

# Phase Equilibria and Molecular Solutions

Jan G. Korvink and Evgenii Rudnyi  
IMTEK  
Albert Ludwig University  
Freiburg, Germany



ALBERT-LUDWIGS-  
UNIVERSITÄT FREIBURG

## Learning Goals

- ◆ Phase Equilibria
  - ◆ Phase diagrams and classical thermodynamics
  - ◆ Simulations of phase equilibria
- ◆ Molecular solutions
  - ◆ Quantum chemistry: molecule in the solution
  - ◆ Simulating molecule in the solution

## References

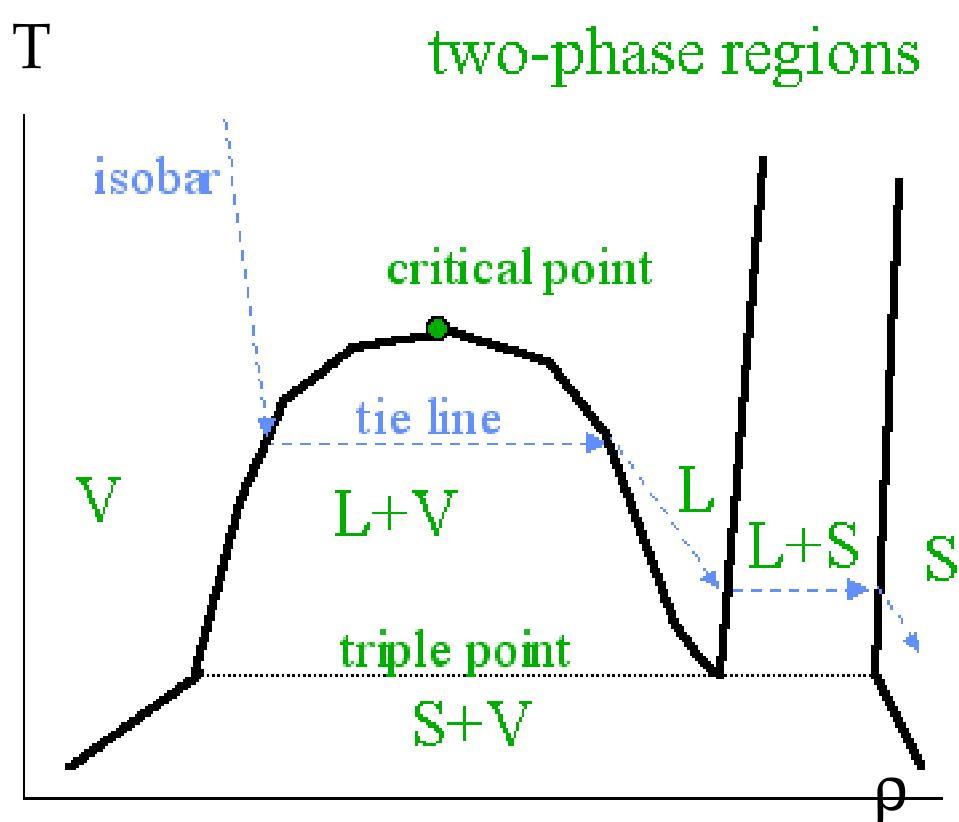
- ◆ Leach, A.R., Molecular modelling: principles and applications, 2001



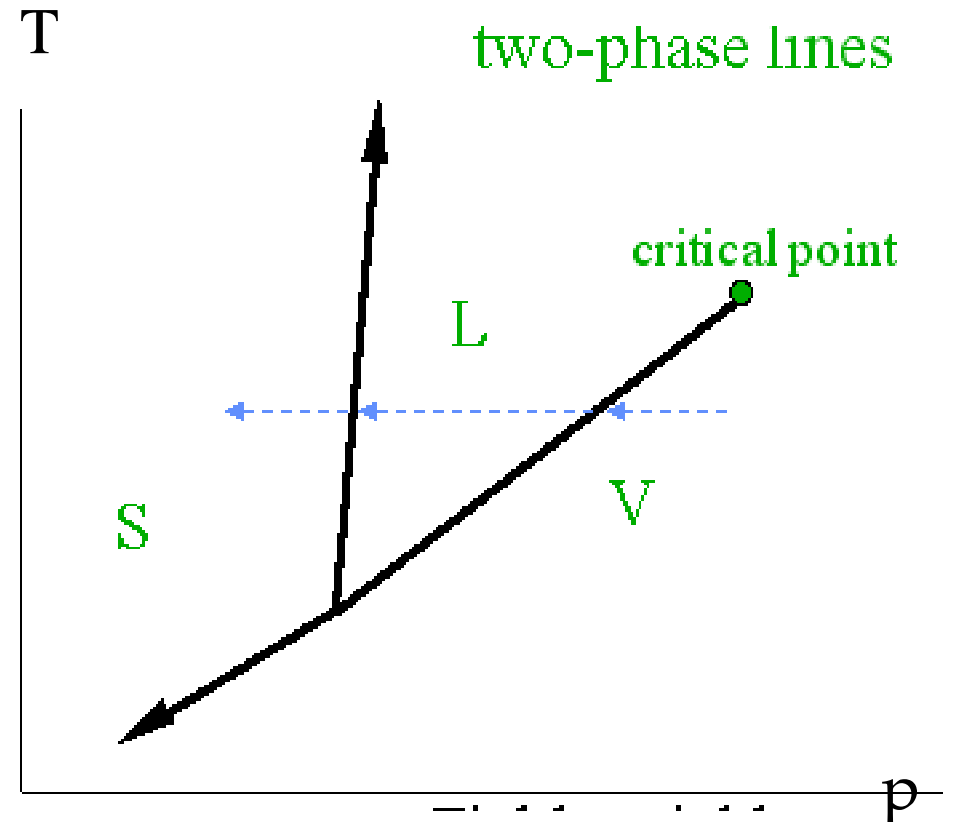
- ◆ <http://kea.princeton.edu/papers/index.html>
  - ◆ Reviews of A.Z. Panagiotopoulos
    - ◆ Monte Carlo Methods for Phase Equilibria of Fluids
    - ◆ Gibbs Ensemble Techniques
    - ◆ Molecular simulation of phase equilibria
- ◆ Free Energy Simulations  
<http://www.biochem.vt.edu/courses/modeling/deltaG.html>
- ◆ Introduction to Continuum Electrostatics, with Molecular Applications (Mike Gilson)  
<http://www.biophysics.org/biophys/society/btol/compute.html>

