Computation of Forces Arising from the Linear Poisson-Boltzmann Method in the Domain Decomposition Paradigm

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Joint work with M.Nottoli (Università di Pisa, Pisa), C. Quan (SUS Tech, China),

and B. Stamm (Universität Stuttgart, Stuttgart)

Outline

Solvation Models

- Ionic Solvation Models [1]
  - Explicit Solvation Models
    - Adopts molecular representation of both solute and solvent
    - Accurate results
    - Computationally expensive

[1] Zhang et. al.: JCTC, 13, 1034-1043, 2017

[2] Tomasci, Persico: CR 94, 2027-2094, 1994

[3] Honig, Nicholls: Sci. 268, 1144-1149, 1995

Solvation Models

- Ionic Solvation Models [1]
  - Explicit Solvation Models
    - Adopts molecular representation of both solute and solvent
    - Accurate results
    - Computationally expensive
  - Implicit Solvation Models [2,3]
    - Microscopic treatment of solute
    - Macroscopic treatment of solvent using physical properties
    - Less computational cost

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Model Problem

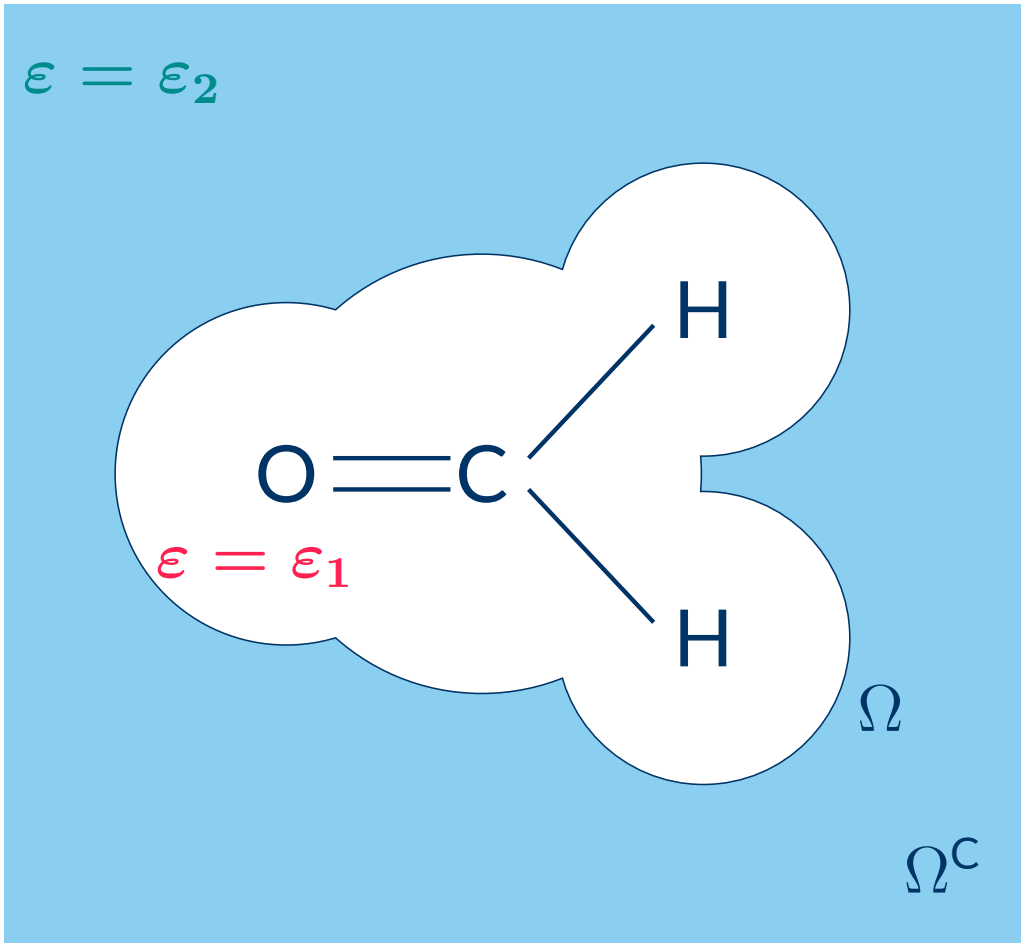

Figure 1: Formaldehyde molecule

- Linear Poisson-Boltzman (LPB) equation

$$-\nabla \cdot [\varepsilon(x)\nabla\psi(x)] + \bar{\kappa}(x)^2\psi(x) = 4\pi\rho_M(x) \quad \text{in } \mathbb{R}^3$$

