Fast algorithms for implicit solvation models

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Ecole des Pontes and INRIA

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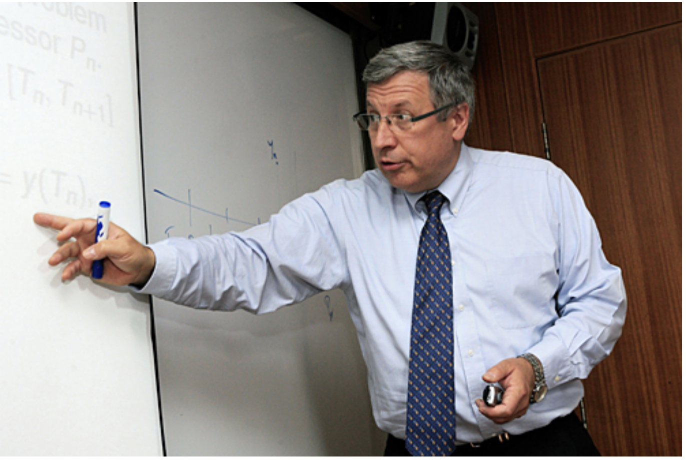
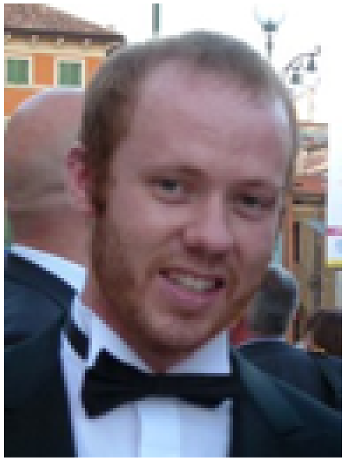
Joint work with

Yvon Maday (Math., Paris 6)



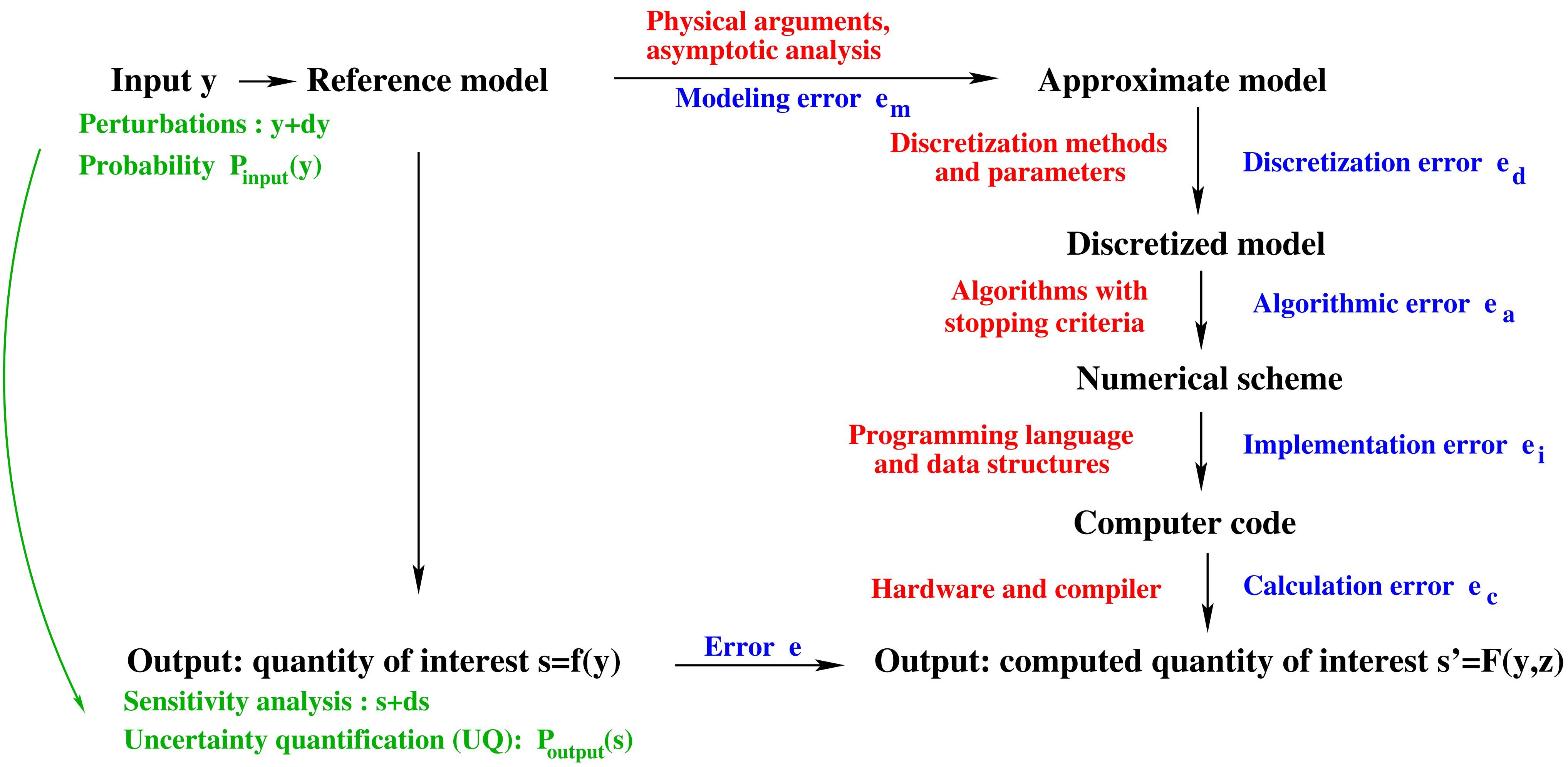
Benjamin Stamm (Math., Paris 6)

Benedetta Mennucci (Chem., Pisa)



Filippo Lipparini (Chem., Paris 6)

Sources of errors in numerical simulations



Input y ⟶ Reference model

Perturbations : y+dy

Probability $P_{input}(y)$

Physical arguments, asymptotic analysis

Modeling error e_m

Approximate model

Discretization methods and parameters

Discretization error e_d

Discretized model

Algorithms with stopping criteria

Algorithmic error e_a

Numerical scheme

Programming language and data structures

Implementation error e_i

Computer code

Hardware and compiler

Calculation error e_c

Output: quantity of interest s=f(y)

Sensitivity analysis : s+ds

Uncertainty quantification (UQ): $P_{output}(s)$

Error e

Output: computed quantity of interest s’=F(y,z)

Global error: $e = s' - s = F(y,z) - f(y) = e_m + e_d + e_a + e_i + e_c$

Modeling error e_{m}

- **Asymptotic limits:**
  - **Born-Oppenheimer approximation (small parameter: $m_{\mathrm{electron}}/m_{\mathrm{nucleus}}$)**
    Single switch trajectory (Lasser et al '10) vs Tully's surface hopping.
  - **Semiclassical limit (large nuclear charge Z, small parameter: Z^{-1})**
    Example: for neutral atoms,

$$|E^{N-\mathrm{body}}(Z) - E^{\mathrm{HF}}(Z)| \leq C_\varepsilon Z^{5/3-\varepsilon} \quad \textbf{(Fefferman '90, Bach '92)}$$

    Useful to construct new XC functionals for DFT (Burke et al.)?

- **Heuristic choices of suitable**
  - **exchange-correlation functional**
  - **solvation model (explicit vs implicit)**
  - **coupling/transfer schemes in multiscale methods.**

Can machine learning help (range of applicability of a model, error bars)?

Discretization error $\mathrm{e_d}$

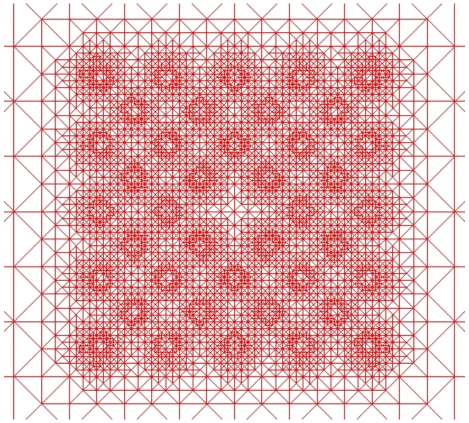
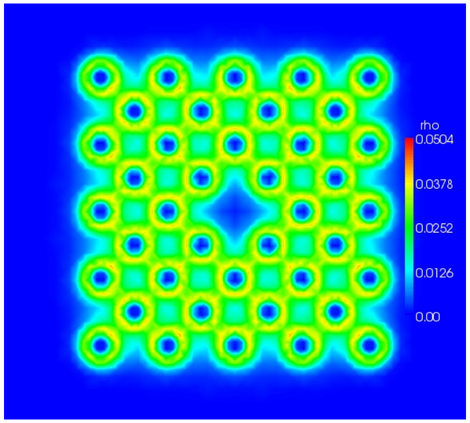
- ***A priori*** **error estimators.**

