Polarizable force-fields

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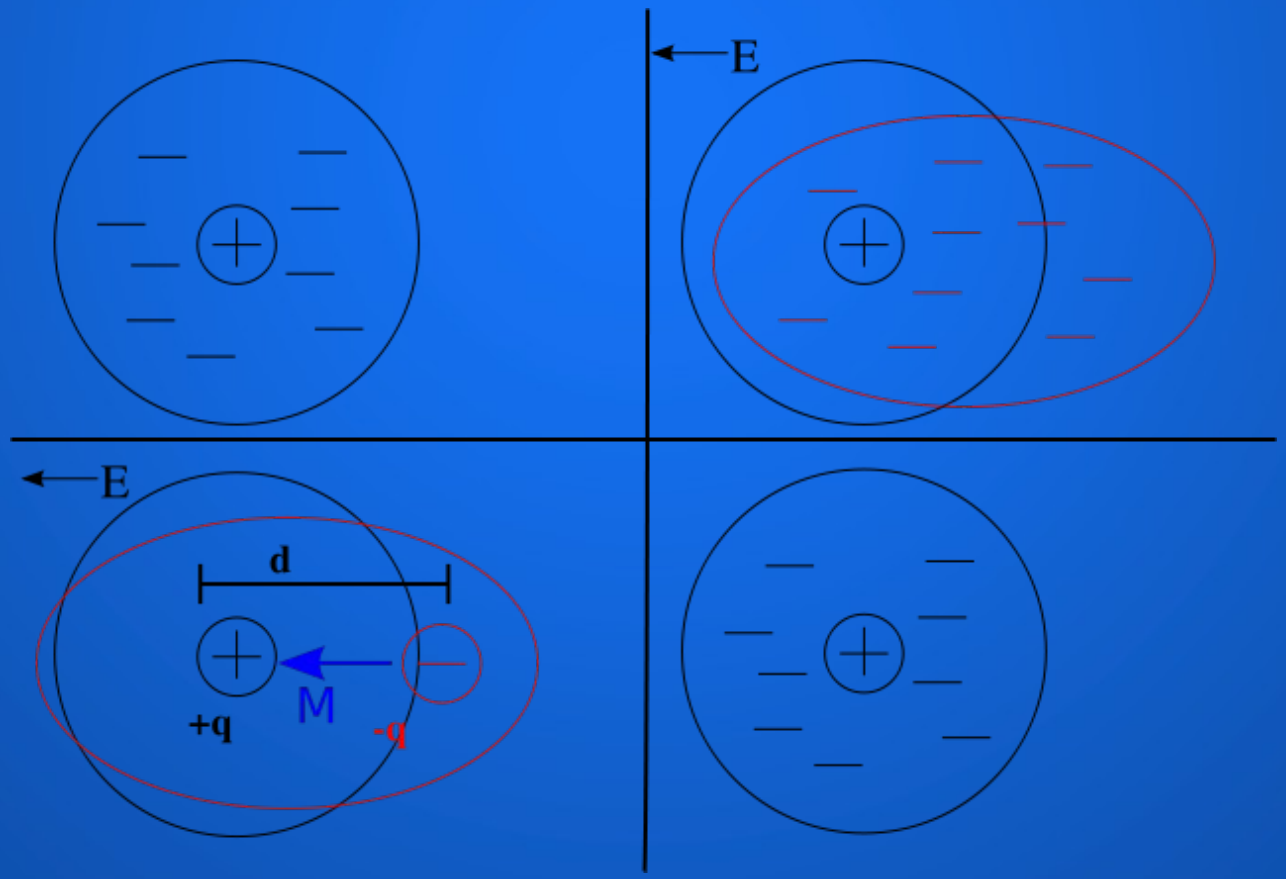
BCMB 610
April 21 2008

Polarization



Classical force-fields

$$V(r^N) = \sum_{\text{bonds}} \frac{1}{2} k_b (l - l_0)^2 + \sum_{\text{angles}} \frac{1}{2} k_a (\theta - \theta_0)^2$$

$$+ \sum_{j=1}^{N-1} \sum_{i=j+1}^{N} \left\{ 4\epsilon_{i,j} \left[\left(\frac{\sigma_{ij}}{r_{ij}} \right)^{12} - \left(\frac{\sigma_{ij}}{r_{ij}} \right)^{6} \right] + \frac{q_i q_j}{4\pi\epsilon_0 r_{ij}} \right\}$$

- additive
- no explicit polarization or lone pairs
- implicit
  - charges scaled up for condensed phase
  - van der Waals

