ω^- and Ω^+, the dielectric constant ϵ and Debye–Hückel parameter κ are discontinuous: $\epsilon=\epsilon^-$ and $\kappa=0$ in Ω^-; $\epsilon=\epsilon^+$ and $\kappa=\bar{\kappa}$ in Ω^+.

To avoid an inaccurate approximation of the singular source term ρ in (1), following the regularization formalism introduced in [3], the potential u is decomposed into a singular part u^s, a harmonic part u^h, and a regular part u^r. We have $u=u^s+u^h+u^r$ and $u^s=u^h=0$ in Ω^+. In Ω^-, the singular component is simply given by Green's function [3,2], $u^s(\vec{x})=\frac{C}{4\pi\epsilon^-}\sum_{j=1}^{N_m}\frac{q_j}{|\vec{x}-\vec{x}_j|}$, and the harmonic component satisfies the Poisson equation

$$-\epsilon^-\Delta u^h=0,\quad \text{in } \Omega^-,\quad \text{and}\quad u^h=-u^s,\quad \text{on } \Gamma. \tag{3}$$

In the present study, this Dirichlet boundary value problem will be discretized by a continuous finite element method. The corresponding variation form is pretty standard and is omitted here.

The solution of the nonlinear PB Eq. (1) thus reduces to a source-free boundary value problem

$$-\nabla\cdot(\epsilon\nabla u^r)+\kappa^2\sinh(u^s+u^h+u^r)=0,\quad \text{in } \Omega,\quad \text{and}\quad u^r=g(\vec{x}),\quad \text{on } \partial\Omega. \tag{4}$$

The same hyperbolic sine nonlinear term is still presented in the present PB Eq. (4), which is known to introduce some instability problem, because the magnitude of the dimensionless potential u could be up to 20 in biomolecular simulations [7,8]. To suppress the nonlinear instability, we will adopt the time splitting scheme developed in [7,8] within the pseudo-transient continuation framework.

We propose to solve the boundary value problem (4) by converting it to a time-dependent form

$$\frac{\partial u^r(\vec{x},t)}{\partial t}=\nabla\cdot(\epsilon\nabla u^r(\vec{x},t))-\kappa^2\sinh(u^s(\vec{x})+u^h(\vec{x})+u^r(\vec{x},t)),\quad \text{in } \Omega, \tag{5}$$

with the same boundary condition $u^r(\vec{x},t)=g(\vec{x})$ for $\vec{x}\in\partial\Omega$. By using a trivial initial value $u^r(\vec{x},0)=0$, one numerically integrates (5) for a sufficiently long time period or until it is convergent. The solution to the original nonlinear PB Eq. (4) is essentially recovered by the steady state solution of the pseudo-time dependent process (5). We note that the sign on the right-hand side of Eq. (5) is the reverse of that of Eq. (4). In principle, a pseudo-time equation with a different sign could yield the same steady-state solution. However, one may experience an instability issue in the numerical integration of an inverse diffusion process. Thus, a regular diffusion process with the positive sign for the Laplacian is considered in the present study.

Consider a uniform grid partition in time with an increment Δt. Denote $t_n=n\Delta t$. A first order time splitting scheme [7,8] will be employed to update (5) in the subinterval $[t_n,t_{n+1}]$

$$\frac{\partial\psi}{\partial t}=-\kappa^2\sinh(u^s+u^h+\psi),\quad \text{with } \psi(\vec{x},t_n)=u^r(\vec{x},t_n),\ t\in[t_n,t_{n+1}], \tag{6}$$

$$\frac{\partial\phi}{\partial t}=\nabla\cdot(\epsilon\nabla\phi),\quad \text{with } \phi(\vec{x},t_n)=\psi(\vec{x},t_{n+1}),\ t\in[t_n,t_{n+1}]. \tag{7}$$

We then have $u^r(\vec{x},t_{n+1})=\phi(\vec{x},t_{n+1})$. The first equation (6) can be integrated analytically. In particular, we note that $\kappa=0$ in Ω^-, while u^s and u^h are vanishing in Ω^+. Thus, when $\vec{x}\in\Omega^-$, we have simply $\psi(\vec{x},t_{n+1})=\psi(\vec{x},t_n)$, while when $\vec{x}\in\Omega^+$, we have analytically [7,8]

$$\psi(\vec{x},t_{n+1})=\ln\left(\frac{\cosh(\frac{1}{2}\bar{\kappa}^2\Delta t)+\exp(-\psi(\vec{x},t_n))\sinh(\frac{1}{2}\bar{\kappa}^2\Delta t)}{\exp(-\psi(\vec{x},t_n))\cosh(\frac{1}{2}\bar{\kappa}^2\Delta t)+\sinh(\frac{1}{2}\bar{\kappa}^2\Delta t)}\right). \tag{8}$$