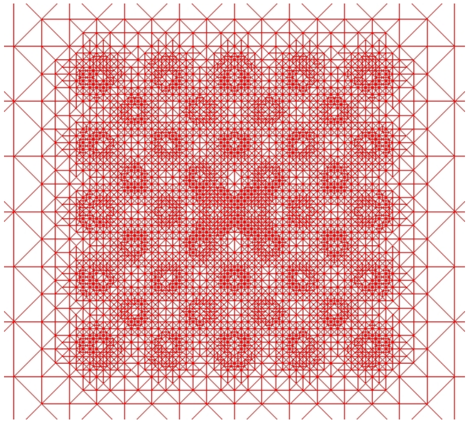
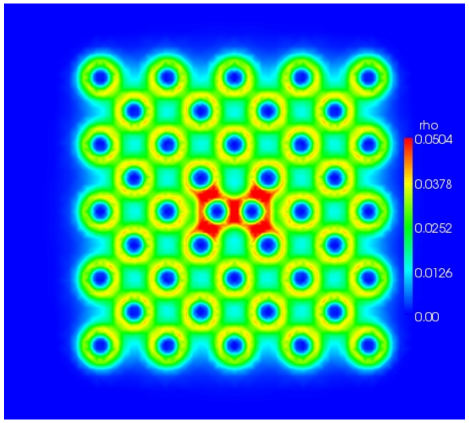
  Example: for planewave Kohn-Sham LDA calculations with Troullier-Martins pseudopotentials (E.C., Chakir, Maday '12),

$$\|\rho^0_{E_{\rm c}} - \rho^0\|_{W^{1,3/2}_{\rm per}} \le CE_{\rm c}^{-2.25} \qquad \|\rho^0_{E_{\rm c}} - \rho^0\|_{L^2_{\rm per}} \le CE_{\rm c}^{-2.75}$$

$$|\varepsilon^0_{i,E_{\rm c}} - \varepsilon^0_i| \le CE_{\rm c}^{-4.5} \qquad |E^0_{E_{\rm c}} - E^0| \le CE_{\rm c}^{-4.5}$$

- ***A posteriori*** **error estimators (courtesy A. Zhou).**

Algorithmic error e_{a}

**DIIS (Pulay ’80, default SCF algorithm in Gaussian 98) vs
EDIIS (Kudin, Scuseria, E.C. ’02, default SCF algorithm in G. 03 / G. 09).**

System	E^{RHF}(initial guess)	Min DIIS (Ha)	Min EDIIS (Ha)	ΔE (kcal/mol)
CH_3-NH-CH=CH-NO_2 6-31G	-374.0038 -322.2373	-375.3869 Does not CV	-375.3869 -375.3869	0 Undefined
Cr_2 6-31G	-2069.5400 -2051.4339	-2085.5449 -2085.4042	-2085.8060 -2085.8060	163.71 251.93
$[Fe(H_2O)_6]^{2+}$ 178 AO	-1700.7596 -1538.7283	-1717.8928 -1717.7355	-1718.0151 -1718.0151	76.68 175.31

Implementation error e_i

- **Human error (bugs): manual/automatic code validation.**
- **Finite arithmetic errors:**
  - **Round-off error: the approximation of the number 0.1 on 24 bits in the internal clock of Patriot missiles lead to a 500 m drift every 100 h.**
  - **Truncation vs round-off: Vancouver stock exchange droped from 1,000 to 520 instead of going up to 1,089 in a few months.**
  - **Overflow error: the Ariane 5 rocket launched on the 4th of June 1996 crashed because of overflow errors during the conversion of 64-bit floating point numbers into 16-bit signed integers.**

Computing error e_c

Resiliency will be one of the toughest challenges in future exascale systems. Memory errors contribute more than 40% of the total hardware-related failures and are projected to increase in future exascale systems. The use of error correction codes (ECC) and checkpointing are two effective approaches to fault tolerance. (Li et al. 2011)

Various aims

1. **Design a converging numerical method: for any tolerance $\varepsilon_{\rm tol}$, find a numerical method such that**

$$\|\mathbf{e}\| \le \varepsilon_{\rm tol}.$$

2. **Minimize the computational cost (CPU, memory) to obtain the desired accuracy.**

3. **Minimize the error for given computational means (do the best you can with what you have at hand).**

These aims require

- **a deep understanding of the models, numerical methods, and coding**
- **error estimators for each component of the error**

$\longrightarrow$ **error equilibration and adaptivity ... in presence of error cancellation**

Outline of the talk

1. Implicit solvation models

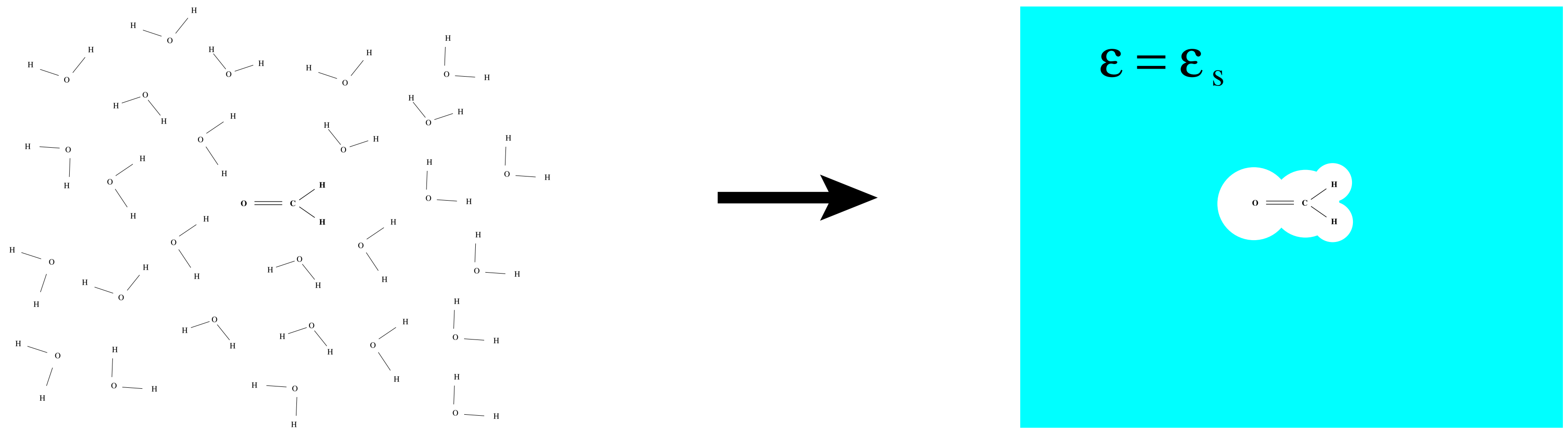
2. Integral equation methods

3. A new domain decomposition approach

4. Conclusion and perspectives

1 - Implicit solvation models

- Solvation is a fundamental phenomenon in chemistry.
- The solvent can tune the solute’s properties and reactivity.
- Most experimental data are measured in solution.



Very costly
explicit solvation model

Cheap (and sometimes accurate enough)
implicit solvation model

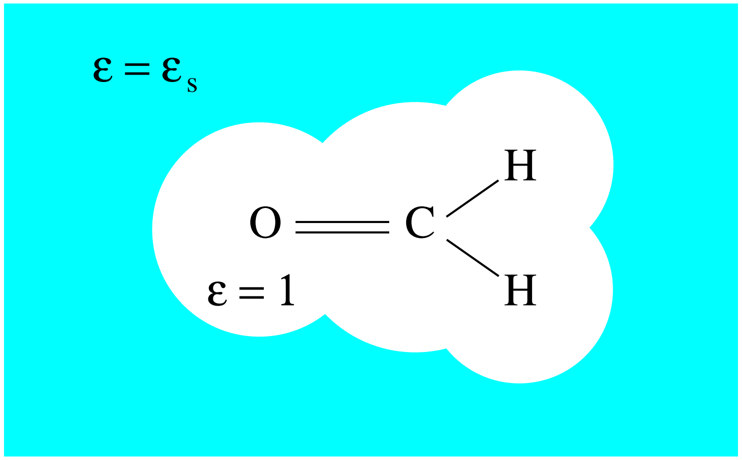
The PCM model

The electrostatic potential is obtained by solving the Poisson equation

$$-\mathrm{div}\left(\varepsilon(\mathbf{r})\nabla V(\mathbf{r})\right) = 4\pi\rho(\mathbf{r}) \quad \textbf{with} \quad \varepsilon(\mathbf{r}) = \left| \begin{array}{ll} 1 & \textbf{inside } \Omega \\ \varepsilon_{\mathrm{s}} & \textbf{outside } \Omega \end{array} \right.$$

where ρ is the charge distribution carried by the solute:

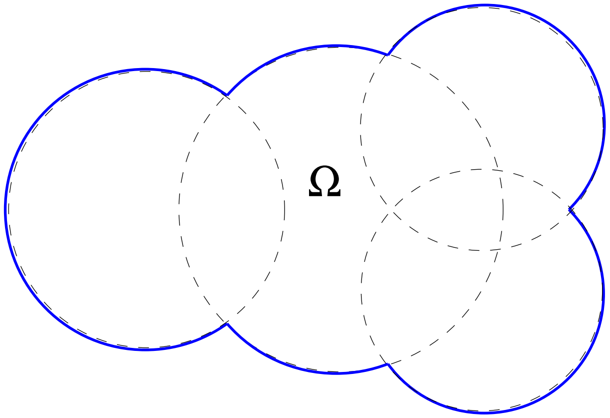
- **point charges and dipoles in classical molecular dynamics**
- **point charges (nuclei) and electronic densities for quantum models.**



Van der Waals molecular cavity

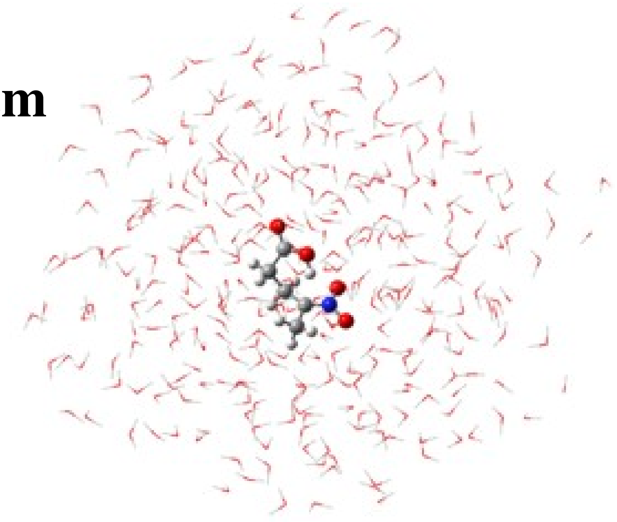
$$\Omega = \bigcup_{i=1}^{M} B(\mathbf{R}_j, r_j)$$