- ◆ Introduction to phase diagrams
- ◆ Equilibria criteria
- ◆ Phase molar Gibbs energy as a thermodynamic model
- ◆ Thermodynamics simulation
- ◆ CALPHAD
- ◆ Problem to compute a partition function

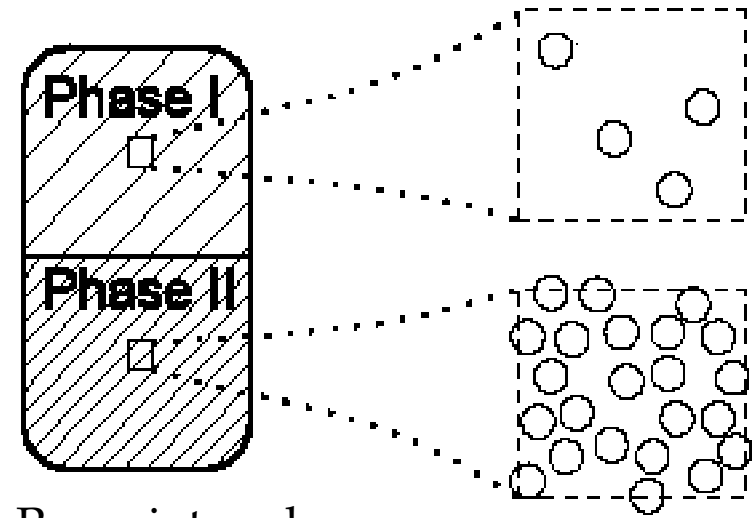
- ◆ One-component phase diagram: S - solid, L - liquid, V - vapor
- ◆ Temperature-density and temperature-pressure



<http://www.cheme.buffalo.edu/courses/ce530/>



- ◆  $U, V \text{ const} \rightarrow \max S$   
 $T, V \text{ const} \rightarrow \min F$   
 $T, p \text{ const} \rightarrow \min G$
- ◆ Phase 1:  $T_1 S_1 = dU_1 + p_1 dV_1 - \mu_1 dn_1$   
 Phase 2:  $T_2 S_2 = dU_2 + p_2 dV_2 - \mu_2 dn_2$
- ◆  $U$  - internal energy,  $V$  - volume,  $n$  - number of moles,  $T$  - temperature,  $p$  - pressure,  $\mu$  - chemical potential
- ◆ Maximize  $S = S_1 + S_2$  at  $U_1 + U_2 = \text{const}$  and  $V_1 + V_2 = \text{const}$
- ◆ Result: thermal  $T_1 = T_2$ , mechanical  $p_1 = p_2$ , and phase  $\mu_1 = \mu_2$   
 equilibria criteria



Panagiotopolus, <http://kea.princeton.edu/>

- ◆ If the molar Gibbs energy function  $G_m(T, p, \vec{x})$  is known for all the phases in question, it is possible to compute all the equilibrium properties {mole fraction  $x_i = n_i / (\sum n_i)$ }
- ◆ Gibbs energy  $G = nG_m$ , entropy  $S = -\frac{\partial G}{\partial T}$ , volume  $V = -\frac{\partial G}{\partial p}$ ,  
enthalpy  $H = G + TS$ , internal energy  $U = H - pV$ ,  
Helmholtz energy  $F = G - pV$
- ◆ Chemical potential  $\mu_i = \frac{\partial G}{\partial n_i}$
- ◆ Phase equilibria by employing the equilibrium criterion

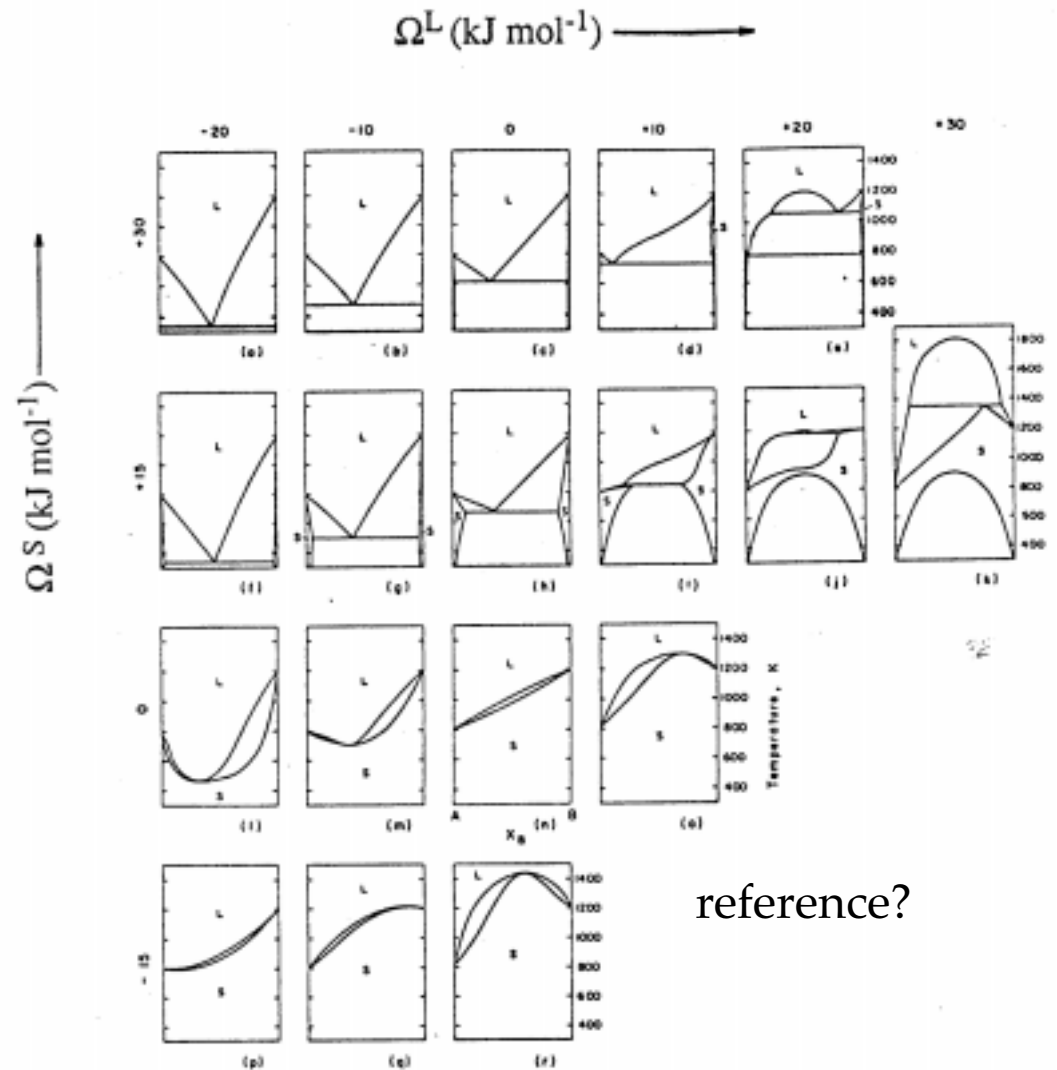
- ◆ Two component systems
- ◆ Two phases: solid solution + liquid solution

