Development and implementation of AMOEBA-IL for classical and QM/MM simulations

G. Andrés Cisneros
Department of Chemistry

2020 ACS Spring Virtual National Meeting

@CisnerosRes; <https://github.com/CisnerosResearch>

Acknowledgements

Group Members

Robert E. Duke
Sehr Naseem-Khan
Erik A. Vázquez-Montelongo
Mark A. Hix
Emmett Leddin
J. Enrique Vázquez-Cervantes
Madison Berger
Miguel Espinoza
Ally Smith
Krithika Ravishankar
Cory Shen

Alumni

Eric G. Kratz (Continental)
Hatice Gokcan (UNC)
Hedieh Torabifard (U. Mich)
Oleg Starovoytov (Southern U. LA)
Yi-Jung Tu (GA Tech)
Alice R. Walker (Stanford/SLAC)

Collaborators

Jean-Philip Piquemal (Sorbonne U.)
Pengyu Ren (UT Austin)
Thomas A. Darden (OpenEye)
Hugo Flores-Ruiz (U. de Guadalajara)
Andy Simmonett (NHLBI)

Computing Time

Funding

Gaussian Electrostatic Model (GEM)

Explicit representation of molecular electronic density

Gaussian Electrostatic Model (GEM)

Explicit representation of molecular electronic density

Separate terms for intermolecular interactions, with energy/force errors ≤ 0.2 kcal/mol

Gaussian Electrostatic Model (GEM)

Explicit representation of molecular electronic density

Separate terms for intermolecular interactions, with energy/force errors ≤ 0.2 kcal/mol

$$\tilde{\rho} = \sum_{tuv} c_{tuv} \Lambda_{tuv}; \quad \Lambda_{tuv} = (\alpha/\pi)^{3/2} (\partial/\partial x)^t (\partial/\partial y)^u (\partial/\partial z)^v \exp(-\alpha r^2)$$

H₂O Molecular Electrostatic potential (ESP)

Gaussian Electrostatic Model (GEM)

Explicit representation of molecular electronic density

Separate terms for intermolecular interactions, with energy/force errors ≤ 0.2 kcal/mol

$$\tilde{\rho} = \sum_{tuv} c_{tuv} \Lambda_{tuv}; \quad \Lambda_{tuv} = (\alpha/\pi)^{3/2} (\partial/\partial x)^t (\partial/\partial y)^u (\partial/\partial z)^v \exp(-\alpha r^2)$$

H₂O Molecular Electrostatic potential (ESP)

Intrinsically finite multipoles $\rightarrow$ GEM-DM

GEM-Distributed Multipoles (GEM-DM)

$$q = hc_{000} \int \Lambda_0 d_r = hc_{000}$$

$$\mu_x = hc_{100} \int \int \int x \Lambda_{100} d_x d_y d_z = hc_{100}$$

$$Q_{x^2} = hc_{200} \int \int \int x^2 \Lambda_{200} d_x d_y d_z = 2hc_{200}$$

$$Q_{xy} = hc_{110} \int \int \int xy \Lambda_{110} d_x d_y d_z = 2hc_{110}$$

J. Chem. Phys. (2006) 125, 184101

J. Chem. Theo. Comp. (2012) 8, 5072

Ionic Liquids

Properties

- High Viscosity
- Low vapor pressure
- Ion Conductive
- Water-immiscible
- Hygroscopic

Chem. Commun., 2012, 48, 7119–7130

AMOEBA-IL Parametrization

- Use of high-level QM intermolecular interaction data (total and energy decomposition analysis)

AMOEBA-IL Parametrization

- Use of high-level QM intermolecular interaction data (total and energy decomposition analysis)

Gaussian → Total intermolecular Energy as a QM reference

RVS/SAPT → Individual Coulomb and Polarization energy

GEM-fit → Distributed multipoles from GEM Hermite

TINKER → Bonded terms and vdW parameters-MM Energies

AMOEBA-IL Parametrization

- Use of high-level QM intermolecular interaction data (total and energy decomposition analysis)