  - $\psi(x)$ – Electrostatic potential

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  - $\psi(x)$– Electrostatic potential
  - $\varepsilon(x)$– Space-dependent dielectric permittivity

$$\varepsilon(x) = \begin{cases} \varepsilon_1 & \text{in } \Omega, \\ \varepsilon_2 & \text{in } \Omega^C := \mathbb{R}^3 \setminus \overline{\Omega} \end{cases}$$

  - Ω– Solute Cavity

Model Problem

- $\bar{\kappa}(\boldsymbol{x})$ – Modified Debye-Hückel parameter

$$\bar{\kappa}(\boldsymbol{x}) = \begin{cases} 0 & \text{in } \Omega, \\ \sqrt{\varepsilon_2}\kappa & \text{in } \Omega^{\mathsf{C}} \end{cases}$$

- κ – Debye-Hückel screening constant

- $\bar{\kappa}(x)$ – Modified Debye-Hückel parameter

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- κ – Debye-Hückel screening constant
- $\rho_M(x)$ – Solute charge distribution

$$\rho_M(x) = \sum_{i=1}^{M} q_i \delta(x - x_i)$$

- M – Number of solute atoms
- q_i – Partial charge on the i^{th} atom

- Boundary Element Method (BEM) [1]

[1] Yoon, Lehnoff: JCC 11, 1080–1086, 1990

[2] Madura et.al.: CPC 91, 57–95, 1995

[3] Chen, Holst, Xu: SINUM 45, 2295–2320, 2007

[4] Cancés, Maday, Stamm: JCP 139, 054111, 2013

[5] Lipparini et.al.: JCP 141, 184108, 2014

[6] Quan, Stamm, Maday: SISC 41, B320–B350, 2019

[7] Lebedev, Laikov: DM 59, 477–481, 1999

Review of numerical methods

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- Boundary Element Method (BEM) [1]
- Finite Difference Method (FDM)[2]
- Finite Element Method (FEM)[3]
- Domain Decomposition Methods [4,5,6]
  - Schwarz decomposition method
  - Does not rely on mesh but quadrature points[7]
  - Computation of forces becomes natural as spheres are centered at nucleus position

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- The LPB equation can be written in two equations

$$-\Delta\psi(x) = \frac{4\pi}{\varepsilon_1}\rho_M(x) \qquad \text{in } \Omega,$$
$$-\Delta\psi(x) + \kappa^2\psi(x) = 0 \qquad \text{in } \Omega^C,$$

with

$$[\![\psi(x)]\!] = 0 \qquad \text{on } \Gamma,$$
$$[\![\partial_{\mathbf{n}}\psi(x)]\!] = 0 \qquad \text{on } \Gamma$$

- Using potential theory the final equations are

$$\begin{aligned} -\Delta\psi_{\mathsf{r}}(x) &= 0 \quad \text{in } \Omega, \\ -\Delta\psi_{\mathsf{e}}(x) + \kappa^2\psi_{\mathsf{e}}(x) &= 0 \quad \text{in } \Omega, \end{aligned}$$

with

$$\begin{aligned} \psi_0 + \psi_{\mathsf{r}} &= \psi_{\mathsf{e}} && \text{on } \Gamma, \\ \sigma_{\mathsf{e}} &= \partial_{\mathsf{n}}\psi_{\mathsf{e}} - \frac{\varepsilon_1}{\varepsilon_2}\partial_{\mathsf{n}}(\psi_0 + \psi_{\mathsf{r}}) && \text{on } \Gamma \end{aligned}$$ [1]

[1] Sauter, Schwab, Springer, Berlin-2011, Thm. 3.3.1

Problem Transformation

- Using potential theory the final equations are

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where

- ψ_{r} – Reaction potential in Ω
- ψ_0 – Potential generated by ρ_{M} satisfying,

$$-\Delta\psi_0 = \frac{4\pi}{\varepsilon_1}\rho_{\mathsf{M}}$$

[1] Sauter, Schwab, Springer, Berlin-2011, Thm. 3.3.1

Problem Transformation

- ψ_e – Extended potential from Ω^C to Ω
- σ_e – Charge density generating ψ_e satisfying

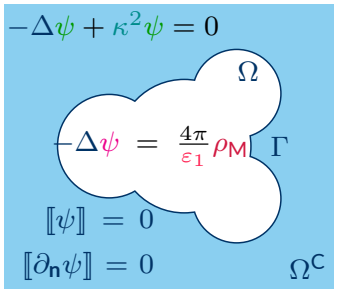
$$S_\kappa \sigma_e(x) := \int_\Gamma \frac{\exp\left(-\kappa|x-y|\right)\sigma_e(y)}{4\pi|x-y|} = \psi_e \quad \forall\, x \in \Gamma$$