- ◆ Regular solution model

$$\Delta_{mix}G = RT(x_A \ln x_A + x_B \ln x_B) + \Omega x_A x_B$$

- ◆ Each phase characterized by “an interaction parameter” -  $\Omega$ . If it is zero we have an “ideal solution”

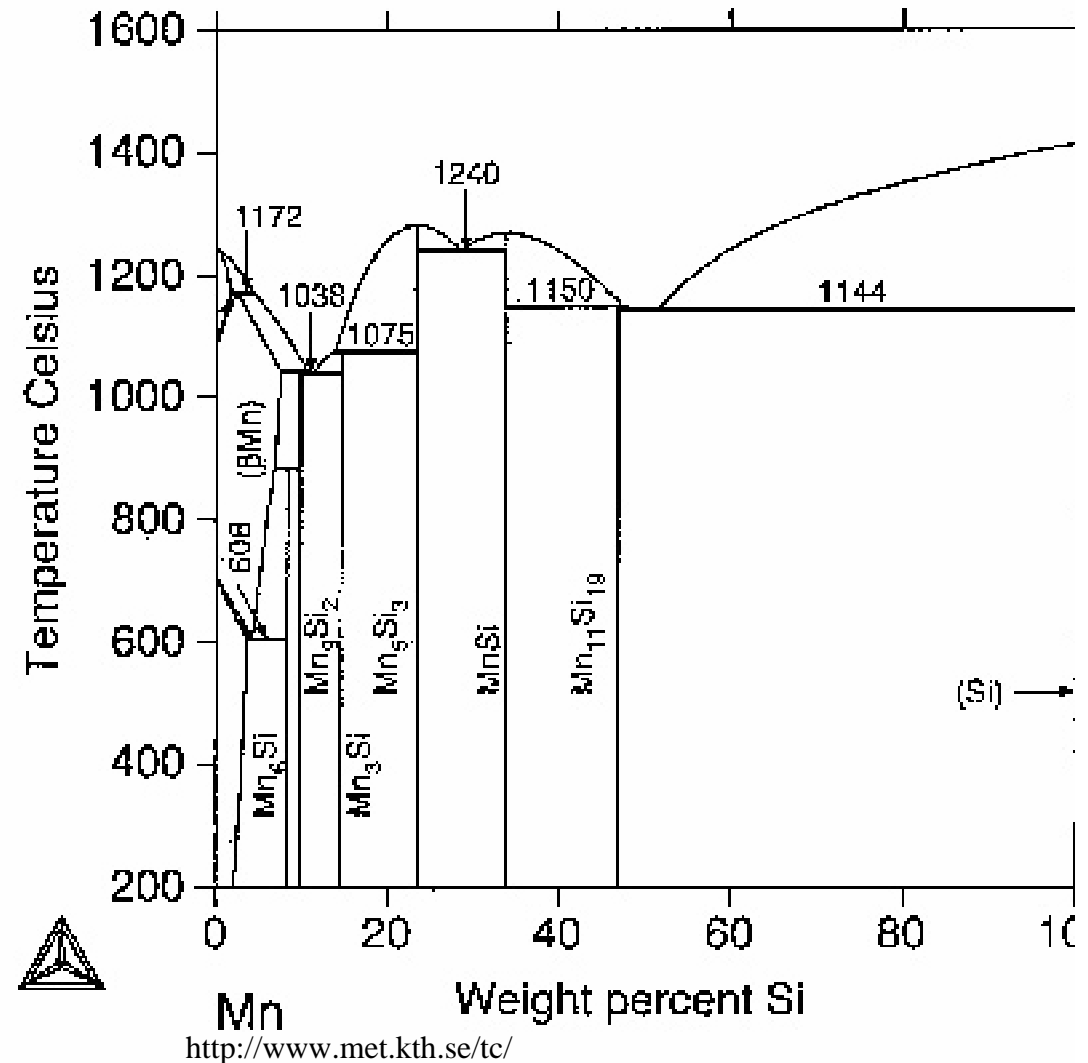
- ◆ Continuous change in  $\Omega$  leads to different topology



reference?



- ◆ Community to produce the databases of molar Gibbs energies to compute the chemical and phase equilibria in the multicomponent systems
- ◆ Phenomenological approach:
  - ◆ to choose an analytical form for the molar Gibbs energy
  - ◆ to determine unknowns parameters from all available experimental results



- ◆ Partition function:  $Z = \frac{1}{h^{dN} N!} \int \exp\{-\beta E\} d\mathbf{p}^N d\mathbf{r}^N$ ,  $\beta = 1/k_B T$

Helmholtz energy:  $F = U_o - k_B T \ln Z$

- ◆ Impossible to compute, Metropolis algorithm can estimate only

$$\langle D \rangle = \frac{\int \exp\{-\beta E\} D(\mathbf{p}^N, \mathbf{r}^N) d\mathbf{p}^N d\mathbf{r}^N}{\int \exp\{-\beta E\} d\mathbf{p}^N d\mathbf{r}^N}$$

- ◆ Trick 1 =  $\exp\{-\beta E\} \exp\{\beta E\}$ , then we can write

$$\frac{1}{Z} = \frac{\int \exp\{-\beta E\} \exp\{\beta E\} d\mathbf{p}^N d\mathbf{r}^N}{\int \exp\{-\beta E\} d\mathbf{p}^N d\mathbf{r}^N} \text{ where } D = \exp\{\beta E\}$$

