Overview of the Domain Decomposition Method for the Linear Poisson Boltzmann Equations

Abhinav Jha

Numerical Mathematics for High Performance Computing, Universität Stuttgart

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Joint work with M.Nottoli (Universität Stuttgart, Stuttgart), A.Mikhalev (RWTH Aachen University, Aachen),

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

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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

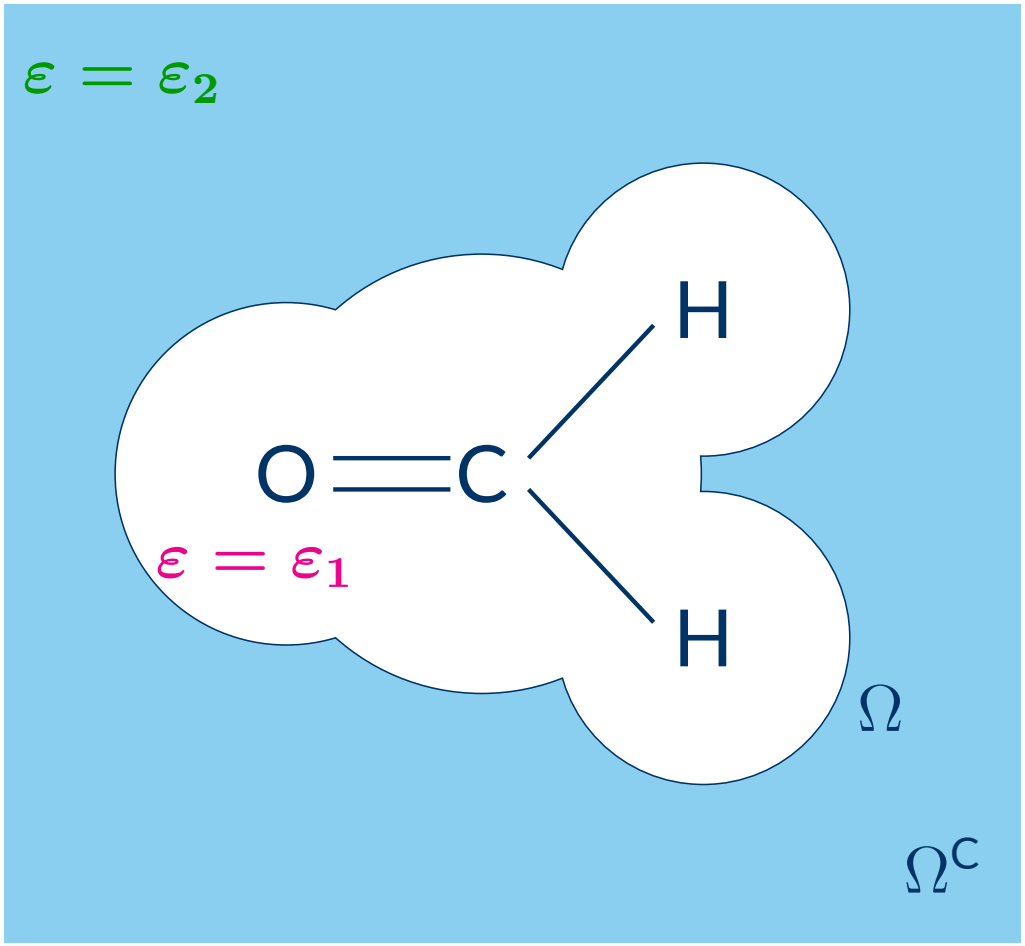

Figure 1: Formaldehyde molecule

- 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

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

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

- κ – Debye-Hückel screening constant

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

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

- 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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- Finite Difference Method (FDM)[2]

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Review of Numerical Methods

- 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

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

- Using potential theory the final equations are

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

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with

$$\begin{aligned} \psi_0 + \psi_r &= \psi_e \quad \text{on } \Gamma, \\ \sigma_e &= \partial_n\psi_e - \frac{\varepsilon_1}{\varepsilon_2}\partial_n(\psi_0 + \psi_r) \quad \text{on } \Gamma \end{aligned}$$

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Problem Transformation

- Using potential theory the final equations are

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with

$$\begin{aligned} \psi_0 + \psi_r &= \psi_e \quad \text{on } \Gamma, \\ \sigma_e &= \partial_n\psi_e - \frac{\varepsilon_1}{\varepsilon_2}\partial_n(\psi_0 + \psi_r) \quad \text{on } \Gamma \end{aligned}$$ [1]

where

- ψ_r – Reaction potential in Ω
- ψ_0 – Potential generated by ρ_M satisfying,

$$-\Delta\psi_0 = \frac{4\pi}{\varepsilon_1}\rho_M$$

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

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

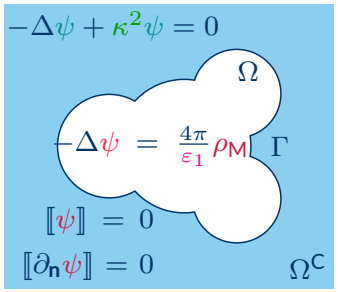
$$S_\kappa \sigma_e(x) := \int_\Gamma \frac{\exp\left(-\kappa|x-y|\right)\sigma_e(y)}{4\pi|x-y|} = \psi_e \quad \forall\, x \in \Gamma$$

