

# Computational biophysics

## Protein's geometry

Centre of mass  $\vec{R}_{cm} = \frac{\sum_{i=1}^N m_i \vec{r}_i}{\sum_{i=1}^N m_i}$

Radius of gyration  $r_g = \sqrt{\frac{\sum_{i=1}^N m_i (\vec{r}_i - \vec{R}_{cm})^2}{\sum_{i=1}^N m_i}}$

$RMSD(t) = \sqrt{\frac{1}{N} \sum_{i=1}^N (\vec{r}_i(t) - \vec{r}_i(0))^2}$

$RMSF_i = \sqrt{\langle \Delta r_i^2 \rangle} = \sqrt{\frac{1}{M} \sum_{f=1}^M (\vec{r}_{i,f} - \langle \vec{r}_i \rangle)^2}$

$B_i = \frac{8\pi^2}{3} RMSF_i^2$

## Semi-empirical force fields

### Bond stretching

Harmonic  $U(r_{AB}) = \frac{1}{2} k_{AB} (r_{AB} - r_{AB,eq})^2$

Anarmonic  $U(r_{AB}) = \frac{1}{2} \left[ k_{AB} + k_{AB}^{(3)} (r_{AB} - r_{AB,eq}) \right] (r_{AB} - r_{AB,eq})^2$

Quartic correction  $U(r_{AB}) = \frac{1}{2} \left[ k_{AB} + k_{AB}^{(3)} (r_{AB} - r_{AB,eq}) + k_{AB}^{(4)} (r_{AB} - r_{AB,eq})^2 \right] \cdot (r_{AB} - r_{AB,eq})^2$

Morse  $U(r_{AB}) = D_{AB} \left[ 1 - e^{-\alpha_{AB}(r_{AB} - r_{AB,eq}^2)} \right]$

### Valence angle bending

Potential  $U(\theta_{ABC}) = \frac{1}{2} k_{ABC} + k_{ABC}^{(3)} (\theta_{ABC} - \theta_{ABC,eq}) + k_{ABC}^{(4)} (\theta_{ABC} - \theta_{ABC,eq})^2 + \dots [(\theta_{ABC} - \theta_{ABC,eq})^2]$

$U(\theta_{ABC}) = \sum_{\{j\}_{ABC}} k_{j,ABC}^{fourier} [1 + \cos(j\theta_{ABC} + \psi_j)]$

Fourier  $k_{j,ABC}^{fourier} = \frac{2k_{ABC}^{harmonic}}{j^2}$

### Torsions

Potential  $U(\omega_{ABCD}) = \frac{1}{2} \sum_{\{j\}_{ABCD}} V_{j,ABCD} [1 + (-1)^{j+1} \cos(j\omega_{ABCD} + \psi_{j,ABCD})]$

Improper  $U(\omega_{ABCD}) = \frac{1}{2} \sum_{\{j\}_{ABCD}} V_{j,ABCD} [1 + (-1)^{j+1} \cos(j\omega_{ABCD} + \psi_{j,ABCD})]$

### Van der Waals

Lennard-Jones  $U(r_{AB}) = 4\epsilon_{AB} \left[ \left( \frac{\sigma_{AB}}{r_{AB}} \right)^{12} - \left( \frac{\sigma_{AB}}{r_{AB}} \right)^6 \right]$

Morse  $U(r_{AB}) = D_{AB} \left[ 1 - e^{-\alpha_{AB}(r_{AB} - r_{AB,eq}^{\lambda})} \right]^2$

Hill  $U(r_{AB}) = \epsilon \left[ \frac{6}{\beta_{AB} - 6} e^{\beta_{AB} \frac{1 - r_{AB}}{r_{AB}}} - \frac{\beta_{AB}}{\beta_{AB} - 6} \left( \frac{r_{AB}}{r_{AB}} \right)^6 \right]$

### Electrostatic interactions

Distribution of charges  $U_{AB} = \sum_A \sum_{B>A} \vec{M}^{(A)} \vec{V}^{(B)}$