- ◆ Does not help: it is necessary to sample high energy regions



- ◆ Computing difference between two free energies
- ◆ Particle insertion
- ◆ Direct simulation
- ◆ Gibbs ensemble method
- ◆ More tricks
- ◆ Example: water

- ◆ Two systems: reference  $U_1$  and in question  $U_2$
- ◆ Coupling parameter between two systems  $U(\lambda) = (1 - \lambda)U_1 + \lambda U_2$
- ◆ Partition function depend on  $\lambda$   $Z = \int \exp\{-\beta U(\lambda)\} d\mathbf{r}^N$
- ◆ 
$$\left(\frac{\partial F}{\partial \lambda}\right)_{NVT} = \frac{\int \exp\{-\beta E\} (\partial U(\lambda) / \partial \lambda) d\mathbf{r}^N}{\int \exp\{-\beta E\} d\mathbf{r}^N} = \left\langle \frac{\partial U}{\partial \lambda} \right\rangle, \langle \rangle$$
-ensemble average
- ◆ Then, thermodynamic integration:  $F_2 - F_1 = \int \left\langle \frac{\partial U}{\partial \lambda} \right\rangle d\lambda$
- ◆ Run a series simulation at different  $\lambda$ , then estimate integral numerically

- ◆ Two systems: reference  $U_1$  and in question  $U_2$
- ◆  $F_2 - F_1 = -k_B T \ln(Z_2/Z_1)$
- ◆ Write expression for  $Z$  and use  $1 = \exp\{-\beta_1 U_1\} \exp\{\beta U_1\}$
- ◆ Thermodynamic perturbation
- ◆ Monte-Carlo over the system 1:  $F_2 - F_1 = -k_B T \ln \left\langle \exp\left(-\frac{U_2 - U_1}{k_B T}\right) \right\rangle_1$
- ◆ Monte-Carlo over the system 2:  $F_2 - F_1 = -k_B T \ln \left\langle \exp\left(-\frac{U_1 - U_2}{k_B T}\right) \right\rangle_2$
- ◆ In principle, this is equivalent, but in practice, this is not.

- ◆ First state -  $N$  particles, second state -  $N+1$  particles

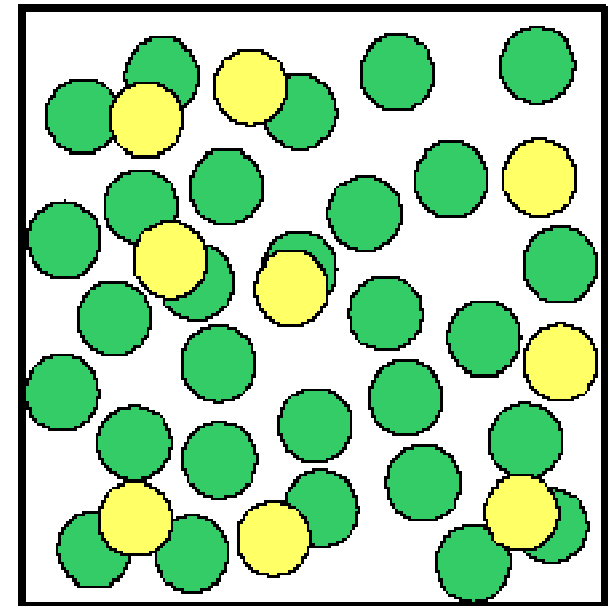
- ◆ 
$$\mu = \left( \frac{\partial F}{\partial n} \right)_{TV} = F_2 - F_1 = -k_B T \ln(Z_{N+1}/Z_N)$$

- ◆ Because of change in the number of particles

- ◆ 
$$\mu_{ex} = \mu - \mu_{id} = -k_B T \ln \left\langle \exp \left( -\frac{U_{test}}{k_B T} \right) \right\rangle_1$$

- ◆ It is possible to derive similar for the particle deletion, but the performance is worse

- ◆ Problem with crystals: no place to insert a particle



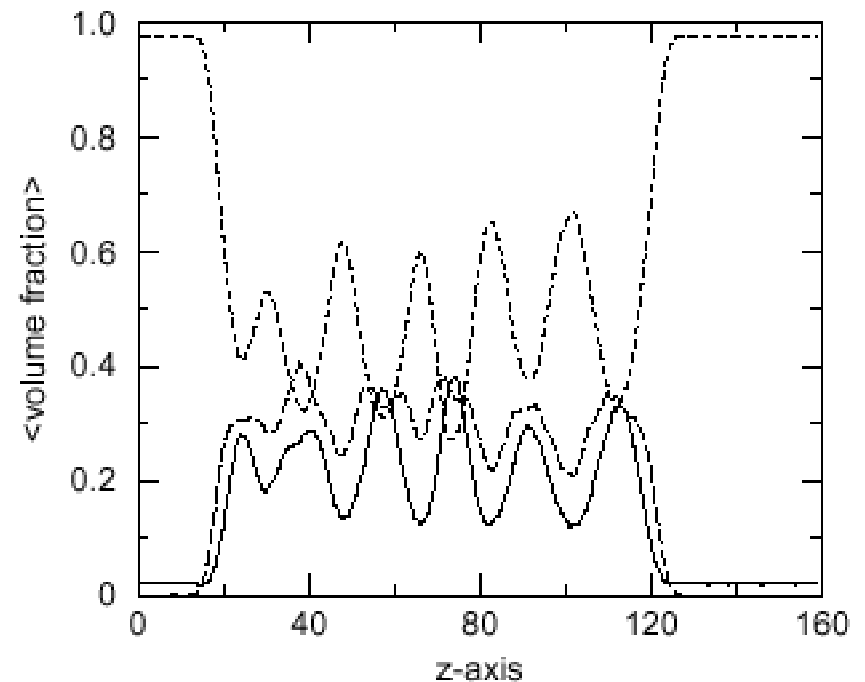
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- ◆ The main problem is introducing interface