- 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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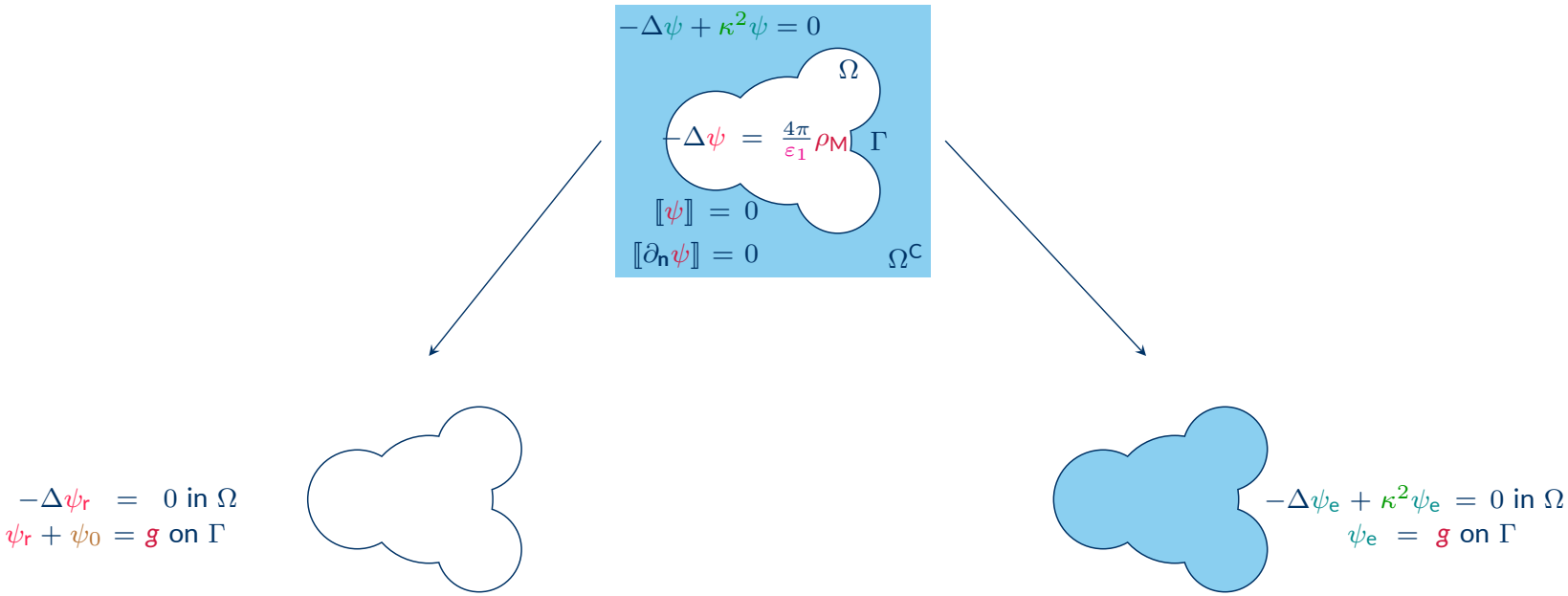

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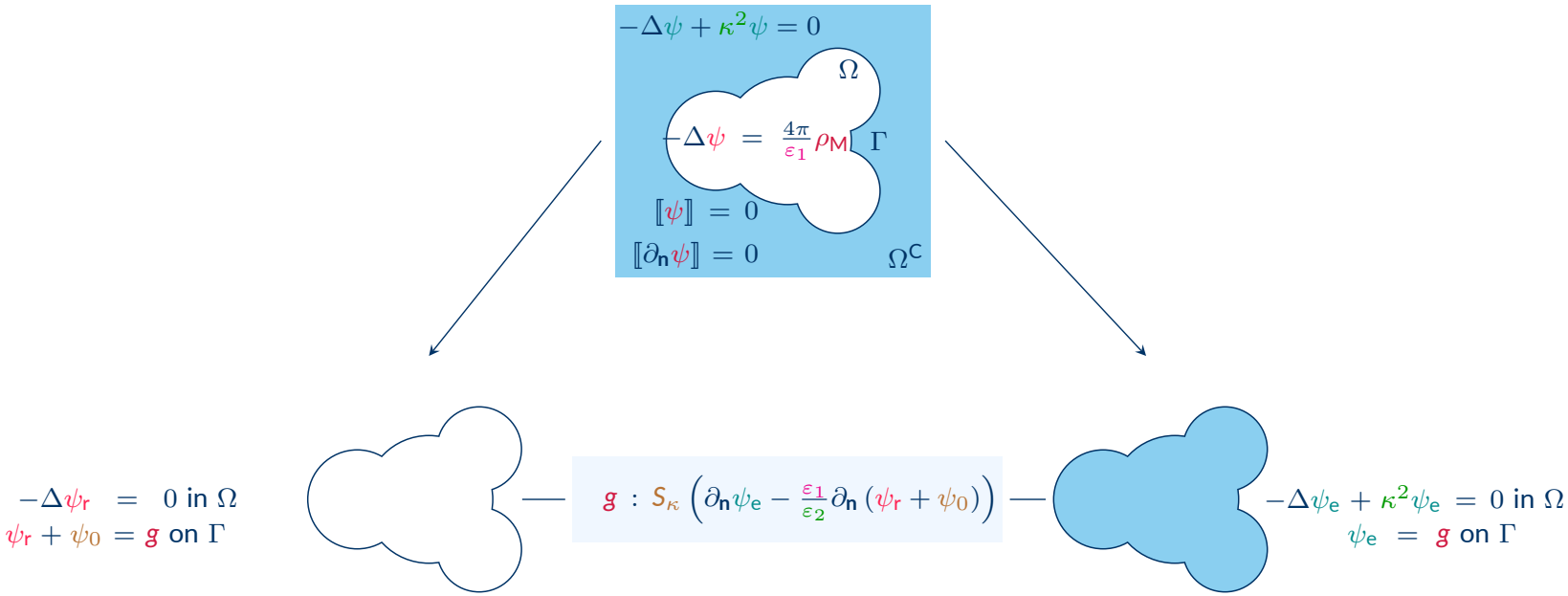