Point like  $U_{AB} = \frac{q_A q_B}{\epsilon_{AB} r_{AB}}$

Dipolar interactions  $U_{AB/CD} = \frac{\mu_{AB} \mu_{CD}}{\epsilon_{AB/CD} r_{AB/CD}^3} (\cos \chi_{AB/CD} - 3 \cos \alpha_{AB} \cos \alpha_{CD})$

### Parameterization

Parameters  $Z = \sqrt{\sum_i \frac{\text{observables occurrences}}{j} \sum_j \frac{(\text{calc}_{i,j} - \text{expt}_{i,j})^2}{w_i^2}}$

$\sigma_{AB} = \sigma_A + \sigma_B$

$\epsilon_{AB} = \sqrt{\epsilon_A \epsilon_B}$

## Classical mechanics

### Newton's laws

$\vec{F} = m\vec{a}$   $\vec{F}_{BA} = -\vec{F}_{AB}$

$\vec{v}(t) = \frac{d\vec{r}}{dt}$   $\vec{a}(t) = \frac{d\vec{v}}{dt} = \frac{d^2\vec{r}}{dt^2}$   $m \frac{d^2\vec{r}}{dt^2} = \vec{F}$

Force acting on atom  $\vec{F}_i(\vec{r}_1, \dots, \vec{r}_N, \vec{r}_i) = \sum_{j \neq i} \vec{F}_{ij}(\vec{r}_i - \vec{r}_j) + \vec{F}^{(ext)}(\vec{r}_i, \vec{r}_i)$

Bond stretching:  $U = \frac{k_b}{2} (l - l^0)^2$

Bond bending:  $U = \frac{k_\theta}{2} (\theta - \theta^0)^2$

Bond torsion:  $U = k_\phi [1 + \cos(n\phi - \phi^0)]$

Van der Waals interactions:  $U = \left[ \frac{a_{ij}}{r_{ij}^{12}} - \frac{b_{ij}}{r_{ij}^6} \right]$

Electrostatic interactions:  $U = \frac{332 q_i q_j}{\epsilon r_{ij}}$

$\vec{p}_i = m_i \vec{v}_i = m \dot{\vec{r}}_i$   $\vec{F}_i = m_i \ddot{\vec{r}}_i = \dot{\vec{p}}_i$

$\vec{x}(t) = \{\vec{r}_1(t), \dots, \vec{r}_N(t), \vec{p}_1(t), \dots, \vec{p}_N(t)\}$

### Lagrangian formulation

$\vec{F}_i(\vec{r}_1, \dots, \vec{r}_N) = -\Delta_i U(\vec{r}_1, \dots, \vec{r}_N)$

$W_{AB} = \int_A^B \vec{F}_i d\vec{l} = U_A - U_B = -\Delta U_{AB}$   $\oint \vec{F}_i d\vec{l} = 0$

Kinetic energy  $K(\dot{\vec{r}}_1, \dots, \dot{\vec{r}}_N) = \frac{1}{2} \sum_i m_i \dot{\vec{r}}_i^2$

$\mathcal{L}(\vec{r}_1, \dots, \vec{r}_N, \dot{\vec{r}}_1, \dots, \dot{\vec{r}}_N) = K(\dot{\vec{r}}_1, \dots, \dot{\vec{r}}_N) - U(\vec{r}_1, \dots, \vec{r}_N)$

Euler-Lagrange  $\frac{d}{dt} \left( \frac{\partial \mathcal{L}}{\partial \dot{r}_i} \right) - \frac{\partial \mathcal{L}}{\partial r_i} = 0$

$E = \frac{1}{2} \sum_i m_i \dot{\vec{r}}_i^2 + U(\vec{r}_1, \dots, \vec{r}_N)$

$quad \frac{dE}{dt} = 0$

### Generalized coordinates

$q_\alpha = f_\alpha(\vec{r}_1, \dots, \vec{r}_N)$   $\alpha = 1, \dots, 3N$   $\vec{r}_i = \vec{g}_i(q_1, d, \dots, q_{3N})$   $i = 1, \dots, N$

$\dot{\vec{r}}_i = \sum_{\alpha=1}^{3N} \frac{\partial \vec{r}_i}{\partial q_\alpha} \dot{q}_\alpha$   $\mathcal{L}(q, \dot{q}) = \frac{1}{2} \sum_{\alpha=1}^{3N} \sum_{\beta=1}^{3N} G_{\alpha\beta} \dot{q}_\alpha \dot{q}_\beta - U(q_1, \dots, q_{3N})$