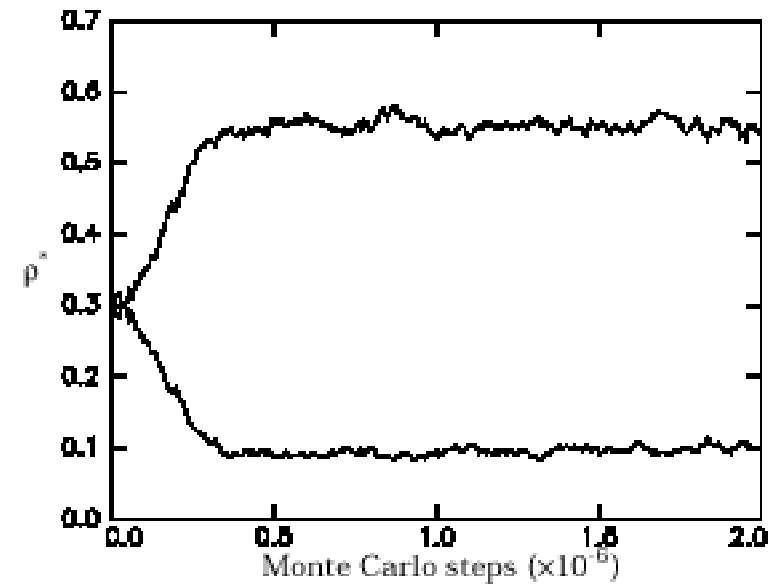
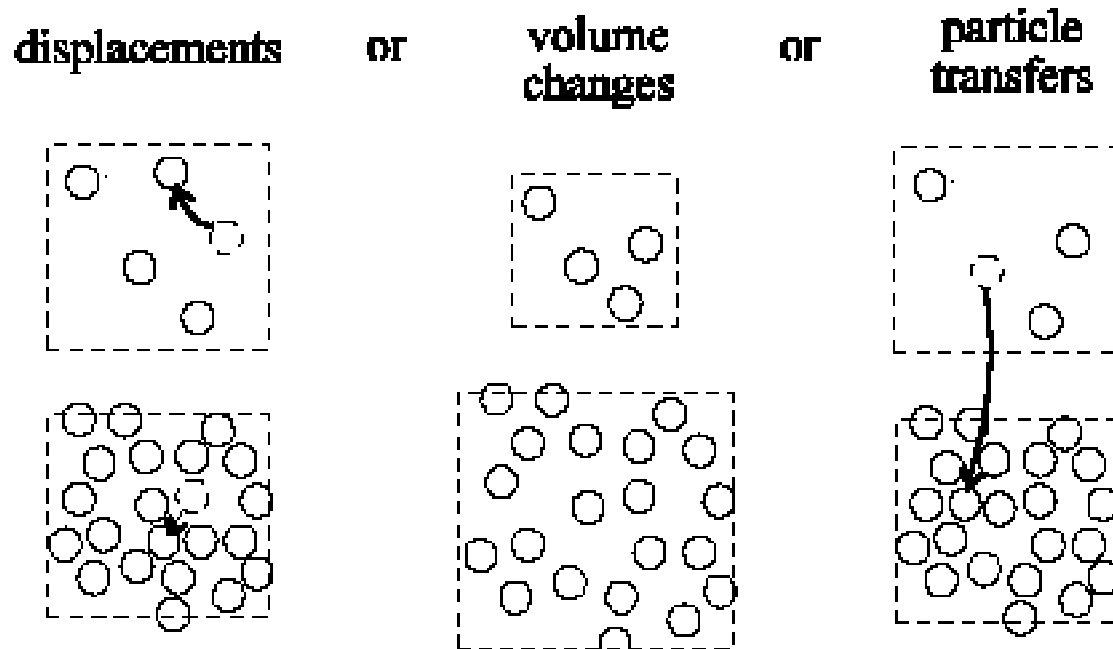
Table 1: Percentage of particles in the interface of a cubic domain (from Frenkel&Smit)

N	125	1 000	64 000	1 000 000
$P_{\text{int}}$	78%	49%	14%	6%

- ◆ The equilibration time is too long
- ◆ The metastable states (overcooled liquid or oversaturated vapor)
- ◆ Computationally expensive
- ◆ Example: two-phase three component system (Panagiotopoulos, J. Phys.: Condens. Matter 12 (2000) R25)



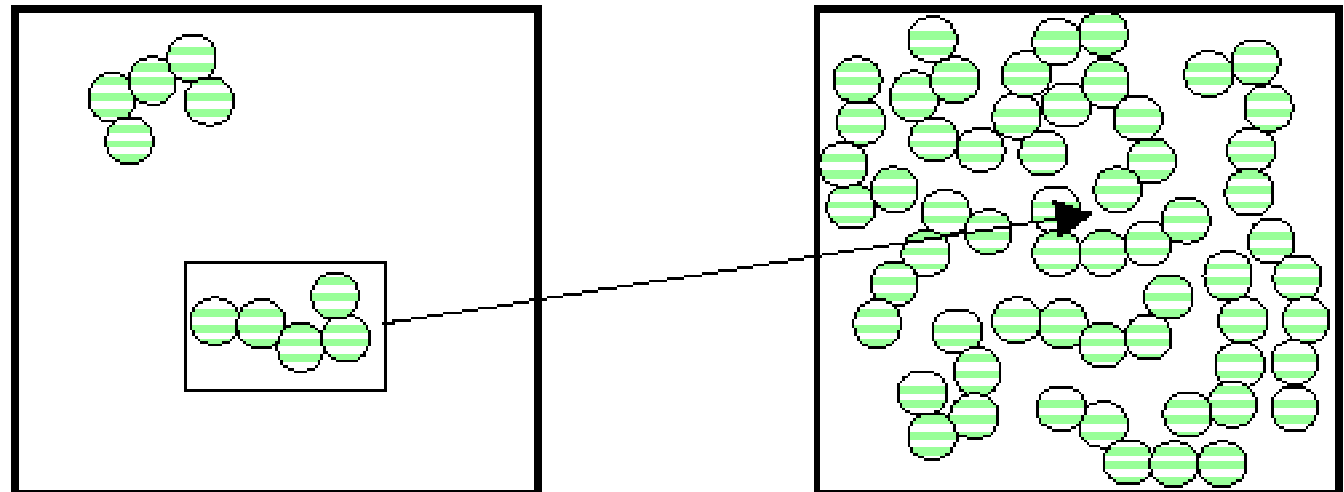
- ◆ Simulating two-phase equilibria without interface
- ◆ Two different boxes at given temperature