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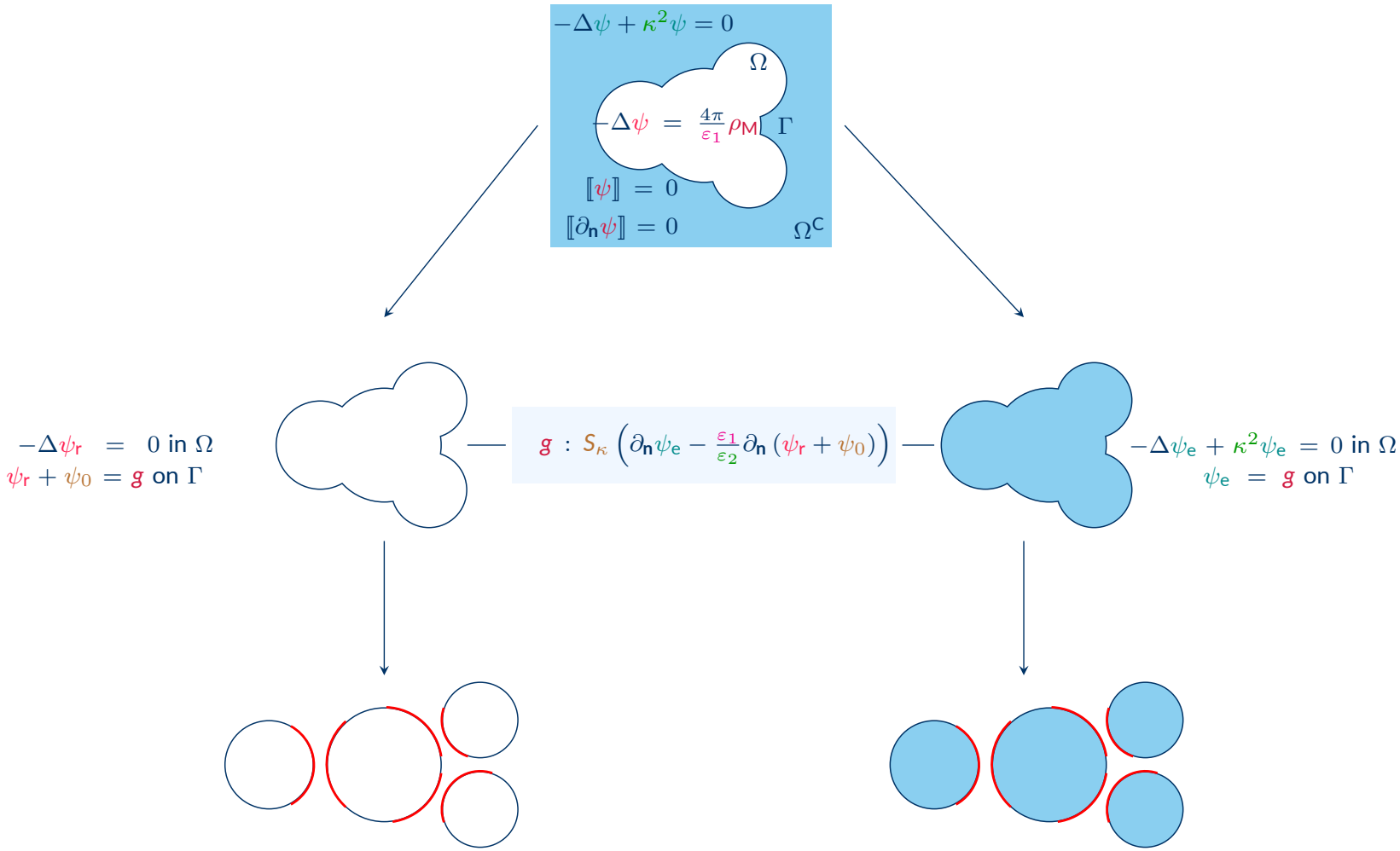
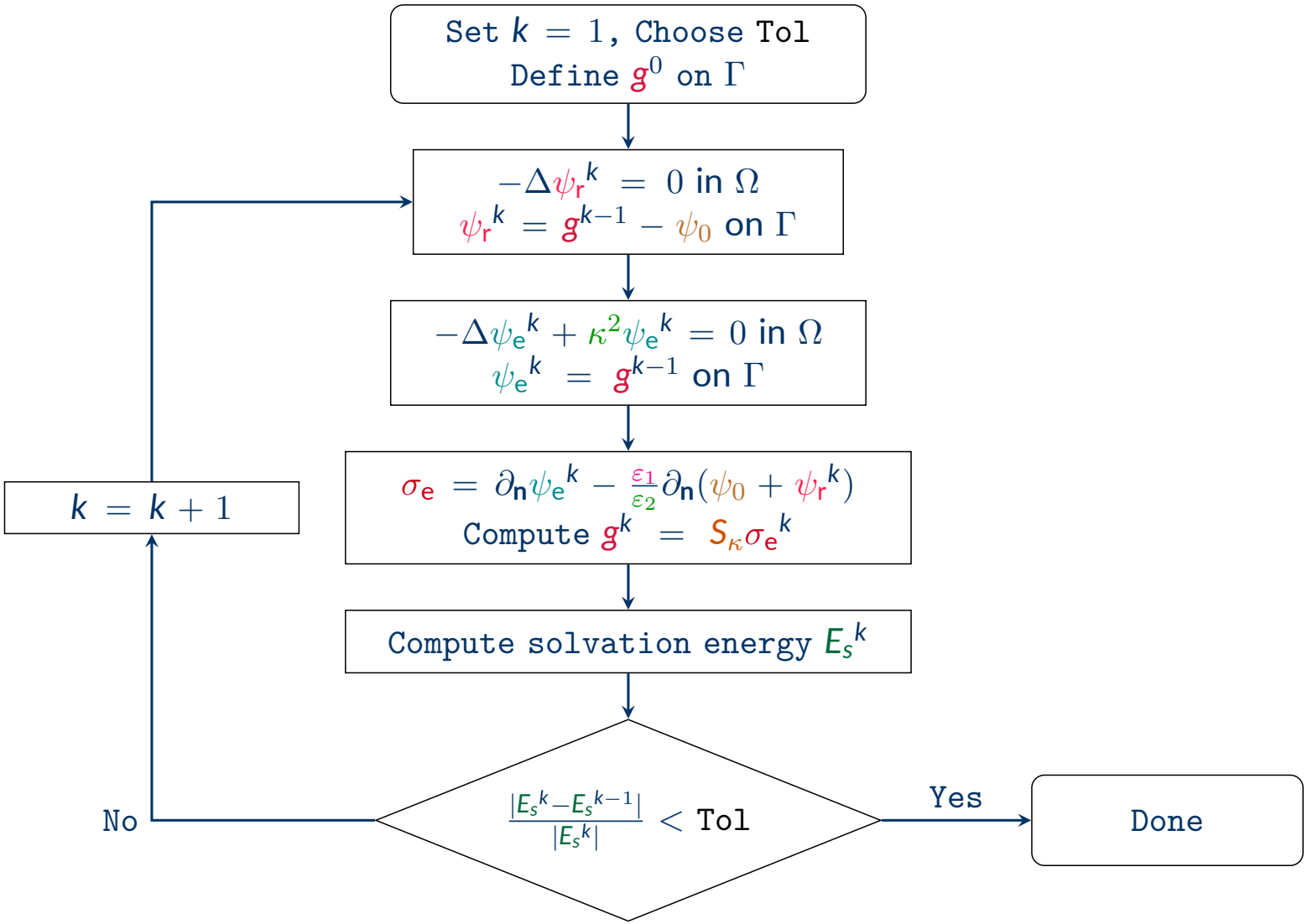


Global strategy



- According to definition of Ω

$$\Omega = \bigcup_{j=1}^{M} \Omega_j, \quad \Omega_j = B_{r_j}(x_j)$$

- Laplace equation restricted to Ω_j

$$\begin{aligned} -\Delta \psi_r|_{\Omega_j} &= 0 && \text{in } \Omega_j, \\ \psi_r|_{\Gamma_j} &= \phi_{r,j} && \text{on } \Gamma_j \end{aligned}$$

where

$$\phi_{r,j} = \begin{cases} \psi_r & \text{on } \Gamma_j^i, \\ g - \psi_0 & \text{on } \Gamma_j^e \end{cases}$$

Domain Decomposition Scheme

- HSP equation restricted to Ω_j

$$\begin{aligned} -\Delta\psi_e|_{\Omega_j} + \kappa^2\psi_e|_{\Omega_j} &= 0 && \text{in } \Omega_j, \\ \psi_e|_{\Gamma_j} &= \phi_{e,j} && \text{on } \Gamma_j \end{aligned}$$