## Classical mechanics (contd)

### Legendre transforms

$s = f'(x) \equiv g(x)$   $f'(x) = g(x) = s \Rightarrow x = g^{-1}(s)$

$b(g^{-1}(s)) = f(g^{-1}(s)) - sg^{-1}(s) \equiv \tilde{f}(s) = f(x(s)) - sx(s)$

$\tilde{f}(s_1, \dots, s_n) = f(x_1(s_1, \dots, s_n), \dots, x_n(s_1, \dots, s_n)) - \sum_i s_i x_i(s_1, \dots, s_n)$

### Hamiltonian formulation

$\mathcal{H}(\vec{r}_1, \dots, \vec{r}_N, \vec{p}_1, \dots, \vec{p}_N) = -\tilde{\mathcal{L}}(\vec{r}_1, \dots, \vec{r}_N, \vec{p}_1, \dots, \vec{p}_N)$

$\mathcal{H}(\vec{r}_1, \dots, \vec{r}_N, \vec{p}_1, \dots, \vec{p}_N) = \sum_{i=1}^N \frac{\vec{p}_i^2}{2m_i} + U(\vec{r}_1, \dots, \vec{r}_N)$

$\mathcal{H}(q_1, \dots, q_{3N}, p_1, \dots, p_{3N}) = \frac{1}{2} \sum_{\alpha} \sum_{\beta} p_{\alpha} G_{\alpha\beta}^{-1} p_{\beta} + U(q_1, \dots, q_{3N})$

Hamilton equations  $\dot{q}_\alpha = \frac{\partial \mathcal{H}}{\partial p_\alpha}$   $\dot{p}_\alpha = -\frac{\partial \mathcal{H}}{\partial q_\alpha}$   $\frac{\mathcal{H}}{dt} = 0$   $\mathcal{H} = const$

### Some properties

Conservation laws  $\frac{da}{dt} = \frac{\partial a}{\partial x_i} \dot{x}(t) = \{a, \mathcal{H}\} = 0$

Incompressibility  $\nabla_x(x) = 0$

Symplectic structure  $M = J^T M J$   $J_{kl} = \frac{\partial x_k(t)}{\partial x_l(0)}$

## Theoretical foundations of statistical mechanics

### Thermodynamics

Equilibrium  $g(N, P, V, T) = 0$  First law  $\Delta E = \Delta Q + \Delta W$

State function  $f(n, P, V, T)$  Entropy  $\Delta S = \int_1^2 \frac{dQ_{rev}}{T}$

Reversible work  $dW_{rev} = -PdV + \mu dN$

Heat  $dQ_{rev} = CdT$

### The ensemble

Average  $A = \frac{1}{2} \sum_{\lambda=1}^N a(x_\lambda) \equiv \langle a \rangle$

Microstate  $x_0 = (q_1(0), \dots, q_{3N}(0), p_1(0), \dots, p_{3N}(0))$

Phase space volume  $dx_t = J(x_t; x_0) dx_0$   $\frac{dx_t}{dt} = 0 \Rightarrow J(x_t; x_0) = 1 \Rightarrow dx_t = dx_0$

$f(x_t) : \int f(x) dx = 1 \wedge \frac{df(x_t, t)}{dt} = 0 \Rightarrow$

Distribution function  $f(x_t, t) dx_t = f(x_0, 0) dx_0 \Rightarrow$

$\frac{\partial f(x_t, t)}{\partial t} + \{f(x_t, t), \mathcal{H}(x_t, t)\} = 0$

Equilibrium  $A = \int a(x) f(x, t) dx \Rightarrow \frac{\partial f(x, t)}{\partial t} = 0 \wedge \{f(x, t), \mathcal{H}(x, t) = 0\} \Rightarrow$

$f(x) \propto \mathcal{F}(\mathcal{H}(x))$

$Z = \int dx \mathcal{F}(\mathcal{H}(x)) \Rightarrow f(x) = \frac{1}{Z} \mathcal{F}(\mathcal{H}(x))$