- ◆ Panagiotopoulos, <http://kea.princeton.edu/>
- ◆ Chemical potential in the implicit form



- ◆ Non-Boltzman distributions
  - ◆ Sampling high energy states: Umbrella sampling
  - ◆ Configuration bias Monte-Carlo
  - ◆ Cluster moves
- ◆ Histogram-re-weighting method: Grand Canonical Monte-Carlo

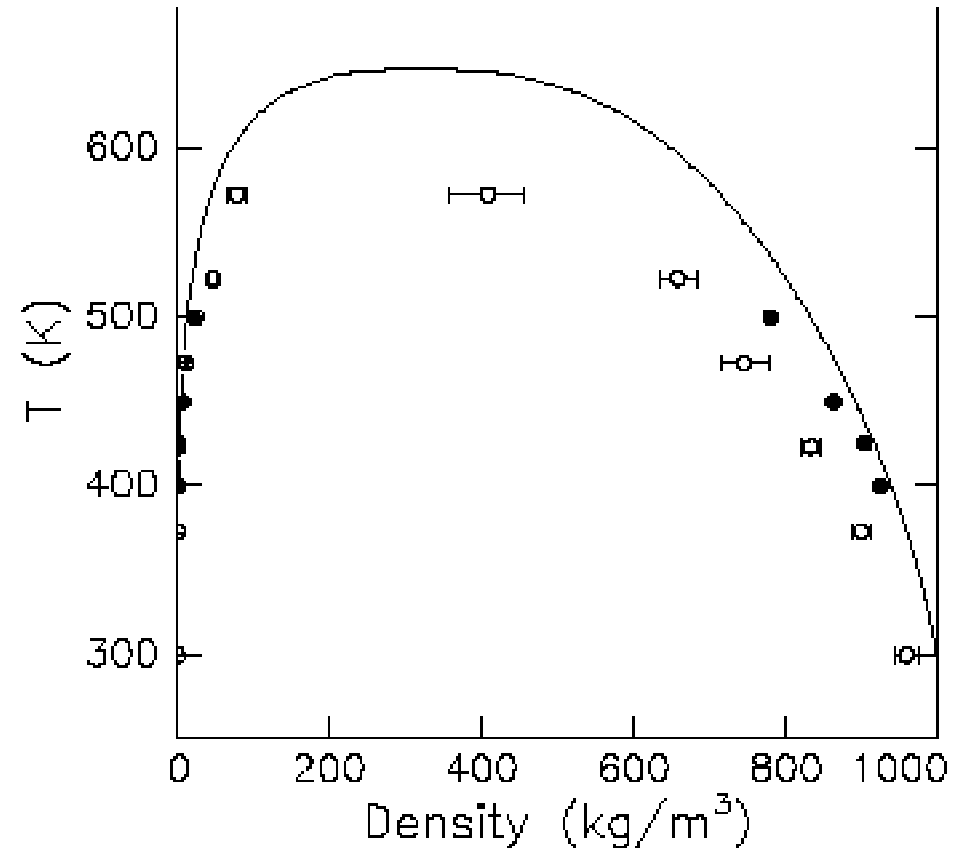


<http://kea.princeton.edu/>

◆ It is necessary to derive specialized force fields

Table 1: Comparison of thermodynamic properties of fixed point charge water models. Simulation data are from Errington and Panagiotopoulos (1998) for the SPC, SPC/E and Exp-6 models and from Vlot *et al.*, (1999) for the TIP4P model.

Model	$T_c$ (K)	$\rho_c$ (kg/m <sup>3</sup> )	$P_{vp}$ (bar) at $T=373$ K
SPC	594 ± 1	271 ± 6	1.0 ± 0.2
SPC/E	639 ± 2	273 ± 9	0.37 ± 0.06
TIP4P	561 ± 3	290 ± 50	1.4 ± 0.1
Exp-6	646 ± 1	297 ± 5	0.95 ± 0.01
Experimental	647	322	1.01



Panagiotopoulos, 2000

Figure 9. Phase diagrams for SPC (○) and TIP4P (●) models for water [48,44] compared to experimental results (—).



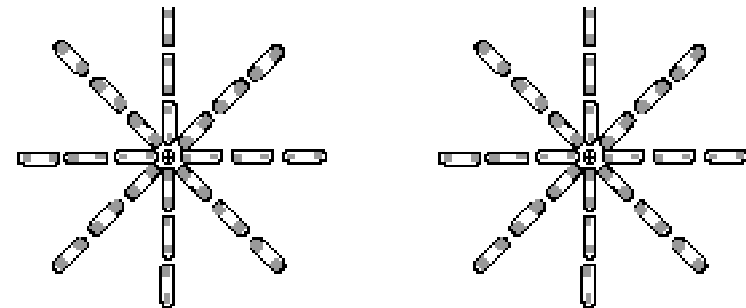
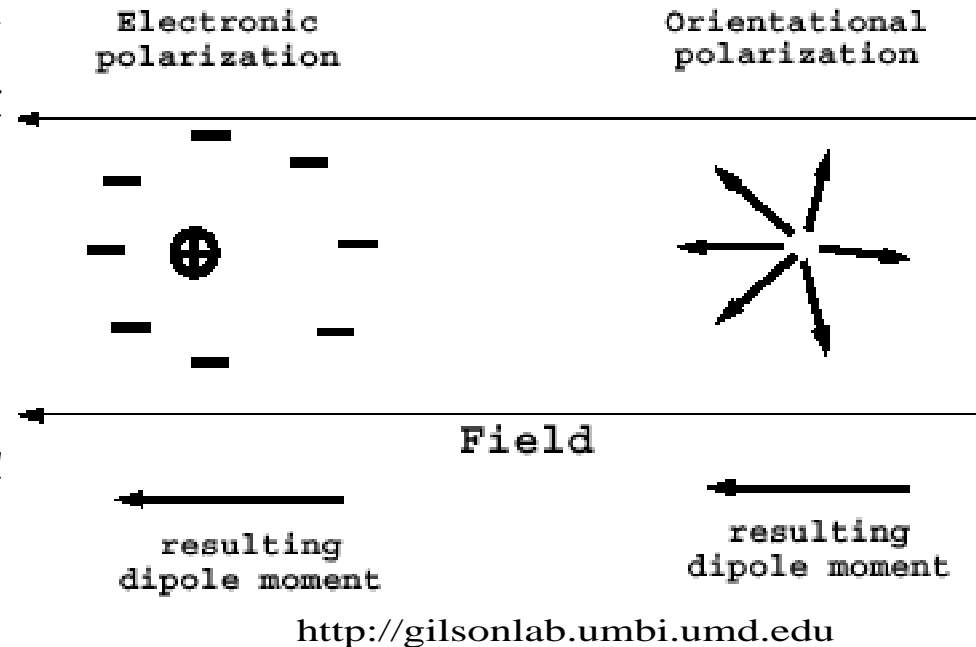
- ◆ Molecules in the electrical field
- ◆ Extreme case
- ◆ Macroscopic continuum models
- ◆ Electrostatic energy
- ◆ Discrete modeling of the solvation shell