A nodal based DG scheme [9] will be constructed to solve the 3D heat Eq. (7) in Ω subject to a boundary condition $\phi(\vec{x},t)=g(\vec{x})$ for $\vec{x}\in\partial\Omega$. Based on discontinuous basis functions, it is quite easy to handle complex geometries of protein systems in the DG variational formulation. Moreover, by properly designing the numerical flux, the non-smoothness of the electrostatic potential solution across the dielectric interface can be accurately captured and well preserved in the DG computations. In the following, a brief introduction to the proposed DG method will be offered. To save the space, we will refer to Refs. [9,10] for more details on constructing nodal finite elements, computing numerical flux, etc.

We first rewrite the heat Eq. (7) into a system of first order equations

$$\frac{\partial\phi}{\partial t}=\nabla\cdot(\sqrt{\epsilon}\vec{Q}),\quad \vec{Q}=\sqrt{\epsilon}\nabla\phi \tag{9}$$

where $\vec{Q}=[Q^x,Q^y,Q^z]^T$. Suppose the domain Ω has been discretized to Ω_k, which consists of k nonoverlapping tetrahedra, i.e. $\Omega\approx\Omega_k=\cup_k D^k$. In each element D^k, we assume $(\phi,\vec{Q})$ can be expanded

in terms of the Lagrange bases $l^k(\vec{x})$ defined on some nodal points of D^k. The DG semi-discretization of (9) in the strong form is given as

$$M^k \frac{d\phi^k}{dt} = \tilde{S} \cdot \vec{Q}^k - \int_{\partial D^k} \vec{n} \cdot ((\sqrt{\epsilon}\vec{Q}^k) - (\sqrt{\epsilon}\vec{Q}^k)^*) l^k(\vec{x}) ds \tag{10}$$

$$\bar{M}^k \vec{Q}^k = \bar{S}\phi^k - \int_{\partial D^k} \vec{n}((\sqrt{\epsilon}\phi^k) - (\sqrt{\epsilon}\phi^k)^*) l^k(\vec{x}) ds, \tag{11}$$

where the superscript k denotes the restriction to the k element, and the superscript $*$ denotes the numerical flux. The vectors are defined as

$$\vec{n} = \begin{pmatrix} n^x \\ n^y \\ n^z \end{pmatrix}, \qquad \bar{M}^k = \begin{pmatrix} M^k & 0 & 0 \\ 0 & M^k & 0 \\ 0 & 0 & M^k \end{pmatrix}, \qquad \tilde{S}_{ij} = \begin{pmatrix} \tilde{S}^x_{ij} \\ \tilde{S}^y_{ij} \\ \tilde{S}^z_{ij} \end{pmatrix}, \qquad \bar{S}_{ij} = \begin{pmatrix} S^x_{ij} \\ S^y_{ij} \\ S^z_{ij} \end{pmatrix}, \tag{12}$$

where the entries are calculated as $M^k_{ij} = \int_{D^k} l^k_i(\vec{x}) l^k_j(\vec{x}) dv$, $\tilde{S}^x_{ij} = \int_{D^k} l^k_i(\vec{x}) \frac{\partial(\sqrt{\epsilon} l^k_j(\vec{x}))}{\partial x} dv$, $S^x_{ij} = \int_{D^k} \sqrt{\epsilon} l^k_i(\vec{x}) \frac{\partial l^k_j(\vec{x})}{\partial x} dv$. Other entries $\tilde{S}^y_{ij}$, $\tilde{S}^z_{ij}$, S^y_{ij}, and S^z_{ij} are computed similarly. In the present study, central flux has been used for both ϕ and $\vec{Q}$:

$$(\sqrt{\epsilon}v)^* = \frac{\sqrt{\epsilon^-}v^- + \sqrt{\epsilon^+}v^+}{2}, \qquad (\sqrt{\epsilon}\vec{Q})^* = \frac{\sqrt{\epsilon^-}\vec{Q}^- + \sqrt{\epsilon^+}\vec{Q}^+}{2}. \tag{13}$$

Because the overall temporal order for the present time splitting procedure is first order, the forward Euler scheme is employed to integrate the DG semi-discretized equations.