- $B(\mathbf{R}, r)$ **is the ball of** $\mathbb{R}^3$ **with center** R **and radius** r**,**
- $\mathbf{R}_j \in \mathbb{R}^3$ **is the position of the** j^{th} **atom (or nucleus),**
- $r_j = 1.2 \times r_j^{\mathrm{VdW}}$ **(for neutral solutes).**



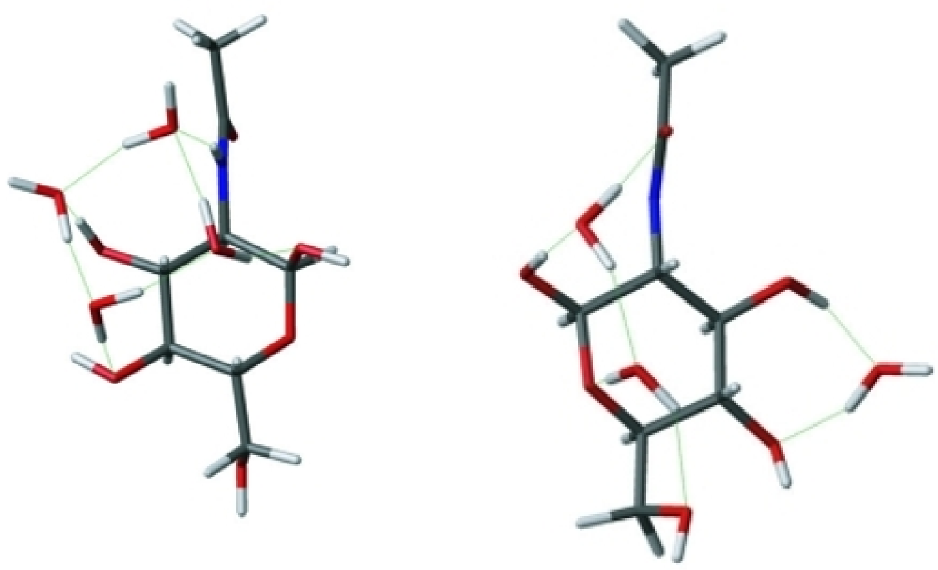
Other kinds of molecular cavities: **solvent accessible surfaces, solvent excluded surfaces, isodensity surfaces, ...**

Pros and cons of implicit solvation models



- dramatic reduction of the size of the simulated system
- no need to sample the phase space
- account for long-range electrostatic effects
- easy to couple with MD, QM, QM/MM, TDDFT

- empirical models
- work poorly in the presence of specific interactions between solute and solvent molecules (e.g. Hydrogen bonds).

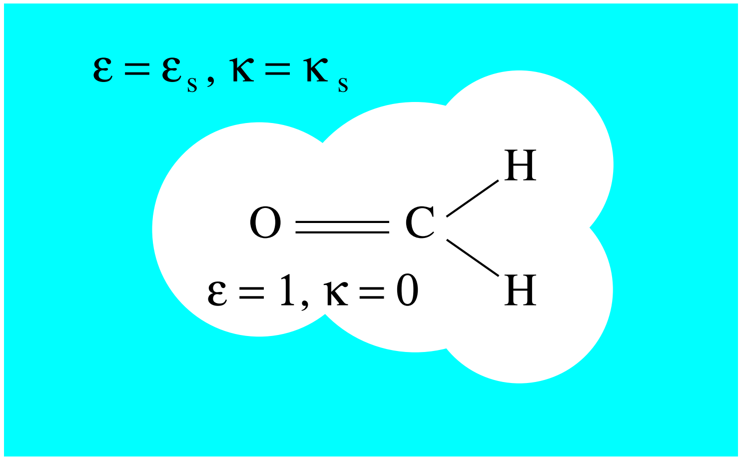


It is however possible to include a few explicit solvent molecules in the simulated system.

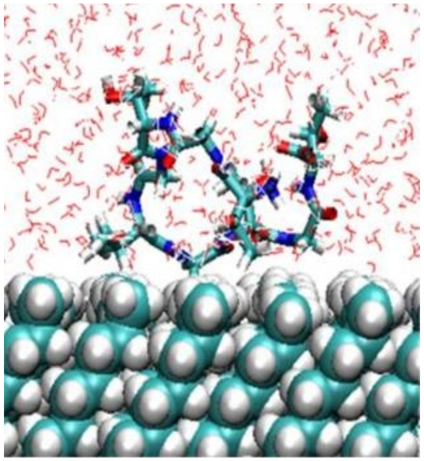
More sophisticated implicit solvation models for

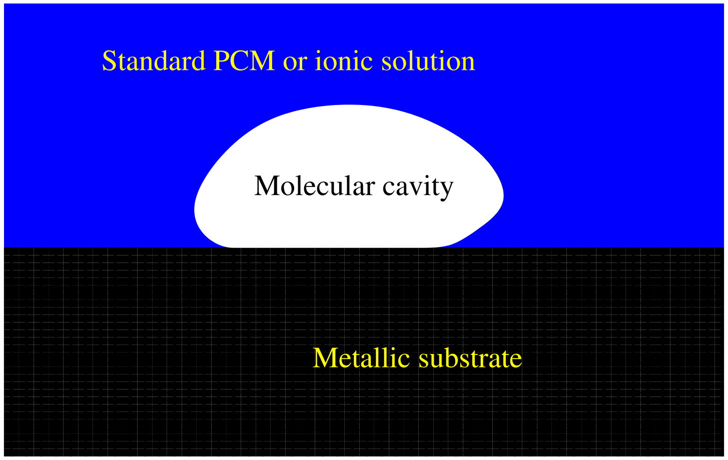
- **Ionic solutions:**
  - **nonlinear Poisson-Boltzmann equation**
  - **Debye-Hückel model (linearized PB equation)**
  - **finite-size effects of the ions (Li et al.)**
- **strong fields: nonlinear PCM for dipolar liquids (Arias et al.)**

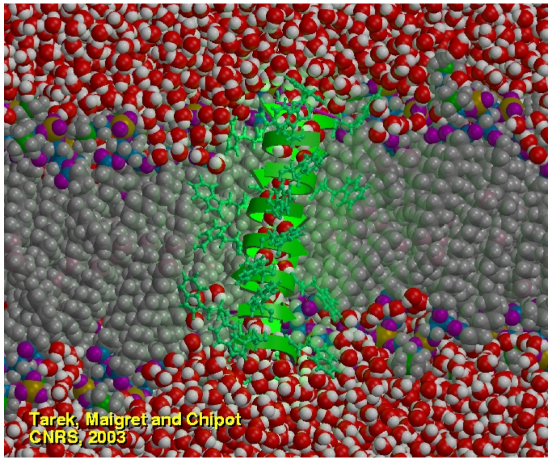
Ex.: Debye-Hückel model $-\mathrm{div}\left(\varepsilon(\mathbf{r})\nabla V(\mathbf{r})\right) + \varepsilon(\mathbf{r})\kappa(\mathbf{r})^2 V(\mathbf{r}) = 4\pi\rho(\mathbf{r})$

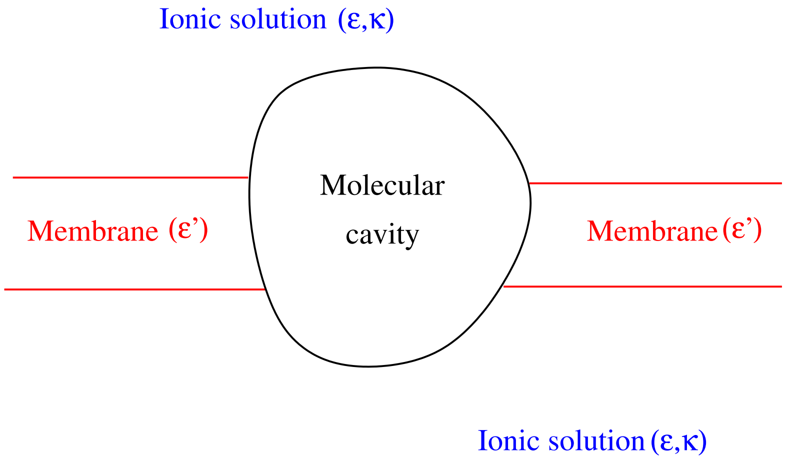


Complex environments with several interfaces



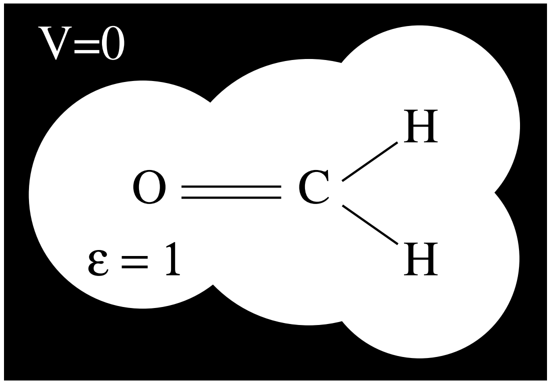



Tarek, Maigret and Chipot
CNRS, 2003



**COnducting-like Screening MOdel (COSMO, Klamt & Schüürmann '93)
Also called C-PCM (see talk by Sharon Hammes-Schiffer)**

$$\begin{cases} -\Delta V = 4\pi\rho & \textbf{in } \Omega, \\ V = 0 & \textbf{on } \Gamma = \partial\Omega, \end{cases}$$



$$\begin{cases} -\Delta W = 0 & \textbf{in } \Omega \\ W = -\Phi & \textbf{on } \Gamma \end{cases}$$