- ◆ Electrical field leads to the molecule polarization (non-zero net dipole moment)
- ◆ The field of these dipoles runs against the inducing field
- ◆ Macroscopic result - dielectric

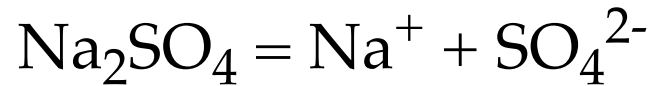
$$\text{constant } U = \frac{q_1 q_2}{4\pi\epsilon\epsilon_0 r_{12}}$$

hexane - 1.9, benzene - 2.3, water - 78

- ◆ The electronic distribution in the molecule in the solution is different

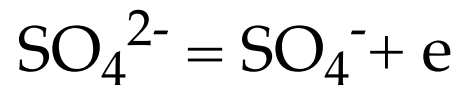


- ◆ Solution chemistry



- ◆ However,  $\text{SO}_4^{2-}$  is not stable in the gas phase

- ◆ Second electron affinity is negative



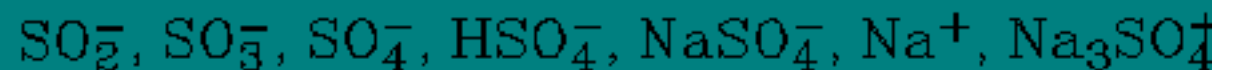
- ◆ Quantum chemistry (or force field) of individual  $\text{SO}_4^{2-}$  is of no use

Multi-charge negative ions do not exist in the gas phase

<http://www.chem.msu.su/~rudnyi/ions/>

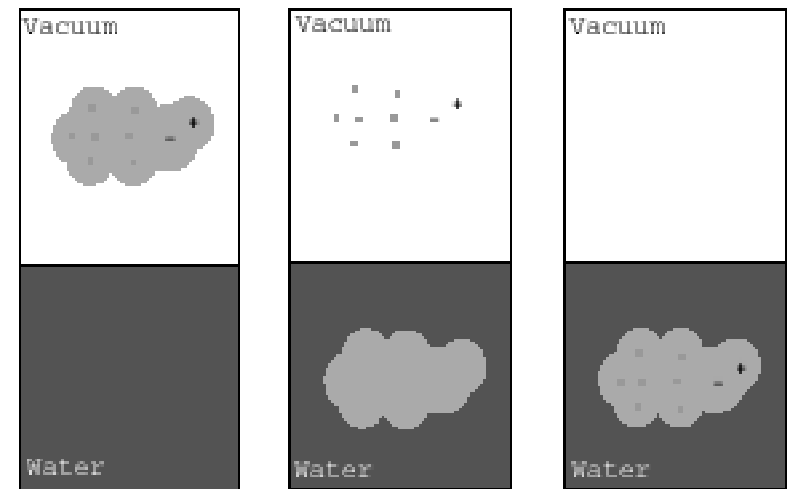
sodium sulphate  $\text{Na}_2\text{SO}_4$

- ◆ ion-molecule equilibria
- ◆ field desorption
- ◆ secondary ion mass spectroscopy
- ◆ fast atom bombardment
- ◆ laser desorption
- ◆ field desorption from solution



$\text{SO}_4^{2-}$  is not found

- ◆  $E = E_o + E_s$ , total = isolated molecule + solvation energy
- ◆  $E_s = E_{es} + E_{disp} + E_{cav}$ , solvation = electrostatic + dispersion + cavity
- ◆ If we can not use  $E_o$ , then let us solve Schrödinger equation with modified Hamiltonian  $H = H_o + U$
- ◆ Problems:
  - ◆ Whether we can use macroscopic  $\epsilon$  near cavity
  - ◆ We take solvent at some temperature ( $\epsilon$  depend on T), but we describe ground molecule energy
  - ◆  $E_s$  - solvation energy or Gibbs solvation energy



<http://gilsonlab.umbi.umd.edu>

- ◆ Kirkwood, molecule - N point charges  $\{Q_i, r_i\}$ , spherical cavity

$$E_{es} = \frac{1}{2} \sum_n \frac{(n+1)(1-\epsilon)}{n+(n+1)\epsilon} \sum_{ij} Q_i Q_j \frac{(r_i r_j)^n}{a^{2n+1}} P_n(\cos \Theta_{ij}),$$

n - multipole expansion, a - cavity radius, P - Legendre polynomial

- ◆ n = 0, monopole, Born solvation energy for the ions,

$$E_{es} = -\frac{Q^2}{2a} \left(1 - \frac{1}{\epsilon}\right)$$

- ◆ n = 1, dipole, Onsager's reaction field  $E_{es} = -\frac{1}{2} \left[ \frac{2(\epsilon-1)\mu^2}{2\epsilon+1 a^3} \right]$

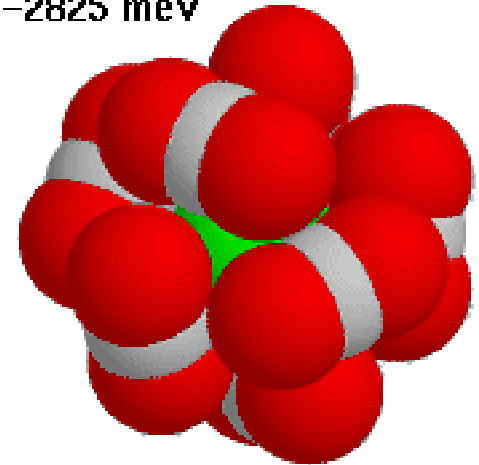
- ◆ For non-spheric cavities, solve Poisson equation