3. Numerical results

We consider a benchmark test [7] to validate the proposed DG method for solving the NPB equation. Consider a one-atom system with a charge at the origin. Here Ω^- is a sphere of radius R, and $\Omega = \Omega^- \cup \Omega^+$ is a large enough box containing the sphere. The source term and analytical solution are chosen to be [7]

$$\rho = \begin{cases} 4\pi\epsilon^-\delta(\vec{x}), & \|\vec{x}\| \le R \\ \bar{\kappa}^2 \sinh\left(\frac{1}{\eta\|\vec{x}\|}\right), & \|\vec{x}\| > R \end{cases} \qquad u = \begin{cases} \frac{1}{\eta R} - \frac{1}{R} + \frac{1}{\|\vec{x}\|}, & \|\vec{x}\| \le R \\ \frac{1}{\eta\|\vec{x}\|}, & \|\vec{x}\| > R \end{cases} \tag{14}$$

where $\eta = \epsilon^+/\epsilon^-$. This benchmark example preserves both the singularity in the source term and the same non-smoothness in the potential solution as in the usual biomolecular studies. Thus, it is ideal to examine the performance of the proposed DG method with special treatments of singular source and nonlinear term. In our computations, the Dirichlet boundary condition (2) is simply derived from the exact solution (14) on $\partial\Omega$ and the piecewise linear nodal basis functions ($p = 1$) are used. The model parameters are chosen as: $R = 1$, $\bar{\kappa} = 1$, $\epsilon^- = 1$, and $\epsilon^+ = 80$. Three grid levels are considered for a domain $\Omega = [-2.5, 2.5] \times [-2.5, 2.5] \times [-2.5, 2.5]$. The number of elements is 1169, 9352, and 74816, respectively, for grid level 1, 2, and 3. All integrations will be carried out until $t = 1$.

The stability analysis is conducted first. We consider an initial solution which is simply obtained by scaling the exact solution (14) with a factor A. We note that when the amplitude of u is large, the value of the nonlinear term $\sinh(u)$ will be exponentially large. If the nonlinear term is treated explicitly in an explicit or semi-implicit time integration, Δt has to be exponentially small for a stable computation. Thus, such an integration will quickly become *unconditionally unstable* when A increases [7]. In the present study, different Δt values will be examined so that we can numerically determine a critical Δt value for which the computation is still stable. We recast this critical value into the stability condition form: $\Delta t \le (\min\{h\})^2/M$,

Table 1
Critical Δt and M values of the DG method for a different scaling factor A.

A	Δt	M	Δt	M	Δt	M
	$\min\{h\} = 0.2814$		$\min\{h\} = 0.1287$		$\min\{h\} = 0.0541$	
1	2.2E−5	3600	6.0E−6	2761	1.4E−6	2091
10	2.2E−5	3600	6.0E−6	2761	1.2E−6	2440
20	2.2E−5	3600	6.0E−6	2761	1.2E−6	2440

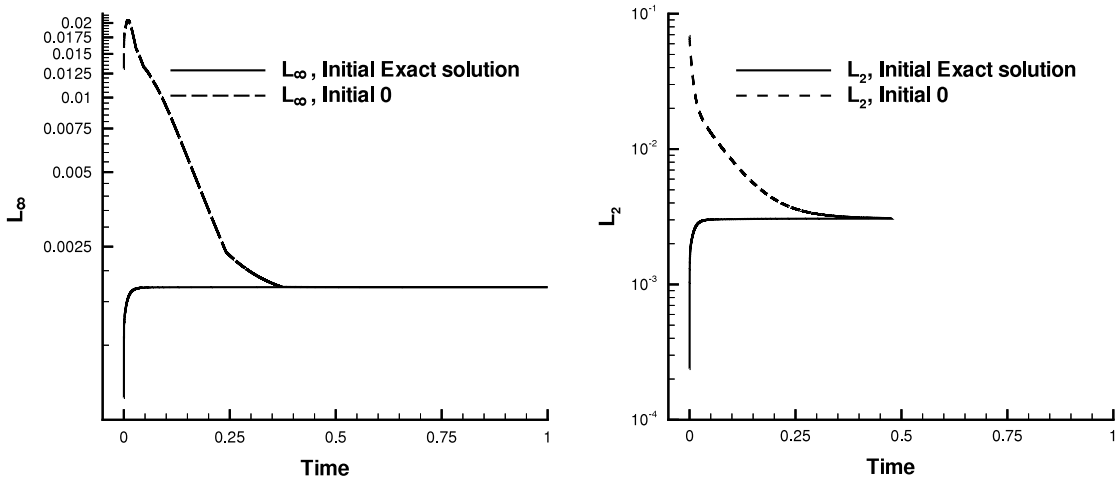

Fig. 1. The L_∞ (left) and L_2 (right) errors of the DG method with respect to the time t. Here the initial solution is chosen as zero or the exact solution (14).

where $\min\{h\}$ is the minimal edge length of a finite element grid. For three tested grid levels, we have $\min\{h\} = 0.2814$, 0.1287, and 0.0541, respectively. By considering $A = 1$, 10, and 20, the stability results are reported in Table 1. It can be seen that by using the forward Euler scheme in time, one has to choose a small Δt for a stable computation. Nevertheless, for each grid, the same or very close stability constrains are observed for tested A values. This indicates that the nonlinear term will not affect the stability, thanks to our analytical treatment in the pseudo-time framework.