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and

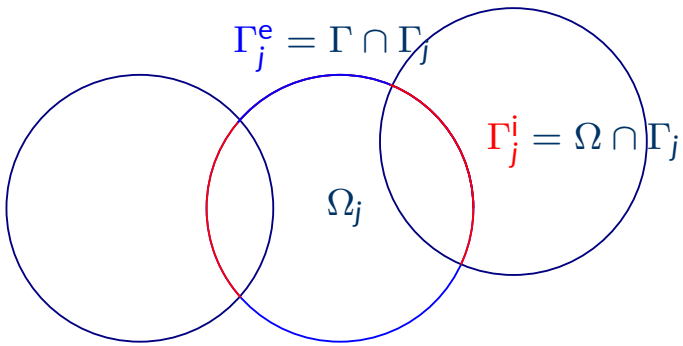

Figure 2: 2-D schematic diagram of Γ_j^i and Γ_j^e

- Laplace equation in unit ball

$$\begin{aligned} -\Delta u_r &= 0 \quad \text{in } B_1(0), \\ u_r &= \phi_r \quad \text{on } \mathbb{S}^2 \end{aligned}$$

- Unique solution in $H^1(B_1(0))$

$$u_r(r,\theta,\varphi) = \sum_{\ell=0}^{\infty} \sum_{m=-\ell}^{\ell} [\phi_r]_\ell^m r^\ell Y_\ell^m(\theta,\varphi)$$

for $0 \leq r \leq 1,\ 0 \leq \theta \leq \pi,\ 0 \leq \varphi < 2\pi$

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for $0 \leq r \leq 1,\ 0 \leq \theta \leq \pi,\ 0 \leq \varphi < 2\pi$
where

  - Y_ℓ^m – (Real orthonormal) spherical harmonics of degree ℓ and order m on $\mathbb{S}^2$
  - $[\phi_r]_\ell^m$ – Real coefficient of u_r corresponding to Y_ℓ^m

$$[\phi_r]_\ell^m = \int_{\mathbb{S}^2} \phi_r(s) Y_\ell^m(s) ds$$

- u_r can be numerically approximated by $\tilde{u}_r$

$$\tilde{u}_r(r,\theta,\varphi) = \sum_{\ell=0}^{\ell_{max}} \sum_{m=-\ell}^{\ell} \left[\tilde{\phi}_r\right]_\ell^m r^\ell Y_\ell^m(\theta,\varphi)$$

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where

  - ℓ_{max} – Maximum degree of Y_ℓ^m
  - $\left[\tilde{\phi}_r\right]_\ell^m$ – Numerical approximation of $[\phi_r]_\ell^m$

$$\left[\tilde{\phi}_r\right]_\ell^m = \sum_{n=1}^{N_{leb}} \omega_n^{leb} \phi_r(s_n) Y_\ell^m(s_n)$$

  - $s_n \in \mathbb{S}^2$ – Lebedev quadrature points
  - ω_n^{leb} – Lebedev quadrature weights
  - N_{leb} – Number of Lebedev quadrature points

- HSP equation in unit ball

$$\begin{aligned} -\Delta u_e + \kappa^2 u_e^2 &= 0 \quad \text{in } B_1(0), \\ u_e &= \phi_e \quad \text{on } \mathbb{S}^2 \end{aligned}$$

- Unique solution

$$u_e(r,\theta,\varphi) = \sum_{\ell=0}^{\infty} \sum_{m=-\ell}^{\ell} [\phi_e]_\ell^m i_\ell(r) Y_\ell^m(\theta,\varphi)$$

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for $0 \le r \le 1,\ 0 \le \theta \le \pi,\ 0 \le \varphi < 2\pi$
where

- $[\phi_e]_\ell^m$ – Coefficient of Y_ℓ^m
- $i_\ell(r)$ – Bessel functions of the first kind

- u_e can be numerically approximated by $\tilde{u}_e$

$$\tilde{u}_e(r,\theta,\varphi) = \sum_{\ell=0}^{\ell_{max}} \sum_{m=-\ell}^{\ell} \left[\tilde{\phi}_e\right]_\ell^m \frac{i_\ell(r)}{i_\ell(1)} Y_\ell^m(\theta,\varphi)$$

for $0 \leq r \leq 1,\ 0 \leq \theta \leq \pi,\ 0 \leq \varphi < 2\pi$

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where

- $\left[\tilde{\phi}_e\right]_\ell^m$ – Numerical approximation of $[\phi_e]_\ell^m$

$$\left[\tilde{\phi}_e\right]_\ell^m = \sum_{n=1}^{N_{leb}} \omega_n^{leb} \phi_e(s_n) Y_\ell^m(s_n)$$

- Rewriting the coupling equations as

$$\psi_r|_{\Gamma_j}(x) - \sum_{i \neq j} \omega_{ji}(x)\psi_r|_{\Omega_i}(x) = \chi_j^e(x)(g(x) - \psi_0(x)) \quad \forall x \in \Gamma_j$$

and

$$\psi_e|_{\Gamma_j}(x) - \sum_{i \neq j} \omega_{ji}(x)\psi_e|_{\Omega_i}(x) = \chi_j^e(x)g(x) \quad \forall x \in \Gamma_j$$

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where

- $\chi_j^e(x) := \begin{cases} 1 & \text{if } x \in \Gamma_j^e, \\ 0 & \text{if } x \in \Gamma_j^i. \end{cases}$, $\omega_{ji}(x) := \dfrac{\chi_i(x)}{\sum_{k \neq j} \chi_k(x)}$

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- $\chi_j^e(x) = 1 - \sum_{i \neq j} \omega_{ji}(x) \quad \forall x \in \Gamma_j$

- Reformulating the global coupling condition over each sphere Γ_i

$$g(x) = \sum_{i=1}^{M} \tilde{S}_{\kappa,\Gamma_i} \left[\chi_i^e \left(\partial_{\mathbf{n}} \psi_e - \frac{\varepsilon_1}{\varepsilon_2} \partial_{\mathbf{n}} (\psi_0 + \psi_r) \right) \right] (x) \qquad \forall x \in \Gamma$$

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where

  - $$\tilde{S}_{\kappa,\Gamma_i} \sigma_e(x) := \int_{\Gamma_i} \frac{\exp(-\kappa |x-y|) \sigma_e(y)}{4\pi |x-y|} \qquad \forall x \in \mathbb{R}^3$$

- Using $x\ (\in \Gamma_j) = x_j + r_j s$ for $s \in \mathbb{S}^2$, the coupling equation is

$$\psi_r|_{\Gamma_j}(x_j + r_j s) - \sum_{i \neq j} \omega_{ji}(x_j + r_j s)\psi_r|_{\Omega_i}(x_j + r_j s)$$
$$= \chi_j^e(x_j + r_j s)\left(g(x_j + r_j s) - \psi_0(x_j + r_j s)\right)$$