- ◆ To model solvation shell, add point charges around the molecule in question
  - ◆ Advantage
    - ◆ More real interactions
    - ◆ No cavity geometry
    - ◆ No macroscopic parameters
  - ◆ Problems
    - ◆ How to construct the solvation shell
- ◆ Solve Schrödinger equation for a cluster of the solute molecule and several solvent molecules
  - ◆ Optimize geometry

## Solvation of Cl<sup>-</sup> by CO<sub>2</sub>

-2825 meV



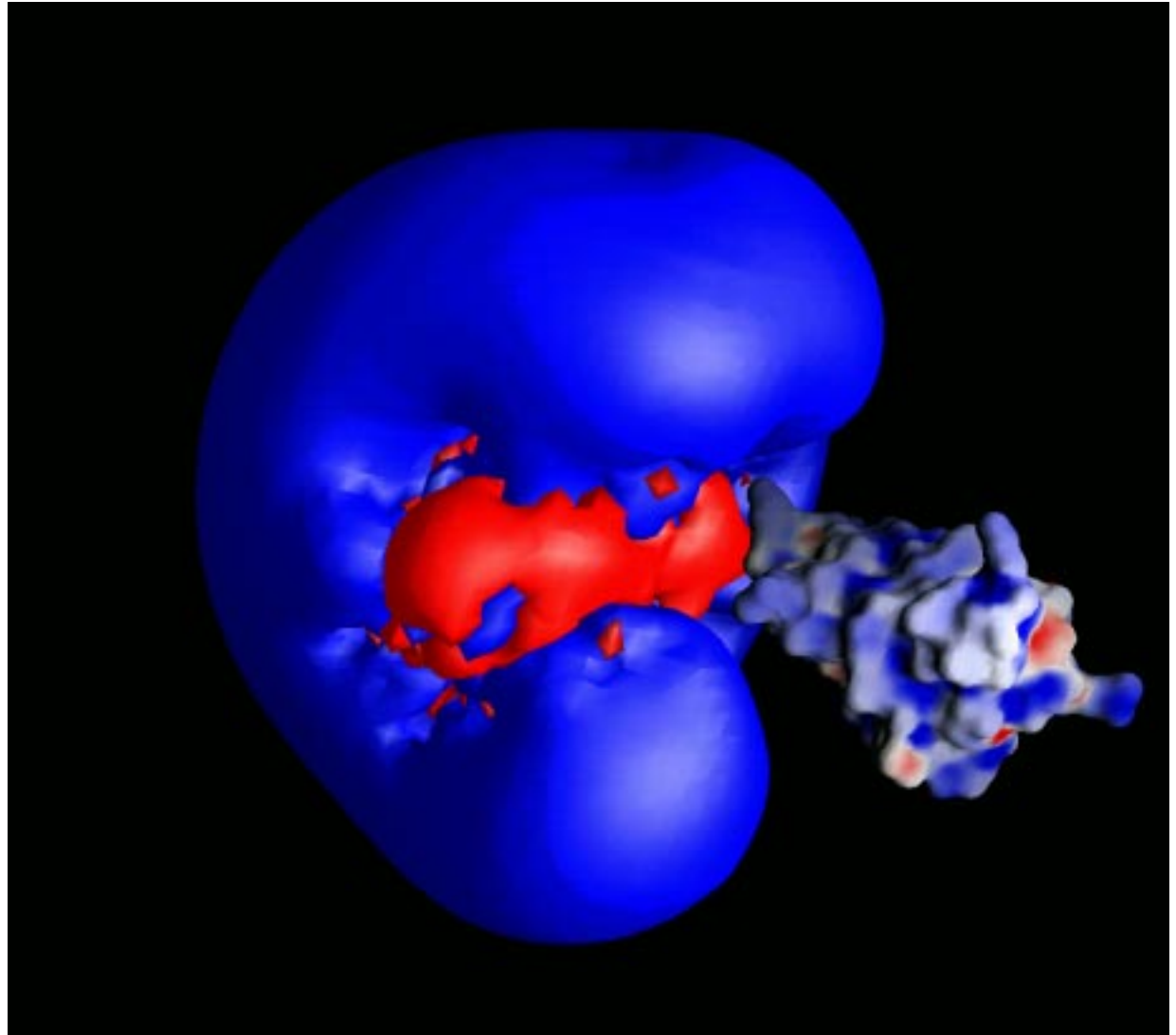
<http://www.weizmann.ac.il/chemphys/faeder/Gallery/>



- ◆ Continuum models: Poisson-Boltzmann equation
- ◆ Example: trypsin
- ◆ Stochastic mechanics

- ◆ Take protein and make a cavity based on van der Waals radii of atoms
- ◆ Write Poisson equation  $\nabla \varepsilon \nabla \phi = -4\pi\rho$
- ◆ Use  $\varepsilon$  for solvent out of the cavity, and  $\varepsilon=2-4$  within the cavity to take into account the polarization of the atoms
- ◆ Model a concentration of the mobile ions by Boltzman equation  
$$n = n_{bulk} \exp(-Q\phi / (k_B T))$$
- ◆ Combine and, to make life simple, linearize  $\nabla \varepsilon \nabla \phi - k\phi = -4\pi\rho$   
 $k$  is related to Debye-Hückel radius
- ◆ Solve by the boundary element method or the finite difference method

- ◆ From Leach's book
- ◆ 3D Electrostatic isopotential contours around trypsin [Marquart et al 1983]. Contours are drawn at  $-1\text{kT}$  (red) and  $+1\text{kT}$  (blue). The trypsin inhibitor is also shown with its electrostatic potential mapped onto the molecular surface.



- ◆ One solute molecule + a number of solvent molecules
- ◆ Non-periodic, stochastic boundary conditions
- ◆ Langevin dynamics  $M\ddot{x} + C\dot{x} + \nabla V(x) = D\dot{W}(t)$ 
  - ◆ Kinetic energy: mass matrix and acceleration
  - ◆ Dissipation energy to surrounding: dumping matrix and velocity
  - ◆ Potential function
  - ◆ RHS: normalized white noise,  $W(t)$  - Wiener process
- ◆ Fluctuation-dissipation theorem  $DD^T = 2k_B TC$
- ◆ Typically dumping matrix is modeled as  $C = \gamma M$

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