The convergence of the proposed DG algorithm is examined next. By choosing the level 1 grid and $\Delta t = 2.2E{-}5$, the L_∞ and L_2 errors of the DG method with respect to the time t are plotted in Fig. 1. To illustrate the robustness, two initial solutions are considered here, i.e., a trivial zero solution and the exact solution of the time independent NPB equation given in (14). It can be seen that both solutions converge to the same place and the convergence of the pseudo-transient continuation approach is fairly quick.

Finally, we investigate the order of accuracy of the DG method. The L_∞ and L_2 errors of the DG method are listed in Table 2. For each grid level, the critical Δt is used. The same numerical errors are obtained if we used an even smaller Δt. For mesh refinements in Table 2, the spatial rate of convergence is also calculated. It can be seen that the proposed DG method achieves a second order of accuracy in space, in terms of the L_2 norm. A slice plot of the DG potential solution on the plane $z = 0.5$ is shown in the left chart of Fig. 2. The corresponding absolute error is depicted on the right. Obviously, the maximum error is located at the interface of two dielectric materials.

4. Conclusion

A novel discontinuous Galerkin (DG) method is developed in this work for solving the Poisson–Boltzmann (PB) equation. To the authors' knowledge, this DG method is the first three-dimensional DG solver in the

Table 2
Spatial order of convergence of the DG method.

Grid	# of elements	Δt	L^2	Rate	L_∞	Rate
Level 1	1 169	2.2E−5	3.06e−3		1.72e−3	
Level 2	9 352	6.0E−6	7.21e−4	2.09	5.52e−4	1.64
Level 3	74 816	1.4E−6	1.86e−4	1.95	1.80e−4	1.62

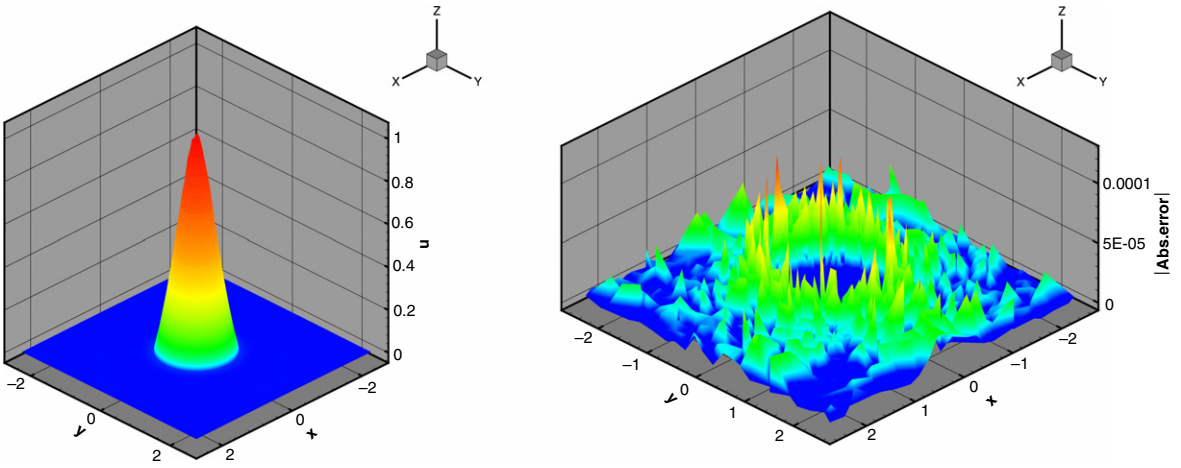

Fig. 2. Left: the slice plot of the DG solution u on the plane $z = 0.5$; Right: the corresponding absolute error.

literature for the fully nonlinear PB equation. Based on a regularization formulation and a pseudo-transient method, both the singular source term and nonlinear term are treated analytically in the proposed DG algorithm. Numerically, the DG scheme is found to be stable, convergent, and of second order of accuracy in space. The further development of the DG method for electrostatic energy analysis of solvated proteins will be reported in the future.

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