- Multiplying by Y_ℓ^m and integrating over $\mathbb{S}^2$

$$\left\langle \psi_r|_{\Gamma_j}(x_j + r_j \bullet) - \sum_{i \neq j} \omega_{ji}(x_j + r_j \bullet)\psi_r|_{\Omega_i}(x_j + r_j \bullet), Y_\ell^m(\bullet) \right\rangle_{\mathbb{S}^2}$$
$$= \left\langle \chi_j^e(x_j + r_j \bullet)\left(g(x_j + r_j \bullet) - \psi_0(x_j + r_j \bullet)\right), Y_\ell^m(\bullet) \right\rangle_{\mathbb{S}^2} \quad \forall\, j, \ell, m$$

- Moving from unit ball to Ω_i

$$\psi_r|_{\Omega_i}(x_i + rs) = \sum_{\ell'=0}^{\ell_{\max}} \sum_{m'=-\ell'}^{\ell'} [X_r]_{i\ell'm'} \left(\frac{r}{r_i}\right)^{\ell'} Y_{\ell'}^{m'}(s), \quad 0 \le r \le r_i,\ s \in \mathbb{S}^2$$

and

$$\partial_n \psi_r(x_i + rs) = \sum_{\ell'=0}^{\ell_{\max}} \sum_{m'=-\ell'}^{\ell'} [X_r]_{i\ell'm'} \left(\frac{\ell'}{r_i}\right) Y_{\ell'}^{m'}(s), \quad x_i + r_i s \in \Gamma_i^e$$

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  - $[X_r]_{j\ell m}$ – Unknown coeffecients of the mode Y_ℓ^m

- Using Lebedev quadrature the final linear system of equations are

$$[\mathbf{A}X_r]_{j\ell m} = [\mathbf{G}_X]_{j\ell m} + [\mathbf{G}_0]_{j\ell m} \quad \forall j, \ell, m$$

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where

- $\mathbf{A}-$ $\mathrm{M}(\ell_{\max}+1)^2 \times \mathrm{M}(\ell_{\max}+1)^2$ matrix

$$[\mathbf{A}X_r]_{j\ell m} = [X_r]_{j\ell m} - \sum_{i\neq j}\sum_{\ell',m'} \left(\sum_{n=1}^{N_{\text{leb}}} \omega_n^{\text{leb}} \omega_{ji} (x_j + r_j s_n) \left(\frac{r_{ijn}}{r_i}\right)^{\ell'} Y_{\ell'}^{m'}(s_{ijn}) Y_\ell^m(s_n) \right) \times [X_r]_{i\ell' m'}$$

- $(r_{ijn}, s_{ijn})-$ Spherical coordinates of $x_j + r_j s_n$ associated with Γ_i

$$x_j + r_j s_n = x_i + r_{ijn} s_{ijn} \quad \text{with} \quad s_{ijn} \in \mathbb{S}^2$$

- $[\mathbf{G}_X]_{jlm} = \sum_{n=1}^{N_{\text{leb}}} \omega_n^{\text{leb}} \chi_j^e(x_j + r_j s_n) g(x_j + r_j s_n) Y_\ell^m(s_n)$
- $[\mathbf{G}_0]_{jlm} = -\sum_{n=1}^{N_{\text{leb}}} \omega_n^{\text{leb}} \chi_j^e(x_j + r_j s_n) \psi_0(x_j + r_j s_n) Y_\ell^m(s_n)$

- Similarly for the 2^{nd} coupling equation

$$[\mathbf{B}\mathbf{X}_e]_{j\ell m} = [\mathbf{G}_X]_{j\ell m} \quad \forall j, \ell, m$$

- $[\mathbf{G}_X]_{jlm} = \sum_{n=1}^{N_{\text{leb}}} \omega_n^{\text{leb}} \chi_j^e(x_j + r_j s_n) g(x_j + r_j s_n) Y_\ell^m(s_n)$
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where

$$[\mathbf{B}X_e]_{j\ell m} = [X_e]_{j\ell m} - \sum_{i \neq j} \sum_{\ell', m'} \left(\sum_{n=1}^{N_{\text{leb}}} \omega_n^{\text{leb}} \omega_{ji}(x_j + r_j s_n) \left(\frac{i_{\ell'}(r_{ijn})}{i_{\ell'}(r_i)} \right) Y_{\ell'}^{m'}(s_{ijn}) Y_\ell^m(s_n) \right) \times [X_e]_{i\ell' m'}$$

- Linear System

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

- Using definition of g

$$\mathbf{G}_X = \mathbf{F}_0 - \mathbf{C}_1 X_r - \mathbf{C}_2 X_e$$

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- $\mathbf{F}_0$ – Associated with $\partial_{\mathbf{n}}\psi_0$
- $\mathbf{C}_1$ – Associated with $\partial_{\mathbf{n}}\psi_r$
- $\mathbf{C}_2$ – Associated with $\partial_{\mathbf{n}}\psi_e$

- Using the global strategy

$$\begin{bmatrix} \mathbf{A} & 0 \\ 0 & \mathbf{B} \end{bmatrix} \begin{bmatrix} {X_r}^k \\ {X_e}^k \end{bmatrix} = - \begin{bmatrix} \mathbf{C}_1 & \mathbf{C}_2 \\ \mathbf{C}_1 & \mathbf{C}_2 \end{bmatrix} \begin{bmatrix} {X_r}^{k-1} \\ {X_e}^{k-1} \end{bmatrix} + \begin{bmatrix} \mathbf{G}_0 + \mathbf{F}_0 \\ \mathbf{F}_0 \end{bmatrix}$$

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

- 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,

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

and

$$\langle X, Q \rangle_j = \sum_{\ell} [X]_{j\ell} [Q]_{j\ell} .$$

[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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- $\mathsf{L}X = g$ 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 $\nabla^\lambda X$

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

- Accuracy of the Discretisation

[1] Mikhalev,Nottoli, Stamm: JCP : 157(11),114103 , 2022

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

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

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- Accuracy of the Discretisation
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  - Comparison with other software[2,3]

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

[1] Herbst, J., Lipparini, Mikhalev, Notolli, Stamm, ddX: https://github.com/ddsolvation/ddX