## Microcanonical ensemble

### State and distribution function

State function  $dS = \frac{1}{T} dE + \frac{P}{T} dV - \frac{\mu}{T} dN$

$\left( \frac{\partial S}{\partial E} \right)_{V, N} = \frac{1}{T}$   $\left( \frac{\partial S}{\partial V} \right)_{N, E} = \frac{P}{T}$   $\left( \frac{\partial S}{\partial N} \right)_{V, N} = \frac{\mu}{T}$

Boltzmann relation  $S(N, V, E) = k \ln \omega(N, V, E)$

$\Omega(N, V, E) = M_N \int d\vec{p} \int_{D(V)} d\vec{r} \delta(\mathcal{H}(\vec{r}, \vec{p}) - E)$

Distribution function  $= M_N \int dx \delta(\mathcal{H}(x) - E)$

$M_N = \frac{E_0}{N! h^{3N}}$

$A = \langle a \rangle = \frac{M_N}{\Omega(N, V, E)} \int dx a(x) \delta(\mathcal{H}(x) - E) = \frac{\int dx a(x) \delta(\mathcal{H}(x) - E)}{\int dx \delta(\mathcal{H} - E)}$

$\left\langle x_i \frac{\partial \mathcal{H}}{\partial x_j} \right\rangle = \frac{M_N}{\Omega(N, V, E)} \frac{\partial}{\partial E} \int_{\mathcal{H}(x) < E} dx x_i \frac{\partial (\mathcal{H} - E)}{\partial x_j}$

### Virial theorem

$\left\langle x_i \frac{\partial \mathcal{H}}{\partial x_j} \right\rangle = \delta_{ij} \frac{\Sigma(E)}{\frac{\partial \Sigma(E)}{\partial E}}$

$\Sigma(N, V, E) = \frac{1}{N! h^{3N}} \int dx \theta(E - \mathcal{H})$

$\Omega(N, V, E) = E_0 \frac{\partial \Sigma(N, V, E)}{\partial E}$   $\left\langle x_i \frac{\partial \mathcal{H}}{\partial x_j} \right\rangle = \delta_{ij} \left( \frac{\ln \Sigma(E)}{\frac{\partial \Sigma(E)}{\partial E}} \right)^{-1}$

$S(N, V, E) = k \ln \Omega(N, V, E) \simeq k \ln \Sigma(N, V, E) = \tilde{S}(N, V, E)$

$\left\langle x_i \frac{\partial \mathcal{H}}{\partial x_j} \right\rangle \simeq \delta_{ij} \left( \frac{S(E)}{\frac{\partial S(E)}{\partial E}} \right)^{-1} = kT \delta_{ij}$

### Thermal contact

$\Omega(N, V, E) = M_N \int dx \delta(\mathcal{H}_1(x_1) + \mathcal{H}_2(x_2) - E)$

$\Omega(N, V, E) = \int dE_1 \Omega_1(N_1, V_1, E_1) \Omega_2(N_2, V_2, E - E_1)$

$S(N, V, E) = k \ln \Omega_1(N_1, V_1, E_1) + k \ln \Omega_2(N_2, V_2, E - E_1)$

$= S_1(N_1, V_1, E_1) + S_2(N_2, V_2, E - E_1)$

$T_1 = T_2$

## Introduction to molecular dynamics

### Verlet algorithm

$\vec{r}_i(t + \Delta t) = 2\vec{r}_i(t) - \vec{r}_i(t - \Delta t) + \frac{\Delta t^2}{m_i} \vec{F}_i(t)$

$\vec{v}_i(t + \Delta t) = \vec{v}_i(t) + \frac{\Delta t}{2m_i} \left[ \vec{F}_i(t) + \vec{F}_i(t + \Delta t) \right]$

Initial conditions  $f(v) = \sqrt{\frac{m}{2\pi kT}} e^{-\frac{mv^2}{2kT}}$   $f(x) = \frac{1}{\sqrt{2\pi\sigma^2}} e^{-\frac{x^2}{2\sigma^2}}$

## Introduction to molecular dynamics (contd)

### Action integral

$Q \equiv \{q_1, \dots, q_{3N}\}$   $\dot{Q} \equiv \{\dot{q}_1, \dots, \dot{q}_{3N}\}$

