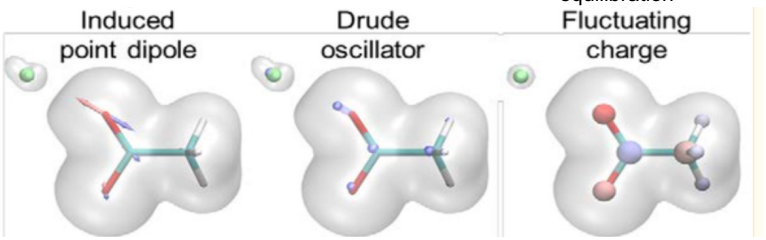
Polarizable Force Field Models



$\mu^{ind} = \alpha E$

μ^{ind}: induced atomic dipole
α: atomic polarizability
E: electric field

$\alpha = q_D^2 / k_D$

q_D: charge of Drude particle
k_D: harmonic spring constant

atomic charges redistributed to equalize electronegativity at each site

$$\chi_\alpha = \left(\frac{\partial E_\alpha}{\partial q_\alpha}\right) = \chi_\alpha^* + 2\eta_\alpha^* q_\alpha + k \sum_{\beta \neq \alpha} \frac{q_\beta}{R_{\alpha\beta}}$$

X: electronegativity; η: chemical harness

Energy needed for charge redistribution E_{self}

$$E_{self}^{Ind} = \sum_i \frac{1}{2} \alpha_i^{-1} \boldsymbol{\mu}_i^2 \qquad E_{self}^{Drude} = \sum_i \frac{1}{2} k_{D,i} \mathbf{d}_i^2 \qquad E_{self}^{FQ} = \sum_i \left(\chi_i q_i + \eta_i q_i^2\right)$$

26

AMOEBA (atomic multipole optimized energetics for biomolecular applications)

(Ponder et al. J. Comp. Chem. 23, 1497 (2002)

Induced dipole model

$$U = U_{bond} + U_{angle} + U_{b\theta} + U_{oop} + U_{torsion} + U_{vdW} + U_{ele}^{perm} + U_{ele}^{ind}$$

Bond and angle potentials include anharmonicity effects through higher order terms:

$$U_{bond} = K_b (b - b_0)^2 [1 - 2.55(b - b_0) + (7/12)2.55(b - b_0)^2]$$

$$U_{angle} = K_\theta (\theta - \theta_0)^2 [1 - 0.014(\theta - \theta_0) + 5.6 \times 10^{-5}(\theta - \theta_0)^2 - 7.0 \times 10^{-7}(\theta - \theta_0)^3 + 2.2 \times 10^{-8}(\theta - \theta_0)^4]$$

Additional bond-angle coupling terms and

$$U_{b\theta} = K_{b\theta}[(b - b_0) + (b' - b_0')](\theta - \theta_0)$$

$$U_{oop} = K_\chi \chi^2$$

potentials to keep sp^2 carbons planar

standard torsion potential

$$U_{torsion} = \sum_n K_{n\phi}[1 + \cos(n\phi \pm \delta)]$$

Van der Waals interactions: buffered 14-7:

$$U_{vdw}(ij) = \varepsilon_{ij} \left(\frac{1.07}{\rho_{ij} + 0.07}\right)^7 \left(\frac{1.12}{\rho_{ij}^7 + 0.12} - 2\right)$$

$\rho_{ij} = R_{ij} / R_{ij}^0$

27

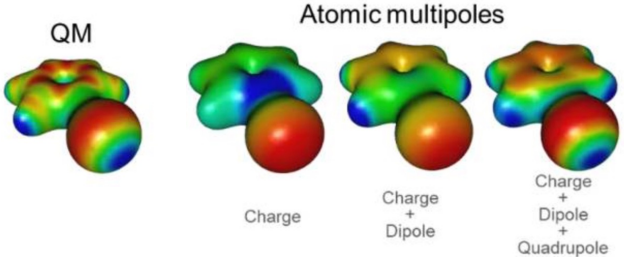
AMOEBA Electrostatic Interactions

$$U_{\text{ele}}^{\text{perm}} = U_{\text{ele}}^{\text{perm}} + U_{\text{ele}}^{\text{ind}}$$

q: atomic charge
μ: atomic dipole moment
Q: atomic quadrupole moment

$U_{\text{ele}}^{\text{perm}}$ via atomic multipole expansion $\mathbf{M} = [q, \mu_x, \mu_y, \mu_z, Q_{xx}, Q_{xy}, Q_{xz}, ..., Q_{zz}]^{\mathrm{T}}$

Atomic multipoles



Coulomb interactions of permanent multipole moments: charge-charge, charge-dipole etc..

Induced dipoles

$U_{\text{ele}}^{\text{ind}}$

$\mu^{\text{ind}} = \alpha E$

E: total electric field generated by all other permanent atomic multipoles and induced dipoles

$$U_{\text{ele}}^{\text{ind}} = -\frac{1}{2}\sum_i (\mu_i^{\text{ind}})^T E_i$$

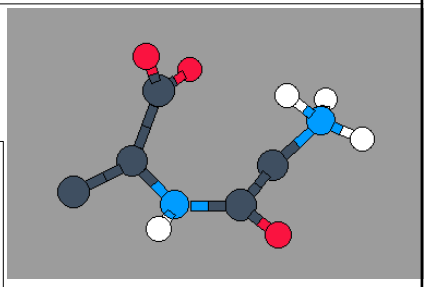
=> has to be solved self-consistently

28

Are Polarization Effects Important?