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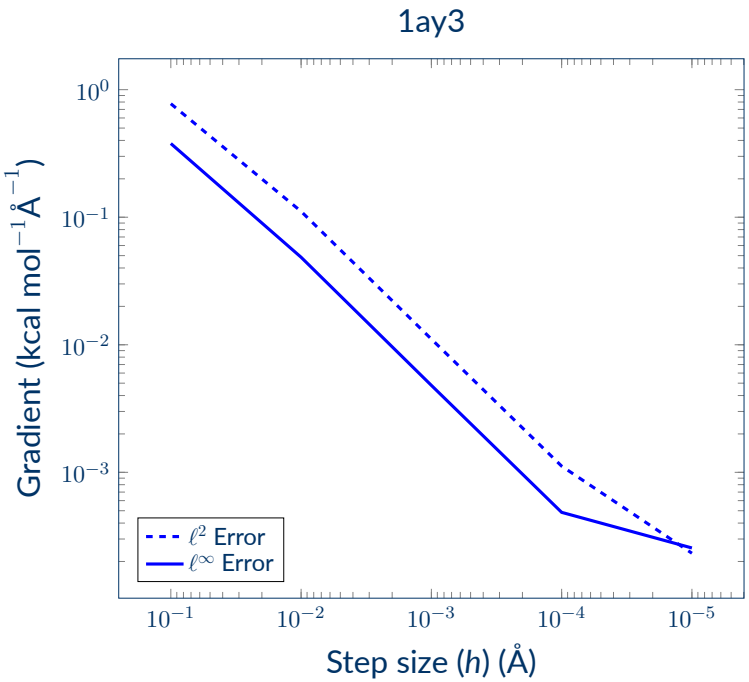
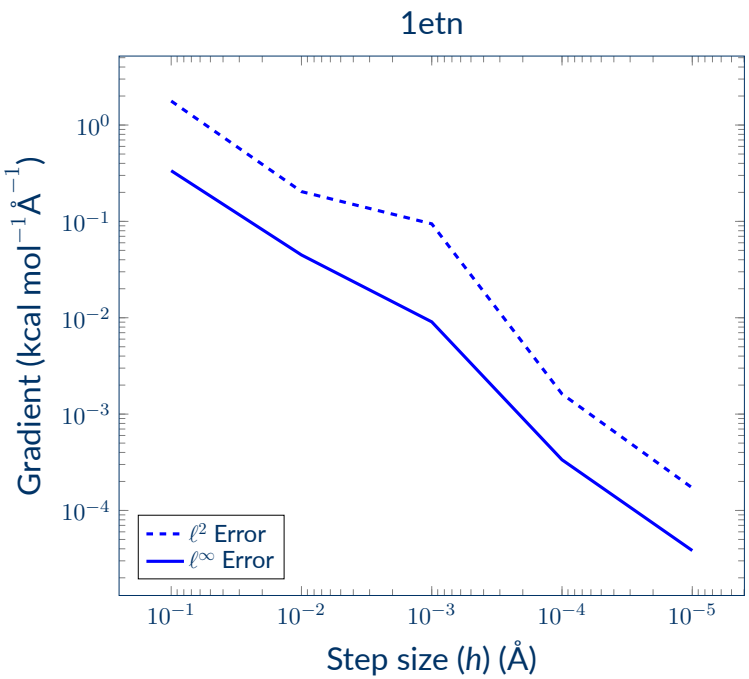
- Test Structures[2]

PDB Code	M	Name
1ay3	25	Nodularin
1etn	180	Enterotoxin
1du9	380	Scorpion toxin
1d3w	2049	Ferredoxin
1jvu	3964	Ribonuclease A
1qjt	9046	EH1 domain
1a3n	10087	Human haemoglobin
1ju2	20260	Hydroxynitrile lyase

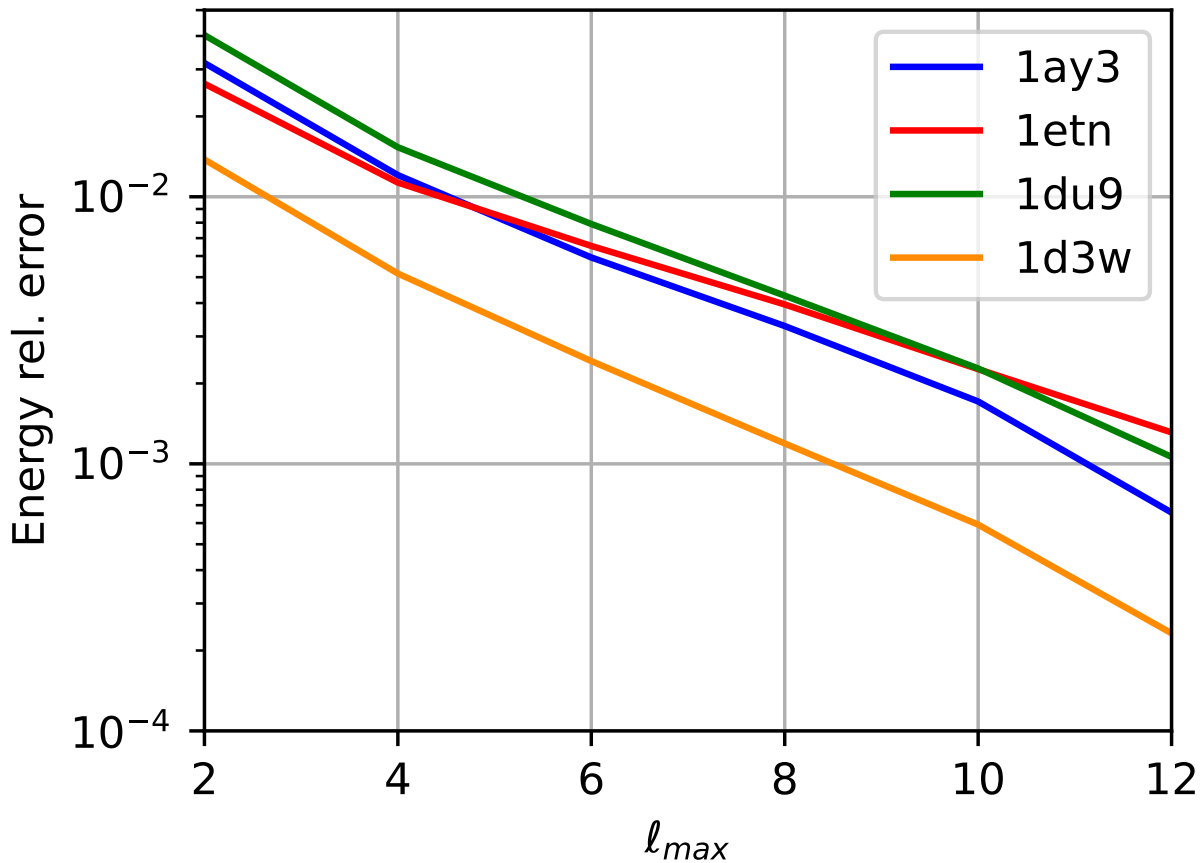
[2] Berman et. al. : NAR 28, 235-242, 2000