$A[Q] = \int_{t_1}^{t_2} \mathcal{L}(Q(t), \dot{Q}(t)) dt$

$\delta Q(t_1) = \delta Q(t_2) = 0$   $\delta \dot{Q}(t_1) = \delta \dot{Q}(t_2) = 0$

$\delta A = \int_{\alpha=1}^{3N} \frac{\partial \mathcal{L}}{\partial \dot{q}_\alpha} \delta q_\alpha(t) \Big|_{t_1}^{t_2} dt + \int_{t_1}^{t_2} \sum_{\alpha=1}^{3N} \left[ \frac{\partial \mathcal{L}}{\partial q_\alpha} \delta q_\alpha(t) - \frac{d}{dt} \left( \frac{\partial \mathcal{L}}{\partial \dot{q}_\alpha} \right) \delta q_\alpha(t) \right] dt = 0$

### Constraints

$\sum_{\alpha=1}^{3N} a_{k\alpha} dq_\alpha + a_{kt} dt = 0, k = 1, \dots, N_C$

Holonomic  $a_{k\alpha} = \frac{\partial \sigma_k}{\partial q_\alpha}$   $a_{kt} = \frac{\partial \sigma_k}{\partial t}$

$\frac{1}{2} \sum_i m_i \dot{\vec{r}}_i^2 - C = 0 \Rightarrow \frac{1}{2} \sum_i m_i \dot{\vec{r}}_i d\vec{r}_i - C dt = 0$

Non-holonomic  $\Rightarrow a_{1i} = \frac{1}{2} m_i \dot{\vec{r}}_i \wedge a_{1t} = -C$

Lagrange multiplier  $\frac{d}{dt} \left( \frac{\partial \mathcal{L}}{\partial \dot{q}_\alpha} \right) - \frac{\partial \mathcal{L}}{\partial q_\alpha} = \sum_{k=1}^{N_C} \lambda_k a_{k\alpha}$

$\dot{q}_\alpha = \frac{\partial \mathcal{H}}{\partial p_\alpha}$   $\dot{p}_\alpha = -\frac{\partial \mathcal{H}}{\partial q_\alpha} - \sum_{k=1}^{N_C} \lambda_k a_{k\alpha}$   $\sum_{\alpha=1}^{3N} a_{k\alpha} \frac{\partial \mathcal{H}}{\partial p_\alpha} = 0$

Simulation  $m_i \ddot{\vec{r}}_i = \vec{F}_i + \sum_{k=1}^{N_C} \lambda_k \nabla_i \sigma_k$   $\dot{\sigma}_k = \sum_{i=1}^N \nabla_i \sigma_k \cdot \dot{\vec{r}}_i = 0$

Velocity Verlet  $\vec{r}_i(\Delta t) = \vec{r}_i(0) + \Delta t \vec{v}_i(0) + \frac{\Delta t^2}{2m_i} \vec{F}_i(0) + \frac{\Delta t^2}{2m_i} \sum_k \lambda_k \nabla_i \sigma_k(0)$

$\vec{r}_i(\Delta t) = \vec{r}_i + \frac{1}{m_i} \sum_k \tilde{\lambda}_k \nabla_i \sigma_k(0)$   $\tilde{\lambda}_k = \frac{\Delta t^2}{2} \lambda_k$

$\sigma_l \left( \vec{r}_1^{(1)}, \dots, \vec{r}_N^{(1)} \right) + \sum_{i=1}^N \sum_{k=1}^{N_C} \frac{1}{m_i} \nabla_i \sigma_k \left( \vec{r}_1^{(1)}, \dots, \vec{r}_N^{(1)} \right) \cdot \nabla_i \sigma_k \left( \vec{r}_1(0), \dots, \vec{r}_N(0) \right) \delta \tilde{\lambda}_k \approx 0$

## Direct translation

### Liouville operator

Computable on  $a : \frac{da}{dt} = \{a, \mathcal{H}\}$

$iL = \sum_{\alpha} \left[ \frac{\partial \mathcal{H}}{\partial q_\alpha} \frac{\partial}{\partial q_\alpha} - \frac{\partial \mathcal{H}}{\partial q_\alpha} \frac{\partial}{\partial p_\alpha} \right] \Rightarrow iLa = \{a, \mathcal{H}\} \Rightarrow \frac{da}{dt} = iLa \Rightarrow a(x_t) = e^{iLt} a(x_0)$