Importance

- Polarization can influence
  - geometry
  - energetics of molecular recognition
- Interfaces
- dipole moments vary 10-20% between bulk water and non-polar pocket env.
- “not one charge fits all”

Models 1/3

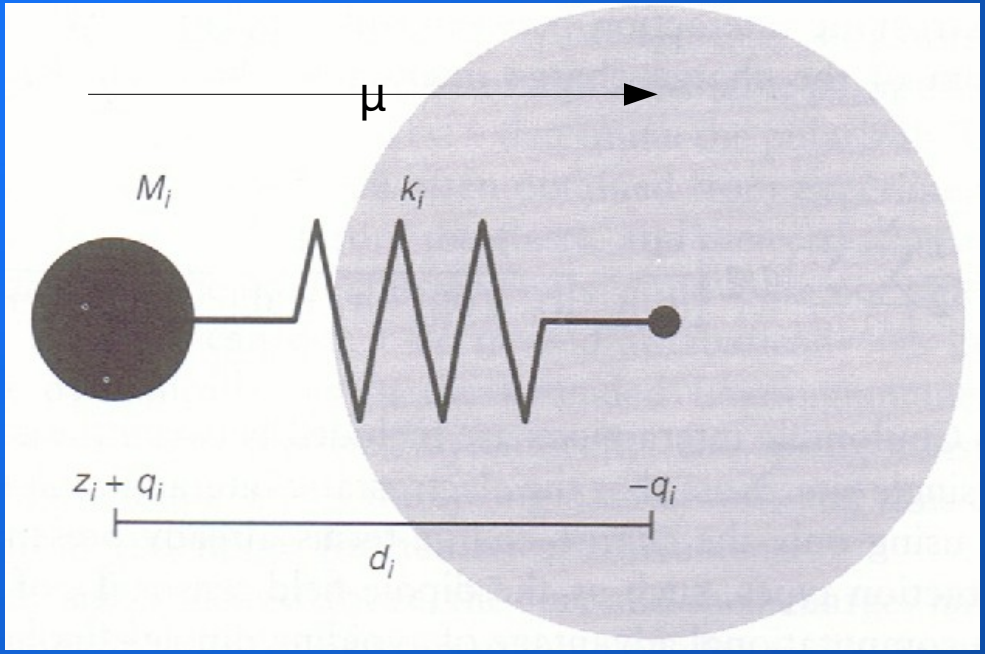
- Polarizable point dipoles
  - point inducible dipoles on some or all atomic sites
  - $\mu_i = \alpha_i E_i = \alpha_i \cdot [E_i^0 - \sum_{j \neq 1} T_{ij} \mu_j]$
  - μ: induced dipole moment, α: polarizability
  - E: electric field, T: dipole field tensor
  - $U_{ind} = U_{stat} + U_{\mu\mu} + U_{pol}$
  - polarization catastrophe

Dipoles coupled

- Self consistence method needed
  - Solving matrix equation $O(N^3)$
  - Iterative (steps=2..10)
  - Predictive (numerical integration)
  - Lagrange (eqn of motion with virtual mass)
- Lagrange long believed to be fastest
- Wang, Skeel 2005: Iterative fastest
- only 2x MD without polarization

Models 2/3

- Drude/Shell Model
  - z+q: core charge
  - -q: shell charge
  - k: spring constant



$$U_{ind} = U_{stat} + U_{\mu\mu} + U_{pol}$$

$$\alpha = q^2/k \quad , \quad U_{pol} = kd^2$$

  - same as point dipoles for k=∞
  - van der Waals anchored on shell

Models 3/3

- Fluctuation Charge (FQ) or Electronegetivity Equalization
- $U_i = E_i^0 + \chi_i^0 q_i + \frac{1}{2} J_{ij} q_i^2 + \sum_{j \neq i} J_{ij}(r_{ij}) q_i q_j = E_i^0 + q_i \chi_i$
- χ: electronegativity, J: hardness
- no explicit dipoles
- overestimated charge transfer
- geometry constraint by charge sites

Results

- Most tests on water
  - FQ constrained to plane
  - lone pairs required for good agreement
  - can reproduce water/gas interface
- small molecules
  - better charge fitting – reduced side-effects
- necessity for protein not yet proven
  - QM calc. to compare become available
  - for flexible molecules in general difficult

Conclusions

- Necessity
  - certain in special cases, unclear otherwise
- Performance (used to be) an issue
- Significant recent progress
- Proteins
  - No well tested, universal agreed FF yet
  - most significant of next generation FFs
  - not enough tested (long timescale tests)