- S_κ – Invertible single-layer potential operator [1]

$$S_\kappa : H^{-1/2}(\Gamma) \to H^{1/2}(\Gamma)$$

[1] Sauter, Schwab, Springer, Berlin-2011, 101-181

ddLPB-Method



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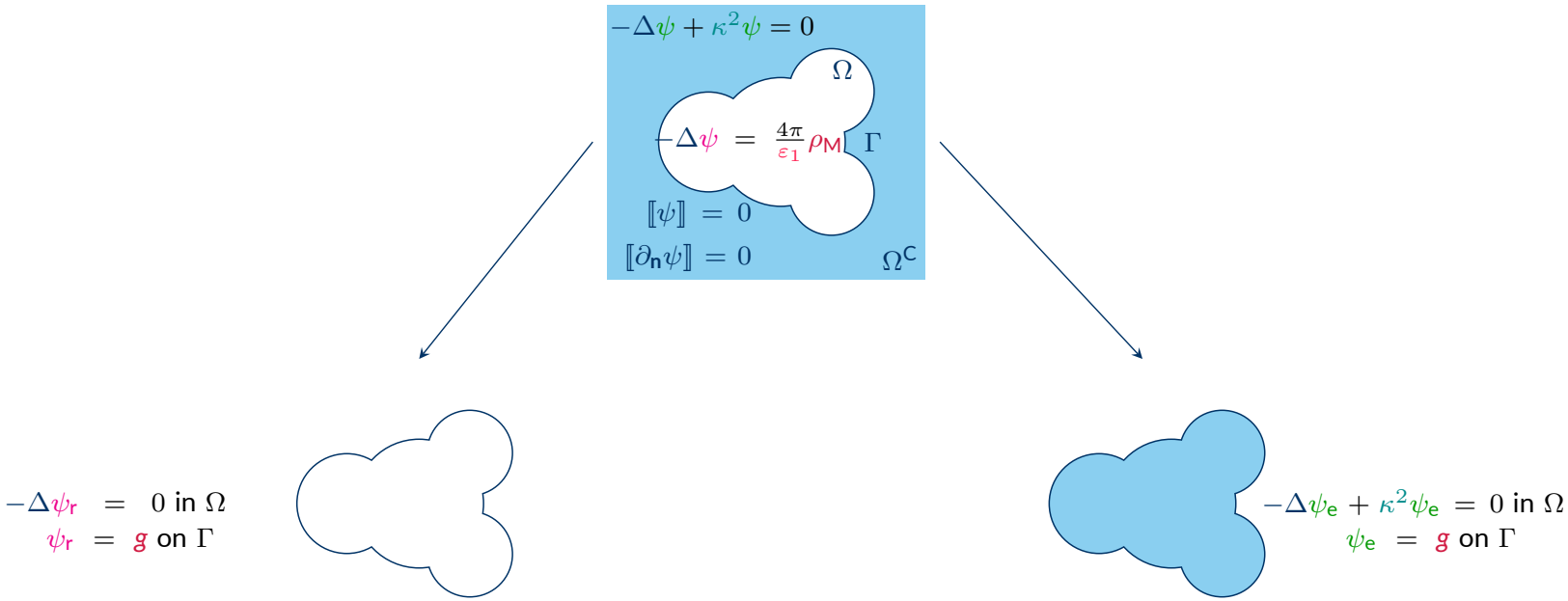