Gaussian → Total intermolecular Energy as a QM reference

RVS/SAPT → Individual Coulomb and Polarization energy

GEM-fit → Distributed multipoles from GEM Hermite

TINKER → Bonded terms and vdW parameters-MM Energies

$$U_{vdW} = U_{Tot}(BSSE) - U_{Coul}(EDA) - U_{Pol}(EDA)$$

Polarization Energy

- Polarization

Redistribution of the electron density in presence of an external electric field

$$\vec{\mu}_{ind} = \alpha E$$

$$\vec{\mu}_{ind} = \alpha(E_{perm} + E_{ind})$$

$$U_{pol} = -0.5 \sum (\vec{\mu}_{ind}) E$$

Pyrrolidinium-based ionic liquids

1 Polarizable Group
1G

3 Polarizable Groups
3G

$[\text{sPyr}^+][\text{BF}_4^-]$ Electrostatic Energy

$[\text{sPyr}^+][\text{BF}_4^-]$ –Total Energy

Total Energy (kcal/mol)-1G

$$f(x) = 1.588x + 33.272$$
$$R^2 = 0.971$$

Total Energy (kcal/mol)-3G

$$f(x) = 1.461x + 27.224$$
$$R^2 = 0.905$$

Simulation Details

- **gem.pmemd** (in AMBER18/20) simulation package
- NPT ensemble ($P=1$ bar)($T=300-500\text{K}$); 216 ion pairs; 10–20 ns production
- non-bonded cutoff = $8 \text{ \AA}$, sPME, 1 fs timestep
- Berendsen thermostat/barostat

Density

Experimental Melting Point: 448 K

Lanthanide Water Exchange in ILs

Motivation

- Understanding of dynamics of ligand exchange on Lanthanides is important for catalysis

Motivation

- Understanding of dynamics of ligand exchange on Lanthanides is important for catalysis
- ^{17}O -NMR Experiments have shown that H_2O exchange rates of lanthanide ions in water is opposite to that in water/[EMIm][EtSO₄]

Motivation

- Understanding of dynamics of ligand exchange on Lanthanides is important for catalysis
- ^{17}O -NMR Experiments have shown that H_2O exchange rates of lanthanide ions in water is opposite to that in water/ $[\text{EMIm}][\text{EtSO}_4]$
- Exchange mechanism is unknown

Motivation

- Understanding of dynamics of ligand exchange on Lanthanides is important for catalysis
- ^{17}O -NMR Experiments have shown that H_2O exchange rates of lanthanide ions in water is opposite to that in water/[EMIm][EtSO₄]
- Exchange mechanism is unknown
- Use polarizable classical MD ...

Parametrization of Lanthanides

Polarizabilities from Marjolin *et al.*, *CPL*, **563**, 25-29, 2013

Metal ions	α ($\text{\AA}^3$)	a	R ($\text{\AA}$)	ϵ (kcal/mol)
Gd ³⁺	0.790 ^a	0.146	3.30 ^b	8.5 ^b
Dy ³⁺	0.728 ^a	0.140	3.23	15.0
Ho ³⁺	0.702 ^a	0.136	3.20	20.0

Parametrization of Lanthanides

Polarizabilities from Marjolin *et al.*, *CPL*, **563**, 25-29, 2013

Metal ions	α ($\text{\AA}^3$)	a	R ($\text{\AA}$)	ϵ (kcal/mol)
Gd ³⁺	0.790 ^a	0.146	3.30 ^b	8.5 ^b
Dy ³⁺	0.728 ^a	0.140	3.23	15.0
Ho ³⁺	0.702 ^a	0.136	3.20	20.0

Metal ions		Current Work	Experiment ^c
Gd ³⁺	CN	8.8	8.7
	Ln-O _{ox}	2.38	2.42
Dy ³⁺	CN	8.6	8.5
	Ln-O _{ox}	2.36	2.38
Ho ³⁺	CN	8.7	8.4
	Ln-O _{ox}	2.35	2.36

Simulation Details

- **gem.pmemd** (AMBER18/20) simulation package
- NPT ensemble ($P=1$ bar; $T=300\text{K}$); 1 lanthanide, $\text{H}_2\text{O}=511$; mixtures 83:150 $\text{H}_2\text{O}:[\text{EtSO}_4]$ molar ratio (1:19 v/v); 99:180 $\text{H}_2\text{O}:[\text{OTf}]$ molar ratio (1:19 v/v); 10–20 ns production
- non-bonded cutoff = 8 Å, sPME
- Berendsen thermostat/barostat