- Analytical Forces vs Finite Difference

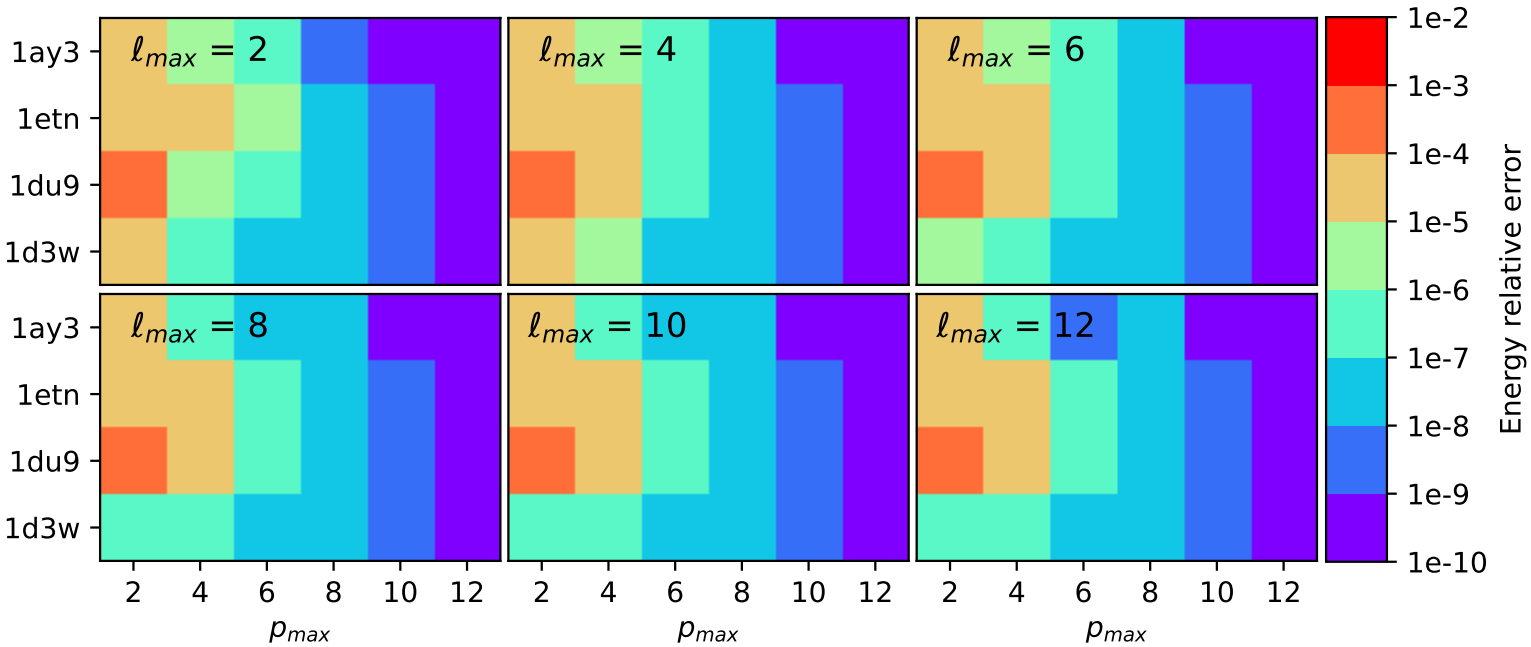




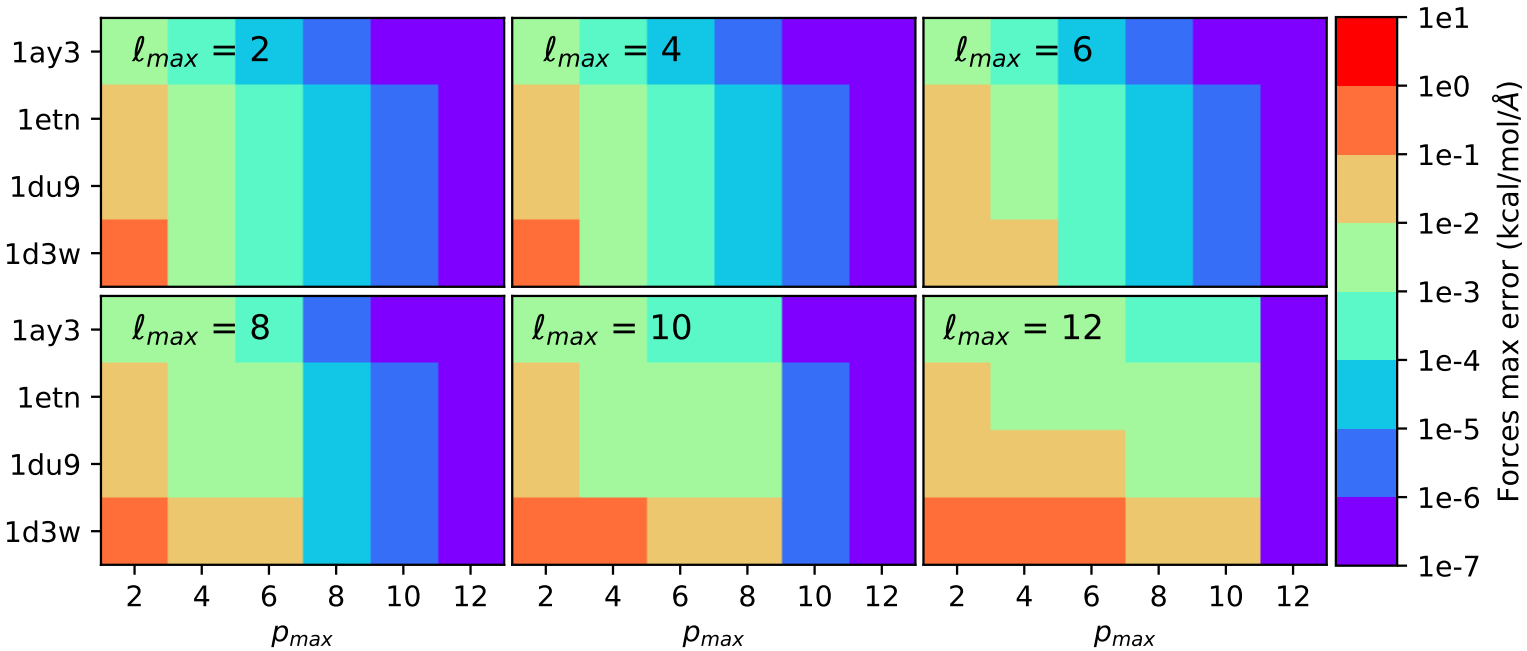
- Relative error of the Energy



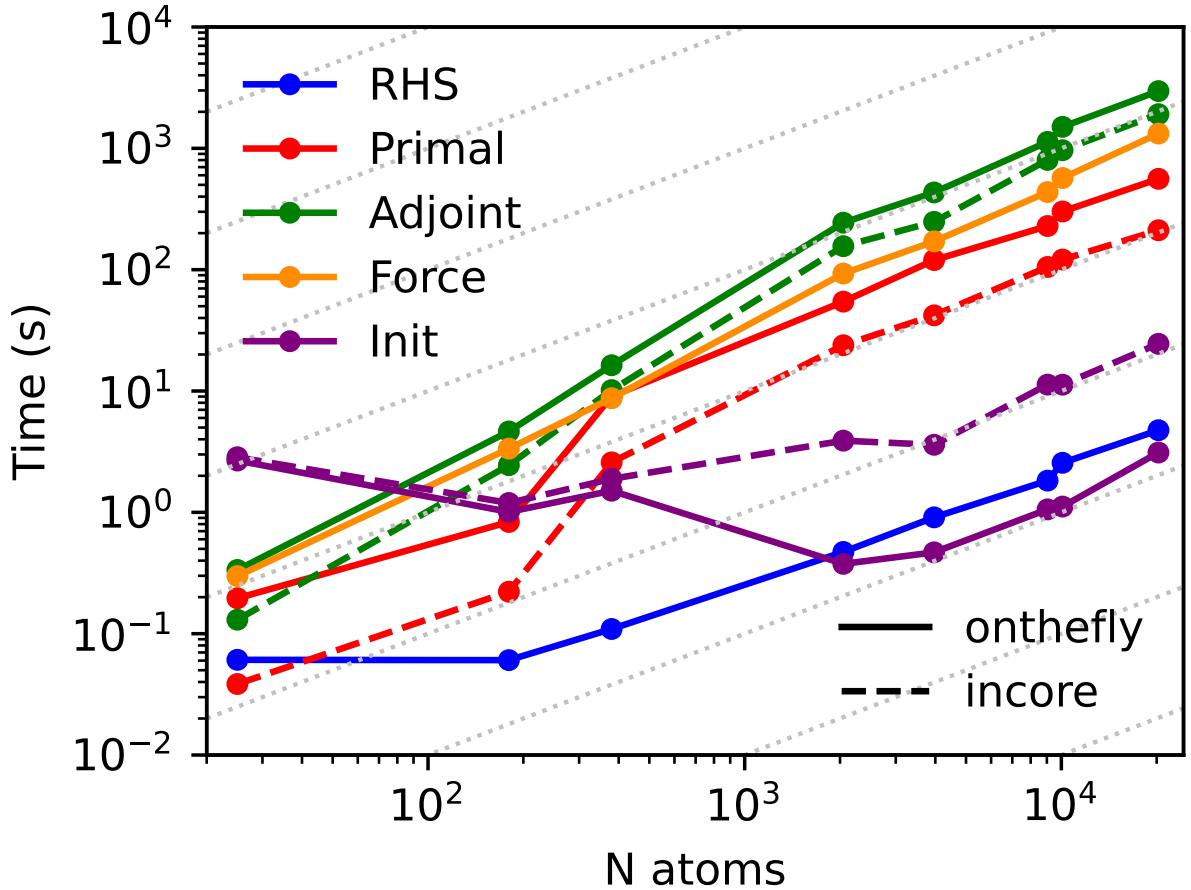
- Absolute error of the Energy



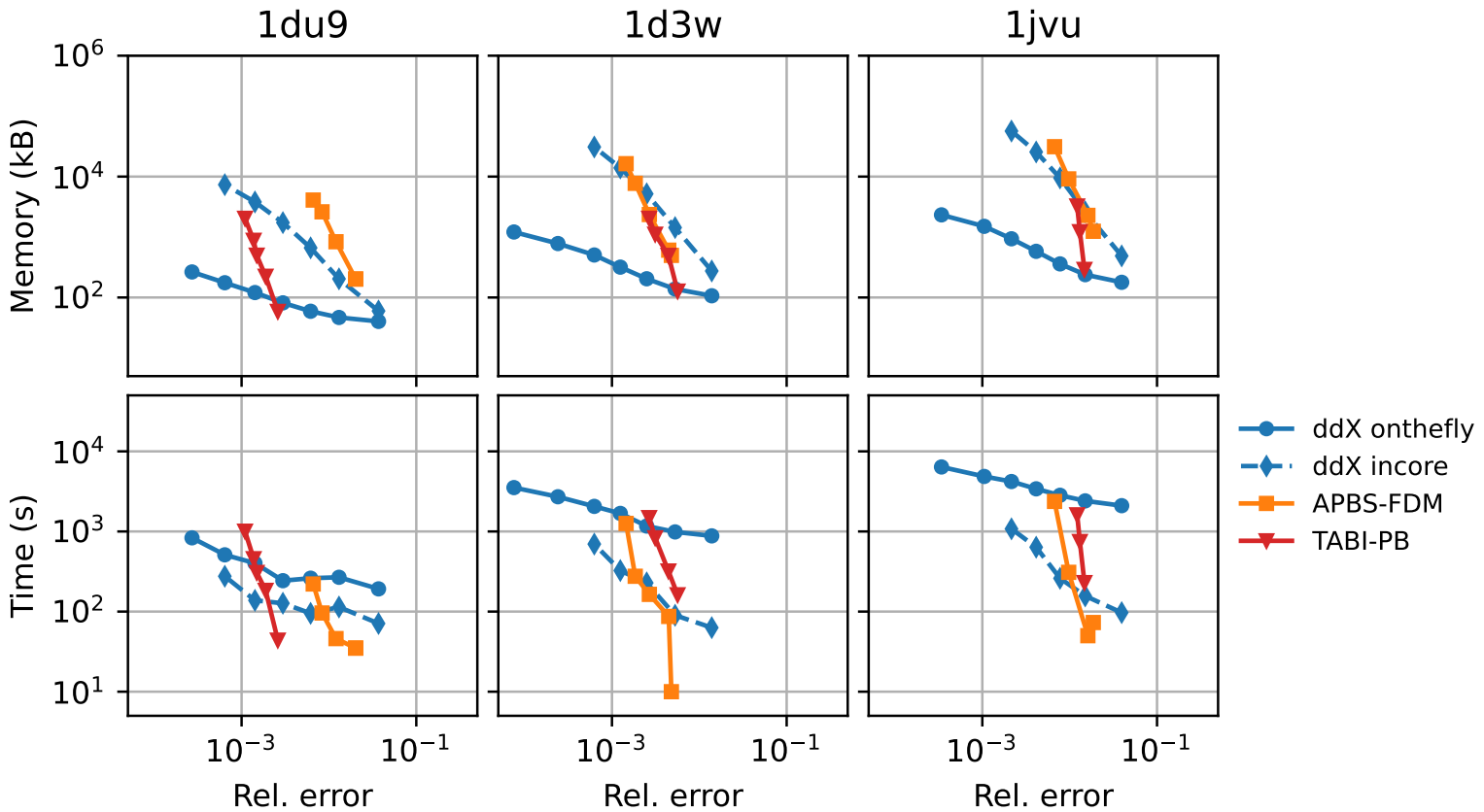
- Maximum Absolute error of the Forces



- Time and Memory for one ddLPB calculation



- Comparison with other Software



Conclusions and Outlook

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

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