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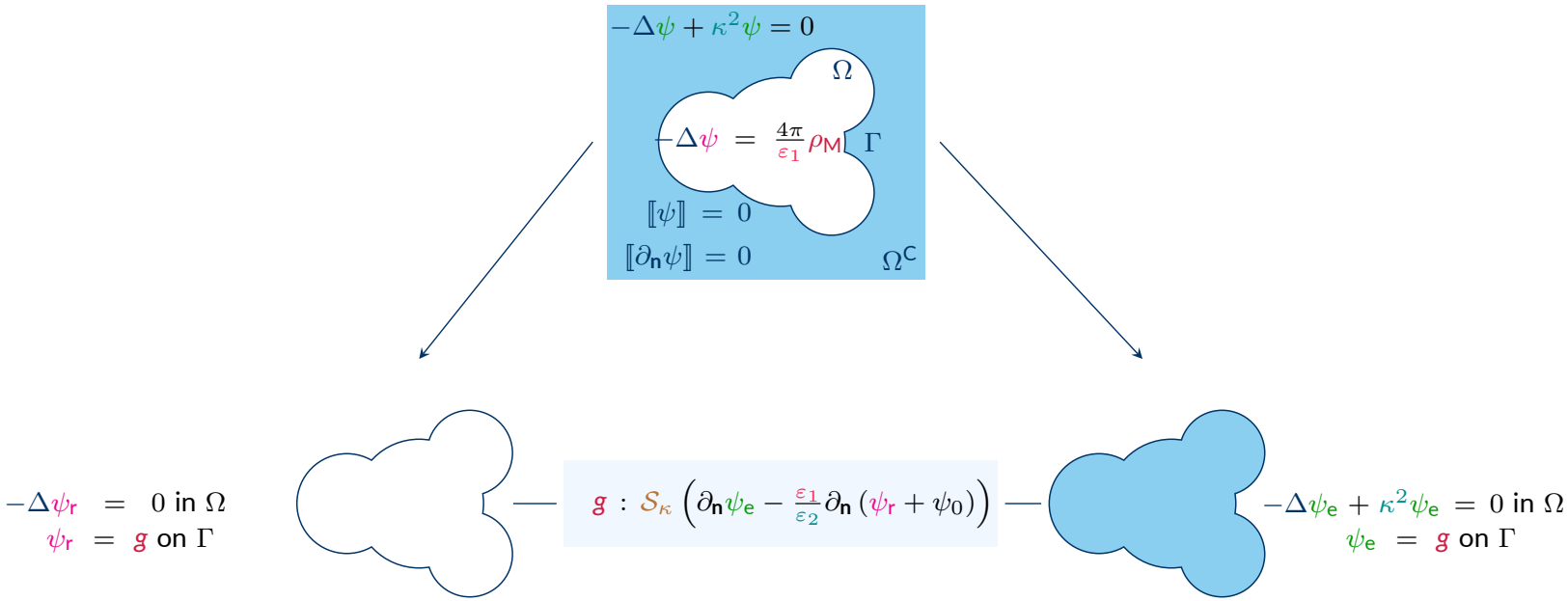