Potential generated by ρ in the vacuum: $\Phi(\mathbf{r}) = \int_{\mathbb{R}^3} \frac{\rho(\mathbf{r}')}{|\mathbf{r}-\mathbf{r}'|}\, d\mathbf{r}'$**.**

Reaction potential: $W = V - \Phi$

Electrostatic component of the solvation energy: $E_{\mathrm{C}}^{\mathrm{s}} = \frac{1}{2} f(\varepsilon_{\mathrm{s}}) \int_{\Omega} \rho W$

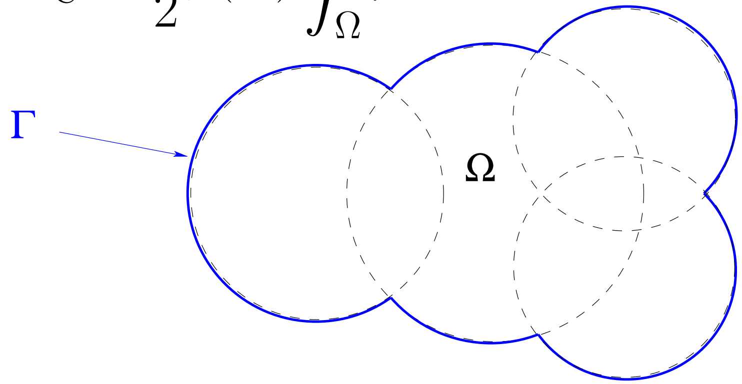
$$f(\varepsilon_{\mathrm{s}}) = \frac{\varepsilon_{\mathrm{s}} - 1}{\varepsilon_{\mathrm{s}} + 1/2}$$

COSMO is equivalent to PCM in the limit $\varepsilon_{\mathrm{s}} = \infty$ ($\varepsilon_{\mathrm{s}} \simeq 78$ for water).

2 - Integral equation methods

Integral equation method for COSMO:

$$E_{\rm C}^{\rm s} = \frac{1}{2} f(\varepsilon_{\rm s}) \int_\Omega \rho W.$$



$$\begin{cases} -\Delta W = 0, & \textbf{in } \Omega \\ W = -\Phi & \textbf{on } \Gamma, \end{cases}$$

$$\Phi(\mathbf{r}) = \int_{\mathbb{R}^3} \frac{\rho(\mathbf{r}')}{|\mathbf{r}-\mathbf{r}'|} \, d\mathbf{r}'.$$

The function $W \in H^1(\Omega)$ being harmonic in Ω, it can be represented by a single layer potential: there exists a unique function $\sigma \in H^{-1/2}(\Gamma)$ s.t.

$$\forall \mathbf{r} \in \overline{\Omega}, \quad W(\mathbf{r}) = \int_\Gamma \frac{\sigma(\mathbf{s}')}{|\mathbf{r}-\mathbf{s}'|} \, d\mathbf{s}'.$$

The surface charge density σ is obtained by solving the integral equation

$$\forall \mathbf{s} \in \Gamma, \quad \int_\Gamma \frac{\sigma(\mathbf{s}')}{|\mathbf{s}-\mathbf{s}'|} \, d\mathbf{s}' = -\Phi(\mathbf{s}),$$

and $$E_{\rm C}^{\rm s} = \frac{1}{2} f(\varepsilon_{\rm s}) \int_\Omega \rho(\mathbf{r}) \left(\int_\Gamma \frac{\sigma(\mathbf{s}')}{|\mathbf{r}-\mathbf{s}'|} d\mathbf{s}' \right) \, d\mathbf{r} = \frac{1}{2} f(\varepsilon_{\rm s}) \int_\Gamma \sigma(\mathbf{s}') \Phi(\mathbf{s}') \, d\mathbf{s}'.$$

$\mathbb{P}_0$ boundary element method

1. Build a mesh $(K_i)_{1\leq i\leq N}$ of Γ (with possibly curved triangles).

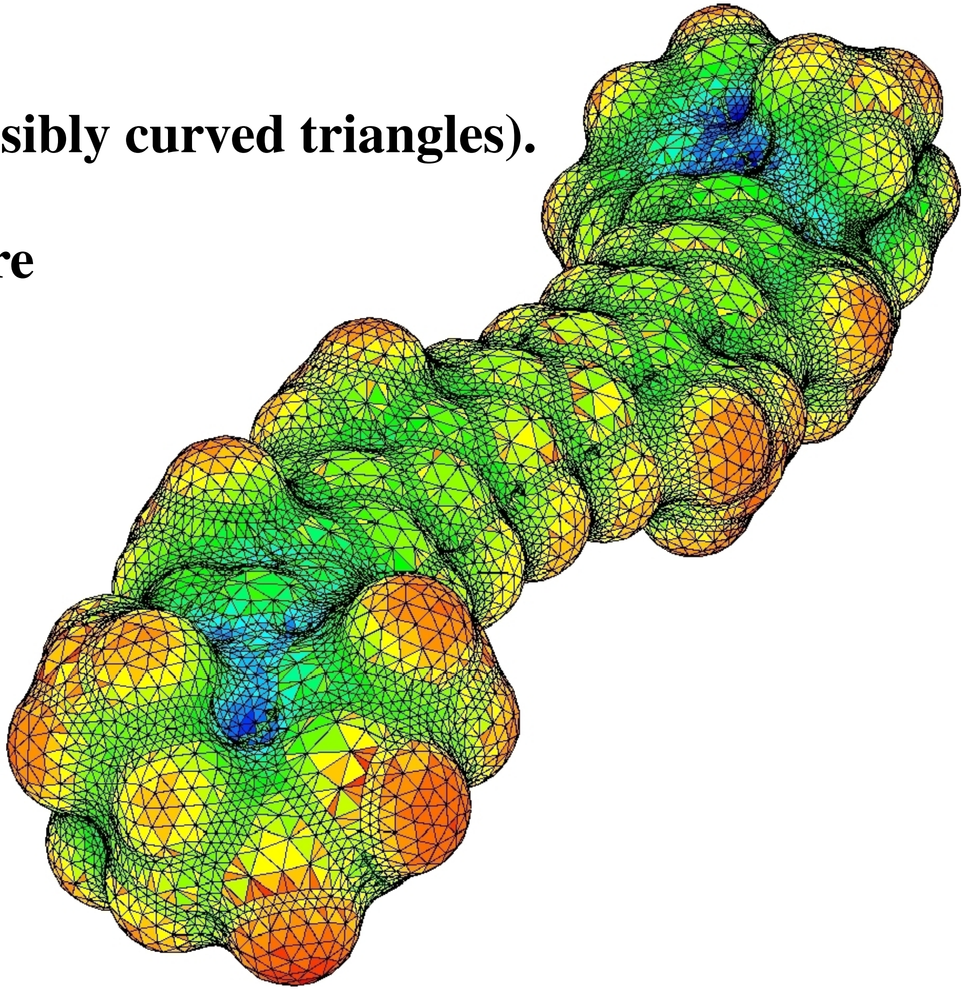
2. Solve the linear system $\mathbf{S}\varsigma = -\varphi$ where

$$[\mathbf{S}]_{ij} = \int_{K_i}\int_{K_j} \frac{1}{|\mathbf{s}-\mathbf{s}'|}\, d\mathbf{s}\, d\mathbf{s}'$$

$$[\varphi]_i = \int_{K_i} \Phi(\mathbf{s})\, d\mathbf{s}.$$

3. Compute the solvation energy

$$E_{\mathrm{C}}^{\mathrm{s}} = \frac{1}{2} f(\varepsilon_{\mathrm{s}}) \varsigma^T \varphi.$$



Surface mesh of the molecular surface of the carotene molecule obtained with the BLSURF software (Courtesy P. Laug, INRIA)

2 - Integral equation methods

Limitations of the boundary element method

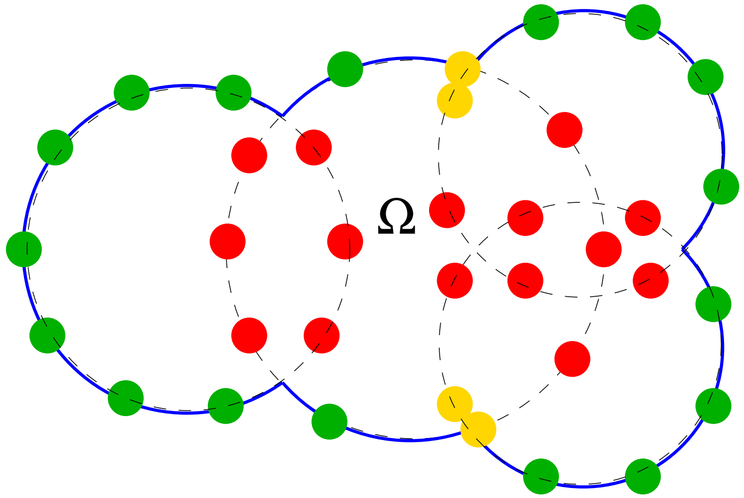
- requires a mesh
- requires Fast Multipole Methods (FMM) to scale linearly
- potential energy surfaces are not smooth, sometimes not well-defined

Non-conformal variational methods using Gaussians (Gaussian 09, QChem, ...)

