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

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

Valence angle bending

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

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

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

Torsions

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

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

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 $Z = \sqrt{\sum_i^{observables} \sum_j^{occurrences} \frac{(calc_{i,j} - expt_{i,j})^2}{w_i^2}}$

$\sigma_{AB} = \sigma_A + \sigma_B \qquad \epsilon_{AB} = \sqrt{\epsilon_A \epsilon_B}$

Classical mechanics

Newton's laws

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

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

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

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

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

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

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

Lagrangian formulation

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

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

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

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

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

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

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

Generalized coordinates

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

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

Classical mechanics (contd)

Legendre transforms

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

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

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

Hamiltonian formulation

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

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

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

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

Some properties

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

Incompressibility $\nabla_x \dot{(x)} = 0$

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

Theoretical foundations of statistical mechanics

Thermodynamics

Equilibrium $g(N, P, V, T) = 0$

State function $f(n, P, V, T)$

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

Heat $dQ_{rev} = CdT$

First law $\Delta E = \Delta Q + \Delta W$

Entropy $\Delta S = \int_1^2 \frac{dQ_{rev}}{T}$

The ensemble

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

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

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

Distribution function $f(x_t) : \int f(x) dx = 1 \wedge \frac{df(x_t, t)}{dt} = 0 \Rightarrow f(x_t, t) dx_t = f(x_0, 0) dx_0 \Rightarrow \frac{\partial f(x,t)}{\partial t} + \{f(x,t), \mathcal{H}(x,t)\} = 0$

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

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

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

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

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

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

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

Virial theorem

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

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

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

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

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

Thermal contact

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

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

$S(N, V, E) = k \ln \Omega_1(N_1, V_1, \bar{E}_1) + k \ln \Omega_2(N_2, V_2, E - \bar{E}_1)$

$= S_1(N_1, V_1, \bar{E}_1) + S_2(N_2, V_2, E - \bar{E}_1)$

$T_1 = T_2$

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

Introduction to molecular dynamics (contd)

Action integral

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

$A[Q] = \int_{t_1}^{t^2} \mathcal{L}(Q(t), \dot{Q}(t)) dt$

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

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

Constraints

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

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

Non-holonomic $\frac{1}{2} \sum_i m_i \dot{\vec{r}}_i^2 - C = 0 \Rightarrow \frac{1}{2} \sum_i m_i \dot{\vec{r}}_i d\vec{r}_i - C dt = 0 \Rightarrow a_{1i} = \frac{1}{2} m_i \dot{\vec{r}}_i \wedge a_{1t} = -C$

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

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

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

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

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

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

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

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

Trotter theorem

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

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

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

Trotter algorithm

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

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

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

RESPA

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

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

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