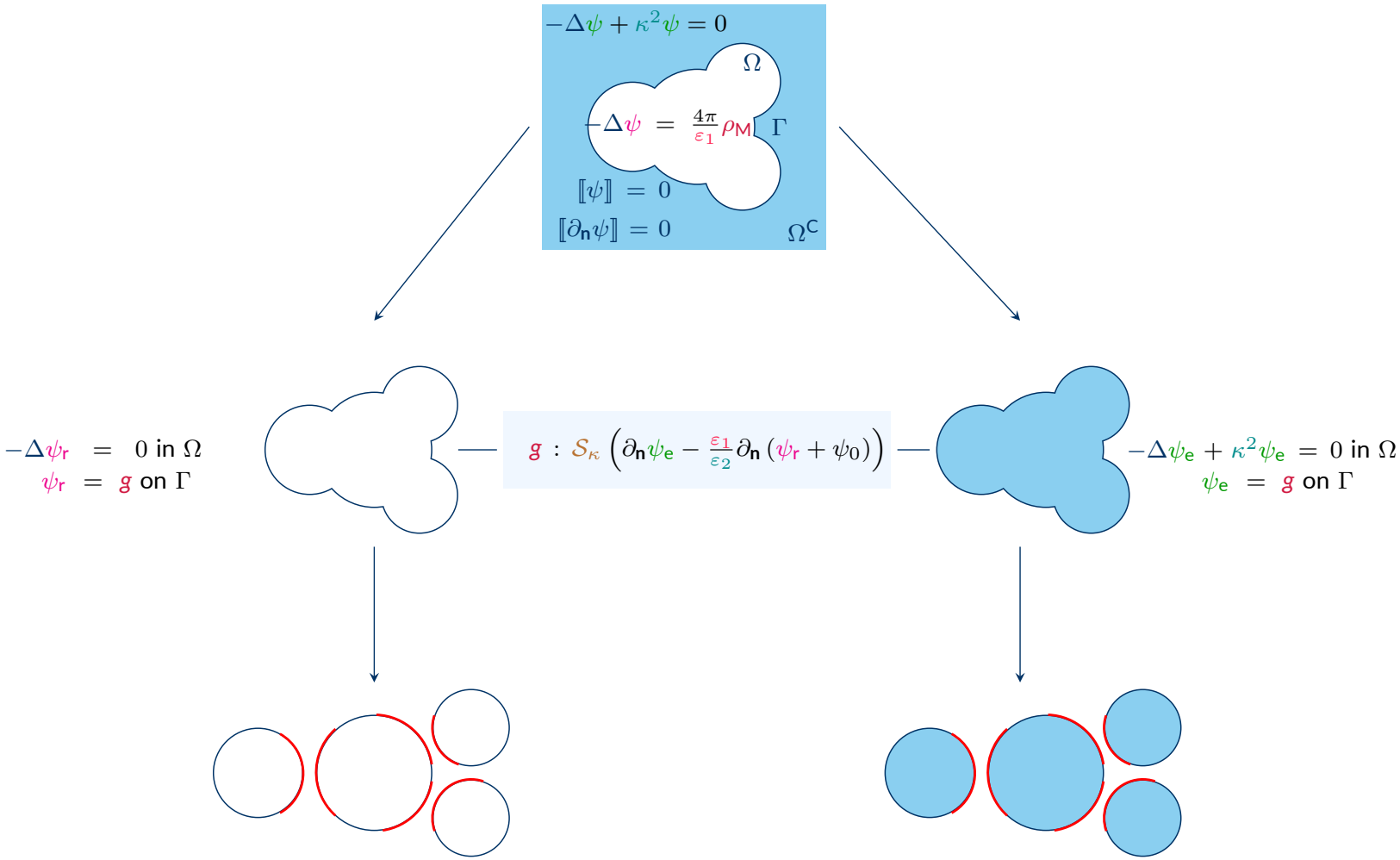
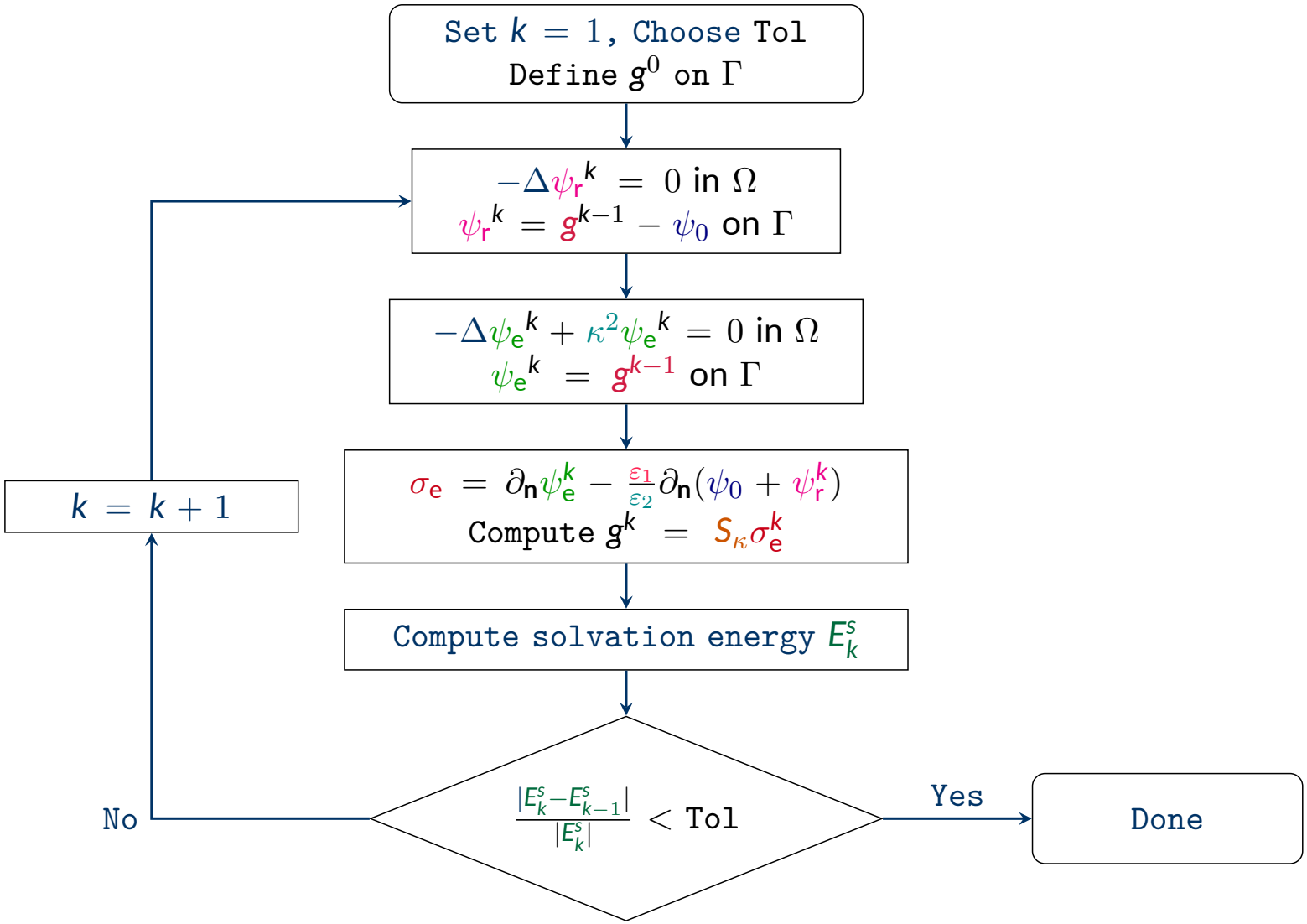