Exchange Rates

Solvent	Metal ion	k_{calc}^{exch}, s^{-1}	k_{exp}^{exch}, s^{-1}
H ₂ O	Gd ³⁺	1.30×10^9	8.30×10^8
H ₂ O	Dy ³⁺	7.72×10^8	4.34×10^8
H ₂ O	Ho ³⁺	4.75×10^8	2.14×10^8
H ₂ O/[EMIm][EtSO ₄]	Gd ³⁺	2.96×10^7	5.08×10^6
H ₂ O/[EMIm][EtSO ₄]	Dy ³⁺	4.94×10^7	3.64×10^7
H ₂ O/[EMIm][EtSO ₄]	Ho ³⁺	8.86×10^7	4.61×10^7
H ₂ O/[EMIm][OTf]	Gd ³⁺	1.30×10^8	1.3×10^7
H ₂ O/[EMIm][OTf]	Dy ³⁺	2.00×10^8	1.4×10^8
H ₂ O/[EMIm][OTf]	Ho ³⁺	2.60×10^8	1.5×10^8

Tu Y.J., Allen M.A., GAC, PCCP, **18**, 30323, 2016;

Tu Y.J., Lin Z., Allen M.A., GAC, JCP, **148**, 0244503, 2018

Exchange Mechanisms in H_2O and $[\text{EMIm}][\text{EtSO}_4]$

Exchange Mechanisms in H₂O and [EMIm][EtSO₄]

Tu Y.J., Allen M.A., GAC, PCCP, **18**, 30323, 2016;

Tu Y.J., Lin Z., Allen M.A., GAC, JCP, **148**, 0244503, 2018

Exchange Mechanisms in [EMIm][OTf]

Tu Y.J., Allen M.A., GAC, PCCP, **18**, 30323, 2016;

Tu Y.J., Lin Z., Allen M.A., GAC, JCP, **148**, 0244503, 2018

Liquid-liquid extraction of Benzene

a) Benzene

+

Dodecane

b) [DMIM]

+

[BF4]

c) [EMIM]

+

[BF4]

E.A. Vázquez Montelongo, GAC, H. Flores Ruiz, J. Mol. Liq. DOI: 10.1016/j.molliq.2019.111846

Simulation Details

- MD with TINKER/OpenMM for AMOEBA
- Ternary systems: 500 molecules each (IL; benzene; dodecane), 300(150) ns production [EMIm]([DmIm]) $x = y = 4.5$ nm, $z = 19.0$ nm
- Binary systems 500 molecules IL; 200 molecules solute (benzene or dodecane), 200 ns production
- NPT ensemble, 10 Å cutoff for nonbonded, 2 fs timestep,

[DMIm][BF₄] Density Profile

E.A. Vázquez Montelongo, GAC, H. Flores Ruiz, J. Mol. Liq. DOI: 10.1016/j.molliq.2019.111846

[EMIm][BF₄] Density Profile

E.A. Vázquez Montelongo, GAC, H. Flores Ruiz, J. Mol. Liq. DOI: 10.1016/j.molliq.2019.111846

Cation SDF

Anion SDF

LICHEM: Layered Interacting CHEmical Models

LICHEM: Layered Interacting CHEmical Models

<https://github.com/CisnerosResearch/LICHEM>

Kratz E. *et al.*, JCC, **37**, 1019, 2016; Gokcan H. *et al.*, JCTC, **15**, 3056, 2019

Aniline protection in [EMIm][BF₄]

1)

2)

Simulation Details

- Initial MD with TINKER/OpenMM for AMOEBA, 7410 H₂O, 189[EMIm][BF₄], 1 aniline, 1 (Boc)₂O; NPT, 2 ns production
- QM/MM: 146 or 155 QM atoms; 26688 MM atoms; ω B97X-D/6-31G(d)
- QSM path optimization; LREC/PME for long-range electrostatics
- 0.001 Å RMSD, 0.005 au/Bohr force RMS, 0.02 au/Bohr max force

Importance of Polarization in QM/MM

Importance of Polarization in QM/MM

Summary

- `gem.pmemd`: MD platform for advanced FFs (experimental GEM implementation)

Summary

- `gem.pmemd`: MD platform for advanced FFs (experimental GEM implementation)
- GEM distributed multipoles may be used in multipolar FF: AMOEBA-IL