Split  $iL_1 = \sum_{\alpha} \frac{\partial \mathcal{H}}{\partial p_\alpha} \frac{\partial}{\partial q_\alpha}$   $iL_2 = -\sum_{\alpha} \frac{\partial \mathcal{H}}{\partial q_\alpha} \frac{\partial}{\partial p_\alpha}$

$iL_1 iL_2 \phi(x) \neq iL_2 iL_1 \phi(x) \Rightarrow iL_1 iL_2 - iL_2 iL_1 \equiv [iL_1, iL_2] \neq 0$

### Trotter theorem

$[iL_1, iL_2] \neq 0 \Rightarrow e^{iLt} \neq e^{iL_1 t} e^{iL_2 t}$

$e^{A+B} = \lim_{P \rightarrow \infty} \left[ e^{\frac{A}{2P}} e^{\frac{B}{P}} e^{\frac{B}{2P}} \right]^P$   $e^{iLt} = \lim_{P \rightarrow \infty} \left[ e^{\frac{iL_2 t}{2P}} e^{\frac{iL_1 t}{P}} e^{\frac{iL_2 t}{2P}} \right]^P$

$e^{iLt} \approx e^{\frac{iL_2 \Delta t}{2}} e^{iL_1 \Delta t} e^{\frac{iL_2 \Delta t}{2}}$

### Trotter algorithm

Exponential operator  $e^{c \frac{\partial}{\partial x}} g(x) = g(x + c)$

$\begin{pmatrix} x(\Delta t) \\ p(\Delta t) \end{pmatrix} = \begin{pmatrix} x(0) + \frac{\Delta t}{m} \left( p(0) + \frac{\Delta t}{2} F(x(0)) \right) \\ p(0) + \frac{\Delta t}{2} F(x(0)) + \frac{\Delta t}{2} F \left( x(0) + \frac{\Delta t}{m} \left( p(0) + \frac{\Delta t}{2} F(x(0)) \right) \right) \end{pmatrix}$

$x(\Delta t) = x(0) + v(0) \Delta t + \frac{\Delta t^2}{2m} F(0)$   $p(\Delta t) = v(0) + \frac{\Delta t}{2m} [F(0) + F(\Delta t)]$

### RESPA

$iL = \frac{p}{m} \frac{\partial}{\partial x} + [F_{fast}(x) + F_{slow}(x)] \frac{\partial}{\partial p} = iL_{fast} + iL_{slow}$   $\mathcal{H}_{ref} = \frac{p^2}{2m} + U_{fast}(x)$

$e^{iL \Delta t} = e^{iL_{slow} \frac{\Delta t}{2}} e^{iL_{fast} \Delta t} e^{iL_{slow} \frac{\Delta t}{2}}$

$e^{iL_{fast} \Delta t} = \left[ e^{\frac{\Delta t}{2} F_{fast} \frac{\partial}{\partial p}} e^{\delta t \frac{p}{m} \frac{\partial}{\partial x}} e^{\frac{\delta t}{2} F_{fast} \frac{\partial}{\partial p}} \right]^n$   $\delta t = \frac{\Delta t}{n}$

## Evaluation of energy and forces

### Periodic boundary condition

Non bonded interaction  $U_{nb}(\vec{r}_1, \dots, \vec{r}_N) = \sum_{i < j \in nb} \left\{ 4\epsilon_{ij} \left[ \left( \frac{\sigma_{ij}}{r_{ij}} \right)^{12} - \left( \frac{\sigma_{ij}}{r_{ij}} \right)^6 \right] + \frac{q_i q_j}{r_{ij}} \right\}$

Error function  $erf(x) = \frac{2}{\sqrt{\pi}} \int_0^x e^{-t^2} dt$   $\lim_{x \rightarrow \infty} erf(x) = 1$   $erf(0) = 0$

Complement error  $erfc(x) = 1 - erf(x) = \frac{2}{\sqrt{\pi}} \int_x^\infty e^{-t^2} dt$   $\lim_{x \rightarrow \infty} erf(x) = 0$