ddLPB-Method



Global strategy



- Energy for LPB equations[1]

$$E_s = \frac{1}{2} \langle \psi_r, \rho_M \rangle = \frac{1}{2} \sum_{j=1}^{M} \langle X, Q \rangle_j \,,$$

where,

$$[Q]_{j\ell m} = \begin{cases} q_j \delta_{\ell 0} \delta_{m 0}, & \text{if } 1 \leq j \leq M, \\ 0 & \text{if } M < j \leq 2M. \end{cases}$$

and

$$\langle X, Q \rangle_j = \sum_i [X]_{ji} \, [Q]_{ji} \,.$$

[1] Fogolari, Brigo, Molinari: JMR 15, 2002

Computation of Forces

- Force with respect to λ

$$F_\lambda = \nabla^\lambda \left(E_s\right) = \frac{1}{2}\left(\left\langle \nabla^\lambda X, Q\right\rangle + \left\langle X, \nabla^\lambda Q\right\rangle\right) = \frac{1}{2}\left\langle \nabla^\lambda X, Q\right\rangle$$

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- Let $\mathsf{L}X = g$ be the ddLPB system

$$\begin{aligned} \nabla^\lambda \mathsf{L}X + \mathsf{L}\nabla^\lambda X &= \nabla^\lambda g \\ \nabla^\lambda X &= \mathsf{L}^{-1}\left(\nabla^\lambda g - \nabla^\lambda \mathsf{L}X\right). \end{aligned}$$

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- Substituting $\nabla^\lambda X$

$$\begin{aligned} F_\lambda &= \frac{1}{2}\left\langle \mathsf{L}^{-1}\left(\nabla^\lambda g - \nabla^\lambda \mathsf{L}X\right), Q\right\rangle \\ &= \frac{1}{2}\left\langle \left(\nabla^\lambda g - \nabla^\lambda \mathsf{L}X\right), \left(\mathsf{L}^{-1}\right)^* Q\right\rangle \\ &= \frac{1}{2}\left\langle \left(\nabla^\lambda g - \nabla^\lambda \mathsf{L}X\right), X_{\text{adj}}\right\rangle \end{aligned}$$

System of Equations

- Linear System

$$LX = g,$$

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where

$$\mathbf{L} = \begin{bmatrix} \mathbf{A} & 0 \\ 0 & \mathbf{B} \end{bmatrix} + \begin{bmatrix} \mathbf{C}_1 & \mathbf{C}_2 \\ \mathbf{C}_1 & \mathbf{C}_2 \end{bmatrix}, \quad X = \begin{bmatrix} X_r \\ X_e \end{bmatrix}, \quad \text{and} \quad g = \begin{bmatrix} \mathbf{G}_0 + \mathbf{F}_0 \\ \mathbf{F}_0 \end{bmatrix}$$

  - $\mathbf{G}_0$ – Associated with ψ_0
  - $\mathbf{F}_0$ – Associated with $\partial_{\mathbf{n}}\psi_0$
  - $\mathbf{C}_1$ – Associated with $\partial_{\mathbf{n}}\psi_r$
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- Using the global strategy

$$\begin{bmatrix} \mathsf{A} & 0 \\ 0 & \mathsf{B} \end{bmatrix} \begin{bmatrix} {X_\mathsf{r}}^k \\ {X_\mathsf{e}}^k \end{bmatrix} = - \begin{bmatrix} \mathsf{C}_1 & \mathsf{C}_2 \\ \mathsf{C}_1 & \mathsf{C}_2 \end{bmatrix} \begin{bmatrix} {X_\mathsf{r}}^{k-1} \\ {X_\mathsf{e}}^{k-1} \end{bmatrix} + \begin{bmatrix} \mathsf{G}_0 + \mathsf{F}_0 \\ \mathsf{F}_0 \end{bmatrix}$$

where

  - k – Iteration

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where

  - k – Iteration
- $\mathbf{A}, \mathbf{B}$ are sparse
- $\mathbf{C}_1, \mathbf{C}_2$ are not sparse

- Comparison of Results

[1] Jurrus et. al. : Protein Sci. 27 (1), 112-128, 2018

Numerical Studies

- Comparison of Results
  - Adaptive Poisson-Boltzmann Solver[1]
    - Energy
    - Memory

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$$\mathrm{Err}_{j,\alpha}(h) = D_h[E_s](x_{j,\alpha}) - \frac{\partial E_s}{\partial x_{j,\alpha}},$$

with

$$\mathbf{x}_j = (x_{j,1}, x_{j,2}, x_{j,3})^T$$

[1] Jurrus et. al. : Protein Sci. 27 (1), 112-128, 2018

- Constants in the Model
  - $\varepsilon_1 = 1, \varepsilon_2 = 78.54$
  - $\kappa = 0.104$ Å^{-1}