Summary

- `gem.pmemd`: MD platform for advanced FFs (experimental GEM implementation)
- GEM distributed multipoles may be used in multipolar FF: AMOEBA-IL
- “bottom-up” approach using *ab initio* data provides accurate parameters for AMOEBA-IL

Summary

- `gem.pmemd`: MD platform for advanced FFs (experimental GEM implementation)
- GEM distributed multipoles may be used in multipolar FF: AMOEBA-IL
- “bottom-up” approach using *ab initio* data provides accurate parameters for AMOEBA-IL
- AMOEBA-IL predicts phase transition of [SPyr]₄ at 453 K, experimental melting pt. = 448 K

Summary

- `gem.pmemd`: MD platform for advanced FFs (experimental GEM implementation)
- GEM distributed multipoles may be used in multipolar FF: AMOEBA-IL
- “bottom-up” approach using *ab initio* data provides accurate parameters for AMOEBA-IL
- AMOEBA-IL predicts phase transition of [SPyr]₄ at 453 K, experimental melting pt. = 448 K
- Water exchange rate trends on lanthanides reproduced by IL; MD shows exchange mechanism is associative in H₂O, and dissociative in IL/H₂O

Summary

- `gem.pmemd`: MD platform for advanced FFs (experimental GEM implementation)
- GEM distributed multipoles may be used in multipolar FF: AMOEBA-IL
- “bottom-up” approach using *ab initio* data provides accurate parameters for AMOEBA-IL
- AMOEBA-IL predicts phase transition of [SPyr]₄ at 453 K, experimental melting pt. = 448 K
- Water exchange rate trends on lanthanides reproduced by IL; MD shows exchange mechanism is associative in H₂O, and dissociative in IL/H₂O
- [DMIM][BF₄] predicted to be a possible solvent for liquid-liquid extraction of benzene from gasoline

Summary

- `gem.pmemd`: MD platform for advanced FFs (experimental GEM implementation)
- GEM distributed multipoles may be used in multipolar FF: AMOEBA-IL
- “bottom-up” approach using *ab initio* data provides accurate parameters for AMOEBA-IL
- AMOEBA-IL predicts phase transition of [SPyr]₄ at 453 K, experimental melting pt. = 448 K
- Water exchange rate trends on lanthanides reproduced by IL; MD shows exchange mechanism is associative in H₂O, and dissociative in IL/H₂O
- [DMIM][BF₄] predicted to be a possible solvent for liquid–liquid extraction of benzene from gasoline
- LICHEM enables combination of unmodified QM and MM codes

Summary

- `gem.pmemd`: MD platform for advanced FFs (experimental GEM implementation)
- GEM distributed multipoles may be used in multipolar FF: AMOEBA-IL
- “bottom-up” approach using *ab initio* data provides accurate parameters for AMOEBA-IL
- AMOEBA-IL predicts phase transition of [SPyr]₄ at 453 K, experimental melting pt. = 448 K
- Water exchange rate trends on lanthanides reproduced by IL; MD shows exchange mechanism is associative in H₂O, and dissociative in IL/H₂O
- [DMIM][BF₄] predicted to be a possible solvent for liquid-liquid extraction of benzene from gasoline
- LICHEM enables combination of unmodified QM and MM codes
- Polarization effects are important for QM/MM reactivity calculations in highly charged media

Acknowledgements

Group Members

Robert E. Duke
Sehr Naseem-Khan
Erik A. Vázquez-Montelongo
Mark A. Hix
Emmett Leddin
J. Enrique Vázquez-Cervantes
Madison Berger
Miguel Espinoza
Ally Smith
Krithika Ravishankar
Cory Shen

Alumni

Eric G. Kratz (Continental)
Hatice Gokcan (UNC)
Hedieh Torabifard (U. Mich)
Oleg Starovoytov (Southern U. LA)
Yi-Jung Tu (GA Tech)
Alice R. Walker (Stanford/SLAC)

Collaborators

Jean-Philip Piquemal (Sorbonne U.)
Pengyu Ren (UT Austin)
Thomas A. Darden (OpenEye)
Hugo Flores-Ruiz (U. de Guadalajara)
Andy Simmonett (NHLBI)

Computing Time

Funding