York and Karplus ’99, Scalmani and Frisch ’10, Lange and Herbert ’10

- meshless
- requires FMM to scale linearly
- smooth PES
- not very well understood mathematically

$$\sigma(\mathbf{r}) = \sum_{j=1}^{M} \sum_{n=1}^{N} \sigma_{j,n} \frac{e^{-|\mathbf{r}-(\mathbf{R}_j+r_j\mathbf{s}_n)|^2/(2\tau^2)}}{(2\pi\tau^2)^{3/2}}$$



3 - A new domain decomposition approach

COSMO, **van der Waals cavity**, $\rho(\mathbf{r}) = \sum_{j=1}^{M} q_j \delta_{\mathbf{R}_j}(\mathbf{r})$

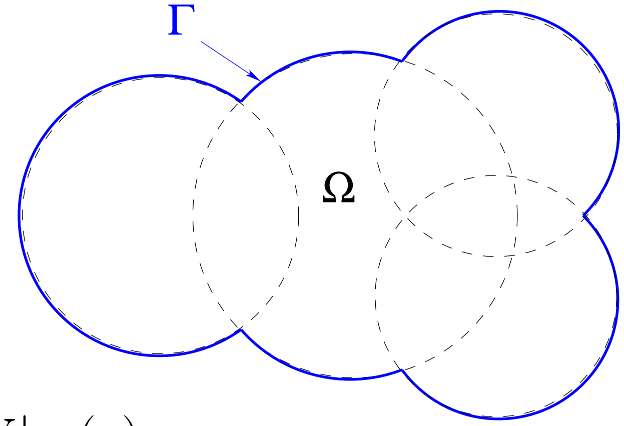
E.C., Y. Maday and B. Stamm, *Domain decomposition for implicit solvation models*, J. Chem. Phys. 139 (2013) 054111.

F. Lipparini, B. Stamm, E.C., Y. Maday and B. Mennucci, *A fast domain decomposition algorithm for continuum solvation models: energy and first derivatives*, J. Chem. Theory Comput. 9 (2013) 3637-3648.

3 - A new domain decomposition approach

An old idea: Schwarz alternating method (1870)

$$\begin{cases} -\Delta W = 0 & \textbf{in } \Omega \\ W = -\Phi & \textbf{on } \Gamma \end{cases}$$

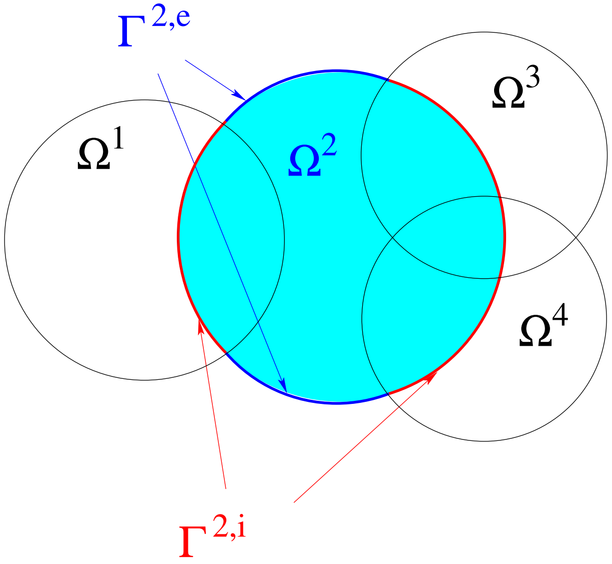


Domain decomposition: $\Omega = \bigcup_{j=1}^{M} \Omega^j, \quad W^j(\mathbf{r}) := W|_{\Omega^j}(\mathbf{r})$

(with overlapping domains)

$$\forall 1 \leq j \leq M, \qquad \begin{cases} -\Delta W^j = 0 & \textbf{in } \Omega^j, \\ W^j = -\Phi & \textbf{on } \Gamma^{j,\mathrm{e}}, \\ W^j = W^j_{\texttt{Neighbors}} & \textbf{on } \Gamma^{j,\mathrm{i}}, \end{cases}$$

$$W^j_{\texttt{Neighbors}}(\mathbf{s}) = \frac{1}{|N(j,\mathbf{s})|} \sum_{k \in N(j,\mathbf{s})} W^k(\mathbf{s})$$

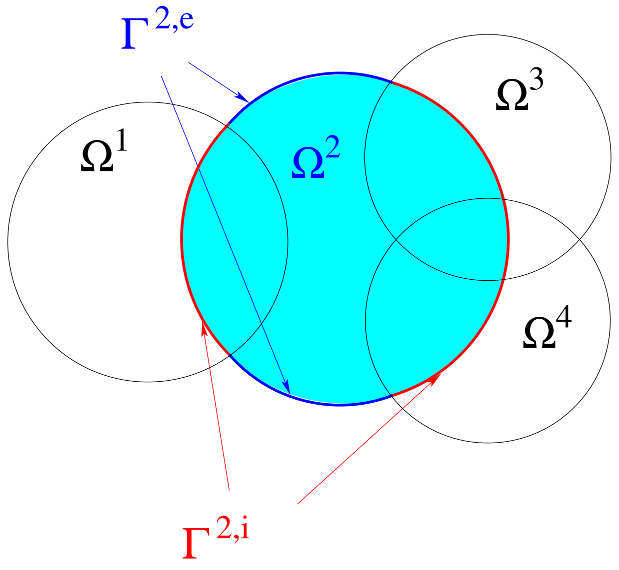


3 - A new domain decomposition approach

Jacobi iterative algorithm (convergence proof in P.-L. Lions '88)

$$\forall 1 \leq j \leq M, \quad \begin{cases} -\Delta W_n^j = 0 & \textbf{in } \Omega^j, \\ W_n^j = -\Phi & \textbf{on } \Gamma^{j,\mathrm{e}}, \\ W_n^j = W^j_{\texttt{Neighbors},n-1} & \textbf{on } \Gamma^{j,\mathrm{i}}, \end{cases}$$

$$W^j_{\texttt{Neighbors},n-1}(\mathbf{s}) = \frac{1}{|N(j,\mathbf{s})|} \sum_{k \in N(j,\mathbf{s})} W^k_{n-1}(\mathbf{s}) \qquad \forall \mathbf{s} \in \Gamma^{j,\mathrm{i}},$$



3 - A new domain decomposition approach

Our approach:

1. Merge Schwarz and integral equation methods

$\longrightarrow$ coupled system of integral equations on M copies on the unit sphere.

2. Smooth out the interface $\Gamma^{j,\mathrm{i}}$/$\Gamma^{j,\mathrm{e}}$.

3. Discretize with real spherical harmonics.

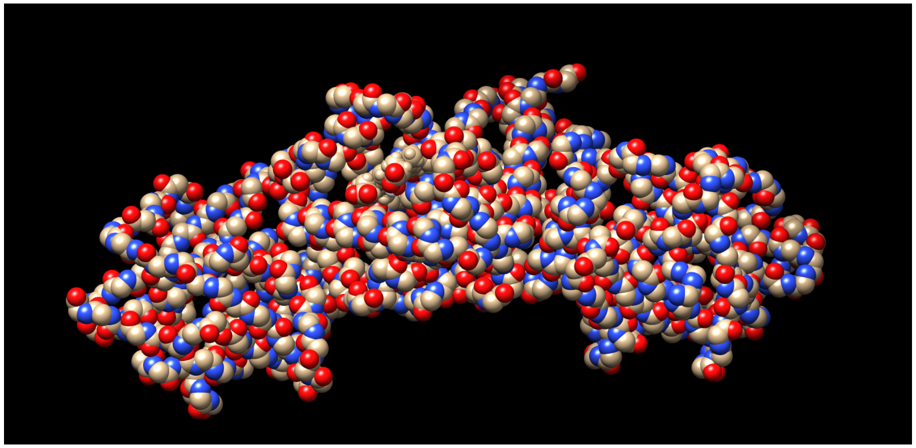
4. Perform numerical integration methods with Lebedev points.

5. Iterate with DIIS (instead of Jacobi or Gauss-Seidel).

6. Compute the forces with adjoint methods (analytical derivatives).

Systematically improvable numerical method generating smooth PES.