$erf(0) = 1$

$\frac{1}{r} = \frac{erfc(ar)}{r} + \frac{erf(ar)}{r}$   $U_{nb} = U_{short} + U_{long}$   $\vec{r}_{ij} = |\vec{r}_i - \vec{r}_j + \vec{S}|$   $\vec{S} = \vec{m}L$

$U_{short}(\vec{r}_1, \dots, \vec{r}_N) = \sum_{\vec{S}} \sum_{i > j \in nb} \left\{ 4\epsilon_{ij} \left[ \left( \frac{\sigma_{ij}}{r_{ij, \vec{S}}} \right)^{12} - \left( \frac{\sigma_{ij}}{r_{ij, \vec{S}}} \right)^6 \right] + \frac{q_i q_j erfc(a r_{ij, \vec{S}})}{r_{ij, \vec{S}}} \right\}$

$U_{long}(\vec{r}_1, \dots, \vec{r}_N) = \sum_{\vec{S}} \sum_{i > h \in nb} \frac{q_i q_h erfc(a r_{ij, \vec{S}})}{r_{ij, \vec{S}}}$

### Short range forces

$\vec{U}_{short} = U_{short}(\vec{r}_{ij}) S(\vec{r}_{ij})$   $S(r) = \begin{cases} 1 & r < r_C - \lambda \\ 1 + \left( \frac{r - r_C + \lambda}{\lambda} \right)^2 (2 \frac{r - r_C + \lambda}{\lambda} - 3) & r_C - \lambda \leq r < r_C \\ 0 & r > r_C \end{cases}$

## Evaluation of energy and forces (contd)

### Long range forces

$C_{\vec{g}} = \frac{4\pi}{|\vec{g}|^2} e^{-\frac{|\vec{g}|^2}{4\alpha^2}}$   $\frac{1}{V} \sum_{\vec{g}} C_{\vec{g}} e^{i\vec{g} \cdot \vec{r}} = \frac{1}{V} \sum_{i \neq j} q_i q_j \sum_{\vec{g} \in S} \frac{4\pi}{|\vec{g}|^2} e^{-\frac{|\vec{g}|^2}{4\alpha^2}} e^{i\vec{g} \cdot (\vec{r}_i - \vec{r}_j)}$

$U_{long} = \frac{1}{V} \sum_{i, j} q_i q_j \sum_{\vec{g} \in S} \frac{4\pi}{|\vec{g}|^2} e^{-\frac{|\vec{g}|^2}{4\alpha^2}} e^{i\vec{g} \cdot (\vec{r}_i - \vec{r}_j)} - \frac{1}{V} \sum_i q_i^2 \sum_{\vec{g} \in S} \frac{4\pi}{|\vec{g}|^2} e^{-\frac{|\vec{g}|^2}{4\alpha^2}}$

$U_{long} = \frac{1}{V} \sum_{\vec{g} \in S} \frac{4\pi}{|\vec{g}|^2} e^{-\frac{|\vec{g}|^2}{4\alpha^2}} |S(\vec{g})|^2 - \frac{\alpha}{\sqrt{\pi}} \sum_i q_i^2$

### Particle-particle particle-mesh Ewald

$\rho(\vec{r}) = \sum_i q_i \delta(\vec{r} - \vec{r}_i)$   $\rho(\vec{g}) = \int d\vec{r} \rho(\vec{r}) e^{i\vec{g} \cdot \vec{r}} = \sum_i q_i e^{i\vec{g} \cdot \vec{r}_i}$

$\nabla^2 \phi(\vec{r}) = -\nabla \cdot \vec{E} = -4\pi \rho(\vec{r})$   $g^2 \phi(\vec{g}) = -4\pi \rho(\vec{g}) = 4\pi S(\vec{g})$

## Canonical ensemble

### Thermodynamics

Helmholtz free energy  $A(N, V, T) = E(N, V, T) - TS(N, V, T)$

$dA = SdT - PdV + \mu dN$   $S = -\left( \frac{\partial A}{\partial T} \right)_{N, V}$   $P = -\left( \frac{\partial A}{\partial V} \right)_{N, T}$   $\mu = \left( \frac{\partial A}{\partial N} \right)_{V, T}$