[1] ddX: https://github.com/ACoM-Computational-Mathematics/ddX

[2] Berman et. al. : NAR 28, 235-242, 2000

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  - GMRES Tol$= 10^{-8}$
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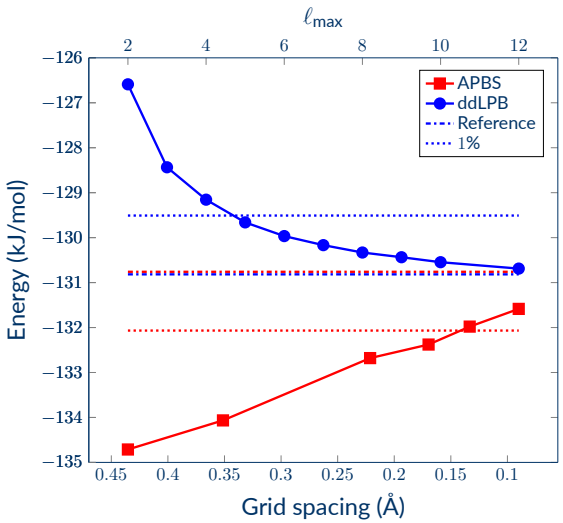
  - Tol$= 10^{-10}$
- Test Structure[2]

PDB Code	M	Name
1ay3	25	Nodularin
1etn	180	Enterotoxin
1qjt	9046	EH1 Domain

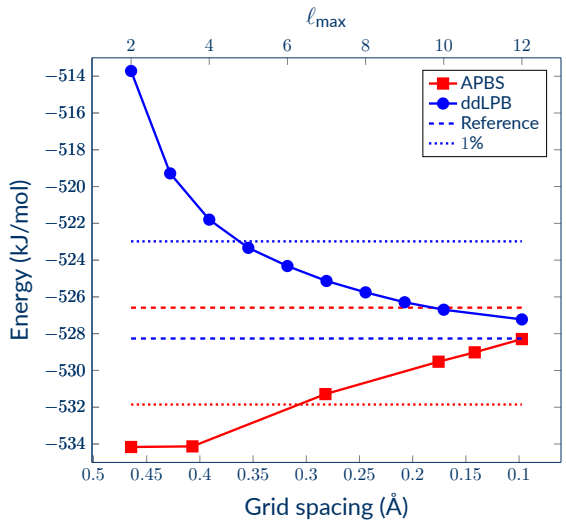
[1] ddX: https://github.com/ACoM-Computational-Mathematics/ddX