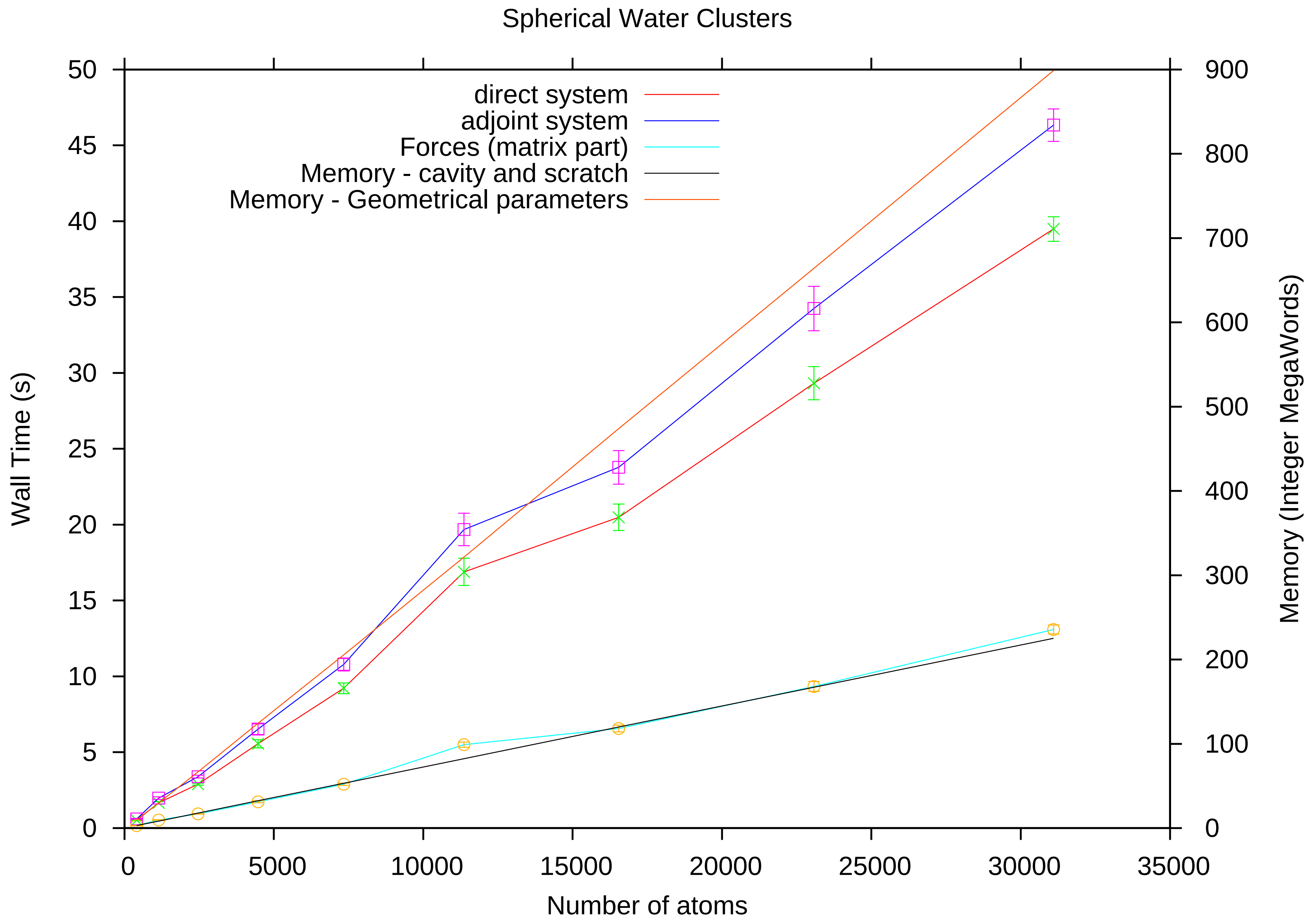
Comparison with the York-Karplus discretization: Myoglobin (2,861 atoms)



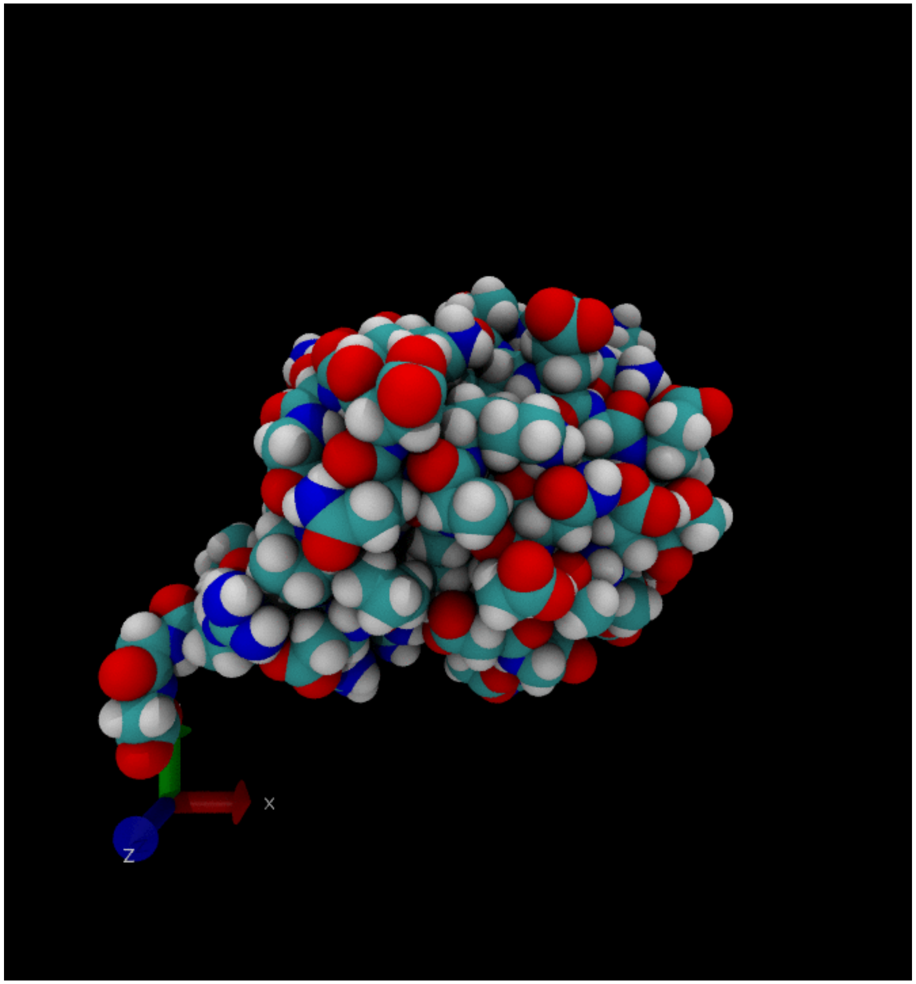
	York-Karplus	ddCOSMO
Basis functions	130,291	346,181
Integration points	130,291	864,022
Convergence Threshold	10^{-6}	10^{-7}
Polarization Energy	-3.05	-3.20
Number of iterations	109	25
(Total) Elapsed time[1]	5 h ($\sim$ 15 min with FMM - instable!)	15 s

[1] On 2*Xeon X5690 @3.47GHz (12 cores), 24GB DDR3 1333MHz

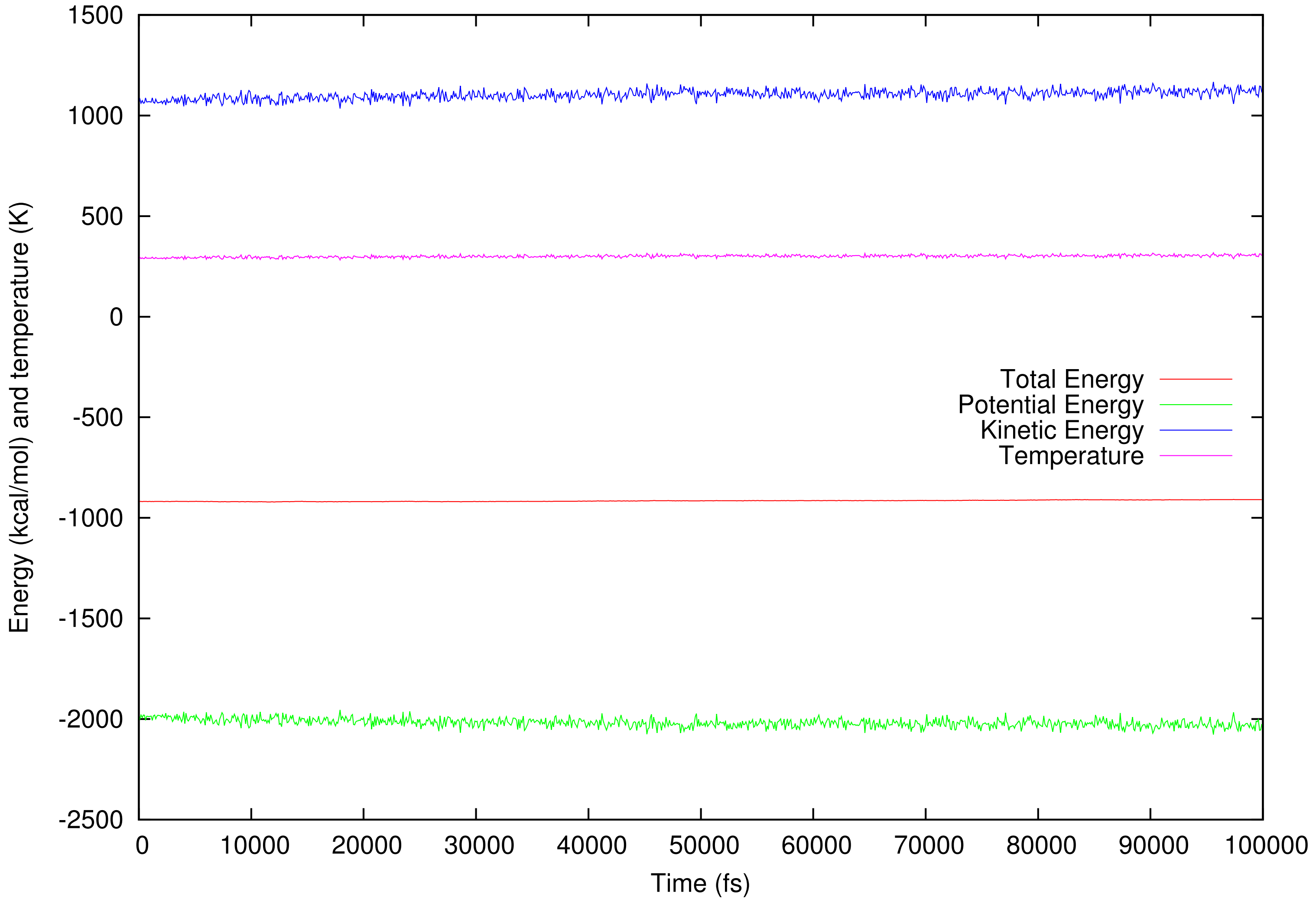
Linear scaling for globular (truly 3D) systems



Molecular dynamics of solvated molecules Ubiquitin (1,231 atoms)
(joint work with L. Lagardère and J.-P. Piquemal, Paris 6)



Long-time behavior of the MD trajectories



Conclusion and perspectives

Conclusion and perspectives

Features of the domain decomposition method:

- it allows one to compute solvation energies for large molecules (10^4 atoms) in a few seconds on a single processor;
- it is easily parallelizable and scales linearly, even for globular systems;
- it is meshfree and systematically improvable;
- it generates smooth potential energy surfaces.