Standard Deviation of the Electrostatic Potential

$$SD(t) = \frac{1}{T}\int_0^T dt' \sqrt{\frac{\sum_{j\in MM}\left(\sum_{i\in QM}\frac{q_i^{ESP}(t)}{r_{ij}(t')} - V_j(t')\right)^2}{\sum_{j\in MM} V_j(t')^2}}$$



Gly-Ala in Water (SPC), QM Based MD 10ps, 300K

Potential:	
AMBER95:	6-13 %
GROMOS96:	9-16 %
D-RESP:	6-8 %
D-RESP(pol):	5 %

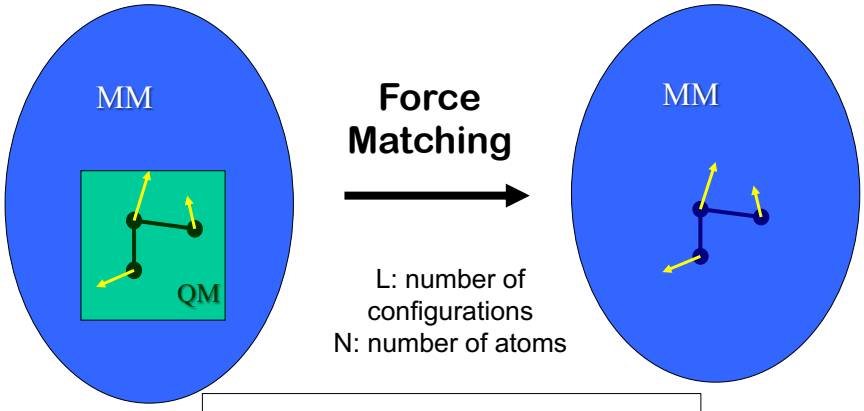
Dipole Moment:	
AMBER95:	6 %
GROMOS96:	7 %
D-RESP:	3 %
D-RESP(pol):	2 %

H. Hugosson et al., J.Comp. Chem. 27, 672 (2006); P. Maurer, et al. JCTC (2007)

29

Automatized Generation of Force Fields

Force field parameters σi fitted to minimize difference between reference and force field forces on each atom



L: number of configurations
N: number of atoms

$$\{\sigma_i\} = \arg\min \Lambda(\{\sigma_i\}) = \frac{1}{L \cdot N} \sum_{l=1}^{L} \sum_{\alpha=1}^{N} |F_{l\alpha}^{\mathrm{MM}}(\{\sigma_i\}) - F_{l\alpha}^{\mathrm{QM/MM}}|^2$$

30

Machine Learning Potentials

Recent review: Unke et al. Chem. Rev. 121, 16, 10142 (2021)

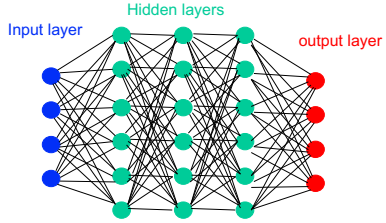
Kernel Methods:

$$E_A = \sum_{I \in A} \epsilon_{\mathrm{local}}(\boldsymbol{M}_I) = \sum_I \sum_J \alpha_J k(\boldsymbol{M}_J, \boldsymbol{M}_I) = \sum_I \boldsymbol{k}_I \boldsymbol{\alpha}$$

$$\boldsymbol{F}_L = -\frac{\partial}{\partial \boldsymbol{R}_L}[E_A] = -\frac{\partial}{\partial \boldsymbol{R}_L}[E_A] = -\sum_I \frac{\partial}{\partial \boldsymbol{R}_L}[\boldsymbol{k}_I]\,\boldsymbol{\alpha} = -\sum_I \sum_J \alpha_J \frac{\partial}{\partial \boldsymbol{M}_I} k(\boldsymbol{M}_J, \boldsymbol{M}_I) \frac{\partial \boldsymbol{M}_I}{\partial \boldsymbol{R}_L}$$

M: descriptor of chemical environment of atom I

Neural Networks:



- Descriptor Based NNs
- End-to-end (input atomic charges and coordinates)

31

Machine Learning Potentials

Important to impose physical constraints:

- Energy conservation (consistency of energy and forces)
- Translational invariance
- Rotational invariance
- Permutational invariance

Advantages:

- Do not need to know anything about interactions/form of the potential
- Automatized: no tedious FF development
- Can also be used for chemical reactions & charge transfer phenomena

Disadvantages:

- Have to generate enough training data
- 1-3 orders of magnitude slower than FF based MD
- Can become unreliable when getting into regions far from training set
- Makes no use of physical knowledge even when it would be available

Software packages for ML-FFs:

AMP (⇔ ASE)
Aenet
DeePMD(⇔LAMMPS)
PhysNet
TensorMol

32