### Thermal contact

Microcanonical  $\Omega(N, V, E) = M_N \int dx_1 dx_2 \delta(\mathcal{H}_1(x_1) + \mathcal{H}_2(x_2) - E)$

Distribution function  $\ln f(x_1) = \ln \int dx_2 \delta(\mathcal{H}_1(x_1) + \mathcal{H}_2(x_2) - E)$

$\ln f(x_1) \approx \ln \int dx_2 \delta(\mathcal{H}_2(x_2) - E) - \frac{\partial}{\partial E} \ln \int dx_2 \delta(\mathcal{H}_2(x_2) - E) \mathcal{H}_1(x_1)$

$Q(N, V, T) = \frac{1}{N! h^{3N}} \int dx e^{-\beta \mathcal{H}(x)}$   $\beta = \frac{1}{kT}$

### From micro to macro

$A = E - \beta \left( \frac{\partial A}{\partial \beta} \right)_{N, V}$

$E = \langle \mathcal{H} \rangle = \frac{1}{N! h^{3N}} \frac{\int dx \mathcal{H}(x) e^{-\beta \mathcal{H}(x)}}{\int dx e^{-\beta \mathcal{H}(x)}} = -\frac{Q(N, V, \beta)}{Q(N, V, \beta)} \frac{\partial Q(N, V, \beta)}{\partial \beta} = -\frac{\partial \ln Q(N, V, \beta)}{\partial \beta}$

$A + \frac{\partial \ln Q}{\partial \beta} + \beta \frac{\partial A}{\partial \beta} = 0 \Rightarrow \ln Q(N, V, \beta) = -\beta A(N, V, \beta)$

$A(N, V, T) = -kT \ln Q(N, V, T)$   $C_N = \frac{1}{N! h^{3N}}$

Energy  $E = \langle \mathcal{H} \rangle = \frac{1}{Q} \frac{\partial Q}{\partial \beta} = 0$

Temperature estimator  $\mathcal{T}(x) + \frac{1}{3Nk} \sum_i \frac{\vec{p}_i^2}{m_i}$   $T = \langle \mathcal{T}(x) \rangle = \frac{C_N \int dx \mathcal{T}(x) e^{-\beta \mathcal{H}(x)}}{C_N \int dx e^{-\beta \mathcal{H}(x)}}$

Energy fluctuation  $\Delta E^2 = \frac{\partial^2 \ln Q}{\partial \beta^2} = kT^2 C_V$   $\frac{\Delta E}{E} \sim \frac{1}{\sqrt{N}}$

Pressure estimator  $\mathcal{P}(\vec{r}, \vec{p}) = \frac{1}{3V} \sum_i \left[ \frac{\vec{p}_i^2}{m_i} + \vec{F}_i \cdot \vec{r}_i \right]$

## Thermostats

$$\begin{aligned} \text{Covariance matrix } C_{ij} &= \overline{(x_i(t) - \bar{x}_i(t))(x_j(t) - \bar{x}_j(t))} \\ \text{Correlation matrix } R_{ij} &= \frac{\overline{(x_i(t) - \bar{x}_i(t))(x_j(t) - \bar{x}_j(t))}}{\sigma_{x_i} \sigma_{x_j}} \\ PC_k(t) &= \sum_{i=1}^N \tilde{d}_i(t) \cdot \tilde{u}_i^k \quad c_k = \frac{2}{T_{sim}} \left( \int_0^{T_{sim}} \cos\left(\pi \frac{kT}{\lambda_k T}\right) PC_k(t) dt \right)^2 \left( \int_0^{T_{sim}} PC_k^2(t) dt \right)^{-1} \\ \Omega_{A,B} &= 1 - \left[ \frac{\sum_{k=1}^{3N-6} (\lambda_k^A + \lambda_k^B) - 2 \sum_{k=1}^{3N-6} \sum_{j=1}^{3N-6} \sqrt{\lambda_k^A \lambda_j^B} (\tilde{u}_k^A \cdot \tilde{u}_j^B)^2}{\sum_{k=1}^{3N-6} (\lambda_k^A + \lambda_k^B)} \right]^{\frac{1}{2}} \end{aligned}$$