On-going projects:

1. implementation in the AMBER package with polarizable force fields (joint work with L. Lagardère and J.-P. Piquemal, Paris 6);
2. extension to quantum charge distributions (with Gaussian Inc.);
3. MPI parallel implementation, GPUs;
4. extension to PCM, linearized Poisson-Boltzmann model, ...;
5. extension to other molecular cavities (solvent excluded surface, ...).

Appendix

Integral equation formulation

The function $W^j \in H^1(\Omega_j)$ being harmonic in Ω^j, it can be represented by a single layer potential: there exists a unique function $\sigma^j \in H^{-1/2}(\Gamma^j)$ s.t.

$$\forall \mathbf{r} \in \Omega^j, \quad W(\mathbf{r}) = W^j(\mathbf{r}) = \int_{\Gamma^j} \frac{\sigma^j(\mathbf{s}')}{|\mathbf{r} - \mathbf{s}'|}\, d\mathbf{s}' = r_j \int_{\mathbb{S}^2} \frac{\sigma_j(\mathbf{s})}{|\mathbf{r} - (\mathbf{R}_j + r_j\mathbf{s})|}\, d\mathbf{s}$$

with

$$\forall \mathbf{s} \in \mathbb{S}^2, \quad \sigma_j(\mathbf{s}) = r_j \sigma^j(\mathbf{R}_j + r_j\mathbf{s})$$

Therefore

$$\begin{aligned} E_{\mathrm{C}}^{\mathrm{s}} &= \frac{1}{2} f(\varepsilon_{\mathrm{s}}) \sum_{j=1}^{M} q_j W(\mathbf{R}_j) = \frac{1}{2} f(\varepsilon_{\mathrm{s}}) \sum_{j=1}^{M} q_j W^j(\mathbf{R}_j) \\ &= \frac{1}{2} f(\varepsilon_{\mathrm{s}}) \sum_{j=1}^{M} q_j r_j \int_{\mathbb{S}^2} \frac{\sigma_j(\mathbf{s})}{|\mathbf{R}_j - (\mathbf{R}_j + r_j\mathbf{s})|}\, d\mathbf{s} = \frac{1}{2} f(\varepsilon_{\mathrm{s}}) \sum_{j=1}^{M} q_j \int_{\mathbb{S}^2} \sigma_j(\mathbf{s})\, d\mathbf{s} \end{aligned}$$

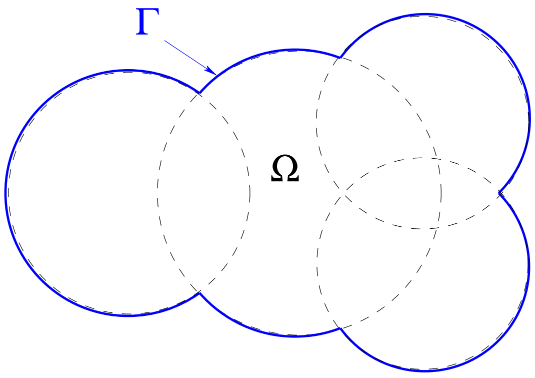
Appendix

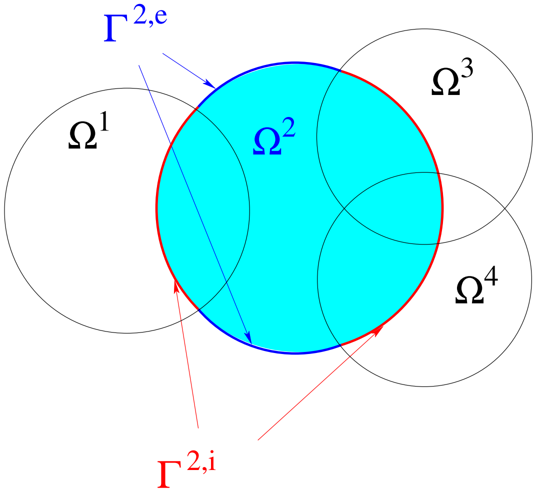
The functions σ_j are solutions to a linear system of the form: $\forall 1 \le j \le M$

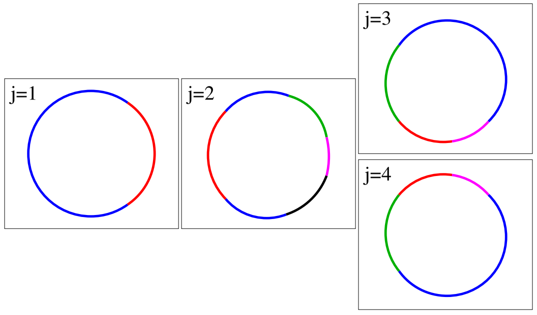
$$\forall \mathbf{s} \in \mathbb{S}^2, \quad \left(\mathcal{S}\sigma_j\right)(\mathbf{s}) - \sum_{k \in \mathcal{N}^j(\mathbf{s})} \omega^{jk}(\mathbf{s}) \left(\widetilde{\mathcal{S}}_{jk}\sigma_k\right)(\mathbf{s}) = -\left(1 - \sum_{k \in \mathcal{N}^j(\mathbf{s})} \omega^{jk}(\mathbf{s})\right) \widetilde{\Phi}_j(\mathbf{s})$$

set on M copies of the unit sphere.

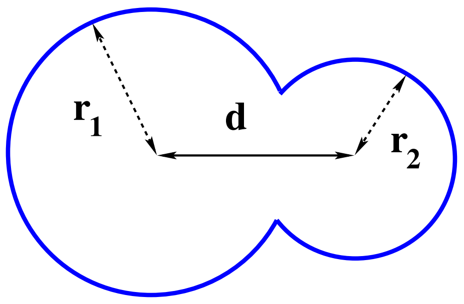
- **Discretization: real spherical harmonics**
- **Numerical integration: Lebedev grid points**
- **Iterative method: Jacobi, Gauss-Seidel or DIIS.**

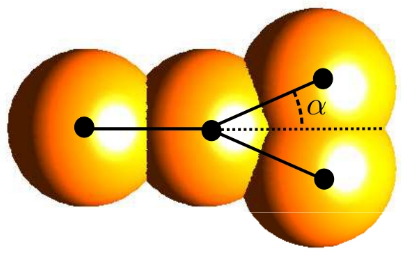


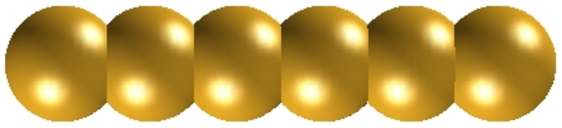




Calibration of the numerical parameters







- Smoothing parameter $0 \leq \eta \ll 1$
- Discretization parameter N (number of spherical harmonics)
- Numerical integration parameter N_{g} (number of Lebedev points)
- Stopping criterion of the iterative scheme (e.g. DIIS) `Tol`

DD-COSMO equations

$$\boxed{\forall \mathbf{s} \in \mathbb{S}^2, \quad \left(\mathcal{S}\sigma_j\right)(\mathbf{s}) - \sum_{k \in \mathcal{N}^j(\mathbf{s})} \omega^{jk}(\mathbf{s}) \left(\widetilde{\mathcal{S}}_{jk}\sigma_k\right)(\mathbf{s}) = -\left(1 - \sum_{k \in \mathcal{N}^j(\mathbf{s})} \omega^{jk}(\mathbf{s})\right) \widetilde{\Phi}_j(\mathbf{s})}$$

where

$$\forall \mathbf{s} \in \mathbb{S}^2, \quad (\mathcal{S}\sigma)(\mathbf{s}) = \int_{\mathbb{S}^2} \frac{\sigma(\mathbf{s}')}{|\mathbf{s} - \mathbf{s}'|} \, ds', \quad (\widetilde{\mathcal{S}}_{jk}\sigma)(\mathbf{s}) = \int_{\mathbb{S}^2} \frac{\sigma(\mathbf{s}')}{|t^{jk}(\mathbf{s})\mathbf{s}^{jk}(\mathbf{s}) - \mathbf{s}'|} \, ds'$$

$$t^{jk}(\mathbf{s}) = \frac{|\mathbf{R}_j + r_j\mathbf{s} - \mathbf{R}_k|}{r_k} \in \mathbb{R}_+ \quad \textbf{and} \quad \mathbf{s}^{jk}(\mathbf{s}) := \frac{\mathbf{R}_j + r_j\mathbf{s} - \mathbf{R}_k}{|\mathbf{R}_j + r_j\mathbf{s} - \mathbf{R}_k|} \in \mathbb{S}^2,$$

$$\mathcal{N}^j(\mathbf{s}) := \left\{ k \neq j \,|\, t^{jk}(\mathbf{s}) := \frac{|\mathbf{R}_j + r_j\mathbf{s} - \mathbf{R}_k|}{r_k} < 1 \right\},$$

$$\omega^{jk}(\mathbf{s}) = \frac{\chi^I_{jk}(\mathbf{s})^2}{\sum_{k' \in \mathcal{N}^j(\mathbf{s})} \chi^I_{jk'}(\mathbf{s})}, \qquad \textbf{with} \qquad \chi^I_{jk}(\mathbf{s}) = \chi(t^{jk}(\mathbf{s})) \; \textbf{and} \; \chi(t) = \left| \begin{array}{ll} 1 & \textbf{if } t < 1, \\ 0 & \textbf{if } t \geq 1. \end{array} \right.$$

$$\widetilde{\Phi}_j(\mathbf{s}) = \sum_{k=1}^{M} \frac{q_k}{|(\mathbf{R}_j + r_j\mathbf{s}) - \mathbf{R}_k|}.$$