[2] Berman et. al. : NAR 28, 235-242, 2000

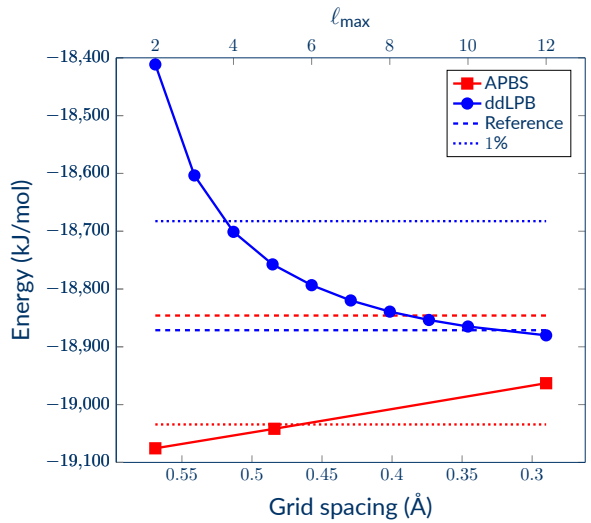
- Energy



(a) 1ay3



(b) 1etn



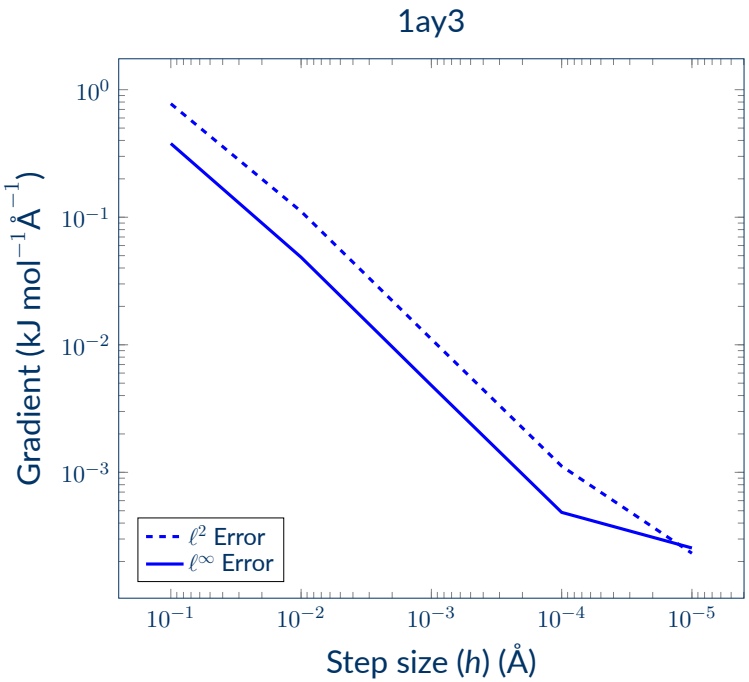
(c) 1qjt

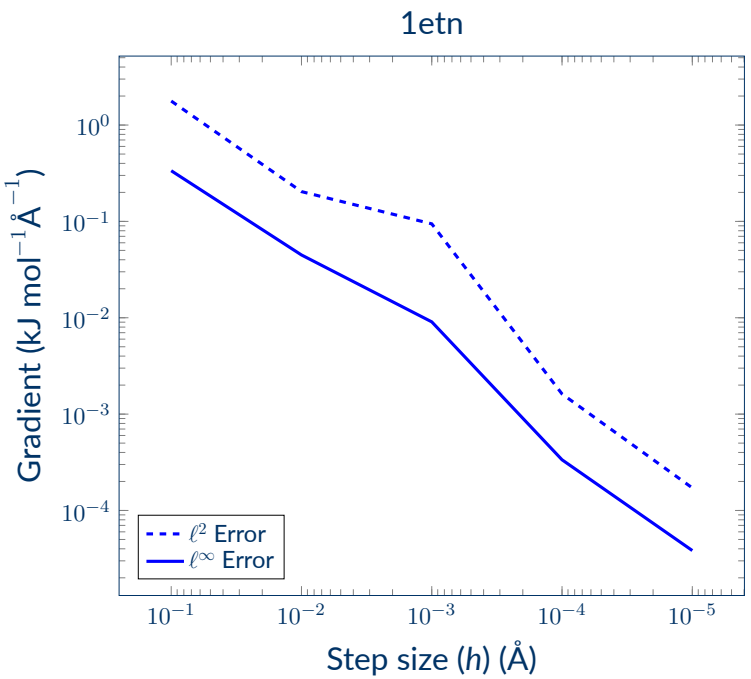
Numerical Studies

- Memory

PDB Code	ddLPB					APBS			
	ℓ_{max}	Energy (kJ/mol)	Rel. En.	Mem. (GB)	Iter.	h (Å)	Energy (kJ/mol)	Rel. En.	Mem. (GB)
1ay3 (25)	2	−126.5891	0.0323	0.0347	5	0.4353	−134.7127	0.0302	0.0215
	3	−128.4347	0.0182	0.0463	6	0.0127	−134.0656	0.0253	0.0218
	4	−129.1554	0.0127	0.0416	6	0.2213	−132.6796	0.0147	0.0638
	5	−129.6607	0.0088	0.0473	6	0.1697	−132.3780	0.0124	0.1244
	6	−129.9653	0.0065	0.0569	6	0.1333	−131.9791	0.0093	0.2448
	7	−130.1668	0.0050	0.0752	6	0.0900	−131.5849	0.0063	0.7906
	8	−130.3308	0.0037	0.0922	6				
	9	−130.4356	0.0029	0.1249	6				
	10	−130.5462	0.0021	0.1525	6				
	12	−130.6886	0.0010	0.2873	6				
1qjt (9046)	2	−18 411.4422	0.0244	1.2203	6	0.5690	−19 075.6126	0.0122	2.9358
	3	−18 603.4737	0.0142	3.1045	8	0.4840	−19 041.8281	0.0104	4.7910
	4	−18 701.0889	0.0090	6.9332	9	0.2900	−18 962.9862	0.0062	24.8033
	5	−18 757.4013	0.0060	13.7357	10				
	6	−18 793.3707	0.0041	24.7674	10				
	7	−18 819.8066	0.0027	41.5118	11				
	8	−18 839.1510	0.0017	65.6922	11				
	9	−18 853.5883	0.0009	99.2852	11				
	10	−18 864.8898	0.0003	144.5051	11				
	12	−18 880.1518	0.0005	279.6300	11				

- Analytical Forces vs Finite Difference





Conclusions and Outlook

- Conclusions[1]
  - Derivation of analytical forces for the ddLPB numerical method using the adjoint method

[1] J.,Nottoli, Quan, Stamm: arXiv : 2203.00552 , 2022

[2] ddX: https://github.com/ACoM-Computational-Mathematics/ddX

[3] Mikhalev,Nottoli, Stamm: chemrxiv : 10.26434 , 2022

[4] Geng,Kransy: JCP, 247, 62-78, 2013

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[1] J.,Nottoli, Quan, Stamm: arXiv : 2203.00552 , 2022

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