Discretization method

$$\forall 1 \leq j \leq M, \quad \forall \mathbf{s} \in \mathbb{S}^2, \quad \sigma_j(\mathbf{s}) \simeq \sigma_j^{\eta,N,N_g}(\mathbf{s}) = \sum_{l=0}^{N} \sum_{m=-l}^{l} [X_j]_l^m \, Y_l^m(\mathbf{s})$$

- **the characteristic function χ is smoothed out**

$$\chi_\eta(t) = \left| \begin{array}{ll} 1 & \textbf{if } t \leq 1-\eta, \\ p_\eta(t) & \textbf{if } 1-\eta < t < 1, \\ 0 & \textbf{if } t \geq 1, \end{array} \right. \qquad \textbf{with} \qquad p_\eta(t) = \eta^{-4}(t-1)^2(t-1+2\eta)^2,$$

with $0 < \eta \ll 1$ a numerical parameter

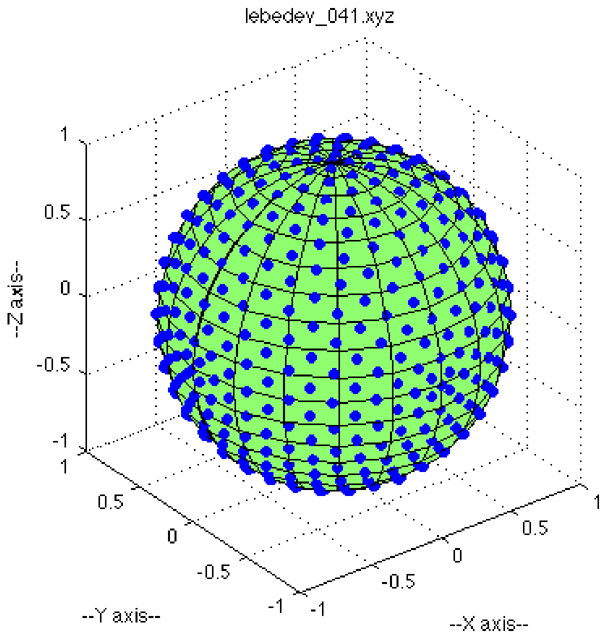
$\longrightarrow$ **smooth potential energy surfaces**

- **$\sigma_j(\mathrm{s})$ is discretized on a set of $(N+1)^2$ real spherical harmonics;**
- **integrals on $\mathbb{S}^2$ are performed with N_g quadrature points.**

Lebedev quadrature rule of order L_g

$$\forall f \in \mathbf{Span}(Y_l^m,\ 0 \le l \le L_g), \quad \int_{\mathbb{S}^2} f(\mathbf{s})\, d\mathbf{s} \overset{\text{exact}}{=} \sum_{n=1}^{N_g} w_n f(\mathbf{s}_n).$$

$(\mathbf{s}_n)_{1\le n\le N_g} \in (\mathbb{S}^2)^{N_g}$: **Lebedev points**
$(w_n)_{1\le n\le N_g} \in \mathbb{R}^{N_g}$: **associated weights**



L_g	17	19	21	23	25	27	29	31	...	131
N_g	110	146	170	194	230	266	302	350	...	5810

Matrix formulation of the problem: **the vector** $(\mathbf{X}_1, \cdots, \mathbf{X}_M)$ **is solution to**

$$\begin{pmatrix} \mathbf{L}_{11} & \cdots & \mathbf{L}_{1M} \\ \cdot & \cdot & \cdot \\ \cdot & \cdot & \cdot \\ \cdot & \cdot & \cdot \\ \mathbf{L}_{M1} & \cdots & \mathbf{L}_{MM} \end{pmatrix} \begin{pmatrix} \mathbf{X}_1 \\ \cdot \\ \cdot \\ \cdot \\ \mathbf{X}_M \end{pmatrix} = \begin{pmatrix} \mathbf{g}_1 \\ \cdot \\ \cdot \\ \cdot \\ \mathbf{g}_M \end{pmatrix}$$

where

$$\begin{aligned} [\mathbf{L}_{jj}\mathbf{X}_j]_l^m &= \frac{4\pi}{(2l+1)}[X_j]_l^m, && \\ [\mathbf{L}_{jk}\mathbf{X}_k]_l^m &= -\sum_{l'=0}^{N} \frac{4\pi}{(2l'+1)} \sum_{m'=-l'}^{l'} [c_{jk}]_{ll'}^{mm'}[X_k]_{l'}^{m'}, && \textbf{if } \Omega^j \cap \Omega^k \neq \emptyset, \\ [\mathbf{L}_{jk}\mathbf{X}_k]_l^m &= 0, && \textbf{if } \Omega^j \cap \Omega^k = \emptyset. \end{aligned}$$

For large molecules, the matrix is block-sparse.
The diagonal blocs are themselves diagonal.

Iterative methods:

- **block Jacobi's or block Gauss-Seidel's algorithms (convergence proved)**
- **DIIS (seems more efficient / convergence not proved).**

$[c_{jk}]_{ll'}^{mm'}$ **not stored in memory, nor even computed.**

$[\mathbf{L}_{jk}\mathbf{X}_k^n]_l^m$ **computed on the fly using an optimal rearrangement of the various summations (**$\mathbf{X}_k^n$**: approximation of** $\mathbf{X}_k$ **at the** n^{th} **iteration).**

Stopping criterion:

$$\mathtt{inc}_n \le \mathtt{Tol} \qquad \textbf{where} \qquad 0 < \mathtt{Tol} \ll 1$$

$$\mathtt{inc}_n = \left(\frac{\displaystyle\sum_{j=1}^{M} \|\sigma_j^{\eta,N,N_g;n} - \sigma_j^{\eta,N,N_g;n-1}\|^2_{H^{-1/2}(\mathbb{S}^2)}}{\displaystyle\sum_{j=1}^{M} \|\sigma_j^{\eta,N,N_g;n-1}\|^2_{H^{-1/2}(\mathbb{S}^2)}} \right)^{1/2} = \left(\frac{\displaystyle\sum_{j=1}^{M}\sum_{l=0}^{N}\sum_{m=-l}^{l} \frac{|[X_j^n]_l^m - [X_j^{n-1}]_l^m|^2}{l+1}}{\displaystyle\sum_{j=1}^{M}\sum_{l=0}^{N}\sum_{m=-l}^{l} \frac{|[X_j^{n-1}]_l^m|^2}{l+1}} \right)^{1/2}$$

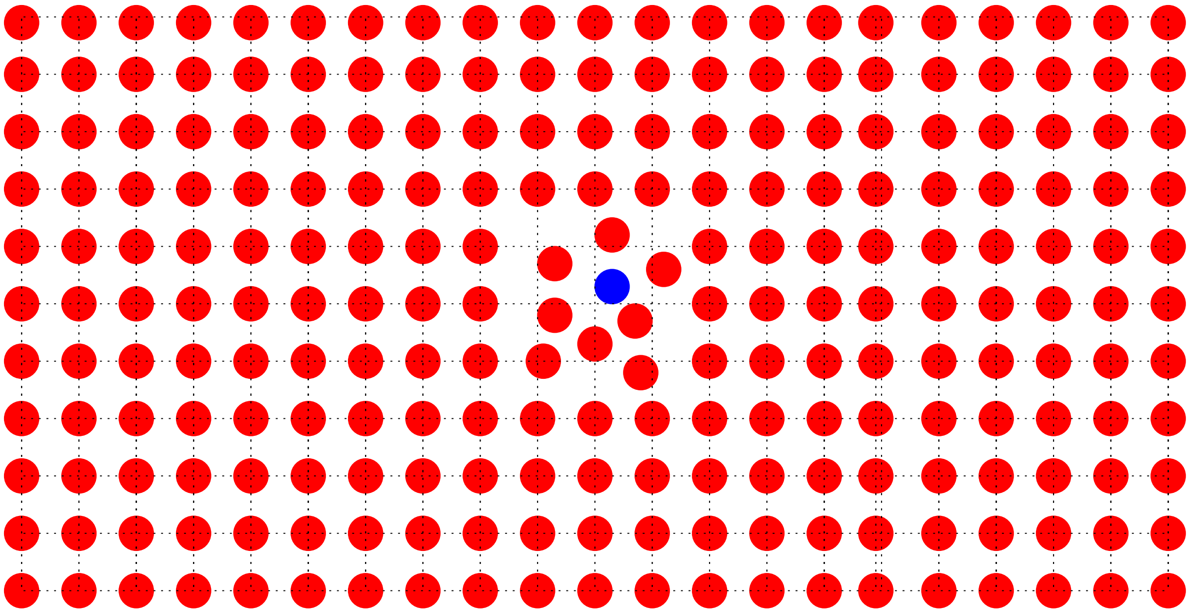
Appendix

Big challenge: rigorous derivation of embedding models for solvated molecules

for instance in the spirit of

- E.C.-Deleurence-Lewin, CMP ’08, J. Phys.: Cond. Matter ’08
- E.C.-Lewin, Arch. Rat. Mech. Anal. ’10
- E.C.-Ehrlacher, Arch. Rat. Mech. Anal. ’11

(embedding of local defects in perfect crystals)



Appendix

Defect = quasi-molecule embedded in the host crystal

$$\rho^{\mathrm{nuc}} = \rho^{\mathrm{nuc}}_{\mathrm{per}} + m \qquad \gamma^0 = \gamma^0_{\mathrm{per}} + Q^{m,\varepsilon_{\mathrm{F}}} \qquad \rho^0 = \rho^0_{\mathrm{per}} + \rho^{m,\varepsilon_{\mathrm{F}}}$$

Goal: find a way to directly compute $Q^{m,\varepsilon_{\mathrm{F}}}$ and $\rho^{m,\varepsilon_{\mathrm{F}}}$

Nuclear charge m of the quasi-molecule